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the margin of success

in asthma therapy, it's the expectorant in Bronkotabs

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[1] Spielman, A. D.: Evaluation of a Combination Tablet of Theophylline, Ephedrine Sulphate, Phenobarbital, Thenyldiamine and Glyceryl Guaiacolate in the Treatment of Chronic Asthma, Ann. Allergy 18:281 (Mar.) 1960.

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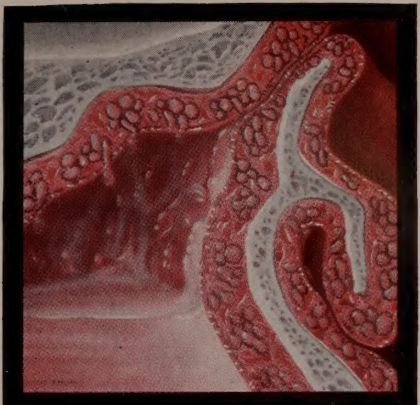
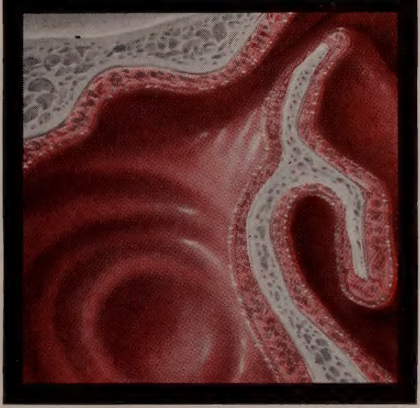


The clogged sinus
In sinusitis, the mucous membrane becomes hyperemic and edematous, lymph glands and goblet cells hyperactive. Ostium is closed by edema and secretions cannot drain freely.



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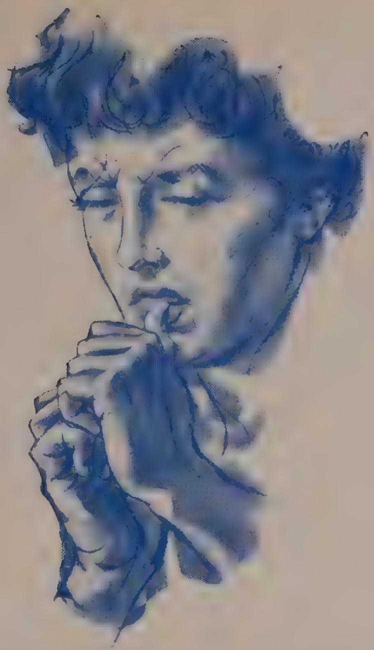

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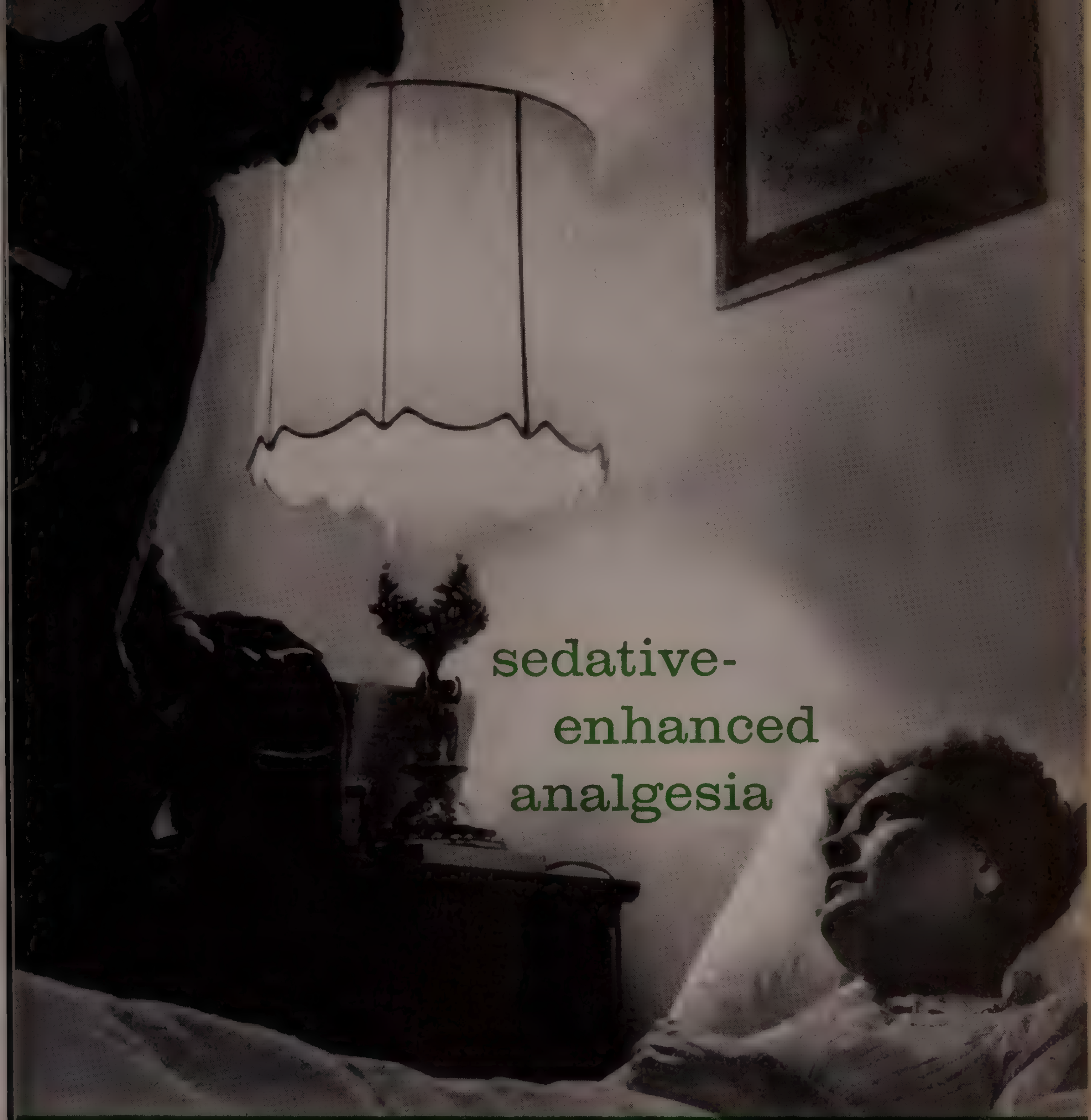

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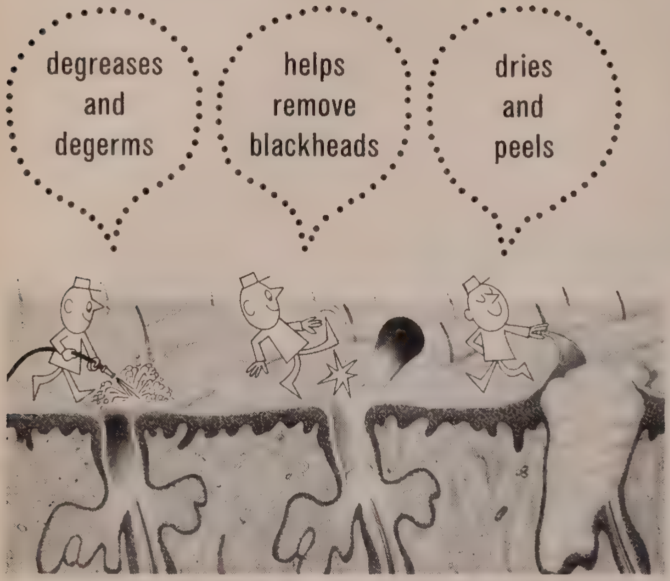

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***Only Fostex contains this unique combination of anti-acne agents:** Sebulytic® (3 surface-active agents—sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, sodium dioctyl sulfosuccinate), micropulverized sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

Supplied—Fostex Cake, bar form. Fostex Cream, 4.5 oz. jars. Also used as a therapeutic shampoo in dandruff and oily scalp which often accompanies and aggravates acne.

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Buffalo 13, N. Y.

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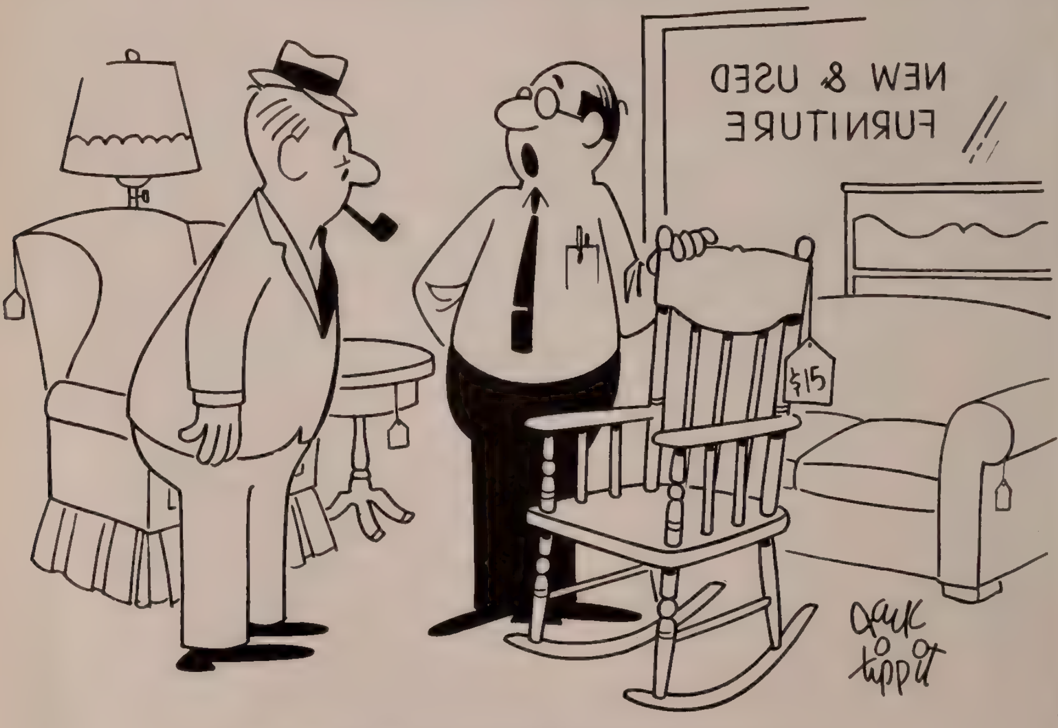

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During the past seven years, 'Thorazine' has become the treatment of choice for moderate to severe mental and emotional disturbances, because it is:

- specific enough to relieve underlying fear and apprehension
- profound enough to control hyperactivity and excitement
- flexible enough so that in severe cases dosage may be raised to two or three times the recommended starting level

Experience in over 14,000,000 Americans confirms the reassuring fact that, in most patients, the potential benefits of 'Thorazine' far outweigh its possible undesirable effects.

Of special value in mental and emotional disturbances: Tablets for initial therapy; Injection (Ampuls and Vials) for prompt control; Spansule® sustained release capsules for all-day or all-night therapy with a single oral dose.

Thorazine® brand of chlorpromazine

a fundamental drug in both
office and hospital practice
Smith Kline & French Laboratories

posed by professional models

'THORAZINE' PRESCRIBING INFORMATION

Because of its pronounced calming effect, 'Thorazine' is an outstanding agent for patients with mental and emotional disturbances, particularly those with symptoms of agitation and hyperactivity. In severe cases, initial use of intramuscular administration may be desirable to control symptoms promptly.

Before prescribing 'Thorazine' for other indications than those given below, the physician should be familiar with the dosage, side effects, cautions and contraindications for such uses. This information is available in the *Thorazine® Reference Manual* and *Physicians' Desk Reference,* and from your SK&F representative or your pharmacist.

ADMINISTRATION AND DOSAGE

Dosage should always be adjusted to the response of the individual and according to the severity of the condition. It is important to increase dosage until symptoms are controlled or side effects become troublesome. In emaciated or senile patients, dosage increases should be made more gradually than in other patients.

ADULT DOSAGE

Mental and Emotional Disturbances (e.g., agitation, excitement, or anxiety)—*Starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. After a day or two, dosage may be increased by increments of 20 mg. to 50 mg. daily, at semiweekly intervals, until maximum clinical response is achieved. Continue dosage at this level for at least two weeks; then it can usually be reduced to a maintenance level. A daily dosage of 200 mg. is "average," but some patients may require substantially higher dosages. Discharged mental patients, for example, may require daily dosages as high as 800 mg. *Starting intramuscular dose* is 25 mg. (1 cc.). If necessary, and if no hypotension occurs, repeat the initial dose in one hour. Subsequent dosages should be oral, starting at 25 mg. to 50 mg. t.i.d.

Alcoholism—Severely agitated patients: *Starting intramuscular dose* is 25 mg. to 50 mg. (1-2 cc.). Repeat initial dose if necessary and if no hypotension occurs. Start subsequent oral dosages at 25 mg. to 50 mg. t.i.d. **Agitated but manageable patients:** *Starting oral dose* is 50 mg., followed by 25 mg. to 50 mg. t.i.d. For ambulatory patients with withdrawal symptoms or sober chronic alcoholics, *starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Patients in a stuporous condition should be allowed to sleep off some of the effects of the alcohol before 'Thorazine' is administered.

CHILDREN'S DOSAGE

For Behavior Disorders—*Oral dosage* is on the basis of ¼ mg./lb. of body weight q4-6h, until symptoms are controlled (i.e., for 40 lb. child—10 mg. q4-6h). *Rectal dosage* is on the basis of ½ mg./lb. of body weight q6-8h, p.r.n. (i.e., for 20-30 lb. child—half of a 25 mg. suppository q6-8h). *Intramuscular dosage* is on the basis of ¼ mg./lb. of body weight q6-8h, p.r.n. In children up to 5 years (or 50 lbs.)—not over 40 mg./day; in children 5-12 years (or 50-100 lbs.)—not over 75 mg./day except in extreme unmanageable cases. In severe cases, higher dosages than those recommended above may be necessary. In such cases, 50-100 mg. daily has been used and, in older children, as much as 200 mg. daily or more may be required.

IMPORTANT NOTES ON INJECTION

Except for acute ambulatory cases, parenteral administration should generally be reserved for bedfast patients. Parenteral administration should always be made with the patient lying down and remaining so for at least ½ hour afterward because of possible hypotensive effects. The injection should be given *slowly, deep* into the upper outer quadrant of the buttock. If irritation and pain at the site of injection are problems, dilution of 'Thorazine' Injection with physiologic saline solution or 2% procaine solution may be helpful. Subcutaneous administration is not advisable, and care should be taken to avoid injecting undiluted 'Thorazine' Injection into a vein. Intravenous administration is recommended only for severe hiccups and surgery.

'Thorazine' Injection should not be mixed with other agents in the syringe. Because contact dermatitis has been reported with 'Thorazine', nurses or others giving frequent injections should avoid getting the solution on hands or clothing. 'Thorazine' Injection should be protected from light, since exposure may cause discoloration. Slight yellowish discoloration will not alter potency or efficacy. If markedly discolored, the solution should be discarded.

SIDE EFFECTS

The drowsiness caused by 'Thorazine' is usually mild to moderate and disappears after the first or second week of therapy. If, however, drowsiness is troublesome, it can usually be controlled by lowering the dosage or by administering small amounts of dextro amphetamine.

Other side effects reported occasionally are dryness of the mouth, nasal congestion, some constipation, miosis in a few patients and, very rarely, mydriasis.

Mild fever (99°F.) may occur occasionally during the first days of therapy with large intramuscular doses.

Some patients have an increased appetite and gain weight, but usually reach a plateau beyond which they do not gain.

CAUTIONS

Jaundice: The over-all incidence of jaundice due to 'Thorazine' has been low—regardless of indication, dosage, or mode of administration. It appears to be related to duration of therapy. Few cases have occurred in less than one week or after six weeks. The jaundice that has occurred mimics the obstructive type, is without parenchymal damage, and is usually promptly reversible upon the withdrawal of 'Thorazine'. Although the mechanism is not clearly understood, most investigators conclude that it is a sensitivity reaction in susceptible individuals.

There is no conclusive evidence to indicate that pre-existing liver disease makes the patient more susceptible to jaundice. (Patients with known alcoholic cirrhosis have been treated with 'Thorazine' without further alteration of liver function.) Nevertheless, 'Thorazine' should be used with due consideration in a patient with liver disease.

If a patient on 'Thorazine' suddenly develops fever with grippe-like symptoms, his serum should be tested for increased bilirubin or his urine for the presence of bile. If any of these tests are positive, 'Thorazine' should be discontinued.

Because detailed liver function tests of 'Thorazine'-induced jaundice give a picture which mimics extrahepatic obstruction, exploratory laparotomy should be withheld until sufficient studies confirm extrahepatic obstruction.

Agranulocytosis: Agranulocytosis, although rare, has been reported. Patients should be observed regularly and asked to report at once the sudden appearance of sore throat or other signs of infection. If white blood counts and differential smears give an indication of cellular depression, the drug should be discontinued, and antibiotic and other suitable therapy should be instituted.

Because most reported cases have occurred between the fourth and the tenth weeks of treatment, patients on prolonged therapy should be observed particularly during that period.

A moderate suppression of total white blood cells, sometimes observed in patients on 'Thorazine' therapy, is not an indication for discontinuing 'Thorazine' unless accompanied by other symptoms.

Potentiation: 'Thorazine' prolongs and intensifies the action of many central nervous system depressants such as anesthetics, barbiturates and narcotics. Consequently, it is advisable to stop administration of such depressants before initiating 'Thorazine' therapy. Later the depressant agents may be reinstated, starting with low doses, and increasing according to response. Approximately ¼ to ½ the usual dosage of such agents is required when they are given in combination with 'Thorazine'. (However, 'Thorazine' does not potentiate the anticonvulsant action of barbiturates. In patients who are receiving anticonvulsants, the dosage of these agents—including barbiturates—should not be reduced if 'Thorazine' is started. Rather, 'Thorazine' should be started at a very low dosage and increased, if necessary.)

Hypotensive Effect: Postural hypotension and simple tachycardia may be noted in some patients. In these patients, momentary fainting and some dizziness are characteristic and usually occur shortly after the first parenteral dose, occasionally after a subsequent parenteral dose—very rarely after the first oral dose. In most cases, prompt recovery is spontaneous and all symptoms disappear within ½ to 2 hours with no subsequent ill effects. Occasionally, however, this hypotensive effect may be more severe and prolonged, producing a shock-like condition.

In consideration of possible hypotensive effects, the patient should be kept under observation (preferably lying down) for some time after the initial parenteral dose. If, on rare occasions, hypotension does occur, it can ordinarily be controlled by placing the patient in a recumbent position with head lowered and legs raised. If a vasoconstrictor is required, 'Levophed' and 'Neo-Synephrine'⋆ are the most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

Antiemetic Effect: The antiemetic effect of 'Thorazine' may mask signs of overdosage of toxic drugs and may obscure diagnosis of conditions such as intestinal obstruction and brain tumor.

Dermatological Reactions: Dermatological reactions have been reported. Most have been of a mild urticarial type, suggesting allergic origin. Some appear to be due to photosensitivity, and patients on 'Thorazine' should avoid undue exposure to the summer sun.

Neuromuscular (Extrapyramidal) Reactions: With very high doses of 'Thorazine', as frequently used in psychiatric cases over long periods, a few patients have exhibited neuromuscular (extrapyramidal) reactions which closely resemble parkinsonism. Such symptoms are reversible and usually disappear within a short time after the dosage has been decreased or the drug temporarily withdrawn. These reactions can also be controlled by the concomitant administration of an anti-parkinsonism agent (see *Physicians' Desk Reference*). Depending on the severity of the symptoms, suitable supportive measures such as maintaining a clear airway and adequate hydration should be employed. When 'Thorazine' is reinstituted, it should be at a lower dosage.

Lactation: Moderate engorgement of the breast with lactation has been observed in female patients receiving very large doses of 'Thorazine'. This is a transitory condition which disappears on reduction of dosage or withdrawal of the drug.

CONTRAINDICATIONS

'Thorazine' is contraindicated in comatose states due to central nervous system depressants (alcohol, barbiturates, narcotics, etc.) and also in patients under the influence of large amounts of barbiturates or narcotics.

SUPPLIED

Tablets, 10 mg., 25 mg., 50 mg. and 100 mg., in bottles of 50, 500 and 5000; 200 mg., for use in mental hospitals, in bottles of 500 and 5000. (Each tablet contains 10 mg., 25 mg., 50 mg., 100 mg., or 200 mg. of chlorpromazine hydrochloride.)

Spansule® capsules, 30 mg., 75 mg., 150 mg. and 200 mg., in bottles of 30, 250 and 1500; also 300 mg., in bottles of 30 and 1500. (Each 'Spansule' capsule contains 30 mg., 75 mg., 150 mg., 200 mg., or 300 mg. of chlorpromazine hydrochloride.)

Ampuls, 1 cc. and 2 cc. (25 mg./cc.), in boxes of 6, 100 and 500. (Each cc. contains, in aqueous solution, 25 mg. of chlorpromazine hydrochloride; 2 mg. of ascorbic acid; 1 mg. of sodium bisulfite; 1 mg. of sodium sulfite; 6 mg. of sodium chloride.)

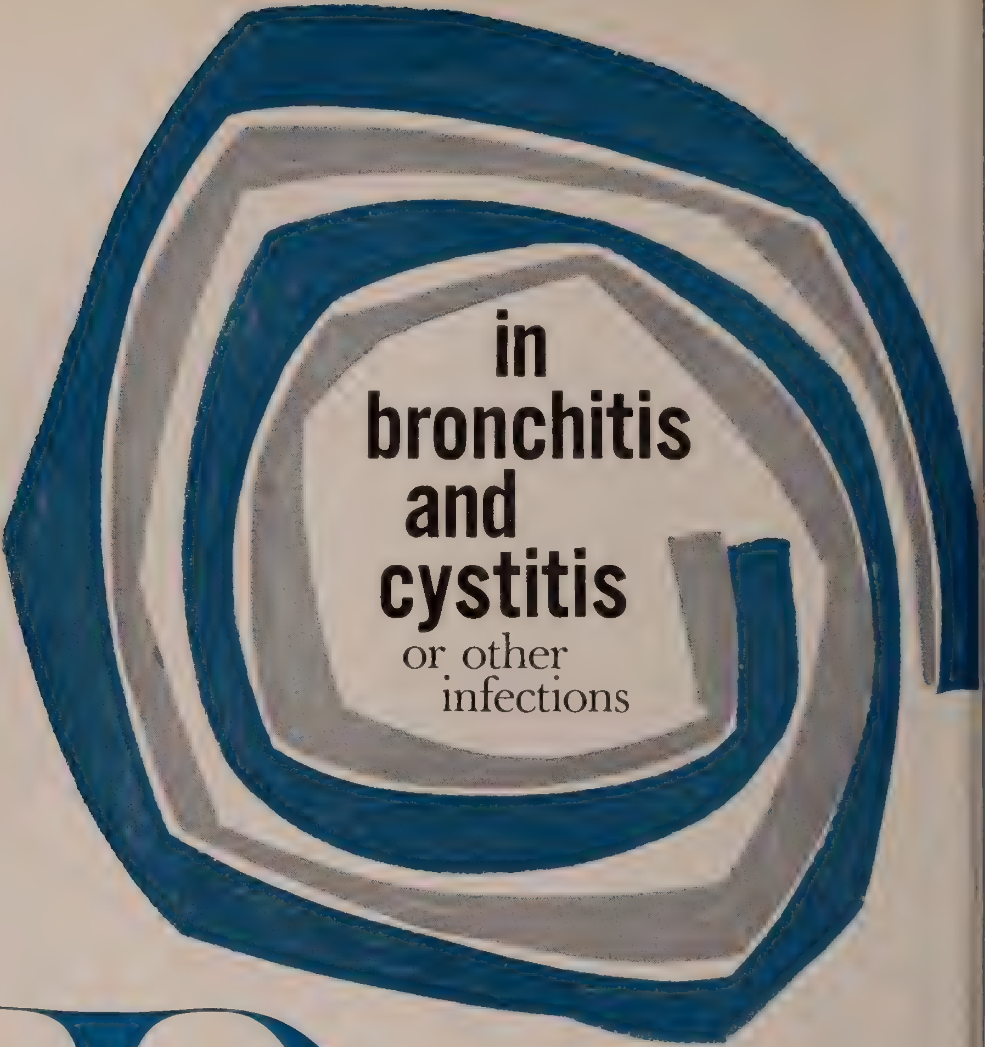
Multiple-dose Vials, 10 cc. (25 mg./cc.), in boxes of 1, 20 and 100. (Each cc. contains, in aqueous solution, 25 mg. of chlorpromazine hydrochloride; 2 mg. of ascorbic acid; 1 mg. of sodium bisulfite; 1 mg. of sodium sulfite; 1 mg. of sodium chloride; 2% benzyl alcohol as preservative.)

Syrup, 10 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. (Each 5 cc. contains 10 mg. of chlorpromazine hydrochloride.)

Suppositories, 25 mg. and 100 mg., in boxes of 6. (Each suppository contains 25 mg. or 100 mg. of chlorpromazine; glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids, lecithin.)

Concentrate (for hospital use), 30 mg./cc., in 4 fl. oz. bottles, in cartons of 12 and 36, and in gallon bottles. (Each cc. contains 30 mg. of chlorpromazine hydrochloride.)

⋆'Levophed' and 'Neo-Synephrine' are the trademarks (Reg. U.S. Pat. Off.) of Winthrop Laboratories for its brands of levarterenol and phenylephrine respectively.



DECLO

antibiotic therapy with an

CAPSULES, 150 mg., 75 mg. *Dosage:* Average infections—150 mg. four times daily. Severe infections—Initial dose of 300 mg., then 150 mg. every six hours.

PEDIATRIC DROPS, 60 mg./cc. in 10 cc. bottle with calibrated, plastic dropper. *Dosage:* 1 to 2 drops (3 to 6 mg.) per pound body weight per day—divided into four doses.

SYRUP, 75 mg./5 cc. teaspoonful (cherry-flavored). *Dosage:* 3 to 6 mg. per pound body weight per day—divided into four doses.

PRECAUTIONS — As with other antibiotics, DECLOMYCIN may occasionally give rise to glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis or dermatitis. A photodynamic reaction to sunlight has been observed in a few patients on DECLOMYCIN. Although reversible by discontinuing therapy, patients should avoid exposure to intense sunlight. If adverse reaction or idiosyncrasy occurs, discontinue medication.

Overgrowth of nonsusceptible organisms is a possibility with DECLOMYCIN, as with other antibiotics, and demands that the patient be kept under constant observation.

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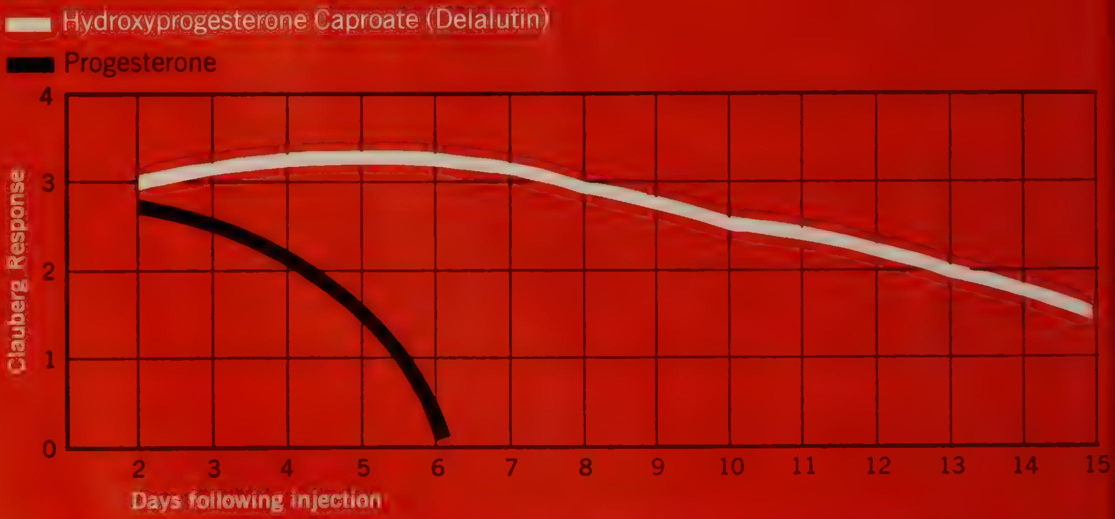
Comparative effect of single subcutaneous injection of Delalutin and progesterone on the progestational changes (Clauberg Test) in the rabbit uterus.

Borman, A.: Laboratory Report on the Duration of Action of 17-Alpha-Hydroxy-progesterone-n-Caproate (Delalutin). The Squibb Institute for Medical Research, May 17, 1955.



Supply: Vials of 2 and 10 cc., each cc. containing 125 mg. of hydroxyprogesterone caproate in sesame oil with 35% benzyl benzoate. Vials of 5 cc., each cc. containing 250 mg. of hydroxyprogesterone caproate in castor oil with 61% benzyl benzoate. **References:** 1. Boschann, H. W.: Ann. New York Acad. Sc. 71:727 (July 30) 1958. 2. Reifenstein, E. C., Jr.: Ann. New York Acad. Sc. 71:762 (July 30) 1958. 3. Castelazo Ayala, L., et al.: Gin. y Obstet. de Mexico 14:249 (May-June) 1959. 4. Plotz, E. J.: Abortion (Hemorrhage of Early Pregnancy), in Conn, H. F.: Current Therapy — 1960, Philadelphia: W. B. Saunders Co., 1960, pp. 613 ff. 5. Wright, H. L., Withers, R. W., and Ingram, J. M.: Am. Pract. & Digest Treat. 10:1544 (Sept.) 1959.

Complete information on administration and dosage is supplied in the package insert and in your Squibb Product Reference and Product Brief.

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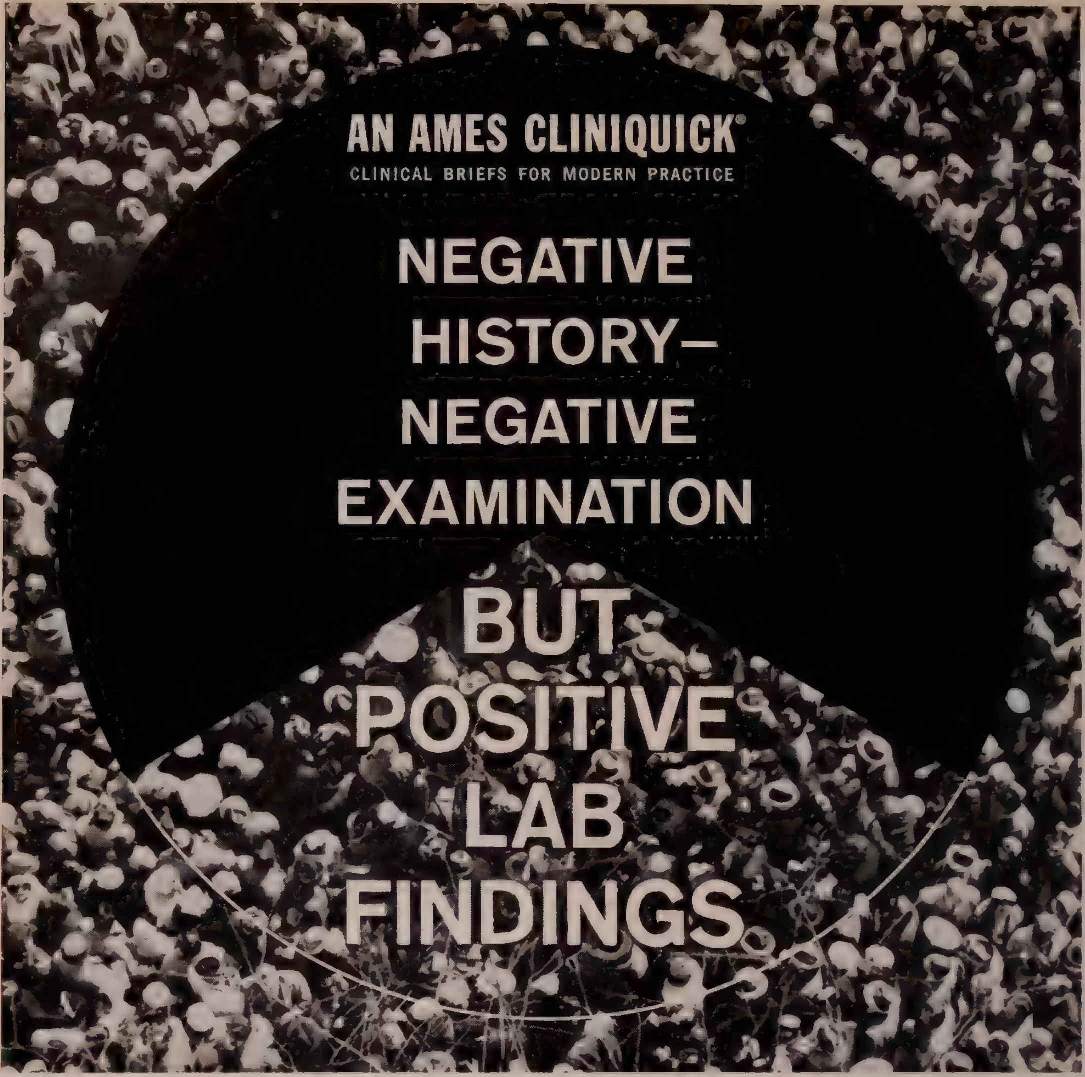
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*Schenthal, J. E.: J.A.M.A. *172*:1 (Jan. 2) 1960.

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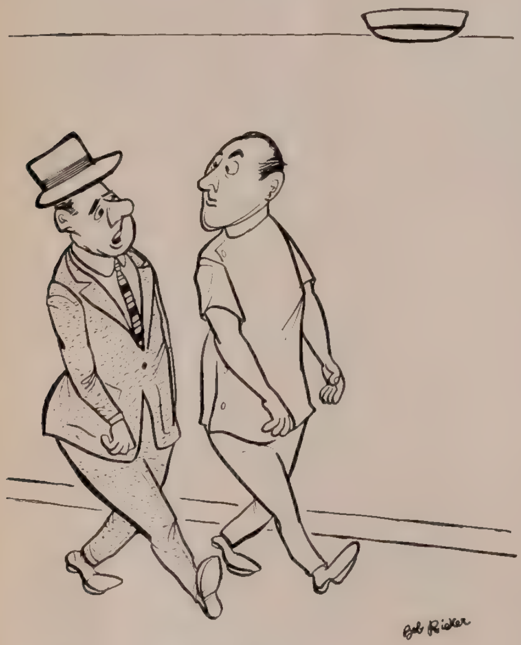

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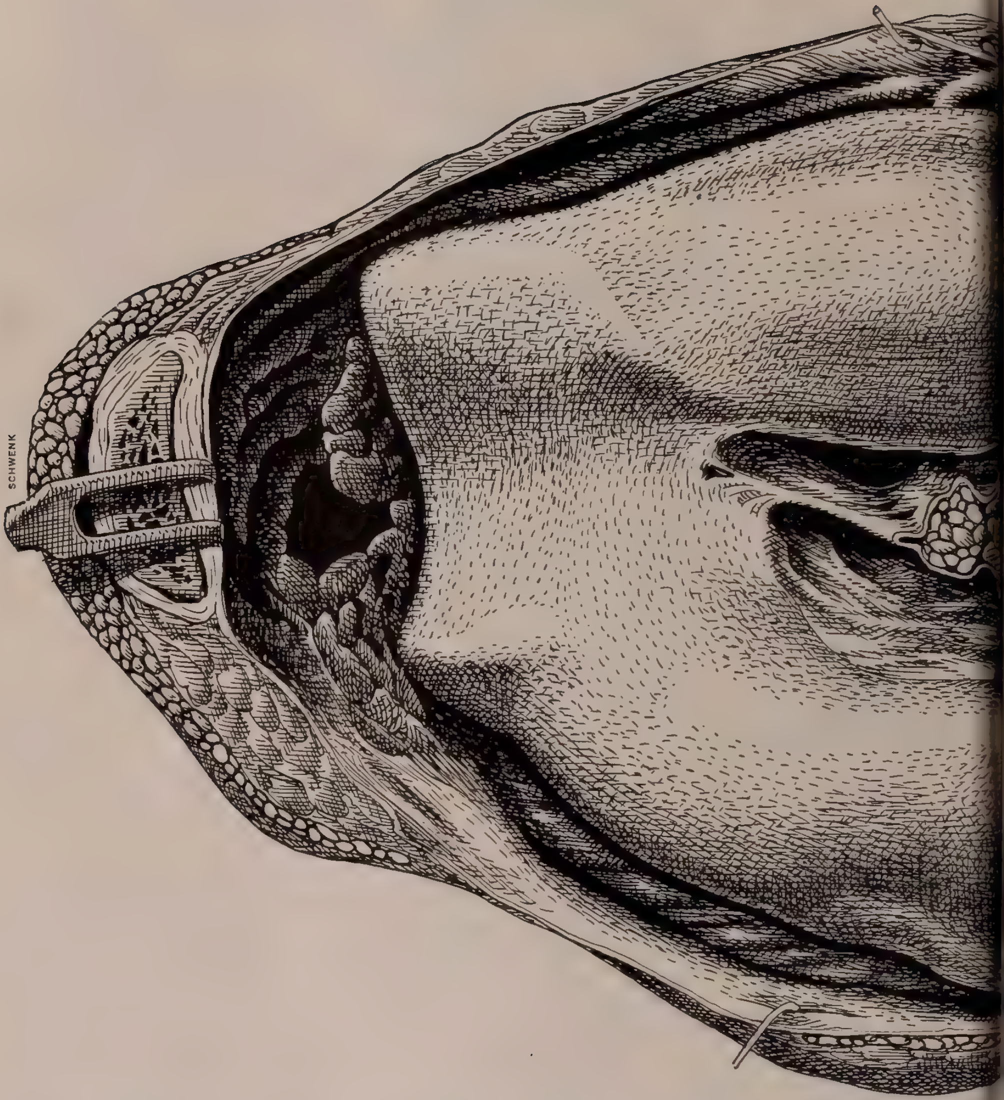

because patients are more than arthritic joints…

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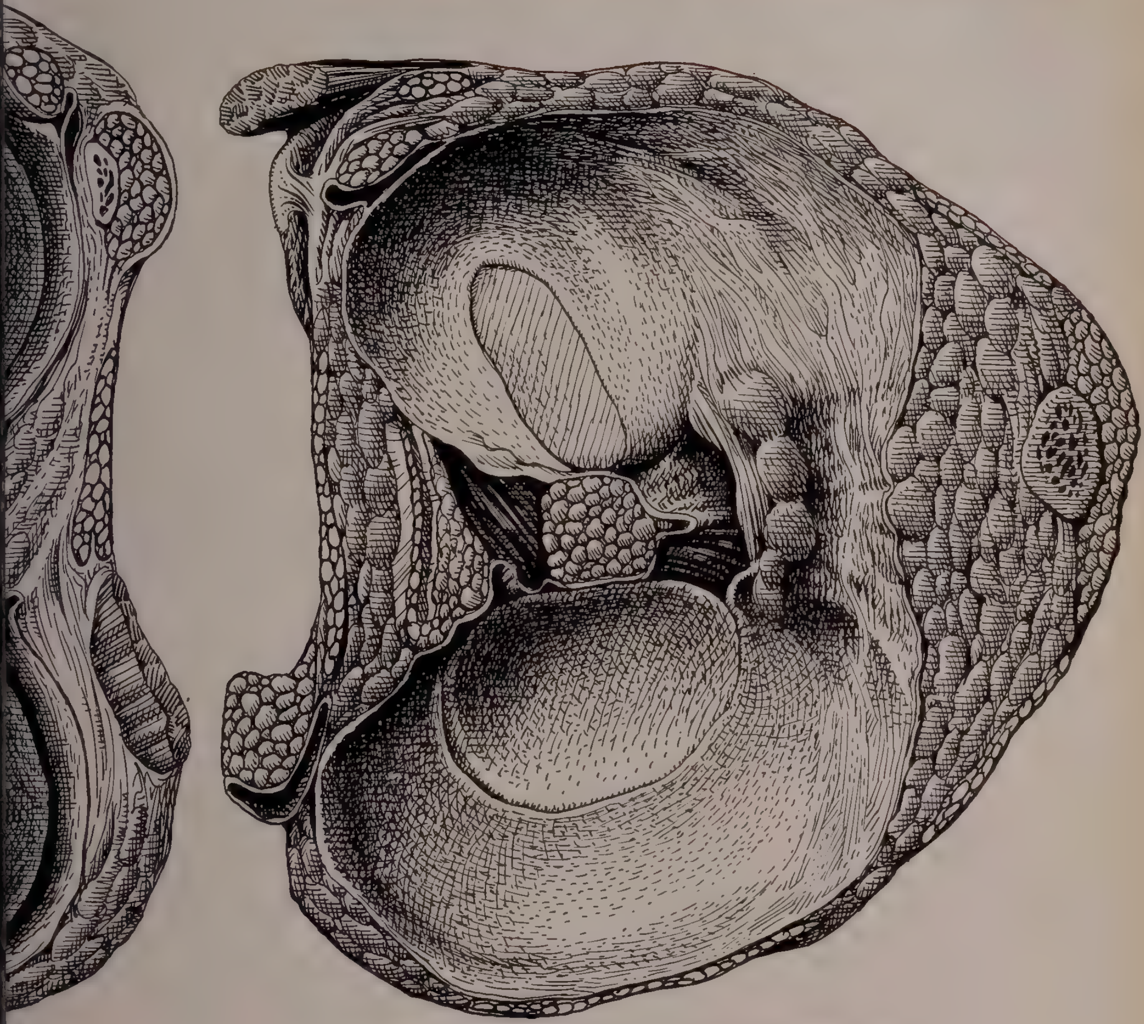

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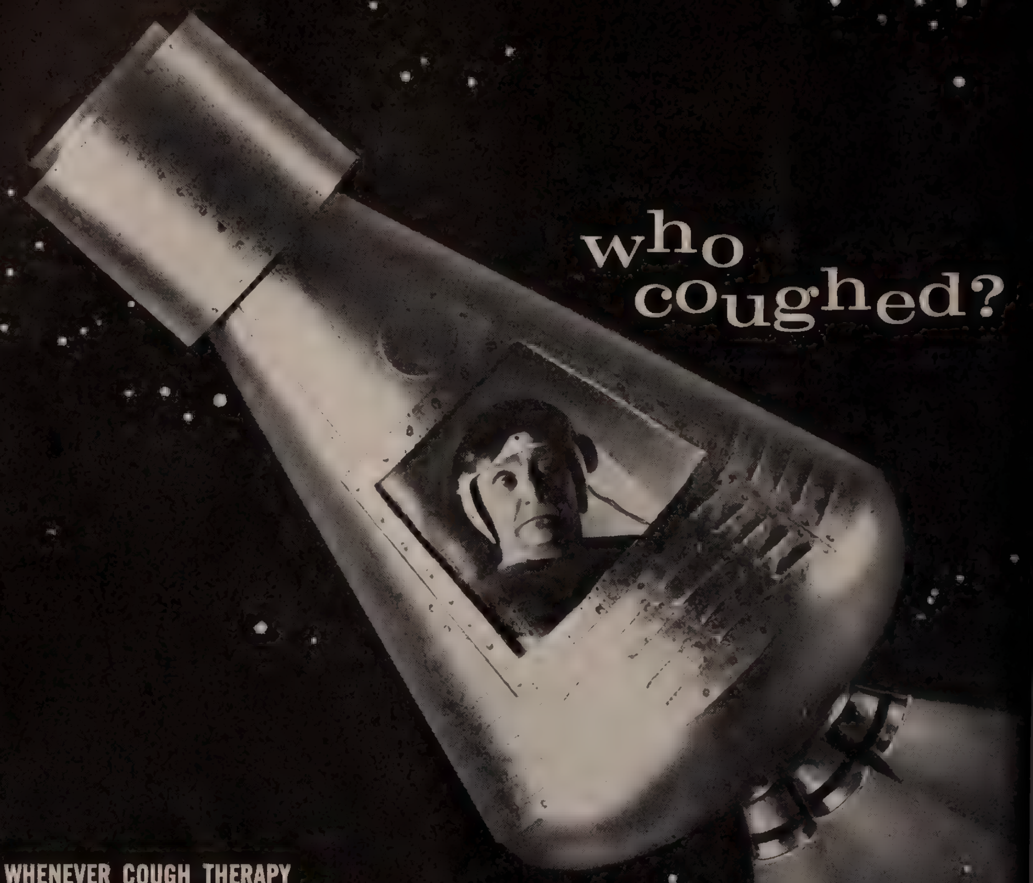
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Dihydrocodeinone Bitartrate (Warning: May be habit-forming)	5 mg.	6.5 mg.
Homatropine Methylbromide	1.5 mg.	
Pyrilamine Maleate		12.5 mg.
Phenylephrine Hydrochloride		10 mg.
Ammonium Chloride		60 mg.
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Literature on request
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In bacterial tracheobronchitis

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promptly

to gain precious therapeutic hours

Panalba your broad-spectrum antibiotic of first resort

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Panalba is effective (in vitro) against 30 common pathogens, including the ubiquitous staph. Use of Panalba from the outset (even pending laboratory results) can gain precious hours of effective antibiotic treatment.

Supplied: Capsules, each containing Panmycin* Phosphate (tetracycline phosphate complex), equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin,* as novobiocin sodium, in bottles of 16 and 100.
Usual Adult Dosage: 1 or 2 capsules 3 or 4 times a day.
Side Effects: Panmycin Phosphate has a very low order of toxicity comparable to that of the other tetracyclines and is well tolerated clinically. Side reactions to therapeutic use in patients are infrequent and consist principally of mild nausea and abdominal cramps.
Albamycin also has a relatively low order of toxicity. In a certain few patients, a yellow pigment has been found in the plasma. This pigment, apparently, a metabolic by-product of the drug, is not necessarily associated with abnormal liver function tests or liver enlargement.

Urticaria and maculopapular dermatitis, a few cases of leukopenia and thrombocytopenia have been reported in patients treated with Albamycin. These side effects usually disappear upon discontinuance of the drug.
Caution: Since the use of any antibiotic may result in overgrowth of nonsusceptible organisms, constant observation of the patient is essential. If new infections appear during therapy, appropriate measures should be taken.
Total and differential blood counts should be made routinely during prolonged administration of Albamycin. The possibility of liver damage should be considered if a yellow pigment, a metabolic by-product of Albamycin, appears in the plasma. Panalba should be discontinued if allergic reactions that are not readily controlled by antihistaminic agents develop.

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offers the speed, the certainty,

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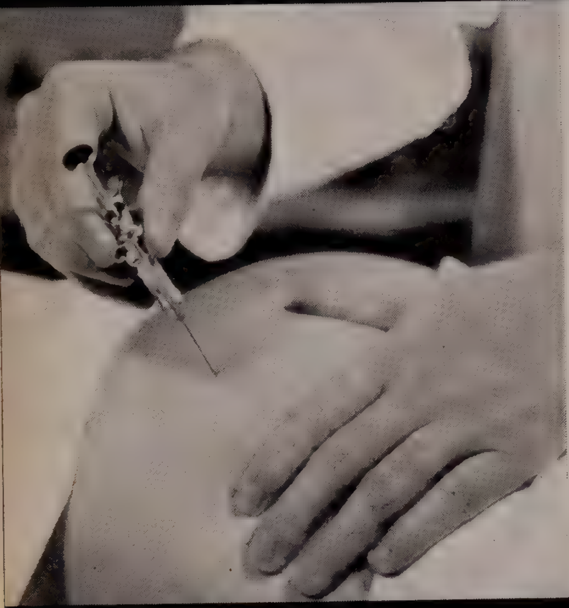

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COMPOCILLIN®-VK

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BECAUSE potassium penicillin V (Compocillin-VK) offers excellent absorption[1,2,3,4]—fast, predictable levels of antibacterial activity enter the blood stream and quickly reach the site of infection. *Absorption takes place high in the digestive tract and is virtually unaffected by gastric media.*

Antibacterial levels are so predictable that, in many cases, *Compocillin-VK may be prescribed in place of injectable penicillin.* This is especially appreciated by younger patients and—as you know—oral administration is considered far safer than injectable.

Compocillin-VK is well tolerated and may be used in treating mild, severe, and in high dosage ranges, even critical cases involving penicillin-sensitive organisms. It comes in stable, palatable forms for every patient—every age.

There are tiny, easy-to-swallow Filmtab® tablets—125 mg. and 250 mg. (200,000 units and 400,000 units), a tasty, cherry-flavored suspension (each 5-ml. teaspoonful contains 125 mg.) and two combinations (Filmtab and suspension) with the triple sulfas. Depending on severity of infection, dosage for Compocillin-VK is usually 125 mg. or 250 mg. three times a day. Won't you try Compocillin-VK?

1. R. Lamb and E. S. Maclean, Penicillin V—A Clinical Assessment After One Year, *Brit. M. J.*, July 27, 1957, p. 191-193. **2.** J. I. Burn, M. P. Curwen, R. G. Huntsman and R. A. Shooter, A Trial of Penicillin V, *Brit. M. J.*, July 27, 1957, p. 193. **3.** J. Macleod, Current Therapeutics, *The Practitioner*, 178:486, April, 1957. **4.** W. J. Martin, D. R. Nichols and F. R. Heilman, Observations on Clinical Use of Phenoxymethyl Penicillin (Penicillin V), *J.A.M.A.*, p. 928, March 17, 1956.

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when your tongue blade points to respiratory infection

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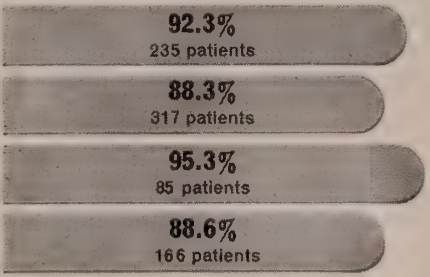

Tonsillitis*

Acute Streptococcus Pharyngitis*

Bronchitis* (Bacterial Complications)

Pneumonia*

*References supplied on request.

The usual dosage for infants and for children under twenty-five pounds is 5 mg. per pound every six hours; for children twenty-five to fifty pounds, 125 mg. every six hours.

For adults and for children over fifty pounds, the usual dosage is 250 mg. every six hours.

In more severe or deep-seated infections, these dosages may be doubled.

Ilosone is available in three convenient forms: Pulvules®—125 and 250 mg.†; Oral Suspension—125 mg.† per 5-cc. teaspoonful; and Drops—5 mg.† per drop, with dropper calibrated at 25 and 50 mg.

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New York State Journal of Medicine

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Editorials

The lady discards her high-buttoned shoes

The New York State Journal of Medicine was born in 1901 and, having attained an abundant middle age according to our present standards, had an urge natural to this time of life to smarten up her appearance. Her mirror told her that though her skin was still firm and her figure presentable perhaps there were things that could be subtly done to enhance the gifts of nature. Perhaps this man Dior . . . . So with shy bravado she consulted a beauty counselor. Dazzling, exciting, and sometimes downright alarming were the recommendations she received. Knowing the love her family bore her and the respect she had among her friends she had to choose carefully from among this tempting array of suggestions.

After much heart-burning thought she chose a few—a new foundation of course, the old one was overstretched in places; a new hairdo, not a beehive but the man said buns were definitely out; a new dress with slimmer cleaner lines and the touch of red she always fancied raised a bit higher on the bodice. She did not take up the henna rinse and the green eye-shadow recommended—after all she is no skittish young thing and what would the family say?

So it is that your Journal appears with this first issue of the new volume 62 in an updated cover which is cleaner and less cluttered. There is a new text type known as Century Schoolbook which is bolder and heavier. It makes the print look blacker and the white spaces whiter and enhances readability. The titles, headings, and subheadings are changed from Bodoni to News Gothic, a type face more in keeping with this half of the twentieth century and one that harmonizes well with the text face. A slightly heavier paper is being used, which makes the text type stand out better and delights the advertisers because their plates reproduce better and there is little or no showthrough from the advertising on the other side of the page. This much for skin-deep beauty.

The character beneath all this is our paramount interest. We shall continue to work up the finest scientific material obtainable and, as usual, have it passed on by the most competent authority obtainable, before presentation. We have both of these and will develop them further.

We introduce short abstracts at the head of articles as an aid in directing your interest. We will repeat the abstracts including reference citations in the back of the Journal, arranged in such a way that they can be cut out and pasted on library cards for filing.

We will publish summaries in Interlingua for the benefit of our Latin readers.

The index to advertisements will show these grouped according to therapeutic indications, making for readier reference.

The Lady goes forth this New Year's Day, 1962, strong as ever in substance and in the mode. With all her respectability, deep down we suspect she would not resent a wolf whistle.

The medical journal and its advertising pages

Most medical journals as we know them today are a triangular composite formed by the journal itself at the apex and the readers and advertisers at the angles at the base. Each is dependent on the other, and each is of equal importance.

If the quality of the material published is not such as to attract and hold its readers then the journal has failed in its principal function. A journal which is the scientific publication of an organization and provides a service for its members has a particular obligation to furnish high quality. Everything starts from here.

Production costs being at an all-time high, subsidy by membership generally is insufficient, and outside income is required. This income comes from the advertisers, largely of the pharmaceutical industry. There is no compulsion on them to use the journal. It is purely a business proposition which serves the function of calling attention to a drug about which the doctor has already been informed. We believe it is to the further advantage of the industry to keep worth-while medical journals going for the publication of unprejudiced descriptions of new, effective drugs and their clinical trials. Where else can this be done?

During the past year and a half the pharmaceutical industry has been reassessing its advertising policy. Also new government regulations on testing have slowed down the flow of new drugs to the market, with a consequent slowing of new drug advertising. As a result there has been a cutback in medical journal advertising ranging from 10 to 30 per cent over this period. All the medical journals have felt this and can but hope that any new policy which may be adopted will give due weight to the value of advertising in their pages.

Progress on a difficult problem

The work previously reported in September, 1960,* by Seneca, Zinsser, and Lattimer, on the enzymatic suppression effect of a mercurial, chlormerodrin, on the bacterially produced enzyme urease has been further extended by these investigators. Following up their observation that resistant organisms such as Klebsiella aerogenes and Bacillus proteus exhibit high enzyme activity, the investigators, with the addition of Donovan, found that when this activity was inhibited by chlormerodrin and other mercurials the bacteria often became susceptible to the commonly used antibiotics. In some of the cases studied, persistent infection was cleared up by the first application of this method. In one case where B. proteus infection of the urinary tract had existed for two years the method was successful. Paradoxically, the investigators also discovered that if these enzyme inhibitors are used on bacteria susceptible to the conventional drugs, they sometimes cause a reverse effect; that is, they may make sensitive bacteria become resistant. Thus this method should be reserved for urea-splitting infections which are resistant to ordinary drugs.

As so often happens in scientific investigation one backfire does not necessarily negate the worth of an experiment. Every piece of information fits into its rightful place, and the final result can have far-reaching and useful effects.

This work opens up a whole new line of attack on the problem of antibiotic-resistant infections. We look forward hopefully to further developments in this field.

---

* Seneca, H., Lattimer, J. K., and Zinsser, H. H.: The chemotherapy of urease- and citrase-producing bacteria of the urinary tract, Ann. Int. Med. 53: 468 (Sept.) 1960.

Taps for tattooing

Another element of raffishness in our largest city has joined the list of things beyond the pale. According to a board rule of the City of New York Board of Health, tattooing, except for medical reasons, has been banned from the City since November 1, 1961.

The tattoo parlors which nestled close to the Navy yard and the public dance halls must join burlesque and other colorful memories of civic adolescence in the sad skeleton closet of our past.

No longer may our youth in the first flush of love have the one's initials encircled by a heart placed permanently on his manly breast. No more will serpents writhe or dancers undulate as manly muscles ripple beneath the artist's fair creation.

And all because after two years of trial it proved impossible to indoctrinate the artists in sterile technic. With definite knowledge that a number of cases of infectious hepatitis were traceable to tattooing the Board of Health was forced to take drastic action.

The Board in its wisdom left an out, when it said "except for medical reasons." Shall some of us develop a side line of sterile, medical tattooing? The designs have limitless possibilities from the staff of Aesculapius to the formula for desoxyribonucleic acid.

Progress is inevitable, and we are for it, but being human we cannot avoid a fond look backward as we are swept along.

Editorial comment

Education in hospital costs. Medical students at Jefferson Medical College Hospital, Philadelphia, learn to consider the cost of as well as the need for diagnostic tests ordered for hospitalized patients.

William A. Sodeman, M.D., and John A. Nelson describe such a program in *Hospitals*, the journal of the American Hospital Association.

Each student, as he worked as a ward clerk, was given a list of the standard charges for various procedures and tests. On at least two of his patients he kept a running chart of the costs of tests and procedures ordered.

"The program was eminently successful in demonstrating cost factors in the care of hospital patients," the authors said. A glance at the running chart dramatized for each student how the total cost added up. Group discussions of the cost factor helped sharpen the analysis of indications for a procedure and the benefits to be obtained by ordering it.

This concern for cost helped stimulate discussion of the nature of the disease, distribution of lesions, and matters of differential diagnosis, the authors said, adding, "The simple questions, 'Do we need it?' and 'Why?,' are not dissociated from an understanding of the disease process and the pathologic physiology of the disease."

In addition to stimulating discussion about disease processes, the cost discussions also illustrated for the student that tests, such as blood chemical studies, should be used selectively for individual patients. When ordering studies of any sort, the student learned to consider the total state of the patient, including his financial situation.

In summary, the authors said the program serves "not only to acquaint students with the costs of patient care, but also to stimulate them to consider, through realization of charges, the need for the procedure or service under discussion. . . . Real benefits in evaluation of indications for, and selection of, alternative procedures resulted."

This pioneering work bears repetition in all our hospitals, whether there is a teaching program or not. Attending staffs as well need this indoctrination.

the first comprehensive regulator of female cyclic function

ENOVID®

(brand of norethynodrel with ethynylestradiol 3-methyl ether)

...unfettered

THE BASIC ACTION

Enovid closely mimics the balanced progestational-estrogenic action of the functioning corpus luteum. This action is readily understood by a simple comparison. In effect, Enovid *induces a physiologic state which simulates early pregnancy—except that there is no placenta or fetus.* Thus, as in pregnancy, the production or release of pituitary gonadotropin is inhibited and ovulation suspended; a pseudodecidual endometrium ("pseudo" because neither placenta nor fetus is present) is induced and maintained.

Further, during Enovid therapy, certain symptoms typical of normal pregnancy may be noted in some patients, such as nausea—which is usually mild and disappears spontaneously within a few days—breast engorgement, some degree of fluid retention, and often a marked sense of well-being. There is no androgenicity. Enovid *is as safe as the normal state of pregnancy.*

THE BASIC APPLICATIONS

1. Correction of menstrual dysfunction. *Emergency* treatment of severe dysfunctional uterine bleeding is promptly effective following the administration of Enovid in larger doses. *Cyclic* therapy with Enovid controls less severe dysfunctional uterine bleeding. In amenorrhea *cyclic* therapy with Enovid establishes a pseudodecidual endometrium providing the patient has endometrial tissue capable of response.

2. Ovulation suppression (to suspend fertility). For this purpose Enovid is administered *cyclically,* beginning on day 5 through day 24 (20 daily doses). The ovary remains in a state of physiologic rest and there is no impairment of subsequent fertility. When Enovid is prescribed for this *cyclic* use over prolonged periods, a total of twenty-four months should not be exceeded until continuing studies indicate that its present lack of undesired actions continues for even longer intervals. Such studies are now in their seventh year and will regularly be reviewed for extension of the present recommendation.

3. Adjustment of the menses for reasons of health (impending hospitalization for surgery, during treatment of Bartholin's gland cysts, acute urethritis, rectal abscess, trichomonal or monilial vaginitis), or other special circumstances considered valid in the opinion of the physician. For this purpose Enovid may be started at any time in the cycle up to one week before expected menstruation. Upon discontinuation, normal cyclic bleeding occurs in three to five days.

4. Endometriosis. *Continuous* therapy with Enovid corrects endometriosis by producing a pseudodecidual reaction with subsequent absorption of aberrant endometrial tissue.

5. Threatened and habitual abortion. Enovid should be used as *emergency* treatment in *threatened abortion* although symptoms may occur too late to be reversible. *Continuous* therapy with Enovid in *habitual abortion* is based on the physiology of pregnancy. Enovid provides balanced hormone support of the endometrium, permitting continuation of pregnancy when endogenous support is otherwise inadequate.

6. Endocrine infertility. Enovid has been used successfully in *cyclic* therapy of endocrine infertility, promoting subsequent pregnancy through a probable "rebound" phenomenon.

THE BASIC DOSAGE

Basic dosage of Enovid is 5 mg. daily in *cyclic* therapy, beginning on day 5 through day 24 (20 daily doses). Higher doses may be used with complete safety to prevent or control occasional "spotting" or breakthrough bleeding during Enovid therapy, or for rapid effect in the *emergency* treatment of dysfunctional uterine bleeding and threatened abortion.

Enovid is available in tablets of 5 mg. and 10 mg. Literature and references, covering more than six years of intensive clinical study, available on request.

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LIFTS DEPRESSION ...AS IT CALMS ANXIETY

"I feel like my old self again!" Thanks to your balanced Deprol therapy, her depression has lifted and her mood has brightened up – while her anxiety and tension have been calmed down. She sleeps better, eats better, and normal drive and interest have replaced her emotional fatigue.

Brightens up the mood, brings down tension

Deprol's balanced action avoids "seesaw" effects of energizers and amphetamines. While energizers and amphetamines may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression and emotional fatigue.*

These "seesaw" effects are avoided with Deprol. It lifts depression as it calms anxiety – a balanced action that brightens up the mood, brings down tension, and relieves insomnia, anorexia and emotional fatigue.

Acts rapidly – you see improvement in a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly – *often within a few days.* Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver or blood damage. Deprol does not cause liver toxicity, anemia, hypotension, psychotic reactions or changes in sexual function – frequently reported with other drugs.

▲Deprol▲®

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be increased gradually up to 3 tablets q.i.d. With establishment of relief, the dose may be reduced gradually to maintenance levels.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

CD-5859

WALLACE LABORATORIES / *Cranbury, N. J.*

Inborn Errors of Amino Acid Metabolism Associated with Dermatologic Manifestations

SAMUEL WEINBERG, M.D.
Massapequa, New York
MAURICE J. COSTELLO, M.D.
New York City
JAMES P. ROTCHFORD, M.D.*
Spokane, Washington

From New York University Medical Center,
New York City

ERRORS IN AMINO ACID METABOLISM *which are transmitted by heredity are manifested dermatologically in such disorders as: phenylketonuria, a disturbance in the metabolism of phenylalanine which causes mental retardation and the presence of phenylpyruvic acid in the urine; alkaptonuria, a disturbance in the metabolism of phenylalanine and tyrosine which results in the excretion of homogentisic acid in the urine; total albinism, a disturbance in the metabolism of tyrosine which causes the complete absence of pigment in the skin, eyes, and hair; partial albinism, a disturbance in the metabolism of tyrosine which is characterized by a congenital absence of pigment in various regions of the body; and Hartnup disease, a disturbance in the metabolism of indican, tryptophan, and indolacetic acid which results in a pellagroid eruption, cerebellar ataxia, mental deficiency, and amino-aciduria. Diagnosis of these conditions is made on the basis of clinical manifestations aided by such technics as paper and ion-exchange chromatography on the urine and blood plasma. In most cases the treatment is symptomatic, although the diagnosis and treatment of phenylketonuria, preferably before one year of age, is essential if mental retardation is to be prevented.*

IN RECENT YEARS the study of amino acid metabolism has increased greatly with the newer methods of determination of the individual amino acids both in plasma and urine. Paper chromatography and, more recently, ion-exchange chromatography[1] and microbiologic and enzymatic technics have enhanced our knowledge of these diseases. At times the skin manifestations of some of these conditions may be the clue to the diagnosis. It is the purpose of this paper to present to the physician those diseases of inborn errors of amino acid metabolism which may present some evidence of skin manifestations.

Phenylketonuria

Phenylketonuria is a disturbance in the metabolism of phenylalanine which causes mental retardation and the presence of phenylpyruvic acid in the urine.

Heredity. This disease is transmitted by a rare recessive autosomal gene and is present in 1 per 20,000 births in the United States. The carriers of this gene exist in 0.5 to 1 per cent of the normal population.

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Dermatology and Syphilology, May 9, 1961.

* By Invitation.

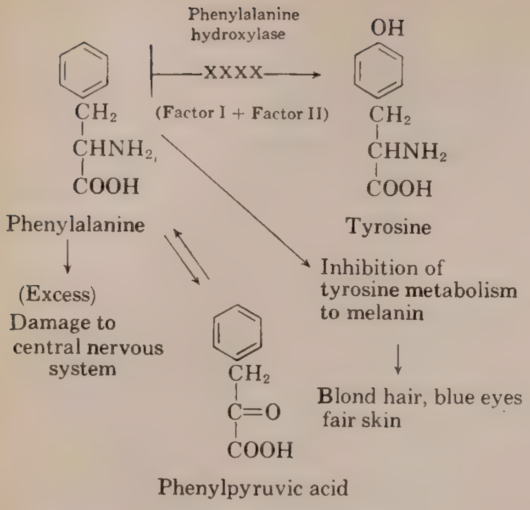
Phenylalanine hydroxylase
XXXX
(Factor I + Factor II)
OH
CH2
CHNH2
COOH
Phenylalanine
Tyrosine
(Excess)
Damage to central nervous system
Inhibition of tyrosine metabolism to melanin
Blond hair, blue eyes fair skin
C=O
Phenylpyruvic acid

FIGURE 1. Pathogenesis of phenylketonuria.

This condition is responsible for approximately 1 per cent of the institutionalized mentally defective persons.

Phenylalanine tolerance tests may reveal the heterozygous carriers of the phenylketonuric gene.

The defect in the enzyme system phenylalanine hydroxylase is related to a deficiency of factor I which is present normally only in the liver (Fig. 1). The result is an excessive accumulation of l-phenylalanine in the blood and spinal fluid.

Clinical manifestations. In a fairly large percentage of cases, the individuals affected have blue eyes, blond hair, and fair skin. This is especially so in the young children with this disease. Xerosis and various eczematous eruptions are present in approximately 25 to 30 per cent of cases.

The neurologic findings are those of mental retardation with an I.Q. usually below 30; however, some cases have been reported associated with a normal intelligence and occasionally with a high intelligence.

Other associated findings may be convulsions, abnormal electroencephalogram tracings, accentuation of deep and superficial tendon reflexes, agitated behaviorisms, and minor chorea-athetosis.

Diagnosis. The diagnosis is made by an awareness of this condition, the previously cited clinical manifestations, and a laboratory examination of the blood and urine.

In the urine, the presence of phenylpyruvic acid indicates this disease. This can be determined by the simple method of acidifying the urine with a few drops of tenth-normal hydrochloric acid and then adding a few drops of fresh 10 per cent ferric chloride solution. An intense blue-green color indicates the presence of phenylpyruvic acid. False positive reactions may occur with the presence of phenothiazine and its derivatives, bile, alkaptonuria, catecholamines, maple syrup urine disease, diacetic acid, melanin, and salicylates.

A reagent strip (Phenistix) dipped into the urine gives similar results.

In the blood, the finding of a phenylalanine level markedly above the normal, which is 0.2 to 1.5 mg. per 100 ml., is diagnostic.

Paper chromatography of the urine and blood plasma reveals an increased amount of phenylalanine and its derivatives.

Treatment. The prevention of mental retardation is accomplished only if treatment is instituted as early as possible in infancy. Screening tests of the urine with ferric chloride should be done on all infants after three weeks of age and repeated at six and eight weeks of age, especially in blond-haired, blue-eyed, fair-skinned children with or without an eczematous eruption.

In the infants born of families with a history of phenylketonuria or those carrying the phenylketonuric gene, the blood plasma level of phenylalanine should be tested in the first week of life to determine the presence of this condition.

Treatment which is instituted after one year of age will probably have little effect on the mental status of the individual, but it may enhance the resolution of some of the skin manifestations.

Definitive treatment consists of a low phenylalanine diet consisting of especially prepared milks such as Lofenalac or Ketonil, 1 per cent protein fruits and vegetables, gluten-free bread, vitamins, and minerals.

Alkaptonuria

Alkaptonuria is a disturbance in the metabolism of phenylalanine and tyrosine

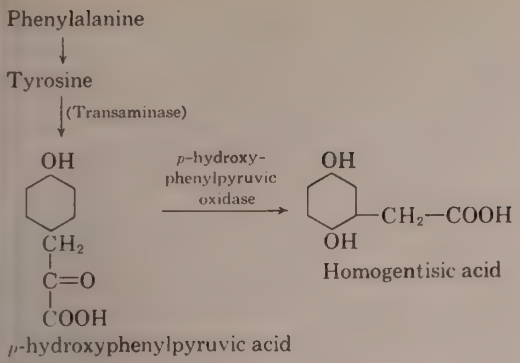
Phenylalanine
Tyrosine
(Transaminase)
OH
CH₂
C=O
COOH
p-hydroxyphenylpyruvic acid
p-hydroxy-
phenylpyruvic
oxidase
OH
CH₂—COOH
OH
Homogentisic acid

FIGURE 2. Pathogenesis of alkaptonuria.

resulting in the excretion of homogentisic acid in the urine (Figs. 2 and 3).

Heredity. This condition is transmitted either by a single recessive gene in the majority of cases or as a simple dominant gene.

The defect in the enzyme system homogentisic oxidase results in the accumulation of homogentisic acid in the blood and its deposition in the tissues and excretion in the urine.

Clinical manifestations. In the skin, ochronosis occurs; it consists of the presence of bluish black deposits which are most prominent in the scleras on either side of the corneal limbus, in the cartilages of the nose and ears, and in the superficial tendons of the hands. A brownish discoloration of the sweat may occur.

Arthritis, usually of a deforming type, may be present along with a kyphosis of the spine.

A blackish discoloration of the urine may be noted by the patient or physician after standing.

A biologic false positive serologic test for syphilis has been reported occasionally in this condition.

Diagnosis. The presence of the preceding clinical manifestations as well as certain laboratory examinations will reveal this disease. In the urine, the presence of homogentisic acid can be determined by alkalinization with sodium hydroxide or ammonium hydroxide. A dark brown or black color will result. The addition of a few drops of a 10 per cent ferric chloride solution to a specimen of urine will result in the appearance of an evanescent blue color.

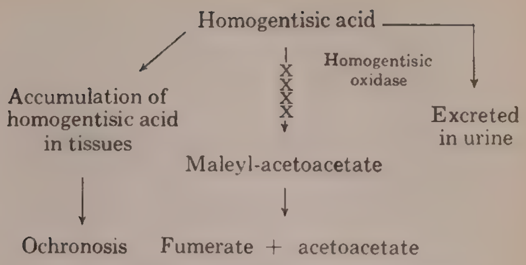
Homogentisic acid
Accumulation of
homogentisic acid
in tissues
Homogentisic
oxidase
Excreted
in urine
Maleyl-acetoacetate
Ochronosis
Fumerate + acetoacetate

FIGURE 3. Action of homogentisic acid.

The addition of a strong alkali and shaking of the sample will result in a dark color.

Roentgenograms of the spine reveal a typical calcification of the intervertebral disks with thinning.

A biopsy at the site of ochronosis reveals a light brown pigment in the dermis. The pigment does not stain with silver nitrate as melanin does but stains black with polychrome methylene blue.[2,3] Treatment is symptomatic.

Total albinism

Total albinism is a disturbance in the metabolism of tyrosine causing the complete absence of pigment in the skin, eyes, and hair (Fig. 4).

Heredity. This condition is transmitted as a simple recessive gene. It occurs in all races. Twenty to 30 per cent of the cases result from marriages between cousins.

Although the total number of melanocytes is normal, the absence of the enzyme tyrosinase within the melanocytes prevents the conversion of tyrosine to melanin. This inhibition of melanin formation occurs even

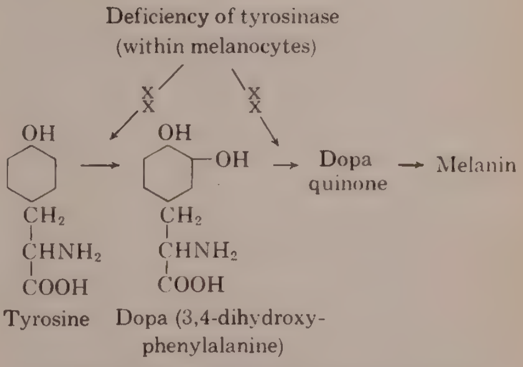
Deficiency of tyrosinase
(within melanocytes)
OH
CH₂
CHNH₂
COOH
Tyrosine
OH
OH
CH₂
CHNH₂
COOH
Dopa (3,4-dihydroxy-
phenylalanine)
Dopa
quinone
Melanin

FIGURE 4. Pathogenesis of total albinism.

in the presence of dopa (dihydroxyphenylalanine), since both dopa and tyrosinase are necessary for the conversion of tyrosine to melanin.

CLINICAL MANIFESTATIONS. At birth, this condition is evident by the presence of a white or pinkish-white skin and unpigmented hair which may be white or yellowish and silky. The eyes present a pink iris, red pupils, nystagmus, astigmatism, and photophobia. These symptoms persist throughout life. Occasionally, mental retardation may occur in this condition.

Keratoses, cutaneous horns, and epitheliomas are complications which may arise later in life in individuals with total albinism.

DIAGNOSIS. This condition is usually obvious from birth with the presence of the preceding clinical manifestations. On laboratory examination of the skin and hair, the dopa reaction is negative. No tanning of the skin occurs on exposure to sunlight.

TREATMENT. The treatment of this condition is purely symptomatic requiring the prevention of exposure to sunlight and the protection of the eyes from light, especially from the bright sun.

Partial albinism

Partial albinism is a disturbance in the metabolism of tyrosine which is characterized by a congenital absence of pigment in various regions of the body.

HEREDITY. This condition may be transmitted as a simple dominant gene; however, in partial albinism of the eye alone, a sex-linked recessive gene may be the cause.

PATHOGENESIS. The defect is probably due to the absence of the enzyme tyrosinase within the melanocytes in certain localized areas.

CLINICAL MANIFESTATIONS. In the skin, patchy well-defined areas of lack of pigmentation, with no surrounding hyperpigmentation, are present from birth. In the hair, pigmentation may be affected with a white forelock or piebald. Albinism of the eye alone may occur and is characterized by a hypoplasia of the macula, astigmatism, nystagmus, photophobia, amblyopia, and head nodding. The irises are pink, and the pupils may be red. These clinical features of the skin, hair, and eyes may occur individually or in combination.

DIAGNOSIS. The clinical features, as well as a history of heredity, will indicate this diagnosis.

TREATMENT. The use of various cosmetic preparations may be tried to make a more acceptable appearance of the skin involved. The sites of involvement should be protected from exposure to sunlight. In the presence of ocular albinism, the eyes must be protected from light.

Hartnup disease

Hartnup disease is a disturbance in the metabolism of indican, tryptophan, and indolacetic acid resulting in a pellagroid eruption, cerebellar ataxia, mental deficiency, and amino-aciduria.

HEREDITY. This condition is believed to be transmitted as an autosomal recessive gene.

PATHOGENESIS. The defect is believed to be in the conversion of tryptophan to nicotinic acid. A disturbance in the utilization of nicotinic acid results in the pellagroid eruption and in a disturbance of indole metabolism which may cause the presence of cerebellar ataxia and mental retardation and also an increased excretion of indican, tryptophan and indolacetic acid in the urine.

CLINICAL MANIFESTATIONS. The skin changes have been noted in early childhood with a pellagroid eruption of the light exposed areas of the legs, arms, hands, and face. A generalized xerosis may be present. Various neurologic symptoms which are frequently noted include cerebellar ataxia, nystagmus, ptosis, tremor, increased deep tendon reflexes, and mental deficiency.

DIAGNOSIS. The clinical manifestations of this condition associated with the presence of a gross amino-aciduria will reveal this diagnosis. Paper chromatography of the urine exhibits an increase of indican, tryptophan, indolacetic acid, and other indole products.

TREATMENT. The use of nicotinamide or nicotinic acid in fairly large doses may prove to be somewhat effective.[4,5] The avoidance of sunlight may diminish the appearance of the pellagroid eruption.

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Discussion

Elmer H. Tuttle, M.D., *Rochester, New York:* I am sure that most of us who were present at the recent meeting of the American Academy of Dermatology in Chicago are grateful for this second opportunity to review this interesting topic of "Inborn Errors of Amino Acid Metabolism." The scientific exhibit presented in Chicago by Dr. Weinberg and his associates was a good one, but for many of us the pressures exerted by the many exhibits and other papers precluded a satisfactory assimilation of their exhibit.

It is unfortunate that in our medical school days we had insufficient background knowledge of the importance of the amino acids and at that time were content to limit our knowledge of them to a memorization of the 10 essential acids aided by some off-color phrase long since forgotten. We were somewhat content to accept as adequate a conclusion that laboratory rats fed on diets deficient in these amino acids in some way didn't grow as well as the controls. Thus, today, confrontation with clinical problems involving these same amino acids requires that we engage in renewed and further study of them.

For background in this subject I would like to direct your attention to an excellent book written by Hsia.[a] Lipid, carbohydrate, and other metabolic diseases are also covered in this easily readable book. In his preface Hsia comments that to understand these inborn metabolic diseases requires a knowledge of genetics and a fairly specialized biochemistry: "During the past few years so many additions have been made to the inborn errors of metabolism that we (as clinicians) are really pressured into extending our knowledge of them. Much has been learned; much more remains to be explored and elucidated."

The advances in knowledge in this field reminds me of the time clocks shown at many sites of geologic interest which note man's existence as a few seconds in comparison with the hours of the age of the universe. We are, it seems to me, a few seconds along in our understanding of amino acid chemistry.

In the past few years many highly technical, but interesting, papers have appeared in the *Journal of Biochemistry* and elsewhere on the mechanism of the enzymatic conversion of phenylalanine to tyrosine and its further conversion to melanin and other products.

On reading them one gets the feeling that perhaps we already have in the literature some tools or know-how which would enable the clinician to manipulate beneficially the clinical disorders encountered. Perhaps we need only the bridge between the biochemist and the clinician.

Kaufman[b] reported that two enzymes appeared to be required for the conversion of phenylalanine to tyrosine plus a nonprotein cofactor. This was not a new observation, but he found that tetrahydrofolic acid could replace the cofactor and on further study found that a portion of the folic acid was more active than the whole folate.

Of some interest to us might be his finding that folic acid antagonists such as Aminopterin are fairly potent inhibitors of the enzymatic conversion of phenylalanine to tyrosine. Does this hold a clue to our treatment of psoriasis with a folic acid antagonist?

Can we influence phenylketonuria or alkaptonuria or albinism with folic acid or the more potent tetrahydrofolates? Probably not.

As dermatologists we are interested in the xerosis and the various eczematous eruptions occurring in about one fourth of patients with phenylketonuria. The relative rarity of the disorder and the superficial discussion in the literature of the skin manifestations makes me uncertain as to whether or not a cause-and-effect relationship exists between the phenylketonuria and the dermatitis. It may be that the increased skin sensitivity is that shared by most fair-skinned persons with or without phenylketonuria.

Alkaptonuria with the accumulation of homogentisic acid in the tissues which we know as ochronosis is not usually very spectacular in respect to skin changes. We have recently seen at Strong Memorial Hospital a brother and sister, middle-aged, showing ochronosis in the scleras and cartilages of the ears. However, the dominating clinical problem was an advanced disabling arthritis with spinal involvement. In these 2 patients the diagnosis was first made by the radiologist who noted the pathognomonic changes in the spinal column. As soon as the diagnosis was suspected the other and less conspicuous manifestations were noted.

The biochemistry of the conversion of phenylalanine and tyrosine to dopa quinone and melanin has been postulated for quite a few years. The biochemists have been able to demonstrate this phenomenon in vitro and in a number of ways have been able to manipulate it adversely and/or beneficially. However, the bridge of clinical application to albinism, total or partial, still eludes us. A tyrosinase deficiency has been postulated as the cause of albinism. However, recently Hu[c] has demonstrated the presence of tyrosinase in albinos. His work has not yet been confirmed by others.

Lerner and Fitzpatrick[d] have an excellent monograph on the biochemistry of melanin formation. This monograph lists several in vitro inhibitors of melanin formation and factors which enhance melanin formation. A rereading of this monograph is well worth while.

It would appear that Hartnup disease which was first reported by Baron, *et al.* in 1956[e] was restricted to one family. No other cases that I know of have been reported.

The symptoms were: a pellagra-like skin rash; neurologic changes suggesting cerebellar ataxia; and amino-aciduria suggesting a disturbance of nicotinic acid utilization. All of the amino acids were increased in the urine except proline. Since the plasma levels were normal it was assumed that the amino-aciduria was renal in origin.

In conclusion I enjoyed hearing Dr. Weinberg's paper and the privilege of discussing it.

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[d] Lerner, A. B., and Fitzpatrick, T. B.: Biochemistry of melanin formation, Physiol. Rev., 1950.

[e] Baron, D. N., *et al.*: Hereditary pellagra-like skin rash with temporary cerebellar ataxia, constant renal amino-aciduria, and other bizarre biochemical features, Lancet **2:** 421 (Sept. 1) 1956.

Identical twins suffer identical ills

A pair of seventy-nine-year-old identical twin women have suffered six identical ailments, according to a report by Lewis M. Schiffer, M.D., Matthew Zucker, M.D., and Eugene L. Lozner, M.D., in the November 4, 1961, issue of the *Journal of the American Medical Association.* The authors said the two women had a "unique combination of illnesses."

They both now suffer anemia, partial paralysis of the face, an abnormality of the small bowel, and hernia of the colon. In addition, both women also had a benign tumor of the breast and probable toxemia of pregnancy.

Although anemia in identical twins is not unique, the physicians could find no previous record of the incidence of the other disorders in twins.

The phenomenon suggests the possibility of a defect in one or more of the patients' chromosomes, although no chromosome abnormality was observable.

Recent Advances in the Medical Treatment of Glaucoma

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THERE HAVE BEEN *important improvements in the drugs used in glaucoma. The carbonic anhydrase inhibitors, of which acetazolamide (Diamox) has been the most widely used, are useful in chronic simple glaucoma and secondary glaucoma associated with uveitis, and preoperatively in the acute phase of angle-closure glaucoma. The cholinesterase inhibitors, of which water-soluble phospholine iodide and demecarium bromide are the most important contributions, produce marked miosis, decrease in intraocular pressure, and improvement in the facility of aqueous outflow. Epinephrine and the epinephrine-like drugs are useful to lower the intraocular pressure in chronic simple glaucoma. All of the drugs mentioned are definitely contraindicated in narrow-angle glaucoma. The most common side-effects are mild to moderate, but more severe toxic effects may occur. A most useful ocular hypotensive agent recently introduced is intravenous urea which brings the intraocular pressure down to normal temporarily in almost all types of glaucoma so that the appropriate surgical procedure may be performed. As most of these drugs are contraindicated in angle-closure glaucoma, the importance of a careful accurate initial diagnosis with gonioscopy and tonography must be emphasized.*

THE DRUGS WE EMPLOY for the management of glaucoma assume an increasingly important role when we realize that the present-day treatment of choice for both chronic simple and most secondary glaucomas is primarily medical. For this reason a considerable effort has been made during the last decade to improve the drugs employed in glaucoma therapy; several new agents have been added to our armamentarium of antiglaucomatous medications, and, what is even more important, the older drugs are utilized to a much better advantage because of recent advances in the entire field of glaucoma diagnosis, pathogenesis of the disease, and a better understanding of the mechanism of action of the drugs employed in therapy.

The most noteworthy contributions in this field were those concerning the carbonic anhydrase and cholinesterase inhibitor compounds, the epinephrine-like drugs, and the ocular hypotensive agents.

Carbonic anhydrase inhibitors

Acetazolamide (Diamox), the first carbonic anhydrase inhibitor employed in ophthalmology, has now been used extensively in all types of glaucoma, and its indications and contraindications are well defined. In chronic simple glaucoma it should be used mainly as an adjunct to miotic drops; in this type of glaucoma it often can be employed safely as a long-term medication. It is very useful in secondary glaucoma associated with uveitis, where miotics are contraindicated and acetazolamide is often the only available medication to lower the ocular pressure.

In the treatment of angle-closure glaucoma acetazolamide should be employed only in the acute phase to control the acute attacks; that is, to help bring the pressure down to normal limits. However, once the pressure is normal acetazolamide therapy should be discontinued, and surgery should be considered. As a matter of fact, for the long-term treatment of narrow-angle glaucomas, acetazolamide is definitely contraindicated.

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The most common side-effects, such as numbness, tingling of the hands and feet, and mild gastrointestinal upsets, are very frequent, but fortunately they are also mild to moderate in nature. However, more severe toxic effects, such as extensive skin reactions, and possible renal calculi formations, should be kept in mind because they do occur occasionally, and naturally under those circumstances the drug should be discontinued immediately.

Besides acetazolamide, dichlorphenamide (Daranide), methazolamide (Neptazane) and ethoxzolamide (Cardrase) are useful carbonic anhydrase inhibitors also. Their pharmacologic action is similar to that of acetazolamide, and they should be employed mainly if the side-effects of acetazolamide are too severe and the drug is not tolerated by the patient. Otherwise dichlorphenamide, methazolamide, and ethoxzolamide do not offer any advantages over acetazolamide.

Recent laboratory investigations have cast some doubt on the exact mechanism of action of the carbonic anhydrase inhibitors on the intraocular pressure. However, while the mechanism of action of this group of compounds is still not well explained, their clinical usefulness in the treatment of glaucoma has been accepted almost universally, and these drugs, in spite of their occasional shortcomings, are here to stay.

Cholinesterase inhibitors

In the field of cholinesterase inhibitor compounds, the water-soluble phospholine iodide (echothiophate iodide) and demecarium bromide (B.C. 48) are the most important contributions to the medical treatment of glaucoma. These are irreversible inhibitors of cholinesterase; they are water-soluble, white crystalline solids. They do not cross the blood-brain barrier readily, and for this reason alone the systemic side-reactions are less severe and less dangerous than those seen with DFP (isoflurophate). These drugs produce marked miosis, a decrease in intraocular pressure, and an improvement in the facility of aqueous outflow both in normal and glaucomatous eyes. Following topical instillation there is some systemic absorption, but most of the systemic side-effects are minimal or rare. Ocular side-effects, however, are much more common, and they consist of injection and tenderness of the globe, severe ciliary spasm resulting in pain in the eyes, brow-ache, and often a generalized headache.

These two compounds should not be used in narrow-angle glaucoma because they can cause ciliary spasm and edema of the entire uveal tract which in turn can trigger off an angle-closure episode and a typical acute attack. This unfortunate course of events was seen a number of years ago when DFP was first introduced in the treatment of glaucoma; at that time several acute attacks had been produced by DFP in angle-closure cases. For this reason DFP was relegated mainly to the treatment of aphakic glaucoma where edema and ciliary spasm are less likely to embarrass the angle. However, more recent clinical evidence indicates that the average case of chronic simple glaucoma with wide angle can tolerate the use of these drugs in most instances. Therefore, gonioscopy should be carried out on all eyes where the use of these powerful miotics is contemplated to rule out the potential angle-closure cases and thus prevent the most severe and embarrassing complications encountered with these drugs.

Phospholine iodide and demecarium bromide also have the practical advantage of being long-acting compounds, and as a rule a once-daily administration is sufficient; they are water-soluble and stable which gives them a considerable practical advantage over DFP which has to be dissolved in peanut oil and is inactivated by contact with water. One disadvantage of phospholine iodide is that it requires storage in the refrigerator to retard loss of activity in aqueous solution; at room temperature approximately one fourth of its activity is lost in the course of two months. In general, phospholine iodide and demecarium bromide are superior to DFP in the treatment of glaucoma. However, they are not the ideal miotic because of their local and sometimes even systemic side-reactions, and so the search for better miotics continues.

Epinephrine-like drugs

It has been known for many years that epinephrine or epinephrine-like compounds lower the intraocular pressure of many eyes with various types of glaucoma. A number of such drugs are currently employed in the treatment of glaucoma, such as epinephrine, epinephrine bitartrate, epitartrate, 1-epinephrine, and Neo-Synephrine. They reduce the ocular pressure apparently by inhibiting to some extent the secretory mechanism of the ciliary body and thus decreasing the amount of aqueous humor being formed. They are ideally suited to the treatment of chronic simple glaucoma when miotic drops by themselves are not sufficient to normalize the tension; in many of these patients the addition of epinephrine-like compounds, in various combinations with the miotics, will bring the pressure to within normal limits. The most frequently seen side-reactions are mild to moderate local irritation in the eye. However, the most severe and most important side-reaction is the possibility of precipitating an acute attack in the narrow-angle glaucoma. Therefore, with this medication, it is important to rule out all angle-closure cases with a complete diagnostic work-up including careful gonioscopy. As a matter of fact, epinephrine or, as it was known in the 1920's, Glaucosan, received its bad reputation because it produced numerous acute attacks due to its widespread, indiscriminate use at that time. Nowadays, however, since we are more careful to differentiate between chronic simple glaucoma and the narrow-angle glaucoma, the acute attacks can and should be prevented by excluding the potential angle-closure cases from treatment with the epinephrine compounds.

Ocular hypotensive agents

The most useful ocular hypotensive agent recently introduced in the field of glaucoma therapy is urea. This compound is administered intravenously to bring the intraocular pressure down to normal in recalcitrant cases; in practically all types of glaucoma, be it primary or secondary, intravenous urea will normalize the tension and thus allow the appropriate surgical procedure to take place at the time that the ocular tension is normal. This is of considerable clinical importance, since operating on a so-called very hard eye is always a risky business. Thus, intravenous urea is a useful adjunct in the treatment of acute glaucomas. However, we must remember that in itself it does not influence the cause of the acute attack; it only brings the pressure down to normal temporarily, and therefore it should be followed immediately with the appropriate surgical procedure to treat the cause of the acute attack.

Summary

The use of carbonic anhydrase and cholinesterase inhibitor compounds, epinephrine-like drugs, and ocular hypotensive agents in the treatment of glaucoma was outlined. The principal pharmacologic actions of these agents was discussed; their main clinical indications and also contraindications were emphasized.

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Discussion

Robert E. Kennedy, M.D., *Rochester, New York:* Dr. de Roetth has presented an interesting discussion of the pharmacologic action and main clinical indications and contraindications of several of the newer agents which are being accepted into use as antiglaucomatous medications. I have nothing of a critical nature regarding this paper but only wish to amplify some of the points which I feel are of significance.

During the discussion of carbonic anhydrase inhibitors it was mentioned that acetazolamide definitely is contraindicated for the long-term treatment of angle-closure glaucoma. It may mask the patient's symptoms so that unrecognized minor episodes of angle closure may occur even while he is under acetazolamide therapy and may result in synechias and a loss of function of the trabecula. This may necessitate a filtering procedure instead of the use of a more simple peripheral iridectomy. Carbonic anhydrase inhibitors should be given in proper dosage as prolonged use at a lower dosage may result in the development of drug adaptation and lack of responsiveness. Six years ago before this meeting there was speculation that acetazolamide might alter lens metabolism harmfully and predispose to cataract formation. Time and its widespread use have shown this to be of no concern. Because of the many general medical side-effects it is well to advise the patient's medical doctor that a carbonic anhydrase inhibitor has been prescribed. There are times when he may prescribe a similar drug also, such as Diuril for hypertension which can result in an additive effect or a significant sulfonamide dosage which may call for a change in the total medical treatment of the patient.

The cholinesterase inhibitors were noted to have local and systemic side-effects. These side-effects are extensive enough so that 15 to 20 per cent of patients are unable to use these drugs. Topically the uncomfortable side-effects are usually tolerated after the drug has been used for from four to seven days. However, fibrinous iritis has occurred, and bilateral retinal detachments have been reported after the use of both Humorsol and phospholine iodide. Iris cysts at the pupillary margin have been noted with the prolonged use of these drugs. These tend to disappear after the drug has been stopped. They occur about half as frequently as cyst formation with the use of DFP.

Dr. de Roetth points out the contraindications for the use of these cholinesterase inhibitors in angle-closure glaucoma which has not been operated on because of the danger of precipitating an acute attack. If this occurs inadvertently, or if a paradoxical elevation of intraocular pressure occurs, the use of the antidote pralidoxime iodide (Protopam) administered subconjunctivally may abort an attack or may be used in the presence of severe local symptoms from the use of these cholinesterase inhibitors. These drugs have their effect on the ocular tension without depending on the miosis induced. Therefore, it is safe in chronic simple glaucoma to use phenylephrine hydrochloride 10 per cent to examine the fundi without decreasing the outflow facility or raising the intraocular tension. This should be done at intervals, at least once a year, to break up any posterior synechias, and to inspect the lens, disk, macula, and peripheral fundus, particularly with any decrease in vision. Also, visual fields may be verified to rule out field changes due to a small pupil with increased lens opacities. Because of the systemic side-effects the drug should be used with caution or is contraindicated in vagotonia, vasomotor instability, bronchial asthma, spastic gastrointestinal disturbbances, hypotension, myocardial infarction, and so forth. The systemic use of atropine or Pro-Banthīne will counteract these side-effects. Again with this group of drugs it is wise to advise the patient's medical doctor that these potentially toxic drugs have been prescribed since their side-effects may cause symptom complexes which could result in unnecessary medical and x-ray studies.

Epinephrine-like drugs were mentioned and again contraindicated in angle-closure glaucoma. Their use in neovascular and hypersecretive glaucoma may be beneficial especially when they are combined with carbonic anhydrase inhibitors.

Ocular hypotensive agents, specifically urea, were mentioned. It is well to remember their contraindication in uremia and renal damage, dehydration, and intracranial bleeding.

Since it has been pointed out that most of these newer agents are contraindicated in angle-closure glaucoma, the importance of a careful accurate initial diagnosis with gonioscopy and tonography must be emphasized again. Only in this way can these potent newer agents be used with better rationale.

Essential Differences Between Cancer in Children and Cancer in Adults

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CANCER IN CHILDREN *differs from cancer in adults in quantitative and qualitative aspects. The usual pattern of childhood cancer is stable because the usual distributor of cancerogens, the fetal blood circulation, is a constant, whereas the location and distribution of primary tumors in adults are variables determined by exposures and experiences during the course of life. In adults about one half of all cancers consist of carcinomas in the cover tissues, which in postnatal life are the only areas directly accessible to exogenous cancerogens. In children, however, leukemia accounts for almost one half of all cancer, as in intrafetal life the cancerogens carried by the maternal blood stream first come in contact with the vascular endothelium. In the author's opinion the cephalocaudal law of physiologic growth and development and the cephalocaudal law of childhood cancer are accounted for by the same peculiarities of the fetal blood circulation. The author suggests that there may be an acquired immunity factor in the development of cancer. There is no sharp demarcation line in the age curve between pre- and postnatally induced cancers. The latency period of prenatally induced cancers varies within the limits of birth and thirty odd years, and the cancer latency varies with organ and system.*

CANCER IN CHILDREN differs from cancer in adults in quantitative and qualitative aspects: in its incidence and distribution by histology, system, organ, and region of the body; in the existence of special tumor forms; in its clinical course; in the shape of the age curve; and in the fact that its main statistical features are stable, while in adults they are highly pliable. The implication of these differences is twofold: (1) The epidemiology of childhood cancer is independent of the environment in which we live, and (2) at the core of all deviations exists one all-embracing mechanism.

Of the older theories, none even pretends to explain more than a specific sector of the features of childhood cancer. This is true of Warren,[1] Bashford,[2] Thiersch,[3] Cohnheim,[4] and Ribbert.[5]

If for the explanation of a stable array of complex phenomena it is necessary to employ several hypotheses, usually none hits the nail on the head. A satisfactory theory should demonstrate that the whole complex of essential features must be as it is and should tell also under what circumstances a change may occur.

Yet none of the theories, including Virchow's,[6] required leukemia to be the leading cancer form of childhood (Table I) nor did any theory state why leukemia occurs more frequently in children than all types of sarcoma together. It is twice the sum of all sarcomas combined. No theory required that a large number of childhood cancers

TABLE I. Distribution by age of cancers in white persons in the United States in 1957 to 1958

Site	Children (Per Cent)		Adults* (Per Cent)	
Cover tissues	2.0		46.8	
Leukemia	48.3	84.8	3.9	12.2
Lymphosarcoma	9.4		4.4	
Central nervous system and eye	20.8		2.1	
Kidney	6.3		1.8	
All others	13.2		41.0	
TOTALS	100		100	

* Over thirty years of age.

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TABLE II. Number of deaths from cancer in white persons in the United States in 1952 to 1958

Site	Number of Children	Number of Adults*
Mouth and pharynx	132	33,007
Stomach	40	139,666
Brain and eye	5,524	29,615
Leukemia	11,925	55,091

* Over thirty years of age.

TABLE III. Approximative distribution of cancers by histology

Condition	Children (Per Cent)	Adults* (Per Cent)
Leukemia and sarcoma	60 to 70	9 to 10
Glioma and neuroblastoma	20 to 21	2
Carcinoma	10 to 16	88 to 89

* Over thirty years of age.

develop in the brain (actually about one fifth of the total) and that the cerebellum harbor more primary malignant conditions than the so much larger cerebrum. Nor did any theory require that mouth and pharynx cancer in children exceed stomach cancers numerically (Table II), nor that eye cancers develop in the retina but not in the lens or iris.

I will now present a unitarian theory which fits all of the principal findings and fulfils the desiderata stated previously.

Intrafetal cancerogenesis

Childhood cancer is the response to cancerogens that acted prior to birth and yet from the embryo's point of view were predominantly exogenous. Ordinarily, these exogenous cancerogens have only one source, maternal blood; one invasion route, the placenta; and one distributory mechanism, the intrafetal blood circulation. At definite periods during the development, in certain organs exogenous cancerogens are complemented by hormonal products, as in the fetal testis, and by products of mass disintegration. Depending on the local circulatory conditions, these products either act in situ as in the testis and kidney or are transported to the place of action as in the eye and adrenal gland. Occasionally, intrafetal cancerogenesis is supplemented by penetrating rays. They reach the target on a straight line, regardless of blood circulation.

The usual pattern of childhood cancer must be stable, because the usual distributor of cancerogens, the fetal blood circulation, is a constant.

Since the early 1920's when I was studying the influence of pregnancies and deliveries on later cancer, I have demonstrated repeatedly that the location and distribution of primary tumors in an adult population are variables, determined by exposures and experiences during the course of life. In general, in adults about one half of all cancers consist of carcinomas in the cover tissues, that is, in the epidermis and the epithelium of the alimentary and respiratory tracts and the uterine cervix. The reason is simple: These epithelia are in postnatal life the only areas directly accessible to exogenous cancerogens. In children, however, these same areas harbor less than 2 per cent of all cancers, while leukemia alone accounts for almost one half of all cancers. This quantitative relation puts in doubt postnatal induction as a major factor in childhood cancer, while the theory of prenatal induction is in agreement with and substantiated by it.

Having entered the embryo or fetus, cancerogens first come in contact with the vascular endothelium, which up to the fourth month is actively lymphocytopoietic, retains its embryonal potentialities throughout the fetal period, according to Fischel,[7] and remains in control of the reticuloendothelial system. The endothelium's exposure results in leukemia and perhaps also in some lymphosarcomas. Thus, the very same principle, namely, that the tissues which are met first carry the brunt of the impact of the exogenous cancerogens, is valid for both adults and children. But it leads to a distribution of malignant conditions which differs radically between these two age groups.

Having passed the fetal capillary walls, cancerogens are brought foremost into the mesenchymal tissues where only sarcomas can be induced. This junction in addition to leukemia is the reason for the high proportion of mesenchymal malignant conditions in childhood (Table III).

Since in the fetal central nervous system, in the nasopharyngeal mucosa, thyroid, liver,

TABLE IV. Approximative topographic division of nonleukemic cancers in white persons in the United States in 1957 to 1958

Site	Children (Per Cent)	Adults (Per Cent)
Upper part* of the body	59	21
Lower part† of the body	41	79
TOTALS	100	100
Proportion of leukemia to totals	100.6	4.2
Proportion of rest to totals**	7.6	6.2

* Head, thyroid, breast; two thirds of skin and lymphosarcomas; one third of bone and connective tissue tumors.

† All other cancers specified, except leukemia.

** Other specified sites and unspecified sites.

and adrenal medulla, the capillaries border on neuroectodermal, ectodermal, or entodermal cells, these structures are affected first of all. Hence, there is a high ratio of nonmesenchymal childhood cancers in these organs. The relevancy of distance between a tissue and its capillaries is attested also by the rarity of mesotheliomas in the serosa of the pleura, pericardium, and peritoneum.

In the fetus, for purely mechanical distributive reasons, only a very small fraction of exogenous cancerogens is delivered to those tissues which in the extrauterine period are called cover tissues. Since an organ's share in all cancers is among others a function of the fraction of the stimuli it received and absorbed, the cover tissues are but seldom the seat of childhood cancers.

Cephalocaudal law

There can be no explanation of the large proportion of cancers in the cephalic part of the child (Table IV) unless cancerogenesis is correlated with the nonmixing of the blood of the two cavae in the fetal right atrium. According to Haller[8] and Sabatier[9] the stream of the cava inferior, carrying all of the blood from the placenta and the venous blood from the caudal part of the body, leaves via the foramen ovale for the left heart and the ascending aorta, while the purely venous blood of the cava superior and the coronary veins leaves during the atrial systole via the tricuspid, right ventricle, pulmonary artery, and ductus botalli for the descending aorta. With many others[10-12] I concur in this view, which has been supported by experiments on the fetal heart and on confluent streams in veins.

The arterialized placental blood is diluted twice when it arrives in the ascending aorta and for a third time in the descending aorta when the unused portion of the blood that pours down from the upper aorta is joined by the purely venous blood flowing in from the ductus botalli. This second component is the same blood that had supplied the heart, head, neck, and the upper extremities with maternal oxygen, nutrients, and cancerogens, and which now, largely stripped of all three, returns to the aorta. Thus, compared with the upper part of the fetal body, the caudal part gets blood that carries per unit of volume less oxygen, less nutrients, and less cancerogens.

In my opinion, both (1) the cephalocaudal law of physiologic growth and development and (2) the cephalocaudal law of childhood cancer are accounted for by the same peculiarities of the fetal blood circulation.

Other differences in the amount and route of cancerogens

Again, for reasons of fetal blood circulation, Wilms tumors are many times more frequent than children's bladder cancers which are sarcomatous (Table V). Physiologically, in the fetus glomerular function is very scanty and late. Therefore, most if not all cancerogens delivered to the kidney remain there and, probably enhanced by the disintegration of vestigial vesicles and tubules, act on the primitive and multipotential tissue. Hardly any cancerogens reach the fetal bladder via the urine; they are carried mainly by the vesical arteries and deposited in the bladder wall. Hence, malignant conditions in the bladder in children are scarce and are sarcomas.

Analogous differences, in both the amount of cancerogens and their route, account for the differences between children and adults in the incidence and histology of cancer of the gastrointestinal and respiratory tracts.

In the child's adrenals most cancers arise from ganglion cells, although this is the least frequent cell form and one that in the central nervous system rarely gives rise to malignant

TABLE V. Number of deaths from kidney and bladder tumors in white persons in the United States in 1952 to 1958

Site	Children	Children 15 to 29 (Years)	Adults	Proportion of Children to Adults
Kidney	1,609	228	26,661	1:16
Bladder	73	40	46,377	1:635
Proportion of kidney to bladder tumors	22:1	6:1	0.6:1	

conditions. On the other hand, malignant pheochromocytomas and adenocarcinomas are scarce, especially in young children. Three items contribute to this picture. First, adrenal ganglion cells lack protection against contact with capillaries, while in the central nervous system, in the paraspinal ganglia, and in the eyes they are protected by glia cells, by nets of fibers, or by distance. Second, because of the one-way blood flow through the adrenals, only the medulla but not the permanent cortex is flooded with the cancer-relevant products of the disintegration of the tremendous mass, called the "fetal adrenal cortex." Third, at the time of this flood, the ganglion cells are only partly differentiated and are thus much more responsive than the already differentiated pheochromocytes.

Acquired immunity

In 1950 to 1958, 35.7 million babies were born alive in the United States. At least 900 of them have developed retinoblastoma, but only 476 deaths were listed. Now think of the survivors from former years and of those abroad, and you arrive at a substantial figure. Even if only one fifth or one sixth of the children with retinoblastoma reached maturity, a considerable number of them could later develop a second primary cancer elsewhere, were it not for an acquired immunity. However, such instances of multiplicity are exceptionally rare. A case, published last year in England by Levene[13] may be mentioned. A woman, who lost both eyes in infancy, at the age of forty developed a fatal vaginal botryoid sarcoma. This is a rare embryonal tumor of early childhood. What kept the tumor anlage dormant for forty years? In agreement with the cephalocaudal law of childhood cancer the eyes received so much more cancerogens than the vagina that the retinoblastoma developed earlier. It was cured early enough to prevent the manifestation of the rhabdomyosarcoma at the usual age of birth to five years. Four decades later, her immunity broke down, and the dormant sarcoma anlage started growing.

Whether or not this interpretation, based on my research work on human cancer since 1933, is pertinent can be proved only by a systematic, coordinated study in which the observation of cases is confronted with correctly assessed expectation.

I should like to touch on one more item. Comparing the ratios and rates of cancers of various systems and organs at the age of fifteen to twenty-nine with both adjacent age groups, I realized that at the age of fifteen to twenty-nine most leukemias, lymphosarcomas, brain and kidney tumors, and bone sarcomas were still of prenatal origin, while the other cancers were induced postnatally.

Conclusion

To conclude (1) in the age curve there is no sharp demarcation line between pre- and postnatally induced cancers, (2) the latency period of prenatally initiated cancers varies within the limits of birth and thirty odd years, and (3) cancer latency varies with the organ and system.

For more details I have to refer you to my recent book.[14]

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 14 to 18, 1962, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1962*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

ALFRED A. ANGRIST, M.D., *Chairman*
Committee on Prize Essays

Steatorrhea

Clinical Approach to Diagnosis and Management

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STEATORRHEA is defined as the presence of increased amounts of fat in the stool. Although it is generally considered a somewhat uncommon entity, recent isotopic technics have revealed that it is present much more frequently than is realized.

The purpose of this report is to summarize the over-all approach to the patient in whom this condition is either suspected or proved.

Causes of steatorrhea

Two basic causes for the presence of elevated fecal fat are generally recognized: a digestive or an absorptive defect. Occasionally both may be present.

Impaired digestion may occur when there is a deficiency of one or more of the substances necessary for normal fat absorption, such as bile salts and pancreatic enzymes. Thus, steatorrhea is common in obstructive jaundice, biliary cirrhosis, and in various diseases of the pancreas, both benign and malignant.

On the other hand, normal amounts of bile and fat-splitting enzymes may be present but may not mix adequately with the ingested food. This is thought to be a factor in the steatorrhea associated with a postgastrectomy state.[1] More recently, steatorrhea has been reported in cases of the Zollinger-Ellison syndrome possibly resulting from an inactivation of the pancreatic enzymes by the gastric hyperacidity that is present in this condition.[2,3]

Absorption defects as a cause of increased fecal fat may result from a variety of conditions which affect the intestinal lining, either directly or indirectly. Thus, diseases of the mucosa (sprue, amyloidosis, and reticulosis) and of the submocosa (regional ileitis, Whipple's disease, and scleroderma) may be associated with steatorrhea. Recently we[4] and others[5,6] have found that increased fecal fat excretion occurs in some patients with congestive heart failure. The impairment of both neutral fat and free fatty acid absorption as detected by isotopic lipid technics suggests that a mucosal component (edema?) as well as a digestive one (enzyme insufficiency due to pancreatic congestion?) may be responsible. The occurrence of steatorrhea following the administration of neomycin sulfate is also thought to result from primary changes in the absorbing surface of the small intestine produced by the administration of the antibiotic.[7,8]

Indirectly, the accumulation of large amounts of mucus as a result of abnormal bacterial flora in cases of the blind-loop syndrome, strictures, and diverticulosis may impede fat absorption.[9]

A decrease in the absorbing surface of the intestine following surgical resection or with abnormal communications, such as gastrojejunocolic fistulas, are frequently accompanied by increased fat excretion, even when pancreatic enzymes and bile are adequate. Similarly, a decreased time of contact with a normal intact intestinal mucosa in cases of diarrhea from various causes, functional[10] or infectious,[11,12] may lead to steatorrhea.

Fat malabsorption also has been described in certain endocrinopathies, notably adrenal and pituitary insufficiency.[13] Although the exact mechanism is not known, a primary mucosal defect has been postulated.

Presented as a scientific exhibit of the Section on Gastroenterology and Proctology at the 110th Annual Meeting of the American Medical Association, New York City, June 25 to 30, 1961.

Work-up of patient with suspected steatorrhea

To ESTABLISH PRESENCE OF STEATORRHEA. The presence of elevated fecal fat should first be established by gross and microscopic examination of the stool. A gray, greasy, malodorous stool is highly suggestive, as is the daily excretion of more than 400 Gm. The microscopic demonstration of an appreciable amount of fat droplets after staining with suitable dyes is also of diagnostic importance.

Occasionally it may be necessary to perform a fat balance study. It is generally accepted that the chemical determination of the fecal fatty acids on a dietary intake of more than 50 Gm. of fat daily is the most accurate means to detect the presence of steatorrhea. However in the majority of cases the use of a test meal of radioactive triolein using a quantity of fat based on the body weight with the determination of the radioactivity in a forty-eight- to seventy-two-hour stool collection will give valid information.[14]

DETERMINATION OF BASIC DEFECT—ABSORPTIVE OR DIGESTIVE. Having established the presence of steatorrhea, it is important to determine whether the malabsorption is due to a digestive or to an absorptive defect.

Specific function tests to measure the adequacy of the pancreatic secretions, such as enzymes and bicarbonate, involve duodenal intubation technics. These are difficult and tedious to perform and even in the most experienced hands are frequently not definitive in their results.

Inferential procedures to assess pancreatic sufficiency include various tolerance tests whereby fat or fat-soluble test meal substances (vitamin A and carotene) are administered and their postprandial blood levels measured. Each of these technics is subject to many limitations, however, which restrict their value.

In our experience, the differential use of radiotriolein and/or oleic acid has been the simplest method to distinguish these two types of malabsorption.[15] A low blood radioactivity curve with elevated fecal radioactivity after the administration of radio-oleic acid indicates a primary absorptive defect. Normal postprandial blood and stool activity with low blood and increased stool values following the administration of radiotriolein indicates a primary defect in digestion (Table I, Figs. 1 and 2).

STEATORRHEA, THE PRESENCE *of increased amounts of fat in the stool, is more common than is generally realized. It may be caused by a digestive defect, associated with such disorders as obstructive jaundice, biliary cirrhosis, and various diseases of the pancreas. It may be caused also by an absorption defect, in diseases of the mucosa and submucosa and other conditions which decrease the absorbing surface of the intestine. The presence of elevated fecal fat should be established by gross and microscopic examination of the stool; it may be necessary to perform a fat balance study. The authors feel that the most effective way of determining whether the defect is a digestive one or an absorptive one is the differential use of radiotriolein and/or oleic acid. A low blood radioactivity with elevated fecal activity after administration of radio-oleic acid indicates a primary absorptive defect. Low blood and increased stool values following administration of radiotriolein indicate a primary defect in digestion. A complete history and physical examination, sigmoidoscopy, and radiologic studies are required to determine the specific etiology of the process causing the disorder; biopsy and surgery may be necessary also. In certain cases the use of a therapeutic trial may be indicated. In the management of steatorrhea, a high-calorie diet is essential, with iron and calcium given orally or by injection. A gluten-free diet is effective in nontropical sprue; tropical sprue is frequently improved by the administration of vitamin* B_{12} *or folic acid. The administration of steroids, antibiotics, and pancreatic enzymes has been effective in the treatment of some diseases with malabsorption.*

DETERMINATION OF SPECIFIC ETIOLOGY OF PROCESS CAUSING STEATORRHEA. A carefully taken history and a complete physical examination must be done on every patient

TABLE I. Use of radioactive lipid absorption tests in differential diagnosis of steatorrhea

I^{131}-Triolein		I^{131}-Oleic Acid		
Blood RA*	Fecal RA	Blood RA	Fecal RA	Interpretation
Normal	Normal	Normal	Normal	Normal
Decreased	Increased	Normal	Normal	Digestive defect
Decreased	Increased	Decreased	Increased	Absorptive defect

* RA = radioactivity.

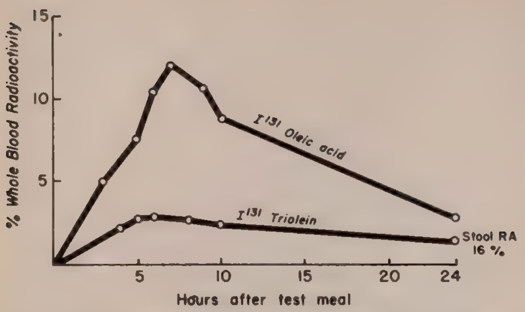

FIGURE 1. Radioactive lipid absorption patterns in steatorrhea due to pancreatic disease.

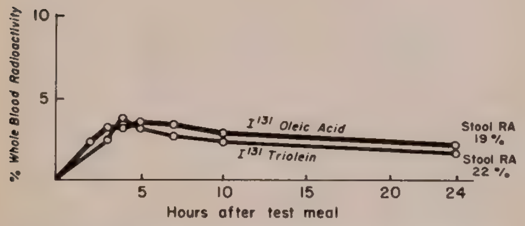

FIGURE 2. Radioactive lipid absorption patterns in steatorrhea due to sprue.

with steatorrhea, and in many cases these will furnish the necessary diagnostic clues. Sigmoidoscopy should also be performed routinely prior to any x-ray procedure.

Radiologic studies should encompass the entire gastrointestinal tract: an upper gastrointestinal series, a small bowel progress meal, and a barium enema. Failure to include this may result occasionally in a failure to demonstrate a gastrocolic fistula.

Of late a variety of small intestinal biopsy technics have been developed which make it possible to obtain tissue specimens for diagnosis.[16-21] An increasing number of reports attest to the value of these procedures in establishing a definitive diagnosis in many cases of nonspecific steatorrhea.

And finally, in specific instances surgery may be necessary to determine the origin of the malabsorption state when all other means have failed.

Therapeutic trial. In a certain number of cases where the clinical picture and the laboratory and x-ray findings are not clear cut, the use of a therapeutic trial may help resolve the problem.

Thus, the demonstration of marked improvement following the administration of a gluten-free diet, wide-spectrum antibiotics, or pancreatic supplements is good evidence that the disease process at hand is nontropical sprue, a bacterial malabsorption (blind loop, diverticulosis, or stricture), or a pancreatic insufficiency.

Management

General measures. A high-calorie diet with adequate amounts of all the vitamins, especially D and K, is essential in each case. Iron and calcium should be given either orally or by injection. Fat restriction, as previously recommended, is no longer necessary since specific or replacement therapy enables almost normal amounts of dietary fats to be absorbed in many cases.

Specific therapy. The use of a gluten-free diet usually affords dramatic improvement in nontropical sprue.[22-25] Since recovery may occasionally be delayed, this diet should be continued for at least a three-month period before a final decision is rendered as to its effectiveness. Often nonresponse is due to failure to follow the diet strictly, and so it is of prime importance that one become thoroughly familiar with the many gluten-containing foodstuffs.[26]

Patients with tropical sprue frequently will show clinical and laboratory improvement with the administration of vitamin B_{12} or folic acid.[27,28]

Recent studies have shown that adrenal cortical hormones may induce clinical improvement in many patients with sprue who do not respond to conventional therapy.[29-33] Although the exact mechanisms involved are not apparent, tolerance tests have demonstrated increased absorption of glucose, fat, iron, and vitamins A and B_{12} in these cases during the administration of cortisone or other steroids.

The use of these agents in other diseases with malabsorption, notably Whipple's disease, has also been recommended.[34,35]

An improvement in fat absorption in cases of the blind-loop syndrome or of small intestinal diverticulosis may occur following therapy with one of the broad-spectrum antibiotics.[9]

The steatorrhea present in patients with pancreatic insufficiency may be decreased by the administration of pancreatic enzymes in large enough doses. The use of a new pancreatic extract with standardized lipase activity* has resulted in excellent clinical improvement together with increased radioactive fat absorption[36] (Fig. 3).

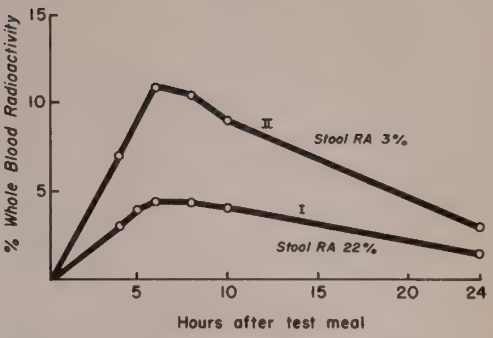

FIGURE 3. Improvement in radioactive fat absorption in patient with chronic pancreatitis during treatment with a pancreatic extract. I = initial study; II = during treatment with pancreatic extract.

Summary

The causes of steatorrhea, the mechanisms involved in its pathogenesis, the clinical application of radioactive tagged lipids in its diagnosis, and the approach to management have been outlined.

Since in all cases the presence of increased fecal fat is merely a manifestation of some underlying disease state, it is necessary that a specific etiologic diagnosis be made in order that the proper treatment may be applied.

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* Cotazym.

Surgical Experiences in the Eye Camps of India

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From the New York Eye and Ear Infirmary

THE LURE OF INDIA with its vast clinical and surgical material is a dream world to any ophthalmologist. However surgical experiences in India can present some very distressing aspects to those of us who are accustomed to the refinements of the American operating theater, but the work and the results are gratifying. The surgeon newly arrived in India faces the problem of accustoming himself to the strangeness of the country, the heat, and the food and also to the differences in attitudes and to the complexities of Indian society and life. The lack of electricity, running water, and sanitary facilities, which we take for granted, requires a period of personal adjustment. When translating these conditions to a medical setup, that is, an eye camp where patients are to be examined and operated on, these primitive circumstances make the work even more difficult.

The four eye camps which I conducted recently in India were located in the rural areas on the Western coast from Gujerat in the North to Kerala in the South. The camps themselves were located at Gargoti, Mithapur, Ankola, and Chottanikara in areas far removed from urban centers. Many of the patients were so feeble that they had to be carried or transported by bullock cart for many miles, and many were so poor that they came on foot.

Each camp was set up for a period of from ten to twelve days and was temporary in nature. In some instances temporary shelters had to be constructed to house the patients. In other areas a school building was put to this use. In some of the areas no other medical facilities were available. Many of the patients had never had any contact with modern medicine. Whatever medical care they had had consisted of herbal, tribal, or folklore medicine administered by medicine men or women.

It seemed rather remarkable that these people who are ridden with superstition and religious taboos would even be willing to come for care from a stranger. As a matter of fact I was amazed at the number of people who presented themselves for surgery or other eye care in each camp. Perhaps it would be better to say that I was overwhelmed rather than amazed. In each camp almost a thousand patients appeared, accompanied by their relatives, so that the initial impact was even greater. The prospect of giving these patients eye care in a period of four or five days without a large staff of assistants overwhelms one mentally as well as physically. However, once they have arrived at the camp one feels the moral and human obligation to see them all.

Function of eye camp

An eye camp is not an eye hospital and cannot function as such. It is basically able to relieve curable blindness due to cataracts and early glaucoma. It cannot provide all the ophthalmic services such as treatment of other eye diseases or refractions. The examination process is basically a rapid screening process for the cases which are to be operated on within the first four or five days of the camp. In view of the fact that a camp lasts a maximum of twelve days, a certain period of postoper-

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ative care must be allowed for. All surgery must stop on the fifth day. Naturally, the patients who were totally blind owing to bilateral cataracts were given priority. If there were any beds left over, unilateral cataracts were admitted. Acute medical eye problems were admitted for treatment. Minor surgery was performed on an ambulatory basis. Patients with glaucoma which was fairly advanced were rejected because of the lack of ophthalmic facilities once the camp was disbanded.

Conditions

During the screening process a great many interesting and unusual conditions were encountered. The clinical material in any one of the camps would satisfy the intellectual curiosity of any ophthalmologist. Many of the problems encountered were completely new to me despite the fact that I have seen a great deal of clinical material in Western Europe, the United States, and the Caribbean. At times I wished for more adequate clinical facilities for the study of these unusual patients. A slit lamp could have made life not only easier, but also, from a scientific point of view, more interesting. My equipment was a flashlight and a loupe. The lack of laboratory facilities was at times frustrating. The operating room usually was a converted screened schoolroom. This did not prevent flies and insects from wandering in to observe the goings-on. Illumination was a major problem. Surgery was performed with the aid of a large flashlight. At no time was the illumination adequate.

Asepsis was also a problem. There was neither running nor even clean water. Ordinary unboiled water was used for scrubbing up. Surgical gowns were limited in number and the luxury of changing gowns between cases was, of course, impossible. Gloves were not used. The large number of cases to be operated on each day did not permit scrub-ups between cases. However, all the material used was sterilized by means of a portable autoclave. The heat for this autoclave was provided by portable heaters. The solutions used were also sterilized in this manner. The instruments were boiled and the sharp instruments were immersed in alcohol.

THE AUTHOR CONDUCTED *four eye camps in India, each of which lasted for from ten to twelve days. The examination process was a rapid screening for cases of curable blindness due to cataracts and early glaucoma to be operated on within the first four or five days, as a period of postoperative care had to be provided. A total of 3,306 patients were seen in the four camps; 255 operations were performed, of which 207 were cataract operations on adults. The other 48 operations were for glaucoma, congenital cataracts, ptosis, squints, removal of tumors, dacryocystectomies, and plastic procedures. The technic for cataract operation had to be modified because of the large number of surgical cases; despite the simple procedure, the number of complications was extremely small. In spite of the primitive operating rooms, poor asepsis, inadequate illumination, and poor physical condition of the patients, the results were excellent and the complications minimal.*

These camps were also designed to serve as a pilot project for the establishment of future, small, improved eye camps. Future camps were to have adequate provisions for postoperative care and follow-up. In the meantime Indian eye surgeons from not too distant areas were drawn in to assist. Under Indian conditions what we would consider "not too distant" often meant one or two days of travel for the "local" men. These surgeons not only assisted with the surgery but also took care of the follow-up. It was arranged that the patients who had been operated on be returned to a site near the camp two weeks and one month following surgery. Follow-up visits meant sacrifice both for the patients and for the doctors because of the transportation difficulties.

The number of patients seeking care varied from camp to camp. At the first camp only 600 patients presented themselves, whereas at the fourth camp over a thousand appeared. The total number of patients seen in the four camps was 3,306. In three of the camps—that is Gargoti, Ankola, and Mithapur—the patients requiring surgery far outnumbered the available beds. In the last camp, despite the large registration of over a thousand, the number of curable blind patients was much smaller. The majority of the patients who came there were hopelessly blind.

Methods

A total of 255 operations were performed in the four camps. Of this total, 207 were cataract operations on adults. The other 48 operations were for glaucoma, congenital cataracts, ptosis, squints, removal of tumors, dacryocystectomies, and plastic procedures.

The technic used for cataract operations had to be modified in consideration of the large number of surgical cases. Only three consecutive days were actually available for cataract surgery to allow sufficient time for postoperative care. In the first camp, I attempted to operate on the cataracts with a keratome section and three corneoscleral sutures. This turned out to be too time-consuming. The procedure then used was a cataract knife section with one preplaced suture. The section was made as large as possible to avoid the need for enlarging the incision. A total iridectomy was performed in all cases. After the cataract was removed, air was injected. Only the operated eye was bandaged, and the patients were allowed to get up two days after surgery.

This procedure might seem somewhat primitive at this stage of our refined cataract surgery. However, time was of the essence and refinements were a luxury. Despite this simple procedure, the number of complications was extremely small. There was a total of 5 iris prolapses and 3 patients had postoperative hyphema. The iris prolapses were successfully repaired and all the hyphemas absorbed. Remarkably, there were only 2 postoperative infections, both on the same day in the second camp. These infections were in cases which I had considered rejecting, but because of the desperate need for surgery, operations were performed. It is of interest to note that these 2 patients were the last to have operations performed at that camp.

Results

From a surgical point of view, the results obtained on these undernourished and frequently disease-ridden people were most remarkable. Particularly is this true in view of the lack of a careful preoperative work-up. The medical check-up consisted merely of a urine examination for sugar and a taking of blood pressure. Except for those obvious cases of advanced malnutrition, only diabetic and the extremely hypertensive persons were rejected. It was also obvious that many of the patients on whom operations were performed suffered from intestinal infections of various types. However, these patients had not been eliminated on that score.

As to the visual results, all the cataract patients were given plus 10 spheres as glasses. Obviously, they were not properly refracted. But in view of the fact that the patients were totally blind prior to surgery, they were perfectly happy with their vision. This information I obtained from the doctors who were responsible for the follow-up. Certainly it would be of interest to find out what the long-term results were, but that is an impossibility because of the difficulties of transportation and communication.

Comment

The clinical material also presented a great number of interesting cases. There were many congenital lesions. The number of patients with retinitis pigmentosa was astounding in all four camps. Many patients were seen with microphthalmia. One or 2 patients were seen who appeared to have anophthalmia. The large number of congenital lesions can possibly be explained on the basis of the Indian caste system with its concomitant intermarriages.

A great number of hopelessly blind patients were seen whose blindness resulted from preventable causes. For example, out of the total 3,306 patients seen, 210 were totally and permanently blinded by vitamin A deficiency. By the time they arrived in the camps they had phthisis bulbi or staphylomas of the cornea or a combination of both. Many patients were seen with bilateral staphylomas of the cornea as a result of smallpox infection. Minor injuries and infections led to total destruction of the globes. Frequently, this was not due to the lack of resistance but to the ministrations of medicine men and to the use of all kinds of home remedies.

In the last camp, 3 patients presented themselves with microphthalmia and large cyst-like formations in the lower orbit. On exploring one of these, a cornea was found with an almost normal-sized globe. Another one was removed for pathologic examination. The results of this examination I hope to receive in the near future. All these interesting anomalies will, I hope, be the subject of a future paper.

The attitude and faith of the patients in my ability to restore vision to those who had been blind for many years was both touching and frustrating. It also spoke for their naïvete and lack of knowledge. On the other hand, the acceptance of their fate when surgery was not possible spoke of a resignation resulting from the hardships and deprivations under which these people live, rather than from the Karma concept of their religion.

Their lives in the villages are extremely primitive. Mud huts with only a door and perhaps one window are characteristic. The constant struggle for food is a major problem. The Indian concept of Karma means resignation, but not resignation without any effort at self-help. But all their efforts at self-help cannot provide sufficient protein and fats because of the large population and the insufficiencies of available food. Despite these difficulties, the Indians are very wiry and appear to endure physical hardship to a greater degree than would seem possible.

Ideally, surgery should be performed under conditions equal to our own. Realistically, this is impractical. In an eye camp one must be satisfied with much less and be willing to improvise and compromise. Rigid adherence to preset standards would make an eye camp impossible. Considering the circumstances which did exist—the primitive operating rooms, the poor asepsis, the inadequate illumination, and the poor physical condition of the patients—it was to me most remarkable that the results were excellent and the complications minimal.

The lure of India for ophthalmologists consists of the wealth of clinical material and the mass of surgical cases available. The four eye camps I conducted only touched the surface. There is a tremendous amount of material still waiting for each of you. The reward is more than the mass of surgery accomplished. The human experiences and values to surgeon and patient alike more than compensate for the difficulties of living and working in Indian eye camps.

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Warning signs not rare in stroke victims

Warning signs are not uncommon in persons who suffer strokes, according to an article by Charles E. Wells, M.D., in the November, 1961, issue of *Archives of Neurology*, published by the American Medical Association.

Of 120 patients whose medical records were studied, 19 gave a history of premonitory signs. It is probable that the incidence of warning signs would have been even higher had examining physicians made a special search for them.

Headache was the most common warning symptom, appearing to be related to the subsequent stroke in 10 patients. In 5 of these patients, the headache was localized to the side of the head in which blockage of a cerebral blood vessel later occurred, and in the other 5 the headache was generalized.

Six other patients experienced various neurologic dysfunctions such as numbness, weakness, slurred speech, and disorientation. The other 3 patients described neurologic symptoms in the days or weeks preceding the appearance of the stroke, but it was difficult to assess their significance.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

The Lutheran Medical Center,
Brooklyn, New York
March 9, 1961

Conducted by ISRAEL DIAMOND, M.D.

Discussed by EDWARD REILLY, M.D.

Recurrent Infections and Diarrhea in an Infant

Case history

Marshall Ause, M.D.: A two-year-old white male was admitted to the hospital because of severe diarrhea, vomiting, inability to retain feedings, and lethargy of three days duration. The child was the product of an uneventful pregnancy and a normal, spontaneous delivery. The birth weight was 6 pounds, 10 ounces. The first four months of life were uneventful. At four months of age the infant contracted the first of a series of infections, a respiratory infection beginning as a nasopharyngitis and developing into a full-blown pneumonia caused by Hemophilus influenzae. Recovery was rather slow in spite of proper treatment; no sooner had he been discharged from the hospital than he developed a suppurative otitis media caused by a pneumococcal infection. A myringotomy and the use of antibiotics resulted in prompt clearing of the infection. At eight months of age a common diaper rash developed into staphylococcal pyodermia which responded rather slowly to local applications and systemic antibiotic therapy. At one year of age the patient had a bout of fever and diarrhea, but no investigations were done at that time although hospitalization was necessary. A subsequent bout of diarrhea two months later necessitated protracted intravenous fluids, and this time pathogenic Escherichia coli and Bacillus proteus were cultured from the stools. The child remained ostensibly well until nineteen months of age when there was another bout of pneumonia necessitating hospitalization and intensive therapy. No single organism was incriminated.

This child had four siblings ranging from four to eleven years of age. The three eldest were in good health. The four-year-old had had a somewhat similar course during the first three years of life, but was now alleged to be well. The family history was otherwise noncontributory.

A physical examination on admission revealed a dehydrated, poorly-nourished, poorly-developed, febrile, and lethargic child. The temperature was 101 F., pulse 100 per minute, respirations 32 per minute, and weight 21 pounds. Both the ear drums were slightly reddened, and on the left side some fluid could be discerned. The mucous membranes of the nose and throat were reddened. On the tongue, soft palate, and buccal mucosa a few scattered lesions of thrush were seen. The gingivae were swollen, and the teeth showed slight caries. No lymph nodes were palpable in the neck. A few tiny, firm lymph nodes were palpable in the axilla and inguinal areas. The thorax appeared questionably increased in the anteroposterior diameter. A Harrison's groove was present, but there was no beading of the costochondral junctions. The heart and lungs did not appear remarkable. The liver edge was palpable 4 cm. below the costal margin. The spleen was not palpable. The abdomen was moderately distended, and gurgling sensations were elicited freely on palpation. There was virtually no panniculus over the abdominal wall, and the subcutaneous veins were easily visible. The external genitalia were well formed, and there was slight edema of the scrotum and prepuce. Perianal excoriation was slight. There was slight pitting edema over the sacrum. The extremities appeared wasted. Pallor was moderate. There was no cyanosis or jaundice. A neurologic examination was unrevealing.

The urine contained 2 plus albumin, and the sediment contained a few granular casts, a few leukocytes, and numerous red blood cells. The hemoglobin was 9.5 Gm. per 100 ml., the red cell count 3 million per cubic millimeter, and the white cell count 5,000 per cubic millimeter with 14 per cent polymorphonuclear leukocytes, 77 per cent lymphocytes, and 10 per cent monocytes. No immature cells were seen. The hematocrit was 34, the corrected sedimentation rate 56 mm. per hour, blood platelets 250,000, bleeding and clotting times normal, prothrombin time 18 seconds, and control 14 seconds. The fasting blood sugar was 80 mg. per 100 ml., urea nitrogen 17 mg., calcium 8.1 mg., phosphorus 3.5 mg., and serum bilirubin 1 mg. The alkaline phosphatase was 4 Bodansky units. The thymol turbidity and cephalin flocculation tests showed normal findings. The total serum protein was 5.5 Gm. per 100 ml. with 3.5 Gm. albumin and 2 Gm. globulin. The serum electrophoretic pattern was abnormal. A blood culture was positive on one occasion for Salmonella paratyphi C. The same organism was recovered from the stool and from rectal swabs on several occasions. Rectal smears yielded inflammatory cells, red cells, and, on occasion, fungal forms. On two occasions Monilia was cultured from the stool. Routine urine cultures were negative. Urinary cytology did not reveal inclusion bodies.

Admission x-ray films of the abdomen showed gaseous distention and confirmed the finding of hepatomegaly. The chest film showed increased pulmonary markings, and there was some question regarding the presence or absence of a miliary infiltrate. Nasopharyngeal cultures yielded Staphylococcus aureus hemolyticus and Monilia. Intravenous pyelography showed findings within normal limits.

This patient was treated intensively with penicillin and Chloromycetin. For the first week he received nothing by mouth and was maintained on parenteral fluids including Amigen. He also received nystatin (Mycostatin) topically to the oral lesions. The diarrhea diminished but did not disappear. During the second week oral feedings were begun, and nystatin was given systemically. The patient's course was afebrile after the first few days but spiked sharply at the beginning of the third week when he appeared to have relapsed. The diarrhea became profuse, the abdomen again became distended, and breathing became labored. The liver was no longer palpable. Slight jaundice developed. A chest x-ray film showed scattered, prominent, irregular densities throughout both lungs. Oliguria ensued with azotemia. Death occurred shortly thereafter.

Discussion

EDWARD REILLY, M.D.: The history of this child is a story of repeated infections and growth arrest. The infections were many and varied, beginning in the fifth month of life. There is a good deal of useful bacteriologic information. The child had at one time or another had infections caused by H. influenzae, S. aureus, E. coli, B. proteus, and terminally S. paratyphi C and Monilia. At two years of age the child weighed 21 pounds. The average expected weight at that age is 28 to 30 pounds, so this child was about 25 to 30 per cent underweight. I know of only three underlying conditions which need to be seriously considered as the etiologic background against which this picture might develop. These are congenital absence of the spleen; mucoviscidosis, or cystic fibrosis of the pancreas; and hypo- or agammaglobulinemia, either congenital or acquired.

The most striking physical finding in this child who had so many bacterial infections is the lack of any peripheral lymph node enlargement. Even a normal, healthy child of two years has palpable cervical lymph nodes. Children who have had recent severe, or even mild, infections often have enlarged lymph nodes which may persist for some time, even to the point of provoking some clinical concern regarding the possibility of neoplasia of lymphoid tissue.

Equally striking is the observation that the spleen was never palpated. In a child so thin, even debilitated, one should be able to feel the tip of the spleen from time to time, particularly with a history of recurrent infection. An intriguing finding is the moderate enlargement of the liver at the time of admission which seemed to abate shortly before death. One normally expects to feel the liver edge a bit below the costal margin, but 4 cm. is beyond normal limits. If we assume that the disappearance of hepatomegaly is a valid observation, then this uncommon occurrence must be accounted for.

Let us first consider the possibility that this is an example of congenital absence of the spleen. This condition is associated with two phenomena, a heightened susceptibility to infection and associated congenital cardiovascular malformations. While I cannot discard this diagnosis with assurance, the absence of any sign or symptom of cardiac anomaly is strong evidence against it. Interestingly enough, this child had a mild, slightly macrocytic anemia. If we calculate the mean corpuscular volume on the basis of a hematocrit of 34 and a red cell count of 3 million, we get an index of 113 cubic microns, a slight but definite macrocytosis. In addition, there is a granulocytopenia. This is not the peripheral blood picture seen in congenital absence of the spleen. In such patients the peripheral blood resembles that seen following splenectomy; one would expect to find target cells, decreased red cell fragility, Howell-Jolly bodies, occasional nucleated red cells, siderocytosis, leukocytosis, and a variable degree of thrombocytosis. I can find no support for a diagnosis of congenital splenic agenesis.

It is difficult to entertain seriously the idea of mucoviscidosis. We are told that this child's difficulties began after the first four months of life. While it is possible for mucoviscidosis to have a later onset, it is extremely unlikely, and in a two-year-old child succumbing to the complications of this disease, one might reasonably expect an early onset of both the intestinal and respiratory elements of this entity. Parenthetically, although this child did have recurrent respiratory infections and growth arrest, there is no suggestion of a celiac syndrome, at least no steatorrhea. The protocol says nothing about sweat sodium and chloride or about tryptic activity of the duodenal contents or stool. We may reasonably infer that the attending physicians did not seriously entertain this diagnosis, nor shall I.

We are now left to consider a defect in the child's ability to manufacture protein, specifically gamma globulins with antibody activity. Everything in the clinical protocol is compatible with this diagnosis. The only question the protocol does not answer in this respect is whether the defect is congenital or acquired. Let us review the protocol with the idea of hypogammaglobulinemia or agammaglobulinemia in mind. We are told that the first four months of life were uneventful. This is a characteristic finding, since in the congenital form of the disease the child "coasts" on a supply of maternal gamma globulin obtained transplacentally. The repeated infections were characterized by their severity and frequency. Of particular note is the diaper rash developing into a staphylococcal pyoderma. True pyoderma is extremely uncommon at this age and bespeaks the difference in this child's ability to respond to infection compared with a normal infant. The family history is significant. We are told that the three eldest siblings were in good health but that a four-year-old sibling, presumably his next senior, had had a similar course during his first three years of life. Like hemophilia, agammaglobulinemia is probably transmitted by a sex-linked recessive gene and except for one instance has been found only in males. Do we know the sex of any of this child's siblings?

Dr. Ause: No, we do not have this information.

Dr. Reilly: This is worth looking into. The statement that the child's four-year-old sibling is now well need not be true; he may be merely between infections.

I should like to return to the matter of lymph nodes. Characteristically, in gamma globulin deficiency there is a striking reduction in lymphoid tissue throughout the body. The nonpalpable spleen ceases to be mysterious for this reason. What about the hemogram? The peripheral blood picture is perfectly compatible with gamma globulin deficiency insofar as the erythroid series is concerned. Cases of agammaglobulinemia with an increased mean corpuscular volume have been reported. Likewise, anemia secondary to repeated infection is almost always found. Since agammaglobulinemia is associated with a reduction in lymphoid tissue, the presence of 77 per cent lymphocytosis in a peripheral white cell count of 5,000 poses a problem for which I have no ready explanation. However, in view of the possibility of disseminated moniliasis, one might wonder whether this child did not in fact have an agranulocytosis in the presence of overwhelming terminal infection. I take comfort in the 13 per cent neutrophil proportion since this is certainly indicative of depleted granulocytes.

I find support for a diagnosis of hypo- or agammaglobulinemia in the statement that the serum protein electrophoretic pattern was abnormal. I assume that this abnormality will be disclosed in due course, and I predict that the gamma globulin peak will be at most a mere foothill. I would be interested in knowing whether or not this child showed natural and acquired antibodies, particularly with respect to his blood grouping antibodies.

In conclusion, I will commit myself to a diagnosis of hypo- or agammaglobulinemia, most likely of the congenital type. I further believe that in addition to his Salmonella infection he also had disseminated moniliasis. These are amply documented in the protocol which describes thrushlike lesions on the tongue and palate and positive stool cultures for Monilia and S. paratyphi C. This latter organism also was cultured from the blood. I would expect to find monilial lesions in the upper gastrointestinal tract and probably in the lung. I hope that lesions of Salmonella enteritidis also will be demonstrated.

John Monfort, M.D.: An additional diagnostic feature which may be helpful in this sort of case where lymphatic tissue is generally reduced is a lateral x-ray film of the nasopharynx to determine the amount of adenoid tissue. In a normal child one can see a sizable amount of it projecting into the nasopharynx as a soft tissue shadow. In children with agammaglobulinemia the radiolucency of the air-filled nasopharynx shows as a wider passage without projecting soft tissue shadows.

Nicholas Chiara, M.D.: What is your explanation for the reduction in the size of the liver from 4 cm. below the costal margin to being nonpalpable?

Dr. Reilly: In a normal child of two years one expects to feel the liver edge at or just slightly below the costal margin unless the child is unduly well nourished. It may have been enlarged because of a certain amount of passive congestion, or it may have had some degree of fatty metamorphosis associated with repeated infection. I would attribute its subsequent shrinkage to starvation since the infection became chronic, and the child's nutritional status deteriorated gradually.

Arthur Keith-Swenson, M.D.: Dr. Reilly raised a point about the child's iso-agglutinins. Was there time for these to be studied?

Dr. Ause: Unfortunately, we thought about this in retrospect only. The general rule is that infants and children with agammaglobulinemia have low to absent anti-A and anti-B titers.

Grace Altenau, M.D.: Could you say a few words about the management of such patients? Is it possible to increase their serum gamma globulins by parenteral injections of gamma globulin? If so, is it advisable to do so? Do children with hypogammaglobulinemia or agammaglobulinemia derive any real benefit from such injections?

Dr. Reilly: I am sure that the last chapter in the management of these children is still to be written. Certainly they require close supervision and energetic antibiotic therapy whenever they contract a bacterial infection. Insofar as gamma globulin is concerned, a minimal plasma level of 150 mg. per 100 ml. seems to be required for demonstrable benefit. This necessitates monthly injections of from 100 to 150 mg. of gamma globulin per kilogram of body weight. The injections may have to be given at shorter intervals. The treatment is painful and expensive but seems to be effective.

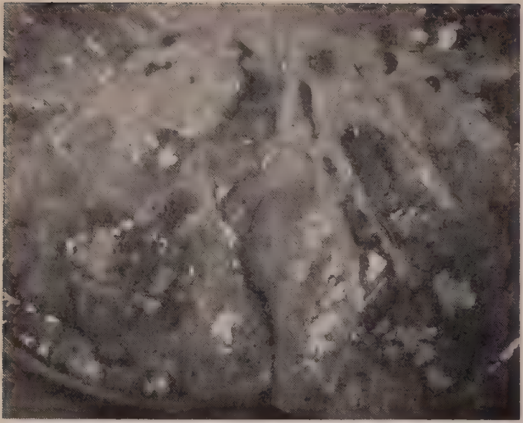

FIGURE 1. Lung, cut surface, showing foci of moniliasis.

Dr. Ause: Would you care to comment further on the lymphocytosis?

Dr. Reilly: It is a mystery to me. One certainly would not expect lymphocytosis in the peripheral blood in a disease which is pathologically noted for its generalized depletion of lymphoid tissue. Perhaps the Salmonella infection had something to do with it.

Clinical diagnoses

(1) Agammaglobulinemia; (2) salmonellosis; (3) moniliasis, disseminated.

Dr. Reilly's diagnoses

(1) Hypogammaglobulinemia or agammaglobulinemia, congenital; (2) salmonella enteritis and bacteremia; (3) moniliasis, nasopharynx, respiratory tract, and upper gastrointestinal tract.

Pathologic report

Israel Diamond, M.D.: The postmortem examination revealed an emaciated child exhibiting slight edema and jaundice. The anteroposterior diameter of the chest was increased, and there was beading of the ribs and flaring of the costal angle. The lungs were voluminous, heavy, and retained their shape. They were dark red and stippled with fine yellow dots. This appearance was seen externally and on the cut surface (Fig. 1). In some places the yellow foci coalesced to form larger lesions measuring 2 to 3 mm. in diameter. Microscopically these yellow lesions corresponded to colonies of Moniliae embedded in necrotic parenchyma (Fig. 2). The hyphae could be seen spreading from the margins of the colonies through the surrounding tissue, including blood vessels, with little or no accompanying inflammatory reaction. A number of the pulmonary veins showed intimal lifting by masses of monilial hyphae. Typical monilial lesions studded the tongue, pharynx,

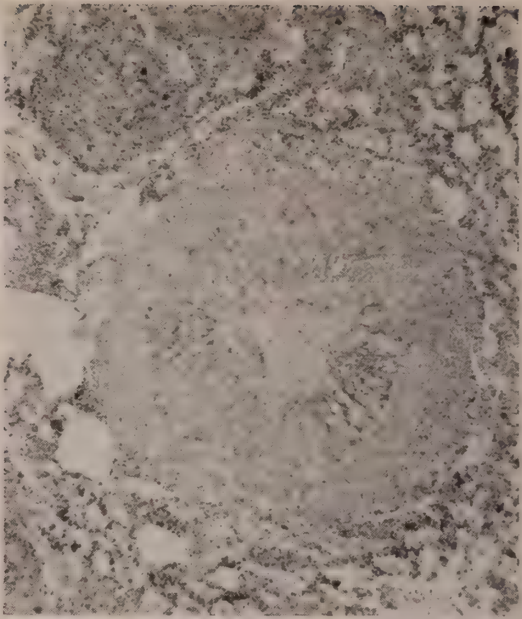

FIGURE 2. Lung showing a colony of Monilia. Note the radial hyphae within the necrotic focus.

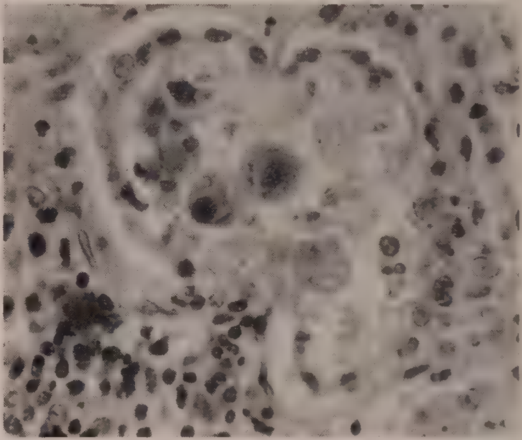

FIGURE 3. Lung showing two cells with typical intranuclear cytomegalic inclusions.

FIGURE 4. Lung showing a cyst of Pneumocystis carinii containing eight organisms. Five are in sharp focus, three are just out of the focal plane. Adjacent, is one free-lying organism (Gomori methenamine silver stain).

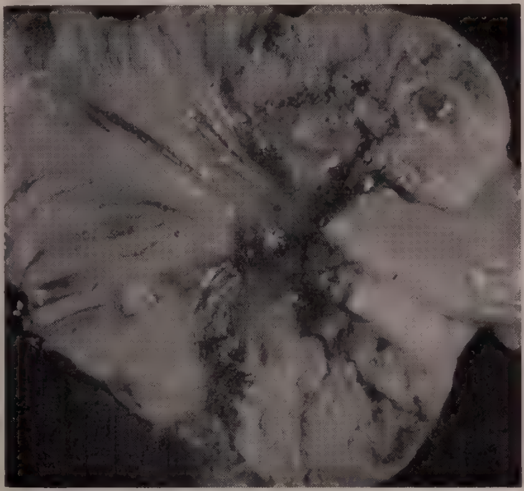

FIGURE 5. Ileocecum showing extensive pseudomembrane formation in the cecum.

esophagus, and stomach. In the latter two organs the fungus produced extensive ulcerations and large, semidetached sloughs. Characteristic yellow monilial foci also were found in the kidneys and in the liver.

To return to the lungs, there were extensive additional and equally interesting lesions. Mainly in alveoli around the monilial foci were found enlarged free-lying cells in whose nuclei were the typical basophilic large inclusions of cytomegalic inclusion disease (Fig. 3). Cells with similar inclusions were found in other portions

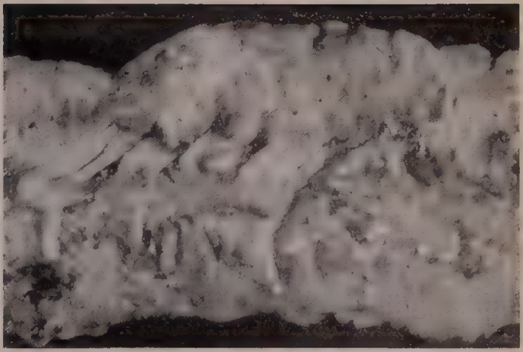

Figure 6. Colon showing severe edema and ulceration.

of the lung but in much smaller numbers. Evidence of cytomegalic inclusion disease also was present in the adrenals and in the salivary glands. In the adrenals there was no associated inflammation or necrosis. In the salivary glands there were focal lymphatic infiltrates around the affected ducts.

The inflammatory reaction of the lungs was generalized but with some variation from area to area. A few of the bronchi and bronchioles were acutely inflamed and showed plugging by masses of neutrophils. The majority of these passages showed only chronic inflammation with infiltration by lymphocytes. Most of the alveolar walls were thickened markedly by infiltration by plasma cells with a smaller number of admixed lymphocytes. The alveolar lumens contained macrophages or fibrin, or both. In some spaces edema fluid was seen. The presence of plasma cells raised the suspicion of Pneumocystis carinii infection although no characteristic foamy exudate was seen. Free-lying organisms and cysts of Pneumocystis carinii were found within alveolar lumens, particularly in those situated near the monilial lesions (Fig. 4). The organisms exhibited characteristic morphology and staining properties.

The small and large intestines showed severe acute inflammation with varying amounts of ulceration (Figs. 5 and 6). In the small intestine reddening and edema were diffuse. Ulceration was confined to the tips of the mucosal folds. In the colon there was extensive ulceration with pseudomembrane formation. Microscopically the lesions were focal and diffuse and fre-

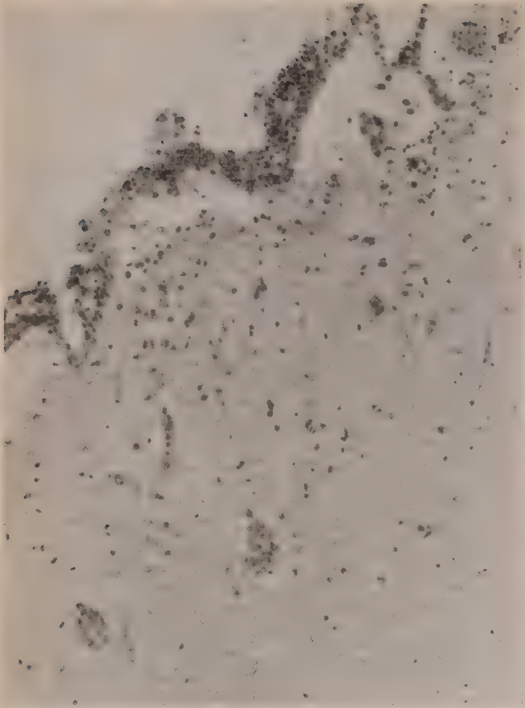

FIGURE 7. Cerebral cortex showing meningitis. Note the cuffing of intracerebral vessels.

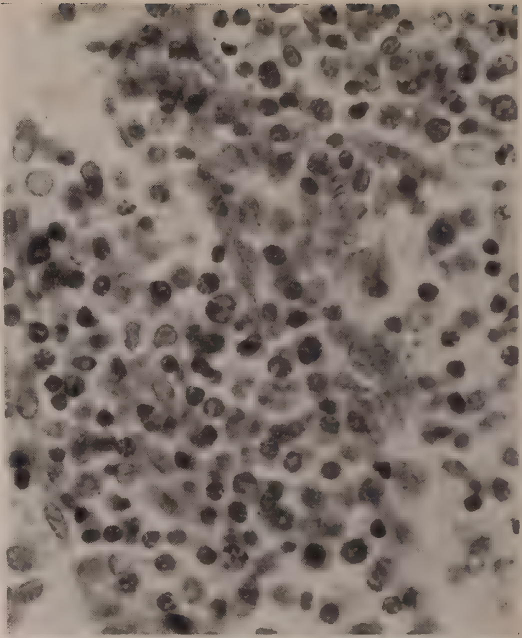

FIGURE 8. Lymph node showing plasma cells. The large and small cells with typical "cart wheel" nuclei denote active formation.

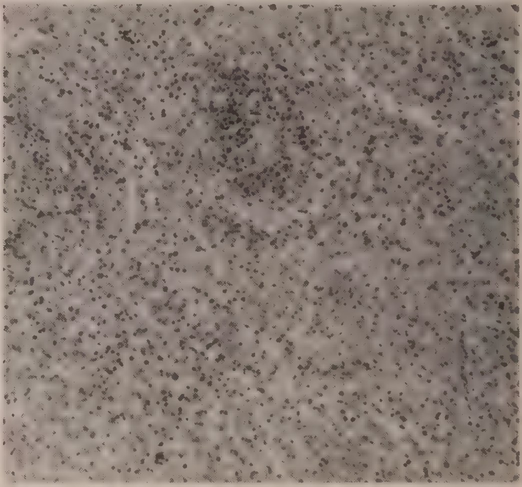

FIGURE 9. Spleen showing severe reduction in lymphoid tissue. The small aggregate surrounding the central arteriole is all that constitutes the malpighian body.

quently involved the entire thickness of the bowel wall. Inflammatory exudate contained fibrin, red cells, macrophages, and lymphocytes; polymorphonuclear leukocytes were rare or absent. These changes are attributed to the Salmonella infection; there were no associated monilial organisms in the large and small bowels. Focal necroses, also devoid of monilial organisms, were numerous in the spleen and liver and also were seen in lymph nodes, bone marrow, and the testes. I am inclined to attribute these to the Salmonella infection. Grossly, the brain and spinal cord did not appear remarkable. Microscopically, there was a meningeal exudate composed of lymphocytes and histiocytes which extended along the spaces of Virchow-Robin into the substance of the brain (Fig. 7). I believe this, too, may be attributed to the Salmonella.

As expected, the lymphatic tissue was reduced markedly in volume throughout the body. The spleen was very small, and the lymph nodes were tiny indeed. Microscopically, they showed an unexpected finding which already has been hinted at by the predominating infiltrating cell in the pulmonary interstitial inflammation. The lymph nodes showed many plasma cells and numerous foci of plasma cell formation (Fig. 8). While the nodes showed severe lymphoid depletion, lymphocytes were still the predominant cells; germinal centers were encountered rarely and, when present,

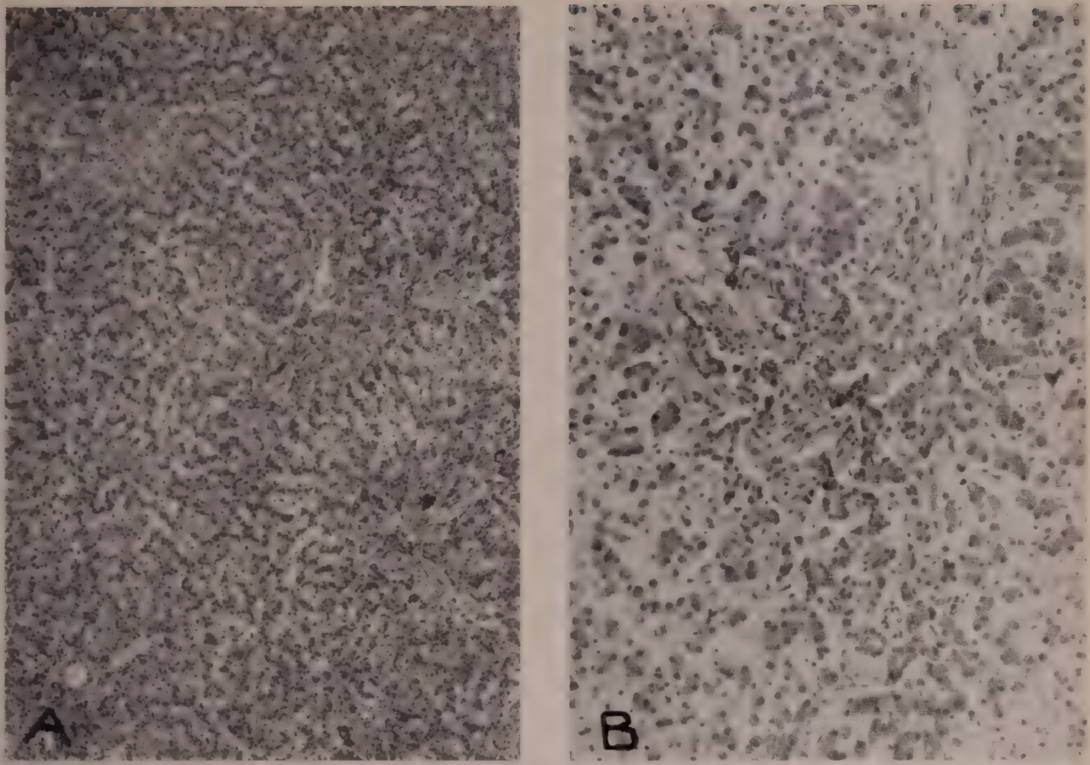

FIGURE 10. (A) Liver showing disorganization and attenuation of the liver cell cords. Only the periportal cells appear intact. (B) Liver showing periportal scarring with bile duct proliferation.

were small; the lymphoid component of the lymph nodes was chiefly in cords. In the spleen, it was difficult to identify malpighian bodies since only a few strands of lymphoid tissue remained (Fig. 9). The bone marrow showed a marked reduction in granulocytic activity. Foci of erythropoiesis were frequent. Most of the hematopoietic tissue consisted of histiocytic cells with admixed lymphocytes and plasma cells. Megakaryocytes were present in normal quantity.

In addition to the acute focal necroses due to Salmonella and the lesions of disseminated moniliasis, the liver revealed a diffuse parenchymatous lesion. The hepatic lobules showed severe, centrilobular and midzonal necrosis and atrophy (Fig. 10A). Only at the periphery of the lobules did some of the liver cells contain rare fatty vacuoles. The portal areas were increased in size and cellularity and showed stellate scarring with mild proliferation of the small bile ducts (Fig. 10B). The observations in the portal areas were similar to those observed in kwashiorkor and may provide an explanation for the curious change in liver size which was noted clinically. The findings suggest that there may have been a fatty liver, presumably the consequence of malnutrition, at some time before the onset of the terminal illness. The reduction in size probably was caused by an aggravation of the malnutritional state by the combination of infections resulting not only in a protein deficiency but also in a reduction in total caloric intake. In this circumstance, fat is mobilized out of the liver; an enlarged fatty liver develops only when the caloric intake is high and there is an associated specific set of nutritional deficits.

The laboratory findings leave no doubt that this child had severe gamma globulin deficiency or possibly absence since the paper electrophoretic studies of the serum showed no gamma globulin (Fig. 11). The morphologic findings are of no help in determining whether we are dealing with the acquired or congenital form of the disease, but the patient's history and the family history suggest a diagnosis of congenital agammaglobulinemia.

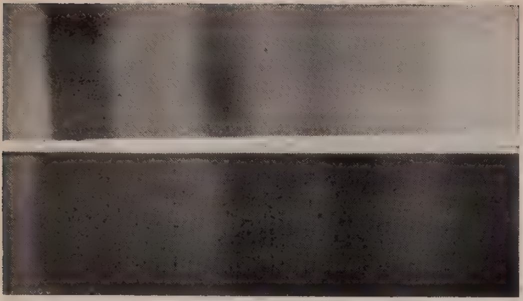

FIGURE 11. Paper electrophoresis pattern of serum proteins. The upper strip is from the patient; the lower, from a normal control.

This case is interesting for a number of reasons. It is popularly believed that plasma cells are absent in congenital agammaglobulinemia, and it is true that almost all of the cases show a striking absence of these cells. However, the presence of plasma cells has been described. The 2 cases of agammaglobulinemia with Pneumocystis carinii pneumonia reported by Bird and Thompson[1] had plasma cells. Russell[2] described the same concomitance of these two diseases in a female infant who exhibited no plasma cells. A similar case in a male was reported by McKay and Richardson.[3] The unusual feature of a lymphocytosis has been described by Dolan, McCullough, and Gibson[4] in a case of hypogammaglobulinemia with an associated Salmonella Newport infection. Possibly in their case and in ours the lymphocytosis was the direct result of the Salmonella infection.

Pneumocystis carinii pneumonia is a relatively new disease in this country. Gajdusek's 1957[5] review of the European experience with this disease was timely since a small but increasing number of reports have appeared since. The association of Pneumocystis carinii pneumonia with cytomegalic inclusions has been noted.[6] It is interesting that the first case of Pneumocystis carinii pneumonia in England, described by Baar,[7] had salivary gland inclusions. The occurrence of monilial infection with Pneumocystis carinii infection[5] and with cytomegalic inclusion disease[8] also has been described. One wonders whether or not these various concomitances are merely an expression of debility since these diseases frequently occur singly as a terminal complication in a debilitated patient. On this basis the impressive combination of disseminated moniliasis, Pneumocystis carinii pneumonia, and cytomegalic inclusion disease if nothing else would indicate severe debility. Severe debility certainly was present, and the agammaglobulinemia and Salmonellosis are more than sufficient to account for it.

Anatomic diagnoses

(*1*) *Agammaglobulinemia, probably congenital;* (*2*) *salmonellosis, paratyphi C, with enterocolitis, bronchiolitis, meningitis, and focal necroses of liver, spleen, lymph nodes, bone marrow, and testes;* (*3*) *moniliasis, disseminated, involving lungs, kidney, liver, esophagus, stomach, tongue, and pharynx;* (*4*) *cytomegalic inclusion disease, involving lungs, salivary glands, and adrenals;* (*5*) *Pneumocystis carinii pneumonia;* (*6*) *lymphoid depletion, severe, with associated plasmacytosis;* (*7*) *granulocytic hypoplasia, bone marrow.*

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Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Role of Zinc and Other Trace Metals In Diabetes Mellitus

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IN CONTRAST to the well-recognized role and importance of trace metals in plant physiology and animal husbandry,[1] their significance in human pathology has been investigated incompletely. It is only recently that reliable data have become available on the trace metal content of normal human organs.[2] The purpose of this review is to present information concerning the relationship of carbohydrate metabolism and trace metals. It must be recognized that some data, obtained with older technics, are difficult to interpret and judgment of their value may have to await repetition of the work with modern methods.

Insulin, pancreas, and zinc

The discovery by Scott[3] in 1934 that crystalline insulin prepared by various methods always contained zinc and that amorphous insulin could not be crystallized without the presence of either Zn^{++}, Co^{++}, Cd^{++} or Ni^{++}, led to a series of investigations and speculations concerning the relationship of insulin to trace metals. Ash estimations of crystalline insulin showed constant values for whichever of the three metals (Zn^{++}, Co^{++}, Cd^{++}) was used for its crystallization and the ash content was proportional to the atomic weight of the metal.[4] This was interpreted as indicating that the metals were chemically combined constituents and not impurities. The solubility of insulin was compared with that of zinc insulin, utilizing radioactive zinc in the system. Crystallization and zinc content appeared to vary with the ionic strength and pH of the reaction mixture.[5,6] Tanford and Epstein[7,8] determined the number and position of reactive groups on the insulin molecule and postulated that two imidazole groups participated in the binding of one zinc ion. The confirmation of an imidazole-zinc-type linkage as well as further clarification of the factors influencing such binding came from the studies of Cunningham and his group.[9] These investigators demonstrated that there are two types of binding of zinc to insulin, and that only the type I or irreversible binding (which is the imidazole-zinc type) changes the sedimentation constant and electrophoretic mobility of the insulin molecule. According to their calculations with crystalline zinc-insulin, 0.28 to 0.55 mol of zinc is bound per mol of insulin. They also found that Co^{++} is bound to insulin but this binding is reversible and does not cause profound changes in the physicochemical properties of the molecule. A practical application of the change in solubility of insulin when combined with zinc has been utilized in the preparation of a long-acting insulin.[10]

Interest in the role which zinc might play in the action of insulin was heightened by the observation that the pancreas contained significant amounts of zinc.[11] It was shown that the quantity of extractable insulin bore no simple relation to the amount of zinc in the glands. The pancreas of fetuses and young animals contained much more insulin but no more zinc.[12] The zinc content of the pancreas, as determined by emission spectrography, was in agreement with the older data.[2] It also confirmed the observation that insignificant amounts of cobalt and nickel occur in this gland. The zinc content of the pancreas is not significantly different from that found in other organs, such as the liver and spleen. Considering that islet tissue accounts for only about 2 per cent of the total pancreas, conclusions for or against the physiologic role of zinc in this organ cannot be drawn on the basis of its concentration. The carboxypeptidase of pancreatic tissue contains fair amounts of zinc[13] and probably accounts for the greater part of this metal in the pancreas. Scott and Fisher[14] have reported that the diabetic pancreas contains only half of the zinc concentration and one quarter of the insulin content of normal glands, but this was disproved when reexamined in a larger series and subjected to statistical analysis.[15] The fact that neither the feeding of large amounts of nonradioactive zinc to cats[16] nor the prolonged administration of Zn^{65} to rats[17] produced injury to the islets with the development of diabetes serves to emphasize further the complexity of this question.

Experimental diabetes

One of the strong arguments in favor of the association of zinc and insulin has been the demonstration that several organic reagents which produced diabetes in the experimental animal also showed a strong affinity for zinc. Following the demonstration by Okamoto that the islets of Langerhans can be stained with dithizone, a number of studies have been performed to demonstrate a relationship between the chemical formula and the diabetogenic property of several compounds.[18–21] In these investigations it was found that of several structurally similar compounds only dithizone and oxine (8-hydroxyquinoline) produced diabetes, and it also was demonstrated that the diabetes produced by these compounds was similar to alloxan diabetes. The destruction of beta cells closely paralleled the course and appearance of hyperglycemia. Also it was shown that various species exhibited different degrees of sensitivity to these compounds. Root and Chen[22] were less successful in producing oxine diabetes but were able to enhance the effect of the drug by the prior injection of methylene blue. The explanation for this was thought to be the reoxidation of a reduction product of 8-hydroxyquinoline. A similar effect of methylene blue was found earlier in conjunction with alloxan. Finally it also was demonstrated that giving alloxan and 8-hydroxyquinoline together in doses which were not diabetogenic for either compound resulted in diabetes.

Investigations concerning the diabetes produced by dithizone were extended by Maske and his collaborators.[23–28] In addition to using the Okamoto histochemical staining method, these authors developed an in vivo method of staining the islets with dithizone. The same injection which caused selective staining of the islets if the animal was sacrificed ten minutes after injection caused diabetes if the animal was allowed to live. It was shown that there was less staining of the islets in well-fed animals than in starved ones and still less staining was found if the animals were fed repeatedly with glucose. The occurrence of alloxan diabetes also was decreased with prior glucose feeding or with a previous injection of adrenalin. Both chemicals produced destruction of beta cells, while the alpha cells remained intact. Following dithizone injection, zinc dithizonate could be extracted from the pancreatic islets of several species but not from the guinea pig. This animal has no histochemically demonstrable zinc in the islets and is resistant to the diabetogenic action of both alloxan and dithizone.

The experiments of Shibata and Ibaraki[21] cast doubt on the central role assigned to zinc in experimental diabetes. These authors demonstrated that alloxan, oxine, or dithizone diabetes can be prevented by the prior injection of some zinc-binding compounds which are nondiabetogenic. If this observation can be confirmed, it will prove to be of great significance in our understanding of experimental diabetes. It indicates either that diabetogenic action and metal chelating ability do not have to go hand in hand, or that some zinc must be present to produce diabetes with alloxan, dithizone, or oxine.

Chelation, an important biologic phenomenon,[2,29] is the explanation given for the glycosuria following the administration of amithiozone, an antituberculous compound.[30] Further proof that chelation rather than structural similarity is the essential factor in finding diabetogenic compounds comes from the interesting observation of Iwamoto and Adams.[31] These authors described glycosuria and hyperglycemia in experimental animals after the injection of hematoxylin, a compound which is a metal chelator but structurally quite dissimilar from alloxan.

Adding to the complexity of the question regarding the role of zinc in the pancreas was the discovery that glucagon, too, was apparently associated with zinc. It had been shown by Best[32] that duck pancreas is extremely rich in alpha cells. This observation was confirmed and extended to other avian species and it was found that the pancreas of all birds (with the exception of the screech owl and the kestrel) contains ten times more glucagon than the gland of mammals.[33]

Runge, Muller, and Ferner[34] investigated the alpha and beta cells of the duck following the injection of dithizone. Since in this animal the alpha cells occur in macroscopically recognizable brown islets, it could be shown with the naked eye that both the alpha- and beta-cell islets showed red staining. Microscopically the red zinc dithizonate was visible only on the capillary side of the alpha cells, while the alpha granules filled the entire cell. Further investigation[32] showed that the zinc content of the alpha and beta cells was approximately the same in the duck's pancreas. The alpha cells were shown to have glucagon activity. It is claimed that zinc combines both in insulin and in glucagon with the imidazole ring of the histidine residue. The suggestion has been made that the histidine occurs at the amino end of the peptide chain of glucagon. Although glucagon has been crystallized free of zinc and found to be biologically active, the possibility that a recombination with zinc in vivo may be important for its action has not been ruled out. The same argument pertains to insulin.

Two recent investigations, both utilizing Zn^{65}, bear on the relationship of zinc, diabetes, and insulin. Lowry, Baldwin, and Harrington[35] compared the radioactivity in the pancreata and kidneys of normal and alloxan-diabetic rats following an injection of Zn^{65}. They found that the diabetic pancreas contained only one eighth of the specific activity of the normal gland, while the kidneys showed higher specific activity in the diabetic animals. McIsaac[36] injected normal rats with Zn^{65} chloride and compared the exocrine and endocrine portions of the pancreas by means of radioautography. The acinar cells showed high activity early, but this declined rapidly. In contrast, islet tissue demonstrated a remarkable constancy of radioactivity over the period of observation. By calculating the asymptote he found that 50 per cent of the injected isotope is excreted rapidly, while 42 per cent enters a compartment in which the turnover is very slow. It was assumed that the islets, which in the rat consist mostly of beta cells, are part of the compartment with the slow turnover rate.

Zinc in human diabetes

Several investigators[37–39] compared the serum zinc levels of diabetic individuals with those of normal subjects and noted no significant differences in mean serum zinc concentration between the two groups. The diabetic patients showed no diurnal variations in their serum zinc levels. A correlation between serum zinc and severity, degree of control, or duration of the disease could not be demonstrated. The total zinc intake from zinc-insulin preparations was calculated in a group of diabetic patients but had no apparent effect on plasma zinc levels. Tolbutamide failed to influence the plasma zinc concentration in one patient. Dimercaprol (BAL) produced some changes in blood glucose and urinary zinc levels but the results were inconsistent. Our own observations[40] thus far have failed to reveal an apparent change in serum zinc levels either in uncomplicated diabetic patients or in patients with diabetic retinopathy, nephropathy, or neuropathy.

A notable exception to all these negative findings is the observation of Constam, Leemann, and Almasy[41] that urinary excretion of zinc in diabetic patients is significantly higher than in normal subjects. They also report a parallelism between degree of diabetic control and urinary elimination of zinc. The range of values observed in their cases is very great and one must await further confirmation of these findings. Even if it should be established definitely that diabetic individuals have increased urinary excretion of zinc, this does not necessarily shed any light on the pathogenesis. Other diseases, particularly porphyria, are known to be associated with high urinary zinc excretion. Chelating agents have been employed in the treatment of this disease[42] but the results are equivocal.*

Trace metals in intermediary metabolism

It is not within the scope of this paper to give a review of intermediary metabolism, since this was done in an earlier paper of this series.[43] It seems, however, appropriate to call attention to some of the steps in intermediary metabolism which require the presence of trace metals in an obligatory fashion. The fact that thus far very few clinical entities are known in which trace metal deficiency or excess plays an important role does not detract from the great theoretical interest of these possibilities. In fact, the interpretation of clinical disease entities depends on the availability of biochemical information.

The most thoroughly investigated trace element is zinc and much of our knowledge stems from the studies of Vallee[13] and his collaborators. This metal is known to be an essential component of the molecule of several enzymes connected with carbohydrate or protein metabolism. The dehydrogenases listed in the following paragraphs are all diphosphopyridine nucleotide-dependent and form metalloenzymes with zinc. These metalloenzymes are characterized by a definite stoichiometric ratio between metal and protein when highly purified. The activity of these enzymes is irreversibly lost if treated with metal chelating agents.[44]

Alcohol dehydrogenase. Alcohol dehydrogenase (ADH) has been obtained from brewer's yeast and from horse liver. Both enzymes have been shown to contain zinc.[45] Alcohol dehydrogenase from yeast acts on ethanol, while the enzyme from horse liver acts on higher alcohols as well. Ethanol is oxidized through the action of this enzyme to acetaldehyde which, catalyzed by pyruvate carboxylase, is being formed from pyruvate, in the presence of thiamine pyrophosphate. All the reactions mentioned are reversible.[46] Alcohol dehydrogenase is an important enzyme of the Embden-Meyerhof glycolytic cycle.

Lactic dehydrogenase. Lactic dehydrogenase (LDH) participates similarly in the glycolytic pathway, as it catalyzes the redox interconversion of lactate and pyruvate. The enzyme isolated from rabbit skeletal muscle was found by Vallee and Wacker[47] to contain zinc. Although it is now well established that lactic dehydrogenase consists of several isozymes[48] and it is possible that not all of these contain zinc, this does not militate against the importance of this trace metal in the enzyme. On the contrary, if it should become established definitely that some lactic dehydrogenases contain zinc and others do not, this would emphasize even more strongly the specificity of each isoenzyme and the role the metal plays to assure such specificity.

L-glutamic dehydrogenase. L-glutamic dehydrogenase catalyzes the oxidative deamination of the amino acid (L-glutamic acid) to its corresponding keto acid, alpha-ketoglutaric acid.[49] This enzyme is widely distributed and has been crystallized from beef liver. It was found to contain zinc in significant amounts.[50]

The reactions and enzymes discussed thus far lead to end products (pyruvate and

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* A rough calculation will show that serum zinc cannot be expected to show any variations in diabetic patients. The pancreas is assumed to contain about 3,000 micrograms of zinc, of which about 2 per cent or 60 micrograms are in the islets (assuming uniform distribution). The total zinc in the circulating volume of serum is also about 3,000 micrograms. It is obvious that even significant variations in islet zinc would have no reflection on the serum zinc levels.

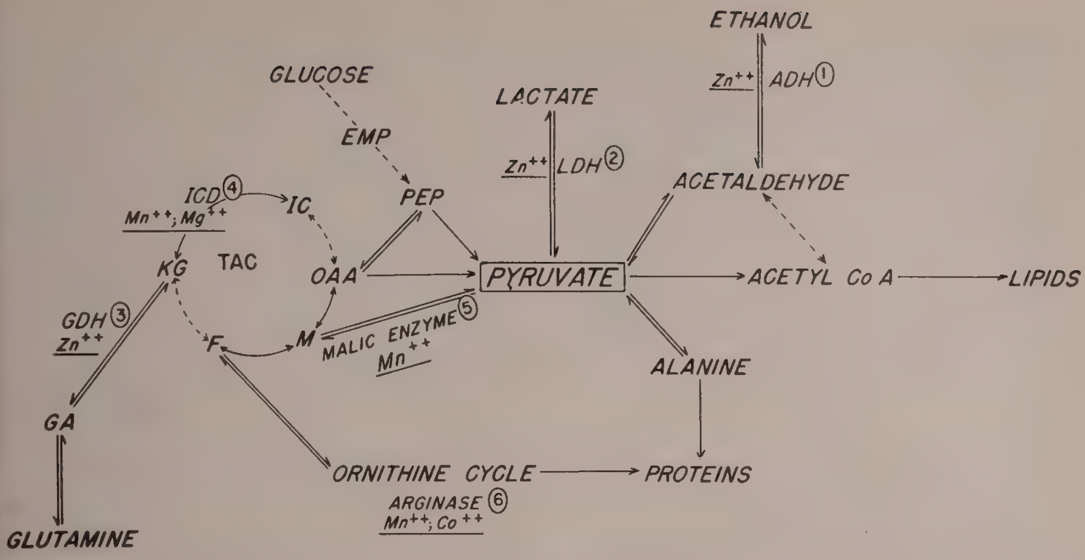

FIGURE 1. Trace-metal-dependent-enzymes of intermediary metabolism. The central role of pyruvate is emphasized. Broken lines mean that intermediary products have been omitted.

Abbreviations: ADH, alcohol dehydrogenase; LDH, lactic dehydrogenase; GDH, L-glutamic dehydrogenase; ICD, isocitric dehydrogenase; EMP, Embden-Meyerhof Pathway; PEP, phospho-enol-pyruvate; TAC, tricarboxylic acid cycle; OAA, oxalacetate; M, malate; F, fumarate; KG, alpha-ketoglutarate; IC, isocitrate; GA, glutamic acid.

alpha-ketoglutarate) which have a central role in the intermediary metabolism of carbohydrates, proteins, and fats. Three enzymes and their reactions, which are equally important and are, in fact, closely linked with the reactions already described, will be discussed briefly in the following paragraphs. These enzymes require manganese for their action, although the metal requirement may not be as specific as it was found for zinc in the previously mentioned enzymes.

Isocitric dehydrogenase. Isocitric dehydrogenase participates in the tricarboxylic acid cycle, catalyzing the conversion of d-isocitrate to alpha-ketoglutarate. Two varieties of the enzyme have been described: one is triphosphopyridine nucleotide-dependent, the other diphosphopyridine nucleotide-specific; the former occurs mostly in the cytoplasm, the latter in mitochondria. Besides its dependence on pyridine nucleotides, this enzyme requires the divalent cations Mn^{++} or Mg^{++} for its action.[49]

"Malic enzyme." The "malic enzyme" is one of three participating in the so-called Wood-Werkman reaction.[46,49] This reversible reaction involves the enzymatic fixation of carbon dioxide and thereby formation of 4-carbon dicarboxylic acids from 3-carbon compounds. The end products of the reaction are: malate, oxalacetate, and succinate; again compounds which participate in the tricarboxylic acid cycle. The enzyme in question catalyzes the formation of malate from pyruvate whereby reduced triphosphopyridine nucleotide is oxidized to triphosphopyridine nucleotide. Manganese is obligatory for the action of this enzyme.

Arginase. Arginase causes in ureotelic animals the hydrolytic cleavage of L-arginine to L-ornithine and urea; hence it is most abundant in the liver. Arginase is activated by Mn^{++} or Co^{++}. The breakdown of arginine occurs in the reaction chain known as the ornithine cycle. The ornithine cycle is, in turn, connected with the citric acid (or tricarboxylic acid) cycle, via fumarate, a compound which is formed in both cycles.

It is abundantly clear from the brief description of the reactions mentioned that the enzymes with a requirement for Zn^{++} or Mn^{++} participate in the cleavage or formation of compounds which play a central role in carbohydrate, protein, and fat metabolism. Pyruvate is probably the most important compound—it represents one of the end products of glycolysis and at the same time is an important link to energy release (Krebs cycle), protein metabolism (alanine), and fat metabolism (acetyl coenzyme A) (Fig. 1). The other compounds, through their participation in the tricarboxylic acid cycle or the ornithine cycle, also connect the various pathways of intermediary metabolism.

Comment

The essential role of trace metals in certain enzymatic reactions of the carbohydrate cycle, the suggestive evidence for the association of zinc and insulin, and the work on experimental diabetes are important and interesting data. The translation of these data into human physiology and their relationship to the pathogenesis of diabetes in man undoubtedly will be attained by future investigation.

Addendum

Since this manuscript was submitted for publication, attention has been called to the possible role of another trace element, trivalent chromium, in glucose utilization.[51] The mechanism of action of this metal in carbohydrate metabolism has not been elucidated.

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Number thirty in a series of articles on Current Concepts in Diabetes Mellitus

On waste in hospitals

Any casual observer can notice the same almost planned waste around any hospital. Nurses put out far too many dressings on the dressing table or towel, and generally the excess dressings are wasted. The waste of adhesive tape is also very significant. A great saving could be made by proper preparation and utilization of ordinary gauze squares for sterile dressings. Proper hospital administration could cut down a great deal of waste time among the servant class employes of a hospital. Another frightful waste of time is the so-called "coffee break." If a nurse wants a cup of coffee, I see no reason why she shouldn't have it on the floor. Waste does not mean much to patients because Blue Cross will pay for it. If they stop to think, they would realize that the more hospital waste, the higher their Blue Cross premiums will go.—*Amos R. Koontz, M.D., Current Medical Digest, October, 1961*

Medical Diagnostic Clinics

A series of special articles on rare but important disease entities or medical esoterica

Prepared by the Department of Medicine, St. Vincent's Hospital, New York City

WILLIAM J. GRACE, M.D., Editor
MATTHEW J. FERGUSON, M.D., Associate Editor

A Medical Diagnostic

Protocol

A twenty-three-year-old white unemployed waitress visited the hospital outpatient department complaining of heaviness and numbness of both upper extremities. She had been well until two years before when she noted the onset of chronic fatigue, occasional low-grade fever, and inability to gain weight. One year before she had been dismissed from her job because she frequently dropped trays and dishes. Since then, she stated, her arms tired easily and even hurt after moderate activity. In addition to this, she complained of periods of dizziness and giddiness and her family said she had "passed out" on several occasions. The development of all these symptoms was coincident with unusually severe emotional problems.

A superficial physical examination was unremarkable. She was referred to the psychiatric clinic where she was followed for six months. Despite a resolution of her emotional problems, she continued to voice her original complaints.

Diminished vision in the right eye prompted an ophthalmologic consultation. A cataract was present on the right eye, and retinal spasms and peripapillary arteriovenous anastomoses were described in the left eye. Surgery was advised but was deferred to await medical clearance because of coexistent symptoms.

That same day, while walking home, she developed a transient left-sided weakness. This recurred several times in the next few days until finally a left hemiparesis and dysarthria became evident. She was then admitted to the hospital.

Physical examination. A physical examination revealed a thin, well-developed, fairly well-nourished female who was dysarthric and had an obvious left-sided paresis. The blood pressure could not be obtained in the right arm. It was 80/70 mm. Hg in the left arm. The blood pressure was somewhat elevated in the lower extremities. The pulse was regular at 90 per minute. The temperature was 99.6 F. There appeared to be a right facial atrophy. An ulcer was present on the nasal septum. The teeth were loose and many were missing. The eye findings were as reported previously. The heart was not enlarged and the sounds were of good quality. A systolic murmur was heard over the manubrium sterni radiating into the right side of the neck and a thrill was felt in the right neck. The remainder of the examination was within normal limits.

Course. In sixteen hours the patient recovered completely from the paretic episode. The spinal fluid was normal. She signed out of the hospital against advice on the third hospital day. It was later learned that during the next month she had several more episodes of hemiparesis and her vision became progressively worse. Four weeks after leaving the hospital she collapsed while climbing some stairs. She was brought to the hospital and was dead on arrival. A medical examiner's postmortem examination was performed.

(Elucidation will be found on page 92)

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

BENJAMIN J. CILIBERTI, M.D., Chairman
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Obstruction of the Airway in the Intubated Patient

The obstruction of the airway in the endotracheally intubated patient is not rare. One should not feel entirely secure or relax his vigilance during the time that a respiratory obstruction may occur following the insertion of an endotracheal catheter. The difficulties which arise are mostly mechanical. The most common causes of respiratory obstruction in such cases are kinking of the endotracheal tube, intubation of the right main bronchus, overinflation of a cuff situated close to the bevel of the tube, or the bevel of the tube displaced close to or against the wall of the trachea. The obstruction of endotracheal catheters also may be caused by secretions, debris, loose tissue, and blood or pus originating directly from an involved lung or coming indirectly from the contralateral lung by manipulation. The signs of hypoxia, difficult manual ventilation, wheezing, or labored breathing should raise the suspicion of respiratory obstruction.

The failure to recognize these problems increases the morbidity and mortality associated with anesthesia during surgery. The following is a case of respiratory obstruction with an endotracheal tube in place during an exploratory thoracotomy. The favorable postoperative outcome was attained through efforts in determining and relieving its cause. However, the patient succumbed on the third postoperative day from a cause probably not related to anesthetic management.

Case report

This fifty-four-year-old, white male came to surgery for an exploratory operation because of an x-ray diagnosis of cancer of the right lung. A previous bronchoscopy did not help in establishing a definite diagnosis. The patient received 10 mg. of morphine and 0.4 mg. of atropine one hour before the expected time of surgery. A complete blood count; urinalysis; sodium, potassium, and chloride values; combining power of carbon dioxide; total proteins; albumin-globulin ratio; and urea nitrogen were within normal limits. Anesthesia was induced with 350 mg. of thiopental sodium in a $2^1/_2$ per cent solution. Forty mg. of succinylcholine were administered intravenously, and after proper oxygenation rapid endotracheal intubation was performed with a cuffed number 40 Murphy tube. The cuff was inflated to secure a tight fit. Anesthesia was maintained with halothane, nitrous oxide, and oxygen. The concentrations of halothane varied from between 0.6 and 0.9 per cent during maintenance. The patient was placed in the left lateral decubitus position following the return of normal res-

Presented and discussed at a conference held at Bellevue Hospital, New York City, September 11, 1961. Clinical anesthesia conferences are held on the first Monday of each month.

pirations. On opening the chest the middle and lower lobes of the lung were found to be collapsed. The respirations were assisted. During exploration a gradual rise in blood pressure was noticed, the pulse became pounding, and some cyanosis appeared. These changes coincided with pressure applied to the collapsed lobes by the surgeon. On searching for the reason for the unexpected changes it was found that the right lung could be inflated with ease, but the left side of the chest did not show any movements even with excessive bag pressure. It was obvious that the left main bronchus was obstructed, and no gas mixture was able to enter or leave that lung. Surgery was discontinued temporarily, and every effort was made to relieve the obstruction. The cuff was deflated, and the tube was retracted slightly. A suction catheter was passed without any improvement in the obstruction. The tube then was removed, and a number 42 cuffed Murphy tube was inserted with the patient in the left lateral position. Immediately on exchanging the tube there was a marked improvement in the patient's condition, and inflation of the left side of the chest became possible. Since some cyanosis persisted after ten minutes it was decided to close the chest after the biopsy. The biopsy did not show a malignant condition, and the diagnosis of abscess of the right lung was made. After the patient was placed in the supine position, a bronchoscopy was done. Some debris and pus in the left main bronchus was removed, following which the cyanosis cleared completely.

On inspection of the removed endotracheal tube a clump of tissue made up of debris and pus was found to be attached to the opening of the Murphy tube opposite to the bevel. This apparently lodged in the opening and extended to the left main bronchus. The patient's recovery from anesthesia was uneventful. On the third postoperative day, while dangling his legs, he suddenly collapsed. The patient was pronounced dead within a few minutes. An autopsy showed an embolism in the left lung.

Comment

An ever-present danger during anesthesia is respiratory obstruction with an endotracheal tube in place. Such a complication should be recognized and treated effectively without delay. A failure to do so may result in a fatality which might have been prevented. Although the preoperative clinical diagnosis was lacking on this patient, it illustrates that the anesthesiologist must be prepared for any emergency which may arise during surgery. After unsuccessful attempts to relieve the obstruction by checking the possible causes, it was decided to remove the tube and replace it with another. This maneuver improved the ventilation of the left lung. An inspection of the removed tube illustrated that debris and secretions can be sufficiently large and extensive to occlude one of the openings of a Murphy tube. Any endotracheal catheter which causes obstruction or becomes obstructed and evades correction should be replaced. This case also illustrates the advantage of being able to perform intubation with patients in the lateral position. Time-saving measures are essential in such emergencies. Although bronchoscopy suction was performed at the termination of surgery for remaining secretions in this case, it may be necessary to do this at any time during the operative procedure to relieve an obstruction.

Patients with excessive tracheobronchial secretions or lung abscesses present the problem of flooding and obstructing the respiratory passages. The recommended solutions to this problem consist of endobronchial intubation of the unaffected lung, bronchial tamponade, positioning of the patient to confine secretions to dependent parts of the lung as recommended by Overholt, and Woods* and the use of bronchial blockers. The major contribution, when feasible, may come from the surgeon by the proper handling of tissues and clamping the involved bronchus as early as possible to avoid spillage.

Not infrequently, medical patients with respiratory problems have endotracheal tubes inserted to improve the airway and aid in the removal of secretions. Such tubes can and do become obstructed after a period of time from inspissated material adhering to the inner surfaces. When this occurs, the tube's primary purpose is lost, and it actually becomes dangerous. Frequent inspections and changing of such tubes are necessary.

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* Overholt, F. H., and Woods, F. M.: The prone position in thoracic surgery, J. Internat. Coll. Surgeons **10:** 216 (Mar.-Apr.) 1947.

Number one hundred fifteen in a series of clinical anesthesia conferences

Accidental Chemical Poisonings

From the Poison Control Center,
The City of New York Department of Health

A series prepared by
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The City of New York Department of Health;
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Iron Intoxication

INCIDENT 1

Agent	*Age*	*Sex*
Ferrous sulfate, molybdenum oxide	22 months	Male

The patient's father was painting the medicine cabinet in the bathroom and put the medications in the bedroom including a box containing iron pills which were prescribed for the victim's mother to take during pregnancy.

The child obtained the pills and swallowed four of them, thinking they were candy. He became nauseous and vomited and was taken to a hospital for treatment. In the hospital the patient's stomach was lavaged in the emergency room, and he was admitted to the inpatient service for further observation and treatment. In addition to nausea and vomiting he also developed diarrhea and became stuporous. He was treated with intravenous fluids and was retained in the hospital for four days at which time he made a complete recovery.

INCIDENT 2

Agent	*Age*	*Sex*
Ferrous sulfate	2 years	Male

The patient's mother related to the interviewing public health nurse that the medication was prescribed for her in a prenatal clinic. She placed the medication in a bedroom drawer. While the mother was cleaning in the kitchen, the child apparently obtained the drug and swallowed about ten 5-grain tablets. The mother was unaware of the occurrence until she heard a noise. On entering the bedroom she found the child with the empty bottle. The mother also told the nurse that she thought of the medication as vitamins and not as poisonous. Two hours following ingestion the patient began to vomit and was taken to a nearby hospital. On admission to the hospital, in addition to recurrent vomiting, the patient also appeared stuporous. He vomited several times, and the stomach was lavaged with water two and one-half hours following the ingestion. He was hospitalized for four days, treated symptomatically, and discharged as symptom-free.

INCIDENT 3

Agent	*Age*	*Sex*
Ferrous sulfate	15 months	Male

The patient's mother, who was pregnant, was instructed to take this medication because of a secondary anemia. She kept the medication in her pocketbook so that she could always take it as prescribed.

On the day of the accident she placed her pocketbook on the bedroom dresser, but an older sibling removed it and put it on a chair. While all the other members of the household were in the living room watching television, the patient obtained the handbag, removed the box containing the iron medication, and swallowed eight 5-grain tablets.

When the mother returned to the bedroom she found the patient playing with the pocketbook and the box containing the tablets.

On admission to the hospital the patient presented the symptoms of nausea, recurrent vomiting, diarrhea, and stupor. His stomach was lavaged with sodium bicarbonate and after four days of hospitalization and supportive and dietary therapy, he made a complete recovery.

INCIDENT 4

Agent	*Age*	*Sex*
Ferrous sulfate, molybdenum oxide	1 Year	Male

This drug was prescribed for the mother of the patient because of pregnancy. She placed the medication in the bathroom medicine cabinet. According to the mother, the child climbed on a chair, obtained the medication, and swallowed an unknown number of 5-grain tablets. When his mother found him (the exact time following the ingestion is unknown) he was vomiting repeatedly and soon began to convulse.

The child was taken immediately to the Kings County Hospital emergency room where the stomach was lavaged with saline. The gastric contents contained a pinkish-red material. The patient was given intravenous fluids and milk of magnesia and was put on a soft diet after the acute symptoms subsided. He was observed in the hospital for three days and discharged symptom-free but with instructions to return to the outpatient department for follow-up care.

INCIDENT 5

Agent	*Age*	*Sex*
Ferrous sulfate	2 Years	Male

The patient's father informed the public health nurse that the child's grandmother had a box of pills in her handbag which she left hanging on a doorknob in the living room. The child apparently removed the box from the handbag and swallowed 32 3-grain tablets. The box was entirely empty, and only three tablets were found on the floor. The child vomited six or seven times beginning about one-half hour following the ingestion. He became drowsy and was rushed to City Hospital at Elmhurst where he was treated heroically for three weeks until recovery ensued.

We are indebted to Manfred Weichsel, M.D., Director of Pediatrics, for the following excellent summary.

> This is a short report on the case of the two-year-old child with severe iron poisoning. On his admission to the hospital on March 18, 1961, it was stated that the child had vomited about five to seven times and suddenly became very drowsy. The vomitus consisted of greenish material and later became "coffee ground." There was no diarrhea. The child appeared pale, cold, semiconscious, and reacted weakly to painful stimuli. The extremities were flaccid, and the temperature was 97.2 F. The pulse was rapid, almost imperceptible, and the respirations were rapid and shallow. The patient was given stimulants and oxygen, and an immediate gastric lavage was performed when a history of ingestion of some unknown substance was obtained. Chocolate-colored material was obtained from the stomach. Plain water and later milk were used for the lavage. At the same time, very loose, watery stools were gushing out continuously; later they contained fresh and clotted blood.
>
> At this time the information was obtained that the child had swallowed 32 tablets of 3 grains each (0.2 Gm.) of ferrous sulfate prior to his admission to the hospital. The grandmother had been treated for anemia and apparently left the medicine bottle in a place where the baby was able to ingest the entire contents. Treatment with intravenous fluids and ethylenediamine tetra-acetate was continued, but in view of the seriousness of the situation we decided to perform an exchange transfusion. Fifteen hundred cc. of compatible blood was used by means of a saphenous vein cut-down. Subsequently, fluids were continued, and undiluted evaporated milk was given by mouth.
>
> I am happy to report that the child made an uneventful recovery and was discharged in good condition three weeks after the accident.
>
> Pre-exchange serum iron: 386 mg. per 100 ml.
>
> Postexchange serum iron: 248 mg. per 100 ml.

Incident 6

Agent	*Age*	*Sex*
Ferrous sulfate, molybdenum oxide	$2^1/_2$ years	Female

The drug was prescribed for the patient's mother, who was pregnant. She placed the bottle containing the medicine in her housecoat, which she hung in the living room without removing the bottle. Apparently there was a hole in the coat, and the bottle fell on the floor. While the parents were asleep, the patient apparently obtained the bottle in the early morning and swallowed 14 or 15 tablets. When the mother awoke, she found some of the tablets in the child's crib. Within fifteen minutes after the mother awoke, the child began to vomit and was taken to the Kings County Hospital. Her stomach was lavaged with water, and after one day of observation she looked well and symptom-free.

Incident 7

Agent	*Age*	*Sex*
Ferrous sulfate	1 year	Male

The mother had just returned from a prenatal clinic where she received some ferrous sulfate tablets in a box which she put in her purse. She placed the purse on a low dresser near the infant's crib. Apparently when the child awoke he obtained the purse, removed the iron tablets from the box, and swallowed approximately half of the contents, fifteen 20-grain tablets. The patient began to vomit "and his eyes looked weak." His mother gave him some fruit juices but to no avail. She called the hospital and was told to bring the child immediately to the hospital. His stomach was lavaged with normal saline, and the patient was admitted to the inpatient service for observation. After three days of supportive therapy he made a complete recovery.

Comment

It is of interest that in all accidental ingestions in children, the families related to the public health nurses that they were unaware that these tonics or vitamins were harmful. They looked on such medications as "health-promoting" agents. Since none of these medications bear any precautionary label, we wrote a letter on the subject to the company which manufactures ferrous sulfate, a widely-used product which is often incriminated in accidental poisonings. We are very happy to publicize their wholehearted cooperation as indicated in the following letter:

> Thank you for your recent letter about the labeling of ferrous sulfate tablets and the lack of an appropriate warning for storing.
>
> We can well understand your concern about the lack of an appropriate warning to keep these tablets out of the reach of children, and I'm sure you'll be pleased to know that a change has been made. Bottles of 100 tablets are now being manufactured with a label reading, "Keep this and all medicines out of the reach of children." This new label was first used in December, 1959. Undoubtedly, the bottle you saw was from stock manufactured before that date. I should like to mention that the larger package of 1,000 tablets does not yet bear a warning label, but arrangements have been made for the change.
>
> We appreciate your writing to us and if we can be of service at any time, please let us know.

Number eighty-two in a series of Accidental Chemical Poisonings

Medical Care Insurance

A series of articles on health insurance prepared by the Associated Blue Shield Plans of New York State

LEONARD J. RAIDER, M.D., Editor

The Medical Profession and the Federal Employe Health Program

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Chairman, Professional Relations Committee,
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On July 1, 1960, American medicine became an active partner with the United States government in providing prepaid medical care for more than 4 million Federal employes and dependents.

For the first time, the Federal government, as the nation's largest employer, appropriated direct Federal subsidies to help its workers purchase prepaid medical and hospital care.

For the first time, each individual member of a large employed group was given the opportunity to choose his own favored prepayment program from a wide choice of approved plans negotiated for him by the Civil Service Commission.

For the first time, by long-considered action of Congress, the United States government became a participant in the voluntary prepayment medical and hospital programs which had long been ignored or derided by many politicians and bureaucrats.

Significance

The Federal Employe Health Program is a proving ground for the voluntary system of health care prepayment in America. Blue Cross-Blue Shield has been freely selected by a majority of the Federal workers, and this program will put the medical profession and our voluntary hospital system to a crucial test.

The independent medical profession, working through its own prepayment mechanism, is challenged to demonstrate its efficiency and integrity in the care of those who work for the Federal government. If it should fail this test, the profession might never have another opportunity to prove the soundness of the voluntary prepayment system.

Historical background

On September 28, 1959, President Eisenhower signed Public Law 86-382, known as the Federal Employes Health Benefits Act of 1959. Prior to this enactment, health insurance on a group basis with payroll deduction had never been available to the great majority of Federal employes. Even more important, there had never been any provision for employer contribution to the cost of any prepayment protection that the Federal worker might obtain on his own initiative.

Bills to accomplish this purpose had been introduced in every session of Congress since 1947, but it took twelve years for Congress to determine whether or not, and in what manner, the United States government might do for its employes what nearly every private employer has long since undertaken on a voluntary basis.

A subsequent enactment has provided for the inclusion of Federal employes who retired prior to July 1, 1960, newly retiring employes having been included in the original measure.

Characteristics of the legislative act

The enabling legislation, while giving the Civil Service Commission great latitude in developing the program and establishing regulations, nevertheless spells out fairly precisely the broad outlines of the prepayment program to be provided for Federal workers.

Thus the Commission was authorized to "contract for or approve" one government-wide service benefit plan (offering two levels of benefits); one government-wide indemnity benefit plan (again offering two levels of benefits); employe organization plans which were in operation on July 1, 1959; group-practice prepayment plans, where available; and individual-practice prepayment plans with a comprehensive scope of benefits.

The inclusion of a service benefit plan in the Act as a specific type (in fact, the first-mentioned specific type) was done explicitly to enable a contract to be negotiated with Blue Cross and Blue Shield. The Act defines a service benefit plan as one "under which payment is made by a carrier under contracts with physicians, hospitals, or other providers of health services for benefits . . . or, under certain conditions, payment is made by a carrier to the employe . . . ." An indemnity benefit plan is defined as one "under which a carrier agrees to pay certain sums of money, not in excess of the actual expenses incurred . . . ."

The Act prescribes the general scope of benefits to be offered by any approved program and provides for the free choice of plan by each employe and for a change of plan if desired, according to regulations to be set up by the Civil Service Commission.

The Act further prescribes how the Commission may contract for the several programs to be offered; provides that rates shall be reviewed periodically and adjusted on an experience-rated basis for the group as a whole; and sets forth the range of allowable Federal contributions to the premiums to be charged for the several programs.

Among various other provisions of the Act is a requirement that "The Commission shall transmit to the Congress annually a report concerning the operation of this Act." Thus the details of a program involving the medical care of some 4 million citizens, supported in considerable part by tax funds, are brought under the scrutiny of Congress.

Initial enrollment

The Blue Cross Association and the National Association of Blue Shield Plans acted as the contracting parties for their respective member plans in negotiations with the Civil Service Commission. Aetna Insurance Company acted as contracting agent for the commercial insurance companies in negotiating the indemnity benefit plan, and in all, the Commission approved 36 carriers, all of which, except Blue Cross-Blue Shield and Aetna, operate within limited geographic areas.

A total of 54 per cent of all Federal employes who chose any plan at all chose Blue Cross-Blue Shield in the initial selection period ending July 1, 1960. Twenty-seven per cent chose the indemnity program, and 19 per cent elected local employe association or comprehensive plans. Of those enrolling since July 1, 1960, 68 per cent have chosen Blue Cross-Blue Shield; 19 per cent chose the indemnity program; and 13 per cent selected other approved plans. This reflects an increasing recognition of the superior quality of the Blue Cross-Blue Shield program.

During the first weeks in October, 1961, each Federal worker had an opportunity to decide whether he wished to keep the plan he then had or change to one of the alternatives available to him.

Although the program is administered in Washington, D.C., each Blue Cross and Blue Shield Plan is responsible for the delivery and direct administration of the basic benefits for Federal employes served by physicians or hospitals within that Plan's area of operation, and Plans in 27 states presently are underwriting and servicing the supplemental benefit portion of the program.

One of the many uniquely significant factors in this program is the fact that while the Federal employes constitute the largest single group covered by Blue Cross-Blue Shield, the individual employe makes the choice of carrier and decides whether or not to change his carrier. Therefore, the Plans are dealing primarily with individuals rather than with a group. The Civil Service Commission has specifically prohibited any approved carrier from making a direct "sales appeal" to the potential individual subscribers. Enrollment representatives for Blue Cross-Blue Shield may interpret or explain their program, but they may not "sell."

This means, of course, that each program offered the Federal employes under this Act will ultimately stand or fall on its record of performance.

Outline of coverage

Each Federal employe who chose Blue Cross-Blue Shield also had a choice between two programs—the high option and the low option. And both of these options were made up of a basic benefit program and a supplemental (major medical) benefit program.

The Blue Shield basic high option program (selected by 82 per cent of all who elected a Blue Cross-Blue Shield program) includes benefits for the following services: surgical procedures; obstetric procedures; inhospital medical care; anesthesia; diagnostic x-ray films, both inhospital and when provided in a doctor's office or as an outpatient benefit within seventy-two hours of an accident; laboratory and pathologic services (for hospital bed patients only); radiation therapy; and physical therapy (for hospital bed patients only).

Where benefits are provided on a service benefit basis, local fee schedules and applicable income limits are used; where indemnity benefits are provided, a national fee schedule applies.

The surgical benefits apply in or out of hospital; medical benefits begin on the first day of medical hospitalization and apply up to one hundred and twenty days per admission. Up to thirty days care per year is allowed for pulmonary tuberculosis or mental or nervous treatment.

Standard exclusions apply, but there are no waiting periods or exclusions for preexisting conditions.

The low option basic program limits medical care in the hospital to thirty days per admission and tuberculosis and mental care to ten days per year. The principal difference is the provision of a lower income limit and a lower schedule of payments.

The supplemental benefits formerly provided required (for the high option subscriber) payment of a $100 deductible, after which 80 per cent of additional allowable expenses up to $20,000 is paid by the Plan ($10,000 per benefit period). Allowable expenses included reasonable and necessary expenses for any kind of medical, hospital, nursing, laboratory, or ambulance service, including braces, artificial limbs, rental of special equipment, physiotherapy, transfusions, blood, and so forth. Cosmetic surgery and dental work were limited to the care of accidental injuries; mental and nervous treatment had to be received as an inpatient (outpatient care for mental and nervous being covered only to 50 per cent of costs).

The low option supplemental benefits called for a deductible of $200 and for 75 per cent of the additional allowable expenses to be paid by the Plan.

On November 1, 1961, these supplemental benefits were increased in several important respects. Under the high option program, maximum benefits were raised from $20,000 to $30,000. Under the low option program the maximum was increased from $5,000 to $10,000. For a single benefit period the maximum benefits under the low option program were increased from $2,500 to $5,000, and the low option deductible was reduced from $200 to $150. Benefits for certain diagnostic services and for special nursing care were liberalized, and services for the treatment of nervous and mental conditions were expanded to include treatment in mental hospitals and elsewhere, under the low option program (as had already been provided under the high option plan).

In addition, the provision which ended a supplemental benefit period if a subscriber had no covered expenses for over ninety days was eliminated. A benefit period now continues for twelve consecutive months.

Basic Blue Shield benefits were expanded also as of November 1, 1961. Benefits for cesarean delivery and for complications of pregnancy were increased.

Benefits for oral surgery were extended also, and basic benefits for a physician's charges for emergency first-aid treatment within seventy-two hours of an accident will now be provided even when surgery is not involved.

Retired persons may have the same benefits as active workers and at no greater cost. Surviving annuitants of an employe or retired person who is covered may continue their coverage at the same rates, after the death of the enrolled employe or the retired person.

Conclusion

In a masterpiece of understatement, the Department of Health, Education, and Welfare has declared that "a program whose combined cost to employes and the government will be about $260 to 270 million (per year) is of interest in itself. The program will have an impact on the economics of medical care."

The nature of this impact and its consequences will be determined largely by the quality of interest shown by each practicing physician in the Federal Employe Health Program.

Number fifteen in a series of special articles on Medical Care Insurance

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Vitamins neither a food nor an energizer

Vitamins are not a food substitute, nor will they give a healthy person any extra nutritional benefits when taken in addition to an adequate diet, according to an article by Gaynor Maddox in the November, 1961, issue of *Today's Health*. Vitamins are regulating chemicals needed for growth and the control of body activities. Well-balanced meals provide all the vitamins and other nutrients the body needs or can use.

According to Clement A. Smith, M.D., many parents equate vitamin pills with food. "They have been deceived by skillfully misleading advertisements into believing vitamin pills will take care of the family's nutrition. Children don't gain pep by taking vitamin pills, and parents must understand clearly that no vitamin, either in food or in pill form, is a tonic or stimulant. Nor does giving a child more vitamins than he needs for normal growth speed up his growth rate."

William B. Bean, M.D., said: "There is not one iota of scientific information which suggests that people who have an adequate balanced diet and have no diseases that interfere with digestion gain any benefit from self-prescribed vitamin or mineral supplements." In a study involving about 1,000 healthy Army men, some of whom took vitamins in addition to their rations, Dr. Bean found no difference in performance, fitness, or health between those who took vitamins and those who had the same rations and no vitamins.

Dr. Charles Glen King said a vitamin deficiency can be identified only by a competent physician and added that there is good evidence that the average American's diet contains adequate supplies of all vitamins known to be needed, along with the other essential nutrients.

It was also pointed out that there is no medical proof that any vitamin supplement on the market can prevent colds, nor is there any need for adding supplemental vitamins to a well-planned low-calorie reducing regimen.

ELUCIDATION

Continued from page 82

At a Japanese Ophthalmological Society meeting in 1908, Takayasu[1] described a young woman with a cataract and unusual retinal vascular changes. At the same meeting Onishi and Kagoshima[2] described 2 similar patients and noted the absence of a radial pulse in one. Over the next four decades a half score of such patients with eye signs and abnormalities of the great arteries of the aortic arch were reported in the Japanese literature. It seemed to be exclusively an Oriental disease until the early 1950's when several patients were described in the Scandinavian countries.[3] In 1952 Caccamise[4] reported the first American case. Now there are reports from all over the globe and Occidental patients predominate.[5]

Takayasu's disease or pulseless disease—also known as brachial arteritis, aortic arch arteritis, obliterative brachiocephalic arteritis, and hypersensitivity arteritis—is found, with few exceptions, in young women, ages ten to forty-five years. Essentially, it is an arteritis of the arch of the aorta and its great branches. This arteritis leads to narrowing, thrombosis, and obliteration of these vessels, with consequent ophthalmologic, cerebral, and upper-extremity symptomatology.

The patient's clinical picture will depend on the circulation of the specific vessels involved. Some authors have noted nonspecific symptoms such as fever, malaise, weight loss, anemia, elevated sedimentation rate, and abnormal serum protein. The more specific symptoms and signs may be listed as follows:

Ophthalmologic. Blurring of vision aggravated by exertion and relieved by rest ("intermittent claudication of vision"), amblyopia, and spots before the eyes are the most common eye symptoms. An examination may reveal cataracts and atrophy of the retina and iris. Funduscopic changes include retinal spasm, atrophy of the retina, and the classic peripapillary arteriovenous anastomoses described by Takayasu.

Neurologic. Headache, exertional giddiness and dizziness, syncope, convulsions, hemiparesis, and even hemiplegia have been described. The syncope seems to be related to hypersensitive carotid sinuses.

Soft tissue pathologic. Chronic ischemia induces various trophic changes such as facial atrophy, ulcers on the tip of the nose, perforation of the nasal septum, and loss of teeth and hair.

Upper-extremity. Involvement of the subclavian arteries leads to easy fatigability and even pain. There may be decreased skin temperature and muscular atrophy. Because of collateral circulation, trophic changes such as those seen in Buerger's and Raynaud's disease do not occur.

Cardiovascular. The carotid pulses may be decreased or absent. Murmurs and thrills produced by stenotic vessels are sometimes heard high in the chest or neck. Murmurs heard over the precordium are thought to be due to collateral circulation.

Pathologically the lesion begins as a periarteritis and progresses to a panarteritis. Plasma cells and lymphocytes infiltrate the adventitia. There is disruption of the muscle and elastica of the media. The intima becomes thickened and fibrous, predisposing the patient to intraluminal thrombosis.

The etiology is unknown. Tuberculosis was once incriminated, as were syphilis and streptococci. Hypersensitivity is now intriguing students of the disease. Its predominance in females suggests a hormonal factor.

The prognosis is poor. The disease may be acute or chronic with a duration ranging from one to twenty years. Cerebral ischemia is the usual cause of death. Treatment is unsatisfactory. Steroids and anticoagulants are the drugs of choice at this time.

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Case Reports

Complete Heart Block Associated with Subacute Bacterial Endocarditis

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THE OCCURRENCE of complete heart block during the course of subacute bacterial endocarditis is extremely rare. In his review of subacute bacterial endocarditis, Kerr[1] noted that only 7 such cases with this complication had been reported by 1955. The following case report concerns a patient with complete heart block and probable subacute bacterial endocarditis with recovery from both entities. None of the previously reported cases have survived.

Case report

A forty-seven-year-old white male was hospitalized on March 31, 1960, with the complaints of weakness, fainting, and slow pulse. Seven years previously the patient had several episodes of fainting and weakness. He was found to have a pulse rate as low as 20 per minute and was hospitalized and treated with ephedrine for a short time only. He apparently recovered completely and was not told of heart disease when he was discharged. In the intervening years he received several physical examinations and was informed that he had no evidence of heart disease.

In February, 1960, the patient had a fever of up to 104 F. with chills and malaise. This illness subsided without therapy. Six weeks prior to his hospital admission the patient had several dental fillings done. He had a recurrence of fever, chills, and malaise and was given chloramphenicol (Chloromycetin) for a few days. Two days prior to his admission the patient noted that his pulse was slow and irregular, but he was asymptomatic. An electrocardiogram one day before his admission revealed a complete heart block. On the day of admission the patient vomited and had several syncopal episodes. The patient denied any knowledge of rheumatic fever, and the rest of the history was noncontributory.

PHYSICAL EXAMINATION. A physical examination revealed a temperature of 100 F., pulse 32 per minute, and a blood pressure of 90/60 mm. Hg. The patient appeared acutely and critically ill. The pharynx was moderately injected. Jugular venous pulsations were clearly visible and were disassociated from the arterial pulse. There were fine rales at the base of the left lung posteriorly. The point of maximum cardiac impulse was diffuse with a heaving thrust at the anterior axillary line in the fifth intercostal space. M_1 was greater than M_2. A_2 equaled P_2. There was a regular ventricular rhythm at a rate of 32. Atrial sounds were audible occasionally at the apex. There was a harsh, blowing, Grade IV systolic murmur heard best at the apex and transmitted to the left axilla. There were no other abnormalities noted.

The laboratory findings included a hemoglobin of 14 Gm., hematocrit 44, white blood count 19,500 with 83 per cent polymorphonuclear leukocytes, and a sedimentation rate of 44 mm. per hour. The initial urine examination was entirely within

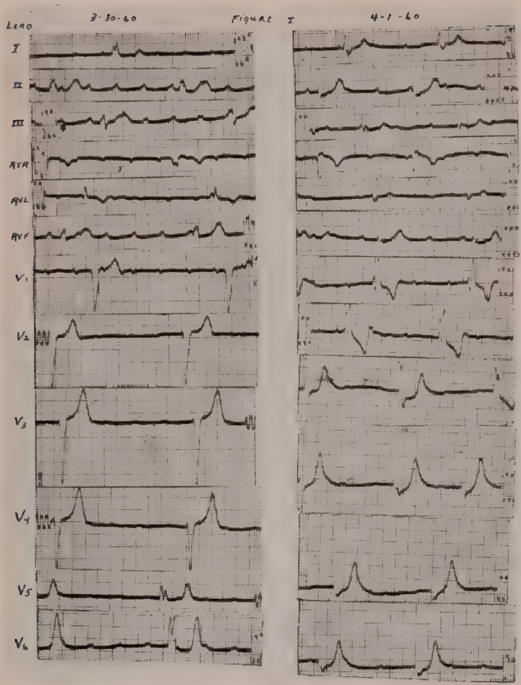

FIGURE 1. Electrocardiogram showing supraventricular tachycardia with complete heart block.

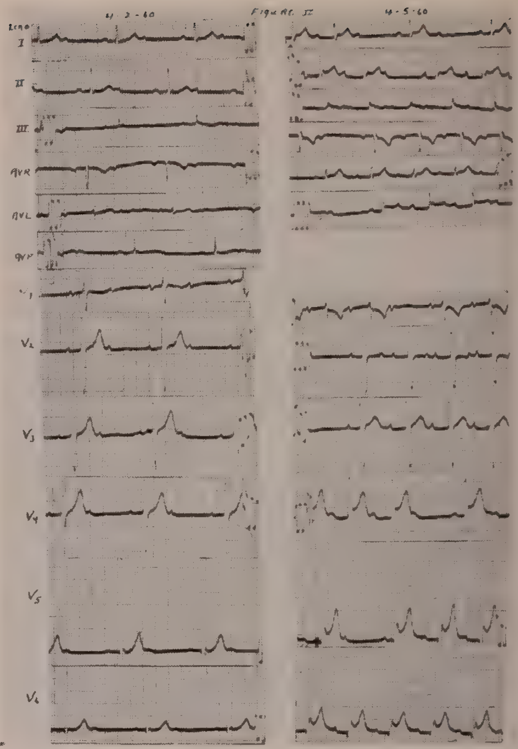

FIGURE 2. Electrocardiogram showing sinus rhythm and first degree block.

normal limits. The initial blood urea nitrogen was 25 mg. per 100 ml. and rose to 38 mg. per 100 ml. in twenty-four hours. The carbon dioxide was 22.5 mEq., chloride 98 mEq., sodium 131 mEq., and potassium 4.7 mEq. per liter. The serum glutamic oxaloacetic transaminase was 22, and the serum glutamic pyruvic transaminase was 10. An electrocardiogram on admission revealed a supraventricular, probably sinus, tachycardia with an atrial rate of 130 and complete heart block with an idioventricular rate of 28 (Fig. 1).

Hospital course. The patient was treated with intravenous isoproterenol hydrochloride (Isuprel), 2 mg. per 1,000 cc., at a rate sufficient to keep his pulse above 40 but below 50. Because of minimal signs of congestive heart failure, the patient was given Digoxin. He also received four 5-mg. doses of prednisone because of an admitting diagnosis of acute rheumatic fever. The prednisone was discontinued after twenty-four hours. On April 1, 1960, the patient still had a supraventricular tachycardia with complete heart block, but the idioventricular rate had increased to 40 (Fig. 1). At this time the patient began to complain of pleuritic chest pain and of transient arthralgias of several joints lasting for about forty-eight hours.

On April 2 the patient had a sinus rhythm with a 2-1 auriculoventricular block (Fig. 2). The patient's initial hospital course was complicated by a persistent fever with spikes to 101 to 102 F. daily. Because of the possibility of pneumonia in this critically ill patient who was complaining of pleuritic chest pain, a blood culture was obtained but never was reported because of a technical error. The patient was started on chloramphenicol 1 Gm. per day and penicillin 2.4 million units per day intramuscularly. These antibiotics had no apparent effect on his fever curve. The patient continued to complain of migratory, transient arthralgias of the ankles, knees, and interphalangeal joints and paroxysmal pleuritic chest pain.

For the first three days of his hospitalization his heart rate was maintained at approximately 45 beats per minute by an intravenous drip of isoproterenol hydrochloride. This fell promptly to the range of 20 to 30 beats per minute if the infusion was stopped. During this time a changing intensity of the first heart sound was present uniformly on auscultation. A diastolic murmur was heard at the apex intermittently after the second hospital day. Late on April 2 the changing intensity of the first heart sounds disappeared although the systolic and diastolic murmurs were still present. On April 3, while receiving isoproterenol hydrochloride, it was noted that the patient would occasionally exhibit 1:1 auriculoventricular conduction with Wenckebach's phenomenon. At this time a single sublingual dose of 10 mg. of isoproterenol hydrochloride caused an acceleration of the ventricular rate to 90 with a normal 1:1 auriculoventricular conduction. On this day the patient was noted to have petechiae over his shoulders and upper part of the chest and a splinter hemorrhage in a nail bed. Splenomegaly never was observed. All antibiotics were stopped, and in the next thirty-six hours throat, urine, and 11 blood cultures were obtained. All of these cultures were sterile. On April 5 the patient had a sinus rhythm with a first degree block and occasional episodes of Wenckebach's phenomenon (Fig. 2).

On April 6 the patient was started on 18 million units of intravenous penicillin per day, and this therapy was continued for twenty-one days. He also received 1 Gm. of streptomycin daily. His temperature remained elevated for the first week of therapy with spikes of over 100 F. every day until April 12. The patient returned to 1:1 conduction on April 4, and isoproterenol hydrochloride was stopped at that time. After the first week of antibiotic therapy the patient had gradual but definite clinical improvement. The diastolic murmur was not noted after this time. No new petechiae occurred. The patient had no further episodes of joint or chest pain, and he remained afebrile until his discharge on April 26, 1960. The final diagnosis was subacute bacterial endocarditis superimposed on old rheumatic heart disease with mitral regurgitation.

Comment

Subacute bacterial endocarditis is rarely complicated by complete heart block. In a group of 278 patients with complete heart block studied by Rowe and White in 1958,[2] no case was considered to be the result of subacute bacterial endocarditis. In a study of 251 cases of complete heart block by Penton, Miller, and Levine,[3] the authors found only 1 case in which there was a possible relationship. They wrote, "A 50 year old man had a chest cold, lassitude, aching, chills, fever, and night sweat for three weeks. Three days after admission to the hospital he developed complete heart block and syncope and died eleven days later. Postmortem revealed vegetations in the right ventricle and a necrotic cavity in the interventricular septum." This seems most likely to be an example of acute bacterial endocarditis.

Whitaker in 1952[4] described a thirty-five-year-old man with subacute bacterial endocarditis and aortic stenosis who had intermittent complete heart block and died from Stokes-Adams seizures. Cates and Christie,[5] in their study of 442 cases of subacute bacterial endocarditis, mentioned 1 case of heart block without specifying the degree. Antenucci and Eckhardt in 1942[6] described an eighteen-year-old boy with subacute bacterial endocarditis in the presence of an interventricular septal defect in whom complete heart block with Stokes-Adams seizures developed. The patient reverted to a normal sinus rhythm before his death. Stenström[7] described a case of complete heart block which converted to a regular sinus rhythm with first degree heart block before death. Blood cultures were not obtained, but a postmortem examination showed findings of subacute bacterial endocarditis.

Zettner and Irmiere in 1959[8] described a forty-eight-year-old male with transient complete heart block. The patient had negative blood cultures before therapy, and an autopsy showed aortic valve vegetations with an interatrial septal abscess. It was felt that the patient had acute bacterial endocarditis superimposed on old rheumatic heart disease. In 1926, Wilson[9] reported a fatal case of subacute bacterial endocarditis complicated by complete heart block and Stokes-Adams syncope. In 1935, Kidd[10] reported a case with a fatal outcome and mentioned 1 similar case which was seen by Warren Cooksey, M.D. Fatal cases also were reported by Perry in 1936,[11] Lemierre and Rudolf in 1929,[12] and Saphir and Katz in 1950.[13]

Doubt always arises as to the validity of the diagnosis in any patient suspected of having subacute bacterial endocarditis with negative blood cultures. The presence of a persistently negative blood culture in 10 to 20 per cent of cases of proved subacute bacterial endocarditis is well known.[1,14,15] In the present case, the use of penicillin and chloramphenicol for suspected pneumonia prior to obtaining the blood cultures may account for the negative cultures. The evidence for subacute bacterial endocarditis included petechiae, a splinter hemorrhage, changing organic heart murmurs, migratory arthralgias, positive findings in a Rumpel-Leede test, transitory pleuritic chest pain, and fever which responded only after one week of intensive intravenous penicillin therapy. The patient had had known dental work done six weeks prior to his admission which may have provided the portal of entry for the infection.

It is difficult to evaluate the history of a slow pulse which began seven years previously. A complete heart block may have been present, reflecting some damage to the auriculoventricular conduction system which then spontaneously reverted to a normal sinus rhythm. It is possible that in the presence of subacute bacterial endocarditis the previously damaged conduction system failed transiently again.

Summary

A case of transient complete heart block associated with, and in all likelihood caused by, subacute bacterial endocarditis is presented.

The use of dilute solutions of isoproterenol hydrochloride (Isuprel) intravenously controlled the patient's ventricular rate adequately. This is apparently the first reported instance of recovery from subacute bacterial endocarditis complicated by complete heart block.

Acknowledgment. The author wishes to thank Walter Street, M.D., Richard Greene, M.D., and G. R. Lewis, M.D., for the opportunity to see this patient. The author also wishes to thank Richard H. Lyons, M.D., and J. A. Abildskov, M.D. for their constructive criticism.

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Peutz-Jeghers Syndrome with Jejunal Carcinoma

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IN CHILDREN adenomatous polyps of the small intestine are usually associated with other stigmas of the Peutz-Jeghers syndrome.[1] This syndrome is a hereditary condition characterized by the occurrence of pigmented zones of the face, oral mucosa, and hands and feet and by gastrointestinal polyposis. A comprehensive account of the syndrome was given by Jeghers, McKusick, and Katz in 1949.[2] Our case is interesting because an intestinal polyp appearing in a child was malignant, and the patient showed the diagnostic features of the Peutz-Jeghers syndrome.

Case report

An eleven-year-old white girl entered the emergency department of the Hospital Departmental Universitario with a chief complaint of abdominal pain. Prior symptoms of skin pallor, anorexia, and constipation had started two months before admission. Pain started six days prior to admission and was followed by postprandial vomiting. For three days she did not defecate.

She was a well-developed, well-nourished, acutely ill girl with pallor of the skin and mucous membranes. The abdomen was slightly distended and painful to palpation, especially around the umbilicus where a hard intra-abdominal mass was palpable. The peristalsis was hyperactive. An examination of other systems failed to reveal any abnormalities.

Roentgenograms showed an abdominal mass that filled the hypogastrium. The patient was given intravenous therapy which included electrolytes and blood transfusions to improve her general condition. On the second hospital day an exploratory laparotomy was performed, and an intussusception of the jejunum was found. Because the intestinal wall appeared gangrenous the surgeons decided to perform a segmental resection of the jejunum with an end-to-end anastomosis. The patient had an uneventful postoperative period.

The examination of the jejunum revealed a hemorrhagic peritoneal surface with areas of necrosis and fibrinopurulent exudate. The invaginated portion of the intestine measured 3 cm. in length. Attached to the leading portion was a 2-cm. polyp with a 1-cm. pedicle. No other lesion, polypoid or otherwise, was present.

Microscopically the bulk of the tumor was composed of numerous glands lined with columnar epithelium which had hyperchromatic nuclei. Mitosis occurred approximately one per high-power field. The glands were of irregular shape and size; some large ones contained pools of mucus. The tumor had infiltrated through the muscularis propria to reach the serosa (Fig. 1). Scattered gland spaces were found in the mesenteric adipose tissue beneath the peritoneum (Fig. 2A). The glands were solitary and showed no evidence of associated mucosal structures, although the cells were not pleomorphic (Fig. 2B). The pattern of growth was interpreted as being that of a malignant tumor. It was distinguished from a diverticulum by the absence of mucosal stroma; similarly the absence of associated mucosal structures distinguished this from congenital deformities and hamartomas. An area of calcification was prominent in the stroma. This feature is an unusual finding in carcinoma of the small intestine. A diagnosis of carcinoma arising in a jejunal polyp was made.

Several postoperative roentgenographic

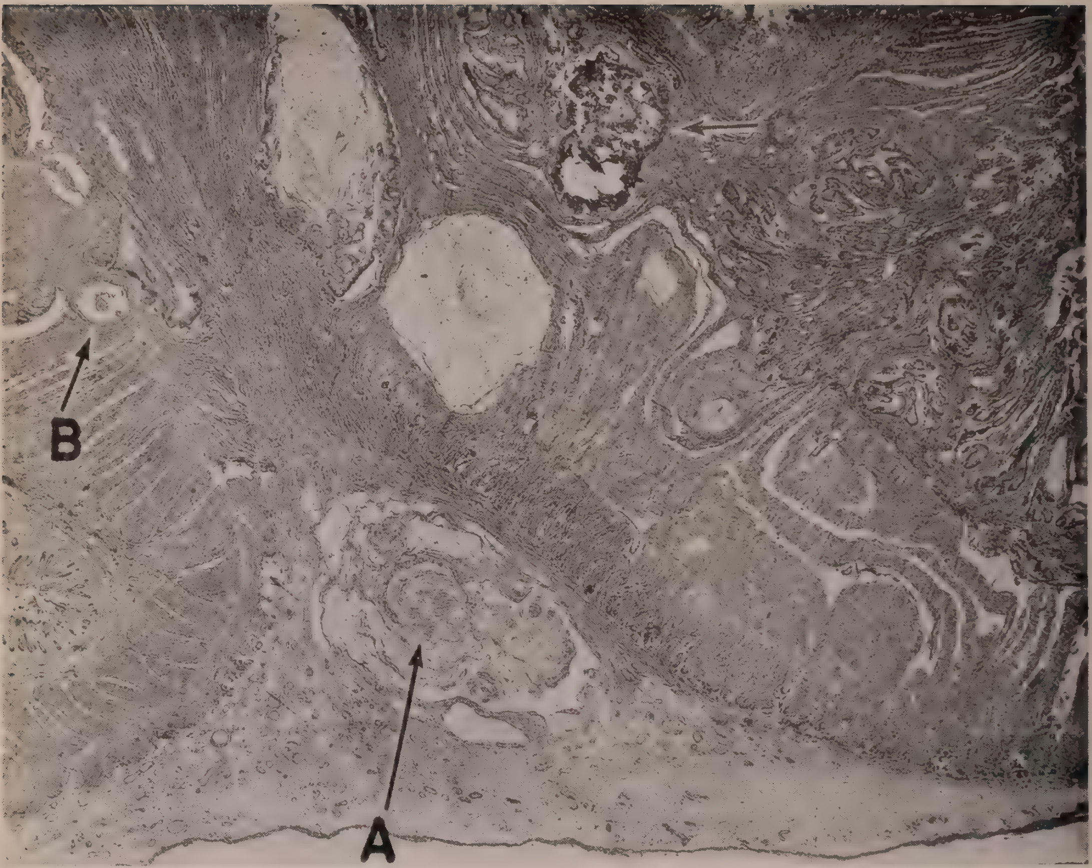

FIGURE 1. Panoramic view showing base of polyp with penetration of distorted muscularis by cancer. Note calcification at area C.

studies failed to show any other intestinal lesions, but additional features of the Peutz-Jeghers syndrome—many freckles on the face, particularly around the mouth, and pigmentations of the mucous membrane of the lips and cheeks—were found.

The family history was re-examined to determine whether or not other members had stigmas of the disease. Physical examinations and roentgenographic studies of the child's immediate relatives were carried out. The study revealed the following: The child's father had many "freckle-like" pigmentations in the skin of the face, thorax, and limbs and in the mucous membrane of the left cheek and lips; he had no gastrointestinal symptoms. Her mother had neither gastrointestinal symptoms nor pigmentations. Her maternal grandfather had no pigmentations or gastrointestinal symptoms. Her three younger sisters and one brother were all normal individuals. She had an aunt who apparently died of intestinal obstruction.

Comment

In the Peutz-Jeghers syndrome the most common initial symptoms are those of intestinal obstruction resulting from intussusception appearing in the second decade of life. The existence of melanotic spots is practically pathognomonic of gastrointestinal polyposis when they are found in a patient complaining of abdominal pain of gastrointestinal origin. These spots usually are found around the mouth, on the skin of the hands and feet, and in the mucous membrane of the lips and cheeks. They have never been described on the tongue. In some cases the pigmentations are numerous,[3] and in others only a single pigmented spot is found.[4] The

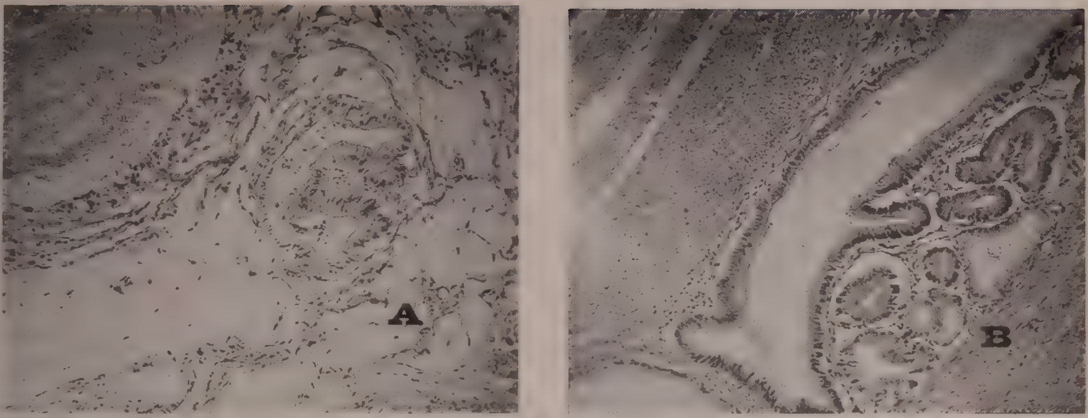

FIGURE 2. (A) Area A in Figure 1 showing high-power view of glandular elements in serosa. (B) Area B showing lack of pleomorphism of the cells, but uniformity of cell type.

spots have been noted shortly after birth,[5] but most commonly six months to a year elapse before they are noticed. Berkowitz[6] states that for the most part they are very dark and that the degree of pigmentation does not vary with exposure to sunlight. Occasionally they have been mistaken for the pigmentations seen in Addison's disease.[7]

Polyps in this syndrome are found most frequently in the small intestine but may be located in the stomach, colon, or even the appendix.[8,9] Malignant conditions developing in polypoid lesions in adults affected with the Peutz-Jeghers syndrome have been reported. According to Bartholomew, Dahlin, and Waugh[10] the reported incidence of malignant degeneration is from 20 to 25 per cent of all resected cases. However, they mention also that no documented case of death from carcinoma associated with the Peutz-Jeghers syndrome has been reported.

This last point is an important one since it is possible that the atypical changes which are seen so commonly in adenomatous polyps may have been interpreted mistakenly as carcinoma. The case reported by Berkowitz and his coworkers[6] was diagnosed as malignant solely on the basis of the presence of mitoses and some atypical glands. In another case an illustrative figure by Basu[11] shows only the features of adenomatous polyp. Bartholomew and his coworkers[10] in their review concluded that the evidence for malignant conditions in many of the reported cases is not entirely convincing. The theory suggested by Bartholomew, Dahlin, and Waugh[12] that the polypoid lesions found in this syndrome actually represent hamartomas rather than true neoplasms is ruled out in the present case, since only one type of cell was predominant and no Paneth's cells were found as would be expected in a hamartoma of the small bowel. The smooth muscle in the region of the polyp showed only the natural distortion expected in an intussusception. Both layers, however, appeared clearly demarcated.

The presence of unmistakable carcinomatous changes in a child of this age renders the present case even more unique since carcinoma of the small bowel in children is said not to occur.[13]

Summary

A case of Peutz-Jeghers syndrome has been reported in an eleven-year-old girl. She had both skin and mucous membrane pigmentations. The most interesting feature, however, was the presence of a carcinoma arising in the jejunal polyp.

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Strategic placement

Out of the heat of sun-drenched Rome, the cool auditorium of the palazzo was a place to relax after lunch while the array of distinguished persons on the distant stage went through the movements of Opening a Congress. Earphones on, we switched the selector knob to hear which of the translators was winning the race with the speaker and watched the photographers wandering to-and-fro, up and down the aisles, across the platform, behind, between, round and in front of the speakers. Public speaking is thirsty work; how thoughtful then was one of the cameramen. He had arranged to have a crate of mineral water brought to the platform. A bottle was discreetly put at the elbow of each of the distinguished presidents, secretaries, leaders of delegations, and glasses filled for them. More photographs, but just before each picture the bottle was quietly placed forward to the front of the table, label square to the camera. Watching the skill with which it was shown in black and white that distinguished medical men prefer a certain water relieved the tedium of a rather dull ceremony. The only drawback was that having no field glasses to read the label I still do not know which bottled water to drink to give me at least renal distinction, if no more.—*The Lancet, October 21, 1961, page 927*

Hypercalcemia in Neoplastic Disease Without Bone Metastases

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HYPERCALCEMIA MAY OCCUR with various clinical entities including hyperparathyroidism, sarcoidosis, hypervitaminosis D, multiple myeloma, the milk-alkali syndrome, immobilization, and, rarely, hyperthyroidism.[1] Metastases to bone, especially from mammary carcinoma, are also frequently accompanied by elevated serum calcium levels.[2] Very infrequently cases of neoplasia without a demonstrable osseous spread may manifest this mineral disturbance (Table I). The case to be described apparently is the only case report in the English literature of carcinoma of the urinary bladder associated with hypercalcemia in the absence of apparent bone invasion.

Gutman, Tyson, and Gutman in 1936[3] reported a case of bronchogenic carcinoma without evidence of bone destruction in which hypercalcemia and initial hypophosphatemia were noted. This case also showed an isolated area of Paget's disease which the author believed to be unrelated to the elevated serum calcium. In 1953 a case of hemangiosarcoma of the liver with hypercalcemia and hypophosphatemia was reported from the Massachusetts General Hospital.[4] Again, the bones were free of disease. Connor, Thomas, and Howard in

TABLE I.—Summary of reported cases of hypercalcemia in neoplastic disease without bone metastases

Author	Type of Neoplasm	Serum Calcium (Mg. per 100 Ml.)	Serum Phosphorus (Mg. per 100 Ml.)	Parathyroid Glands
Gutman, Tyson, and Gutman[3]	Bronchogenic carcinoma	13.4 to 18.9	2.1 to 4.5	Not described
Case Records of the Massachusetts General Hospital[4]	Hemangiosarcoma of liver	12.7 to 15.6	2.6 to 5.0	Normal
Connor, Thomas, and Howard[5]	Bronchogenic carcinoma	Hypercalcemia (Exact values not given)	Hypophosphatemia	Not described
Plimpton and Gellhorn[6]	Kidney, ovary, lung, uterus, and lymphoma	12.0 to 23.0	1.9 to 3.6	Normal
Myers[7]	Urinary bladder	Approximately 11.5	Not given	Not described
Case Records of the Massachusetts General Hospital[8]	Bronchogenic carcinoma	11.8 to 13.6	2.6	Secondary hyperparathyroidism
Schatten, Ship, Pieper, and Bartter[9]	Vulvar carcinoma	8.2 to 19.0	1.7 to 2.6	Normal
Abouav, Berkowitz, and Kolb[10]	Ovarian carcinoma	14.0 to 17.6	1.5 to 2.9	Not described
Gold and Shnider[11]	Bronchogenic carcinoma	15.5 to 17.4	3.0 to 4.0	Normal
Case Records of the Massachusetts General Hospital[12]	Renal cell carcinoma	12.0 to 12.8	2.7 to 3.3	Normal

1956[5] reported 2 cases of bronchogenic carcinoma with apparent bone metastases in which serum calcium levels were elevated markedly in association with decreased phosphorus levels. In these 2 cases the calcium levels returned to normal following resection of the tumor. In 1 case a recurrence of disease was associated with a concomitant rise in serum calcium levels. Plimpton and Gellhorn in 1956[6] reported a series of 10 cases representing carcinoma of the kidney, ovary, lung, and uterus and retroperitoneal lymphomatous disease. All cases were accompanied by hypercalcemia and most of them were accompanied by hypophosphatemia. Apparently these tumors had not invaded the bone, and with a successful resection in 3 cases the calcium and phosphorus levels returned to normal. In 1 case recurrent disease was associated with rising serum calcium. Myers[7] in 1956 mentioned briefly 6 cases of malignant disease without evident osseous spread in which hypercalcemia occurred. This group included uterine, mammary, lymphomatous, renal, cervical, and urinary bladder tumors. More recently another case was reported from the Massachusetts General Hospital,[8] and it was noted that this was only the second case of carcinoma associated with hypercalcemia in the absence of bone disease seen at that hospital. This was a case of bronchogenic carcinoma, and at autopsy it also manifested parathyroid hyperplasia. Schatten *et al.* in 1958[9] reported a case of vulvar carcinoma associated with hypercalcemia and hypophosphatemia in the absence of osseous spread. The abnormal serum chemistries returned to normal following the excision of the tumor. In 1959 Abouav, Berkowitz, and Kolb[10] reported a case of nonmetastatic ovarian tumor with hypercalcemia and hypophosphatemia. These values also returned to normal following a resection of the neoplastic lesion. Gold and Shnider[11] mentioned a case of bronchogenic carcinoma without bone metastases in which hypercalcemia occurred. Most recently a case of renal cell carcinoma with hypercalcemia and hypophosphatemia was reported from the Massachusetts General Hospital in which the calcium and phosphorus levels returned to normal following nephrectomy.[12] There was brief mention in this report of a case of urinary bladder carcinoma with elevated serum calcium and depressed serum phosphorus which returned to normal following the excision of the tumor and which at autopsy manifested normal parathyroid glands.

Case report

A sixty-two-year-old married woman was admitted to the Montefiore Hospital on August 10, 1959. She had been in good health until six months prior to admission when she experienced the onset of persistent gross hematuria. On June 1, 1959, she was admitted to another hospital where a tumor of the urinary bladder was seen on cystoscopy. On histologic section, epidermoid carcinoma was found. Only a partial resection was possible, but the patient remained without symptoms for the next six weeks when hematuria recurred. She also began to experience anorexia with weight loss and lower back and abdominal pains. Her condition deteriorated rapidly and she was finally admitted to the Montefiore Hospital in a stuporous condition. There was no history of headache, convulsions, or other central nervous system symptoms.

A physical examination revealed a semicomatose and chronically ill white female with a pulse rate 140 per minute, a temperature of 104 F., (40 C.) and a blood pressure of 160/90 mm. Hg. No masses were felt in the neck. Bilateral basilar rales were present. The heart was unremarkable. There was a suprapubic abdominal scar bearing two fistulas which were draining urine and blood. The liver and spleen were not felt. Bilateral costovertebral tenderness was present and both kidneys were palpably enlarged. A pelvic examination revealed that the anterior walls of the vagina and uterus were fixed. Except for a lateral deviation of the right eye (which apparently had been present for many years) and the obtunded mental state, the neurologic examination was within normal limits.

An examination of the blood showed a hematocrit of 34 which fell subsequently to 23, with white blood counts of 24,200 and 6,100 per cubic millimeter. A urinalysis revealed a specific gravity of 1.012, an acid reaction, a 2 plus albumin, a trace of sugar, and many red blood cells. The blood urea nitrogen was 42 mg. per 100 ml. on admission and 93 mg. per 100 ml. terminally. The serum creatinine was 3.8 mg. per 100 ml., and the fasting blood sugar was 102 mg. per 100 ml. Serum electrolyte studies showed the sodium to range from 123 to 149 mEq. per liter, the potassium from 3.8 to 4.4 mEq. per liter, the chloride from 84 to 114 mEq. per liter, and the carbon dioxide content from 27.9 to 21.7 mEq. per liter. The serum calcium was 13.3 mg. per 100 ml. initially and 16 mg. per 100 ml. terminally. The serum phosphorus determinations were 4.6 and 4.3 mg. per 100 ml. respectively. The serum alkaline phosphatase was 2.6 Bessie-Lowry units. A roentgen examination of the chest showed discoid atelectasis, mainly at the left base. A flat film of the abdomen revealed an inhibition ileus and a soft tissue mass in the true pelvis. An excretory urogram resulted in poor visualization of the upper urinary tracts bilaterally. No evidence of metastatic disease was noted in the shoulder girdles, ribs, lumbar spine, or pelvis on the roentgenograms. Cultures from the bladder fistulas grew out pseudomonas and Escherichia coli. The cerebrospinal fluid was not remarkable.

The patient was given intravenous fluids and antibiotics (chloramphenicol, penicillin, and later streptomycin). Over the next twenty-four to forty-eight hours the temperature fell, but the urinary output decreased and a cystoscopy was performed. The tumor had involved the bladder diffusely, and the trigone could not be visualized. The patient's condition was considered too poor to tolerate operative intervention. The blood urea nitrogen rose gradually, the urinary output remained poor, and the patient expired shortly thereafter.

A postmortem examination revealed epidermoid carcinoma arising in the urinary bladder and involving the anterior uterus, the vagina, the sigmoid colon, and the abdominal wall. The kidneys showed bilateral hydronephrosis and acute pyelonephritis. A gross examination of the skull, multiple vertebra, ribs, and sternum demonstrated no evidence of osseous metastases or bone resorption. A histologic examination of the spine was likewise unremarkable. The two parathyroid glands that could be identified were normal both on gross and on histologic examination.

Comment

Hypercalcemia in neoplastic states not involving the skeletal system is a rare occurrence. With the frequently associated hypophosphatemia the picture may be quite suggestive of hyperparathyroidism, and several patients have been explored for parathyroid adenomata.[6,9,12]

The mechanism by which these various neoplasms evoke such profound changes in the serum calcium and phosphorus levels is at best conjectural. It has to be borne in mind that most of the tumors reported to be associated with hypercalcemia in the absence of apparent osseous involvement are those which frequently metastasize to bone. Bronchogenic carcinoma and hypernephroma comprise a large portion of such cases, and it may be that areas of skeletal invasion exist, although they are not revealed by x-ray study. Many cases of osteolytic metastasis, especially to the spine, even when fairly extensive, may not appear at all on roentgenography.[13] Furthermore, it is not possible to scrutinize a truly representative portion of the skeletal system during postmortem examinations.[8] The fact that several such neoplasms have been resected with a concomitant fall in the elevated serum calcium levels, however, might indicate the elaboration of a humoral substance by the tumor. Again, there are tumors whose metastases regress following a resection of the primary site.

The hypothesis that the tumor may be producing a parathyroid-like hormone is certainly attractive, although thus far no such agent has been isolated. In the case of Abouav, Berkowitz, and Kolb[10] urinary total resorbable phosphorus studies were within normal limits. These results suggested to these investigators that a hormone with solely hypercalcemic activity was produced by the tumor and that the phosphaturic activity of whole parathyroid extract was lacking. On the other hand, Stewart and Bowen[14] have shown that certain thymic and splenic extracts have a phosphaturic action. This might imply that tissues other than parathyroid have a similar action, and Schatten *et al.*[9] seem to have demonstrated it. Their case of vulvar carcinoma manifested a lowered maximal tubular capacity to reabsorb phosphate, which returned to normal following an excision of the lesion. In an effort to elucidate the nature of a possible hormone, these investigators infused 100 cc. of their patient's serum into a parathyroidectomized dog but could obtain no rise in urinary phosphorus. In addition, they had a large section of tumor extracted and analyzed for parathyroid hormone activity with negative results. Unfortunately, such studies were not done on our case, nor have they been reported in any other cases.

In a case of bronchogenic carcinoma without apparent bone metastases reported from the Massachusetts General Hospital[8] the parathyroid glands were hyperplastic. This change was thought to be secondary to the effects of a humoral substance produced by the tumor, and the associated hypercalcemia and hypophosphatemia were considered a function of a hyperparathyroid state. In the other cases reported the parathyroid glands, when described, were normal.

It has also been suggested that these rare neoplasms may produce a vitamin D-like substance which enhances enteric absorption of calcium similar to that postulated in sarcoidosis.[6] Successful balance studies exploring this possibility in neoplastic disease have not been reported.

The finding of hypercalcemia in urinary bladder carcinoma is most unusual. In 2 reports a brief mention was made of cases in which the serum calcium level was elevated.[7,12] The degree of elevation was approximately 11.5 mg. per 100 ml. in the first report and was not stated in the second one. The serum calcium level in our case reached 16 mg. per 100 ml. In 38 cases of carcinoma of the urinary bladder without bone metastases that came to autopsy at Montefiore Hospital in the past eleven years in which serum calcium levels were recorded, 2 had slightly elevated levels of 11.4 mg. per 100 ml.

Summary

Hypercalcemia in neoplastic states not involving the skeletal system is an infrequent occurrence. A case of epidermoid carcinoma of the urinary bladder failed to reveal any evidence of osseous metastatic disease or parathyroid abnormality by roentgen and autopsy examination. The serum calcium in this case reached 16 mg. per 100 ml. It should be borne in mind that minute areas of skeletal invasion may actually exist, although they are not demonstrated on x-ray films or at necropsy. However, several reported tumors exhibiting hypercalcemia without apparent metastases to bone have been resected with a corresponding fall in the elevated serum calcium levels to normal. The exact mechanism by which neoplasms without bone metastases evoke such profound changes in the serum calcium level has not yet been found.

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Neurilemmoma Of the Vagus Nerve

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Although specific nerve sheath tumors involving peripheral and certain cranial nerves have been described with increasing frequency, the neurilemmoma of the vagus nerve remains an infrequent pathologic finding which is, nevertheless, a worthy point in the differential diagnosis of a cervical mass.

Since we have found only 11 documented cases of neurilemmoma arising from the vagus nerve in the neck, it seems worth while to add another.[1-7]

Case report

A twenty-six-year-old white married male public accountant was admitted to Strong Memorial Hospital for the first time on September 26, 1958, complaining of an enlarging mass high on the right side of his neck. First noted about five years before, this mass began enlarging slowly two years before the present admission at which time it was thought to represent an inflammatory node secondary to chronic tonsillitis. A tonsillectomy at that time failed to arrest the steady and relentless enlargement of the mass. The patient remained relatively asymptomatic except for a slight increase in the pitch of his voice. Ten months prior to the present admission a surgical approach had been made to excise the lesion. However, because of technical problems, the incision was closed after a bit of tissue was removed for a biopsy. On microscopic study this tissue proved to be from a lymph node with chronic inflammatory changes. Since that time the lesion had continued to enlarge without invoking new symptoms.

The past history gave negative information except for the irradiation of an enlarged thymus when the patient was an infant. The radiation dose is not known.

On admission he appeared to be a well-developed, well-nourished white male of the stated age of twenty-six years. The positive physical findings were limited to the neck where a regular, firm, nontender 8 by 8 cm. mass lay posterior to the angle of the right mandible and apparently beneath the sternocleidomastoideus. The skin was fixed to the mass only at the site of the previous biopsy incision. The lesion was slightly movable in the horizontal plane but not in the vertical. The body of the right parotid was apparent above, but by palpation the mass could not be defined distinctly from the tail of this gland. The thyroid was distinct and within normal limits. No other masses were palpable on either side of the neck.

The impression at this time was that the lesion most probably represented a mixed tumor of the tail of the parotid. Hence a superficial parotidectomy was planned.

Operation. When an endotracheal tube for anesthesia was introduced, both vocal cords were seen to move. A Y-shaped incision was laid out on the neck, the upper limbs embracing the lobe of the ear and the long lower limb running parallel with the sternocleidomastoideus and encompassing the previous biopsy scar. With the lobe of the ear reflected upward and the skin-platysma flaps laid back, the facial nerve was exposed as it emerged from the skull. The sternocleidomastoideus then was split in the direction of its fibers to expose the superficial surface of the mass. It presented a smooth, shiny surface with a definite capsule along which a dissection plane was established readily. The local relationships were distorted by the space occupation, but there was no invasion.

Superiorly, the mass was bounded by and adherent to the tail of the parotid. Along its anterior surface lay the carotid sheath. As sharp extracapsular dissection progressed, it became apparent that the mass was intimately involved in the sheath of the vagus nerve, the latter structure having been displaced quite far posteriorly from its normal relationship to the carotid artery and the jugular vein. To complete the excision it was necessary to divide the vagus; this was done by sacrificing only a few millimeters of nerve. Then an end-to-end suture of the vagus was carried out with 6-0 silk. No change in pulse, blood pressure, or respiration was observed on sectioning the vagus.

Following the excision the field was explored carefully for other masses; none were found. The incision was closed in layers using interrupted 6-0 silk and 6-0 Nylon in the skin. A $^1/_4$ -inch Penrose drain was left in the lower angle for two days.

PATHOLOGY. The excised mass measured 6.4 by 4 cm., was firm, tan in appearance, and presented an intact shiny capsule. The cut surface was lobulated irregularly with a tan mucoid appearance. Microscopic sections revealed a pink fibrillar stroma with numerous vascular spaces. The nuclei varied considerably in shape from flat to round to lobular vesicular forms. Numerous collections of nuclei appeared in palisade formation. Several areas of recent and old hemorrhage were present. A pathologic diagnosis of neurilemmoma was made.

POSTOPERATIVE COURSE. As the endotracheal tube was removed, the cords were again visualized; the right cord had little or no motion. The following day the patient's voice was higher pitched but clear. A right Horner-Bernard syndrome was present which has cleared only partially. The vocal cords were examined again two months following the operation; the right cord appeared fixed. A re-examination one year after the operation revealed a nearly normal excursion of the right cord. This was associated with a return of the voice toward normal. The wound healed without problems and there has been no evidence of recurrence.

Comment

First described histologically by Verocay in 1908[8] and named a "neurinoma" by him in 1910,[9] the specific nerve sheath tumor has been called variously "schwannoma," "perineural fibroblastoma," "peripheral glioma," and now "neurilemmoma" since Stout's excellent description and naming of the lesion in 1935.[10] The variance in nomenclature reflects the differing views on the histogenesis of the tumor. Masson[11] and Murray and Stout[12] feel that the lesion arises from the nerve sheath cell or Schwann cell and is therefore an ectodermal tumor, supporting this position by tissue-culture evidence. Penfield,[13] on the other hand, contends that the morphology suggests a fibroblastic origin.

Excellent histologic descriptions appear in most standard pathology texts. Grossly the lesion is usually clearly encapsulated, has a yellowish-gray appearance, and is either soft or, at times, fluctuant representing characteristic cystic degeneration. The fibers of the associated nerve may lie displaced along one side of the tumor or splayed out on its surface. Microscopically two cellular patterns are generally recognized. Type A presents a palisading effect of sheets of cells interwoven by a wavy reticulum of collagen. Coexistent with this orderly pattern a second tissue pattern, Type B, often is found. The palisading here is completely lacking and is replaced by a disorderly cellular architecture interspersed with many small vacuoles. Collagen is rare or absent. These two forms may exist in the same section but are separated rather sharply.

The malignant degeneration of these tumors has not been described. Complete surgical excision is curative. Since the diagnosis is difficult to establish preoperatively and since these lesions respond poorly to radiation, surgical extirpation is the treatment of choice. Although the tumor does not involve the nerve fibers, it has been the experience of many authors that the lesion is associated so intimately with the nerve proper that an adequate resection cannot be accomplished short of sectioning the nerve trunk to include the involved segment. The principle disability following a high unilateral vagotomy is paralysis of the homolateral vocal cord. Altany and Pickerell[7] advise resuturing the nerve when possible, although for technical reasons, they were unable to do so in their 3 cases. In the remainder of the cases where the nerve was divided no mention is made of resuturing, and cord paralysis was permanent. The recovery of cord function after one year in our case, where it was possible to resuture the nerve, emphasizes the desirability of this maneuver.

A second frequent postoperative occurrence is a homolateral Horner-Bernard syndrome. Trauma at surgery has been advanced as the explanation for this phenomenon.[14] This is borne out by the uniform disappearance of the syndrome in a few months.

Summary

A case of neurilemmoma of the vagus nerve treated by excision has been reported. The nerve was divided and resutured with subsequent recovery of vocal cord function.

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Shot-put and discus throw approved for junior high school

The shot-put and discus throw are suitable sports for junior high school students if the lighter shot and discus are used and strict supervision is provided, according to an article by Dr. Fred V. Hein in the October 21, 1961, issue of the *Journal of the American Medical Association.* A necessary safety measure would be to screen the thrower from other members of the group with a strongly constructed backstop. In addition, an area wider than the angle within which the discus usually will land should be kept clear of other persons.

A properly supervised and planned program of weight-training aimed at conditioning and development rather than competition also is considered an appropriate part of physical education for this age group. Dr. Hein added: "Until a few years ago, there was a fear on the part of some physicians, physiologists, and physical educators that it would lead to a muscle-bound condition, but this fear has been largely dispelled."

Estimated Effects of Nuclear Detonations of Various Megaton Yields

From the Atomic Energy Commission
and the Department of Defense

THE FOLLOWING ESTIMATES of the possible effects of nuclear detonations of various megaton yields are subject to many uncertainties. It is impossible to predict with any assurance of accuracy the effects of actual detonations of very high yields, particularly if they were to occur at a high altitude.

Blast effects

The blast wave of a 5-megaton surface detonation would be capable of causing severe damage to residential-type structures up to a distance of about 6 miles from ground zero (8 miles for a 10-megaton surface burst, 10 miles for a 20-megaton surface burst, 12 miles for a 30-megaton surface burst, 14 miles for a 50-megaton surface burst, and 17 miles for a 100-megaton surface burst). A 5-megaton surface detonation would cause severe blast damage to reinforced concrete structures out to about 4 miles (5 miles for a 10-megaton, 6 miles for a 20-megaton, 7 miles for a 30-megaton, 8 miles for a 50-megaton, and 10 miles for a 100-megaton). For an optimum air burst for air blast effects these ranges of blast damage could be increased by from 30 to 40 per cent.

A 5-megaton detonation above about 35 miles (44 miles for a 10-megaton, 50 miles for a 20-megaton, 60 miles for a 30-megaton, 75 miles for a 50-megaton, and 100 miles for a 100-megaton) would cause insignificant blast damage on ground structures.

Thermal effects

A 5-megaton surface detonation or an air burst below 50,000 feet on a clear day could cause first-degree burns to exposed skin out to a slant range of about 25 miles (35 miles for a 10-megaton, 45 miles for a 20-megaton, 55 miles for a 30-megaton, 70 miles for a 50-megaton, and 100 miles for a 100-megaton) and second-degree burns to exposed skin out to about 17 miles (25 miles for a 10-megaton, 32 miles for a 20-megaton, 40 miles for a 30-megaton, 50 miles for a 50-megaton and 70 miles for a 100-megaton). Paper and various similar materials would ignite at distances of about 20 miles (30 miles for a 10-megaton, 39 miles for a 20-megaton, 47 miles for a 30-megaton, 60 miles for a 50-megaton, and 85 miles for a 100-megaton). Above about 50 miles the thermal effects on the earth's surface of a 20-megaton detonation would be negligible (60 miles for a 30-megaton, 75 miles for a 50-megaton, and 110 miles for a 100-megaton). These distances would apply only on clear days and would be materially lessened when the thermal radiation is attenuated, such as on cloudy or hazy days.

Initial radiation

The initial gamma and neutron radiation expected from a nuclear explosion in the range of 5 to 100 megatons at or near the surface of the earth is not expected to be of significance when compared with the radius of damage from other effects, such as blast damage or thermal radiation effects.

Electromagnetic effects on world communications

Communication blackouts due to low-altitude, high-yield explosions are probably too localized to be of interest. If the cloud stabilizes at an altitude of about 25 miles, however, the possibility exists of producing observable effects on radio waves over distances of about 100 miles from air zero.

As a result of a 50-megaton detonation at an altitude of about 50 miles, large-scale, high-frequency communications blackouts could be expected within a region of 2,500 miles radius and for a time span of about a day. At 30 miles altitude the radius of effect would be about 1,000 miles.

For detonations at the same altitudes as previously mentioned but with yields of less than 50 megatons, the results would be similar, but the radius of effect as well as the duration of blackouts would be less. Conversely, a 100-megaton detonation at the same altitudes as discussed for the 50-megaton burst would have a larger effects radius and a longer duration of communications blackout.

It is important to note that for a radio wave to be affected the wave must pass through the disturbed region. Detonations in the Soviet Union of these yields at high altitudes probably would affect some North America-to-Europe communications. By increasing the altitude of detonation beyond 50 miles the radius of effects would be increased, but the duration of such communications blackouts should decrease. For a detonation of high yield at an altitude of 600 miles, the radius of the communications blackout effect may extend to 4,000 miles.

Local fallout

For a 20-megaton surface burst, for example, assuming 50 per cent fission yield and 40-knot winds, local fallout of 450 roentgens would be expected at 360 miles downwind (higher exposures at lesser distances) for persons fully exposed for ninety-six hours following the start of fallout at that place (450 roentgens would be expected at 415 miles downwind for a 30-megaton detonation, at 500 miles downwind for a 50-megaton detonation, and at 620 miles downwind for a 100-megaton detonation). It is expected that exposure to 450 roentgens would result in 50 per cent deaths.

For detonations at altitudes such that the fireball does not approach the ground there would be very little local fallout. The fireball for a 20-megaton nuclear explosion would be about $3^1/_2$ miles in diameter (about 4 miles for 30-megaton, about 5 miles for 50-megaton, and about 7 miles for 100-megaton).

World-wide fallout

Assuming that these detonations took place in the atmosphere so that the fireball did not approach the ground and that the fission yield was 50 per cent of the total yield, then a 20- or 30-megaton detonation would produce less fission products than the current U.S.S.R. tests to date (excluding, of course, the detonation of October 23 which is estimated to have been about 25 megatons and the detonation of October 30 which is estimated to have been about 50 megatons), and the 100-megaton detonation might produce more than twice this amount.

The debris spread world-wide (as distinguished from local) from all past nuclear tests of all nations prior to the resumption by the Soviets of atmospheric tests on September 1, 1961, is estimated to have been the equivalent of 60 megatons of fission yield. Thus, for example, a 100-megaton detonation (50 megatons of fission) might produce almost as much world-wide radioactivity as all past tests to November 3, 1958.

The distribution of fallout from such high-yield detonations is not known with certainty. However, it is estimated that if they were fired in the lower atmosphere, at most, three fourths of the world-wide fallout might occur in the 30- to 60-degree northern latitude zone. If the detonation took place at higher altitudes (greater than 20 miles), the amount of world-wide fallout of long-lived radionuclides would be more equally partitioned between the northern and southern hemispheres.

A 5-megaton detonation in the lower atmosphere fired north of 30 degrees north latitude might deposit about 4 millicuries of strontium-90 per square mile in the United States, and the 100-megaton shot might scale up to about 75 millicuries of strontium-90 per square mile. There were about 70 millicuries of strontium-90 per square mile deposited in the United States before the current U. S. S. R. tests.

It is estimated that increasing the current level of strontium-90 in the United States by manyfold would still result in less strontium-90 in the bones than that permitted by radiation exposure guides now in effect for the general public for normal peacetime operations.

Water waves

Water waves produced by high-yield nuclear detonations could be of appreciable magnitude hundreds of miles from a deep underwater burst. A 50-megaton burst at a depth of 2,700 feet in deep water would generate wave heights of from 20 to 50 feet at a range of 100 miles and 5 to 12 feet at 400 miles. A 100-megaton burst at about 4,000 feet in deep water would generate wave heights of about 28 to 70 feet at a range of 100 miles and 3 to 7 foot waves at 1,000 miles. For lesser burst depths the waves would be of lesser magnitude.

In all cases bottom profiles in shallow water and shoreline characteristics could greatly affect wave heights. The increase in the water level at the shoreline from a deep underwater high-yield burst could be higher than that of the deep water waves at the same distance from the detonation.

An explosion of 50 megatons at the surface of the ocean would produce waves of a height of about 1 to 10 feet at 100 miles and 3 inches to $2^1/_2$ feet at 400 miles. For an above-surface explosion at 10,000 feet altitude it is predicted that the waves produced would be less than half those produced by the surface explosion. For higher altitudes the wave produced would not be of significant height. All of these figures are based on a depth of water in the area of generation of about 16,000 feet. For shallower depths the wave heights would be less. In general, it is expected that the wave heights would vary as the square root of the yield.

Retinal burns

If a person were looking at the point of burst from any of these detonations, burns to a portion of his retina causing some visual loss might be received at ground distances up to 500 miles away on a clear day with no cloud cover for a burst occurring at a 30-mile altitude. A burst at 60 miles altitude might produce the same result at 700 miles. As the altitude of burst increases, the severity of retinal damage decreases. However, the severity of retinal damage increases at night.

For a 50-megaton burst in the lower atmosphere on a clear day, for example, retinal burns may be possible out to 250 miles (out to 210 miles for a 20-megaton burst, out to 290 miles for a 100-megaton burst).

Other effects

From any of these detonations at high altitude (30 miles to 1,000 miles) widespread and spectacular aurorae could be visible at distances from ground zero to 1,000 miles, and for the larger yields, perhaps out to 2,000 miles for the higher-altitude bursts. These aurorae would not be harmful to human beings. The air glow in the ionosphere produced by the shock wave also may be visible for more than 1,000 miles.

For bursts in deep space, 50,000 miles or more, there would be one sharp pulse of light that might be noticeable only to a person looking directly at the burst. On the basis of current knowledge, it is not expected that there would be any other observable effects to the unaided eye at the earth's surface.

Treatment of Tuberculosis in General Hospitals*

A CONFERENCE on "Tuberculosis Treatment in General Hospitals" was held to discuss the practicability and advisability of treating tuberculosis patients in voluntary and municipal general hospitals in New York City and, more particularly, in Brooklyn. The Conference afforded an opportunity to review the changes in treatment and care of the disease which have taken place in the past two decades. The attendance was limited primarily to representatives of Brooklyn hospitals who had expressed an interest in discussing this subject.

A panel of city and national experts joined local physicians, hospital administrators, nurses, and social workers at the Conference. Among those leading discussions, in addition to the Chairman, Harold A. Lyons, M.D., Professor of Medicine, College of Medicine, State University of New York, were: Carl Muschenheim, M.D., Professor of Clinical Medicine, Cornell University; Biagio Battaglia, M.D., Attending Physician, The Brooklyn Hospital; Benjamin Burbank, M.D., Attending Physician, Long Island College Hospital; Sidney Dressler, M.D., Chief of Staff, National Jewish Hospital, Denver, Colorado; I. D. Bobrowitz, M.D., Director, Tuberculosis, Department of Hospitals, City of New York; Mr. Joseph Terenzio, Executive Director, The Brooklyn Hospital; Mr. Emanuel Hayt, Counsel, Greater New York Hospital Association; James W. Raleigh, M.D., Medical Director, American Thoracic Society; Aaron D. Chaves, M.D., Supervisor of Clinics, Bureau of Tuberculosis, Department of Health, City of New York; and Mr. Vernon Stutzman, Director, Methodist Hospital.

Why the general hospital should treat tuberculosis

At the end of the last decade, the advent of chemotherapy made tuberculosis less a disease for long-term hospitalization and more of a short-term hospital problem. The medical care of the disease began to be shared more and more with the general practitioner, the internist, and the pediatrician. Therefore, it behooves those concerned especially with tuberculosis to disseminate the recently acquired knowledge about the disease to every level of medical practice and to determine and promote the changes in therapy which are now recommended. Patients in general are not only responding more rapidly to treatment, but also there is increasing evidence that the communicability of their disease is extremely low, if at all, when they are conforming to a proper drug treatment regimen.

Local community hospitals in Brooklyn are founded on the basis of service to the community, very frequently to a sectional area. The people residing in each neighborhood look to them for help and care in time of illness. Patients are spared some of the anxieties which placement in a separate institution may create, and relationships between the hospital and the community are strengthened when tuberculosis patients are admitted for treatment.

The tuberculosis patient frequently has concomitant illnesses, and the diagnostic facilities of a general hospital make it the most favorable place for his total treatment.

When the general hospital accepts tuberculosis patients, staff teaching about the pathogenesis and the course of the disease and its proper treatment is more effective. Greater emphasis is given to the relationships of tuberculosis to other diseases and to case-detection programs among groups of patients with high incidence rates. The opportunity is afforded to provide training to nurses, house staff, and ancillary personnel in the management of communicable diseases.

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* A digest of the discussions in an all-day Conference sponsored by the Brooklyn Tuberculosis and Health Association at the College of Medicine, University of the State of New York, June 21, 1961. The Conference developed from a recommendation by the Association's Nursing Advisory Committee late in 1959 to its Medical Advisory Committee.

Both the patient and the hospital benefit when tuberculosis treatment is provided in the general hospital.

Considerations and concerns of the hospital

Today, it is generally admitted that tuberculosis patients need the same kind of hospital care and facilities as other patients. The few additional requirements which should be met if the disease is to be treated in general hospitals can easily be defined, namely:

1. There must be a willingness of hospital administrators and medical boards to regard tuberculosis as a disease which should be cared for in general hospitals.
2. The patients will need to be grouped in one ward or section of a ward where the necessary protective precautions (which need not be overelaborate) can be carried out readily and medical supervision by experienced attending physicians can be given.
3. An organized system of group conferences and hospital rounds needs to be set up to review the patients' progress and to decide methods of continued treatment, whether surgery is indicated, and similar questions.
4. A consultation service on tuberculosis and pulmonary problems should be provided for the entire hospital.
5. The outpatient department should include a chest clinic which will operate in very close liaison with the inpatient service.
6. The tuberculosis or chest unit should function as an integral part of the medical service.
7. Laboratory facilities, equipped and staffed to function competently and effectively, must be available to all treatment services.
8. The reimbursement for tuberculosis treatment made by the city to voluntary hospitals should be equivalent to the medical-surgical rates allowed for general care patients. The current practice is to pay a much lower per diem rate for tuberculosis inpatient treatment than for general medical-surgical care.

The manning of tuberculosis units with adequate house and visiting staff and ancillary personnel has not been a special problem of private hospitals: The Brooklyn, Long Island College, and New York Hospitals. Their experiences show that physicians and nurses are indeed interested in tuberculosis when they become indoctrinated about the disease and opportunities are provided to work with other nontuberculous diseases as well. Many of the tuberculosis patients are in the older-age group and have many medical and surgical complications which require a staff with a wide variety of competencies such as those found in the general hospital.

The problems of compensation, formerly a major concern of hospital administrators where tuberculosis treatment was provided, have receded almost to the vanishing point because the communicability of the disease, when adequate and appropriate antimicrobial therapy is given has been greatly reduced.

Even though the hazards may be negligible, the hospital will wish to be covered with appropriate compensation insurance. It may also wish to consider the advisability of including coverage for volunteers, either by including them as employes or as a third-party liability. These people, through gratis services, make a substantial contribution to the hospital. New York State is quite liberal in its interpretation of occupational disease laws, and all an employe needs to prove to be entitled to Workmen's Compensation is that he had contact in the hospital with a tuberculosis patient.

Insurance compensation rates are based on the hospital's experience record. If no claims are presented to the insurance company on the basis of someone's contracting tuberculosis as a result of service to those patients, there is no increase in premium.

The hospital which has a definite program of tuberculosis control, exercises precautions, and has definite procedures which are followed by the staff is probably in less hazard of being involved in a law suit for possible administrative negligence than the hospital which admits only an occasional tuberculosis patient.

Middle-income tuberculosis patients have been aided greatly by the extension of major medical plans to include tuberculosis treatment for periods up to three months. This period permits an evaluation of the disease, the initiation of therapy, the education of the patients and of their families, and an opportunity to arrange for continued hospital care if it is indicated. Patients who continue treatment at home can then be readmitted to the hospital as necessary for short periods of evaluation and for surgery where it is advisable.

Unfortunately, the continuity of medical care is sometimes interrupted if the patient with limited income requires a long period of drug therapy after his hospital discharge. Since drugs are not available from the City for their outpatient treatment, the voluntary hospital physicians refer these patients in New York to local health department chest clinics. The Department of Welfare reimburses for drugs used in the treatment of welfare clients, but the City makes no similar provision for patients with marginal incomes.

The problems which are now present when tuberculosis treatment is given by general voluntary and municipal hospitals are not insurmountable and can readily be eliminated. Some of them are already in the process of being corrected.

Changing New York City picture

In 1953, the average ward census in the tuberculosis services of the Department of Hospitals of the City of New York was 5,200 patients. Now it is about 1,800. The reduction in beds occurred in hospitals devoted principally to the care of tuberculosis and not in general hospital centers. With the effectiveness of the antimicrobial drugs and the earlier discharge of hospital patients, ambulatory care became increasingly important. In 1953, few patients were on chemotherapy in the Department of Hospitals' 12 chest clinics. Now close to 3,800 receive drug treatment there.

A major shift has been an increase in older male patients. In New York City, whereas 56 per cent of all patients with tuberculosis are over the age of forty-five, two thirds of the men are over forty-five and only 29 per cent of the women are in this age group. This type of patient population raises various problems. Older people have a higher incidence of emphysema, pulmonary insufficiency, and other nonpulmonary conditions such as heart disease, diabetes, and neoplasms. The use of thoracic surgery is often limited because of the existing complications, and the antituberculosis drugs produce toxic reactions in the aged more frequently than in younger persons. Many are homeless or have poor home or family situations.

Whereas fifteen years ago only 7 per cent of known active cases of tuberculosis who died in New York had a nontuberculous cause of death, now almost half the tuberculous patients who die have a primary cause of death which is not tuberculosis. The treatment of these significant and numerous associated diseases requires not only the basic medical, nursing, and ancillary staff, but also the clinical and laboratory facilities and the consultation services available in a general hospital.

Sixty per cent of the patients with tuberculosis have had no previous hospitalization, and 62 per cent never had antituberculosis drug therapy. Effective original treatment of these patients represents a tremendous opportunity for reducing the treatment failures and the potential reservoirs of infection in the community.

Chemotherapy and its effects on treatment

The use of antituberculosis drugs has made it possible for patients to be more active and not to be confined to bed for long periods of time. The desirable and allowable increase in activities, which individuals under antimicrobial therapy are permitted, requires rehabilitation services. At National Jewish Hospital in Denver, Colorado, tuberculous and nontuberculous patients attend some social functions together; for all other purposes both services are separate. On the pediatric service, children with primary tuberculosis and with reinfection tuberculosis who do not cough are not separated from the others with nontuberculous conditions. In the experience of this and other pediatric centers where this kind of program is followed, there has been no documented evidence that tuberculosis has been communicated to a nontuberculous child.

There is a need for a continuous program of orientation and education so that patients will understand not only how to protect themselves, but also how to protect others in the community. In addition to educating the patient to the great importance of continuing therapy until he can be discharged safely from medical supervision, he must be taught how he can prevent the spread of tuberculosis. When patients show they appreciate their responsibility, practice good personal hygiene, and conduct themselves appropriately, greater freedom of movement in the hospital community is permissible and desirable. Out-of-hospital privileges can also be expanded.

Sidney Dressler, M.D., Chief of Staff at National Jewish Hospital, where a program such as that already described is in operation, reported on ten years of experience in preplacement and periodic tuberculin testing in routine health examinations of the staff. In all these years, representing about 3,000 to 3,400 people, there have been only 30 documented conversions of the tuberculin test. At least six months of therapy with isoniazid or isoniazid plus para-aminosalicylic acid was recommended for most of these employes, and as far as is known, all have remained well.

New questions on therapy are arising; some of them need to be answered, for example:

What should be done about the individual excreting resistant tubercle bacilli or who shows persistently positive test results and is beyond what modern chemotherapy and surgery can offer? Some of these patients are capable of physical activity and indeed of vocational activities. Should special activities and services be established for treating and accommodating these long-term patients?

To what extent can these chronically disabled tuberculosis patients share in programs arranged for other chronically disabled individuals?

The definition of what constitutes a resistant tuberculosis organism is a confused one. Laboratories are using various methods to determine resistance. Methods may differ in the type of medium used, the amount of drug put into the medium and the size of the inoculum, and whether subcultures or direct susceptibility tests are used. This question should be clarified.

Recommended tuberculosis control measures in employe health program

One of the most important things in planning for tuberculosis control in a health program for hospital employes is that one individual, a physician, be given the responsibility and authority to carry out the program. A specific written plan, applying to all employes, should be developed so that it may serve as a definite norm.

The preplacement physical examination should include a chest x-ray examination and a tuberculin test. Frequent changes should not be made in the tuberculin testing procedures used, so that a valid appraisal of the program may be made in the year-by-year evaluations and comparisons.

The exclusion of individuals from employment or from enrollment as students of nursing or medicine merely because they have a history of tuberculosis is no longer justified. There should be room for the tuberculosis control officer to make exceptions and individual determinations. Most tuberculosis experts no longer consider that a BCG vaccination is necessary for those who have tuberculin-negative reactions and presumably have negative chest film results at the time of employment. Other experts, while maintaining that these individuals need not be sheltered from work in the tuberculosis unit, are inclined to recommend BCG vaccination, to give the employes some protection against primary infection with drug-resistant organisms rather than relying on treating the recent converter with isoniazid.

Tuberculin testing of nonreactors to tuberculin is recommended at three- or six-month intervals, depending on the intimacy of the contact. When a change from a negative to a positive skin test result occurs, an x-ray film should be obtained immediately; and if the findings are negative for evidence of tuberculosis, the x-ray should be repeated three months later, again six months later, and then at six-month intervals. Although the scientific evidence is not yet available, isoniazid prophylaxis is quite generally recommended for recent converters from negative to positive tuberculin reactions. Usually, about every six months chest x-ray films of employes with positive tuberculin reactions are taken.

Good case-detection programs for patients who have been admitted to inpatient and outpatient services are part of the tuberculosis control program of the hospital and are a protection to employes. Unknown exposure to patients with active tuberculosis is greatly reduced. The detection procedures used by hospitals should vary with the prevalence of the disease in the areas or groups which they serve.

An inservice program for the proper indoctrination of all employes in protective measures against tuberculosis is a final important part of this health program. Some of the so-called protective technics now followed by hospitals need to be reexamined and evaluated from the point of view of air hygiene, the patient's responsibilities, and the new developments in treatment.

The American Society's Thoracic Committee on Therapy recently issued a statement on "Tuberculosis Control Programs for Hospital Personnel." It is an outline of certain general principles, and the details of their implementation must be decided by the individual hospital, nursing school, and medical school.

Public health implications

A tuberculosis program in a general hospital, from a public health point of view, should include a tuberculosis detection program for hospital admissions as an important start. There are always cases which can be discovered from the community, in addition to those sent in by physicians and public health authorities.

When tuberculosis patients are treated in a general hospital, the only real problem is the management of the patient with infectious or suspected infectious disease. Certain groups of tuberculous patients, in the opinion of well-respected medical experts, can be cared for in an open ward; namely, patients with inactive and noninfectious disease, patients with active nonpulmonary tuberculosis, and children with any form of tuberculosis other than the rare open cavitary form.

The hospital should have specified isolation procedures. The approach to the care of tuberculous patients should be one which stresses the education of the patient, covering the mouth with paper napkins, disposal of paper napkins, and the use of masks by patients when there is going to be exposure to hospital personnel or others. The protective measures followed should be based on sound principles and not on the traditionally ritualistic methods that are so difficult to remove.

There are many areas in which the City of New York Department of Health can be of service to general hospitals. No formal association between the two groups now exists, but there is no reason why such an association cannot be developed with respect to tuberculosis if enough general hospitals undertake this type of work.

Since the reporting of active tuberculosis is mandatory, the Department of Health receives notice that someone has infectious tuberculosis. Special consultations can be arranged. The machinery for finding contacts, which includes examining them and doing follow-up procedures, the exchange of information, and the review of special problems, can all be accomplished.

Summary

Today, the treatment of tuberculosis in voluntary and municipal general hospitals is feasible, practical, and advisable. When hospitalization is indicated for patients, with tuberculosis the arrangements should be made so that they will be near their homes. Continuity in medical treatment is important, and hospital and outpatient care should be integrated closely throughout the course of the disease. Reimbursement by the city to voluntary hospitals for inpatient and outpatient tuberculosis treatment should be equivalent to the medical-surgical rates allowed for general care patients.

Antimicrobial drug therapy and the new findings in air hygiene now make it necessary to take a new view of treatment schedules; rehabilitation services; and the education of patients, their families, and the public.

Woman's Auxiliary

The public image of the doctor's wife

As the doctor often is made into a public figure by public fancy, his wife often becomes a public figure also. As a member of the Woman's Auxiliary to the Medical Society of the State of New York she works on her own level to correct any false impressions the community may have.

Doctors' wives often act as a buffer for their husbands. They assume and dispatch many of the social obligations that befall busy men; they represent the families to good advantage on countless public occasions to spare the busy doctor both time and effort. Auxiliary membership prepares them to do this, and an Auxiliary member who is well informed can bring the cause of medicine to the attention of her community in a straightforward and enlightened way.

Parent-teacher associations are a natural contact for Auxiliary members who are mothers of school-age children. Many Auxiliary members work with health organizations and on fund-raising drives. The members of these groups are receptive to the story of medicine in its proper perspective.

Women's clubs and study groups comprise another large segment of the thinking population. All of such organizations put much emphasis on their programs. No one is better able to present authoritative information on current medical topics to such groups than the well-informed Auxiliary member who is identified with the group concerned. When one of these groups does undertake such a program, the member who is also an Auxiliary member can provide information, expert speakers, and well-planned study program material.

Hospital auxiliaries are one of the public's closest associations with the medical profession outside of the doctor-patient relationship. Therefore Medical Society Auxiliary members should become members of hospital auxiliaries and work along with other interested women, but at the same time they should guard against assuming control or too much voice in leadership. Hospitals need all the public interest and support that they can garner from the com munity; the wider the base of interest, the wider the area of support.

Many Auxiliary members find gratification in working with handicapped persons, visiting aged individuals, reading to blind persons, bringing recreation and music to shut-ins, or operating a bookmobile. Some Auxiliary members teach their adolescent children to work along with them in providing some of these services.

Doctor's wives play large individual roles in the community also. Among Auxiliary members are lawyers, accountants, nurses, professional social workers, librarians, artists, writers, and teachers. Even this partial list shows the extent to which Auxiliary members are integrated in their communities and the good influence they strive to bring to the community.

All Auxiliary members work to promote the aims and purposes of the Medical Society. Auxiliary members would welcome any suggestions from Medical Society members for a fuller or more expanded Auxiliary program.

Mrs. Isadore Zadek

New Rochelle, New York

Gallstones and diabetes

According to an article by Fred L. Turrill, M.D., Margaret M. McCarron, M.D., and William P. Mikkelsen, M.D., in the August, 1961, issue of the *American Journal of Surgery*, diabetes mellitus adds greatly to the gravity of complications of cholelithiasis. The over-all mortality in the entire series was fivefold greater in the diabetic person. And, mortality among the diabetic patients was nearly twentyfold greater than in the nondiabetic person.—*Current Medical Digest, October, 1961*

These corrections are on gummed paper and may be cut out and pasted over the original entries in the 1961 Medical Directory.

1961 Medical Directory Errata

Corrections of erroneous biographic material in the 1961 *Medical Directory of New York State* are listed below. Changes have been made in material received prior to the closing date of July 1, 1960.

Δ★**BERNSTEIN, Harold,** 128 De Mott Av. Rockville Centre, N.Y. 1–3, 7–8 except Wed Fri Sat evenings; Sun by appt. Tel Rockville Centre 6-0058. RCP&S Edinburgh 1940. SJM-4, 16. FACA. FCCP. FACC. Am Ger; Milit Sur US; NY Cardiol; Al St Cath. Asst Phy Periph Vas Dis Queens Hosp Cent OPD; Adj Phy Meml Long Beach; Staff So Nassau Com Oceanside.

Δ★**BLAU, Abram,** Mount Sinai Hospital, 1176 Fifth Av. New York, N.Y. by appt. Tels Atwater 9-0075, Trafalgar 6-1000. McGill 1931. D-PN (P; N; ChiP). QP. SI. Am Group Psychother; Am Psych (F); Am Ac Child Psych; Am Psychoan; Am Psychosom; Am Orthopsych; Res Nerv & Ment Dis; Ac Med; NY Psychoan; NY Neur; NY Clin Psych; Psychoan Assn NY; Al Mt Sinai; Al Bell. Psych & Psych-in-Chg Child Psych Mt Sinai.

Δ★**BROWN, Walter J.** Orchard Rd. Mount Kisco, N.Y. by appt. Tel Mount Kisco 6-9601. P&S NY 1940. D-R. SD. MACR. NY Roent. Dir Radiol No Westchester; Asso Radiol Grasslands.

Δ★**CRISTO, Eduardo,** 35-05 30 St. Astoria, N.Y. 12–2, 6–8. Tels Empire 1-1732, 1733. Xavieran Bogota 1954. XM-5.

Δ★**DOONEIEF, Alfred S.** 14 Smith Ave. Mount Kisco, N.Y. by appt. Tel Mount Kisco 6-6062. NY Univ 1938. D-IM. SJM-2. FACP. FCCP. Am Trudeau; Intl Int Med; NY Thor Sur; NY Int Med; Ac Med. Phy Pulmon Dis Monte; Asso Phy Grasslands & No Westchester.

Δ★**FEITELBERG, Abraham,** 1835 Grand Concourse, Bronx, N.Y. 10–1 by appt. Tel Tremont 8-0505. Cornell 1923. X. Am Ger; Al New York. Phy Hebrew Chronic.

Δ★**FISHMAN, Stanley Irving,** 20 Eighth Ave. Brooklyn, N.Y. by appt. Tel Main 2-3500. Cincinnati 1946. D-IM. SJ. AFCCP. Am Trudeau; Am Ger; Bkln Thor; Al Kings Co. Asst Phy Kings Co & St Johns; Asso Phy & Phy-in-Chg Pulmon Function Jew; Asso Phy Bkln Womens & Unity.

Δ★**FREUND, H. Robert,** 142 Joralemon St. Brooklyn, NY. by appt. Tel Triangle 5-3244. P&S NY 1940. D-S. SA. FACS. Bkln Sur. Sur St Giles, Kings Co & LIC; Chief Head & Neck Sur LIC OPD; Cons Head & Neck VAH; Dir Head & Neck Sur Bkln E&E.

Δ★**GINSBURG, Selig Moses,** 70 E 77 St. New York, N.Y. by appt. Tel Yukon 8-2444. 130 W 89 St. Cornell 1950. NB. D-IM. SJ. Clin Soc NY Diabet; Al Phila Genl; Al Monte; Al Mt Sinai. Clin Asst Phy Mt Sinai & Bell; Phy New York OPD; Asst Phy French OPD.

Δ★**GREENBERG, Louis,** 460 E 17 St. Brooklyn, N.Y. Tel Buckminster 2-4551. P&S NY 1908. D-OL. SF. Cons Otolar Maimonides.

★**HALPERN, Nathaniel Philip,** 10 Post Av. New York, N.Y. 12–1, 6–7. Tel Lorraine 7-3144. Univ & Bell 1927. D-OL. XF. Clin Asst Phy Knicker.

Δ★**HYSLOP, George Hall,** 129 E 69 St. New York, N.Y. by appt. Tel Rhinelander 4-0112. Cornell 1919. D-PN. QP. SI. Am Ac Comp Med (F); Am Neur; Res Nerv & Ment Dis; Milit Sur US; Ac Med; NY Clin Psych; NY Neur. Neur (Inactive) Presby; Cons Neur Nyack & St Agnes White Plains; Emerit Cons Neur Meml.

Δ★**KRASNER, Frank,** 30 E 60 St. New York, N.Y. by appt. Tel Plaza 5-1294. State Univ Bkln 1954. NB. D-D. SH. Am Ac Derm & Syph; Invest Derm; Al Maimonides; Al Bell. Asst Derm Goldwater Meml & Knicker; Asst-in-Derm Univ.

★**LOEWE, Walter Ralph,** 1 E 69 St. New York, N.Y. 9–12 by appt. Tel Butterfield 8-1303. Tufts 1917. D-O. SE. FACS. PAMA; Am Ac Ophth & Otolar; NY Clin Ophth; Al City. Cons Ophth Met & Coler Meml; Asst Attd Ophth Flower & Fifth Ave; Cons Ophth City, Elmhurst.

★**McCANN, Thomas P. Sr.** Seaford, N.Y. by appt. Tel Sunset 5-4412. Fordham 1915. XM-5.

★**MESSER, William,** 4711 12 Av. Brooklyn, N.Y. 1–4, 6–8 Mon Wed Fri; 10–1 Sat by appt. Tel Gedney 6-5656. LIC Hosp 1925. D-IM (Al). SJM-12. FACAL. Am Ac Alg (F). Sr Clin Asst Ped Alg Mt Sinai; Asst Attd Phy Maimonides; Asst Attd Alg Maimonides OPD.

Δ★**MUSACCHIO, Tito,** 1452 75 St. Brooklyn, N.Y. 12–2, 6–8. Tel Beachview 2-5716. Marquette 1955. XM-5.

Δ★**ROTHBARD, Bernard,** 9000 Kings Highway. Brooklyn, N.Y. by appt. Tel Dickens 2-1440. Also Manhattan. NY Med 1939. NB. SM-10. Am Pub Health; NY Ind Med; Al Coney Isl. Med Dir Unit WM & M Med Cent.

Δ★**ROTHBARD, Bernard,** 842 Broadway. New York, N.Y. by appt. Tel Gramercy 3-5781. Also Brooklyn. NY Med 1939. NB. SM-10. Am Pub Health; NY Ind Med; Al Coney Isl. Med Dir Unit WM & M Med Cent.

★**SPIER, Robert,** 191 W North St. Buffalo, N.Y. by appt. Tels Garfield 2122, 2123. Penn 1951. D-S. SA. Al New York. Jr Clin Asst Sur Genl; Asso Sur Child.

Δ★**STERMAN, Max M.** 272 W 90 St. New York, N.Y. 5:30–7 by appt. Tel Trafalgar 3-3040. P&S NY 1919. XJM-5. Am Pub Health; Am Trop Med & Hyg; NY Trop Med; Al Beth Israel. Phy Daughters Israel; Asso Phy Trop Dis City, Elmhurst; Asso Ped Trop Dis & Parasit Knicker.

★**VEENEMA, Ralph James,** 180 Fort Washington Av. New York, N.Y. by appt. Tel Wadsworth 3-2500. NJ State Soc. Jefferson 1945. D-U. FACS. NY Urol. Asst Attd Urol Presby; Cons Urol Valley Ridgewood NJ.

★**WOLFERMAN, Adolph,** 153 Pierrepont St. Brooklyn, N.Y. by appt. Tel Main 5-6707. Geneva 1941. NB. D-OL. SF. Am Ac Ophth & Otolar. Asst ENT Jew; Sr Clin Asst ENT Bkln E&E; Asst ENT Poly.

Medical News

New ophthalmologic society

The ophthalmologists of Rockland County have announced that they have instituted the Rockland County Ophthalmological Society. For information concerning the new society write to: Frank J. Errico, M.D., Secretary-Treasurer, 95 Washington Avenue, Suffern, New York.

Course in uses of radioactive isotopes

A four-months course in the medical uses of radioactive isotopes will be offered at the Queens Hospital Center by the Radiation Medicine Department. The course will commence on Tuesday, February 6, and will consist of weekly five-hour sessions covering lectures, laboratory exercises, and clinical management of patients. Enrollment will be limited.

Apply to: Philip J. Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York.

Basic criteria for blood transfusion

The Joint Blood Council, Inc., has released a basic criteria for blood transfusion. The new brochure will be distributed to all known hospitals in the United States. It will also be used in the Council's planned program for adding to the information of interns, students, and residents.

Grants for study of tuberculosis

The New York Tuberculosis and Health Association has announced its 1962 research grant and fellowship program for the study of tuberculosis and other pulmonary diseases. For full information concerning the program write to: New York Tuberculosis and Health Association, 260 Park Avenue South, New York 10, New York.

Review of dermatology

The Division of Dermatology, Department of Medicine, State University of New York Downstate Medical Center, has announced a general review of dermatology for the practitioner to be held on Wednesdays from 1:00 to 2:30 P.M., during the months of February and March. One hour of category 1 credit will be granted for each session by the American Academy of General Practice.

Applications and requests for further information should be addressed to: The Office of Postgraduate Education, State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

Poison Prevention Week

Representatives of 21 professional, industrial, and service organizations and Federal agencies met in Washington, D.C., in November to plan for the first National Poison Prevention Week, to be observed March 18 through 24.

A recent act of Congress authorized the President to designate the third week of March each year as National Poison Prevention Week. The November meeting was called by the National Clearinghouse for Poison Control Centers of the U.S. Public Health Service and the American Pharmaceutical Association. Protection against accidental poisoning of children under five years of age will be the prime target of the organizations. More than 302,000 children under the age of five suffer accidental poisoning every year.

Essay prize offered

The American Therapeutic Society has announced its prize essay contest for 1962. An award of $500 plus travel expenses will be presented to the author of the best essay in the field of therapeutics and clinical pharmacology.

Any scientist or physician in residency or fellowship status or within three years following residency or fellowship is eligible for the award. The essay should be an original manuscript describing work done by the essayist alone or as an important member of a research team.

The manuscript and a letter from the chief of service or laboratory indicating his approval of the material being entered in competition must be in the hands of the Secretary, Oscar B. Hunter, Jr., M.D., 915 19th Street, N.W., Washington, D.C., by March 1.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that the next scheduled examinations (Part II), oral and clinical, for all candidates, will be conducted at the Edgewater Beach Hotel, Chicago, Illinois, April 9 through 14. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates.

Candidates participating in the Part I examination will be notified of their eligibility for the Part II examinations as soon as possible.

Current bulletins of the Board outlining the requirements for application may be obtained by writing to the Secretary: Robert L. Faulkner, M.D., 2105 Adelbert Road, Cleveland 6, Ohio.

Personalities

Awarded. Joost A. Meerloo, M.D., New York City, a peace award from the American Association for Social Psychiatry.

Elected. Sheppard Siegal, M.D., New York City, as president of the New York Allergy Society.

Appointed. Samuel J. Gelman, M.D., Brooklyn, as executive director of the Jewish Hospital of Brooklyn . . .Vaughan Mason, M.D., New York City, as chairman of a committee organized by the New York Urban League to survey discriminatory practices against Negroes in the medical profession . . .Aubre de L. Maynard, M.D., New York City, as director of surgery at Harlem Hospital.

Honored. Isidore Snapper, M.D., Brooklyn, at a dinner sponsored by the Beth El Hospital of Brooklyn in honor of his fiftieth anniversary as a physician . . .Janet G. Travell, M.D., New York City and Washington, D.C., as Medical Woman of the Year by the New York State branch of the American Medical Women's Association.

Speakers. Lionel S. Auster, M.D., New York City, in November on the subject of cancer therapy before hospital staffs in Tel Aviv, Jaffa, and Jerusalem, Israel . . .Howard W. Potter, M.D., New York City, on November 17 before the staff of the Veterans Administration Hospital, Northport, Long Island, on the topic "Dynamic Implications of Hospital Life" . . .Alfred Schick, M.D., New York City, before a meeting of the Association for the Advancement of Psychotherapy, Inc., on December 15, on the topic "Etiological Aspects of Psychiatric Disorder and Their Implications on Therapy."

Medical Meetings

Tillie S. Bergman Memorial Lecture

The Tillie S. Bergman Memorial Lecture will be held on Thursday, January 4, at 9:00 P.M. in the Murray Cohen Auditorium of Lebanon Hospital, Grand Concourse and Mt. Eden Parkway, Bronx 57, New York. Owen H. Wangensteen, M.D., professor of surgery, University of Minnesota, and chairman, Department of Surgery, University of Minnesota Hospitals, will be the guest speaker. His topic will be "Facets of the Peptic Ulcer Problem."

American Society of Facial Plastic Surgery

The American Society of Facial Plastic Surgery will hold a meeting on January 19 at the Hotel Elysee, 60 East 54th Street, New York City.

For information contact: Samuel M. Bloom, M.D., Secretary, American Society of Facial Plastic Surgery, 123 East 83rd Street, New York 28, New York.

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis, Inc., will sponsor a lecture by Dr. Georgene H. Seward, professor of psychology of the University of Southern California, on January 24, at the New York Academy of Medicine, 103rd Street and Fifth Avenue, at

8:30 P.M. Dr. Seward's topic will be "The Relation Between Psychoanalytic 'School' and Value Problems in Therapy."

For information contact: B. Joan Harte, M.D., Chairman, Public Relations Committee, Association for the Advancement of Psychoanalysis, Inc., 329 East 62nd Street, New York 21, New York. Telephone PLaza 2-5267.

American College of Radiology

The American College of Radiology will hold its thirty-eighth annual convention February 7 through 10 at the Roosevelt Hotel in New York City.

For further information write to: The American College of Radiology, 20 North Wacker Drive, Chicago 6, Illinois.

The Heart Association of Southeastern Pennsylvania

The Heart Association of Southeastern Pennsylvania announces a two-day scientific session on the application of computers in cardiovascular disease to be held at the Sheraton Hotel, Philadelphia, Pennsylvania, February 27 and 28. Experts in computer analysis and programing, together with physicians and members of other life sciences, will discuss how best to use the so-called "electronic brains" to conquer heart and circulatory diseases.

For information write to: The Heart Association of Southeastern Pennsylvania, 318 South 19th Street, Philadelphia 3, Pennsylvania.

M. D. Anderson Hospital and Tumor Institute

The University of Texas M. D. Anderson Hospital and Tumor Institute will present its sixteenth annual symposium on fundamental cancer research, March 1 through 3, entitled "Conceptual Advances in Immunology and Oncology."

For further information write to: Editorial Office, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston 25, Texas.

New York State Society of Internal Medicine

The New York State Society of Internal Medicine will hold its third annual internists' day at the Savoy Hilton Hotel in New York City, on Saturday, March 3. A feature of the meeting will be a symposium on the subject "Diseases of the Thyroid Gland; Recent Advances."

For further information write to: Maxwell Spring, M.D., Program Chairman, Third Annual Internists' Day, 800 Grand Concourse, Bronx 51, New York.

Alumni Association of the New York Eye and Ear Infirmary

The annual spring meeting of the Alumni Association of the New York Eye and Ear Infirmary will be held April 9 through 12. Pertaining to the eye, symposia will be offered on preoperative workup, surgical management, and complications of cataract surgery. There will also be courses and a closed circuit television demonstration of surgical procedures.

Pertaining to the ear, nose, and throat, there will be symposia on complications of stapes surgery and significance of a mass in the neck as well as lectures and a closed circuit television demonstration of surgical procedures.

For further information write to: Vincent Carter, Jr., M.D., Secretary-Treasurer, Alumni Association, The New York Eye and Ear Infirmary, 218 Second Avenue, New York 3, New York.

American College of Surgeons

The American College of Surgeons will hold its final 1962 sectional meeting in Washington, D.C., April 16 through 18. Headquarters hotel will be the Sheraton-Park. Subjects to be included are: occlusive arterial disease, gastrointestinal bleeding, endocrine disorders, coordinated care in severe trauma, surgery of the biliary-pancreatic tract, and new developments in pediatric and geriatric surgery.

For further information write to: American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.

Council on Medical Television

The fourth annual meeting of the Council on Medical Television will be held on May 15 and 16 at the Clinical Center, National Institutes of Health, Bethesda, Maryland. The Council meeting will be followed immediately by the annual medical-dental TV workshop held on May 16 and 17 at the National Naval Medical Center, also in Bethesda and adjacent to the National Institutes of Health.

For further information contact: Institute for Advancement of Medical Communication, 33 East 68th Street, New York 21, New York.

American College of Obstetricians and Gynecologists

Districts I and II of the American College of Obstetricians and Gynecologists will meet at the Queen Elizabeth Hotel, Montreal, Canada, October 11 through 13. For further information contact: Martin L. Stone, M.D., New York Medical College, Fifth Avenue at 106th Street, New York, New York.

Necrology

Samuel Edson Appel, M.D., of Dover Plains, died on August 17, 1961, at Sharon (Connecticut) Hospital at the age of seventy-five. Dr. Appel graduated in 1911 from New York University and Bellevue Hospital Medical College. The second medical examiner in Dutchess County, he was an attending physician in surgery at Harlem Valley State Hospital in Wingdale and a consultant in surgery at Wassaic State School and Sharon Hospital. President of the Dutchess County Medical Society in 1933 and a vice-president of the former Dutchess-Putnam Medical Society, Dr. Appel was a Fellow of the American College of Surgeons and a member also of the Medical Society of the State of New York and the American Medical Association.

Percy Edward Banks, M.D., of Newburgh, died on September 3, 1961, at the age of eighty-three. Dr. Banks graduated in 1904 from Long Island College Hospital Medical School. He was a member of the Orange County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

S. Muriel Baron, M.D., of Forest Hills, died on August 13, 1961, at Memorial Hospital at the age of sixty-one. Dr. Baron graduated in 1924 from Woman's Medical College of Pennsylvania, Philadelphia, and interned at Columbia-Presbyterian Medical Center (Neurological Institute). She was an associate attending physician in neuropsychiatry at Queens Hospital Center and an associate clinical professor of neurology and neuropsychiatry at New York Medical College. For thirty years Dr. Baron was a member of the board of directors of the Child Service League and was a cofounder of its Turkey Mountain summer camp project for teenagers and the first honorary president of the organization. Dr. Baron was a Diplomate of the American Board of Psychiatry and Neurology, a Member of the American Psychiatric Association, and also held memberships in the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Bernard Blutstein, M.D., of Corning, died on August 26, 1961, at the age of forty-one. Dr. Blutstein graduated in 1944 from Tulane University of Louisiana School of Medicine. He was an attending physician in radiology at Corning Hospital. Dr. Blutstein was a Diplomate of the American Board of Radiology, a Member of the American College of Radiology, and also held memberships in the Steuben County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Florence Brush, M.D., of White Plains, died on October 25, 1961, at St. Agnes Hospital at the age of eighty-two. Dr. Brush graduated in 1907 from Woman's Medical College of Pennsylvania, Philadelphia. She was a former resident physician at the Burke Foundation in White Plains.

Ray Douglas Champlin, M.D., of Guilford, died on September 1, 1961, at his home at the age of sixty-seven. Dr. Champlin graduated in 1917 from the University of Maryland School of Medicine and College of Physicians and Surgeons. For twenty-four years he was Oneonta District Public Health Officer and in 1948 he was promoted to Regional State Health Director at Syracuse, retiring from this post in 1955. Dr. Champlin was a member of the American Public Health Association.

Harold R. De Pue, M.D., of Canton, died on November 3, 1961, at the A. Barton Hepburn Hospital, Ogdensburg, at the age of seventy-nine. Dr. De Pue graduated in 1911 from the University of Vermont College of Medicine. He had served as St. Lawrence County Jail physician, St. Lawrence County Home physician, and at one time as St. Lawrence University physician. Dr. De Pue was a member of the St. Lawrence County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James Bertram Dowd, M.D., of Brooklyn, died on November 2, 1961, at the age of eighty-two. Dr. Dowd graduated in 1900 from Long Island Hospital Medical School. He was an emeritus physician in obstetrics and gynecology at the Lutheran Medical Center and had been the organizer of the obstetrical department there. Dr. Dowd was a Fellow of the American College of Surgeons and a member of the Brooklyn Gynecological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Stuart Irving Gurman, M.D., of New York City, died on August 26, 1961, at Danbury, Connecticut, at the age of forty. Dr. Gurman graduated in 1950 from Syracuse University School of Medicine. He was an assistant attending physician in radiology at The Mount Sinai Hospital. Dr. Gurman was a Diplomate of the American Board of Radiology and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Kurt Kaiser, M.D., of Gloversville, died on August 16, at 1961, the North Adams Hospital at the age of sixty-two. Dr. Kaiser received his medical degree from the University of Berlin in 1922. He was an attending physician in obstetrics and gynecology at the Nathan Littauer Hospital. Dr. Kaiser was a Fellow of the International College of Surgeons and a member of the Fulton County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Paul Kaufman, M.D., of Far Rockaway, died on August 27, 1961, at the age of seventy-seven. Dr. Kaufman received his medical degree from the University of Budapest in 1909. He was a consulting physician at Goldwater Memorial Hospital. Dr. Kaufman was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ferenc Kornis, M.D., of Bellmore, died on October 18, 1961, at the age of sixty-four. Dr. Kornis received his medical degree from the University of Budapest in 1922. He was a member of the Nassau County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Hans S. Krakauer, M.D., of Boston, died on October 28, 1961, at Buffalo General Hospital at the age of fifty-five. Dr. Krakauer received his medical degree from the University of Heidelberg in 1929. He was an associate attending physician at Deaconess Hospital in Buffalo. Dr. Krakauer was a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Raphael Kurzrok, M.D., of New York City, died on November 25, 1961, at his home at the age of sixty-six. Dr. Kurzrok graduated in 1920 from Columbia University College of Physicians and Surgeons. He was a consulting physician in endocrinology at Morrisania Hospital. Dr. Kurzrok was a Diplomate of the American Board of Obstetrics and Gynecology and a member of the Society for Experimental Biology and Medicine, the International Fertility Association, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York and the American Medical Association.

Henry Lake, M.D., of Brooklyn, died on October 26, 1961, at the age of seventy. Dr. Lake graduated in 1915 from Long Island College Hospital Medical School. He was a member of the American Academy of General Practice, the American Geriatrics Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Carey Lee, M.D., of Norwich, died on October 23, 1961, at Robert Packer Hospital, Sayre, Pennsylvania, at the age of seventy-one. Dr. Lee graduated in 1916 from Fordham University School of Medicine.

Frank Leon Okoniewski, M.D., of Auburn, died on October 15, 1961, at Auburn Memorial Hospital at the age of fifty-five. Dr. Okoniewski graduated in 1931 from the University of Buffalo School of Medicine. He was chief of the medical staff and chief of the X-Ray Department at Mercy Hospital and an associate attending physician in x-ray at Auburn Memorial Hospital. Dr. Okoniewski was a member of the Radiological Society of North America, Inc., the Radiological Society of New York State, the Central New York Roentgen Ray Society, the Cayuga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Everett Norman Perkins, M.D., of Gloversville, died on August 1, 1961, at his home at the age of fifty-five. Dr. Perkins graduated in 1931 from Albany Medical College. He was an attending physician in anesthesiology at Nathan Littauer Hospital and from 1949 to 1960 had served as health commissioner for Gloversville. A former president of the Fulton County Medical Society, Dr. Perkins was a member also of the American Society of Anesthesiologists, Inc., the Medical Society of the State of New York, and the American Medical Association.

Elliott DeWitt Root, M.D., of Jamestown, died on September 7, 1961, at the Jamestown General Hospital at the age of fifty-four. Dr. Root graduated in 1932 from Northwestern University College of Medicine. He was a member of the medical staff of the Jamestown General Hospital and an attending physician in eye, ear, nose, and throat at the Woman's Christian Association Hospital. Dr. Root was a Fellow of the American College of Surgeons and a member of the Chautauqua County Medical Society and the Medical Society of the State of New York.

Edward A. Rosenberg, M.D., of Manhasset, died on July 23, 1961, at the age of eighty-five. Dr. Rosenberg graduated in 1898 from Columbia

University College of Physicians and Surgeons.

Julio Samper, M.D., of Mount Kisco, died on October 27, 1961, at his home at the age of seventy-three. Dr. Samper received his medical degree from the University of Morelia in 1912. A former director of the Good Samaritan Clinic in Mexico City, Dr. Samper was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harold Lawson Stein, M.D., of Hawthorne, died on August 7, 1961, at the age of thirty-seven. Dr. Stein graduated in 1950 from George Washington University School of Medicine.

Joseph Tenopyr, M.D., of Cutchogue, died on November 18, 1961, at Long Island Jewish Hospital at the age of seventy-six. Dr. Tenopyr graduated in 1908 from Long Island College Hospital Medical School and interned at Kings County Hospital. He was a consulting surgeon at the Jewish Chronic Disease Hospital, the Kings County Hospital, the Central Suffolk Hospital Association (Riverhead), the Eastern Long Island Hospital Association (Greenport), and a senior consultant in surgery at Caledonian Hospital. Former president of the Kings County Medical Society and president of the Caledonian Hospital medical board in 1934, Dr. Tenopyr started the first tumor clinic in Brooklyn at the Caledonian Hospital, and was also a governor of the American College of Surgeons. Dr. Tenopyr was a Diplomate of the American Board of Surgeons, a Fellow of the American College of Surgeons, and a member of the Associated Physicians of Long Island, the Brooklyn Surgical Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph A. Zepf, M.D., of Watervliet, died on August 13, 1961, at Albany Veterans Hospital at the age of sixty-two. Dr. Zepf graduated in 1926 from Georgetown University School of Medicine. He was a consultant in surgery at Leonard Hospital in Troy. Dr. Zepf was a member of the Rensselaer County Medical Society and the Medical Society of the State of New York.

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Scientific Exhibits

Applications for space for scientific exhibits should be made directly to the Chairman, Scientific Exhibits Subcommittee of Convention Committee:

William L. Watson, M.D.
340 East 72nd Street
New York 21, New York

No applications can be considered after January 15, 1962.

Awards will be made in two groups:

Group I: Awards are made for exhibits of individual investigation which are judged on the basis of originality and excellence of presentation.

Group II: Awards are made for exhibits which do not exemplify purely experimental studies and which are judged on the basis of presentation and correlation of facts.

Abstracts

Weinberg, A., Costello, M. J., and Rotchford, J. P.: Inborn errors of amino acid metabolism associated with dermatologic disorders, New York State J. Med. **62:** 43 (Jan. 1) 1962.

Errors in amino acid metabolism which are transmitted by heredity are manifested dermatologically in such disorders as: phenylketonuria, a disturbance in the metabolism of phenylalanine which causes mental retardation and the presence of phenylpyruvic acid in the urine; alkaptonuria, a disturbance in the metabolism of phenylalanine and tyrosine which results in the excretion of homogentisic acid in the urine; total albinism, a disturbance in the metabolism of tyrosine which causes the complete absence of pigment in the skin, eyes, and hair; partial albinism, a disturbance in the metabolism of tyrosine which is characterized by a congenital absence of pigment in various regions of the body; and Hartnup disease, a disturbance in the metabolism of indican, tryptophan, and indolacetic acid which results in a pellagroid eruption, cerebellar ataxia, mental deficiency, and amino-aciduria. Diagnosis of these conditions is made on the basis of clinical manifestations aided by such technics as paper and ion-exchange chromatography on the urine and blood plasma. In most cases the treatment is symptomatic, although the diagnosis and treatment of phenylketonuria, preferably before one year of age, is essential if mental retardation is to be prevented.

De Roetth, A., Jr.: Recent advances in the medical treatment of glaucoma, New York State J. Med. **62:** 49 (Jan. 1) 1962.

There have been important improvements in the drugs used in glaucoma. The carbonic anhydrase inhibitors, of which acetazolamide (Diamox) has been the most widely used, are useful in chronic simple glaucoma and secondary glaucoma associated with uveitis, and preoperatively in the acute phase of angle-closure glaucoma. The cholinesterase inhibitors, of which water-soluble phospholine iodide and demecarium bromide are the most important contributions, produce marked miosis, decrease in intraocular pressure, and improvement in the facility of aqueous outflow. Epinephrine and the epinephrine-like drugs are useful to lower the intraocular pressure in chronic simple glaucoma. All of the drugs mentioned are definitely contraindicated in narrow-angle glaucoma. The most common side-effects are mild to moderate, but more severe toxic effects may occur. A most useful ocular hypotensive agent recently introduced is intravenous urea which brings the intraocular pressure down to normal temporarily in almost all types of glaucoma so that the appropriate surgical procedure may be performed. As most of these drugs are contraindicated in angle-closure glaucoma, the importance of a careful accurate initial diagnosis with gonioscopy and tonography must be emphasized.

Peller, S.: Essential differences between cancer in children and cancer in adults, New York State J. Med. **62:** 53 (Jan. 1) 1962.

Cancer in children differs from cancer in adults in quantitative and qualitative aspects. The usual pattern of childhood cancer is stable because the usual distributor of cancerogens, the fetal blood circulation, is a constant, whereas the location and distribution of primary tumors in adults are variables determined by exposures and experiences during the course of life. In adults about one half of all cancers consist of carcinomas in the cover tissues, which in postnatal life are the only areas directly accessible to exogenous cancerogens. In children, however, leukemia accounts for almost one half of all cancer, as in intrafetal life the cancerogens carried by the maternal blood stream first come in contact with the vascular endothelium. In the author's opinion the cephalocaudal law of physiologic growth and development and the cephalocaudal law of childhood cancer are accounted for by the same peculiarities of the fetal blood circulation. The author suggests that there may be an acquired immunity factor in the development of cancer. There is no sharp demarcation line in the age curve between pre- and postnatally induced cancers. The latency period of prenatally induced cancers varies within the limits of birth and thirty odd years, and the cancer latency varies with organ and system.

Berkowitz, D., and Glassman, S.: Steatorrhea; clinical approach to diagnosis and management, New York State J. Med. **62:** 58 (Jan. 1) 1962.

Steatorrhea, the presence of increased amounts of fat in the stool, is more common than is generally realized. It may be caused by a digestive defect, associated with such disorders as obstructive jaundice, biliary cirrhosis, and various diseases of the pancreas. It may be caused also by an absorption defect, in diseases of the mucosa and submucosa and other conditions which decrease the absorbing surface of the intestine. The presence of elevated fecal fat should be established by gross and microscopic examination of the stool; it may be necessary to perform a fat balance study. The authors feel that the most effective way of determining whether the defect is a digestive one or an absorptive one is the differential use of radiotriolein and/or oleic acid. A low blood radioactivity with elevated fecal activity after administration of radio-oleic acid indicates a primary absorptive defect. Low blood and increased stool values following administration of radiotriolein indicate a primary defect in digestion. A complete history and physical examination, sigmoidoscopy, and radiologic studies are required to determine the specific etiology of the process causing the disorder; biopsy and surgery may be necessary also. In certain cases the use of a therapeutic trial may be indicated. In the management of steatorrhea, a high-calorie diet is essential, with iron and calcium given orally or by injection. A gluten-free diet is effective in nontropical sprue; tropical sprue is frequently improved by the administration of vitamin B_{12} or folic acid. The administration of steroids, antibiotics, and pancreatic enzymes has been effective in the treatment of some diseases with malabsorption.

Kronenberg, B.: Surgical experiences in the eye camps of India, NEW YORK STATE J. MED. **62:** 62(Jan. 1) 1962.

The author conducted four eye camps in India, each of which lasted for from ten to twelve days. The examination process was a rapid screening for cases of curable blindness due to cataracts and early glaucoma to be operated on within the first four or five days, as a period of postoperative care had to be provided. A total of 3,306 patients were seen in the four camps; 255 operations were performed, of which 207 were cataract operations on adults. The other 48 operations were for glaucoma, congenital cataracts, ptosis, squints, removal of tumors, dacryocystectomies, and plastic procedures. The technic for cataract operation had to be modified because of the large number of surgical cases; despite the simple procedure, the number of complications was extremely small. In spite of the primitive operating rooms, poor asepsis, inadequate illumination, and poor physical condition of the patients, the results were excellent and the complications minimal.

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Scientific Motion Pictures

William J. Sullivan, M.D., Chairman, Scientific Motion Picture Subcommittee of the Convention Committee, is interested in hearing from members who have 16-mm. motion picture films suitable for presentation at the 1962 convention.

For applications, write to WILLIAM J. SULLIVAN, M.D., 132 Pondfield Road, Bronxville, New York.

Abstracts in Interlingua

Weinberg, A., Costello, M. J., e Rotchford, J. P.: Innate errores del metabolismo de amino-acido in association con disordines dermatologic, New York State J. Med. **62:** 43 (1 de jan.) 1962.

Errores in le metabolismo de amino-acido que es transmittite per hereditate se manifesta dermatologicamente in disordines del typo de phenylcetonuria (un disturbation in le metabolismo de phenylalanina que causa un retardo mental e le presentia de acido phenylpyruvic in le urina), alkaptonuria (un disturbation in le metabolismo de phenylalanina e tyrosina que resulta in le excretion de acido homogentisic in le urina), albinismo total (un disturbation del metabolismo de tyrosina que causa le absentia complete de pigmento in le pelle, le oculos, e le capillo), albinismo partial (un disturbation in le metabolismo de tyrosina que es characterisate per le absentia congenite de pigmento in varie regiones del corpore), e morbo de Hartnup (un disturbation in le metabolismo de indicano, tryptophano, e acido indolacetic que resulta in un eruption pellagroide, ataxia cerebellar, deficientia mental, e amino-aciduria). Le diagnose de iste conditiones se face a base del manifestationes clinic, con le adjuta de technicas del typo de chromatographia a papiro o a excambio de iones in le urina e in le plasma del sanguine. In le majoritate del casos le tractamento es symptomatic. In le caso de phenylcetonuria, le establimento del diagnose e le initiation del therapia es urgente e deberea preferibilemente esser complite ante que le patiente attinge un etate de un anno pro prevenir retardo mental.

De Roetth, A., Jr.: Recente progressos in le tractamento medical de glaucoma, New York State J. Med. **62:** 49 (1 de jan.) 1962.

Es a notar importante meliorationes in le drogas usate in glaucoma. Le inhibitores de anhydrase carbonic—inter le quales acetazolamida es le plus extensemente usate—es utile in chronic glaucoma simplice e in glaucoma secundari associate con uveitis, preoperativemente etiam in le phase acute de glaucoma a clausura de angulo. Le inhibitores de cholinesterase—inter le quales hydrosolubile ioduro de phospholina e bromuro de demecarium es le plus importante—resulta in marcate grados de miosis, un reduction del pression intraocular, e un meliorate libertate de effluxo aquose. Epinephrina e le drogas epinephrinoide es utile in reducer le pression intraocular in chronic glaucoma simplice. Omne le drogas mentionate es definitemente contraindicate in glaucoma a angulo restringite. Le plus commun adverse effectos secundari es de character leve o moderate, sed plus sever effectos toxic pote occurrer. Un utilissime agente de hypotension ocular, de introduction recente, es urea intravenose que reduce le pression intraocular temporarimento al nivello normal in quasi omne typos de glaucoma, de maniera que le appropriate intervention chirurgic pote esser effectuate. Viste que le majoritate de iste drogas es contraindicate in glaucoma a clausura de angulo, le importantia de un meticulose e precise diagnose initial, effectuate con le uso de methodos gonioscopic e tonographic, non pote esser exaggerate.

Peller, S.: Differentias essential inter cancere in juveniles e cancere in adultos, New York State J. Med. **62:** 53 (1 de jan.) 1962.

Cancere in juveniles differe ab cancere in adultos in aspectos quantitative e qualitative. Le configuration usual del canceres de pueritia es stabile proque le distributor usual del cancerogenos—le circulation sanguinee fetal—es un constante, durante que le sito e le distribution de tumores primari in adultos es variabiles determinate per le experientias e le expositiones occurrente in le curso del vita. In adultos circa un medietate de omne le canceres consiste de carcinomas in le tissus tegumental, le quales—in le vita postnatal—es le sol areas directemente accessibile a exogene cancerogenos. In juveniles, del altere latere, leucemia representa quasi un medietate de omne le canceres, proque in le vita fetal le cancerogenos portate in le materne circulation de sanguine arriva a continger primemente le endothelio vascular. In le opinion del autor, le lege cephalocaudal del crescentia e disveloppamento physiologic e le lege cephalocaudal de cancere del pueritia es basate in le mesme peculiaritates del fetal circulation de sanguine. Le autor suggere que il existe possibilemente un acquirite factor de immunitate in le disveloppamento de cancere. Il non existe un linea clar de demarcation in le curva de etate inter cancere de induction prenatal e illo de induction postnatal. Le periodo de latentia de canceres de induction prenatal varia inter zero e plus que trenta annos (a partir del nascentia), e iste periodo varia etiam ab un organo o systema al altere.

Berkowitz, D., e Glassman, S.: Steatorrhea; diagnose e therapeutica ab le puncto de vista clinic, New York State J. Med. **62:** 58 (1 de jan.) 1962.

Steatorrhea, i.e. le presentia de augmentate quantitates de grassia in le feces, es plus commun que lo que es generalmente recognoscite. Le condition pote esser causate per un defecto digestive—associate con disordines del genere de jalnessa obstructive, cirrhosis biliari, e varie morbos del pancreas—sed illo etiam pote esser causate per un defecto absorptive, lo que occurre in morbos del tunica mucose e submucose e in altere conditiones que reduce le superficie de absorption del intestino. Le presentia de elevate nivellos de grassia fecal deberea esser demonstrate per examines macro- e microscopic del feces. In certe casos il es necessari executar un studio de balancia del grassia. Le autores opina que le plus efficace maniera de determinar si le defecto es digestive o absorptive es le utilisation differential de radiotrioleina e/o de acido oleic radioactive. Un basse radioactivitate in le sanguine in le presentia de elevate valores radioactive in le feces, observate post le administration de acido oleic radioactive, indica un defecto absorptive primari. Basse valores radioactive in le sanguine e altes in le feces post administrationes de radiotrioleina indica un defecto primari in le digestion. Un complete documentation anamnestic e un detaliate examine physic, insimul con studios sigmoidoscopic e radiologic, es requirite pro determinar le etiologia specific del processo que causa le disordine. Biopsia e chirurgia es necessari in certe casos. A vices le uso de un therapia experimental es indicate. In le tractamento de steatorrhea, un dieta a alte valor caloric es indispensabile. Ferro e calcium es administrate per via oral o per injection. Un dieta libere de glutine es efficace in sprue non-tropic. Sprue tropic es frequentemente meliorate per le administration de vitamina B_{12} o acido folic. Le administration de steroides, de antibioticos, e de enzymas pancreatic ha essite efficace in le tractamento de certe morbos que es associate con malabsorption.

Kronenberg, B.: Experientias chirurgic in le "campos de oculopathia" de India, New York State J. Med. **62:** 62 (1 de jan.) 1962.

Le autor hac onducite quatro "campos de oculopathia" in India de durationes de dece a dece-duo dies. Le processo examinatori esseva un rapide identification del casos de curabile cecitate causate per cataractas e glaucoma precoce, con operationes effectuate in le curso del prime quatro o cinque dies a causa del necessitate de provider un periodo de assistentia post-operatori. Un total de 3.306 patientes esseva examinate in le quatro campos. Esseva effectuate 255 operationes, incluse 207 pro cataractas in adultos. Le remanente 48 esseva pro glaucoma, cataractas congenite, ptosis, strabismo, excision de tumores, dacryocystectomia, e chirurgia plastic. Le technica usate in le operation pro cataractas debeva esser modificate a causa del grande numero de casos. In despecto del simplification technic, le numero del complicationes esseva extrememente basse. Le primitive character del salas de operation, le inadequate provisiones de aseptica e de illumination, e le pauco favorabile stato physic del patientes non preveniva le resultatos de esser excellente e le complicationes de remaner minime.

Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the New York State Journal of Medicine from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the Journal, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

Books Received

The following books were received during the month of October, 1961

The Origin of Medical Terms. By Henry Alan Skinner, M.B. Second edition. Quarto of 437 pages, illustrated. Baltimore, The Williams & Wilkins Company, 1961. Cloth, $12.50.

Immunity. By Sidney Raffel, M.D. Second edition. Octavo of 646 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $10.

Boys in White, Student Culture in Medical School. By Howard S. Becker, Blanche Geer, Everett C. Hughes, and Anselm L. Strauss. Octavo of 456 pages, illustrated. Chicago, The University of Chicago Press, 1961. Cloth, $10.

Practical Pediatric Dermatology. By Morris Leider, M.D. Second edition. Quarto of 437 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $13.75.

Differentiation Between Normal and Abnormal in Electrocardiography. By Ernst Simonson, M.D. Quarto of 327 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $13.50.

Surgery, A Concise Guide to Clinical Practice. Edited by George L. Nardi, M.D., and George D. Zuidema, M.D. Octavo of 1,034 pages, illustrated. Boston, Little, Brown and Company, 1961. Paper, $8.50. Cloth, $12.

Medical Physiology. Edited by Philip Bard, Ph.D. Eleventh edition. Quarto of 1,339 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $16.50.

Mechanisms of Disease, An Introduction to Pathology. By Ruy Perez-Tamayo, M.D. Quarto of 512 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $14.

Introduction to Anesthesia. By Robert D. Dripps, M.D., James E. Eckenhoff, M.D., and Leroy D. Vandam, M.D. Second edition. Octavo of 413 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $8.00.

Clinical Diagnosis. By Rustom Jal Vakil, M.D., and Aspi F. Golwalla, M.D. Octavo of 412 pages, illustrated. New York, Asia Publishing House, 1961. Cloth, $12.

Appraisal of Current Concepts in Anesthesiology. Edited and assembled by John Adriani, M.D. Duodecimo of 279 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $7.75.

Progress in Medicinal Chemistry. Volume 1. Edited by G. P. Ellis, Ph.D., and G. B. West, Ph.D. Octavo of 262 pages, illustrated. London, Butterworth & Co. Ltd., 1961. Cloth, $11.25.

Ciba Foundation Symposium on Somatic Stability in the Newly Born. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. With 63 illustrations. Octavo of 393 pages. Boston, Little, Brown and Company, 1961. Cloth, $10.

Clinical Obstetrics. By Benjamin Tenney, M.D., and Brian Little, M.D. Octavo of 440 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $8.50.

One for a Man, Two for a Horse. By Gerald Carson. Folio of 128 pages, illustrated. Garden City, N. Y., Doubleday & Company, Inc., 1961. Cloth, $6.50.

A Manual of Neurology and Psychiatry in Occupational Medicine. By Ralph T. Collins, M.D. Octavo of 244 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $6.50.

Executives' Health Secrets. By William P. Shepard, M.D. Octavo of 268 pages. New York, The Bobbs-Merrill Company, Inc., 1961. Cloth, $4.95.

Rehabilitation of A Child's Eyes. By Herbert M. Katzin, M.D., and Geraldine Wilson, R.N. Third edition of Scobee's "Rehabilitation of A Child's Eyes." Octavo of 107 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $3.75.

Experiments in Survival. Compiled and edited by Edith Henrich. Commentary by Leonard Kriegel. Octavo of 199 pages. New York, Association for the Aid of Crippled Children, 1961. Cloth, $3.50.

David Edwardes Introduction to Anatomy 1532. By C. D. O'Malley and K. F. Russell. Octavo of 64 pages, illustrated. Stanford, Calif., Stanford University Press, 1961. Cloth, $2.75.

The Medical Clinics of North America. Nationwide Number. September, 1961. Arthritis and Rheumatism. J. Sydney Stillman, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bi-monthly (six numbers a year). Cloth, $18 net; paper, $15 net.

Clinical Obstetrics and Gynecology, Volume 4 Number 3. September 1961. Cardiovascular-Renal Problems in Pregnancy. Edited by Russell R. De Alvarez, M.D. **Ovarian Tumors.** Edited by Langdon Parsons, M.D. Octavo of 316 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Published quarterly (four numbers a year). Cloth, $18 per year.

Heredity, An Introduction to Genetics. By A. M. Winchester. Octavo of 269 pages, illustrated. New York, Barnes & Noble, Inc., 1961. Paper, $1.75.

Research into road safety. Report on the first international meeting on Research into Road Safety, organized by O.E.E.C. at the Road Research Laboratory, Langley (United Kingdom), July, 1960. Octavo of 54 pages, illustrated. France, O.E.E.C. Publications.

Books Reviewed

Modern Occupational Medicine. Edited by A. J. Fleming, M.D., and C. A. D'Alonzo, M.D. Associate Editor J. A. Zapp, Ph.D. Second edition. Octavo of 587 pages, illustrated. Philadelphia, Lea & Febiger, 1960. Cloth, $12.

This volume is divided into eight sections. The first section is devoted to the evaluation of medical services in industry, history of industrial medicine, administration, functions, location, personnel, layout, equipment, medical history and records, and physical examinations.

The second section describes industrial preventive medicine and contains chapters on research, toxicologic methods, protective clothing, engineering, functions of the industrial hygiene laboratory, and immunizations in industry.

The third section describes physical environment, work, stress, and occupational health. Section four details services allied to occupational medicine. Section five is devoted to psychiatric problems in industry. Section six is concerned with toxicology. Section seven describes acute poisoning. Section eight is devoted to biostatistics in occupational medicine.

The thirty-five chapters which make up the book are authoritative monographs by the contributing authors, sixteen of whom work in one or more of the medical departments of E. I. du Pont de Nemours & Company. Four nonmedical department contributors, it is stated, are closely associated with the medical division of the company. The text is concise, meaty, and in an easily read form. It represents the collective experiences of a well-organized group working as a team, all well qualified by training and experience.

The chapters on medical history and physical examinations and the medicolegal aspects of occupational medicine are highly recommended to all physicians in or out of industry.—S. LOUIS HORNSTEIN, M.D.

The Structure and Dynamics of the Human Mind. By Edoardo Weiss, M.D. Octavo of 472 pages. New York, Grune & Stratton, 1960. Cloth, $8.75.

The author of this book is a private practitioner of psychoanalysis in Chicago and has served on the staff of the Chicago Institute for Psychoanalysis. The volume is dedicated to the memory of his teachers, Sigmund Freud and Paul Federn.

This book is a collection of previously published papers of the author throughout his lifetime. Some of them were published originally in Italian, German, or English. Through the

continued on page 134

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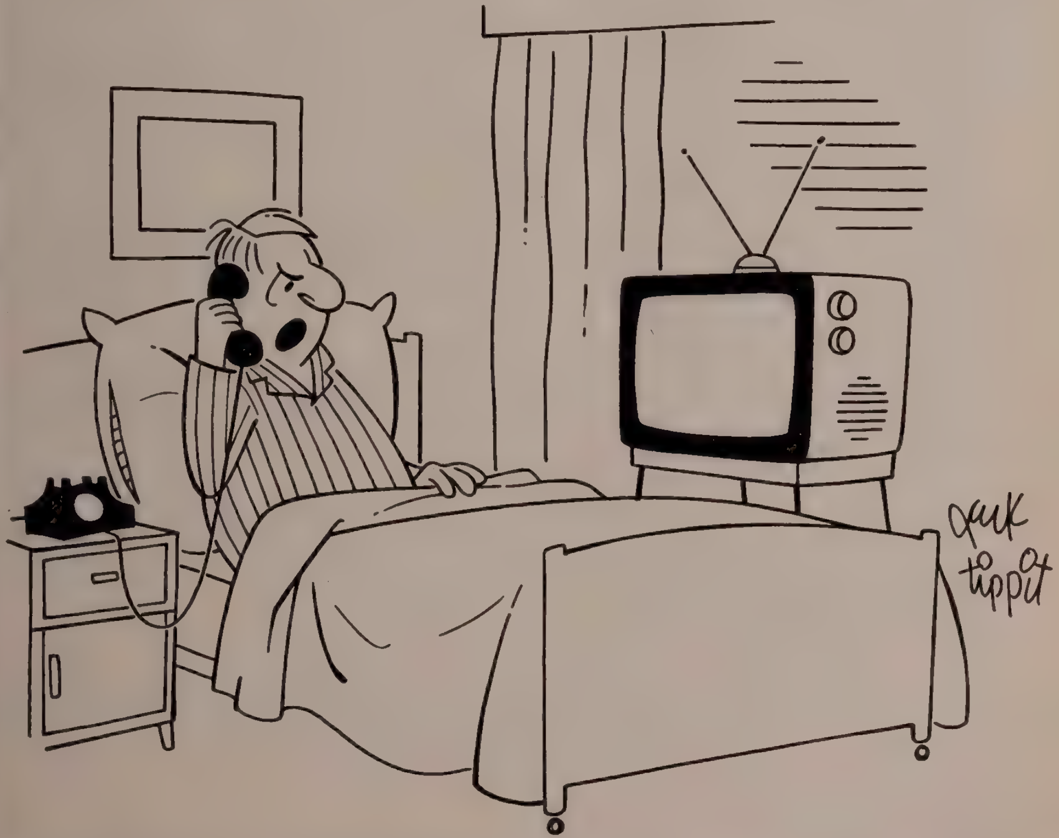

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years, however, they have been subject to the modification of earlier concepts in keeping with revised thinking and practice.

The purpose of the treatise is that of a psychoanalytic guide for students and others interested in this aspect of psychiatric practice. In America, at least, the psychoanalyst is first and essentially a medical practitioner who later specializes in psychiatry, and, if his inclination so develops, he takes special training for this subspecialty of psychoanalysis. In this first volume is a general presentation of the structure and dynamics of the human mind. A later volume is in preparation which concerns the psychologic approach to neuroses and psychoses, along with treatment technics. The classic psychoanalytic technic is emphasized for the psychoneuroses. The author also has in mind methods other than classical psychoanalysis for neuroses and psychoses.

This volume is of primary interest to the practitioner of psychoanalysis. Psychoanalysis of course has various schools of thought which by no means are in complete agreement. This, however, is hopeful inasmuch as it keeps the door open for more practical helpful means of treating the vast majority of mentally ill persons who cannot afford classical psychoanalytic methods, which, indeed, are not necessary when you look at the total psychiatric picture.

Practicing psychoanalysts and those concerned with psychodynamics will find much food for thought in this lifelong sampling of presentations of a seasoned practitioner in this subspecialty of psychiatry.—FREDERICK L. PATRY, M.D.

Management of Hypertensive Diseases. By Joseph C. Edwards, M.D. Octavo of 439 pages, illustrated. St. Louis, The C. V. Mosby Company, 1960. Cloth, $15.

The author states that in 1955 49.5 per cent of all natural deaths in the United States and 93 per cent of the 810,200 deaths from cardiovascular disease were due to arteriosclerosis and hypertension, and 11 per cent were due to hypertension alone.

The new normal range of hypertension at different age levels is discussed. There is an excellent chapter on the electrocardiogram in hypertension, and the subject is discussed at length with illustrations of electrocardiograms.

There is a detailed table dealing with the management of the patient with hypertension, including the use of the newer drugs alone or in combination. The recommended doses and their action are given in other tables. Hypertension associated with pregnancy is discussed by Monat and Edwards with detailed methods of treatment. Special types of hypertension are discussed at length.

The final chapter is on etiology. For the student there are some 1,622 references on hypertension at the end of the book. —VINCENT ANNUNZIATA, M.D.

Clinical Applications of Cardiopulmonary Physiology. By M. Henry Williams, Jr., M.D. Octavo of 233 pages, illustrated. New York, Paul B. Hoeber, Inc., Medical Division of Harper & Brothers, 1960. Cloth, $7.50.

Dr. Williams, associate professor of medicine and physiology at the Albert Einstein College of Medicine, is well qualified to write this small but complete monograph. All but the highly trained specialist will learn much from him about the clinical application of the newer technics for assessing heart and lung function. The diagrams and tables are few but good, as is the index. The references could have been updated.—MILTON PLOTZ, M.D.

Ciba Foundation Symposium on Haemopoiesis: Cell Prodution and its Regulation. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. Octavo of 490 pages, illustrated. Boston, Little, Brown and Company, 1960. Cloth $11.

This work is a compilation of various efforts in the field of hemopoiesis by outstanding American and European investigators.

This symposium is actually the brain child of Professor J. M. Yoffey of Bristol, England. It would seem that the "stem cell" totipotent for a rich variety of further research is the ultimate objective of this congress of workers in hemopoiesis. Thanks are due to the Ciba Foundation for affording the means for calling into intimate contact the foremost investigators in the field.

Thus an opportunity is afforded students of hemopoiesis to actually sit at the feet of the masters and absorb the gems of wisdom, which may stimulate them to increased efforts.—MAURICE MORRISON, M.D.

The Practitioner's Handbook. Edited by William A. R. Thomson, M.D. Octavo of 711 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1960. Cloth, $12.50.

This easily read, meaty edition is meant for any individual who treats man. It has an excellent index. The need for advice in the treatment of the "ordinary run of ailments" by English physicians returning to civilian practice in 1945 resulted in a series of articles by "The Practitioner." Nearly three hundred articles were written and are now revised in this volume. They supply the general practitioner with an authoritative, concise, and practical review of methods of diagnosis and treatment that can not be surpassed anywhere. The aim of this book is to survey the best features of our therapeutic armamentarium rather than the latest news of the newest drug.—BERNARD SELIGMAN, M.D.

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PREVENTS LACTATION AND BREAST ENGORGEMENT / just one injection at the end of the first stage of labor / optimally balanced, long-acting combination of gonadal steroids for easy injection through small-gauge needle because of low viscosity / virtually eliminates need for analgesics[1] / essentially eliminates withdrawal reaction and secondary breast engorgement sometimes associated with oral medication[1] / does not affect involution of uterus or restoration of normal ovarian function[2].

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Supply: Each cc. of Deladumone 2X provides 180 mg. testosterone enanthate and 8 mg. estradiol valerate dissolved in sesame oil. Vials of 2 cc. Dosage: 2 cc. given as a single intramuscular injection preferably at the end of the first stage of labor or else immediately upon delivery. For full information see your Squibb Product Reference or Product Brief. References: 1. Watrous, J. B., Jr., et al.: J.A.M.A. 169: 246 (Jan. 17) 1959. 2. Lo Presto, B., and Caypinar, E.Y.: J.A.M.A. 169:250 (Jan. 17) 1959.

Announcing CAPLA™–

to lower blood pressure

Only Capla acts directly on the brainstem centers that control blood pressure

This central action reduces peripheral resistance, lowers pressure.

Capla is a new kind of drug to treat hypertension. Chemically, Capla is 2-methyl-2-*sec*-butyl-1, 3 propanediol dicarbamate. It is unrelated chemically to any other antihypertensive agent.

New therapy

Capla is effective alone in the treatment of mild to moderate hypertension, and can be combined with diuretics or peripherally acting antihypertensives in more severe cases.

Exceptionally well tolerated

Capla acts rapidly, producing substantial blood pressure reduction within two hours, yet does not produce postural hypotension. It has proved exceptionally well tolerated in clinical use and has no known contraindications. Capla has not produced changes in renal, hematological, hepatic or endocrine function.

Compatible with other drugs

Hypertensive patients with other disorders can receive Capla along with other medications.

For example, patients with congestive heart failure, angina, and diabetes mellitus can receive Capla along with such medications as digitalis, nitrates, and insulin—without aggravating these other disorders.

a new drug that works in a new way without serious side effects

Capla lowers blood pressure without serious side effects

In 755 hypertensive patients treated with Capla, the only side effect observed with any frequency was mild, usually transient, drowsiness.

Capla is effective therapy without the unpleasant and serious side effects which often cause patients to abandon treatment. Side effects, when they do occur, are mild and usually transient. Transient drowsiness sometimes occurs, usually at higher dosage.

Patients on Capla often report a mild calming effect which, together with Capla's unusual freedom from side effects, makes therapy gratifying for both patient and physician.

Effective in clinical use

Average reductions in systolic and diastolic blood pressure reported with Capla. (755 patients)

	BEFORE	AFTER
MILD (403 patients) (Diastolic B.P. up to 100 mm. Hg)	183/93	159/85
MODERATE (249 patients) (Diastolic B.P. from 101 to 115 mm. Hg)	187/108	169/94
SEVERE (103 patients) (Diastolic B.P. over 116 mm. Hg)	208/120	162/99

Usual dose, Capla 300 mg., q.i.d.—duration of therapy, 3 weeks to over 1 year. These data show Capla reduces both systolic and diastolic pressure, usually in proportion to initial pre-treatment elevations.

Recommended Dosage: **One 300 mg. tablet three or four times daily, before meals and at bedtime. Dosage should be adjusted to individual requirements.**
Composition: **Each white, scored tablet is 300 mg. of Capla (mebutamate, Wallace).**
Supplied: **Bottles of 100 tablets.**

Clinical and Pharmacological Reports 1. Berger, F.M., Douglas, J.F., Kletzkin, M., Ludwig, B.J., and Margolin, S. The Pharmacological Properties of 2-methyl-2-sec-butyl-1, 3-propanediol dicarbamate (mebutamate, W-583) a New Centrally Acting Blood Pressure Lowering Agent. J. Pharmacology. In press, 1961. **2.** Berger, F.M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W-583). Fed. Proc. *20*. 113 1961. **3.** Bohensky, F.S.: Mebutamate, a New Drug for the Treatment of Hypertension, N. Y. State J. Med. In press, 1961. **4.** Diamond, S. and Schwartz, M.: Blood Volume in Uncomplicated Essential Hypertension. Modern Med. In press, 1961. **5.** Douglas, J. F., Ludwig, B. J., Ginsberg, T. and Berger, F. M.: Studies on W-583 Metabolism, Fed. Proc. *20*: 113 1961. **6.** Duarte, C., Brest, A. N., Kodama, R., Naso, F., and Moyer, J. H.: Observation on the Antihypertensive Effectiveness of a new Propanediol Dicarbamate (W-583). Curr. Therap. Res. *2*: 148-52 May, 1960. **7.** DuChez, J. W., Scientific Exhibit, American Medical Association, New York, 1961. **8.** Holloman, J. L. S., Jr. Treatment of Hypertensive Patients with Mebutamate, a new Antihypertensive drug—A Preliminary Report. J. Nat. Med. Assoc. In press, 1961. **9.** Kletzkin, M., and Berger, F.M.: A Centrally Acting Antipressor Agent. Fed. Proc. *20*: 113 1961. **10.** Leslie, C.H.. The Efficacy of Mebutamate, A New Antihypertensive Drug, in the Treatment of Refractory Geriatric Hypertensive Patients—A Preliminary Report. J. Am. Geriatrics Soc. In press, 1961. **11.** Mulinos, M G., Scientific Exhibit, Amer. College of Cardiology, New York May. 1961. **12.** Mulinos, M G., Saltefors, S., Boyd, L.J., and Cronk, G.A.: Human Pharmacology Studies with W-583. Fed. Proc. *20*: 113 1961. **13.** Shubin, H., Scientific Exhibit, American College of Cardiology, New York, 1961. **14.** Turek, L H. Clinical Evaluation of Mebutamate, an Antihypertensive Agent: Preliminary Report. Clinical Med. *8*: 7 1961.

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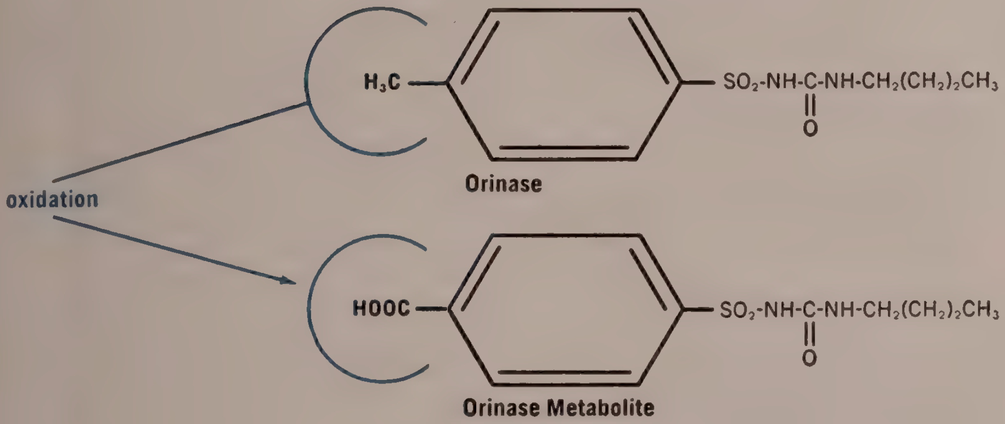
Why is the methyl "governor" in Orinase so important?

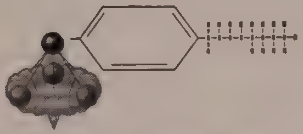
One of the most significant advantages of Orinase therapy is the rarity of associated hypoglycemic reactions.

This widely-reported clinical benefit is a function of the exclusive Orinase methyl "governor." Lending itself to ready oxidation (principally, it is thought, a hepatic process), the methyl group ensures prompt metabolic inactivation of the Orinase molecule. What actually happens is that a rapidly- and continuously-excreted carboxy-metabolite is produced that has no hypoglycemic activity at the existing levels.

As a result of the oxidation of its methyl group, Orinase shows a decline in activity soon after it reaches its effective peak in the plasma. Maintenance dosage serves to reduce blood sugar levels to normal, but rarely below that point, and there is no reported problem of accumulation.



Orinase*



An exclusive methyl "governor" minimizes hypoglycemia

Indications and effects: The clinical indication for Orinase is stable diabetes mellitus. Its use brings about the lowering of blood sugar; glycosuria diminishes, and such symptoms as pruritus, polyuria, and polyphagia disappear.

Dosage: There is no fixed regimen for initiating Orinase therapy. A simple and effective method is as follows: *First day*—6 tablets; *second day*—4 tablets; *third day*—2 tablets. The daily dose is then adjusted — raised, lowered or maintained at the two-tablet level, whichever is necessary to maintain optimum control.

Patients receiving insulin (less than 20 units)—discontinue insulin and institute Orinase; (20 to 40 units)—initiate Orinase with a concurrent 30 to 50% reduction in insulin dose with a further careful reduction as response to Orinase is observed; (more than 40 units) — reduce insulin by 20% and initiate Orinase with a further careful reduction in insulin dosage as response to Orinase is observed. In candidates for combined Orinase-insulin therapy, an individualized schedule is usually obtainable during a trial course of two or more weeks.

Contraindications and side effects: Orinase is contraindicated in patients having juvenile or growth-onset, unstable or brittle types of diabetes mellitus; history of diabetic coma, fever, severe trauma or gangrene.

Side effects are mild, transient and limited to approximately 3% of patients. Hypoglycemia and toxic reactions are extremely rare. Hypoglycemia is most likely to occur during the period of transition from insulin to Orinase. Other untoward reactions to Orinase are usually not of a serious nature and consist principally of gastrointestinal disturbances, headache, and variable allergic skin manifestations. The gastrointestinal disturbances (nausea, epigastric fullness, heartburn) and headache appear to be related to the size of the dose, and they frequently disappear when dosage is reduced to maintenance levels or the total daily dose is administered in divided portions after meals. The allergic skin manifestations (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) are transient reactions, which frequently disappear with continued drug administration. However, if the skin reactions persist, Orinase should be discontinued.

Clinical toxicity: Orinase appears to be remarkably free from gross clinical toxicity on the basis of experience accumulated during more than four years of clinical use. Crystalluria or other untoward effects on renal function have not been observed. Long-term studies of hepatic function in humans and experience in over 650,000 diabetics have shown Orinase to be remarkably free of hepatic toxicity. There has been reported only one case of cholestatic jaundice related to Orinase administration, which occurred in a patient with pre-existing liver disease and which rapidly reversed upon discontinuance of the drug.

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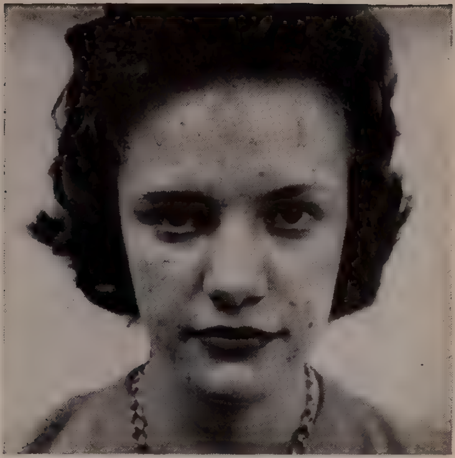

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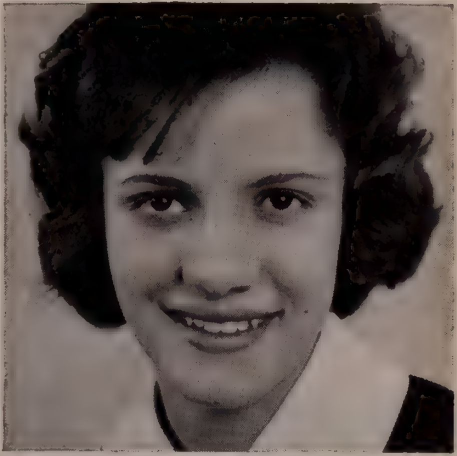

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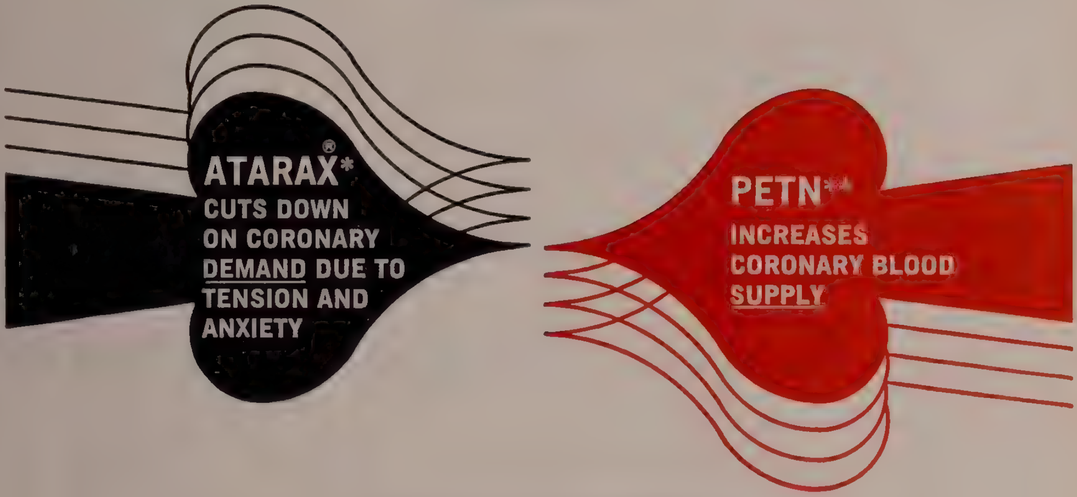
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1. Clark, T. E., and Jochem, G. G.: Angiology **11**:361 (Aug.) 1960.

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full antibiotic activity ● lower milligram intake per dose ● up to 6 days' activity with 4 days' osage ● uniformly high, sustained peak activity ■ **syrup** (cherry-flavored), 75 mg./5 cc. tsp., ottles of 2 and 16 fl. oz. Dosage: 3 to 6 mg./lb./day—in four divided doses. **pediatric drops,** 0 mg./cc., 3 mg./drop, 10 cc. bottles with calibrated dropper. Dosage: 1 to 2 drops/lb./day—n four divided doses

RECAUTIONS: As with many other antibiotics, DECLOMYCIN may occasionally give rise to glossitis, stomatitis, proctitis, nausea, iarrhea, vaginitis or dermatitis. A photodynamic reaction to sunlight has been observed in a few patients on DECLOMYCIN. Although eversible by discontinuing therapy, patients should avoid exposure to intense sunlight. If adverse reaction or idiosyncrasy occurs iscontinue medication. Overgrowth of nonsusceptible organisms is a possibility with DECLOMYCIN, as with other antibiotics. The patient hould be kept under observation.

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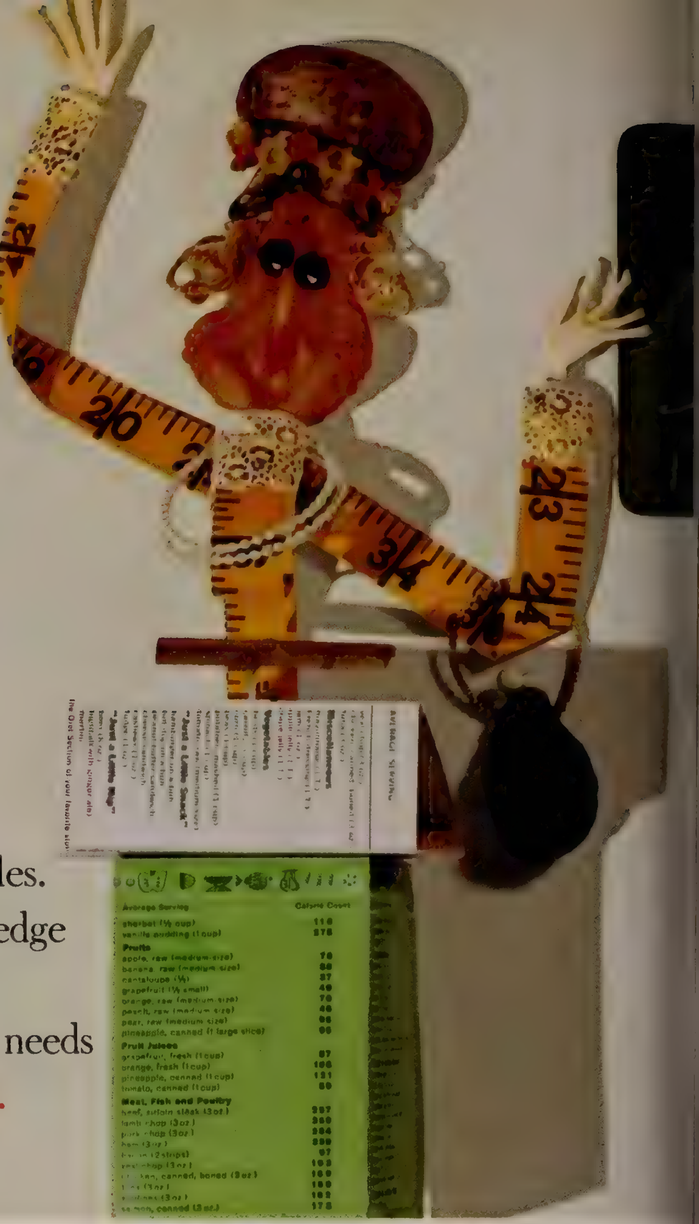

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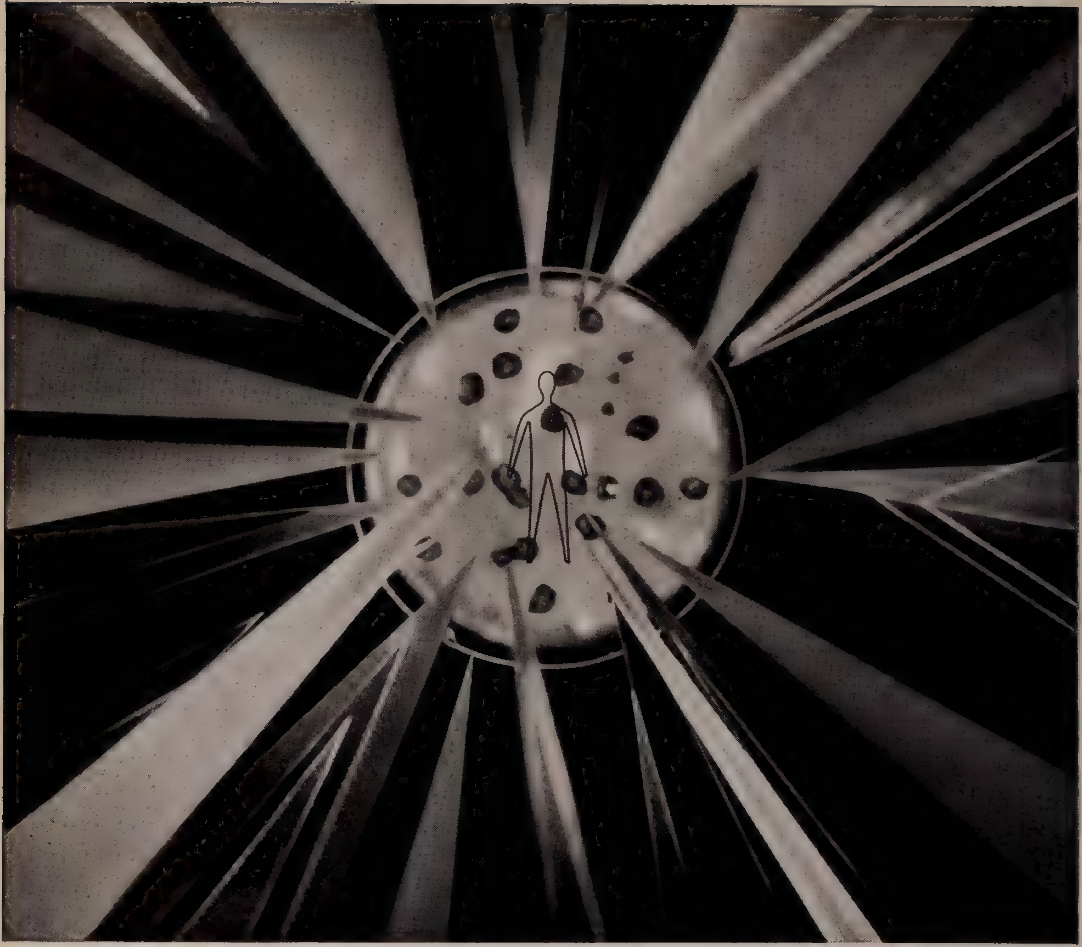

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because... it contains Fungizone, the antifungal antibiotic,
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Robert A. Hardt, President

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lifts the facade of TENSION/ANXIETY New Listica allays tension/anxiety in as many as 89% of cases,[2-13] by selectively inhibiting impulses through internuncial pathways of the central nervous system. Whether the patient's tension/anxiety is psychosomatic or a complication of somatic disorder, Listica reduces or eliminates the excess impulsivity seen in tension/anxiety states.

maintains normal acuity Unlike many drugs, Listica does not affect unconditioned response or normal motor activity. Thus, Listica allays tension and anxiety without inducing apathy or impairing acuity; patients are able to pursue normal activities, such as driving, reading, writing, etc., without interference from drug therapy.

enhances physician-patient rapport As it removes tension/anxiety, fear and frustration, LISTICA PROMOTES EUNOIA*—"a normal mental state." It bares the patient's true somatic condition, and facilitates diagnosis and therapy. Patients are more tractable to concomitant drug therapy, respond better, faster.

without known toxicity or contraindications Listica is safe, as well as effective. Chronic studies[14] in rats (12 months) and dogs (6 months) were free of toxic manifestations at oral dosage levels as high as 200 mg./kg./day (approximately 10 times the recommended human dosage). No macroscopic or microscopic changes in tissues, organs or blood indicative of toxicity were observed, even at doses up to 320 mg./kg. In humans, there have been no adverse blood, urine or cardiac changes; liver profiles were negative, and jaundice has not been noted.

without serious side effects or habituation During three and one-half years of clinical study in 1,759 patients,[2-13] Listica has produced no serious side effects. Less than 4% of patients experienced any side effects, and these were invariably minor and transient. Most frequent (38 cases) was mild drowsiness, which disappeared after the first few days of Listica therapy. Habituation, cumulative effects, or withdrawal symptoms have not been noted, even in patients taking Listica as long as two years.

with convenient dosage and availability One Listica tablet, q.i.d., is the recommended dosage. Listica is supplied in bottles of 50 tablets on prescription only, by pharmacies everywhere. Each tablet contains 200 mg. of Hydroxyphenamate, Armour.

References:

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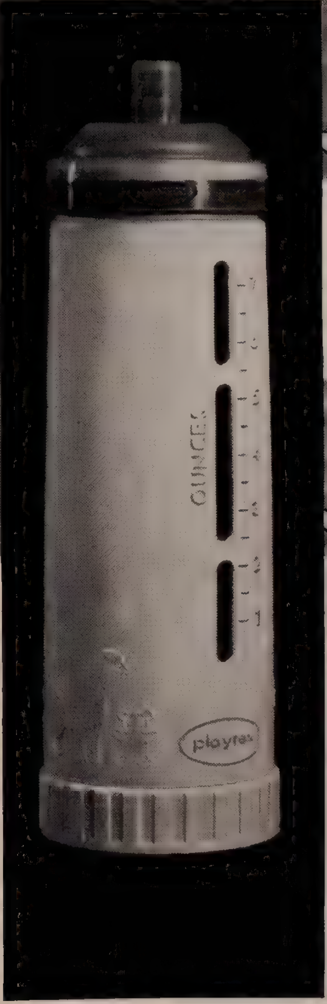
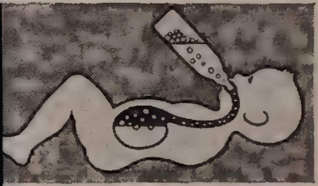
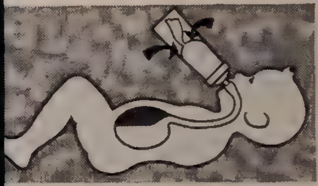
Because the disposable bottle is pre-sterilized, *it eliminates the possibility of contamination through improperly sterilized bottles.*





With conventional bottle *air has to get inside bottle for milk to come out. Nipple often collapses and baby has to suck harder, so more air gets into his stomach. Both overfeeding and underfeeding can ensue, along with the aerophagia and flatulence which can produce colic, spitting up, and after feeding distress.*



Natural design nipple *of Playtex Nurser assures even flow. Its pliable inner bottle contracts with atmospheric pressure as formula is consumed. Baby takes more nourishing formula, less swallowed air to cause discomforting spitting up and colic.*

dramatically reduces spitting up and colic

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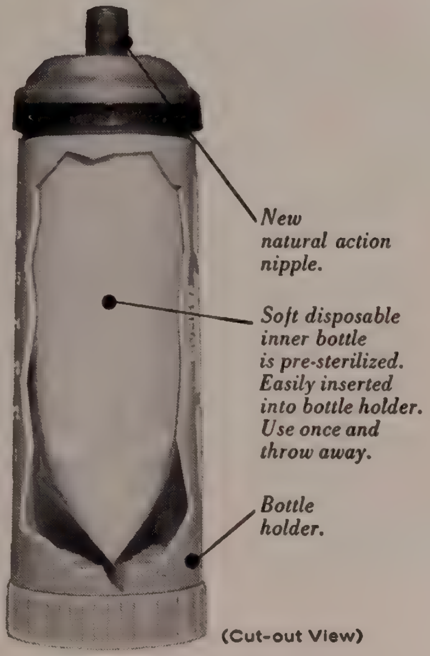
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Bottle holder.
(Cut-out View)

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...or, to be exact, a total of 2,106 ounces in his first two years. And how much he'll need during his first twenty years would have to be measured by the truckload, because the need for the nutrients contained in Florida orange juice continues throughout life.

How our little "limey" or any of your other patients obtain the vitamins and nutrients found in citrus fruits is important to them and to you. There are so many wrong ways, so many substitutes and imitations for the real thing.

For a way that combines real nutrition with real pleasure, there's nothing better than the oranges and grapefruit ripened under Florida's own sunshin

It's *good* nutrition to encourage people to drink th juices and eat the fruits watched over by the Florid Citrus Commission. These men set the world's highes standards of quality in fresh, frozen, canned, or car toned citrus products.

When you suggest to your patients that they hav a big glass of orange juice for breakfast, or for snack, the deliciousness of Florida orange juice wi assure you that they'll *want* to carry out your recom mendation. You'll be helping them to the finest drin there is—by the glassful or the barrel.

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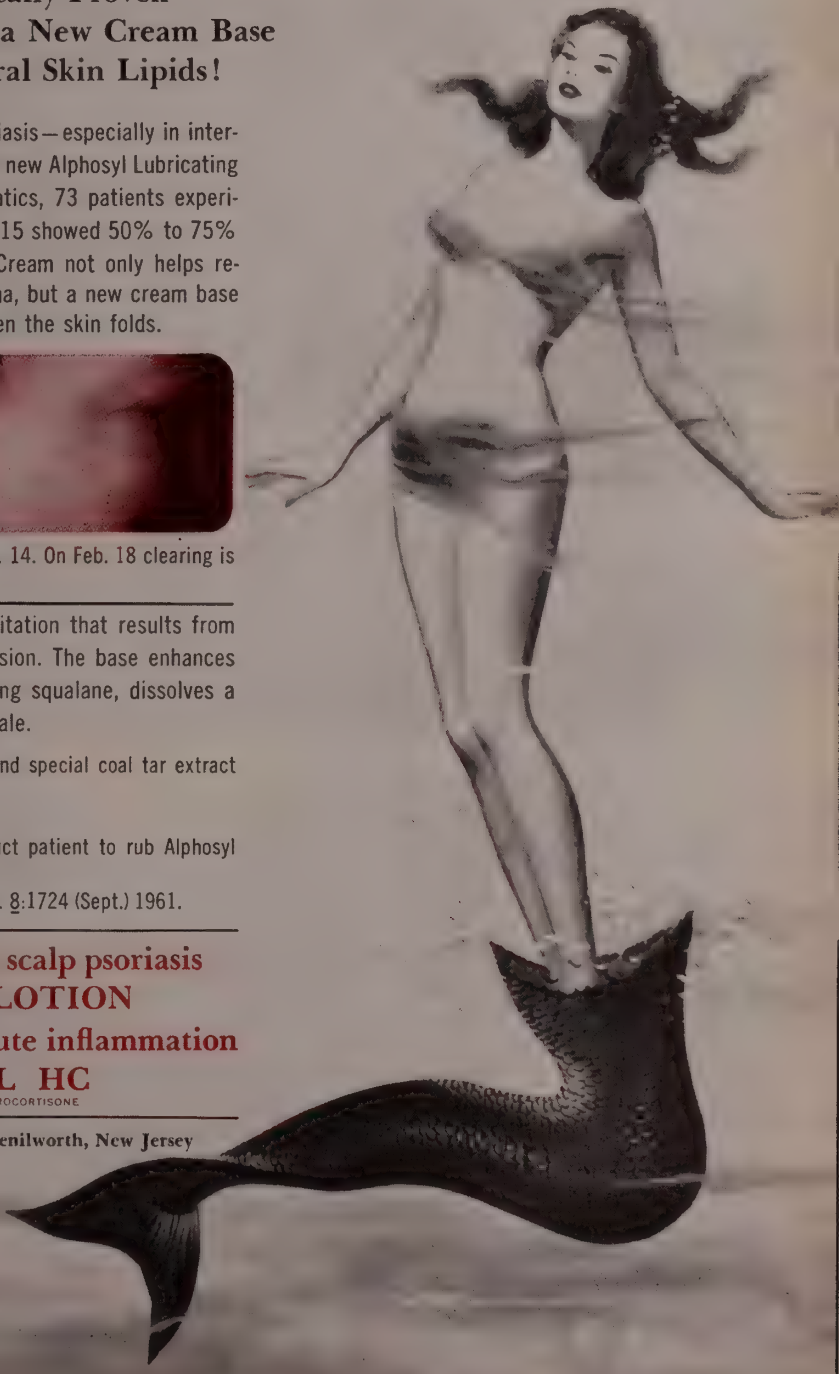
OR PSORIASIS—ESPECIALLY IN INTERTRIGINOUS AREAS

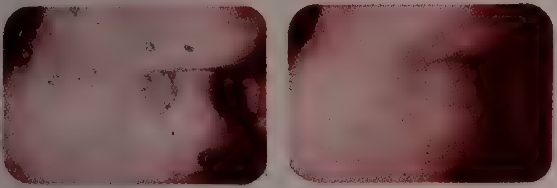
ALPHOSYL® LUBRICATING CREAM

REMOVES SCALES! REDUCES ERYTHEMA! RELIEVES IRRITATION!



Now! The Clinically Proven LPHOSYL Formula in a New Cream Base that Simulates Natural Skin Lipids!

Marked success in treating psoriasis—especially in intertriginous areas—is reported with new Alphosyl Lubricating Cream.[1] In a study of 96 psoriatics, 73 patients experienced 75% to 100% clearing—15 showed 50% to 75% clearing.[1] Alphosyl Lubricating Cream not only helps remove scales and reduce erythema, but a new cream base affords added lubrication between the skin folds.



Patient E. C. Treatment started Jan. 14. On Feb. 18 clearing is almost complete.

Thus, it prevents the painful irritation that results from the rubbing of lesion against lesion. The base enhances moisture retention and, containing squalane, dissolves a cement substance in psoriatic scale.

Active Ingredients: Allantoin 2% and special coal tar extract (Tarbonis®) 5%.
Supplied: In tubes of 60 Gm.
Important Therapeutic Note: Instruct patient to rub Alphosyl vigorously into the skin.
Reference: 1. Bleiberg, J.: Clin. Med. 8:1724 (Sept.) 1961.

For generalized and scalp psoriasis
ALPHOSYL LOTION
For psoriasis—with acute inflammation
ALPHOSYL HC
LOTION WITH 0.25% HYDROCORTISONE

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asthma attack averted
. . . in minutes

patient protected
. . . for hours

Nephenalin®
(the dual-action anti-asthmatic tablet)

. . . works with nebulizer speed—provides four-hour protection

One Nephenalin tablet provides: *air in a hurry*—through sublingual isoproterenol HCl, 10 mg. *air for hours*—through theophylline, 2 gr.; ephedrine, ⅜ gr.; phenobarbital, ⅛ gr.
Dosage: Hold one Nephenalin tablet under the tongue for five minutes to abort the asthmatic attack promptly. Then swallow the tablet core for four full hours' protection against further attack. Only one tablet should be taken every four hours. No more than five tablets in 24 hours.
Supplied: Bottles of 50 tablets. For children: Nephenalin Pediatric, bottles of 50 tablets.
Caution: Do not administer Nephenalin with epinephrine. The two medications may be alternated at 4-hour intervals. Nephenalin should be administered with caution to patients with hyperthyroidism, acute coronary disease, cardiac asthma, limited cardiac reserve, acute myocardial damage, and to those hypersensitive to sympathomimetic amines. Phenobarbital may be habit forming. Thos. Leeming & Co., Inc., New York 17, N.Y.

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you feel
lately, Mrs. K?" *"Well, Doctor, some customers still 'get on my nerves'... but somehow this doesn't bother me as much... I feel better now and people seem easier to get along with..."* "Feel sleepy?" *"No, nothing like that."*

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LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York Lederle

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satisfactory results in 88% of cases

comments: "In practically every instance... the patients experienced relief from dryness and pruritus."

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INDICATIONS

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senile pruritus
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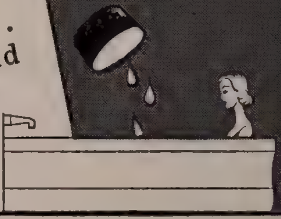
soap dermatitis
ichthyosis



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Patients appreciate pleasant, convenient SARDO.
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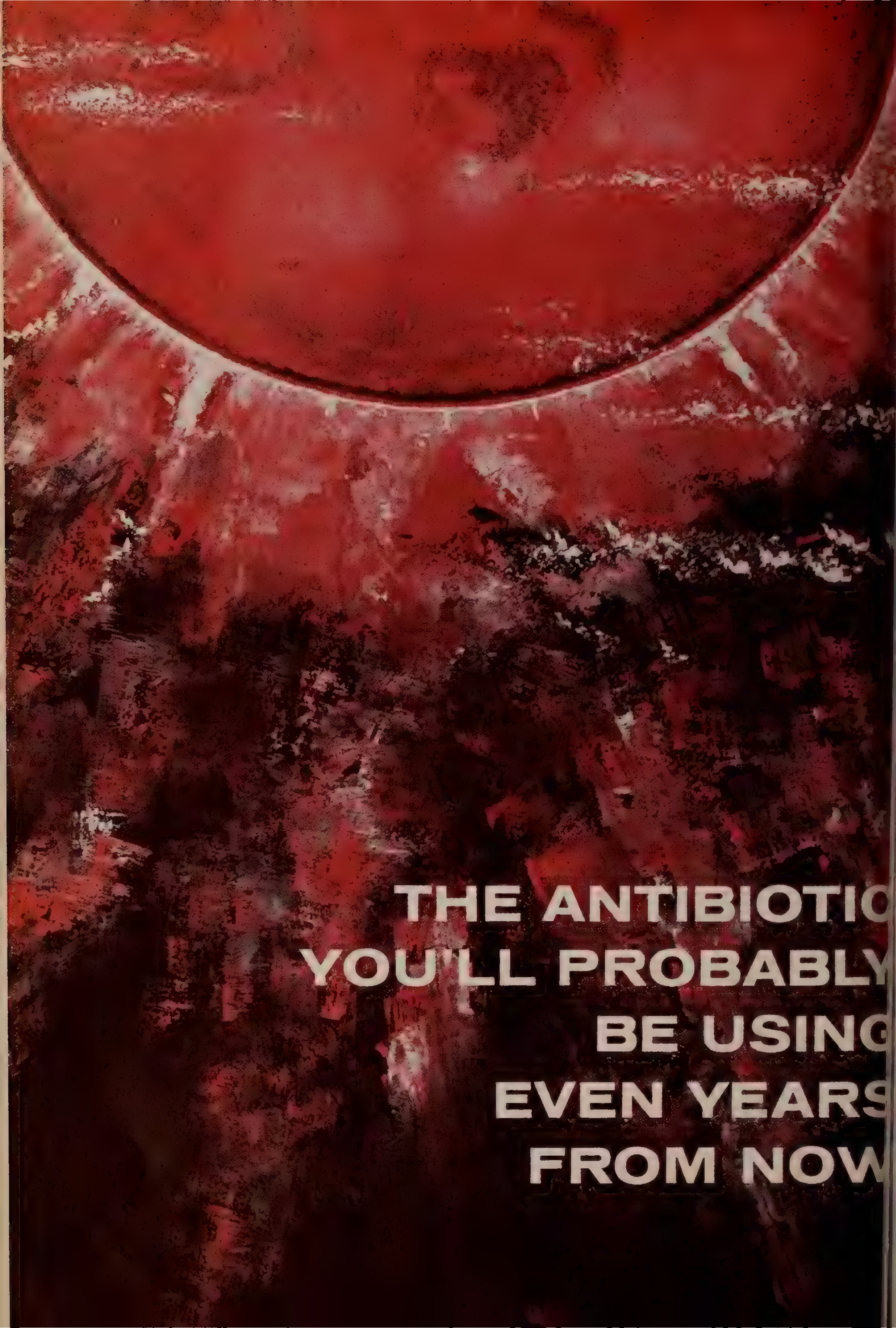

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YOU'LL PROBABLY
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Tao's antimicrobial spectrum includes many Gram-positive and some Gram-negative bacteria—busy pathogens which often cause commonly seen infections. Thus, Tao provides a rapid and decisive response in a wide range of common respiratory, dermatologic, soft tissue and genitourinary infections. Also effective against many resistant Staph. And after four years of clinical experience, Tao continues to be effective against many resistant staphylococci and has been found to be particularly useful in pediatric streptococcal infections.

For effectiveness in antibiotic therapy of common infections, you can count on Tao: ". . . a markedly effective antibiotic agent for general clinical use."[1]

Available as Tao Capsules, 250 and 125 mg.; Ready Mixed Oral Suspension, 125 mg. per 5 cc.; Pediatric Drops, 100 mg. per cc. of reconstituted liquid; Intramuscular or Intravenous, as oleandomycin phosphate. Usual adult dose: 250 to 500 mg., four times daily, depending on severity of infection. Usual pediatric dose: 3 to 5 mg./lb. body weight every 6 hours.

References: 1. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy 5:527 (Aug.) 1958.

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Ready Mixed • Raspberry Flavored • For Pediatric Use

And for nutritional support **VITERRA®** Vitamins and Minerals formulated from Pfizer's line of fine pharmaceutical products

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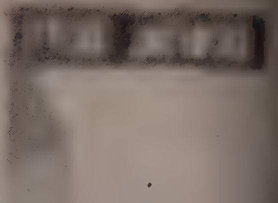

when urinary tract infections present a therapeutic challenge...

CHLOROMYCETIN®

(chloramphenicol, Parke-Davis)

Often recurrent...often resistant to treatment, urinary tract infections are among the most frequent and troublesome types of infections seen in clinical practice.[1,2] In such infections, successful therapy is usually dependent on identification and susceptibility testing of invading organisms, administration of appropriate antibacterial agents, and correction of obstruction or other underlying pathology.

Of these agents, one author reports: "Chloramphenicol still has the widest and most effective activity range against infections of the urinary tract. It is particularly useful against the coliform group, certain Proteus species, the micrococci and the enterococci."[1] CHLOROMYCETIN is of particular value in the management of urinary tract infections caused by *Escherichia coli* and *Aerobacter aerogenes*.[3] In addition to these clinical findings, the wide antibacterial range of CHLOROMYCETIN continues to be confirmed by recent *in vitro* studies.[4-6]

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is available in various forms, including Kapseals® of 250 mg., in bottles of 16 and 100. See package insert for details of administration and dosage.

Warning: Serious and even fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, granulocytopenia) are known to occur after the administration of chloramphenicol. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. Bearing in mind the possibility that such reactions may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used when other less potentially dangerous agents will be effective, or in the treatment of trivial infections, such as colds, influenza, or viral infections of the throat, or as a prophylactic agent. *Precautions:* It is essential that adequate blood studies be made during treatment with the drug. While blood studies may detect early peripheral blood changes, such as leukopenia or granulocytopenia, before they become irreversible, such studies cannot be relied upon to detect bone marrow depression prior to development of aplastic anemia.

References: (1) Malone, F. J., Jr.: *Mil. Med.* **125**:836, 1960. (2) Martin, W. J.; Nichols, D. R., & Cook, E. N.: *Proc. Staff Meet. Mayo Clin.* **34**:187, 1959. (3) Ullman, A.: *Delaware M. J.* **32**:97, 1960. (4) Petersdorf, R. G.; Hook, E. W.; Curtin, J. A., & Grossberg, S. E.: *Bull. Johns Hopkins Hosp.* **108**:48, 1961. (5) Jolliff, C. R.; Engelhard, W. E.; Ohlsen, J. R.; Heidrick, P. J., & Cain, J. A.: *Antibiotics & Chemother.* **10**:694, 1960. (6) Lind, H. E.: *Am. J. Proctol.* **11**:392, 1960.

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relieve U. R. I. distress rapidly

- relieve sneezing, runny nose
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- lift depressed feelings
- reduce fever, chills

For complete details, consult latest Schering literature available from your Schering Representative or Medical Services Department, Schering Corporation, Bloomfield, N. J.

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Each CORIFORTE Capsule contains:

CHLOR-TRIMETON® (brand of chlorpheniramine maleate)	4 mg.
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phenacetin	0.13 Gm.
caffeine	30 mg.
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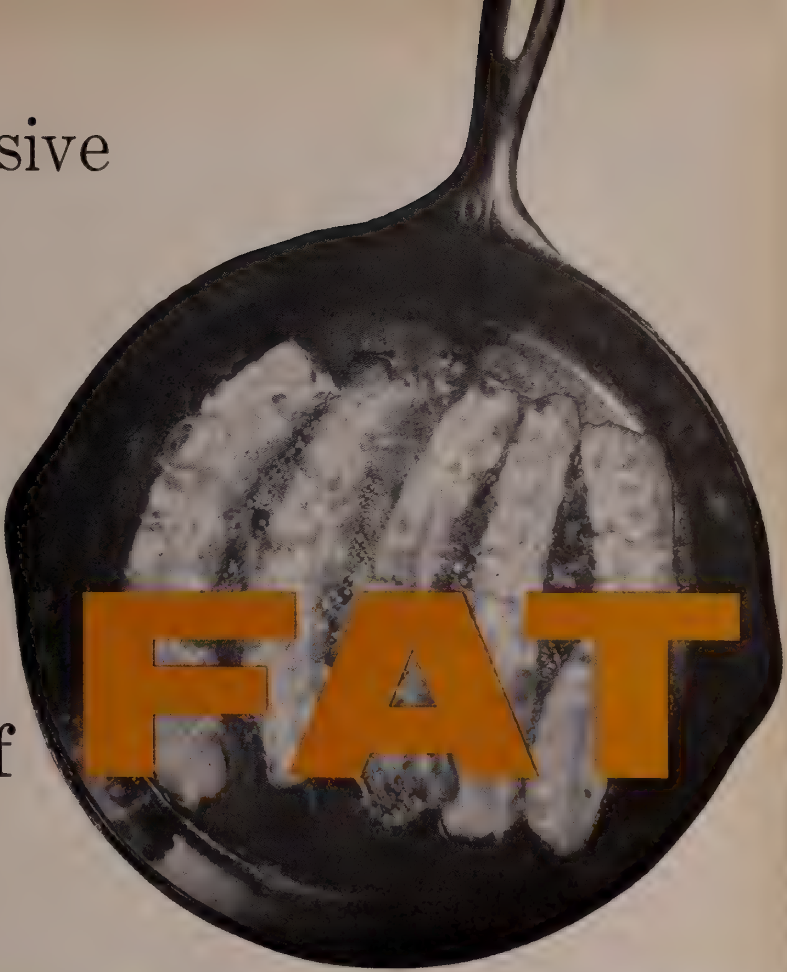

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Dosage: 1 or 2 tablets with water just before each meal.

Supply: Bottles of 48 tablets.

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Lipancreatin Bile Salts Cellulase

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**The Significance of Lipancreatin* (Pancreatic Enzymes Concentrated 'Organon')

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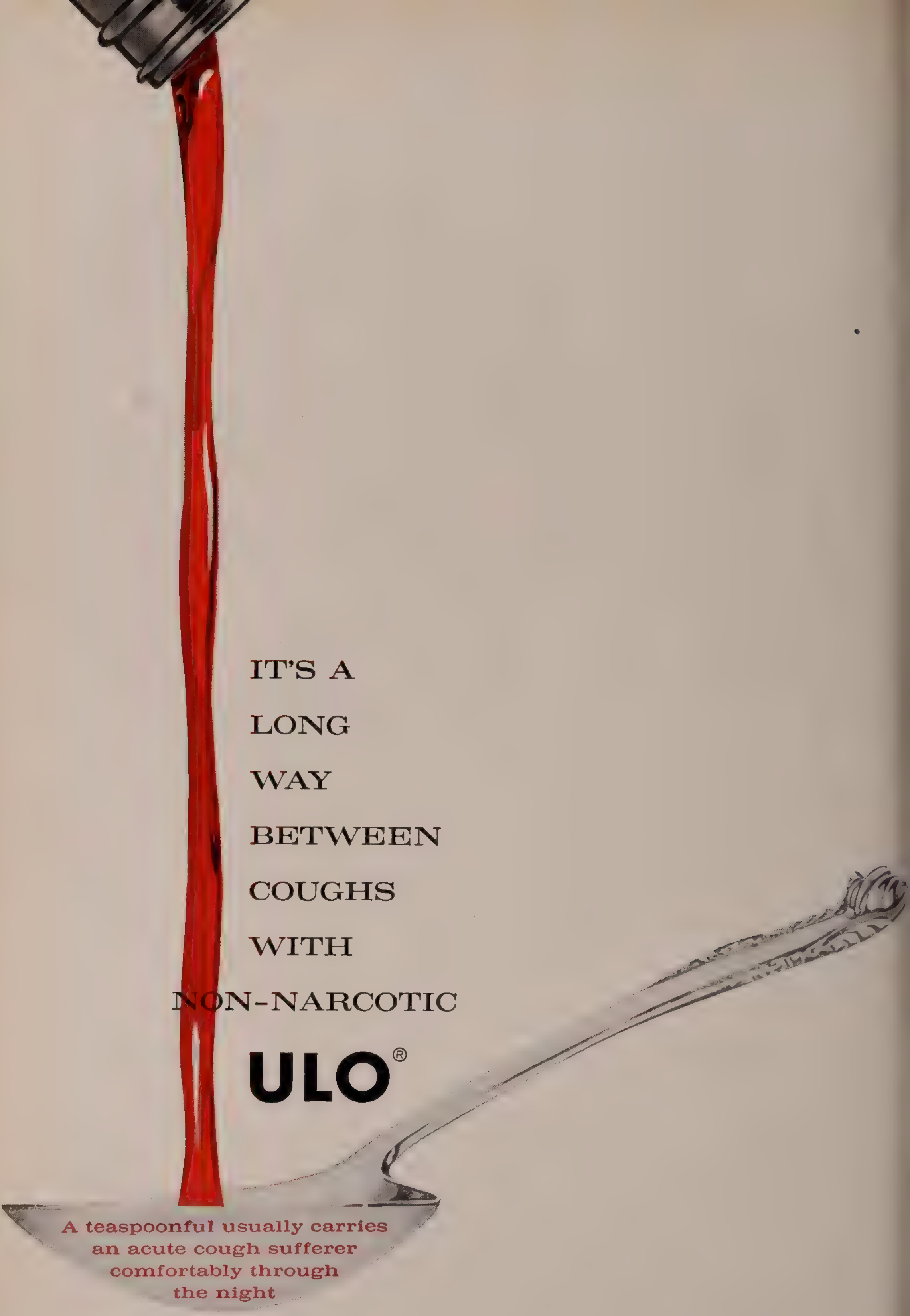
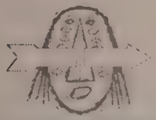

IT'S A
LONG
WAY
BETWEEN
COUGHS
WITH
NON-NARCOTIC
ULO®
A teaspoonful usually carries
an acute cough sufferer
comfortably through
the night

FOR CONTROL OF ACUTE COUGH AND COLD DEMONS

ULO®
syrup for control of acute cough



ULOMINIC®
syrup for control of acute cough
with allergic reactions

ULOGESIC®
tablets for control of acute cough
and relief from associated aches, pain, and fever

INHIBITS COUGH IMPULSE FOR 4 TO 8 HOURS Non-narcotic ULO equals the cough suppressant action of narcotics; maintains its effect far longer; and avoids the limitations and side effects of narcotics.	**ULO®** non-narcotic molecule chlophedianol HCl
COUNTERACTS IRRITATION IN PHARYNX, LARYNX, TRACHEA, AND BRONCHI	**DIAFEN®** fast-acting antihistaminic diphenylpyraline HCl
RELIEVES CONGESTION	**PHENYLEPHRINE HCl** sympathomimetic
MAKES VOLUNTARY COUGH MORE PRODUCTIVE	**GLYCERYL GUAIACOLATE** expectorant and demulcent
ALLEVIATES ASSOCIATED ACHES AND DISCOMFORTS AND ABORTS FEVER	**APAP** analgesic and antipyretic

INDICATIONS:
For acute cough associated with:
Upper Respiratory Infections
Common Cold
Influenza
Pneumonia
Pertussis
Pleurisy
Bronchitis
Tracheitis
Laryngitis
Croup
Allergies (Ulominic and Ulogesic)

CONTRAINDICATIONS:
Although no contraindications for Ulominic or Ulogesic are known, they should be used only for acute cough.

CAUTION:
Since Ulominic and Ulogesic contain an antihistaminic agent, drowsiness may occur. As they also contain a sympathomimetic agent, they should be used with caution in coronary artery disease, glaucoma, hypertension, and hyperthyroidism.

SIDE EFFECTS:
ULO
These occur only occasionally and have been mild. Nausea and dizziness have occurred infrequently; vomiting and drowsiness rarely. As with all centrally acting drugs, an infrequent case may develop excitation, hyperirritability and nightmares. The symptoms disappear within a few hours after the drug is discontinued. In three cases (1 adult and 2 children) where the drug was continued in large or even excessive amounts after stimulation was present, hallucinations developed. Upon withdrawal of the medication, the patients recovered rapidly within a few hours.

ULOMINIC and ULOGESIC
Side effects from ULOMINIC or ULOGESIC occur occasionally and are mild. Nausea, dizziness, and dryness of the mouth occur infrequently; vomiting and drowsiness rarely.

DOSAGE:
ULO
Adults: 25 mg. (1 teaspoonful) 3 or 4 times daily as required.

Children: 6 to 12 years of age — 12.5 to 25 mg. (½ to 1 teaspoonful) 3 or 4 times daily as required.

2 to 6 years of age — 12.5 mg. (½ teaspoonful) 3 or 4 times daily as required.

ULOMINIC
Adults: One teaspoonful (5 cc) four times daily.

Children: 6 to 12 years — ½ teaspoonful (2.5 cc) 4 times daily.

2 to [illegible] years — ¼ teaspoonful (25 drops) 4 times daily.

ULOGESIC
Adults: Two tablets 4 times daily.

Children: [illegible] to 12 years — one tablet 4 times daily.

AVAILABILITY:

ULO SYRUP Bottles 12 oz.

ULOMINIC SYRUP Bottles 1 pint.

ULOGESIC TABLETS
Bottles of 100 tablets.

CAUTION: Federal Law prohibits dispensing without prescription.

FORMULAS:

ULO SYRUP — Each 5 ml. teaspoonful contains:

chlophedianol HCl* [alpha-(2-dimethylaminoethyl)-o-chlorobenzhydrol • HCl]	25 mg.
chloroform, U.S.P.	0.001 ml.

Alcohol 6.65 per cent in a pleasant flavored syrup base

ULOMINIC® SYRUP — Each teaspoonful (5cc) contains:

chlophedianol HCl* [alpha-(2-dimethylaminoethyl)-o-chlorobenzhydrol • HCl]	15.0 mg.
diphenylpyraline HCl (1-methyl-4-piperidyl-benzhydryl ether • HCl)	1.0 mg.
phenylephrine HCl	5.0 mg.
glyceryl guaiacolate	100.0 mg.
alcohol	6%

ULOGESIC® — Each tablet contains:

chlophedianol HCl* [alpha-(2-dimethylaminoethyl)-o-chlorobenzhydrol • HCl]	7.5 mg.
diphenylpyraline HCl (1-methyl-4-piperidyl-benzhydryl ether • HCl)	0.5 mg.
phenylephrine HCl	2.5 mg.
glyceryl guaiacolate	25.0 mg.
acetaminophen	162.5 mg.

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NORTHRIDGE, CALIFORNIA

*PATENTS PENDING

when your tongue

blade points to respiratory infection

Ilosone® works

to speed recovery

Through the years, Ilosone has built an impressive record as an effective antibiotic in common bacterial respiratory infections. Numerous published clinical studies attest to excellent therapeutic response with Ilosone. Decisive recovery has become a matter of record.

Efficacy of propionyl erythromycin and its lauryl sulfate salt in 803 patients with common bacterial respiratory infections

92.3% 235 patients	Tonsillitis*
88.3% 317 patients	Acute Streptococcus Pharyngitis*
95.3% 85 patients	Bronchitis* (Bacterial Complications)
88.6% 166 patients	Pneumonia*

*References supplied on request.

The usual dosage for infants and for children under twenty-five pounds is 5 mg. per pound every six hours; for children twenty-five to fifty pounds, 125 mg. every six hours.

For adults and for children over fifty pounds, the usual dosage is 250 mg. every six hours.

In more severe or deep-seated infections, these dosages may be doubled.

Ilosone is available in three convenient forms: Pulvules®—125 and 250 mg.†; Oral Suspension—125 mg.† per 5-cc. teaspoonful; and Drops—5 mg.† per drop, with dropper calibrated at 25 and 50 mg.

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Editorials

The Faraway Island

This is the name the mainland Indians gave to the island of Nantucket, lying 30 miles out to sea from the coast of Massachusetts.

Imagine a northern Bermuda increased in size from 19 square miles to 47 square miles. Despite differences in climate, vegetation, and building materials, there are many similarities between Nantucket Island and Bermuda. The same clean, sea-swept air, narrow, winding roads bordered by high, close-clipped hedges, flower-covered cottages, and swarms of cyclists everywhere give one a feeling of having seen this somewhere before. The long stretches of untrammeled beach and lonely central moors of bracken and broom bring thoughts of other islands.

In spite of wars and pestilence and drastic economic changes, rugged men and women have lovingly tended and thrived on Nantucket for more than three hundred years.

The town of Nantucket, the business and civic center of the island where the off-islander disembarks, retains a strong flavor of having gained its livelihood from the sea. Here are preserved impressive memorials of the pioneers, of the great whaling days, and of succeeding efforts to maintain the island's life. From the humblest cottage to the most aristocratic mansion tender and scholarly care has been expended to keep history burnished bright.

Of particular interest to the physician visitor are the medical affairs of this distant island community. With a year-round population of 3,500 which swells enormously to more than 10,000 in the summer, one asks immediately how medical care is provided.

There are six doctors who live and practice on the island. Doctors who are summer residents on the island are available during this period for consultation if it is requested. Of the six practicing physicians five are general practitioners; three of these perform the major surgery, and all practice obstetrics. There is one nose and throat specialist.

There is no referring back and forth between the general men since each is competent, through necessity, to handle any situation which arises. Anesthesia and x-ray and electrocardiographic interpretation are no problem because these men have been doing these things ably themselves all their professional lives. It is refreshing for the spoiled city doctor to know such men exist.

Behind these men stands the Nantucket Cottage Hospital of 50 beds, founded in 1912, expanded and modernized five years ago at a cost of $1.5 million, and now fully paid for. This hospital is the equal in plant and equipment to any of comparable size on the mainland anywhere. The hospital is accredited and has an actively functioning tissue committee. It has a full-time lay director who works closely with the trustees and the medical staff. An arrangement exists with the Peter Bent Brigham Hospital whereby highly specialized medical help is called down from Boston at any time for any patient who requires it and is too ill to be moved.

There is no house staff and no nursing school for neither is feasible nor necessary. The nursing staff consists of 20 nurses, mostly registered, living on the island, who can give enough part-time care for adequate coverage. There is no nursing problem in the summer months because many recent graduates like to combine work and vacation on the island.

Anyone interested in hospital management could learn much from the solvency of the Cottage Hospital's operation. A working combination of Yankee thrift and ingenuity with excellent public relations makes this possible. The annual deficit of about $60,000 is made up half from interest on endowment and half from an annual stand-by appeal. Summer residents have much pride in their hospital and interest in their medical care. They assist the permanent residents greatly both in raising capital funds and in the annual deficit-clearing appeal.

Nantucketers, whether they be full or part-time residents, go about their medical affairs wisely and quietly in a manner befitting their beautiful island home—The Faraway Island

Operations of the Food and Drug Administration

Commissioner George P. Larrick of the United States Department of Health, Education, and Welfare in a recent speech to the American Petroleum Institute described his department as follows:

> The Food and Drug Administration is a part of the Department of Health, Education, and Welfare. Our responsibilities include the enforcement of the Federal Food, Drug, and Cosmetic Act and the Federal Hazardous Substances Labeling Act. We have over 2,200 employes, of which two thirds are stationed in 18 district offices and 40 Inspection Stations in principal cities throughout the country.
>
> Our Washington office includes administrative, research, and technical units. In enforcing these Acts, our inspectors make periodic investigations of establishments where products subject to the laws are manufactured, held, or sold, to determine their compliance with the law. They collect samples from interstate shipments, and our scientists examine the samples to determine whether or not the shipments are legal.
>
> Both laws provide for seizure through the Federal courts of illegal products to remove them from the market. Persons responsible for introducing such products into commerce may be prosecuted. Injunctions may be obtained to restrain individuals and firms from further violation of these laws.
>
> We review evidence submitted as to the safety of new drugs before they are placed on the market, and determine the safety of color additives used in foods, drugs, and cosmetics. Batches of insulin and five of the most important antibiotic drugs and their derivatives are checked for purity and potency before they are sold. The law provides for the establishment of the amount of pesticide residues that may safely remain on food. Regulations are issued stating safe conditions for using food additives. Imports are examined to determine that they meet the requirements of the United States laws.
>
> Our basic philosophy is to employ preventive measures rather than punitive enforcement but where necessary we vigorously pursue enforcement in the courts.

As government offices go this is a comparatively small staff. It has a tremendous job on its hands already. Proposed legislation would add to its responsibilities. In the matter of providing uniformity in generic-named drugs alone the administrative process would be staggering. The therapeutic efficacy of a drug cannot be fully determined by U.S.P. assay. Most pharmaceutical products contain ingredients other than the active drug, and in addition the manufacture of these products involves a series of operations—mixing, filtering, temperature control, compressing, and coating.

Any of these operations if improperly controlled can affect the usefulness of the product adversely without chemical assay showing any deviation from "official standards."

Uniform quality control in all its minute details is a large order. It can be accomplished only by the pharmaceutical industry and government bureaus working understandingly together.

They have done so in the past, and after the present sound and fury is over they will do so in the future. Fairness for all is but another way of saying "equal justice under law."

Knowledge and evil

A frontier has been defined as wherever men face facts. Ever since the first military fission bomb was discharged at Alamogordo in 1945 we have been on a frontier of gigantic power for destruction.

It is important for all thinking persons to have some understanding of this power. We present, therefore, as a special article in this issue a presentation on this subject by 50 scientists of the New York area released by the New York Academy of Sciences. This report on the results of a 20-megaton thermonuclear explosion on Columbus Circle is based on unclassified information available to anyone. From time to time we have presented in the pages of this JOURNAL articles on the constructive uses of atomic energy. We feel it our stern duty now to present this article on the destructive uses of the same power. By knowledge we can circumvent evil. Knowing the devastating effects of this weapon we can understand the problems of civil defense and appreciate the awesome responsibility of the President of the United States. Knowing this evil we can back up our national and world leaders more intelligently in their heroic attempts to outlaw this horror.

Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the NEW YORK STATE JOURNAL OF MEDICINE from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the JOURNAL, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

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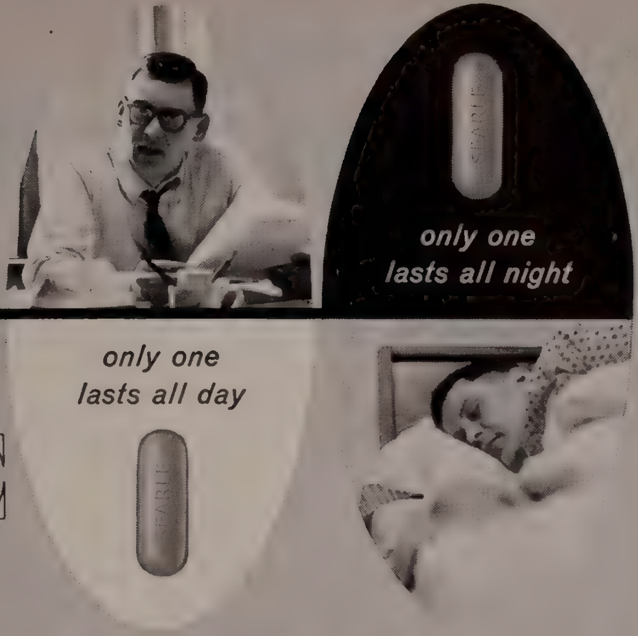

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*Cass, L. J., and Frederik, W. S., Am. Pract. Dig. Treat., 2:844, 1951.

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Ultrafiltration with a Parallel Flow, Straight Tube Blood Dialyzer

Introduction and Historical Review

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VARIOUS METHODS *of extracorporeal ultrafiltration of the blood, which permits the extraction of a protein-free solution from the blood, have been tried since 1947. A dialyzer-ultrafilter has proved to be more effective as a method of removing intractable edema fluid than dialysis with a hypertonic solution or peritoneal lavage. The MacNeill blood dialyzer has been in use by the authors since 1954. With this apparatus ultrafiltration may be carried out simultaneously with dialysis or exclusively. Ultrafiltration without the simultaneous use of washing fluid was used successfully in 7 patients with intractable edema due to congestive heart failure. Three main groups of patients achieve important benefit from the use of extracorporeal ultrafiltration of the blood: patients with congestive heart failure who become unresponsive to salt restriction, diuretic therapy, digitalis, and other more usual forms of therapy; patients with congestive heart failure who can undergo corrective cardiac surgery if their decompensation can be brought under control temporarily; and patients with acute and chronic renal failure who become significantly overhydrated. Care must be exercised so that fluid will not be extracted so rapidly as to cause hemoconcentration, dehydration, hypovolemia, hypotension, and shock. More extensive analyses of ultrafiltrates obtained in this manner are indicated; the procedure opens the way to study of diffusible substances which appear in low concentration in the blood; this may be of particular value in the elucidation of the chemical causes of the uremic syndrome.*

In 1947, Malinow and Korzon[1] suggested that extracorporeal ultrafiltration of the blood might be a useful approach to the investigation of clearances. Observing that ultrafiltration permits the extraction of a protein-free solution from the blood, these investigators recognized this technic as a new approach to the study of bound and unbound constituents of the blood. They sought to compare the effects of a synthetic ultrafilter with human renal clearance. With this objective in mind they developed an apparatus which could be used in an attempt to prolong the lives of uremic animals. Because it was considered to be of consistent porosity and highly reproducible, cellophane was chosen as the filter membrane. Other advantages of this membrane were its neutral reaction, its ability to withstand high pressures when supported, and the lack of change in its permeability following sterilization with steam.

A description of the apparatus was published in the original article by Malinow and Korzon.[1] It was composed of a vacuum chamber, a filter complex, a blood pump, and associated tubing. The capacity of a single tube was 30 ml., and its surface area was 0.04 M². With a blood flow of between 15 and 100 ml. per minute and under a filtration pressure of 800 mm. Hg, about 60 ml. of ultrafiltrate could be obtained from a single tube in an hour. The cellophane tubing employed* was probably similar to the membrane then being used by Kolff[2,3] for dialysis.

Many different maneuvers were carried out by Malinow and Korzon with this apparatus, up to 20 cellophane tube units being used at one time. Ultrafiltration was carried out following sterilization of the membrane with steam at 250 F. for fifteen minutes. The process was carried out continuously over periods of up to ten hours. The blood flow in these experiments varied from 15 ml. to 100 ml. per minute. Liquids of different viscosities were used in the blood chambers, for example, blood versus saline solution. In none of these experiments was hemolysis observed, and in no case did a change in the filtration rate take place. The application of higher pressure within the blood chamber, however, resulted in an increase in the rate of ultrafiltration. The ultrafiltrates obtained from both human and dog blood were found to be free of protein and usually contained amounts of chloride, urea, and nonprotein nitrogen identical to those in the blood.

The limitations of this method in the control of uremia were quite obvious in that the urea clearance values were very low compared with those reported at that time for extracorporeal hemodialysis.[4,5] However, this apparatus had clear advantages: ease of sterilization, lack of hemolysis, and the extraction of relatively large amounts of ultrafiltrate. While the authors recognized that the technic offered an important approach to the study of bound and unbound constituents of the blood, they did not mention the potential value of the method in the removal of edema fluid.

Grandjean in 1951[6] carried out ultrafiltration studies with Rehberg membranes. The latter, however had different characteristics from those of the Visking membrane with which this paper deals principally.

In 1951, Skeggs, Leonards, and Kahn[7] carried out successful experiments with the ultrafiltration of the blood of normal and edematous dogs. In the apparatus they used, the Skeggs-Leonards artificial kidney, a high-pressure system is used to circulate the subject's blood through an arrangement of multiple, paired, short, broad sheets of cellophane, which are placed between firm rubber pads. The blood is pumped between the cellophane sheets while the dialyzing fluid flows the opposite way along grooves in the rubber pads.

In 1952, Lunderquist[8] described the efficacy of Alwall's dialyzer-ultrafilter which was intended for human use. The design had been described earlier by Alwall.[9,10] In this device the cellophane tubing (1.6 M². cellophane surface area) through which the blood flows is wrapped around the exterior surface of a longitudinally grooved metal cylinder placed within another cylinder which has grooves on its inner surface. On the application of a vacuum on the outer surface of the tubing, ultrafiltration is effected. In his report Lunderquist included a preliminary description of ultrafiltration treatments. From 2 edematous patients who were treated for two hours each, the yield of ultrafiltrate was approximately 700 ml. per hour. From another patient, 7,400 ml. of ultrafiltrate were extracted during a nine-hour treatment period; the symptoms of edema disappeared during ultrafiltration. The same patient later underwent ultrafiltration for a seventeen-hour period; 8,600 ml. of ultrafiltrate were obtained.

Using the apparatus of Alwall, in 1952 Bernard, Fischer, and Bassett[11] showed that acute overhydration in renal insufficiency may be alleviated by the use of the extracorporeal hemodialyzer. These experiments were carried out in dogs in which the removal of water from the circulating blood by ultrafiltration resulted in a definite decrease in cerebrospinal fluid pressure. Confirmatory evidence of the removal of fluid was found in weight measurement and in hematocrit values.

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* Visking Corporation, Chicago, Illinois.

Kolff and Leonards in 1954[12] dealt with the reduction of edema in patients who had been resistant to common methods of treatment or in patients in whom the usual forms of treatment were contraindicated. They described three methods of removing edema fluid by dialysis-ultrafiltration: dialysis with a hypertonic solution (the addition of 2 to 5 per cent glucose to the usual dialyzing bath was recommended to augment the osmotic pressure of the washing fluid and thus attract water from the blood); peritoneal lavage using a hypertonic solution; and ultrafiltration, using the dialyzer of Skeggs, Leonards, and Heisler.[13]

Kolff and Leonards presented an example in which a weight loss of 2.7 Kg. was effected in one treatment, using dialysis with a hypertonic solution and the rotating drum-type artificial kidney. Earlier, Lewis *et al.*[14] and others[2,15,16] had reported the reduction of pulmonary edema by the use of the artificial kidney employing a hypertonic bath fluid. Lewis had reported a weight loss of 4 Kg. in six hours using concentrations of glucose of up to 5 per cent in the rinsing fluid. He found the method unpredictable and usually not so potent as one would wish.

When the latter procedure is used, the glucose concentration of the blood returning to the patient is very much increased. Several investigators have found that the blood glucose level may rise to more than 700 mg. per 100 ml.[12,16-18] Among them, Kolff has attempted to combat the high blood sugar levels with insulin intravenously. Ten to 20 units every half-hour sometimes have been necessary. Water shifts (fluid retention by the patient) have been found by some of these observers to follow the rapid diffusion of glucose into the patient.

Alwall *et al.*,[19] in experiments with rabbits, found that the use of hypertonic glucose solutions to extract water from the blood was far less efficient than ultrafiltration and could result in dangerous hyperglycemia.

Kolff and Leonards' second method for the removal of edema fluid by peritoneal lavage, using a rinsing fluid made hypertonic by the addition of from 2 to 10 per cent glucose, has been successful in some patients. Encouraging results with this method have been seen by Girard *et al.*[20] Kolff and Leonards described a case in which 4 L. of fluid were removed in ten hours of lavage. Their peritoneal dialysis was carried out continuously, according to the method of Legrain and Merrill.[21]

The third method of fluid extraction recommended by Kolff and Leonards was the application of the artificial kidney of Skeggs, Leonards, and Heisler.[13] The cellophane membranes were supported by stationary fine ridges, and negative pressure was applied from a water aspirator to the outflow tube of the rinsing fluid while the inflow tube, carrying the bath to the dialyzer, was partially clamped. By this means it was possible to remove from 1 to 1.2 L. of ultrafiltrate per hour from the blood while dialysis was being accomplished. In the laboratory, the investigators found that normal dogs could be killed by the rapid removal of about 800 ml. of fluid from the blood stream. This finding prompted them to caution against dehydrating a patient too rapidly. They recommended that blood pressure and hematocrit readings be determined frequently. In their series 4 patients underwent ultrafiltration; in each instance temporary improvement was obtained.

In 1 case the remaining edema fluid was rapidly and spontaneously eliminated. Another of the patients showed continued improvement. The avoidance of postdialytic oliguria in 1 case may have been due in part to the addition of urea to the rinsing fluid. So that rapid reaccumulation of fluid in the patient would not occur, these investigators employed fluid restriction during the first few days after ultrafiltration.

Using the same type of apparatus as that employed by Kolff and Leonards, Keitzer, Ford, and Miller in 1954[22] described the successful treatment of a forty-nine-year-old white male with anasarca which had been refractory to treatment with salt restriction and mercurial diuretics.

In 1955, Elkinton and Danowski[23] reported a case in which 1,500 ml. of fluid were removed via ultrafiltration with the Skeggs-Leonards dialyzer from an overhydrated patient in acute renal failure. There was concomitant clearing of the clinical signs of pulmonary edema. Also using this apparatus, Anthonisen *et al.*[24] found that by varying the gradient of hydrostatic pressure between the blood and the bath fluid, the rate of fluid extraction could be regulated. They pointed to the achievement of a weight loss of from 500 to 600 Gm. per hour using such manipulations. Broadbent and Odel,[25] who also employed the Skeggs-Leonards dialyzer, found that 250 ml. of fluid were removed from the blood each hour during a standard dialysis as a result of the "normal" ultrafiltration occasioned by the elevated pressure within the blood chamber of the dialyzer. They replaced the fluid loss with isotonic sodium chloride solution which was administered intravenously at the rate of 250 ml. per hour.

One of the disadvantages of the Kolff-Brigham artificial kidney, according to Shackman and Milne,[26] is the lack of ultrafiltration during dialysis. They found that from 500 to 600 ml. of fluid are transferred into the patient during a six-hour period of dialysis. In more than 1 of the patients they reported on in 1957, pulmonary edema developed during dialysis; in 1 case this undesired eventuality appeared to contribute to the fatal outcome. The osmolarity of the bath fluid used by these investigators was approximately 300 milliosmols per liter and was prepared to match closely the osmolarity of normal blood. They emphasized, however, that the osmolarity of the blood of a patient with a blood urea nitrogen of 500 mg. per 100 ml. is approximately 370, and hence, in the dialysis of such a patient with the Kolff-Brigham device, some water will be transferred inevitably from the relatively low osmotic pressure zone represented by the bath to the relatively high osmotic pressure compartment represented by the blood. They concurred in the opinion earlier expressed by Alwall *et al.*[19] that the addition of large amounts of glucose to the bath would not be eminently successful because this solute passes so rapidly across the cellophane barrier into the blood.

Following its introduction in 1956, the Kolff twin-coil "kidney" was studied considerably in regard to its ultrafiltration capabilities.[27,28] In this apparatus high pressure is used to force blood through two long, flattened coils of cellophane tubing which are held tightly between plastic-covered Fiberglas screens housed in a metal container. The dialyzing bath is forced under pressure through an opening in the bottom of the container and overflows freely at the top. Since the effective pressure within the blood chamber of this device is considerably greater than the hydrostatic pressure surrounding the cellophane tubing, water can be transferred from the blood to the bath in appreciable quantities. It has been said that fluid can be transferred at rates of between 700 and 1,000 ml. per hour.[29]

In their work with the Kolff twin-coil kidney, Meyer *et al.*[30] found that when the blood is pumped through the apparatus under a pressure of from 180 to 300 mm. Hg, the hydrostatic pressure gradient causes the ultrafiltration of from 200 to 500 ml. of water per hour.

Pierce[31] reported an interesting group of ultrafiltration investigations in 1958. These experiments were carried out in dogs, using the Skeggs-Leonards dialyzer. The data indicated that all fluid extracted by ultrafiltration with an isosmotic bath is obtained from the extracellular fluid compartment, little or no cell water being removed. Moreover, it was demonstrated that if ultrafiltration is carried out while a hyperosmotic dialyzing bath is used, some intracellular water as well as extracellular fluid will be extracted. Overhydrated animals which had not yet reached the state of cardiac decompensation tolerated fluid removal by ultrafiltration quite well. Poor results were observed when cardiac decompensation had occurred. As in the experiments of Kolff and Leonards,[12] it was found in Pierce's studies that the removal of excessive amounts of fluid brought about the death of the animal. The extraction of fluid representing more than from 5 to 7 per cent of the total body weight of the dog, by ultrafiltration during dialysis, led to fatality. It was noted that hypotension would develop before death and that if the weight loss were replaced immediately by intravenous Ringer's solution, the animal would survive.

A new hemodialyzer with a cellophane surface area of 1 M^2. was described in 1959 by Kupfer and Rosenak.[32] In this device, Lucite rods are inserted through the entire lengths of 36-inch cellophane tubes. The rods support the tubes, which are mounted in parallel fashion and placed in a large tank containing a standard dialyzing solution, which is agitated. The authors demonstrated ultrafiltration of the fluid from the blood chamber in vitro (using aqueous solutions), augmenting the pressure by increasing the constriction of the outflow blood tube. During this procedure the cellophane tubes become progressively distended. It was found that the rate of ultrafiltration increased, curvilinearly, from 0 to 7.8 ml. per minute, as the intraluminal pressure was increased from 0 to 120 mm. Hg.

Lemmon *et al.*[33] have reported the use of the Kolff twin-coil kidney for what they term "renal dialysis" in a patient with intractable edema. Renal dialysis is not a legitimate name for the procedure used, which involved the standard technic for dialysis-ultrafiltration with this apparatus, plus the use of a hyperosmotic dialyzing bath to enhance ultrafiltration. The success of the technic in this case was especially rewarding, in that the patient was so much improved that she was able to undergo cardiac surgery. The repair of her cardiac defect effected a complete cure.

Materials and methods

Prior to the work of Malinow and Korzon, one of us (A.E.M.) in 1942 drew up several designs for membrane blood oxygenators. These designs were based on the principle of the transfer by diffusion of dissolved respiratory gases across the membrane, to and from the blood. Very compact arrangements were needed for such a membrane interface, not only so that the total size of the apparatus might be manageable, but also to reduce to a minimum the amount of blood required to fill the blood channels.

One of these designs was revived in 1948 in the development of a study of laboratory dialysis. Units were constructed and exhibited in 1949 and 1953.[34–36]

The successful use of dialyzing technics with other apparatuses by Kolff,[2] Merrill *et al.*,[16,37] Murphy *et al.*,[38] Skeggs, Leonards, and Heisler,[13] Alwall,[9] Kyle *et al.*,[39] Doolan, *et al.*,[40] and others, served as encouragement to the continued development of this very compact blood dialyzer. The small blood volume requirement of the apparatus, together with its portability, appeared to offer a practical means to the extension of the blood dialyzer technic into a wide range of investigative situations.

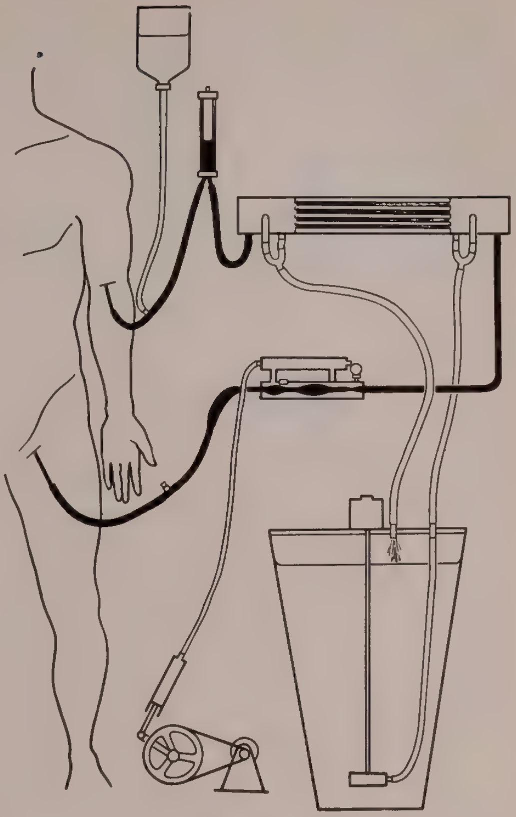

FIGURE 1. The complete MacNeill dialyzer circuit. The blood is removed from the inferior vena cava via a saphenous vein cannula. The piston-powered blood pump circulates the blood through the cellophane tubes in the dialyzer whence the blood flows through the flow meter and then returns to the patient's circulation via an antecubital vein cannula. Simultaneously the dialyzing bath is propelled through the outer chamber of the dialyzer by the bath pump. The fluid falls back into the bath reservoir by gravity. Blood samples can be removed and drugs and fluids administered via the blood access connectors.

The MacNeill blood dialyzer has been in regular clinical use by our group since the time of its initial application in 1954. A complete description of the structural details of the apparatus has been published.[41] A diagram of the entire dialyzing system is presented in Figure 1.

The cellophane membrane used in the

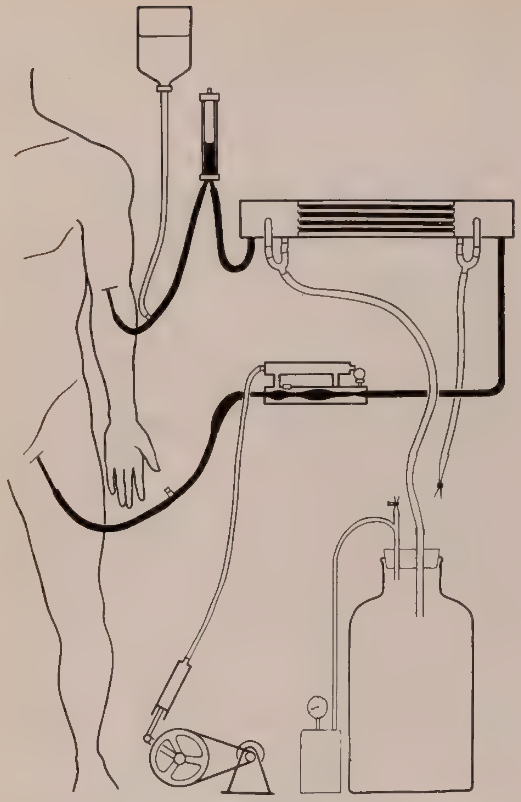

FIGURE 2. The complete MacNeill ultrafiltration circuit. The blood is removed from the inferior vena cava via a saphenous vein cannula. The piston-powered blood pump circulates the blood through the cellophane tubes in the dialyzer whence the blood flows through the flow-meter and then returns to the patient's circulation via an antecubital vein cannula. Simultaneously, suction is applied by means of a vacuum pump to the outer chamber of the dialyzer. The ultrafiltrate is trapped in a collection bottle. Not shown is a warm bath in which the efferent blood line of the dialyzer rests. This bath maintains a constant temperature in the blood returning to the patient. Blood samples can be removed and drugs and fluids administered via the blood access connectors.

MacNeill-Collins dialyzer is seamless, regenerated cellulose tubing made by the Viscose* process. The average pore radius of this cellophane is only 20 angstrom units (2.4 millimicrons). The membrane is permeable to water and will allow compounds of low molecular weight in aqueous solution to diffuse across it, while refusing passage to higher molecular-weight materials, including protein, viruses, and bacteria. Steam sterilization will not harm the membrane, but the film should not be allowed to dry out after such handling since the subsequent shrinkage will modify the original properties. Cellulolytic microorganisms will attack the membrane, especially when it is wet. Therefore, wet tubing must be stored in water containing benzoic acid or formaldehyde or it must be refrigerated. The tubing has a wall thickness of 0.008 inch (approximately 20 microns); when the tubing is wet, the thickness is increased. Similar tubing is used in the dialyzers of Alwall and Lunderquist,[10] Kolff,[2] and Kolff and Watschinger.[27]

Included in Figure 1 is a diagrammatic representation of the MacNeill blood pump which was first introduced in 1955.[42] The great virtue of this pump is the lack of significant hemolysis associated with its in vivo application. The introduction of the blood pump allowed the use of a vein-to-vein circuit and permitted much faster blood flow rates than could be obtained in an artery-to-vein circuit with no extracorporeal pump.

We early found it to be a distinct advantage to be able to remove fluid from overhydrated or edematous patients via ultrafiltration. In a previous publication we described briefly the adjunctive use of ultrafiltration in a series of patients with acute and chronic renal failure.[43]

Ultrafiltration is made possible by the fact that the bath chamber of the dialyzer itself can be sealed off completely and made airtight. A Pyrex bottle is substituted for the plastic-vat bath reservoir as indicated in Figure 2. Two ports in the heavy rubber stopper of the bottle accommodate tubes for the inflow and outflow of the rinsing fluid. A third port in the stopper contains a tube which is attached to a vacuum pump. When a vacuum is applied to the sealed bath circuit, the pressure there can be reduced to as much as minus 700 mm. Hg. Fluid can then be extracted from the blood in appreciable amounts.

In the renal failure series, using the vacuum method of ultrafiltration for periods of up to five and one-half hours, as much as 1,785 ml. of fluid were extracted.[43] In 1 patient in this group, thirst was noted after a period of dialysis and ultrafiltration. Thirst, in relation to hypertonicity of the plasma, has been commented on by Wolf.[44]

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* Visking Corporation, Chicago, Illinois.

Ultrafiltration was carried out in the renal failure series simultaneously with dialysis. That is, the dialytic process was not stopped while ultrafiltration was added. Subsequently, we found that when ultrafiltration alone is carried out with the MacNeill apparatus, much larger amounts of fluid can be extracted. Concomitant circulation of the dialyzing fluid apparently limits the amount of ultrafiltrate extracted.

Seven patients with intractable edema due to congestive heart failure have been subjected to ultrafiltration without the simultaneous use of washing fluid. The data obtained from the study of this group of patients are presented in the following case reports and in the subsequent comment.

It should be noted that in all cases except Case 6, the MacNeill dialyzer with a cellophane surface area of 2 M^2. was used exclusively. In Case 6 a MacNeill 1.5 M^2.-membrane area dialyzer was used part of the time. In all cases except in Case 7 a vein-to-vein circuit was employed with the MacNeill blood pump. In Case 7 an artery-to-vein circuit, with the blood pump, was used for the ultrafiltration procedure.

Case reports

Case 1. A forty-four-year-old white female was first observed by the dialysis team during the course of a long hospitalization for congestive heart failure. She had had rheumatic valvular heart disease for many years and had been in a state of constant cardiac decompensation for nearly six months. Her edema had failed to clear with the use of acetazolamide, mercurial diuretics, ammonium chloride, and salt restriction and what appeared to be adequate digitalization.

The physical examination revealed an edematous, middle-aged white female whose weight was 130 pounds. The neck veins were distended, and an examination of the chest revealed moist rales at both lung bases on auscultation as well as dullness to percussion in these areas. The heart was found to be enlarged to the left and to the right and revealed systolic and diastolic murmurs at the apex as well as a systolic murmur of loud intensity, maximally, at the fourth right interspace. Auricular fibrillation and tachycardia were present. A further examination revealed hepatomegaly, ascites and generalized edema, moderate cyanosis, and an increased rate of respiration. The diagnoses were: (1) inactive rheumatic heart disease, (2) tricuspid insufficiency, (3) mitral stenosis, (4) mitral insufficiency, and (5) auricular fibrillation.

The electrocardiogram revealed right axis deviation and digitalis effect. The chest x-ray film showed cardiac enlargement involving all the chambers and congestion of the lung fields.

Because of a lack of response of the edema to the use of any of the aforementioned agents it was decided to employ dialysis and ultrafiltration.

The first procedure was carried out for a six-hour period, pure ultrafiltration being used for the first five hours. A total of 3,320 ml. of fluid were removed. During the procedure the patient's temperature fell, and for a short period of time she experienced a shocklike episode. This was obviated at the fifth hour by employing a dialysis bath for the remainder of the procedure to warm her blood. This was the first instance of a fall in body temperature that we had observed during an ultrafiltration. Dialysis was carried out simultaneously with ultrafiltration for the final hour of the procedure.

During the procedure the patient's weight declined from 130 pounds to 116 pounds (59.1 Kg. to 52.7 Kg.). Afterwards, she began to respond once again to the injection of mercurial diuretics.

Two weeks later a second ultrafiltration procedure was carried out for a six-hour period. This time, however, a dialysis bath was used for the first five hours and pure ultrafiltration for the final hour. The measured extraction of fluid during this treatment was 2,760 ml. The patient showed a weight loss of 8 pounds (3.6 Kg.). Once again mercurial diuretics were employed effectively following the dialysis ultrafiltration.

The patient was discharged from the hospital two weeks following the second ultrafiltration procedure; her weight at that time was 85 pounds (38.6 Kg.). She was edema-free and much improved over her preadmission condition.

The use of elastic bandages on the legs of this patient appeared to be of help in mobilizing the edema fluid while the ultrafiltration procedure was being carried out. In this last hour of the second treatment a pure ultrafiltrate became available for analysis. Figure 3 demonstrates graphically the effect of ultrafiltration and shows the patient's weight responses to mercurial diuretics following each procedure. The blood flow through the dialyzer-ultrafilter in these procedures averaged 200 ml. per minute, and the amount of vacuum applied to the exterior of the cellophane tubes averaged 20 inches Hg (510 mm. Hg). The hematocrits were measured each hour throughout. In the first procedure only the blood entering the dialyzer was measured for the hematocrit value, except for the second hour, when the

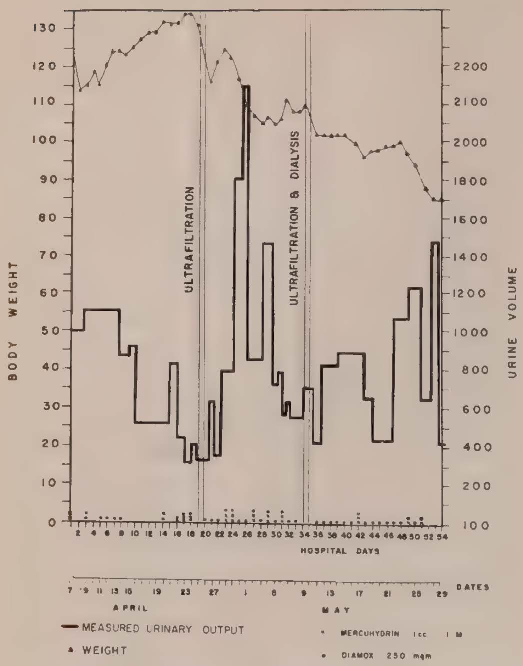

FIGURE 3. Graphic representation of changes observed in a patient with intractable edema during fifty-four days of hospitalization. Note weight loss afforded by ultrafiltration and increased responsiveness to diuretic therapy following ultrafiltration.

blood leaving the dialyzer was measured simultaneously with that entering. In this instance there was an increase of from 43.5 to 45 as the blood passed through the dialyzer. The blood at the start of the first ultrafiltration procedure showed a hematocrit of 45.5, and at the end it was 43. The plasma hemoglobin levels were measured hourly throughout this maneuver and showed no change from a normal value of 1.8 mg. per 100 ml., indicating that the process caused no important hemolysis.

In the second dialysis-ultrafiltration hematocrits were measured on the blood entering the dialyzer as well as on that leaving the apparatus, at hourly intervals. At the first hour the blood entering the dialyzer had a hematocrit of 34, while the blood going out gave a value of 36.5. At the end of the procedure the hematocrit of the blood entering the dialyzer was 35, and that of the blood leaving the machine was 36.5. Plasma hemoglobin measurements were carried out each hour and revealed an increase from 1.7 mg. per 100 ml. to 4.3 mg. per 100 ml. at the end of the procedure. This represents insignificant hemolysis, any value below 30 mg. per 100 ml. having no clinical importance.

Blood and ultrafiltrate samples were analyzed and gave approximately equal values for urea nitrogen, sodium, potassium, and chloride. Four samples of the ultrafiltrate obtained in the first procedure were analyzed in the laboratory for glycosides and gave an average value of 0.3 mg. per liter.

Case 2. A sixty-three-year-old white male civil servant was seen during the course of a long period of hospitalization. He had had numerous previous admissions to the hospital for chronic bronchitis, pulmonary emphysema, and periodic exacerbations of these conditions following acute respiratory infections. He had been found to have arteriosclerotic heart disease and cor pulmonale and had been under treatment with digitalis and diuretics for some years. His response to these agents had been good in the past. Auricular fibrillation had been persistent for nearly two years. He had a mild case of diabetes but had been well controlled on dietary measures.

Two and one-half months before he was seen by the dialyzing team the patient had been admitted to the hospital because of sudden severe dyspnea. On admission he was thought to be suffering from another episode of acute pneumonitis superimposed on his chronic cardiopulmonary disease. His response to bronchodilators and appropriate antibiotics was good, but as the hospitalization progressed, cardiac failure, predominantly right-sided, became an increasing problem. Cardiac drugs and diuretics, which previously had been satisfactory, now elicited no effect. Drastic sodium restriction, ammonium chloride, and organomercurial administration in many combinations were disappointing, as was the use of other agents. Abdominal paracentesis had been used on several occasions to relieve discomfort and had been useful in reducing weight. At the time the patient was evaluated for ultrafiltration, however, his weight, which had been 139 pounds at the lowest, had reached a level of 159 pounds (72.2 Kg.).

A physical examination revealed a chronically ill white male who did not appear to be cyanotic. The neck veins were distended when the patient was in a semirecumbent position. The chest was almost fixed in an inspiratory position. There was a decrease of breath sounds in both lung fields. The expiratory phase was prolonged, and the diaphragms were low and moved poorly. A few basilar rales were heard on both sides as well as diffuse sibilant rhonchi throughout the lung fields. The heart was enlarged to 1 cm. beyond the midclavicular line on the left. The right border could not be percussed. The rhythm was grossly irregular, with a ventricular rate of 120. A harsh apical systolic murmur was present. The blood pressure was 130/60. There was a moderate amount of ascites, and the liver was palpable 6 cm. below the right costal margin and was slightly tender. There was massive edema involving the lumbosacral area, the lower portion of the abdomen, the genitalia, and both lower extremities in their entirety. Healing ulcers were observed at the sites of previously introduced

Southey's tubes. A chest x-ray film revealed chronic, moderately severe pulmonary emphysema with vascular congestion, cardiomegaly, and minimal calcification in the aortic arch. Electrocardiograms showed rapid auricular fibrillation and suggested cor pulmonale.

A six-hour dialysis-ultrafiltration procedure was carried out. Suction amounting to 18 inches Hg (485 mm. Hg) was exerted on the dialyzing bath compartment. During the course of the procedure the patient's weight fell from 159 pounds to 150 pounds (72.2 Kg. to 68.1 Kg.). The measured amount of fluid extracted was 4,000 ml. By the end of the procedure there was an obvious decrease in the amount of peripheral edema, and the abdomen appeared softer. The patient was breathing more easily and felt more comfortable. There was no change in the blood chemistry during dialysis. The nonprotein nitrogen remained somewhat elevated, and the electrolytes remained nearly normal.

Disappointingly, the patient sustained further fluid retention over the ensuing few days, and his response to the administration of diuretics was not improved. Cardiac failure continued to be a major problem during the remainder of his period of hospitalization. He was not again subjected to dialysis-ultrafiltration. The long and complicated illness was terminated some six months following the experimental treatment when the patient expired following the sudden exacerbation of all symptoms and a rapid decline.

At autopsy the principal findings were those of chronic pulmonary emphysema, bronchitis, cor pulmonale, arteriosclerotic cardiovascular disease, myocardial fibrosis, and coronary sclerosis.

CASE 3. A fifty-seven-year-old white male government inspector was referred to the hospital in a state of congestive heart failure for the consideration of dialysis and ultrafiltration. Twenty-four years prior to his admission he had had rheumatic fever; heart murmurs had been present since that time. There was a vague history of a "heart attack" five years prior to his admission. During the five months before the patient was seen in the hospital he had experienced progressive weakness, ankle edema, paroxysmal nocturnal dyspnea and ever-worsening orthopnea, and severe dyspnea on exertion. Despite apparently adequate digitalis dosage and the judicious use of mercurial diuretics, the symptoms had progressed recently to a point where the patient was unable to move from a chair or to sleep in bed. The edema had become massive, and ascites had appeared, requiring a number of abdominal paracenteses to relieve discomfort and respiratory impairment.

A physical examination revealed an emaciated, fatigued white male sitting upright in a cardiac chair. The optic fundi showed some arteriolar narrowing. Neck vein distention was apparent. An examination of the lung fields revealed a few basilar rales on auscultation. The heart was enlarged to the anterior axillary line in the left sixth interspace; auricular fibrillation was present. There was a thrill and a harsh murmur over the aortic area, transmitted into the neck. Distinct systolic and diastolic murmurs were present at the apex. The blood pressure was 120/20. The abdomen was distended with fluid. Since the patient could not be examined in the supine position because of respiratory distress, the liver could not be outlined. There was 4 plus edema of the legs and mild cyanosis of the nail beds.

Laboratory findings included hemoglobin 11.7, white blood count 10,000, bands 7, filaments 71, lymphocytes 15, and monocytes 7. A urinalysis revealed a specific gravity of 1.011, 2 plus albumin, no glucose, 5 to 10 white blood cells, and occasional red blood cells. The fasting blood glucose was 120 mg. per 100 ml., and the blood urea nitrogen was 20 mg. per 100 ml. The serum albumin was 4 Gm. per 100 ml., while the globulin was 1.7 Gm. per 100 ml. The serum chemistry included uric acid, 5.7 mg. per 100 ml., calcium 11 mg. per 100 ml., sodium 127 mEq. per liter, potassium 5.2 mEq. per liter, chloride 83 mEq. per liter, and carbon dioxide 21 mEq. per liter.

The chest x-ray film revealed cardiac configuration of mitral stenosis and cardiomegaly, but the lung fields were clear. The electrocardiogram showed auricular fibrillation, left ventricular hypertrophy, and digitalis effect.

Hemodialysis was carried out for a short time and then discontinued, whereupon ultrafiltration was begun and continued for a six-hour period. Approximately 4,300 ml. of fluid were extracted during the procedure, using a vacuum of 20 inches Hg (510 mm. Hg). The patient's weight fell from 127 to 116 pounds (57.7 to 52.2 Kg.) during the six-hour period, and the peripheral edema decreased noticeably. The blood chemistries remained at predialysis levels.

Over the next several days the patient was able to maintain his weight with the use of mercurial diuretics and chloride supplements. However, two weeks following the ultrafiltration procedure his weight again had climbed to 124 pounds (56.3 Kg.). At this time a second dialysis-ultrafiltration procedure was carried out, and 2,800 ml. of ultrafiltrate were extracted. The patient's body weight was lowered to 118 pounds (53.6 Kg.), and again subjective improvement and renewed responsiveness to mercurial diuretics were noted. The patient was able to be up and about to a limited extent for the first time in several months. He was discharged four days following the second procedure in an improved condition. About one month later the patient expired suddenly in a bout of acute ventricular failure.

CASE 4. A forty-three-year-old housewife

TABLE I. Hour-to-hour fluid loss in Case 4

Time (Hour)	Amount of Fluid Extracted (Ml.)	Vacuum (Inches)
First	1,620	25
Second	1,150	25
Third	1,010	25
Fourth	965	25
Fifth	940	25
Sixth	795	25
Total	6,480	

TABLE II. Levels of urea nitrogen in the ultrafiltrate in Case 4

Time (Minutes)	Mg. Per 100 Ml.
120	108.1
130	114.1
160	100.0
220	113.5
280	86.6
340	111.8
360	112.6

was seen by the dialysis team on her ninth hospital admission. She had had hypertensive cardiovascular disease and congestive failure for at least one and one-half years. Peripheral edema had become gradually worse during this period, lessening, however, during periods of hospitalization. The patient had been known to have diabetes mellitus for about twenty-one years and had received insulin for a number of years but recently had been controlled with dietary measures alone. Edema had become worse during the week prior to admission. She became very short of breath and was unable to ambulate during the two days before coming to the hospital.

There had been a gradual diminution in the urine volume during the two months prior to hospital admission. Voiding had become less frequent during this time, and for twenty hours prior to admission she had not voided at all. On the day of admission a sharp, aching pain developed in the region of the left kidney.

A physical examination revealed a well-developed, well-nourished forty-three-year-old white female in respiratory distress. Her face appeared slightly puffy. The right optic fundus revealed arteriolar narrowing with arteriovenous nicking and a small hemorrhage. The left optic fundus was not visualized because of lenticular opacity. The neck veins were moderately distended. Auscultation of the chest revealed a few scattered rales at the level of the seventh rib on the left and the ninth rib on the right posteriorly, and percussion revealed flatness below these levels. The heart was enlarged to the left. The rhythm was regular. The blood pressure was found to be 235/120. The abdomen was obese, and the liver was found to be enlarged 4 cm. below the right costal margin and was slightly tender. Ascites and marked left costovertebral angle tenderness were present. The lower part of the body from the level of the fifth lumbar vertebra downward was grossly edematous. Several thoracenteses were carried out on the right side during the first eight days of hospitalization. The total amount of straw-colored fluid extracted was 2,800 ml. The administration of aminophylline and Mercuhydrin led to some reduction of the edema. Fluid continued to reaccumulate, however, and by the end of two weeks the patient was again grossly edematous. At this time multiple skin punctures of both lower extremities were carried out. This maneuver resulted in considerable drainage of fluid and appreciable weight loss.

However, four weeks after admission considerable edema persisted. She did not appear to be responding to the diuretics and still maintained a level of pleural fluid up to the sixth rib bilaterally by percussion. Ascites was still present, and edema of the lower extremities extended up to the iliac crest. It was then decided to use ultrafiltration.

The ultrafiltration procedure was carried out for a six-hour period with an especially rapid blood flow rate (600 ml. per minute). Also, a greater than usual amount of suction was used on the dialyzing fluid compartment of the apparatus, 25 inches Hg vacuum (638 mm. Hg) being employed. The measured amount of ultrafiltrate extracted was 6,480 ml. The weight loss in the patient was 16 $^{3}/_{4}$ pounds (7.6 Kg.). She tolerated the procedure very well and exhibited a considerable decrease in edema throughout her body. The night following the ultrafiltration procedure the patient slept, for the first time in years, with the head of her bed down.

The hour-to-hour fluid loss in this case showed a progressive diminution in the amount of ultrafiltrate extracted (Table I).

With the judicious use of diuretics she maintained her gains, and peripheral edema became further diminished. One week following the ultrafiltration procedure pleural fluid appeared to have disappeared on the left side and was barely detectable at the right pulmonary base. Following ultrafiltration the body weight was 149$^{1}/_{2}$ pounds (67.9 Kg.), and eleven days later the weight was 143$^{1}/_{4}$ (65.1 Kg.). At that time it was felt that the patient was improved enough to be discharged to private home medical care.

During the ultrafiltration procedure the serum sodium was reduced from 146 to 140 mEq. per liter. Other blood chemistry remained at approximately predialysis levels. At hourly intervals during the procedure hematocrits were measured on the blood entering the dialyzer and on the blood leaving the machine. At the end of the first hour an increase in the hematocrit from 28 to 39 was detected as the blood traversed the dialyzer. However, at no other hourly interval to the termination of the procedure did the increase in the hematocrit exceed 3 mm. Prior to ultrafiltration the urinary output had averaged less than 600 ml. daily; after ultrafiltration the urinary output averaged well above 1,000 ml. daily.

Of special interest are the figures for the levels of urea nitrogen in the ultrafiltrate at various times throughout the period of treatment (Table II).

CASE 5. A fifty-nine-year-old white housewife was admitted to the hospital because of congestive heart failure manifested by extensive edema, pulmonary congestion, and ascites. Three weeks prior to admission the patient developed malaise, myalgia, headache, a nonproductive cough, fever, and shaking chill. Three days prior to admission she suddenly sustained pain in the left side of the chest associated with shortness of breath, nausea, vomiting, and anorexia. It was noted that the patient had had at least 15 previous admissions to the hospital because of rheumatic heart disease with congestive heart failure and edema. A history of diabetes mellitus was of long standing.

A physical examination revealed a lethargic, obese, white female who appeared acutely ill. Her breath had a fruity odor. The optic fundi did not appear to be abnormal. Distention of the neck veins was apparent. An examination of the chest revealed an elevation of the diaphragm. Auscultation of the lung fields revealed fine rales in both pulmonary bases. Percussion of the chest demonstrated no abnormalities. The heart was enlarged, but the rhythm was regular. A loud, high-pitched systolic murmur was detected at the cardiac apex. The abdomen was distended, and the presence of ascites was demonstrable. It was impossible to palpate any abdominal organs because of the ascites. Marked edema of the abdominal wall extended to above the umbilicus. There was also considerable edema of the back up to the lower thoracic region. The patient's legs were grossly edematous with large areas of ulceration and weeping. Her hands and arms were edematous up to the elbows.

The diagnoses were rheumatic heart disease, inactive, with mitral insufficiency, aortic stenosis, and cardiac insufficiency and diabetes mellitus with renal intercapillary glomerulosclerosis.

In the past the patient's cardiac insufficiency had responded to digitalis, ammonium chloride, acetazolamide, and other diuretics, but ten days after admission the vigorous use of these agents had failed to elicit a response. A laboratory evaluation revealed depressed serum sodium, potassium chloride, and carbon dioxide, while the blood urea nitrogen was elevated.

Sixteen days after admission hemodialysis and ultrafiltration were carried out for a seven-hour period. A total of two hours of dialysis and a sum of five hours of ultrafiltration were carried out. The vacuum applied to the outer chamber of the dialyzer averaged 20 inches Hg (510 mm. Hg). The blood flow averaged 500 ml. per minute. During periods of dialysis the bath flow was 3,300 ml. per minute, but when ultrafiltration was being carried out, the bath flow was stopped. The patient was unresponsive prior to the procedure, and although there was no real change in the level of consciousness during the dialysis-ultrafiltration, she tolerated the procedure well. The measured amount of ultrafiltrate extracted during the maneuver was 5,470 ml. The blood urea nitrogen fell somewhat during dialysis, and the serum carbon dioxide-combining power rose during the procedure while levels of serum sodium, potassium, calcium, and chloride remained at relatively normal levels. The levels of urea nitrogen in the ultrafiltrate (mg. per 100 ml.) were found to be 64.5 at the second hour, 84.4 at the third hour, 84.1 at the fourth hour, and 76.7 at the fifth hour.

TABLE III. Hour-by-hour ultrafiltrate extraction in Case 5

Period of Time	Amount of Ultrafiltrate (Ml.)	Vacuum (Inches)
1 hour	1,000	18 to 20
30 minutes	0	0 (dialysis)
1 hour	1,130	15 to 20
30 minutes	0	0 (dialysis)
1 hour	1,140	19
30 minutes	0	0 (dialysis)
1 hour	1,100	18 to 20
30 minutes	0	0 (dialysis)
1 hour	1,100	18 to 21
Total	5,470	

The periods of ultrafiltration and dialysis were regularly staggered. The hour-by-hour ultrafiltrate extraction is shown in Table III.

A comparison of chest x-ray films taken before and after the procedure showed considerable clearing of the pulmonary edema and pleural effusion which had been present prior to ultrafiltration (Fig. 4).

However, the patient remained restless and unresponsive, and despite the improvement sustained from the procedure she became comatose on the second day following dialysis and expired on the third day.

CASE 6. A thirty-one-year-old white male office worker first became aware of heart disease when he was twenty-seven years old, at which time he was hospitalized for "irregular heart" and placed on quinidine with a good effect. The diagnoses of rheumatic endocarditis, inactive, with mitral stenosis, tricuspid insufficiency, and cardiac insufficiency were established. He was reasonably well for almost four years until two months prior to the time that

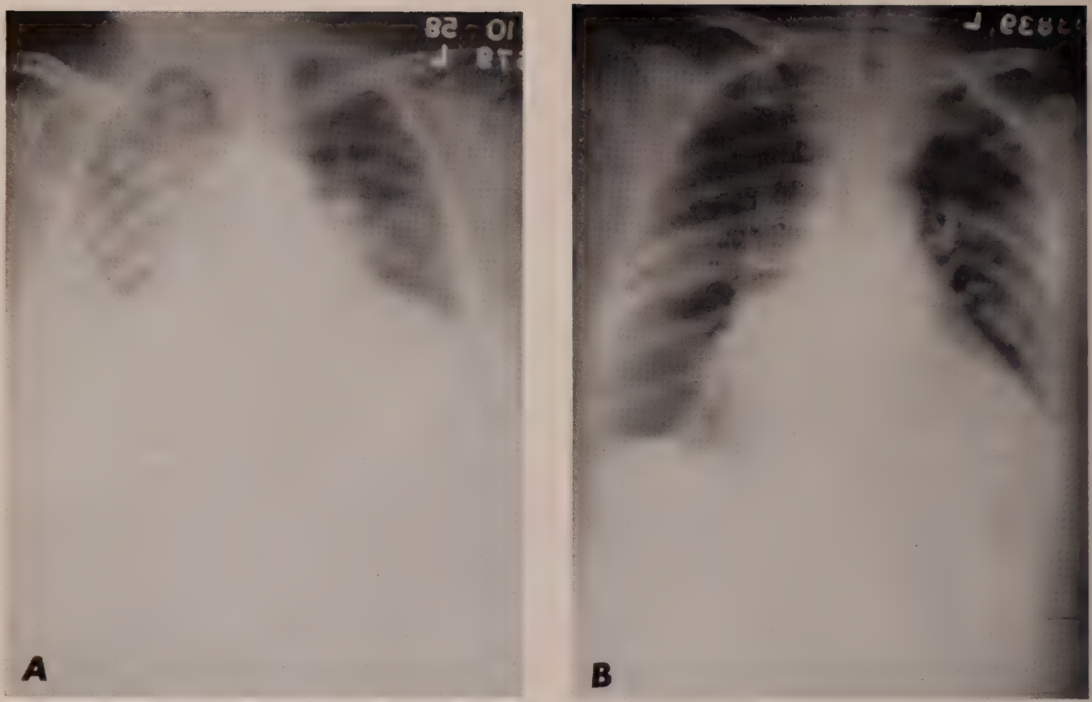

FIGURE 4. Case 5. (A) Chest roentgenogram taken the day prior to the ultrafiltration procedure. (B) Chest roentgenogram the day following the ultrafiltration procedure.

he was evaluated by the dialysis team, when he was again hospitalized for one month with ankle edema. At that time he was placed on a digitalis preparation. After a month in the hospital he was well enough to return home, where he stayed for approximately four weeks.

Ankle edema again developed, accompanied by moderate exertional dyspnea, and hospitalization again was necessary. A physical examination revealed a chronically ill-appearing, thirty-one-year-old white male who was slightly cyanotic. Venous distention in the neck was apparent as was venous pulsation synchronous with systole. An examination of the lung fields revealed no abnormalities. The cardiac apex was found to be to the left of the midclavicular line in the fifth interspace, but the heart was enlarged to the right. A Grade V systolic murmur was loudest over the tricuspid area, radiating toward the apex and the left sternal border. An early diastolic rumble was detected near the apex. The cardiac rhythm was irregular. An examination of the abdomen revealed no evidence of edema or ascites. There was pitting edema of the feet and ankles.

Three days after admission, catheterization of the right side of the heart and puncture of the left side of the heart were accomplished and confirmed the diagnosis. Following this procedure the patient developed an elevated temperature for several days, vomited several times, and occasionally became cyanotic. The liver, which had been found to be enlarged on admission, remained large and tender. The feet

TABLE IV. Amount of ultrafiltrate extracted in Case 6

Period of Time (Hours)	Fluid Extracted (Ml.)	Vacuum (Inches Hg)	Concentration of Glucose in Dialyzing Bath (Mg. per 100 Ml.)	Cellophane Surface Area of Dialyzer (M.^{2})
1	105	0 (dialysis)	400	2.0
1	300	0 (dialysis)	400	2.0
1	0	0 (dialysis)	100	1.5
$1\frac{1}{4}$	0	0 (dialysis)	100	1.5
$1\frac{1}{4}$	750	21	No bath	1.5
1	260	0 (dialysis)	400	1.5
$\frac{1}{2}$	300	20	No bath	1.5

remained swollen, but there was no calf tenderness. The heart sounds remained unchanged. Slight jaundice appeared, and peripheral edema had increased by the eleventh hospital day. At this time the urinary output had fallen, and serum sodium and chloride showed very low values.

On the twelfth hospital day dialysis and dialysis-ultrafiltration were carried out for five and one-quarter hours and ultrafiltration for one and three-quarter hours. An apparatus with 2 M^2. cellophane surface area was used for two and one-half hours and then because of technical difficulties was replaced with an apparatus containing 1.5 M^2. cellophane surface area. The patient lost about 300 ml. of blood in the exchange of dialyzers. The blood flow varied from 160 to 400 ml. per minute. The total measured amount of ultrafiltrate extracted was 1,715 ml., and was collected as shown in Table IV.

During the course of the dialysis-ultrafiltration the blood urea nitrogen dropped from 50 to 42 mg. per 100 ml. while the carbon dioxide-combining power rose very slightly from 18.5 to 19.4 mEq. per liter. The serum potassium increased slightly above the normal range, but the serum sodium increased from a level of 112 to 128 mEq. per liter and the chloride from 76 to 105 mEq. per liter.

Prior to dialysis the urine sodium content had been too low to determine, and it remained so three days after dialysis. At this later time the urine chloride excretion was found to total 0.97 Gm. in a twenty-four-hour period (1,632 ml. urine). This figure is, of course, far below the normal level.

Two days following the treatment the patient was still fatigued, had edematous legs, and was beginning to show sacral edema. A few rales were heard in the left axilla, and there were diminished breath sounds on auscultation of the right pulmonary base. Seven days following dialysis the patient was more dyspneic although his edema remained at about the same level. Twelve days after dialysis, on the twenty-fourth hospital day, little if any improvement had been noted, and Southey's tubes were inserted in the legs. A modest amount of fluid was extracted in this way. Two days later multiple incisions into the subcutaneous space in the lower extremities were carried out. Four L. of fluid were drained from these incisions, but the patient's condition became progressively worse. On the twenty-eighth hospital day he expired.

Case 7. A thirty-eight-year-old white male was evaluated by the dialysis team. He had been known to have albuminuria since the age of five years.

A review of the past history also revealed that he had had diphtheria at the age of eighteen months and scarlet fever in his teens. At the age of twenty-two years he was studied at the Mayo Clinic, where a diagnosis of chronic glomerulonephritis was made. It also was noted that he had aplasia of the left kidney. Thereafter, the patient was limited in his activity because of easy fatigability. He was fairly well, however, until the age of thirty-six, when he was first admitted to a hospital in a nearby city because of blurring of vision in his left eye.

In the next six months he had several admissions to this neighboring hospital because of symptoms of chronic renal insufficiency. When he developed persistent convulsions and markedly altered blood chemistry, including a blood urea nitrogen of 132 mg. per 100 ml., he was transferred to the Buffalo General Hospital for consideration of hemodialysis.

At that time a physical examination revealed a well-nourished, well-developed white male who appeared chronically ill. He was fairly alert and cooperative but somewhat restless and nauseated. The skin exhibited pallor, and his face appeared to be somewhat puffy. The optic fundi showed marked vessel spasm, no hemorrhages or exudates, and no papilledema. An examination of the chest and lung fields revealed no abnormalities. The heart was not enlarged and exhibited regular sinus rhythm. There were no murmurs, and a friction rub was not present. The abdomen was slightly obese, soft, and revealed no tenderness. The liver edge could be felt 2 cm. below the right costal margin. There was an appendectomy scar in the right lower quadrant of the abdomen. Some tenderness was elicited in both lumbar regions. There was no sacral or peripheral edema. There were subcutaneous nodules at both elbows; the nail beds were slightly pale.

Over the next four months this patient underwent dialysis three times in attempts to correct the abnormal blood chemistry and control the symptoms of uremia and acidosis. Three days following the first dialysis he experienced a bout of acute pulmonary edema following the infusion of 250 ml. of packed blood cells. He responded rapidly to the administration of oxygen, morphine, intravenous Digoxin, and the application of tourniquets to the extremities. During the period following the second dialysis there developed sacral and lower extremity edema. The peripheral edema persisted following the third dialysis.

His general condition remained fairly stable, however, and he was discharged on gitalin, sodium bicarbonate, aminophylline, Compazine, Sparine, and calcium chloride.

The patient was readmitted to our hospital six days later with massive swelling of the feet and legs and shortness of breath. He was placed in a cardiac chair and given intravenous aminophylline. This and other measures effected improvement during the next several days. The blood pressure was 210/130. The eye grounds revealed a flame hemorrhage on the left side; there was considerable narrowing and spasm of the retinal vessels on both sides. While the lung fields were mostly clear to auscultation, there were a few crackling rales in the bases of both lungs.

TABLE V. Rate of fluid extraction during ultrafiltration in Case 7

Hour	Fluid Extracted (Ml.)	Vacuum (Inches Hg)
First	1,200	20
Second	900	20
Third	750	20
Fourth	900	20
Fifth	650	20
Sixth	750	20

TABLE VI. Total ultrafiltrate values in Case 7

Ultrafiltrate	Values Mg. per 100 Ml.	mEq. per Liter
Urea nitrogen	122	...
Creatinine	7.2	...
Sodium	...	119
Potassium	...	6.1
Calcium	5.9	3.0
Chloride	...	88
Phosphate	9.6	5.8

Five days following this second admission the patient was subjected to a seven-hour period of hemodialysis and ultrafiltration. An artery-to-vein flow was used, the vessels cannulated being the left radial artery and the left basilic vein. The blood flow averaged from 200 to 250 ml. per minute. The bath flow rate was 3,600 ml. per minute, but the dialyzing fluid was circulated for only one hour. Ultrafiltration was carried out for the remaining six hours of the treatment, with a vacuum pump applying suction to the outer chamber of the dialyzer to the extent of 20 to 23 inches Hg (510 to 586 mm. Hg). Again, 2 units of packed red blood cells were transfused during the procedure. The measured amount of ultrafiltrate extracted from the patient's blood during this maneuver was 5,550 ml. Prior to ultrafiltration the patient's body weight was 172$^1/_4$ pounds (78.3 Kg.), and following ultrafiltration it was 159-$^3/_4$ pounds (72.6 Kg.).

The rate at which fluid was extracted during the six-hour period of ultrafiltration is shown in Table V.

A complete analysis of the total ultrafiltrate was carried out in this case and revealed the values shown in Table VI.

Remarkable subjective improvement was noted following the ultrafiltration. Two days after the procedure the patient had lost an additional 3$^1/_4$ pounds (1.5 Kg.). The lung fields were quite clear to auscultation with only occasional rales at the bases. The peripheral edema was then limited to the ankles and lower legs and did not exceed 1 plus. Slight edema remained around the pelvic region. It was decided to allow the patient to go home.

Two and one-half weeks later he was admitted to the hospital for the last time. Again he had developed persistent nausea, emesis, and some mental disturbance. The edema had not returned since the ultrafiltration treatment. The optic fundi revealed additional vascular changes, another hemorrhage in the right eye, and increased narrowing of the vessels bilaterally. A chest examination revealed rales at both pulmonary bases, the heart demonstrated a gallop rhythm, and the abdomen showed slight distention. There was 1 plus edema of the lower back and sacral area. The blood pressure was 200/120. During the next two days the patient's condition deteriorated rather rapidly; he became somnolent and exhibited considerable muscle twitching. A pericardial friction rub became pronounced, and the neck veins became distended. Edema of the lower trunk and the lower extremities increased rapidly, and rales at the pulmonary bases became more numerous. Distention of the abdomen with fluid supervened, and peripheral cyanosis developed. In the evening of the third hospital day he expired.

It is of interest that only a slight degree of hemoconcentration occurred during the ultrafiltration procedure carried out during the patient's third period of hospitalization. This was demonstrated by an increase in the hematocrit from a value of 25 mm. prior to ultrafiltration to a level of 29 mm. at the end of the procedure. Differences in hematocrit values were measured hourly between the blood entering the dialyzer and that leaving the apparatus, and at no time was there an increase greater than 1 mm. in the hematocrit value. A summary of the results of ultrafiltration in this series appears in Table VII.

Comment

Many patients in congestive heart failure become unresponsive to salt restriction, diuretic therapy, digitalis, and other more usual forms of therapy. Some patients in congestive heart failure can undergo corrective cardiac surgery if their decompensation can be brought under control temporarily. Certain patients in acute and chronic renal failure become significantly overhydrated. These constitute the three main groups which achieve important benefit from the use of extracorporeal ultrafiltration of the blood.

All of the important work in clinical ultrafiltration which has been carried out by American investigators in the past decade has been summarized in the preceding historical review. It is now apparent that ultrafiltration is a thoroughly workable

TABLE VII. Results of ultrafiltration in 7 patients with congestive heart failure

Case	Procedure Number	Cellophane Area (M².)	Amount of Vacuum Used (Inches Hg)	Length of Ultrafiltration (Hours)	Blood Flow (Ml. per Minute)	—Weight (Pounds)—		Measured Amount of Fluid Extracted (Ml.)
						Before Dialysis	After Dialysis	
1	1	2	20	6	150	130	116	3,320
1	2	2	20	6	150	108	100	2,760
2	3	2	20	6	?	159	150	4,000
3	4	2	16	6	200	127	116	4,300
3	5	2	20	6	200	125	118	2,800
4	6	2	25	6	600	166.25	149.5	6,480
5	7	2	20	5	500	...	...	5,470
6	8	1.5	20	2.5	160 to 400	...	...	1,715
7	9	2	20 to 30	6	200 to 250	172.25	159.75	5,550

variation of the standard technic of extracorporeal hemodialysis. It is important to emphasize, however, that a satisfactory ultrafiltration apparatus must provide for the rigid support of the cellophane membrane, that it should contain a large cellophane surface area, and that it should be so constructed that the application of a high degree of negative pressure to the external surface of the cellophane membrane can be withstood.

Concentrated glucose solutions have been used selectively in our ultrafiltration experiments because of previously mentioned disadvantages of this method and largely to confirm the observations of others that the method is inefficient.

Kolff and Leonards,[12] Lewis *et al.*,[14] Alwall *et al.*,[19] and Darmady,[17] working in different places with dissimilar apparatuses and under diverse working conditions, have reached essentially the same conclusion: While ultrafiltration achieved by the use of hypertonic glucose bath solutions is possible, it is unpredictable and not as potent as one would desire. Moreover, the great increase in blood sugar levels seen with this approach is highly undesirable and should be avoided.

While the removal of fluid from edematous patients has been accomplished successfully by peritoneal lavage by Kolff and Leonards,[12] Girard *et al.*,[20] and others, the potential hazards of this technic should give one pause in recommending its application, especially in view of the fact that safe and efficient methods for extracorporeal ultrafiltration of the blood are now available.

The use of the Kolff twin-coil "kidney" entails the mandatory loss of fluid during dialysis by ultrafiltration. That is, using the standard technic of hemodialysis with this device, fluid is lost to the dialyzing bath because of the high pressure in the proximal portion of the blood circuit. The amount of fluid involved in this inevitable transfer has been characterized by Meyer *et al.*[30] as from 200 to 500 ml. per hour. The application of negative pressure to the bath compartment of the twin-coil "kidney" is not possible with the standard arrangement for dialysis. The unavoidable fluid loss seen with the use of this dialyzer is sometimes disadvantageous since it cannot be controlled easily. The application of high pressures to the blood compartment should be avoided; such avoidance is not possible with the Kolff twin-coil kidney. The requirement for blood priming of the coil kidney is another undesirable feature.

It is apparent also that the use of the Skeggs-Leonards artificial kidney is associated with a certain amount of inevitable fluid loss. Here again, the high blood pressure in the proximal part of the circuit is responsible for the mandatory fluid extraction. One of the virtues of the Skeggs-Leonards dialyzer is that ultrafiltration can be increased by the application of suction to the dialyzing bath compartment of the machine. However, this device also requires blood priming, which of course increases the hazard associated with its use.

The MacNeill blood dialyzer provides rigidly supported short lengths of flattened cellophane tubes which contain blood under low pressure; there is no extraction of fluid from the blood during the course of the standard dialyzing procedure. When a vacuum pump is added to the bath circuit of this device, as shown in Figure 2, it is possible to regulate carefully the extraction of fluid simply by varying the amount of negative pressure applied to the exterior surface of the cellophane film.

It is quite apparent from our own studies herein reported, and from the preceding review of the ultrafiltration experience of other groups, that the extraction of fluid from exteriorized blood is technically feasible and therapeutically potentially highly beneficial in selected cases. The extraction of amounts of fluid up to 8,600 ml. in a single dialysis-ultrafiltration procedure has been reported. The latter figure represents a loss in body weight of some 19 pounds. It should be remembered that the fluid measured may not be an exact reflection of the total amount of fluid extracted since some water may be lost by evaporation.

In the case reported by Keitzer, Ford, and Miller[22] it was suggested that convulsions may have been terminated by the reduction in cerebral edema effected by ultrafiltration. The increase in plasma protein concentration and the elevation of hematocrit during the ultrafiltration process must contribute to the movement of water from the interstitial and intracellular compartments. Lowered blood pressure, within limitations, will enhance the effectiveness of the increased osmotic pressure occasioned by the heightened concentration of plasma proteins and cellular elements. It is quite apparent, however, that one should not attempt to dehydrate too rapidly. The experience of Kolff and Leonards[12] and of Pierce,[31] who found that dogs died when fluid amounts corresponding to from 5 to 7 per cent of the body weight were extracted rapidly, should be ample evidence that rapid fluid extraction is undesirable. It is certainly important, then, to measure the hematocrit frequently lest it increase too much in one passage across the dialyzer. Frequent measurements of blood pressure also are exceedingly important inasmuch as too-rapid dehydration will reduce the circulating blood volume and lead to hypotension and shock. Frequent measurements of body temperature also are indicated, especially when dialyzing fluid is not used to bathe the external surface of the cellophane membrane. When washing fluid is not used during ultrafiltration, provision should be made for rewarming the blood as it re-enters the body.

It is of especial interest to note that when we allowed half-hour periods of straight dialysis between hourly periods of ultrafiltration (Case 5) the amounts of ultrafiltrate obtained per hour did not diminish with time.

In our own studies, amounts of vacuum applied to the external chamber of the dialyzer, up to 27 inches Hg, have been used. It is not technically easy to achieve higher degrees of vacuum. Indeed, it may not be desirable to use more negative pressure than this since the cellophane membrane and its connections may be overstressed.

We have found that the application of elastic bandages to the lower extremities during a course of dialysis-ultrafiltration is useful in mobilizing edema. The bandages should be removed frequently and replaced during the course of the treatment so that adequate pressure will be maintained. These bandages also should be kept in place for many days following the completion of ultrafiltration to hinder the reaccumulation of fluid in the extremities. The recommendation of Kolff and Leonards[12] of fluid restriction for the first few days after treatment is a valuable one. We, also, have found that the limitation of fluid intake prevents the reaccumulation of edema during this period. Kolff and Leonards have noted the spontaneous elimination of the remaining edema fluid following ultrafiltration, and we have found that mercurial diuretics have become effective again, postdialysis, in previously refractory subjects.

Hemolysis has been so slight with the clinical use of the MacNeill dialyzer-ultrafilter as to be insignificant, the plasma hemoglobin value never having exceeded 8 mg. per 100 ml. at any time it was measured. The hematocrit tended to increase (range from 1 mm. to 5 mm.) on a single passage of the blood through the dialyzer-ultrafilter. An increase of the hematocrit value in the patient's blood, however, from the beginning to the end of the procedure, did not exceed 3 mm., indicating that severe dehydration of the circulating blood did not occur.

In general, values for urea nitrogen and for sodium, potassium, and chloride in the ultrafiltrate closely resembled those in the blood and serum. The concentration of calcium in the serum was compared to that of the ultrafiltrate in 2 cases. In 1 case the serum calcium was 9.1 mg. per 100 ml., while the corresponding ultrafiltrate value was 6 mg. per 100 ml. In another instance the serum calcium was 7.9 mg. per 100 ml., and the ultrafiltrate calcium was 5.2 mg. per 100 ml. In each instance the filtered calcium appeared to represent about two thirds of the total serum calcium. Considering the possibility that the fluid measured may not be all of the fluid extracted (since some water may be lost in evaporation), we cannot be entirely certain that we were not dealing with slightly hypertonic variants of the true ultrafiltrates.

Four samples of the ultrafiltrate obtained in the first analysis in Case 1 were analyzed in the laboratory for glycosides and gave an average value of 0.3 mg. per liter. This patient was fully digitalized and was receiving 0.1 mg. of digitoxin daily.

More extensive analyses of ultrafiltrates obtained in this manner are indicated. The availability of pure ultrafiltrates of the blood opens the way to the study of diffusible substances which appear in low concentrations in the blood. Such study may be of particular value in the elucidation of the chemical causes of the uremic syndrome. Such substances cannot be measured easily in standard samples of blood or serum. Some trace materials cannot be measured at all by ordinary technics.

Summary

1. The history of the development of ultrafiltration technics is reviewed.
2. The method of blood dialysis with the MacNeill apparatus is reviewed briefly, and the addition to it of a technic of ultrafiltration is described.
3. The advantages of the technic of dialysis-ultrafiltration with the MacNeill equipment are emphasized.
4. The case histories of 7 patients with congestive heart failure and intractable edema are described. The successful use of ultrafiltration in each of these patients is discussed. Each of 2 patients underwent ultrafiltration twice. The other 5 patients were each treated once with this technic.
5. The technical superiority of extracorporeal hemodialysis-ultrafiltration over dialysis with hypertonic glucose solutions and peritoneal lavage is underscored. The superiority of the therapeutic result with the MacNeill system over results with other methods is established. Caution must be exercised so that fluid will not be extracted so rapidly as to cause hemoconcentration, dehydration, hypovolemia, hypotension, and shock.
6. Some of the characteristics of a pure ultrafiltrate of the blood are described. More extensive analyses of these ultrafiltrates is indicated.
7. The extraction of digitalis glycosides was demonstrated in 1 case.

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Mystery of the throat swab

Of all the mysteries of medicine to the lay person, one of the greatest is the value of the throat swab. Our child gets a temperature and inflamed tonsils, and my husband, a conscientious pediatrician, orders an antibiotic and takes a throat swab. The throat swab is sent to the laboratory, and I arm myself with a bottle and teaspoon and prepare for a week of disturbed nights. After five days my husband says the antibiotic was not the best one according to the report and we are to change to eight-hourly administration of another type. After a few days he takes another throat swab. Why, I ask—so that we may know in a week's time how he was today? I get a pitying smile.—*The Lancet, October 21, 1961, page 927*

Surgical Treatment of Biliary Tract Disease

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BILIARY TRACT DISEASE *occurs in many areas of the world. It is associated significantly with pregnancy: In the author's experience, of every 5 patients with biliary tract disease, 4 are women, of whom 3 have been pregnant, and 1 is a man. The disease is relatively rare in children and more frequent in the older-aged group than in the general population. In North America gallstones are associated with the majority of disorders of the biliary tract. An adequate explanation of the formation of gallstones is lacking. The most common clinical manifestation of the disease is the complaint of "indigestion," from mild to severe. The disease may go unrecognized for years and result in liver damage. Cholecystography and cholangiography make possible an accurate diagnosis. The definitive treatment of biliary tract disease is surgical. Elective cholecystectomy has become more common over the past thirty years with the reduction in risk of operation and decrease in complications. Biliary tract disease may be divided into four stages; the stage at which the operation is undertaken determines whether the procedure is to be cholecystectomy, common duct exploration, correction of biliary-enteric fistula, or right lobectomy for carcinoma of the gallbladder. The gallbladder containing stones should be removed irrespective of the stage of biliary tract disease, unless there is overriding contraindication that renders the procedure hazardous.*

BILIARY TRACT DISEASE is prevalent in many areas of the world as well as in North America.[1] The incidence in Central and South America is estimated to be slightly less than it is in this country. Northern Europe and the Scandinavian countries probably have a higher incidence, whereas that in Central Europe, including Great Britain, is about equal to ours. Statistical data from Russia are lacking, but it is known that operations on the biliary tract are among those most frequently done in the hospitals of that country. Available reports indicate the incidence to be much less in Southern Asia, India, China, and Japan. Australia and New Zealand and certain areas in South Africa parallel the incidence in Central Europe and North America.

Within the United States there appears to be little difference as to geographic distribution. Disease of the biliary tract is believed, but not actually demonstrated, to occur less often in the Negro than in the white population. The Navajo Indians have an incidence slightly above that of the United States as a whole. Attempts at finding some variation in diet among different religious groups have been unrewarding. Jews, Protestants, and Catholics appear to have no such differences.

One factor is associated significantly with gallstone formation: pregnancy. In our experience, for each 5 patients with biliary tract disease 4 will be women and 1 a man, and 3 of the women will have been pregnant. The incidence in men and in women who have not been pregnant seems to be parallel. Biliary tract disease is relatively rare in children and is most often associated with severe infection with bacteremia and blood dyscrasias such as familial hemolytic jaundice.[2] An incidence higher than that of the

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total population has been observed among the older-aged portion of our population.[3] This is indicative that gallstones may cause little disability for years but eventually give rise to difficulty and even to catastrophe.

Etiology

Gallstones are associated with the majority of disorders of the biliary tract encountered among the people of North America. Thus, in considering biliary tract disorders, one may best present a comprehensive picture of the subject by reviewing the clinical course associated with gallstones and noting specifically the differences among those in whom calculi are not involved.

The mechanism whereby stones are formed in the gallbladder and biliary ductal system is poorly understood.[4] Much study has been devoted to this problem. Many isolated and easily comprehended facts have been revealed. Many more associated and complex fragments of information which are difficult to interpret have been brought forth by numerous investigators. No single theory provides an adequate explanation for all gallstone formation. Perhaps the most satisfactory concept is that stone formation is the result of general variations from the normal functioning of the liver and biliary system. These may be the result of disturbances in metabolism, infection, stasis, and obstruction. Stasis and infection appear to play an important role in this change in bile concentration. Much investigation and study have failed to demonstrate a direct and constant relationship between the cholesterol content of bile and that of the blood serum. In pregnancy, however, it is common for both to be elevated, but all pregnant women do not develop gallstones. While some defect in cholesterol metabolism probably accounts for many instances of gallstone formation, we cannot be specific as to just where in the long and intricate chemical process it occurs.

Clinical manifestations

The symptoms that cause a patient with gallstones to seek the physician's help vary, ranging from vague and minimal complaints to attacks of prostrating pain. The term "indigestion" is most common and indicates a lack of well-being after eating, a sense of having eaten too much, followed by belching and slight regurgitation. Pain may be intermittent or constant and is usually in the midepigastrium or the right upper quadrant. Intense and excruciating pain is associated with acute inflammation and obstruction.

The most frequently encountered example of chronic cholecystitis is that of the patient who for months or years has had indigestion manifested by discomfort after eating. If a larger amount of food than usual is ingested, or if food high in fat content is included, there are, in addition, belching and regurgitation for several hours. These symptoms may increase, to be followed by pain and colic with nausea and vomiting. The duration of such episodes may be short or prolonged over hours or days. Many of these patients have had repeated episodes of acute cholecystitis. Some, however, may never have had an acute inflammatory process involving the gallbladder. Rather, the condition is believed to result from calculi in the gallbladder associated with a persistent low-grade infection.

In early adult life, the symptoms may be of little concern to a patient when they first appear. Over a few years, they may increase so insidiously that the exact time at which they began to cause actual disability is difficult to determine. Under such circumstances, patients tend to accept their symptoms as something they can and should tolerate. They learn to keep them to a minimum by avoiding overeating and by abstaining from an ever-increasing number of foods that they believe correctly or incorrectly cause their complaints. Many patients tolerate these symptoms throughout their more robust years of life. During this period, the changes of biliary tract disease—namely, increase in number and size of calculi, scarring of the gallbladder wall, and reduction in functional efficiency of the gallbladder—progress, and, what is probably of greater significance, the liver sustains injury which may range from negligible damage to frank cirrhosis. Undoubtedly there are instances in which the process seems to subside and the patient is symptom-free for years. As stones increase in number and size, the patients become likely candidates for an obstructive type of acute cholecystitis, which is one of the most frequent conditions leading to abdominal operation in persons over sixty-five years of age. Thus many individuals, unaware of the significance of their symptoms, have progressive injury to their liver and, if this has been considerable, may be poor operative risks when they present themselves for surgery. Such situations are frequent because many patients with chronic cholecystitis are able to tolerate their symptoms for years, and only when the degree of disability becomes marked and they experience an acute attack do they seek relief.

Diagnosis

The diagnosis of gallstones was greatly simplified by Graham, Cole, and Copher in 1924[5] with their development of cholecystography. Direct and indirect evidence obtained by this means provides over 95 per cent accuracy in the diagnosis of gallbladder disease. Within the past decade, the utilization of radiopaque material to visualize the intact ductal system has added materially to the evaluation of the biliary tract disease.

A careful history and physical examination together with cholecystography and cholangiography establish the diagnosis of biliary tract disease. The evaluation and exclusion of other conditions as a cause of symptoms provides for a degree of accuracy attained in few diagnoses.

Treatment

The treatment of biliary tract disease is surgical. Ninety-five per cent of patients with biliary tract disease have gallstones; the other 5 per cent of acalculous disease are associated primarily with infection and neoplasia.

The evolution of the present-day surgical treatment is significant. So-called medical treatment and management has gradually been replaced by operative procedures since Bobbs of Indianapolis in 1867[6] unwittingly performed a cholecystostomy. Eleven years later another American surgeon, J. Marion Sims, M.D.,[7] performed the first planned cholecystostomy. Four years later, July 5, 1882, Langenbuch[8] in Germany did the first cholecystectomy. There is some question as to who first removed calculi from the common duct successfully. Courvoisier[9] probably performed the first planned and successful choledocholithotomy on January 21, 1890. The first surgical removal of a common duct stone through choledocholithotomy by Kümmell,[10] on the other hand, antedates Courvoisier's operation by several years. Kümmell's operation, however, was not planned and the patient died. By 1900 the three procedures—cholecystostomy, cholecystectomy, and choledochotomy—had become established but were utilized chiefly in advanced disease and its complications. The common belief among the medical profession was that biliary tract disease was well tolerated by most patients and that there was considerable risk associated with surgery. Osler,[11] in an early edition of his famous textbook, subscribed to this view. The morbidity of complications and the mortality rate following surgery was high, the latter being estimated well above 10 per cent at the turn of the century.

With the increased accuracy of preoperative diagnosis made possible by cholecystography, a greater number of patients with gallstones were encouraged by their physicians to have a cholecystectomy. Over the past thirty years general advances in surgery and particularly in anesthesiology have made possible a reduction in the risk of operation, so that the anticipated mortality rate is now about 0.5 per cent for elective cholecystectomy. This has been accompanied by a comparable decrease in nonfatal complications. Of no little importance has been the ease from the patient's point of view with which operations on the biliary tract can be accomplished. The general over-all good results of cholecystectomy for cholecystitis and cholelithiasis and the safety and ease with which the operation is now associated as compared with the unpredictable and often dismal outlook for patients treated by medical management have led to wide acceptance of the surgical approach by general practitioners and internists as well as surgeons.

In recent decades there has developed an increased awareness that one cannot predict what complications will occur or when they will occur in any particular individual with gallstones. It has also become evident as experience has increased, that the majority of patients with gallstones who live into the older-age group will sustain significant liver damage as well as develop those grave sequelae and complications that contribute to the morbidity and mortality of the disease.

Classification

In an attempt to outline the natural course of calculous biliary tract disease and the complications that most commonly occur, a classification has been proposed. The results in the surgical treatment of disease of the biliary tract depend chiefly on the duration and severity of the disease, together with the age and general physical status of the patient. The least risk, the lowest mortality rate, and the smallest incidence of nonfatal complications occur among those patients who are under fifty years of age and whose histories suggest that biliary calculi have not been associated with complications, such as common duct stone or episodes of acute cholecystitis. The outstanding examples are those women who develop gallstones during the years of their early pregnancies.[12] For these women, undelayed cholecystectomy is accomplished with little risk, and in our experience follow-up studies made from twenty to twenty-five years later indicate approximately 95 per cent good results with surgical interruption of the disease.

This has prompted us to attempt to differentiate and classify biliary tract disease into groups according to changes believed to indicate its duration and rate of progress. Specifically, we have divided biliary tract disease into four stages. Each stage is defined readily and is not reversible. An acute phase can be superimposed on any stage without necessarily changing it.

STAGE I. In Stage I cholecystography reveals that the gallbladder fills readily and empties following a fat meal; stones are present. At operation the wall of the gallbladder is almost normal in appearance; the wall is thin, perhaps slightly thickened, and blue or gray. Histologically, there is only a mild chronic inflammatory response within the wall of the gallbladder. This stage is usually seen in young women in the third decade of life who have recently been pregnant, or in a slightly older group of women who have not been pregnant, or in men in the third to fifth decades of life.

STAGE II. In Stage II cholecystography visualizes the gallbladder faintly and shows that it empties incompletely following a test fat meal. Stones have been present for a longer time than in Stage I. The gallbladder wall at operation is thickened and gray, and histologically there is scarring within the liver. There is an increased incidence of choledocholithiasis. This stage occurs in a wider age range, and symptoms have been present for a longer period of time. Almost two thirds of the patients operated on by us were in this group.

STAGE III. In Stage III cholecystography reveals that the gallbladder no longer functions. It is rarely visualized. Stones have been present for a long time. At operation the wall of the gallbladder is thickened, white, and contracted down about its contained stones. There is a much higher incidence of choledocholithiasis, and there may be more scarring within the liver. Symptoms have been long-standing, and often the episode just preceding admission to the hospital has been characterized by pain and biliary colic that is described as moderately severe and is followed by jaundice. This stage of the disease is seen in the older-age group, especially in persons sixty years of age and older. The incidence of morbidity and mortality is higher, and the disease may well be fatal in patients with major degenerative illnesses; patients should not be allowed to progress to this stage.

STAGE IV. In Stage IV are included conditions and complications associated with long-standing and advanced biliary tract disease. In this category are biliary-enteric fistula, cirrhosis of the liver, benign stenosing fibrosis of the ductal system, and neoplasms of the gallbladder and bile ducts.

The particular stage at which operation is undertaken for biliary tract disease to some extent determines just what is to be done, that is, whether the procedure is to be a cholecystectomy, a common duct exploration, a correction of a biliary-enteric fistula, or a right lobectomy for carcinoma of the gallbladder.

Surgical procedures

If the disease is limited to the gallbladder, cholecystectomy is indicated. If the common duct contains stones, they should be removed. Scarring and stenosis of the sphincter of Oddi may be overcome by incising the involved part, or the common duct may be transected and anastomosed anew to the duodenum. Tumors that involve the ampulla of Vater require resection of a segment of the duodenum and partial pancreatectomy. For nonresectable cancer involving the extrahepatic ductal system and producing obstructive jaundice, palliative procedures that provide a bypass are indicated.[13]

The gallbladder containing stones should be removed irrespective of the stage or phase of biliary tract disease, unless there is some contraindication that renders the procedure hazardous. The patient's general condition and the inflammatory reaction that distorts the anatomic relationship may, for example, be reasons for doing a lesser procedure. Although cholecystectomy is the procedure of choice in acute cholecystitis, the surgeon should keep an open mind as to just what is to be done until he has evaluated the findings at operation. Cholecystostomy, a lesser procedure, may be indicated in the presence of a peritonitis following a perforation of the gallbladder. Later, within a matter of weeks or months when circumstances are more favorable, the gallbladder should be removed. It has been observed that over half the patients who have stones removed and only a cholecystostomy done will develop additional stones within two years.[14] In almost every instance of biliary tract disease that is not in an acute phase, cholecystectomy can be done. The removal of a gallbladder should include the removal of the cystic duct to within 5 mm. of its true junction with the common duct. Remnants of the cystic duct may be the site of stone formation and reproduce the clinical picture of cholelithiasis. In removing the gallbladder, care should be exercised not to injure the common duct or the blood supply to the liver. If the right hepatic artery is ligated mistakenly instead of the cystic artery, this may be fatal. The incidence of anatomic variations of the blood vessels and bile ducts in the subhepatic area sufficient to be called anomalies is estimated at from 10 to 15 per cent.

Comment

On the basis of a five-day week, it is estimated that in the United States there were over 1,600 operations performed daily on the biliary tract during the current year. For some, perhaps the majority, it was a planned and an elective procedure directed at the relief of symptoms and a wide range of disability. A small proportion of these operations, perhaps 10 per cent, were done as urgent or emergency procedures because of the complications of biliary tract disease. They were undertaken in an attempt to prevent or combat a grave situation that might be fatal. The disability of those with biliary tract disease is not readily estimated. That it is considerable there is no doubt. The common symptoms of indigestion and pain are tolerated well by some, while others are incapacitated and are unable to work. The complications of acute cholecystitis and jaundice due to common duct obstruction, of course, may result in the patient being confined to bed. Autopsy figures are the basis for estimating that over 10 per cent of our adult population have gallstones. There is great variation in the extent of the complaints and the disability they cause, some being asymptomatic. Of those patients who are operated on for biliary tract disease, about 95 per cent have gallstones. Are they the disease, the cause of the disease, or the result? Evidence might be advanced in support of each of the three concepts.

Whether or not the incidence of biliary tract disease is increasing in this country is difficult to determine. Progress has been and continues to be made in the early recognition of the condition and in the reduction of the time delay between diagnosis and surgical therapy. The risk of operation and the burden of operation on the patient are constantly being lessened. In our experience with surgery for nonmalignant disease of the biliary tract from September 1, 1932, to September 1, 1960, at The New York Hospital-Cornell Medical Center, we have a mortality rate of 0.7 per cent for patients undergoing cholecystectomy, that is, there were 33 deaths among 4,309 cases; there was a mortality rate of 12.4 per cent for cholecystostomy, or 17 deaths among 137 patients; and a mortality rate of 4.1 per cent for choledochotomy, with 39 deaths among 933 patients. These results are commendable but this is not good enough. Gallstones can surely be prevented. Think how this would contribute to the avoidance of disability and be the possible extension of life, to say nothing of the saving of the cost of this disease in dollars from loss of time from work, ineffectiveness in effort, and medical care.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 14 to 18, 1962, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1962*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

ALFRED A. ANGRIST, M.D., *Chairman*
Committee on Prize Essays

Natural History of Aneurysm of Ventricle

ALBERT H. DOUGLAS, M.D.
Jamaica, New York
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From the Department of Medicine, Queens Hospital Center

THE MOST COMMON VARIETY of aneurysm of the ventricle occurs as a sequel of myocardial infarction. Of 4,427 consecutive autopsies at the Queens Hospital Center, 524 cases of myocardial infarction were found (12 per cent); 45 of these had ventricular aneurysm (1.02 per cent of the total number of autopsies and 8.7 per cent of the patients with myocardial infarction). To this series were added 6 patients who were followed clinically. In the series there was a great difference between the incidence of ventricular aneurysm in patients with myocardial infarcts as reported by the pathologist at autopsy (8.7 per cent) and the incidence reported by the clinician, chiefly on the basis of x-ray film study (1.7 per cent); thus 3 out of 4 cases were missed clinically. Ventricular aneurysm should be suspected when myocardial infarction is associated with an increase in cardiac dullness, maximum pulsation internal to the left cardiac border, or paradoxical pulsation. A localized bulge on x-ray film yields a diagnosis in a minority of cases only. In this series 60 per cent of the infarcts were located anteriorly. The authors believe that the combination of a transmural anterior wall myocardial infarct with or without a localized bulge on x-ray film, but with cardiomegaly which develops subsequent to the lesion and which cannot be explained by hypertension or associated valvular disease is very suggestive. The results of operation on 35 cases of ventricular aneurysm following myocardial infarction, with a maximum follow-up of three years, have been most encouraging. Further investigation of the control of paradoxical pulsation by means of a prosthesis, with or without excision of the infarcted myocardium, seems indicated.

THE DRAMATIC ADVANCES in cardiac surgery during the past decade have made it necessary for the internist to acquaint himself more accurately with the natural history of cardiac lesions that may be correctable. What the surgeon has to offer must be weighed against the probable course on medical therapy alone. In this report it is our purpose to examine current concepts concerning aneurysm of the ventricle and the prognostic implications of the diagnosis. We shall limit our study to the most common variety of ventricular aneurysm which occurs as a sequel of myocardial infarction.

That aneurysm of the heart is not a rare disease has been well demonstrated by Schlichter, Hellerstein, and Katz[1] who found 102 cases in a series of 512 patients with myocardial infarction, an incidence of 20 per cent. They selected their cases from 5,836 consecutive autopsies, constituting 1.8 per cent of the total patients. These figures contrast sharply with the relative infrequency with which the diagnosis is made during life. Thus, a recent textbook of medicine[2] devotes only a small paragraph to the subject and states that they "are usually of little clinical importance." Considering the frequency and importance of myocardial infarction, a complication which appears so often at postmortem examination and which is missed so often clinically, this condition deserves careful re-evaluation if it can be demonstrated that the lesion affects cardiac function significantly and if specific therapy is possible.

Material

The autopsy files of the Queens Hospital Center, for the period from 1954 to 1960, were studied. The authors are indebted

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* By invitation.

TABLE I. Age and sex in ventricular aneurysm

Age (Years)	Male	Female	Total
40 to 44	1	0	1
45 to 49	2	0	2
50 to 54	4	0	4
55 to 59	2	0	2
60 to 64	6	1	7
65 to 69	8	6	14
70 to 74	9	4	13
75 to 79	3	1	4
80 to 84	0	1	1
85 to 89	1	1	2
90 to 94	0	1	1
TOTALS	36	15	51

TABLE II. Duration of life after onset of ventricular aneurysm

Interval	Number of Cases	Percentage
Months		
0 to 5	11	35
6 to 11	4	. . .
12 to 23	3	. . .
24 to 35	2	30
36 to 47	0	. . .
48 to 59	3	. . .
Years		
Over 5	5	. . .
Over 10	2	. . .
Over 15	1	35
TOTAL	31	

to Alfred Angrist, M.D., and Gertrude Silverman, M.D., for the postmortem data. Of 4,427 consecutive autopsies, 524 cases of myocardial infarction were found (12 per cent) and ventricular aneurysm was reported in 45 cases, an incidence of 1.02 per cent. In this series 8.7 per cent of the patients with myocardial infarction had ventricular aneurysm. To this series we added 6 patients who were followed clinically.

The ages of the patients ranged from forty to ninety-four years. There were 36 males and 15 females (Table I). Sixteen patients died from noncardiac causes, including 6 who died from cerebrovascular disease. Embolism was found in 2 cases, and rupture of the ventricle was found in 1 case (four days after the onset of myocardial infarction). Fifteen patients died of myocardial infarction, and 6 patients had terminal congestive heart failure.

In 31 instances the history permitted an approximation of the duration of the lesion following myocardial infarction. Six deaths occurred within the first week, 8 occurred within a month, and 11 occurred within five months (Table II). Eight patients lived longer than five years, and 3 lived for ten or more years. The longest survival time was fifteen years.

A review of the records indicated that 18 of the 45 autopsied cases had had chest x-ray films. The roentgenologist reported an enlargement of the heart or an increase in the transverse diameter in 13 patients, a hypertensive configuration in 3 patients, a calcification in 1 patient, and a left pleural effusion in 1 patient. It is evident from these figures that the characteristic localized bulge that makes an aneurysm of the ventricle easy to recognize in the x-ray film is uncommon. Clinical search for such obvious saccular enlargements of the cardiac silhouette yielded only 6 cases from among 360 patients with myocardial infarction, an incidence of 1.67 per cent.

Electrocardiograms were available for 40 patients of our series. The pattern of anterior wall myocardial infarction was found in 24 patients (60 per cent) and of posterodiaphragmatic infarction in 5 patients (12.5 per cent). The remainder of the patients showed atypical patterns, interpreted as left bundle branch block or left ventricular hypertrophy.

Studies of hospital charts after a postmortem diagnosis cannot yield as accurate a clinical picture as that obtained by the physician who has had the opportunity to observe the patient personally over a period of years. It was considered worth while, therefore, to present briefly the course of the 6 patients in whom a clinical and x-ray film diagnosis of ventricular aneurysm was made.

Case reports

CASE 1. A seventy-one-year-old normotensive man sustained an anterior wall myocardial infarction at the age of sixty years. He was treated with Dicumarol for four weeks, and his course was uncomplicated except for transient left-sided failure. His electrocardiograms are

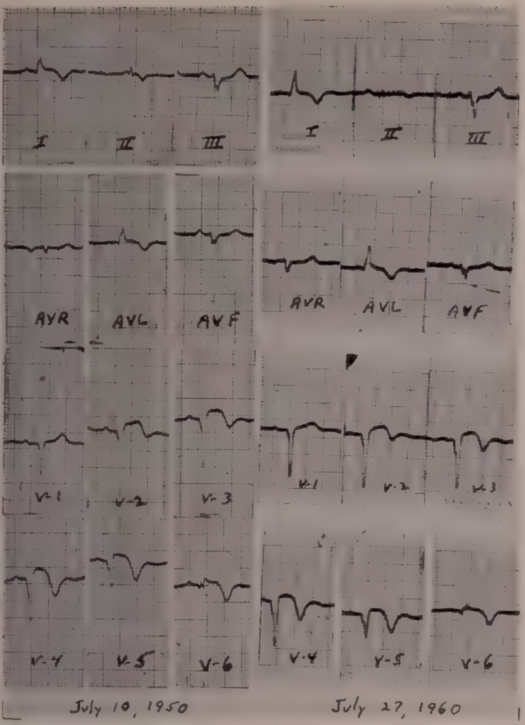

FIGURE 1. Case 1. Ten-year-old calcified ventricular aneurysm.

presented in Figure 1. When he was re-examined three months after his coronary attack, the patient showed roentgen evidence of an aneurysm of the left ventricle (Fig. 2). The patient subsequently returned to a program of normal activities. Frequent re-examinations over a ten-year period have revealed no evidence of impaired cardiac reserve, nor has the patient complained of chest pain or dyspnea with effort.

A calcification of the wall of the aneurysm has been well illustrated.

This case shows that life expectancy is not always shortened, nor is morbidity always increased, even when the ventricular aneurysm is large. It may well be that the calcification provides protection against loss of ventricular contractile force associated with paradoxical pulsation.

Case 2. A fifty-eight-year-old male developed an anterior wall myocardial infarction. He returned to work at the betting window of a race track after four days. He presented himself at the office of one of us (A. D.) five months after the onset of a history of chest pain. Roentgen studies showed a typical aneurysm of the left ventricle. The electrocardiograms are presented in Figure 3. There was no history of antecedent hypertension, but the blood pressure range during six and one-half years of observation was from 140/70 to 170/90.

This patient was able to perform his usual duties at work, including travel between the various race tracks along the eastern seaboard, until his sudden death, six and one-half years after the onset of his illness. A postmortem examination revealed extensive anterolateral infarction with aneurysm of the ventricle and widespread coronary artery sclerosis.

Clinically, this patient's course was com-

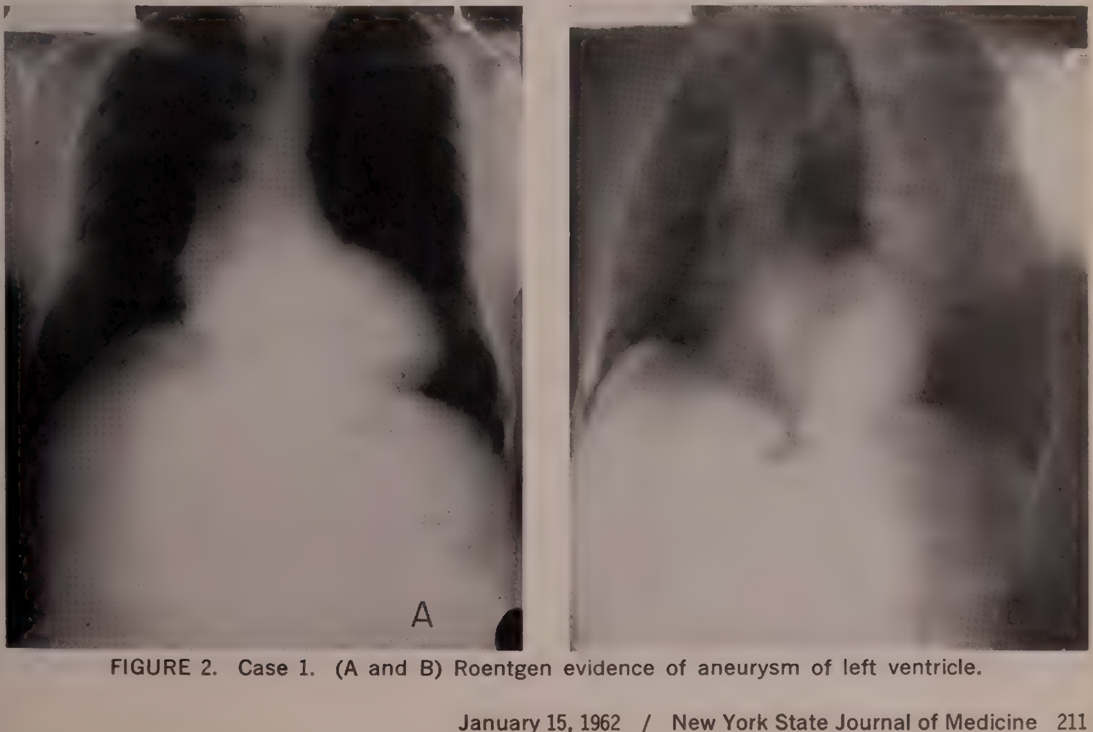

FIGURE 2. Case 1. (A and B) Roentgen evidence of aneurysm of left ventricle.

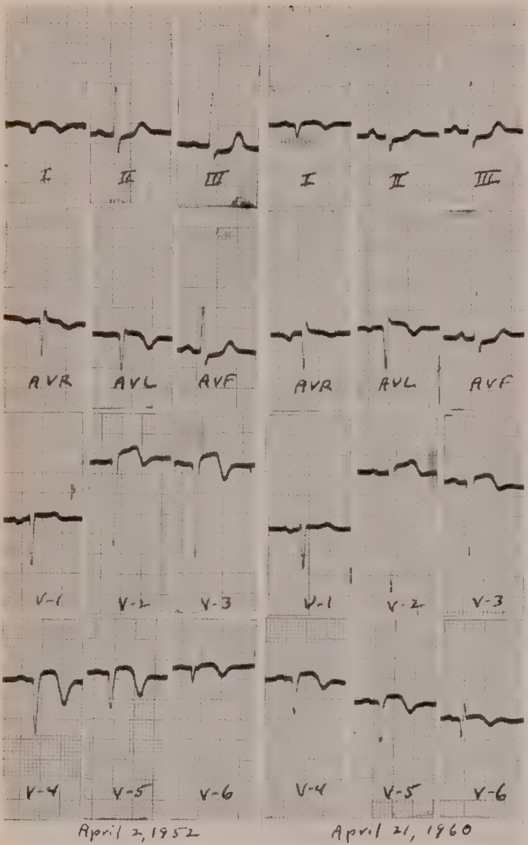

FIGURE 3. Case 2. Electrocardiogram of patient who expired six and one-half years after onset of aneurysm.

plicated by mild congestive failure, angina, and ventricular premature contractions. However, his symptoms were well controlled by medical therapy and did not incapacitate him.

CASE 3. A fifty-year-old merchant sustained an anterior wall myocardial infarction and was found to have a ventricular aneurysm when he was re-examined a year after the onset of his illness. There was no history of hypertension. The coronary attack was a severe one and was followed by angina with effort and a shoulder-hand syndrome. The patient had five months of rest before he returned to sedentary work.

Four years later the patient sustained a second myocardial infarct, located inferiorly and with electrocardiographic changes suggestive of a nontransmural lesion. At this time long-range anticoagulant therapy was started. Following this attack his angina decreased in frequency, and the patient was able to return to work and to indulge in moderate effort without distress. He expired suddenly six years after his first coronary episode. A postmortem examination was not done. The electrocardiograms in this case are presented in Figure 4.

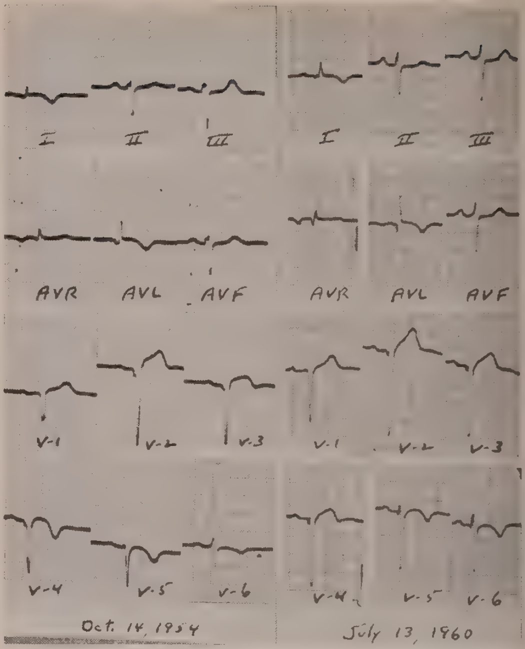

FIGURE 4. Case 3. Electrocardiogram of patient who expired six years after onset of aneurysm.

CASE 4. A forty-eight-year-old dress salesman developed an anteroseptal infarct, followed by a severe shoulder-hand syndrome. There was no hypertensive history, and the postcoronary blood pressure range was from 88/68 to 130/80. After four weeks of bed rest, a cautious increase in activities was permitted. X-ray studies three months after the attack suggested an aneurysm of the ventricle. Long-range anticoagulant therapy was prescribed. Dyspnea and occasional chest pain with effort required appropriate therapy, but the patient was able to return to work. Five years after the initial myocardial infarct, this patient had a second infarct, located anterolaterally. He is now convalescing from this illness and is doing relatively well. His electrocardiograms are shown in Figure 5.

CASE 5. A forty-four-year-old salesman of canned goods was treated for an anteroseptal myocardial infarct and made a good recovery. When he presented himself for routine reexamination three years later he had roentgen evidence of ventricular aneurysm. He had no hypertensive history, and a month of rest in the hospital was followed by a gradual resumption of activities without symptoms. Six years have passed since the onset of the patient's heart disease. He leads a normal life and requires no therapy. His electrocardiograms are presented in Figure 6.

CASE 6. A fifty-four-year-old sheet metal worker was hospitalized because of an extensive myocardial infarct. Electrocardiograms (Fig.

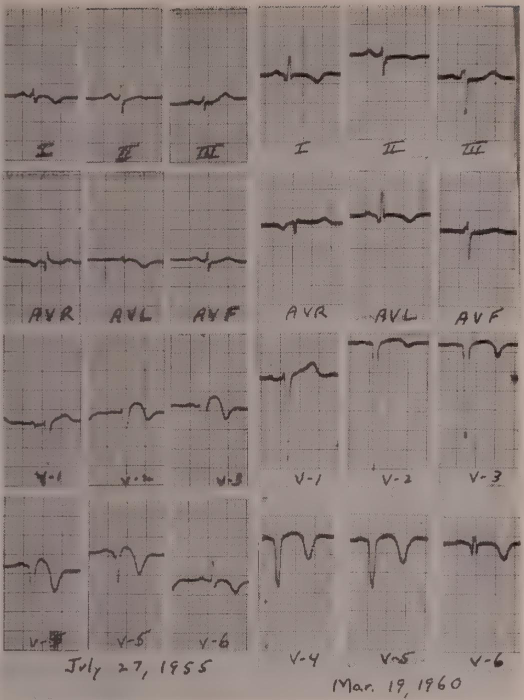

FIGURE 5. Case 4. Electrocardiogram of patient who survived five years.

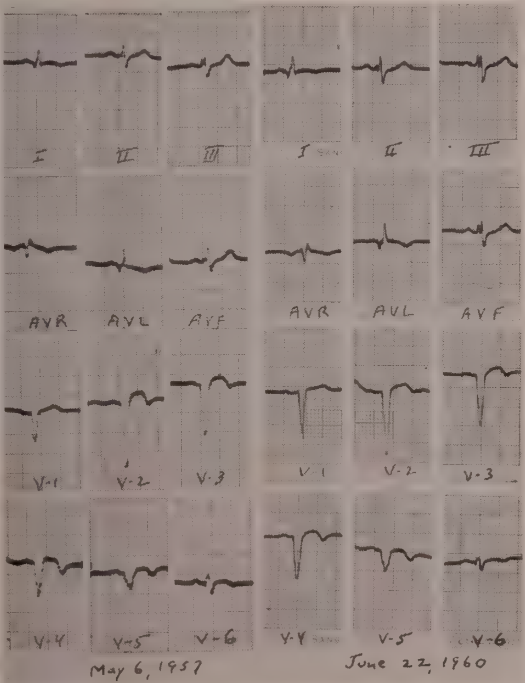

FIGURE 6. Case 5. Electrocardiogram of patient who survived over six years.

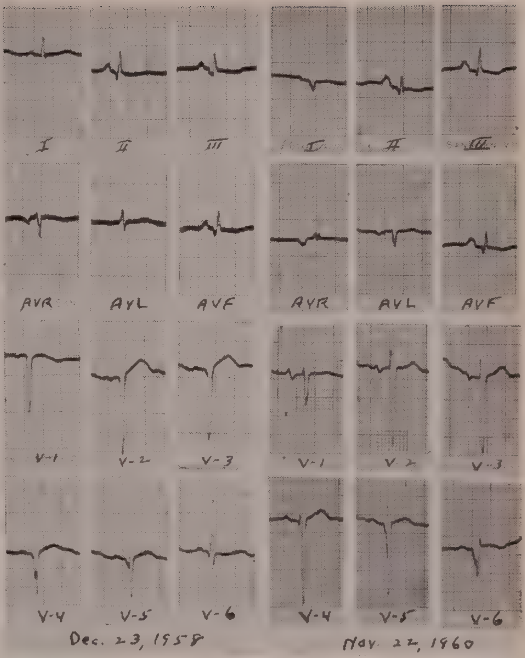

FIGURE 7. Case 6. Electrocardiogram of patient who survived two years.

7) suggested an involvement anteroseptally and inferiorly. The patient was critically ill and required therapy for shock, pulmonary edema, and bronchopneumonia. A loud pericardial rub was audible during the first week. However, he was discharged from the hospital after a month and returned to work after three months. There was no history of hypertension, and the postcoronary blood pressure has averaged 120/90. X-ray studies a month after the onset of illness suggested ventricular aneurysm.

This patient did heavy work for two weeks after the onset of pain in the left upper extremity and returned to heavy work against advice. His clinical course has been complicated by claudication due to peripheral arteriosclerosis and congestive failure which requires digitalis and diuretics, but the patient has continued with a "work as usual" program. He now has marked cardiomegaly and is an example of the probable role of "too much and too early" exertion in the pathogenesis of the lesion in some cases.

In summary, 2 of 6 patients with ventricular aneurysm who were followed clinically were alive and well six and ten years later respectively. Three cases had further coronary thrombotic episodes. Congestive failure was significant in only 1 instance.

Comment

In our series there is a striking difference between the incidence of ventricular aneurysm in patients with myocardial infarcts as reported by the pathologist at autopsy (8.7 per cent) and the incidence reported by the clinician, chiefly on the basis of x-ray film study (1.7 per cent). It would appear that we are missing 3 out of 4 cases, and this is a serious matter if specific therapy is available.

In the literature there are relatively few studies that permit an analysis of large numbers of these cases. For the most part isolated cases[3-5] or small series of 10 or fewer cases[6,7] are described. This is strange, since myocardial infarction accounts for an ever-increasing percentage of deaths,[8] and our hospitals are bulging at the seams with coronary cases. The most complete postmortem review is that of Schlichter, Hellerstein, and Katz.[1] These authors found that 20 per cent of their myocardial infarcts showed ventricular aneurysm, but they agree that this figure is higher than that reported by most investigators. On clinical evidence, presumably x-ray-film enlargement, Master *et al.*[9] have reported an incidence of 5.7 per cent in a series of 209 patients with myocardial infarcts who were listed as Class 1 from a functional point of view, with a higher incidence in those more seriously handicapped. In these reports there is no indication of the criteria for clinical diagnosis. As indicated, we have limited our diagnosis to those patients in whose chest x-ray films there was an obvious localized bulge.

Perhaps the present generation of physicians is to be criticized for paying inadequate attention to information obtained by percussion and auscultation. There is little doubt that the astute clinician occasionally can suspect ventricular aneurysm when myocardial infarction is associated with an increase in cardiac dullness, with maximum pulsation internal to the left cardiac border, or even a rare instance where paradoxical pulsation might be considered to exist.[10] It is quite clear that Roentgen's discovery of the x-ray made the diagnosis much easier. However, our data indicate that a localized bulge on x-ray film yields a diagnosis in a minority of cases only. This information must, therefore, be supplemented. In all probability, more frequent use of angiocardiography following myocardial infarction would increase diagnostic accuracy, but this technic has been used little for this purpose up to the present. Dolly, Dotter, and Steinberg[5] demonstrated in 1 case that radiopaque material can delineate clearly an aneurysm of the ventricle.

Because the lesion pulsates paradoxically, use has been made of roentgen kymography[11] electrokymography,[7,12] and kinetocardiography[13] to make more accurate diagnoses. It is not within the scope of this report to consider these methods in detail. Their weakness is inherent in the fact that paradoxical pulsation can be demonstrated in the absence of anatomic aneurysm and even in the absence of myocardial infarction.[13]

Considerable attention has been paid to the electrocardiographic patterns in ventricular aneurysm, and several authors have called attention to the frequency with which the displacement of the S-T segment persists in these cases.[6] Others have stressed a small R-I associated with a deep S in leads II and III and a tall R in aVr as diagnostic.[14] It has become clear, however, that there is no electrocardiographic pattern which can be considered characteristic of the lesion.[1] However, the frequency with which anterior wall infarcts are found has been impressive in the series reported in this commentary and in the literature.[3-7] Perhaps these figures are misleading and mean nothing more than an increased difficulty in the recognition of aneurysms located posteriorly or inferiorly. This does not seem probable, however, when postmortem correlation shows such a marked difference. In our material 60 per cent of the infarcts were located anteriorly. We believe, therefore, that the combination of a transmural anterior wall myocardial infarct with or without a localized bulge on x-ray film, but with cardiomegaly which develops subsequent to the lesion and which cannot be explained by hypertension or associated valvular disease, is very suggestive.

An accurate diagnosis of ventricular aneurysm is important only if it affects the prognosis and treatment. We have confirmed the report of others to the effect that an aneurysm of the ventricle, even when it is large, need not shorten life expectancy.[1,3] However, Schlichter, Hellerstein, and Katz[1] have reported that 73 per cent of 66 cases died within three years, and 88 per cent died within five years. In our series 8 of 31 cases (26 per cent) survived for more than five years.

It is evident that the great majority of patients with ventricular aneurysm die within five years. An analysis of the causes of death indicates recurrent myocardial infarction in 33 per cent and congestive heart failure in 13 per cent of our series of 45 cases. The group that showed congestive heart failure is of particular interest because surgical therapy has been limited thus far to these cases. Crucial questions concern the mechanism of failure in these patients. Why does failure occur in one instance and not in another with an anatomic lesion of comparable extent? Why can an excision of a ventricular aneurysm cure congestive heart failure? The assumption that paradoxical pulsation is the villain seems to explain all the facts best. Thus, one can understand why a calcified segment of the ventricle which cannot contract interferes less with ventricular output than does a thin zone which balloons outward with each systole. In other words, no contraction is better than paradoxical pulsation. Data obtained from the relatively small number of cases treated surgically (Table III) support this conclusion. Thus, Templeton *et al.*[15] and Cooley *et al.*[16] found a significant increase in the cardiac output and in the cardiac index following excision. It may well be that the organization of an endocardial thrombus lining the aneurysm, possibly with calcification at a later stage, serves as a protective patch. The rapidity with which aneurysmal dilatation takes place is another factor that must be considered. Some thirty years ago Shookhoff and Douglas[17] had occasion to report a case of aneurysm of the ventricle within a few days after the onset of myocardial infarction. This was considered uncommon at the time, but it has since been shown to be a frequent occurrence.[1] In our present study 6 of 41 patients died within a week, and 8 died within a month.

The prognosis, then, appears to be determined by the following factors: (1) the extent of myocardial damage and its effect on cardiac output by paradoxical pulsation; (2) the protection afforded by subendocardial thrombosis, when the thrombus is firmly adherent, and the danger of embolization when the thrombus is fragile; (3) the rapidity with which dilatation of the aneurysmal sac occurs; (4) the condition of the uninfarcted myocardium; and (5) the condition of the coronary supply to the intact myocardium.

TABLE III. Surgical results in postinfarction ventricular aneurysm

Author	Number of Patients	Number of Survivors	Maximum Follow-Up Reported
Templeton *et al.*[15]	3	3	26 months
Cooley *et al.*[16]	10	8	14 months
Bailey *et al.*[19]	6	5	3 years
Petrovskii[20]	15	14	?
De Camp[21]	1	0	. . .
TOTALS	35	30	

Up to the present time about 35 cases of ventricular aneurysm following myocardial infarction have been operated on, with a follow-up to a maximum of three years.[15–20] As indicated in Table III, the results have been most encouraging. They emphasize the importance of an increased awareness of ventricular aneurysm as a physiologic rather than an anatomic entity.

If there is a significant reduction in the cardiac output because of paradoxical pulsation, the presence of an anatomic aneurysm would seem to be of less importance than the presence of a physiologic aneurysm. With our present knowledge, it seems reasonable to believe that an excision of a myocardial infarct may cure refractory congestive failure even when a localized bulge is not demonstrable on x-ray film. In this regard, it is pertinent to refer to the classic experiments of Murray[18] who demonstrated that an excision of an acute myocardial infarct in the dog is feasible. Bailey *et al.*[19] repeated Murray's experiments and concluded that such an excision was followed by a congestive failure attributed to the small size of the repaired ventricle. One wonders what the results would be if a myocardial infarct were excised and replaced by a prosthesis that would maintain the ventricular size. If the assumption that "no pulsation is better than paradoxical pulsation" is valid, such experiments should succeed and may pave the way for similar surgery in human beings.

Summary

1. Of 4,427 consecutive autopsies at a large municipal hospital, myocardial infarction was found in 524 or 12 per cent. In 45 (8.7 per cent) of the coronary group a diagnosis of ventricular aneurysm was made.

2. A review of clinical material yielded 6 cases with an obvious localized bulge on x-ray film in a series of 360 cases of myocardial infarction, an incidence of 1.7 per cent. Many cases, therefore, are missed clinically.

3. Thirteen of 18 chest x-ray films of patients with ventricular aneurysm, proved at autopsy, showed only diffuse cardiomegaly, without an obvious localized bulge.

4. Of the electrocardiograms of the proved cases of ventricular aneurysm 60 per cent showed the pattern of anterior wall myocardial infarction.

5. When myocardial infarction is followed by cardiomegaly not explained by hypertension or valvular disease, the presence of ventricular aneurysm must be suspected. This is particularly true if the electrocardiogram suggests anterior localization. In these cases refractory congestive heart failure may be amenable to surgical therapy.

6. The concept that "no pulsation is better than paradoxical pulsation" is suggested by the long survival of some patients with large calcified aneurysms. The natural history of aneurysm of the ventricle, therefore, gives a clue to further investigation, directed to the problem of control of paradoxic pulsation by means of a prosthesis, with or without the excision of the infarcted myocardium.

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Hypothermia: Ventricular Fibrillation During Hyperventilation

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VENTRICULAR FIBRILLATION can occur spontaneously during hypothermia or as the result of mechanical stimulation. Acidosis and respiratory alkalosis predispose the heart to ventricular fibrillation. The occurrence of ventricular fibrillation can be reduced by controlling the pH of the blood through the alteration of ventilation. A study was undertaken on 10 dogs to determine the temperature at which ventricular fibrillation would occur when respiratory alkalosis was induced. Marked hyperventilation was used to produce alkalosis; surface cooling was used to lower the temperature of the animals. Five of the animals were unprepared; 5 had the plasma potassium level lowered slightly by diet and sodium exchange resin. Hypothermia and hyperventilation produced the following results: The minute volume of respiration varied from 21 to 27 L. per minute. The blood pH level rose in all the animals; the highest level was 8.1. Five of the 10 dogs developed ventricular fibrillation above 20 C.; the highest temperature at which ventricular fibrillation occurred was 24.2 C. An Osborn S-ST wave occurred in all but 1 of the animals. The arterial carbon dioxide pressure was reduced by hyperventilation and hypothermia from an average of 45 mm. Hg at normothermia preventilation to an average of 2.1 mm. Hg at the lowest temperatures at which the samples were taken.

DURING HYPOTHERMIA ventricular fibrillation can occur spontaneously, or it can be precipitated by mechanical stimulation, such as cardiotomy. Acidosis increases the incidence of ventricular fibrillation.[1-3] The occurrence of ventricular fibrillation can be reduced by controlling the pH of the blood through the alteration of ventilation.[1-11] If the pH of the blood is normal, asystole instead of ventricular fibrillation may occur in deep hypothermia.[7,11] Curiously enough, respiratory alkalosis due to hyperventilation also appears to predispose the heart to ventricular fibrillation.[10,12]

This study was undertaken to determine the temperature at which ventricular fibrillation would occur when respiratory alkalosis was induced. Marked hyperventilation was used to produce the alkalosis. Surface cooling was used to lower the temperature of the animals.

Method

Ten dogs were studied. The first 5 were unprepared. The second 5 were kept on a low-potassium diet for from one week to ten days and gavaged daily with 5 Gm. per kilogram of ion-exchange resin in the sodium cycle.

The animals were young, adult, 9- to 16-Kg., male and female mongrel dogs. Each animal was anesthetized with 30 mg. per kilogram of pentobarbital sodium administered intravenously. A tracheal catheter was introduced.

A catheter was inserted in the proximal end of a transected carotid artery for the taking of blood samples and for the continuous determination of the blood pressure. The blood pressure was recorded with a strain gauge and a photographic recorder. A catheter was placed in the external jugular vein, and the tip was advanced to the junction of the superior and inferior vena cavae. The position of the catheter was verified at autopsy. Venous samples were taken from this catheter. Electrocardiographic leads were placed as subcutaneous needles so that apical or standard lead II records could be made. A thermistor probe was placed in the esophagus at the level of the heart to observe the temperature.

After the preparation of the animal, the

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TABLE I. Effect of hyperventilation during hypothermia.

Dog No.	Kg.	Ventilation O_2L / Min.	pH ** at low Temp.	K		Temperature			Partial pressure CO_2 in blood	Buffer Base
				before	low temp	Appearance of S-ST wave	VF Temp.	Diff.		
1	9.5	22	7.63	5.7	5.3	28.0	Not at 20			
2	11.5	26	7.62	6.3	5.0	37.0	22.4	14.6		
3	15.4	28	7.67	4.4	4.7	30.0	Not at 20			
4	16.1	27.5	7.79	4.5	4.0	32.0	22.5	9.5	P_aCO_2 46→2.4	42.8→34.0
5	10.0	21.2	8.12	3.8	3.4	28.0	Not at 20		P_aCO_2 52→1.6	
*6	10.0	21	7.90	3.3	3.2	28.5	Not at 19.5			
*7	12.0	27	7.75	4.4	4.3	32.0	23	9.0	P_aCO_2 47→2.6	44.2→33.2
*8	10.7	21	7.73	3.7	3.8	37.0	22.5	14.5	$P_aCO_2 45 \rightarrow \left\{\begin{matrix} Pa\ 1.9 \\ Pv\ 5.0 \end{matrix}\right.$	39.3→30.0
*9	9.5	26	7.90	4.0	3.4	none	Not at 16		$P_aCO_2 49 \rightarrow \left\{\begin{matrix} Pa\ 1.4 \\ Pv\ 3.1 \end{matrix}\right.$	40.5→30.8
*10	12.1	27	7.50	2.6	2.0	38.0	24.2	13.8	$P_aCO_2 33 \rightarrow \left\{\begin{matrix} Pa\ 2.6 \\ Pv\ 10.8 \end{matrix}\right.$	41.7→ 30.0

* LOW K DIET + ION EXCHANGE RESIN, SODIUM CYCLE

** CORRECTED FOR TEMPERATURE

tracheal catheter was connected to a Palmer pump with a rate of 60 per minute and a stroke volume of 380 to 500 cc. The inspiratory pressures were 18 to 25 mm. Hg, and the expiratory pressures were 4 to 7 mm. Hg. The minute volume of respiratory exchange was measured before immersion and at 25 C. with the Bennett ventilometer. One hundred per cent oxygen was administered throughout the experiment. The animal was given 0.8 to 1 mg. per kilogram of curare to prevent shivering. Cooling was accomplished by immersing the entire animal in ice water. The temperature was lowered until ventricular fibrillation occurred or until it reached 20 C. One animal was followed to asystole at 16 C. Each animal was sacrificed at the end of the experiment.

The pH of the blood was determined with the Holaday pH meter.[13] The pH was read at 37 C. and was corrected to the temperature of the blood at the time the sample was taken. The carbon dioxide content was determined by the method of Holaday and Varosky.[14] The carbon dioxide pressure was calculated by using the Singer and Hastings[15] nomogram. The potassium concentration was determined by the use of the Patwin flame photometer with an internal standard.

Results

Table I summarizes the observations in the 10 dogs. The minute volume of respiration varied from 21 to 27 L. per minute. The pH of the arterial blood at the lowest temperature prior to fibrillation or discontinuation of the experiment varied from 7.50 to 8.12. The average precooling level of potassium in the arterial plasma of the untreated dogs was 4.9 mEq. per liter. The average precooling level of potassium in the treated dogs was 3.6 mEq. per liter. The plasma level of potassium fell in 8 of the 10 dogs during cooling. Of the 2 dogs with an elevation of plasma potassium during cooling, 1 was in the untreated group and the other in the treated group.

The temperature of only 1 dog was followed below 20 C. Five of the 10 dogs developed ventricular fibrillation above 20 C. The highest temperature at which ventricular fibrillation occurred was 24.2 C. The Osborn or S-ST wave (Fig. 1) occurred in every instance except in the

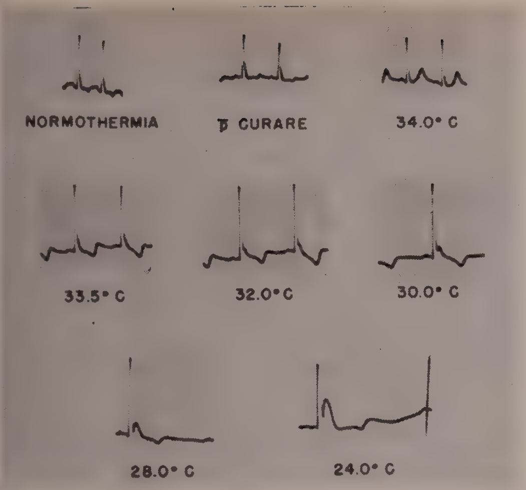

FIGURE 1. The Osborn or S-ST wave developed gradually as the temperature fell.

animal that was followed to asystole at 16 C.[2,5] The arterial carbon dioxide pressure was reduced by hyperventilation and hypothermia from an average of 45 mm. Hg at normothermia preventilation to an average of 2.1 mm. Hg at the lowest temperatures at which the samples were taken.

The atrioventricular carbon dioxide pressure difference at the low temperatures averaged 4.3 mm. Hg.

Comment

The minute volume of ventilation remained relatively constant for each animal. It was common for the temperature to drop several degrees shortly after hyperventilation was started. It is possible that the movement of the oxygen at room temperature produced a local cooling effect on the trachea and esophagus.

Niazi and Lewis[10] found a marked alkalosis with normal or slight hyperventilation. In this study, even with gross overventilation, the average pH at the lowest temperatures was 7.76. Perhaps a metabolic acidosis prevented a further rise of pH. There was no evidence of shivering to produce a metabolic acidosis. However, the blood pressure usually fell markedly after the administration of curare, and it remained low thereafter. Peripheral stasis might then have occurred with a resulting metabolic acidosis. The buffer base fell from an average precooling level of 42.2 to 33.5 at the lowest temperature at which samples were taken. The tongue veins were bright pink, and the chest wall veins oozed pink blood when cardiac resuscitation was performed.

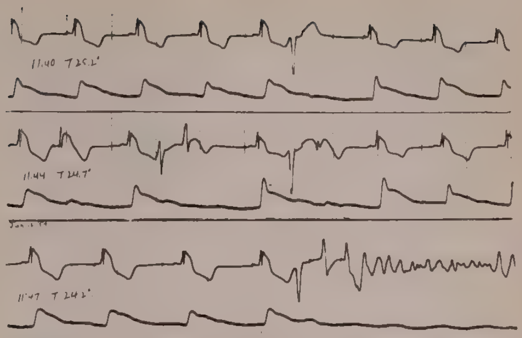

FIGURE 2. Upper tracing is the electrocardiogram. Lower tracing is the arterial pulse. The extrasystoles occurred in the vulnerable period and finally produced ventricular fibrillation as the temperature fell.

Hyperventilation and hypothermia produced a marked fall in the blood carbon dioxide pressure levels. The arteriovenous carbon dioxide pressure differences indicate that the bodies of the animals were producing carbon dioxide and that the lungs were effectively excreting it.

The animal which had ventricular fibrillation at the highest temperature was also the animal with the lowest initial potassium level. However, the 1 animal that did not have the wave premonitory of ventricular fibrillation was also in the low potassium diet group.[5] The plasma level of potassium does not reflect the intracellular level of potassium during hypothermia and hyperventilation.[3,4,16]

Figure 2 is the electrocardiogram of the animal that showed fibrillation at 24.2 C. The extrasystoles did not produce heart beats, although the electrical configurations are similar to the extrasystoles that do produce ventricular contractions. The abnormal ventricular patterns occurred in the "vulnerable" period and finally precipitated ventricular fibrillation when the threshold had been sufficiently lowered in the myocardium.[6,17,18]

Summary

Ten dogs were studied. Five of these

had the plasma potassium level lowered slightly by diet and sodium exchange resin. Hypothermia and hyperventilation produced the following changes:

1. The blood pH level rose in all the animals. The highest level was 8.1.
2. The arterial carbon dioxide pressure level fell in all the animals. The lowest level was 1.4 mm. Hg.
3. All the animals except 1 developed an S-ST wave.
4. Five of the 10 dogs fibrillated above 20 C.
5. The highest temperature at which ventricular fibrillation occurred was 24.2 C.

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Discussion

LOUIS R. ORKIN, M.D., *Bronx, New York.* The normal physiologic requirements for the hypothermic state remain undefined. The hypothermic state is itself unphysiologic for man. It is difficult, therefore, to determine what should or should not exist in relationship to pH, carbon dioxide pressure, oxygen pressure, electrolytes, and so forth. The behavior of blood and its constituents at 20 C. is different from its behavior at room temperature. The oxygen-hemoglobin dissociation curve and the carbon dioxide and pH relationships normally derived and made into nomograms for 37 C. do not apply to the hypothermic state. The Singer-Hastings nomogram cannot be used to calculate carbon dioxide pressure. The corrected values would be higher than those presented by Dr. Wycoff but nevertheless low enough to prove the points that hyperventilation, low carbon dioxide pressure, and high pH do not prevent ventricular fibrillation.

Changes occur during hypothermia which have been related to ventricular fibrillation. While the heart is slowed and cardiac output is decreased slightly, the work of the heart is increased 30 per cent at 30 to 32 C. In the heart muscle itself sodium decreases and potassium increases, but serum potassium may fall and serum sodium remain unchanged. The arteriovenous oxygen difference and carbon dioxide production do not indicate that gas transport is the basic problem, nor is endogenous epinephrine a primary fibrillating factor. The average carbon dioxide pressure at 20 C. should equal 12 to 20 mm. Hg, and the pH should be 7.5 to 7.7. Part of this relationship must be the metabolic acidosis and must be related to tissue hypoxia. This is compensated by hyperventilation which also prevents the sudden rise in pH from the very low levels that would otherwise occur.

The etiology and prevention of ventricular fibrillation is not clear. Although it is less of a problem during cardiovascular surgery since defibrillation is feasible, it still remains a problem for extrathoracic surgery. In such instances temperatures below 30 C. do not seem justified.

Phenobarbital Idiosyncrasy

Avoidance by Use of Phenobarbital-Niacin

IDIOSYNCRATIC REACTIONS *to phenobarbital may be caused by an inherent sensitivity, or they may develop as an acquired idiosyncrasy, especially in persons with an allergic background. Phenobarbital, iodide, and bromide idiosyncrasies are caused by poisoning of the oxidative coenzymes I and II. Niacin supplies the essential portion of the pyridine nucleus necessary for the reconstitution of both coenzymes. A study was undertaken to determine the efficacy of phenobarbital-niacin (Barba-Niacin) for idiosyncrasy to phenobarbital. The group consisted of 44 cases of known phenobarbital idiosyncrasy. The nature of the idiosyncrasy was neurologic in 23 cases, cutaneous in 15, and bizarre in 6. The symptoms included lassitude in 14, depression in 13, pruritus in 11, skin rash in 8, irritability in 4, daydreaming in 2, and panic in 1. The substitution of phenobarbital-niacin for phenobarbital in identical dosage over an average period of five weeks proved to be free of all untoward reactions in 40 of the 44 cases (91 per cent). In 4 cases the idiosyncratic reactions were of equal degree under the two medications.*

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IDIOSYNCRATIC REACTIONS to phenobarbital in therapeutic dosage are many and varied. They may be caused by an inherent or natural sensitivity to the drug or they may develop as an acquired idiosyncrasy on repeated usage, especially in persons with an allergic background.[1]

A natural idiosyncrasy most often manifests itself in an abnormal response of the central nervous system to the drug. It may take the form of lassitude or prolonged depression and hangover. Toxic effects, most frequently involving the nervous system, were observed in 2.2 per cent of 1,000 cases in which phenobarbital was administered.[2]

A phenobarbital sensitivity syndrome characterized by an erythematous rash, high fever, mental confusion, and toxic damage of parenchymatous organs following therapeutic doses of phenobarbital has been reported. There were 3 cases, and 2 of the patients died.[3]

Skin eruptions due to acquired sensitivity are the most common type of allergic reaction and may follow a single dose of phenobarbital. They may take the form of pruritus, urticaria, generalized morbilliform rash, bullous erythema multiforme, discrete coin-sized violaceous macules, or universal exfoliative dermatitis.[1] The cutaneous eruptions often are associated with sharp febrile reactions, mucous membrane involvement, and glandular swellings.[4]

Several investigators have reported fatal exfoliative dermatitis and idiosyncratic skin eruptions following the use of phenobarbital.[5–7] In another almost fatal sensitization reaction to phenobarbital, universal exfoliative dermatitis was complicated by hepatitis, severe jaundice, decided leukocytosis, and depletion of the serum albumin.[8]

Occasionally an idiosyncrasy to phenobarbital has been manifested by amaurosis, albuminuria, or ataxia.[9] In addition to these rather specific classifications, there is an unclassified group of bizarre reactions to phenobarbital.

Relation to iodism and brominism

We were impressed with the similarity between the manifestations of phenobarbital idiosyncrasy and those of iodism and brominism, in both of which niacin (nicotinic acid) and niacinamide (nicotinamide) exert a specific protective action.

It has been established that idiosyncrasies to iodides, bromides, and phenobarbital all are caused by poisoning of the oxidative coenzymes I and II. Niacin supplies the essential portion of the pyridine nucleus necessary for the reconstitution of both coenzymes.

Our previous studies have shown that when potassium iodide is combined with niacinamide hydroiodide, the drug may be administered in full dosage over long periods of time without inducing iodism.[10,11] These results have been confirmed by other investigators.[12,13]

In related studies we found niacinamide hydrobromide equally effective in preventing and clearing up brominism in susceptible persons who were receiving a full dosage of bromide medication.[14,15]

The specificity of the niacin and niacinamide combinations in the prevention of iodism and brominism is similar to their action in the prevention and correction of pellagra. Accordingly, we were encouraged to develop a combination of niacin with phenobarbital and to test its efficacy for idiosyncrasy to that barbiturate.

Phenobarbital-niacin

Phenobarbital-niacin* is a combination of phenylethylbarbituric acid (phenobarbital) with niacin. Its physical constants are an empirical formula of $C_{18}H_{15}N_3O_4$, a molecular weight of 337, and a melting point of 165 to 167 C. It contains 64 per cent carbon, 4.5 per cent hydrogen, 12.5 per cent nitrogen, and 19 per cent oxygen.

Because of the reconstitution of the oxidative coenzymes, the therapeutic index (ratio of therapeutic to lethal dose) of phenobarbital-niacin is greatly improved. The reduction of toxicity by the oxidative coenzymes results in a relatively nontoxic barbiturate.

Clinical data

The group studied comprised 44 cases of known phenobarbital idiosyncrasy. It included 20 men and 24 women. The average age was forty-eight years (range from twenty-three to sixty-six), weight 153 pounds (range from 124 to 214), and height 65.2 inches (range from 53 to 73).

The primary diagnosis and indication for the use of phenobarbital was a neurosis in 30 cases, hypertension in 3, insomnia in 3, menopausal syndrome in 2, male climacteric in 2, and 1 each of hyperthyroidism, angina pectoris, duodenal ulcer, and hay fever.

The daily dosage of phenobarbital which produced the idiosyncratic reaction was 90 mg. in 27 cases, 60 mg. in 12, 30 mg. in 3, 15 mg. in 1, and undetermined in 1 (average 76 mg.).

The nature of the idiosyncrasy was classified as neurologic in 23 cases, cutaneous in 15, and bizarre in 6. The symptoms observed included lassitude in 14 cases, depression in 13, pruritus in 11 (pruritus ani and pruritus vulvae in 1 case each), skin rash in 8, irritability in 4, daydreaming in 2, and panic in 1.

Phenobarbital-niacin was substituted for phenobarbital in identical dosage based on the quantity of phenobarbital. The period of treatment with phenobarbital-niacin averaged five weeks (range from one to twelve weeks).

In 40 of the 44 cases (91 per cent) all of the idiosyncratic reactions previously observed in the same patients receiving the equivalent dosage of phenobarbital were completely absent when phenobarbital-niacin was substituted. In 4 cases (9 per cent) lassitude, depression, irritability, and daydreaming were of equal degree under both phenobarbital and phenobarbital-niacin medication.

In 29 cases the symptoms of phenobarbital idiosyncrasy, which were present when the medication was changed, disappeared during the continued administration of phenobarbital-niacin in equivalent dosage. The untoward symptoms corrected by this switch included depression in 10 cases, lassitude in 9, pruritus in 8, skin rash in 6, irritability in 3, and daydreams and panic in 1 case each.

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* Supplied as Barba-Niacin tablets by Cole Chemical Company, St. Louis, Missouri.

In a blind test on a woman with pruritus ani the itching was aggravated every time she took phenobarbital but never after she took phenobarbital-niacin.

In another blind test a woman developed a rash across the chest and under the arms every time she took phenobarbital for several days. She repeated this experience many times, always with the same result. When she changed to phenobarbital-niacin, repeating its use frequently, no skin rash ever developed.

Summary

Forty-four cases of known phenobarbital idiosyncrasy are reported, classified as neurologic in 23 cases, cutaneous in 15, and bizarre in 6. The symptoms included lassitude in 14 cases, depression in 13, pruritus in 11, skin rash in 8, irritability in 4, daydreaming in 2, and panic in 1.

Evidence is adduced to show that phenobarbital idiosyncrasy is caused by the same mechanism as iodism and brominism, namely, poisoning of the oxidative coenzymes I and II. Niacin supplies the essential portion of the pyridine nucleus necessary to reconstitute both of these coenzymes.

In a controlled comparison on 44 patients with demonstrated phenobarbital idiosyncrasy, the substitution of phenobarbital-niacin in equivalent dosage proved to be free from all untoward reactions in 40 cases (91 per cent). In only 4 cases (9 per cent) was there a lack of difference between phenobarbital and phenobarbital-niacin with respect to idiosyncrasy.

In 29 cases the symptoms of phenobarbital idiosyncrasy, which were present when the medication was changed, disappeared during the continued administration of phenobarbital-niacin in equivalent dosage.

The use of phenobarbital-niacin in preference to phenobarbital adds considerably to the safety of that sedative and avoids most of the idiosyncratic reactions.

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Rehabilitation in Radical Head and Neck Surgery

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Extirpative surgery alone is no longer an adequate concept in the attack on tumors in the head and neck. Many aspects of radical excisional surgery in the head and neck have become well established, and an increased interest in the rehabilitation of these wounds has developed. The removal of vital organs in this area, associated with serious alterations in functional capacity and the attendant mutilation, have placed increased responsibilities on the operating surgeon. It has become essential to incorporate in the original operative plan the nature of the wound that will be created by the removal of the tumor and a concept of rehabilitation of this wound. This planning should include the maximum amount of rehabilitation to be carried out during the excisional phase of the operation. Such deterrents as poor tissue bed, post-irradiation fibrosis and atrophy, and excessively large extirpative operations compromise the type and quality of reconstruction that can be carried out at the time of the original operation. Under these circumstances additional staged operations frequently promote further improvement.

The essential aspects of this review will deal with resurfacing and reconstitution by the various technics of free-skin grafting, regional flap transposition, bone grafts, dermal-fat-fascial grafts, nerve grafts, and artery grafts.[1,2]

Free-skin grafting

Free-skin grafting has become the most utilitarian method of rehabilitating wounds in the head and neck. It may serve as a wound dressing or as a permanent covering for the wound, depending on requirements. It has been found to grow readily on the pia of the brain, the dura, the scalp, the face and neck, in the maxillary and oral cavities, and on the tongue, the pharynx, larynx, and cervical esophagus.[3-7] With the advent of the Browne dermatome, the procurement of great and varied sizes of free skin became a routine procedure. The application of this free-skin graft may solve the wound problem forthwith. It may prevent scar tissue contraction and enhance the function of the residual organs, and it may prevent the necessity for additional operations. There is, indeed, very little reason today for an open, raw wound to be established intentionally.

The incidence of "take" of the skin graft under operative conditions at these sites in the head and neck is comparable to that of controlled, external skin grafting in other sections of the body.

Regional tissue flaps

The regional flap does not have as broad usefulness as skin-grafting technics, but it contains a specific and important application. This technic provides that in a single-stage procedure a segment of tissue adjacent to the wound can be transposed with the intention of accomplishing resurfacing, thus providing additional contour and increasing the physiologic support to the area. As much as 240 cm.[2] of tissue may be transposed onto the face[8] or the neck in a one-stage technic. These flaps may be applied on the scalp,[9] face,[10,11] neck,[8,12,13] eyelids,[6,14-16] nose and lips,[17-19] and by rotation from an adjacent site.[13,20-23] The tongue[24] and the mucous membrane[25-27] of the oral and pharyngeal cavities often are appropriate and expedient donor sites for flaps to these immediate areas. The suitability of such flaps is limited by the arterial and venous blood flow, the quality of the transposed tissue, and the viability of the recipient tissue bed. Acceptable relative factors for the length and width of transposed tissue are of the order of two to one and three to one.

In instances of severe x-ray damage or of perforation by cancer, resurfacing of the entire neck with a regional flap [12] from either the nape of the neck or the anterior chest has proved a distinct advance over all other technics. This resurfacing facility provides considerable protection to the carotid artery system. When used to augment the closure of a pharyngostome or esophagostome, this generous addition of healthy skin in the area facilitates subsequent reconstruction of the gullet and trachea.[3,7,28-33]

In the vast majority of instances the immediate regional flap transposition has supplanted the technics of the development of skin tubes and the delayed, staged transposition from distant sites on the body. Modifications of these latter technics still are required, however, in rehabilitating massive deficiencies of the lower third of the face.[34]

Bone grafts

The reconstitution of the mandibular arch is the principal application of the technic of bone transplantation in the head and neck.[35-38] This is best accomplished by the implantation of an appropriately modeled bone graft held in position by either internal wiring or metal plates and screws.[39,40] Internal wiring has proved to be better tolerated, and it less frequently requires removal due to foreign body reaction.[41] When the temporomandibular joint has been destroyed, a compromise reconstruction is inevitable. Bone grafts to deficiencies of this magnitude will provide moderate improvement in contour, although only slight improvement in function.

Autogenous bone is preferred over homologous bone or inert substances.[42] In young children, in whom the development of bone is incomplete at the time of surgery, homologous bone is indicated. The ambitious use of inert materials in the mandible, particularly close to the surface in areas sustaining the trauma of movement, almost invariably results in perforation and externalization of the prosthesis, demanding eventual removal. Excessively large wounds and postirradiated tissue beds understandably reduce the warranty for bone-grafting technics.

Deficiencies about the frontal and maxillary regions are less frequent and may be rehabilitated by the implantation of bone, cartilage, or prosthetic material. Where the areas of deficiency are not required to endure the phenomenon of stress, satisfactory reconstruction in bony tissue usually is accomplished by onlay grafting. The absorption factor in diced bone and cartilage often is disappointingly high. Inert prostheses have a reasonable chance of success in establishing contour and support in certain conditions about the quiet areas of the orbit, zygoma, maxilla, and frontal regions. Lyophilized and despeciated bone are under investigation.

Dermal-fat-fascial grafts

Soft-tissue replacement is best accomplished by the implantation of fascia or dermis in small defects and by the dermal-fat-fascial graft where the deficiency is large.

Depressions resulting from the loss of subepithelial supportive and filling structures are most adaptable to this technic. The so-called "sandwich" grafts composed of dermis and fascia lata on either side of a medial segment of fat, procured en masse from the lateral thigh, may be molded into shapes and forms appropriate to the face. They are soft to the touch and serve to rehabilitate deformities resulting from extirpative surgery as well as those occasioned by arrested development of the face secondary to irradiation in childhood or to congenital deficiencies. Such grafts also have been used successfully to form a new soft tissue mandibular contour or as a recipient tissue bed for subsequent, delayed bone grafting at this site. As much as 240 cc. of free tissue have been transplanted into prepared tunnels and pockets for recontouring. One must anticipate the absorption of as much as 50 per cent over an interval of a year in the planning.

Facial nerve repair

Considerable progress has been made during the past ten years in the management of the facial nerve in radical surgery of the temporal bone,[43] ear, parotid gland,[44,45] and face.[46] The technics of direct approximation, nerve grafting,[47,48] and nerve crossing have assisted considerably in alleviating the distressing results of the loss of portions of this nerve pathway.[49] The most propitious time for the rehabilitation of the facial nerve is during the first extirpative operation when the wound is open and all structures are readily available. The resection of a portion of the terminal peripheral filaments of the facial nerve system causes a minor deficiency in esthetics and function. The loss of the principal superior or principal inferior division of the nerve usually results in a down-grading of facial function to the extent of approximately 10 to 20 per cent.

Direct approximation may be carried out when the nerve deficiencies are not over 1 to 2 cm. in length, with an excellent chance for this technic to effect a significant return of facial movement.

Immediate nerve grafting should be carried out when the peripheral aspect of the main trunk and its immediate divisions have been resected in radical parotid extirpation. The sensory cervical plexus provides a graft with four or five ramifications. Used as a free transplant, it is carefully sutured to the main trunk and peripheral segments with number 000,000 atraumatic silk. A nourishing tissue bed enhances the possibility of a successful graft. In approximately 70 per cent of the cases some type of return may be anticipated.

When the proximal trunk of the seventh cranial nerve has been destroyed in temporal bone resection, rehabilitation may be effected by nerve crossing. Under these circumstances the hypoglossal nerve is split and sutured to the peripheral stump in the face. The return of movement under these circumstances occurs in approximately 80 per cent of the cases, and the movement on the whole is of better quality than that obtained with nerve-grafting technics.

The spontaneous return of movement of the face after the resection of a portion of the peripheral aspects of the seventh nerve has been reported. The possibility of such spontaneous return should not be substituted for a definitive rehabilitative technic.

The movement resulting from these surgical technics is always inferior to the natural facial movement. Usually there is a lack of selectivity in motion, and several muscles contract with a mass movement quality. This motion is always superior, however, to no movement at all, and it is also preferable to rehabilitation by the technic of static suspension. The degree of success depends on the accuracy of the anastomosis, the affluence of the intercommunications of the network of peripheral facial nerve fibers, and the patient's ability to recognize and exploit the elements responsible for the movement, through concentration and practice.

Blood vessel replacement

The common and internal carotid arteries are the only blood vessels in the neck that may be considered inviolate and may demand replacement on the basis of their function to supply blood to the brain.[50] All other blood vessels encountered in the field of head and neck surgery may be considered resectable. Carotid artery continuity may be maintained by vessel suturing,[51] vessel patching, ipsilateral anastomosis of the internal to the external carotid arteries,[52] and vessel replacement using autogenous vein[53] or homologous artery grafts.[54,55] The inert prosthetic substitution of arteries is rarely applicable in radical head and neck surgery.[56] The technics to maintain the integrity of these vital blood vessels have specific significance when a resection or ligation might prove fatal or might result in hemiplegia.

Obviously, all individuals undergoing carotid artery ligation and resection do not require reconstitution of the vascular pathway. Those comprising this fortunate group may be identified by angiography, analysis of the circle of Willis, identification of the dominant artery, direct measurements of the arteries, and evaluation of intra-arterial pressures before and after temporary ligation of the artery. These technics have cast some scientific light on this perplexing situation and help to clarify the circumstances in which artery grafting might be considered meddlesome. Although the preoperative analysis is helpful, it is no guarantee against serious complications when the carotid artery is resected.

The use of an intra-arterial or external "bypass" has proved helpful in critical cases where ligation of the dominant carotid artery would result in immediate and critical cerebral hypoxia. The surgical planning should be of such caliber as to obviate the necessity for carotid artery resection except for the invasion of the vessel wall by cancer.[12,13] The prognosis under these circumstances is grave, and such factors as potential infection, postirradiation damage, and surgical devitalization of the tissue bed all lessen the chances of success.

These improvements in rehabilitating these serious wounds in the head and neck have alleviated some of the distress attendant on this type of extirpative surgery. The extensions of many of the more radical technics have reached the perimeters of acceptability in relationship to mutilation, function, and curability. Advances in reconstruction will follow the adoption of the concept of massive and maximum immediate rehabilitation, a careful analysis of the altered physiology of crippling in this area, and a solution to the homotransplantation problem.

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Case of depression traced to parathyroid tumor

A drastic change in the personality of a thirty-eight-year-old man was traced to a tumor of the parathyroid gland by Ralph F. Reinfrank, M.D., writing in the October, 1961, issue of *Archives of Internal Medicine*, published by the American Medical Association.

The patient was found to be suffering from hyperparathyroidism, although he did not demonstrate two of the major symptoms of this disorder, kidney stones and bone disease.

The patient's main symptoms were a loss of interest in his surroundings, loss of appetite, weight loss, depression, and suicidal inclinations. Exploratory surgery revealed the presence of the tumor which was removed with prompt disappearance of the patient's mental depression. The manner in which parathyroid tumors cause mental aberrations is not understood. However, mental depression should be considered as another possible symptom of hyperparathyroidism.

Clinicopathologic Conference

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Conducted by MICHAEL S. BRUNO, M.D., AND
WILLIAM B. OBER, M.D.

Discussed by FURMAN M. JONES, JR., M.D.

Heart Failure, Arrhythmias, and Embolic Phenomena

Case history

SALVATORE BALDINO, M.D.: A fifty-four-year-old Japanese male was admitted to Knickerbocker Hospital for the fifth time on April 18, 1961, because of cough, shortness of breath, and orthopnea of long duration.

FIRST ADMISSION. In February, 1959, the patient was first admitted with a four-week history of illness that followed a mild infection of the upper respiratory tract. The patient stated that he had been having shortness of breath with such effort as stair climbing. Walking three blocks or more required him to stop and rest. In addition, he noted that he was comfortable only when sleeping with two pillows, and on several occasions he was awakened from sleep by shortness of breath that responded to sitting up. He did not complain of chest pain, pain on effort, or ankle swelling. The past history included only typhoid fever at fourteen years of age and diphtheria at the age of eighteen. He denied rheumatic fever, rheumatic heart disease, diabetes, hypertension, syphilis, and tuberculosis. A system review was unremarkable.

A physical examination revealed a well-developed and well-nourished Oriental male with a blood pressure of 98/80, temperature of 98 F., and a respiratory rate of 18. Pertinent physical findings included an irregular ventricular rhythm with a rate of 128 per minute. The thyroid was not felt, and the chest was clear.

The hemoglobin was 13 Gm. per 100 ml., and the white blood count was 7,000. The erythrocyte sedimentation rate was 19 mm. per hour. A urinalysis and serum transaminase showed normal results. The protein-bound iodine was 6.7 micrograms per 100 ml. A chest x-ray film revealed minimal generalized cardiac enlargement. The electrocardiogram demonstrated atrial flutter with varying block.

The patient was given digitalis and subsequently quinidine to the point of toxicity without conversion of his arrhythmia. However, he improved symptomatically and was discharged from the hospital on digoxin (0.75 mg. daily) with an atrial flutter still present.

Following his discharge the patient converted spontaneously to a normal sinus rhythm. The atrial flutter recurred several times over a period of the next year while he was being followed by his private physician. These episodes were controlled readily, and the patient reverted to sinus rhythm either spontaneously or with digitalis.

The patient was maintained on digitalis and a sodium-restricted diet.

Second admission. In November, 1959, the patient developed burning on urination following catheterization for urinary retention. A cystoscopy revealed an acute cystitis which responded to Gantrisin.

Third admission. In October, 1960, the patient was admitted with a history of persistent cough of two weeks duration with hemoptysis on one occasion, mild difficulty in swallowing, and several days of abdominal cramps and diarrhea.

A physical examination revealed a blood pressure of 110/80 and a temperature of 98.6 F. The neck veins were flat, and the liver was not palpable. The chest was clear. The heart was enlarged to percussion, and the rhythm was irregular. No murmur was heard.

A urinalysis showed normal results. The white blood cell count was 9,200 with 77 per cent polymorphonuclear leukocytes. A sputum culture yielded Streptococcus viridans and Aerobacter aerogenes. Sputum specimens for acid-fast bacillus, culture, and cytologic study were negative. A chest x-ray revealed minimal cardiac enlargement and no evidence of intrapulmonic disease. Both an upper gastrointestinal series and a barium enema produced negative findings.

The patient improved on tetracycline and expectorants.

Fourth admission. Following the patient's discharge from the hospital, a severe cough recurred with episodes of frank hemoptysis. He had received antibiotics and antihistaminic treatment without benefit. He also complained of shortness of breath, difficulty in swallowing, and a 20- to 30-pound loss of weight. A physical examination revealed a blood pressure of 98/60 and an irregular pulse at 88 per minute. Heart sounds were described as distant with the first mitral sound accentuated and "hollow sounding." There were rales at the base of the right lung. The liver was palpated 3 fingerbreadths below the right costal margin.

A chest x-ray film demonstrated no intrapulmonic disease. On fluoroscopy it was noted that the heart was slightly enlarged generally, and the cardiac pulsations were described as feeble. A barium swallow showed some delay in the passage of barium which remained in the esophagus for a relatively long time; there was no intrinsic disease of the esophagus, however. X-ray films of the upper gastrointestinal tract and a barium enema again showed negative results. The electrocardiogram revealed atrial fibrillation with a ventricular response of 80 per minute. A sputum examination for eosinophils, acid-fast bacilli, and tumor cells showed negative results. A bronchoscopic examination was reported as unremarkable.

While in the hospital, the patient developed mild pitting ankle edema which cleared with Mercuhydrin and later HydroDiuril. He was continued on this medication and digoxin 0.75 mg. per day. He improved symptomatically.

Final admission. Cough, shortness of breath, and dysphagia recurred, and the patient was readmitted in April, 1961. All observers were struck by the progressive downhill course of the patient's illness in spite of vigorous therapy with diet, digitalis, diuretics, and supportive care. He appeared debilitated and chronically ill. In the few months prior to his admission he was unable to do any physical work, and at this time he was distressed and short of breath even at rest. The hemoptysis had subsided.

The examination was little changed. The blood pressure remained about 100/70. The heart rate was 80 per minute and regular. A protodiastolic gallop was heard at the apex along with a soft systolic murmur. The first mitral sound was described as "hollow and tamboric in quality." The liver was enlarged.

The hemoglobin was 14 Gm. per 100 ml. with a white blood cell count of 7,000 and a normal differential. The nonprotein nitrogen was 43 mg. per 100 ml. A urinalysis showed normal results and a serology gave negative results. An admission electrocardiogram revealed a sinus rhythm with a P-R interval of 0.28 seconds. A chest x-ray film demonstrated some increase in cardiac size with mild congestive changes in the lungs. An upper gastrointestinal study again showed a delay in the passage of barium through the esophagus which seemed to localize to an area just below the aortic knob. The motor function of the esophagus seemed disturbed.

Ten days after admission the patient had a sudden onset of numbness in both legs and feet below the knees. There was definite rubor and discoloration of the right foot and leg up to the knee with coolness in the same area. The femoral pulses were present bilaterally, but the posterior tibial and dorsalis pedis pulses were absent on the right. The next day the right foot and leg were bluish with a zone of demarcation in the upper calf. Within a short time the patient's blood pressure became unobtainable, and moist crackling rales appeared in both lung fields. He expired on the eleventh hospital day.

Discussion

Furman M. Jones, Jr., M.D.: This fifty-four-year-old Japanese male had five admissions to the hospital over a two-year period. Except for his second admission, which was for acute cystitis, the major symptoms were cardiorespiratory in nature. Exertional dyspnea, orthopnea, and paroxysmal nocturnal dyspnea were prominent. Later in his course he also complained of persistent dysphagia and episodes of hemoptysis. I can see nothing in the protocol that gives any evidence that he had hypertension, chest pain, rheumatic fever, or lues which might point to the etiology of his heart disease. At no time was a significant heart murmur ever heard. The most prominent feature of the case from its inception was the presence of a variety of arrhythmias, which were paroxysmal and punctuated by long intervals of normal sinus rhythm. Nonetheless, the arrhythmias appeared to be relatively refractory to therapy. Despite intensive therapy, his course was relentlessly downhill. By the time of his last admission he had lost 20 to 30 pounds in weight and was obviously failing rapidly. The terminal event was clearly an embolic arterial occlusion in the right leg.

The laboratory data do not give any immediate clue to a specific diagnosis. His cardiac problem was not compounded by anemia, nor is there anything to implicate an active rheumatic process, thyrotoxicosis, or myocardial infarction. The chest x-ray film showed generalized cardiac dilatation without enlargement of any one chamber (Fig. 1). There was no unusual calcification within the cardiac silhouette nor of the pericardium. The configuration of the aortic knob and pulmonary conus was not remarkable. Fluoroscopy showed that the cardiac excursions during systole were reduced significantly in amplitude. There was nothing to suggest a restrictive pericarditis, mitral stenosis or insufficiency, or a congenital malformation. These diagnoses are unlikely on purely historical grounds as well.

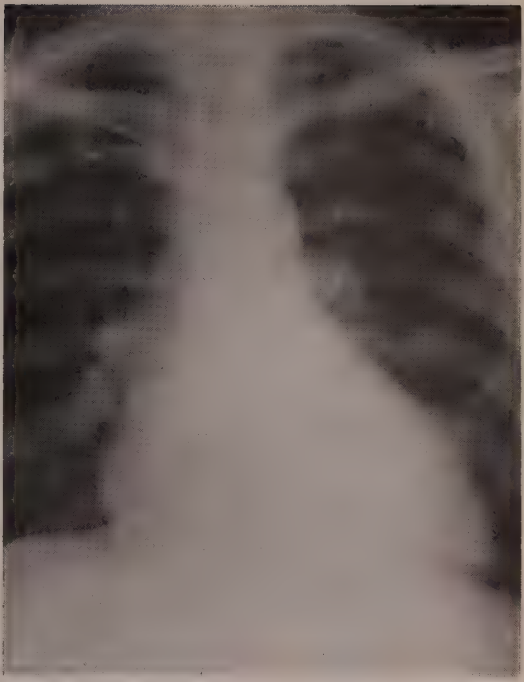

FIGURE 1. Roentgenogram of chest showing a marked degree of generalized cardiac enlargement without disproportionate enlargement of any one chamber.

Apparently the symptom of dysphagia caused considerable concern. Was this symptom as constant as it appears from the protocol?

Michael S. Bruno, M.D.: Yes, it was. For the last nine or ten months of his life it was one of the main complaints. I observed him on several occasions while he was eating. He had a great deal of difficulty swallowing, but there was no regurgitation of food.

Dr. Jones: I would infer, then, that the possibility of scleroderma was considered and that the barium swallow was ordered in an effort to see if this diagnosis could be supported.

DR. BRUNO: That was our line of reasoning.

DR. JONES: I would infer from the radiologist's report that there was some delay in the passage of barium but that there was still active peristalsis in the wall of the esophagus. I cannot feel that this is typical of scleroderma. Also, the absence of characteristic changes or even suggestive changes in the subcutaneous tissue is against it. I take it that there were no Raynaud's phenomena?

DR. BRUNO: That is right. There were no Raynaud's phenomena.

DR. JONES: Try as I may, I cannot muster enough evidence to support the diagnosis of scleroderma heart disease, and I shall have to discard it.

Parenthetically, I can find no evidence in the protocol of any sort of angina or unusual chest pain. There is nothing to suggest coronary artery disease, indeed nothing to suggest any significant degree of arteriosclerosis anywhere in the body.

Since I can eliminate the basic cause of this man's cardiac difficulties as being in the pericardium, the coronary arteries, the heart valves, or due to hypertension or a congenital malformation, by the process of elimination I am left with the diagnosis of primary myocardial disease. Typically, primary myocardial disease is difficult to analyze both clinically and pathologically. Weakness, fatigue, and exertional breathlessness are common as early features of disease of the heart wall itself. Often these are mistaken for iatrogenic heart disease or psychosomatic cardiac complaints. It is only after the patient is observed for a few weeks that the very real nature of the disease becomes apparent. Later in the course of primary myocardial disease, as signs of congestive failure develop, the symptoms are usually far out of proportion to those seen in failure secondary to other forms of heart disease.

There are a few specific observations in the protocol which are observed commonly in myocardial disease. The blood pressure of 98/80 is very helpful. In the absence of aortic stenosis, the narrow pulse pressure certainly suggests a weakened cardiac muscle. Likewise, the decreased amplitude of the systolic contraction on fluoroscopy and the distant heart sounds on auscultation are consistent with diffuse myocardial damage. Peripheral embolization and paroxysmal arrhythmias likewise are consistent with primary myocardial disease, although certainly not specific for it.

While there is nothing specific about the auscultatory findings in primary myocardial disease, a protodiastolic gallop usually is present as the condition progresses. With generalized cardiac dilatation the murmurs of relative mitral and tricuspid insufficiency also may be detected.

Recently, Mattingly* has proposed a classification of primary myocardial disease based on its etiologic factors and its clinical forms. I would like to repeat this classification (reproduced with the permission of the American Heart Association and the author) and see where this patient fits into the picture.

MYOCARDITIS: ACUTE, SUBACUTE, CHRONIC
  Myocarditis due to infectious etiologic agents
  Idiopathic myocarditis
  Myocarditis of collagen vascular diseases
  Myocarditis of physical and metabolic origin
OBSCURE MYOCARDIAL DISEASES (PROBABLY HEALED MYOCARDITIS)
  Fibroelastosis
  Endomyocardial fibrosis
  Idiopathic cardiac hypertrophy
  Familial cardiomegaly
MYOCARDIAL DISEASES ASSOCIATED WITH SYSTEMIC DISEASES
  Amyloidosis
  Hemochromatosis
  Sarcoidosis
  Carcinomatosis
  Anemias
  Glycogen storage disease
  Friedreich's ataxia
  Progressive muscular dystrophy
PRIMARY MYOCARDIAL TUMORS

In acute myocarditis pain often is a prominent feature, even simulating the pain of myocardial infarction; conversely, the process may be painless and insidious, with death occurring before the illness can be recognized. In the chronic form cardiac dilatation and hypertrophy result from the actual deterioration of the heart muscle. In the noninfectious form of primary myocardial disease pain is not common. When present, it is usually due to coronary insufficiency secondary to decreased cardiac output.

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* Mattingly, T. W.: Clinical features and diagnosis of primary myocardial disease, Mod. Concepts Cardiovas. Dis. **30:** 677 (Aug.) 1961.

Arrhythmias and conduction disorders usually are observed at some period during the course of the illness. Ectopic rhythms of supraventricular, ventricular, or nodal origin are seen. A sinus tachycardia out of proportion to any existing fever, not associated with any endocrine disorder, not associated with any other systemic disease, and associated with mild heart failure should make one suspicious of myocarditis. Intraventricular conduction disturbances and bundle branch block are the most common electrocardiographic abnormalities.

Having thus limited the field of our inquiry, let us proceed to entertain other diagnostic categories. If there were good evidence for a specific infectious agent or a specific type of infection, the diagnosis of infectious myocarditis would be easy. However, there is nothing in the patient's history to suggest rheumatic carditis or bacterial, fungal, rickettsial, or viral infection. The symptoms did develop following a respiratory infection, but this episode is not defined, and I cannot place much weight on it. A history of antecedent respiratory infection often is obtained in idiopathic myocarditis, the so-called Fiedler's myocarditis. Theories have been advanced that the myocardial infiltration is the reaction to bacterial toxins or a type of hypersensitivity, but the evidence is far from convincing. The concept of idiopathic myocarditis is not sufficiently well defined for me to be able to assign a given case to that category except by exclusion and negative evidence. However, I shall not make a diagnosis of myocarditis in this case because of the clinical course; usually, myocarditis is fatal in a matter of weeks or months; this patient survived for two and one-half years.

We already have found insufficient evidence for a diagnosis of scleroderma, the most likely of the collagen-vascular diseases. There is even less evidence for either lupus erythematosus or periarteritis nodosa. By the same token, there is no evidence of physical or metabolic injury to the heart. There was no diabetes, thyrotoxicosis, or beriberi.

Of the various systemic diseases which may produce myocardial damage, I can see no evidence for carcinomatosis, sarcoidosis, hemochromatosis, glycogen storage disease, Friedreich's ataxia, or progressive muscular dystrophy. The patient was never anemic. Amyloidosis must be considered. However, the absence of any macroglossia, or of any urinary findings or evidence of renal damage, and the absence of significant hepatic damage make primary amyloidosis unlikely. If this patient had amyloidosis, it would be fairly well confined to the heart itself and diagnosable only by biopsy. Also, the absence of a Congo-red test or a serum protein electrophoresis makes me suspect that amyloidosis is a poor choice.

This leaves me with the group of obscure myocardial diseases to discuss. It is difficult to distinguish among the members of this group in Mattlingly's classification on purely clinical grounds. Most frequently the diagnosis is made at autopsy. However, in the absence of a positive family history I feel safe in eliminating heredofamilial cardiomegaly. I shall not make the diagnosis of idiopathic cardiomegaly; it is a classification to be used when all other possibilities are exhausted. The clinical and pathologic features of endocardial fibroelastosis and endomyocardial fibrosis overlap a good deal. The former is more common in infants and children, and the latter is common in Uganda. Neither of these two observations is helpful in the case of a fifty-four-year-old Japanese male. Both entities are characterized by relentlessly progressive cardiac failure punctuated by embolic episodes and variable arrhythmias. Both are extremely rare, but fibroelastosis is somewhat more commonly reported, if one can judge by the current literature. On this basis, I shall offer a diagnosis of endocardial fibroelastosis. It is a disease of obscure pathogenesis; that is, the pathologists are still arguing about it. In adults, valvular lesions are uncommon, but in infants and children the valves fre-

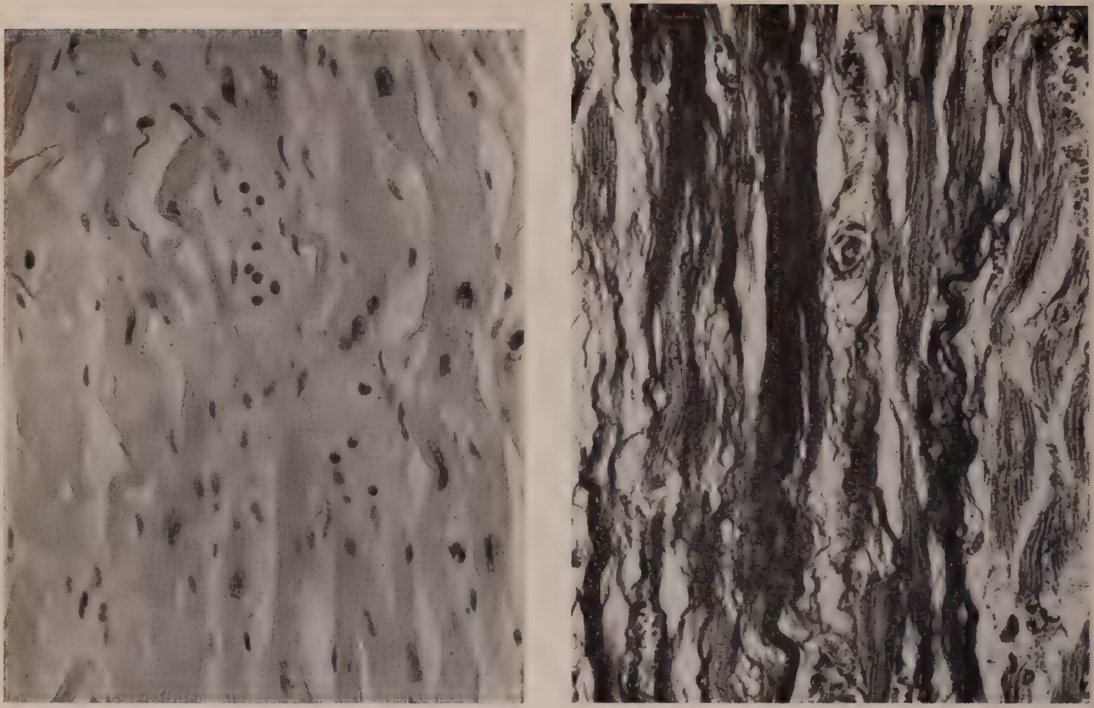

FIGURE 2. (Left) Sparse accumulations of leukocytes between myocardial fibers. (Right) Fibrosis of individual myocardial fibers (Masson's trichrome method).

quently are involved. Beyond this point I cannot safely venture.

Maxwell L. Gelfand, M.D.: A generation ago a case of this sort would have been diagnosed unhesitatingly as chronic myocarditis or Fiedler's myocarditis. However, with the evolution of greater insight into the role of coronary arteriosclerosis in the pathogenesis of myocardial scarring, including such concepts as focal myocytolysis, the term chronic myocarditis became taboo. To make such a diagnosis a decade ago would stamp one as hopelessly old-fashioned. However, in recent years the pendulum has swung back a little, and we recognize the fact that chronic myocarditis is a clinical and pathologic entity even though it still can be difficult to diagnose, even though in most cases we cannot pin-point a specific etiologic agent.

Mardoqueo I. Salomon, M.D.: Admittedly, segregation of cases of this sort into nosologic entities is difficult. Mattingly's classification is as helpful as any, but one often has the impression that some entities are artificially separated and that actually there is more overlap than such a refined classification appears to allow. For example, I am not really convinced that endocardial fibroelastosis and endomyocardial fibrosis are really different diseases.

Dr. Bruno: This case is a good deal easier to analyze in retrospect with a knowledge of the clinical course than it was when the patient was first admitted. As Dr. Jones pointed out, arrhythmias and some nonspecific symptoms were the significant findings early in his illness. When he was first seen, his cardiac failure was minimal and seemed to be secondary to his disordered rhythm. However, arrhythmias per se usually are not a sufficient cause for cardiac failure in the patient of this age who is otherwise well. However, as his illness progressed it became apparent that he had significant cardiovascular disease, and we began to look for an etiologic factor. We went through much the same process as Dr. Jones did. By a process of eliminating the more common varieties of heart disease, and in the light of the developing clinical picture, we, too, felt reasonably certain that he had primary myocardial disease, probably with some degree of fibrosis. During the last few months of life the patient was a cardiac cripple; although he had only minimal failure when he was first seen, over a two and one-half year period his cardiac reserve became progressively reduced until it was negligible.

Clinical diagnoses

(1) *Primary myocardial disease with myocardial fibrosis, possibly fibroelastosis;* (2) *congestive heart failure;* (3) *thrombo-embolic occlusion, right popliteal artery, terminal.*

Dr. Jones's diagnoses

(1) *Primary myocardial disease, probably endocardial fibroelastosis;* (2) *congestive heart failure;* (3) *thrombo-embolic arterial occlusion, right leg.*

Pathologic report

William B. Ober, M.D.: The heart weighed 490 Gm. and was considerably dilated. The myocardium was uniformly light brown and extremely flabby. The coronary artery tree was singularly free from arteriosclerotic changes. There was a partly organized thrombus in the left auricle. The picture of congestive heart failure was completed by pulmonary edema, bilateral pleural effusions, a moderate degree of ascites, and central congestion of the liver. The terminal episode was the result of a fresh thrombo-embolus lodged in the right popliteal artery. A healed renal infarct indicated that the thrombo-embolic process, although intermittent, was of long standing.

A microscopic examination of the heart revealed an inflammatory process of some duration. It was characterized by a sparse interstitial infiltrate of leukocytes and the conversion of individual myocardial fibers into fibrous scars (Fig. 2). Capillary engorgement was prominent throughout, and the blood in capillaries contained a large proportion of leukocytes (Fig. 3). There was also a slight infiltration of lymphocytes in the epicardial fat. The simplest morphologic label for this process is chronic interstitial myocarditis with fibrosis. One usually infers that this sort of myocarditis is postinfectious, and the history of the onset of cardiac symptoms in the wake of a significant respiratory infection is consistent with such an interpretation. However, we are unable to assign a specific pathogen to this process. Occasionally, in a case of acute myocarditis, bacteriologic or virologic studies will demonstrate the etiologic agent, but in cases which progress to chronicity, we are rarely so fortunate.

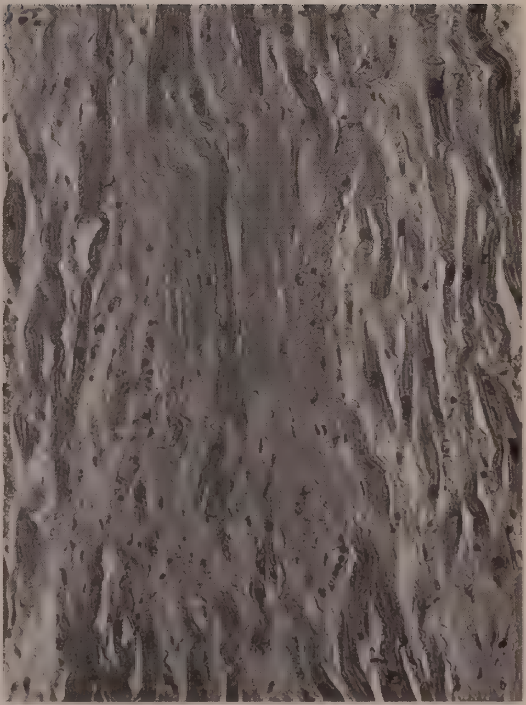

FIGURE 3. Dilated capillaries containing increased leukocytes in areas of focal myocardial scarring.

Anatomic diagnoses

(*1*) *Chronic interstitial myocarditis with fibrosis, postinfectious type;* (2) *cardiac dilatation and hypertrophy;* (3) *mural thrombosis, left auricle;* (4) *pleural effusions, bilateral;* (5) *pulmonary congestion and edema;* (6) *chronic passive congestion of viscera;* (7) *healed renal infarct;* (8) *thrombo-embolic occlusion, right popliteal artery, terminal.*

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MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Spontaneous Hypoglycemia

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SEVERAL YEARS have elapsed since the publication of the last comprehensive review of spontaneous hypoglycemia.[1] During this interval, knowledge of carbohydrate metabolism has advanced rapidly. Although such advances have been concerned primarily with increasing our understanding of diabetes mellitus, they are concomitantly of great import in the comprehension of states of abnormal depression of the blood sugar. Simultaneously, rapid advances have been made by investigators who have concentrated predominantly in the study of spontaneous hypoglycemia. Significant contributions have been achieved in: (1) the study of extrapancreatic neoplasms associated with hypoglycemia; (2) the precipitation of hypoglycemia by amino acids; (3) the use of new diagnostic aids for the detection of functioning islet-cell tumors; (4) the possible genetic etiology of insulinomas occurring in association with adenomas of other endocrine sites; and (5) the recognition of spontaneous hypoglycemia as an early manifestation of diabetes mellitus.

It is the purpose of this article to emphasize the salient diagnostic and therapeutic considerations of spontaneous hypoglycemia in the light of our present knowledge and to incorporate the advances of the past few years in our understanding of this problem.

Definition of terms

The early literature concerned with spontaneous hypoglycemia is complicated by a profusion of terms used to describe both identical and unrelated phenomena. One encounters reference to hyperinsulinism and dysinsulinism,[2] absolute and relative hypoglycemia,[3] and nervous and reactive hypoglycemia.[4,5] It is necessary therefore to have a precise definition of terminology. Spontaneous hypoglycemia is an all-inclusive phrase employed to denote a characteristic symptom complex associated with an abnormal depression of the glucose content of the extracellular fluid as determined by actual measurement of the plasma level. A blood sugar depression below 55 mg. per 100 ml. by the Folin-Wu method[6] or 40 mg. per 100 ml. by the Nelson modification of the Somogyi method[7] is acceptable evidence of hypoglycemia. Spontaneous hypoglycemia is not a single disease but rather a manifestation of an altered state of carbohydrate utilization or replenishment that may accompany many seemingly unrelated abnormalities. The recognition of a group of symptoms as examples of spontaneous hypoglycemia is only the initial achievement in alleviating such complaints. The precise etiology must then be determined before rational and successful therapeutic measures can be instituted.

Relative hypoglycemia is a phrase that has been used to characterize the occurrence of symptoms resembling the usual manifestations of spontaneous hypoglycemia but in the absence of demonstrable absolute depression of the blood glucose. It has been suggested that a sudden decline of the blood sugar, although not of sufficient magnitude to reach subnormal values, may nevertheless be the cause of alarming symptoms. We are reluctant to accept this explanation although by no means wishing to imply that such a phenomenon may not occur. However, it must be recognized that conclusive evidence for the existence of relative hypoglycemia is conspicuous by its absence. Indeed concomitant hyperventilation and hypocalcemia have been offered as possible explanations for the pseudohypoglycemic symptoms.[8,9] Until further information becomes available, this term should be discarded.

Spontaneous hypoglycemia excludes the occurrence of blood-sugar depression effected by the self-administration of hypoglycemic agents. A constant awareness, however, must be maintained to recognize such instances of factitious hypoglycemia. Suspicions are warranted immediately when hypoglycemia is encountered in medical personnel or relatives of diabetic patients. Such individuals possess the required knowledge of administration and have access to hypoglycemic preparations. Although self-administration of insulin has been the most frequently encountered cause of the variety of hypoglycemia, the arlysulfonylurea compounds are similarly offending agents. Both tolbutamide[10] and chlorpropamide[11,12] are capable of severe blood-sugar depression when they are administered in sufficient dosage to normal individuals. Phenformin (DBI) does not possess hypoglycemic activity in the nondiabetic subject. We are aware[13] of a patient who closely mimicked the characteristics of an islet-cell tumor by the daily ingestion of tolbutamide. Discovery of the true cause of the hypoglycemia was accomplished only shortly before contemplated pancreatic exploration. The acidification of this patient's urine specimen produced a heavy precipitate which subsequently was identified as l-butyl-3-p-carboxyphenylsulfonylurea, the primary excretion product of tolbutamide.[14]

The patient with self-induced hypoglycemia rarely is able to reproduce the characteristic repetitive pattern of symptoms and objective findings which serve to identify true endogenous spontaneous hypoglycemia. The hypoglycemic agent seldom is administered at regular intervals and hence the resultant blood-sugar depression bears little relationship to those events which precipitate episodes of true spontaneous hypoglycemia. This lack of recognized periodicity of symptomatology and of objective findings affords an important clue to the true nature of the disorder. The methods employed by these patients to secrete their drug sources have been ingenious[15] and the exposure to multiple pancreatic explorations has been accepted without hesitation.[16] It is naïve to assume that confronting such severely emotionally disturbed individuals with suggestive evidence of self-induced hypoglycemia will result in their ready admission of drug administration. Psychiatric aid must be sought by more subtle approaches.

Spontaneous hypoglycemia is not synonymous with hyperinsulinism. The latter term implies an absolute increase in endogenous insulin secretion, a mechanism which is operative in only some instances of spontaneous hypoglycemia. Definitions of other frequently used terms will be given in appropriate later sections of this review.

Symptoms of spontaneous hypoglycemia

The symptoms of spontaneous hypoglycemia are well defined. They are best assembled into two categories. Complaints of faintness, weakness, tremulousness, palpitations, diaphoresis, hunger, and nervousness constitute one pattern of symptoms. It is readily apparent that these manifestations resemble the effects of overdosage of rapid-acting soluble insulin. In addition, such symptoms are closely reproduced by the administration of epinephrine. There is good reason to believe that hyperepinephrinemia is actually the mechanism responsible for the symptom complex. The demonstration of increased circulating "sympathins" during induced hypoglycemia was observed by Houssay in 1924.[17] With the development of more precise methods of analysis, Goldfien has shown the augmentation of plasma epinephrine levels following insulin administration in dogs[18] and man.[19,20] The urinary excretion of adrenalin also rises under these circumstances,[21] and the depletion of adrenal medullary stores occurs simultaneously.[22,23] Greater difficulty has been experienced in demonstrating increased norepinephrine release in response to insulin-induced hypoglycemia. Since this latter amine is a product primarily of sympathetic neural formation, it is presently assumed that the sympathetic neural contribution to induced hypoglycemia is considerably less than that of the adrenal medulla. Luft and Von Euler[24] have shown that an intact anterior hypophysis is not a prerequisite for the rise in urinary epinephrine excretion following hypoglycemic episodes. Apparently the activating mechanism involves a hypothalamic-adrenal medullary axis. The increased adrenal medullary discharge offers a rapid, protective response to the challenge of blood-sugar depression. Epinephrine enhances the hepatic mobilization of glycogen and inhibits peripheral glucose utilization.[25] Although increased adrenocortical secretion as evidenced by rising plasma cortisol levels also occurs in response to induced hypoglycemia,[26] it is doubtful that such a mechanism affords significant immediate amelioration of the hypoglycemia.

The second pattern of symptoms associated with spontaneous hypoglycemia is indicative of central nervous system derangement.[27] Headache, confusion, visual disturbances, motor weakness, palsies, ataxia, and marked personality disturbances may be encountered. The progression to loss of consciousness, convulsive seizures, and coma is not unusual. It is apparent that this group of symptoms closely resemble the manifestations of overdosage of long-acting insulin. It is entirely possible to encounter patients whose symptoms may merge from the more benign manifestations of hyperepinephrinemia into the alarming neurologic complaints. Several factors appear to determine which pattern of symptoms may be experienced. A rapid fall of the blood sugar to levels which are not maximally depressed and a short duration of the hypoglycemia favor the occurrence of reactive hyperepinephrinemia. A slow descent of the blood glucose to extremely low levels and a long duration of the hypoglycemia precipitate the cerebral manifestations. We have been impressed also by the predilection of the elderly to exhibit neurologic symptoms. It appears probable

TABLE I. Etiologic Classification of Spontaneous Hypoglycemia[28]

- Organic—recognizable anatomic lesion
  - Hyperinsulinism
    - Pancreatic islet-cell adenoma: single, multiple, aberrant, associated with other endocrine adenomas
    - Pancreatic islet-cell carcinoma
    - Generalized hypertrophy and hyperplasia of the islets of Langerhans
  - Hepatic Disease
    - Ascending infectious cholangitis
    - Toxic hepatitis
    - Carcinomatosis
    - Fatty metamorphosis
    - Laennec's cirrhosis
    - Viral hepatitis
    - Chronic passive congestion
    - Glycogen storage disease
  - Hypopituitarism
    - Destructive lesions (adenoma, craniopharyngioma)
    - Atrophy and degeneration
    - Surgical hypophysectomy
  - Postpartum infarction (Sheehan's syndrome)
    - Pituitary myxedema
    - Severe inanition
    - Postoperative hypoglycemia
  - Adrenocortical hypofunction
    - Idiopathic cortical atrophy
    - Destructive granulomas
    - Destructive neoplasms
    - Congenital adrenal hyperplasia
  - Extrapancreatic neoplasms (fibromas and sarcomas)
  - Central nervous system lesions (hypothalamus or brain stem)
- Functional—no recognized anatomic lesion
  - Hyperinsulinism—nervous or reactive hypoglycemia
  - Alimentary hyperinsulinism—postsurgical, totally or partially excluding the pyloric sphincter
  - Idiopathic spontaneous hypoglycemia of infancy
    - Leucine sensitive
    - Leucine insensitive
  - Renal glycosuria
  - Hypoglycemia of early diabetes
  - Lactation
  - Severe continuous muscular work

that cerebrovascular damage may render this group more vulnerable.

Regardless of the pattern of symptoms that the patient with spontaneous hypoglycemia may experience, it must be emphasized that the complaints are episodic and repetitive. Although the tempo and severity of attacks may vary, the same patient will most often experience the same symptom complex. Variations in threshold sensitivity, however, do occur. The same degree of blood-sugar depression will not necessarily provoke a symptomatic response at different times. Recognition of the episodic nature of the patient's symptoms is of diagnostic importance and often is the first clue enabling the physician to suspect the true nature of the disorder. It will be demonstrated that the type of symptom complex also affords a valuable diagnostic clue to the cause of the spontaneous hypoglycemia.

Etiologic classification of spontaneous hypoglycemia

The maintenance of normoglycemia is dependent on physiologic mechanisms which are far too complex to elaborate in this brief review. It will suffice to indicate that gastrointestinal absorption of carbohydrate, pancreatic insulinogenesis, hepatic storage, and the release of glucose and peripheral utilization of sugar are prominent components. A modifying influence is effected by the central and vegetative nervous system, the anterior hypophysis, the thyroid, the adrenal cortex and medulla, and in experimental animals by gonadal secretions. Table I presents an etiologic classification of spontaneous hypoglycemia. It has been adopted with minor additions from the work of Conn.[28] It is to this investigator that full credit must be given for bringing order and reason to an area where chaos reigned previously.

A perusal of Table I may immediately leave the physician with a sense of confusion and futility in attempting to determine the etiology of the individual example of spontaneous hypoglycemia. Such is by no means the true state of affairs. Many of the listed causes of spontaneous hypoglycemia are extremely rare and seldom encountered. In other instances, the hypoglycemia constitutes only one facet of a disease that is recognized by more obvious signs. Diagnostically it has proved of great value to reclassify the causes of spontaneous hypoglycemia on the basis of the time of occurrence of the blood-sugar depression. Three categories are recognized:

Fasting hypoglycemia. Within the group with fasting hypoglycemia the lowest level of the blood sugar is achieved following the maximum interval after food ingestion. For individuals consuming three meals daily, this period is the early morning hours prior to breakfast. The most important examples of fasting hypoglycemia are: (1) hepatogenic hypoglycemia; (2) anterior hypophyseal insufficiency; (3) adrenocortical insufficiency; and (4) extrapancreatic neoplasms—fibromas and sarcomas.

Stimulative hypoglycemia. Within the group with stimulative hypoglycemia the lowest level of the blood sugar is achieved in from two to four hours after food ingestion. In contrast to the fasting hypoglycemias, long intervals without food do not precipitate blood-sugar depression. The most important examples of stimulative hypoglycemia are functional hyperinsulinism and alimentary hyperinsulinism.

Combined fasting and stimulative hypoglycemia. Within the group with combined fasting and stimulative hypoglycemia a severe depression of the blood sugar may occur both in the fasting state and after food ingestion. The most important examples of combined hypoglycemia are organic hyperinsulinism and the idiopathic spontaneous hypoglycemia of infancy.

When one considers the observed frequency of the various causes of spontaneous hypoglycemia it becomes abundantly clear that less than 10 per cent of the cases are ascribed to the more esoteric abnormalities. It is precisely in this group that other manifestations of the underlying disorder are detected without difficulty. The remaining large majority of patients with spontaneous hypoglycemia will be examples of three diseases: functional hyperinsulinism, hepatogenic hypoglycemia, and organic hyperinsulinism. The following measures have proved to be of great assistance in

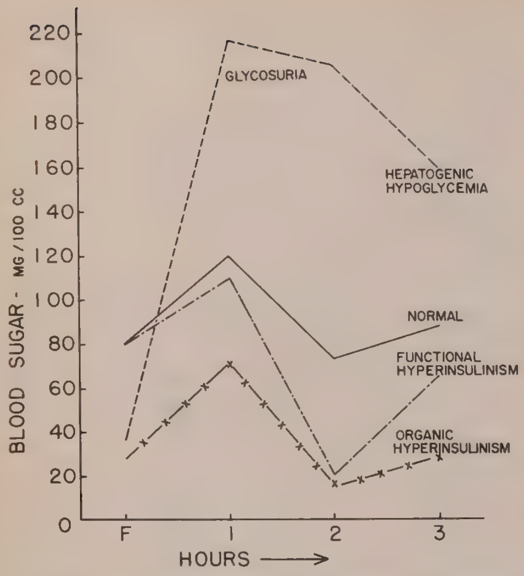

FIGURE 1. Three types of glucose tolerance curves in spontaneous hypoglycemia.[28]

differentiating these three causes of spontaneous hypoglycemia: (1) the history of the type of symptom complex experienced, the time of the occurrence of the episodes, and the tempo of the attacks; (2) the level of the fasting blood sugar determined on several occasions with the patient on a normal and restricted carbohydrate intake; (3) the configuration of the glucose tolerance curve after a standard preparatory diet[29]; (4) the results of a battery of liver-function tests; and (5) the response to the intravenous administration of tolbutamide.

Functional hyperinsulinism

Functional hyperinsulinism is the most frequently encountered cause of spontaneous hypoglycemia. It is a disease intimately related to psychosomatic pathogenesis. It occurs with much greater frequency among females. The typical individual shows many manifestations of great emotional lability. The complaints which are caused by the depression of the blood sugar are frequently only a part of a multitude of somatic symptoms. Such patients experience the symptom complex of hyperepinephrinemia. Central nervous system derangement is seldom encountered. It is most important to ascertain carefully the exact nature of episodes which may be termed "fainting spells" or loss of consciousness. True loss of consciousness, convulsions, sphincter relaxation, and self-injury do not occur with functional hyperinsulinism. The attacks of hypoglycemia are not progressive in their severity or frequency. Indeed periods of freedom from symptoms may occur when environmental or other emotional stresses are alleviated. The episodes of spontaneous hypoglycemia occur from two to four hours after food ingestion. They do not occur in the fasting state. Occasionally patients with functional hyperinsulinism will experience symptoms in the early morning hours prior to breakfast. A close interrogation will reveal that nighttime snacks have been consumed. Muscular exercise does not precipitate blood-sugar depression. The fasting blood sugar is invariably normal and the restriction of carbohydrate does not produce objective hypoglycemia. The liver function is not altered. The true nature of the defect becomes apparent by inspection of the glucose tolerance curve (Fig. 1). This study will demonstrate a normal fasting blood sugar with a normal postabsorptive elevation. Between the second to the fourth hour, however, the blood sugar will fall to hypoglycemic levels. Concomitantly the patient will experience symptoms identical to the spontaneous episodes. The blood-sugar depression is transitory and not severe. Values below 45 mg. per 100 ml. (Folin-Wu) are unusual. The blood sugar returns to normal levels within fifteen to thirty minutes following the hypoglycemic phase. Synonyms that have been used by various authors to describe this form of spontaneous hypoglycemia have been: reactive hypoglycemia, hypoglycemia fatigue, nervous hypoglycemia, and functional hypoglycemia. The term functional hyperinsulinism as initially introduced by Conn[30] appears preferable since it alludes to the probable causative mechanism. Several studies[31,32] have documented the fact that the primary stimulus for insulin release from the islets of Langerhans is the glucose content of the pancreatic arterial blood. Since the postabsorptive rise of the blood sugar in functional hyperinsulinism is within the expected normal range, the subsequent precipitous fall to hypoglycemic levels has been considered evidence of increased responsitivity of the islet tissue to the normal stimulus for insulin secretion. This excessive functional response of the islets apparently involves changes in the fine autonomic regulatory mechanisms. This mechanistic concept is in direct contrast to the postulated pathogenesis of spontaneous hypoglycemia following gastrointestinal surgery which excludes the pyloric sphincter. In the latter instance, the absorptive surface of the small bowel is exposed rapidly to ingested carbohydrate with a resultant greater than normal rise of the blood sugar. Although the subsequent release of insulin is sufficient to produce hypoglycemia, this magnitude of response occurs following a supernormal stimulus. Alimentary hyperinsulinism is therefore a normal islet-cell response to a greater than normal insulinogenic stimulus. Strong evidence indicating the importance of the pyloric spincter in the genesis of alimentary hyperinsulinism is afforded by studies of normal subjects with duodenal intubation.[33] Typical alimentary hyperinsulinism may be reproduced by the tubal administration of carbohydrate. Alimentary hyperinsulinism should be differentiated from the "dumping syndrome" which may also follow gastric surgery. Symptoms of epigastric fullness, sweating, weakness, and palpitations may be experienced when large amounts of hyperosmolar jejunal contents rapidly draw fluid into the intestinal lumen. These manifestations of the "dumping syndrome" have their onset shortly after meals and subside prior to the occurrence of the symptoms of alimentary hyperinsulinism.

It should be appreciated that the postulates implicating increased insulinogenesis must still be considered theoretical since studies of plasma insulin have not been reported in such cases. These studies would now appear eminently appropriate.

The relief of functional hyperinsulinism is best achieved by a strict reduction of the carbohydrate content of the diet.[34] The physician thus attempts to minimize the postprandial rise of the blood sugar and the subsequent islet-cell response. It is often necessary to reduce the carbohydrate intake to 75 to 100 Gm. daily evenly distributed with the three meals. Emphasis must be placed on carbohydrate diminution and not on the accompanying protein augmentation. The use of supplementary feedings is not advocated since it rarely is possible to exclude additional carbohydrate. The substitution of other carbohydrates for the more simple sugars is doomed to failure since these substances have been shown to produce a comparable glycemic response when administered in isoglucogenic quantity.[35] Although the use of cholinergic drugs to abolish vagal influences has been advocated,[36] this form of treatment has met with minimal acceptance. Berry[37] has recently described a group of patients with spontaneous hypoglycemia closely resembling functional hyperinsulinism. Although male patients predominated, emotional instability, apprehension, and insecurity were prominent characteristics, and the published glucose tolerance tests were identical in configuration to the curve of functional hyperinsulinism. Abstinence from tobacco was curative. Further observations would seem warranted.

Spontaneous hypoglycemia: early manifestation of diabetes mellitus

Seltzer, Fajans, and Conn[38] recently have drawn attention to a group of patients who demonstrate the symptoms of functional hyperinsulinism, but in whom the glucose tolerance curve suggests early diabetes mellitus. These patients demonstrate a fasting blood sugar which is normal or slightly elevated. Following the administration of glucose the blood sugar rises to a hyperglycemic peak which is maintained for from two to four hours. Between the third to the fifth hour the blood glucose falls to hypoglycemic levels with accompanying symptoms. A compensatory rise then follows. The presence of a normal or elevated blood sugar, the lack of evidence of hepatic disease, and the terminal compensatory rise of the blood glucose distinguishes this curve from the variety encountered in hepatogenic hypoglycemia.

The authors postulate that this variety of spontaneous hypoglycemia may represent an early manifestation of diabetes mellitus. The initial diabetic defect is therefore regarded as a diminution in the immediate release of insulin in response to the stimulus of a rising blood sugar. The capacity of the islets to produce insulin is not impaired in this early phase of diabetes and the hyperglycemia affords a supernormal stimulus. The islets then discharge sufficient insulin to produce transient hypoglycemia. Recent observations of Yalow and Berson[39] with an immunologic assay for plasma insulin support these postulates. In patients with mild diabetes mellitus they have demonstrated a delay in the normal rapid release of insulin after the administration of glucose followed by a supernormal discharge of the hormone.

Hepatogenic hypoglycemia

The recognition of the central role of the liver in the maintenance of normoglycemia was first emphasized by Mann and Magath.[40] These investigators demonstrated the gradual diminution of the blood glucose culminating ultimately in convulsions and death which follows experimental hepatectomy. It is now well established that the liver is the main contributor to the blood glucose during the fasting state.[41] The normal liver possesses the ability to convert absorbed glucose and other hexoses into glycogen (glycogenesis); it is able subsequently to break down this complex branched polysaccharide and release glucose to the periphery (glycogenolysis); it converts protein precursors into carbohydrate (gluconeogenesis); and it possesses proteolytic mechanisms for the degradation of insulin.[42]

Spontaneous hypoglycemia in severe hepatic disease appears to be related to deficient glycogen storage and inadequate conversion into glucose.[43] In classic glycogen storage disease, a specific enzymatic defect has been demonstrated.[44] A lack of glucose phosphatase results in the severe attenuation of glycogen breakdown. No examples of hepatogenic hypoglycemia have yet been ascribed to abnormalities in insulin-degrading mechanisms.

When one considers the large number of patients with far-advanced hepatic disease, it is surprising that spontaneous hypoglycemia is not encountered more frequently. Nevertheless it is entirely possible that manifestations of the basic liver disorder occupy the physician's primary interest, and episodes of symptomatic hypoglycemia may pass unrecognized or masquerade as other phenomena. Tumulty and Mellinkoff[45,46] have emphasized the occurrence of spontaneous hypoglycemia secondary to congestive hepatomegaly in long-standing myocardial failure. Episodes of disordered behavior, coma, and convulsions usually attributed to anoxemia, cerebrovascular disturbance, or drug intoxication may actually have their genesis in spontaneous hypoglycemia. Similarly, mental aberrations and torpor in the course of severe hepatic disease may be incorrectly ascribed to protein encephalopathy. Nevertheless, it must be admitted that spontaneous hypoglycemia is not a common complication of liver disease, and alterations of carbohydrate metabolism producing clinically alarming manifestations are unusual.

Hepatogenic hypoglycemia is characterized symptomatically by cerebral phenomena. The symptom pattern of hyperepinephrinemia is encountered rarely. Blood-sugar depression occurs in the fasting state. It may be precipitated by food omission, carbohydrate restriction, or strenuous muscular exercise. Hypoglycemic episodes do not occur in the immediate postabsorptive period. Although the secretion of insulin directly into the portal system following carbohydrate ingestion has been shown by Madison *et al.*[47] to diminish the hepatic release of glucose, the elevation of the blood sugar from the absorbed carbohydrate far overshadows the immediate effects on the liver.

The diagnosis of hepatogenic hypoglycemia is facilitated by the usually abundant evidence of severe liver disease and only rarely is the underlying disorder more difficult to discern. The glucose tolerance curve (Fig. 1) demonstrates a low fasting blood sugar with a rise to a hyperglycemic peak following carbohydrate administration. The blood sugar then falls slowly to severe hypoglycemic levels from between the fourth to the seventh hour. Hypoglycemic unresponsiveness is maintained unless additional food is ingested.

It is not unusual for hepatogenic hypoglycemia to parallel the course of the hepatic disease. An improvement in liver function will be accompanied by the amelioration of the hypoglycemia. The prognosis of hepatogenic hypoglycemia is therefore dependent on the nature of the hepatic lesion. The treatment of hepatogenic hypoglycemia is limited to the use of a high carbohydrate diet with frequent feedings, in addition to the measures employed for therapy of the liver disorder. It is advisable to administer a bedtime or midnight feeding to avoid early morning attacks.

The occurrence of spontaneous hypoglycemia in association with primary liver cell carcinoma will be considered under the topic of extrapancreatic neoplasms.

Organic hyperinsulinism

The most profound examples of spontaneous hypoglycemia are enountered with anatomically demonstrable lesions of the islets of Langerhans which are hormonally active and produce excess insulin. These lesions are most commonly adenomas, either single or multiple; less frequently they are diffuse hyperplasia or carcinoma. Since surgical removal of an insulinoma results in a dramatic cure of an often catastrophic illness, physicians are eager to advise pancreatic exploration in suspicious cases. Unless rigid diagnostic criteria are maintained closely, many unnecessary surgical procedures will be recommended with an unavoidable morbidity and mortality.

The patient with organic hyperinsulinism may demonstrate the symptoms of both hyperepinephrinemia and cerebral dysfunction. Although neurologic manifestations may be the sole complaint, it is extremely rare to encounter only the symptom complex of augmented epinephrine release. This combination of symptoms is readily explained by the rapid fall of the blood sugar that follows excess insulin discharge. In contrast to patients with functional hyperinsulinism, however, in whom counter-regulatory mechanisms are adequate to prevent severe hypoglycemia and resultant neurologic disturbances, the excessive discharge of insulin from a functioning tumor is frequently of sufficient magnitude to overwhelm the counter-regulatory defenses. Profound and prolonged hypoglycemia will result. The episodes of hypoglycemia occur both in the fasting state and from two to four hours after meals. The latter observation suggests that insulinomas are not necessarily autonomous neoplasms but may respond as does normal islet tissue to the glycemic postprandial stimulus. The omission of meals, a diet low in carbohydrate, or excessive muscular work may precipitate the hypoglycemia. The contribution of muscular exercise in effecting blood sugar depression has been clarified recently by new observations in the diabetic patient. Although it has long been recognized that physical activity will increase glucose utilization, the mechanism of this phenomenon has been understood poorly. Morgan *et al.*[48] has shown that local hypoxia such as that which occurs with muscular exercise will increase glucose penetration into the cell as well as augment phosphorylation. Glucose utilization is thereby facilitated. Goldstein *et al.*[49–51] have suggested that muscular exercise may provoke the release of a humoral hypoglycemic factor. These views still remain controversial.[52]

The attacks of spontaneous hypoglycemia are progressive in organic hyperinsulinism. Although the initial episode may be mild, both the tempo and the severity of the attacks become intensified as the disease persists. The patient may make the observation that increased food consumption offers a gratifying relief of symptoms and hence obesity not infrequently complicates an ultimate surgical exploration.

The glucose tolerance curve in organic hyperinsulinism (Fig. 1) shows a depressed fasting blood sugar with a normal or subnormal postabsorptive elevation. There then occurs a sharp fall to extremely depressed values between the second and the fifth hour. Occasionally a tolerance curve with a postabsorptive hyperglycemic plateau is encountered. The curve will then be identical to the configuration seen in hepatogenic hypoglycemia. In such an instance it has been assumed that the abnormal source of insulin has depressed normal islet-cell function.[53] The hyperglycemic peak is the result of the failure of the anatomically normal but functionally depressed islet tissue to respond with insulinogenesis to the stimulus of the administered carbohydrate. Pollen, Grodsky, and Di Raimondo[54] have reported studies of the insulin content of a functioning adenoma and adjacent normal pancreas which tend to validate this concept of impaired hormonal release. Ordinarily one can restore normal islet-cell responsiveness by feeding the patient a high carbohydrate diet for several days. A second glucose tolerance curve will then lack the hyperglycemic peak. Gittler *et al.*[55] have reported the rare occurrence of the amelioration of diabetes mellitus by a proved insulinoma. In this case obliteration of the hyperglycemic peak of the tolerance curve could not be achieved by carbohydrate feeding since the non-neoplastic islet tissue was unable to respond because of the prior diabetic defect.

Although little difficulty may be expected in the diagnosis of severe organic hyperinsulinism, considerable problems are presented by the patient who has sustained occasional episodes suggestive of severe hypoglycemia and who demonstrates normal fasting blood sugar levels and a normal glucose tolerance curve. Such objective information is by no means sufficient to exclude organic hyperinsulinism, and measures to precipitate hypoglycemia must then be instituted. These technics involve various degrees of caloric and carbohydrate restriction combined with physical exercise. Conn and Seltzer[1] have advocated the use of a provocative diet containing 50 Gm. of carbohydrate and 50 Gm. of protein with a total of 1,200 calories. If fasting hypoglycemia is not reproduced by the end of three days, the patient abstains from all food on the fourth day and is exercised on the fifth morning. Such severe and time-consuming procedures may now be outmoded by the recent studies of Fajans *et al.*[56] These investigators have characterized a unique response of insulinomas to the intravenous administration of sodium tolbutamide. In patients with functioning islet-cell tumors, tolbutamide produces a profound decrease in the concentration of the blood sugar with persistence of the hypoglycemia for several hours. In normal subjects tolbutamide will cause a fall of the blood glucose within thirty to forty-five minutes, followed by a secondary rise toward normal by ninety to one hundred and eighty minutes. It is to be emphasized that persistence of the blood-sugar depression and not the absolute level of hypoglycemia is the diagnostic characteristic of the response of an insulinoma to tolbutamide. Yalow and Berson[57] employing the immuno-assay of plasma insulin have corroborated the hypothesis that tolbutamide is indeed able to produce an insulin discharge from islet-cell tumors. Although the elevation of plasma insulin may not persist as long as the blood sugar depression, it is entirely probable that diminished hepatic release of glucose effected by the discharge of insulin to the portal circulation may contribute to the hypoglycemic unresponsiveness. In functional hyperinsulinism, early diabetes with hypoglycemia, adrenal insufficiency, and the majority of patients with hepatic disease, sodium tolbutamide does not cause hypoglycemic unresponsiveness to the degree found in organic hyperinsulinism. It should be emphasized that the use of sodium tolbutamide is superfluous in patients who already demonstrate fasting hypoglycemia.[58] Under such circumstances the administration of this drug may provoke severe hypoglycemic reactions.[59]

Although it might be anticipated that studies of plasma insulin concentration would be of ultimate diagnostic value in establishing the existence of hyperinsulinism, the observed results unfortunately have shown considerable variability. In 18 proved cases of insulinomas, Willebrands and Groen[60] were able to show high levels of plasma insulin-like activity in only 10 cases. Wright[61] has reported similar results with plasma levels determined during demonstrable hypoglycemia. It therefore does not appear warranted to suggest that temporary quiescence of tumor-insulin secretion would explain the normal values. The possibility of inhibitors present within the plasma specimen which might affect the bio-assay procedure is an alternative explanation. Nevertheless Yalow and Berson[62] utilizing the immuno-assay have noted normal fasting plasma insulin in 2 proved cases of islet-cell tumors. One may conclude that regardless of the methodology, a single normal plasma insulin level does not exclude the diagnosis of organic hyperinsulinism.

The treatment of organic hyperinsulinism requires surgical extirpation of the hypersecreting pancreatic lesion. Patients are prepared for laparotomy by the use of a high carbohydrate diet combined with the administration of ACTH or glucocorticoids. Although the primary intent of these measures is to achieve normoglycemia at the time of exploration, a secondary benefit is the diminution in postoperative hyperpyrexic crisis that may complicate pancreatic surgery.[63] The surgeon must be prepared to perform a detailed inspection of the whole pancreas since adenomas may reside in the head, body, or tail of the gland.[64] The identification of these lesions is complicated further by their small size which rarely exceeds 5 cm. in diameter.[65] Although the tumors may be superficially located in the body or the tail of the pancreas, those which occur within the head of the gland often are buried deep within the parenchyma. Multiple adenomas are found in 10 to 15 per cent of the reported cases. Recently we have encountered a patient who harbored eight islet-cell tumors.[66] In instances of multiple tumors, the surgeon may be aided by a determination of the blood sugar before and after the removal of all suspicious tissue. A significant rise of the blood sugar within ninety minutes following resection is indicative of the absence of additional functioning adenomas. This technic has proved successful in 5 reported cases.[55,66–69] Although the procedure may prolong operative exposure, undoubtedly it is preferable to the risk of a second exploration. Prolonged steroid administration may be justified in the patient who refuses surgical aid. Permanent relief should not be anticipated. In the rare instance of islet-cell carcinoma with metastases, intensive steroid treatment is warranted. Glucagon administration also may reduce the frequency of hypoglycemic attacks and decrease the requirement for exogenous glucose.[70,71] The administration of alloxan has been unsuccessful in controlling hypoglycemic episodes in such patients.[72]

Although islet-cell tumors most frequently exist as a sole endocrine abnormality, their association with adenomas of other endocrine sites has been re-emphasized by Underdahl, Woolner, and Black.[73] The frequency of the simultaneous occurrence of tumors of the pancreatic islets, anterior hypophysis, and parathyroid glands makes it mandatory that a search for such multiple abnormalities be performed whenever one site is the locus of tumor formation. Wermer[74] has called attention to the frequent association of peptic ulceration in patients with multiple endocrine adenomatosis. His studies would suggest that there is a strong familial tendency. It is possible that the peptic ulceration in these patients may be determined genetically and not necessarily attributed to the hormonally active tumors. The relationship of this group of patients to those with the ulcerogenic noninsulin-producing tumors of the pancreatic islets (Zollinger-Ellinson syndrome) awaits further clarification.[75]

Spontaneous hypoglycemia of infancy

In 1954 Mc Quarrie[76] reported a group of 25 infants and children who manifested severe fasting hypoglycemia of unknown origin. He termed this syndrome "idiopathic spontaneous hypoglycemia of infancy." It constitutes the most common form of spontaneous hypoglycemia which is encountered in infancy and early childhood. Its onset may occur from shortly after birth to the early prepubertal years. The hypoglycemia is frequently profound and may result in permanent brain damage. Although fasting hypoglycemia is the prominent abnormality, the glucose tolerance curve does indicate a postabsorptive stimulative component. The curve may therefore be identical to the configuration seen in organic hyperinsulinism. Since islet-cell tumors may occur in early childhood,[77] the differential diagnosis assumes great importance. It is noteworthy that Mc Quarrie reported a familial incidence of hypoglycemia in siblings and cousins of the patients which he studied. The history of an affected kinship is therefore of aid in distinguishing idiopathic infantile hypoglycemia from organic hyperinsulinism. The response to sodium tolbutamide may similarly be of assistance in this differential diagnosis. Grumbach and Kaplan[78] and Fajans *et al.*[56] have reported normal responses to tolbutamide administration in idiopathic hypoglycemia.

Mc Quarrie[76] has shown that the attacks of hypoglycemia are self limited and subside spontaneously after several years. During the active phase of the disturbance he has suggested treatment with corticotrophin. Although glucocorticoids may be employed, they appear to be less efficacious than ACTH gel.

Although Mc Quarrie's characterization of the clinical features of this syndrome constituted a significant advance, his stimulation of subsequent investigations attempting to elucidate the mechanism of the blood-sugar depression has opened a new chapter in the study of spontaneous hypoglycemia. Initially Mc Quarrie reported an absence of alpha cells in the islet tissue of 2 siblings affected with idiopathic hypoglycemia. He therefore postulated a congenital deficiency of glucagon secretion as the primary etiologic defect. This hypothesis, however, proved untenable when subsequent pancreatic biopsies failed to substantiate a diminution of alpha cells. No further light was shed on the mechanistic dilemma until 1956 when Cochrane *et al.*[79] observed that some infants with idiopathic hypoglycemia have an intensification of the abnormality when they are treated with a high-protein diet. Since casein was the major protein constituent of the diet, these investigators next demonstrated that casein alone possessed hypoglycemic activity. Gelatin, however, proved inert. The amino acid composition of casein shows a higher content of leucine and tyrosine than is present in gelatin. Feedings of l-leucine and not tyrosine reproduced the hypoglycemia. Not all patients who manifest the idiopathic hypoglycemia of infancy are sensitive to l-leucine, indicating a degree of heterogeneity among this group of patients. Cochrane[80] suggests that approximately 60 per cent of infants with this syndrome demonstrate leucine sensitivity.

The hypoglycemic activity of other amino acids has been investigated with many conflicting reports.[78,81–83] Although the data are insufficient to warrant definite conclusions, the apparent discrepancies may result from yet undefined differences within the group of leucine-sensitive patients. Similar difficulties have been encountered in determining the hypoglycemic potency of the known catabolites of l-leucine.[84]

Regardless of which additional amino acids or their intermediary metabolites may precipitate hypoglycemia, the mechanism of blood-sugar depression appears to be mediated via beta-cell stimulation. Plasma insulin and insulin-like activity are increased following the administration of leucine.[78,79,85,86] Although an increased release of endogenous insulin appears to be the major mechanism of leucine hypoglycemia, the potentiation of insulin activity is a possible secondary effect.[87]

The treatment of patients with leucine-sensitive hypoglycemia is similar to that described previously for idiopathic hypoglycemia. In addition, the dietary regime ideally would eliminate leucine. This amino acid, however, is essential for normal growth and most proteins contain substantial amounts of leucine. Cow's milk is richer in its leucine content than human milk. Additional carbohydrate feedings in the immediate postabsorptive stage are indicated to counteract the stimulative component of the hypoglycemia. The performance of a partial pancreatectomy has been reported[88] to improve 15 of 25 children with idiopathic hypoglycemia. Although some reports have emphasized the finding of islet-cell hyperplasia, pancreatic resection appears appropriate only when the disease is not amenable to other therapeutic modalities.

Although leucine is devoid of hypoglycemic activity in normal adults, Fajans *et al.*[89] have been able to demonstrate leucine sensitivity in such subjects by pretreatment with chlorpropamide. These observations suggest that normal islet tissue, when stimulated to increased hormonal activity, also will show augmented insulinogenesis when challenged with leucine. Similarly leucine sensitivity has been demonstrated in patients with proved insulinomas.[90–92]

Hypoglycemia and extrapancreatic neoplasms

The association of fasting hypoglycemia and extrapancreatic tumors was reported by Doege[93] in 1930. In the following thirteen years 3 additional cases were described.[94-96] No further study of extrapancreatic neoplasms and hypoglycemia appeared until the report of Skillern *et al.* in 1954.[97] This investigator described two instances of sarcoma-like tumors associated with spontaneous hypoglycemia. In both cases the removal of the tumor was accomplished successfully and the hypoglycemia was relieved. In the first patient the neoplasm was located within the right thorax intimately related to the diaphragm and the lower lobe of the lung. In the second case the tumor was a large encapsulated nodular mass in the upper abdomen which was attached posteriorly in the region of the pancreas. Histologically the neoplasms were similar in appearance and consisted of two cell types: (1) small spindle cells with sparse cytoplasm, oval nuclei, and long processes; and (2) round, oval, prismatic or polyhedral cells with a faint rim of cytoplasm. Occasional intracellular material with the staining characteristic of insulin granules was demonstrated. Skillern *et al.*[97] believed that the tumors were of epithelial origin and represented atypical extrapancreatic insulinomas. These neoplasms differed in location from the rare ectopic islet-cell tumor which usually is situated adjacent to the pancreas in the duodenal wall or splenic hilum.

In the seven years following Skillern's communication, 23 additional cases have been studied.[98-101] A review of these reports indicates important case similarities. The hypoglycemia associated with such tumors is severe and occurs in the fasting state. No stimulative component has been demonstrated. When surgical removal of the neoplasm was accomplished, the blood-sugar depression was ameliorated. The reappearance of the hypoglycemia heralds the recurrence or metastases of the original tumor. Invariably the growths are of great size and average over 2,000 Gm. There is a definite predilection for occurrence within the pleural cavity and the retroperitoneal areas, although a not insignificant number of these lesions have occurred intraperitoneally. Microscopically 80 per cent of the tumors were classified as malignant, and although histologic diagnoses were quite diversified (for example: fibrosarcoma, spindle-cell sarcoma, leiomyosarcoma, rhabdomyofibroma, and mesothelioma) it is apparent that most pathologists considered the lesions to be of mesenchymal origin.

Although the clinical characteristics of these tumors have been well defined, considerable disagreement exists concerning the mechanism of the blood-sugar depression. Seckel[96] suggested initially that the tumors by virtue of their location and size interfered with the sympathetic neural receptors in the liver, adrenal, and pancreas. The lack of sympathetic activity diminished glycogen mobilization and produced hypoglycemia. This hypothesis does not appear reasonable in view of the absence of hypoglycemia as a complication of surgical sympathectomy and the failure to encounter hypoglycemia with other large intra-abdominal or thoracic tumors. An alternate explanation proposed by Scholz, Woolner, and Priestley[102] is that the neoplasms inhibit insulin degradation and thus permit enhanced endogenous insulin activity. No evidence to substantiate this hypothesis has been forthcoming. Excessive metabolic activity with high glucose consumption or tumor production of a hypoglycemic substance appear to be the two most plausible theories. The persistently large size of the neoplasms and the significant glycogen storage within some of the tumors has been cited as evidence in favor of increased glucose consumption. The fasting nature of the hypoglycemia also is consistent with this viewpoint. August and Hiatt[103] first presented evidence that these tumors may produce a substance with insulin-like activity. Although previous attempts to demonstrate hypoglycemic activity in tumor tissue had met with little success, technical problems often vitiated the assay procedure. August and Hiatt, however, were able to show insulin activity in tumor extracts in an amount calculated to be three times that reported for the normal pancreas. Three additional studies also have been successful in demonstrating insulin activity from tumor tissue or patient's serum.[102,104,105] Conversely Sellman *et al.*[106] have reported an extraordinarily well-studied patient in whom insulin activity could not be shown in extracts from the tumor or the patient's serum.

Karsh, Freedman, and Blumenthal[107] had the opportunity to study a unique case of functional islet-cell carcinoma which metastasized to the liver as a spindle-cell tumor. Although the possibility exists that some of the reported instances of mesenchymal tumors and hypoglycemia might actually be metastatic islet-cell carcinomas in which the primary lesion has been overlooked, it does not appear probable that such an explanation is applicable to many of the reported cases. Since the removal of the demonstrable tumor cures the hypoglycemia, one must postulate an extremely low level of hormonal activity for the primary pancreatic neoplasm which remains in situ. This view is not consonant with previous experiences with islet-cell carcinomas. The isolated spread of such a tumor to the retroperitoneal and intrathoracic areas also would be most unusual.

Although emphasis has been placed on the connective tissue origin of these tumors, 5 examples of adrenocortical carcinoma,[108] 1 of cortical adenoma,[109] and 2 cases of pseudomyxoma peritoneii[110] have been associated with hypoglycemic attacks. Mc Fadzean and Yeung[111] and others[112] have noted the occurrence of spontaneous hypoglycemia with primary liver-cell carcinoma. Conn[112] believes that these tumors act similarly to other extrapancreatic neoplasms in producing hypoglycemia.

Summary

The subject of spontaneous hypoglycemia has been reviewed in the light of the significant contributions of the past several years. Emphasis has been given to the modification of prior concepts in consideration of this newly acquired knowledge. In addition, the more recent advances have been discussed and incorporated with previous information.

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Number thirty-one in a series of articles on Current Concepts in Diabetes Mellitus

Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the New York State Journal of Medicine from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the Journal, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

Nutrition Excerpts

Prepared with the cooperation of the faculty of the Graduate School of Nutrition, Cornell University, Ithaca, New York

R. A. NELSON, Editor

Cutaneous Vitamin D

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Ithaca, New York

ADULT HUMAN BEINGS normally do not require an exogenous source of vitamin D,[1] and the requirement for vitamin D by adults of many animals is variable or demonstrated with difficulty. The formation of vitamin D_3 by sunlight irradiation of cutaneous provitamin D_3 (7-dehydrocholesterol) appears to be a major endogenous source of the vitamin as first suggested by Bills.[2] The higher dietary requirement of vitamin D by individuals whose skin is generally not exposed to sunlight indicates a substantial synthesis of vitamin D in skin.

Three factors are essential for the formation and utilization of cutaneous vitamin D: provitamin D must be present in the skin; provitamin D must be sufficiently close to the skin surface for effective radiation; and the newly-formed vitamin D must become available by reassimilation. These three steps will be discussed in this report.

Presence and formation of cutaneous provitamin D

The presence of provitamin D_3 has been demonstrated in a number of animal tissues. The concentration appears to be higher in skin than in the internal tissues. Festenstein and Morton[3] isolated provitamin D from a number of tissues and reported its concentration in swine skin to be as high as 3 per cent of the extracted sterols. The provitamin also has been found in the skin of human beings as well as in the skin of rats, mice, guinea pigs, and a number of other laboratory and farm animals.[4]

Because the provitamin occurs only as a trace companion of cholesterol in most internal tissues and appears to be absent from the serum, a substantial proportion of the cutaneous sterol is probably synthesized within the skin. The biosynthesis of the provitamin in skin may take place in two ways: The synthesis of the sterol may occur totally from small molecules or by a conversion of previously-formed cholesterol to the provitamin. Each pathway has been demonstrated in animal tissues. There is substantial evidence for the presence in skin of the enzymes which catalyze the synthesis of sterols from acetic acid. Provitamin D is synthesized from acetic acid in slices of rat and mouse skin.[5] The formation of the provitamin occurs rapidly, and radioactive data indicate a substantial synthesis of this product. The second biosynthetic pathway (that is, the conversion of cholesterol to provitamin D) has not been demonstrated in the skin. However, the formation of 7-dehydrocholesterol from cholesterol in a number of other tissues is well documented.[6] The specific enzyme which carries out the one-step conversion of cholesterol to the provitamin has been found in the intestinal mucosa. Presumably the same enzyme could be present in skin and utilize serum or cutaneous cholesterol as a precursor of provitamin D. Because the synthesis from small molecules involves more than two dozen reactions which must occur in sequence, the one-step conversion would be more efficient and more immediately responsive to demands for changes in the rate of formation of provitamin D in the skin.

Irradiation

The irradiation of provitamin D to the vitamin form is the second step which must occur. The ultraviolet wave lengths of light which are absorbed by the provitamin must be of suitable intensity to initiate the conversion to the vitamin. Because the radiation of these same wave lengths is absorbed effectively by the proteins, nucleic acids, and pigments of skin, the provitamin must be sufficiently close to the surface for irradiation. Reinertson and Wheatley[7] observed most of the provitamin in the malpighian layer of human epidermis. Other companion sterols were localized in the stratum corneum and the sebaceous glands. The same workers concluded that the concentration of the provitamin in the malpighian layer of human epidermis was sufficiently high to provide the daily vitamin requirement by irradiation of only a few square inches of skin even though the provitamin is in the lower strata of the epidermis.[8]

Biosynthetic evidence supports the occurrence of provitamin D in the malpighian layer of the epidermis. Patterson and Griesemer[9] reported a rapid synthesis of sterols in slices of human epidermis. Squalene was formed in the dermis and the sebaceous glands. Similar experiments with rat skin demonstrated a substantial formation of sterols in both the epidermis and the sebaceous glands. Most of the activity which was associated with the formation of provitamin D was noted in the slices which contained the epidermis and not in the sebaceous glands.[10]

These observations indicate that the provitamin is formed and stored in the malpighian layer of human epidermis, and this layer is sufficiently close to the skin surface for effective irradiation of the provitamin. The intracellular localization eliminates the need for further translocation of the provitamin onto the skin surface prior to irradiation.

Reassimilation

To be of value the newly-formed vitamin must be carried to various tissues. This is accomplished in lower aminals by preening and licking of the skin and hair. In the human being, the newly-formed vitamin must be reassimilated directly from the epidermis. Unfortunately, little information is available on the assimilation of vitamin D from the cells of human skin. Topical applications of the vitamin penetrate skin readily,[11] and the fatty nature of this vitamin suggests a transfollicular rather than a percutaneous absorption process. If the newly-formed vitamin D is actually intracellular as suggested, however, the reassimilation of the vitamin may not be analogous to the absorption of topical doses of vitamin D.

Presumably, the intracellular vitamin may penetrate into the hair follicles analogously and be carried to the capillaries of the dermis. On the other hand, absorption of the vitamin into the extensive vascular system of the upper dermis would be more direct. This latter process is much less likely to occur with topical applications of the vitamin.

Comment

Many inferences have been drawn from studies on the nutritional requirement of vitamin D and the occurrence of provitamin D in the skin of various species. Certainly, a strong case may be argued for the nutritional significance of cutaneous vitamin D. The presence of the provitamin in skin, however, is not adequate to interpret its role in the supply of vitamin D to the whole animal. As discussed in this report, the irradiation and reassimilation of the provitamin may also be significant factors in the vitamin D economy of human beings and other animals. When manipulations are developed to separate these phases of vitamin D production in the skin, the parameters other than just the concentration of cutaneous provitamin D may be studied.

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Number twenty-five in a new series of Nutrition Excerpts

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 14 to 18, 1962, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1962*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

ALFRED A. ANGRIST, M.D., *Chairman*
Committee on Prize Essays

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

BENJAMIN J. CILIBERTI, M.D., Chairman
VALENTINO D. B. MAZZIA, M.D., Cochairman
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Prolonged Succinylcholine Apnea

APNEA IN THE COURSE of anesthesia may be caused by different mechanisms. These may be central, affecting the brain and spinal cord, or peripheral, affecting the neuromuscular junction. In clinical practice more than one mechanism may be operating in the same patient. The prolonged cessation of respiration extending to the postoperative period is undesirable. With the use of muscle relaxants this complication, with its inherent dangers, has led some authorities to suggest that it is wiser to use assisted than controlled respiration. It also has been stated that the only safe and certain prevention of prolonged postoperative apnea is the prevention of prolonged apnea during anesthesia.

The following case report illustrates the failure of an attempt to terminate apnea during surgery by discontinuing both anesthetic agents and succinylcholine for a seventy-minute period. The apnea persisted for an additional three hours postoperatively.

Presented and discussed at a conference held at Bellevue Hospital, New York City, September 11, 1961. Clinical Anesthesia Conferences are held on the first Monday of each month.

Case report

This thirty-four-year-old, white female who was rather obese had nothing significant in her medical history. She entered the hospital for the removal of a large fibroid uterus. One hour before the contemplated time of surgery she received 75 mg. of meperidine hydrochloride and 0.4 mg. of atropine intramuscularly. She arrived in the operating room well sedated but not depressed. Her blood pressure was 120/80, pulse 80 beats per minute, and respirations 18 per minute. The induction of anesthesia was accomplished with the intravenous administration of 200 mg. of thiopental sodium in a $2^1/_2$ per cent solution. Forty mg. of succinylcholine were given, and the patient was oxygenated. A number 38 cuffed Murphy tube was inserted into the trachea under direct vision. Anesthesia was maintained with intermittent cyclopropane and oxygen. Muscular relaxation was obtained with a 0.2 per cent succinylcholine drip at a rate of about 15 drops per minute with respiratory effort being maintained. After fifteen minutes of surgery the patient was put into the Trendelenburg position, and the respirations continued to be assisted. About twenty-five minutes after the start of surgery it was noticed that spontaneous respiration ceased despite no increase in the drip rate of the relaxant. Extreme relaxation was present, and the lungs could be inflated with ease, suggesting that the apnea was due to succinylcholine.

The blood pressure and pulse remained stable while manual artificial respiration was performed adequately. To exclude a narcotic effect, 0.5 mg. of levallorphan tartrate was given intravenously. The apnea remained unchanged. The respirations were controlled, and the peritoneum was closed in about seventy minutes after the onset of the apnea. During the apneic period the patient received only oxygen. Cyclopropane and succinylcholine were discontinued on cessation of spontaneous respirations. Periodic attempts were made to permit the patient to initiate spontaneous breathing. On completion of the peritoneal closure a test dose of 10 mg. of edrophonium chloride was given to antagonize a possible nondepolarization block sometimes caused by succinylcholine. There was no improvement. Three hours after the completion of surgery spontaneous respiratory efforts were noticed. The patient recovered in four and one-half hours after succinylcholine and cyclopropane were discontinued. The endotracheal tube was then removed. Oxygen was given by mask for a brief period and then by nasal catheter for an additional hour. The postoperative course was uneventful. There was complete amnesia for the entire apneic period.

Comment

As previously mentioned, apnea may be produced by several causes.[1,2] An overdose of relaxant drugs is a common cause. Anesthetic agents that affect the myoneural junction may produce a summation with nondepolarizing muscle relaxants resulting in a prolonged apnea. Patients with atypical or low-level plasma pseudocholinesterase may have delayed destruction of succinylcholine. Low-serum potassium has been associated with prolonged respiratory paralysis following the use of relaxant drugs. Myasthenic patients have been affected in a similar manner. In addition, overdose or increased sensitivity to hypnotic, analgesic, or anesthetic drugs; hypoventilation with prolonged acidosis; prolonged hypoxia, hyperventilation, and the resultant reduction in the normal carbon dioxide tension; and prolonged stimulation of the pulmonary stretch receptors during positive pressure-controlled respiration may lead to persistent apnea. The mere presence of an endotracheal tube in some individuals has been known to inhibit respirations reflexly.

A review and evaluation of the anesthetic technic employed may lead to revealing evidence in pinpointing the principle factor. The electrical stimulation of a peripheral nerve, such as the ulnar, and observing the response may aid in differentiating a central or peripheral mechanism as the cause of apnea.[3] The premedication and amount of thiopental sodium used for induction did not appear to be unduly excessive for this patient although an unwarranted degree of sensitivity to these or to the anesthetic agent may have been present.

A single dose-response determination has been recommended at the beginning of anesthesia to avoid prolonged apnea. This patient received 40 mg. of succinylcholine initially. Subsequent relaxation was maintained by the drip method during which respiratory efforts were being maintained. A single dose-response may or may not have been evaluated fully in this patient. Assisted respirations during the use of the muscle relaxant were assumed to be adequate, and hypoventilation was not considered a factor. Periodic attempts during apnea to permit the patient to initiate spontaneous breathing and accumulate carbon dioxide seemed to eliminate hyperventilation as its cause. One must avoid the excessive build-up of carbon dioxide during this trial period. The arterial carbon dioxide tension or end expiratory carbon dioxide concentration may be determined to confirm these clinical impressions of hypo- or hyperventilation.

A specific antidote can be used to antagonize nondepolarizing muscle relaxants. Edrophonium chloride was tried in this case on the basis that large doses of a depolarizing block may resemble a nondepolarizing-type block. The results indicated that this did not occur in this patient. The desire to eliminate the narcotic effect led to the administration of levallorphan tartrate as an antagonist. This also did not improve respiratory activity for this patient.

There was some speculation as to the possible central effect of succinylcholine since this patient remained unconscious and had complete amnesia with only 100 per cent oxygen being administered for several hours. There has been no reported evidence for this although some fragile evidence that d-tubocurarine may pass directly into the brain cells and depress their activity has been stated.[4] "Habit apnea" may have developed from prolonged stimulation of the Hering-Breuer reflex. Occasionally, requesting or commanding the apneic patient to breathe may initiate spontaneous respirations.

It was felt that this patient's prolonged apnea was due to succinylcholine and most likely was on the basis of a low or atypical plasma cholinesterase. The use of edrophonium chloride and levallorphan tartrate may have aided in prolonging the apneic period. Respiratory stimulants and anticholinesterases are contraindicated in such cases.[5] Adequate artificial ventilation, circulatory support if necessary, and infinite patience are required.

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Number one hundred sixteen in a series of Clinical Anesthesia Conferences

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Scientific Exhibits

Applications for space for scientific exhibits should be made directly to the Chairman, Scientific Exhibits Subcommittee of Convention Committee:

William L. Watson, M.D.
340 East 72nd Street
New York 21, New York

No applications can be considered after January 15, 1962.

Awards will be made in two groups:

Group I: Awards are made for exhibits of individual investigation which are judged on the basis of originality and excellence of presentation.

Group II: Awards are made for exhibits which do not exemplify purely experimental studies and which are judged on the basis of presentation and correlation of data.

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Antihistamine Intoxications

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Toxic Agent	*Age*	*Sex*
Chlorpheniramine Maleate	5 years	Male

The patient suffered from croup and was given penicillin and chlorpheniramine maleate by his family physician. He had a violent reaction to the drug and repeatedly banged his head against the wall.

His parents told the interviewing public health nurse that the child became exceedingly hyperactive to the extent that he seemed bent on self-destruction by constantly banging his head against the wall. This patient was affected with mongolism and had an I.Q. of 21.

After two days in the hospital the patient made a complete recovery.

INCIDENT 2

Toxic Agent	*Age*	*Sex*
Chlorpheniramine Maleate	2 years	Female

The child obtained a box containing the medication while the house was in a state of confusion when the family was moving to another apartment, and she swallowed 2 tablets. Vomiting was induced immediately on the advice of the Poison Control Center, and the patient did not suffer any ill effects.

INCIDENT 3

Toxic Agent	*Age*	*Sex*
Chlorpheniramine Maleate	18 months	Male

While the family was moving into a new apartment, a bottle of chlorpheniramine tablets was left on the floor in the bedroom in a box with other materials. The parents were totally unaware that the child had found the box and had swallowed 16 Gm. of the medication. When the mother returned to the bedroom she found the child playing with the box and realized what had happened. He was taken to a hospital emergency room where the only symptom on admission was drowsiness. Vomiting was induced with the aid of ipecac, and after a short period the patient became symptom-free.

INCIDENT 4

Toxic Agent	*Age*	*Sex*
Chlorpheniramine Maleate	3 years	Female

This child obtained the box containing the medication and ingested 8 tablets.

Although the patient was symptom-free, the physician lavaged the child's stomach with sodium bicarbonate within thirty minutes following the ingestion.

Incident 5

Toxic Agent	*Age*	*Sex*
Dexchlorpheniramine Maleate	2 years	Female

This patient is the daughter of a registered nurse. The child swallowed ten 4-mg. tablets. The mother called the Poison Control Center, and the Center advised that vomiting be induced. The patient vomited one and one-half hours following the ingestion. The mother relates that, "The bottle of tablets was left on a dresser after my husband tried to get my son to take one. My husband forgot the bottle, and the baby apparently pulled over the rocking horse, climbed up, and ate the pills. It was discovered when my husband went to get something out of the dresser."

Comment

These incidents are cited to indicate that accidents happen to unsuspecting children because of the mishandling of drugs by adults.

The products involved in the incidents are manufactured by the same company. Chlorpheniramine maleate is supplied in 4-mg. tablets, as repetabs in 8 and 12 mg., with sodium pentobarbital 50 mg., and also as a syrup. It is a potent antihistamine.

Dexchlorpheniramine maleate is supplied as an expectorant in various doses, as a general antihistamine in repetabs of 4 and 6 mg., in tablets of 2 mg., and in the form of a syrup.

The chief side-effects are drowsiness and dizziness. In spite of claims by pharmaceutical manufacturers, all antihistamine drugs are capable of producing side-reactions. However, there is a marked individual variation to susceptibility and tolerance. There is also a marked individual variation as to the tolerance of an individual to a given drug.

The most common side-effects of antihistamines are drowsiness, lethargy, dizziness, confusion, inability to concentrate, and disturbed coordination. They also may produce dryness of the mouth, nose, and throat.

Antihistamine drugs in some individuals also have caused excitation, tremors, palpitation, and convulsions. A few of the rare manifestations are muscular weakness and gastrointestinal disturbances, such as nausea, vomiting, and diarrhea.

The treatment of acute poisoning and particularly the drowsiness, if not cleared by the elimination of the drug through induced vomiting and lavage, may require a cerebral stimulant, such as amphetamine. In general, the treatment is symptomatic and supportive.

The wide variety of antihistamine drugs and the practice of some manufacturers of producing the same drug under different names is regrettable. It is confusing to the physician in regard to treatment when he is confronted with side-effects following its use.

We questioned this, but apparently unsuccessfully, in a letter to the editor of a leading medical journal.

> The modern physician is beset by a multiplicity of names for the same drug, and must distinguish and remember the trade, generic, and often the chemical name.
>
> Meanwhile, the journal itself assists in this confusing situation when two ads for "Polaramine" describe it as a brand of dexchlorphiramine maleate, and dextro-chlorphiramine maleate, while in the same issue "Demazin" is described as a mixture of chlorprophenpyridamine maleate and epinephrine.
>
> From these ads, what average physician would know or deduce (1) that chlorphiramine maleate and chlorphenpyridamine maleate are identical, (2) that both are just his old Chlor-Trimeton, (3) "Polaramine" is only the dextro form of Chlor-Trimeton?
>
> If "Polaramine" is called dex or dextro chlorphiramine, consistency should dictate that the physician should be informed that "Demazin" contains chlorphiramine.
>
> Until the path through the present morass of drug nomenclature is found, a closer scrutiny of drug advertising copy is indicated.

We received the following reply from the advertising committee chairman of the journal.

> Thus far the advertising committee has held that both the U.S.P. synonym (chlorprophenpyridamine) and the U.S.P. name (chlorpheniramine) may be used as generic or common names for the drug introduced as Chlor-Trimeton. Similarly, the dextro isomer, marketed as Polaramine, has been permitted to be advertised with either the generic designation, dexchlorpheniramine, or the variant dextro-chlorpheniramine. Ideally, chlorpheniramine and dexchlorphenir-

amine would seem to be the only common names needed to identify these two drugs, and in the future we shall try to see to it that these names are employed in conjunction with advertising.

Table I shows a report on poisonings during a recent weekend.

TABLE I. Incidents in which aid was requested from the Poison Control Center during a recent weekend

Substance Ingested	Age (Years)	Sex
Ajax and bleach	$1^1/_2$	F
Alcohol (isopropyl)	38	F
Alcohol (isopropyl)	$1^1/_3$	M
Alcohol (rubbing)	35	M
Anacin	40	F
Aspirin	3	F
Aspirin	4	F
Aspirin	$2^1/_2$	M
Aspirin	3	M
Aspirin	$2^1/_2$	F
Aspirin and quinine	25	M
Barbiturates	25	F
Bleach	38	M
Camphor	18	F
Cheracol (cough medicine)	3	M
Cheracol (cough medicine)	$2^1/_2$	F
Charcoal lighter	2	F
Cigaret	1	F
Cleanser	37	F
Cleanser	$1^1/_2$	F
Clorox (bleach)	$1^1/_2$	M
Clorox (bleach)	22	F
Creosote	$1^3/_4$	F
Detergent	$3^1/_2$	F
Detergent	2	F
Deodorant	2	M
Dexamyl	14	F
Diuretic	3	Unknown
Dye	$1^1/_2$	M
Electric paste (rodenticide)	$2^1/_2$	M
Electric paste (rodenticide)	21	M
Even-Flo cleaner	Unknown	M
Feather	2	F
Fluorescent bulb (fumes)	35	M
Furniture polish	2	M
Glue	2	M
Hair dye (scalp burns)	41	F
Hair spray	1	Not reported
Hair spray (in eyes)	19	F
India ink	2	M
Insect repellent	2	M
Insect repellent	4	M
Insect repellent	$1^1/_2$	F
Insect spray	$^1/_2$	M
Insect spray	6	F
Insect spray	$1^1/_2$	M
Iodine	26	F
Lead paint scraps	2	F
Lighter fluid	2	M
Lysol (germicide)	6	F
Makeup	1	M
Medicated powder	$4^1/_2$	M
Mercurochrome	2	M
Mice-Seeds	$2^1/_2$	M
Miltown	25	F
Mr. Clean (detergent)	$1^1/_2$	M
Muriatic acid (in eyes)	Unknown	M
Nail polish	$1^1/_4$	M
Naphthalene	3	M
Narcotics	20	F
Noxon (metal cleaner)	1	M
Nussew glue	$2^1/_2$	F
Paint (rubber-base)	$1^2/_3$	F
Paint (Aluminium)	2	F
Paint	28	F
Paint (water color)	2	F
Paint (water color)	1	F
Paint (water color)	3	F
Pencil (water color)	$1^1/_6$	M
Penny	2	M
Perfume	3	F
Perfume	2	F
Perfume	$1^2/_3$	M
Pine oil	35	F
Pine oil	16	F
Potassium permanganate	15	F
Sani-Flush (lye) (in eye)	2	Not reported
Sedative	31	F
Shampoo	1	F
Sominex (sleeping pill)	20	M
Sting ray (bite)	23	M
Suntan oil	1	F
Thallium	$^2/_3$	M
Transmission fluid	$3^1/_2$	M
Transmission oil	3	F
Tricoloid (ammonium compound)	2	F
Turpentine	$^5/_6$	F
Warfarin (anticoagulant)	2	F
Windex (window cleaner)	3	M
Witch hazel	2	M
Worm medication	4	M
Unknown	24	F
Unknown	25	F

Number eighty-three in a series of Briefs on Accidental Chemical Poisonings

Case Report

Adrenal Cyst

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ADRENAL CYSTS are rare and seldom diagnosed preoperatively. An excellent recent review of the literature by Abeshouse, Goldstein, and Abeshouse[1] reported 155 cases from the world literature, including 3 of their own. We are adding another verified case and 3 more from the world literature, for a total of 159 cases. The clinical obscurity of this condition is brought out by the fact that in Abeshouse's review, 88 of the 155 cases had no known symptoms and had been found unexpectedly at autopsy. Correct diagnoses preoperatively were made in 9 cases. The diagnoses were made by Levison,[2] Ellis[3] (3 cases), Parker,[4] Siceluff,[5] Hancock,[6] and Abeshouse[1] (2 cases). Anderson, Roberts, and Smith[7] reported on a calcified cyst of the adrenal cortex without endocrine symptoms. A case of calcification in an adrenal neoplasm was reported,[8] as was a case of a calcified adrenal tumor.[9] The case reported here was considered preoperatively to be a pancreatic cyst.

Case report

A fifty-three-year-old white fireman was admitted to the Long Island Jewish Hospital on February 1, 1960, with a chief complaint of transient fullness after meals. For the past several years he had had recurrent epigastric pain associated with pain in the left shoulder. About six months prior to admission these episodes appeared after each meal, and at that time he first sought medical aid.

Prior to admission a scout abdominal roentgenogram, a gastrointestinal series, and an intravenous pyelogram were done. A calcified mass was identified in the left upper quadrant of the abdomen. Because of a tentative diagnosis of splenic artery aneurysm, he was admitted for aortography. There were no associated symptoms, and a review of his systems was noncontributory. His past history and family history were negative. A physical examination revealed a well-developed, well-nourished white male in no distress. His blood pressure was 150/90, his pulse 86, his temperature 99 F., and his respiration 20. All findings were negative except for the abdomen, where a bruit was heard distinctly and localized in the left upper quadrant. A blood count and urinalysis were normal.

X-RAY FINDINGS. A plain film of the abdomen revealed a rounded area of calcification, about 7 cm. in diameter, in the left paravertebral region. Several smaller calcareous opacities were seen within and cephalad to the larger one. A gastrointestinal radiographic examination revealed that the calcific density caused extrinsic pressure on the posterior aspect of the lesser curvature of the stomach; this was best visualized on the "spot" films and lateral projections (Fig. 1). Four hours later no deformity or extrinsic pressure on the transverse colon was noted, and the stomach was empty. An intravenous urogram showed normal kidneys without displacement (Fig. 2). A translumbar aortogram showed that the abdominal aorta together with its visceral branches filled satisfactorily. The splenic artery was identified and did not enter the previously described calcification

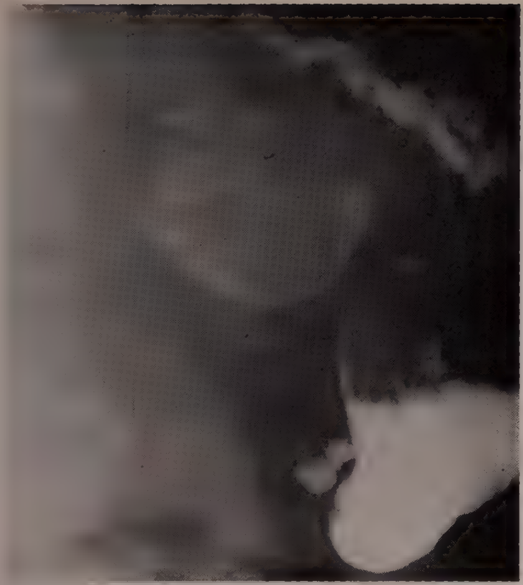

FIGURE 1. Left posterior oblique projection of stomach demonstrating calcific density causing extrinsic pressure on posterior aspect of lesser curvature of the stomach.

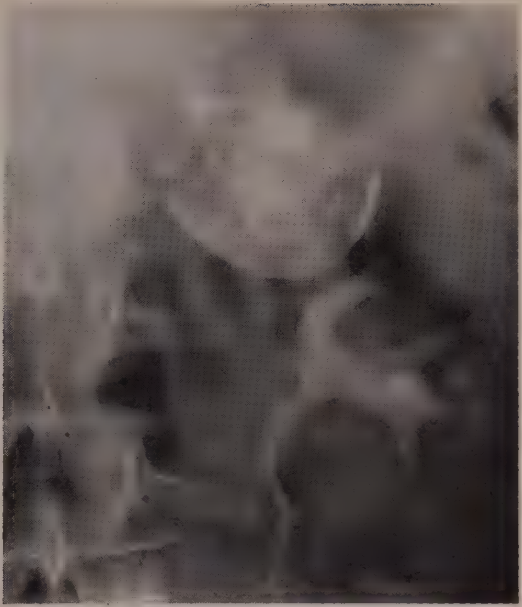

FIGURE 2. Fifteen-minute excretory urogram showing calcific density causing no displacement of left kidney.

in the left hypogastrium (Fig. 3). No abnormality of the abdominal aorta or its branches was noted. A splenic artery aneurysm with calcification thereby was ruled out. Other possibilities considered included calcified cyst of the pancreas, spleen, left kidney, or left adrenal gland; calcification within a tumor of the previously named organs; and calcification of a parasite (echinococcus cyst) of the spleen.

A surgical exploration revealed that the peritoneal cavity was normal except for a cystic mass about 4 inches in diameter in the left adrenal region. In spite of some compression the adrenal tissue on the left appeared normal. The cyst was removed intact, together with a portion of adrenal gland which appeared normal. The aorta and its branches pulsated normally and revealed no sclerosis.

PATHOLOGIC FINDINGS AS REPORTED BY NORBERT PLATT, M.D. The specimen consisted of a cystic mass weighing 50 Gm. and measuring 7 by 4.5 by 3 cm. in greatest dimensions. The surface was multilobulated because of the presence of numerous cystic cavities exhibiting prominence on the surface (Fig. 4). A cut section revealed the presence of a multiloculated cystic cavity which presented a remnant of adrenal tissue in the periphery. The largest cavity was occupied by necrotic hemorrhagic material. The rest of the cavities were lined interiorly by a very thin and smooth fibrous membrane presenting numerous areas of deposits of calcium. The relationship of the adrenal tissue to these cavities was that of the adrenal cortex covering the cystic cavities, especially the largest of them.

The microscopic description was as follows: The cyst wall consisted mainly of dense fibrous tissue showing irregular calcification, displaying small remnants of adrenal cortical tissue. The inner surface of the cyst was lined in places by fibrosing granular tissue displaying small areas with many hemosiderin-laden macrophages. In other places it was lined by granular eosinophilic debris displaying many cholesterol clefts and small groups of foamy histiocytes. All these findings led to the interpretation of the end results of necrosis, hemorrhage, cystification, and organization without any obvious primary mechanism. The diagnosis was adrenal cyst showing fibrosis, necrosis, and disruption of the

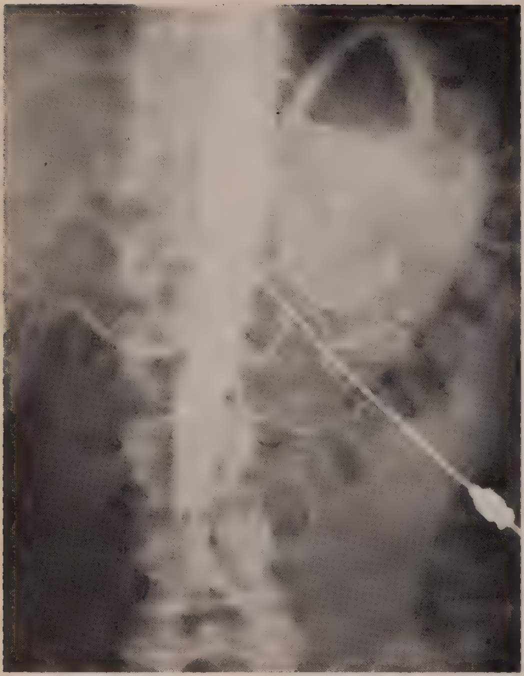

FIGURE 3. Translumbar aortogram; splenic artery is noted to bypass the calcific density.

adrenal glands.

Postoperative course. The patient recovered uneventfully and was discharged on the eleventh postoperative day. On April 9, 1960, he was free of all the symptoms of which he had complained prior to the operation. It was also interesting to note that the bruit which had been present preoperatively was now gone. The disappearance of the bruit was attributed to the relief of the compression of an adjacent artery.

Comment

Adrenal cysts are rarely diagnosed benign entities with unknown etiology. A correct diagnosis is difficult since most are asymptomatic. When present, the symptoms often are related to the gastrointestinal tract and are produced by pressure. On occasion, as in pancreatic conditions, the symptoms are so vague as to suggest neurosis. Differential diagnosis includes calcified cysts and malignant tumors of the liver, spleen, pancreas, and kidney; empyema of the gallbladder on the right; calcified aneurysm of the aorta, splenic artery, and adrenal artery; and echinococcus cysts of the liver, spleen, and pancreas. The possibility of carcinoma of the adrenal with cystic changes exists, and for this reason alone they should be removed.

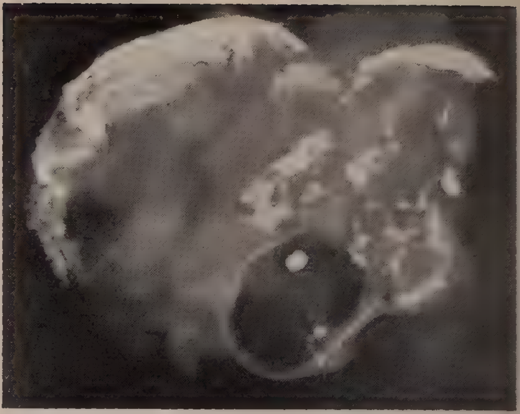

FIGURE 4. Pathologic specimen demonstrating calcified cystic mass which is multiloculated and contains a remnant of adrenal tissue.

Summary

An additional case of adrenal cyst is reported. Such cysts are difficult to diagnose. Surgical excision offers cure and is the treatment of choice.

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Special Articles

Utilization and Improvement of Patient Care in Morrisania City Hospital*

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THE AVERAGE AMERICAN today spends almost one day for each year of his life in a general hospital. The rate of hospital utilization—the number of patient days per 1,000 population—has increased about 20 per cent in the past quarter century.

The present trend in utilization is a product of two divergent factors, a rise of almost 80 per cent in admission rates over the past twenty years contrasted with a decrease of about one-third in the average length of stay per patient. Clearly, the rise in admissions reflects the growing importance of hospitals for almost all types of medical care and is a major reason behind recent medical progress. The decline in the average length of stay per patient is very much the result of new medical knowledge, early ambulation following surgery, new medical and surgical procedures, and new drugs.†

Similarly, in the past quarter of a century hospital costs also have risen to an all-time high. The steadily rising hospital admissions and hospital costs have focused increased attention by spokesmen for the public and for the hospital insurance agencies on how efficiently hospitals are operated and how each bed is used.

Richard L. Johnson, Secretary of the American Hospital Association's Council on Research and Education, predicts a national average daily bed cost of $50.28 by 1969. "I am assuming," he adds "that in 1964 hospital costs will go on rising at the steady 7 per cent annually that has prevailed since 1946, and that the rate of increase will drop to 3$^1/_2$ per cent thereafter." If Johnson's assumed drop-off does not materialize, the price of a day in the hospital will rocket past $60 by the end of the decade.

Hospital costs in some states are climbing even faster. Ray E. Trussel, M.D., Commissioner of the Department of Hospitals, found that out in the fall of 1960. Previously he had headed a team of experts investigating hospital costs in New York State. His official report to Governor Rockefeller indicated that New York hospital costs, as published for 1957, would rise 50 per cent in ten years. But before the 383-page report could be printed, striking unions increased wages in several New York City hospitals, affecting the estimate and causing certain hospital authorities to project a new estimate of a 50 per cent increase in five years rather than ten. This predicated that New York per diem bed cost would jump 50 per cent in five years from $27.91 to $41.87 by 1962.

Method of operation

To carry out better the administrative responsibilities for facility utilization, which might reduce per diem bed cost and produce better patient care, the Medical Superintendent of Morrisania City Hospital in 1955

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* Report of the activities of the Committee on Utilization and Improvement of Patient Care.

† Health Insurance Foundation Trends in Use of General Hospitals Progress in Health Services, Vol. 8, (Oct.) 1959.

Presented to the Hospital Administrators' Club of New York at the Columbia University Club of New York City, October 9, 1961.

organized a Committee on Improvement of Patient Care. The Committee consisted of the Medical Superintendent, the Assistant Administrator, the Deputy Medical Superintendent, the Director of the Outpatient Department, the Director of Radiology, the Director of Pathology, the Director of House Staff Education, who is a member of the Medical Board, the chief residents of the clinical services, the Chief of the Admitting Service, the Superintendent of Nurses, the Nursing Supervisors of the Clinical Services, and the Director of Social Service. Recently another important member has been added to our Committee. He is a representative of our lay advisory board who represents the community and therefore even the patient.

We have conducted regularly-scheduled monthly meetings every third Wednesday of each month. The objectives of these meetings are: to improve relations between the house staff and nursing staff throughout the hospital; to discuss any and all problems affecting both the medical and nursing care of patients; to present recommendations to the administration for the improvement of service; to iron out any difficulties and resolve any service problems that might directly or indirectly affect stay in the hospital and patient care; and to follow through with implementing on the various services these recommendations, policies, or regulations approved by the administration.

During the past five years the agenda of these meetings comprised a wide range of problems. Some of the problems discussed were (1) unnecessary admissions to hospitals, (2) delays in taking and reporting on x-ray films, (3) delays in taking and reporting on laboratory procedures, (4) unnecessary laboratory requests, (5) delays in taking and reporting on electrocardiograms, (6) delays in operations and scheduling problems in the operating room, (7) delays in answering consultations, (8) the prevention of excessive use of diagnostic facilities, (9) elective case admissions, (10) anesthesia problems, (11) formulary for hospital and the ordering of special drugs, (12) the nursing shortage, (13) ways of increasing the autopsy per cent, and (14) record room problems.

Also discussed were (15) recommendations of the Joint Commission on Accreditation of Hospitals, (16) attendance and rounds of visiting staff; (17) blood donations and other blood bank problems; (18) notice of intentions to discharge patients; (19) the problem of the transfer of the custodial and chronic patient; (20) delays in the transfer of the home care, nursing home, and welfare patients; (21) shortage of hospital personnel, equipment, and supplies; (22) proper utilization of hospital personnel; (23) delays in repair requisitions; (24) delays in elevator service; and (25) laundry problems, such as a linen shortage on weekends.

We also have conducted time and motion studies in the processing of admissions, laboratory reports, and messenger service. We have noticed a significant improvement in the time element between the moment a patient arrives in our admitting unit and the time he is admitted to the ward. We have installed in our emergency division a special elevator emergency bell so as to expedite the transportation of an acutely ill person to his respective ward or operating room. The elevator proceeds at once to the floor of the emergency unit.

The Director of House Staff Education conducts the meeting in the capacity of chairman. Complete and accurate minutes are kept of the various proceedings at the meetings by a duly appointed secretary. The services or divisions involved are asked to conduct a careful and thorough follow-up of the recommendations regarding the solutions of the various problems made at the previous meeting. At subsequent meetings the members involved report back and give full details as to the steps taken with a view to rectifying or improving the situation discussed. The meetings are conducted in an informal manner and last about one hour.

The Administrator, who is a member of this Committee, must at all times exercise caution not to accept any new suggestions too readily unless they are feasible. We are fully aware of the fact that discussing a problem and resolving it creates a better relationship among doctors, nurses, and hospital personnel. This approach is geared to and could have only one result, better patient care.

The Administrator, who is required to supervise the various services, its personnel, and items of equipment and supplies essential to maintain the services of his patient for the proper care of the patient, is limited to a great extent by the inflexibility of the budgetary allotment by the City of New York. These meetings form a basis and aid in determining the budgetary requirements for the following year.

We also wish to point out that the Administrator's attitude at these meetings plays a very important role. Many of the complaints voiced can be settled in an amicable manner to the satisfaction of all concerned.

Problems and complaints are discussed on a give-and-take basis, and then decisions are made which either resolve or improve the problem. The chiefs of the various diagnostic services, such as x-ray, laboratory, and electrocardiography, are present at these meetings and are confronted with the complaints and statistics regarding their individual departments. This leads to a quicker solution of these delays. These chiefs are then instructed to report at subsequent meetings the progress and improvement in their respective departments.

We at Morrisania, through our Committee on Utilization and Improvement of Patient Care, have tried to clear the hurdles and bottlenecks and have made several inroads into some of our difficult problems.

We have utilized our diagnostic clinic for ambulatory patients. A work-up on patients is done thoroughly and expeditiously with the patients on an ambulatory basis. This eliminates the prolonged and costly period of hospitalization and releases sorely-needed beds, which are made available for those requiring hospital care.

All patients who are ambulatory and who enter our emergency room are screened very carefully by our admitting physicians and the resident on the particular service to determine whether the patient should be admitted directly to the hospital for care or given an appointment to the diagnostic clinic or to the specialty clinic for a complete work-up.

We also have tried to overcome the bottleneck in our laboratory division by appointing additional technicians in our blood bank division on a twenty-four hour basis. These technicians do the routine urinalysis, blood count, Wasserman test, typing, and cross-matching and also a blood sugar determination on a diabetic patient on every admission before a patient is admitted to the hospital wards. This expedites some of the work which is so important for the completion of the patients' record to decrease the length of stay in the hospital.

We also are planning to have a twenty-four-hour coverage in our x-ray department. We are requesting two additional technicians in our 1962 budget. Since the beginning of 1961 we have been taking large chest x-ray films on all cases prior to their admission to the medical wards. This reduces the hospital stay in those chest cases where diagnosis plays an important role. It also minimizes the transportation of the patient and saves many hours of messenger service. New equipment and more space in the x-ray department are to be provided shortly. All these measures will help break the bottleneck in that division.

To prevent many unnecessary admissions from the emergency room or outpatient department, all pediatric, orthopedic, surgical, medical, and obstetric patients for admission are screened and checked more completely by their respective residents. This also has reduced the number of admissions to the hospital.

The Home Care Program, as carried out by our Home Care Staff, is maintained on the highest plane of efficiency. All of its members cooperate to carry out the standards set by the department and also to develop ways and means of increasing our home care census so as to reduce hospital stay.

The increasing number of custodial and chronic patients has become an additional problem in all our wards. We are trying to overcome this situation by checking with relatives and friends and trying to establish some arrangements whereby they will accept the responsibility to care for these patients. We have established a chronic and custodial female ward. Other than that we are still trying to evacuate these patients to other city institutions for chronic conditions to make available much-needed beds for acutely ill patients.

To equalize our existing facilities so that they may do the most good for patient care and overcome crowded conditions on some wards, we have reallocated some of our specialty divisions. We have achieved this by moving male urology, which had its own ward, to the orthopedic-surgical ward. We also moved Neurosurgery, Plastic Surgery, and Eye, Ear, Nose, and Throat to the general surgical ward which was less crowded. This gave us an additional ward to be utilized for an Intensive Care Unit. This unit, unlike other wards, holds both male and female patients. It has 20 beds and is equipped to meet the needs of our critically ill patients who require twenty-four-hour medical supervision and nursing care. It provides optimal centralization of physicians, nurses, and equipment which has saved many lives and shortened their stay. The concentration of the seriously ill patients in one ward lightens the work load of other nursing units, an important factor in the current nursing shortage.

This 20-bed unit has an adjacent recovery room for 6 postoperative patients. The advantage of such a set-up is that when a patient leaves the recovery room and still needs constant medical and nursing supervision, he may be placed directly in the intensive care unit.

Our hospital, as others throughout the country, is faced with a critical and acute shortage of nurses. To attract and maintain our nursing personnel we are exerting all means to make their lot a happier one. The chief resident meets every morning with the head nurses on their respective wards, and they prearrange and map out the day's work. The reason for the adoption of this procedure is the fact that we have to cope with the acute shortage of afternoon and evening nursing personnel so that all necessary nursing procedures and treatments can be carried out on the morning shifts.

The house staff is also urged to do all they possibly can to alleviate the burden of the nursing personnel, due to this acute shortage. The residents are urged to perform as many treatments as they can themselves without assistance from the nursing personnel. They also are urged, whenever possible, to make rounds by themselves and only bring to the attention of the head nurse any problems they may be confronted with during their rounds.

In reviewing the agenda of the meetings and also some of the problems discussed, one can see readily that our Committee on Improvement of Patient Care, which has been functioning since 1955, was really a utilization committee with some additional objectives. The Committee, which met on August 30, 1961, felt that the former Committee on Improvement of Patient Care should be renamed the Committee on Utilization and Improvement of Patient Care.

A utilization record form was developed (Fig. 1). This form will be completed by the physician discharging the patient and will be sent down with the regular chart to the record room. The librarian in the record room will remove the form from the chart and send it to the office of the Deputy Medical Superintendent, who will review it and make the necessary statistical tabulations. These tabulations then will be referred to the Committee on Utilization and Improvement of Patient Care for further analysis and disposition.

Summary

The Committee on Utilization and Improvement of Patient Care is another administrative tool that has proved successful in our institution.

It has tried to eliminate unnecessary hospital admissions and to reduce protracted hospital stays.

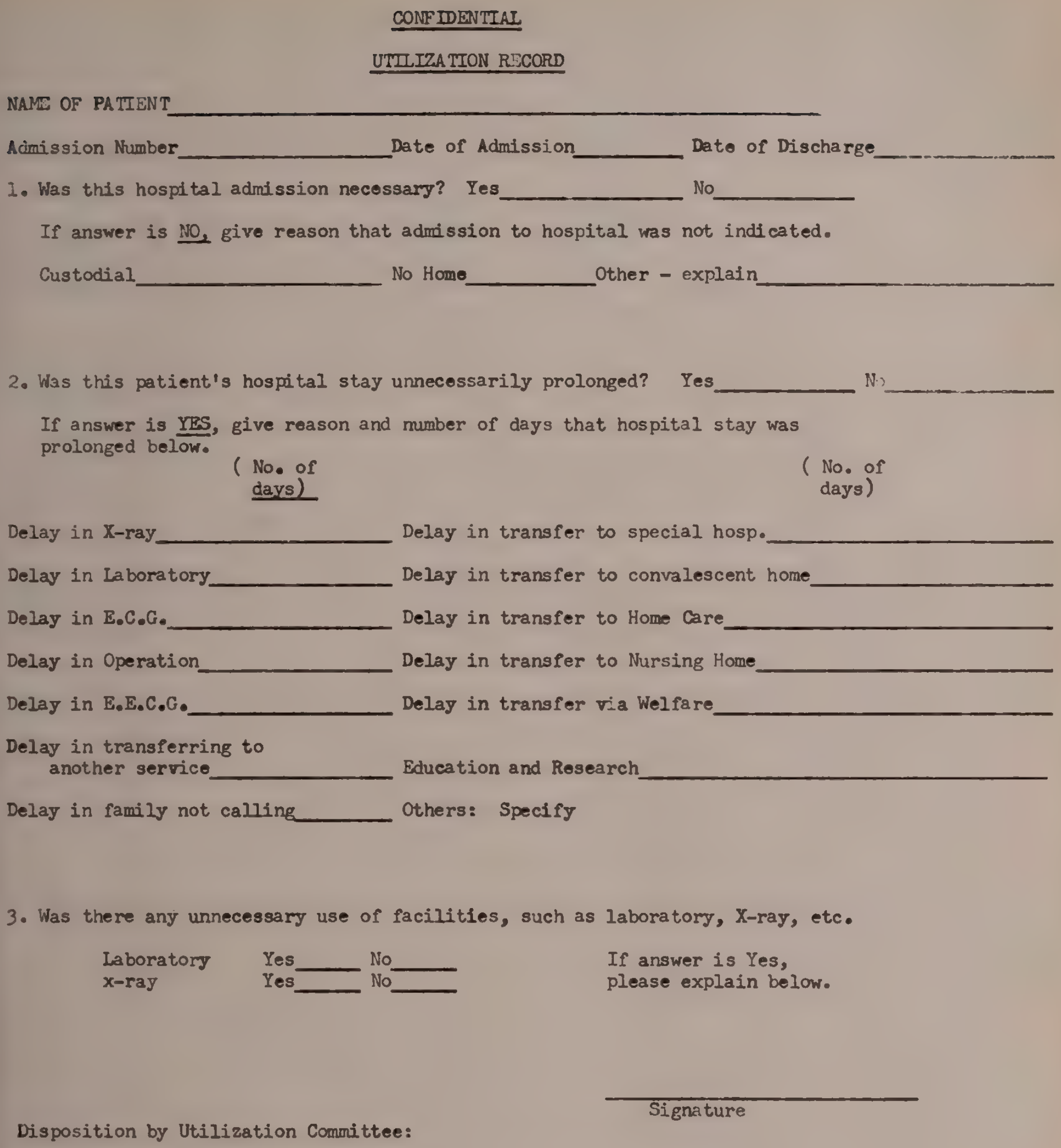
It not only looked into the question of utilization but also was greatly concerned with its responsibility to assure the public of high quality hospital care without waste or abuse.

It aided in determining the budgetary requirements for the following year.

Through these meetings, the medical, nursing, laboratory, administration, and other divisions of the hospital have an opportunity for the confrontation and discussion of the problems and inadequacies of each department.

It affords the opportunity for the administration to bring its thinking directly to the individuals concerned with patient care and allow for an exchange of views and ideas.

As a result of these meetings many of these problems have been improved or



CONFIDENTIAL

UTILIZATION RECORD

NAME OF PATIENT____

Admission Number______________ Date of Admission__________ Date of Discharge____________

1. Was this hospital admission necessary? Yes____________ No__________

If answer is NO, give reason that admission to hospital was not indicated.

Custodial______________ No Home__________ Other - explain________________

2. Was this patient's hospital stay unnecessarily prolonged? Yes__________ No__________

If answer is YES, give reason and number of days that hospital stay was prolonged below.

(No. of days) (No. of days)

Delay in X-ray______________ Delay in transfer to special hosp.______________

Delay in Laboratory______________ Delay in transfer to convalescent home______________

Delay in E.C.G.______________ Delay in transfer to Home Care______________

Delay in Operation______________ Delay in transfer to Nursing Home______________

Delay in E.E.C.G.______________ Delay in transfer via Welfare______________

Delay in transferring to another service______________ Education and Research______________

Delay in family not calling__________ Others: Specify

3. Was there any unnecessary use of facilities, such as laboratory, X-ray, etc.

Laboratory Yes______ No______

x-ray Yes______ No______

If answer is Yes, please explain below.

____
Signature

Disposition by Utilization Committee:

FIGURE 1. Utilization record form.

resolved, resulting in better patient care and better utilization of existing facilities.

No one member of the Committee can do the job alone. The most effective help that can be given to a patient is through a team operation, when each member recognizes the contribution of each of the other professions and helps to integrate knowledge and skills in the interest of the total care of the patient.

Effects of a 20-Megaton Thermonuclear Explosion on Columbus Circle

From the Scientists' Committee for Radiation Information,
New York Academy of Sciences, New York City

THIS SUMMARY will describe in some detail what would happen to the New York metropolitan area and its residents if a single, 20-megaton bomb hit Columbus Circle in midtown Manhattan. Any analysis of a nuclear explosion depends on the assumptions made. In this case, the assumptions were that the size of the bomb would be 20 megatons. Columbus Circle was selected because it is a well-known landmark. Obviously, the bomb might be larger or smaller, there might be several bombs, and they might be dropped elsewhere. For the purposes of analysis, a single bomb makes calculations easier.

While it is not possible to make precise predictions for some types of damage, estimates are possible, using the evidence from test explosions and the atomic drops on Hiroshima and Nagasaki and various published material. All estimates are based on unclassified information with three major sources.[1–3]

The explosion and its aftermath

As the bomb explodes, the sky would fill with a bluish-white glare. A man standing 60 miles away would see a fireball 30 times brighter than the noonday sun—a fireball as hot as the center of the sun.

The fireball would expand rapidly, sucking up millions of tons of pulverized earth and debris, until it is three and one-half miles wide. As it expands, the fireball would begin to rise, scorching an ever-widening area.

Exploded in the air on a clear day, the heat would ignite a man's clothing 21 miles away and would burn exposed skin seriously at 31 miles. (A contact surface burst would cut the distances to 13 and 19 miles.)

The matter sucked up by the fireball in a surface burst would start to condense on reaching upper air layers, 5 to 10 miles up. It would spread out, forming a radioactive, mushroom cloud of fallout.

Meanwhile, an intense pressure wave, or shock front, traveling faster than sound, would spread out from the center of the explosion, crushing almost everything in its path until it gradually loses its force.

Following the shock front would come the wind of more than 1,000 miles per hour. As it moves outward, the wind would diminish and a giant vacuum develop. Then the surrounding air would rush in, fanning the fires started by thermal radiation and initial blast damage.

Soon these fires would join and develop into a firestorm that could cover a circular area of anywhere from 30 to 50 or more miles across, destroying all that will burn—structures and living things.

The blast itself, from a surface burst, would create a hole 240 feet deep at its deepest point and a half mile across. Within a radius of 7.7 miles the destruction would be severe. Up to 15 miles the damage would still be heavy.

The casualties could include 5 to 6 million dead out of 8 million New Yorkers within the first few days. In the 17-county New York-New Jersey metropolitan area fatalities and injuries could claim about 9 million out of the population of 13 million.

The population would face seven different types of hazards, each of which must be coped with successfully for survival. The effects would vary somewhat, depending on whether the bomb drop were a contact surface burst or an air burst. A surface burst produces greater local blast damage and heavy local fallout. An air burst produces little local fallout, more world-wide fallout, greater danger of firestorm, and more widespread blast damage.

The seven types of hazards are as follows: (1) immediate thermal effects; (2) immediate nuclear radiation; (3) blast effects; (4) firestorm; (5) fallout; (6) economic and social disruption; and (7) long-term effects.

Immediate thermal effects

The fireball would give off a tremendous amount of heat, or thermal energy. The extent of this damage can be predicted by noting the number of calories per square centimeter of surface a given object would receive if exposed to the flash of the bomb. For example, about 4 calories per square centimeter (cal. per $cm.^2$) will ignite shredded newspaper; 13 cal. per $cm.^2$ will ignite deciduous leaves. At 23 cal. per $cm.^2$ most clothing will ignite.

Flash burns are an even greater danger than the burning of clothing. At Hiroshima and Nagasaki, burn casualties from flash and flame burns were the major problem in medical care, accounting for more than half of all deaths.

A surface burst would produce less thermal damage than an air burst. There is less thermal energy to start with, and heat rays near the ground would not travel as far because they are absorbed and scattered by dust, water vapor, and carbon dioxide. A high air burst, for example, 20 miles up, where there is practically no atmosphere, would produce even greater fire damage on earth.

On a clear day, a 20-megaton (MT) low air burst would produce these injuries to exposed skin: third degree burns (12 cal. per $cm.^2$) 27 miles from the explosion; second degree burns (10 cal. per $cm.^2$) 31 miles away; and first degree burns (4 cal. per $cm.^2$) 45 miles away. For a surface burst these distances would drop by 40 per cent.

Unless medical supplies and facilities were spared somehow, the second and third degree burns would probably result in death. Such burns nearly always become infected. And radiation further reduces the chances of recovering from even minor infections.

A person actually seeing the flash of the bomb burst would suffer a burn on the retina which could lead to blindness. The seriousness of the burn would depend on its size and its location on the retina. For a high burst as opposed to a surface burst the flash would be seen further away. Only sparse information about retinal burns has been declassified. However, it has been disclosed that "a megaton detonation" 40 miles high produced retinal burns in rabbits 340 miles away.

Immediate nuclear radiation

With a small bomb, for example, 20 kilotons (KT), nuclear radiation is an important hazard. With a large bomb, such as 20 megatons, immediate nuclear radiation may be ignored because the blast and heat effects of a 20-megaton weapon are so great that they would far outweigh the immediate radiation danger. For example, 2.5 miles from ground zero the radiation intensity would be about 300 r, a lethal dose for 3 to 18 per cent of those exposed. However, the blast force at that distance on an unshielded man would be 40 pounds per square inch (psi) overpressure. This blast pressure and the heat, plus flying debris, are likely to kill him.

Blast effects

Blast damage to a building or other structure may result from one or several causes. First, the shock front squeezes everything in its path. A building may collapse because it is being blown over or because the external pressure is suddenly so great that all four walls collapse inward.

Right behind the initial shock front are the drag forces, in the form of a strong wind. Telephone poles and radio towers that may resist the squeezing effect of the shock front are quite vulnerable to being blown over. This wind pressure may last for many seconds, whereas the initial shock front passes by in a few seconds.

Following the shock front and drag forces, there is a reversal in pressure. Buildings now experience a partial vacuum and afterwinds which blow back toward the center of the explosion. The stress is less, but it can add to damage on an already weakened structure. Also, the ground shock itself can knock a building down as an earthquake does.

A surface burst on Columbus Circle would produce a mammoth hole. It would cover a 20-block area and be deep enough to hide a 20-story building. The hole would extend from 55th to 63rd Streets and from east of Seventh Avenue to west of Columbus Avenue. The subway systems, which are interconnected in the midtown area, would be penetrated.

Any midtown 20-megaton hit is likely to penetrate at least one of the subway tunnels. The deepest tunnel is the BMT 60th Street tunnel under the East River which is down 113 feet. Since all three systems are interconnected in the midtown area, the blast wave would sweep with lethal intensity through a large part of the system. Blast waves in a tunnel maintain their intensity over a longer distance since they cannot spread out.

Within a 7.7-mile radius of Columbus Circle, the blast would produce severe structural damage. At the outer edge of this circle, most unreinforced brick or wood-frame houses would be completely demolished, the result of a peak overpressure of 5 pounds per square inch. Brick apartment buildings would probably still be standing but would need major repairs. However, within a 6.4-mile radius, they too would collapse. An air burst would extend the major damage radius to 10 miles.

Within a 15-mile radius, the damage would be less severe but extensive. At the edge of the circle, a wood-frame house might remain standing but would need such major repairs that restoration would not be economical. The peak overpressure at the 15-mile line would be 1.9 pounds per square inch. This is still enough to tear entrance doors off their hinges, breaking them into pieces, to send window glass flying through the house, and to dislodge window frames.

Up to 40 miles away there would be some damage, such as window breakage, in the majority of structures. And under some conditions a New York City explosion could produce shattered windows in Wilmington, Delaware. That would be the result of meteorologic factors which could enable the shock front to advance by bouncing back and forth between the earth and the air, causing damage at regularly spaced intervals.

The inner circle (7.7-mile radius) of severe blast damage would include, at its outer edges, in Brooklyn: Gowanus Bay, half of Prospect Park, Ebbets Field, and the Bedford-Stuyvesant and Bushwick sections.

In Queens it would include Ridgewood, the western tip of Forest Hills, Corona, and the western edge of the Whitestone section. In the Bronx it would include Sand View Park, Crotona Park, and New York University. Only the tip of Manhattan above the Cloisters would not be inside this area.

In New Jersey, this zone of mass destruction would include most of Jersey City, Leonia, Ridgefield Park, Teterboro Airport, and half of Kearny. The Palisade ridge would probably not provide much protection since blast waves move around such objects.

The 15-mile radius (1.9 pounds per square inch) from Columbus Circle would include all of New York City, except the area beyond Staten Island Airport and a very small corner of Far Rockaway. In Nassau County the eastern portion of the circle would be marked by Elmont, Floral Park, Manhasset, and Port Washington. Most of New Rochelle and almost all of Yonkers would be within the circle. In New Jersey these cities would be along the perimeter: Ridgewood, Paterson, Caldwell, West Orange, Union, and Linden.

It should be noted that not all brick houses would collapse within the inner circle, nor would all brick houses remain standing beyond the outer circle. There would be individual variations depending on construction differences and variations in the local behavior of the shock front.

While these primary blast effects undoubtedly would produce casualties, the secondary blast effects are much more important in this regard. Secondary effects would probably account for more initial casualties (within the first few minutes) than any other factor.

The mass destruction of buildings and other objects would have produced an immense quantity of flying debris. It has been determined that chunks of flying glass and masonry could cause casualties up to 17 miles from ground zero. (A casualty is defined as "an individual sufficiently injured to be unable to care for himself who thus becomes a burden to someone else.") It should be noted that small glass fragments lodging in the eye could produce casualties at distances much greater than those cited.

There would also be a third type of blast effect—displacement, such as picking up a man and smashing him into a wall. This could occur as far away as 15 miles from ground zero. A significant number of head and skeletal injuries would occur, with the extent of the injury depending on the distance traveled prior to impact.

Firestorm

A prime threat to urban populations after a thermonuclear explosion is the firestorm. The storm develops when a mass of fresh air breaks into an area with a high density of fires and replaces the hot rising air. This mass of fresh air may move with hurricane velocity. The wind causes the fires to merge and become a raging storm of fire.

The fires can start in two ways. First, thermal radiation would ignite trash, window curtains, dry grass, leaves, and, toward the interior of the fire zone, many less flammable materials. Second, the blast would upset stoves, cause electrical short circuits, break gas lines, and burst underground oil storage tanks. All of these would become ignition points.

For an air burst, when the threat of firestorm is greatest, the heat would be sufficient to ignite clothing on an exposed person 21 miles from ground zero. At that distance, the heat would register 23 cal. per cm.^2 It should be recalled that 13 cal. per cm.^2 is enough to cause third degree burns and 4 cal. per cm.^2 is enough to ignite newspaper. This raises the important question of how large an area a single 20-megaton bomb could convert into a completely inflamed area.

Within the radius of 21 miles from Columbus Circle, it is probably conservative to predict an average of 10 ignition points per acre in every part of the city (except for the southern half of Staten Island, which is outside this line and is partly shielded by the terrain). Since New York City covers about 200,000 acres, this would result in nearly 2 million fires in the city. The fire department could hardly cope with such a staggering number, even if it were prepared. In this case, most of the force would be unable to respond, most equipment would be unusable, water pressure would be inadequate, and many rubble-lined streets would be impassable.

How likely is a firestorm? It is most likely with an air burst and probable with a surface burst. The air burst would create wider fire damage, of course. In view of the density of combustible material in many parts of the city, a firestorm seems inevitable. (The contents of a fireproof building are combustible, even if the building is not.)

At Hiroshima, where a smaller bomb (20 kilotons) was dropped, a firestorm developed and eventually covered a radius of about 1.2 miles. In Nagasaki no firestorm developed because apparently natural winds carried the fire into an area where there was nothing to burn. Still, all buildings in Nagasaki within 1.25 miles of ground zero were destroyed by flames.

There are not enough data to justify quantitative predictions of the firestorm area. However, as noted earlier, it could cover a circular area of anywhere from 30 to 50 miles or more across.

The most complete data on firestorm casualties come from Hamburg, Germany, where a firestorm occurred July 27, 1943, after prenuclear incendiary air raids. Some 60,000 persons were killed, almost as many as in the atomic bomb drop on Hiroshima.

Hamburg police engineers estimated that temperatures in the burning city blocks were as high as 800 C. (about 1,500 F.). Wind velocity exceeded 150 miles per hour. Hundreds of persons were seen leaving shelters as the heat became unbearable. They ran into the streets and slowly collapsed. Many were found naked. It is not known whether the intense heat disintegrated their clothing without actual burning or whether flames consumed the clothing, singing the skin. Days after the raids ended, as some shelters were opened, there was enough heat remaining inside for the influx of oxygen to cause the shelters to burst into flames. Bodies had been cremated or melted in the general debris.

Death from intense heat can occur in ways other than burning or disintegration. Heat stroke can occur in a temperature of

140 F. Inhalation of hot air may cause severe damage to the respiratory passages. Exterior damage can close off ventilation in a sheltered area.

Also, carbon monoxide poisoning would be one of the chief types of injuries expected. In World War II it was a common cause of death in public air raid shelters and improvised home shelters. Carbon monoxide casualties are nearly always expected in flaming buildings, where exits have been blocked by rubble. Under such conditions, a cellar protected from the blast could become a tomb. In Hamburg it is estimated that 70 per cent of all casualties not caused by mechanical injuries or burns were brought on by carbon monoxide.

In World War II it was typical to find shelter victims of such poisoning in peaceful positions, suggesting a complete lack of knowledge of the imminent danger.

It is unclear what precautions could be taken to meet the potential threat of firestorm.

Fallout

The hazard of fallout is at least as uncertain and much more difficult to predict in detail than any of the hazards discussed in the preceding sections.

The fallout begins in a circular area around ground zero. Within the first hour the heavier particles in the mushroom begin to descend. The lighter particles take longer to come down and are carried out of the immediate circle by the wind. How far any given particle travels depends on its size, the height it reaches before descent, and the wind patterns. The lightest particles will not return locally but will become part of worldwide fallout.

One estimate indicates that a 10-megaton weapon would contaminate an area of 2,500 square miles sufficiently to provide a lethal dose for 50 per cent of the unshielded population (LD_{50}). Such a lethal dose for human beings is generally considered to be about 450 r, but some scientists believe it is lower.

Some scientists have estimated that 80 per cent of the radioactive material produced would return to earth as local fallout. But this could vary, depending on atmospheric conditions and the type of fallout. All information on fallout has been obtained from kiloton bursts on silicate or megaton bursts on coral sand. The fallout from a surface burst in a built-up city on granite, such as New York, might possess quite different properties and produce different results. It is also possible that the firestorm would modify local fallout.

Once fallout has been deposited, it is subject to weathering, although the precise behavior of the fallout particles when they land on various surfaces, such as building material, roads, and soil, is not known. These many uncertainties make it difficult to predict accurately what the fallout situation would be in any specific New York locality if a 20-megaton bomb hit Columbus Circle.

However, it is possible to take an example. During the Holifield hearings, New York was assumed to be attacked on a day when the winds were west-southwest with an average velocity of 40 miles per hour. In such a situation, Long Island would be inundated with fallout. One might expect a 4,000-square-mile area to contain sufficient radioactivity to deliver a dose of 9,100 r to the unshielded population between the end of the first hour and the end of the second day after the detonation. This dose exceeds the lethal dose for 50 per cent of the unshielded population by a factor of 20. Since the winds could blow in another direction, the danger area might be in Westchester and Rockland counties, or in Connecticut, or in New Jersey.

Within the contaminated areas it is probable that farmers could not work their land for several weeks. In a situation like the one cited, physicist Ralph Lapp has estimated that it would take about two years before the radioactivity would drop to levels that are considered safe. ("Safe" refers to the currently acceptable peacetime standards for atomic industrial personnel of 50 milliroentgens in a forty-hour week.)

Exposure to radiation lowers man's resistance to infection. Infection associated with minor burns and cuts, therefore, would be aggravated by exposure to fallout and in the absence of proper care could lead to death.

The effects of inhaled radioactive particles are not fully known. In human beings and animals, the principal effects of radiation to the respiratory tract are pneumonitis and fibrosis and, in experimental animals, cancer. It should be remembered that in the event of an air burst, which maximizes the blast and increases the thermal effects, fallout would be less of a hazard than in a ground burst.

Disruption of physical facilities

Careful consideration of problems that arise from the wide breakdown of physical facilities and social services in the event of a nuclear explosion is vitally important to any discussion of survival. Such consideration, however, leads beyond the competence of the Scientists' Committee for Radiation Information. At best, this segment of the report can suggest problems of physical disruption that deserve more systematic study.

In all previous American experience with large-scale disaster, relief and reconstruction assistance poured in from other community, state, national, or international agencies. It is probable that in the event of a 20-megaton nuclear explosion on New York City the consequences of disruption of community facilities would turn on the availability of help from external sources. In the following observations two underlying assumptions are made: first, that no organized assistance would be available from outside agencies within the first two weeks; and second, that the weapon is a 20-megaton air burst with a relatively small amount of local fallout.

TRANSPORTATION FACILITIES. The problem of transportation facilities may be regarded in three categories: thoroughfares, fuel, and machines. Throughout the area of the 15-mile radius from ground zero, debris would clog streets with little hope of clearance within the first two weeks. No vehicle could be expected to pass. It is probable that bridges would not be serviceable and that tunnel entrances in Manhattan would be blocked. Rail and subway lines would most likely suffer commensurately. Transportation equipment remaining after blast and fire would find extremely limited fuel since local supplies would probably have been ignited in the firestorm. Equipment depending on central electrical generators and transmission facilities would have no available power. Repair facilities, personnel, and parts, if available, would be severely taxed to cope with the extensive destruction. This dearth of transportation would affect the conduct of most other vital social services.

WATER SUPPLY. It seems probable that many water storage tanks, some mains, filtering and purification equipment, and pumps would be destroyed or would become inoperable. The contamination of water in reservoirs would be high in a ground burst or in the case of an air burst would be accompanied by rain or snow.

FOOD SUPPLY. The question of food supply can be examined in two categories: first, that food which is stored in the city, and, second, that food which is produced outside. Food stored under normal conditions would be subject to blast and fire. Food processing plants and storage and refrigeration facilities would be affected by blast and fire also. Metropolitan food supplies are heavily dependent on transportation. Sheltered food supplies, if they were available after extensive ruin, might provide sustenance for a limited period. Outside the metropolitan area the extent of damage to stock, produce, and arable land would vary with the altitude of the blast, with respect to fire and the quantity of immediate fallout.

HOUSING AND HOME FUEL SUPPLIES. It seems probable that few, if any, of New York City's approximately 2.5 million dwelling units would provide adequate shelter for survivors, even if the firestorm did not consume everything. It is more difficult to predict what would happen in the suburbs. Widespread blast damage would extend in an 18-mile radius around Columbus Circle. Even at 27 miles (1 pound per square inch) some blast damage would occur. (The firestorm, a probability within a 15-mile radius and possibly beyond, could create further havoc.) Those fortunate enough to have dwelling units remaining, and with a manageable radiation problem, would have a hard time during cold weather. Local supplies of fuel would probably have been destroyed, and the breakdown of transportation would curtail further deliveries. Human exposure during the winter months is an inevitable source of casualties.

Medical facilities. It seems clear that most of the city's hospitals and related facilities would be destroyed or unusable, since the bulk of medical facilities lie within the 18-mile radius of destruction. The millions of dead and injured would include a sizable proportion of doctors and other trained personnel. Those hospitals and centers of medical personnel still able to function would be faced with enormous problems arising from the general destruction, since medical services are heavily dependent on city-wide physical facilities and transportation. Few hospitals, for example, have auxiliary power sources sufficient for more than emergency periods. The destruction of city power plants and limited fuel supplies would therefore limit an important component of hospital services. Insufficient power would affect not only light, x-ray, and other machines, but also refrigeration necessary for important drugs. Problems arising from the destruction of transportation of medical supplies and the presumed lack or limitation of water, raising problems of general sanitation, suggest further complications of medical service in the event of a 20-megaton nuclear explosion.

Sanitation and public health. The sources of epidemic characteristically include: uncollected refuse, sewage, uncontrolled vermin, contaminated water and food supplies, and lack of medical facilities. The collection and disposal of corpses would require large numbers of workers and adequate transportation facilities. Public health problems created specifically by an extensive radioactive environment have not been experienced so far. Persons suffering from exposure to radiation, however, are particularly susceptible to infection, and a population of weakened and injured survivors, as in all comparable crises, would seem to invite epidemic.

Long-term effects

The hazards discussed in earlier sections would occur largely within days, weeks, and months after the explosion. There would also be longer-term radiation effects of two types: those that affect the exposed individual (somatic effects) and those that affect his descendants (genetic effects).

These effects are not fully understood by scientists. The knowledge that does exist has been studied exhaustively, but interpretations vary and are not conclusive. The uncertainties of the biology are compounded by uncertainty about radiation doses. While these effects will not be discussed in detail here, certain observations are possible.

Virtually all scientists agree that excess exposure to radiation will have harmful effects on subsequent generations. The disagreements concern the relative incidence of the harmful effects. These genetic effects might include abortions, stillbirths, neonatal deaths, congenital malformations, reduced mental and physical vigor, feeblemindedness, and a host of physiologic diseases or malfunctions, any one of which might lead to the disablement or death of an individual.

The evidence indicates that it is unlikely that long-term exposure to radiation would result in the genetic extinction of the human species, whatever the other harmful effects might be.

There is concern about the effects of sterility on the present male generation. Men exposed to a moderately high dose of radiation, followed by a continuous low dose over a period of time, are likely to exhibit sterility and reduced fertility for years. The gonads are among the most sensitive to radiation of all human organs.

Among other possible somatic effects are: increased incidence of leukemia and other forms of cancer, increased incidence of degenerative diseases, shortening of the life span, development of cataracts, and various changes in physical growth and development, such as a decrease in body weight.

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Questions and Answers on Health Insurance

Prepared by the New York State Professional Relations Committee of the Health Insurance Council, New York City

FRANCIS T. CRAWLEY, Editor

How does an insurance company determine the amount of a reasonable or customary charge in major medical expense insurance?

Insurance companies do not set fees nor do they intend to. However, generally by their contract language they do agree to recognize only what is a customary and usual charge. Years of experience in settling claims naturally have given insurance companies an insight into doctors' fees, but this is not to be relied on when one is faced with a need for advice concerning the doctors' charges. Some of the medical profession have recognized this, and, after considering it and other important factors, several medical societies have established review committees. To these committees providers of financial protection may turn when seeking advice, particularly in the area of fees. These committees are, of course, in their experimental stages, but they most certainly should provide considerable help to those groups interested in obtaining guidance.

What is a "review" committee? What is the difference between it and existing "grievance" committees?

A review committee is a group of physicians appointed by a state or county medical society to advise in matters introduced to it by such agencies as insurance companies, Blue Shield Plans, or independent plans. Requests for review of a matter, the nature of which, for example, might be an unusual fee, an unnecessary procedure, or an unduly prolonged hospital stay, normally would come from the insuring organization but also may come from the physician or public.

The doctors constituting such a committee would be representative of the various specialities; objectivity of viewpoints and continuity of liaison are two principles inherent in such a mechanism. The advice of the review committee guides the insuring organization, or whoever seeks such advice, toward a sound disposition of its problems.

The fundamental difference between a "grievance" committee and a "review" committee is that a review committee is established as an advisory mechanism without an accusation of wrongdoing. A grievance committee, on the other hand, refers to any committee, whatever its title, which receives and assists in the adjustment of complaints from the public against individual physicians or the medical profession generally.

Why is there not a fee for filling out every form, as there is a fee from some companies for completion of forms?

If the doctor will recognize that in health insurance he may be asked for two types of statements, the fee question will be better understood: (1) A claim statement is a request by his patient for a statement which is submitted to his insurance company to get his claim paid; no fee is paid by the insurance company; and (2) an underwriting statement is a request by the insurance company for information to enable the company to determine the insurability of an applicant for insurance; a fee usually is paid by the company.

The Health Insurance Council has helped the doctor in his task by making claim forms uniform. The HIC symbol at the lower right of the attending physician's statement indicates that the uniform form is one used by companies having in force the vast majority of health insurance coverage. It was devised by the industry and approved by the American Medical Association, in an effort to lighten the doctor's paper work load.

Doctors reading this column are encouraged to send in their questions to the Health Insurance Council, 750 Third Avenue, New York 17, New York.

Abstracts

Doyle, J. E., Anthone, S., Anthone, R., and MacNeill, A. E.: Ultrafiltration with a parallel flow, straight tube blood dialyzer, New York State J. Med. **62:** 185 (Jan. 15) 1962.

Various methods of extracorporeal ultrafiltration of the blood, which permits the extraction of a protein-free solution from the blood, have been tried since 1947. A dialyzer-ultrafilter has proved to be more effective as a method of removing intractable edema fluid than dialysis with a hypertonic solution or peritoneal lavage. The MacNeill blood dialyzer has been in use by the authors since 1954. With this apparatus ultrafiltration may be carried out simultaneously with dialysis or exclusively. Ultrafiltration without the simultaneous use of washing fluid was used successfully in 7 patients with intractable edema due to congestive heart failure. Three main groups of patients achieve important benefit from the use of extracorporeal ultrafiltration of the blood: patients with congestive heart failure who become unresponsive to salt restriction, diuretic therapy, digitalis, and other more usual forms of therapy; patients with congestive heart failure who can undergo corrective cardiac surgery if their decompensation can be brought under control temporarily; and patients with acute and chronic renal failure who become significantly overhydrated. Care must be exercised so that fluid will not be extracted so rapidly as to cause hemoconcentration, dehydration, hypovolemia, hypotension, and shock. More extensive analyses of ultrafiltrates obtained in this manner are indicated; the procedure opens the way to study of diffusible substances which appear in low concentration in the blood which may be of particular value in the elucidation of the chemical causes of the uremic syndrome.

Glenn, F.: Surgical treatment of biliary tract disease, New York State J. Med. **62**: 203 (Jan. 15) 1962.

Biliary tract disease occurs in many areas of the world. It is associated significantly with pregnancy: in the author's experience, of every 5 patients with biliary tract disease, 4 are women, of whom 3 have been pregnant, and 1 is a man. The disease is relatively rare in children and more frequent in the older-aged group than in the general population. In North America gallstones are associated with the majority of disorders of the biliary tract. An adequate explanation of the formation of gallstones is lacking. The most common clinical manifestation of the disease is the complaint of "indigestion," from mild to severe. The disease may go unrecognized for years and result in liver damage. Cholecystography and cholangiography make possible an accurate diagnosis. The definitive treatment of biliary tract disease is surgical. Elective cholecystectomy has become more common over the past thirty years with the reduction in risk of operation and decrease in complications. Biliary tract disease may be divided into four stages; the stage at which the operation is undertaken determines whether the procedure is to be cholecystectomy, common duct exploration, correction of biliary-enteric fistula, or right lobectomy for carcinoma of the gallbladder. The gallbladder containing stones should be removed irrespective of the stage of biliary tract disease, unless there is overriding contraindication that renders the procedure hazardous.

Douglas, A. H., Sferrazza, J., and Marici, F.: Natural history of aneurysm of ventricle, New York State J. Med. **62:** 209 (Jan. 15) 1962.

The most common variety of aneurysm of the ventricle occurs as a sequel of myocardial infarction. Of 4,427 consecutive autopsies at the Queens Hospital Center, 524 cases of myocardial infarction were found (12 per cent); 45 of these had ventricular aneurysm (1.02 per cent of the total number of autopsies and 8.7 per cent of the patients with myocardial infarction). To this series were added 6 patients who were followed clinically. In the series there was a great difference between the incidence of ventricular aneurysm in patients with myocardial infarcts as reported by the pathologist at autopsy (8.7 per cent) and the incidence reported by the clinician, chiefly on the basis of x-ray film study (1.7 per cent); thus 3 out of 4 cases were missed clinically. Ventricular aneurysm should be suspected when myocardial infarction is associated with an increase in cardiac dullness, maximum pulsation internal to the left cardiac border, or paradoxical pulsation. A localized bulge on x-ray film yields a diagnosis in a minority of cases only. In this series 60 per cent of the infarcts were located anteriorly. The authors believe that the combination of a transmural anterior wall myocardial infarct with or without a localized bulge on x-ray film, but with cardiomegaly which develops subsequent to the lesion and which cannot be explained by hypertension or associated valvular disease is very suggestive. The results of operation on 35 cases of ventricular aneurysm following myocardial infarction, with a maximum follow-up of three years, have been most encouraging. Further investigation of the control of paradoxical pulsation by means of a prosthesis, with or without excision of the infarcted myocardium, seems indicated.

Wycoff, C. C.: Hypothermia: ventricular fibrillation during hyperventilation, New York State J. Med. **62:** 217 (Jan. 15) 1962.

Ventricular fibrillation can occur spontaneously during hypothermia or as the result of mechanical stimulation. Acidosis and respiratory alkalosis predispose the heart to ventricular fibrillation. The occurrence of ventricular fibrillation can be reduced by controlling the pH of the blood through the alteration of ventilation. A study was undertaken on 10 dogs to determine the temperature at which ventricular fibrillation would occur when respiratory alkalosis was induced. Marked hyperventilation was used to produce alkalosis; surface cooling was used to lower the temperature of the animals. Five of the animals were unprepared; 5 had the plasma potassium level lowered slightly by diet and sodium exchange resin. Hypothermia and hyperventilation produced the following results: The minute volume of respiration varied from 21 to 27 L. per minute. The blood pH level rose in all the animals; the highest level was 8.1. Five of the 10 dogs developed ventricular fibrillation above 20 C.; the highest temperature at which ventricular fibrillation occurred was 24.2 C. An Osborn S-ST wave occurred in all but 1 of the animals. The arterial carbon dioxide pressure was reduced by hyperventilation and hypothermia from an average of 45 mm. Hg at normothermia preventilation to an average of 2.1 mm. Hg at the lowest temperatures at which the samples were taken.

Feinblatt, T. M., and Ferguson, E. A., Jr.: Phenobarbital idiosyncrasy; avoidance by use of phenobarbital-niacin, New York State J. Med. **62:** 221 (Jan. 15) 1962.

Idiosyncratic reactions to phenobarbital may be caused by an inherent sensitivity, or they may develop as an acquired idiosyncrasy, especially in persons with an allergic background. Phenobarbital, iodide, and bromide idiosyncrasies are caused by poisoning of the oxidative coenzymes I and II. Niacin supplies the essential portion of the pyridine nucleus necessary for the reconstitution of both coenzymes. A study was undertaken to determine the efficacy of phenobarbital-niacin (Barba-Niacin) for idiosyncrasy to phenobarbital. The group consisted of 44 cases of known phenobarbital idiosyncrasy. The nature of the idiosyncrasy was neurologic in 23 cases, cutaneous in 15, and bizarre in 6. The symptoms included lassitude in 14, depression in 13, pruritus in 11, skin rash in 8, irritability in 4, daydreaming in 2, and panic in 1. The substitution of phenobarbital-niacin for phenobarbital in identical dosage over an average period of five weeks proved to be free of all untoward reactions in 40 of the 44 cases (91 per cent). In 4 cases the idiosyncratic reactions were of equal degree under the two medications.

Abstracts in Interlingua

Doyle, J. E., Anthone, S., Anthone, R., e MacNeill, A. E.: Ultrafiltration del sanguine, effectuate per medio de un dialysator rectitubal a fluxo parallel, New York State J. Med. **62:** 185 (15 de jan.) 1962.

Depost 1947, varie methodos ha essite essayate pro effectuar un ultrafiltration extracorporee del sanguine que permitterea le extraction ex le sanguine de un solution sin contento de proteina. Le uso de un dialysator-ultrafiltro se ha provate plus efficace in le separation de liquido edematic in casos alteremente intractabile que dialyse con solution hypertonic o que lavage peritonee. Le autores utilisa depost 1954 le dialysator de sanguine de MacNeill pro iste objectivo. Con le dialysator de MacNeill, ultrafiltration pote esser effectuate simultaneemente con dialyse o sin dialyse. Ultrafiltration sin le uso simultanee de un liquido lavatori esseva usate a bon successo in 7 patientes con intractabile edema causate per congestive disfallimento cardiac. Tres major gruppos de patientes obtene significative beneficios ab le uso de ultrafiltration extracorporee del sanguine. Illes es (1) patientes con congestive disfallimento cardiac qui ha cessate responder a restriction de sal, therapia a diureticos, digitalis, e altere formas plus usual de therapia; (2) patientes con congestive disfallimento cardiac qui esserea preste a esser subjicite a correction cardio-chirurgic si lor discompensation poteva esser reprimite temporarimente; e (3) patientes con acute o chronic disfallimento renal qui ha devenite significativemente hyperhydratate. Attention debe esser prestate que le extraction de liquido non progrede satis rapidemente pro causar hemoconcentration, dishydratation, hypovolemia, hypotension, e choc. Plus extense analyses del ultrafiltratos obtenite per medio de iste methodo remane desirabile. Le methodo promitte esser applicabile al studio de diffundibile substantias que es presente in le sanguine in basse concentrationes. Isto va possibilemente esser de valor particular in le clarification del causas chimic del syndrome uremic.

Glenn, F.: Tractamento chirurgic de morbo de via biliari, New York State J. Med. **62:** 203 (15 de jan.) 1962.

Morbo de via biliari occurre in multe areas del mundo. Su association con pregnantia ha un incidentia significative. In le experientia del autor, 4 de omne 5 patientes con morbo de via biliari es feminas, e 3 de illas ha essite pregnante. Solmente 1 de omne 5 tal patientes es un masculo. Le morbo es relativemente rar in patientes pediatric. Illo es plus frequente in le gruppos de etates plus avantiate que in le population general. In Nord-America calculos biliari es associate con le majoritate del disordines del vias biliari. Il non existe un adequate explication del formation de calculos biliari. Le plus commun manifestation clinic del morbo es le gravamine de "indigestion"—leve o sever. Il occurre que le morbo es presente, sin esser detegite, durante un numero de annos e que illo resulta alora in lesiones del hepate. Cholecystographia e cholangiographia rende possibile un accurate diagnose. Le tractamento definitive de morbo de via biliari es un intervention chirurgic. Cholecystectomia elective ha devenite plus commun in le curso del passate trenta annos, in parallela al reduction del risco inherente in le operation e del incidentia de complicationes. Morbo de via biliari pote esser describite in terminos de su progresso per quatro stadios. Le stadio al qual le operation es interprendite determina si iste operation va esser cholecystectomia, exploration del ducto commun, correction de un fistula biliario-enteric, o lobectomia dextere pro carcinoma del vesica biliari. Si le vesica biliari contine calculos, illo debe esser excidite sin reguardo al stadio del morbo de via biliari—excepte in le presentia de un pesantissime contraindication que rende le intervention hasardose.

Douglas, A. H., Sferrazza, J., e Marici, F.: Historia natural de aneurysma de ventriculo, New York State J. Med. **62:** 209 (15 de jan.) 1962.

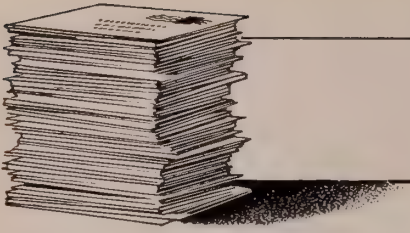
Le plus commun varietate de aneurysma del ventriculo occurre como sequella de infarcimento myocardial. In un serie de 4.427 necropsias successive effectuate al Centro Hospitalari Queens, il esseva constatate que in 524 (12 pro cento) il se tractava de infarcimento myocardial. Quaranta-cinque del patientes in iste gruppo habeva aneurysmas ventricular (1,02 pro cento del serie total e 8,7 pro cento del casos de infarcimento myocardial). A iste serie sex patientes esseva addite qui esseva tenite sub observation clinic. Intra le serie un grande differentia esseva notate inter le incidentia de aneurysma ventricular in patientes con infarcimento myocardial a base del reporto necroptic del pathologo (8,7 pro cento) e illo reportate per le clinico, principalmente a base de studios de radiographias 91,7 pro cento). Assi 3 inter 4 casos escappava al detection clinic. Aneurysma ventricular deberea esser suspicite quando le infarcimento myocardial es associate con un augmento del matitate cardiac, un maximo de pulsation intra le margine cardiac sinistre, o un pulsation paradoxe. Un localisate extrusion in le radiographia es le base del diagnose in solmente un minoritate del casos. In le presente serie, 60 pro cento del infarcimentos esseva situate in locos anterior. In le opinion del autores, le diagnose de aneurysma ventricular es fortemente suggerite per le combination del presentia in le pariete anterior de un transmural infarcimento myocardial (sin o con protrusion local in le radiogramma) con un cardiomegalia que se disveloppa in subsequentia al lesion e que non pote esser explicate per hypertension o un associate morbo valvular. Le resultatos de operationes in 35 casos de aneurysma ventricular post infarcimento myocardial ha essite multo incoragiante. Le duration maximal del observation post-operatori ha essite tres annos. Pare esser indicate investigationes additional del regulation de pulsation paradoxe per medio de un prosthese, con o sin excision del infarcite myocardio.

Wycoff, C. C.: Hypothermia: fibrillation ventricular durante hyperventilation, New York State J. Med. **62:** 217 (15 de jan.) 1962.

Fibrillation ventricular pote occurrer spontaneemente durante hypothermia; illo etiam pote occurrer como resultato de stimulation mechanic. Acidosis e alcalosis respiratori predispone le corde a fibrillation ventricular. Le occurrentia de fibrillation ventricular pote esser reducite per le regulation del pH del sanguine per medio de alterationes in le ventilation. Esseva effectuate un studio in 10 canes pro determinar le temperatura al qual fibrillation ventricular occurrerea quando alcalosis respiratori esseva inducite. Marcate grados de hyperventilation esseva usate pro producer alcalosis. Frigidation superficial esseva usate pro reducer le temperatura del animales. Cinque del animales non esseva preparate specialmente. In le altere 5, le nivello de kalium esseva reducite levemente per medios dietari e le uso de resina a excambio de natrium. Hypothermia e hyperventilation produceva le sequente resultatos: Le volumine respiratori per minuta variava inter 21 e 27 L. Le nivello de pH del sanguine montava in omne le animales. Le nivello maximal esseva 8,1. Cinque del 10 canes disveloppava fibrillation ventricular a temperaturas de plus que 20 C. Le plus alte temperatura al qual fibrillation ventricular occurreva esseva 24,2 C. Un unda S-ST de Osborn occurreva in omne le animales con un sol exception. Le pression arterial de bioxydo de carbon esseva reducite per hyperventilation e hypothermia ab un valor medie de 45 mm de Hg sub conditiones normothermic pre-ventilatori ad un valor medie de 2,1 mm de Hg al plus basse temperatura al qual specimens esseva prendite.

Feinblatt, T. M., e Ferguson, E. A., Jr.: Reactiones idiosyncratic a phenobarbital; evitation de illos per le uso de phenobarbital-niacina, New York State J. Med. **62:** 221 (15 de jan.) 1962.

Reactiones idiosyncratic a phenobarbital pote occurrer como effecto de un sensibilitate inherente, sed illos etiam pote disveloppar se como un idiosyncrasia acquirite, specialmente in subjectos con antecedentes de allergia. Reactiones idiosyncratic a phenobarbital, a ioduro, e a bromuro es causate per le invenenamento del oxydative coenzymas I e II. Niacina forni le portion essential del nucleo de pyridina que es necessari pro le reconstitution del duo coenzymas. Esseva interprendite un studio pro determinar le efficacia de phenobarbital-niacina (Barba-Niacin) in prevenir reactiones idiosyncratic a phenobarbital. Le gruppo consisteva de 44 casos de cognoscite reactivitate idiosyncratic a phenobarbital. Le natura del reactiones esseva neurologic in 23 casos, cutanee in 15, e bizarre in 6. Le symptomas includeva lassitude in 14, depression in 13, pruritus in 11, eruption cutanee in 8, irritabilitate in 4, sonios in stato de evelia in 2, e panico in 1. Le substitution de phenobarbital-niacina pro phenobarbital in dosage identic durante un periodo medie de cinque septimanas resultava in le complete absentia de adverse reactiones in 40 del 44 casos (91 pro cento). In 4 casos, le grado del reactiones idiosyncratic esseva le mesme sub le duo regimes.



Letters to the Editor

The Potemkin village

To the Editor: The New York Times of October 15, 1961, on page 9 of the first section, devotes an entire column to the factual description of the Russian medical exhibit which had just opened in Chicago. The Russian vice-minister of health, Victor Zhdanov, is quoted as stating that Russia has "400,000 doctors—twice as many as in the United States." Also, there is the further quote that Russian schools "graduate 25,000 doctors annually" (as against our 8,000).

It has been pointed out that Russians deliberately blur their statistics by lumping together the middle and upper medical personnel: the "vrach," physician, is equated with the doctor.[1] This results in calculated confusion; a very invidious "Potemkin village" façade is reiterated often enough to become accepted as truth.

The phrase, Potemkin village, has a very special meaning in Russia. During the reign of Catherine II, 1762 to 1796, much of what is now the Ukraine (borderland) was conquered. Her favorite, Prince Potemkin, was appointed to colonize the fertile, unpopulated steppes. In time, the sovereign expressed a desire to tour her most recent acquisitions. Prince Potemkin went to the enormous trouble of gathering together secretly a huge cast of actors and a fantastic quantity of props. As he had charge of the Empress' itinerary, he was able to send the actors ahead of the imperial entourage. The stagehands would set up entire villages complete with all the trimmings. When the Empress traveled by day, she would observe in the distance scenery that gave the illusion of complete settlements, baronial estates, and other items to be expected in the flourishing land. At dusk she would reach a splendid group of habitations; processions of obsequious local dignitaries and well-dressed happy peasants would greet her. She would pass the night in splendidly comfortable quarters.

So marvelous was the performance by Prince Potemkin's troupe that, to the end of her days, the Empress failed to realize that she had been looking at a façade. This incredible feat of deception has gone into the Russian language. To any educated Russian of today, the term Potemkin village means a stage front concealing a rather differing substantive reality.

Please note also that the beholder deceives himself. He is permitted to "observe" to his heart's content; no one tells any direct lies. This very specific meaning is at the very heart of this unique term.

Today, the Russians avoid the outright lie. It is the foreign visitor who is "perfectly free to see and observe" and yet who—by not such a strange coincidence—manages to see the very sights to which he is steered by his obliging hosts.

The vice-minister of health does not state that Russia graduates 25,000 Doctors of Medicine annually. He merely lumps together the physicians and the doctors; as translated into English they are all doctors. He did not say so; the reporters assumed the translation as being so. It is this self-deception that creates the Potemkin village; this is the reason for the present letter.

It is necessary to reiterate that only some 10 per cent of the stated figure represents (as of today) actual Doctors of Medicine. If we fail to grasp this simple fact, we build Potemkin villages and draw totally unwarranted conclusions as to Russian progress in medical education.

This is not to say that the Russians are stagnating and that we can draw fatuous satisfaction from still being in the van. The Russians are making tremendous headway. Still, they are not nine feet tall, and they have not leapfrogged past us in the present decade. The Potemkin village concept is not an outmoded cliché when we accept without correction such tremendous self-imposed distortions of the truth.

Before closing, there might be room for asking whether or not the Russian methods of medical education have anything constructive to offer for our consideration. In essence, Hudson[2] raises the question of medical assistants. Without lowering medical standards for doctors, can we train assistants who would perform under proper supervision the mundane, repetitive chores of daily practice, thus freeing the doctor for more creative tasks. This would permit fewer doctors to serve more people.

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[1] Lieberman, A.: Comments on Soviet medicine, New York State J. Med. **61**: 1771 (May 15) 1961.

[2] Hudson, C. L.: Expansion of medical professional services with nonprofessional personnel, J.A.M.A. **176**: 839 (June 10) 1961.

Necrology

Antonio La Duca Barone, M.D., of Buffalo, died on July 6, 1961, at the age of seventy-one. Dr. Barone graduated in 1914 from the University of Buffalo School of Medicine.

Philip Buchholtz, M.D., of Brooklyn, died on August 3, 1961, at the age of sixty-four. Dr. Buchholtz graduated in 1921 from New York University and Bellevue Hospital Medical College. He was a consulting physician at Sea View Hospital. Dr. Buchholtz was a Fellow of the American College of Chest Physicians and a member of the Kings County Medical Society and the Medical Society of the State of New York.

Rose Carmel Cacchillo, M.D., of New York City, died on July 9, 1961, at the age of forty. Dr. Cacchillo graduated in 1948 from the Woman's Medical College of Pennsylvania, Philadelphia. She was an assistant surgeon at the New York Eye and Ear Infirmary and an assistant in ophthalmologic surgery at Greenpoint Hospital. Dr. Cacchillo was a Diplomate of the American Board of Ophthalmology and a member of the Pan American Association of Ophthalmology, the American Academy of Ophthalmology and Otolaryngology, the Morgagni Medical Society of New York, the Brooklyn Ophthalmological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

E. Martin Freund, M.D., of Nassau, retired, died on July 18, 1961, at the age of seventy-one. Dr. Freund graduated in 1916 from Albany Medical College. He was former chief of the eye, ear, nose, and throat section of the Veterans Administration Hospital Outpatient Department, Albany. Dr. Freund was a Diplomate of the American Board of Otolaryngology and a member of the American Academy of Ophthalmology and Otolaryngology and the Eastern New York Eye, Ear, Nose and Throat Association.

Jacob Goldmann, M.D., of New York City, died on April 26, 1961, at the age of sixty-seven. Dr. Goldmann received his medical degree from the University of Heidelberg in 1911. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry Theodore Hagstrom, M.D., of Brooklyn, died on December 2, 1961, at the Methodist Hospital of Brooklyn at the age of sixty-seven. Dr. Hagstrom graduated in 1922 from Harvard University Medical School and interned at Sloane Hospital and Methodist Hospital of Brooklyn. He was a consultant in gynecology cytology at the Methodist Hospital of Brooklyn and a former medical director for the *New York Herald Tribune*. Dr. Hagstrom was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, and a member of the Brooklyn Gynecological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James McAndrew Happell, M.D., of Salamanca, died on November 6, 1961, at his home at the age of eighty-four. Dr. Happell graduated in 1903 from the University of Buffalo School of Medicine. He was an honorary physician and obstetrician at Salamanca District Hospital and until May 1, 1961, had served as county coroner for ten years. Dr. Happell was a member of the Cattaraugus County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Edward Lane, M.D., of Poughkeepsie, died on November 7, 1961, at his home at the age of seventy-seven. Dr. Lane graduated in 1908 from New York Homeopathic Medical College and Flower Hospital. From January 1, 1925, to December 31, 1957, he had served on the local board of health and from 1914 to March 31, 1954, he was physician at the county jail. Dr. Lane was a member of the International Academy of Proctology, the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ferdinand J. Lehr, M.D., of Carmel, died on April 21, 1961, at the Northern Westchester Hospital, Mt. Kisco, at the age of sixty-four. Dr. Lehr received his medical degree from the University of Berlin in 1923. He was a member of the Putnam County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Sol Sydney Lichtman, M.D., of New York City, died on June 15, 1961, at Polyclinic

Hospital at the age of sixty-two. Dr. Lichtman graduated in 1921 from Cornell University Medical College. He was an assistant attending physician at New York and the Mount Sinai Hospitals. Dr. Lichtman was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Edward Harvey Marsh, M.D., of Chappaqua, died on December 6, 1961, at his home at the age of seventy-five. Dr. Marsh graduated in 1909 from Cornell University Medical College. In 1952 he retired as deputy health commissioner of Westchester County. Dr. Marsh was a member of the American Public Health Association, the Association of Military Surgeons of the United States, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Albert Rankin McFarland, M.D., of Rochester, died on October 23, 1961, at his home at the age of sixty-nine. Dr. McFarland graduated in 1918 from the University of Pennsylvania School of Medicine. He was a consultant in dermatology at St. Mary's Hospital, an honorary member of the medical staff of Highland Hospital of Rochester, and a consultant in dermatology and syphilology at Rochester General and Genesee Memorial Hospitals. Dr. McFarland was a Diplomate of the American Board of Dermatology, Inc., and a member of the American Academy of Dermatology and Syphilology, the American Dermatological Association, the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Austin G. Morris, M.D., of Rochester, died on October 14, 1961, at the age of seventy-seven. Dr. Morris graduated in 1908 from Syracuse University College of Medicine. Former president of the Monroe County Medical Society, he was an honorary member of the medical staff of Highland Hospital of Rochester and an honorary physician in laryngology, rhinology, and otology at Rochester General Hospital. Dr. Morris was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the American Laryngological, Rhinological and Otological Society, the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Phillips, M.D., of New York City, died on August 3, 1961, at the age of seventy-seven. Dr. Phillips graduated in 1906 from Columbia University College of Physicians and Surgeons. He was a Fellow of the International College of Surgeons and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Russell Purcell, M.D., of Mechanicville, died on November 16, 1961, at the age of fifty-one. Dr. Purcell graduated in 1936 from Albany Medical College. He was a former health officer for the City of Mechanicville and during World War II served on the Selective Service Board. Dr. Purcell was a member of the Saratoga County Medical Society and the Medical Society of the State of New York.

Armand Salmon, M.D., of Brooklyn, retired, died on March 12, 1961, at the age of ninety-one. Dr. Salmon graduated in 1895 from Long Island College Hospital Medical School. He was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Adolf Schaefer, M.D., of New York City and Astoria, died on January 27, 1961, at the age of fifty-one. Dr. Schaefer graduated in 1935 from New York Homeopathic Medical College and Flower Hospital. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Harry M. Shapiro, M.D., of the Bronx, died on April 5, 1961, at the age of sixty-six. Dr. Shapiro graduated in 1919 from Fordham University School of Medicine. He was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Bronx Pediatric Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Eugene Svecenski, M.D., of Wingdale, died on August 17, 1961, at the age of sixty-four. Dr. Svecenski received his medical degree from the University of Vienna in 1924. He was supervising psychiatrist at Harlem Valley State Hospital. Dr. Svecenski was a member of the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frederick Max Wertheim, M.D., of New

York City, died on June 5, 1961, in Sydney, Australia, at the age of seventy-two. Dr. Wertheim received his medical degree from the University of Bonn in 1913. He was a member of the Rudolf Virchow Medical Society.

Clarence Edison Winter, M.D., of Richmond Hill, died on February 25, 1961, at the age of eighty-three. Dr. Winter graduated in 1900 from Long Island College Hospital Medical School.

Medical Meetings

Buffalo Academy of Medicine

"Manifestation of Connective Tissue Disease" is the subject of a panel discussion scheduled for the February 7 meeting of the Buffalo Academy of Medicine. The moderator of the program will be Evan Calkins, M.D., Boston. Panelists will be: Albert Dorfman, M.D., University of Chicago; Lewis Thomas, M.D., New York University Medical Center and New York University School of Medicine; and Theodore B. Bayles, M.D., Robert Breck Brigham Hospital, Boston.

The Buffalo Academy of Medicine meets on the first Wednesday of each month at the University of Buffalo. Cocktails are served at 6:00 P.M., at the Faculty Club, dinner at 7:15 P.M., at Norton Hall, and the meeting is held at 8:30 P.M., at the Medical School. Guests are invited to attend.

For information and reservations write to: H. Paul Longstreth, M.D., Secretary, Buffalo Academy of Medicine, 193 Mt. Vernon Road, Buffalo 26, New York.

Symposium on infertility

The New York University Medical Center in conjunction with the American Society for the Study of Sterility will present a symposium on infertility February 8 through 10.

For a detailed program and application forms write to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

Michigan Association of the Professions

The Michigan Association of the Professions, an organization representing more than 30,000 persons in the professions of architecture, dentistry, engineering, law, medicine, pharmacy, and veterinary medicine will hold its third annual congress of the professions at Michigan State University in East Lansing, Michigan, Friday and Saturday, February 9 and 10.

For further details write to: Michigan Association of the Professions, 120 West Saginaw, East Lansing, Michigan.

Medical News

Section on Ophthalmology, Nassau Academy of Medicine

The first joint meeting of the Section on Ophthalmology, Nassau Academy of Medicine, and the Long Island Ophthalmological Society was held on November 27, 1961, at the Academy with the Section as the host organization.

Ben S. Fine, M.D., Washington, D.C., was the guest speaker. His topic was "Electron Microscopy of Ocular Tissues."

The next meeting of the Section will be on Monday, January 22.

Doctors' Gun Club

The Doctors' Gun Club, a rifle and pistol club composed of physicians and dentists in the Metropolitan New York area, has recently been organized. Excellent range facilities are available, and all those interested in guns are invited to join. For information contact: William Greenfield, D.D.S., 110 East 36th Street, New York 16, New York. Telephone MU 3-0367.

American Society for the Study of Sterility

The American Society for the Study of Sterility announces the following awards and grants to be given in 1962:

The Ortho Medal—The Ortho Medal and the sum of $1,000 is to be awarded to a recipient chosen by the Awards Committee of the Society on the basis of highly significant work related to fertility and sterility during the previous three years. The money awarded is to be used by the recipient for expenses in visiting medical and research centers of his interest.

The Rubin Award—The Rubin Award, consists of a certificate of merit and the sum of $250 and is to be awarded to the author whose paper is deemed by the Awards Committee to be the most significant contribution of those appearing in *Fertility and Sterility* from the March-April through the November-December 1961 issues.

The Carl G. Hartman Grant-in-Aid—The Carl G. Hartman Grant-in-Aid in the amount of $500 is available for research in fertility and sterility or related subjects in 1962. Applications should be sent to the chairman of the Awards Committee of the American Society for the Study of Sterility, Michael Newton, M.D., 2500 North State Street, Jackson 6, Mississippi. The application must be accompanied by six copies of a brief outline of the project for which the grant is being sought.

Study on care of children

A broad research study of the care of children in the United States will be established on February 1 at the international headquarters of the American Academy of Pediatrics, Evanston, Illinois.

The study will be operated under the Joint Committee on Pediatric Practice, Research, and Education, whose members represent the Academy, the American Board of Pediatrics, the Pediatric Section of the American Medical Association, the Society for Pediatric Research, and the American Pediatric Society.

The study will be directed by Alex J. Steigman, M.D., of Louisville, Kentucky. The purpose of the study is to ascertain the status of practice, research, and teaching in child health and to find the most effective use of medical and paramedical manpower in child care in the community and in research and teaching in universities and institutes.

Practical nurses must be licensed

A warning to the public to guard against employment of women who call themselves "practical nurses" but are not licensed by the State Education Department has been issued by Licensed Practical Nurses of New York, Inc., a state-wide membership organization.

Licensure of practical nurses is mandatory in New York State and it is a misdemeanor for anyone to practice nursing who is not legally permitted to do so.

Inquiries concerning activities of the organization or the qualifications for membership should be sent to: Mrs. Christine B. Quell, Executive Secretary, Licensed Practical Nurses of New York, Inc., 250 West 57th Street, New York 19, New York.

Papers on ophthalmology sought

The Section on Ophthalmology and Otolaryngology of the Southern Medical Association announces that it will now accept papers to be considered for presentation before the next annual meeting at Miami Beach, Florida, November 12 through 15. Papers will be accepted for consideration until May 15.

For further information write to: Albert C. Esposito, M.D., Secretary, Section on Ophthalmology and Otolaryngology of the Southern

Medical Association, Suite 1212, First Huntington National Bank Building, Huntington 1, West Virginia.

Course in pediatric oncology

The Pediatric Department of Memorial Sloan-Kettering Cancer Center, New York City, announces its annual comprehensive three-day course in pediatric oncology for pediatricians, general practitioners, and health officers to be held April 25 through 27.

Current developments and established methods in diagnosis, differential diagnosis, and management of benign and malignant tumors, Hodgkin's disease, leukemia, and reticuloendothelioses in childhood, are included.

Twenty members of the attending staffs of Memorial Hospital for Cancer and Allied Diseases and the Memorial Sloan-Kettering Cancer Center will be on the faculty.

For information write to: Chairman, Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, 444 East 68th Street, New York 21, New York.

St. Francis Hospital gets grant

The Nassau County Heart Fund has announced that it has given a $3,470 research grant to St. Francis Hospital in Roslyn, Long Island, to develop a more accurate and simple technic of diagnosing heart defects.

William J. Noble, M.D., medical director, and John Billows, M.D., director of radiology, at the hospital will supervise the program.

American Medical Association Education and Research Foundation

The American Medical Education Foundation was established in 1951 for the purpose of providing financial assistance to medical schools. The American Medical Research Foundation was established in 1957 for broader purposes, including the provision of financial assistance to medical schools.

Effective January 1, 1962, the programs of AMEF and AMRF were consolidated within the framework of a single Foundation—the American Medical Association Education and Research Foundation. At the same time these programs have been expanded and a concerted effort made to provide increased financial assistance to medical schools in addition to financing the other projects of the Foundation.

The Foundation is incorporated under the laws of the State of Illinois as an educational, scientific organization. All contributions to the AMA-Education and Research Foundation are tax deductible under Section 501 (c) (3) of the U.S. Internal Revenue Service Code.

The affairs of the Foundation are managed by a Board of Directors elected annually by and from the membership of the Board of Trustees of the American Medical Association.

At present, the Board of Directors and officers are: Hugh H. Hussey, Jr., M.D., Washington, D.C., president; Raymond M. McKeown, M.D., Coos Bay, Oregon, vice-president; James Z. Appel, M.D., Lancaster, Pennsylvania, secretary-treasurer; Leonard W. Larson, M.D., Bismarck, North Dakota, and Gerald D. Dorman, M.D., New York City.

At the present time, the Foundation is seeking funds to support the following programs: unrestricted financial assistance to medical schools; a medical journalism fellowship program; a research grants program for medical research workers; a study of perinatal mortality and morbidity; and a study of continuing medical education.

During 1962 the Foundation will also undertake to raise funds to assist in the financing of medical scholarships and for loans to medical students, as well as to physicians in internships and residencies.

Plastic surgery and dermatology

A discussion in "Plastic Surgery in Relation to Dermatology" will be held under the auspices of the Division of Dermatology, Department of Medicine, State University of New York Downstate Medical Center, on Friday, March 2, from 10:00 to 11:30 A.M., in the E Building Auditorium of Kings County Hospital, 451 Clarkson Avenue, Brooklyn 3, New York. Lawrence Frank, M.D., professor of dermatology at the Medical Center, will be the moderator and Howard Rasi, M.D., attending plastic surgeon, Methodist Hospital will deliver the address.

New obstetric society formed

The American Society for Psychoprophylaxis in Obstetrics has been formed by physicians interested in using, promulgating, and investigating the psychoprophylactic method (Lamaze) in this country. For further information write to: Alfred Tanz, M.D., F.A.C.S., The American Society for Psychoprophylaxis in Obstetrics, 2 Grace Court, Brooklyn, New York.

Course on emotional problems in medical practice

The New York Academy of Medicine will present the third in an annual series of courses on "Emotional and Psychiatric Problems in Medical Practice" starting on Monday, January 29. Deadline for the receipt of applications for registration is Monday, January 15.

The objective of the course, which is open to all physicians in both general and specialty practice, is to link the practice experience of the student-physician with current psychiatric conceptions of human behavior so as to facilitate more effective patient care and greater satisfaction for the doctor.

For information contact: Executive Secretary for Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Fight for Sight grants

The National Council To Combat Blindness, Inc., announces that a total of 76 Fight for Sight grants and fellowships have been awarded to support eye research for the 1961 period. These awards, totaling $257,512 will be administered during 1961–1962 at medical colleges, hospitals, and eye centers throughout the nation and in foreign countries.

Included in the total are 34 grants-in-aid, 12 postdoctoral research fellowships, and 26 student fellowships for research into degenerative diseases of the retina, cataracts, glaucoma, the eye in old age, blindness due to diabetes, eye infections and other problems that cause defective vision, and partial or total blindness.

Four special grants have been made—three supporting clinical service projects and one to assist in the dissemination of information to investigators concerned with electroretinography studies.

All grants and fellowships are reviewed and approved by members of the organization's Scientific Advisory Committee, which includes in New York: Charles A. Perera, M.D., Columbia University College of Physicians and Surgeons; Goodwin M. Breinin, M.D., New York University Medical Center; Arthur G. DeVoe, M.D., Institute of Ophthalmology, the Presbyterian Hospital; Dan M. Gordon, M.D., and John M. McLean, M.D., New York Hospital, Cornell Medical Center; Samuel L. Saltzman, M.D., New York Medical College, Flower and Fifth Avenue Hospital; and George K. Smelser, Ph.D., Columbia University, College of Physicians and Surgeons.

Applications for 1962 awards are now being received by the office of the National Council To Combat Blindness, 41 West 57th Street, New York 19, New York. March 1, is the closing date for application.

Personalities

Honored. Edmund Prince Fowler, M.D., New York City, as guest of honor at the fiftieth anniversary dinner of the New York League for the Hard of Hearing at which he was presented with a scroll in appreciation for his contributions in the field of otology.

Elected. Joseph P. Alvich, M.D., Bronx, as president of the medical board and director of surgery at Fordham Hospital.

Awarded. Edith Klemperer, M.D., F.A.P.A., New York City, a fellowship by the Society for Clinical and Experimental Hypnosis.

Appointed. Leonard C. Lang, M.D., Buffalo, as assistant commissioner in charge of community services for the New York State Department of Mental Hygiene.

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Scientific Motion Pictures

William J. Sullivan, M.D., Chairman, Scientific Motion Picture Subcommittee of the Convention Committee, is interested in hearing from members who have 16-mm. motion picture films suitable for presentation at the 1962 convention.

For applications, write to WILLIAM J. SULLIVAN, M.D., 132 Pondfield Road, Bronxville, New York.

Medical Schools

Albany Medical College

Appointment. Ernst Jurgen Plotz, M.D., associate professor of obstetrics and gynecology, University of Chicago School of Medicine, and attending obstetrician and gynecologist, Chicago Lying-In Hospital and the Argonne Cancer Research Hospital, has been appointed chairman, Department of Obstetrics and Gynecology, to become effective February 1.

College of Physicians and Surgeons

Clark Foundation Gift. The Clark Foundation of New York has presented the College with $10,000 in honor of Dr. Aura E. Severinghaus, associate dean and professor of anatomy and a trustee of the Mary Imogene Bassett Hospital in Cooperstown. The gift will be used primarily for financial assistance to students and for strengthening the College's teaching program at the Bassett Hospital. Dr. Severinghaus, a specialist in cytology of the endocrine glands, has been a member of the faculty since 1927 and has served as associate dean since 1943 and as secretary of the faculty since 1942.

Renewed Grant. A new method to visualize viruses inside cells will be utilized by medical scientists at the College under a renewed National Foundation-March of Dimes grant of $41,293. Harry M. Rose, M.D., John E. Borne Professor of Medical and Surgical Research and chairman, Department of Microbiology, will direct the work. Associated with Dr. Rose in this work are Councilman Morgan, M.D., Calderon Howe, M.D., Gabriel C. Godman, M.D., Arline D. Deitch, M.D., Alice W. Knox, M.D., and Herbert Rosenkranz, M.D.

New York Medical College

Award. Dr. Karl Meyer, professor of biochemistry, Columbia University College of Physicians and Surgeons, received the New York Medical College Award on November 30 "in recognition of distinguished achievement and service to science, medicine and humanity" for his pioneering work in the field of the mucopolysaccharides. The award was presented at a Mucopolysaccharides Seminar held at the College under the auspices of the Department of Biochemistry.

Two-Week Course. A two-week course on the rehabilitation of the chronically ill patient for registered nurses, occupational therapists, physical therapists, and social workers will be held on April 23 through May 4 at Bird S. Coler Hospital. The teaching staff includes members of the faculty of the College, professional staff of the Medical Center, and noted guest lecturers. Application should be made to Raymond C. Lerner, M.S.S.W., coordinator, PostGraduate Education, Department of Physical Medicine and Rehabilitation, New York Medical College, 1 East 105th Street, New York 29, New York.

State University of New York Downstate Medical Center

Symposium. A two-day symposium on December 6 and 7, 1961, at the Center presented a comprehensive review of the psychiatric problems related to asthma in children. Principal speakers were: Murray Peshkin, M.D., consulting allergist, The Mount Sinai Hospital; John Lamont, M.D., director, Child Psychiatry, Massachusetts General Hospital; Henry I. Schneer, M.D., director, Division of Child and Adolescent Psychiatry, Downstate Medical Center; Harold A. Abramson, M.D., consultant, Research Psychiatry, Central Islip State Hospital; George J. Mohr, M.D., Sheldon Selesnick, M.D., and Bernice Augenbraun, M.D., Mount Sinai Hospital, Los Angeles; Edward Lipton, M.D., Murray Lieberman, M.D., and Melitta Sperling, M.D., Downstate Medical Center's psychiatry department; Lewis Bernstein, M.D., director, Psychological Services, Jewish National Home for Asthmatic Children, Denver; Lucie Jessner, M.D., professor of psychiatry, University of North Carolina School of Medicine; and Peter Knapp, M.D., research professor of psychiatry, Boston University College of Medicine.

Radio Conference. William Dock, M.D., professor of medicine, and Elaine T. Feldman, M.D., assistant professor of medicine, presented a two-way radio conference on heart disease for physicians at 36 hospitals in five states on December 12, 13, and 15, 1961. The conference was on "Metabolic Factors in the Management of Coronary Heart Disease."

1960–1962 Honor Scholarships. Medical students named winners of the 1961–1962 Honor Scholarships on November 28, 1961, were: Vincent Barresi, the Brooklyn Gynecological Society Honor Scholarship; Harvey Cohen, and AMEF Honor Scholarship; Barry

Jacobs, the Norman S. Goetz Honor Scholarship; Allen P. Kaplan, the Dave Luckman Honor Scholarship; David Mahon, Thomas Mulvaney, Elliott Reichbach, and Allen Shevach, AMEF Scholarships; and Steven Stein, the Woman's Auxiliary to the Medical Society of the County of Kings Honor Scholarship.

Upperclassmen receiving scholarships were: Phillip Charney, David Howitt, Theodore Weinstein, Yasoma Challenor, Barry Edelstein, Frank Gutmann, and Berton Zbar, AMEF scholarships; and Robert Oberhand, the Class of 1934 Honor Scholarship, and Michael Bromer, the Alumni Association Honor Scholarship.

Research Grants. Nineteen research grants totaling $304,756 were received during September and October, 1961. Four of the grants represented continuations of previous projects and in addition a grant was awarded by the United States Public Health Service to the Department of Surgery to support an undergraduate training program in cancer.

Appointments. Clinical assistant professors in the Department of Pediatrics are Philip J. Kozinn, M.D., and Jacob L. Stein, M.D.; Raymond Nadell, M.D., has been named clinical assistant professor of psychiatry, and Jacob Levitt, M.D., has been appointed lecturer in pediatrics.

Promoted. From lecturer to associate professor of psychiatry, Jan Frank, M.D.; and promoted from clinical instructor to clinical assistant professor, Abbott Lippman, M.D.

Joint Research Program. The obstetrics departments at the Downstate Medical Center and at the University of Aberdeen, Scotland, are planning a joint research program on the epidemiology of human reproductive problems. The National Institute of Neurological Diseases and Blindness has granted an initial sum of $4,836 to set up the project. Principal investigators will be Sir Dugald Baird, chairman, Department of Midwifery and Gynaecology, and Schuyler Kohl, M.D., associate professor of obstetrics and gynecology.

State University of New York Upstate Medical Center

Postgraduate Course. The twelfth annual postgraduate course in ophthalmology was held on December 1 and 2, 1961. James McGraw, M.D., professor and chairman, Department of Ophthalmology, was chairman. Guest speakers were: Harold Whaley Brown, M.D., clinical professor of ophthalmology, New York University College of Medicine; Irving H. Leopold, M.D., professor and chairman, Department of Ophthalmology, Graduate School of Medicine, University of Pennsylvania, Philadelphia; Joseph A. C. Wadsworth, M.D., associate clinical professor of ophthalmology, Columbia University College of Physicians and Surgeons.

Visiting Professor. Dr. Geoffrey Harris, Fellow, Royal Society and professor of anatomy, Oxford University, England, was the Merck Sharp and Dohme Visiting Professor until November 20, 1961. On November 15, 1961, Dr. Harris delivered a lecture on "Central Nervous System Control of Endocrine Function."

MEND Lecturer. George Hyatt, M.D., professor, orthopedic surgery, Georgetown University School of Medicine, Washington, D.C., was the MEND Lecturer on November 29, 1961. Dr. Hyatt spoke on "The Role of the Tissue Bank in a Catastrophe."

Lecture. Morris Fishbein, M.D., lectured on "Fifty Years of Medical Progress" on December 13, 1961. The lecture was sponsored by the Student American Medical Association chapter.

University of Rochester School of Medicine and Dentistry

Honored. George H. Whipple, M.D., dean emeritus, was presented with a certificate of merit by the American College of Dentists on November 30, 1961, for his "distinguished services to the dental profession." Under Dr. Whipple as dean in 1929 a pioneering experiment in dental education has produced more dental school deans, teachers, department heads, and research directors than any comparable graduate training program in the country.

Lewis P. Ross Professor of Physiology. Dr. William D. Lotspeich, professor and chairman of the physiology department has been designated Lewis P. Ross Professor of Physiology. Dr. Lotspeich came to the University as chairman of the Department of Physiology in 1959 from the University of Cincinnati College of Medicine, to succeed Wallace O. Fenn, M.D., who retired from the chairmanship but continued as Distinguished Senior Professor of Physiology.

Books Reviewed

The Management of Fractures and Soft Tissue Injuries. By the Committee on Trauma, American College of Surgeons. Based on *An Outline of the Treatment of Fractures*, seventh edition, and *Early Care of Acute Soft Tissue Injuries*, second edition. Octavo of 372 pages, illustrated. Philadelphia, W. B. Saunders Company, 1960. Cloth $5.00.

Combined in one volume are the formerly published *Outline of the Treatment of Fractures*, seventh edition, and *Early Care of Acute Soft Tissue Injuries*. The material is very well presented; the field of surgery of trauma is widely covered.

The book will be of value to all who have occasion to treat any acute injury.—MAYER E. ROSS, M.D.

Progress in Neurology and Psychiatry. Volume XV. Edited by E. A. Spiegel, M.D. Octavo of 619 pages, illustrated. New York, Grune & Stratton, 1960. Cloth, $12.75.

This fifteenth volume of annual review of the neurologic and psychiatric literature covers effectively the years 1958 and 1959.

The 1959 contributions do a creditable job of sometimes reviewing and sometimes just listing published articles in the field. The volume is useful to gain a bird's-eye view of what is going on and as a reference guide. It is of course not suitable for study in depth.

Some of the reviews are narrative and describe the discussed reports in sufficient detail; others are telegraphic in style and hardly do more than to touch on the subject matter. The latter are much less useful, although this is unavoidable in view of limitations of space.

This book will be welcomed, as before, by those in the field who wish to remain informed and those who want a guide list of references in any problem in neurology, psychiatry, and neurosurgery.—L. P. HINTERBUCHNER, M.D.

Urology in General Practice. By Ian Parton, M.B. Octavo of 293 pages, illustrated. London, Butterworths, 1960. Cloth, $9.00.

Dr. Parton, the author of this text, is assistant urologist at Auchland Hospital and a member of the Royal College of Surgeons of Australia. It is of extreme interest to note that the principles of urology as set forth in this text by Dr. Parton over 10,000 miles away from our medical center are in no way different from the principles as practiced in our area. There was not one major point of disagreement between this text and those precepts in general acceptance in American urology. The text is a well-itemized and well-indexed reference for general practitioners as it includes the acute as well as the chronic urologic conditions that the general practitioner is faced with in his office or during home visits.

Beside the general elucidation of urologic principles, Dr. Parton has elaborated on the problems that the general practitioner often must deal with: urinary incontinence, chronic male infertility, and the treatment of congenital anomalies. More frequently than not these are chronic conditions, and the first physician in consultation is not the urologic surgeon. Implicit directions are given for the home treatment of renal colic and chronic urinary retention and overflow and for the care of the helpless patient with an advanced malignant condition that has to be treated at home. In addition, there is a section on emergency operation that would be useful to those who are forced to do these procedures when the patient is at a distance from a urologic center.

Because of its brevity and itemized style the text is a bit too advanced for the medical student. However, it is ideal for the practicing physician, for it covers all the problems of urology that are seen by those who practice any branch of medicine.—SIDNEY R. WEINBERG, M.D.

Fundamentals of Nerve Blocking. By Vincent J. Collins, M.D., with the assistance of Emery Andrew Rovenstine, M.D. Octavo of 354 pages, illustrated. Philadelphia, Lea & Febiger, 1960. Cloth, $9.50.

This small book contains a wealth of information. Although its title suggests that the motif is technic, the author discusses pain syndrome, vascular lesions, and autonomic blockade. The book covers the pharmacology and chemistry of local anesthetic agents and outlines the applicable history in concise, almost outline form.

The author has incorporated most of the present thinking in nerve block therapy, making this book valuable to practitioners in almost all branches of medicine. However, the conciseness exacts its toll by making some of the block technics difficult to follow and understand.

This book deserves to be on the library shelf of every doctor.—IRVING M. PALLIN, M.D.

Cerebrospinal Fluid Dynamics in Health and Disease. By David Bowsher, M.D. Octavo of 80 pages, illustrated. Springfield, Charles C Thomas, 1960. Cloth, $4.75.

This compact, small volume by an English lecturer in anatomy deals concisely with the production, absorption, and hydrodynamics of the cerebrospinal fluid in animals and human beings in health and disease. Much of the review is based on investigations of other workers, some on the author's own. Although some of the conclusions (such as the routes of absorption) must be read with certain reservations, this volume contains much useful information condensed in a small space.

The text is easy to read and will be of interest primarily to neurologists and neurosurgeons.—L. P. Hinterbuchner, M.D.

Ciba Foundation Symposium Jointly with Committee for Symposia on Drug Action on Adrenergic Mechanisms. Editor for the British Pharmacological Society, J. R. Vane, B.Sc. Editors for the Ciba Foundation G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. With 163 illustrations. Octavo of 632 pages. Boston, Little, Brown and Company, 1960. Cloth, $12.50.

The less we know about a phenomenon the greater the number of explanations are hypothesized to explain it. An example of a disease is cancer, an example of a pervading phenomenon is life, and there are those who believe that life is essentially the balance between adrenergic and cholinergic functions. Obviously, any one explanation is a gross oversimplification. Nonetheless, the numerous areas in the functioning of living organisms and the very many functions which adrenergic mechanisms modify, influence, initiate, or control, invite intensive attention to that mechanism. The advent of new drugs in the field does not reduce, but in fact increases, the need of attention to it; for new drugs do not create new pathways of activity but exert their action through existing physiologic mechanisms.

The coins of exchange in this mechanism are enzymes and their -ases, acronyms such as dopa or triphosphopyridine nucleotides and structures and processes as mitochondria, chromaffin cells, sympathetic nerve fibers, methylation and depolarization, liberation of epinephrine at synapse in response to stimulation by a nerve impulse. Despite these apparently arcane activities adrenergic mechanisms are involved very practically in hypertension, in the control of blood sugar levels, in cerebral function, in certain endocrinologic states, in infection and inflammation, and in a variety of symptoms or conditions due to the somatopsychic factors that call them forth.

These highly complex and interrelated adrenergic mechanisms are encompassed under sections exploring the formation and activation of adrenergic transmitters; the storage of catecholamines; the adrenergic mechanisms and their inhibition; and the action of epinephrine, norepinephrine, and other sympathomimetic amines. There is little clinical material here, but the mechanisms discussed enable the grasp of a greater familiarity with the clinical effect of these substances. The interrelationship to other substances, as adenosine triphosphate, also fundamentally concerned in numerous physiologic functions, is the subject of other chapters.

This text is recommended to those who wish to have a current and more than superficial explication of these factors.—Erwin Di Cyan, Ph.D.

The Medical Clinics of North America Chicago Number. January, 1961. Clinical Problems in Gynecology and Obstetrics. Herbert E. Schmitt, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bi-monthly (six numbers a year). Cloth, $18 net; Paper, $15 net.

This is an interesting and informative issue, edited by the late Herbert E. Schmitt, M.D., and completed just before his untimely death. It represents, according to the introduction, the current teaching and practice of the Chicago group.

Most of the articles are excellent and worth while; a few are superficial and trivial. I recommend it to the specialist and to practitioners interested in obstetrics and gynecology.—Robert E. Gordon, M.D.

The Out-patient Treatment of Schizophrenia. A Symposium. Edited by Sam C. Scher and Howard R. Davis. Octavo of 246 pages, illustrated. New York, Grune & Stratton, 1960. Cloth, $5.75.

The organizers of this timely symposium are to be congratulated. There is no problem in psychiatry today demanding more attention for its understanding and solution than the so-called "schizophrenias."

This symposium is pointed essentially to the interests of psychiatrists. Herein one will find diversified views concerning diagnostic principles with emphasis on description and clinical matters of delineation including process.

Whereas theory and therapy are in the foreground, much is said about the need of further research. All agree that there is such an entity concept as schizophrenia, but there is a great diversity of opinion about the details of its classification, especially from the understanding of the process and the diversification of treatment methodologies.

It is hoped that the U.S. Public Health Service will continue to make grants for similar symposia on psychiatric subjects about which there is divergent opinion and therefore need of further light. The panels composing the symposium are the "top drawer" of American psychiatry. Any interested person could do no better than to browse in a very discriminating manner through this diversified presentation.—Frederick L. Patry, M.D.

continued on page 292

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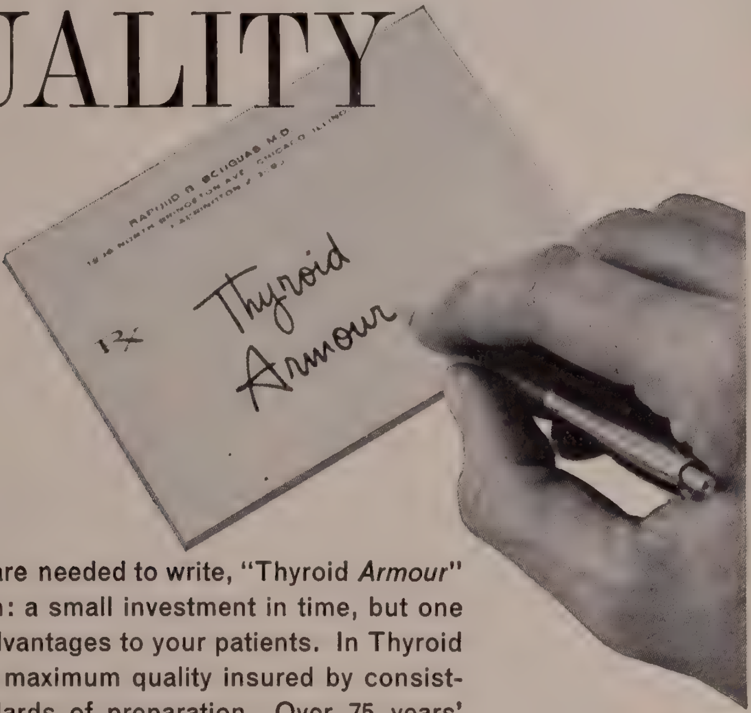

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continued from page 290

Letters to My Son. By Wendell J. S. Krieg, Ph.D. Sextodecimo of 82 pages. Evanston, Ill., Brain Books, 1960. Cloth, $3.00.

This eminent neuroanatomist has written a well-received, frank, and inspirational series of articles of advice to a fictional son. This "son" has chosen to follow in the footsteps of his adopted father and become a professor of medical science in a businessman's world. Finances and advances in position are stressed. Advice on how to cope with the duties, demands, and frustrations placed on the teacher, including his investigative, administrative, and political challenges, is given. Advice on the importance of being a man of parts and the enjoyment of life is given. Touched on is the inherent desire and ability of the enviable scholar who on his own can reach great heights to the glory of the university. Our standards of education need a fresh viewpoint.—BERNARD SELIGMAN, M.D.

Hypothermia for the Neurosurgical Patient. By Antonio Boba, M.D. Octavo of 124 pages, illustrated. Springfield, Ill., Charles C Thomas, 1960. Cloth, $6.00.

This monograph may be divided into three basic sections: hypothermia in general, the anesthetic management of a neurosurgical patient under hypothermia, and the technical aspects of hypothermia.

The first section is the most instructive. The physiologic deviations in the entire patient which are produced by hypothermia are outlined with illustrative tables and graphs.

Anesthesiologic procedures from premedication to the recovery room are described minutely. The reviewer cannot accept the author's statement, "cyclopropane cannot be used because it is explosive (the cautery is invariably used), but ether, which is also explosive, may be administered using certain safe precautions." The latter are not mentioned, apparently because they do not exist. The reviewer considers such practice dangerous and illegal. The text is marred by many misspelled words and poor proofreading.

This book is most useful to the anesthesiologist who needs detailed description of the management of a patient with an intracranial vascular tumor or anomaly.—SAMUEL BERKOWITZ, M.D.

Ciba Foundation Colloquia on Endocrinology. Volume 13 Human Pituitary Hormones. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Cecilia M. O'Connor, B.Sc. With 86 illustrations. Octavo of 336 pages. Boston, Little, Brown and Company, n.d. Cloth, $9.50.

This is our best foot forward in an attempt to define, delineate, and purify various fractions of the pituitary gland. The attempt is made to understand the "cross over" reactions of the metabolins and gonadotropins as well as their effect on target organs and metabolic processes. It is fascinating.

Thirty-two international authorities with nine American scientists discuss our knowledge of the pituitary gland. Especially noteworthy are the immunologic studies of the human growth hormone, the structure of the melanocyte-stimulating hormone by Iruan Harris, and the purification of the growth hormone by Li.—BERNARD SELIGMAN, M.D.

Pharmacology. The Nature, Action and Use of Drugs. By Harry Beckman, M.D. Second edition. Quarto of 804 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $15.50.

Now in its second edition, this text is addressed primarily to the medical student. Because of its adaptability to quick reference and its informativeness, it can be useful also for general reference to refresh a point or to obtain a quick, although boldly drawn, picture of a particular therapy. It is not, nor is it purported to be, a substitute for the more comprehensive pharmacology texts as Goodman & Gilman's (Macmillan) or Drill's (McGraw-Hill) when a detailed exposition of a subject is sought. But the book is more articulate and contains more information than Oldham's *Essentials of Pharmacology*, one of the better of the short texts.

The book is organized by the pharmacologic effect of drugs on organs and drug effects. Chapters include titles such as drugs that effect improvement in anemias (hematinics), drugs that lessen blood coagulability (anticoagulants), and drugs that increase the production of urine (diuretics). The remainder of the book conforms to that pattern.

The practicing physician will find quite useful and interesting a 10-page chapter on the untoward effects of drugs which contains a list of 100 commonly used drugs. That list provides data on pharmacologic action, therapeutic use, and the most serious side-effects, although these are not the most frequently encountered side-effects. This book is as creditable as the first edition, brought up to date.—ERWIN DI CYAN, PH.D.

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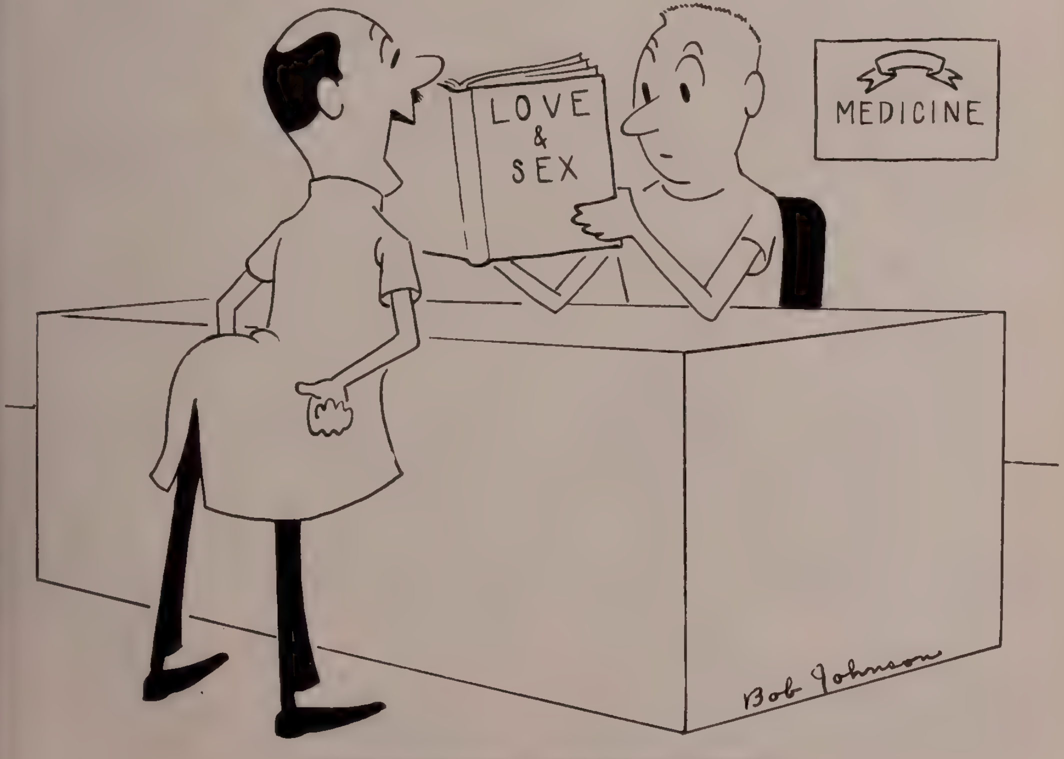

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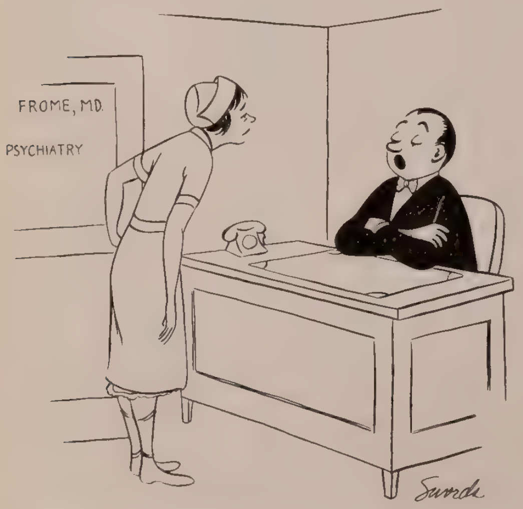

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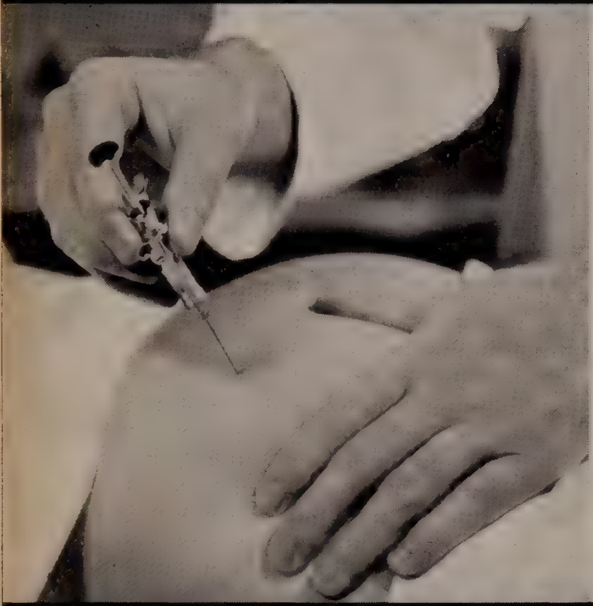

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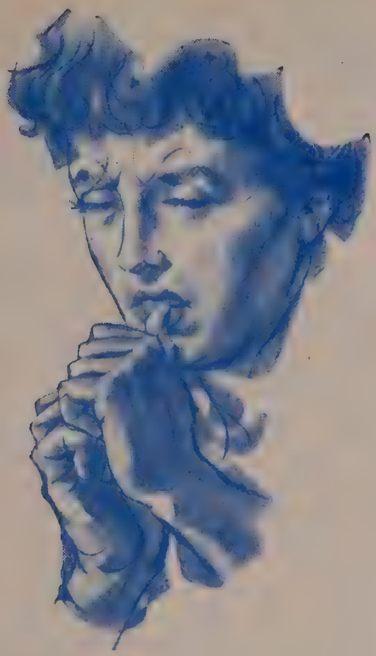

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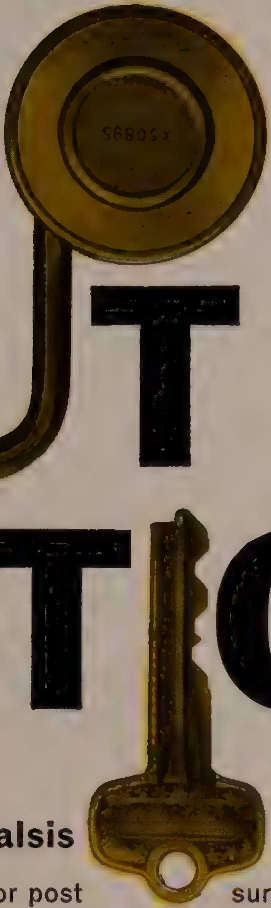

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*eunoia: A normal mental state (Stedman's Medical Dictionary).

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Vitamin B-1 (Thiamin Mononitrate)	10 mg.
Vitamin B-2 (Riboflavin)	10 mg.
Niacinamide	150 mg.
Vitamin B-6 (Pyridoxine HCL)	1 mg.
Calcium Pantothenate	10 mg.
Vitamin C (Ascorbic Acid)	150 mg.
Vitamin E (Succinate)	12 Int. Units
Rutin	25 mg.
Citrus Bioflavonoid Complex	25 mg.
Choline Bitartrate	50 mg.
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Vitamin K (Menadione)	1 mg.
Nucleic Acid	25 mg.
Yeast Enzymatic Hydrolysate	25 mg.
Glutamic Acid	12.5 mg.
Glycine	12.5 mg.
Cysteine HCL	12.5 mg.
Iron (from Ferrous Gluconate)	20 mg.
Manganese (from Manganese Sulfate)	1 mg.
Copper (from Copper Sulfate)	0.45 mg.
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SUPPLIED: in bottles of 100 Tablets.

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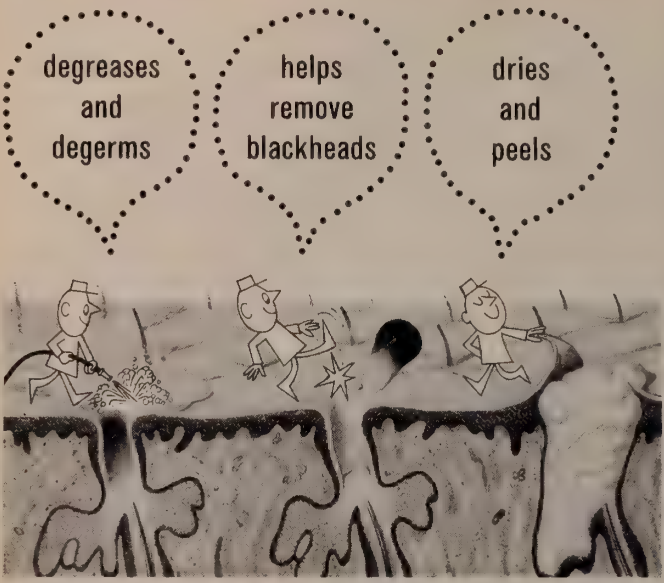

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Supplied—Fostex Cake, bar form. Fostex Cream, 4.5 oz. jars. Also used as a therapeutic shampoo in dandruff and oily scalp which often accompanies and aggravates acne.

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The physician can measure the basal metabolic rate by means of oxygen consumption. But he has no instrument—no objective test—for measuring comfort.

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Each tablet contains Alphadrol (fluprednisolone) 0.75 mg. or 1.5 mg.
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Precautions and contraindications

Patients on Alphadrol will usually experience dramatic relief *without* developing such possible steroid side effects as gastrointestinal intolerance, weight gain or weight loss, edema, hypertension, acne or emotional imbalance.

As in all corticotherapy, however, there are certain precautions to be observed. The presence of diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, renal insufficiency, or active tuberculosis necessitates careful control in the use of steroids. Like all corticosteroids, Alphadrol is contraindicated in patients with arrested tuberculosis, peptic ulcer, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia, or varicella.

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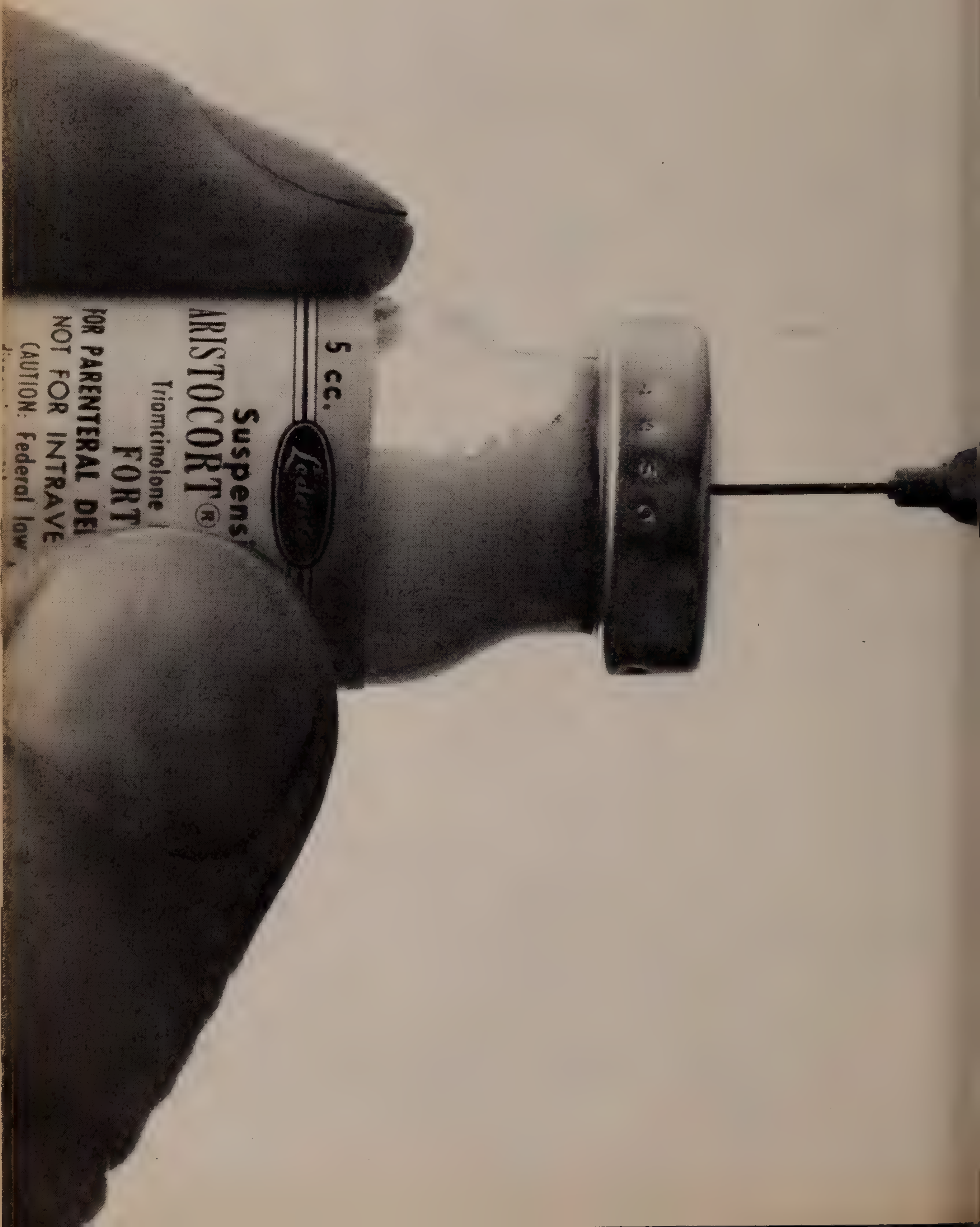
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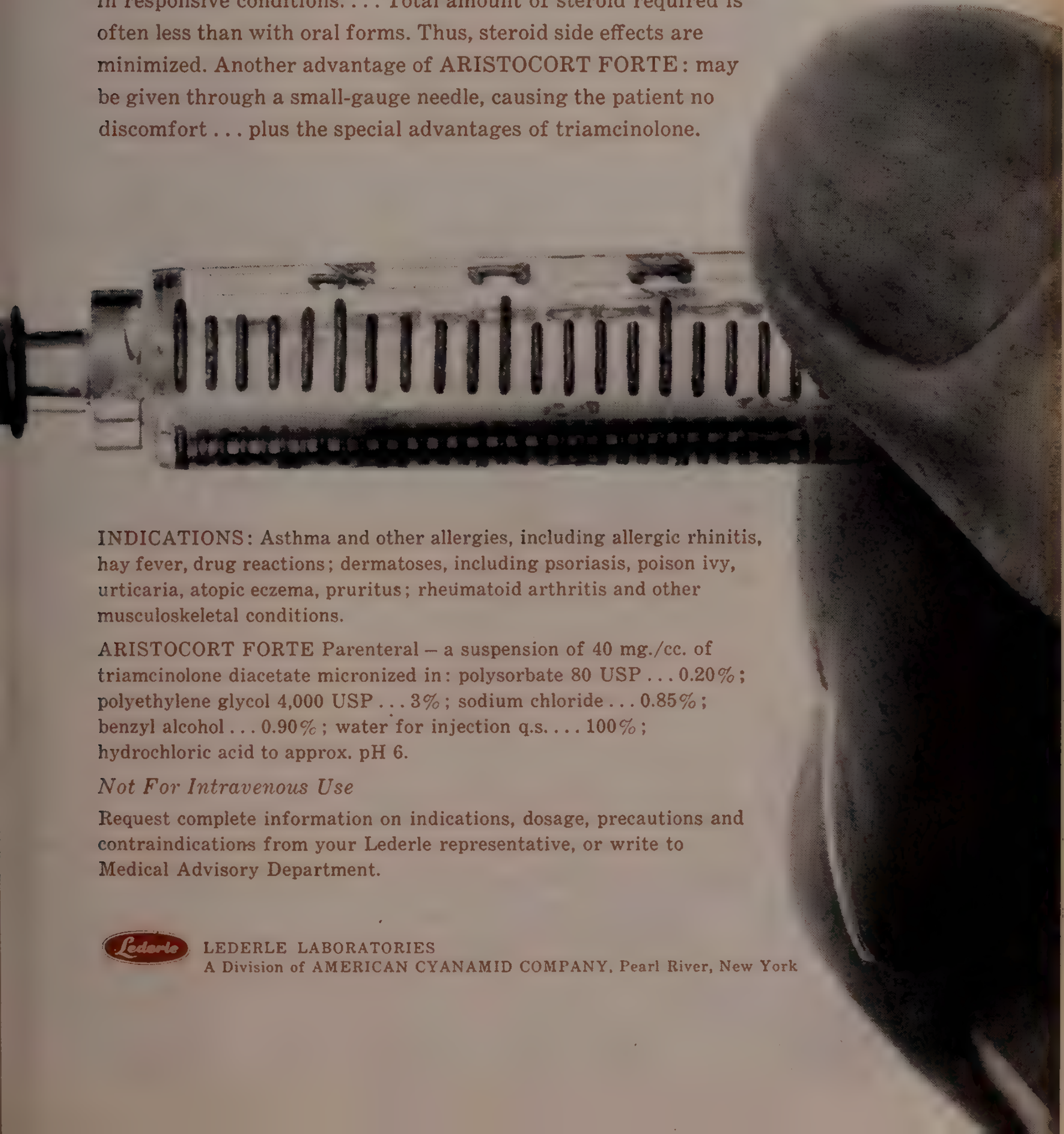

INDICATIONS: Asthma and other allergies, including allergic rhinitis, hay fever, drug reactions; dermatoses, including psoriasis, poison ivy, urticaria, atopic eczema, pruritus; rheumatoid arthritis and other musculoskeletal conditions.

ARISTOCORT FORTE Parenteral—a suspension of 40 mg./cc. of triamcinolone diacetate micronized in: polysorbate 80 USP . . . 0.20%; polyethylene glycol 4,000 USP . . . 3%; sodium chloride . . . 0.85%; benzyl alcohol . . . 0.90%; water for injection q.s. . . . 100%; hydrochloric acid to approx. pH 6.

Not For Intravenous Use

Request complete information on indications, dosage, precautions and contraindications from your Lederle representative, or write to Medical Advisory Department.

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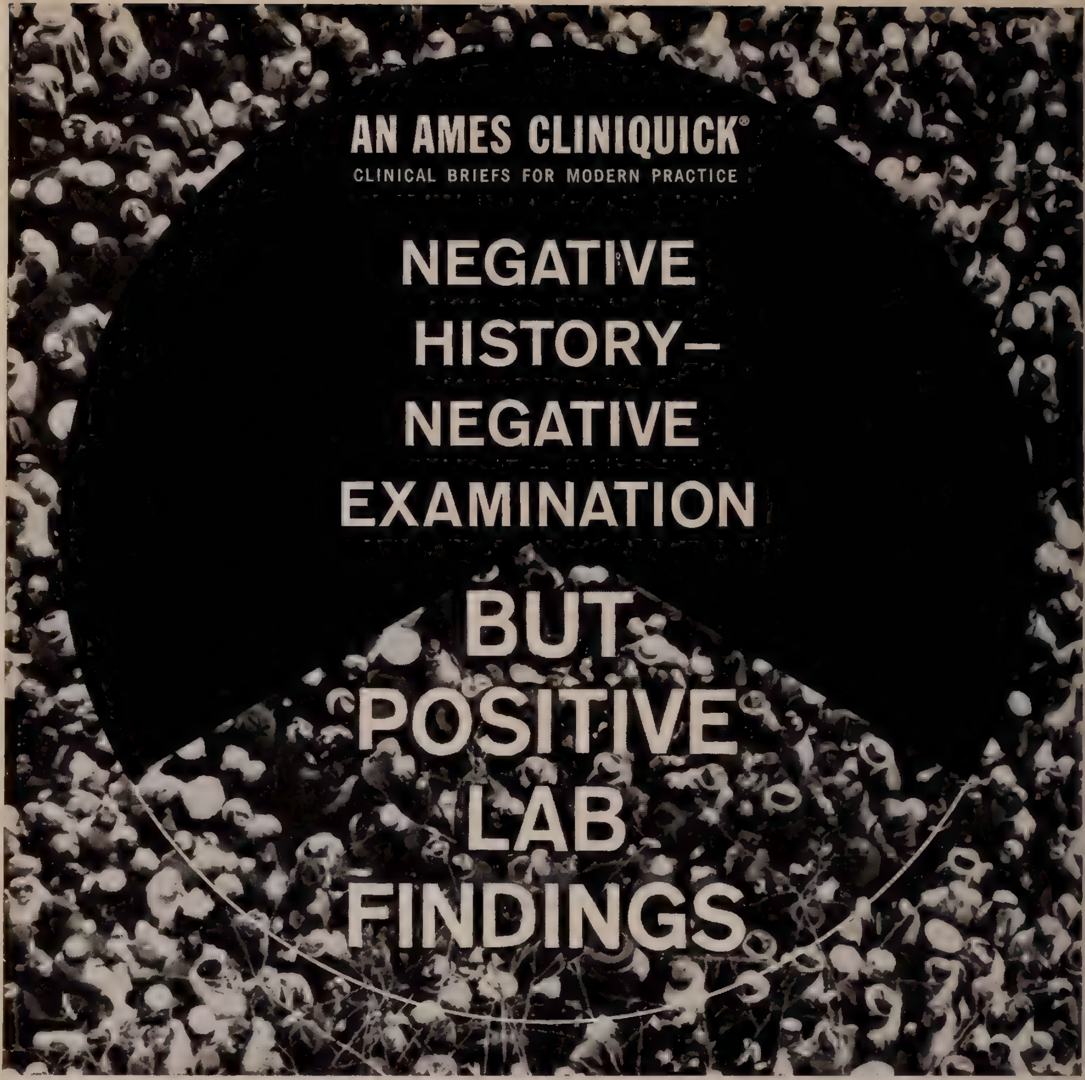
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BUT POSITIVE LAB FINDINGS

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*Schenthal, J. E.: J.A.M.A. *172*:1 (Jan. 2) 1960.

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Niedelman, M.L.: Am. Pract. & Digest Treat., 10:1001, 1959.

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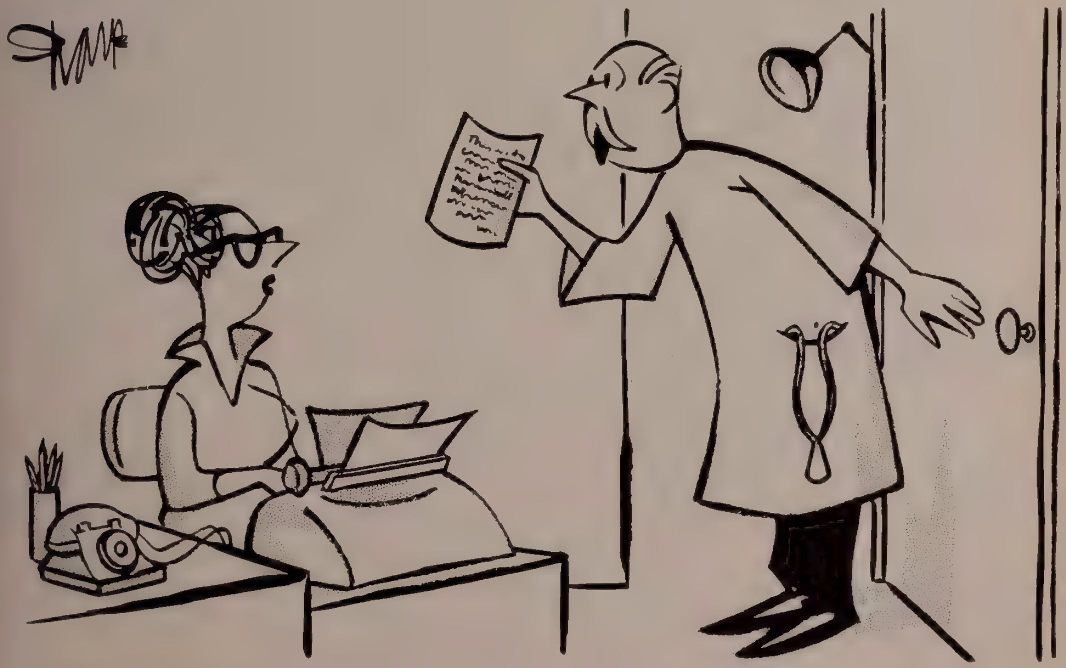

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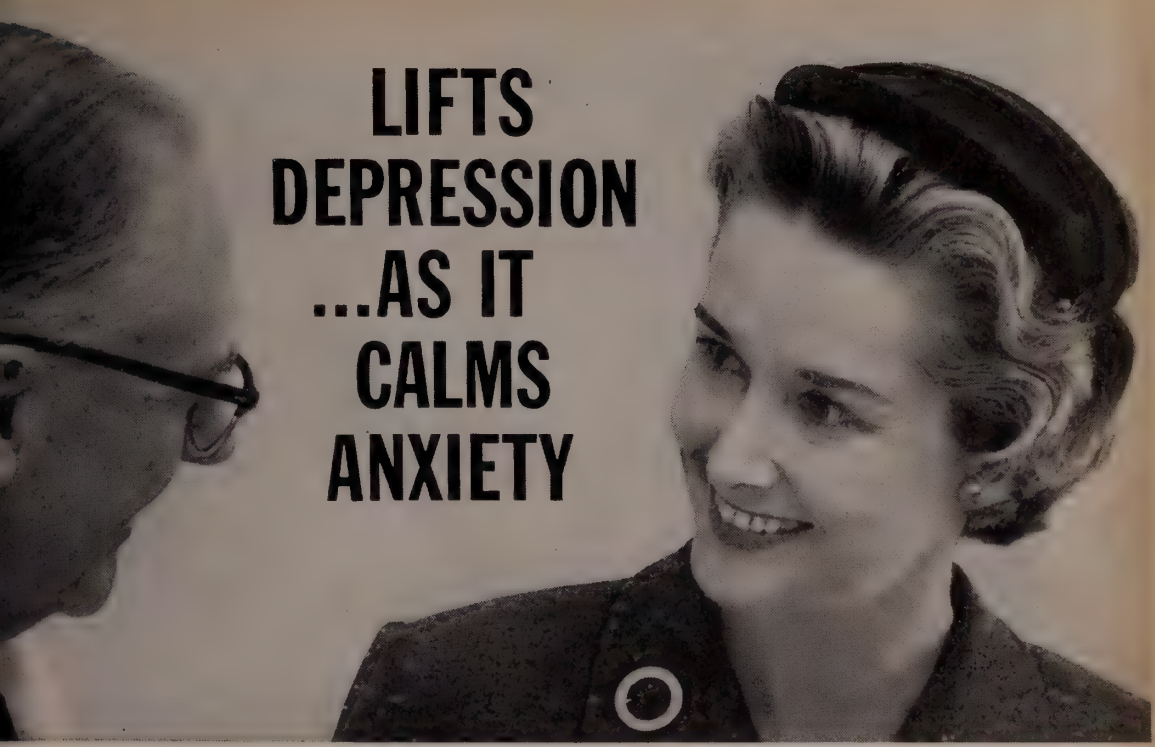

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Deprol's balanced action avoids "seesaw" effects of energizers and amphetamines. While energizers and amphetamines may stimulate the patient – *they often aggravate anxiety and tension.*

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Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

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or other
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. . . for hours

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*Ayd, Frank J., Jr.: Drug-induced Extrapyramidal Reactions: Their Clinical Manifestations and Treatment with Akineton. Psychosomatics 1:143 (May-June) 1960.

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The reason Capla has no serious side effects is the unique way it works. Unlike other agents, Capla acts on the blood pressure control centers in the brainstem to lower peripheral resistance, without upsetting the autonomic nervous system or electrolyte balance. Therefore, it cannot produce the side effects of Rauwolfia, ganglionic blocking agents or the diuretics.

In 755 hypertensive patients treated with Capla, the only side effects observed with any frequency were mild, usually transient, drowsiness, which usually disappeared spontaneously or after a minor dosage reduction and occasional lightheadedness.

DOSAGE: the recommended dose of Capla is one 300 mg. tablet three or four times daily, before meals and at bedtime. The dosage should be adjusted to individual requirements; for example, older patients may require lower dosage.
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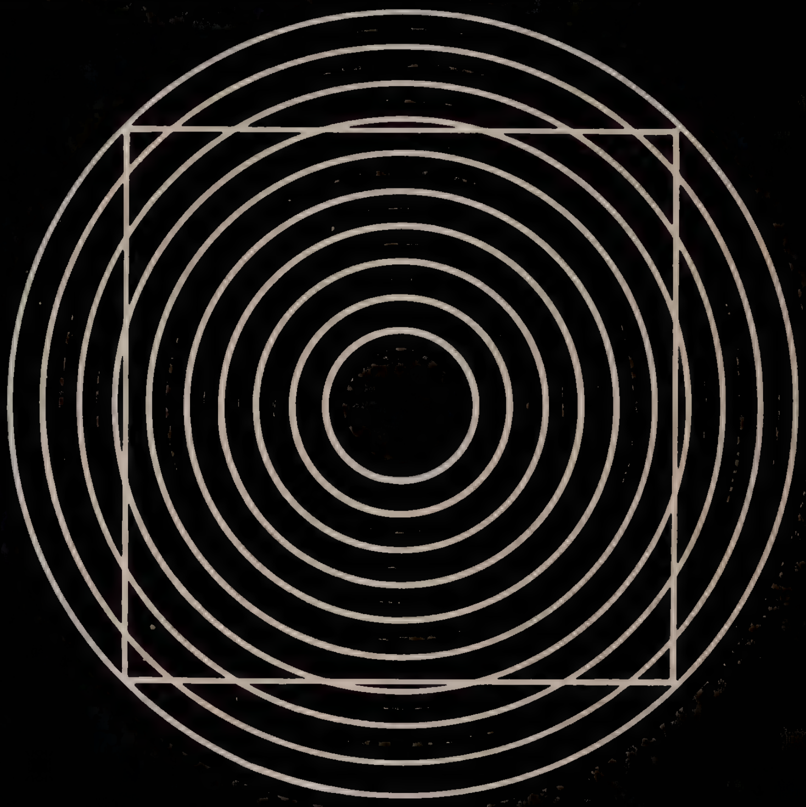

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[1] Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.

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Fancies, fallacies, and pharmacology

Of drugs we have an abundance—this is a matter of gratification not a cause for complaint. The problem does not lie in having many drugs but in selecting the optimum drug for treatment. Fortunately, patients are not placed into a Procrustean bed to fit the symptoms or conditions which are prescribed on the labeling of a drug and which it purports to treat; conversely, the drug—especially a new drug—is viewed from the standpoint of how it may serve the patient. This is the heart of the problem in selecting the drug to prescribe. And in making the selection, the physician depends in great measure on the literature supplied by the manufacturer of a given drug.

The literature tells the truth. It is compelled to do so by a law enforced by criminal penalties. But that does not solve the problem of selection. The literature which is supplied is essentially a collection of facts on which one must perforce depend.

In putting his trust in the literature accompanying or relating to a drug, the physician puts a great deal of weight on the objectivity with which the evidence was collected. In his determination the physician looks for the conventional devices which are used in the attempt to reduce subjective impressions and to enhance objectivity in reported results. Among these devices are the test methods, which are used toward the aim of enhancing objectivity. The use of placebos and double-blind designs of experiment are reputed to intensify an objective result. Charts and graphs are highly prized to help one gain an objective view. Tests done by the use of radioactive tracers are highly esteemed; they lend prestige and a scholarly air to an investigation.

In that milieu the terms objective, control, and statistically significant set off a series of pleasant signals; these are good labels and may be called "purr" symbols. Conversely, such terms as side-effect or psychogenic set off a series of cacophonous signals; these are bad labels or "slur" symbols.

We normally react to "purr" symbols as well as to "slur" symbols. The net result is a reaction to a label rather than to the substance to which the label is affixed. This self-delusional system will continue—and will grow worse—as long as we allow ourselves to remain conditioned and to respond to labels before we examine whether or not the label a drug wears fits it.

It is unfortunate that methodology has been sold so widely and well that it becomes an end in itself. Many investigators devote their productive lives to the development of methods. Indeed, it is imperative that we have reliable methods; advances were frequently delayed until an accurate method was developed by which a change could be demonstrated. But the user, in this case the prescribing physician, is pulled along the stream of methodology as such, whereas he should ask himself what the method, which is cited so authoritatively, adds to the pertinent use of the drug.

For example, a report that a given substance has been studied clinically by the use of radioactive isotopes—a valuable "purr" symbol—does not mean necessarily that the substance so studied is utilized by the body. And if it is utilized and converted, does it cause an amelioration or improvement in the condition in which it was used?

This is not readily apparent from a summary of an article. The whole paper must be read. Then it must be considered whether what is demonstrated by the clinical account is a relevant result or a display of radiotracers used like fireworks.

This question suggests itself: Has the investigator or reader discarded an observation which, although subjective, is pertinent, in favor of an objective result that is not?

Another method deals with graphs—also a "purr" symbol. Bar graphs may be so reproduced that, although they reflect the truth, they may be visually misleading. One neat method is to cut out the middle of a bar graph which may then show that in a comparison between two substances A is twice as good as B. This illusion is produced by showing that at the top the end of bar A is twice as tall as bar B, whereas the full-length bars may show only a slightly greater height of A as compared to B. The figures are there, and the facts are given, but the visual impression is grossly misleading.

The fallacy of the big number is one to which we readily succumb in our delusional system. There is almost automatically greater confidence reposed in a study of 1,000 patients than in one of 25 patients. Unquestionably, the greater the number of trials, the more representative the sampling, and the greater opportunity exists for a more thorough, hence more valid, evaluation. But the mere existence of a large number does not confer, ipso facto, a virtue. Fallacies may be embodied in a large study which may vitiate its validity.

This question suggests itself: What opportunity was taken to take advantage that a large number offers?

It was pointed out that the term psychogenic is a "slur" symbol. True as that may be in pharmacology, where the effect of a drug is expected to be the result of interaction between the drug and metabolism, the term itself is not a stigma. It should not be regarded as a bad label. For example, the results of treatment by psychotherapy, especially analysis, are psychogenic. In a recent Congressional hearing it was brought out that the salubrious effect of the physician's person in his relation to his patient is psychogenic, because the patient's confidence in his physician is " . . . a factor that is extremely necessary in the effective treatment of disease."* To affix a bad label to the term psychogenic in this context is self-contradictory and incongruous. It is just as incongruous to shrug off as psychogenic, side-effects or lack of effect reported by a patient from a drug given to him by a physician with whom there is a hostile relationship. It may be psychogenic, but it is thoroughly real.

The deprecatory connotation of the placebo gives rise to an extraordinary contradiction in the concept of the placebo itself. This is clear in the case of the hypnotic agents or so-called tranquilizers that are available for over-the-counter sale. Laymen are warned that only tranquilizers which are available on prescription are active tranquilizers. Indeed, tranquilizers which are sold over the counter are not tranquilizers at all. But in such a highly suggestible situation as tension, placebos can be as active as more powerful drugs. A wealth of clinical data as well as the experience of every physician support that notion. To state that tension-allaying drugs available over the counter are inactive—true as that may be pharmacologically—destroys the foundation of the placebo concept. The reason is that clinical studies using placebos are based on the premise that an effect is exerted even by inactive drugs.

By logical extension the so-called tranquilizers sold over the counter should be among the safest of drugs since inactive drugs have no toxic side-effects. Yet activity for their intended purpose may be achieved by psychogenic means. They are at least as active as lactose.

Other controls—whether they be devices or inherent in the structure of the design of an experiment—are generally regarded with a great deal of security; but recognition must be given to the possibility that they may be false prophets not worthy of the blind faith with which homage is paid to them.

Controls aid, but they never assure that the answer they supply is determinative, or even helpful. For example, anticoagulants have been assessed by the use of elaborate and adequate controls. But views on their usefulness are now divided about evenly. One would expect well-controlled tests to be determinative and conducive to a preponderance of one opinion rather than to evenly divided opinions. And certainly, monitored by prothrombin-type determinations, the effect of anticoagulants cannot be suspected at all of being psychogenic.

Controls are always tested against various pitfalls which may arise. Often they are not tested against one criterion: clear thinking. There is something casuistic when thinking is delegated to gimmicks called objective evidence, or double-blind tests, or placebos, or statistical significance, or radioactive tracers, or anything else. When nihilistic investigators make the smug comment that with many diseases placebos are as effective as the drugs themselves, this question suggests itself: Is there anything wrong with the method, with drugs themselves, with placebos, or with the investigators? The abdication of further curiosity bespeaks uncertainty in interpreting findings.

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* Washington News: Dangers of controlled drug advertising explained, J.A.M.A. **177**: 25 (Sept. 9) 1961.

There is no objection to the use of placebos per se or methodology per se. Methods of study have far-reaching implications in medicine. But further productiveness does not lie in a refinement of placebos or other methods but in a re-evaluation of our thinking and knowing. Contradictory findings take place when method becomes an end in itself and takes precedence over substance, or when pushing decimal points one more space in the attempt to be more precise becomes an end in itself. When that occurs, perhaps the remedy may lie in a fundamental re-evaluation of our thinking.

One objective of this editorial is to threaten the dependence we place on labels. Another objective is to serve as a reminder that placebos, control structures, radioactive isotopes, statistics, graphs, and so forth are merely instruments for evaluation. They represent a method, a means to an end. Therefore, one should not be so impressed by method as to lose sight of the objective. An example where method becomes an end would be the discarding of a subjective finding that is relevant in favor of an objective one that is not. ERWIN DI CYAN, PH.D.

The risk of snow shoveling

Although definite actuarial statistics are not available on deaths attributable to the exertion of snow shoveling there are indirect ways to measure this problem. The United States Weather Bureau has matched up climatologic data with newspaper accounts of deaths and has kept a running record of these over the years. Following a snowstorm on January 7, 1957, it was recorded for the New England area that 6 deaths were attributed to coronary accidents brought on by embattling snow. A similar storm on January 10, 1957, in the New York area matched up with at least 2 deaths from heart failure, 1 from shoveling snow and the other from the exertion of putting chains on a car. From Missouri during a snowstorm on January 22, 1957, it was reported that 6 men died of heart attacks brought on by exertion in the storm.

On January 12, 1960, Massachusetts reported 16 deaths during the snowstorm of that day, attributable to snow shoveling and pushing stalled cars. During that same storm New Jersey reported 52 deaths due to exposure, exhaustion, and heart attacks from overexertion.

As a result of a heavy snowstorm on January 2 to 3, 1961, 5 deaths were recorded in the press in Illinois as due to the exertion of shoveling snow, and in Pennsylvania in the extremely heavy snowstorm of January 3 to 4, 1961, the claim was made that all the reported deaths except those due to motor accidents were caused by overexertion while shoveling snow.

We as physicians can reinforce this inferential data with personal knowledge of cases that perhaps did not get into the newspapers. We can also serve our patients by warning them of the danger inherent in the spontaneous exertion involved in walking in deep snow, shoveling it, pushing cars in it, and trying to stretch tight chains on overinflated tires.

It is better for the unconditioned person to "let George do it." Anyone over forty who does not walk a mile a day regularly ought not to contemplate even lifting the shovel out of the corner.

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Further, during Enovid therapy, certain symptoms typical of normal pregnancy may be noted in some patients, such as nausea—which is usually mild and disappears spontaneously within a few days—breast engorgement, some degree of fluid retention, and often a marked sense of well-being. There is no androgenicity. Enovid *is as safe as the normal state of pregnancy.*

THE BASIC APPLICATIONS

1. Correction of menstrual dysfunction. *Emergency* treatment of severe dysfunctional uterine bleeding is promptly effective following the administration of Enovid in larger doses. *Cyclic* therapy with Enovid controls less severe dysfunctional uterine bleeding. In amenorrhea *cyclic* therapy with Enovid establishes a pseudodecidual endometrium providing the patient has endometrial tissue capable of response.

2. Ovulation suppression (to suspend fertility). For this purpose Enovid is administered *cyclically,* beginning on day 5 through day 24 (20 daily doses). The ovary remains in a state of physiologic rest and there is no impairment of subsequent fertility. When Enovid is prescribed for this *cyclic* use over prolonged periods, a total of twenty-four months should not be exceeded until continuing studies indicate that its present lack of undesired actions continues for even longer intervals. Such studies are now in their seventh year and will regularly be reviewed for extension of the present recommendation.

3. Adjustment of the menses for reasons of health (impending hospitalization for surgery, during treatment of Bartholin's gland cysts, acute urethritis, rectal abscess, trichomonal or monilial vaginitis), or other special circumstances considered valid in the opinion of the physician. For this purpose Enovid may be started at any time in the cycle up to one week before expected menstruation. Upon discontinuation, normal cyclic bleeding occurs in three to five days.

4. Endometriosis. *Continuous* therapy with Enovid corrects endometriosis by producing a pseudodecidual reaction with subsequent absorption of aberrant endometrial tissue.

5. Threatened and habitual abortion. Enovid should be used as *emergency* treatment in *threatened abortion* although symptoms may occur too late to be reversible. *Continuous* therapy with Enovid in *habitual abortion* is based on the physiology of pregnancy. Enovid provides balanced hormone support of the endometrium, permitting continuation of pregnancy when endogenous support is otherwise inadequate.

6. Endocrine infertility. Enovid has been used successfully in *cyclic* therapy of endocrine infertility, promoting subsequent pregnancy through a probable "rebound" phenomenon.

THE BASIC DOSAGE

Basic dosage of Enovid is 5 mg. daily in *cyclic* therapy, beginning on day 5 through day 24 (20 daily doses). Higher doses may be used with complete safety to prevent or control occasional "spotting" or breakthrough bleeding during Enovid therapy, or for rapid effect in the *emergency* treatment of dysfunctional uterine bleeding and threatened abortion.

Enovid is available in tablets of 5 mg. and 10 mg. Literature and references, covering more than six years of intensive clinical study, available on request.

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Combined Oral Hypoglycemic Therapy

To Improve Control of Diabetic Patients Unresponsive to Single Agents

MORTON LINDER, M.D.
Valhalla, New York
CHARLES WELLER, M.D.
Larchmont, New York
ALICE I. MACAULAY, M.D.
Valhalla, New York

From the Metabolic Clinic and the Department of Internal Medicine, Grasslands Hospital

THERE HAVE BEEN *many primary and secondary failures in oral hypoglycemic therapy. Because recent work has suggested that the two classes of oral hypoglycemic agents, the sulfonylureas and the biguanides, exert their effects at different sites and in different manners, a study was undertaken of the effectiveness on 40 cases of maturity-onset diabetes mellitus of combined therapy with the sulfonylurea, chlorpropamide (Diabinese), and the biguanide, phenformin (DBI). All of the cases were primary or secondary failures to chlorpropamide or phenformin used alone or were intolerant of one of the compounds. The maximum daily dosage level during the study was 150 mg. of phenformin and 500 mg. of chlorpropamide. The follow-up periods ranged from one to eighteen months, averaging seven and one-half months. Twenty-seven of the 40 previously inadequately controlled patients showed good or fair control while on the combined therapy, a salvage rate of 68 per cent. Ten patients exhibited poor control and were changed to insulin; the combined therapy was discontinued in 3 patients because of intolerance, although they were well controlled chemically. To date no secondary failures have occurred. When used together, the combination of chlorpropamide and phenformin can minimize potential toxicity and/or side-effects because smaller doses of each can be used for increased therapeutic effectiveness.*

OPTIMISM CONCERNING the introduction of the newer oral hypoglycemic agents was bolstered by the initial favorable response of large numbers of patients to one or another of the recently available agents. This continued, although there were many primary failures. Unfortunately, as the duration of the therapy lengthened, the incidence of secondary failures in sulfonylurea-treated patients increased to a disturbing extent. The rate of occurrence of secondary failure has been calculated by one group to be 3 per cent per month.[1,2] Similarly, the barriers of primary and, later, secondary intolerance or toxicities supervened, ranging from nausea to jaundice. As defined by Williams,[3] the term "primary failure" often has been applied when the therapeutic response has been poor within the first one to four weeks. "Secondary failure" is said to occur when the patient has been under satisfactory control for several weeks and then fails to respond adequately. Owing to the increasing incidence of therapeutic failure and intolerance, we are beginning to see a shrinking segment of the diabetic population

TABLE I.—Criteria for degree of diabetic control

Control	Fasting Blood Sugar Range* (Mg. per 100 Ml.)	Remarks
Good to excellent	From 100 to 130	Free from symptoms, no persistent glycosuria.
Fair	From 130 to 190	Free from symptoms, no persistent glycosuria.
Poor	Over 190	And/or ketonuria, persistent glycosuria, and persistent symptoms of diabetes.

* Folin-Wu method.

which is responsive to oral therapy. In many quarters the earlier optimism has given way gradually to guarded conservatism.

Recent work has suggested that the two classes of oral hypoglycemic agents in current use exert their effects at different sites and in different manners. The sulfonylureas are dependent on functioning pancreatic beta cells for their action, which seemingly is the release of additional endogenous insulin into the blood stream.[4,5] The biguanides, on the other hand, can exert their predominantly peripheral effect even in the absence of intact pancreatic beta cells by a mechanism which is not as yet completely known.[6,7] Both sulfonylureas and biguanides may exert additional effects on the liver.[6]

In view of the differing actions of the sulfonylureas and biguanides, it seemed desirable to study the combined effects of these two classes of compounds in patients who had exhibited primary or secondary failure or intolerance to any of the compounds used singly. A study of this type was first reported in the literature by Beaser,[8] who found such combinations of drugs helpful. Recent reports show similar favorable results.[9,10]

The following is a report of 40 cases of diabetes mellitus studied under combined therapy with the sulfonylurea, chlorpropamide (Diabinese), and the biguanide, phenformin (DBI). Although we are aware of the slightly increased incidence of toxicity observed with chlorpropamide as compared with tolbutamide, we felt that the increased potency and longer duration of action of chlorpropamide warranted its use in this study.

Materials and methods

Forty maturity-onset diabetic patients, 37 of whom were ketoacidosis-resistant, were chosen from the metabolic clinic of a large county general hospital. All of them were primary or secondary failures to chlorpropamide or phenformin used alone, as defined by the criteria described earlier, or were intolerant of one of the compounds. The patients were screened throughout the study period for other diseases. They were evaluated for their reliability with regard to dietary adherence and prescribed oral hypoglycemic agent intake, emotional or social factors which might conceivably influence their carbohydrate metabolism, concomitant nondiabetic therapy, and other pertinent factors.

The patients who did not respond to adequate doses of chlorpropamide had phenformin added to their previous regimes. Conversely, those patients who failed to respond to adequate doses of phenformin had chlorpropamide added to their regimes. Fasting blood sugar, urinary glucose, urinary acetone, body weight, and other significant clinical findings were recorded at each visit. Laboratory determinations were made at frequent intervals. These determinations included hemograms, complete urinalyses, blood urea nitrogen, a cephalin flocculation test, alkaline phosphatase, chest x-ray films, and electrocardiograms.

Drug dosages were titrated according to the patients' needs and tolerance. On the basis of our own previous experience and other published reports, maximal dosage levels of 150 mg. of phenformin daily and 500 mg. of chlorpropamide daily were established arbitrarily as both safe and well tolerated. Patients whose control was found inadequate on maximal doses of both drugs were considered failures in control and were transferred to insulin therapy.

There is a lack of unanimity among workers in the field as to what constitutes good control of diabetes, and the words "good, fair, and poor" are meaningless unless they are defined numerically. Our

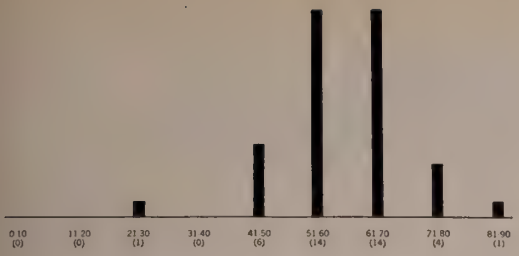

FIGURE 1. Age range of patients.

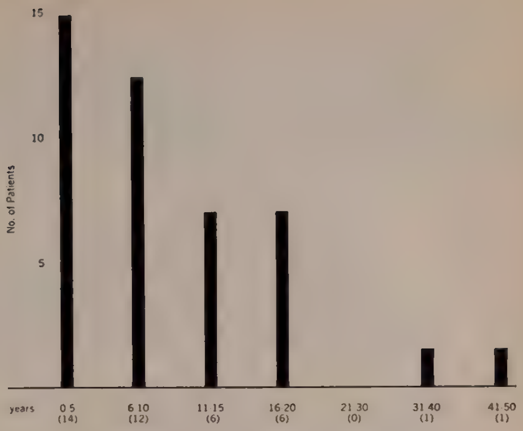

FIGURE 2. Duration of diabetes.

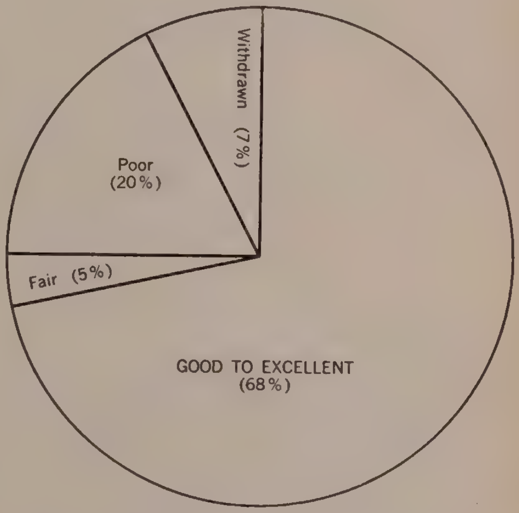

FIGURE 3. Control of combined therapy.

criteria for evaluation are outlined in Table I.

Results

On previous single therapy there were 42 therapeutic failures: 16 patients treated with phenformin and 26 patients treated with chlorpropamide. Two patients failed on both drugs singly. Thirty-seven of the patients were of ketoacidosis-resistant type, and 3 patients had occasional slight acidosis. Physically, 16 patients were obese, 6 were asthenic, and 18 were of average proportions. Twenty-seven patients were female, and 13 patients were male. Additional patient data are given in Figures 1 to 3.

The following are 2 typical case histories.

Case reports

Case 1. A sixty-year-old obese woman with ketoacidosis-resistant diabetes of fifteen years duration had been maintained on dietotherapy for thirteen years. She developed vascular disease of her lower extremity, necessitating the amputation of her left leg. Insulin was needed during and following the stress of her surgery, and she was unable to achieve good diabetic control on either phenformin or chlorpropamide singly. Combined therapy was started with 75 mg. of phenformin and 100 mg. of chlorpropamide. The chlorpropamide was soon raised to 200 mg. for three months, then lowered to 100 mg. daily as a maintenance dose. Her fasting blood sugar remained between 100 to 140 mg. per 100 ml. for the duration of the study. This patient's record of treatment is shown in Figure 4.

Case 2. A sixty-five-year-old ketoacidosis-resistant obese male with diabetes of eleven years duration had required 15 units of NPH insulin for control of his diabetes during the first ten years of his disease. The patient failed to respond to either sulfonylurea or biguanide therapy when those drugs were given singly and refused to take insulin for control. Relatively small doses of 100 mg. of chlorpropamide and 12.5 mg. of phenformin three times a day readily controlled his diabetes. He was able to maintain his fasting blood sugar levels within the desired range. The patient's treatment data are shown in Figure 5.

Comment

The follow-up periods in this study ranged from one to eighteen months, averaging seven and one-half months. Twenty-seven of our 40 previously inadequately controlled patients showed good or fair control while on the combined therapy, a salvage rate of 68

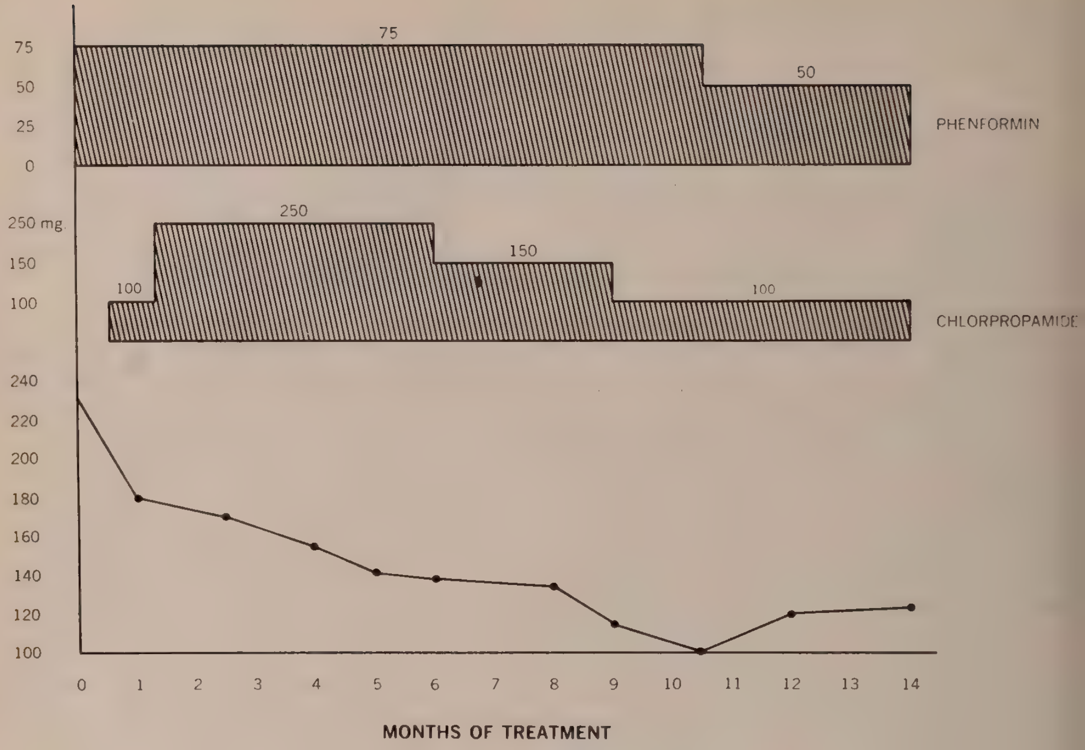

FIGURE 4. Case 1. Data of treatment.

per cent. Ten patients exhibited poor control and were changed to insulin therapy. The combined regime was discontinued in 3 patients, although they were well controlled chemically. These were included in our results and were reported as failures. Two of these patients displayed gastrointestinal intolerance while they were on their combined therapy. The third patient, with chronic alcoholism, developed abnormal liver function tests, at which time the chlorpropamide was withdrawn as a precautionary measure. His dose of chlorpropamide had been 250 mg. daily.

Our longest follow-up in this study was eighteen months. This period is too early to predict the emergence of secondary failures to this regime, but to date none have appeared. The large percentage of patients who exhibited improvement in the control of their diabetes with the combination of chlorpropamide and phenformin suggests the usefulness of the combination of these drugs in selected patients. This type of therapy could be used in patients starting treatment with oral hypoglycemic agents to utilize the combined "therapeutic target" effect of both drugs. When used together, these compounds can minimize potential toxicity and/or side-effects because smaller doses of each can be used for increased therapeutic effectiveness. Patients who require large doses of a single oral hypoglycemic agent may be changed to smaller doses of both drugs. Similarly, patients who are sulfonylurea failures may respond effectively to the combined therapy.

Summary

Forty maturity-onset diabetic patients were studied, all of whom had been primary or secondary therapeutic failures to either phenformin or chlorpropamide alone. Since sulfonylureas and biguanides, as represented in this study by chlorpropamide and phenformin respectively, seemingly exert their metabolic effects in different manners, it

seemed desirable to study the effects of the combined administration of these drugs.

With submaximal doses of each drug in effective combination 27 of the 40 patients achieved good or fair regulation with good tolerance, a salvage rate of 68 per cent. All 40 patients previously had been therapeutic failures with either chlorpropamide or phenformin alone. Observation periods ranged from one to eighteen months at the time of the study, averaging, seven and one-half months. Ten patients were therapeutic failures within the limitation of our arbitrarily chosen dosage ceiling. Three patients were withdrawn from the combined regime despite excellent-to-good chemical control, 2 were withdrawn because of gastrointestinal intolerance to their drugs, and the third was withdrawn because of abnormal liver function tests not related to their treatment.

This method of therapy in selected patients who exhibited primary or secondary therapeutic failures to a single oral hypoglycemic agent appears to be an additional means of improving the degree of diabetic control in the maturity-onset diabetic patient.

This combination of oral agents is suggested in patients who currently require large doses of a single oral hypoglycemic agent and, additionally, in those patients in whom oral hypoglycemic therapy is about to be initiated. This method should insure the maintenance of, or improvement in, the control of their diabetes and at the same time bring the hazards of potential toxicity and/or side-effects to a minimum.

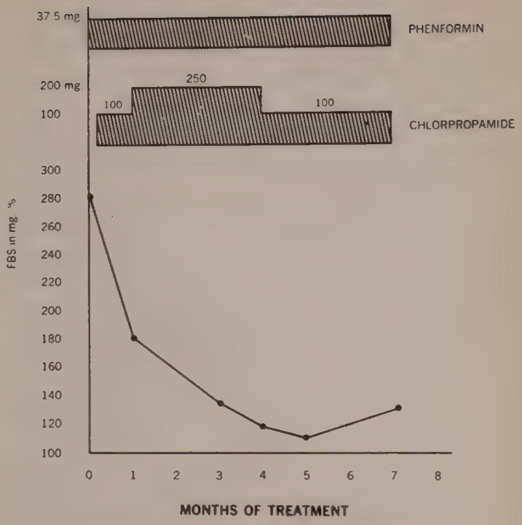

FIGURE 5. Case 2. Data of treatment.

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Vaginal Bleeding Secondary to Spontaneous Complete Rupture of Umbilical or Placental Vessels

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THIS PAPER is presented primarily to remind general physicians practicing obstetrics that vaginal bleeding late in pregnancy is not necessarily of maternal origin. Placenta previa, abruption, and carcinoma are stressed repeatedly in the literature, in medical schools, and in postgraduate training as the primary etiologic factors in third trimester bleeding, which indeed they are. However, only a scant literature recognizes that vaginal bleeding may be from a fetal source. Included are vasa previa, which has received some attention, and the relatively rare condition of a complete spontaneous rupture of the cord or placental vessels. Herein is a brief review of the latter problem with the addition of a case to the literature.

A review of the general pathology of the cord and placenta with their respective vessels may be found in Baden's[1] discussion and in Nesbitt's[2] textbook. Detailed studies of vasa previa likewise are available in the standard textbooks and to some extent in the literature.[3,4] With the mention of vasa previa as the major cause of fetal hemorrhage in the third trimester, further attention will be turned to the second remaining known cause of fetal bleeding, namely, the rupture of the cord and placental vessels. This latter problem may be subdivided as follows:[1]

1. Partial rupture, defined as bleeding into Wharton's jelly with the formation of a hematoma under the amniotic covering of the cord and placenta.
2. Complete rupture, disruption of both the cord vessel and amniotic covering.

Either complete or partial abruption of the cord or placental vessels may occur in vessels which are histologically normal or abnormal, for example, varicosities, aneurysms, and so forth.

Partial rupture of the cord and placental vessels is rare. Dippel[5] reviewed the literature and added 2 cases of his own in 1940 which brought the total of reported cases to 36. At Johns Hopkins Hospital he determined an incidence of 1 in 5,505 term or premature deliveries. The incidence of immediate fetal mortality in this series was 47 per cent, and with 2 additional perinatal deaths the mortality rose to 58 per cent. In 31 of the 36 cases in which the ruptured vessel was identified, rupture of the vein occurred in 28 and rupture of the artery in 3.

The complete rupture of a cord or placental vessel is more rare, there having been found 1 case of rupture of both umbilical arteries,[6] 1 of complete rupture of a single artery,[7] and 9 of complete venous rupture,[3,8-13] for a total of 11 cases to date. The case herein reported would appear to be the twelfth such report. Of the 12, only 2 infants reportedly survived the perinatal period. Of these 12 cases, including this one, 7 were associated with a velamentous insertion of the cord as the only noted pathologic condition. Cases of complete rupture occurred in association with each of the following pathologic findings: 2 cases of ruptured umbilical vein varicosity,[11,13] umbilical vein tear in association with a short cord or marginal insertion of the cord,[12] a placental vessel aneurysm,[8] and finally, a simple dilatation of the cord arteries on histologic examination.[6]

Short cord, inflammation,[1,14] trauma, or the sudden escape of excessive amniotic fluid have been mentioned as predisposing causes of umbilical vessel rupture along with velamentous insertion. Aneurysms, varicosities, and other histologic abnormalities of the vessels are mentioned rarely. A review of the problem as presented in the literature substantiates only velamentous insertion as the primary predisposing cause of abruption, with histologic abnormalities being the second most common cause. It would seem appropriate, therefore, to mention at this point that velamentous insertion of the cord has a noted incidence of between 0.5 and 1 per cent of all placentas.

It might be noted further that Torrey,[3] in his review of the problem of vasa previa noted the fact that although vasa previa had not been reported more than 100 times between 1801 and 1952, the "true incidence of vasa previa could not even be guessed." In view of the 1 per cent incidence of velamentous insertion (which is almost always associated with vasa previa), a higher incidence of both vasa previa and complete abruption of cord vessels might be suspected.

The signs and symptoms of the cord or placental vessel rupture obviously are determined by two facts, namely, whether the rupture is partial or complete and whether the amniotic sac is intact or ruptured.

In the partial rupture of a vessel with either intact or ruptured amniotic membranes (not to be confused with amniotic covering of the cord or placenta), the signs are those of fetal distress. How extensively these signs develop will depend entirely on the size of the hematoma formed and to what extent it mechanically obstructs the cord circulation. Partial rupture, therefore, is to be considered in a differential diagnosis of fetal distress when the more common causes have been excluded.

The complete rupture of the cord and placental vessels with the membranes intact produces signs of rapidly progressive fetal distress without any evidence of change in the maternal vital signs. Fetal death results promptly unless the infant is delivered either from below or by cesarean section. A careful examination of the cord and placenta after the delivery which demonstrates a tear of a vessel confirms the diagnosis. A diagnosis prior to delivery may be only suspected along with other causes of fetal distress.

VAGINAL BLEEDING *late in pregnancy is not necessarily always of maternal origin. It may be from a fetal source: vasa previa or complete spontaneous rupture of the cord or placental vessels. There have been only 36 reported cases of partial rupture of the cord and placental vessels and 12 of complete rupture. However, in view of the 1 per cent incidence of velamentous insertion, which is associated almost always with vasa previa, a higher incidence of vasa previa and complete abruption of cord vessels might be suspected. Rupture of the cord or placental vessels may occur in vessels which are histologically normal or abnormal. Complete rupture of the cord or placental vessels after the amniotic membranes have ruptured produces painless vaginal bleeding either prior to the onset of labor or in its first or second stages. This is usually not associated with any significant change in maternal vital signs but is associated with signs of rapidly increasing fetal distress. The presence in vaginal blood of large numbers of fetal red blood cells may be an indication of fetal bleeding. If, in the presence of the previously mentioned clinical findings, a live but extremely pallid, flaccid, nonbreathing or shallow-breathing infant is born in the absence of any known Rh factor problem, the diagnosis of hemorrhagic fetal shock should be considered immediately. The authors suggest that a smear of vaginal blood be taken during labor. The presence of nucleated fetal red blood cells in a relatively large quantity in the smear would focus attention on the necessity of prompt attention to the infant at delivery. Consultation is necessary to determine whether or not a cesarean section is indicated. In case of fetal hemorrhage, prompt transfusion is essential.*

A complete rupture of the cord or placental vessels after the membranes have ruptured produces painless vaginal bleeding either prior to the onset of labor or in its first or second stages. This is usually not associated with any significant change in the maternal vital signs, such as blood pressure, pulse rate, and so forth, but is associated with signs of rapidly increasing fetal distress. It was thought at one time that an examination of the vaginal blood for the presence of nucleated fetal red blood cells might confirm the diagnosis of fetal bleeding. Recently, it has been reported that nucleated fetal red blood cells may be found in the postpartum maternal circulation in varying concentrations.[15] Whether or not they also are found in the maternal circulation prior to the beginning of labor was not determined.

However, when one considers the fact that fetal red blood cells are responsible for the production of maternal antibodies in the Rh factor problem, it would seem logical to conclude that these same cells may be circulating prior to and during labor. In this event, the presence in vaginal blood of small numbers of fetal red blood cells may not at all confirm the source of bleeding as fetal. On the other hand, should they be found in large quantities, it certainly would point a finger in this direction. If, in the presence of the previously mentioned clinical findings, a live but extremely pallid, flaccid, nonbreathing or shallow-breathing infant is born in the absence of any known Rh factor problem, the diagnosis of hemorrhagic fetal shock should be considered immediately. Again, a prompt and thorough evaluation of the cord and placenta postpartum usually will provide all the evidence necessary to make an accurate diagnosis of a complete rupture of the cord or placental vessel, and thereby the treatment of the infant with replacement of blood becomes obvious.

Case report

A twenty-five-year-old white female, para 1, gravida 2, whose last menstrual period was April 12, 1959, was seen for the first prenatal visit on June 18, 1959. A vaginal examination revealed a small amount of blood-tinged vaginal discharge with no obvious bleeding from the endocervical canal. The uterus was consistent in size with the date, and a tentative diagnosis of threatened abortion was made. The patient was started on Hesper-C, and her activities were limited. The bleeding stopped, but on June 30, 1959, following a 100-mile motor trip, she noticed a steady spotting of three days duration, which terminated spontaneously. Thereafter, she had an unremarkable prenatal course, being checked a total of 12 times.

She was admitted to the hospital at 11:30 P.M. on January 25, 1960, with the membranes intact and contractions every four minutes, lasting thirty seconds. Between the admission and 3:40 A.M. when she was taken to the delivery room, she had a total of four rectal examinations by the nurses and two vaginal examinations by the operator. The latter were performed shortly after admission and just prior to taking the patient to the delivery room. At neither time were vessels, pulsating or otherwise, palpable across the os, nor was there any evidence of a low-lying placenta. The fetal heart tones in the right lower quadrant of the abdomen ranged between 120 and 132. The membranes ruptured spontaneously seventy-five minutes after admission; there was no blood noted at that time.

After the patient had been prepared and draped and put under medical relaxation with small whiffs of Trilene, a vaginal examination revealed a left occipitoposterior presentation with the cervix fully dilated and the vertex at a plus 1 station.

A pudendal block with 1 per cent Xylocaine hydrochloride was started on the patient's right side, and it was during this procedure that an estimated 100 cc. of rather dark blood was noted escaping swiftly past the presenting vertex. The needle tip was palpated carefully to confirm its location near the spine. An immediate tentative diagnosis of partial abruption was made, and the pudendal block procedure was discontinued. The baby was delivered promptly at 3:58 A.M. by low forceps over a median episiotomy from the posterior position.

At birth an anatomically normal, completely white and flaccid female with shallow breathing was noted. She neither breathed nor cried spontaneously. After suction produced no improvement, the baby was mouth-breathed, and in approximately three to four minutes the cry became weak, the respirations slightly improved, and she became less pallid. An immediate check of the lungs, heart, and fontanel suggested no abnormalities, and the impression of fetal anoxia secondary to partial abruption persisted. The baby was placed in a warm incubator with oxygen.

In reattending the mother, it was noted that the cord seemed to tear in extracting the placenta from the cervical os. A velamentous insertion with the placenta intact was noted but was not associated with the second stage of vaginal bleeding or the infant's condition. The repair of the episiotomy was without incident.

In the nursery with 40 per cent oxygen, the infant continued to have relatively shallow, rapid breathing; marked pallor; felt cold to the touch; and she yawned frequently. It was at this point that the thought of the bleeding

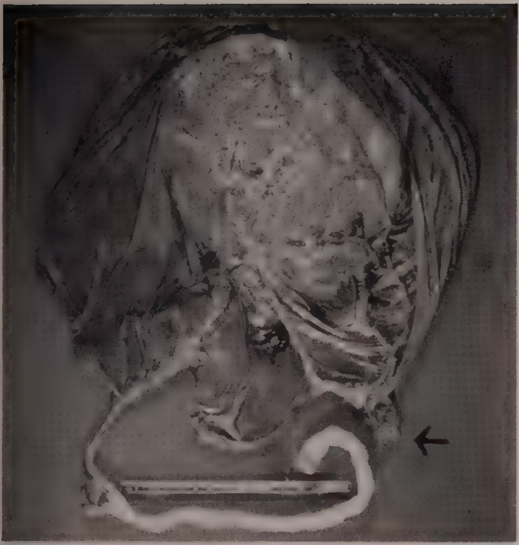

FIGURE 1. Placenta with attached umbilical cord. Arrow shows point of rupture.

having been fetal in origin rather than maternal was first considered. A stat hemoglobin revealed 12.5 Gm. following which a femoral puncture was performed for blood type and crossmatch. Three hours and thirty-seven minutes after the delivery a transfusion was started, but the infant expired during this procedure.

An autopsy report revealed that the placenta was discoid, measured 16 by 3 cm., and had a total weight of 590 Gm. The maternal surface was spongy, red-gray, and not particularly remarkable. The usual shagginess and sponginess of the tissue was noted with normal cotyledons. The compacta and spongiosa were within normal limits, and on sections the marginal sinus was seen well at different points. Attached to the placenta was a segment of cylindrical gray-white umbilical cord 48 by 1.5 cm. The umbilical vessels did not show the customary central or pericentral attachment to the placenta but rather bifurcated and followed a tortuous course through the amniotic sac. No abnormalities were noted proximal to the attachment of the vessels in the amniotic sac. However, 2.5 cm. from the point of initial bifurcation of the cord vessels into the amnius, a rupture of one vessel with complete transection occurred (Fig. 1).

As one followed the path of this vessel into the amniotic sac, two additional points of rupture (also with complete transection) were noted. Grossly, it could not be determined if the vessel in question represented an artery or a vein. The amniotic sac was translucent, gray-white, and fairly intact for the most part except at the point of fetal exit and at the previously described points of vascular rupture (Fig. 2). A diagnosis of velamentous insertion of umbilical vessels was made.

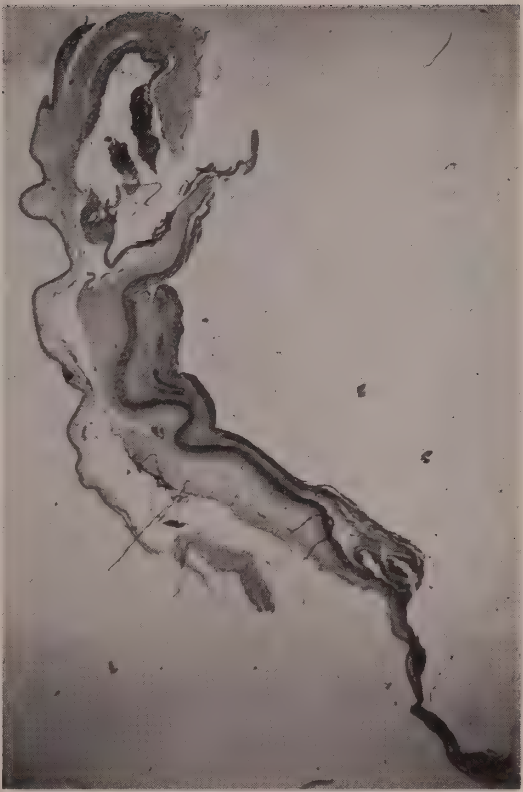

FIGURE 2. Amniotic sac showing points of rupture.

At the time of the autopsy the infant was pale, well developed, and showed no anatomic abnormalities of any significance outside of a patent ductus arteriosus and patent foramen ovale. A microscopic examination of the sections of the ruptured vessel that had been noted grossly revealed them to be parts of the umbilical vein.

Treatment

The differential diagnosis of vaginal bleeding in the third trimester still includes the familiar placenta previa, abruptio placenta, carcinoma of the cervix, and our subject, fetal hemorrhage. Obviously, in the presence of a dead fetus, a conservative management bearing in mind the possibility of afibrinogenemia is to be preferred.

However, given a fetus at term, painless vaginal bleeding (and I might add a rather dark venous blood rather than a bright oxygenated blood), with no change in the maternal vital signs, but rapidly progressive signs of fetal distress, the diagnosis of spontaneous complete rupture of an umbilical or placental vessel must be considered. This is not to infer that the three aforementioned causes of maternal bleeding may be ruled out by any one or combination of the previously mentioned signs and symptoms, since it is a well-known fact that any of them, especially early in their respective syndromes, may present identical signs and symptoms. However, stress is given to the concept that this combination of signs and symptoms clearly rules in the possibility of vasa previa or a complete spontaneous rupture of vessels, rather than ruling out more common causes of vaginal bleeding in late pregnancy or labor.

The presence of nucleated fetal red blood cells in a relatively large quantity in a smear of the vaginal blood might add further evidence that the bleeding is fetal rather than maternal in origin. Certainly this procedure would seem worth while performing while waiting for a room to be set up for the examination of the mother and possible cesarean section. Should they be found in quantity, regardless of whether or not cesarean section is performed eventually, attention would be focused on the necessity of prompt attention to the infant at delivery rather than to the mother. In this hospital we feel that vaginal bleeding in the third trimester or in labor demands prompt consultation with our colleagues in obstetrics, especially when there are signs of significant fetal distress. Further vaginal examination by a general practitioner would appear to be contraindicated in view of the continued possibility at this time that the suspected complication could be vasa or placenta previa or an abruption. Similarly, we hold that consultation is necessary in the event that there are signs and symptoms of increasing fetal distress prior to the rupture of the amniotic membranes and especially so when the vertex is out of reach of a low forceps delivery.

Thus, in consultation a decision is made as to whether or not a cesarean section is indicated in the event of fetal distress with or without painless vaginal bleeding. However, when, as in this case, the vaginal bleeding occurs in the last moment prior to delivery, the only procedure available to the general practitioner is the prompt delivery of the baby from below.

One then turns his attention to the infant, since as in this case, the hemorrhage had not involved the maternal circulation. An infant in acute shock, regardless of the cause, is an obvious pediatric emergency. When recognized as such and when it is possible, the case again demands the general practitioner's prompt consultation with the specialist. Until his arrival, drawing of cord blood for type, crossmatch, and hemoglobin is indicated, together with the usual forms of treatment of shock. Michaels in 1955[8] suggested the following: "10 cc. of blood per pound of body weight should be drawn at once from the mother and should she be Rh positive, given to the infant preferably through the umbilical vein by means of a #17 polyethylene catheter. If the mother is Rh negative, a plasma infusion should be instituted until Rh negative blood is obtained." In the face of an obvious diagnosis of fetal hemorrhage, prompt transfusion prior to the arrival of the pediatrician will be lifesaving. Unless there is a dire emergency, type and crossmatch and a transfusion with matched blood is to be preferred.

Summary

The case of fetal intrauterine hemorrhage secondary to complete, spontaneous abruption of the cord or placental vessels is studied, and the classification and etiology is reviewed. A scan of the American and British literature is presented with the signs and symptoms, means of diagnosis, and treatment. A case is added to the literature.

Finally, the thought occurs to the authors, stimulated by Michaels' comment in 1955, that perhaps in view of a 1 per cent incidence of velamentous insertion, the incidence of fetal hemorrhage is higher than was suspected previously. A suggestion is made to a large obstetric center interested in a research problem that in all cases of vaginal bleeding in the third trimester or in early labor, the mother should be subjected to the simple procedures of venipuncture and the preparation of a vaginal blood smear to determine the presence and

quantity of nucleated fetal red blood cells. Perhaps this would serve to establish both the frequency of fetal bleeding and the degree of invasion of maternal circulation by fetal red blood cells prior to delivery.

If a higher-than-suspected incidence of fetal bleeding is determined, a higher fetal salvage might result by prompt transfusion to the newborn infant in cases of third trimester and intrapartum vaginal bleeding.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 14 to 18, 1962, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

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Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1962*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Total Sympathetic Blockade as an Adjunct to Anesthesia

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EARLY EXPERIENCE *taught that prolonged anesthesia, necessitated by radical surgical procedures, was not tolerated well by poor-risk patients, blood loss was often profuse, and circulation remained inadequate despite rapid blood replacement. It has been shown that hypothermia and vasodilation are possible solutions to this problem. The authors report 125 cases in which total sympathetic blockade was produced, 79 with total epidural analgesia, 4 with high spinal, 20 with hexamethonium (Bistrium), and 12 with trimethaphan camphorsulfonate (Arfonad). The blockade was attained by a catheter placed in the epidural space. Almost all of the patients had at least one serious medical condition before operation; 38 had cardiac conditions. Most of the cases were radical interventions for cancer. In 27 cases the procedure lasted eight hours or more; only 8 lasted three hours or less. Forty-four of the patients were over seventy. Using the epidural technic it was not difficult to lower the blood pressure if enough anesthetic solution was injected, the patient was positioned so that gravity helped to distribute the drug, and there were no epidural adhesions. The clinical results were satisfactory. Postoperatively, hemoglobin, hematocrit, blood pressure, and urinary output were at preoperative levels despite the magnitude of the operative procedures and the age and condition of the patients. Total sympathetic blockade, produced by epidural analgesia as an adjunct to anesthesia, has made possible light anesthesia with excellent relaxation, minimal blood loss, ease of production of hypothermia, absence of shock, and a means of monitoring blood volume changes by following the blood pressure. It may be applicable also to further studies of cardiovascular physiology.*

MANY ANESTHETIC METHODS have been developed for radical surgical procedures in poor-risk patients. Early experience taught us that prolonged anesthesia, even of moderate depth, was tolerated poorly by such patients. In addition, blood loss was often profuse, and long periods during which the circulation was inadequate were unavoidable despite rapid blood replacement. Therefore, a technic was sought to provide anesthesia with adequate relaxation which would be better tolerated by poor-risk patients. This method should make possible a better estimate of blood loss and adequacy of replacement, and it should afford some protection against hemorrhagic shock. Others have shown that both hypothermia[1] and vasodilation[2] were possible solutions to this problem.

In the hypothermic state there is a decreased oxygen demand, affording the vital organs protection against short periods of inadequate circulation. It has been shown by many workers, including Hershey,[3] that the irreversible ravages of hemorrhagic shock can be prevented by the prophylactic use of ganglionic blocking agents. The hypotension following sympathetic blockade, whether produced by interruption of impulses at the ganglia or by paralysis of the sympathetic nerves as they emerge from the spinal cord, has the advantage of reducing blood loss from small vessels.[4] The degree of hypotension which results from blockade also provides an indication

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of the adequacy of the blood volume before operation and of subsequent changes in the blood volume during operation.[5,6]

One hundred twenty-five cases are reported in which total sympathetic blockade was produced, 79 with total epidural analgesia, 4 with high spinal, 20 with hexamethonium (Bistrium), and 12 with trimethaphan camphorsulfonate (Arfonad). Any of these methods produce a hypotension equivalent to that of the epidural. The latter will be described since this has evolved from the others and has been found to be the most satisfactory.

Method

Originally blocking agents were used to attain sympathetic blockade. Now we use a catheter placed in the epidural space. Once a sensory level has been demonstrated, the patient is given a minimum of thiobarbiturate and succinylcholine for endotracheal intubation and is carried thereafter on 2:1 nitrous oxide and oxygen. After the airway has been established, additional local anesthetic agent is given epidurally. Sometimes 50 to 60 ml. of solution are required to produce total blockade. We have not seen convulsions with initial amounts of lidocaine (Xylocaine) as high as 800 mg., probably because our patients are anesthetized. Total blockade is considered to have been established when the patient has ceased spontaneous respirations, his pulse rate is about 60 beats per minute, and his blood pressure has fallen to a plateau level. If the initial fall in blood pressure is below 70 to 80 mm. Hg, the range which we consider safe, he receives plasma expander or blood to raise it to that level. A pulse pressure of 10 to 15 mm. Hg can be expected.

Artificial ventilation is maintained throughout the procedure by manual compression of the breathing bag or the mechanical respirator. The electrocardiograph is monitored. Hypothermia is induced by means of a child's water mattress or ice bags over the superficial large arteries. The temperature attained ranges between 28 and 33 C.

The sympathetic blockade is maintained by adding a third of the original amount of solution of local anesthetic every thirty to forty minutes. We found that an anesthetic solution without epinephrine must be used because, in the amounts we inject, enough epinephrine is absorbed into the systemic circulation to produce blood pressure changes. Plain lidocaine from 1 to 2 per cent has proved satisfactory. To achieve a high level of analgesia with a minimum of anesthetic agent, the patient is positioned so that gravity assists in the distribution of the drug.

As the surgical procedure progresses, reductions in blood pressure are treated by transfusion to maintain the systolic pressure at 70 mm. Hg.

About an hour before the end of the procedure, lidocaine injections are withheld. At closure, the patients are breathing well and are conscious when nitrous oxide has been discontinued. Blood pressures return to preoperative range within an hour after surgery.

At the conclusion of the procedure, the catheter may be left in place for postoperative analgesia, should it be advisable to avoid narcotics.

Postoperatively, as hypothermia recedes, if shivering supervenes, 25 to 50 mg. of chlorpromazine (Thorazine) or promazine (Sparine) are given intravenously and may be repeated every three or four hours, as needed. Minimal circulatory depression is seen, since none of the usual depressant drugs have been used during anesthesia.

Almost all of our patients, especially in the older-age group, had at least one serious medical condition before operation, and many of them had several. There were 38 patients with cardiac conditions, ranging in severity from nonspecific electrocardiographic changes to recent decompensation. These included 3 frank patterns of previous infarction as well as 18 hypertensive patients. In addition, of the 38 patients 9 had emphysema, 3 had cirrhosis, and 1 had a history of epilepsy.

Nine of the patients had liver disease of considerable severity. Four had kidney disease, including 1 who had had a nephrectomy. There were many more with ureteral obstruction due to carcinoma of the cervix. Twenty-six had some form of compromising pulmonary disease, many were cachectic, and 4 were notably obese. There were 3

TABLE I. Previously existing medical conditions

Disease	Number of Patients
Cardiac or cardiovascular disease from nonspecific electrocardiographic changes to decompensation	38
Hepatic insufficiency	9
Renal disease	4
Respiratory disease	26
Metabolic disease (diabetes, cachexia, obesity, alcoholism)	15
Neurologic disease (epilepsy, Parkinsonism)	2

diabetic patients and several alcoholic persons in the series (Table I).

TABLE II. Type of operation

Operation	Number of Patients
Exenteration	13
Radical hysterectomy or trachelectomy	20
Radical vulvectomy	2
Radical mastectomy	14
Pulmonary resection	2
Radical head and neck procedures	24
Radical nephrectomy	3
Radical cystectomy	5
Radical prostatectomy	3
Abdominoperineal resections	10
Colectomy and gastrectomy	
Vascular shunts and aneurysm repair	7
Exploratory laparotomy	22
Craniotomy	
Relatively minor procedures	
TOTAL	125

Results

Most of the 125 cases reported were radical interventions for cancer (Table II). Both the surgical operation and the anesthesia were performed by residents with the help of the attending staff.

Twenty-seven operations lasted eight hours or more, 3 of these over twelve and 1 over thirteen hours. Only 8 of the 125 lasted three hours or less (Table III).

Forty-four of the patients were over seventy and 3 over eighty. One of the octogenarians had a ten-and-a-half-hour procedure (Table IV).

Using the epidural technic, it was not difficult to lower the blood pressure if enough anesthetic solution was injected, the patient was positioned so that gravity helped to distribute the drug, and there were no epidural adhesions. When total sympathetic blockade had been achieved, 56 per cent of our patients had pressures of 70 mm. Hg or higher and received no volume expander. Of the others, 40 per cent needed 500 ml., and 4 per cent were given up to a liter, but none required more to bring his pressure up to this level.

Once hypotension had been established, there was rarely any oozing from small vessels, but large vessels bled so that they could easily be identified. It is our impression that less blood was needed than would have been required without hypotension, but this has not been documented specifically.

Hemoglobins and/or hematocrits studied in 50 unselected cases were within normal ranges immediately postoperatively regardless of the magnitude of the blood replacement. No patient of the 125 showed any signs of overtransfusion, although 5 who survived received between 10 and 20 units of blood.

Of the 11 deaths associated with surgery, 1 was frankly anesthetic. Cardiac arrest occurred while dressings were being applied after an uneventful anesthetic course. The anesthesiologist, miscalculating the length of the procedure, had continued the epidural too long and then allowed the patient to hypoventilate. This patient had had a lobectomy for tuberculosis some years before and could not tolerate the hypoxia. This could have occurred had the patient been paralyzed by any other means. Another patient whose death could have been caused by prolonged hypotension, died in ventricular fibrillation on the second postoperative day after a total cystectomy lasting thirteen hours. The fibrillation was preceded by several short tonic seizures. However, he had an unexplained hypercalcemia which was thought to have contributed to his death.

No cerebral vascular accidents occurred, and there were no proved cases of myocardial

TABLE III. Length of operation

Duration (Hours)	Number of Patients
8 or more	27
7	9
6	29
5	17
4	18
3	17
Less than 3	8
TOTAL	125

TABLE IV. Age of patients

Age (Years)	Number of Patients
Over 80	3
75 to 80	2
70 to 75	9
65 to 70	17
60 to 65	13
55 to 60	15
50 to 55	20
45 to 50	20
40 to 45	15
35 to 40	11
TOTAL	125

infarction in the postoperative period. One patient who had had a seven-hour operation did very well, despite cirrhosis with ascites, diabetes mellitus, and an old myocardial infarct, until the twelfth postoperative day when he died suddenly while sitting in a chair. Since no autopsy was obtained, it was not known if this was a myocardial infarct or a pulmonary embolus.

The urinary output of those patients who survived forty-eight hours was adequate except for 1 patient who for ten days had a persistently low output due to hyponatremia which was not treated for fear of cardiac decompensation. This was early in our experience.

Two patients died from uncontrollable hemorrhage on the table. The signs of shock, however, did not appear in these or in other patients who bled profusely, even though at times their circulation must have been inadequate.

One patient, when the sympathetic blockade wore off, exhibited the classic signs of hemorrhagic shock. He was a patient with a severe cardiac disorder whose excessively low blood pressure under blockade was not corrected with transfusion at the surgeon's insistence. This is an example of the accuracy of the method, because it was clear at operation from blood pressure readings that the patient needed more blood. When he finally received it ten hours later his shock was already irreversible.

Another patient did very well for four days after total exenteration but went into shock and died on the fifth day, having received no replacement for the inevitable constant oozing of serum from the large denuded area created by this operation. Other patients who have survived have required six or seven units of plasma in the first few days to normalize rising hematocrits. This patient was inadequately treated.

Three other patients also died weeks postoperatively, from frank surgical complications.

Comment

Total sympathetic blockade, produced by epidural analgesia as an adjunct to anesthesia, has made it possible to achieve many of the ideals others have sought. Light anesthesia with excellent relaxation, minimal blood loss, ease of production of hypothermia,[7] and absence of shock all result from the technic.

Most important of all, however, it has provided a means of monitoring blood volume changes by following the blood pressure. Enderby in 1953[4] mentioned that under ganglionic blockade small amounts of hemorrhage were reflected by a decrease in blood pressure. Freis, *et al.*[8] reported that in experiments performed for another purpose they had found that under sympathetic blockade "the withdrawal of a relatively small amount of blood by venesection, that is, 100 cc. or 2 to 3 per cent of the total volume, resulted in a perceptible decrement in the arterial pressure." That the converse is true, that pressures rise under sympathetic blockade when more than the normal blood volume is transfused, was shown by Frye and Braunwald.[9] They demonstrated that without blockade the introduction of 1,500 cc. of blood caused no change in blood pressure, a 10 per cent rise in cardiac output, with the central blood volume and stroke volume decreasing by 1 per cent and 3 per cent respectively. When the transfusion was preceded by sympathetic blockade, however, the blood pressure rose progressively as the blood was transfused: The cardiac output rose 44 per cent, the central blood volume rose 36 per cent, and the stroke volume rose 53 per cent.

What physiologic factors made this possible? The blood pressure is the resultant of five forces: the pumping action of the heart, the peripheral resistance, the blood volume, the elasticity of the arterial walls, and the viscosity of the blood.[10] The last two factors do not change significantly under sympathetic blockade.[11] Since the work of the heart is reduced as much as 75 per cent when the peripheral resistance is at a minimum,[12] the pumping action is favored by blockade, and since the heart is pumping against a reduced but unchanging peripheral resistance, its efficiency tends to remain constant, providing the heart rate and the filling in the right side of the heart are unchanged and there is adequate oxygenation of the cardiac musculature.

The heart rate, when it is relieved of its sympathetic control, is under vagal domination and, with total sympathetic blockade, stabilizes at about 60 per minute, decreasing as the patient becomes cold. When blood is then lost, the rate remains unchanged, but the volume of the pulse diminishes.

Coronary filling occurs principally during diastole and depends on the mean blood pressure.[13] During sympathetic blockade, if the blood volume is adequate, the mean pressure is about 65 mm. Hg, and the diastolic phase is long.

Under the conditions of this method, four of the five determinants of blood pressure remain at an established plateau, unaffected by reflex action. The one remaining factor which influences blood pressure and fluctuates during the surgery is the blood volume. Changes in volume, therefore, are reflected immediately in the blood pressure reading.

At the induction of total sympathetic blockade, a fall in systolic blood pressure to approximately 70 mm. Hg is seen in normally healthy individuals. A fall below this level is probably indicative of a reduced blood volume. Patients who then receive plasma expander or blood stabilize at a systolic pressure of 70 mm. Hg or above. Thus, with blockade maintained, changes in blood pressure indicate changes in blood volume. Replacement needs can be judged and overtransfusion avoided.

Blood flows have been measured in the vital subsidiary circulations under ganglionic blockade and high spinal analgesia, but the influence of initial blood volume measurements has not been considered. In 15 normotensive subjects who presumably were normovolemic since their average mean arterial pressure was 63 mm. Hg after a level to the first thoracic segment under spinal, there was no change in cerebral blood flow or oxygen consumption, and cerebral vascular resistance fell.[14] Cerebral blood flow was found to be reduced in 3 out of the 4 hypertensive patients in this study. Other investigators[4,8,15] have found hypertensive patients more sensitive than normotensive patients to ganglionic blocking drugs. This agrees with our experience in that, in these patients, the initial pressure fall is precipitous and usually to a level low enough to require the infusion of 200 to 500 ml. of volume expander to bring the systolic pressure up to 70 mm. Hg. Once this has been done, however, hypertensive patients can be treated like normotensive patients, suggesting that prolonged vasoconstriction may have contracted the blood volume.[16,17]

There is no direct effect on the cerebral vessels consequent to sympathetic blockade. Secondarily, however, a fall in systemic blood pressure to 50 per cent or below of the initial pressure resulting from blockade may be reflected in the cerebral blood flow,[15] since the arteriovenous pressure difference is the "driving force" of cerebral blood flow. Because cerebral venous pressure is very low, approximating atmospheric, only a small pressure difference is needed to circulate blood through the brain when the cerebral vascular resistance is low. Sokoloff and Kety[18] found that the critical arterial pressure is about 50 mm. to 70 mm. Hg.

Cardiac output has usually been found reduced[19] probably due to the slowed venous return,[20] but Lynn and his coworkers[12] found that ventricular work was reduced 75 per cent because of the reduced peripheral resistance. Coronary flows, though reduced, are sufficient in view of the decreased work, since arteriovenous oxygen differences are unchanged or decreased.[21]

Renal hemodynamics have been studied often. Some of the earliest work was done under high spinal analgesia by Smith, *et al.* in 1939.[22] They found, as have others,[23] that there is a momentary decrease in urinary output following an acute reduction of blood pressure, but that intrinsic compensatory mechanisms supervene to return function to normal. This was found to be true even in patients with arteriosclerotic vascular disease.

Measurements of mesenteric and hepatic blood flows and splanchnic resistance are contradictory. They are generally accepted as reduced and dependent on the venous pressure, but some investigators have found the resistance to be elevated. Trapold,[24] at first reported the resistance increased but later published results which showed that the system which he used to measure the vascular resistance interposed a resistance of its own which was being interpreted falsely as that of the splanchnic bed. Here again, the measurements have been made without considering the role played by blood volume in a low pressure system, and this may account for the varied results.

If hemodilution occurred rapidly following operative blood loss in these patients, the method described for estimating blood volume would be less valid. Chien[11] found, however, that hemodilution occurred much more slowly, and to a considerably less extent, in sympathectemized than in normal dogs responding to hemorrhage. He concluded that an intact sympathetic system is necessary for "normal" hemodilution. Probably some degree of hemodilution does take place in patients who have had total sympathetic blockade for several hours and who have had hemorrhage and transfusion, but it cannot be of significant magnitude since postoperative hematocrits are within the normal range when the criteria for blood replacement as described herein have been followed.

If the postulates of this concept are correct, an explanation has been found for the hypotension of spinal and epidural anesthesia. At the Francis Delafield Hospital now, when pressures fall below the range expected for a given analgesic level, a plasma expander or blood is used to restore the pressure, unless the procedure is minor, in which case a vasopressor is used to help the patient regain the degree of compensation which was present before his sympathetic blockade removed a portion of his vasoconstriction and revealed his hypovolemia.

There are surely many other phenomena which may be clarified by observation of the behavior of the vascular system when its compensatory mechanisms are prevented from functioning.

Summary

A report is made of 125 patients in whom total sympathetic blockade was produced by ganglionic blocking drugs or regional analgesia. Many of these patients were also cooled. The clinical results were satisfactory. Postoperatively, hemoglobins, hematocrits, blood pressures, and urinary outputs were at preoperative levels, despite the magnitude of the operative procedures and the age and condition of the patients.

The regional method with total epidural block is described. A constant relationship between the blood pressure and the blood volume when all cardiovascular reflex activity is removed by sympathetic blockade is described and discussed. The additional advantages accruing from high regional analgesia are mentioned.

It is concluded that this method is useful as a clinical tool for monitoring blood volume changes during operative procedures and may be applicable to further studies of cardiovascular physiology.

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Discussion

ROBERT G. HICKS, M.D., *New York City.* In Crile's* original thesis of anoci-association emphasis centered on the abolition of noxious afferent stimulation and the bombardment of the central nervous system with disturbing cardiovascular responses which were initiated over efferent autonomic pathways. Afferent stimuli were blocked by regional anesthetic technics. Almost forty years passed before investigators of the 1950's again approached the autonomic system to compromise its role under anesthesia and surgery with the thought of minimizing blood loss. The methods used were total spinal block and ganglionic blocking agents. Recently the method of sympathetic blockade has been employed to vitiate peripheral resistance especially as it relates to the splanchnic bed. In this way it was hoped to overcome tissue hypoxia from the ischemia and decreased organ perfusion attendant to shock.

Dr. Henley and Dr. Kritchman obviously have employed the technic to great advantage in a group of elderly and infirm patients with disease in whom more complications might have been expected. Clinically, however, it is difficult in this series to assess the value of sympathetic blockade as compared with that achieved through hypothermia. Certainly with any significant degree of hypothermia, a depression of cellular metabolism and a redistribution of circulating fluid volume are well recognized. The authors have emphasized their demonstration of a basal blood pressure as a measure of the adequacy of blood volume in hypotension produced by this method. This may become a very useful guide for blood replacement. I respectfully suggest that before it does each parameter of such a study should be defined thoroughly and then explored systematically.

The apparent overshooting of a modified Gillies technic with an end point of cessation of respiration in achieving total sympathetic blockade leaves much to be desired. Immediately, one wonders with the aggregate amounts of lidocaine deployed in the epidural space what influence on central nervous system thresholds have been achieved and how in turn this might have influenced cardiac output, cerebral flow, renal flow, and, perhaps most important, hepatic flow.

It is in the conjecture associated with the interplay between portal and systemic circulations in relation to hepatic ischemia and catabolite formation that we find fascination in the use of sympathetic blockade and hypothermia in enhancing patient homeostasis during periods of stress. Indeed, is there a mechanism, perhaps an effector cell, in the hepatic bed which responds to a portal outpouring of the product of visceral sympathetic stimulation, norepinephrine? And does this then set the stage for the death of the organism?

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* Crile, G. W.: Nitrous-oxide anesthesia and a note on anoci-association, a new principle in operative surgery, Surg. Gynec. & Obst. **13:** 170 (Aug.) 1911.

Should the postulates of this presentation be verified, the contribution of such a clinical blood volume guide would become significant. It would greatly lighten the burden of the anesthesiologist who is often disturbed by the time lag between present clinical and laboratory estimates of blood loss when faced with the urgency of a rapid decision concerning replacement in the face of hypotensive status. Notwithstanding, the eventual contribution of this paper might be greater in providing another building block in research avenues for the eventual solution of the basic physiologic provocations.

Health of Canadians among best in world

The health of Canadians, judged by their longevity, ranks among the best in the world, according to statisticians of the Metropolitan Life Insurance Company.

Official data show an average length of life of 67.6 years for males and 72.9 years for females in 1955 to 1957.

The pattern of health improvement in Canada is also very similar to other countries in the Western world. Canadian females—as is true in the United States—not only have lower death rates than males, but also have experienced a greater rate of improvement. For females the death rate fell from somewhat over 10 per 1,000 in 1940 to less than 7 in 1954 to 1959. The corresponding decline for males was from nearly 12 to about 9.4 per 1,000.

The trend of mortality from the leading causes in Canada is similar to that in other Western nations. For example, the death rate from cardiovascular-renal diseases has increased from an annual average of 392 per 100,000 in 1941 to 1945, to 402 in 1959. The mortality rate from cancer also rose during the same period from 123 to 128 per 100,000. Notable factors in both increases are the growing proportion of aged persons and the improved diagnosis of these diseases.

On the other hand, striking reductions have occurred in the number of deaths from tuberculosis and the principal communicable diseases of childhood. The rate from tuberculosis fell from 50 per 100,000 in 1941 to 1945 to only 5.5 in 1959; the rate for the communicable diseases was down from 8.7 to 0.8.

Other remarkable improvements have been recorded in infant and maternal mortality, which have declined by half and by 90 per cent, respectively, since 1940. The infant mortality rate in 1940 was nearly 60 per 1,000 live births, whereas the figure for 1959 was 28 per 1,000. More dramatic was the drop in maternal deaths—from 40 per 10,000 live births in 1940 to 5.5 in 1957 to 1959.

A much more gradual downward trend is in evidence for accident mortality. There were 60.5 accidental deaths per 100,000 population in 1941 to 1945 and 54.1 in 1959.

"Current major health tasks in Canada are the control of the chronic diseases of middle and late life and measures to reduce accidents. Another important health problem is the relatively high levels of perinatal and infant mortality in some areas, particularly in the eastern Provinces," the statisticians concluded.

Scientific session held at the
Hotel Beekman Tower,
New York City, March 29, 1961
JOSEPH FRIES, M.D.,
President, Chairman

PROCEEDINGS

New York Allergy Society

SHEPPARD SIEGAL, M.D., AND MURRAY DWORETZKY, M.D., Editors

Delayed Bacterial Allergy, Homograft Sensitivity, and Auto-Immune Disease

Expressions of the Immunologic Origins and Consequences of Individuality

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New York City

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As YOU ARE all aware, the origin of the studies which I will discuss was with the observations of Dr. Merrill W. Chase on the transfer of tuberculin sensitivity in animals by means of cells from a sensitive to a nonsensitive guinea pig. With this technic we had at our disposal for the first time the nearest replica to an antibody-like system for allergies of the delayed tuberculin type.

Our observations began with the question as to whether or not leukocytes from a tuberculin-sensitive human being would also possess the capacity to transfer systemic tuberculin hypersensitivity. This was found to be exactly the case.

The material or materials in sensitive human leukocytes we have since come to designate "transfer factor," to describe the biologic activity responsible for making another individual sensitive to tuberculin or to the specific test material under study. This designation is a convenient shorthand, for we realize that there may be more than one factor involved in this transaction. I hope to show that there is evidence that we are transferring not only the instrument or effector reagent of tissue damage observed in delayed allergy, but also the machinery that for prolonged periods of time continues to make the recipient respond as the donor to the specific test material.

The other line of observation which I will develop would suggest the view that the common meeting ground for tuberculin allergy, for homograft sensitivity, and for certain types of autoimmune disease may be a transfer factor.

The known types of allergic inflammatory response are divided into early and delayed. In the "early" category is found reaginic antibody with which you are especially familiar. We would suggest that this type of altered immune response may be a characteristic peculiar to the genetically susceptible few.

The other early response is found in Arthus or anaphylactic-type reactions, a predominantly man-made sensitivity. Both of these "early" responses are separated from the "delayed" type by the easy accessibility of an antibody which is detectable in the serum of appropriately sensitive individuals.

The delayed type of response, which I will delineate more fully, is perhaps unique, insofar as it is the more widespread and enduring: All human beings, on exposure to the appropriate agent (such as bacteria, viruses, fungi, spirochetes, or simple chemical compounds), cannot help but respond with the development of the specific delayed allergy. Under "delayed responses," as Dr. Chase has done, I would include allergic encephalomyelitis and homograft rejection phenomena.

In respect to delayed reactions I'd like to focus your attention on the fact that so far there has not been an antibody detectable in the serum or, so far, in cells and that the transfer of this sensitivity has thus far been accomplished only with cells of the leukocyte series and not with serum.

I might say, before going on, that the table we have formulated is just a convenient scaffold on which alterations are going on, I hope, all the time.

Material and methods

In the protocol for the transfer experiments leukocytes are isolated from the peripheral blood of the sensitive donor and injected into the shoulder of the negative recipient. Twenty-four hours later the opposite forearm is challenged, and within twenty-four hours the recipient becomes tuberculin-positive, when that is the specific test material under study. Intact leukocytes are used in early experiments, and when this material is injected into the shoulder, there is a variable degree of an inflammatory response in the various intradermal sites. We have illustrations to show the tuberculin test in the forearm of a formerly negative and now positive recipient about three days after transfer and twenty-four hours after the skin test.

William S. Tillett, M.D., and I were originally attracted to the cell transfer system because we thought that rheumatic fever was, perhaps, a disease that resembled tuberculosis more than it did serum sickness and that delayed allergy mediated an integral part of the prolonged tissue damage following certain streptococcal infections.

Following the demonstration that tuberculin sensitivity could be transferred in human beings, we adapted this finding to streptococcal sensitivity and found that the subjects reacted to a streptococcal substance (type I) twenty-four hours after a skin test and about two weeks after the transfer.

In every respect the findings in human beings confirmed the earlier findings of Dr. Chase, which have been further confirmed in animal species as well. As he found, we also noted that the critical variables which condition transfer are the degree of delayed sensitivity of the donor and the dosage of leukocytes used to transfer such sensitivity.

However, some differences from the animal system began to appear in human beings. The departures centered around the minute doses of leukocytes needed and the prolonged duration of sensitivity, often one to two years in man as compared with animals in whom sensitivity may wane within a week. However, depending on the care with which the sensitization and transfer are done, as shown by Dr. Chase, sensitivity could be made to endure in animals for periods of months.

Because of these differences and for reasons which we need not detail now, we thought we could lyse cells completely with distilled water and freeze and thaw the cells through from seven to ten cycles. When leukocyte extracts prepared in this fashion are injected, we find that streptococcal or tuberculin sensitivity is transferred with the same intensity and follows the same pattern as has been observed using viable cells.

A sample protocol shows the transfer of delayed streptococcal M-substance sensitivity by water lysed or frozen and thawed leukocyte extracts. The leukocyte extract is lysed by distilled water, all the feulgen-positive nuclear material is centrifuged out, and only the remaining cytoplasmic supernatant is injected. This test demonstrates that cytoplasmic materials alone are capable of transferring sensitivity.

A reaction to streptococcal M substance appears twenty-four hours after a skin test and three days after a transfer. A more intense skin reaction to streptococcal M substance follows a transfer using the cytoplasmic supernatant injected into the shoulder.

Because Dr. Chase and so many other workers had shown beyond question and had confirmed repeatedly the observation that if one extracted cells in the guinea pig, transfer was abolished, the unique finding in man made it our responsibility to be sure that our observation was not in error, no matter how well intentioned, and to confirm it with other test systems repeatedly. A protocol using frozen and thawed leukocyte extracts to transfer tuberculin sensitivity confirmed the findings observed with streptococcal M substance as a test material.

As had been found using intact leukocytes, leukocyte extracts obtained from tuberculin-negative reactors are unable to transfer tuberculin sensitivity.

Case report

Of interest is a student nurse recipient who had remained tuberculin-negative after BCG inoculation but who did become tuberculin-sensitive following a transfer with leukocyte extracts. When cells, in turn, were obtained from her at the height of her maximum sensitivity and injected into another patient, he also became sensitive.

We have tried this type of serial transfer only on two occasions. On both occasions, it has shown positive results. The exact meaning of this remains to be evaluated by further experimental studies.

The reactions in the recipient about twenty-one days after transfer and twenty-four hours after a skin test, using 1 mg. of "old tuberculin," to which she had shown repeated negative reactions, as well as to 0.005 mg. of purified protein derivative in the opposite forearm, were as follows:

After 60 consecutive successful transfers, there seemed to emerge two patterns of response. In pattern 1, the recipient became maximally sensitive within a matter of hours or days and retained that sensitivity either for a long period, upwards of a year, or she would revert to negative reactions again, in some instances in a matter of weeks or months, or the curve would gradually fall off in intensity.

The more interesting phenomenon is that of pattern 2 where, although the recipient became definitely but minimally sensitive within a day or week, the sensitivity remained at a low level (10 by 10 mm. reaction) anywhere from two to six or eight weeks, and then there would be a sudden upsurge of reactivity to maximum (40 by 40 mm. reactions or greater).

Etiology of reactions

We felt that this uncovered a recipient contribution to the transaction and began to think in terms of the possibility that pattern 1 represented donors who had more of a readily available antibody-like material, if you will, in their leukocytes, and pattern 2 represented donors who had less of this readily available material and more of a template, which required further processing by the recipient before the full impact of it became manifest.

Moreover, the injection of a minute amount of biologically active material that changes the entire reaction capacity of an adult human being for prolonged periods of time, to the extent that he acquires the specific characteristics of the donor, evoked a possible analogy to the operation of a mammalian-type of pneumococcal-transforming principle, where the desoxyribose nucleic acid was of great importance, or perhaps a cytoplasmic genetic particle, or perhaps a phenomenon akin to transduction in bacterial cells.

To test this assumption, we treated the frozen and thawed extracts with desoxyribonuclease to inactivate all of the desoxyribose nucleic acid and other extracts with ribonuclease to inactivate ribonucleic acid in the hope of abolishing transfer sensitivity. There was no difference in the capacity to transfer seen following the injection of frozen and thawed extracts alone, or desoxyribose nucleic acid-treated extracts, or ribonuclease-treated extracts.

The great difficulty in assessing negative results is the limited conclusion one can draw: Transfer-factor activity doesn't appear to depend on highly polymerized desoxyribose nucleic acid. This conclusion is based on the enzymatic depolymerization and on the physical separation of the desoxyribose nucleic acid.

The negative results following treatment with ribonuclease leave one with the conclusion that enzyme was added in tremendous excess under the most propitious circumstances. However, this was no guarantee that it reached or inactivated or de-polymerized its substrate. Therefore, experiments with this enzyme do not permit any firm conclusions to be drawn, particularly in the face of negative results.

Application in other areas

About this time Dr. Pappenheimer and I adapted these findings to the diphtheria toxoid system with which we had worked some years earlier, in the hope of trying to make some conventional immunologic sense out of this rather unusual immune system. We found that we could, indeed, transfer both tuberculin and toxoid sensitivity with leukocyte extracts. We also observed that we could not detect an antibody of the conventional type in the extracts that were used to transfer sensitivity nor in the sera or skin of the recipients, following transfer, at the time of their maximum delayed skin reactivity to toxoid.

We were left with the conclusion that if an antibody of the conventional type were present, it had escaped detection by a most sensitive biologic test, the rabbit skin neutralization test.

In an attempt to detect antitoxin in the site of delayed reactivity following cell transter, we injected toxin into the sites of delayed reactions that had been transferred, and in each instance the toxin was not neutralized. We had hoped to find conventional antibody here, if anywhere, but again were disappointed in this regard.

We did some other experiments at this time, trying to neutralize the transfer factor with antigen (tuberculin or diphtheria toxoid) without success. However, a more interesting finding was observed whereby the incubation of sensitive leukocytes with antigen resulted in a translocation of all of the transfer activity to the cell-free supernatant. The cells were now desensitized and, therefore, no longer able to transfer sensitivity. However, in the control tube all of the transfer activity remained in the cells, and none was liberated into the supernatant.

The technical problems posed by this sort of experiment we had also shown, related to the fact that transfer factor can leak out of poorly handled or damaged cells nonspecifically. Because of the way these experiments were designed, we were unable to conclude that there was an immunologically specific release of transfer factor. However, the one fact we can conclude is that the cells are definitely desensitized. This observation has been confirmed in vivo by Oliviera-Lima, who desensitized human cell donors who had both streptococcal and tuberculin sensitivity. Before desensitization the donors transferred both modalities, but when each donor was desensitized to tuberculin, then his cells could transfer only streptococcal sensitivity.

One of the difficulties with transferring tuberculin and streptococcal sensitivities in man is that one cannot be sure that the transfer is not elevating a latent sensitivity. To attempt an assessment of this possibility we undertook a combined study with Oscar Rappaport, M.D., Russell G. T. Millar, M.D., and Charles E. Smith, M.D. in Berkeley, California. Leukocytes were collected in the San Joaquin Valley from coccidioidin-sensitive donors, frozen, and flown east. Following the injection of desoxyribose nucleic acidase-treated leukocyte extracts, coccidioidin sensitivity was transferred to negative volunteers who had never been away from the eastern seaboard. As a result of this extensive study, good evidence was made available that a transfer factor can initiate sensitivity de novo and not merely elevate a latent state.

I think the transfer of homograft sensitivity which I will discuss establishes this fact clearly, since one cannot postulate that an individual may be exposed to another's skin without knowing about it. I might refer here to another fact of interest, both from our own studies with coccidioidin and with diphtheria toxoid and from Good's studies on transfer to agammaglobulinemic agents: The peripheral blood leukocyte of human beings can transfer only the capacity for delayed allergy and cannot transfer the capacity for serum antibody formation.

Properties of transfer factor

The transfer factor endows the recipient with the specific sensitivity of the donor, the sensitivity is systemic, the onset is early, in a matter of hours, and the duration is long, from months to one or two years. A minute dosage of white cells is effective; the capacity to transfer depends on the degree of donor sensitivity and the dosage of leukocytes used. Negative donors are incapable of this feat. Extracts or cell-free supernates are as effective as viable cells in human species, and so far we have been unable to cross the species barrier, that is, to transfer sensitivity from man to guinea pig, which would be very convenient.

The study of the biochemical properties of the transfer factor is just beginning. The factor seems to be very hardy. One can work at 25 or 37 F. for six hours and suffer no loss of activity. It can be deep frozen at least as long as a year and either the cells or their extracts are still active. I have reservations about the negative results when ribonuclease is added to extracts.

The immunologic properties of the transfer factor may be of interest: It interacts with but is not neutralized by antigen. The white cells are desensitized in the presence of antigen. Nonsensitive white cells incubated with antigen are capable of transfer, and we have been unable to detect an antibody of the conventional type.

I do not think the results of transfer represent active sensitization because of the early onset or nonpassive sensitization because of the long duration. Although repeated tests with antigen will increase the intensity and the duration of the transferred sensitivity, we went out of our way to show with the coccidioidin system that in the absence of antigen in the environment the duration of sensitivity depended on the degree of sensitivity transferred originally.

Application to homograft problem

I should like to proceed to the application of this system to the homograft problem. Our real aim in transferring accelerated homograft rejection is to try to delineate the antibodies involved in this process. I think perhaps the most pressing problem involved in the homograft rejection phenomenon today is the clear definition of the antigen or the antigens that induce this response and the antibody or antibodies that mediate it.

By comparing the tuberculin type of sensitivity with homograft rejection, we hope to view the homograft problem that arises when the host is infected with tissue cells that have different metabolic properties, say, from tubercle bacilli, but whose mechanisms of handling and disposal are the same as those of the tubercle bacillus.

Intact bacterial and intact tissue cells are still the most efficient means of inducing both types of sensitivity in nature. The latent period is the same in both. The Koch phenomenon results when one tests for tuberculin sensitivity; accelerated rejection, we would think, results when one tests for homograft sensitivity. In tuberculin allergy the specificity is for the bacteria; in homograft sensitivity the specificity is for the specific donor.

The presence of serum antibody is variable in both tuberculin and homograft sensitivity, and nowhere has there been a parallelism demonstrated between the titer of serum antibody and the degree of tissue damage in either. The transfer sensitivity with serum has been negative in both types of sensitivity with the exception of Stetson's serum transfer of local sensitivity in the rabbit ear homograft.

However, what concerns us a great deal is the fact that both modalities are transferable by means of cells. The studies to be described were done in collaboration with Dr. Rappaport, Dr. Converse, and Dr. Tillett.

Methods of transfer

The transfer of homograft sensitivity represented the first occasion we had to sensitize our donors actively; at all other times, donors were taken as they occurred in nature, without any artificial sensitization. To do this, we had to take skin from an individual, A, and sensitize another individual, B; thus, B would be sensitive to A's skin. It was postulated that the sensitized subject, B, had in his leukocytes a transfer factor directed against A's skin, and therefore B's sensitized leukocyte extract was injected into a third individual, C.

To test this hypothesis, skin homografts were placed on C, from subjects A and D, with whom he had not had contact before. We would expect, ordinarily, that C would accord skin from A and D a first-set response, that is, the graft would survive for at least eight to ten days.

We found that by giving subject C desoxyribonuclease-treated leukocyte extract from donor B sensitized to A's skin, that C would reject A in accelerated (four to six days) fashion, indicating that sensitivity had been transferred.

Another series showed that there are fairly exacting conditions for the transfer, and that placing two grafts on an individual in sequence was enough to sensitize a person for a local but not for a systemic transfer. If we wanted to effect a systemic transfer (that is, putting the cells in the shoulder and the skin graft on the forearm some three weeks later), then the donor required four sequential exposures to the specific skin. In this experiment the test graft was rejected in from four to five days, whereas the control graft went through its usual first-set rejection after a period of eight days.

I think the interesting part of the transfer of homograft sensitivity is the fact that the desoxyribonuclease-treated leukocyte extract can be injected into the shoulder and some three weeks later both test and control grafts put on the forearm, and the individual will respond to the test graft as if he had met it before, while the control graft is accorded a first-set response.

Of interest also was the finding that sensitization and desensitization could occur in parallel, and that whichever factor was in the ascendancy at any point in time governed the effectiveness of the transfer. If sensitization is in the ascendancy, then the transfer is effective.

Comment

In an attempt to try and make some general biologic sense out of the homograft reaction and out of the transfer of delayed allergy, and prodded by the unprecedented behavior of the transfer factor, we have proposed a hypothesis. I would like to preface it with the statement that I do have an acute awareness of the short half-life of hypotheses, particularly those that are designed to provoke experiments, and I hope that is what this one will do. Moreover, the pathways to any unknown and uncharted area are bound to be littered with discarded hypotheses. I'll be happy to discard this one as promptly as we have discarded some of the others along the way, as soon as it provokes the experiments that it should.

This is based on a suggestion that Thomas made, following a discussion of Medawar's paper, that if homograft sensitivity had been discovered before tuberculin allergy, we would be as busy trying to explain tuberculin allergy in terms of homograft sensitivity as we are currently trying to show the reverse.

Thomas suggested that tuberculin allergy is not an effective mechanism for coping with the tubercle bacillus; he also suggested that tuberculin allergy did not evolve in the usual sense, in an evolutionary way, to anticipate the unlikely event that one man would place skin on another. He suggested further that both homograft rejection and tuberculin allergy utilize a mechanism that was evolved for quite another purpose, and this purpose may be related to the disposal of mutant cells, cells that have undergone mutation and are, perhaps, a safeguard against neoplasia.

With this viewpoint and the acknowledged immunologic reality and biologic implications of acquired tolerance, one could view the induction of tuberculin-type hypersensitivity in a new way. For example, where one sees strong delayed allergy in nature, the bacterium is usually a preferential intracellular parasite, such as tubercle bacillus, typhoid, or brucella; or in viral infection, where delayed allergy is found wherever tested, the microorganism is an obligatory intracellular parasite; and in delayed allergy to simple chemicals, as Eisen has shown, the chemical must complex the host's own tissues before it can function as a delayed allergen.

We would propose the view that interaction between macrophages and the ingested tubercle bacillus or its degradation products may result in a complex formed between the tubercle bacillus and the host's own tissues which we call "self."

As such macrophages when dead or dying are in turn phagocytosed by whatever reticuloendothelial recognition centers there may be, this interaction could constitute an event that may be recognized as slightly out of the ordinary. One's own tissue, then, may be recognized as foreign tissue to the extent that X has altered the self components. This circumstance may result in an immune response, whereby the host's leukocytes are sensitized and a transfer factor is induced against the "self plus X" complex. A homely example of this may be given by patients with caseating cavitary pulmonary tuberculosis who in an attempt to reject the tubercle bacillus are inadvertently caused to reject portions of their own pulmonary tissue as well, in consequence of the mechanism proposed. Tuberculin-sensitive individuals ordinarily react to their tissues as belonging to themselves and do not undertake a reaction against them.

However, when the sensitive reactor's cells are coated with an intradermal test with tuberculin, we would suggest that such cells coated with antigen be recognized as a local group of "self plus X" complexes and that we actually witness a modified type of homograft rejection, in which the tested individual attempts to reject a portion of his own skin as if it belonged to another. This response occurs following an interaction between sensitized leukocytes bearing transfer factor and antigen-coated cells, causing sickness or the death of each.

Unfortunately, we are not yet in a position to define the transfer factor or to describe its exact mechanism of action. However, in a biologic sense we are transferring both the prompt effector reagent of delayed allergy and the machinery which continues to make the recipient respond as the donor for prolonged periods of time.

The self plus X hypothesis brings us to a consideration, a very brief one, of possible mechanisms involved in the genesis of certain auto-immune diseases.

For example, in allergic encephalomyelitis, following a viral infection or immunization with smallpox vaccine and after an incubation period, one sees the individual afflicted with rather extensive inflammatory disease of the brain. I would like to suggest in this instance that the virus functions as X and causes the patient to react to his own brain constituents as if they belonged to someone else. In attempting to reject such altered tissues as if they were indeed a homograft, the individual may have set in motion the events that result in disease.

In the laboratory, this situation is much more easily reproduced by incorporating one animal's brain in Freund's adjuvant and injecting the mixture into another.

Perhaps, in diseases like thyroiditis, rheumatoid arthritis with its rheumatoid factor, and disseminated lupus with its lupus erythematosus phenomenon, the serum factors are signals that an earlier immunologic event has occurred and are not the instruments of tissue destruction. I would suggest that the instrument of tissue destruction may be a cell-bound factor, such as a transfer factor, and that it is this that somehow triggers the damage, which liberates the thyroglobulin or the other tissue constituents to which the host produces serum antibody. Whether or not some as yet unknown X materials change the antigenic constituents of an individual's tissues to the extent that he undertakes this type of response is a matter of conjecture at this time.

Discussion

Dr. Merrill W. Chase, *New York City*. The importance that is placed now on delayed-type allergies has been emphasized to you. We see this as an apparent operating principle also in the rejection of skin in transplantation from man to man or between animals of one species or in organ transfer.

Delayed-type reactions have been opened to investigation because through good fortune in the laboratory, we recognize that the white cell is the key element in these transfers. Delayed-type reactions, as you know, have all the criteria of specificity, although they appear to develop independent of the serum antibodies when these are present. These reactions are subject to the recall phenomenon and to desensitization, so that they seem to reflect genuine, perhaps embryonic-type, stimuli to and response from the immunologic apparatus.

My own role, as you know, has been to look for universal principles in this area. Dr. Lawrence, in the study of hypersensitive man, has found phenomena or principles that so far have not been duplicated in the guinea pig or in other laboratory animals. His studies have led him to emphasize the role of a "transfer factor."

The question before us, then, I suggest, is this: Do we, when we receive a suitable stimulus, such as a bacterial infection of no especial duration, acquire a dermal reactivity which is long-continuing because we have elaborated a factor under the initial stimulus, it has stayed with us, and it sensitizes each new cell generation to such an extent that we retain a self-perpetuating memory of an experience that happened long ago? Is this exactly what is happening?

When a cell transfer is made successfully from one human being to another with the use of extracts of leukocytes, this may be the case, and the concept of a "transfer factor" may be cogent. Nonetheless, it might be worth while to look at some other experiences that make us ask whether this concept is to be regarded as the working principle that we need for our thinking.

Dr. Lawrence, I believe, has had some experiences that would indicate that the principle of the "transfer factor" does not operate always and easily. For example, in Dr. Lawrence's transfer of the capacity to reject homografts, there is a rather critical time during which he may take the cells from the donor and still succeed in obtaining successful rejection in the recipient by means of transferring cellular extracts.

Now, why should there be a critical period in this experiment? If a "transfer factor" is the thing that functions to maintain one's own hypersensitivity, why can't we take cells at any time and do the experiment?

What Dr. Lawrence has done is magnificent, and I have no inclination to cast any doubts on his actual results; but I would like to show you some of the other items that make me pause in judging what the final assessment will be.

Study of transfer. I wish to point out that, by means of whole cell transfer from guinea pig to guinea pig, we can transfer sensitivity equally well to tuberculin and to contact with chemical allergens. If a particular donor has been sensitized to a chemical allergen, such that he will undergo a contact reaction to it, a guinea pig receiving white cells from the donor will show the same contact reactivity. If we sensitize the donor so that he possesses tuberculin hypersensitivity, we can transfer tuberculin hypersensitivity with white cells. If the donor possesses both types of hypersensitivity, we transfer both types.

Now, curiously, in man the cellular transfer of delayed-type bacterial hypersensitivity occurs easily, but the cellular transfer of hypersensitivity to chemical allergens encounters great difficulty. At present we do not understand what the difference is.

For example, in our studies an animal served as the recipient of cells taken from guinea pigs that were sensitized to picryl chloride. The recipient animal was then tested by contact on three successive days. Twenty-four hours after the first contact, we saw an area that showed a brawny edema and a marked erythematous response; the vessels were filled. This illustrates the kind of response that we get on a guinea pig that has not been sensitized directly but has been prepared by means of the cells of other individuals.

In 1 of 2 recipient guinea pigs a transfer of tuberculin hypersensitivity was effectuated, and in the other, on the same transfer day, a sensitivity to 2:4 dinitrochlorobenzene was effectuated. The 2 animals were then tested with several different tuberculins. Only the animal receiving cells from tuberculin-sensitive donors reacted to the tuberculins. The other animal, receiving cells not capable of transferring tuberculin hypersensitivity, showed no reactivity. With converse testing a contact test with the chemical allergen showed negative results in the first guinea pig and positive with the second recipient.

These responses are specific. It is very difficult to comprehend why one cannot, by means of cellular transfer, attain this goal of sensitizing to chemical allergens between human beings with the same readiness as one does with guinea pigs. In both species, cellular transfer of tuberculin hypersensitivity can be attained readily.

Each test showing the responses of guinea pigs after the transfer of cells is read on the day following the transfer, since we are dealing with delayed reactions.

With living cells we get a rather uniform pattern from one experiment to another. But the same cell pool that imposed hypersensitivity when living cells were injected failed to do so when it was simply heated for fifteen minutes at 48 C.

The other cell pool transferred hypersensitivity typically, but when we froze the cells there was no transfer; in many other similar experiments we have not found it possible to transfer hypersensitivity with frozen-and-thawed cells.

COMMENT. With guinea pig cells we have tried all the technics that Dr. Lawrence has used with human white cells. We have frozen, we have lyophilized, we have done desoxyribonuclease treatment, we have used sonication, and we have tried water lysis. In my laboratory, Mr. Barry Bloom has devoted himself to finding out whether or not it is possible to get from the cells of guinea pigs a "transfer factor" that would transfer hypersensitivity either to chemical allergens or to tuberculin.

We now feel that the only report presently in the literature alleging that extracts from guinea pig cells are capable of effecting transfer was in error, and we think we know the source of the difficulty. But these experiences will serve to dramatize the differences in handling the cells of guinea pigs and man; that a "transfer factor" is missing from or is labile in the guinea pig requires an explanation if we desire to stress a biologic common denominator for men and animals.

Again, tuberculin hypersensitivity that is transferred from guinea pig to guinea pig by means of living white cells is not a sustained hypersensitivity but diminishes with time, unless the recipient guinea pig is genetically like the donor. In one recipient guinea pig, there was a persisting hypersensitivity, since the recipient was of the same inbred genetic strain as the cell donors; the test was made on the twenty-sixth day after transfer and was read at twenty-four hours. When another part of the same cell pool was injected into a guinea pig of another strain, by the twenty-sixth day there was hardly anything but some vestige of toxicity.

Now, so far as "transfer factor" is involved, such pairs of guinea pigs are not genetically further apart than is true in cellular transfer from man to man as Dr. Lawrence practices it. Dr. Lawrence finds long-term hypersensitivity in randomly chosen human recipients: wherefore, in part, the concept of "transfer factor." With randomly chosen guinea pig recipients, we find short-term hypersensitivity and long-term hypersensitivity only under special conditions.

With an inbred line of guinea pigs, in which lymph node cells were transferred between individuals (transfer ratio 1:1, that is, the lymph nodes of one animal into one recipient), even on the hundredth day there was still tuberculin reactivity, which hardly persists in transfers between guinea pigs of common stocks.

Finally, we may mention another situation that is curious as regards the concept of a "transfer factor." When we have a guinea pig that has been rendered incompetent immunologically to undergo sensitization to a particular chemical allergen, and one uses it as a recipient for cell transfer, the "pattern" of transfer is very much inhibited.

In another test study, 2 normal guinea pigs were recipients, 1 being given 0.29 ml. of cells, the other 0.33 ml. At each test, reactions were obtained over a twenty-six-day test period.

In contrast, 4 other recipient animals were rendered tolerant to the sensitizing effects of the same chemical allergen. The cell transfer produced positive reactions, but the inhibited recipients lost this donated hypersensitivity fairly quickly. Only when we got up to 0.42 ml. of cells for transfer did we find a reaction persisting at the fourteenth day.

Now, as I said before, these comments are not intended to damage the position of Dr. Lawrence's scientific work for which I have enormous respect, but I cannot help feeling that the last word has not yet been said about delayed-type hypersensitivity. If I had omitted to detail another kind of experience and had only complimented Dr. Lawrence, as I so richly and sincerely do, I think you would not see the magnitude of this problem that still confronts those who study the general area of delayed-type hypersensitivity.

Question and answer period

Joseph Fries, M.D.: Thank you, Dr. Chase. I believe we have a few minutes for questions. I don't think we ought to make it too long, and, as a matter of convenience, wonder if I may present the first question or questions.

If these studies must be done on human beings, are there any hazards, and has there been any confirmation of these studies? Dr. Lawrence.

Dr. Lawrence: The only hazard to these studies is the possibility of transmitting homologous serum hepatitis. We circumvent this by using cells obtained from donors who have shown that they do not transmit hepatitis, after having given blood to patients who needed a transfusion and by following such patients.

The second question concerns the confirmation of these results. Following the publication of the report of transfer with viable cells, there was a series of rapid confirmations of this fact by Urbach *et al.*, by Good and his group, and by several other laboratories.

The real question at issue, though, was, "Is it true that leukocyte extracts will transfer sensitivity?," and there was a period during which no one attempted to confirm this observation. Recently, Maurer has transferred delayed allergy to denatured human serum proteins by means of leukocyte extracts. Sanford has transferred tuberculin allergy by means of leukocyte extracts; Friedman, Fisher, and Cooke transferred delayed allergy to tuberculin using frozen and thawed or Seitz-filtered leukocyte extracts; and most recently Eisen, in some unpublished studies, was able to transfer delayed allergy to tuberculin, but since he used cells from a doubly sensitive donor he was unable to transfer delayed allergy to dinitrofluorobenzene by means of leukocyte extracts. The latter result again points up the distinctions that Dr. Chase made, that although bacterial allergy seems to be very readily transferable in human beings, there is some question about the ease of transfer of contact allergy of the delayed type.

Dr. Fries: Are there any questions?

Samuel J. Prigal, M.D.: I would like to ask Dr. Lawrence a few questions. In the first place, does complement play any role in this transfer? There seem to be some contentions that where a destruction of tissue occurs in this manner there must be some role for complement.

Second, can you tell us whether you are able to differentiate the type of leukocyte which is involved in this.

Then there is one question which particularly concerns those who are resorting to the repository method of treating hay fever. Isn't there a possible induction of delayed-type sensitivity, as has been shown by Samuel Feinberg, M.D.?

Again, a very fundamental and basic question to us: What role does the delayed type of hypersensitivity play in general, in terms of disease?

Dr. Lawrence: I would be glad to try and answer some of your questions. Concerning the role of complement, we have no information on it. In the experiments that Dr. Pappenheimer and I did, incubating sensitive cells with antigen, we assumed that complement was necessary and took great pains to use fresh serum to insure its presence. We have not deliberately eliminated complement from the system to see if this interaction would occur, and so I have no information on that.

The type of leukocyte: Dr. Chase would be a better one to answer this question, and I would quote from him a remark made at a symposium where a similar question was asked about which leukocyte was responsible for transfer, and he said he wasn't a lymphomaniac.

I have followed this very good precept, and we have, perhaps, gone out of our way not to designate a cell type. There are good reasons for this. In cytotoxicity experiments and from results of other studies, it is possible, for instance, that only 4 per cent of the cells may be responsible for the biologic function that we see reflected in the recipient, and these could be mononuclear cells.

We thought that the more sensible approach was to try to define the transfer factor biochemically and immunologically and then hope to backtrack to delineate the cell or cells involved.

Moreover, there may be more than one

cell population involved, and there is suggestive information that cells other than leukocytes may participate in this.

I am really well prepared to discuss the induction of delayed sensitivity with the adjuvant treatment since Dr. Chase discussed this at the dinner table with us. Perhaps he would care to say a word on this now. Those individuals who are engaged in the production of a serum antibody to a pollen stimulus would most likely continue this immunologic function. They may not develop delayed allergy to the material with which they are engaged in the production of serum antibody. However, the incorporation in an adjuvant mixture of a new material to which one is not producing serum antibodies is an ideal way of inducing delayed allergy to that other material to which the patient may not have been sensitive or may not have formed an immune response. I think that this possibility is still to be evaluated as a risk in such studies.

The last question concerns the role of delayed allergy in disease. I think the best example is afforded by tuberculosis, in which the pathogenesis of the lesions, the prolonged course, the symptomatology, indeed even the refractoriness to antimicrobial agents are direct reflections of the delayed allergy induced in the recipient. This is particularly true in patients who are subject to a growing population of microorganisms producing tuberculin. The caseating necrosis which we see in this disease and the clinical and pathologic course are manifestations of delayed allergy to the tubercle bacillus and its products.

There are other examples of the role of delayed allergy in disease. Spink has shown in patients with brucellosis that all of the symptoms of this disease can be produced by exposure to an adequate amount of antigen to which the patient has a delayed allergy.

I think there is little question of that relationship. The question I would pose relates to the role of delayed allergy in diseases that are postulated as being autoimmune. I think this area remains to be evaluated.

Dr. Fries: Matthew Walzer, M.D.

Matthew Walzer, M.D.: As to the ability of white cells in human beings to transfer reaginic allergy, I'd like to say that I have succeeded in an ascaris sensitivity experiment. In this case, with an extract of circulating cells, I transferred not only the delayed allergy but also a 4 plus immediate reaction. In another case recently published, I succeeded in transferring the immediate reaction without transferring the delayed sensitivity, and here again I obtained a 3 or 4 plus immediate reaction on transfer.

If I may take a moment, I would like to tie together what has been said about delayed allergy with what most of us are interested in, namely, the immediate type of hypersensitivity. Dr. Lawrence has tended to separate sharply the immediate and the delayed forms. I am in a position now where I think that they are not as separate as they appear to be.

For the last twelve years I have been interested in the leukocytic transfer of immediate sensitivity. I haven't the large supply of material that Dr. Lawrence has, and it was difficult to get volunteers if I also transferred the delayed sensitivity with ascaris. I tried to separate them to make sure that I would transmit only the immediate type.

The cases we studied first were of the atopic type, that is, as in ragweed sensitivity. These transfers were all slight and, of course, weren't good enough since there has been considerable doubt that they were actually specific.

I believe I have proof that they were specific, but I had to approach the subject from a somewhat different viewpoint. I proceeded to do sensitization experiments in human beings, and although I obtained leukocytic transfers of immediate sensitivity with 2, 3, and 4 plus wheal transfers specific in the subject, I found that I could not get such transfers unless the donors had delayed sensitivity as well as immediate sensitivity.

The more I have worked with this problem, the more have I found that the success of my transfer depended more on the intensity of the delayed sensitivity than it did on the intensity of the immediate sensitivity manifested by the donor. There is therefore no sharp demarcation between delayed sensitivity and the immediate type with circulating antibodies.

I think that as this work goes on we will find that the two forms of allergy are connected in a very much closer fashion than we deem possible today. May I say that the presentation of Dr. Lawrence and the discussion by Dr. Chase have been very exciting.

Dr. Fries: If the audience isn't too tired, I thought we could have another question or two.

Isidore D. Mechaneck, M.D.: Is there any relationship between the delayed type of reaction in skin testing and this delayed type of sensitivity we have been talking about?

Dr. Lawrence: Any relation between the delayed types of reaction to pollen antigen and the bacterial type of delayed allergy? I don't know. I would suspect that there may be.

Dr. Chase: Returning to the guinea pig as model, if one injects ovalbumin, for example, in the skin, one will find antibody shortly. But if the amount of ovalbumin is dropped down to a really small concentration, let us say 3 micrograms, and injected intracutaneously, a delayed type of reaction to ovalbumin will be found and will be present for from ten to twenty-one days before an antibody appears.

In my opinion this would be strong presumptive evidence that the delayed type of reaction should be expected to occur in man in consequence of receiving a repository injection containing a foreign protein. The appearance as a delayed reaction would be analogous to the delayed reaction as we see it in the tuberculin-tuberculosis relationship, although probably it would be infinitely weaker. The tuberculin hypersensitivity, which often can be elicited by 0.02 microgram of purified protein derivative in the first test dose or by 5 micrograms of purified protein derivative on the second, is, of course, rather a strong response to such small test doses.

But in the case of repository injections of emulsion, if I follow your thinking rightly, you are more concerned with the chances of finding a local slough because of the onset of delayed-type hypersensitivity than with the question of the relative intensity of the delayed type of reaction.

I believe that the Church holds one position on dogma, and it also has something that is called theological opinion; I wonder whether I could speak on the subject of "theological opinion?"

If I had a repository injection to make in the guinea pig and I didn't want to increase my chances for establishing a delayed type of reactivity, then when I filled the syringe I would put on a clean needle and I would leave its shank unfilled. I wouldn't displace air and load it to the tip as we customarily do with fluid prior to injection. I would enter this unfilled shaft through the skin to the position I wanted, I would make the depot, and as I withdrew the needle I would pull back on the plunger and pinch the skin together in a fold so that the needle would be wiped by the compressed deeper tissue as I withdrew the shaft of the needle. With the guinea pig, at least, by means of such tricks one can accomplish a great deal with relative safety.

Now, the problem as to whether or not these tricks are applicable to the injection of human beings I will turn over to you bishops.

Max Grolnick, M.D.: I will just take a moment to return to a question that Dr. Prigal raised concerning so-called depot therapy using pollen antigen. We were able to demonstrate that the delayed sensitivity in a few instances was followed by an immediate reaction. This accords with the findings of those who reported that there is a hazard in sensitizing an individual who originally is not actually sensitive to the antigen.

Arthur A. Goldfarb, M.D.: I wonder whether Dr. Lawrence or Dr. Chase would comment about the possibility of the repository technic being nonspecifically a stimulant. Would the adjuvant in itself, without any ragweed or grass in it, actually give a nonspecific stimulation of all the antibodies?

Dr. Chase: If I understand your question, you feel that if a so-called "blank emulsion" were given, where you had, let us say, a buffer, presumably pH 7.1 or 7.2, as the aqueous phase and also Drakeol as the paraffin oil phase, you would stimulate the immunologic apparatus to produce several varieties of antibodies such as it had produced in the past. I am of the opinion that this is not likely to happen at all. If we had a rabbit that had produced an antibody a year ago to the typhoid organism and were to measure the amounts of agglutinins in the circulation, an injection of such "blank emulsion" into the rabbit would give rise to no antibody response. I would see no reason to assume that you would incite the production of an antibody by making an injection in which the specific stimulus is missing.

Dr. Prigal: May I answer that question? This is a question that intrigues me. I have had some evidence which has suggested that perhaps the very medium that we use does exert some effect, and probably through the reticuloendothelial system.

In experiments which I have been doing with endotoxins, emulsifying them and thereby being able to give larger doses to our mice, we were able to demonstrate long periods of survival and survival to a high degree when these animals were challenged with a staphylococcus, which otherwise would have killed them, because 114 of 115 control animals died.

In one of the series of controls we used the identical emulsion minus the polysaccharide. These animals were also challenged in exactly the same way. We found, very much to our amazement, that the animals will not die in the same fashion. They are protected in some degree, as though one had injected them with a new dose of polysaccharide. My feeling is that perhaps we are coming closer to an explanation of this phenomenon.

Maury D. Sanger, M.D.: We are talking in terms of patients who are not sensitive to an antigen, and they are given the depot antigen. Can the same phenomenon occur in a patient who is known to be sensitive? In a ragweed-sensitive patient who is given an emulsion injection, can you produce a delayed hypersensitivity in that individual?

Dr. Chase: Do I understand you to ask whether a patient already sensitive to ragweed, receiving ragweed in an emulsion form, would be likely to develop a delayed-type hypersensitivity to the same material?

To such a question a little hedging is needed in answering. Ragweed extract contains several allergens and one particular patient might be sensitive, "reaginically speaking," to only one among the several. I don't think there is too much evidence for such an assumption. But it is conceivable. I believe that once you have started the antibody-producing mechanism so that one is producing serum antibody, you cannot impose a delayed-type hypersensitivity to the same material. Under marginal conditions, it might prove to be possible.

Now, could I say something about Dr. Prigal's remark?

The mouse that is given antitoxin has an acute physiologic change and reacts in various ways to many different materials. So does the mouse given two doses of pertussis vaccine, the mouse starved for four to twelve hours, and the mouse given three intraperitoneal injections of saline. Now, the respective alterations are of different magnitudes. An entire thesis developed in studies made in Columbia University was negated because mice receiving three injections of saline intraperitoneally acted precisely like an immunized group in which a virus served as the antigen.

Therefore, I think that the change in the physiologic response of an animal, by means of a material that is new to it, may well be the important part of Dr. Prigal's experience as I understand him, rather than that one has discovered a clue to the action of Freund's adjuvant that is long-lasting in its effects, not short-acting.

Usually such mice will rather shortly (with antitoxin, perhaps in three or four weeks, with other stimuli perhaps a shorter time) return to their pristine state.

Dr. Fries: In closing, may I express the feelings of the New York Allergy Society and myself in offering to you our warm thanks for a most informative evening.

Technic of the Sagi Test*

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FURTHER IMPROVEMENTS *and standardizations have been made in the technic of a test for malignant conditions which differentiates blood serum by its configuration on contact with various strengths of phenol solution, labeled as levels 1 to 5. A quantitative procedure has been developed. Blood is drawn in the postabsorptive period. A control is used with each unknown. A drop of negative serum forms a round pellet almost immediately; at about the fifth minute it begins to shrink gradually and eventually disappears. A drop of positive serum expands either immediately or shortly after its release, or it may flatten to a thin film or disintegrate more or less completely within a short period. Sera with negative reactions in level 1 are eliminated and reported as negative; sera with positive reactions in level 1 are tested through the lower levels using the same procedure. If the serum is positive only on level 1, it is recorded as 1 plus; if it is positive on all levels, as 5 plus. In a series of 4,000 sera from a cancer detection clinic, all were drawn during the absorptive period. In 1,800 of these which were cloudy, there were 402 positive test results. Eighty of these were repeated on a fasting stomach; 16 results were still positive, and 64 became negative. Further studies of the lipid fractions are in progress. It is not known if the degree of positivity of this test has any correlation with the clinical stage of disease, but a definite correlation has been found between the degree of positivity of the test and the duration of gestation.*

IN A PREVIOUS ARTICLE[1] the technic of a test which differentiates blood serum on phenol has been described. Various modifications have been made since then. This article will detail them. They consist in improvements and standardizations and in the development of a quantitative procedure.

Reagents

In a measuring cylinder 37.5 ml. of liquefied phenol (preferably Mallinckrodt), 2.5 ml. of a 10 per cent solution of sodium hydroxide, and 10 cc. of glycerin, chemically pure, are placed. The cylinder is shaken and inverted until the mixture becomes homogeneous without traces of streaks. The pH of this mixture is 8.1. To determine this pH, 5 per cent solutions in distilled water are made, and an electric pH meter is used. This solution is known as a level 1 reagent. Level 2 reagent is prepared by adding to 8 ml. of level 1 a mixture of 2 ml. of phenol and glycerin in the ratio of 3:1. This reagent now has a pH of 8. Levels 3, 4, and 5 are now prepared by adding 6, 4, and 2 ml. respectively of level 1 to 4, 6, and 8 ml. of the phenol-glycerin mixture. The respective pH values of these lower concentration levels are 7.9, 7.7, and 7.5. Reagents should be prepared one or two hours before using.

Apparatus

The apparatus consists of a pipet fitted with a needle, a support for the pipet, agglutination slides, a precooler, a platform for the slide, and a pan for cool water.

PIPET. One end of a glass tube, 15 cm. long, with an inner diameter of 7 mm., is drawn into a cone and ground. To the cone is affixed a 26-gauge hypodermic needle

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* This study has been supported by a grant from the Cancer Research Institute of New York, Inc., New York City.

† Deceased.

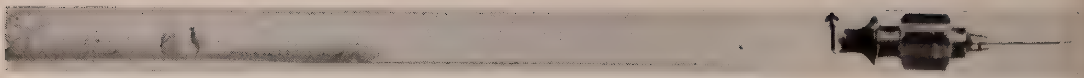

FIGURE 1. Pipet and hermetically sealed needle.

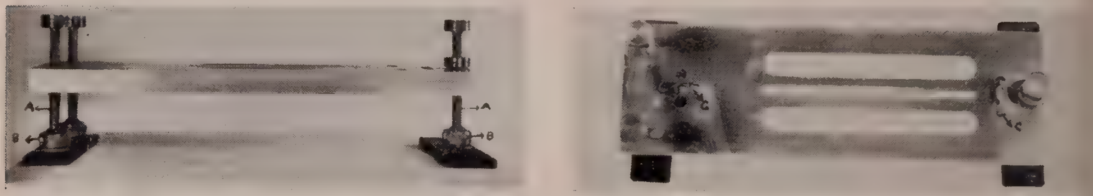

FIGURE 2. (Left) Support for pipet, side view. Three legs (A) support the stand. Cap bolts (B) may be adjusted to vary height. (Right) Support for pipet, view from above. Two water scales (C) allow for leveling the plate.

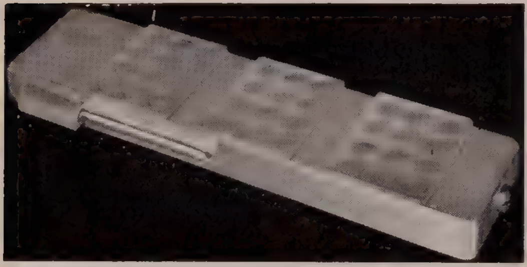

FIGURE 3. The precooler with thermometer in place and 3 agglutination slides being prepared.

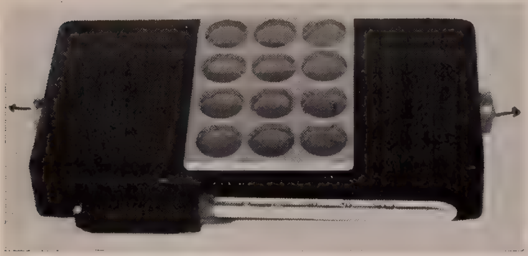

FIGURE 4. Platform for slide shows thermometer in place and one agglutination slide on black lacquer background.

with a shaft of 12 mm. in length. The needle is hermetically sealed to the pipet by a cement such as Sealit. In the other end of the pipet is inserted a tightly packed column of cotton, about 6 cm. long, leaving a free space of about 6 cm. at the lower end (Fig. 1). This both prevents the flow of saliva into the lower part of the pipet and slows down and regulates the formation of the drop of serum at the tip of the needle. The needle tip is kept sharp and regular. Any irregularity detected by touch or by the magnifying glass is corrected by applying 0/1 sandpaper. When it is not in use, the pipet is placed in a normal saline solution.

Support for the pipet. The support is a stainless steel plate 3 cm. thick, with two legs on one side and one on the other (Fig. 2). These legs (A) are of the screw type, affixed to the plate by cap bolts (B). The bolts may be loosened, allowing the height of the support to be adjusted. Two water scales (C) in the plate assure its being horizontal, which is regulated by the screws in the legs. In the plate are cut 3 parallel grooves. The middle groove is 3 mm. wide and 12 cm. long and serves to suspend the pipet by its contact with the quadrangular portion of the needle The two outer grooves permit better observation of the needle in relation to the cavity on the slide and of the formation of the drop.

Agglutination slide. The conventional agglutination slide with 12 cavities is used (Fig. 3).

The precooler. The precooler (Fig. 3) is a hollow metal block, 30 cm. long, 7.5 cm. wide, and 2.5 cm. high. A hole and a screw cap are present at either end, allowing it to be filled with cool water. There is also a slot for the insertion of a thermometer. The precooler serves as a stand for the slides while they are being filled with the reagent and for keeping them cool until they are ready for use.

Platform for slide. The platform (Fig. 4) is a hollow metal block, 15 cm. long, 7.5 cm. wide, and 2.5 cm. high. It is finished with a black lacquer and contains the same provisions for temperature control as the precooler.

Pan for cool water. The pan should be sufficiently large to keep the required number of test tube racks in cool water.

Procedure

Blood is drawn and prepared as originally described.[1] It is well to note that blood should be taken in the postabsorptive period, as results obtained with blood taken within eight hours of eating are valid only if the findings are negative, no matter whether the serum is clear or cloudy. If such a serum gives a positive result, a repetition with fasting blood is necessary.

The room temperature is kept between 20 and 23 C. by an air-conditioning unit. If this is not available, a temperature of about 20 C. of the sera should be maintained by placing the tubes in a water bath.

Four agglutination slides are placed on the precooler adjusted to a temperature of from 15 to 17 C. Three drops of the desired reagent are now placed in each cavity by a pipet which releases 30 drops to each milliliter. One slide, so loaded, is placed on the platform for the slide, which is adjusted to a temperature of from 15 to 19 C. Temperatures of both the precooler and the platform are regulated by immersing them in a bath of ice water and then allowing them to warm to the desired temperature.

The support for the pipet is placed directly above the platform for the slide, the latter being perfectly horizontal. The support is brought into a horizontal position by manipulating the screws if the water scales show any deviation. The distance between the top of the slide and the top surface of the support should be 19 mm. and should be adjusted if necessary by manipulating the legs of the support.

Serum is now drawn into the pipet, which is placed in the middle groove perpendicular to the plane of the support, and the needle is aimed at the center of a cavity. The drop is now released. If its formation is retarded, slight pressure with the finger tip on the top orifice of the pipet is exerted. The same pipet is used continually for all sera, but it should be rinsed once or twice with each serum, and these rinsings should be discarded.

A control is used with each unknown. This control is made up of a pool of from 8 to 10 previously inactivated sera. Such sera have been exposed to a temperature of 58 C. for half an hour, rendering them negative even though they may previously have been positive. One drop of the unknown is released to each of 2 cavities and a drop of the control to the third.

A drop of negative serum forms a round pellet almost immediately with a smooth circumference and a regular shape on the surface of the phenol reagent. Gradually it begins to shrink at about the fifth minute after release, eventually disappearing.

A drop of positive serum either expands immediately or shortly after its release, or it may flatten to a thin film or disintegrate more or less completely within a short period. As the fate of the drop is partly a function of time, five minutes are allowed to pass between the release of the last drop and the reading of the result. A trained person can release 4 unknown sera and 4 controls on an agglutination slide in about five minutes. Thus, one slide is read at the completion of the loading of the next slide. Comparison in size is made by contrasting the unknown drop with the control drop against a dark background. Figure 5A illustrates a negative and 3 types of positive reactions after five minutes with reagent level 1, while Figure 5B shows the same sera with reagent level 5.

If the 2 drops of the unknown differ from each other, the test is repeated until these drops agree. Sera with negative reactions in level 1 are eliminated and reported as negative. Sera with positive reactions in level 1 are tested through the lower levels, using the same procedure. If the serum is positive only on level 1, it is recorded as 1 plus; if it is positive on all levels, as 5 plus.

Comment

In a series of 4,000 sera from a cancer detection clinic, all were drawn during the absorptive period. About 1,800 of these sera were cloudy in various degrees up to gross lactescence. In this 1,800 there were 402 positive test results. Eighty of these

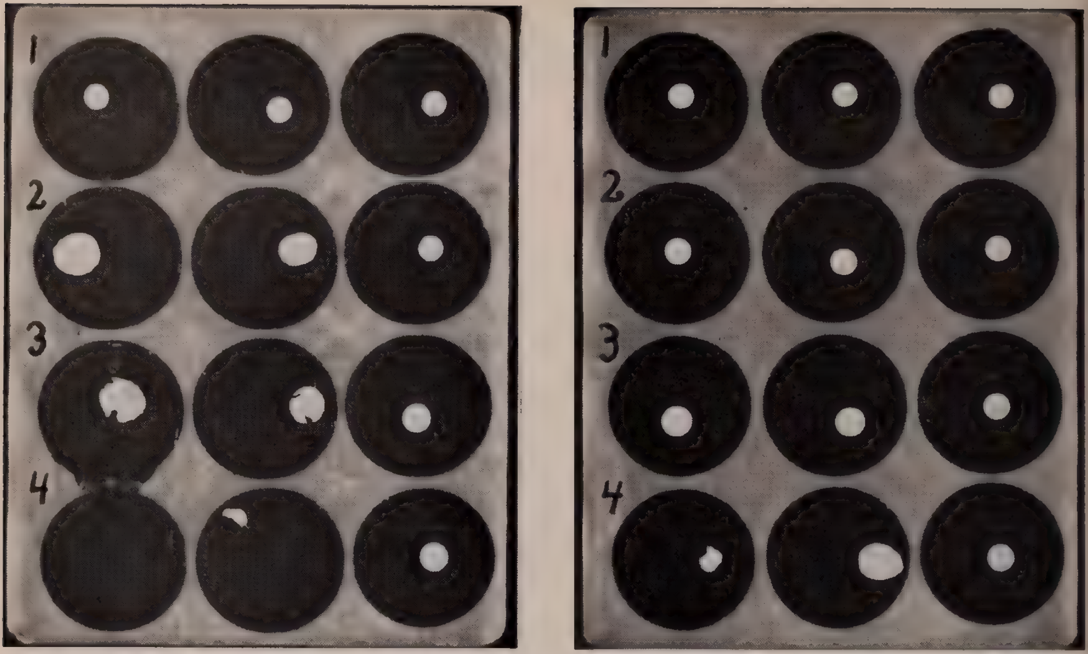

FIGURE 5. (Left) Various reactions after five minutes with level 1 reagent: 1 = negative reaction; 2, 3, and 4=different types of positive reactions. (Right) Various reactions after five minutes with level 5 reagent. These are the same sera as those illustrated at left. At this level only serum 4 shows a strong positive reaction.

were repeated on a fasting stomach, and 16 results were still positive and 64 became negative. Some sera with a 5 plus positivity reverted to negative on a fasting blood. One can understand why cloudy sera with innumerable suspended fat globules may be less resistant to penetration by phenol and consequently may dissolve more freely. This may cause the drop to spread and disintegrate. However, occasionally even grossly lipemic sera give negative results, and at present there is no explanation for this phenomenon. Experiments are now in progress to attempt to identify which lipid fractions may be responsible for positive results in transparent sera containing more than 500 to 700 mg. of lipids per 100 ml.

It is not known if the degree of positivity of this test has any correlation with the clinical stage of disease. A definite correlation has been found to exist between the degree of positivity of the test and the duration of gestation.[2]

Summary

Details concerning the preparation of reagents, the apparatus, the procedure, and the reading of results of the Sagi test have been enumerated. A short discussion concerning some of the factors involved in lipemic sera has been given. Future studies and the incomplete results of some of the programs now in progress have been mentioned.

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Ureteral Ectopy Without Incontinence in Reduplicated Kidneys

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THE MOST FREQUENT SIGN *of ureteral ectopy is intermittent urinary incontinence despite normal micturition. Infection usually is present and adds to the patient's distress. In the absence of urinary incontinence, this disease cannot be recognized solely by its clinical picture. An ectopic ureter may be symptomless if it is uncomplicated by infection. The diagnosis is the result of x-ray examination which is requested for an unexplained and stubborn urinary infection or as part of a work-up for vague abdominal pains. The final diagnosis rests on the identification of the ectopic ureteral orifice, which can be facilitated by intravenous injection of indigo carmine. Repeated examinations are usually necessary. Two cases of ectopic ureters without incontinence in reduplicated kidneys are presented. A greater awareness of this condition would result in more frequent diagnoses. The treatment of the condition should be specific according to the individual findings, as illustrated by the different surgical procedures employed in the 2 cases presented.*

THE GENITOURINARY system abounds in various modalities of maldevelopment. The detection of these malformations often will elude our most critical diagnostic methods, and the clinical manifestations often depend soley on their complications.

The following 2 cases illustrate a less common form of ureteral anomaly and the individualism that should be retained in the attempt at surgical correction.

Case reports

CASE 1. An eleven-year-old white female was admitted to the Albany Hospital in November, 1959, because of fever and abdominal pains.

She had a history of recurrent episodes of hematuria and pyuria associated with fever and vague abdominal pains for the past two years. Conservative treatment with sulfa drugs and antibiotics by her family physician brought only slow and partial relief of her symptoms. The past history and physical examination on admission revealed no other pertinent findings.

The laboratory studies showed a hemoglobin of 11.8 Gm., a white blood count of 11,200 with a normal differential count, fasting blood sugar of 77 mg. per 100 ml., and blood urea nitrogen of 10 mg. per 100 ml. A urinalysis was within normal limits.

Excretory urography before admission suggested the possibility of a reduplication of the left collecting system (Fig. 1).

Cystoscopy was performed under general anesthesia. An examination of the vulva showed it to be normal, as were the bladder walls and mucosa. Normally placed ureteral orifices were identified. Alerted to the possibility of a reduplication of the left ureter by the previous intravenous pyelogram, the examiner, hoped to visualize the double ureters by filling them from below with the Braasch bulb. This method failed to reveal two ureters. Therefore, indigo carmine was given intravenously, and close scrutiny of the trigone and the bladder neck was rewarded by the identification of a ureteral orifice directly in the middle of the floor of the urethra proximal to the external sphincter as blue ejaculate was seen to originate from it. A ureteral catheter was introduced immediately, and studies were done. The pyeloureterogram showed a moderately hydronephrotic superior group of collecting cavities.

A conservative surgical correction was done three days later. Because of good function on the intravenous pyelogram and a mild degree of hydronephrosis, the ectopic ureter was sectioned as low as feasible through a left Gibson

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* By invitation.

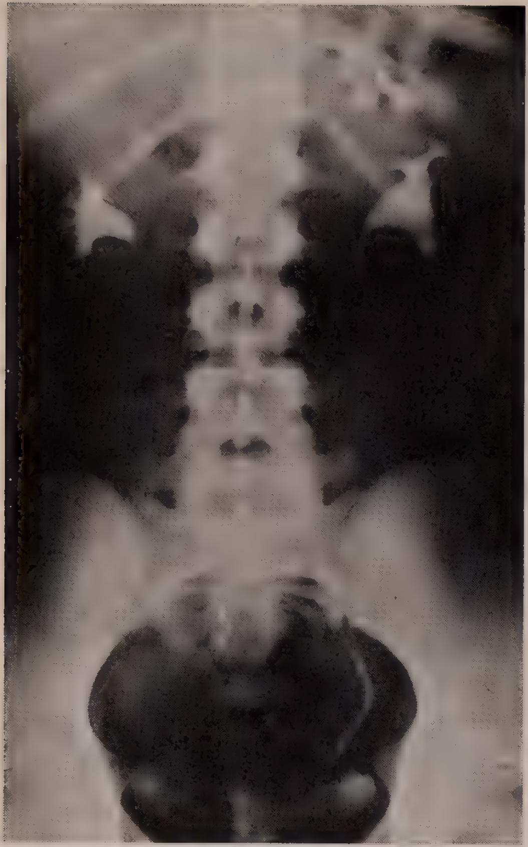

FIGURE 1. Case 1. Intravenous pyelogram taken preoperatively.

incision and was reimplanted into the bladder using the Leadbetter technic to prevent reflux.

The patient made an uneventful recovery and was discharged thirteen days later with a few pus cells in the urine.

Three months following her discharge from the hospital the patient was still free from symptoms. The pus cells disappeared from the urine. An intravenous pyelogram showed good dye concentration in the ectopic group of calyces and a decrease in the hydronephrosis. A culture at that time was negative. There was no evidence of reflux.

Check-up films done one year postoperatively showed marked improvement in the hydronephrotic upper half and no evidence of reflux (Fig. 2). The patient was free of symptoms.

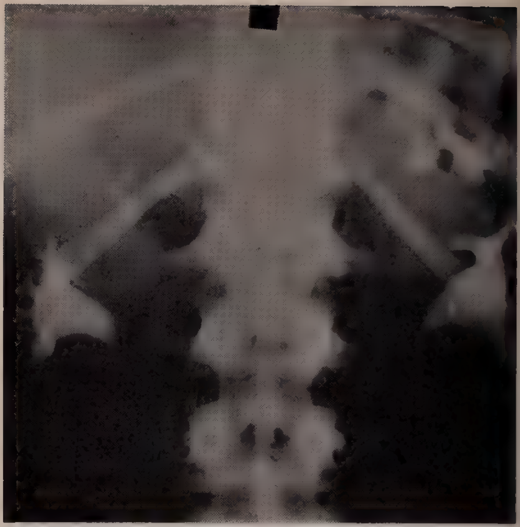

FIGURE 2. Case 1. Pyelogram taken one year postoperatively.

Case 2. A twenty-one-year-old white female nurse was admitted to the Albany Hospital in August, 1959, with the chief complaint of left flank pain, frequency, and a low-grade fever.

The patient was born with a cleft lip and palate on the left side which necessitated repeated surgical intervention for adequate correction.

Since the age of ten years she had complained of an intermittent, dull pain in the left flank. Routine urinalyses on her many hospital admissions showed a progressive increase in the number of white blood cells and albumin. There were occasional episodes of fever and urgency, but these bouts never were severe enough to warrant a hospital admission up to the time of the 1959 admission. The attention was always focused on the correction of her more apparent deformities.

On admission she complained of moderately severe left flank pain without radiation. She had frequency, urgency, and dysuria with some nausea and vomiting.

The urinalysis showed many white blood cells and a 3 plus albuminuria. No acid-fast bacilli were found in the urines, and the lupus erythematosus preparation was negative. C-reactive protein could not be detected.

An intravenous pyelogram showed normal findings. A cystoscopy and a pyelogram on August 7, 1959, failed to demonstrate any abnormality. Once again the antibiotics cleared her urinary infection, and she was discharged.

Three months later she was again admitted with a recurrence of her urinary tract infection. The urinalysis revealed many white blood cells. The blood urea nitrogen determination was 14 mg. per 100 ml. Intravenous pyelograms again showed normal findings except for one delayed film which gave a slight suggestion of dye above the normal left pyelogram (Fig. 3). In view of this the cystoscopic examination was repeated, and after thorough observation an ectopic ureteral orifice was found, opening on the floor of the urethra, proximal to the external sphincter. A ureteral catheter was introduced, and a retrograde pyelogram revealed a hydronephrotic

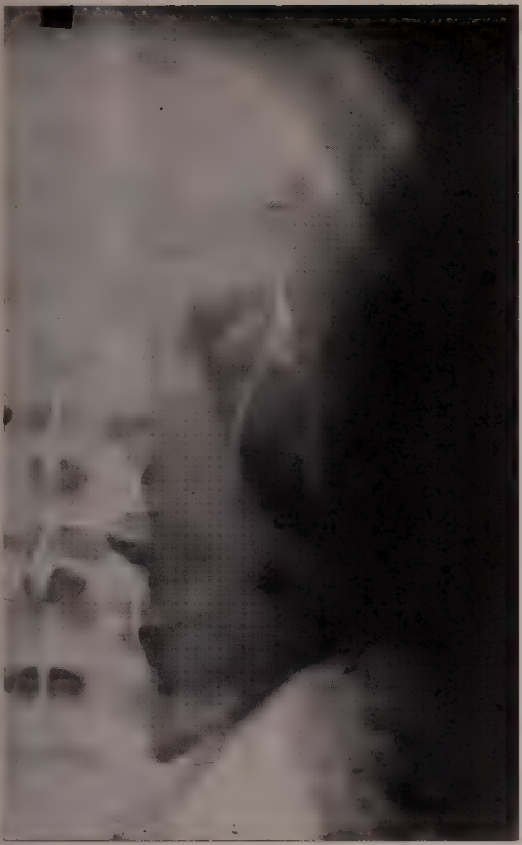

FIGURE 3. Case 2. Preoperative intravenous pyelogram showing a suggestion of dye above the normal pyelogram.

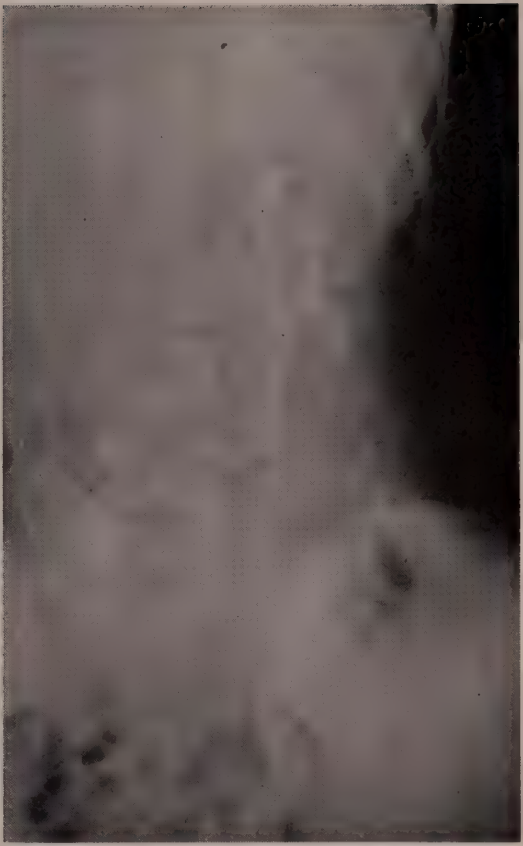

FIGURE 4. Case 2. Ureteropyelogram showing double kidney.

club-shaped upper collecting system on the left side with a widely dilated ureter (Fig. 4). There was no phenolsulfonphthalein excretion in one hour.

The absence of function from the ectopic elements and the presence of persistent infection made conservative surgery unjustified. On November 23, 1959, a left partial nephroureterectomy was carried out. The ectopic kidney tissue measured 3 cm. and had a separate blood supply. The ureter was removed entirely. The patient recovered without incident and was discharged six days later. Since then she has had sterile urine and has remained free of urinary symptoms for over a year.

Comment

The most frequent sign of ureteral ectopy is intermittent urinary incontinence despite normal micturition. As with most congenital anomalies of the urinary tract, infection usually is present and further adds to the patient's distress. Patients will peddle their malodorous handicap from one doctor's office to another for many years before the condition is recognized. The relative infrequency and inconsistency and perhaps even the unfamiliarity with this anomaly explains the failure by the examiners to make an early diagnosis in most cases.

In the absence of urinary incontinence, obviously this disease cannot be recognized solely by the clinical picture. An ectopic ureter opening proximal to the urethral sphincter may be symptomless if it is uncomplicated by infection. The diagnosis is purely a roentgenologic finding, the x-ray examination being requested for an unexplained and stubborn urinary infection or as part of a work-up for vague abdominal pains. Both cases reported fit into this category.

The reduplicated kidney was obvious in 1 case since the functioning parenchyma excreted enough dye to demonstrate clearly the anomalous tract, but the reduplication in the second patient was not evident. The long-standing infection resulted in the destruction of most of the functioning nephrons, and little, if any, dye could be seen above the normal lower kidney segment. Presumptive evidence of the condition was entertained solely on the basis of an extended kidney shadow without evidence of collecting cavities.

The final diagnosis rests on the identification of the ectopic ureteral orifice. This can be facilitated by the intravenous injection of indigo carmine, followed by careful observation of all the lower urinary tract and vulva. The escaping dye may help to spot the anomalous opening. However, the theoretic value of this adjunct is seldom substantiated in practice, since the ectopic kidney is usually too diseased to concentrate enough material to make it visible. Therefore, one must scrutinize the mucosal surface, gently probing each little dimple in the hope that one of them will be the stray orifice. Repeated examinations are necessary, as a rule, before the search is successful.

Most reported cases of ectopic ureters emptied distal to the external sphincter; less commonly the orifices will open on the floor of the posterior urethra.

This condition is by no means rare. Its occurrence in 2 consecutive cases makes it interesting, and we cannot but wonder if the second case would have been diagnosed if the first one had not been found such a short while before. The greater awareness of this condition certainly results in more frequent diagnoses.

The treatment of a condition should be specific according to the individual findings. This is well illustrated by the different surgical procedures done on each of these cases. Definitive treatment, of course, should be the goal. The blind removal of diseased organs, although curative, may sacrifice normal tissue. The extent of the destruction must be weighed against the recuperative power of the kidney. The first case was certainly worth salvaging. The second case necessitated the removal of a nonfunctioning, infected, upper portion of the left kidney.

The follow-up is perhaps too short for us to make any comments on the effectiveness of the management, but we cannot discount the patients' freedom from urinary symptoms and complete well-being.

Summary

1. Two cases of ectopic ureters without incontinence in reduplicated kidneys have been presented.
2. The individual case warranted different surgical correction.

Discussion

Edgar A. Slotkin, M.D., *Buffalo, New York.* The authors have brought to our attention the necessity for careful urologic investigation in cases of ectopic ureters. The frequency of diagnosis is directly proportionate to the amount of interest, awareness, persistence, and care exerted by the examiner. The symptoms, pathology, and the corrective surgery depend on where the ureter terminates as well as the amount of damage to the renal element that is involved.

About 75 per cent of all the recorded cases involve the incontinent female. The 2 cases presented today are not in this category and are of further interest because of their management and the good surgical judgment exercised.

I would like to call attention to several points. First, ureteral ectopy usually is associated with duplication of the renal pelvis and ureter, and the orifice drains the ureter which connects the upper renal pelvis. This is the Weigert R. Meyer law, in other words, the ectopic ureter drains the upper renal pelvis or segment, and the orifice is located in the more caudal position. Second, the termination of the ureter in order of frequency in the female is the vestibule, urethra, vagina, uterus, and rectum. In the male, in order of frequency, the ureter terminates in the posterior urethra, seminal vesicle, prostatic utricle, ejaculatory ducts, and the vas deferens.

Hypoadrenocorticism and Endocrinologic Treatment of Meniere's Disease

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HYPOADRENOCORTICISM *exists in the general population to a greater degree than has been recognized. Individuals with this condition react poorly to stress because of hormonal imbalance or lack. The disease may be inherited or acquired as the result of cortisone therapy or repeated stress. Patients with inherited hypoadrenocorticism have many common characteristics. A diagnosis is possible by means of a careful endocrine history and physical examination. The four-hour glucose-tolerance test is the most important laboratory test for hypoadrenocorticism. It is the author's belief that Meniere's disease is a localized vasomotor reaction to a general series of external influences on a body predisposed by an abnormally reacting autonomic nervous system. The major factor in this abnormality is hypoadrenocorticism. In 75 cases treated by the author, 90 per cent have shown good responses to the use of whole adrenal cortical extract and other glandular therapy. The avoidance of stress and the importance of diet are emphasized. Adrenocortical therapy leads to the repair of the capillary system and the resorption of the transudate and diminishes the tendency to angiospasm. Of the three main symptoms, vertigo is improved markedly in from two to four weeks, and tinnitus is relieved after from two to three months, but hearing loss improves much more gradually, if at all. There are no contraindications to use of the whole physiologically balanced adrenal cortical extract in doses ranging from 1 to 100 cc.*

THE PROBLEMS OF STRESS and lowered adrenal cortex function, allied with other endocrine disturbances as related to otolaryngology, were presented at the Fifth Pan American Congress in 1956 in San Juan, Puerto Rico, and the Sixth International Congress in 1957 in Washington, D.C.

We studied the effects of faulty adrenal function in viral infections, infectious mononucleosis, vasomotor rhinitis, allergies, certain types of headaches, recovery from surgery, and in Meniere's syndrome. The results in our treatment of endolymphatic hydrops have been so encouraging that it was deemed worth while to study this aspect in fuller detail. By establishing that the cause of this condition is of endocrinologic origin, I believe that we can treat the disease so that we not only alleviate symptoms, but also re-establish the endocrine balance and thus permanently help this condition. At the present time the various other methods of treating Meniere's syndrome aim only at treating symptoms. Of course, as in all endocrinologic dysfunctions, prolonged treatment may be necessary to re-establish and maintain homeostasis.

Most investigators seem to agree that there is some dysfunction present in Meniere's disease which interferes with fluid and electrolyte metabolism in the inner ear. There must be some general mechanism disordered by many types of stimuli. Williams[1] states the following:

> The precipitating factors are those which produce stress or tendency toward alteration in either the organism's external or internal environment.
>
> The evidence appears to suggest, therefore, that the physiologic mechanism by which the

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organism resists stress of all types is a mechanism which has become increasingly more elaborate but which retains as one of its fundamental factors a typical autonomic reaction consisting of arteriolar spasm and capillary dilation.

It is on the hypothesis that this condition is due to a dysfunction of the normal autonomic defense mechanism which includes the peripheral vascular bed, that most successful treatments of Meniere's syndrome, whether consciously or unconsciously have been based.

Menkin[2] has demonstrated that adrenal hormones decrease capillary permeability and normalize it.

Effects of faulty adrenal function

About six years ago I learned that some intense studies had been made on the hypoadrenocortical state or what I prefer to call Tintera's syndrome. Interestingly enough, in his studies of 200 patients Tintera[3] had found tinnitus in 3 per cent, vertigo in 20 per cent, anorexia in 34 per cent, and epigastric distress in 51 per cent. These findings led to our collaboration in the treatment of Meniere's disease and of various other otolaryngologic conditions due to hypoadrenocorticism.

A state of hypometabolism, that is, hypoadrenocorticism, exists in the general population to a far greater degree than has been recognized heretofore. These patients react poorly to stress situations because of a lack of hormonal production or an imbalance of these hormones. Any stress elicits increased demands for adrenocortical hormones to meet the increased needs for cellular activity. The sudden demands may be enormous at times. Each of the groups of adrenal hormones bears its own role in nourishing the tissues and in maintaining electrolyte balance and vasomotor stability. The increased secretion of these hormones is essential for resistance to stress. Homeostasis is maintained by proper integration of the two important systems of the body, the hormonal and autonomic nervous systems. An involvement of one system upsets the function of the other. Nervous stimuli may, therefore, result in hormonal imbalance or, conversely, hormonal imbalance may be manifest in nervous aberrations, such as vasospasm.

The capillary system in normal individuals is well adapted to meet the emergency calls imposed by the stress reactions. However, once the capillary wall is altered and increased capillary fragility is evidenced, the capillary system can no longer withstand the burden of the stress reaction. We feel that whole adrenocortical therapy leads to repair of the capillary system and the resorption of the transudate, thus diminishing the tendency to angiospasm. Gonadal therapy further relieves the vasomotor instability through the autonomic nervous system.

We found that of these many problem patients were treated in an unsatisfactory fashion or referred to psychiatrists because of symptoms which were considered vague or emotional in origin and which were frequently disregarded. With an understanding of certain endocrinologic precepts, the basis of many of these complaints can be put on a definite physiopathologic etiology.

Hypoadrenocorticism itself may be inherited or acquired. Acquired hypoadrenocorticism may be due to cortisone therapy or to repeated stress such as severe infectious diseases, injuries, exposure to extremes of weather, surgical procedures, or emotional situations. All patients of the inherited type usually are very meticulous and conscientious. They are perfectionists in all their activities and drive themselves to exhaustion, not knowing what it means to relax. Generally, their intelligence is above average, but they usually are of a nervous, irritable, and apprehensive temperament. They frequently complain of excessive weakness, fatigue, depression, sluggishness, and faintness. A frequent complaint is the inability to fall asleep readily and waking after a few hours, due to hypoglycemia, occasionally complaining of headaches and dizziness. Indeed, this is probably often the basis of chronic alcoholism. On awakening in the morning, the patients feel more tired than on retiring and need several cups of coffee to "get going."

In women the menarche has its onset later than average. In one third of the cases the flow of menses ceases on the fourth day, then starts up again. Eighty-five per cent of the women have premenstrual tensions, nervousness, emotional instability, severe headaches, and an increased craving for carbohydrates which may take the form of alcohol. Dysmenorrhea is a frequent complaint. Most of the women in our Meniere's disease list are in their late thirties and early forties. When questioned closely, they disclosed that they were beginning to have symptoms of the menopause without realizing it. Werner[4] noted that tinnitus and vertigo are not uncommon before, during, or after the menopause.

The appearance of hypoadrenocortical patients is very typical. The women are of the thin asthenic type, most often flat chested, and with long, thin necks. They have fainting spells and palpitations. Men are often the lean, smooth-bearded, intellectual types. Both sexes usually have a full head of fine abundant hair. The extremities are proportionately longer than the torso. Bercovitz[5] has remarked that after some familiarity with this type of patient, one can recognize them when they walk through the door. In males the hair on the lower lateral two thirds of the legs is usually absent with little or no hair on the chest, and there is often a delay in the start of shaving. However, variations in the functioning abilities of the pituitary, thyroid, ovarian, or androgenic hormones may alter the makeup of the pure hypoadrenocortical type of patient.

There is an easy bruisability, as a result of an increased capillary fragility. In general, all these people fall into the allergic diathesis group. An orthostatic hypostatic hypotension is usually found, accounting for the inability to fall asleep readily and the feeling of dizziness on suddenly assuming the erect position. Some patients may have a marked puffiness of the lower lids on awakening. This subsides after a few hours. The nasal turbinates are enlarged and many patients complain of nasal stuffiness.

Diagnosis

A diagnosis is possible by means of a careful endocrine history and a physical examination rather than by elaborate laboratory tests.

Of all diagnostic laboratory tests for hypoadrenocorticism, the four-hour glucose-tolerance test is the most important. Of significance is the low fasting blood sugar, with a slight rise after from one to two hours, and a subsequent fall to hypoglycemic levels. The hypoglycemia is generally thought to be due to hyperinsulinism and is often confused with tumors of the pancreas, but actually it is due to the faulty regulatory mechanism of the adrenal cortex on the pancreas. In younger individuals we usually find a flat curve, with a dropping off between the third and fourth hours.

In almost all of these cases we find a low metabolic rate of minus 11 to minus 15, and the protein-bound iodine determination is normal. A low basal metabolic rate is not necessarily an indication of thyroid deficiency or for thyroid medication. These patients have been found to be extremely sensitive to thyroid extract. Where necessary, small doses ($^1/_4$ grain) should be given. Because of the lowered basal metabolic rate these patients have been labeled atypical hypothyroid patients. However, with the availability of the protein-bound iodine and radioactive iodine tests it is readily recognizable that these patients may have a lowered metabolism but certainly not on a thyroid basis. The use of adrenocortical extract regulates the thyroid-adrenal axis. Thyroid activity is temporarily depressed and later resumes normal activity. During this period, the small doses of thyroid extract are useful for a short time.

Liothyronine (Cytomel) is only a fraction of the whole thyroid hormone. However, any beneficial results from a fraction of the thyroid hormone have been due to an immediate temporary effect on the thyroid-adrenal axis in its ability to stimulate the adrenal cortex. This explains why symptoms recur quickly when liothyronine is discontinued. An examination of the blood reveals a lympocytosis and an eosinophilia. Many women have been treated for anemia. Another indication of adrenal involvement is the low titer of the 17-ketosteroids. However, higher levels are possible if the determination is made at a time of stress or strain.

A combination of ascorbic acid plus natural bioflavonoids is useful to protect the capillaries against damage by maintaining the integrity of the capillary walls and intercellular cement. When protected by adequate amounts of ascorbic acid and the natural bioflavonoids, the capillaries are better adapted to meet the emergency calls of the alarm reaction and are thus better adapted to withstand the burden of stress reactions.

Comment

There have been a multitude of concepts in the therapy of Meniere's syndrome. Dederding[6] and Cawthorne and Fawcett[7] restricted fluids. Furstenberg and his associates[8] advocated a low-sodium, high-potassium diet and ammonium chloride. Dohlman,[9] Derlacki,[10] and Dean[11] felt that many cases were on an allergic basis. Atkinson[12] grouped his patients into vasoconstrictor and allergic groups, depending on their reaction to intradermal histamine. Wright[13] felt that focal infection was an important cause of Meniere's syndrome. Some authors[14] have incriminated an avitaminosis or dietary deficiency. Histamine therapy has been advised in the past.[15]

It is my belief that endolymphatic hydrops is a localized vasomotor reaction to a general series of external influences on a body predisposed by an abnormally reacting autonomic nervous system response. The major factor in this abnormality is a subclinical Addison's disease, that is, hypoadrenocorticism or Tintera's syndrome. The therapeutic application of this concept with the use of whole adrenal cortical extract plus other glandular therapy has substantiated this line of reasoning. Of our 75 cases, 90 per cent have unfailingly shown good responses and have recovered. Treatment on an individual basis is necessary and cannot be routinized.

Treatment

In treating these patients it is very important to give them some explanation of the nature of their illness. They are told why they must avoid fatigue, worry, infections, and other stresses. The importance of their diet is stressed, especially the avoidance of excessive carbohydrate intake. Its relationship to fatigue and weakness is explained.

The primary aim is to relieve the adrenal cortex of excess stress, thus suppressing adrenal cortical hyperstimulation and give it an occasional "refractory period" to allow the cells to return to a better functioning state if this is possible, that is, to provide a cortical reserve so that response to stress is not manifested by abnormal vasomotor reactions. Sufficient amounts of whole adrenal cortical extract are given so that the target organs, depending on these hormones, are adequately supplied to produce a normal physiologic response. It must be emphasized that this is not a replacement form of treatment but an adjunct to the normal physiologic response of the glands to stress. Depending on the severity of the condition, 10 cc. of whole adrenal cortical extract are administered intravenously slowly at varying intervals ranging from every four hours initially to as long as once a week. Two cc. of Benadryl hydrochloride solution are added to the intravenous infusion in the severe cases. As the signs of adrenal cortical insufficiency diminish, the interval between injections is gradually increased. Adrenocortical therapy thus leads to the repair of the capillary system and the resorption of the transudate and diminishes the tendency to angiospasm. Of the three main symptoms, vertigo is the first symptom to be relieved and is improved markedly in from two to four weeks. Tinnitus is relieved after from two to three months. Hearing improves much more gradually, if at all.

There are absolutely no contraindications to the use of the whole physiologically balanced adrenal cortical extract in doses ranging anywhere from 1 to 100 cc. Electrolytic disturbances are never encountered, provided the patient eats a sufficient amount of salt.

Although whole adrenal cortical extract is possibly the main implement of our armamentarium, it is very definitely only a part of the therapy. There is never a situation of a pure glandular dysfunction without the involvement of the entire glandular system. For example, many ramifications are seen in an upset of the thyroid-adrenal axis. The ultimate improvement of one gland may be accomplished through extracts of another gland. The younger women almost invariably have symptoms of an ovarian deficiency. Their manifest symptoms of fluid retention (ankle edema) are corrected if the proper dose of estrogen and progesterone are given, for instance, in the failure of corpus luteum development. Very often deficiencies of either of these hormones are the causes of general edema, especially prior to the menstrual period. This gonadal therapy relieves their vasomotor instability through the autonomic nervous system. In males, on the other hand, the greater proportion of testosterone and its analogues are produced in the adrenal cortex. The testosterone thus helps to restore the normal function of the adrenals and testes, and at the same time it decreases hypophysial gonadotropins. The pituitary responds to any deficiencies of the glands in the endocrine symphony by producing excessive amounts of all trophic hormones accounting for hypertension, and so forth.

The autonomic nervous system undoubtedly plays a major part in converting emotional stimuli into symptoms. An autonomic nervous system stabilizer, Bellergal, has been of value in obtaining the normal integration and stabilization between the nervous and glandular systems. Thus the role of emotions in the production of functional symptoms is minimized.

We cannot overemphasize the importance of diet in conjunction with therapy. Patients will usually adhere to the prescribed diet once they realize from careful discussion and personal experience that any dietary indiscretions, although slight, will cause an exacerbation of their symptoms. Dietotherapy is aimed at alleviating the stress imposed by readily absorbable carbohydrates and also at obviating sudden rises in blood sugar with subsequent sudden falls. Such foodstuffs are considered "adrenotoxic." It is the hypoglycemia which precipitates many of the symptoms enumerated previously, and it is with this sudden fall in blood sugar that symptoms in the autonomic nervous system are generally found. Between-meal feedings of milk or fruit are advised to prevent any slackening-off of blood sugar levels which are prone to occur from two to three hours after eating. This point is stressed very strongly. Salt is allowed in unrestricted amounts because of a tendency to sodium depletion. A diet high in protein, moderate in fat, and low in carbohydrates is advised. For the first month the diet is reviewed repeatedly. It must be very strictly adhered to for the first year.

ACTH has been recommended but with little success and is only indicated where cortisone has been used previously since it is the trophic hormone for the glucosteroids. The adrenal cortex may be stimulated to greater secretions, but the result is temporary and not curative. Cortisone is primarily a glucose-regulating hormone and therefore has little effect on the other groups of adrenal steroids except in causing salt and fluid retention which is just what we do not want. Their therapeutic application is not without danger as I have pointed out in previous reports,[16] whereas whole adrenal cortical extracts aid in the recovery of the endocrine system.

Summary

It is believed that all types of Meniere's disease have a common capillary dysfunction, namely, a localized expression of a basic hypometabolic state due mainly to a lowered adrenal cortical function but always accompanied by some other endocrinologic involvements.

By familiarizing the otolaryngologist with its symptoms and history an attempt is made to help him recognize hypoadrenocorticism without the necessity for complicated laboratory procedures. However, some knowledge of endocrinology is essential. Roberts[17] has shown how useful this knowledge can be to the otolaryngologist. Tintera[3] has pointed out how an unbalanced or lowered adrenocortical function is related to stress. The role of stress in Meniere's syndrome has been shown repeatedly.

Endolymphatic hydrops frequently has been treated symptomatically. It is felt that the method of treatment outlined re-establishes a normal balance to the whole endocrine system. There are absolutely no contraindications to the use of the whole adrenal cortical extract as used, and there are no further endocrinologic involvements. These cases have responded so well in treatment of this basic hypoadrenocortical state that I now believe that Meniere's syndrome is a localized expression of a lowered adrenal cortical funcation.

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Discussion

GEORGE A. HILLEMAN, M.D., *Rochester, New York.*—It should be stated promptly that most of us who have been compelled to resort to surgical destruction of the labyrinth to relieve vertigo believe that the methods of physical or chemical destruction leave much to be desired. Any nonoperative therapy that is successful for this chronic disease is far more advantageous. The pathologic changes that involve one side can, at a future date, involve the other cochlea and labyrinth. Therefore, the destruction of one labyrinth in some patients could be extremely unfortunate.

In 1861 Meniere[a] described a clinical entity that bears his name. According to him, the symptoms include repeated attacks of vertigo, accompanied by nausea and vomiting occurring intermittently over weeks, months, and years. The patients are healthy between attacks except for a unilateral or bilateral loss of hearing of the cochlear type. The low frequencies are involved more than the high ones. This gives us the rather frequently described "upward slanting audiogram curve." In addition, there is usually tinnitus in the affected ear.

One worker suggested the actual pathologic changes in 1871 when he compared it to ocular glaucoma. Very little was added to Meniere's original description until Shambaugh and Knudsen[b] attracted attention to the frequent presence of diplacusis. Fowler,[c] in 1937, described the existence of the recruitment of loudness in this disease as compared with the absence in other forms of neurosensory loss. In 1938, Crowe[d] noticed the marked fluctuation in the hearing impairment. Recently it has been observed that speech discrimination is poor during an attack.

For the sake of brevity, let us assume that the outstanding pathologic change in endolymphatic hydrops is an increased volume of endolymph. Arteriolar spasm and capillary dilatation cause the increased permeability in the stria vascularis. This is reputedly caused by food and inhalant allergies, foci of infections, or vasomotor dysfunction. Some people believe that the cause may be a delay in the absorption of endolymph in locations such as the endolymphatic sac.

We have felt that in many patients with vertigo the metabolic balance has been upset by infections rather than by the presence of physical obstruction of the eustachian tube due to mucous membrane edema. This has led us to the use of prednisone and the indicated antibiotic drugs. We have assumed that those infections due to fairly clear-cut emotional stress are due to depression of the thyroid-stimulating hormone by the action of the hypothalamus on the pituitary gland.

Accordingly, we have laid a fair amount of emphasis on the action of the thyroid gland. I have been impressed with Godlowski's[e] results with the use of liothyronine in patients with a normal estimate of the protein-bound iodine but a lowered metabolic rate under sedation. He believes that the thyroid hormone disturbance is at the level of the tissue cell or in the blood and not in the hypothalamus, adenohypophysis, nor the thyroid gland. This explains why dessicated thyroid will not give relief. In a few stubborn cases good results with liothyronine have been reported. Dr. Goldman apparently has found a slightly lowered basal metabolic rate together with a normal protein-bound iodine determination.

We have not abandoned histamine desensitization. The ambulant patient is instructed how to use it under the tongue. The method, suggested by Shambaugh,[f] is followed fairly closely, and it has been found satisfactory in a great number of patients. We have not abandoned Dramamine, Bonamine, nor nicotinic acid. We urge the complete abstinence from smoking and the reduction of the sodium intake. Occasionally, we supplant sodium chloride with potassium chloride. Inhalant and food allergies are sought out and avoided or desensitization is started.

Dr. Goldman's use of the whole extract of adrenal cortex apparently offers fairly quick relief to the incapacitated patient. Undoubtedly it is a very valuable supplement to our already abundant therapeutic armamentarium. It does away with sodium restrictions. I presume that the extract should be used with caution in the diabetic, gastric ulcer, and arteriosclerotic patient. The restriction of carbohydrates in the diet will probably prove a very valuable adjunct in the treatment of Meniere's disease.

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Carbon monoxide poisoning

Faulty home heating units and automobile exhaust systems are responsible for many accidental carbon monoxide deaths each year. In 1960, 45 carbon monoxide deaths were reported in New York State, according to figures compiled by the New York State Department of Health.

Although accidental carbon monoxide poisoning is a hazard throughout the year, the incidence of such poisoning is greater during the winter months.

The State health department reports that a few simple precautions will remove most of the dangers of carbon monoxide poisoning.

1. Home heating systems should be checked to make certain the heating and venting units are in proper working condition. A serviceman should be called to correct any unsatisfactory conditions. Homes today are more nearly airtight, and this increases the likelihood that carbon monoxide poisoning may occur in cases where the home heating units is not functioning properly.

2. A dependable means of supplying fresh air continuously (to replenish the air depleted by burning) must be provided for the operation of furnaces, fireplaces, space heaters, and water heaters.

3. Automobile exhaust systems should be checked regularly to eliminate conditions which might result in the leakage of carbon monoxide, and when driving, a window should always be kept open, even in cold weather.

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Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Malignant Melanoma

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UNTIL RECENT YEARS the diagnosis of malignant melanoma was considered to be the equivalent of passing a death sentence on a patient. It was believed generally that no more than from 5 to 10 per cent five-year survivals could be obtained regardless of the method of treatment. However, since the late 1940s, more and more interest has been directed at this tumor. The clinician has found that this tumor attracts him because of its serious import for his patient. The research worker has found that this tumor is of interest because it can be grown in vitro in tissue culture and because malignant melanoma cells can be isolated from the circulating blood of its victims. The chemotherapeutist has become interested in this tumor because in some instances favorable responses have been reported from the use of chemotherapeutic agents that are presently available.

In this discussion the term melanoma will be used as the equivalent of the term malignant melanoma. The opinions which follow are based on the experiences of the past fifteen years with slightly more than 300 such cases.

Relation of benign nevus to melanoma

A nevus is noted to be the precursor of a melanoma in about 70 per cent of the reported cases.[1,2] A nevus is a benign tumor which may or may not be pigmented. It is composed of a collection of nevus cells in the dermis or epidermis. There is more or less agreement among observers that the nevus is a forerunner of the melanoma. The type of nevus most often named in this connection is the "junction nevus." This junction nevus is so named because the nevus cells are found at the junction between the dermis and the epidermis. The cause of the change from a benign nevus to a malignant melanoma has been a subject of much speculation. It has been ascribed variously to acute trauma, chronic irritation, or to the hormonal changes that accompany puberty and pregnancy.

If a nevus has not been noted previously at the location of a melanoma, it is still possible that a microscopically small collection of nevus cells were present at the site, even if they were not visible.

The occurrence of the change from a nevus to a melanoma must be a very infrequent one. Nevi are very common (15 to 25 per person in this country), and melanomas fortunately are relatively uncommon.[3] Melanomas represent less than 2 per cent of all malignant tumors of the skin.

In general, it is considered advisable to remove nevi by excision from areas which are subject to injury or irritation. When possible, this should be done before puberty.

Diagnosis

Melanomas are usually single in number, brown in color, and not particularly large. However, on occasion, more than one melanoma has been found on the skin of the same patient, arising as apparently separate primary tumors. Thus, it is possible to have multiple primary foci present. A melanoma may occur anywhere on the skin of the body. It may be found at times in a subungual location (melanotic whitlow). Melanomas also may be found on the mucous membranes near the body orifices. The eye (choroid and ciliary body) is a common location. Primary melanomas are said to have been found also in the adrenal glands, bowels, and meninges. In deeply pigmented individuals, such as Negros, they appear to occur most frequently where the pigment is least. The nail matrix, soles of the feet, and oral cavity are examples of such locations.

The primary melanoma is usually not a large tumor. Often it is no more than 1 to 2 cm. in size. Its appearance may be very disarming. There is a great variation among melanomas. Primary tumors actually may measure many centimeters in diameter. Pigmentation at times may be absent completely, and then it takes a keen observer indeed to make the diagnosis. The presence or absence of pigment appears to have no prognostic value. The primary tumor may have no observable pigment, while the metastases may be deeply pigmented. The reverse is also true. Where an unpigmented tumor exists which is thought possibly to represent a melanoma, the "dopa" reaction performed on a bit of fresh tissue which has not been fixed may be used to clarify the diagnosis. This is an enzymatic reaction which will develop latent pigmentation in the tumor cells.

Whenever a pre-existing, apparently benign nevus exhibits any one of the following signs, the observer should conclude that a melanoma already may be present, and it should be treated accordingly. These five signs are: (1) increase in size, (2) change in color, (3) bleeding, (4) ulceration, and (5) infection.

Methods of metastasis

Possibly melanomas are so deadly because of their methods of distant spread. Local extension does not play an important part in their growth. Rather, they have a predilection for spread by means of both the blood stream and the lymphatics. It appears to be mainly the hematogenous method of spread which is the one that limits the number of survivals that present-day methods of treatment can produce. It is not possible to tell clinically by even the most careful palpation of the regional lymph nodes whether or not they contain a tumor, unless they already are involved grossly. In most instances there is an error of approximately 30 per cent each way. The observer says the nodes show negative findings when on subsequent microscopic examination they are found to show positive findings, and vice versa.[4,5] This is the basis for advising the excision of regional lymph nodes even before they are enlarged clinically.

Treatment

Once a patient is suspected of having a melanoma, care must be taken that nothing is done to encourage the distant spread of the tumor. A total excision biopsy of a suspected lesion is the preferred method of diagnosis. This type of biopsy is considered less apt to produce distant metastases than is an incisional biopsy. Therefore, whenever possible, the entire suspected lesion is removed for examination. Incisional biopsies are reserved for doubtful lesions in areas where a cosmetic or disabling defect would not be justified without a definite diagnosis.

Once the diagnosis has been established and no sign of distant metastases can be found, the biopsy site is very widely and deeply excised. The fascia of the underlying muscles is removed with this specimen wherever possible. A graft often is necessary to close the defect.

Where the primary tumor is so situated that the regional lymph nodes can be removed in continuity with the tumor site itself, this is done. Where removal in continuity of the regional lymph nodes is not practical, these lymph nodes then are removed by radical excision as a separate procedure shortly after the primary site of the melanoma has been handled adequately. No disadvantage has been found in doing these two operations as separate, discontinuous procedures in cases with clinically negative findings in lymph nodes which this writer has observed. Others feel differently on this point. However, when lymph nodes are involved grossly, the results are poor no matter what the method of treatment.

One of the fundamental points in dealing with this disease is that regional lymph nodes must be considered to be involved with this tumor even when they are not clinically enlarged. It is for this reason that their removal is usually recommended. The results to date appear to show that this approach is correct. Over four times as many patients survived five or more years when the lymph nodes were removed before gross involvement became evident than when the nodes removed already were obviously grossly involved with tumor. Regional lymph node dissections, however, may be deferred when the patient's age is great, his general physical condition is poor, distant metastases already exist which are not surgically accessible, or the primary tumor site is in such a position that it may drain to more than two sets of regional lymph nodes.

A word should be said about the treatment of melanomas arising in certain specific areas of the body. When a melanoma occurs in the eye, the treatment is enucleation of this organ. When a melanoma occurs on the hard or soft palate, it is treated by a wide excision of the involved tissue, and a cervical lymph node dissection also is recommended. A melanoma of a finger or a toe often is treated best by an amputation of this member, followed by a regional lymph node dissection. A melanoma of the anal canal would be treated by an abdominoperineal resection and a bilateral dissection of the inguinal lymph nodes. The outlook for a patient with this latter type of lesion is a very dim one.

Chemotherapeutic agents, such as TSPA (triethylene thiophosphoramide) and PAM (phenylalanine mustard) have been given at the time of definitive surgery.[6] This is done to diminish the chances of tumor cells which may have been released into the blood stream at the time of surgery from remaining viable.

Results of treatment

The results of the previously mentioned methods of treatment have been as follows: Approximately 50 per cent of the patients in this series have survived five or more years after regional lymph node dissections have been performed where the lymph nodes were thought to be clinically free of tumor, even though many of these patients were reported as having lymph nodes which showed microscopic nests of melanoma cells in them. Where the regional lymph nodes were both grossly and microscopically involved, the five-year survival rate was 13 per cent. The experience of others has been similar, or slightly less favorable.[1,7,8]

An added advantage to these outlined methods of treatment has been that the need for procedures such as interscapulothoracic amputation or hemipelvectomy has been reduced greatly. These two procedures are reserved for those cases where a mass of involved lymph nodes has become firmly adherent to the essential vascular or nervous structures of an extremity and there is still no sign of more distant metastases. These procedures also may be indicated where a large number of recurrent melanotic nodules have occurred on an extremity that previously has had the primary site of the tumor and/or the regional lymph nodes removed and where there is no evidence of more distant metastases.

Chemotherapeutic methods of therapy

Isolation-perfusion technics recently have been used in the treatment of melanomas of the extremities. A tourniquet is placed proximally on the affected extremity to isolate its circulation from the remainder of the body. This is done so that the toxic drugs which are used for therapy will not affect the entire body as a whole but only that portion which has been isolated by the tourniquet. Then the main artery and vein have catheters inserted, and an extracorporeal circulation is established. This closed system is then perfused for a period of time with a tumorocidal chemotherapeutic agent, such as Thio-TEPA or phenylalanine mustard. Some investigators have reported favorable results without serious systemic effects occurring from the leakage of the chemotherapeutic agent into the general circulation during the perfusion.[9] It is this author's opinion that with the chemotherapeutic drugs presently available the therapeutic results which can be expected from this method of treatment are modest. However, it is an excellent method of screening the new chemotherapeutic drugs.

Treatment of advanced cases

When a patient is seen with widespread disseminated malignant melanoma involving not only the surface of the body with subcutaneous nodules but also many organs, such as the lungs, liver, spleen, brain, and so forth, the only presently available method of treatment is the use of x-rays or of chemotherapeutic agents. These chemotherapeutic agents usually are Thio-TEPA or phenylalanine mustard.[10] At best, however, only palliation can be expected. While x-ray therapy usually is of little advantage in this disease, there are times when a melanoma may be unexpectedly sensitive to this modality, especially metastases to the brain, lungs, and liver.

When a patient is seen with a small, surgically accessible reappearance of malignant melanoma, such as one or two subcutaneous nodules, these lesions should be excised surgically. Numerous cases have been observed by this author and others in which after the excision of one or more subcutaneous nodules no other signs of a reappearance subsequently developed. While, unfortunately, this is not a common occurrence, the fact that patients can remain well after the excision of such lesions is an encouragement to continue to treat such cases this way. At the same time, patients who do have a reappearance of malignant melanoma might receive maintenance doses of chemotherapeutic agents with the slim hope that this will lessen the chance of other metastases developing. It always should be borne in mind that, as with most malignant tumors, unexplained spontaneous regressions have been reported occasionally.[11]

Growth of melanoma in vitro

In recent years it has been found possible to grow human melanoma tissue in vitro. Its growth characteristics and cytology have been studied carefully.[17] In addition, portions of the tumor growing in vitro have been exposed to the effects of various chemotherapeutic agents and/or x-ray therapy. In far-advanced cases this enables the patient to be treated with a chemotherapeutic agent to which his own particular tumor appears to be most sensitive in vitro. While favorable results have ensued from this method, these results have been modest and temporary.[6,10]

Juvenile melanomas

A word should be mentioned about melanomas in childhood. There is a variety of compound nevus that occurs usually before puberty but may occur in adults as well. This is the so-called juvenile melanoma. Histologically it closely resembles the adult melanoma, but it has several characteristics microscopically that allow it to be identified.[12,13] This is important because it does not act like a malignant lesion and does not metastasize. It can be treated as a benign lesion. Therefore, its identification is essential. On the other hand, true melanomas may occur in childhood and produce metastases and death just as in adults. These true melanomas in childhood should be treated exactly as melanomas in adults.[12]

Pregnancy

The effect of pregnancy on patients with melanoma has long been thought to be adverse. Most clinicians can recall cases in which the occurrence of pregnancy appeared to be the trigger which caused a nevus to begin to grow or otherwise undergo a change which resulted in a melanoma. In addition, the prognosis has been deemed worse in pregnancy.[14] Recently, a study of 115 patients with melanoma was reviewed. The five- and ten-year survival time in this particular group of women was judged to be no worse than in a control group which was not pregnant.[15,16] In this writer's experience women who became pregnant after a melanoma had been removed surgically did not appear to run an increased risk of a reappearance of this tumor.

Comment

As the reader can discern, much is still to be learned about the treatment of malignant melanomas. One of the great limiting factors in the present methods of therapy is the hematogenous method of spread. The present methods for dealing with this are the early diagnosis and surgical removal of the primary melanoma, the avoidance of undue trauma in handling the melanoma, and the use of chemotherapeutic agents which still are far from effective in their results.

The lymphatic method of spread can be dealt with reasonably well by removing regional lymph nodes prior to their becoming obviously involved with melanomas. The local method of spread usually can be handled by the wide and deep local excision of the primary site of these tumors.

However, even in removing the primary site of a melanoma widely and extirpating the regional lymph nodes before they are involved clinically, and even in the absence of obvious hematogenous spread of the melanoma, problems still arise. An example of this is an extremity which may become studded with melanotic nodules after all the previously mentioned procedures have been done in what appears to be a proper manner. Possibly lymphatic stasis after regional node dissection may encourage this. Another example is that of a reappearance of a melanotic nodule at the margin of a skin graft which was placed at the site of a wide and deep excision of the primary site of the tumor. These and numerous other occurrences remain a constant stimulus for the search for new and better methods of handling this disease. However, knowing that a sizable number of patients may be saved by present modalities of therapy should encourage physicians not to lose heart.

Conclusion

1. Nevi should be removed from areas subjected to injury or irritation. This should be done prior to puberty when possible.
2. Whenever a nevus increases in size, changes in color, bleeds, becomes ulcerated, or becomes infected, it should be suspected of already being a melanoma.
3. When a biopsy of a suspected melanoma is indicated, a total excision biopsy ordinarily should be done. Incisional biopsies are reserved for special situations.
4. Regional lymph nodes usually should be removed without waiting for them to become enlarged clinically.
5. Chemotherapeutic agents are of modest value at present in the treatment and the palliation of this disease.

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Current Concepts in Diabetes Mellitus

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Dental and Oral Considerations in Diabetes Mellitus

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There is a relationship between diabetes and dental disease, and in this article that relationship will be explored.

Diabetes mellitus in its interaction with the teeth and mouth may be discussed in four sections: (1) The effect of diabetes mellitus on the dental and oral tissues; (2) the effect of dental disease on diabetes; (3) the interaction of dental and medical therapy in the diabetic patient; and (4) oral and dental manifestations as clues to the presence of diabetes and prediabetes.

Effect on teeth and oral tissues

Physicians have long been familiar with the fact that oral symptoms may be the first to suggest the presence of diabetes. Dry mouth is a frequent primary presenting symptom.[1] It has been suggested that the dry mouth, burning mouth, hyperemic and swollen mucous membranes, and loss of filiform papillae of the tongue occurring in the uncontrolled diabetic subject may be related to an associated vitamin B complex deficiency rather than to the direct effects of the impairment of carbohydrate tolerance.[2] Oral changes may be found even in well-controlled patients, and hypertrophy of the lingual filiform papillae is one of the most consistent of these.[3] Enlargement of the tongue resulting in indentations of the teeth on the lateral borders is not uncommon in diabetes. In xanthoma diabeticorum, xanthomatous nodules similar to those on the skin also may be found on the tongue.[4]

Relationship to caries. Uncontrolled diabetes may be associated with a marked increase in the incidence of dental caries.[5–7] Since diminished salivary flow leads uniformly to greater caries activity in man and animals,[8] this has been postulated as the probable explanation in uncontrolled diabetes.[7] There is some suggestive recent evidence to indicate that the parotid saliva may reflect elevated blood glucose.[9,10] Mandel and his associates[11] in assaying the free and protein-bound carbohydrate in human parotid saliva have indicated that the only free sugar present is glucose. Using the glucose-oxidase method they found the order of magnitude to be about 0.5 mg. of glucose per 100 cc. of saliva.[10,11] Whether or not the elevated carbohydrate in the saliva in this microrange is related to the accelerated dental caries rate remains to be investigated. Experimentally, in the albino rat, there is no difference in caries experience between alloxan-diabetic animals and normal controls when they are fed a cariogenic diet.[12] This limited animal experimentation, therefore, is in disagreement with clinical experience. Furthermore, the alloxan-diabetic rat metabolizes varying levels of fluoride as well as his normal counterpart.[13] The fluoride, in turn, has no effect on the level of blood glucose or the incidence of cataracts in the diabetic animals.

There is general agreement that treated diabetic patients do not have a greater than normal dental caries incidence. The dispute is whether or not the incidence is less than in other population samples. The classic work of Boyd and Drain[14] and Boyd's follow-up studies[15-17] indicate that juvenile diabetic patients on carefully controlled diets show a reduced incidence of dental caries. Later investigators[5,18,19] find contrary evidence, but this may be explained by a difference in the rigidity of the dietary control among the various diabetic groups under investigation.

RELATIONSHIP TO PERIODONTAL DISEASE. *Uncontrolled diabetes.* In uncontrolled diabetes an unusually high incidence of periodontal disease is noted and a significant number of these cases are severe.[6,7,20-28] The periodontal tissues are the supporting and surrounding tissues of the teeth, gingivae, periodontal membrane, and alveolar bone, and they may all be involved in the inflammatory and degenerative disease processes, ranging from a simple gingivitis to an advanced suppurative periodontitis (pyorrhea).[7,26,27,29,30] These periodontal changes are similar to those found in nondiabetic patients,[30-32] and the difference is chiefly in the prevalence of early onset and the severity of the process.

Glickman[32] has shown that in alloxan-diabetic rats there are no gingival changes peculiar to the diabetes, and gingival inflammation is seen as frequently in the control as in the diabetic animals. The severity of the hyperglycemia is not reflected in the degree of severity of gingival disease. A tendency toward varying degrees of nonspecific osteoporosis of alveolar bone unrelated to gingival changes is a feature in individual cases of diabetes mellitus.[32,33] Thirty-nine per cent of the diabetic animals showed bone resorption. When marked pathologic changes occur throughout the alveolar bone in diabetic animals, comparable alterations are observed in other bones of the skeletal system.[32]

Yerganian[34] has noted severe periodontal disease, apparently similar in all respects to that occurring in human patients,[35] in many of his strain of Chinese hamsters which have developed spontaneous genetically determined diabetes.

Treated diabetes. Both periodontal disease and diabetes become more prevalent with advancing age, which makes the evaluation of any relationship between them extremely difficult in the older-age groups. However, if the advanced type of periodontal disease generally associated with older individuals—resorption of alveolar bone, tooth mobility, and pocket formation—is seen with greater than expected frequency in young diabetic patients, the possibility of causal relationship is suggested. Between the ages of eighteen and forty diabetic individuals manifest a higher incidence of more severe periodontal bone resorption than can be attributed to local causes alone.[3,6,36-40] Below the age of eighteen there appear to be no premature resorptive bone changes attributable to diabetes.[19,30,37,38,41,42] Above the age of forty it becomes increasingly difficult to evaluate the correlation because so many patients are edentulous[6,37] (in itself possibly significant), but in those who are not edentulous there appears to be no uniform relation between diabetes and alveolar bone resorption.[36]

It is regrettable that most of the clinical investigations of diabetes-periodontal disease association, with certain notable exceptions,[36,38,39] are either inadequate or not objective and thus are of limited value. However, despite certain serious weaknesses, such as the limitations on their comparability, the absence of controls or the assumption of normality in the selection of controls, and the lack of a reliable reproducible method of scoring periodontal disease, careful critical evaluation of this group of reports suggest the following conclusions. There seem to be two clinical periodontal syndromes related to diabetes. The first is the acute fulminating form found most frequently in the undiscovered and uncontrolled diabetic subject, particularly in the juvenile type, and characterized by gingival inflammation ranging from marginal gingivitis to acute suppurative periodontitis, mobility of teeth, pain on percussion of teeth, rapid loss of bone, granular subgingival proliferations, and multiple gingival abscesses. With control of the diabetes this group of symptoms may be expected to lessen in severity and occasionally to subside. The second is that of gradual resorption of the alveolar bone. This is a more chronic degenerative change which seems to be related significantly to the duration of diabetes. The concurrence of several workers in finding more frequent and more advanced bone loss in the twenty- to forty-year-old age groups where the diabetes may have been present for some years tends to support this thesis. In this dependence on the duration of diabetes for development of bone resorption there is a striking similarity to other so-called complications of diabetes such as nephropathy and retinopathy.[43] The possibility of correlation between the presence of degenerative periodontal breakdown and other diabetic complications would appear to be a fruitful area of investigation and is one which we expect to explore.

One cannot help speculating that the periodontal changes associated with long-term diabetes may be another expression of diabetic microangiopathy. Suggestively characteristic microvascular lesions have been found in such a variety of tissues and organs[44,45] that it is reasonable to assume they also may occur in the periodontium.[46] Studies are in preparation in our laboratory to test this hypothesis.

One microscopic study of the gingivae of diabetic patients mentions that thickening and hyalinization of blood vessel walls was a "frequent occurrence."[31] In this study gingival biopsies of 30 patients ages ten to seventy-one years, with the duration of diabetes ranging from three months to ten years, were examined. The only correlation attempted was between micropathology and degree of control. Unfortunately no notation was made of the relationship between the duration of diabetes and the presence or absence of small vessel disease.

Pathogenesis. Assuming that there is validity in the concept that alveolar bone resorption occurs in long-term diabetic patients more frequently than can be explained by chance alone, what are the possible mechanisms for this phenomenon? If diabetic microangiopathy occurs in the periodontal membrane as suggested, it could conceivably interfere with the nutrition of this connective-tissue structure and decrease its ability to repair normal wear and tear. Since the resorption-deposition balance of the alveolar bone depends on the insertion of viable, functional, periodontal membrane fibers, degeneration of the periodontal membrane would shortly be reflected in resorption of the alveolar bone.

In contrast to the functional concept, a metabolic concept has been advanced. Negative nitrogen balance has been proposed by several workers[26,46,47] as a possible cause of the bone resorption. This would be a reasonable hypothesis in untreated or uncontrolled diabetic subjects who are losing weight but would not explain the bone loss in the long-term controlled diabetic patient.

Gingival inflammation and infection seem to be more prevalent and more severe in the uncontrolled diabetic patient than in either the controlled or the nondiabetic patient. This may be related in part to lowered resistance to infection. Two short reports in the literature mention an alteration in the oral flora in the diabetic individual. Candida albicans[48] and hemolytic streptococcus and hemolytic staphylococcus[49] were isolated more frequently from the saliva of diabetic individuals than from the saliva of nondiabetic individuals.

Effect of dental disease on diabetes

Dental infection has been implicated repeatedly in the worsening of the diabetic state. Its presence will elevate the blood glucose, may cause keto-acidosis, and has been known to precipitate coma. The initial regulation of a newly detected diabetic patient may be rendered difficult or impossible in the presence of active periodontal or apical infection. Furthermore, exacerbation of dental infection may throw a well-controlled diabetic patient out of control. Since in this disease a dental emergency may rapidly become a medical emergency and may endanger the life of the patient,[7] it is of utmost importance that dental and periodontal health be established and maintained.

The presence of rampant dental disease may influence the problem of systemic management by making mastication painful or difficult. The patient may then turn to foods which are easier for him to cope with but which may be dietetically improper. With the loss of many or all of the teeth the masticatory problems are self-evident. Although full dentures may in many cases be completely satisfactory, there is a strong correlation between denture satisfaction and size and form of the alveolar ridge remaining. Most patients suffering from periodontal disease have less than adequate lower edentulous ridges when their teeth are lost, and the impression is gained that most edentulous diabetic patients have become so through periodontal disease. Furthermore, it has been noted that full dentures may not be tolerated well by the diabetic individual, particularly one who is poorly controlled, because of mucosal soreness and the need for frequent relining of the denture. Thus it is wise not to hasten the consummation of the edentulous state in the diabetic patient but rather to make every effort to preserve a healthy, functional, natural dentition so that the proper foods may be chewed efficiently and comfortably.

Interaction of dental and medical treatment

When it is discovered that a patient with advanced dental disease also has diabetes, extractions should not be performed, unless absolutely necessary, until the systemic condition is brought under control. Acute abscesses, however, require immediate drainage.[50] Admittedly, complete regulation may not be possible while dental infection is still present, but the glycemia can be reduced. With the amelioration of the diabetic status there may be dramatic improvement in the acute periodontal condition. The teeth may become firmer, gingival inflammation may subside, suppurative exudate from the gingival crevices may decrease, and soreness and sensitivity may lessen. At this stage dental evaluation may be carried out and necessary treatment instituted. Teeth in a hopeless condition may now be extracted and residual infection and inflammation eliminated. Periodontal therapy may lower the insulin requirement and reduce fluctuating uncontrollable sugar levels to a more manageable state. Thus, the treatment of periodontal disease may facilitate the practical regulation of diabetic patients.[28]

Under good medical control and with enlightened dental care the diabetic patient shows no greater tendency to postdental surgical complications than his nondiabetic counterpart. Dental treatment is in most instances a stressful event and, therefore, certain precautions in the handling of the diabetic dental patient are judicious and advisable. Dental appointments should be in the morning, generally about an hour and a half after breakfast and the administration of the morning insulin.[50–52] Those patients on intermediate and long-acting insulin given in the morning before breakfast may be treated safely in the early afternoon also.[51] Every effort should be made to allay apprehension and minimize pain. The rational administration of sedatives and analgesics preoperatively is strongly advised.

Local anesthesia is the anesthetic modality of choice in oral surgery.[53] There has been some interdiction to the inclusion of epinephrine (Adrenalin chloride) in local anesthetics because of its diabetogenic action, but this is more theoretical than real.[19] As Amies and Park have noted,[19] the minute amount of epinephrine included as a vasoconstrictor with local anesthetics represents only one fifth to one tenth of that used as part of their routine treatment of hypoglycemic coma; and this five to ten times larger amount will only elevate the blood glucose from 30 to 40 mg. per 100 ml.[19] Even if it is injected directly into the blood stream the amount of epinephrine in local anesthetics is insignificant. With the slow release from an injection site, it can be disregarded. Stress-stimulated endogenous epinephrine is of more consequence than the small amounts administered in dental local anesthesia.

Experience at several institutions[28,50,52,54] has demonstrated clearly that when the diabetic patient is under good medical control, oral surgical procedures can be carried out exactly as they would be on a nondiabetic patient both as to extent and technic of the surgery. Procedures as extensive as full mouth extractions[50] and full mouth gingivectomy[28] have been performed at one sitting with no detrimental effect to the patient, although this is not generally recommended even in the nondiabetic individual.

Following dental or oral surgical procedures, attention must be paid to the patient's ability to chew and swallow. The dentist may call on the physician to suggest temporary liquid and semisolid dietary substitutes during the initial healing.

Since the diabetic patient is more subject to infection than the nondiabetic patient[55] and since infection in the diabetic patient represents a serious threat it is wise to overlay every oral surgical episode with adequate antibiotic coverage.

Oral and dental manifestations as clues to presence of diabetes and prediabetes

Recently a series of papers[56-63] emanating from the University of Alabama has reported some interesting, and occasionally startling, findings. A group of 100 patients selected at random from among those who presented themselves for dental treatment at the dental clinic were analyzed by means of the three-hour true-glucose tolerance test (Somogyi-Nelson) by Cheraskin and his associates who found that 26 had glucose tolerance curves with peaks above 150 mg. per 100 ml. which failed to return to below 100 mg. per 100 ml. at the end of the two-hour period.[56] Of these 26 patients only 2 previously were known to have diabetes. Following the criteria established by Mosenthal and Barry[64] and adopted by the American Diabetes Association,[65] these 26 individuals were regarded as having diabetes mellitus. The next group was composed of 17 individuals who had glucose tolerance curves with either a peak value above 150 mg. per 100 ml. or a failure to return to 100 mg. per 100 ml. or below at two hours. These subjects were considered to have moderately decreased glucose tolerance, marginal diabetes, or prediabetes. Thirty-seven patients had normal curves and the remaining 20 had flat curves demonstrating an increased glucose tolerance. The finding of 43 out of 100 individuals with frank or marginal abnormality of the glucose tolerance test results is surprising. The great difference in the frequency of diabetic curves in this Alabama dental patient population compared with other population groups has not as yet been explained. Interestingly, a recent report of a mass survey of 767 hospitalized neuropsychiatric patients by means of the glucose tolerance test disclosed 17.6 per cent with peak levels above 200 mg. per 100 ml. (Folin-Wu).[66]

Other diabetes detection surveys of groups of dental patients using urinalysis,[67] fasting blood sugar,[68,69] or the glucose tolerance test[70] as the diagnostic test have failed to reveal significantly larger numbers of diabetic individuals than in the general population.

Cheraskin and his coworkers analyzed extra-oral and intra-oral symptoms and intra-oral signs in relation to the glucose tolerance curves and found that: (1) Intra-oral symptoms proved more helpful in the detection of possible diabetes mellitus than extra-oral symptoms; a history of dry and burning mouth, gingival tenderness, and pain on tooth percussion occurred more frequently in those with decreased glucose tolerance; (2) some intra-oral signs (lip dryness, loss of gingival stippling, spontaneous gingival bleeding, pocket formation, and tooth mobility and loss) were found with significantly greater frequency in those patients showing evidence of decreased glucose tolerance; (3) the roentgenographic finding of alveolar bone resorption appeared more often in patients with confirmed or possible diabetes; moreover, no patients with frankly diabetic curves had normal alveolar bone crests.

When the original data were re-examined by means of the grouping of patients by the presence or the absence of findings and evaluating the glucose tolerance curves of these groups, it was found that a significantly decreased glucose tolerance was found in those with the following signs and symptoms, singly or in combination: dry mouth, burning mouth, tooth mobility, and alveolar bone loss.[57-63]

If the work of the Alabama group can be reproduced and confirmed it offers another valuable series of clues to the detection of diabetes and prediabetes. Just as increased fetal mortality and the birth of babies weighing more than 10 pounds occur more frequently in prediabetic mothers,[71] just as recurrent hypoglycemia may be an early hint of a subsequently developing diabetes, just as retinopathy, nephropathy, or the absence of deep reflexes[72] may be the initial findings in a patient without overt symptoms of diabetes,[71] so may these dental findings stand in relation to prediabetes and diabetes.

Many questions are raised by the series of papers from the University of Alabama, some of which we hope to answer by repeating the study on a larger scale for greater significance in statistical analysis.

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Number thirty-two in a series of articles on Current Concepts in Diabetes Mellitus

Reading retardation a symptom, not a discrete clinical entity

The determination of the cause of a reading problem in a child is often difficult because of the multiplicity of factors—biologic-neurologic, intellectual potential, family relationship, personality, schooling, social—involved in the learning process. Reading retardation is symptomatic, not a clinical entity, with one of three etiologic possibilities, according to articles by R. D. Rabinovitch in *Neurology and Psychiatry in Childhood* and *American Handbook of Psychiatry*. The three possibilities are: (1) frank brain damage; the impairment of capacity is manifested by clear-cut neurologic deficits; (2) biologic or endogenous causes, reflecting a basic disturbed pattern of neurologic organization—primary retardation; it is manifested by an inability to deal with letters and words as symbols, hence a diminished ability to integrate the meaningfulness of written material; and (3) interference of various exogenous factors, for example, negativism, anxiety, depression, emotional blocking, psychosis, limited schooling opportunity, with an intact capacity to learn to read—secondary retardation.

Where total or severe reading retardation exists in the absence of brain damage, the problem is usually primary. Boys predominate in this group to a proportion estimated to be greater than 10 to 1. In differentiating primary from secondary reading retardation, 5 approaches have been fruitful: psychometric evaluation, achievement testing, psychiatric evaluation, neurologic appraisal, and response to remedial reading therapy.—*Feelings and Their Medical Significance, Ross Laboratories*

Clinical Rehabilitation Conference

Prepared by the Department of Rehabilitation Medicine,
The Albert Einstein College of Medicine,
Bronx Municipal Hospital Center, New York City

EDWARD F. DELAGI, M.D., AND HEINZ I. LIPPMAN, M.D., Editors

Below-Knee Amputation

Edward F. Delagi, M.D.: Today we have a rather specialized prosthetic problem in a patient with a below-knee amputation. This type of problem is becoming of increasing concern to us because of the incidence of vascular disease leading to amputation. Will the student please present the case.

Case history

This is a forty-eight-year-old Negro male patient who had a below-knee amputation in April, 1960, at another hospital, because of a gangrenous ulcer of the foot. It was an open guillotine amputation with a long below-knee stump. In August, 1960, he was transferred to the Department of Rehabilitation Medicine of the Bronx Municipal Hospital Center. A patellar tendon-bearing, full-contact prosthesis was prescribed. When the patient was discharged in September, 1960, he ambulated well. Six months after discharge he had the first of three painless breakdowns over the stump scar. The abrasion at the end of the stump made it necessary for him to stop working and to stay at home for periods of two to three weeks at a time. The latest and third recurrence of stump breakdown was two weeks ago. He is presented to the conference for advice as to how to prevent further breakdown and disability. His diabetes is under control with 40 units of NPH insulin and 2 tablets of chlorpropamide (Diabinese) a day. In the patient's past history there are four other episodes of hospitalization, two for retinal detachment and two for cataract extractions. His vision today is zero on the right eye and 20/30 on the left.

The significant physical findings reveal an obese patient with a right below-knee amputation stump which is 8 inches long (from the lower end of the patella with the knee extended) with a round adherent scar at the end. There is an area of ulceration which is painful and tender about $^1/_4$ inch in diameter in the center of the scar. The range of motion of all joints is normal, and muscular strength is excellent. On the left, all pedal pulses are absent. The left popliteal and femoral pulses are of fair quality. On the amputated right side, both popliteal and femoral pulses are present. Oscillometric readings are confirmatory: trace at the ankle and 4 at left calf level. The stump is warm, and the skin, aside from the area of ulceration, appears to be in good condition. The skin of the left foot is warm and normal in appearance. There are no trophic or postural changes in either leg. Roentgenograms demonstrate a spur in the direction of the scar arising from the medial aspect of the lower end of the tibial stump.

Dr. Delagi: Thank you. May we see the patient? (The patient walks in to the conference wearing his prosthesis.) Dr. Chu, would you demonstrate the end of the patient's stump.

Shun Wu Chu, M.D.: You noticed the patient walked in wearing a total contact limb which formerly was called a UCB (University of California, Berkeley) prosthesis. He limps because of pain. Please, sit down. (Dr. Chu removes the prosthesis and demonstrates the ulceration at the end of the stump. The shoe and stocking are removed from the other extremity.) You notice the skin of the left foot, and the right stump is in good condition.

Alfred Ebel, M.D.: What kind of work do you do?

Patient: I am a fur dresser.

Dr. Ebel: How do you go to work?

Patient: When I am working I go by subway. Unfortunately, I was forced to stop working because of this continuous trouble with the stump.

Dr. Ebel: Do you own a car?

Patient: Yes.

Dr. Ebel: Have you driven it since you received this prosthesis?

Patient: Yes. I drive with my healthy leg.

Dr. Ebel: Have you had your car modified so that you can drive with your left leg?

Patient: No, I use the left foot for gas and to brake and shift.

Dr. Delagi: Thank you. (The patient puts on his prosthesis and walks out.) Dr. Chu, would you discuss this patient's problem and your plans for him.

Management

Dr. Chu: The question arises as to whether the recurrent stump breakdown should be dealt with surgically or conservatively, by removing the spur and revising the stump, or by relieving the pressure and modifying the prosthesis. I suspect the guillotine below-knee type of amputation is responsible for much of the trouble. The tight scar became adherent to the open tibial shaft which in itself may cause breakdown when the patient walks, regardless of the type of prosthesis he wears. Therefore I would suggest that his stump be revised and shortened slightly to try to obtain a nonadherent padded scar such as that seen in most of our patients.

Dr. Ebel: I agree with Dr. Chu. This stump is of more than adequate length, and the loss of one inch or so would enhance rather than damage its functional capacity. I would like to add that I question the wisdom of prescribing a full-contact prosthesis for any stump resulting from a guillotine amputation since there is weight-bearing in the area of the scar as well. For such a prosthesis, a stump without a scar on the end would be preferable. Most recent experience with the total contact leg demonstrates that the shrinkage of the stump after a while leads to more end-bearing and less full-contact distribution of weight. In patients with an adherent scar at the end of the stump this would be particularly hazardous.

Heinz I. Lippmann, M.D.: Both Dr. Chu and Dr. Ebel have presented good arguments against stumps resulting from guillotine below-knee amputation as weight-bearing stumps and also against the fitting of such a stump with a full-contact prosthesis. However, I would like to submit that this patient's difficulties are not related either to the type of amputation or to the type of prosthesis. The main trouble here arises from pressure on the scar by a spur which is the result of ossification of the periosteum which was left behind during amputation. This may occur in any type of amputation, even though the incidence of this complication is quite low, if during amputation the tibial separation is kept clean and attention is paid to handling the periosteum properly.

Dr. Chu: It was always my impression that a guillotine-type amputation was an emergency procedure which was to be followed by definitive revision of a stump at a future date. This was not carried out in our patient, and I am wondering if this is not at least one cause of the patient's difficulty.

Dr. Lippmann: The guillotine procedure you are referring to is the supramalleolar amputation which may indeed be lifesaving as an emergency operation if it is done to ablate a gangrenous infected foot in the presence of toxemia, fever, or bacteremia. Such amputation provides a draining surface until a definitive procedure higher up is safe. Thus the knee can be saved not infrequently while a primary below-knee amputation would have been unsuccessful in the presence of lymphangitis. With our presently available prosthetic devices, a supramalleolar stump can hardly be fitted with a usable limb. In our patient, however, a definitive guillotine amputation was performed at below-knee level, probably because of an infection. This type of amputation used to be the below-knee procedure of choice in preantibiotic days and may result in good stumps for prosthetic ambulation. The procedure should not be forgotten for some cases with bad infection or lymphangitis.

In the open guillotine stump the skin edges surrounding the cut cross section gradually contract and cover the cut surface. A small scar in the center of the stump which adheres to the distal end of the tibia is the result of this type of operation. Most physiatrists concur that an adherent scar in an amputation stump is not ideal for prosthetic weight-bearing. Still, we have seen some good prosthetic results in such stumps. By and large, the padded soft but firm stump with a thin long scar which is the result of primary closure of the below-knee stump as practiced by most surgeons is preferable from the standpoint of prosthetic ambulation.

Resident: Would a conventional below-knee socket in which there is no weight-bearing on or near the end of the stump solve this patient's problem?

Dr. Lippmann: As you indicated there is weight-bearing over a smaller surface of the stump in the conventional below-knee socket than in the full-contact socket. The resulting pull on the skin may cause more trauma to our patient's stump scar. We have a means of minimizing weight-bearing on the stump by varying the length of the thigh corset which is part of the conventional below-knee prosthesis. Thigh corsets have the triple function of suspending the prosthesis, aligning it, and reducing weight-bearing on the stump. A corset of sufficient length may carry as much as 70 per cent of the patient's weight during ambulation.

In the full-contact prosthesis, the weight is usually distributed over the larger area of the whole stump, and a small band suspends the prosthesis. We find the absence of the thigh corset in this kind of prosthesis a great advantage to the patient, in addition to the advantages resulting from the larger surface contacted by the socket. This reduces the weight load and increases the proprioceptive feedback; many patients use this kind of prosthesis with ease and efficiency. I believe that our patient should not be denied the benefit of this prosthesis since he is young and active and needs to to return to work with the least delay. His spur should be removed and his stump revised so that a better scar which is nonadherent and thin results with some shortening of his stump. We will then be able to fit him with a new insert into his present prosthesis. Our limb makers agree with this plan.

Visiting Physician: Wouldn't it be possible to save this patient another operation by building a relief into the present socket so that the pressure is not borne by the scar?

Dr. Lippmann: That might have been done at the first episode of breakdown. In considering the roentgenographic findings and the working time lost to the patient so far, we really should go ahead with a stump revision. The spur will always present a threat to the integrity of the skin at the end of the stump. Temporary healing after relief built into the socket is possible, but it will break down in time. There is the risk that edema may develop at the site of the relief and contribute to breakdown.

Dr. Delagi: We will consult our vascular surgeons and suggest that the patient's stump be revised now and the spur removed. The revision should include shortening of the tibia to the optimum length of $6^1/_2$ to 7 inches below the lower edge of the patella. We anticipate that the patient will return to work thereafter. Thank you.

Follow-up*

Resident: The patient whose below-knee stump was revised because of a spur has now a good stump with a thin nonadherent scar which is well padded and firm. It has shrunk enough to have a new full-contact insert made by the prosthetist which fits into his old prosthesis. He cannot be presented in person since he went to work. He uses public transportation. His diabetes remains controlled, and he follows good foot care for his "healthy" leg.

Dr. Delagi: This case teaches the importance of attention to detail in below-knee amputation and how this can make the difference between very adequate function and severe disability.

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* Two months later.

Number five in a series of Clinical Rehabilitation Conferences

Medical Diagnostic Clinics

A series of special articles on rare but important disease entities or medical esoterica

Prepared by the Department of Medicine, St. Vincent's Hospital, New York City

WILLIAM J. GRACE, M.D., Editor
MATTHEW J. FERGUSON, M.D., Associate Editor

A Cardiac Diagnostic

Protocol

A twenty-four-year-old nun consulted a physician because of several attacks of syncope while she was climbing stairs. During the previous eight months the patient had not been feeling well. She had noted easy fatigability, frequent chest colds, and exertional dyspnea. She had also experienced constricting sensations in the midchest during moderate activity. Orthopnea, paroxysmal nocturnal dyspnea, hemoptysis, and ankle edema were denied. She had always lived in the New York City area. There was no history of rheumatic fever or pulmonary disease. Four years earlier, before she entered the convent, a thorough physical examination had shown normal findings.

A physical examination revealed a slender, well-nourished, well-developed white female who did not appear ill. The blood pressure was 100/85 mm. of Hg, pulse rate 92 per minute, respirations 20 per minute, and temperature 98.6 F. The lungs were clear to percussion and auscultation. The cardiac rhythm was regular. The point of maximal impulse was in the fifth interspace inside the midclavicular line. The second pulmonic sound was loud, split, and palpable. A parasternal heave and increased retrosternal dullness were noted. A short decrescendo diastolic murmur was heard at the pulmonic area. The remainder of the examination was within normal limits.

A laboratory analysis gave normal results. The electrocardiogram showed sinus rhythm, peaked P waves, and right ventricular hypertrophy. A chest film disclosed clear lung fields and a prominent pulmonary artery segment.

Course. Over the next few months her symptoms became increasingly severe, especially the chest discomfort which became more anginal in character. Transient systolic murmurs were heard and rheumatic heart disease was suspected.

At this time, the patient was admitted for pulmonary function studies and cardiac catheterization. The results of the former were normal and the essential findings of catheterization were (1) increased right atrial pressure, (2) markedly increased pulmonary artery pressure, (3) normal pulmonary capillary wedge pressure, (4) an eightfold increase in pulmonary vascular resistance, (5) decreased pulmonary blood flow, (6) decreased cardiac output, and (7) no evidence of a shunt.

The patient was discharged on symptomatic therapy. The slightest activity caused dyspnea. Her voice became hoarse. The lungs remained clear, but ankle edema and hepatomegaly developed. Three months after her discharge she was rehospitalized because of massive edema. She now presented the classic picture of tricuspid insufficiency with a systolic murmur, dilated neck veins, pulsating liver, and ascites.

The failure did not respond to therapy. On the seventh hospital day she became unresponsive and signs of peripheral vascular collapse were evident. She expired suddenly the following day.

(Elucidation will be found on page 406)

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

BENJAMIN J. CILIBERTI, M.D., Chairman
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Polycythemia Vera and Anesthesia

POLYCYTHEMIA VERA is not a common entity and is encountered less frequently than relative polycythemia in the surgical patient. Its recognition is important since this variety is characterized not only by an absolute increase in the number of erythrocytes but also by an increase in the blood volume. Immediate effective therapy is resorted to in the untreated surgical emergent patient, and meticulous attention is demanded in the management to avoid serious complications.

A thrombotic phenomenon is a frequent complication of polycythemia vera. The following case report is based on such a complication and illustrates some of the problems encountered in anesthetic and surgical management.

Case report

This sixty-four-year-old white male with a ruddy purple complexion came to surgery as an emergency case to have an exploration of the left axillary artery because of an acute arterial occlusion. Prior to surgery a stellate ganglion block was performed, but there was very little improvement noted following an apparently successful block. His arm remained cyanotic, and no pulses were palpable.

The preoperative findings revealed a hemoglobin of 22.2 Gm. per 100 ml. and a hematocrit of 64. The white blood cell count was 15,800 per cubic millimeter. His blood pressure was 180/110, and the electrocardiogram showed a sinus tachycardia with a rate of 115 beats per minute. He also had a parietal block with a possible anterior wall infarction. The x-ray film of the chest showed negative findings except for a noted increase in bronchovascular markings. The urinalysis showed a 1 plus albumin, and the blood urea nitrogen was 7 mg. per 100 ml. His blood chemistries were within normal limits.

In the operating room his blood pressure was 200/130, pulse 120, and respirations 26 per minute. Five hundred ml. of blood were withdrawn into an acid citrate dextrose blood flask. The patient was given meperidine hydrochloride 25 mg. and scopolamine 0.2 mg. intramuscularly twenty minutes prior to the induction of anesthesia. The blood pressure at this time was 120/80 and the pulse 100 beats per minute. Four hundred mg. of thiopental sodium were given intravenously for the induction of anesthesia. Halothane and nitrous oxide through an endotracheal tube were used for maintenance. Cyclaine hydrochloride (5 per cent) 2 ml. were instilled into the trachea prior to orotracheal intubation. Although the blood pressure and pulse rate did not vary much from the preoperative levels during surgery, the respiratory rate increased to approximately 44 per minute. There was some wheezing, and the patient's

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Presented and discussed at a conference held at Bellevue Hospital, New York City, November 6, 1961. Clinical Anesthesia Conferences are held on the first Monday of each month.

face appeared somewhat cyanotic and dusky throughout most of the procedure.

The surgical procedure consisted of two brachial arteriotomies and the attempted aspiration of a thrombus. Finally, an axillary arteriotomy was performed with the successful aspiration of the thrombus. Heparin and saline were flushed into the vessel during surgery. The color of the patient's left arm improved. A good axillary and subclavian pulse and a weak radial pulse were noted. The patient received heparin for anticoagulation during the procedure which lasted for four hours.

In the recovery room there was severe oozing from the wound, and the surgical dressings were reinforced. The Lee and White coagulation time was more than sixty minutes. The left arm again appeared cyanotic, and no pulses were palpable. The hemoglobin was now 17.3 Gm. per 100 ml., and the hematocrit was 54. Protamine sulfate was given in fractional doses followed by cessation of the bleeding. The systolic blood pressure had fallen to 90 mm. Hg, and the patient was transfused with 500 ml. of his own blood.

On the following day his arm was swollen and cyanotic below the elbow, and no peripheral pulses were palpable. Anticoagulant therapy was being maintained. On the second postoperative day fibrinolysin therapy was instituted intravenously. Bleeding from the wound and venipuncture site was noted, and fibrinolysin then was discontinued. On the following day the arm was warmer, the color improved, and a good radial pulse was palpable. The large axillary hematoma which occurred following surgery had now disappeared and extravasated over the back and anterior thoracic cage. The platelet count varied between 300,000 and 400,000 per cubic millimeter. Blood volume studies were requested, but because of the recent massive bleeding it was thought best to wait until the patient's condition was stabilized.

At present, the edema of the arm is subsiding, but sensory and motor functions of the hand and forearm have not returned. The impression is that there is involvement of the three main cords of the brachial plexus. The patient is presently receiving physiotherapy.

Comment

The pathologic changes encountered in polycythemia vera are usually the result of increased viscosity of the blood resulting from an increased red cell mass and slow velocity of blood flow. At autopsy the significant findings reported are the changes in bone marrow, splenomegaly, and plethora of all tissues. Coronary artery occlusion and myocardial infarction also are frequent findings in these patients.[1]

The stellate ganglion block performed on this patient was indicated in an attempt to relieve any vasospastic element and improve collateral circulation. When it is performed, it is advisable to complete the procedure prior to anticoagulant therapy.

Methods of therapy such as the use of chemical agents, interval venesections, spray irradiation, and radioactive phosphorus cannot be resorted to prior to emergency surgery because of the time factor. An attempt must be made to bring down the total red cell mass by venesections in the uncontrolled or untreated patient. Although 500 ml. of blood were withdrawn from this patient, the amount most likely was inadequate to be effective. Some physicians recommend the withdrawal of from 2 to 4 pints of blood. A comparable amount of plasma is given to the patient in return. This decreases the red cell mass and also supplies a certain amount of fibrinogen.[2] Determinations of the patient's total red cell volume are more important than the red cell count, hematocrit, or hemoglobin since plasma volume may vary in these patients.

The skin and mucous membranes in polycythemia vera have been described as bluish-red in contrast to the bluish cyanosis associated with other conditions. In general, slowed capillary circulation of the blood with normal oxygen saturation exists. Some of these patients may appear to be pale, however. The depth of color in the skin is due in part to the location and state of distention of the capillaries. Under anesthesia the skin color in this patient gradually changed. The cyanosis became deeper and more bluish. This was evidence of some degree of oxygen unsaturation of the blood even in the presence of a high oxygen concentration in the anesthetic mixture and assisted ventilation. The tachypnea during anesthesia was due to the existing hypoxia. The viscosity of the blood and the retarded circulation through the alveolar capillaries deepened the cyanosis probably by a further disturbance of the ventilation-blood flow ratios. The decrease in elasticity and increased adhesive resistance in the lung may well account for the wheezing noted during anesthesia.

Following pulmonary function studies in patients with polycythemia, Newman, Feltman, and Devlin[3] listed a sequence of events which may occur in some of these patients. The increased blood viscosity and volume cause a decrease in the elasticity and an increase in the viscous resistance of the lungs leading to a decrease in maximum breathing capacity and the vital capacity. Impaired ventilation results, giving rise to a poor correlation between ventilation and perfusion. The high distribution gradient thus created results in arterial oxygen unsaturation, increased arterial carbon dioxide pressure, and respiratory acidosis. In addition, the increased blood viscosity and volume would tend to open the capillary bed of alveoli, which are normally poorly ventilated, and thus increase the distribution gradient and resultant anoxia. The fact that thrombi in alveolar capillaries and respiratory center damage may occur in some patients would impair diffusion and ventilation further and contribute to the anoxia. These patients may go on to pulmonary hypertension and finally right ventricular failure.

The postoperative period was of interest in that the patient continued to bleed and became hypotensive requiring blood replacement by retransfusing his own blood. This technic is justified, but one wonders about giving whole blood to this patient whose hematocrit and hemoglobin values were still above normal. It might have been better to use plasma or an expander at this point.

The improvement of the color and circulation of the patient's arm following the use of fibrinolysin also was of interest. It is difficult to state whether the improvement was due to the intravascular effects of fibrinolysin or the dissolution of the hematoma and the release of external pressure on the axillary artery.

The uncontrolled or poorly treated polycythemic patient presents many hazards during anesthesia. The induction and maintenance of anesthesia are most difficult. It has been recommended that in the presence of hemoconcentration the choice of anesthesia be limited to regional technics when possible.[4] Nevertheless, all such patients should be prepared properly by the reduction in the red cell mass to near-normal levels prior to anesthesia and surgery because of the dangerous complications likely to occur.

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Number one hundred seventeen in a series of Clinical Anesthesia Conferences

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Skin disease linked to internal cancer

There is a significant correlation between the occurrence of internal cancer and a skin ailment known as Bowen's disease, according to an article by Edward S. Peterka, M.D., Francis W. Lynch, M.D., and Robert W. Goltz, M.D., in the October, 1961, issue of *Archives of Dermatology*, published by the American Medical Association.

The authors urged repeated thorough examinations for internal cancer particularly for patients in whom unexposed areas of the skin are affected. Such examinations can contribute to the recognition of internal cancer before its symptoms appear. The authors found internal cancer in 11 of 33 patients with Bowen's disease affecting the trunk, arms, and legs. "Combining these data with information from previous reports one concludes that approximately one third of patients with Bowen's disease develop evident internal cancer at an average of six to ten years after the initial diagnosis of Bowen's disease."

Accidental Chemical Poisonings

From the Poison Control Center,
The City of New York Department of Health

A series prepared by

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Methyl Salicylate Poisoning

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Methyl Salicylate	63 years	Female

Methyl salicylate had been prescribed for the relief of pain to be used by the patient as a topical application.

She misunderstood the instructions and swallowed approximately 10 ml. of the preparation. She immediately experienced a burning sensation of the mouth and vomited. She called her physician who advised her to go to a hospital emergency room service.

On arrival at the hospital her stomach was lavaged with one-sixth molar lactate about two hours following the ingestion. At that time she also complained of abdominal pains, was in a profuse sweat, experienced hyperventilation, and was "feeling poorly all over."

The gastric contents had a salicylate odor. She was observed for several hours and sent home.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	23 months	Female

The mother of the patient told the public health nurse who visited the home that her husband had a virus infection and had used oil of wintergreen for a rubdown. After its use he placed it on a dresser in his bedroom. While the family was in the kitchen, the patient went into the bedroom, obtained the bottle containing the preparation, and drank an unknown quantity.

When the mother realized what had happened, she induced vomiting and took the child to a nearby hospital. On admission to the hospital the patient was dyspneic and had deep and slow respirations. The stomach was lavaged with saline within one hour following the ingestion, and the patient was admitted for observation. After four days of symptomatic and supportive therapy the patient recovered completely.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	16 years	Female

This patient had a coughing spell during the night and went to the bathroom to take some cough medicine from the medicine cabinet. She mistakenly took a bottle containing oil of wintergreen and swallowed about half an ounce. When her mother went into the bathroom she noted the odor of oil of wintergreen. She inquired whether or not the patient took the right medication, and the error was then realized. The mother immediately administered olive oil and 2 quarts of milk as a first aid measure and took the child to a hospital for further care.

On admission to the hospital the patient had abdominal pains, hyperpnea, burning in the mouth and throat, and an odor of oil of wintergreen on her breath.

Her stomach was lavaged with potassium permanganate and charcoal. The gastric contents were positive for salicylates. The blood had a pH of 7.311, and carbon dioxide was 21 volumes per 100 ml. The patient was treated symptomatically, and the electrolyte balance was maintained with one-sixth molar lactate. After four days the patient made a complete recovery.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	9 years	Female

The patient suffered from a cough and mistakenly was given 1 teaspoonful of oil of wintergreen as a cough remedy. The bottle of oil of wintergreen had been placed next to the cough medication in the medicine cabinet.

The patient complained of burning in the mouth and throat, nausea, and abdominal pains. On admission to the hospital the patient also had an odor of oil of wintergreen on her breath and appeared extremely nervous.

In an attempt to induce vomiting the patient inadvertently had been given 15 cc. of ipecac by her mother. At the hospital 150 to 175 cc. of the stomach contents were aspirated by means of a nasogastric tube. Following this the stomach was lavaged with 500 cc. of normal saline with no evidence of bleeding from the gastric mucosa.

After this 30 cc. of Gelusil and 60 cc. of milk were given. The patient soon made a satisfactory improvement and was sent home after four hours, symptom-free.

INCIDENT 5

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	9 years	Male

This patient was playing doctor with his cousin who gave him 2 teaspoonfuls of oil of wintergreen for some imaginary illness in addition to 2 aspirins and tooth paste in 1 ounce of water. On the way home from his cousin's place the patient became very ill and was taken to his family physician. His stomach was lavaged immediately with normal saline, and he was later hospitalized and given supportive therapy.

Since he was symptom-free after twenty-four hours, he was sent home as recovered.

INCIDENT 6

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	19 months	Male

While visiting with his aunt, the patient went into the bathroom and obtained a bottle of oil of wintergreen which was placed on the ledge of a cabinet. The child drank an unknown amount of the preparation.

He immediately cried out as though in pain and complained of burning in the mouth and throat. Since he had a smell of oil of wintergreen on his breath, his aunt realized what had happened. She induced vomiting and took him to a hospital for further care. His stomach was lavaged in the emergency room with sodium bicarbonate within forty-five minutes following ingestion, and he was transferred to the Kings County Hospital where he received symptomatic and supportive therapy.

Comment

Methyl salicylate is perhaps more toxic than the sodium salt and aspirin, and metabolic acidosis is more common. One teaspoonful has been reported as causing a fatality in an infant.

While it has no real value in modern therapeutics, it is still widely used for a variety of conditions. Its ready availability in the home gives rise to many needless accidental poisonings, particularly in children.

The most prominent symptoms of acute poisoning are burning in the mouth and throat, nausea, vomiting, perspiration, hyperpnea, rapid pulse, thirst, irritability, headache, nervousness, lethargy, stupor, convulsions, and coma. Hemorrhagic manifestations also may appear. The urine may contain acetone and albumin, and the ferric chloride test will be positive for salicylates.

The symptoms are chiefly those arising

from the central nervous system stimulation and ultimate depression and from the electrolyte imbalance occasioned by the respiratory alkalosis which is soon followed by a metabolic acidosis, particularly in children.

The treatment is aimed at the removal of the toxic substance, delaying absorption, and the correction of the electrolyte imbalance. In addition to emesis and gastric lavage, the treatment is chiefly supportive and symptomatic. If acidosis is present, and in most cases of salicylate poisoning in children it occurs early, alkalinization is indicated. This can be accomplished best by the use of M/6 sodium lactate or 4 per cent sodium bicarbonate intravenously. A pH determination of the blood should be made to determine whether either alkalosis or acidosis is present. A determination should be repeated every four hours. The intravenous administration of glucose in either saline or water also is recommended for the correction of dehydration or possible hypoglycemia.

Vitamin K also may be administered to combat hemorrhage.

If nephrotoxic symptoms appear and renal shutdown is threatened, hemodialysis may be indicated. Peritoneal lavage and exchange transfusions also have been used profitably. In the majority of cases, however, neither of the previously mentioned procedures are indicated since correct alkalinization will be effective in the treatment of the acidosis in most cases.

Number eighty-four in a series of Briefs on Accidental Chemical Poisonings

Peptic ulcer in children seen as frequent occurrence

A five-year survey of patients treated for ulcers showed x-ray evidence of peptic ulcer in 55 children under sixteen years of age. Their average age was 8.75 years; the youngest was 5.5 months. On the basis of these findings, R. H. Whittlesey, M.D., in an article in the June, 1961, issue of the *American Journal of Surgery*, reports that peptic ulcer "occurs considerably more frequently than was previously believed."

The most common symptom was abdominal pain for three to four weeks, often located in the epigastrium and accompanied by vomiting, less often by nausea and diarrhea. Pain was distinctly less characteristic of ulcers in children than in adults. Furthermore, the relief of pain bore little relationship to the ingestion of regular foods.

Because ulcer symptomatology in children is so atypical, the author stresses that roentgenologic confirmation of diagnosis by the demonstration of the crater is essential. Prominent radiologic features are irritability of the duodenal cap and intermittent pylorospasm.

Symptomatic treatment includes bland diet, frequent administration of milk and cream in small quantities, and appropriate doses of anticholinergics and alkali.

For isolated, intractable cases requiring surgery, the author believes that subtotal gastrectomy may be the treatment of choice.—*Pediatric Currents*, *Ross Laboratories*

ELUCIDATION

Continued from page 399

The patient had primary pulmonary hypertension.

At postmortem examination, the significant pathologic findings were limited to the heart and pulmonary arterial vasculature. The right auricular chamber was markedly enlarged, and the tricuspid ring was widely dilated, resulting in valvular incompetence and accounting for the terminal loud systolic murmur. There was striking hypertrophy of the right ventricle and ectasia of the pulmonary arteries. The pulmonic ring was also dilated and the leaflet closure insufficient, producing the pulmonic diastolic or so-called Graham Steell murmur. The essential microscopic lesion was observed in the muscular pulmonary arteries and arterioles where medial muscular hypertrophy was conspicuous. The intima exhibited fibrosis and this appeared to predispose to thrombosis and occlusion. This generalized impedance to arterial flow in the muscular arteries accounts readily for the increased pulmonary pressures and the consequent strain on the right side of the heart.

It was not until after the advent of cardiac catheterization that an accurate description and understanding of primary pulmonary artery hypertension became available. Prior to this, the disease was sometimes called idiopathic right ventricular hypertrophy. Dresdale, Schultz, and Michtom[1] deserve credit for focusing attention on the true nature of this entity, and their observations are still remarkably accurate.

Primary pulmonary hypertension is a disease of unknown etiology found primarily in females between twelve and forty-five years of age.[2-5] Its possible relationship to childbearing has been discounted because of its frequent occurrence in children and nulliparous women. Schistosomiasis and multiple pulmonary emboli may present a similar clinical and physiologic picture.

The early symptoms of breathlessness, exertional syncope, and angina-like pain are thought to be due to decreased cardiac output and consequently reduced cerebral and coronary blood flow. Increased pulmonary resistance is responsible for the diminished blood flow to the left side of the heart and the low cardiac output.

Cardiopulmonary auscultation reflects the impairment of pulmonary circulation. The pulmonic second sound is loud, often split, and frequently palpable. An ectatic pulmonary artery may result in a left recurrent laryngeal nerve paralysis and hoarseness as it did in the patient presented. A pulmonic diastolic murmur (Graham Steell) is a result of an enlarged pulmonic ring. Increased retrosternal dullness and a parasternal heave indicate right ventricular hypertrophy. In the terminal stages the tricuspid ring may dilate and produce the classic picture of tricuspid insufficiency with its loud systolic murmur, dilated neck veins, and pulsating liver.

The electrocardiogram most often shows sinus rhythm, right ventricular hypertrophy, and peaked P waves. A chest roentgenogram will reveal a prominence of the pulmonary artery segment. The peripheral lung fields are clear. Pulmonary function and blood gas studies are usually within normal limits.

The key to diagnosis is cardiac catheterization which allows the clinician to discard congenital and rheumatic heart lesions that may present pulmonary hypertension. The two most significant findings are an increased pulmonary artery pressure and normal pulmonary capillary wedge pressure. The right atrial pressure and pulmonary resistance are also elevated. There is a decrease in pulmonary blood flow and cardiac output.

The duration of life after the onset of symptoms varies between one month and twenty years. However, the majority of reported cases survive less than two years after the diagnosis. It may terminate in sudden death or in unrelenting failure of the right side of the heart.

Priscoline, acetylcholine, and aminophylline, when injected into the pulmonary artery, cause a drop in the blood pressure. Unfortunately, they are ineffective when administered by any other route. There are two schools of thought on treatment: steroids and anticoagulants by one, therapeutic nihilism by the other. Each has been equally ineffective.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 14 to 18, 1962

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 14 to 18, 1962, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1962*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Abstracts

Linder, M., Weller, C., and Macaulay, A. I.: Combined oral hypoglycemic therapy; to improve control of diabetic patients unresponsive to single agents, New York State J. Med. **62:** 337 (Feb. 1) 1962.

There have been many primary and secondary failures in oral hypoglycemic therapy. Because recent work has suggested that the two classes of oral hypoglycemic agents, the sulfonylureas and the biguanides, exert their effects at different sites and in different manners, a study was undertaken of the effectiveness on 40 cases of maturity-onset diabetes mellitus of combined therapy with the sulfonylurea, chlorpropamide (Diabinese), and the biguanide, phenformin (DBI). All of the cases were primary or secondary failures to chlorpropamide or phenformin used alone or were intolerant of one of the compounds. The maximum daily dosage level during the study was 150 mg. of phenformin and 500 mg. of chlorpropamide. The follow-up periods ranged from one to eighteen months, averaging seven and one-half months. Twenty-seven of the 40 previously inadequately controlled patients showed good or fair control while on the combined therapy, a salvage rate of 68 per cent. Ten patients exhibited poor control and were changed to insulin; the combined therapy was discontinued in 3 patients because of intolerance, although they were well controlled chemically. To date no secondary failures have occurred. When used together, the combination of chlorpropamide and phenformin can minimize potential toxicity and/or side-effects because smaller doses of each can be used for increased therapeutic effectiveness.

Paganelli, V. H., and Galindo, J.: Vaginal bleeding secondary to spontaneous complete rupture of umbilical or placental vessels, New York State J. Med. **62:** 342 (Feb. 1) 1962.

Vaginal bleeding late in pregnancy is not necessarily always of maternal origin. It may be from a fetal source: vasa previa or complete spontaneous rupture of the cord or placental vessels. There have been only 36 reported cases of partial rupture of the cord and placental vessels and 12 of complete rupture. However, in view of the 1 per cent incidence of velamentous insertion, which is associated almost always with vasa previa, a higher incidence of vasa previa and complete abruption of cord vessels might be suspected. Rupture of the cord or placental vessels may occur in vessels which are histologically normal or abnormal. Complete rupture of the cord or placental vessels after the amniotic membranes have ruptured produces painless vaginal bleeding either prior to the onset of labor or in its first or second stages. This is usually not associated with any significant change in maternal vital signs but is associated with signs of rapidly increasing fetal distress. The presence in vaginal blood of large numbers of fetal red blood cells may be an indication of fetal bleeding. If, in the presence of the previously mentioned clinical findings, a live but extremely pallid, flaccid, nonbreathing or shallow-breathing infant is born in the absence of any known Rh factor problem, the diagnosis of hemorrhagic fetal shock should be considered immediately. The authors suggest that a smear of vaginal blood be taken during labor. The presence of nucleated fetal red blood cells in a relatively large quantity in the smear would focus attention on the necessity of prompt attention to the infant at delivery. Consultation is necessary to determine whether or not a cesarean section is indicated. In case of fetal hemorrhage, prompt transfusion is essential.

Henley, J., and Kritchman, M.: Total sympathetic blockade as an adjunct to anesthesia, New York State J. Med. **62:** 348 (Feb. 1) 1962.

Early experience taught that prolonged anesthesia, necessitated by radical surgical procedures, was not tolerated well by poor-risk patients, blood loss was often profuse, and circulation remained inadequate despite rapid blood replacement. It has been shown that hypothermia and vasodilation are possible solutions to this problem. The authors report 125 cases in which total sympathetic blockade was produced, 79 with total epidural analgesia, 4 with high spinal, 20 with hexamethonium (Bistrium), and 12 with trimethaphan camphorsulfonate (Arfonad). The blockade was attained by a catheter placed in the epidural space. Almost all of the patients had at least one serious medical condition before operation; 38 had cardiac conditions. Most of the cases were radical interventions for cancer. In 27 cases the procedure lasted eight hours or more; only 8 lasted three hours or less. Forty-four of the patients were over seventy. Using the epidural technic it was not difficult to lower the blood pressure if enough anesthetic solution was injected, the patient was positioned so that gravity helped to distribute the drug, and there were no epidural adhesions. The clinical results were satisfactory. Postoperatively, hemoglobin, hematocrit, blood pressure, and urinary output were at preoperative levels despite the magnitude of the operative procedures and the age and condition of the patients. Total sympathetic blockade, produced by epidural analgesia as an adjunct to anesthesia, has made possible light anesthesia with excellent relaxation, minimal blood loss, ease of production of hypothermia, absence of shock, and a means of monitoring blood volume changes by following the blood pressure. It may be applicable also to further studies of cardiovascular physiology.

Sagi, E. S., Mackenzie, L. L., and Adler, M. P.: Technic of the Sagi test, New York State J. Med. **62:** 369 (Feb. 1) 1962.

Further improvements and standardizations have been made in the technic of a test for malignant conditions which differentiates blood serum by its configuration on contact with various strengths of phenol solution, labeled as levels 1 to 5. A quantitative procedure has been developed. Blood is drawn in the postabsorptive period. A control is used with each unknown. A drop of negative serum forms a round pellet almost immediately; at about the fifth minute it begins to shrink gradually and eventually disappears. A drop of positive serum expands either immediately or shortly after its release, or it may flatten to a thin film or disintegrate more or less completely within a short period. Sera with negative reactions in level 1 are eliminated and reported as negative; sera with positive reactions in level 1 are tested through the lower levels using the same procedure. If the serum is positive only on level 1, it is recorded as 1 plus; if it is positive on all levels, as 5 plus. In a series of 4,000 sera from a cancer detection clinic, all were drawn during the absorptive period. In 1,800 of these which were cloudy, there were 402 positive test results. Eighty of these were repeated on a fasting stomach; 16 results were still positive, and 64 became negative. Further studies of the lipid fractions are in progress. It is not known if the degree of positivity of this test has any correlation with the clinical stage of disease, but a definite correlation has been found between the degree of positivity of the test and the duration of gestation.

Milner, W. A., Garlick, W. B., Spakowski, W., and Charron, J.: Ureteral ectopy without incontinence in reduplicated kidneys, New York State J. Med. **62:** 373 (Feb. 1) 1962.

The most frequent sign of ureteral ectopy is intermittent urinary incontinence despite normal micturition. Infection usually is present and adds to the patient's distress. In the absence of urinary incontinence, this disease cannot be recognized solely by its clinical picture. An ectopic ureter may be symptomless if it is uncomplicated by infection. The diagnosis is the result of x-ray examination which is requested for an unexplained and stubborn urinary infection or as part of a work-up for vague abdominal pains. The final diagnosis rests on the identification of the ectopic ureteral orifice, which can be facilitated by the intravenous injection of indigo carmine. Repeated examinations are usually necessary. Two cases of ectopic ureters without incontinence in reduplicated kidneys are presented. A greater awareness of this condition would result in more frequent diagnoses. The treatment of the condition should be specific according to the individual findings, as illustrated by the different surgical procedures employed in the 2 cases presented.

Goldman, H. B.: Hypoadrenocorticism and endocrinologic treatment of Meniere's disease, New York State J. Med. **62:** 377 (Feb. 1) 1962.

Hypoadrenocorticism exists in the general population to a greater degree than has been recognized. Individuals with this condition react poorly to stress because of hormonal imbalance or lack. The disease may be inherited or acquired as the result of cortisone therapy or repeated stress. Patients with inherited hypoadrenocorticism have many common characteristics. A diagnosis is possible by means of a careful endocrine history and physical examination. The four-hour glucose-tolerance test is the most important laboratory test for hypoadrenocorticism. It is the author's belief that Meniere's disease is a localized vasomotor reaction to a general series of external influences on a body predisposed by an abnormally reacting autonomic nervous system. The major factor in this abnormality is hypoadrenocorticism. In 75 cases treated by the author, 90 per cent have shown good responses to the use of whole adrenal cortical extract and other glandular therapy. The avoidance of stress and the importance of diet are emphasized. Adrenocortical therapy leads to the repair of the capillary system and the resorption of the transudate and diminishes the tendency to angiospasm. Of the three main symptoms, vertigo is improved markedly in from two to four weeks, and tinnitus is relieved after from two to three months, but hearing loss improves much more gradually, if at all. There are no contraindications to use of the whole physiologically balanced adrenal cortical extract in doses ranging from 1 to 100 cc.

Necrology

Samuel Meyerson Baum, M.D., of New York City, died on December 12, 1961, at Roosevelt Hospital at the age of sixty-seven. Dr. Baum graduated in 1919 from Columbia University College of Physicians and Surgeons. He was an associate in radiology at City Hospital at Elmhurst. Dr. Baum was a Diplomate of the American Board of Radiology, a Member of the American College of Radiology, and also a member of the American Radium Society, the Radiological Society of North America, Inc., the Rudolf Virchow Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ellis Moore Black, M.D., of the Bronx, died on December 25, 1961, at his home at the age of sixty-nine. Dr. Black graduated in 1920 from Harvard Medical School. In 1929 he established Black's Sanitarium which is now known as the Parkchester General Hospital. Dr. Black was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Birney Broad, M.D., of Syracuse, died on December 6, 1961, at his home at the age of ninety. Dr. Broad graduated in 1896 from Syracuse University College of Medicine. He was senior attending in gynecology at Syracuse Memorial Hospital, senior consultant in gynecology at the Hospital of the Good Shepherd (formerly University Hospital), and professor emeritus at Syracuse University College of Medicine. In 1946 a lectureship honoring him was established by the College and since then a George Birney Broad lecture has been given at the College annually by a nationally known gynecologist. Dr. Broad was a Fellow of the American College of Surgeons and a member of the Syracuse Academy of Medicine, the Onondaga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Chester Carmer, M.D., of Lyons, died on December 3, 1961, at the Barber Hospital at the age of seventy-four. Dr. Carmer graduated in 1910 from Cornell University Medical College. Dr. Carmer was a member of the Wayne County Medical Society and the Medical Society of the State of New York.

Frank Mahlon Holcombe, M.D., of Auburn, died on October 31, 1961, at Auburn Hospital at the age of seventy-six. Dr. Holcombe graduated in 1912 from Columbia University College of Physicians and Surgeons. He was an attending physician in general practice at Auburn Memorial Hospital and from 1938 until his retirement in 1955 he served on the medical staff of Auburn Prison. Dr. Holcombe was a member of the American Academy of General Practice, the Cayuga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ralph Louis Icken, M.D., of Long Island City, died on July 13, 1961, at the age of sixty-two. Dr. Icken received his medical degree from the University of Freiburg in 1926. He was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Brien Kaiser, M.D., of Far Rockaway, died on December 13, 1961, at his home at the age of fifty. Dr. Kaiser graduated in 1935 from the University of Buffalo School of Medicine. He was an attending in surgery at St. Joseph's Hospital, Far Rockaway, and an associate attending in surgery at the Queens Hospital Center. Dr. Kaiser was a Diplomate of the American Board of Surgery and a member of the Queensboro Surgical Society, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Martin Joel Loeb, M.D., of the Bronx, died on December 16, 1961, at the age of seventy-eight. Dr. Loeb graduated in 1909 from New York University and Bellevue Hospital Medical College. He was a consultant in urology at the Bronx Municipal Hospital Center. Dr. Loeb was a member of the New York Academy of Medicine, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Preston Macleod, M.D., of New York City, died on June 17, 1961, at the age of eighty-three. Dr. Macleod graduated in 1903 from Harvard Medical School and interned at Bellevue Hospital and Lying-in Hospital. He was a member of the Industrial Medical

Association, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James P. McManus, M.D., of Jamaica, died on December 23, 1961, at Mary Immaculate Hospital at the age of seventy-one. Dr. McManus graduated in 1920 from New York University and Bellevue Hospital Medical College and interned at Bellevue Hospital. He was a consultant in obstetrics at Mary Immaculate Hospital, Mercy Hospital (Rockville Centre), and St. Joseph's Hospital (Far Rockaway). Dr. McManus was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, and a member of the New York Academy of Medicine, the Queensboro Surgical Society, the Queens Gynecological Society, the Brooklyn Gynecological Society, the New York Obstetrical Society, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Eugene Neuwirth, M.D., of Great Neck, died on September 22, 1961, at the age of seventy. Dr. Neuwirth received his medical degree from the University of Budapest in 1915. He was a Diplomate of the American Board of Physical Medicine and Rehabilitation and a member of the American Rheumatism Association, the New York Rheumatism Association, the New York Society of Physical Medicine and Rehabilitation, the Nassau County Medical Society, and the Medical Society of the State of New York.

Wesley Theodore Pommerenke, M.D., of Rochester, died on November 22, 1961, in Chicago at the age of sixty. Dr. Pommerenke graduated in 1930 from Harvard Medical School. He was an associate professor of obstetrics and gynecology at the University of Rochester School of Medicine and an associate attending in obstetrics and gynecology at Strong Memorial Hospital, a consultant in gynecology and obstetrics at Genesee, Wyoming County Community (Warsaw), and the Arnold Gregory Memorial (Albion) Hospitals. Dr. Pommerenke was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American College of Obstetricians and Gynecologists, and a member of the American Society for the Study of Sterility (president in 1956), the American Physiological Society, the International Fertility Association, the Rochester Academy of Medicine, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Nelson Potts, M.D., of Buffalo, died on October 12, 1961, at the age of seventy-one. Dr. Potts graduated in 1912 from the University of Buffalo School of Medicine. A former professor of orthopedic surgery at the University, he was a consultant in orthopedic surgery at Children's Hospital, Buffalo General Hospital, Mercy Hospital, and United States Public Health Service Outpatient Clinic. Dr. Potts was a Diplomate of the American Board of Orthopedic Surgery, a Fellow of the American College of Surgeons, and a member of the American Orthopaedic Association, the American Academy of Orthopaedic Surgeons, the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Stahl, M.D., of the Bronx, died on June 26, 1961, at the age of sixty-seven. Dr. Stahl graduated in 1915 from New York University and Bellevue Hospital Medical College. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Joseph Tenenbaum, M.D., of New York City, died on December 9, 1961, at Maimonides Hospital, Brooklyn, at the age of seventy-four. Dr. Tenenbaum received his medical degree from the University of Lemberg in 1914. Retired, he was a consultant in urologic surgery at Goldwater Memorial Hospital and Maimonides Hospital. Dr. Tenenbaum was a Diplomate of the American Board of Urology, a Fellow of the American College of Surgeons, and a member of the New York Academy of Medicine, the New York Society of the American Urological Association, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harold Williams Trott, M.D., of Hemlock, died on May 17, 1961, at the age of sixty-one. Dr. Trott graduated in 1924 from the McGill University Faculty of Medicine.

Ross Miller Wilson, M.D., of New York City, died on December 11, 1961, at the age of seventy-seven. Retired, Dr. Wilson graduated in 1911 from Long Island College Hospital School of Medicine. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Maredith H. Wyttenbach, M.D., of Elmira, died on November 25, 1961, at the age of fifty-six. Dr. Wyttenbach graduated in 1929 from Indiana University School of Medicine. In 1955 she was elected chairman of the board of directors of the New York State Academy of General Practice and in 1956 she was appointed chairman of the general practice section of the Medical Society of the State of New York. Dr. Wyttenbach was a member of the American Academy of General Practice, the Chemung County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harry Joel Zisk, M.D., of Brooklyn, died on December, 9, 1961, at the Jewish Hospital of Brooklyn at the age of fifty-one. Dr. Zisk received his medical degree from the University of Vienna in 1937. He was an associate attending physician at the Coney Island Hospital and an adjunct physician at the Jewish Chronic Disease Hospital and the Jewish Hospital of Brooklyn. Dr. Zisk was a member of the American Geriatrics Society, the Brooklyn Society of Internal Medicine, the New York Cardiological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical Meetings

Fourth annual Clara Thompson Memorial Symposium

"Problems of Leadership in Psychoanalysis and Everyday Life" will be the topic of the fourth annual Clara Thompson Memorial Symposium on Sunday, February 4, at 1:30 P.M. at the Starlight Roof of the Waldorf-Astoria Hotel, New York City.

Guest speakers will be: Thomas S. Szasz, M.D., professor of psychiatry, State University of New York Upstate Medical Center, Syracuse; Arthur Schlesinger, Jr., special assistant to President Kennedy; F. C. Northrop, Sterling Professor of Law and Philosophy, Yale University; and Richard Revere, Washington correspondent, *The New Yorker* magazine.

Chicago Ophthalmological Society

The Chicago Ophthalmological Society will hold its annual clinical conference on February 16 and 17 at the Drake Hotel in Chicago. Arthur Gerard DeVoe, M.D., New York City, will be among the guest speakers.

Registration may be made by contacting: Mrs. Mary E. Ryan, 1150 North Lorel Avenue, Chicago 51, Illinois.

American Society of Psychosomatic Dentistry and Medicine

The annual meeting of the American Society of Psychosomatic Dentistry and Medicine will be held at the Shoreham Hotel, Washington, D.C., from Friday evening, March 2, to the afternoon of Sunday, March 4. The main theme of the program will be "Patient Relationship, Its Importance and Development in the Clinical Setting of General Practice."

Members of the American Academy of General Practice will receive category II credit for attendance.

For information contact: Philip Ament, D.D.S., 964 Delaware Avenue, Buffalo 9, New York.

Region II Conference of National Association of Blue Shield Plans

Region II of the National Association of Blue Shield Plans will sponsor a professional relations conference at the Hotel Biltmore, New York City, March 28 and 29.

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis, Inc., will sponsor a lecture by Dr. Paul Tillich on the topic "What Is Basic in Human Nature" on Thursday, March 29, at 8:30 P.M., at the New York Academy of Medicine, 103rd Street and Fifth Avenue, New York City.

Month in Washington

The Kennedy Administration and other main supporters of medical care of the aged under Social Security are preparing to make an all-out effort to push the legislation through Congress in the 1962 session.

Their campaign poses a serious challenge to the medical profession and its allies in the fight against such compulsory government health schemes.

It is too early to evaluate the effect on the legislation of changes in House Democratic leadership and House Ways and Means Committee membership. The White House has been exerting pressure in an effort to have a congressman supporting its views named as a replacement for Rep. Frank Ikard (D., Tex.), who resigned. Ikard opposed proposals to put health care under Social Security.

Administration officials from President Kennedy down publicly gave the Administration medical care legislation, the King-Anderson bill, top priority for the 1962 session. During the interim after the adjournment of the 1961 session, the Administration held a political roadshow in key cities in an effort to build up public support for the King-Anderson bill and other Administration proposals that did not fare so well in Congress. At a number of the so-called White House Regional Conferences physicians forcefully expressed the medical profession's opposition to putting health care under Social Security.

The AFL-CIO geared for a renewed fight for the Administration legislation. A new national organization of the elderly has been formed with the main purpose of lobbying for the King-Anderson bill. It is the National Council of Senior Citizens for Health Care Through Social Security. Former Rep. Aime J. Forand (D., R.I.), who sponsored such legislation when he was in Congress, was the leading figure in organizing the group and is national chairman.

On the other side of the fight, there also is a new organization—The American Medical Political Action Committee. It is a nonprofit, voluntary, nonpartisan, unincorporated committee set up last May with the approval of the A.M.A. Board of Trustees. AMPAC—which functions independently of medical organizations and societies whether at the national, state, or local level—was organized to meet "an unmet need, the need of providing the medical profession with an opportunity to assume a more active and effective role in public affairs." In November the A.M.A. Board of Trustees House of Delegates at Denver urged that all physicians, their wives, and interested friends join AMPAC and similar political action committees in their states and communities.

Leonard W. Larson, M.D., A.M.A. president, warned the House of Delegates that physicians "are engaged in a historic struggle to preserve our country's unique system of medical care and our stature as a profession." He said both are "seriously threatened" by such legislative proposals as the King-Anderson bill.

Dr. Larson said that the A.M.A. could expect "even more bitter attacks" than those so far from Administration and AFL-CIO spokesmen. He appealed to physicians to support medicine's friends in Congress with money and personal campaign assistance. He noted that AMPAC provides "a national mechanism through which physicians and their families can channel funds for strategic placement where the money will do the most good."

A leading congressional opponent of health care under Social Security also warned of the seriousness of the fight ahead. Sen. Wallace F. Bennett (R., Utah), a member of the Senate Finance Committee which handles such legislation, told students at Harvard University Medical School that there undoubtedly would be "a determined drive to rush H.R. 4222 (the King-Anderson bill) through the Congress" in 1962.

"The propogandists who are behind the determined drive for a system of socialized medicine have latched on to an emotional appeal in trying to push this legislation through the Congress," Bennett said. "They have tried to create a public image that the A.M.A. and any individual who opposes this plan is motivated by selfish interests.

"As one who is vigorously opposed to compulsory Federal medical care, I resent the tactics used by those who advocate this system of socialized medicine. There is an answer to this problem of meeting the medical needs of our aged, and I frankly believe that it is being honestly met by our present voluntary health insurance programs and by the cooperative Federal-state aid to our needy aged who are incapable of paying their own medical expenses.

"I am opposed to H.R. 4222 or other bills which would open the flood gates to a system of compulsory medical care, directed first to our aged, but which, once instituted, would surely by political pressure be expanded to all of our population. The battle over this legislation in this next Congress is bound to be hectic and monumental. It is a battle we can't afford to lose."

Abstracts in Interlingua

Linder, M., Weller, C., e Macaulay, A. I.: Combinate therapia hypoglycemic oral; pro meliorar le stabilisation in patientes diabetic qui non responde a agentes solitari, New York State J. Med. **62:** 337 (1 de feb.) 1962.

Ha occurrite numerose disfallimentos primari e secundari in oral therapia hypoglycemic. In consideration del facto que recente investigationes suggere que le duo classes de oral agentes hypoglycemic—le sulfonylureas e le biguanidos—exerce lor effectos in differente sitos e in differente manieras, un studio esseva interprendite, in 40 casos de diabete mellite a declaration in etate adulte, del efficacia de un combinate therapia con le sulfonylurea chlorpropamido (Diabinese) e le biguanido phenformina (DBI). Omne le casos esseva casos de disfallimento primari o secundari in le uso de chlorpropamido o de phenformina como agente solitari o esseva intolerante pro un del duo compositos. Le dosage maximal durante le studio esseva 150 mg de phenformina e 500 mg de chlorpropamido per die. Le periodos de observation catamnestic variava inter un e dece-octo menses, con un duration medie de septe menses e medie. Vinti-septe del 40 previemente mal stabilisate patientes monstrava bon o adequate stabilisation sub le conditiones del therapia combinate, lo que representa un salvamento de 68 pro cento. Dece del patientes monstrava un stabilisation non satisfacente e esseva transferite a insulina. Le combinate therapia esseva interrumpite in 3 patientes a causa de signos de intolerantia, sed chimicamente illes esseva ben stabilisate. Usque al tempore del presente reporto, nulle disfallimento secundari ha occurrite. Quando usate in un therapia combinate, chlorpropamido e phenformina pote reducer le risco potential de toxicitate e/o de adverse effectos secundari, proque plus micre doses del un e del altere resulta in un plus grande efficacia therapeutic.

Paganelli, V. H., e Galindo, J.: Sanguination vaginal, secundari a un spontanee e complete ruptura de vasos umbilical o placental, New York State J. Med. **62:** 342 (1 de feb.) 1962.

Sanguination vaginal in un stadio avantiate del pregnantia non es necessarimente e in omne casos de origine materne. Illo pote esser de provenientia fetal, i.e., illo pote esser le resultato de vasos previe o de un complete e spontanee ruptura de vasos umbilical o placental. Il existe in le litteratura solmente 36 reportos de casos de ruptura partial del vasos umbilical e placental e 12 de casos de ruptura complete. Tamen, viste le facto que insertion velamentose ha un incidentia de 1 pro cento e que isto es associate in quasi omne casos con vasos previe, un plus alte incidentia de vasos previe e del complete abruption de vasos umbilical debe esser suspicite. Le ruptura del vasos umbilical o placental pote occurrer in le presentia de vasos que es histologicamente normal o anormal. Le complete ruptura del vasos umbilical o placental occurrente post le rupturation del membranas amniotic resulta in indolor sanguination vaginal ante le declaration del labores o durante le prime o secunde stadio de illos. Usualmente isto non es associate con ulle significative alteration del materne signos vital, sed illo es associate con signos de un rapidemente crescente angustia del parte del feto. Le presentia, in le sanguine vaginal, de grande numeros de erythrocytos fetal pote servir a identificar le origine fetal del sanguination. Si, in le presentia del supra-mentionate constatationes clinic, le neonato vive sed es extrememente pallide e flaccide e sin respiration o con un respiration pauco profunde, alora—providite que nulle problema de factor Rh existe cognoscitemente in le caso—le diagnose de un choc de hemorrhagia fetal deberea esser considerate immediatemente. Le autores suggere que un frottis de sanguine vaginal debe esser obtenite durante le labores. Le presentia de nucleate erythrocytos fetal in relativemente grande quantitates in le frottis signala le necessitate de prestar prompte attention al feto al momento del parturition. Consultation es indicate pro determinar si o non un section cesaree es necessari. Si hemorrhagia fetal ha de facto occurrite, un prompte transfusion es essential.

Henley, J., e Kritchman, M.: Total blocage sympathic como adjuncto al anesthesia, New York State J. Med. **62:** 348 (1 de feb.) 1962.

Jam le prime experientias monstrava que un prolongate anesthesia, del typo requirite per radical interventiones chirurgic, non es ben tolerate per patientes fortemente compromittite. Le perdita de sanguine esseva frequentemente considerabile, e le circulation remaneva inadequate in despecto de un rapide transfusion de reimplaciamento. Il ha essite monstrate que hypothermia e vasodilatation es solutiones possibile de iste problema. Le autores reporta 125 casos in que un total blocage sympathic esseva producite: 79 con total analgesia epidural, 4 con analgesia alti-spinal, 20 con hexamethonium (Bistrium), e 12 con camphorosulfonato de trimethaphan (Arfonad). Le blocage esseva effectuate per medio de un catheter placiate in le spatio epidural. Quasi omne le patientes habeva al minus un serie condition medical ante le operation. In 38, un condition cardiac esseva presente. In le majoritate del casos il se tractava de interventiones radical pro cancere. In 27 casos, le operation durava octo horas o plus. Illo durava tres horas o minus in solmente 8. Le etate de 44 del patientes esseva plus que septanta annos. Con le uso del technica epidural, il non esseva difficile reducer le pression de sanguine per injicer un sufficiente quantitate del solution anesthetic. Le patiente esseva positionate de maniera que le gravitate promoveva le distribution del droga. Il occurreva nulle adhesiones epidural. Le resultatos clinic esseva satisfacente. Post le operation, hemoglobina, hematocrite, tension de sanguine, e rendimento urinari esseva al nivellos pre-operatori in despecto del magnitude del intervention chirurgic e del etate e condition del patientes. Total blocage sympathic, producite per analgesia epidural como adjuncto al anesthesia, ha rendite possibile leve anesthesia con excellente relaxation, minime perdita de sanguine, facile effectuation de hypothermia, absentia de choc, e le opportunitate de surveliar alterationes in le volumine de sanguine per observar le tension del sanguine. Il pare probabile que le methodo es etiam applicabile a studios additional del physiologia cardiovascular.

Sagi, E. S., Mackenzie, L. L., e Adler, M. P.: Le technica del test de Sagi, New York State J. Med. **62:** 369 (1 de feb.) 1962.

Esseva effectuate meliorationes e standardisationes additional in le technica de un test pro conditiones de malignitate le qual permitte le differentiation de seros sanguinee a base de lor configurationes in contacto con varie concentrationes de solution de phenol que es identificate como nivellos 1 a 5. Un technica quantitative esseva disveloppate. Le specimen de sanguine es obtenite in le periodo post-absorptive. Un standard de controlo es usate con omne incognito. Un guttetta de sero negative forma quasi immediatemente un globulo le qual, post circa cinque minutas, comencia contraher se pro disparer gradualmente. Un guttetta de sero positive se expande tosto o mesmo immediatemente, o illo se applatta in un tenue pellicula o se disintegra plus o minus completemente intra un breve periodo de tempore. Seros con comportamento negative al nivello 1 es eliminate e designate definitivemente como negative. Seros con comportamento positive al nivello 1 es testate al altere nivellos in le mesme maniera. Si le sero es positive solmente al nivello 1, illo es designate como "1 plus." Si illo es positive a omne le nivellos, illo es "5 plus." In un serie de 4.000 seros ab un clinica pro le detection de cancere, omnes esseva obtenite durante le periodo absorptive. In 1.800 de istos (que esesva nubilose), 402 habeva un test positive. Octanta del 402 esseva repetite "a stomacho jejun." Decesex persisteva positive, 64 deveniva negative. Studios additional del fractiones lipidic es in progresso. Il non es cognoscite si le grado de positivitate in iste test es correlationate con le stadio clinic del morbo, sed un correlation definite esseva constatate inter le grado de positivitate del test e le duration de gestation.

Milner, W. A., Garlick, W. B., Spakowski, W., e Charron, J.: Ectopia ureteral sin incontinentia in renes reduplicate, New York State J. Med. **62:** 373 (1 de feb.) 1962.

Le plus frequente signo de ectopia ureteral es intermittente incontinentia urinari in despecto de un micturition normal. Usualmente un infection es etiam presente e augmenta le difficultate del patiente. In le absentia de incontinentia urinari, iste morbo non es recognoscibile a base del tableau clinic sol. Un ureter ectopic pote esser asymptomatic si illo non es complicate per un infection. Le diagnose resulta de un studio roentgenologic, del typo requestate pro inexplicate e persistente infectiones urinari o como parte de un examine pro vage dolores abdominal. Le establimento definitive del diagnose require le identification del ectopic orificio ureteral, lo que pote esser rendite plus facile per le injection intravenose de carmino indigo. Repetite examines es usualmente necessari. Duo casos de ureter ectopic sin incontinentia in renes reduplicate es presentate. Plus attention prestate al potentialitate de iste condition resultarea in plus frequente diagnoses de illo. Le tractamento debe esser specific a base del constatationes individual. Isto es illustrate per le distincte methodos chirurgic usate in le un e le altere del casos hic presentate.

Goldman, H. B.: Hypoadrenocorticismo e tractamento endocrinologic de morbo de Meniere, New York State J. Med. **62:** 377 (1 de feb.) 1962.

Hypoadrenocorticismo existe in le population general a grados non previemente recognoscite. Individuos con iste condition reage mal a stress a causa de lor imbalancia o manco hormonal. Le morbo pote esser presente per hereditage o illo pote esser acquirite in consequentia de therapia a cortisona o de stresses repetitive. Patientes con hypoadrenocorticismo per hereditage ha multe characteristicas in commun. Le diagnose es possibile a base de un detaliate studio del antecedentes endocrinologic, insimul con le datos ab le examine physic. Le test del tolerantia pro glucosa a quatro horas es le plus importante test de laboratorio pro hypoadrenocorticismo. Secundo le opinion del autor, morbo de Meniere es un localisate reaction vasomotori a un serie general de influentias externe afficiente un corpore predisponite per un reactivitate anormal del systema nervose au-

tonome. Le factor principal in iste anormalitate es hypoadrenocorticismo. In un serie de 75 casos tractate per le autor, 90 pro cento monstrava un bon responsa al uso de un complete extracto adrenocorticale de altere formas de therapia glandular. Es sublineate le importantia de evitar stress e de regular le dieta. Therapia adrenocortical resulta in le reparo del systema capillari e le resorption del transsudato. Illo reduce le tendentia angiospasmodic. Inter le tres major symptomas, vertigine es meliorate marcatemente in inter duo e quatro septimanas; tinnito es alleviate post duo a tres menses; le perdita del audita se meliora multo plus gradualmente o non del toto. Il existe nulle contraindicationes contra le uso de un complete, physiologicamente equilibrate extracto adrenocortical in dosages de inter 1 e 100 cm^3.

Medical News

Essay contest on geriatrics

The National Geriatrics Society announces its first annual essay contest on the subject "Institutional Care of the Aged." Deadline for entries is March 15.

All papers are to be judged anonymously. Identification numbers may be obtained from: Joseph B. Enos, M.D., President, National Geriatrics Society, P.O. Box 2605, Niles, California. Completed typewritten manuscripts should be sent to the same address.

The awards are as follows: First prize, $500; second prize, $300; third prize, $200; and fourth, fifth, and sixth prizes, $100 each.

Utica to get rehabilitation center

Herman E. Hilleboe, M.D., Commissioner, New York State Department of Health, has announced the establishment of a secondary rehabilitation center at the Children's Hospital Home of Utica.

The center is the fourth in a Statewide program which calls for a network of 12 primary centers affiliated with medical schools and teaching hospitals and 15 secondary rehabilitation centers. Under the terms of an agreement between the Hospital and the State Health Department, the rehabilitation center will receive up to $35,000 a year in support of any deficit resulting from the operation of its outpatient services.

Survey on blood serum cholesterol

Announcement has been made of a national blood serum cholesterol survey to be conducted by the College of American Pathologists.

The measurement of serum cholesterol as presently practiced is considered unsatisfactory because of wide variations in results. This variability is attributable to the use of diverse methods and to the unavailability of an acceptable universal standard.

It is the purpose of the Standards Committee of the College of American Pathologists to characterize a best cholesterol standard for universal use and to recommend an analytical procedure which may serve as a consistent point of reference.

For information write to: Cholesterol Survey, College of American Pathologists, Prudential Plaza, Chicago 1, Illinois.

Seminars on thoracic diseases

The Mount Sinai Hospital, Fifth Avenue and 100th Street, New York City, announces its schedule for its Thursday afternoon seminars on "Current Status of Thoracic Diseases" to be held in Room 3B of the Administration Building from 4:00 to 5:00 P.M.

February 8—"Therapy of Chronic Bronchitis and Emphysema," Mortimer E. Bader, M.D., and Richard A. Bader, M.D.; and "Bullous Disease and Pneumothorax," Paul A. Kirschner, M.D.

February 15—"Therapy of Allergic Asthma," and "Fibrinous Bronchitis," Sheppard Siegel, M.D.

March 1—"Pulmonary Suppuration: Medical and Surgical Aspects," Oscar H. Friedman, M.D., and Gabriel Seley, M.D.

March 8—"Pulmonary Infarction: Pneumonoconiosis," Irving J. Selikoff, M.D.

March 15—"Disseminated Lung Disease, Including Sarcoidosis," Alvin S. Teirstein, M.D., and Louis E. Siltzbach, M.D.

New medical library center

Howard Reid Craig, M.D., New York City, president of The Medical Library Center of New York and director of The New York Academy of Medicine, has announced that an eight-story garage and loft building on East 102nd Street has been purchased to house a new medical library center which will serve medical schools and research institutions in the New York City area.

Grants from the Avalon Foundation, The Commonwealth Fund, The John and Mary R. Markle Foundation, the James Foundation of New York, and the New York City Health Research Council provided the initial financing for the new center.

Treatment of narcotics addicts

A 20-bed unit for the treatment and rehabilitation of narcotics addicts opened at Utica State Hospital, Utica, in December.

The unit, which will provide immediate treatment and long-term rehabilitation, will serve the Upstate area. Admissions will be on both a voluntary and court referred basis.

The unit was established under the direction of Martin Lazar, M.D., director of Utica State Hospital. Heinz G. Cohn, M.D., supervising psychiatrist at the Hospital, is psychiatrist in charge of the facility. The staff includes a head nurse, an occupational therapist, a recreation therapist, and 16 attendants. The ward staffing ratio will be one employe per patient.

Postgraduate course in Philadelphia

The Philadelphia County Medical Society will hold its twenty-sixth annual postgraduate institute at the Bellevue-Stratford Hotel, Philadelphia, March 13 through 16. Edward Annis, M.D., Miami, Florida, representing the American Medical Association, will be the featured speaker on March 15.

For information write to: Malcolm W. Miller, M.D., 301 South 21st Street, Philadelphia 3, Pennsylvania.

Personalities

Speakers. Horace E. Ayers, M.D., New York City, before the Society of Medical Jurisprudence on the subject "Symphy Siotomy—What Is It?" . . . Marie Pichel Warner, M.D., New York City, before the Pacific Coast Fertility Society, Palm Springs, California, on the subject "The Question of Postmaturity-Length of Gestation after Donor Artificial Insemination" . . . Harold Rifkin, M.D., New York City, at the ninth symposium of the Clinical Society of the New York Diabetes Association . . . Howard A. Rusk, M.D., New York City, at a dinner given by the Lotus Club in honor of Mrs. Albert D. Lasker.

Elected. Martin G. Goldner, M.D., Brooklyn, as president of The New York Diabetes Association.

Awarded. Alexander Schiff, M.D., New York City, The James J. Walker Memorial Trophy, by the Boxing Writers Association of New York.

Retired. Arthur G. Rodgers, Jr., M.D., Syracuse, as director of Syracuse State School after forty-two years of State service.

Appointed. Herbert G. Cave, M.D., Mount Vernon, as director of anesthesiology at Harlem Hospital . . . Richard B. Hadley, M.D., Rye, to the membership committee, and Norman E. Johnson, M.D., Syracuse, to the research committee of the American Rhinologic Society . . . William T. Lhamon, M.D., Houston, Texas, as psychiatrist-in-chief of the New York Hospital, as head of the Payne Whitney Psychiatric Clinic, and as professor and chairman of the Department of Psychiatry of Cornell University Medical College . . . Jerome M. Schneck, M.D., New York City, as a contributing editor in psychiatry on the staff of *Psychosomatics*, organ of the Academy of Psychosomatic Medicine . . . Jacob Schneider, M.D., Thiells, as director of Syracuse State School . . . Martin Symonds, M.D., Brooklyn, as honorary police surgeon of the New York City Police Department . . . Ray E. Trussell, M.D., New York City, re-appointed as Commissioner of Hospitals in New York City.

Books Reviewed

Atlas of Obstetric Technic. By J. Robert Willson, M.D. De luxe edition. Quarto of 304 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $14.50.

This is an excellent atlas with clear detailed illustrations of the standard obstetric procedures. The text has been kept to a minimum, and the illustrations supply most of the necessary information.

The Braxton Hicks version might better have been excluded along with the Vorhees bag for the induction of labor. Both procedures are outmoded and dangerous.

This book can be highly recommended to anyone concerned with obstetrics.—Robert E. Gordon, M.D.

Clinical Cardiopulmonary Physiology. Second edition, revised and enlarged. Sponsored by The American College of Chest Physicians. Burgess L. Gordon, M.D., editor-in-chief. Quarto of 1,001 pages, illustrated. New York, Grune & Stratton, 1960. Cloth, $28.50.

This enormous volume (63 chapters, 1,013 pages) has been compiled under the sponsorship of the American College of Chest Physicians. This second edition has been much expanded and is an up-to-date panorama of cardiac and pulmonary physiology and their clinical application.

The first three sections are devoted to cardiovascular physiology; the fourth is on associated functions of the heart and lungs; next are two on pulmonary physiology, three on restrictive and obstructive diseases of the chest, one on the physiologic therapy of pulmonary diseases, one on the diseases of the mediastinum, and a final section on the relation of special environmental influences to cardiopulmonary physiology.

The editorial board headed by Burgess Gordon, M.D., has achieved its aims admirably, and almost all the chapters are very fine. The pulmonary sections are somewhat better than the cardiac ones although note should be taken of the admirable chapters by Sampson on coronary disease and by Bellet on cardiac arrhythmias.—Milton Plotz, M.D.

Surgical Diseases of the Pancreas. By John M. Howard, M.D., and George L. Jordan, Jr., M.D. Quarto of 607 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1960. Cloth, $20.

The authors enlisted the aid of other equally qualified surgeons interested in this subject to concentrate a collective review of current experiences and contributions in diseases of the pancreas.

From a most complete collection of cases, the authors present a concept of the natural course of pancreatitis classified into three distinct entities, namely: gallstone pancreatitis, alcoholic pancreatitis, and postoperative pancreatitis; they point out the different treatment of each. Considerable evidence is presented which casts doubt on old theories of obstruction and reflux in the causation of these diseases.

Physiology, laboratory diagnosis, chronic pancreatitis, cysts, benign and malignant tumors of the pancreas and para-ampullary region, complications, and operative technic are amply documented and discussed.

An unusual bibliography is the rule, as, for example, 78 cases of annular pancreas are reported and 49 ulcerogenous islet cell tumors to 1958. Over 1,000 cases of pancreatitis in 32 hospitals were studied for the presence of gallstones. In 15 hospitals 1,350 patients with pancreatitis were studied to determine an incidence of 26 per cent of alcoholic pancreatitis.

The importance of combined clinical and laboratory findings in diagnosis is stressed. The drawing of blood in the emergency room for amylase studies, refrigerating it until the morning, is advised as the use of opiates for pain and other factors may increase the serum amylase.

The accumulation of current knowledge offered by this book can be recommended to be of great value to all students and clinicians seeking such information.—Ward V. Ceilly, M.D.

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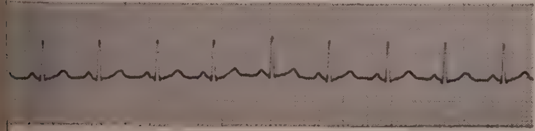

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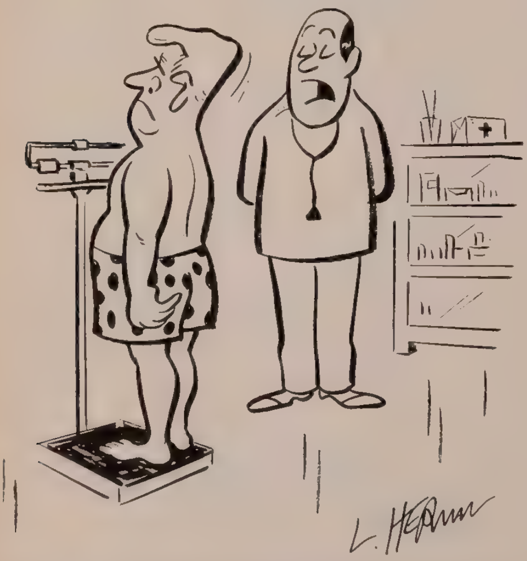

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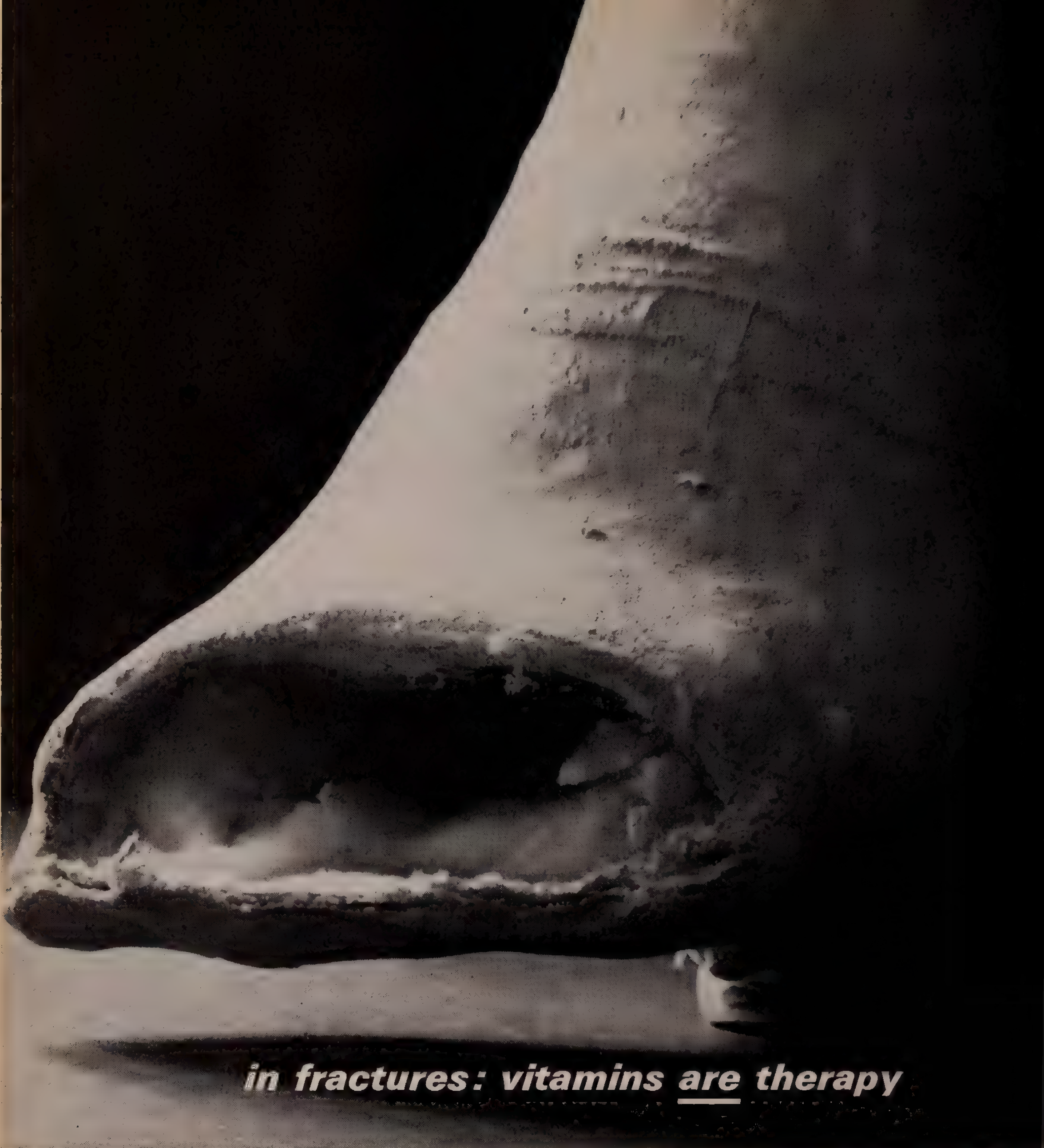

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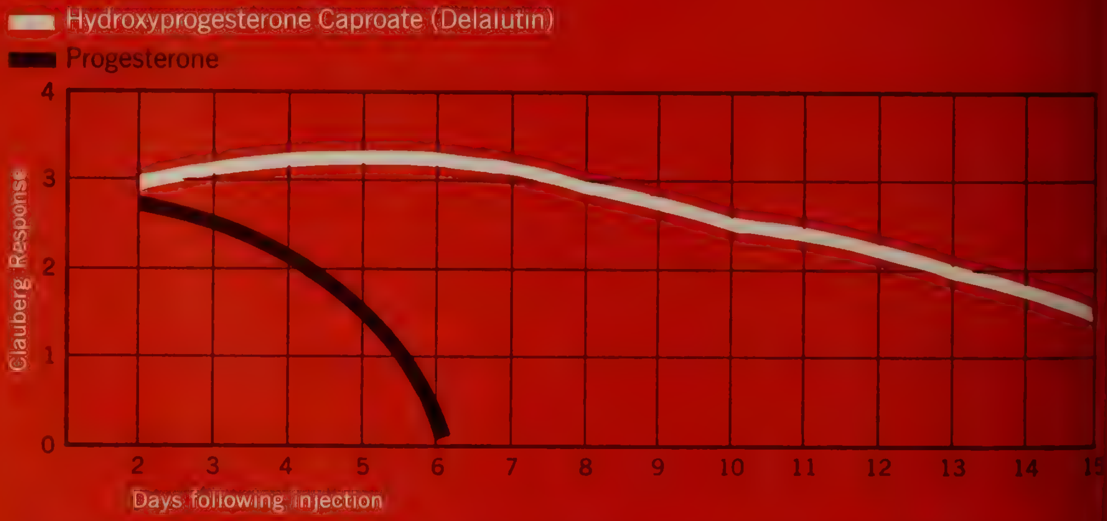

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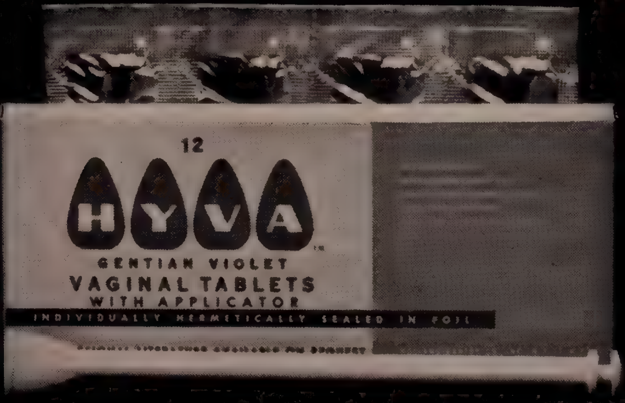
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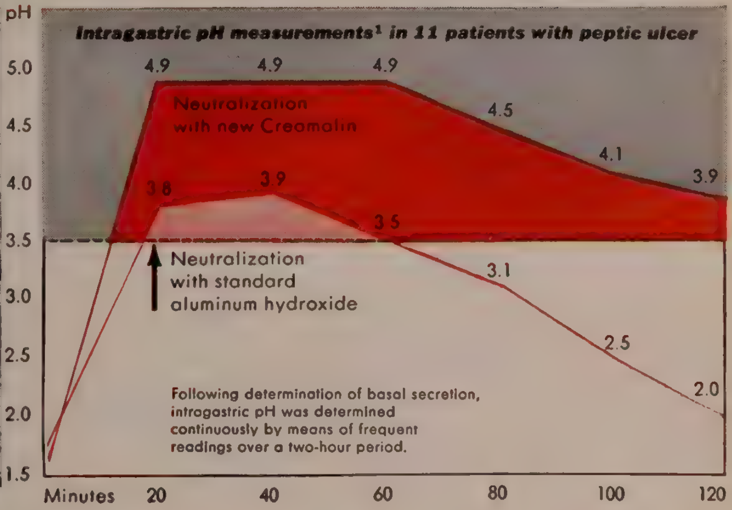
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4.0
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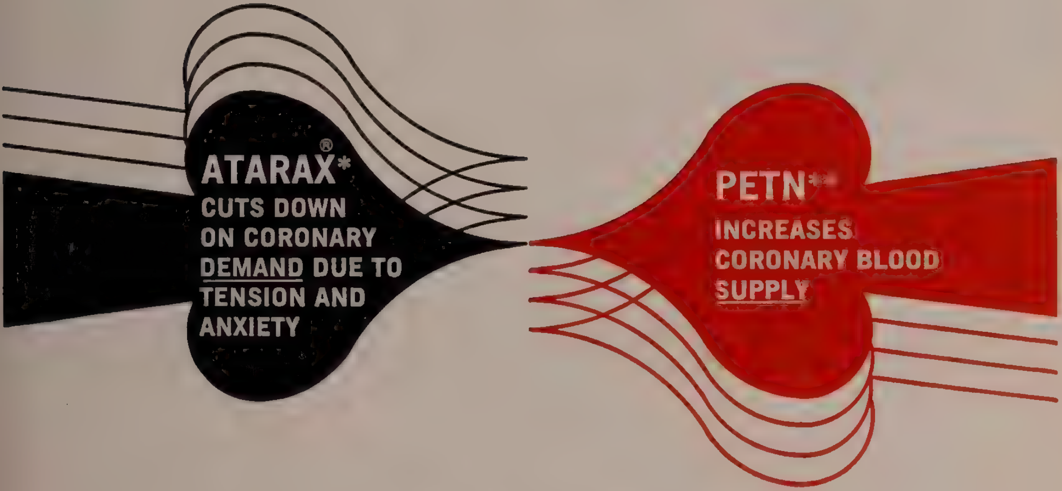
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1. Berger, R.A., Clinical Medicine, Sept. 1961.

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CLINICAL & PHARMACOLOGICAL REPORTS. 1. Berger, F. M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W-583), Fed. Proc. *20*:113 (March) 1961. **2.** Diamond, S., and Schwartz, M., Scientific Exhibit at Ill. State Med. Soc., Chicago, (May) 1961. **3.** Douglas, J. F., Ludwig, B. J., Ginsberg, T., and Berger, F. M.: Studies on W-583 Metabolism. Fed. Proc. *20*:113 (March) 1961. **4.** Duarte, C., Brest, A. N., Kodama, R., Naso, F., and Moyer, J. H.: Observations on the Antihypertensive Effectiveness of a New Propanediol Dicarbamate (W-583). Curr. Ther. Res. *2*:148-52 (May) 1960. **5.** DuChez, J. W., Scientific Exhibit at AMA, New York, (June) 1961. **6.** Holloman, J. L. S., Jr.: Treatment of Hypertensive Patients with Mebutamate, a New Antihypertensive Drug—a Preliminary Report. J. of Nat. Med. Assoc. in Press. 1961. **7.** Kletzkin, M., and Berger, F. M.: A Centrally Acting Antipressor Agent. Fed. Proc. *20*:113 (March) 1961.**8.** Leslie, C. H.: The Efficacy of Mebutamate, a New Antihypertensive Drug, in the Treatment of Refractory Geriatric Hypertensive Patients—a Preliminary Report. J. Am. Geriatric Soc. 1961 in press. **9.** Mulinos, M. G., Scientific Exhibit at Amer. Coll Card. New York, (May) 1961. **10.** Mulinos, M. G., Saltefors, S., Boyd, L. J., and Cronk, G. A.: Human Pharmacology Studies with W-583, Fed. Proc. *20*:113 (March) 1961. **11.** Shubin, H., Scientific Exhibit, Amer. Coll. Card. New York, (May) 1961. **12.** Turek, L. H.: Clinical Evaluation of Mebutamate, an Antihypertensive Agent: Preliminary Report: Clin. Med. *8:7* (July) 1961.

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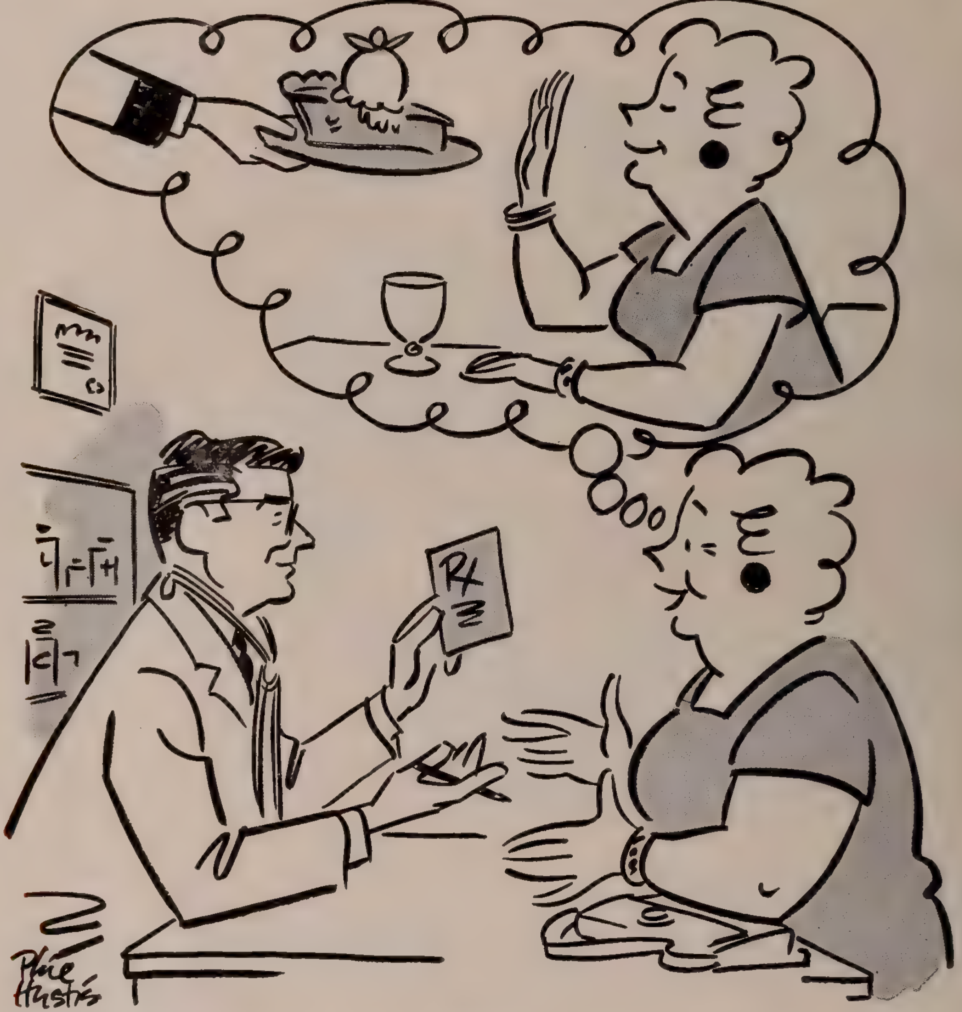

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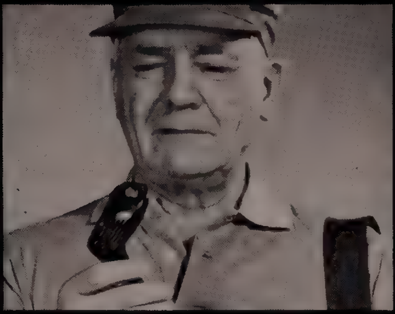

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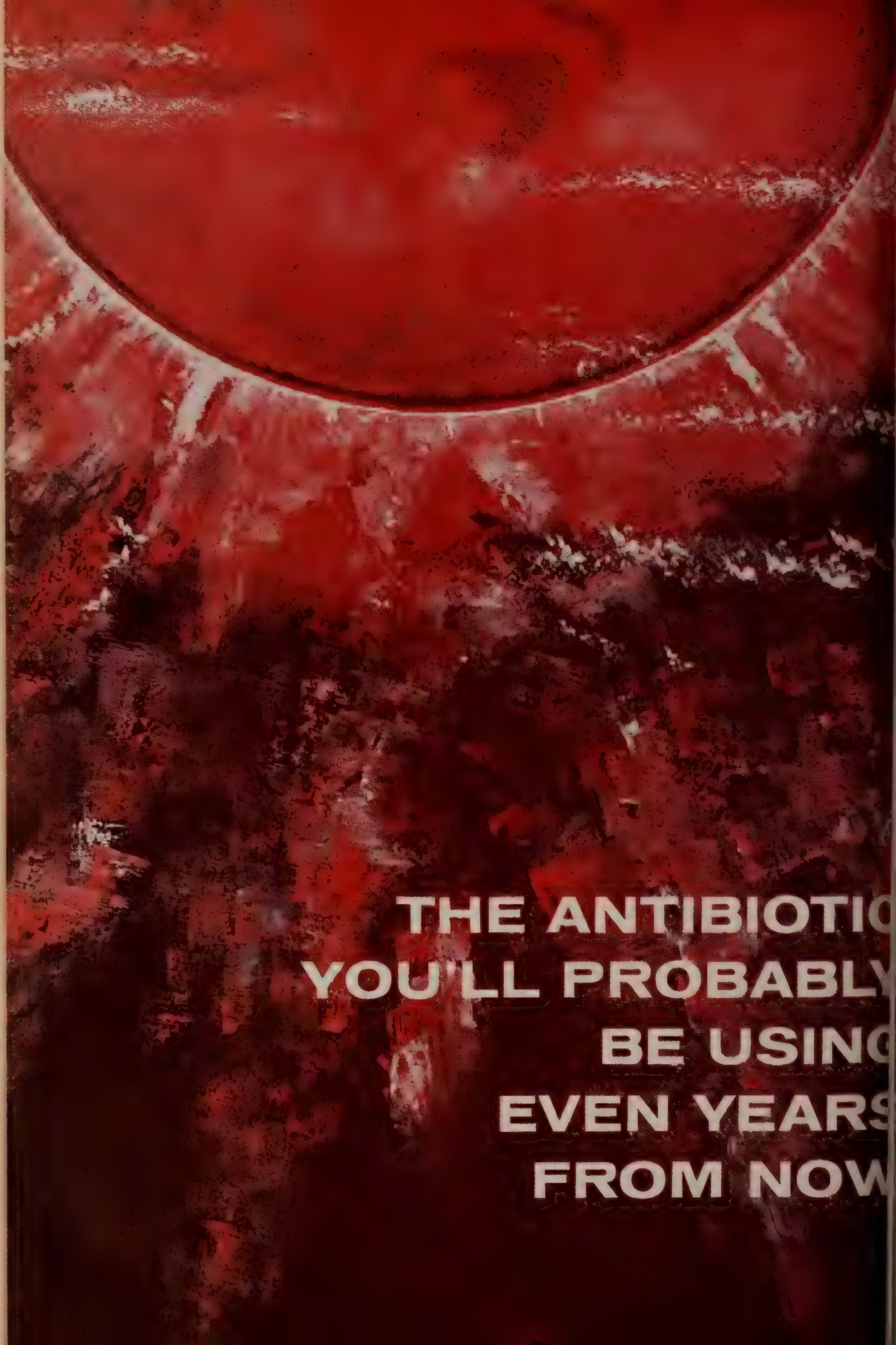
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References: 1. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy 5:527 (Aug.) 1958.

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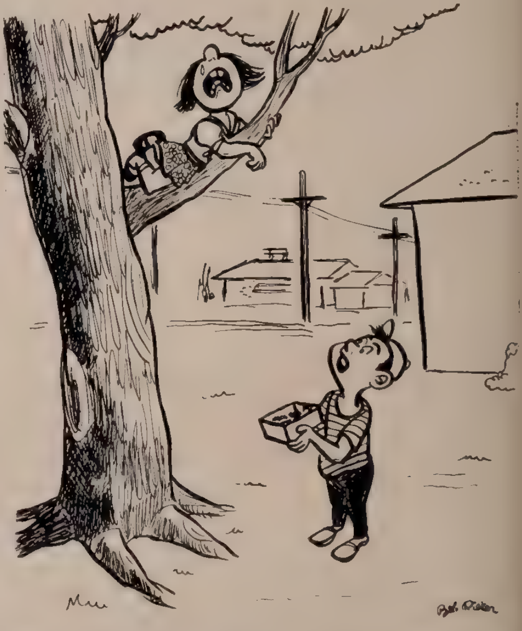

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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GENERAL SESSIONS SCHEDULE

Every Afternoon
Monday Through Friday

MONDAY, MAY 14

1:00–3:00	Albany Medical College of Union University
3:00–5:00	Albert Einstein College of Medicine of Yeshiva University

TUESDAY, MAY 15

1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

FRIDAY, MAY 18

1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
3:30–5:00	New York Medical College

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References: 1. Franko, B.V., and Lunsford, C. D.: "Derivatives of 3-Pyrrolidinols-III. The Chemistry, Pharmacology, and Toxicology of some N-substituted-3-Pyrrolidyl α-substituted Phenylacetates," J. Med. Pharmaceut. Chem. 2:523, 1960. 2. Clinical reports from 42 investigators on file in the Medical Dept., A. H. Robins Co., Mar. 1961. 3. Moeller, H. C.: "Physiological Effect and Clinical Evaluation of Glycopyrrolate in Peptic Ulcer Disease," presented at the N.Y. Acad. Sc., Oct., 1961. 4. Breidenbach, W. C.: investigative clinical report, March 1961.

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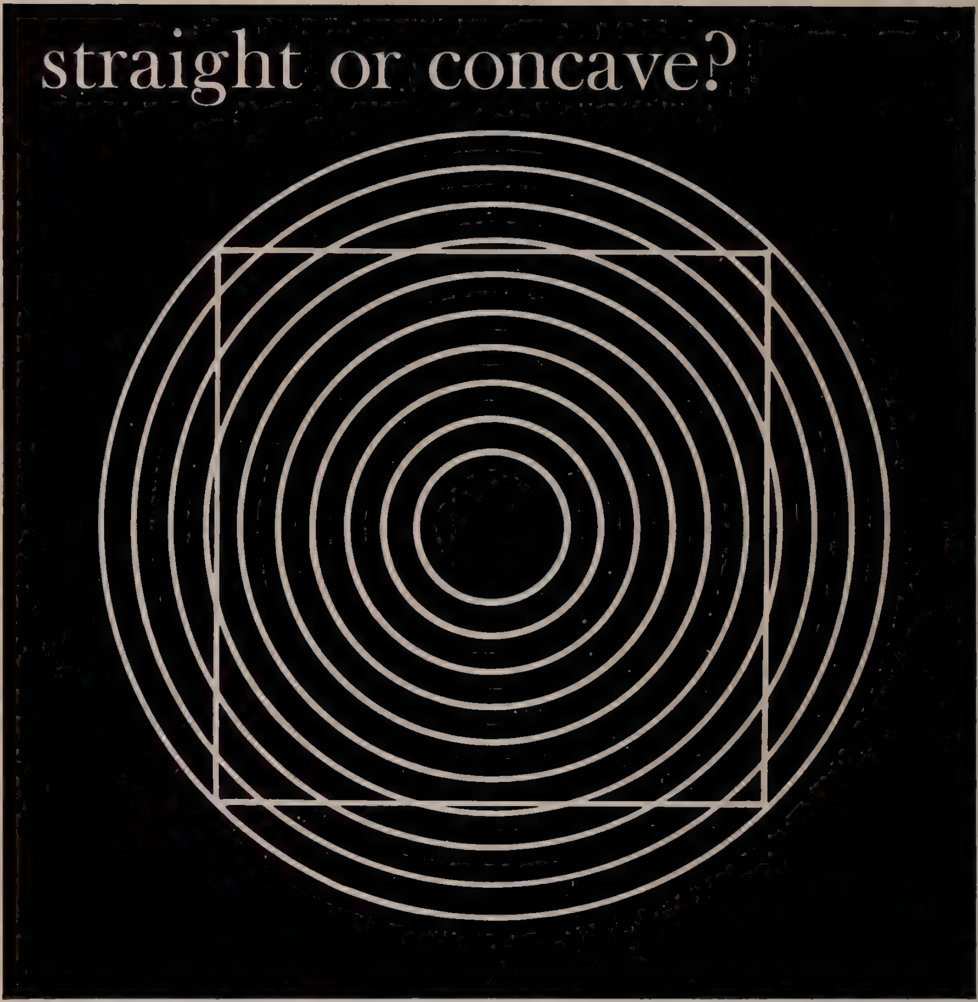
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1. Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.

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February 15, 1962 Volume 62 Number 4

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Editorials

Highlights of State Health Commissioner's Report for 1961

The important developments during this year were in the fields of chronic disease, rehabilitation, and environmental health. The problems of ionizing radiation and lung cancer came to the fore. For the first time lung cancer has become the most common site of malignant disease reported in men in Upstate New York. Since 1943, the incidence rate of lung cancer in men has risen from 12.09 to 46.46 cases per hundred thousand male population. Highly qualified research clearly indicates that lung cancer occurs much more frequently in persons who smoke cigarets than among nonsmokers.

The State of New York Department of Health has one of the finest radiation-surveillance programs in the nation. Modern equipment enables the prompt detection of increases in radioactivity. The results of recent Russian detonations are being followed closely as to effects on milk, water, air, and marine life, and if levels reach a critical point we will know of it at once.

During the past ten years much effort has gone into teaching lay persons the principles of emergency first aid. More than 500,000 people have received information on this, and some 112,000 have been graduated from formal training courses.

In regard to air pollution, Statewide laws to prevent air pollution from new sources have been adopted, and testing has been started on a crankcase-ventilating device which should reduce noxious fumes from motor vehicles by approximately 30 per cent.

Three rehabilitation centers were established during the year which eventually will develop into a network of 12 primary centers affiliated with medical schools and teaching hospitals and 15 associate centers. Primary centers have been established at the Albany Medical Center Hospital and the Hospital of the Good Shepherd (Syracuse University), and an associated center has been established at the Sunnyview Orthopedic and Rehabilitation Center in Schenectady.

There was one outbreak of poliomyelitis in the Syracuse area last August which resulted in 80 cases of paralytic poliomyelitis. Through the combined efforts of health departments, private physicians, nurses, hospitals, and many volunteers, approximately 400,000 persons in the area received Type 1 oral vaccine. This experience points up the fact that poliomyelitis continues to be a health problem and that efforts must continue to vaccinate everyone possible with Salk vaccine. This vaccine is the only one available at the present time which immunizes against all three types of virus.

Fruitful research goes forward at Roswell Park Memorial Institute regarding a possible link between viruses and cancer. At present four new drugs are under study, and a new method for analyzing the hereditary material in the human cell has been developed.

The problem of bat rabies in the State was reported during the summer when several persons were bitten by bats. The State Health Department provides rabies diagnostic facilities, consultation, and advisory services to the physicians faced with this problem. Because healthy bats can carry the rabies virus the State Health Department considers all bats that have bitten persons to be rabid until laboratory tests have shown they are not.

Stricter rules to control the sale of narcotics and safeguard such supplies have been instituted, and all nursing homes which handle narcotics prescribed for patients are required to register and be licensed for this service by the State Health Department.

During the year the form of the birth certificate has been changed so that information in regard to racial or ethnic group is so placed that it cannot be reproduced in the issuing of copies by registrars of vital statistics.

The annual report of the State Health Commissioner, Herman E. Hilleboe, M.D., is a source of great satisfaction because it so clearly indicates that medical knowledge and skill are being used to the full in the public interest.

The public's responsibility in emergency medical service

A recent survey of the experience of the Emergency Medical Service of the Medical Society of the County of Monroe reveals some pertinent facts regarding public attitudes.

The survey covered the first four months of operation of the Emergency Medical Service plan—September, October, November, and December of 1960—and September, 1961, which was used as a check month.

Of 592 calls routed to the Emergency Medical Service during the five-month survey period, the survey showed that 85, or 1 call in 7, was a serious enough emergency to require hospitalization of a patient who contacted the service.

Of 592 calls recorded during the five-month survey period, 286 patients recorded that they had no family doctor. Another 110 of the 592, or 18 per cent more, were from patients who had made no effort to reach their family doctor before calling the Emergency Medical Service. Only 8 per cent of the recorded calls during the survey period—46 out of 592—were from patients who had tried but were unable to reach their family doctor and then called the Emergency Service.

The following guide lines were laid down to define a real emergency: "It is a true emergency if: (1) there is bleeding that won't stop; (2) there is any interference with breathing; (3) there is a convulsive seizure; (4) there is acute pain; (5) there is sudden unconsciousness without quick recovery; (6) there is high temperature with no apparent reason; (7) there is severe coughing."

Abuses of the system disclosed the following:

1. Patients calling while under the influence of alcohol who, while not actually experiencing a medical emergency, force the system to check to make sure of this fact.
2. Failure of parents to instruct baby-sitters adequately in the procedure for contacting the family doctor in the event of a medical emergency with children; also instances in which parents leave seriously ill children with a baby-sitter when the child actually should be under the watchful eye of the parent or family doctor.
3. Patients who have a family doctor but who, for a variety of personal reasons, do not care to call him. In this category come the patients who think their family doctor will not respond to a call because he is aware that their ailment is not a medical emergency.
4. Patients who have a family doctor but who simply do not try to contact him but instead call the Emergency Medical Service, often for routine advice and/or treatment for a problem that does not constitute a medical emergency.

It was stated that: "The conclusion is inescapable from this survey that if people will establish a family doctor relationship, not only their routine normal medical problems but also the emergency situations will be handled better to their satisfaction and well-being and to the benefit of the overall health picture of the community."

Older citizens whose family doctor has retired or died should establish a new relationship with a doctor; likewise newcomers to a community should provide such a relationship.

In regard to emergencies arising among children, baby-sitters should be clearly briefed, preferably in writing, as to where the parent and the family doctor can be reached.

The Medical Society of the County of Monroe is to be congratulated on this survey and the manner in which they have conveyed the facts to the public through the local press—a commendable public service that undoubtedly will save lives.

The day is here

"The night is far spent, the day is at hand." This couplet from the twelfth verse of the thirteenth chapter of *Romans* expresses the feeling and sense of urgency present in the important address of Leonard W. Larson, M.D., President of the American Medical Association, to the House of Delegates at Denver on November 27, 1961.

It is our privilege to present that address in this issue of the JOURNAL. Anyone who feels uninformed on the aims and policies of the American Medical Association in the field of politics, government, and legislation will be completely briefed by reading this.

The program is a positive one. It tells what we are for and why we are for it. Only the alert and informed individual will be able to follow and influence the great upcoming debate in Congress on the extension of the Social Security system into the practice of medicine. We urge you to ponder Dr. Larson's words.

The welfare bite

How much of our income do we really spend for welfare in New York State? An answer to this question was given recently by Commissioner Raymond W. Houston. By comparing figures of income and welfare expenditure for a deep depression year (1936) and two subsequent years ten years apart (1950 and 1960) it appears that the line is being held and that there has been no over-all increase in the ratio of welfare cost to total income.

Despite the gradual decrease in the value of the dollar over this period, the steadily increasing population and steadily rising personal income have made these figures possible. We are fortunate in our highly populous and prosperous State to have the economic base for a progressive welfare program. A progressive welfare program provides for human needs but goes further and studies the reasons for these needs and develops methods to correct them. This requires highly trained staff, skilled by experience. In this State public welfare is not a holding operation; it is a salvage operation and well worth its cost.

	1936	1950	1960
Population New York State	13,145,000	14,914,000	16,857,000
Number of recipients	2,432,219	518,552	512,691
Per cent of population	18.5	3.48	3.04
Total personal income	$10,914,000,000	$28,054,000,000	$48,000,000,000
Relief expenditures (including work relief)	$453,124,000	$236,365,000	$339,057,000
Per cent of personal income	4.15	0.84	0.71

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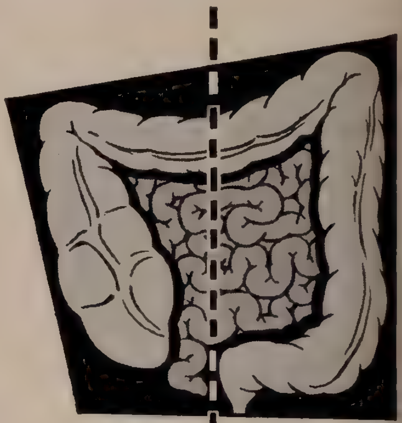

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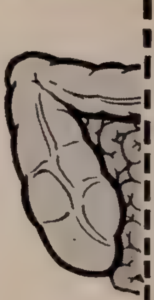

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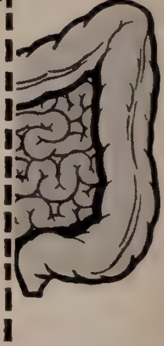

. . . FOR THE OTHER HALF

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Each Modane Tablet contains 75 mg. Danthron (1.8 Dihydroxyanthraquinone) and 25 mg. Calcium Pantothenate. Each Modane Mild Tablet and each teaspoonful Modane Liquid contains 37.5 mg. Danthron and 12.5 mg. Calcium Pantothenate. Dosage — 1 tablet, teaspoonful, or fractional teaspoonful, immediately after the evening meal.

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New York City

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Francis Delafield and Presbyterian Hospitals

EXPERIENCE WITH 50 PERFUSIONS *in 48 patients, all of whom exhibited an advanced stage of cancer, is described. Almost all had undergone unsuccessful conventional therapy. The over-all results were disappointing in terms of prolonged tumor regression or palliation. Of the total series 42 patients were followed long enough to determine accurately the effects of perfusion therapy in terms of tumor response. Of these, 9 (4 genitourinary carcinomas, 1 parotid carcinoma, 1 liposarcoma, and 3 melanomas) demonstrated tumor regression. This was transient in 8 and only "permanent" in 1. However, 9 of 11 patients with intractable pelvic pain were benefited, and where pain was a major factor in tumors of other areas, perfusion achieved similar relief. The 7 complications (1 fatal, 2 serious, and 4 minor) occurred during the first few months of clinical trial when the drug dosages were not firmly established and the methods of vascular isolation were experimental. There are two principal values of perfusion: (1) the possibility of delivering to the area in question concentrations of drug which would be lethal if given systemically; and (2) the symptomatic relief afforded many of the patients. Limitations to perfusion stem from difficulty in achieving adequate vascular isolation in most areas of the body, deficiencies inherent in the drugs themselves, and danger of chemotherapeutic stimulation of tumor growth. Perfusion technics have not been standardized, and there is need for technical improvements, methods to minimize the systemic toxicity of the available chemotherapeutic agents, and a means for long-term exposure of tumor to drug. Tentative criteria for selection of patients for perfusion are proposed.*

THE TREATMENT of advanced localized malignant disease by regional or isolation perfusion technics has received considerable attention during the past two years. Since the orginal provocative report by Creech *et al.* in 1958,[1] relating his preliminary laboratory and clinical experience with perfusion numerous reports have appeared adding to our cumulative knowledge of the role this therapeutic tool may play in the attack on cancer.[2-22]

We are adding our modest experience with clinical perfusion to that which has already been published and are attempting a critical evaluation of existing technics with particular reference to the selection of patients for perfusion. Our volume is not large; to date we have performed 50 perfusions in 48 patients, and the interpretation of the data must perforce be modified by this fact. We have, however, developed certain impressions relative to this modality of treatment which are worthy of report.

Clinical material and technics

Clinical material was drawn from both the Francis Delafield and Presbyterian Hospitals. Virtually all patients exhibited an advanced stage of their cancer; almost

TABLE I. Regional perfusion—tumor types

Tumors	Number of Cases
Carcinoma	
Rectum and sigmoid	6
Cervix (squamous)	3
Vulva (squamous)	1
Anus (muco-epidermoid)	1
Endometrium	1
Urethra	1
Prostate	2
Bladder	1
Lung (metastatic)	2
Parotid	1
Cheek and antrum (squamous)	3
Breast (metastatic)	2
Kidney (metastatic)	1
Groin and iliac fossa (squamous)	1
Sarcoma	
Liposarcoma	1
Fibrosarcoma	1
Fibroxanthoma	1
Melanoma	11
Miscellaneous	
Retinoblastoma	5
Glioblastoma	1
Metastatic carcinoma (? primary)	2
Ewing's tumor	2

TABLE II. Regional perfusion—drugs used

Drug	Number of Perfusions
HN_2*	24
Cyclophosphamide	7
TSPA†	3
Amethopterin**	1
5-FU††	1
Phenylalanine mustard	2
Phenylalanine mustard plus TSPA	9
5-FU plus TSPA	3

* Methyl-bis (B-chloroethyl) amine hydrochloride (nitrogen mustard), supplied through the kindness of Merck Sharp & Dohme, Philadelphia 1, Pennsylvania.

† Triethylene thiophosphoramide (Thio-TEPA)

** 4-amino-$N^{(10)}$ methyl folic acid (methotrexate), generously supplied by Lederle Laboratories Division, American Cyanamid Co., New York City.

†† 5-fluorouracil, supplied through the kindness of Roche Laboratories, Division of Hoffmann-LaRoche, Inc., Nutley 10, New Jersey.

all had undergone unsuccessful conventional therapy in the form of surgery, radiotherapy, or a combination of both, dependent on tumor type. In 3 instances only was perfusion offered the patient as initial therapy; these 3 individuals had malignant melanomas of the lower extremities in which secondary surgical procedures were contemplated. Two additional patients refused amputation, the procedure of choice for their extremity tumors, and were therefore perfused.

The variety of tumor types treated in this series is expressed in Table I. Table II enumerates the drugs used, and the unit dosage in each case is shown in Table III.

Our perfusion technics did not depart significantly from those described initially by Creech *et al.*[1] Extracorporeal perfusion circulation was maintained by two Sigmamotor pumps with an interposed plastic disposable bubble oxygenator.* Bank blood, preserved in anticoagulant acid citrate dextrose solution, was used as the perfusate; warming of this blood initially was accomplished by submerging coiled tubing in a warm bath without monitoring and, more recently, by the use of a Harrison Brown heat exchanger interposed in the arterial line, with the arterial temperature maintained at between 36 to 40 C.

In several instances a venous reservoir was used to control the perfusion rate, but in most cases the perfusion circuit was a closed one. We made no attempt to monitor the perfusion pressure. Flow rates, however, were calculated to effect a pressure somewhat less than the systemic arterial pressure to discourage a "leakage" gradient from the perfused to the general circulation. This leakage factor was determined in a number of cases by the use of chromium-51-tagged red blood cells. The results of this study will be reported elsewhere.

In an effort to protect bone marrow against the toxic action of the chemotherapeutic agents used, autologous bone marrow, removed prior to perfusion in a volume of from 200 to 500 ml. by marrow trochar from the posterior iliac crests and strained through a number 20 needle into a siliconized vessel containing heparin solution, was reinfused intravenously one to three hours after the completion of perfusion. This procedure was reserved for a selected few patients in whom a high leakage factor was anticipated during perfusion and in an additional group of individuals who were receiving systemic chemotherapy.

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*Pulmopaks, Abbott Laboratories, North Chicago, Illinois.

TABLE III. Summary of perfusion cases

Area and Patient	Malignant Tumor	Drug	Unit Dose (Mg. per Kg.)	Maximum White Blood Count Depression (Postoperative Day)	Other Complications	Results
Pelvis						
1	Squamous, cervix	HN_2	0.8	No drop	None	Pain relief. Died 3 months. Massive tumor necrosis at autopsy.
2	Squamous, cervix	HN_2	0.8	2,150 (16)	None	Pain relief. Died 5 months. No apparent tumor response.
3	Squamous, vulva	HN_2	0.8	1,900 (5)	None	Died 3 months. ? Tumor acceleration.
4	Squamous, cervix	HN_2	1.0	3,050 (11)	None	Pain relief for 2 months. Died 6 months of disease.
5	Squamous, groin; iliac fossa	HN_2	0.7	No drop	None	Died 1 month. ? Tumor acceleration.
6	Muco-epidermoid, anus	HN_2	1.0	2,300 (9)	None	Pain relief for 2 weeks only. Died 3 months. No tumor response.
7	Recurrent, rectum	NH_2	0.8	900 (15)	None	No pain relief (drug addiction), or apparent tumor response. Died 8 months of disease.
8	Recurrent, sigmoid	HN_2	0.8	450 (8)	None	Transient softening pelvic mass. Died 15 months of disease.
9	Recurrent, rectum	HN_2	0.8	2,250 (12)	None	Superficial tumor necrosis by biopsy. Died 13 months of disease.
10	Recurrent, sigmoid	HN_2	0.8	No drop	None	Pain relief. Died 11 months.
11	Recurrent, rectosigmoid	HN_2	0.9	1,000 (6)	Passed cast of colonic mucosa via colostomy	Pain relief. Died 4 months of uremia.
12	Recurrent, sigmoid	HN_2	0.8	No drop	None	Died 9 months. No apparent response.
13	Endometrial	5-FU TSPA	15.0 0.6	3,300 (14)	None	No pain relief or tumor response. Died 11 months of disease.
14	Urethra	HN_2	0.8	No drop	None	Pain relief. Slight decrease in size perineal implants. Died 3$^1/_2$ months.
15	Prostate	HN_2	0.8	No drop	None	50 per cent decrease tumor size initially with gradual regrowth. Died 15 months of disease.

Area and Patient	Malignant Tumor	Drug	Unit Dose (Mg. per Kg.)	Maximum White Blood Count Depression (Post-operative Day	Other Complications	Results
16	Prostate	HN_2	0.8	No drop	None	Pain relief for 2 months, 30 per cent decrease tumor size. Gradual regrowth. Alive 19 months post-perfusion.
17	Bladder	HN_2	1.0	1,650 (15)	None	Slight symptomatic relief. Transient 20 per cent decrease in tumor size. Died 2 months.
18	Fibroxanthoma, buttock	HN_2	0.8	2,450 (16)	None	Transient softening of tumor, then rapid growth. Hemipelvectomy.
19	Metastatic melanoma	PAM TSPA	1.2 0.6	200 (13)	None	Immediate softening tumor masses, then rapid growth. Died 4 months of disease.
Brain						
20	Glioblastoma	TSPA	0.5	No drop	None	No apparent response. Died 2 months of disease.
21	Metastatic, (?) primary	TSPA	0.9	No drop	None	Died 8 days of disease.
22	Bronchogenic metastases	TSPA	0.5	No drop	None	Died 6 weeks of disease.
23	Bronchogenic metastases	Cyclophosphamide	35.0	1,100 (10)	Hemorrhage from wound 2 weeks	Started on betatron therapy 3 days post-perfusion. Too recent to evaluate results.
Head and neck						
24	Melanoma, antrum	PAM	0.5	No drop	None	No apparent response. Died 4 months of disease.
25	Parotid	HN_2	0.4	No drop	Aphasia, right hemiparesis, grand mal seizures 24 hours postoperatively	Complete disappearance of visible tumor. Died from pneumonia $2^1/_2$ months post-perfusion.
26	Squamous, cheek	HN_2	0.2	No drop	None	No tumor response. Died 13 months of disease.
27	Squamous, antrum	HN_2	0.3	No drop	None	No apparent tumor response.
28	Squamous, cheek	HN_2	0.3	No drop	None	Died 3 months. No tumor response.
29	Retinoblastoma	Cyclophosphamide	20.0	3,3000 (5)	None	Too recent to evaluate.

Area and Patient	Malignant Tumor	Drug	Unit Dose (Mg. per Kg.)	Maximum White Blood Count Depression (Postoperative Day)	Other Complications	Results
30	Retinoblastoma	Cyclophosphamide	23.0	No drop	None	Too recent to evaluate.
31	Retinoblastoma	Cyclophosphamide	25.0	1,600 (3)	None	Too recent to evaluate.
32	Retinoblastoma	Cyclophosphamide	33.0	No drop	None	No apparent tumor response.
33	Retinoblastoma	Cyclophosphamide	25.0	1,800 (6)	None	No apparent tumor response.
Chest wall						
34	Recurrent melanoma, axilla	PAM TSPA	0.8 0.5	No drop	None	Initial slight decrease in tumor size, then rapid growth. Died 5 months.
35	Recurrent melanomas, axilla	PAM TSPA	1.2 0.8	2,400 (5)	None	Axillary dissection 2 months later. No apparent tumor response.
Extremity						
36	Breast metastases to femur (a)	HN_2	0.75	No drop	None	No x-ray response.
	(b)	5-FU	20.0	No drop	None	Evidence of early callus formation by x-ray film. Died 2 months, following hypophysectomy.
37	Ewing's tumor, leg (a)	Methotrexate	0.6	No drop	None	No response.
	(b)	5-FU TSPA	20.0 1.0	No drop	None	No response.
38	Recurrent melanoma, arm, postexcision	PAM	1.5	No drop	Pain for 2 months, ischemic paralysis of hand (Volkmann type)	No recurrence tumor area. Died of cerebral metastases 12 months.
39	Melanoma, leg	PAM TSPA	1.5 0.8	200 (15)	Died bone marrow depression septicemia	Died 26 days postperfusion. Moderate regression primary tumor and inguinal metastases.
40	Melanoma, leg	PAM TSPA	1.2 0.9	No drop	None	One lesion in thigh quiescent, excised in 10 months. Second lesion of calf disappeared.
41	Metastases, femur	5-FU TSPA	20.0 1.0	No drop	None	Pain relief, but no x-ray evidence of change in tumor. Died 5 weeks.

Area and Patient	Malignant Tumor	Drug	Unit Dose (Mg. per Kg.)	Maximum White Blood Count Depression (Postoperative Day)	Other Complications	Results
42	Melanoma, foot	PAM TSPA	1.2 0.7	No drop	None	Syme amputation 1 month postperfusion. Only slight regression primary tumor. Died metastases 11 months.
43	Recurrent liposarcoma, thigh	HN_2	0.8	No drop	None	Massive necrosis of tumor, with hemorrhage. Completely excised 2 months postperfusion. Died pulmonary metastases 7 months.
44	Metastases, hypernephroma, humerus	Cyclophosphamide	35.0	No drop	Osteoclavicle	Lesion quiescent 10 months.
45	Recurrent melanoma, thigh, postexcision	PAM TSPA	1.2 0.8	3,500 (4)	None	Local recurrence 8 montsh. Scheduled for second perfusion.
46	Fibrosarcoma, thigh	HN_2	0.8	No drop	None	Acceleration of tumor growth. Disarticulation 3 weeks postperfusion.
47	Recurrent melanoma, thigh	PAM TSPA	1.2 0.6	No drop	None	Too recent to evaluate results.
48	Recurrent melanoma, thigh	PAM TSPA	0.9 0.65	250 (11)	None	? Acceleration of tumor growth. Died 7 months.

These data will be dealt with at a later date. Along the same lines, and designed to protect bone marrow, recently we have attempted to provide general hypothermia, by external cooling only, thus creating a significant temperature differential between the tumor-bearing area, perfused with normothermic or hyperthermic blood, and the remainder of the body. The validity of this concept has yet to be evaluated.

Isolation technics have been dictated by the anatomy of the perfused area and have followed closely methods described fully by others. The amount of material to escape from the perfused areas, as measured by Cr^{51}-tagged red blood cells, has approximated that reported by others. Needless to say, complete vascular isolation has been achieved only in extremity perfusions permitting a proximally placed arterial tourniquet; in perfusions of the groin, pelvis, axilla, brain, and neck regions, the monitored leak has been appreciable. This, of course, has imposed limitations on drug type and dosage.

Where possible, serial biopsies of perfused tumors have been obtained in the postoperative period, and in selected cases special staining technics have been employed to determine specific sites of drug action in the cell. A preliminary report of these findings has been published elsewhere.[19]

Results

Table III describes briefly the results of perfusion in each individual case. Attempts to summarize results in a sizable group of cases are often misleading: terms such as "quiescent," "controlled," and so forth are frequently inadequate, and a differentiation between early transient tumor regression and a significant alteration in the course of the disease is not always clearly stated. We have therefore resorted to this more laborious and descriptive form of reporting.

The over-all results are disappointing in terms of prolonged tumor regression or palliation. Of the 19 pelvic perfusion cases, 17 have died from one to fifteen months after the procedure, all from disease progression. The average survival in this group was seven months. The 2 living patients include Case 16, who demonstrated a transient 30 per cent decrease in the size of his prostatic tumor and was still alive nineteen months later, and Case 18, a young man with a malignant fibroxanthoma of the buttock area who underwent hemipelvectomy one month after perfusion and three months later showed signs of recurrent disease. The progress of his malignant condition was not altered. Two patients with recurrent adenocarcinoma of the rectosigmoid showed a transient softening of their tumor masses, with subsequent active growth; all 4 patients with cancer of the genitourinary tract demonstrated from slight to 50 per cent decrease in the size of their tumors. Again, this regression was transient. Brief improvement in Cases 18 and 19 was also noted. In no case, however, can we state with certainty that life has been prolonged significantly.

Of considerable interest, however, has been the pain relief achieved by perfusion in the pelvic cases. Nine of 11 patients who entered operation with severe intractable pelvic or perineal pain demonstrated immediate and dramatic relief of symptoms. This relief was extremely variable in duration, lasting from two weeks to three months. It must be postulated that the mechanism behind this action of HN_2 (nitrogen mustard) is a selective effect on sensory nerve fibers; in no instance did any disturbance in motor function occur. Similar pain relief has been noted in perfused areas other than the pelvis, although the degree and intractability of the pain pattern cannot be compared with that experienced in the pelvic cases.

Little need be said of the brain perfusions. Three of the 4 patients had advanced lesions with profound neurologic changes. No apparent change was noted in any of them following treatment, and autopsy studies failed to reveal any pathologic change which could be attributed to perfusion. The fourth patient (Case 23), with a metastatic bronchogenic carcinoma, received betatron therapy starting three days after perfusion; the results, which are too recent to evaluate accurately, will be impossible to interpret in view of the mixed treatment.

The 3 squamous carcinomas of the head and neck area demonstrated no response to HN_2 perfusion. Five retinoblastomas of infancy, perfused with cyclophosphamide (Cytoxan), have been treated recently;[2] 2 have shown no apparent response, and the others cannot be evaluated accurately at this early date. One patient, with an extensive melanoma of the antrum, showed no apparent tumor regression following head perfusion with PAM (phenylalanine mustard). Only 1 individual (Case 25) in this head and neck group, a man with an advanced recurrent parotid carcinoma, demonstrated tumor regression. After he was perfused with HN_2 at a dose of 0.4 mg. per kilogram, his visible tumor disappeared rapidly and remained at least quiescent until his death from pneumonia ten weeks later.

Two recurrent melanomas of the axilla were treated with PAM and TSPA (triethylene thiophosphoramide), via the axillary vessels, without demonstrable improvement. There was an initial softening of the axillary mass in Case 34, with subsequent rapid regrowth. In Case 35, an axillary dissection two months after perfusion provided us with an opportunity for pathologic study of the treated arm; no histologic evidence of tumor change was present.

Seven extremity melanomas were subjected to perfusion with PAM or a combination of PAM and TSPA. In 3, perfusion represented a component of initial therapy; in 3, perfusion was carried out as "prophylactic" therapy following surgical removal of all gross tumor; and in 1, perfusion was offered for massive thigh recurrence after a dissection of the groin.

All 3 patients with primary melanomas showed some response to perfusion in terms of tumor change. In Case 42, it was minimal. The primary lesion on the foot showed a 20 per cent decrease in size during the first two postperfusion weeks, followed by progressive activity. A subsequent dissection of the groin revealed node metastases, and the patient died from widespread disease eleven months later. Patient 39 had a primary melanoma of large size just below his patella as well as a 6- by 4- by 3-cm. mass in his groin. Perfused via the external iliac vessels, both tumor areas began to regress impressively, the groin lesion somewhat more than the primary, and at the time of this man's death three weeks after perfusion (see "Complications") the inguinal mass had almost disappeared. Autopsy studies showed massive tumor necrosis.

Case 40 was of particular interest. This man had two sizable cutaneous melanomas of the lower extremity, one in the thigh, the other in the lower leg. Following perfusion, the leg lesion began to regress slowly and continued to become smaller over the next ten months, at the end of which time all that remained was a flattened, soft, small area of pigmentation marking the site of the original tumor. This condition prevailed for six months. The thigh lesion, on the other hand, failed to regress, but remained inactive until ten months later, when it was excised. Why there should have been this differential response between the two lesions remains a matter of speculation.

Of the 3 patients with melanoma to whom perfusion was offered as a prophylactic procedure, 1 died twelve months later of brain metastases, but without local recurrence; 1 returned with a local thigh recurrence and was scheduled for a second perfusion; and 1 was apparently disease-free six months after perfusion. This is too short an interval from which to draw conclusions. The remaining patient in the melanoma group, who had extensive lymphatic recurrence in the thigh and groin, not only failed to demonstrate tumor response, but showed instead an apparent acceleration of tumor growth.

Two sarcomas of the thigh were perfused with HN_2. The liposarcoma (Case 43) underwent immediate softening, followed by continuing hemorrhage into the area once occupied by the tumor. A packing procedure was necessitated by the hemorrhage three weeks after perfusion, at which time persistent tumor was found in one small area. It is estimated that 95 per cent of the tumor mass was destroyed by the HN_2. A complete excision was finally achieved, with clear surgical margins, but three months later extensive pulmonary metastases were apparent. It would be of interest to know whether or not the increased vascularity of the tumor area following perfusion contributed to the blood-borne dissemination. In contrast to this case, the patient with the fibrosarcoma of the thigh (Case 46) responded to perfusion with an accelerated tumor activity; three weeks later disarticulation was carried out.

Our experience with bone tumors has been small. A Ewing's tumor in a child (Case 37) was exposed to methotrexate, without response; in a second perfusion, 5-fluorouracil and TSPA were given in combination, again without demonstrable response of the tumor. Aside from a metastatic hypernephroma of the humerus (Case 44), which remained quiescent for ten months following perfusion with cyclophosphamide, all other metastatic bone tumors have failed to respond.

In summary, then, the following facts are clear. Of the total series, 42 patients were followed long enough to determine accurately the effects of perfusion therapy in terms of tumor response. Of these, 9 (4 genitourinary carcinomas, 1 parotid carcinoma, 1 liposarcoma, and 3 melanomas) demonstrated tumor regression. This was transient in 8 and "permanent" in only 1. In other words, only 1 of 50 perfusions succeeded significantly or permanently in altering the course of the patient's disease. In terms of symptomatic relief, however, the results were more impressive. Nine of 11 patients with intractable pelvic pain were benefited, and where pain was a major factor in tumors of other areas, perfusion achieved similar relief.

Complications

The only serious complications of perfusion occurred during the first few months of clinical trial, at which time the drug dosages were not firmly established and the methods of vascular isolation were experimental. The 1 fatality of our series (Case 39) resulted from inadequate isolation. This man was perfused via the external iliac vessels with PAM (1.5 mg. per kilogram) and TSPA (0.8 mg. per kilogram), with a high thigh tourniquet fixed in place above a skin clip fixed in the anterior superior iliac crest. Studies with Cr^{51}-tagged red blood cells revealed a 50 per cent leak in seven minutes from the perfused circuit. Despite fresh blood transfusions, antibiotics, bacterial isolation, and steroids, he died twenty-six days postoperatively from uncontrolled septicemia secondary to a profound leukopenia. It is interesting to note that only 2 other patients of the 15 who underwent extremity perfusion suffered a leukopenia; in both these instances the leg was perfused via the iliac vessels, a technic which allows for some degree of escape from the extremity.

As anticipated, leukopenia was a more frequent sequel in the pelvic perfusions. Twelve of 19 patients in this group suffered a leukocyte drop to a level between 200 and 3,300, maximal depression occurring between the fifth and sixteenth postperfusion days. Far smaller drug doses were employed in the brain, head and neck, and chest wall perfusions because of the known inadequacies of vascular isolation in these areas, and with the exception of the cyclophosphamide-treated cases no leukopenia occurred.

One patient (Case 25) developed aphasia, right hemiparesis, and grand mal seizures following perfusion of the left neck with HN_2 (0.4 mg. per kilogram). Neurologic recovery occurred slowly, but he died from pneumonia ten weeks later. An excessive amount of PAM (1.5 mg. per kilogram) was administered to a well-isolated upper extremity in Patient 38 with consequent edema, erythema, and intense pain lasting approximately two months and resulting in a Volkmann's type of ischemic paralysis of the hand. Although some degree of edema and skin discoloration followed most extremity perfusions, this was the only instance of severe tissue damage.

Following the resection of a small segment of clavicle for perfusion of the upper extremity via the subclavian vessels, Patient 44 developed an osteomyelitis of the clavicle which eventually necessitated the complete removal of the remaining clavicle.

Postoperative hemorrhage occurred in 2 individuals. The first (Case 23), from a neck wound two weeks after a brain perfusion, was due to a technical error; the second (Case 43) appeared in the tumor area of the thigh after a marked regression of the liposarcoma. Bleeding was controlled without difficulty in both cases.

Aside from this total of 7 complications (1 fatal, 2 serious, and 4 minor), perfusion was tolerated well, and I believe it can be said with confidence that we have now arrived at a stage where established technics and drug dosages should permit the safe application of this procedure. With the advent of new chemotherapeutic agents, and during the exploratory phase of using existing agents in combination, some complications must be expected, however.

Comment

The clinical results which have been enumerated are, at face value, disappointing. Of the 48 patients herein reported, a handful only have demonstrated tumor regression, and in these, with rare exception, the improvement has been transitory. In only 1 patient have we effected complete tumor disappearance; the permanence of this response is uncertain. Complications have been infrequent but serious, and in certain patients we are impressed by the apparently accelerated growth of tumor following perfusion. It is not illogical, then, to reexamine carefully our early enthusiasms and to attempt a redefinition of the present and potential usefulness of perfusion technics.

THEORETIC AND DEMONSTRATED VALUE OF PERFUSION TECHNICS. All anticancer drugs today, whether they be alkylating agents, antimetabolites, or antibiotics, depend on a narrow differential response between tumor and normal tissue. To effect an appreciable tumor effect, the drug in question must be "pushed" to the point of systemic toxicity. Unhappily, this point can never be clearly anticipated in any particular patient, and the toll of primary drug deaths is alarmingly high.

The principal theoretic advantage of

perfusion is based on this inherent limitation of presently available chemotherapeutic agents. Through the means of vascular isolation of a tumor-bearing segment of the body, it is now possible to deliver to the area in question concentrations of drug which would be lethal if given systemically. If the isolation is perfect, or nearly complete, the only limiting factor in drug dosage is the tolerance of the normal tissue surrounding the tumor in the perfused area. In effect, this means that a drug concentration perhaps 10 to 20 times higher than the systemically tolerated dose can be brought to bear on a particular tumor.

Although it cannot be postulated that tumor response is invariably a factor of drug concentration, there can be no doubt that this theoretic virtue of perfusion has been realized partially in practice. The remarkable results in the perfusion treatment of malignant melanoma of the extremities, as reported by Stehlin, Smith, and Clark[22] and Creech,[23] must be credited to the technic. Systemically given PAM is not only hazardous, but also rarely results in appreciable tumor regression; the same drug administered by perfusion methods in high concentration to an isolated area achieves a 30 to 40 per cent melanoma regression rate. Of the occasional sarcoma or epithelial tumor which has responded following perfusion, the same may be said; in each instance, an effect was produced which could not have been reproduced by systemically safe drug concentrations. These favorable responses are certainly in the small minority when they are compared with the total number of cases treated by perfusion; but the fact cannot be altered that these results could not have been achieved without the use of the perfusion technic, given our present armamentarium of anticancer drugs.

A second demonstrated value of perfusion which has emerged, and which was totally unanticipated initially, has been the symptomatic relief afforded many of these patients. This first became evident in the perfusions of the pelvis, where intractable nerve root or bone pain so often accompanied the recurrent rectal or cervical carcinoma. Pain relief was immediate and, in most instances, complete, suggesting a direct action of the drug on involved nerves rather than a secondary effect due to a regression in tumor size. This effect has been achieved with high frequency in pelvic perfusion, but somewhat less consistently in other areas. A failure to effect pain alleviation has usually been associated with narcotic addiction. Shingleton, Parker, and Mahaley,[17] in reporting technics for total abdominal perfusion, have been gratified by the symptomatic relief achieved, particularly in carcinomas of the body of the pancreas with associated back pain.

Fortunately, in our experience, pain relief has not appeared at the expense of motor function, but all too often the relief has been transitory. The average duration of pain relief in our pelvic cases has been approximately one month, although reports of others indicate complete freedom from pain up to a year in occasional cases.

LIMITATIONS OF PERFUSION THERAPY. An important limitation to perfusion therapy stems from the difficulty in achieving adequate vascular isolation in most areas of the body. Even the tightly tourniqueted extremity demonstrates a 5 per cent leak into the systemic circulation after one hour of perfusion. The escape from the perfused pelvis, abdomen, chest wall, axilla, brain, or head and neck region is comparably far greater. This has been documented by many investigators, using Cr^{51}-tagged erythrocytes or RISA (radioiodine-tagged serum albumin).[24,25] Our own unpublished data indicate a 50 per cent fifteen-minute disappearance time of Cr^{51} from the pelvis, eight minutes from the head and neck area, and five minutes from the brain. This rapid loss of red cells or plasma does not, of course, reflect necessarily the loss of specific chemotherapeutic agents from the perfusion circuit. It is obvious, from the absence of severe bone marrow depression following pelvic perfusion with large amounts of HN_2 that this drug is rapidly fixed in the perfused tissues. Studies with labelled cyclophosphamide and Thio-TEPA (triethylene thiophosphoramide) show that the detectable loss from the perfusion circuit does not correspond quantitatively to the appearance of radioactivity in the systemic circulation; the most reasonable interpretation is that even these relatively long-acting alkylating agents are being taken up to some degree by the perfused tissues during the first thirty to sixty minutes of exposure. Less is known of the fate of the antimetabolites, although the work of Lawrence[26] would suggest that there is a considerable disparity between the measured appearance of methotrexate in the systemic blood contrasted with Cr^{51} or RISA.

There is little question, however, that a rough correlation exists between the escape of long-acting agents and of tagged blood elements from imperfectly isolated areas. This fact imposes important limitations on the spectrum of anticancer drugs that can be used. Long-acting alkylating agents and antimetabolites have little rationale for use if the effective differential concentration of drug between the perfused and systemic circulations can be maintained for only a short while. Not only are problems of systemic toxicity encountered, but also it is improbable that any appreciable tumor response can be effected by such a short exposure of tumor to drug. We are consequently faced with the necessity of limiting ourselves to the use of short-acting or rapidly "fixed" agents, such as HN_2, in the poorly isolated system.

Little need be said about the limitations of our present armamentarium of chemotherapeutic compounds. It is quite clear that clinical failure is more a measure of drug inadequacy than of technical difficulties concerning vascular isolation. Few, if any, specific drug-tumor relationships have been established. The observed response of melanoma to phenylalanine mustard provides the most convincing example of such a relationship. Rochlin[27] has recently reported encouraging results in the treatment of extremity sarcomas with PAM and actinomycin D in combination. We have been impressed by the response of certain vascular tumors to methotrexate.[28] These, and other reported series, are too small, however, to be anything else but suggestive.

Our basis for drug choice, then, remains largely empiric rather than rationale. Undoubtedly greater clinical experience by the trial-and-error method will provide useful information as to drug action and specificity. Tissue culture screening methods are now being investigated as a possible basis for drug choice in specific human tumors. Golumb[29] has reported an 81 per cent correlation between in vitro sensitivities and clinical response. Unfortunately, not all human tumors can be grown in tissue culture satisfactorily, and the time interval between biopsy and definitive therapy is inordinately long. Improvements in culture technic may, however, make this a practical method for intelligent drug selection.

In addition to the deficiencies inherent in the drugs themselves and our inability to achieve good vascular isolation in many body areas, there is yet another limitation, or rather danger, to perfusion therapy. We have been impressed by the fact that in at least 5 patients, 3 with melanoma, 1 with a squamous carcinoma of the extremity, and 1 with a vulvar carcinoma, tumor growth appears to have been accelerated following perfusion. This observation is impossible to document, but the concept of chemotherapeutic stimulation of tumor growth is supported by the work of others.[30-32] Preliminary work at this institution indicates that skin homograft rejection is greatly delayed in a perfused limb, suggesting a possible alteration in local immunologic factors. If we postulate that certain local or systemic factors are responsible for controlling the behavior of a given tumor rather than the control of growth being autonomous within the tumor itself, then we must accept the contention that altering these host defense factors will allow tumor growth to proceed more rapidly.

The destruction of tumor tissue by chemotherapy may also lead to complicating sequelae. Toxic protein breakdown products may in themselves be lethal. Local vascularity may be increased by perfusion, as in Case 43, perhaps promoting earlier blood-borne dissemination of tumor.

These objections are perhaps speculative and impossible of documentation, but we believe that they should be given consideration when decisions are made concerning forms of therapy. The cliché "Well, at least it can do no harm" is not, in our opinion, invariably applicable to perfusion.

TECHNICAL CONSIDERATIONS. Perfusion technics are by no means standardized as yet, and there are many facets which are now undergoing investigative scrutiny. Although it is conceded by most that whole blood constitutes the most effective perfusate, it is not clear whether oxygenation of the perfusate is necessary or even desirable. The rationale for oxygenation as originally expressed by Creech *et al.*,[1] was based on the similarities of action and tissue response between the alkylating agents and x-radiation and the observed fact that the tissue effects of radiation are augmented by high oxygen levels.[33–35] Ryan *et al.*,[36] using 5-fluorouracil under various oxygen concentrations in the hind limb of the dog, report data which tend to confirm this assumption. More recent work by Krementz, Harlin, and Knudson[37] indicates that increased tissue oxygen tension potentiates the effect of nitrogen mustard on Ehrlich ascites tumor in CFW mice. Ausman *et al.*,[38,39] on the other hand, have arrived at opposite conclusions; they contend that relative hypoxia produces a vasodilation which enlarges the vascular bed available to nitrogen mustard. They suggest a 70 per cent oxygen, 30 per cent carbon dioxide gas mixture to prevent the rise in pH observed in oxygen-saturated perfusates and to maintain maximal vasodilation. This work was done on normal dog limbs, and its relevance with respect to tumor tissue is not clear.

Ideal flow rates and perfusion pressures likewise have not been established. There is fragmentary evidence to suggest that the uptake of HN_2 is augmented by low flow rates;[39] virtually all investigators concur that the pressure in the perfusion circuit (which has a roughly linear relationship to flow rate) should be maintained at a level lower than that of the systemic circulation to avoid any gradient which would allow excessive leak of a drug from the perfused area. Gravity venous drainage is favored by some, the perfusion flow rates being governed principally by the rate of venous return. Such a technic obviates the possibility of vein wall collapse and the subsequent reduction in venous return occasionally encountered in a high pressure closed circuit system, but it should not be necessary when relatively low flow rates are employed.

Other methods to augment the local tumor effects of anticancer drugs are currently under investigation. The use of vasodilators, such as papaverine and priscoline, that are designed to enlarge the vascular bed and effect a wider dispersal of drug, has been described. It is probable that the temperature of the perfusate is of greater importance in this regard. Recent experimental evidence suggests that drug uptake increases with progressive warming of the perfusate, presumably due to heightened tissue metabolism as well as to vasodilatation.[39–41] Heat exchangers have consequently been added to the perfusion circuits in many clinics, the perfusate being maintained at between 37 and 40 C. The use of systemic hypothermia in conjunction with selective normothermia in the regionally perfused area has been recommended,[17,42] based on the fact that some degree of bone marrow protection against drug cytotoxicity is afforded by hypothermia. The contraction of the vascular bed in the cooled tissue likewise creates a barrier to the escape of blood from the expanded bed of the normothermic segment. Our own experience tends to confirm this assumption. We have recently given up to 1.5 mg. per kilogram of nitrogen mustard in the pelvis, using differential temperatures, without subsequent serious marrow depression and with apparently augmented local effects.

The documented leak factor, referred to earlier, has prompted a re-evaluation of existing technics for vascular isolation. The meticulous anatomic isolation of the pelvic circulation has been described by many, and although the leak can be reduced by attention to the inferior epigastric, ovarian or spermatic, lateral circumflex iliac, ileolumbar, and superior and inferior gluteal vessels, it still remains significant. Martin[43] has devised an ingenious apparatus for containing the pelvic circulation, consisting of two supported inflatable rubber cuffs, one inside and one outside the abdominal cavity, that is reported to reduce escape from the dog pelvis to 6 per cent in one hour. Whether this protection will be afforded in man is unknown. Lawrence[26] is now experimenting with a broad abdominal pneumatic tourniquet to achieve the same end; apparently the increased intra-abdominal pressure produced controls the blood flow effectively. Watkins *et al.*,[44] among others, have reported recently on the use of intravascular balloon catheters in pelvic perfusion, thus obviating the need for direct occlusion of the aorta and vena cava via laparotomy. Isolation technics for the extremities, axilla, and head and neck region are reasonably uniform; it does not appear that further mechanical measures in these areas will cut down effectively on drug escape. The leak during brain perfusion is, as expected, of considerable magnitude owing to the technical difficulties in occluding the vertebral vessels. Of interest is Woodhall's observation[45] that leak is no higher with unilateral than with bilateral brain perfusion, indicating the independence of the vascular circuits on either side of the midline. Many investigators are now studying the feasibility of perfusing the isolated lung and liver;[46-50] as yet, the technics are cumbersome and not without risk.

Methods to minimize the systemic toxicity of the available chemotherapeutic agents are likewise under investigation. The use of autologous bone marrow has received much attention. We have had experience with it in some 15 cases, 7 of which were total body perfusions, the others regional in nature. This group of patients received nitrogen mustard or phenylalanine mustard in doses approximately twice the conventional systemic dose. One death occurred from acute hematopoietic depression ten days following perfusion; all the other patients in this series suffered a mild to severe leukopenia, which was reversible. A comparable control series is unobtainable, but we are of the impression that we did not influence bone marrow recovery significantly. Initial dog experiments, using autologous marrow obtained from the femurs, suggest the same thing. Miller and Lawrence[51] have described a method for protecting iliac marrow by using a pneumatic external abdominal tourniquet during nitrogen mustard therapy of tumors in the upper body, aortic and caval flow being occluded by intravascular balloons. The protective action of sodium thiosulfate against HN_2 toxicity is being studied in several centers. To date, no conclusive information is available. Needless to say, if some method could be found for inactivating nitrogen mustard or other alkylating agents in the systemic circulation, it would make it possible to use higher and perhaps more effective drug concentrations in a regionally perfused area, without concern for leak.

We question whether or not technical improvements per se in existing perfusion technics will alter clinical results significantly, given our presently inadequate stock of chemotherapeutic agents. The vascular isolation of certain body areas, although subject to slight improvement, will never be complete; the augmentation of local drug action pharmacologically, by temperature alteration, or by regulation of perfusion flow rates or pressures will not, in our opinion, modify fundamentally the response of a particular tumor to a particular drug. Even the absolute protection of bone marrow against drug cytotoxicity, by a more sophisticated method of autogenous marrow use or by new pharmacologic compounds, will not permit significantly greater concentrations of drug in the perfused area because of the limitations imposed by normal tissue tolerance.

Aside from the obvious need for more specific and less toxic anticancer agents, it would appear to us that the greatest concentration of effort should go toward means for long-term continuous exposure of tumor to drug. It is no more logical to think that a large tumor mass should respond completely to thirty minutes of concentrated drug therapy than to expect pneumonia or any other massive infection to resolve following a single antibiotic injection. Nor have reported clinical perfusion results, with certain obvious exceptions, given us reason to think otherwise. Martin[52] has approached this problem by introducing a dialyzer into the perfusion system and by monitoring the pH and carbon dioxide pressure of the perfusate, such a system being designed for long-term isolation perfusion. His clinical results will be of interest. Sullivan, Miller, and Sikes's work,[53] using continuous intra-arterial infusions of an antimetabolite (methotrexate), while providing systemic protection through intermittent intramuscular injection of metabolite (citrovorum factor), has had much appeal for us, in that it allows prolonged exposure of tumor to drug. His early results have been impressive. In our own small experience with this technic, using not only methotrexate but also 6-aminonicotinamide in combination, the results have not been as convincing, but we feel that more work is warranted along these lines.[54] Again, this technic is circumscribed by drug toxicity; at present, only antimetabolites which have available metabolites for systemic administration can be used. This necessarily excludes many available cytotoxic agents, including the alkylating compounds and the antibiotics, from use in this continuous system. Perhaps the most effective use of available anticancer agents would be realized through the combined application of regional perfusion (alkylating compounds or antibiotics) and subsequent continuous intra-arterial antimetabolite therapy.

Selection of patients for perfusion. Based on our own experience and that of others, we have become more selective in our choice of patients for perfusion. As new improvements in technic emerge, as new chemotherapeutic agents appear for trial, and as new combinations of existing compounds are proposed for evaluation, we shall no doubt alter our criteria for selection. At this time, however, given the existing spectrum of anticancer drugs, we believe that perfusion should be reserved for the following situations:

1. All extremity tumors, providing
    (*a*) The disease is thought clinically to be localized.
    (*b*) There are no preferable standard surgical means of eradicating the tumor.
    (*c*) Amputation or other radical surgical procedures are refused.
    (*d*) The local situation is unmanageable (that is, ulceration, infection, or bleeding), despite the presence of distant metastases.

    Depending on tumor type, location, and extent, perfusion may be used alone or as an adjunct to surgery. We do not subscribe to the opinion that all extremity tumors should be perfused before or at the time of amputation or radical surgical excision. On the other hand, there is increasing conviction that perfusion should become an integral part of the treatment of extremity melanomas, used as an adjunct to appropriate surgical measures.

2. Unresectable pelvic tumors of ovarian, endometrial, or urogenital origin. Carcinomas in the pelvis arising from the cervix or rectum should be perfused only if there is a dominant element of pain.
3. Unresectable carcinomas of the head and neck region which are resistant to tolerance doses of external radiation and which are producing interference of function or unmanageable pain.
4. All soft tissue sarcomas and tumors of vascular origin whose location allows for vascular isolation.

Summary

Our experience with 50 regional perfusions for a variety of locally advanced malignant conditions is described, and problems relating to available drugs and technics are discussed. Tentative criteria for the selection of patients for perfusion are proposed.

Perfusion remains an experimental tool, and its role in the over-all management of cancer cannot be established without considerably wider experience.

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Prevalence of peptic ulcer

Some two and a half million Americans have peptic ulcers, according to *Patterns of Disease*, a Parke, Davis & Company publication for the medical profession. The estimated prevalence of peptic ulcer in the population has risen almost sixfold in the past twenty years. However, part of this rise has been attributed to improved diagnostic accuracy.

Triflupromazine and Fluphenazine as Adjuncts in Anesthetic Management*

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A STUDY WAS UNDERTAKEN *to evaluate the sedative, hypnotic, and antiemetic properties of triflupromazine hydrochloride (Vesprin) and fluphenazine dihydrochloride (Prolixin). Trials were made on 24 patients scheduled for electroconvulsive therapy with thiopental sodium alone and in combination with triflupromazine or fluphenazine. It appears that 6 mg. of triflupromazine and 6 mg. of fluphenazine have approximately the same sedative potency as 50 mg. of pentobarbital sodium. In a group of 160 patients, triflupromazine used alone or with scopolamine hydrochloride as preoperative medication produced well-sedated patients. Fluphenazine proved to be a tranquilizer in doses of 4 to 6 mg. with little sedative effect. Triflupromazine was very useful in relieving apprehension and quieting 28 patients scheduled for bronchospirometry or bronchoscopy under topical anesthesia. In a group of patients under spinal or peridural anesthesia, marked hypotension was frequently seen with small doses of triflupromazine. As an antiemetic, fluphenazine appeared to be more effective than triflupromazine, and a smaller dose was needed. Both drugs were effective in treating emergence delirium, although fluphenazine is preferred because it does not prolong the anesthesia time. Triflupromazine potentiated the general anesthetic effect, but fluphenazine did not. Both drugs are contraindicated in spinal anesthesia. Side-effects were not noted, but the discussant warns against potential side-effects and points out the need for further research on the subject.*

EACH NEW PHENOTHIAZINE derivative has been investigated for its possible role as an adjunct in anesthetic management. Two compounds, triflupromazine hydrochloride (Vesprin) and fluphenazine dihydrochloride (Prolixin) have demonstrated their usefulness as sedatives, tranquilizers, or antiemetics. The sedative or hypnotic properties were quantitatively determined by the method of Orkin and Chun[1] employing the sleep dose of thiopental sodium as a measuring rod in a series of patients scheduled for electroconvulsive therapy. Both triflupromazine hydrochloride and fluphenazine dihydrochloride were used as preoperative medications with a view to providing sedation prior to general anesthesia. Since either drug might exhibit tranquilizing ability, both were used during the course of local or regional anesthesia and in patients scheduled for bronchoscopy or bronchospirometry. Both drugs were also given preoperatively or during the latter hour of surgery if postoperative retching or emesis was to be avoided or expected, as in neurosurgery, ophthalmic, dental, or abdominal surgery. In the recovery room, patients who exhibited emergence delirium or vomiting were given the preparations intravenously.

The dose range, with intramuscular administration, varied from 10 to 20 mg. of triflupromazine hydrochloride; the intravenous dose varied from one to six injections of 2.5 mg. (2.5 to 15 mg.). The peak effect of intramuscular injection was difficult to judge, but on intravenous injection the

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maximum effect was attained in from seven to ten minutes.

Observations

Sedative and hypnotic properties. Each of 24 patients scheduled for electroconvulsive therapy was anesthetized with 2.5 per cent thiopental sodium at the rate of 25 mg. per thirty seconds. Thiopental sodium was administered until the patients failed to respond to the command "Open your eyes" shouted into their ears fifteen seconds prior to the next scheduled dose. At least two trials were made with thiopental sodium alone and two each fifteen minutes following the intravenous administration of triflupromazine hydrochloride or fluphenazine dihydrochloride in doses of 2, 4, or 6 mg. The same patients were used in crossover studies, and the order of administration was randomized. At least three days passed between trials.

Practically no sedation (reduction in thiopental sodium dosage) was seen with 2 mg. of either drug. Fluphenazine dihydrochloride reduced the thiopental sodium requirements 5 per cent with 2 mg., 17 per cent with 4 mg., and 30 per cent with 6 mg. Triflupromazine hydrochloride reduced the thiopental sodium requirements 15.5 per cent with 3 mg., 36.6 per cent with 6 mg., and 58.9 per cent with 12 mg. A previous study with pentobarbital sodium and secobarbital (50 mg. each) indicated a reduction of 38.5 and 29 per cent respectively (Table I).[2] It would thus appear that 6 mg. of triflupromazine hydrochloride and 6 mg. of fluphenazine dihydrochloride have approximately the same sedative potency as 50 mg. of pentobarbital sodium.

Preoperative medication. Triflupromazine hydrochloride alone or with scopolamine hydrochloride produced well-sedated patients. Doses of 10 to 20 mg. administered intramuscularly one hour prior to surgery resulted in patients who appeared tranquil, cooperative, and easily arousable. They would aid movement from the stretcher to the operating table, stating they felt rested and wanted to sleep. In the presence of pain, sedation with triflupromazine hydrochloride was obviously not as effective as with a narcotic. Fluphenazine dihydrochloride proved to be a tranquilizer in doses of 4 to 6 mg. with little sedative effect. Clinically, it did not give evidence of prolonging the sleeping time following a barbiturate. With this medication, psychic sedation was obtained without the postanesthetic depression seen following the administration of meperidine hydrochloride or morphine in short surgical procedures. In the group of 160 patients who ranged in age from twelve to sixty years, there was no significant clinically apparent depression of blood pressure or respiration.

TABLE I. Average per cent reduction in the amount of thiopental sodium necessary to produce sleep in 10 patients with two trials for each dose and drug

Drug	Amount (Mg.)	Reduction (Per Cent)
Triflupromazine hydrochloride	3	15.5
	6	36.6
	12	58.9
Fluphenazine dihydrochloride	2	5.0
	4	17.0
	6	29.8
Pentobarbital sodium	50	38.5
	100	52.8
	200	73.4

Adjunct for local or regional anesthesia. Triflupromazine hydrochloride in our hands has been extremely useful in relieving apprehension and quieting 28 patients who were scheduled for bronchospirometry or bronchoscopy under topical anesthesia. In spite of moderate sedation, these patients were agitated and frightened on arrival in the operating room. Five mg. given intravenously (1 mg. per minute) was the average dose necessary to produce a tranquil attitude. A like regimen was instituted for patients requiring awake intubation, with similar results.

During local or regional anesthesia, when pain is present, a narcotic or analgesia with nitrous oxide-oxygen was usually necessary. Therapy with triflupromazine hydrochloride is effective, when combined with small doses of narcotic, in producing a state of being similar to that expected from larger, but depressant, doses of narcotics. This agent thus alters the individual's response to pain rather than relieves the pain and reduces the amount of analgesic needed by 25 per cent. Fluphenazine dihydrochloride is not as effective.

The patients in this group ranged from ten to seventy years of age. No patient developed a severe respiratory or circulatory depression which necessitated special therapy. Transient tachycardia (increase of 10 to 20 beats per minute) occurred frequently but returned to the preinjection rate in one or two minutes. The tachycardia was seen much more frequently with triflupromazine hydrochloride than with fluphenazine dihydrochloride.

The possibility that triflupromazine hydrochloride would protect against the convulsive effect of local anesthetics was screened in 300 mice. A dose of 10 mg. per kilogram of triflupromazine hydrochloride was injected into the peritoneum of mice fifteen and thirty minutes before the local anesthetic agent. Procaine 450 mg., tetracaine hydrochloride 50 mg., or 2-chloroprocaine 1,000 mg. per kilogram produced convulsions in 95 per cent of the control groups of mice. No significant reduction was found after pretreatment with triflupromazine hydrochloride. Fluphenazine dihydrochloride was not studied.

In a group of patients under spinal or peridural analgesia, marked hypotension was frequently seen with small (2 mg.) doses of triflupromazine hydrochloride. The fall in blood pressure responds to moderately large doses of vasopressor. Phenylephrine hydrochloride (Neo-Synephrine hydrochloride) by continuous infusion was usually necessary to overcome this undesirable side-effect.

Triflupromazine hydrochloride was tried in 10 children between two and twelve years of age for sedation during cardiac catheterization. This agent was inferior to morphine, rectal thiopental sodium, or a combination of meperidine hydrochloride and phenergan hydrochloride.

Antiemetic potency. Either preparation was administered to patients having a history of nausea and emesis following the previous administration of an anesthetic agent or to patients in whom nausea and emesis would seriously disrupt a smooth postoperative course. The prophylactic use of an antiemetic would be indicated only in such circumstances as neurosurgery, intraocular surgery, wiring of mandible, and dehiscence. In 60 such patients, the drugs have been associated with the absence of nausea and vomiting in over half the trials and possibly had the effect of reducing the severity in another 30 per cent. The duration of action is such that in short operative procedures the compound could be given before surgery. In long operative procedures, the drug was given toward or at the end of surgery. In the latter instance the intravenous administration did not reduce the respiration or blood pressure. There was no correlation among the anesthetic agents used. Fluphenazine dihydrochloride appeared to be more effective than triflupromazine hydrochloride and one-third to one-half the dose was needed. Triflupromazine hydrochloride in doses of 5 to 15 mg. appeared to prolong the postanesthetic sleeping time, but fluphenazine dihydrochloride in doses of 2 to 4 mg. did not. Since the administration of fluphenazine dihydrochloride considerably reduces the incidence of nausea and emesis to the same extent as triflupromazine hydrochloride but with much smaller doses, it appears that for this phenothiazine derivative, the antiemetic action is greater than the sedative effect. Further trial is definitely indicated. Significant hypotension was not seen in this small survey with intravenous doses of fluphenazine dihydrochloride ranging to 6 mg. and triflupromazine hydrochloride to 15 mg. Respiratory depression was not noted.

Postoperative recovery room. Emergence delirium was treated, with excellent results. Since a quiet and cooperative patient was desired without undue prolongation of anesthesia time, fluphenazine dihydrochloride appeared to be a better drug than triflupromazine hydrochloride. Doses of 3 or 4 mg. proved adequate in most instances. Occasionally the intravenous administration was repeated in fifteen minutes without untoward effect. The patients became remarkably quiet, cooperative, and indifferent to their surroundings. Here, again, no significant falls in blood pressure were noted.

Potentiation of anesthetic agents. Triflupromazine hydrochloride and fluphenazine dihydrochloride were administered to 25 patients in intermittent doses of 10 and 3 mg. respectively via an intravenous infusion during general anesthesia. Triflupromazine hydrochloride definitely potentiated the general anesthetic effect but fluphenazine dihydrochloride did not. Patients who were anesthetized with thiopental sodium-nitrous oxide anesthesia were lightened by the restriction of the amount of thiopental sodium administered. Anesthesia was deepened easily by a single slow injection (1 mg. per minute) of 10 mg. of triflupromazine hydrochloride. The action of the single injection appeared to be maintained for over an hour. Respiratory depression was not evident clinically. Hypotension did not occur if the patient was anesthetized lightly. Hypotension occurred, however, on three occasions in one patient, who was under the regimen described, while anesthesia was deep. The fall in blood pressure to 90 mm. systolic, normal 140 mm., responded well to phenylephrine hydrochloride by dilute intravenous infusion. Fluphenazine dihydrochloride was not as effective. The recovery time in these patients was prolonged but uniformly smooth.

Comment

The clinical survey that has been outlined indicates that triflupromazine hydrochloride and fluphenazine dihydrochloride are two drugs which have potentials as adjuncts to the armamentarium of the anesthesiologist. Certainly the use of triflupromazine hydrochloride as a sedative and fluphenazine dihydrochloride as an antiemetic deserves further clinical trial and critical investigation.

The antiemetic potency of promethazine has been studied by Eckenhoff[3] who, while demonstrating the excellent effects in this aspect, pointed out that phenothiazines may produce hypotension of an unusual refractory nature to vasopressors. Bowman[4] and Sheiner[5] both used triflupromazine hydrochloride to prevent and treat nausea, retching, and/or vomiting. Bellville[6] critically compared fluphenazine dihydrochloride, triflupromazine hydrochloride, and Marezine hydrochloride. Our results are in major agreement with their opinions. Hypotension in this report was rare following the administration of triflupromazine hydrochloride. Undoubtedly this difference is due to the smaller doses employed herein as compared with the doses investigated by Bellville. Also in agreement is the finding that small doses of fluphenazine dihydrochloride had effective antiemetic properties. Its specific use as an antiemetic therapeutic agent becomes obvious.

Dobkin[7] also evaluated the sedative effect of triflupromazine hydrochloride by utilizing the decrease in thiopental sodium requirements. Although he used the dog as an experimental subject, and man was studied here, the results are quite similar. Any differences can be explained readily by the differences in experimental design.

The desirable effect of preoperative medication is well correlated with the sedative effect. However, the introduction of tranquilizers has paralleled a newer concept of the satisfactory preoperative state. The patients with triflupromazine hydrochloride were sleepy or sleeping but were easily arousable, mentally calm but clear, and most cooperative. Induction was easily accomplished in such patients without the necessity of intravenous medication. Similar findings were described by Zeedick,[8] Stone,[9] and Davies,[10] who also published favorable reports on the use of triflupromazine hydrochloride as a premedication during local, regional, or general anesthesia. This survey demonstrates its usefulness during local anesthesia in calming the agitated patient. However, attempts to employ triflupromazine hydrochloride during spinal anesthesia and the frequent occurrence of refractory hypotension contraindicate its use. Davies[10] did not make this point, but one must remember that he used this agent for one and one-half hours prior to the administration of a spinal anesthetic. The peak effect and probably the potentiating hypotensive effect had already passed prior to spinal anesthesia.

Conclusion

From this clinical and laboratory survey, triflupromazine hydrochloride appears to offer advantages as a drug for sedation, preoperative medication, potentiating general anesthesia and narcotics, and as an antiemetic. Circulatory and respiratory depressions are infrequent in clinically effective dose ranges. The use of the drug during spinal anesthesia is contraindicated. Hypotension occurred with doses of 2 mg. No evidence of hyperactivity of the extrapyramidal system was noted.

Fluphenazine dihydrochloride on the other hand, is a potent antiemetic in doses which do not produce sedation. The antiemetic effect lasted about 50 per cent longer than that of triflupromazine hydrochloride. The incidence of emesis was 4 per cent with fluphenazine dihydrochloride and 10 per cent with triflupromazine hydrochloride. There is no apparent increase in toxicity with the increased potency of fluphenazine dihydrochloride, and postoperative sleeping time was not prolonged. Side-effects were not noted; hypotension, respiratory depression, or extrapyramidal signs were absent. A recommended prophylactic dose of 1.5 to 2.5 mg. is realistic. This dose may be given prior to or during the last hour of surgery or in the recovery room. A few psychotic patients on large doses of fluphenazine dichloride reacted with hypotension during elective surgery.

Both drugs appear to be useful, but either should be used with reasonable clinical judgment where it is indicated. Triflupromazine hydrochloride is useful with an antiemetic and/or when sedative effects are desirable. Fluphenazine dihydrochloride is useful where sedation is not required or desirable.

Summary

1. A clinical and laboratory study demonstrates the possible usefulness of triflupromazine hydrochloride (Vesprin) and fluphenazine dihydrochloride (Prolixin) in anesthesiology.
2. Triflupromazine hydrochloride is a sedative and antiemetic.
3. Fluphenazine dihydrochloride is an antiemetic with few sedative properties.
4. Their use during spinal anesthesia is not recommended.

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Discussion

Herbert L. Erlanger, M.D., *New York City*. This study submits two new additional tranquilizers for consideration. The clinical evidence presented shows that triflupromazine hydrochloride in doses sufficient to counteract vomiting is accompanied by sedation. Fluphenazine dihydrochloride on the other hand can counteract vomiting without sedation.

The method of Orkin and Chun[1] of employing the sleep dose of thiopental sodium as a measuring rod is adequate as a control and avoids the phenomenon of acute and chronic tolerance to thiopental sodium.

In my opinion, some of the conclusions and handling of the data need further proof. Thus the study on sedation shows a positive correlation between increasing doses of triflupromazine hydrochloride and fluphenazine dihydrochloride and decreasing percentages of thiopental sodium. The reliability of the data cannot be assessed since only averages for the groups are given. Individual readings are also necessary to account for scatter and overlap. Similar data of Dobkin's[7] in dogs are analyzed for the significance of the difference between means by the t test.

A placebo might have been included for comparison in the study on regional and local anesthesia in view of the fact that the emotional reactions of patients tends to obscure results.

The section titled "Conclusion" states that the incidence of vomiting with fluphenazine dihydrochloride was 4 per cent, and with triflupromazine hydrochloride it was 10 per cent, yet there are no data in the body of the article relating to these rates. Prophylaxis against vomiting was done when the history or operative site indicated a high probability of an occurrence of vomiting. Vomiting is, however, affected by many parameters, including the anesthetic agent; the age, sex, duration of operation; hypotension; the position on the operating table; and mechanical stimuli including airway insertion. One of our patients, who was maintained on Fluothane-nitrous oxide anesthesia received fluphenazine dihydrochloride, 2.5 mg. intravenously, ten minutes prior to the termination of a tonsillectomy. Immediately following the removal of the endotracheal tube, copious vomiting occurred.

Neither of the phenothiazines has enough specificity of action to avoid potentially severe side-effects entirely. The incidence of hypotension is low, nevertheless the severe hypotension seen occasionally with 2 mg. of triflupromazine hydrochloride given with spinal and epidural anesthesia and the instances of hypotension with deep general anesthesia imply that further stress such as sudden hypovolemia, change of position, or tilt may lead to a dangerous blood pressure fall.

Extrapyramidal side-effects usually are not seen with a single injection, but Bellville[6] reports an oculogyric crisis with one dose of 5 mg. of fluphenazine dihydrochloride that was given to an ambulatory patient. Similarly, Archer* reports dystonias such as tetanus-like reactions, oculogyric crises, and a new syndrome: the face-neck syndrome.

In conclusion this is a new group of potent tranquilizers that differ quantitatively from other phenothiazines by a greater intensity of action at the emetic center and the extrapyramidal system. The observations in Dr. Hyman's and Dr. Orkin's study are worthy of further follow-up.

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Elastic stocking compression and venous blood flow

For some years elastic compression of the lower extremities has been used for prophylaxis of thromboembolism. The procedure has been empirical, based on the rationale that the pressure of elastic bandages or elastic stockings increases the rate of blood flow in the veins. In an investigation reported in the July 16, 1961, issue of the *Lancet*, B. R. Meyerwitz, M.B., and Ann Crook, B.Sc., devised technics to measure the pressure exerted by the appliance on the limb and compare the rate of flow in stockinged and unstockinged legs by injected radioactive tracer material. Of 31 subjects, the stockinged leg had a more rapid venous flow than its unstockinged fellow in all but 2, and in 22 of the subjects (71 per cent) the rate was more than doubled. The authors believe that their results demonstrate that elastic compression of the lower extremities before operation should decrease the morbidity from venous thrombosis with subsequent pulmonary embolus, particularly in patients of middle age and beyond. *Medical Abstract Service.*

Treatment of Emotionally Ill Children

Nature and Management of Initial Resistance Factors

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We are pleased to have the opportunity of presenting a further clinical communication reflecting experience in the Mental Hygiene Clinic of the Westchester Division, Inc., having to do with the diagnosis and treatment of emotionally ill children. As described in a previous report,[1] the Clinic utilizes the skills of the various members of the clinical team—the psychiatrist, the clinical psychologist, and the psychiatric social worker—in a closely collaborative manner in the interest of developing the most effective technics of clinical practice and training.

Children with behavior disturbances show the damaging effects of adverse environmental influences on the course of healthy growth and development. In certain cases some structural damage or maldevelopment of brain tissue may be responsible for behavior problems, but organic brain damage is not a factor in the great majority of cases of emotional disturbance in children. Rather, the abnormal behavior of the child is more likely a symptom of underlying emotional difficulties caused by present or past adverse environmental influences. These adverse influences are for the most part pathogenic attitudes and actions toward the child by one or more significant figures in his life. Thus, to some extent the child's illness may be seen partially as a reaction to the family group and to some extent as an expression of the pathologic condition of broader patterns of social reaction.

The hereditary and constitutional characteristics of the child are also of basic importance, and in general the causes of an emotional illness are to be found in a disturbance of the equilibrium between these various interlocking dynamics. Just as a fever indicates the presence of some disease process in the body, so abnormal behavior indicates that the child is inwardly disturbed because of a pathogenic relationship with someone near him. The primary pathologic process is to be found not in the child, but in the interrelating, emotionally charged interaction between him and another person. The child's symptoms as well as his inner unrest reflect this disturbed bond. In the diagnostic process, however, we need to use caution lest we think of unhealthy attitudes seen in the parents as being the only possible cause rather than realizing that something in the personality make-up of this particular child may have stirred up a negative response in this particular parent, thus setting off a chain reaction of negative feelings.

Seeing abnormal behavior as a result of a deep-seated pathologic process, one can recognize that it is not possible to modify this behavior directly by bribe, by threat, by sedation, or by other manipulation. One must look behind the particular disturbance for its causes, especially in the child's relationships with those around him. When the causes of a behavior symptom are understood and modified, the abnormal behavior diminishes or disappears since the child no

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longer needs to react or to cope with his world in his former ways.

Pathogenic attitudes are seldom seen in pure culture, but may represent various types and degrees of neurotic reactions.

Such attitudes and actions most likely to cause emotional disturbance in the child are: (1) parental rejection; (2) excessive parental demands; and (3) parental overprotection.

Pathogenic attitudes in environment

Parental rejection is not difficult to define: In one way or another the child has been and is being told "I don't want you—I never wanted you—you give me a pain—you disgust me." The rejection may be open and direct, or it may be subtle and disguised. It may be expressed (that is, defended against) by displays of great love, or it may be demonstrated by critical, punitive disparagement. In whatever form it takes it is probably the most noxious and damaging attitude toward the child, since it is most threatening to his security, his well-being, and his sense of worth.

Excessive parental demands means that the parent makes demands of the child which are well beyond the latter's capacities. Such parents ignore the idea that a child's readiness to meet certain expectations is dependent on his level of maturation and development. Such parents are apt to be rigid and authoritarian with their children, demanding strict adherence to unrealistic rules and schedules. They expect "instant" obedience and think of their children in terms of standards of conduct, rather than in terms of the child's emotional needs and satisfactions.

Parental overprotection applies most often to the mother who cannot let the child go and who is with him excessively, fighting his fights and trying to remake the world so that the child will be safe and comfortable. Some mothers in this group control their children at all times so that the child becomes a submissive puppet with no will of his own. Other mothers of this type can exert no control over their child, and he becomes a tyrant who is destructive, egocentric, and given to temper outbursts when he is crossed. Some mothers blow hot and cold in their overprotectiveness, and the child becomes anxious and confused, never knowing what he is capable of doing or what actions will gain acceptance and approval.

IN GENERAL THE CAUSES *of emotional illness in a child are found in a disturbance in the equilibrium between the hereditary and constitutional characteristics of the child and present or past adverse environmental influences. Abnormal behavior indicates that the child is inwardly disturbed because of a pathogenic relationship with someone near him. The pathogenic attitudes most likely to cause emotional disturbance in the child are parental rejection, excessive parental demands, and parental overprotection. The general pathologic reaction patterns are submission, withdrawal, rebellion, and substitutive reactions. However, therapy must be directed to a modification of the pathogenic relationship rather than toward treating the behavior symptom itself. As a result, the concept of family-centered treatment has replaced the child-centered concept of child guidance. Initial resistance in parents who come to a child guidance clinic for help is normal. Proper handling of referral and greater understanding of the parents can help to overcome this resistance. Resistance to introspection occurs frequently, and the child patient displays resistance symptoms also. Overcoming resistance in parents and children is one of the major tasks of the child guidance clinic.*

Maternal overprotection is very difficult to treat because it is often a result of excessive and inappropriate dependency which is mutual. As such it is a satisfactory arrangement to both mother and child. The mother may wish to get rid of the child's symptoms (for example, tantrums), but she is unable to give up her excessively close attachment to him.

The attitudes of other members of the family are also important, especially those of the father, as well as those of siblings and others living in the home such as grandparents, maids, and boarders. Teachers' attitudes can effect a positive or negative influence on the child's behavior also, as can those of other significant figures in the child's life, such as his physician, minister, policeman, and relatives. For the sake of simplicity we are discussing here the parents' attitudes, particularly those of the mother as being significant pathogenic factors in behavior disturbance. To understand more fully the origin of a child's disturbance we would need a complete reconstruction of all the life forces that have had a significant effect on him.

With these pathogenic attitudes in his environment, the child seeks to find a pattern of adaptation and reaction which enables him to maintain himself in spite of these hindrances to his growth. His behavior reaction patterns will depend on the severity of these attitudes, the length of time he has been subjected to them, the presence of modifying or supportive features in his environment, his age, and the health of his emotional "past."

Pathologic reaction patterns

There are of course many possible variations of pathologic reaction patterns, but these patterns may be grouped under four general headings: (1) submission; (2) withdrawal; (3) rebellion; and (4) substitutive reactions.

Submission and withdrawal represent fixations of childlike behavior and are referred to in diagnostic terminology as "habit disturbances." Rebellion is referred to as "conduct disturbance," and substitutive reactions are identified as "neurotic traits."[2]

These reaction patterns come about in response to parental attitudes and actions which undermine normal growth and development. All of these reactions in a moderate or controlled degree are normal responses to certain situations or are a part of a normal child's behavior. However, when they become exaggerated to extreme degrees so that the child is capable of coping with the world in no other way than by this entrenched pattern of reaction, the child can then be considered as being pathologically rigid and overdefended, in effect, incapable of adjusting to a wide range of environmental conditions and stimuli.

These behavior disorders, then, come about in response to pathogenic attitudes and actions of the parent. It has been said that parents can pound, smother, or freeze a child into submission. Similarly they can frighten or bewilder him into a withdrawal into himself and into a world of fantasy; or through overpermissiveness or rejection they can foster the development of a rebellious, disobedient child. Or in response to the anxiety engendered by internal conflicts the child may develop substitutive reactions in an effort to diminish his inner disturbance. The paths leading to these pathologic end states are many and varied. Whatever reaction pattern he uses, the child is attempting to maintain a precarious balance between two struggles: the struggle to maintain and enhance his individuality and his sense of self against the pathogenic attitudes of someone near him and the struggle to secure and preserve his place in his parents' affections—a place that he needs so sorely for his own growth. In all probability the child will compromise himself and his needs and rights to maintain his security in the face of the parents' pathogenic attitudes.

In effect, the child sees that growing up crippled is preferable to not surviving at all. Unless these children can be helped significantly to modify the crippling effects of pathogenic attitudes in their environment, they will grow into warped and troubled adults who, as parents, will relate to their own children in unhealthy and destructive ways. This is inevitable since that is the only way they are able to relate to them, that is, in accordance with some prototype of their own experiential past, and the cycle is thus drawn full circle.

One must bear this in mind when treating the parents of a disturbed child—namely that they handle and relate to him out of their own emotional needs and frustrations of the present and the past, and that many of their attitudes and behavior patterns are determined either unconsciously or partly so. These parents behave as they do, not because they freely choose to do so, but because they have no choice—they know no other way of living or relating, they themselves having pathologic reaction patterns which dictate the child-rearing practices which they employ. It is therefore important to approach parents as sympathetic coworkers who are interested in understanding the problem and to conduct with them a nonjudgmental inquiry into the complex phenomena of their children's behavior and of their own parental attitudes.

And there are no short cuts to such understanding. Sometimes people become angry with parents who show pathogenic attitudes, particularly if such parents seem unable or unwilling to follow out well-intended (and even correct) advice and suggestions. But it helps little to tell a mother to stop leaning on or pounding on her child until she can understand her need for a leaning board or a pounding block. Either a new support or outlet must be substituted, or the parent must change and grow emotionally enough not to need such props or scapegoats. In either instance the effect of the mother's attitudes and behavior must be diverted from the child.

A large part of our work with children, then, consists of efforts to reduce or remove the pathogenic attitudes in their environment and/or to protect them from further danger by environmental pathogenic processes. Second, we work with the children themselves to help create or to recreate favorable conditions for change and new growth. Thus, in the treatment of the child and the parents, in addition to the negative purpose of eliminating emotional suffering, we need to set up the positive goal of activating the full potential of the child in keeping with the basic principles of preventive medicine.

Since the pathologic process in behavior disorders is often to be found in an unhealthy relationship between the child and another person, therapy must be directed to a modification of this relationship rather than toward treating the behavior symptom itself. As a result, the question of who is the "patient" has become somewhat blurred in child guidance work, and the concept of family-centered treatment has come to replace the child-centered concept of child guidance.

In actual practice all the significant participants may become "patients" when the problem is seen as emanating from the disturbed relationships between the child and those around him.

Parental fears and anxieties

When a parent applies or comes to a child guidance clinic for help, he or she has usually been sent by some authoritative person who has informed the parent that her child is in need of psychiatric help.

Most parents arrive feeling on the defensive and often will say that they do not see much of a problem, but that they are willing to go along with so-and-so's recommendations. This defensiveness then is a response to their inner pangs of doubt and guilt about themselves as people and as parents. In treating such parents, one does not hope to agree either with their conscious wish that the problem is slight or with their unconscious fear that it is grave and that they are culpable. Instead the middle road requires as thorough an evaluation as possible of the family dynamics and of the emotional disturbances of the child and of the parents. A summary review with the parents of the diagnostic findings together with recommendations can then be made in a manner that is compatible with their ability to understand what is meant. Usually some of their defensiveness has abated by this time, and they are more ready to look at and work on the difficulties in the home which are reflected in the child.

Diagnosis and treatment cannot be separated in psychiatric disorders. The way in which the whole intake process is handled can be and often is therapeutic in itself since parents appreciate and derive reassurance from the genuine interest shown in searching for causes of the difficulties. The diagnostic process continues throughout the therapy as the interplay of forces is explored and understood. Similarly therapy begins simultaneously with the diagnostic procedures, since one often must deal therapeutically with the fears and anxieties that the parents have about the whole venture of seeking help. Thus treatment and diagnostic inquiry are intimately intertwined.

Treatment in a psychiatric clinic for the emotionally ill child begins in relation to the referral of the child to the clinic. The reactions and attitudes of the parents to the idea of emotional illness in their child and to the recommendation for psychiatric evaluation are characterized invariably by fear or anxiety, the presence of which may be revealed or expressed in many ways. In this study we are concerned with the nature and the initial management of such anxieties as they are expressed in the form of various patterns of "resistance."

Initial resistance

NORMAL, EARLY RESISTANCE. Parents frequently express the idea that they have failed or committed some grievous error which has caused the child's illness, or they may tend to blame someone else for the difficulty. Attitudes such as these may signify one or another of two general types of resistance that may be encountered. The first may be considered as a normal, early resistance which every parent feels in seeking outside help for what he sees as a defect in his child and, even more, as a failure in himself as a parent. Thus the parent is reluctant to accept the pediatrician's or family physician's evaluation of the problem as being primarily emotional and the subsequent referral to a psychiatric or child guidance clinic, even though he may have considerable confidence in the physician. The parent may later be reluctant to follow through on the referral and to go through the various procedures of intake and diagnostic work-up leading to the undertaking of treatment itself. In addition, parents who do seem to accept the referral readily may have followed the doctor's recommendation compliantly, partly to avoid facing their doubts and fears, which, however, are bound to find expression in some less obvious form of resistance.

For example, the mother of a six-year-old girl had been urged by the school psychologist and by her pediatrician to consult the Clinic regarding the child's whispered speech, lack of socialization, and soiling. As the mother herself felt isolated as a newcomer to the community, she misinterpreted her child's teacher's attempts to discourage her overprotectiveness with the result that she hesitated to accept the advice to seek psychiatric help. The child's doctor, however, in observing the mother's inadequate functioning in the home in relation to all of the children was able to convince her of the medical necessity for taking this action.

The important fact to note is that universally parents find it hard to accept the evidence of serious emotional disturbance in their children and, further, to accept the need for psychiatric treatment. There are personal and cultural inhibitions which affect the extent of their initial resistance to such admissions of failure or inadequacy as parents. The very nature of the child's problem may be culturally stigmatized: for example, aggressiveness and violence, which imply the parents' inability to control the child; or withdrawn or bizarre behavior associated with mental illness, which may be seen as being hereditary or as being caused by inadequate parental handling. No matter how concerned the parent is about his child's welfare or how intelligent and well-adjusted and oriented to psychiatric concepts this parent may be, we know that he will have either conscious or unconscious doubts, fears, and misgivings about referral to a psychiatric resource.

Such resistance may be expressed in many ways, either directly or indirectly, so that it may not be apparent to the referring doctor or even at first to the therapist in the psychiatric clinic; it may subside and crop up at a later date, especially if it has not been recognized and handled adequately at the time of referral or in the initial stage of treatment. One parent may argue that his child has had good reason to withdraw or to be rebellious, or that the child will outgrow his problem, or that he would be fine if the other parent treated him differently. As we have seen, the way in which a particular parent shows his resistance to the idea of his child's having an emotional problem and of his needing psychiatric treatment is related to his own personality structure, his own characteristic behavior patterns, and his own way of defending against anxiety.

HANDLING OF REFERRAL. Subsequent treatment can be greatly facilitated by the proper handling of the referral itself, particularly with respect to the parents' negative or mixed feelings about it. Such feelings should be recognized as being universal in parents, whether or not they are expressed openly and directly. The first step in handling them is unavoidably in the hands of the referring person, whether he be the physician, the school psychologist, or another professional or community person to whom the parent has appealed for help. First, he can let the parent know that he realizes it is not easy for him to consider psychotherapy for his child. Second, he can give the parent specific information about how to apply to one or more clinics, in some instances offering to make the initial inquiry for him. At the same time the referring person should promote the active participation of the parent in making his own call—a step which is eventually required of all psychiatric clinics. In discussing the clinic to which the family is being referred, the physician should be careful not to commit the clinic to any particular way of working, nor to lead the family to expect too much too soon. However, the physician may designate the area of help for which they are being referred, while indicating that further exploration will have to be worked out with the clinic itself. The skill with which the referral is made will do much to diminish the initial resistance of the family in getting started with the treatment. In this connection we cannot stress too much the importance of the approach and the attitude of the referring doctor in addition to that of the clinic personnel in these contacts with both parents and child.

To return to the example of the six-year-old child with whispered speech, general lack of socialization, and soiling, the referring doctor had already developed considerable interest in the family's children as well as respect for the mother as an intelligent, responsible person. He accredited her strengths and recognized her burden and frustration in the child's failures in toilet training. The doctor then called the clinic to determine how soon the family could be seen and subsequently gave the mother the name of the social worker to whom she should speak, indicating that he had already told this worker something about her child. He also prepared her for the fact that there would be several weeks delay before an appointment could be given and that in the meantime he would send a written report to the clinic. The doctor also reassured her as to the value of the school report, as requested by the clinic, even though she had felt rejected and misunderstood by the teacher, who had criticized, perhaps too directly, her handling of the child. Thus the mother used the support of her doctor in taking the necessary steps to bring her child to the clinic.

GREATER UNDERSTANDING OF PARENTS. The Clinic staff is frequently called on by referring physicians and others in various professions for assistance in using constructive attitudes toward a greater understanding of parents of children who are showing evidence of emotional problems. In other instances[3] and as noted in *Action for Mental Health* (the final report to Congress of the Joint Commission on Mental Illness and Health), a great many physicians still do not recognize emotional problems or attempt to treat them, seeing them as an "enigma," being indifferent to them, or actually rejecting patients with such problems.

A generation ago many subscribed to the maxim: "There are no problem children, only problem parents." Today we stress parental responsibility, but also show real acceptance of parents themselves, accrediting their strengths and potential. As Hamilton[4] has said, "the essence of the therapeutic aim is to approach the parents, not as obstacles to the child's progress which must be smoothed away, but to enlist them in the search to remove obstacles in the child's path." For example intake interviews recently held in this Clinic for a professional man and his wife as part of the treatment plan for their thirteen-year-old son revealed a severe emotional disturbance in the father characterized by emotional instability with temper tantrums and depressiveness, extreme dependency needs, strong feelings of inadequacy, and almost complete incompatability with his son. However, he was able to participate in the intake interviews only in terms of what he called "the needs of the family" from which at that time he could not isolate himself as a disturbed and disturbing person. Another father and mother were seen for intake interviews at the urgent request of the father because he had learned that his fourteen-year-old daughter had been stealing money in nearby apartments where she had been baby-sitting. In his initial application telephone call he stated that his wife had told him that she would have nothing further to do with the child and that he should "send her to a home." As the parents were interviewed, it became apparent that the father had gradually usurped certain of the mother's prerogatives in her relationship with her daughter, but he was evasive about the patterns of his behavior which eventually led his wife to withdraw from any disciplinary efforts for the child. In this case also, the father needed to shift the responsibility for the problem to his wife because of his own emotional immaturity.

INTAKE INTERVIEW. In recognition of the importance of initial parental attitudes, experience in this Clinic has shown the wisdom of planning and conducting the preliminary or intake interview with great care based on what is learned from the application data. For this reason procedures now to be described are generally utilized for this purpose with such flexibility as may be most useful in the individual case.

At the time of the intake interview the parent or parents are seen briefly first by the physician-in-charge after which they are seen for a more prolonged interview by the psychiatric social worker who discusses the problem in regard to certain aspects of it as follows:

1. A brief descriptive evaluation of the relative.
2. The nature of the problems and their significance from the relative's point of view.
3. Efforts made to cope with the problems to date.
4. An assessment of relative's motivation for treatment.
5. A brief survey of significant factors in the social history if the relative is not to be available for further interviews.
6. The securing of signed waivers for obtaining and releasing clinical information re child patients and the "consent form" for any unmarried patient under age twenty-one (New York State legal ruling).

Following this interview a staff conference is held for the purpose of determining the advisability of further clinical service and the financial eligibility as well as formulating a preliminary diagnostic impression.

The parent is then recalled from the reception room for a "report interview" in which the results of the conference are discussed and plans are made for either a diagnostic study or another appropriate disposition. If the child is accepted for further Clinic service the next step is a diagnostic study and trial of treatment leading to an evaluation conference and, again, a decision relative to continued treatment or other recommendation. It is during this trial-of-treatment period that evidence of the second type of "resistance" begins to be apparent and efforts are made to understand and resolve it.

Resistance in treatment

RESISTANCE TO INTROSPECTION. That resistance which is described most frequently and fully in the psychiatric literature develops within the treatment situation and represents the "internal struggle of a patient against the emergence of unconscious material."[5] The resistance to the treatment itself is a peculiar facet of psychotherapy having no precise analogue in other medical therapies. The patient's reluctance to reexperience in his conscious awareness certain painful emotional reactions associated with previous experiences leads him to oppose or sabotage the treatment which he supposedly desires. Furthermore, since the patient must participate actively in the treatment process, he is in the best position to do this. Psychotherapy in contrast to other medical therapies is not something that can be done to someone. With the therapist's help the patient must engage in an introspective analysis of himself, and he may not like what he sees as he begins to understand himself in his relationships with others. It is this phenomenon, which during the course of treatment makes it difficult for a patient to change his patterns of behavior or emotional reactions, which may be pathogenic and instrumental in the development of a child's illness. Freud[6] identified this reaction technically as "transference resistance," since the patient at first tends to attribute the sources of his disturbed feelings to the therapist until he can tolerate them as representing painful parts of his own experience. He expects the therapist to respond to him as did his mother or father or other significant persons in his past life, that is, with rejection, ridicule, criticism, hostility, dependence, seductiveness, and so forth. This reaction has also been referred to as "everything that prevents the patient from producing material derived from the unconscious . . . ,"[7] and Sullivan[8] has referred to such unpleasant repressed and forgotten memories as the "not—me."

PATTERNS OF RESISTANCE. Uncovering such tender areas in a patient's personality inevitably results in discomfort for him so that treatment is continuously in a state of flux or dynamic balance between two opposing forces: (1) the patient's positive strivings to change, to grow, to feel less at odds with himself, and to be free of his symptoms; and (2) his need to preserve his neurotic system of compromise, to maintain the reassuring effects of his defense mechanisms, and to avoid the painful anxiety of re-experiencing earlier inner conflicts. His resistance may be seen in many forms such as refusal to talk, withholding information, talking too much and in circumstantial or irrelevant ways, forgetfulness, flattery or the reverse, including criticism and antagonism, and in more subtle ways. The patient may express doubts, blame others, or engage in intellectual rationalizations and other philosophic excursions. He may "act out" his resistance by forgetting or cancelling appointments, by being late, or by suffering from various physical symptoms. Such "resistance" patterns may also be seen for brief periods at any time during the course of therapy and frequently will tend to recur temporarily under stressful circumstances even though significant progress has been made in reducing or eliminating them as habitual reactions.[9]

Let it also be noted that each patient has certain expectations and fears of the therapist which are unique to him, and therefore these transference feelings are especially indicative of the kinds of emotional relationships which the patient has had and which have determined the quality of his personality.

In general it is necessary to recognize and to eliminate the resistance symptoms as "the essential work"[7] of the treatment and to do so as soon as possible. This involves psychotherapeutic skill as well as careful attention to timing, as illustrated in part by the following case references having to do with initial phases of treatment:

A thirty-four-year-old woman recently came into treatment in connection with treatment for her nine-year-old stepson because of his withdrawal and excessive daydreaming. She has two children from her first marriage, which ended in divorce shortly prior to her second marriage about four years ago to a widower with two children. Early contacts at the Clinic with this family suggested the possibility of underlying marital conflict, and it was felt therefore that separate therapists for the parents would be preferable.

Although the necessity for regular clinic contact of parents of children in treatment had been discussed with her at intake, the patient indicated her resistance to this at the beginning of her first regularly scheduled contact. In essence she stated that subsequent to having made arrangements for this appointment she had felt troubled all week about why she was coming in, and she denied that she had been informed earlier that she was to be involved in regular contacts. She had no objection to coming in occasionally to discuss material directly relevant to her stepson, nor did she have objection to her husband's regular contacts. She indicated that previously, when her stepdaughter had been in private treatment, her husband had participated in the treatment, but she had not been included. She also mentioned that in connection with problems with her stepdaughter she herself had sought help at a family agency because she had felt the need for this, but basically she had no problems in handling her stepson as he was a good, quiet child and she did not feel the need for help except for some occasional advice. Some of the factors discussed with the patient throughout the course of the interview in an effort to handle her resistance were: (1) the therapist's recognition of her anxiety and the overt reasons for this, such as her not having understood that she was to be involved on a regular basis and the fact that she had not participated actively in her stepdaughter's treatment; (2) clarification of the rationale for including regular participation by one or both parents as part of treatment for the child; (3) the relationships between the child's symptoms and problems within the family; and (4) her extreme anxiety as an indication of probable fear of discussing her own feelings and problems. Although at the end of the first interview the patient agreed to continue regular weekly contacts, both she and the therapist were aware that by no means had this initial resistance been worked through thoroughly.

The second interview, in contrast to the first, presented little evidence of resistance in the patient and, in fact, indicated a beginning involvement of herself. This turn of events appeared to be related significantly to the therapist's questioning her fairly early in the interview as to whether or not her husband was as ready to listen to her problems as she had reported she was always ready to do with him or with the children. This question led to the discussion of how some of her needs were not met by her husband, a discussion of the fact that her children had a right to something as well as his children, and, most significantly, an admission that because she has extended herself constantly for her husband's children some of her initial resistance to involvement at the Clinic was related to this effort which was becoming intolerable—this was a continuation of extending herself for his children and perhaps she had had enough of this. The patient concluded the second interview by stating that she usually never spoke as much as she had just done and that she enjoyed talking to her therapist.

In the third interview, although the patient manifested some difficulty in getting started she soon became involved in meaningful discussion. Resistance came to the fore, however, when the therapist asked for some information concerning her first husband. Even though she had just been discussing many factors concerning her first husband prior to this inquiry, she indicated that she had no objection to discussing him, but she did not see how this could possibly have any relation to her stepson, and she felt this was an area of her life that was "over and done with." Thus, as suggested earlier, despite evidence of a beginning involvement of the patient, deep-seated resistances were still very much a part of the picture, requiring continued treatment effort.

In a second case, a mother applied to the clinic for treatment for her seven-year-old daughter who was completing the first grade. The school principal had suggested treatment in a psychiatric clinic because of the child's performing below her intellectual ability as well as her need of constant praise and reassurance. The mother stated that school testing showed that her child was intensely jealous of her younger sister. In the parents' initial clinic contacts—the mother on the telephone, then both parents coming in together and separately—they made every effort to be cooperative in answering questions about the child and about the family relationships. However, it soon became apparent that their initial resistance to personal involvement had caused them to be extremely guarded in revealing significant family history, including the fact that the child had been conceived prior to their marriage. Also, in the initial presentation of themselves as good parents, with a child whose emotional problems must have sprung from sources outside the family, they attached considerable significance to the child's recent change to another school (because of rezoning) and the fact that this change had separated her from her friends. As soon as the father was seen alone, he revealed his conviction that there was really no problem regarding the child's emotional health and that the current difficulties could be resolved by firmer and more consistent discipline on the part of the mother. It was apparent that both parents were guilty and frightened at the thought that they had produced and reared a child with severe emotional problems. The mother, in panic, called for immediate tangible help: "Return Sally to her original school," "tell me what to say or do" in this or that situation. The father refused to admit that the child was sick. Each parent in his or her own way was showing resistance to the initial laborious and tedious, but very necessary, process of engaging themselves in the revelation of significant data about the child and her family. The therapists, in their early contacts with these parents, recognized how hard it was for them to think of their child being so disturbed, commended them for seeking help, and gradually interpreted the significance of the personal and family information which they were beginning to reveal. In the nonjudgmental and understanding atmosphere of the therapeutic interviews, the parents were gradually able to move into clearer focus and more constructive patterns of reaction in their individual roles as parents as these were seen to relate to the child's problems.

Resistance in the child

Our attention so far has been addressed primarily to resistance factors in the parents' reactions to psychiatric help, but brief mention should also be made of the presence of resistance symptoms in the child as well.

The child patient always has resistance. He did not want to come for treatment in the first place. He was brought, unlike the adult patient who comes because he wants help for himself. The adult patient can see that looking at and working on the things that trouble and upset him will make him happier and better in the future. The child has no such orientation. He knows that talking or thinking about his problems and his discomfort is painful and unpleasant and therefore to be avoided. The child seeks to avoid pain and to gain pleasure or current satisfaction. He does not have the capacity to tolerate present discomfort in the prospect of achieving some future gains or happiness. The child lives in the here-and-now and needs help to approach the sore spots that cause him pain. As he sees in his therapist an ally and a friend, he will gradually accept some discomfort and distress and be able to talk about his troubles. He will also express his buried feelings through various media, that is, play therapy, and come to understand his fears and hates, his wishes and needs. Gradually through the corrective emotional experiences of relating to an accepting and helping parent figure and through increased understanding, he will be able to try out new, more healthy ways of behaving and to give up the fixed pathologic patterns of the past.

A single brief example of resistance symptoms in the child follows:

A child, age seven (to whom we have referred in connection with the resistance of parents), was from the beginning quite active in her play and in her talking with the therapist. However, she did not talk directly of her day-to-day concerns. Much of her activity was used as a smoke screen to prevent the therapist from getting too close to her and to her conflicts. When the doctor raised questions which might be threatening to her, she retreated into play. As seen in her parents, the child used denial as a means of resisting coming too close to problem areas. At times, when the doctor would try to draw her out as to why, for example, she was quiet, she would be evasive in her responses and become preoccupied with a game such as Chinese checkers. Also, symbolic of the child's fear of greater involvement has been her frequent burial of herself in a comic book while waiting for the doctor to approach her in the reception room, at the same time cautiously peering at him from behind the pages of the book. With this child, however, a marked change occurred when she was told of the death of her previous therapist—a fact which had been withheld from her, but which she had vaguely suspected. It was then observed that this freed her to communicate more freely with her therapist and more rapid improvement ensued.

Summary

In considering the general nature of emotional illness in children, a discussion of the principle types of "resistance" symptoms has been presented together with illustrative case material. Emphasis has been placed on the importance of the recognition of symptoms, the manner in which the referral is made in relation to initial parental reactions, and the technics of psychotherapeutic management in clinic practice of the initial resistance during intake visits and of the subsequent "transference" resistance encountered during the early phases of treatment.

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Epithelioma from Single Trauma

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ALTHOUGH THE FIRST SPECULATION about the role of trauma in the appearance of cancer was probably prehistoric, the first report of such an association was in the year 1676.[1] In that year, the great English surgeon, Richard Wiseman, reported 2 cases in which cancer arose at the site of a contusion.

The next two hundred years produced great physicians, but their opinions on the question of trauma and neoplasm could hardly be valid, because the differentiation of cancer from other diseases was inaccurate and the collection and recording of clinical data was scanty. It is sufficient to say that most physicians came to believe that, in some instances, a single injury could result in the development of a malignant tumor. The general public accepted this idea wholeheartedly, just as it does today.

With the work of Rudolf Virchow everything changed. Advances in cellular pathology made the differentiation of cancer more accurate. The appearance in 1863 of Virchow's theory of chronic irritation as a cause of cancer, which was followed soon by Cohnheim's embryonal rest theory, the discovery of spontaneous tumors in laboratory animals, and the surprising fact that they could be transferred, so caught the imagination of the medical world that ideas concerning the connection of simple trauma and cancer seemed unimportant.

At this point, politics took a hand.

Effects of the industrial revolution

The industrial revolution came late to Germany, and its abrupt appearance and rapid development were accompanied by great social upheaval. In addition, by this time the theories of Karl Marx were mature and influential. Faced with such great danger from the left, Chancellor Otto von Bismarck, in an attempt to forestall a dictatorship of the proletariat, sponsored a series of welfare measures which were extremely advanced for the time. The second of these, adopted in 1884, was the Accident Insurance Law, a form of workmen's compensation insurance, paid for entirely by the employer, which covered almost all wage-earning groups.

The question of trauma as a cause of cancer was no longer academic. This new social legislation so aroused interest in the trauma-cancer problem that in the thirteen-year interval from the passage of the Accident Insurance Law to the year 1897, some 2,000 books and papers on the relationship of trauma to tumor formation were published in Germany alone.[2] Many of these publications reported high percentages of cancer arising from injury. By 1900 the crowded court calendars and the mounting confusion in both legal and medical minds over the extent of the employers' responsibility made it clear that something had to be done.

The turning point in evaluating the factor of trauma was reached when von Buengner[3] proposed the standardization of statistics regarding trauma and obtained and published reports from many large German clinics for five-year periods. The effect of this was to reduce immediately the number of reported cases in which trauma was alleged to be responsible for a tumor.

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THE QUESTION *of the role of trauma in the appearance of cancer is a controversial one which is particularly important in workmen's compensation cases. In 1901 the following criteria were established for evaluating the factor of trauma as a cause of skin cancer: previous integrity of the traumatized part; adequate and authenticated trauma; positive diagnosis of a nonmetastatic carcinoma*[3] *origin of the carcinoma at the exact point of injury*[3] *reasonable time interval between trauma and the appearance of the carcinoma; and continuity of signs from trauma to the appearance of the carcinoma. Satisfactory proof for or against the proposition that single trauma can cause cancer is lacking, but the use of the preceding criteria is recommended, and further research using animal experiments and clinical studies is suggested.*

Criteria for establishment of trauma as cause of skin cancer

Jordan, in 1901,[4] was the first to propose postulates which must be fulfilled before a neoplasm could be ruled the result of a single injury. Löwenstein[5] modified these for the use of the German compensation boards. The enactment of compensation laws came much later in the United States, but when they began to appear about 1913, they brought with them the same problems that had attended their passage in Europe, and the same remedies.

Mock and Ellis[6] were chiefly responsible for introducing the German criteria into this country, and they were ably assisted in popularizing them by such eminent authors as Ewing[7] and Knox.[8] These criteria appear in many variations. We present them here as a composite, drawn from several sources.[4-8]

PREVIOUS INTEGRITY OF THE TRAUMATIZED PART. Previous integrity would seem to be the most critical fact to be established. The whole problem revolves around it. But in dermatologic cases, evidence of the skin's complete integrity almost never exists. In practice, the courts often consider it an unreasonable requirement if all of the others have been met.

ADEQUATE AND AUTHENTICATED TRAUMA. Adequate trauma is generally considered a degree of trauma sufficient to produce objective changes, changes which can be seen or felt. The presence of such signs should be authenticated by trained medical personnel.

POSITIVE DIAGNOSIS OF A NONMETASTATIC CARCINOMA. Clearly a certain diagnosis of carcinoma must be made if an award for carcinoma is to be made. The tumor must be of a type which could reasonably arise from the tissues of the injured part. The localization of metastasis in injured tissue is another problem entirely, but by definition metastatic lesions do not take their origin from the tissue in which they are found and, therefore, are not caused by injury to that tissue.

ORIGIN OF THE CARCINOMA AT THE EXACT POINT OF INJURY. The need to establish the origin at the point of injury is self-evident and of great importance in dermatologic cases. It points up the need for medical personnel in industrial facilities to record the location of even trivial injuries with great precision.

REASONABLE TIME INTERVAL BETWEEN TRAUMA AND THE APPEARANCE OF THE CARCINOMA. Determination of the time interval is the most inexact criterion of the group. Maximum times have been set by various authors, but they have no basis in fact and are better ignored. Minimum times are more important. Obviously, an epithelioma 1 cm. in diameter, for example, which was discovered two days after an injury antedated the injury; epitheliomas do not grow that quickly. The generally accepted minimum time limit for the appearance of carcinoma, first set by Thiem,[9] is three weeks.

CONTINUITY OF SIGNS FROM TRAUMA TO THE APPEARANCE OF THE CARCINOMA. Continuing signs are the so-called "bridging signs" which several authors feel make a stronger case for the traumatic origin of a neoplasm. Their presence may increase the likelihood that the relationship of initial inflammation to final tumor is one of cause and effect, but they are not considered essential by the courts.

The weaknesses in the criteria proposed and the difficulty in interpreting them are well known to all concerned. Nevertheless, they are of great importance and represent the best means available, at present, for preventing post hoc ergo propter hoc reasoning from being substituted in the courts for an objective search for the truth. They have been effective in reducing the number of cancers attributed to trauma from estimates as high as 50 per cent in a pre-1900 series[10] to the point where even enthusiasts consider injury only as an uncommon cause of cancer.

Case reports

Two case types with variations present themselves to the dermatologist. The following are examples of these:

Case 1. A forty-five-year-old steelworker was seen in October, 1959, and found to have a basal cell carcinoma on the right cheek which he said had appeared four months earlier. He stated that it began at the site of a blackhead he had squeezed. A biopsy was taken, and the tumor was destroyed by curettage and desiccation. On the second follow-up visit, four weeks later, the patient "remembered" that one week prior to the appearance of the lesion, he had been struck on the exact site by a hot steel chip while working, but had not reported it, as it seemed trivial at the time.

Case 2. In September, 1959, a fifty-three-year-old steelworker was struck on the forehead by a piece of hot slag, sustaining a third degree burn 0.5 cm. in diameter. He was seen immediately at the plant dispensary, where he was given an ointment containing neomycin for topical use. When the lesion failed to heal in a three-month period, while the patient was under constant observation by plant physicians, a biopsy was taken which showed a basal cell epithelioma.

Case 2 meets with all but the first criteria and will usually be awarded compensation, at least in New York State. The claim of Case 1 will usually be denied.

Although these criteria have been established to deal with the problem in a practical way, there are other considerations in the scientific investigation of the evidence for and against the proposition that a single injury can produce a malignant tumor.

Arguments for and against proposition that trauma can cause cancer

For the proposition. The case for the proposition rests almost entirely on clinical reports of time relationships and localization; that is, the time of cancer appearance after injury and cancer appearance at the site of injury. There is no denying that these associations are sometimes strikingly in favor of the proposition. Unfortunately, most of the case reports of this sort are worthless, in that they claim trauma as a cause on the basis of the unsubstantiated history of the patient; they are often prepared and presented with no greater care than the "bruising" report of Wiseman three hundred years ago. It was the preponderance of this type of paper which led Askanazy,[11] a few years ago, to label the whole literature on the subject "a collection of anecdotes." But, aside from these unreliable reports, there are still numerous instances of cases which fulfil all but the first of the criteria, and a few which meet all the criteria.

Against the proposition. The evidence against the proposition can be divided into experimental and indirect.

A number of experimental attempts have been made in the laboratory to produce a cancer in animals by crushing, burning, and otherwise injuring various tissues.[12,13] They have failed; however, in 1931[14] Slye reported the occurrence of malignant tumors arising at points of injury in a strain of mice so highly cancer-prone that practically all of them developed malignant tumors eventually. The injuries were not produced experimentally but were inflicted by the bites of cage mates. The value of Slye's observations in demonstrating trauma as a cause of human cancer or even as a cause of ordinary mouse cancer is highly questionable.

The indirect evidence against the proposition is mostly of a statistical nature. Large studies carried out on injured persons after World War I indicated no increase in the incidence of cancer among them.[15] A similar study has been carried out on individuals injured in sports,[16] likewise showing no increase of cancer in those sustaining injuries. In justice, it must be said that these reports may only indicate that cancer from a single injury is very uncommon.

Thus, with no wholly satisfactory proof available to either affirm or deny the proposition, we are left with two opinions, opposite in nature.

First opinion. A number of clinicians,

impressed by the remarkable time and localization coincidences present in certain cases, conclude that trauma must be considered one of the uncommon causes of cancer. In a much more partisan spirit, compensation attorneys, union officials, and those in general who are expected to do what they can for the worker, tend to believe that a cancer arising at the site of any injury claimed by the worker is caused by that injury until proved otherwise. Negative animal experiments and the failure of physicians and other scientists to explain how trauma might cause cancer have nothing to do with the questions, or, as one group recently put it in the emotional language that sometimes appears in discussions of this problem, "The shortcomings of the medical profession are not to be visited upon the victims of industrial accidents."[17]

SECOND OPINION. The majority of workers in the medical fields, at least those who write, are much more skeptical. With no valid experimental evidence to go by and clinical evidence which is little more than suggestive, they feel that the burden of proof must be on those who seek to establish a connection between a single injury and the appearance of a malignant tumor. Cases presented as traumatic cancer almost always involve a form of post hoc ergo propter hoc reasoning which is unacceptable from the scientific point of view. However imperfect the criteria outlined for the evaluation of these cases may be, they should be followed as rigidly as possible, for they represent the most nearly rational approach to the problem now possible.

Proposals for future research

Research is needed to settle this problem. By present-day standards, the animal experiments previously reported are neither extensive enough nor satisfactorily designed, and they should be redone. Among other things, animal experiments should study the types of atypical overgrowth arising after trauma of various organs, the effect of trauma on various preneoplastic and neoplastic as well as nonneoplastic tissues, the production of growth-stimulating substances by trauma, and the chromosome numbers of normal, traumatized, and neoplastic tissues.

In addition to further laboratory studies, more clinical studies are indicated. Although pre-employment physical examinations and periodic re-examinations with the frequency and precision necessary to yield useful data on the association of trauma and cancer would be impractical as a routine, a pilot study of this type in a selected high-risk industry might yield useful information by recording and following each trauma sustained. Such a study would provide a forward approach rather than the backward historical approach which is used now in case reports to associate tumors with antecedent trauma.

What can be expected from new studies such as these? If, in fact, a single injury can cause a malignant tumor, we can conceive that experiments may be designed which will prove it, perhaps along the lines we have suggested. But if the truth is that single injury cannot cause a malignant tumor, we see little hope in the present imperfect state of science and society of ever establishing such a fact to the satisfaction of everyone. The objections peculiar to negative experiments of this kind will always be present; that is, that the exact conditions which existed when a particular trauma affected a particular worker on a particular spot were not duplicated. It may be that the relationship of trauma to cancer will be explained not by experiments designed to study this specific problem, but rather by an overwhelming clarification of the etiologies of malignant conditions which will appear with continuing basic cancer research.

Summary

1. Historical and sociologic aspects of the problem of the relationship of trauma to cancer are reviewed.

2. Criteria for the establishment of trauma as a cause of skin cancer are presented.

3. Scientific evidence for and against the proposition that trauma can cause cancer is reviewed.

4. Proposals for future research to evaluate trauma as a cause of cancer are made.

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Discussion

HERBERT L. TRAENKLE, M.D., *Buffalo, New York*. Dr. Stoll and Dr. Crissey are to be commended for giving us an historical review and bringing up to date a discussion of this controversial subject.

The results of oncologic investigation, thus far, seem to indicate that neoplasia in any tissue is produced by a constellation of factors, rather than by a single "cause." Thus, the pertinent question here is whether or not trauma of any kind is a factor in the production of cutaneous cancer.

For many years, it has been assumed that chronic irritation, whatever that means, is in some way carcinogenic, and indeed some empiric observations appear to lend support, at least superficially, to this idea. Up to now, however, there is very little, if any, scientific evidence to confirm this concept.

However, recently, perhaps since this paper was written, two investigators reported before the American Academy of Forensic Sciences what they believe is experimental evidence that repeated injury can accelerate the induction and production of mammary cancer in mice. They suggested that trauma may act as a co-carcinogen. Whether or not these findings will be confirmed by others and whether or not such data have any implications regarding human skin are of course as yet unknown.

I am not too much concerned with the fine distinction between so-called single trauma and repeated trauma, or chronic irritation. In many circumstances, such differentiation becomes merely a matter of semantics. For instance, many of us have been confronted in court with the arguments centering around a carcinoma allegedly originating in a nonhealing ulcer produced by a single blow or burn. Is this single trauma, or is the ulcer itself to be regarded as a form of chronic irritation? Time does not permit referring to other examples of the difficulty in definition.

Investigation along the lines recommended by Dr. Stoll and Dr. Crissey is to be encouraged, for it could produce additional data on carcinogenesis as well as the factual knowledge necessary for a rational analysis of litigation claims.

Also, a very essential addition to the present juridical machinery would be the establishment of an impartial panel of experts. Only through such a device can new scientific evidence be utilized in an unbiased fashion. Informative studies are of little medicolegal value if their results are distorted and exploited by one side or the other. It is encouraging that in some regions of the country, such panels are already being tried.

Reflections on Clinical Bacteriology

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I FIRST MET Augustus B. Wadsworth, M.D., in 1922, when he took the trouble to visit me in my laboratory in the University of Cambridge. He came unannounced and told me he wished to talk about the meningococcus. That pleased me as I was at that time taken up entirely with the vagaries of the meningococcus, and it was a treat to discuss the subject freely with someone so well informed and interested as I found Dr. Wadsworth to be. After all, that was to be expected since among his varied contributions to our knowledge was the production and standardization of antimeningococcus serum. And so we spent a very pleasant day that gave me a lasting friendship.

There are many people one meets and quickly forgets, but a few carry some quality that memory never releases. Dr. Wadsworth had many striking attributes and in this place, the site of his outstanding constructive work that is worthily his monument, I don't have to remind you of his strength of character, decisive organizing ability, quick appreciation with a stimulating grasp for the development of research ideas, and of his searching evaluations, all of which were abundantly evident in the easy clarity with which he expressed himself.

But it did seem unnecessary that one so gifted should in addition have a lively manner of light conversation and a strikingly handsome form and demeanor, so that at meetings of societies we other mere ordinary men were jealous. One sometimes wondered, perhaps a little enviously, how his parents ever knew he should be called Augustus.

I am happy to take part in this tribute to the memory of Dr. Wadsworth, and since our conversations often explored the place of the bacteriology laboratory in clinical medicine and because of his interest in diagnostic services, I thought some musings on clinical bacteriology would not be too much out of place.

Functions of bacteriologic laboratory

What is to be expected of the bacteriologic laboratory will depend on whether you look at it from the laboratory end, faced with a specimen collected from an unknown patient and incompletely documented, or whether you view it from the ward, at the bedside of a patient whose condition is not yet diagnosed. The bacteriologist's attitude is colored by the knowledge that the foundations of bacteriology were laid in the clinical laboratory, and that it is still there that the exact diagnosis of infectious disease is made; also that the treatment and management of cases and the prevention of spread of infection are all based on discoveries made in the laboratory.

The clinician, on the other hand, aware of these truths, merges them in a vague mist of history and requires laboratory examinations or tests as aids to diagnosis; and thereafter he believes the case is entirely subject to his knowledge of drugs, diets, nostrums, nursing, and even psychiatry.

In their narrowness both are wrong, and where there is conflict between them progress is impeded or even prevented. Conflict between the laboratory and the ward is not a mere fable, although in well-organized hospitals it is conspicuously reduced today.

Cooperation has been promoted most markedly by the adaptability of bacteria to

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accommodate themselves to circumstances and to take advantage of weaknesses in the technics of our defensive measures. The clinician and the bacteriologist have been brought together by the need to observe the ever-changing sensitivity of pathogens to a multitude of antibiotics and by the prevailing furor over hospital infections.

The contention can arise or be fostered from either end, and sometimes it is fun and games, sometimes malice, and sometimes misunderstanding or stupidity. When I was a young pathologist at Barts (St. Bartholomew's Hospital, London) I remember Dr. James Calvert, writing his clinical diagnosis boldly at the head of the case history and then saying "Now let us see if those gentlemen in the laboratory can confirm our diagnosis."

Very many years later in Montreal I got a letter from Sir Leonard Colebrook, telling me of his work with prontosil on streptococcus and pneumococcus infections, and he sent me some of the drug. I told my clinical colleagues about it, and their immediate response was "Won't that be fine; we shall be able to do without bacteriologists."

This attitude expanded with the introduction of antibiotics to the extent that bacteriologists were eliminated as examiners and bacteriologic questions were reduced to absurdity in the examinations of a number of licensing boards of the United States and of Canada. But this derogation of bacteriology in the practice of medicine, manifestly absurd to start with, is now brought into disrepute by daily procedures everywhere.

However, there is a varying measure of discord between ward and laboratory that grows from an insufficient standing and authority accorded to the bacteriologist and an overweening arbitrariness of the clinician, who alone requisitions on the laboratory. Many bacteriologists and clinicians do not realize how much there is to be learned through consultation at the bedside. To appreciate the varied manifestations of any disease the bacteriologist needs the clinical circumscription of a disease entity and the complicating influences of other disabilities that vary from case to case; and the clinician needs more than the etiologic recognition. For the peculiarities of species and strain of pathogen, the characteristic sites of localization in relation to stages of disease, the possibilities of cellular and immunity responses of the patient, and the interpretation of drug sensitivities of cultures, among other things, all contribute to the proper selection of treatment. But consultation is also well advised before a diagnosis is made, to decide on the way to collect the best specimen for the detection of a suspected kind of infection or for the investigation of a baffling case.

I have received a drop of dried up blood on a slide with the request for a total blood count, a blood culture, and a Widal test! At the same time odd things are worth trying, for I have recovered typhoid bacilli from small samples of blood in capillary tubes sent in for a Widal reaction, and spore bearers are not always killed when they have been gram-stained on a slide. But these are curiosities that should rank as amusements.

In many instances strain with the clinician may be aggravated when the bacteriologist lacks medical training, however competent he may be in the biology of bacteria themselves. This makes his understanding of the clinical problem difficult, and his want of training in pathology seriously limits his interpretation of the process of disease in the patient. Consultation at the bedside is then both reluctant and unfruitful, and to such discouragement you may add the jealous prerogative of medical qualification.

I am convinced that the important work of the bacteriologist for the advancement of our understanding of the processes of infectious disease starts after the diagnosis is made. But this is not a completely independent undertaking, and it is all too seldom that there is thorough correlation of the bacteriologic, pathologic, biochemical, and clinical studies of cases. This results in great individual loss to each of the methods involved, for only their combined aspects truly picture the disease.

It is important to remember that the presence of a pathogenic microorganism is not necessarily accompanied by disease of the host and that disease is a state of illness of the entire patient, in which secondary effects may be paramount in determining the outcome, however essential the specific pathogen may be to initiation of the process.

Need for adequately trained bacteriologists

No one in his senses would disparage or deny the extensive and significant contributions nonmedical bacteriologists have made to the study of infectious disease. But Burnet's thoughtful observation in 1953 is still true, that "The advances in the last twenty years have not been so much in the understanding of the processes of infectious disease as in the provision of agents of extraordinary efficiency for dealing with its practical problems." This rebuke applies most forcefully to those who are medical bacteriologists, whose training should fit them and attract them to the solution of so urgent a problem; but it also points to the limitations of nonmedical bacteriologists.

In the light of what I have said, I condemn those clinicians and hospital administrators who believe that the simple identification of pathogens or the titration of a serum as a diagnostic aid is all that is required of a laboratory, and that this is prefectly satisfactorily done by a technician. There are hospital laboratories in the charge of a technician of limited experience and practically no foundation in bacteriology: of such are the American and the Canadian so-called "medical laboratory technicians," who have been taught a few restricted methods for the recognition of certain common pathogens. This kind of clinical bacteriology is too limited and too unreliable and has brought disrepute to bacteriology. I would much sooner rely on an intelligent guess by a good clinician than depend on the false security of inadequate bacteriologic methods guided by a dangerous "little knowledge." Thus it does not suprise me that on the average the bacteriologist is given less standing and recognition in hospitals than is the pathologist.

It is true that it is difficult for small hospitals to provide for needful bacteriologic work, and sometimes the control of it by the pathologist is not sympathetic or understanding; but perhaps the prevailing scare over hospital infections will promote a scheme and funds for improvement.

In some places public health laboratories are trying to fill the gap by providing a diagnostic service or even attempting the supervision of hospital technicians; this, in a measure, supplies the clinician with the aid to diagnosis he requires. It does not promote the desirable bedside consultation, neither can it control the day-to-day problems which arise, nor can it adequately develop the investigative urge that is so desirable. In rare instances the public health service can insist on standards and have powers of control such as I have heard Dr. Wadsworth expound, but even that requires properly staffed local laboratories to be effective.

The extension of bacteriology into office practice is more difficult, although it is as necessary as it is in the hospital. There are some practitioners who use it extensively, but it needs some encouragement from the laboratory. It is quite likely that the lack of appreciation is because the application of bacteriology to the patient is rarely taught by the bacteriologist in the clinical years in medical schools, and so the subject becomes relegated, in the student's mind, to the limbo of finished things, and few clinical teachers will disabuse them.

Importance of clinical bacteriology

Perhaps more interesting than these generalizations would be instances that have influenced my way of thinking, or which indicate that clinical bacteriology retains an importance greater than some people allow, or which illustrate the ill effects of ignorance or neglect.

In 1916 I was sent to Mesopotamia (now known as Iraq) and posted as bacteriologist to the 33rd British General Hospital at Ashar, near Basrah. The commanding officer received me enthusiastically and took me at once to the laboratory. The whole hospital was under canvas, and one large E.P. tent had a conspicuous label "Laboratory"; inside it was a small folding camp table placed at the little mosquito net window, and on the table was a small folding microscope which belonged to the commanding officer, a small bottle containing a little smear of brownish powder and labeled "Methylene Blue," three very scratched slides, and one coverslip. There was nothing else at all. Having found a piece of thin iron wire I twisted it around a sliver of bamboo and made a loop in the end; at least I had a simulacrum of the emblem of the bacteriologist. I returned in about an hour, after arranging my own tent, but I could not enter the laboratory tent easily for covering the entire floor and out through the two entrances were bedpans, a pavement of bedpans. The requisitions on them read: "query cholera," "query typhoid," "query bacillary dysentery," "query amoebic dysentery." There were a few smaller articles that turned out to be blood smears for malaria and tubes of blood for Widal tests. The demand was great for aids to diagnosis, without any realization of what was needed for it.

Later I moved to the 3rd British General Hospital in the Palace of the Sheik Mohamrah at Basrah, where there was a laboratory that lacked much but where something could be done. The temperature outside rose to from 120 to 130 F. in the shade, and in the laboratory it rose to 140 F. because of the primus stoves used to heat the sterilizers and the homemade still. So you covered your cultures with wet cloths to keep them cool and alive, no incubator was needed, and there was no ice in the whole country.

There was much to interest a bacteriologist, and I still have the cultures I collected there and later used for the serologic classification of dysentery bacilli. Mesopotamia was a dangerously and amusingly interesting place, and when I retire again I may develop a "cacoethes scribendi."

Before the days of "wonder drugs" all cases of subacute bacterial endocarditis died, whether they were due to the viridans or to the enterococcus groups of streptococci. I thought I would titrate the bactericidal power of the blood in a number of such cases and found it increased greatly as the disease progressed. Toward the fatal end the patient's freshly drawn blood when it was allowed to clot, would kill not merely the bacteria it contained but also large numbers added from a freshly isolated culture.

A young moribund man was a volunteer in the Black Watch, and two of his regimental comrades came to the laboratory every day to be bled, so that I could put 200 cc. of fresh serum a day intravenously into the patient. This was to supply complement, as I do not believe it is present in the formed state in the circulating blood.

The patient had a high bactericidal titer, and with the daily increment of complement he showed a spectacular improvement over a couple of months. We had hopes for his recovery, but although the daily blood culture usually became negative, an occasional one gave a few colonies. We found he had an indolent apical abscess under one premolar, and I asked the dentist to drill through the tooth and drain the abscess. Although I asked him particularly not to extract the tooth he did so, and the patient developed uncountable colonies per cubic centimeter of blood within eighteen hours, his skin was peppered with petechiae, and he quickly relapsed and died. Without any meaning or connection, it is strange to note that the dentist died of subacute bacterial endocarditis a few years later.

It is an open question whether the effect I observed was due to antibody, as I suspect, or to properdin, which was not known of then; but it does raise an interesting line for combined clinical and laboratory investigation. The point I wish to make is that I could not persuade the administration to let me retain in the hospital, free of charge, a few selected cases of subacute bacterial endocarditis to investigate this interesting observation further. I often wished that the bacteriologic department could have had six beds in the hospital for its own purposes.

A student, who is now pathologist to a hospital, had a staphylococcal brain abscess in a frontal lobe. This was everted and drained, with complete recovery. But some years later he was troubled by jacksonian symptoms due to the scar, which Dr. William V. Cone, wished to excise. Because it had been a staphylococcus abscess and since there was no great hurry, we spent a couple of months immunizing him with staphylococcus toxoid to a high blood level of antitoxin. Then, for safety, on the operating table he was given a good dose of potent staphylococcus antitoxin horse serum. All went well without incident. I took the excised brain scar tissue back to the laboratory, pulped and cultured half of it, and cut serial sections of the other half. I grew a pure culture of Staphylococcus aureus, and by examining a number of sections stained by the Jensen-Claudius method, I found a few small clumps of gram-positive cocci. He had not developed any symptoms of infection, and the loci of cocci in the sections showed no indication of active inflammation but were deeply imbedded in scar tissue. The second operation was done two years after the first, and it seems that the staphylococcus lay trapped and dormant all that time. But, be that as it may, it is not unreasonable to suppose that this was a fortunate collaboration of clinician and bacteriologist.

It is the responsibility of the clinician to evaluate the numerous tests and examinations that he now requires be made on a patient before the diagnosis is decided, but sometimes consultation would enlighten interpretation. A case that intrigued Dr. Wadsworth illustrates the point. A man in his sixties returned to work for fear of losing his job, although he still had what he called a very bad cold. He had to give in and come to hospital because the pain in his hip was more than he could bear, and he felt very ill. He had a high temperature and a leukocytosis. A blood culture showed a heavy growth of Type 2 pneumococcus, and the x-ray film was said to show Paget's disease of the pelvis. As these reports were not easily reconciled, the examinations were repeated, and again the blood culture gave a heavy growth of Type 2 pneumococcus; but because the x-ray film now was said to show carcinoma of the hip a surgeon was consulted. The surgeon found fluctuation and let out a lot of greenish pus from the region of the hip, which proved to be full of Type 2 pneumococcus. But the man died, and an autopsy showed an extensive unresolved pneumonia and an abscess tracking from the diaphragm along the psoas muscle and down the thigh to the knee, containing more than a quart of Type 2 pneumococcus pus. Unfortunately, bacteria are not recognizable by x-ray film.

Mixed infections and antagonisms

One feature of bacterial infections I have always found to be neglected by both the bacteriologist and the clinician is the interplay of mixed infections. It is true that the pure culture study of bacteria is essential for their identification and for the appreciation of their individual functions. However, the nature of a disease caused by one kind of bacterium often is complicated by the intervention of another kind.

In Mesopotamia we became accustomed to a patient having two and sometimes three separate diseases at the same time, but you seldom hear that possibility discussed in our hospitals. Even minor secondary infections can be active influences that modify the symptoms, the course, the outcome, or the response to treatment of a disease.

The symptoms of phthysis can be aggravated by secondary infection and relieved by treatment that does nothing to the tubercle bacillus. I have seen the pneumococcus replace the meningococcus in meningitis completely in at least 10 cases, and that, before antibiotics were available, was a serious matter. It was interesting to follow the development in such instances, and it gave point to an interest in synergies, antagonisms, and replacements that could be shown in infected wounds, empyemas, and so forth.

A woman had a mixed Staph. aureus and Streptococcus pyogenes infection of the large wound area of a Halsted removal of the breast. Blood cultures were intermittently positive for the streptococcus and never for the staphylococcus, but the spread of mixed infection in the wound area got steadily worse. The patient was given a good dose of staphylococcus antitoxin and later actively immunized with staphylococcus toxoid. The staphylococci steadily reduced in numbers and eventually disappeared; the blood cultures ceased to be positive, although the streptococcus persisted in the wound. Antistreptococcus serum was then used locally and immediately phagocytosis became intense, and within a short time the wound healed completely. The patient was discharged well. But control of the case depended on management of the staphylococcus which held the key position in the infection, and the laboratory played an important part in this.

In later years I saw several mixed Staph. aureus and Str. pyogenes infections that would not respond to sulfonamides until the staphylococcus was brought under control by immunization. This synergistic protection has been observed by others, but it is not in agreement with many statements concerning antagonism by staphylococcus. Perhaps in these days of more and more different antibiotics and mixtures of antibiotics it is difficult to observe synergisms and antagonisms between bacteria in the patient. But I do know of other instances where one kind of bacterium will protect another from the action of antiseptics. There is evidently much to be learned from studies of mixed infections that would enlighten us on the processes of disease and guide our devices for treatment.

There is an interest today in antagonisms, but mixed bacterial cultures give surprising ecologic results. In 1919 we found that mixed cultures of Hemophilus influenzae, Str. pyogenes, and Diplococcus pneumoniae gave much larger yields of each than we could get in pure cultures on the best media we knew. In mixed cultures pneumococcus kills meningococcus, but it grows more profusely and lives longer, perhaps due to the catalase the meningococcus produces, while pneumococcus produces peroxides.

Inoculating animals with mixtures is also surprising; for example, a dose of Str. pyogenes that fails to infect alone will cause fatal septicemia if it is inoculated subcutaneously with Proteus vulgaris, which remains at the site of injection. I have seen a similar state in infected wounds and mastoid infections, when the streptococcus could not be controlled until the Proteus was killed by dressings of lactic acid.

Comment

Straws in the wind, as you might call such random observations, have been the starting points for far-reaching investigations, as the history of bacteriology shows. Therefore I have always maintained that there should never be such a concept as "routine work" in clinical bacteriology, for it destroys interest and perception. But it is hard to maintain ideals when the demand is more than the allotted staff can handle circumspectly, and so it becomes exigent to look for what is expected and ordinarily recognizable rather than to look for what is not known.

Certain faults and failings of the laboratory can be due to complacency, which may apply to the manner of working, to the kind of specimens and their collection, to the circumstances of the laboratory, and to the connection between the clinician and the patient. Complacency is far more deleterious than lack of knowledge or inexperience, which can be corrected in time, for it is an incorrigible source of errors.

It is not uncommon for a culture of Listeria monocytogenes to be thrown out as a "contaminating diphtheroid" through not knowing of the existence of listeriosis, but there is no excuse for a failure to recognise meningococcal meningitis. I have seen a report of 4 children from one family who were in the hospital with serious symptoms and meningococcal meningitis which were not diagnosed until a postmortem was done on one of them; then the doctor is quoted as saying the disease was detected in time to treat the other 3 children. Incompetence can be represented as virtuous skill. And marvelously solicitous precautions can be vaunted, as when two undertakers were given prophylactic penicillin after preparing a meningococcus meningitis corpse for burial.

The protean nature of meningococcus septicemia can cause confusion, and the peculiarities of certain strains can make distinction from the gonococcus difficult. The laboratory identification of a meningococcus blood culture was not accepted clinically and serum treatment was withheld because a patient had orchitis and had given a history of gonorrhea some years before. The man discharged himself from the hospital to take an attractive job but returned two days later with meningitis due to the same type and fermentatively distinctive meningococcus as had been found in his blood.

The laboratory is not without foibles and can lose much by failing to inspire confidence or by an aloof attitude. There is no doubt that much more effective and more appropriate examinations are made when there is a friendly and appreciative cooperation between the bacteriologist and the clinician; and this is improved when the pathologist and biochemist are included. The variability of infectious disease is not determined by the bacteria alone but by an interplay involving the inborn constitutional disposition of the host, and we have too little understanding of this.

Too much stickling for what is called "scientific accuracy" or "statistical significance" can preclude the recognition of something that has not been noticed before. There are real situations and values for which the statistician has no technic or formula, and these are more readily revealed to imaginative curiosity tempered by experience than to a stereotyped methodology.

Fashions come and go in science and medicine and seem at times to give more direction to research than do the dictates of reason or urgency or interest. At times the fashion seems to be shaped by sentimental appeal or the scare tactics most apt to inveigle earmarked funds. The availability of grants, although not always very strictly circumscribed, is an enticement to restrict the range of investigation. I have not heard of any foundation devoted to the installation and development of laboratories in hospitals, although they are essential to the proper practice of modern medicine and are often in need of equipment and an adequate staff for what is expected of them. It is reasonable for the public to be interested in the progress of science which has brought so many advantages, but I dislike the sensational notoriety of indiscriminate publicity, and I deplore the abuse of science as an instrument of political expediency.

I am glad I have worked in a number of widely differing places, before the days of antibiotics, and with people whose sound principles were not soured by austerity or by prudish pretensions. Experience, gained before electronic equipment in the laboratory and therapeutic suppression of infection by antibiotics, gives a certain sense of proportion to events and changes, which is balanced by having known some of the people renowned for their discoveries. To me it seems important to realize that nothing is too trivial to notice and that good work does not depend on having elaborate or costly equipment. Great discoveries have been made under quite simple circumstances, and it is the man who really matters in the laboratory, not the machinery.

There are, too, twists and turns of personality or circumstances that are amusing to remember. At the time the principles of the carrier problem were being established, Sir David Semple was standing in the laboratory at Muktesar holding a sliver of wood on which was a fid of feces from a possible typhoid carrier and saying: "You know, Harvey, some people earn their living in an extraordinary way!" Then I would have you picture Dr. M. H. Gordon, wearing a silk hat with a cutaway coat and striped trousers, scooping up horse manure in a crowded old London street and putting it in a paper bag, to confirm a recent observation that you often could isolate tetanus bacilli from horse dung.

Interest in your work and the search for truth defies social conventions and prejudices. Soon after the gonococcus was discovered, Dr. Wyatt Johnston, made a positive diagnosis and Dr. C. F. Martin, protested that it could not be correct as his patient was one of the most respected citizens of Montreal. "Well!" said Johnston, "It must be an immaculate infection." Sir Howard W. Florey said that his contribution in the penicillin story was that "a man might now contract gonorrhea twice in one day."

As I went with the late Dr. Cone to see a case of osteomyelitis of the skull, he told me the patient was a Roman Catholic monk who spoke only French and feared he would go to hell if he died in a Protestant hospital. When we entered the room the old gentlemen was asleep, and he woke when I touched his shoulder, started violently, and drew the bedclothes over his head exclaiming loudly "O, Mon Dieu, le Diable!" It took me several minutes to persuade him I was not Mephistopheles.

Such opinions of patients and friends make me wonder why I should have been asked to give this Twelfth Annual Augustus B. Wadsworth Lecture.

County Hospital Care of Chronically Ill Patients

From Infirmary to Chronic Disease Hospital

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From Onondaga County Home and Infirmary

ONONDAGA COUNTY is a central New York county with about 400,000 residents. Its only city is Syracuse, with a population of about 250,000. For many years, its medical school was part of Syracuse University, but in 1950 it was purchased by the State University of New York, permitting a great expansion of the facilities, faculty, and number of student admissions.

Despite the presence of a medical school and its teaching hospitals, until recently the county infirmary was no better than comparable institutions through the country. In 1950, however, a series of events started which culminated in a marked upgrading of the institution. The first of these was, as already mentioned, the purchase of the medical school by the State. The second was the appointment of a public health-trained physician as dean of the medical school. The third was a citizens' survey of health and hospital services, which was completed in 1954.[1] Although it was completely unproductive in terms of solving the severe shortage of hospital beds,[2] it had a subcommittee on chronic illness, chaired by the diocesan director of Catholic charities and having the dean of the medical school as a member. This committee, in essence, recommended that a physician with special interest and training in chronic illness be appointed Medical Director of the welfare department and the Onondaga County Home and Infirmary. This position was set up very rapidly as a joint appointment between the County of Onondaga and the College of Medicine and was filled in September of 1954.

Situation in 1954

One of the first tasks of the Medical Director was a survey of the medical care, personnel, and facilities at the County Infirmary, which shortly before had been described by an eminent internist as a "masterpiece of sanitation and neglect." What did this survey reveal?

STAFF. *Medical.* The entire medical staff for some 600 people (about half chronically ill and half residents) was comprised of a full-time general practitioner and a half-time internist. There were no consultants of any type, and all special problems had to be referred to downtown outpatient departments or hospitals (about 6 miles away) with all the attendant problems of personnel time, personal inconvenience to the patients, and lack of communication between staffs of different institutions.

Nursing. The nursing staff, although traditionally oriented and understaffed, provided extremely good nursing care, as evidenced by the fact that patients who had been bedridden twenty-five years or more showed no signs of bedsores. The question as to whether or not the patients should have been bedridden in the first place will be considered later.

Ancillary. There was no ancillary staff to speak of, as only a partly trained dietitian fell into this category.

Administrative. The administration was in the hands of a totally untrained political appointee (a farmer by background) and

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an equally untrained assistant (an undertaker by profession). Except for nursing and medical personnel, almost all staff appointments were political in nature.

Facilities. *Laboratory.* There was in existence a small laboratory which in practice was used for only one purpose: the performance, by the full-time staff physician, of a "ritualistic" admission urinalysis on each new infirmary patient.

Radiology. The institution owned an x-ray apparatus which probably had the original Coolidge tube in it, as evidenced by its appearance, and which had not been used in many years.

Other facilities. Such facilities as physical therapy, dental services, or central sterile supply were undreamed of.

Patient care. *Quantity.* Obviously, by any modern concepts the range of services which should have been available to chronically ill patients was inadequate in the extreme, with the possible exception of nursing. Such items as glasses and prosthetic devices, for example, were not available, except in very unusual circumstances.

Quality. Again, with the one exception of nursing, the quality of care was poor. Only one of the two staff physicians was adequately trained, and of course it was impossible to render adequate medical care with none of the facilities available. The charts were sketchy in the extreme, with rare progress notes.

Community relations. As was to be expected, relationships with the community were poor. The Board of Supervisors, which has both legislative and appropriating functions, was kept very poorly informed and was advised of the situation only at budget time and when a financial crisis threatened, such as the burning down of the barn or a huge plumbing repair bill. Annual reports were sketchy and dealt largely with the amount of produce raised on the county farm.

Community physicians were likewise completely uninformed. It has been almost impossible to locate a physician who had ever visited the institution on a professional basis. Residents conceived of it mostly as a place to "dump" undesirable patients, and hospital administrators were concerned almost entirely with long waiting lists which made local hospital bed shortages even more severe.[3]

TABLE I. Comparison of Onondaga County Home and Infirmary in 1955 and 1960

Item	1955	1960
Basic facts		
Number of beds*	215	415
Number of days care†	209,120	225,546
Number of admissions†	669	1,370
Budget	$932,765	$1,890,080
Miscellaneous facts		
X-ray examinations	0	3,101
Laboratory tests	100 (estimated)	33,837
Physical therapy treatments	0	12,734
Formal teaching programs	0	3**
Research projects	0	25††

* Capacity not achieved until end of year.

† Includes County Home as well as County Hospital.

** Medical students, hospital attendants, and practical nurses.

†† Under way or completed in last six years.

It is difficult to imagine an institution, 6 miles from a medical center and a large university, more isolated from the modern world of medical and social progress.

Progress, 1954 to 1961

As a result of his survey, which included discussions with the dean of the College of Medicine and practically all department chairmen, the Medical Director made a series of recommendations to the Board of Supervisors early in 1955. Although not all of these were adopted immediately, a review of the situation in 1957 showed that 18 out of 19 recommendations had been adopted completely or were in process at that time. By 1961 the situation was radically changed.

Situation in 1961

The two most marked changes between 1954 and 1961 were the more rapid turnover, with admissions more than doubling, and the budget, which also doubled (Table I).

Staff. *Medical.* The attending staff

TABLE II. Staff of Onondaga County Home and Infirmary in 1955 and 1961

Staff	1955	1961
Medical		
Physicians, full-time	1	1
Physicians, part-time	1	6
Specialists, full- or part-time	1	7
Consultants	0	12
Nursing		
Registered nurses	10	39
Licensed practical nurses	33	57
Hospital attendants	47	58
Paramedical, full- or part-time		
Hospital administrator	0	1
Dentist	0	1
Social worker	0	1
Physical therapists	0	3*
Occupational therapist	0	1
Speech therapist	0	1
Pharmacist	0	1
Dietitians	1*	2
X-ray technician	0	1
Laboratory technicians	0	3*
Podiatrist	0	1
Psychologist	0	1

* Not all are fully trained.

has been increased from two to eight, with the changes being primarily in part-time physicians, as one method of getting the quality desired (Table II). All new staff members are board-certified or qualified in their specialty and hold medical school faculty appointments. This includes the consulting staff of 12 as well as the attending physicians.

Nursing. The nursing staff has increased by more than one-third, from 90 in 1954 to 154 in 1961; the significant increases were in the number of licensed nurses, rather than in the number of relatively untrained hospital attendants (Table II). A recent report indicates the amount of time and effort that went into nursing reorganization, definition of functions, and training in geriatric and rehabilitation nursing.[4]

Ancillary. As far as paramedical personnel are concerned, there was an increase from 1 in 1955 to 17 on the 1961 payroll (Table II).

Administrative. The key administrative staff consists of a superintendent, who is still a political appointee but who is an able administrator with many years of experience. He is backed by an assistant who is a trained hospital administrator.

Facilities. *Laboratory.* A complete clinical laboratory is now operating, with three technicians and over 30,000 tests being performed a year. Tests which are not economical to perform are purchased from the University Hospital, but these are decreasing each year.

Radiology. A modern diagnostic x-ray machine is functioning now, and over 3,000 examinations were performed in 1960.

Physical therapy. Physical therapy is one of the key departments in the new program which is heavily geared to rehabilitation; over 12,000 treatments were given in 1960.

Patient services. *Quantity.* It is felt that patient services are quantitatively adequate, with the major exception of psychiatry. This has not been available because of the lack of psychiatric personnel in the community.

Quality. As indicated by the modern charting system, the care is equivalent to that found in many teaching hospitals, and it is believed superior in some areas, particularly in nursing and in the emphasis on rehabilitation.

Community relations. Community relations are now excellent. There has been little trouble in obtaining understanding and financial support from the Board of Supervisors because of a continuous program of information and interpretation. The medical community, the health and social agencies, and the College of Medicine all have supported the institution generously.

Education and research. As seen in Table I, neither education nor research has reached the adequacy of patient service, but both have progressed markedly over the years and should continue to improve.

Philosophy

What is the difference in philosophy between the old and the new program? No philosophy was ever formally stated in the pre-1954 days, but it might have been expressed as follows: Chronically ill people need nursing care, enough medical supervision to ensure the control of disturbing symptoms, and rest. This is all predicated on the idea that nothing constructive is possible in dealing with the chronic illnesses, particularly for the older-age group. One of the results of this policy was the fact that practically no one was discharged except through death.

Today, the philosophy is that everyone who is ill needs adequate medical care, including a careful diagnostic study and any indicated therapy. The maximum physical, mental, and social activity permitted by the patient's age and illness are best for the patient. Activity is offered and encouraged, but not demanded. A major result of this policy is frequent rehabilitation to self-care and discharge to home or to a home substitute.

Principles

Describing the case history of one institution may help to cast some light on what is happening and can happen in other places.[5,6] Some of the major principles in upgrading a county almshouse into a chronic disease hospital are the following (always assuming a favorable community climate):

1. A clear idea as to the function of such an institution and its relationship to the rest of the community.
2. A survey of the current conditions with careful recommendations to the appropriate decision-makers in terms of both short-range and long-range proposals.
3. An educational program for selected community groups (the health professions, hospitals, and health and social agencies, among others).
4. A small demonstration of results.
5. A continued program of interpretation to the appropriating body.
6. A willingness to compromise on short-term but not on long-term goals.

County of Onondaga Department of
Social Welfare, Syracuse 2

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Discussion

John J. Bourke, M.D., *Albany, New York.* Dr. Notkin has described very adequately the results of bringing a carefully worked out medical care program to a county home and infirmary situation. Throughout the years, most county home and infirmary programs have suffered from partial or indifferent medical attention. The introduction of a program closely affiliated with the medical school has made it possible to bring the united effort of a wide variety of medical specialties and paramedical skills to a county home infirmary, with emphasis on rehabilitation and achieving the proper type of motivation in the kinds of personal situations which one finds in this type of institution.

In the administration of the Hill-Burton program in New York State, two of the conditions for the approval of Federal grants to county infirmary projects have been: (1) a written agreement of affiliation between the infirmary and a suitable general hospital prior to the approval of a grant and (2) a signed agreement that registered nurse supervision will be available to the patient in the infirmary twenty-four hours a day.

It is at our better general hospitals, particularly the medical teaching institutions, that the best type of medical organization is to be found. This organization results in a teamwork approach to best meet the varied needs of the older patients usually cared for in the county infirmaries. In addition to the medical skills made available to the infirmary under this type of arrangement, other ancillary services, such as consultation in nutrition, nursing care, physical medicine, and laboratory and radiology services, are possible in many institutions which formerly did not have this type of service needed to provide quality-type medical care.

Dr. Notkin is to be commended for his achievements in Onondaga County which have had a very beneficial effect on other counties in the State of New York.

I would suggest that we should be extremely careful in assigning the title of "chronic hospital" to a county infirmary situation. Those actively concerned with the planning of hospital and related facilities usually define a hospital as having all of the medical and related skills, facilities, and equipment required for the modern diagnosis, treatment, and rehabilitation of disease and disability. This implies operating rooms, extensive laboratory facilities and services, diagnostic and therapeutic radiation facilities, and a host of other services that are to be found in our good community hospitals. This broad array of required personnel, facilities, and services is usually not to be found in even the most modern county infirmaries. Further, from the standpoint of the over-all medical and hospital economy, they should not be duplicated, but we should rely on the proper transfer of patients who require active hospital care, whether it be acute or chronic, to the community general hospital which is fully equipped to meet the needs of the patient. The placing of the title "chronic hospital" on an institution which does not meet these standards has implications with regard to reimbursement, particularly from the standpoint of the third-party payees.

Dr. Notkin has pointed out very wisely that the desired program cannot be achieved with budgets that are geared to the past. To provide high quality service, an adequate budget for the county infirmary is needed as well as the proper type of staff. Paramount to the successful operation of a good county infirmary or nursing home is the proper attitude of the director and the staff toward the patients and the accepted goals of good medical care.

Causes of death in hemolytic disease of newborn infant

Necropsy on 74 fatalities from hemolytic disease established that death in 59 per cent of the cases resulted from the severity of the disease, according to a report by R. Van Praagh, M.D., in the August, 1961, issue of *Pediatrics*. A total of 82 infants died among 882 admitted to the Children's Medical Center, Boston, from January, 1950, to December, 1956, with hemolytic disease.

Eighteen per cent of the 74 deaths resulted from a delay in treatment which led to kernicterus, 3 per cent from profound late anemia, and 20 per cent from conditions not related to hemolytic disease. Significant clinical and pathologic findings were: anemia in 70 per cent; aspiration of amniotic sac content in 55 per cent; pulmonary hemorrhage in 54 per cent; heart failure in 51 per cent; anasarca in 42 per cent; death during or soon after the exchange transfusion in 32 per cent; pneumonia in 19 per cent; kernicterus in 18 per cent; pulmonary hyaline membranes in 12 per cent; rupture of the spleen in 5 per cent; and cerebral intraventricular hemorrhage in 4 per cent.

It was found that the risk of death during or soon after the exchange transfusion—one third of all deaths did occur at this time—was 2 per cent per patient and per procedure, if infants with hydrops or fatal lesions are excluded. The total risk was 4 per cent per patient and 3 per cent per exchange transfusion.—*Pediatric Currents, Ross Laboratories*

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Rectal and Colonic Polyps Occurring in Young People

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In recent years reports have appeared indicating that polyps occurring in the rectum and colon of patients in the first and second decades of life present pathologic features which distinguish them from polyps occurring in the same regions in adults.[1,2] These features include an excess of fibrous stroma in cystlike spaces of varying sizes lined by mucous-secreting epithelial cells. There is a concomitant, greater vascularity and evidence of acute and chronic inflammation. The term "juvenile polyp" is used frequently in referring to polyps with this histologic picture.

The pathologic differences described have caused disagreement as to whether or not "juvenile polyps" are of different etiology from adenomatous polyps as they occur in adults or merely represent adenomas which have become secondarily ulcerated and inflamed. There is also disagreement as to whether or not "juvenile polyps" possess malignant potential.

With these controversies in mind it is the purpose of this paper to review our experience with these lesions and to present our interpretation of them.

TABLE I. Age distribution of patients with polyps

Age Group (Years)	Number of Patients
0 to 5	11
6 to 10	4
11 to 15	4
16 to 20	3

Clinical material

For the period 1954 through 1960, 525 patients of all ages were recorded at The Mount Sinai Hospital as having polyps of the colon or rectum. After excluding those patients with a primary diagnosis of ulcerative colitis with pseudopolyps and those with multiple familial polyposis, 22 patients were below the age of twenty-one years, an incidence of 4.2 per cent.

Eleven cases were recorded for the up-to-five-year age group. Four cases were in the five- to- ten-year age group. There were 3 cases in the fifteen- to twenty-year age group (Table I). The youngest patient was two years old, and the oldest was seventeen years of age. There were 13 males and 9 females.

Eighteen patients had a single polyp each. Of these, 14 were located in the rectum, 3 in the descending colon, and 1 at the splenic flexure. Four patients had multiple polyps. Of these, 3 patients had 2 each, and 1 had 5.

Aided by Grant #2A-5126 from the National Institute of Arthritis and Metabolic Diseases.

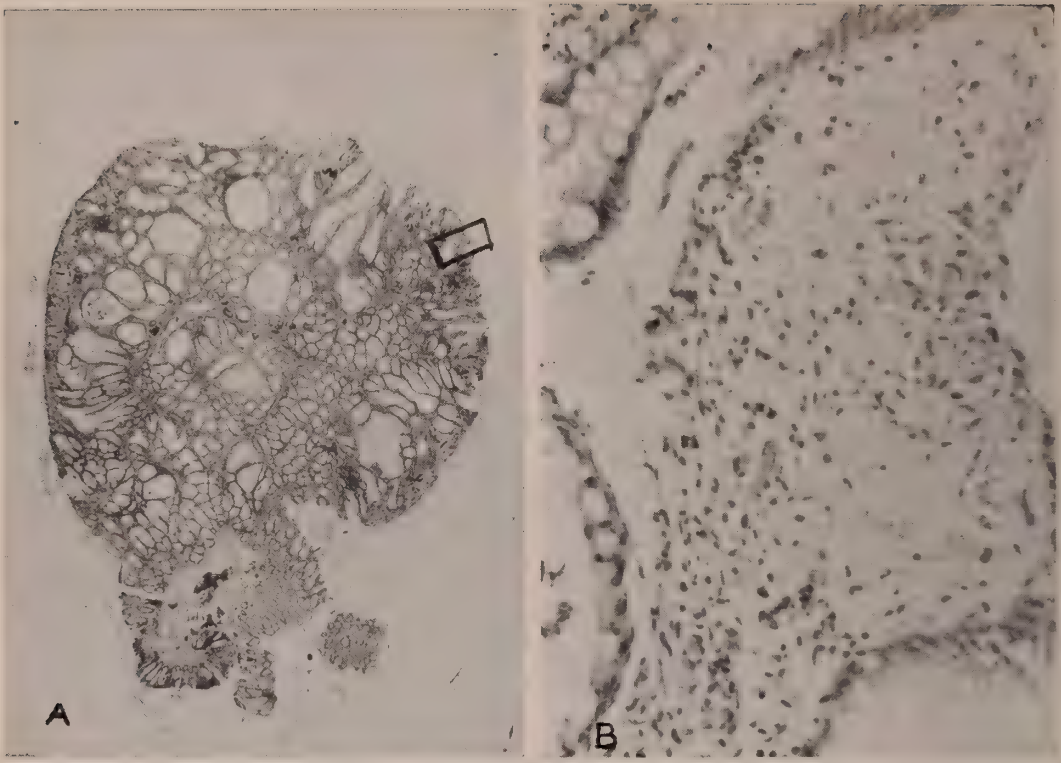

FIGURE 1. (A) Adenomatous polyp with slight surface erosion. (B) Surface erosion with granulation tissue.

When multiple polyps occurred, at least 1 always was located in the rectum.

The most frequent presenting complaint was rectal bleeding, which occurred in 20 patients. The bleeding was never profuse, and a hemoglobin level below 10 Gm. per 100 ml. was recorded in only 1 child, three years of age, who had a level of 8.7 Gm. per 100 ml. In 2 other patients the presenting complaint was a prolapsing rectal mass.

Pathologic material

In 19 patients biopsy material was available for review.

Three biopsies revealed typically adenomatous lesions (Fig. 1). The surface of the polyp was irregular with occasional focal superficial erosions at which areas the mucosal layer was replaced by granulation tissue. The core of the polyp contained numerous glandular elements which showed mild dilatation and a stroma moderately infiltrated with lymphocytes and plasma cells.

Eight specimens showed the changes characteristically associated with "juvenile polyps" (Fig. 2). The surface was smooth, presenting wide areas of erosion. Granulation tissue not only replaced the mucosa but infiltrated the stroma, which was increased in amount and heavily infiltrated with neutrophils and eosinophils. Glandular elements were sparse and markedly dilated. One polyp appeared to be partially infarcted.

Three polyps showed characteristics of both the adenomatous and juvenile form (Fig. 3). Some mucosal irregularity was present, and the surface was partially eroded. The stroma was moderately increased with the extensive formation of granulation tissue and the infiltration of inflammatory cells. The density of glands was reduced, and some of those remaining appeared to be dilated.

In five polyps the inflammatory reaction was so marked that granulation tissue replaced almost the entire polyp, and only a few dilated glands remained (Fig. 4).

There was no evidence of a malignant condition in any of these lesions.

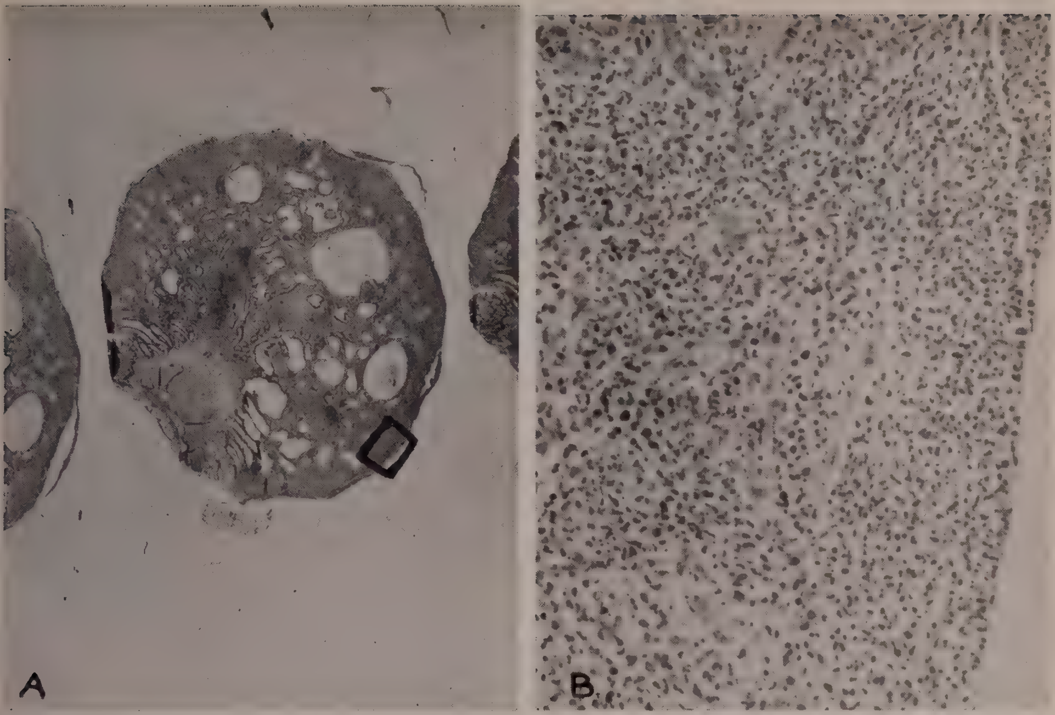

FIGURE 2. (A) "Juvenile polyp." (B) Extensive surface erosion and granulation tissue with acute and chronic inflammation.

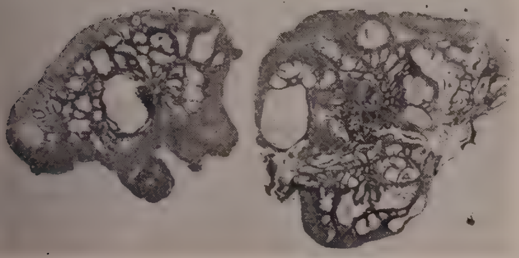

FIGURE 3. Adenomatous polyp with more extensive erosion and inflammation.

Etiology and pathology

Two main theories have been suggested regarding the etiology of "juvenile polyps." One theory holds that these are benign adenomatous neoplasms which may become acutely or chronically inflamed. The other, introduced by Versé in 1908,[3] reiterated by Ewing in 1928,[4] and elaborated by Horrilleno, Eckert, and Ackerman in 1957,[2] contends that the trauma of the fecal stream acting on redundant folds of mucosa causes proliferation of the vascular and connective tissue, hyperplasia of the mucous glands, and chronic inflammation. The orifices of the hyperplastic glands become occluded with epithelial debris resulting in cystic dilatation of the glands.

In analyzing our material it appears that all of the polyps encountered in the juvenile patient actually may be adenomatous in nature. Three specimens were unquestionably adenomatous lesions containing mild histologic evidence of inflammation and erosion. In three others the alterations seen were interpreted readily as the sequelae of increasingly severe inflammation occurring in adenomatous polyps. When the inflammatory process involved the entire polyp and surface erosion extended over the entire lesion, the typical picture of the "juvenile polyp" was seen. Last, in five specimens inflammation was so severe that the glands were virtually replaced by granulation tissue. The surface of those specimens was eroded completely, but their polypoid configuration and occasional glandular remnants suggest their adenomatous origin.

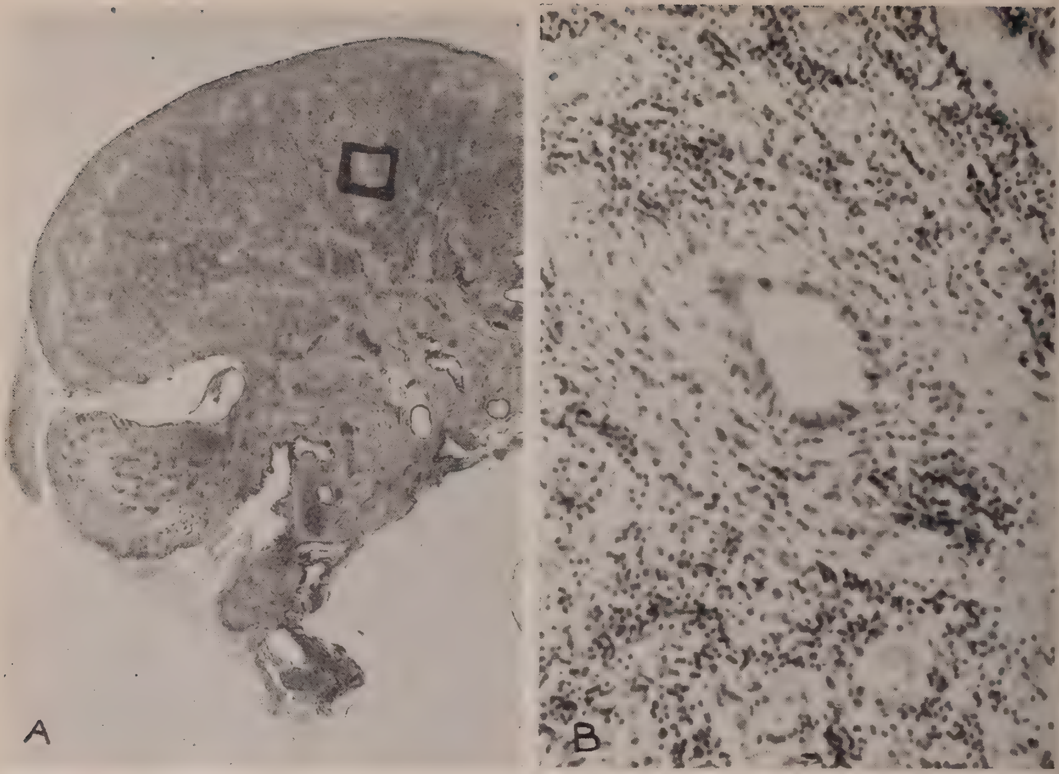

FIGURE 4. (A) Adenomatous polyp almost completely replaced by granulation tissue except for one remaining gland. (B) Close-up of remaining gland.

Thus, the finding of transitional stages from adenomatous polyps with minimal surface erosion to those almost completely replaced by granulation tissue suggests that the "juvenile polyp" is not a different type of tumor but represents a stage in the spectrum of inflammatory alteration.

Incidence

The incidence of rectal and colonic polyps in 449 consecutive autopsies reported by Helwig[5] in patients under the age of twenty-one was 5 cases (1.1 per cent). In 105 asymptomatic children examined sigmoidoscopically, Turell and Maynard[6] found 2 with polyps (1.9 per cent).

Considering a total pediatric case load of 115,398 patients in which only those with proctologic symptoms were examined for the possibility of polyps, Schapiro[7] reported the presence of polyps in 101 children (0.09 per cent). Horrilleno, Eckert, and Ackerman[2] under similar circumstances found 55 polyps among a total of 72,416 patients (0.08 per cent).

The 101 cases of polyps reported by Schapiro were among 2,700 patients with proctologic symptoms. Thus, in the presence of symptoms the incidence was 3.7 per cent.

The higher incidence in those series in which the rectum and colon of all patients were examined compared with those series in which only symptomatic children were studied suggests that many of these polyps do not produce symptoms and may go undetected.

Clinical experience

Our series reveals that most polyps occur in the first decade of life. This age distribution coincides with the experience of others.[5,8,9] The suggestion has been advanced by Knox *et al.*[1] that frequent autoamputation of the polyp may explain the decreased incidence in the second decade.

As in other series, we found that males predominated. We also found that the great majority (81 per cent) of these polyps occurred in the rectum and sigmoid. Knox *et al.*[1] found 65 per cent, and Horrilleno, Eckert, and Ackerman[2] found 91 per cent of polyps in these regions.

Our experience with regard to the clinical picture agrees with that of other groups.[2,6,10-12] Bleeding, usually not accompanied by pain, was by far the most frequent presenting complaint. Four patients complained of abdominal pain, and 2 others had rectal prolapse of the polyp.

Malignant potential

It has been stated by Knox *et al.*[1] that juvenile polyps are not premalignant lesions. However, Kennedy[10] reported that in 18 polyps studied histologically, using Broder's classification, 8 were Grade 1 adenocarcinomas, and 1 was a Grade 2 adenocarcinoma. In another report on colonic polyps in children, Kennedy, Dixon, and Weber[11] stated that 9 of 11 polyps contained adenocarcinoma Grade 1 (75 per cent of all cells differentiated) or low Grade 1 (practically all cells at least partially differentiated). The difficulty in classifying carcinoma is well known, and many pathologists do not accept Broder's classification and would not accept Grade 1 or low Grade 1 as a malignant lesion. Gordon *et al.*[13] reported 9 cases of carcinoma in situ among 58 children in whom the polyps were studied histologically. Their criteria consisted of any three of the following: (1) stratification of epithelial cells with hyperchromatic nuclei, (2) mitotic activity, (3) absence of goblet cells, and (4) presence of large nucleoli. Again, many pathologists would not agree that these criteria are sufficient for the diagnosis of a malignant condition. Schilla[14] reported a carcinoma in a rectal polyp in a two-year-old child. Kerr[9] mentions 2 children whom he thought had developed a malignant growth in what was probably a polyp.

If a malignant growth occurs, it appears to be quite rare. Turell[15] found no evidence of such change in over 150 cases. Harris[16] found none among 70 cases, and Castro[17] also found no evidence of malignant conditions in his 30 cases. Horrilleno, Eckert, and Ackerman[2] found no evidence of malignant changes in 55 patients but stated that on rare occasions they have seen carcinoma develop in an adult-type adenomatous polyp in children.

Since in our view there is no valid distinction between adenomatous and "juvenile polyp," we agree with Turell[15] that "An open mind should be maintained about malignancy in juvenile polyps because theoretically such transformation is a remote possibility."

Summary

In a group of 525 patients of all ages with polyps, 22 patients (4.2 per cent) were below twenty-one years of age. The youngest was two years old and the oldest seventeen. In 18 patients with a single polyp each, 14 polyps were in the rectum or sigmoid colon. When multiple polyps were present, at least one was in these regions.

Rectal bleeding, never severe, was the complaint presented in 20 patients.

A histologic examination revealed both typical adenomatous polyps and "juvenile polyps." Further study revealed that a spectrum of inflammatory alterations was present in this series of polyps and that these polyps appeared to be basically adenomatous in character. All stages of transition were seen, from typically adenomatous lesions with slight surface erosion and mild inflammatory reaction to severely eroded lesions which were replaced almost completely by granulation tissue.

The "juvenile polyp" represents one stage in the reaction of the adenomatous polyp to the inflammatory changes that follow surface erosion.

No evidence of malignant transformation was present in this series. Although reports of such transformation are rare, because of the adenomatous nature of these polyps we feel that an open mind should be maintained on this question.

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Number one hundred ten in a series of Recent Advances in Medicine and Surgery

Mental health in different countries

A continuing study of the factors influencing mental health in different countries, which has taken Cornell University social scientists around the world during the last decade, is being expanded this year with studies of mental health in Sweden and in France.

The Swedish research represents a new approach of the program, for the aim there is to make Swedish data which have already been collected comparable to data collected in earlier Cornell studies in other parts of the world.

The study is being undertaken in an effort to make the data bearing on psychiatric disorder which have been collected in Sweden and in Stirling County, Nova Scotia, comparable. In the French study, new data-collecting technics will be used by Cornell scientists in an effort to learn more about the symptoms of mental distress.

Cornell staff members have been conducting a continuing survey of mental health in different cultures for more than a decade. The most extensive study to date is the extended research program in Nova Scotia. The most recent project in the program is a pilot study of mental health and social factors in the western region of Nigeria, which was made last winter and spring and is now being tabulated.

The scientists are concerned with mental health factors in various cultures. In some places, vast changes taking place within the social systems cause adjustment problems; in others, different factors may influence mental health. Studies are also being conducted in the United States, which can be compared with the results of research in other countries.

The study of mental health in two Swedish parishes was begun in 1947. Ten years later, a follow-up study was completed. The researcher contacted people who had moved from the parishes, consulted records on deceased persons, and interviewed both new and old residents. With these details and the extensive records kept by the Swedish authorities, the scientists have a vast store of information on mental health.

A village in southern France is being studied. A sociologic study was conducted in the village about ten years ago which provides a background for the current research. In this village, an interesting contrast may be evident between the villagers, many of them retired, and the younger people who farm the surrounding country. In addition, many writers and artists who have moved into the village will affect its social structure.

The scientists hope, in these two projects, to compare the data of the Swedish and French studies with those of the Nova Scotian study to determine any contrasts in the results of different research methods and also to discover the differences and similarities of the two areas where mental health factors are concerned.

There is preliminary evidence, for example, that the Swedes are more apt to face conflicts with classical anxiety attacks and that Sweden has a higher suicide rate than either France or Nova Scotia. Cornell scientists hope to learn whether or not this is true and, if so, whether or not society's attitude toward suicide is a factor. In the Swedish village, the responses of newcomers will be compared with those of older residents to determine how valuable the follow-up interview is and how much people remember of events many years before.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Roswell Park Memorial Institute
Buffalo, New York

August 21, 1961

Conducted by JOHN W. PICKREN, M.D.

Discussed by THEODORE NOEHREN, M.D., and
CARLOS PEREZ-MESA, M.D.

Leiomyosarcoma of Epididymis and Cardiac Failure

Case history

A nineteen-year-old Negro male was first admitted to Roswell Park Memorial Institute complaining of shortness of breath and swelling of the neck of one week's duration.

Six months previously a nodule had appeared in the region of the right testis; it grew rapidly, attaining the dimensions of a "chicken egg" in about a week, and an orchiectomy was performed at another hospital. The histologic diagnosis was leiomyosarcoma of the epididymis. A week later a retroperitoneal lymphadenectomy was performed, and lymph nodes containing metastatic tumors were found at the level of the region of the renal vessels. The patient had an uneventful recovery and had no complaints until one week before his first Roswell Park Memorial Institute admission when numerous bilateral roentgenographic densities were found within the lungs.

A physical examination on admission showed a well-developed young man in no apparent distress weighing 78 Kg. The temperature was 98.2 F., and the pulse was 90 per minute. There was a nonpitting, diffuse swelling of the neck and a poorly-defined fixed, fusiform, nontender, left supraclavicular mass about 6 cm. in diameter which was not attached to the overlying skin. The superficial neck veins were distended in both the supine and sitting positions. A few coarse rales were heard in the base of the right lung, and breath sounds were decreased in this area. The heart was within normal dimensions to percussion. The heart sounds were normal, the rhythm was regular, and no murmurs were heard. The blood pressure was 110/70.

The venous pressure was 60 cm. of water in the right arm and 53 cm. in the left arm. A venogram showed compression of the superior vena cava below the azygos vein. Chest films showed blunting of the right costophrenic angle, a lobulated mediastinal mass high on the right side, and a 3-cm. nodular mass adjacent to the left hilum. The cardiac diameter was increased. Fluoroscopy of the heart showed good pulsations, and skull films showed normal findings.

A urinalysis showed a specific gravity of 1.020, 1 plus protein, but no sugar. The urinary sediment contained 30 to 40 leukocytes and 2 to 5 erythrocytes per high power field. The hemoglobin was 13.1 Gm. per 100 ml. The white cell count was 8,600 with 80 per cent neutrophils and 20 per cent lymphocytes. The platelet count was 170,000.

The blood urea nitrogen was 15 mg. per 100 ml., and the blood sugar was 54 mg. per 100 ml. The serum sodium was 142 mEq., potassium 4.3 mEq., and chloride 101 mEq. per liter. The total serum protein was 7.76 Gm. per 100 ml., with albumin 4 Gm. per 100 ml. The serum calcium was 10.1 mg. per 100 ml., serum phosphorus 5 mg. per 100 ml., serum bilirubin 0.9 mg. per 100 ml. at one minute, and 1.1 mg. in thirty minutes, and the alkaline phosphatase was 7.7 King-Armstrong units.

During his hospital stay the patient was treated with nitrogen mustard, receiving a total dose of 0.4 mg. per kilogram of body weight, with some symptomatic relief and a definite decrease in the swelling of the neck and in the size of the pulmonary densities. While in the hospital, he fainted on two occasions immediately after vomiting, and interrogation revealed that several similar episodes had occurred during the previous three months. An electrocardiogram was interpreted as showing sinus tachycardia with a rate of 112 per minute and low voltage throughout, but otherwise the findings were essentially normal. The patient was discharged on the eighth hospital day. During the week following discharge the neck size continued to become smaller, but a cordlike, tender, and pulseless right external jugular vein was palpable.

The patient was admitted for the second and last time twenty-two days after his original admission, complaining of epigastric cramps and nausea associated with vomiting which had appeared suddenly six days previously. He also complained of somnolence. The symptoms were relieved by lying still but were aggravated by walking. They were not related to eating. The neck swelling was less pronounced than it was on the original admission, and the left supraclavicular mass was half its former size. Distention of the neck veins had persisted, and the venous pressure in the left arm was 47 cm. of water. The lung fields were clear to examination with the exception of dullness in the base of the right lung, and the right diaphragm did not seem to move. The heart was definitely enlarged to percussion. On auscultation a Grade II apical systolic murmur was present, and in the pulmonary area the second sound was widely split. The pulmonary component was about twice as loud as the aortic component. The liver was percussed 6 cm. below the right costal margin. The abdominal muscles were tense, but there was no rebound tenderness, and the bowel sounds were normal. No edema of the legs was present.

Roentgenograms of the chest showed a widening of the mediastinum with a mass situated in the paramediastinal region bulging into the left lung field behind the heart and an enlargement of the heart with bulging of the left border. The diaphragm on the right was elevated. Abdominal films revealed enlargement of the liver and questionable ascites. Most of the patient's symptoms disappeared on bed rest. A diastolic gallop was noted by one observer. Electrocardiograms showed no change until the day before death when high and notched P waves appeared. The blood pressure throughout his course varied from 120/100 to 90/70. He was treated with intravenous dichloromethotrexate (7.5 mg. per kilogram of body weight) on the second hospital day. The number of blood platelets decreased from 140,000 to 30,000, and the leukocytes decreased from 4,800 to 3,000. There was no change in the hemoglobin concentration. On the night of the seventeenth hospital day the patient cried out with pain; when seen immediately afterwards, he was cyanotic and in shock, without pulse or blood pressure, and he died shortly thereafter.

Discussion

Theodore H. Noehren, M.D.: Before discussing the clinical problems in this patient I would appreciate it if we could have a short summary of the behavior of leiomyosarcomas of the epididymis. It is a rare tumor, and this is the first one I have seen of this type.

John Phelan, M.D.: Malignant tumors of smooth muscle origin (leiomyosarcomas) may be found in any region of the body where smooth muscle exists. These tumors appear more frequently in the uterus, gastrointestinal tract, and soft tissue of the retroperitoneum. Only rarely have they been reported arising from other soft tissue areas of the body, as represented by the tumor in this protocol.

In 1958 Stout and Hill[1] reported a clinicopathologic study of 36 cases of superficial soft tissue leiomyosarcomas and observed them to be distributed randomly over the entire body, although the thigh area was the

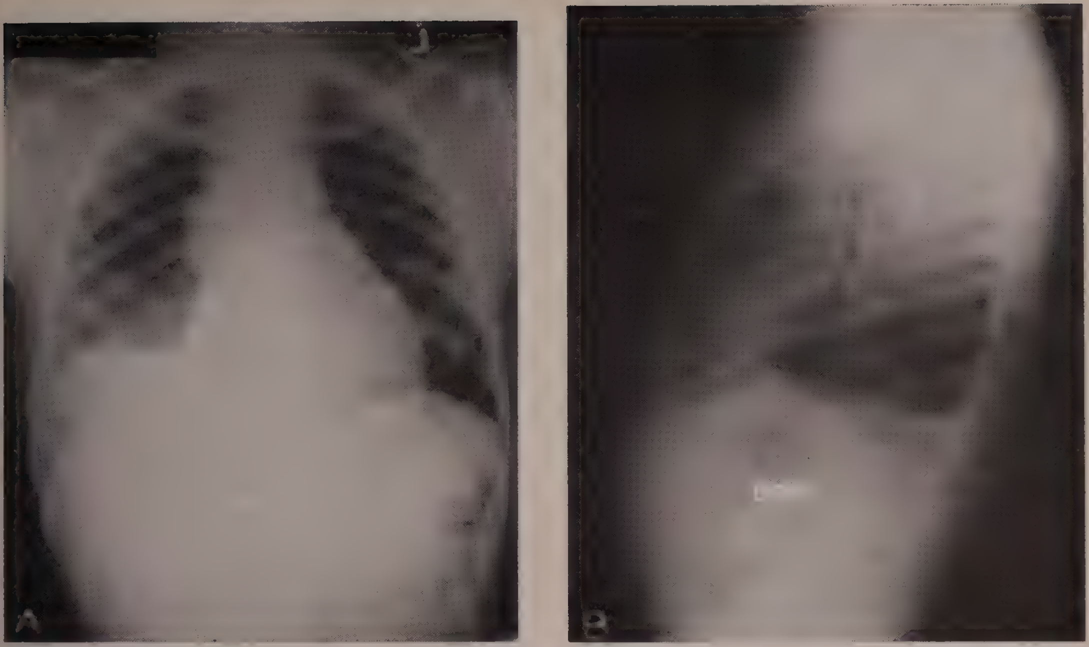

FIGURE 1. (A) Posterior-anterior view of chest on admission shows blunting of right costophrenic angle, a lobulated mediastinal mass in the right side, compression deformity of the trachea, a left hilar mass, and enlargement of the heart. (B) Lateral view shows same findings.

most common site. In addition, he noted that in most of his cases the tumor measured 5 cm. or more in diameter by the time it was removed. He further pointed out that not infrequently these tumors simulated a benign lesion, in that they were movable and circumscribed. Most of these sarcomas were located within the deeper confines of the subcutaneous tissues as contrasted with benign smooth muscle tumors which usually were found within the dermis.

In a recent study of 10 cases of leiomyosarcoma of soft tissue origin at Roswell Park Memorial Institute, a similar clinical pattern was observed. However, we were impressed by two observations: (1) none of the tumors exceeded 7 cm. in greatest diameter, and (2) the tumor frequently mimicked a benign condition. In over 50 per cent of the cases the surgeon simply enucleated the tumor from its bed by finger dissection. In each case when this type of surgical procedure was employed, a local recurrence developed within the first postoperative year; in addition, 2 patients developed lung metastases.

In this respect, Stout and Hill[1] also recorded a high incidence of local recurrence (20 out of 33 patients), while distant lung metastases were observed in 19 patients. Because of this finding, these investigators are of the opinion that inadequate removal of the tumor at the time of initial surgery is the principle cause for this high rate of tumor recurrence. In this respect, it should be pointed out that although soft tissue leiomyosarcomas may appear clinically benign, a microscopic tumor usually extends beyond the tumor's gross boundaries so that in effect, enucleation of the tumor invariably will result in incomplete removal of the tumor. Suffice it to say, the importance of establishing a tissue diagnosis prior to the definitive removal of the tumor is quite apparent. As with all malignant soft tissue tumors, wide excision of the tumor-bearing area along with a generous margin of normal-appearing tissue in all three planes is the procedure of choice. However, this cannot be performed unless the proper histologic diagnosis is established beforehand.

Dr. Noehren: May we see the roentgenograms?

S. J. Kim, M.D.: Posterior-anterior and lateral views of the chest on the patient's first admission show some blunting of the

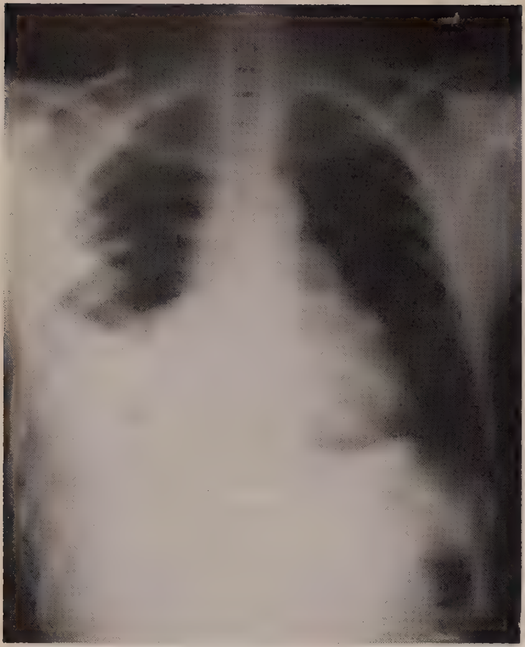

FIGURE 2. Chest film three weeks after admission shows increase in pleural effusion, decrease in size of left hilar and paratracheal masses, but a new mass behind the cardiac shadow.

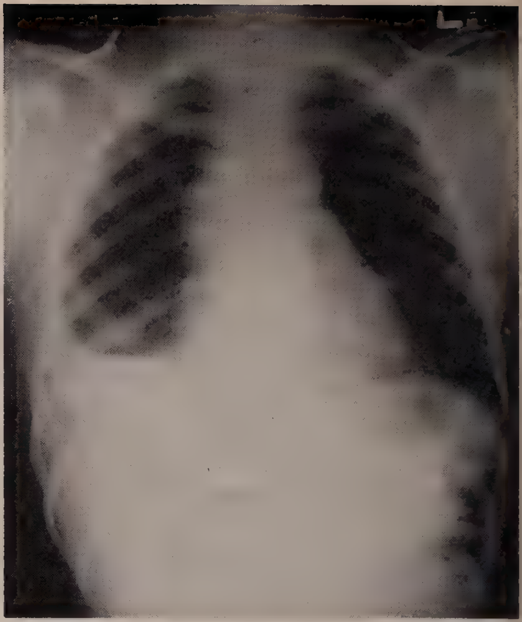

FIGURE 3. Chest film four weeks after admission shows further progression of the pleural effusion and probable growth of the posterior mediastinal mass.

right costophrenic angle area suggestive of a minimal degree of pleural effusion (Fig. 1). A lobulated mediastinal mass in the right side extends from the thoracic inlet down to the right hilum. The trachea is narrowed by extrinsic pressure from this mass. There is also widening of the transverse diameter of the heart with fullness of the left border of the cardiac shadow suggesting cardiac enlargement and rotation of the heart. Adjacent to the left hilum a round nodular mass measures about 3 cm. in diameter. These findings are those of metastatic involvement of the mediastinum.

A re-examination of the chest with posterior-anterior and lateral views after two weeks shows no significant changes in the appearance of the right side of the paratracheal and tracheobronchial mass. However, there is a slight further increase in the size of the cardiac shadow, particularly the left border of the heart. The configuration of the cardiac shadow suggests the accumulation of pericardial fluid in this area. The previously noted round mass adjacent to the left side of the hilum seems to have regressed almost completely on this film. Otherwise, the chest does not seem to be changed.

A re-examination of the chest three weeks after admission shows further increased pleural effusion in the right chest with elevation of the right dome of the diaphragm (Fig. 2). The previously described mass in the right paratracheal and tracheobronchial area on the right side has further regressed. The metastatic nodular mass in the region of the middle field of the left lung adjacent to the left hilum has disappeared almost completely. The configuration of the heart shadow is unchanged. However, there is a large mediastinal mass which is located just behind the cardiac shadow indicating a metastatic mass in the posterior mediastinal area. This mass is not visible in the previous examinations.

Chest x-ray films with posterior-anterior and lateral views after one month demonstrate an extensive degree of pleural effusion in the right side of the chest (Fig. 3). There is displacement of the mediastinal shadow including the cardiac shadow toward the left side. Therefore, the cardiac configuration cannot be evaluated. Due to rotation, the previously described paratracheal and tracheobronchial mass on the right side cannot be evaluated well at the present time. However, the previously described huge posterior mediastinal mass which is behind the heart shadow is again visualized and appears unchanged although it cannot be definitely evaluated since the mediastinal shadow is displaced. One does get the impression that this mass has grown.

DR. NOEHREN: In summary, the patient had a leiomyosarcoma of the epididymis that had metastasized to the retroperitoneal lymph nodes. Roentgenographic evidence of lung and mediastinal metastases is present. Of interest is the regression of the parenchymal lesion while the mediastinal mass persisted after chemotherapy. The question arises, therefore, whether the patient had two types of tumor or whether one can expect several metastases from one tumor to respond differently.

JOSEPH SOKAL, M.D.: This response is not unusual. Our director, George Moore, M.D., has a lantern slide that he uses in his talks to illustrate such divergent responses. In his case, one metastasis disappeared, a second did not change in appearance, and a third actually grew during the course of chemotherapy. The odds are that the patient had one tumor whose individual metastases responded differently to therapy.

DR. NOEHREN: The patient had superior vena cava obstruction; the venous pressure was 60 cm. in the right arm and 52 cm. in the left. The venogram showed compression of the superior vena cava below the azygos vein. This compression is considered to be the result of the metastases. With this information I would agree that one must consider all of these masses secondary to his leiomyosarcoma of the epididymis.

His fainting spells are significant. He fainted on two occasions immediately after vomiting. Interrogation revealed that similar episodes had occurred on several occasions during the previous three months. What are the causes of this fainting? In cough syncope, the patient coughs and then faints momentarily but regains consciousness. For years the explanation has been that the cough caused an excessive Valsava maneuver, preventing the return of blood to the thorax and, diminishing the cardiac output. The patient faints because the peripheral pressure is not maintained. Kerr and Eich,[2] however, questioned this explanation in their recent study of 18 patients. They measured the peripheral blood pressure during the course of cough syncope and found that unconsciousness developed before an adequate fall in peripheral pressure. Furthermore, they maintained that the rapid loss of unconsciousness following a single cough (5.1 seconds) is incompatible with cerebral ischemia. The electroencephalograms made on their patients showed findings similar to those found following cerebral concussion. They postulated that the mechanism of cough syncope was a concussion-like effect from a rapid rise in the cerebrospinal fluid pressure. I wonder if vomiting may cause physiologic changes similar to those from a cough which would explain this patient's episodes of syncope.

What is the relationship of these syncope spells to his sudden death? The patient developed acute cor pulmonale. One of the initial symptoms in primary pulmonary hypertension is fainting. A patient whose chest film shows negative findings but who has increased pulmonary-artery pressure, may have repeated episodes of syncope. Other causes for syncope include certain types of heart disease. The ones most commonly associated with fainting are aortic stenosis, Stokes-Adams syndrome, and septal defects. This nineteen-year-old boy, when first seen, had no evidence of heart disease and no abnormal cardiac findings. Without such findings, I see no reason to consider heart disease as an explanation for his fainting. However, shortly before death his cardiac status was described as abnormal. The heart was enlarged, a Grade II apical systolic murmur was audible, and the second sound in the pulmonic area was split. The pulmonic component was twice as loud as the aortic. In addition, the liver was palpable 6 cm. below the right costal margin. This combination suggests heart failure.

The splitting of the second sound in the pulmonic area can be evidence of several things.[3] The physiology of this phenomenon is related to the closing of the aortic

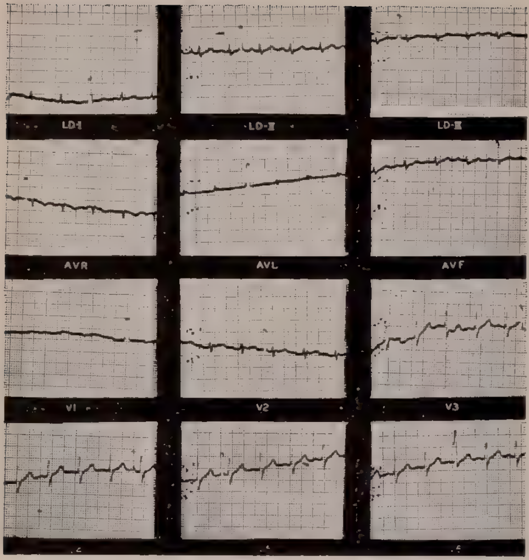

FIGURE 4. Electrocardiogram on first admission shows in the standard leads minimal evidence of right axis deviation.

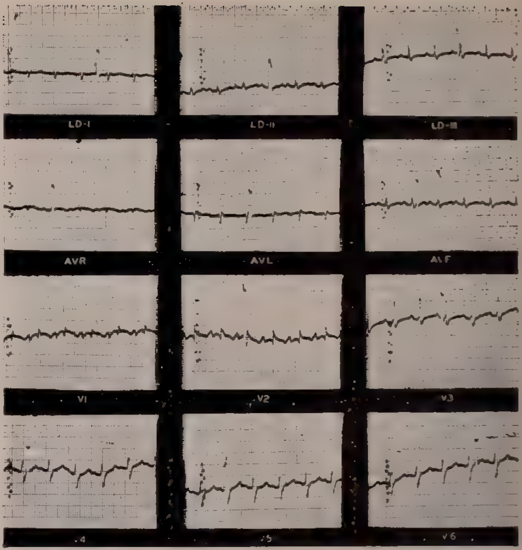

FIGURE 5. Electrocardiogram made the day before death contains deeply inverted T waves in V_1 and V_2, a change in ST segment, and an increase in prominence of P waves.

and the pulmonic valves. A splitting of the second sound actually denotes a temporal separation of the closures of the pulmonic and aortic valves. One can hear this split sound by listening to the heart of a normal individual while he is breathing deeply. Such deep breathing causes an increase in cardiac return, resulting in an increase in the right ventricular stroke volume. Thus, the right ventricle lags behind the left in its contraction. Such delay results in a delayed closure of the pulmonic valve, and the split sound then can be heard. Anything that will cause right ventricular failure also will produce a slower emptying of the right ventricle, causing the right and left ventricle to complete their systole out of phase, with the resulting separation of the two components of the second sound. Right bundle branch block is a common cause of this sign because of the delay in the conduction to the right ventricle.

In our patient with an enlarging heart, the split second sound was not influenced by respirations. There was no evidence of right bundle branch block, but the electrocardiogram showed abnormal findings. In the standard leads there was minimal evidence of right axis deviation on the first admission (Fig. 4). On the second admission there were deeply inverted T waves in both V_1 and V_2, a change in the ST segment, and increased prominence of P waves, which would suggest something abnormal on the right side (Fig. 5). If this were right ventricular cardiac hypertrophy, one would expect that the QRS waves that represent a positive electrical change in that side of the heart would be more increased in the anterior part of the chest leads, such as V_1, V_2, and V_3, but they were not. These changes in the electrocardiogram were noted first the day before death. With such a sudden onset the changes are more suggestive of right ventricular strain than right ventricular hypertrophy. Furthermore, these findings are helpful in estimating the length of time that obstruction has persisted. With slow mediastinal obstruction of the pulmonary artery in a young person, right ventricular hypertrophy would result. In an acute process, findings of right ventricular strain would predominate. Therefore, the cardiographic changes are suggestive of a process of short duration.

Most of the patient's symptoms disappeared on bed rest. He had an enlarged liver and possibly ascites, which would fit in with the right ventricular failure. His systolic blood pressure throughout his course

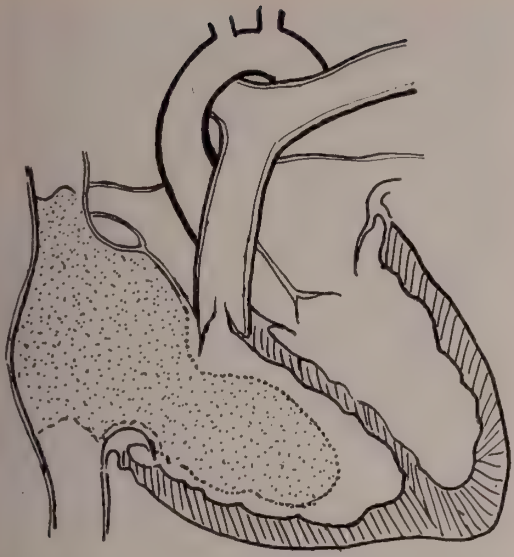

FIGURE 6. Note attachment of the tumor to the intima of the superior vena cava and the prolongation of the mass through the atrium past the tricuspid valve and into the right ventricle.

varied from 120 to 90 mm. He developed pain of unknown origin, became cyanotic and hypotensive, and died shortly thereafter.

Therefore, it seems to me that we were dealing with pulmonary hypertension; an obstruction beyond the right ventricle producing the separation of the two components of the pulmonic sound and the signs of right ventricular strain as seen on the cardiogram. Chronologically, it is not the usual syndrome of primary pulmonary hypertension. A pulmonary embolus or multiple pulmonary emboli are good possibilities. He had a thrombosed vein in the neck and a sudden episode of gastric symptoms before he came into the hospital for the second time. He had what can be a rather acute manifestation of right heart failure. We cannot say whether there were pulmonary emboli underlying the fluid at the base of the right lung, but for him to have peripheral pulmonary emboli which would produce this much failure, I think he would have to have roentgenographic changes considerably greater than those described. A slow extension of the mediastinal mass to include his pulmonary artery or metastatic involvement to the heart or a major blood vessel also can produce these findings. Sarcoma, we know, may involve the heart or vessels. With an acute cor pulmonale, superior vena cava obstruction, and metastatic leiomyosarcoma, I think the logical assumption is that this was a neoplastic obstruction including the pulmonary vascular system. As second, third, and fourth possibilities, a secondary malignant process, major thrombotic emboli, or tumor emboli all would have to be considered.

Clinical diagnoses

(1) Leiomyosarcoma of epididymis with metastases to lung and mediastinum; (2) cardiac failure.

Dr. Noehren's diagnosis

Leiomyosarcoma of epididymis with metastases to lung and mediastinum causing vascular obstruction and cardiac failure.

Pathologic report

Carlos Perez-Mesa, M.D.: At autopsy, multiple confluent neoplastic nodules were present in the posterior mediastinum and extended along the course of the aorta until the origin of the iliac vessels. The largest of these nodules bulged into both pleural cavities, imposed on the left cardiac ventricle, as seen in the roentgenograms, and measured 11 by 8 cm. All were composed of a glistening, yellowish-red, firm tissue with focal areas of hemorrhage, and all had a myxoid appearance. In the posterior mediastinum the tumor was attached to the mid-portion of the esophagus without infiltration of the wall. The wall of the superior vena cava was surrounded and infiltrated by a tumor, and its lumen was occluded. At the level of the right atrial opening the tumor projected into and almost filled the atrial cavity (Fig. 6), extended through the opening of the tricuspid valve into the right ventricle, and occupied the inflow tract of the right ventricle. The base of the polypoid tumor was attached firmly to the infiltrated superior vena cava and for a few millimeters to the neighboring endocardial atrium. The rest of the tumor was free and mobile, acting as a valve. The right atrium was distended, and the wall was thickened. The tricuspid valve was dilated,

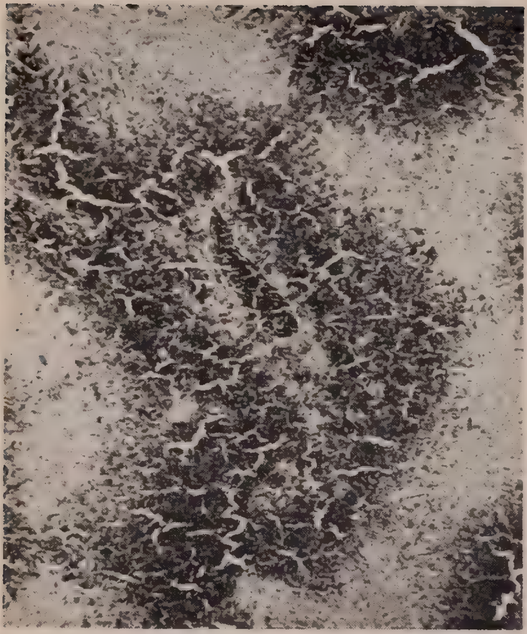

FIGURE 7. Note the extreme congestion of the liver around central veins.

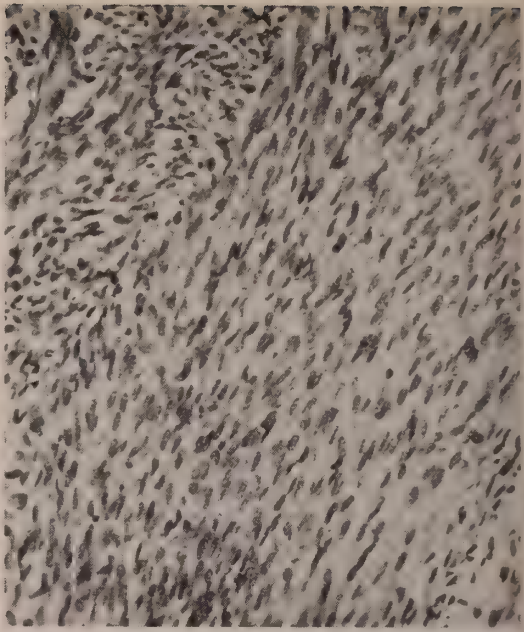

FIGURE 8. Photomicrograph of tumor having characteristics of a leiomyosarcoma.

measuring 15 cm. in circumference. The intracardiac tumor showed the same gross appearance as elsewhere. The heart weighed 425 Gm. The lungs contained a few greyish-white nodules, measuring up to 0.5 cm., distributed mainly around the small vessels. Focal areas of edema also were present. The right pleural cavity contained 100 cc. of cloudy, yellow fluid. The liver was enlarged moderately, and its border was a few centimeters below the costal margin. The liver weighed 1,800 Gm. and showed acute passive congestion (Fig. 7). A tumor also was found in the right side of the groin. Microscopically, the metastatic tumor was similar to the resected primary epididymal lesion. Cellular areas composed of bundles of elongated cells with plump nuclei and increased mitotic activity as well as myxomatous fields were present. The tumor was a leiomyosarcoma (Fig. 8).

The intracardiac tumor acted as a valve; when closed, it produced a temporary partial obstruction to the flow of the blood. Closure more likely occurred when the patient was in the erect position since by gravity the tumor would fall and cover both the opening of the tricuspid valve and the ostium of the inferior vena cava. In the supine position the tumor would fall toward the back and head, allowing more flow of blood. Such a physiologic mechanism may explain in part the patient's bizarre symptomatology in the erect position and his rapid improvement on bed rest. Multiple examples of the bizarre symptoms associated with intracardiac tumors have been reported.[4,5]

Anatomic diagnoses

(1) Leiomyosarcoma of epididymis with metastasis to mediastinum, lungs, and superior vena cava with obstruction of return flow of blood into right side of heart; (2) cardiac failure.

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Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Available Insulins and Insulin Hypoglycemia

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FOLLOWING the discovery of insulin by Banting and Best[1,2] in 1922, efforts to purify the crude insulin led to its crystallization by Abel in 1926.[3] In 1934 Scott[4] showed that insulin could be crystallized readily as the zinc salt thus making its commercial preparation practical. The unmodified insulin had the disadvantage of a short duration of activity, and many attempts were made to prolong its action. In 1936, Hagedorn *et al.*[5] altered the solubility of insulin at the pH of body fluids (7.4) by the addition of protamine. Since then, numerous modifications have been introduced utilizing combinations of insulin with protein precipitants (protamines, histones, globins) or chemicals (hexamine, isocyanate) capable of altering solubility. Hallas-Møller and his associates[6] developed prolonged-acting insulins, without the use of modifying proteins, by precipitating insulin with zinc and resuspending it in an acetate buffer.

There are many preparations of insulin available for clinical use, all having the same basic effect on metabolism but differing from one another in time of onset, peak of activity, and duration of effect (Table I). A prolonged duration of effect has been obtained at the expense of rapidity of onset. Clinically, the major problem has been to select that particular time activity which best fits the needs of the individual patient.

Sanger[7] has demonstrated brilliantly the structural formula of insulin (Fig. 1). It is composed of two polypeptide chains, one of 21 amino acids and the other of 30, joined together by disulfide linkages between their cysteine components. Each position in the structure of insulin is occupied by only one amino acid residue. Preparations from the pancreas of the various species (that is, beef, pork, sheep, whale, and horse) differ in the arrangement of the amino acid constituents of the molecule. The commercial preparations of insulin are made from both beef and pork pancreas. When there is an allergy to the regular preparations, insulin derived from beef or pork pancreas is available. The mechanism of action of insulin will be covered in another article in this series.[8]

Indications for insulin therapy

The indications for the use of insulin therapy are:

1. To control the symptoms and signs of diabetes where they cannot be controlled by diet alone, or by diet plus the oral hypoglycemic agents. Children, young adults with growth-onset diabetes, and older persons with labile diabetes usually require insulin.

2. To treat diabetic ketosis, or other complications of the disease (that is infections, intercurrent disease, surgery, and

TABLE 1. Insulin preparations

Type	pH	Protein Adjuvant (Mg. Per 100 Units)	Zinc Content (Mg. Per 100 Units)	Buffer	Activity			Hypoglycemic Reactions
					Onset	Peak (Hours)	Duration	
Rapidly-acting								
Crystalline zinc (Regular)	3 to 3.5	None	0.02 to 0.04	None	½	2 to 4	6 to 8	Before lunch
Semi-lente (Amorphous zinc)	7.2	None	0.2 to 0.25	Sodium acetate	1	6 to 10	12 to 16	Before lunch
Intermediate								
Globin zinc	3.5 to 3.8	Globin 3.8	0.2 to 0.35	Sodium phosphate	2 to 4	6 to 12	12 to 20	Late afternoon
Lente (70 per cent ultra, 30 per cent semi)	7.1 to 7.4	None	0.2 to 0.25	Sodium acetate	2 to 4	8 to 12	28 to 32	Late afternoon
NPH (Isophane)	7.1 to 7.4	Protamine 0.39 to 0.55	0.016 to 0.04	Sodium phosphate	2 to 4	8 to 12	18 to 30	Late afternoon
Long-acting								
Protamine zinc	7.1 to 7.4	Protamine 1.0 to 1.5	0.2 to 0.25	Sodium phosphate	3 to 6	14 to 20	24 to 36	During night and early morning (before breakfast)
Ultralente	4.8 to 5.7	None	0.20 to 0.25	Sodium acetate	8	16 to 24	36	During night and early morning

trauma). Patients taking the oral hypoglycemic agents often require insulin during acute stress situations.

3. To control hyperglycemia and glycosuria. Arguments have been advanced pro and con as to the necessity or desirability of avoiding hyperglycemia and glycosuria. Joslin and his group[9] recommend strict chemical control of the blood sugar and the maintenance of a sugar-free urine, claiming that laxity in control exposes the patient to the dangers of complications. On the other hand, Tolstoi[10] and others are satisfied with the control of the symptoms of diabetes, the avoidance of ketonuria, undesirable loss of weight, and insulin shock. The conservative school believes that with the available means at hand to control diabetes it is desirable to avoid constant hyperglycemia, glycosuria, ketonuria, and hypoglycemia and to maintain metabolic conditions as close to normal as is possible.[11]

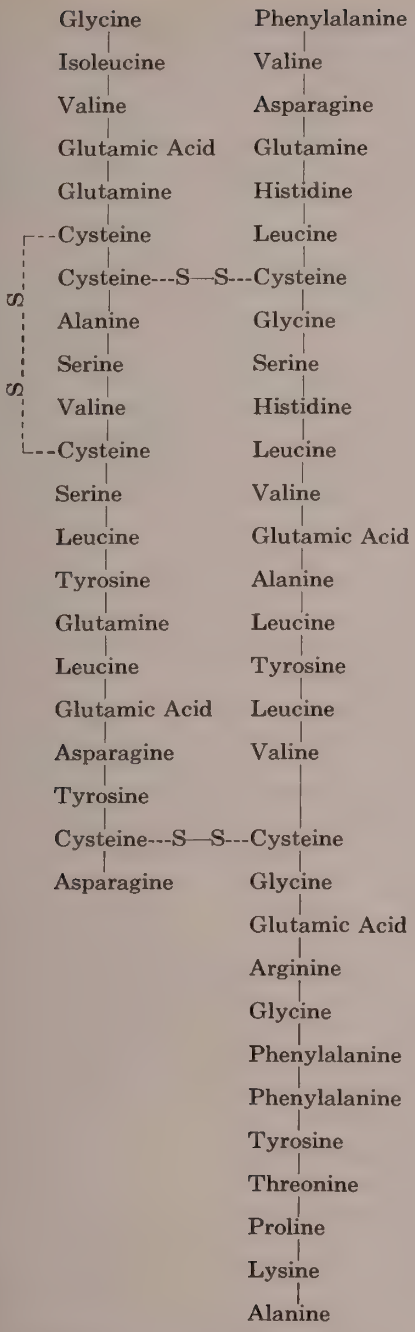
Continuous hyperglycemia has produced hydropic degeneration of the pancreatic islets and complete exhaustion of the beta-cytotropic mechanism resulting in permanent diabetes in animals.[12] Seltzer and Smith,[13] studying plasma insulin-like activity in normal and diabetic subjects before and after glucose loading, found that persistent hyperglycemia at first caused an excessive stimulation of the beta cells which later resulted in the progressive loss of insulin-secreting reserve. The sequelae of unremitting hyperglycemia have been documented experimentally in dogs by Barron and State[14] and in cats by Dohan and Lukens.[12]

Studies with fat tolerance tests have shown that the serum lipids rise to a higher level and remain elevated longer when the blood sugar is elevated.[15] The blood levels of some of the lipids, lipoproteins, and glycoproteins which have been implicated in the atherosclerotic process have been shown to be proportional to the blood sugar levels in some diabetic patients. Since the diabetic individual is so prone to atherosclerosis, it would seem logical to attempt to correct these metabolic abnormalities by maintaining a normal blood sugar level.

An additional reason for controlling the hyperglycemia is the high incidence and rapid progression of infections in the presence of uncontrolled diabetes. Vallance-Owen, Hurlock, and Pease[16] have shown that an insulin inhibitor which is present when the diabetes is uncontrolled is no longer detectable when the blood sugar is in the physiologic range.

Insulin preparations

There are seven types of insulin currently available in the United States. All the in-



Glycine
Isoleucine
Valine
Glutamic Acid
Glutamine
Cysteine
Cysteine---S—S---Cysteine
Alanine
Serine
Valine
Cysteine
Serine
Leucine
Tyrosine
Glutamine
Leucine
Glutamic Acid
Asparagine
Tyrosine
Cysteine---S—S---Cysteine
Asparagine
S
S
Phenylalanine
Valine
Asparagine
Glutamine
Histidine
Leucine
Glycine
Serine
Histidine
Leucine
Valine
Glutamic Acid
Alanine
Leucine
Tyrosine
Leucine
Valine
Glycine
Glutamic Acid
Arginine
Glycine
Phenylalanine
Phenylalanine
Tyrosine
Threonine
Proline
Lysine
Alanine

FIGURE 1. Structure of insulin.[7]

sulin preparations are prescribed in units and are supplied in various concentrations. The international insulin unit is that amount of crystalline preparation required to reduce the blood sugar of a normal twenty-four-hour fasting rabbit of 2 Kg. weight from 120 mg. to 45 mg. per 100 ml. within five hours. The international standard of comparison is a preparation of zinc insulin crystals defined as containing 22 units per milligram. In the United States a U.S.P. (United States Pharmacopeia) standard of reference which has a higher potency is employed. During manufacture, preparations of unknown potency are compared with standard preparations on the basis of production of hypoglycemic convulsions in animals.

Commercially available insulin is supplied in 10 cc. rubber-stoppered vials which are clearly marked U40, U80, and so forth, depending on the number of units per cubic centimeter. A standard color is used for each concentration:

U40 (red) = 40 units per cubic centimeter
U80 (green) = 80 units per cubic centimeter
U100 (orange) = 100 units per cubic centimeter
U500 (brown and white stripes) = 500 units per cubic centimeter

The U40 and U80 concentrations are used most frequently. A 40-unit dose may be given by using 0.5 cc. of U80 or 1 cc. of U40 insulin, the only difference being in the volume of the injection. It is desirable to keep the volume below 1 cc.

Unmodified or regular insulin. The term "unmodified or regular insulin" is used in referring to clear, aqueous solutions of the active antidiabetic principle of the pancreas, whether made from zinc-insulin crystals or from insulin of amorphous origin. Both the unmodified insulins are identical in action and the effects are clinically indistinguishable. Most unmodified insulin is now made from highly purified zinc-insulin crystals. It is a clear solution containing from 0.02 to 0.04 mg. of zinc (as the hydrochloride) per 100 units.

Following a subcutaneous injection of regular or crystalline zinc insulin the hypoglycemic effect is apparent within fifteen to thirty minutes. The peak effect is reached within two hours, and the duration of effect lasts six to eight hours. It is absorbed rapidly and should be given subcutaneously approximately fifteen to thirty minutes before a meal.

Regular insulin is the only insulin that can be used safely intravenously. By this route the onset of action occurs in from ten to fifteen minutes, the peak effect occurs in thirty minutes, and the duration of action is from one to two hours.

Indications for regular insulin. Regular insulin should be used for the treatment of all the emergencies and complications of diabetes (that is ketosis and coma, acute and chronic infections, and surgery and delivery). In these conditions the insulin requirements may change rapidly and a short-acting insulin is the choice.

Regular insulin also is indicated as a supplement to the intermediate and long-acting modified insulins (that is isophane insulin (NPH) and protamine zinc insulin (PZI)) when these insulins are incapable of controlling postprandial hyperglycemia and glycosuria.

When given by any route (intravenous, intramuscular, or subcutaneous) the degree and duration of the hypoglycemic effect varies with the size of the dose.

PROTAMINE ZINC INSULIN. Protamine zinc insulin is a combination of insulin, protamine (a polypeptide obtained from fish sperm), and zinc suspended in a phosphate buffer. It contains 1.25 mg. of protamine and 0.25 mg. of zinc per 100 units of insulin and varies from pH 7.1 to 7.4. The zinc increases the stability of the preparation and the duration of its hypoglycemic effect. At the pH of the tissue fluids, protamine zinc insulin has a low solubility. When injected subcutaneously it is absorbed slowly and has its onset of action in from three to six hours after the injection. The peak activity is reached in approximately sixteen hours (fourteen to twenty) and the duration of action lasts from twenty-four to thirty-six hours. In fasting patients, a hypoglycemic effect has been obtained for as long as forty-eight to seventy-two hours after a single injection.

Indications for protamine zinc insulin. Protamine zinc insulin is useful in replacing regular (unmodified) insulin when multiple injections of the regular insulin are needed for control, or when adequate control cannot be obtained or frequent hypoglycemic reactions occur with the unmodified insulin.

It also is useful in replacing the intermediate insulins (NPH, lente, and globin zinc) in those patients who get late morning or afternoon reactions on small doses (25 units) of these insulins. This is of especial importance in those diabetic patients whose occupations make it essential that they be free of hypoglycemic reactions during the daytime while at work (motor vehicle drivers and so forth).

It is most effective in protecting against nocturnal hyperglycemia. It releases its active insulin at a fairly uniform and constant rate. Because of its slow onset and rate of action it may not protect against postprandial hyperglycemia and glycosuria without the addition of supplementary doses of regular insulin. Doses of protamine zinc insulin large enough to control daytime hyperglycemia and glycosuria may cause nocturnal hypoglycemia. Protamine zinc insulin is unable to cope with the rapidly varying demands of acute emergencies and should not be used alone or to replace rapidly-acting insulin during coma, acute infections, or surgery.

Protamine zinc insulin has an excess of protamine and will convert an equal amount of regular insulin into protamine zinc insulin. Therefore mixtures of protamine zinc insulin and regular insulin should contain an excess of regular insulin, the commonly used ratios being 2:1 and 3:1. When supplementary regular insulin is used in conjunction with protamine zinc insulin it is best that they be given in separate injections. Since the intermediate insulins have become available, the use of protamine zinc insulin with regular insulin has for the most part been discontinued.

Protamine zinc insulin should be given subcutaneously only, never intravenously or intramuscularly.

NEUTRAL PROTAMINE HAGEDORN OR ISOPHANE INSULIN (NPH). NPH insulin is a suspension of crystals containing insulin, protamine, and zinc obtained by mixing carefully a solution of protamine, in accurately measured amounts, with a solution of zinc-insulin crystals.[17] NPH insulin contains 0.5 mg. of protamine per 100 units (as compared with 1.25 mg. of protamine per 100 units of protamine zinc insulin). There is no excess of protamine in the mixture. Each 100 units also contains 0.02 mg. of zinc and sufficient disodium phosphate buffer to maintain the pH between 7.1 and 7.4. After careful mixing, NPH insulin forms a cloudy suspension similar to protamine zinc insulin.

The time action of NPH is intermediate in effect between the rapid, short action of regular insulin and the slow, prolonged action of protamine zinc insulin. It is comparable to a 2:1 mixture of regular and protamine zinc insulin. The onset of activity occurs within two to four hours; the peak of activity occurs within eight to twelve hours, and the duration of effect lasts from eighteen to thirty hours. The duration of activity of NPH insulin is sufficient in most cases to assure an overlap of effect adequate to maintain satisfactory fasting blood sugar levels. The rapidity of its action is prompt enough to control the postprandial hyperglycemia and glycosuria following breakfast in many diabetic patients so that supplemental doses of regular insulin may not be needed. Since there is no excess of protamine, regular insulin can be added to NPH insulin without loss of action of either type provided the mixture is used at the time of mixing. When mixed with regular insulin the proportions are usually 1:1 to 6:1, the larger amount being the NPH insulin.

Indications for NPH insulin. An intermediate-acting insulin such as NPH insulin is indicated for those patients who require multiple injections of regular insulin for control, who cannot be controlled satisfactorily with multiple injections of regular insulin, or who require mixtures of protamine zinc insulin with regular insulin. Because of its rapid onset of action plus its moderate overlapping effect NPH insulin combines the advantages of the short- and long-acting insulins.

It should be given subcutaneously only, never intravenously or intramuscularly.

GLOBIN INSULIN. Globin insulin is an intermediate-acting insulin first prepared and described by Reiner, Searle, and Lang in 1938.[18] It is a clear, yellow liquid in which insulin is combined with a retarding agent, globin (a protein obtained from beef red blood cells), and zinc. Each 100 units of insulin contains 3.8 mg. of globin and from 0.20 to 0.35 mg. of zinc at a pH of 3.5 to 3.8.

Its activity curve is similar to that of NPH insulin except for a somewhat faster peak as well as a shorter duration of effect. The onset of action occurs in from two to four hours, the peak is reached in from six to twelve hours, and the duration lasts for from twelve to twenty hours. With globin insulin as well as with other insulins, the larger the dose, the more intense and prolonged is the effect.

Indications for globin insulin. The indications for the use of globin insulin are the same as for the other intermediate insulins (see NPH insulin).[19] Its advantage is that it is a clear solution. However, it has the disadvantage of an action curve which is less predictable from day to day than that of the other intermediate insulins.

Mixtures of globin insulin with regular insulin are not recommended because of the continuing interaction of the globin and regular insulins which changes the ratio of each, making constancy of dosage difficult to achieve. Globin insulin should not be used if the liquid becomes cloudy or if a sediment forms.

LENTE INSULIN. Hallas-Møller and his associates[6] developed stable preparations of insulin from the action of zinc on insulin under specific chemical conditions without the addition of any modifying chemical agents. By increasing the concentration of zinc to ten times the amount required for the formation of soluble zinc-insulin crystals and by changing the buffer solution from phosphate to acetate, the resulting product was insoluble at the pH of the blood. Two separate forms of the high zinc-insulin compound were produced by the careful adjustment of the pH, one crystalline and one amorphous. The crystalline form has the larger particle size and is much more insoluble (ultralente). The amorphous form has the smaller particle size and is much more soluble (semilente). The mixture of 70 per cent of the ultralente and 30 per cent of the semilente results in lente insulin.

Lente insulin contains 0.2 mg. of zinc per 100 units of insulin. Each cubic centimeter also contains 0.9 to 1.1 mg. of sodium acetate as buffer.

The characteristics of the time action of lente insulin are so similar to that of NPH insulin that they may be used interchange-ably. The onset of activity occurs after two to four hours, the peak is reached in from eight to twelve hours, and the duration of effect is twenty-eight to thirty-two hours.

Indications for lente insulin. The indications for the use of lente insulin are the same as for NPH insulin.[20] The clinical effectiveness of both is the same.

The principal advantage of lente insulin is the absence of protamine or other binding foreign protein. Some feel that since it is the purest modified insulin yet developed it should be used in every diabetic individual in whom it achieves good chemical control without persistent allergy.[21]

It is indicated for all patients who have allergy to other intermediate insulins. In those patients well controlled with NPH, globin, or other insulin, with or without accompanying crystalline insulin, there may be no advantage in shifting to lente insulin.

Lente insulin is considered the insulin of choice by some physicians when insulin treatment is first instituted or when regulation with other types of insulin is difficult.

Allergic reactions to lente insulin have occurred but the incidence of significant reactions is small. Some patients report a transient burning sensation at the site of injection. This may be due to the fact that the preservative, methylparaben, is not anesthetic, while the preservative used with other insulins, tricresol, is a mild local anesthetic.

Lente insulin and crystalline insulin may be mixed in a single injection with preservation of most of the rapid action of the unmodified insulin. They do not combine, nor do they interfere with each other's action as long as the amount of regular insulin does not exceed the amount of lente insulin in the mixture.[22]

Lente insulin has a theoretical advantage over the other two intermediate insulins. Containing no protamine, it cannot, over a long period, have any deleterious effect on blood lipids that might come from protamine, a heparin antagonist.

SEMILENTE INSULIN. Semilente insulin is the rapid-acting form of the stable suspension of zinc insulin crystals in an acetate buffer. It is amorphous and has small particle size and a short action. It contains 0.2 to 0.25 mg. of zinc per 100 units of insulin and its pH is 7.2.

The onset of action occurs in one hour, the peak is reached in from six to ten hours, and the duration of effect is from twelve to sixteen hours. It is midway between regular and NPH insulin in its time of action.

Indications for semilente insulin. The main indication for the use of semilente insulin is to supplement lente insulin when a more rapid action is indicated. When lente insulin alone does not control the postprandial hyperglycemia, semilente insulin may be added to increase the rapidity of action. Since the lente and semilente insulins are identical chemically, they may be mixed in any desired ratio without concern for incompatibility.

ULTRALENTE INSULIN. Ultralente insulin is the crystalline form of the stable, acetate buffered, form of zinc insulin. It has a larger particle size and more prolonged action than lente insulin.

Ultralente insulin contains 0.2 to 0.25 mg. of zinc per 100 units of insulin at a pH of 4.8 to 5.7 (compared with the pH of semilente of 7.2). The onset of action is prolonged (eight hours), the peak of action is from sixteen to twenty-four hours, and the duration of action is greater than thirty-six hours.

Indications for ultralente insulin. The main indication for the use of ultralente insulin is as a supplement to lente insulin to prolong its action and control fasting hyperglycemia. Like semilente insulin it is chemically identical to lente insulin and can be mixed in any desired ratio.

Occasionally it may be used alone on a single-dose schedule to control a patient's diabetes, but this use is rare.

Management of the diabetic patient with insulin

The increasing number of available insulins and the increasing number of combinations that are used may have complicated the problem of insulin therapy. Many methods of therapy have been suggested.[23–27] Some advocate the use of a single dose of protamine zinc insulin as the basic therapy, while others prefer an intermediate insulin with or without supplemental regular insulin. The single most important tenet of insulin therapy is that each patient requires individual management. The type of insulin, number and size of daily doses, time of administration, type of diet, and amount of exercise are problems of management that require continuous medical supervision.

Patients do not always respond in the same manner to a given dose of insulin, since many factors alter this response. There is an increased need for insulin during ketosis, acidosis, infection, burns, endocrine disturbances (such as hyperthyroidism), pregnancy, muscular inactivity, weight gain, and so forth.[28] With the termination or correction of these conditions, the need for insulin decreases.

INSTITUTING THERAPY. A newly discovered diabetic patient may be hospitalized or treated on an ambulatory basis. A short period of hospitalization offers the opportunity for rapid, accurate control as well as a more thorough education of the patient as to the nature of the disease and its complications. It permits a complete evaluation of the cardiovascular, renal, neurologic, and ophthalmologic systems. It affords the patient adequate time for personal instruction and training in diet therapy, testing of urine for sugar and acetone, and administration of insulin.

Except in the case of the new severely diabetic patient or one with complications for whom hospitalization is essential, the entire evaluation, training, and control of the patient can be accomplished in the office or clinic by a physician and staff willing to spend adequate time with the patient. The education of the diabetic individual and his family is essential to success in treatment. They must be taught to correlate diet, exercise, and insulin dosage with various conditions of life.

DIET AND INSULIN. There is a divergence of opinion as to what dietary regimen is best. There is universal agreement, however, that the diet should be well balanced; contain appropriate calories to attain and maintain ideal body weight; supply proper amounts of carbohydrate, protein, polyunsaturated fat, minerals, and vitamins; and be consistent with the local dietary habits and customs.[29]

Dietary control is essential in patients taking insulin to help prevent swings from hypoglycemia to hyperglycemia.[30] Under conditions of usual activity the diet should be relatively constant as to amount, type of food, and time of meals. The diabetic diet is essentially a quantitative diet, and some physicians still advocate the strict weighing of food.[9] However, most physicians now use the list of food exchanges prepared by, and available from, the American Diabetic and American Dietetic Associations in which household measures are used. By this method of diet control the diabetic patient is not restricted in his choice of eating places and is free to eat with other people.

The total caloric intake should be constant in patients taking insulin. If a patient is controlled on a specific dose of insulin, the omission of calories from his diet will result in hypoglycemia, the addition of calories in hyperglycemia. The obese diabetic patient must remain on a low calorie diet to reduce, the underweight diabetic patient must take in enough calories to gain weight, and the diabetic child must ingest sufficient calories to grow normally.

The distribution of caloric intake varies with the type of insulin used—calories being supplied to cover the anticipated time of hypoglycemia, calories being extracted to prevent hyperglycemia.

With regular or short-acting insulin the diet distribution must take into account the rapidity of its peak action and the short duration of its effect. Since the peak effect is reached in from two to four hours, it may be wise to extract a fruit exchange from breakfast and give it at 10:00 A.M. or substitute a slowly absorbed carbohydrate (such as bread or cereal) for the rapidly acting fruit. The intermediate insulins (NPH, lente, globin) have a slow onset of action, and if given before breakfast they reach their peak of activity between 3:00 and 4:00 P.M. A milk and bread allowance may be extracted from the breakfast allowance to be given as the mid-afternoon snack, thus compensating for the slow onset of action and preventing the afternoon hypoglycemia. With globin insulin a night feeding may not be necessary but with lente and NPH insulin a night snack is advocated to prevent nocturnal hypoglycemia.

The long-acting insulins (PZI and ultralente) if given before breakfast require the patient to eat a large dinner and bedtime feeding with a small breakfast. The caloric content of the meal following the injection should be limited to avoid hyperglycemia in the interval between the time of the injection of insulin and its effect. The high caloric intake in the evening and bedtime meals is to prevent hypoglycemia at the time the long-acting insulin is exerting its greatest effect.

The ideal is to have the food distributed so that the properly adjusted dose of insulin will result in good control as manifested by the absence of hypoglycemia, hyperglycemia, and ketonemia. The dietary adjustment of meals must be made individually for each patient according to his work needs and customs.

The newly discovered, uncomplicated, diabetic patient may be given a trial period of from four to five days on diet alone before starting insulin. Seventy-five per cent of the diabetic patients (the obese, maturity-onset type) may need no treatment other than dietary control. The normal-weight diabetic patient of insidious onset may also do well on dietary restriction alone. The juvenile diabetic patient, the thin adult diabetic patient, those patients with complications, and those patients not controlled with diet alone will require insulin.[31]

Observations should be made of the height of the blood sugar, the amount of glycosuria and ketonuria, the presence of symptoms, and the changes in body weight. The need for the administration of insulin will depend on the results of these observations.

INSULIN REQUIREMENTS. The estimation of the insulin requirement of a diabetic patient is purely empiric and must be determined for each patient individually. The adjustment of insulin dosage based only on the determination of urinary glucose is not physiologic, since it gives only gross qualitative information about insulin requirements. However, it remains the most practical method available. The specimens should be collected four times during the day: (1) between bedtime and breakfast, (2) between breakfast and lunch, (3) between lunch and dinner, and (4) between dinner and bedtime. The urines should be examined separately, charted, and used as a guide for the adjustment of insulin dosage. Thus, the presence of excessive sugar in the specimen between breakfast and lunch indicates that the morning dose of insulin should be increased or breakfast decreased in amount. If protamine zinc insulin is being used and the morning urine specimen (bedtime to breakfast) is sugar-free, further increases in dosage are contraindicated since they will probably cause predawn hypoglycemia. If the urine still shows evening glycosuria, there is an indication for supplemental doses of regular insulin or a change to NPH insulin. These fractional urine specimens define the periods of hyperglycemia and enable the physician to judge the effectiveness of the type and dosage of insulin used and to make the necessary changes.

Blood sugar specimens before breakfast or other meals, depending on the type of insulin used, may aid in the management of insulin dosage in newly treated diabetic patients.

MANAGEMENT WITH RAPID-ACTING INSULIN. Some physicians prefer to use rapid-acting insulin (regular insulin) for the early management of newly discovered diabetic patients who require insulin. The usual initial dose is 10 to 15 units fifteen minutes before breakfast. The second dose is then dependent on the blood sugar level and the response to the first dose.

We start with 10 units before the morning and evening meals and increase or decrease the dose by 3 to 5 units every day or two depending on the glycosuria in the corresponding fractional urine specimens of the previous day. Should the morning and evening doses be increased to 20 to 30 units and glycosuria still be present, additional insulin is given before lunch and bedtime.

In most diabetic patients requiring insulin a modified insulin (intermediate) should be substituted as soon as the total daily dose of crystalline insulin necessary for control has been established. We have seen occasional patients who have been treated and controlled for years with regular insulin, and who prefer to continue with multiple doses of insulin, especially when the injections are limited to the morning and evening meals.

MANAGEMENT WITH INTERMEDIATE INSULIN. The most popular insulins used in the management of diabetes are lente and NPH insulin.

In the patient with newly discovered, uncomplicated, and moderately severe diabetes the initial daily dose is usually 10 units given thirty minutes before breakfast. The dose is increased by 3 to 5 units every two to three days depending on the results of the fractional urines and the blood sugar levels until satisfactory control is obtained.

If the patient has been treated previously with crystalline or protamine zinc insulin, he is given slightly less NPH or lente insulin than the total daily dose needed for management (75 to 80 per cent). The dosage is adjusted subsequently depending on the findings.

If the patient was receiving a 2:1 mixture of regular insulin and protamine zinc insulin, the initial dose of intermediate insulin may equal the total dosage of the mixture. The same unit-for-unit substitution prevails when NPH insulin replaces lente or globin insulin, or vice versa. When the fractional urine before the evening meal shows only a trace to 1 plus glycosuria, no further increase in the intermediate insulin is made for fear of inducing mid-day hypoglycemia. If, at this time, the mid-morning control is unsatisfactory (3 to 4 plus glycosuria) a short-acting insulin may be added to the morning dose of intermediate insulin. Five to 10 units of the short-acting insulin may be added to the NPH or lente insulin, and the short-acting insulin may be increased by increments of 3 to 5 units until the noon test is satisfactory. The unmodified insulin may be mixed in the same syringe with NPH insulin. It also may be mixed with lente insulin if the proportion of regular insulin to lente insulin remains 1:1 or less; otherwise it should be given as a separate injection, or semilente insulin, which can be mixed with lente insulin in any proportion, should be used as the short-acting insulin.

If the mixture of intermediate and short-acting insulin is inadequate to control fasting hyperglycemia and glycosuria, additional intermediate insulin may be given before supper or bedtime. One may start empirically with 5 to 10 units of the intermediate insulin before supper and gradually increase or decrease the dose as indicated. The short-acting insulin given in the morning controls the forenoon blood sugar; the morning intermediate insulin controls the afternoon and evening levels; and the evening intermediate insulin controls the overnight levels.

If lente insulin is being used as the intermediate insulin and it controls the daytime glycosuria and hyperglycemia but not the fasting hyperglycemia, ultralente insulin may be added to the lente insulin as a single morning injection. The prolonged action of the ultralente insulin may control the high fasting blood sugar level. The starting dose should be 5 to 10 units of the ultralente insulin, and adjustments should be made depending on the patient's response.

MANAGEMENT WITH LONG-ACTING INSULIN. There are occasional patients who have been taking protamine zinc insulin since its inception who have done well with small doses of it (30 units or less) and who prefer to continue its use. However, because of the defects of the long-acting insulins (the slow onset of action does not control the hyperglycemia following breakfast and the prolonged action may lead to hypoglycemia during sleep) they are infrequently used alone. Even the mixtures of protamine zinc insulin and regular insulin, which were popular prior to the introduction of the intermediate insulins, have been discontinued now that lente and NPH insulins are available.

Ultralente insulin has its greatest use as a modifier of lente insulin in those patients in whom a prolonged action is needed. Since the two compounds are chemically identical, they may be mixed in any ratio.

INSULIN IN COMPLICATIONS OF DIABETES. The use of insulin in special situations, such as diabetic ketosis and surgery, are detailed elsewhere in this series.[32, 33] It is sufficient to say that special technics are necessary.

Technic of insulin administration

Once the need for insulin therapy has been established the patient must acquire the following: (1) an approved insulin syringe; (2) 2 rustless hypodermic needles,

$^5/_8$ or $^3/_4$ of an inch long, 25 or 26 gauge; (3) 70 per cent grain or special isopropyl alcohol; (4) absorbent cotton; and (5) the prescribed insulin.

The insulin syringes are graduated in units with red markings for U40 insulin and green markings for U80 insulin. These are the same colors used to identify the strength of insulin preparations.

The needles should be $^5/_8$ or $^3/_4$ of an inch long, rather than $^1/_4$ to $^1/_2$ of an inch since the shorter needles may result in superficial, poorly absorbed, injections of insulin.

The sterilization of the syringe and needles may be accomplished by boiling them in water for five minutes. Most patients prefer to sterilize their syringes and needles in 70 per cent grain or special isopropyl alcohol. It is safe and much more convenient. It is best to keep the instruments immersed in a container of alcohol between injections. There are available many pocket cases of plastic or metal which permit continuous immersion of the syringe and needle in alcohol while traveling. The alcohol which remains in the barrel of the syringe and in the needle may be removed prior to the injection of insulin by pushing the plunger in and out several times. Any residual alcohol following this will be harmless. Following the injection of insulin, the needle and syringe should be rinsed in cold water and then alcohol.

Insulin is usually administered subcutaneously. In emergencies, regular insulin may be given intravenously. During surgical procedures insulin may be added to the intravenous infusions. The amount added depends on the previous insulin requirements and the number of infusions to be given. The usual dose is 10 to 20 units per 1,000 cc. of 5 per cent glucose in water (or saline). When the insulin is added, the bottle should be inverted and rotated several times to effect an even distribution of insulin throughout the infusion.

The site of injection of subcutanously administered insulin should be varied. This is to prevent fibrosis, induration, atrophy, or hypertrophy and to insure a rapid absorption of the insulin. The most frequently used sites of injection are the thighs, abdomen, and upper arms.

When any of the modified insulins are used, it is essential that the precipitate be distributed evenly throughout the fluid. This can be effected by inverting and rotating the insulin bottle several times immediately before withdrawing the desired amount. The injection should be given soon after withdrawing the insulin to prevent the precipitate from settling in the syringe.

The syringe should be loaded by injecting into the vial a volume of air equal to the volume of the dose of insulin to be used. The insulin is then allowed to flow back into the syringe.

When mixtures of modified and unmodified insulin are to be used, an amount of air equal to the amount of insulin to be removed is first injected into the NPH insulin or protamine zinc insulin bottle and the syringe is removed without removing any insulin from the bottle. Then, the desired amount of unmodified insulin is removed from its vial according to the technic described. The needle is then inserted into the NPH insulin or protamine zinc insulin bottle and the desired amount of insulin is allowed to flow back into the syringe. The two insulins are then mixed in the syringe by drawing back a bubble of air and rotating and inverting the syringe several times before injection.

The skin should be sterilized with alcohol, and the injection should be made at right angles to the skin, which may be pulled taut or pinched up with the fingers approximately 3 inches apart.

Complications of insulin therapy

HYPOGLYCEMIA. Hypoglycemic reactions occur because of an excess of insulin, an inadequate intake of food, an excess of exercise, or a combination of these factors. Symptoms usually appear when the blood sugar level falls to 60 mg. per 100 ml. or below. However, they may occasionally appear when the blood sugar is normal, due to the rapidity of the fall in the blood sugar. The reactions are more frequent in the juvenile and thin adult diabetic patient than in the obese diabetic patient who is relatively insensitive to insulin. The poorly controlled and undernourished patient with an inadequate hepatic glycogen store has

TABLE II. Differential diagnosis of diabetic coma and insulin reactions*

Features	Diabetic Coma	Insulin Reaction	Protamine Zinc Insulin, NPH Insulin, or Lente Insulin Reaction
Clinical			
Onset	Slow (days)	Sudden (minutes)	Gradual (hours)
Causes	Ignorance and neglect Intercurrent disease	Overdosage Delayed or omitted meals Excessive exercise before meals	Overdosage Delayed or omitted meals Excessive exercise before meals
Symptoms	Thirst Headache Nausea Vomiting Abdominal pain Dyspnea	"Inward nervousness" Weakness Sweating Hunger Diplopia, blurred vision Paresthesia Psychopathic behavior Stupor, convulsions	Fatigue Weakness Headache Sweating sometimes absent Dizziness Nausea Diplopia, blurred vision Psychopathic behavior Stupor, convulsions
Signs	Florid face	Pallor	Pallor
	Air hunger	Shallow respiration	Shallow respiration
	Kussmaul breathing		
	Finally, respiratory paralysis		
	Dehydration, dry skin	Sweating	Skin may be dry
	Rapid pulse	Pulse normal	Not characteristic
	Soft eyeballs	Eyeballs normal	Eyeballs normal
	Acetone breath		
	Normal or absent reflexes	Babinski reflex often present	Babinski reflex often present
Chemical			
Urine			
Sugar	Positive	Usually absent, especially in second voided specimen	Usually absent, especially in second voided specimen
Acetone	Positive	Negative	Negative
Diacetic acid	Positive	Negative	Negative
Blood			
Leukocytosis	Present; may be very high		
Sugar	350 ± mg.	60 mg. or lower	60 mg. or lower
CO_2 combining power	Less than 20 volumes	Usually normal	Usually normal
Reponse to treatment	Slow	Rapid; occasionally delayed	May be delayed

* Modified from Joslin.[9]

little protection from hypoglycemic reactions.

The symptoms vary with the type of insulin used. With regular insulin the blood sugar falls rapidly and the predominant symptoms are those of compensatory sympathetic excitation with sweating, weakness, hunger, tachycardia, and "inward trembling" as the major findings. The reaction usually occurs within four hours after the injection of regular insulin.

With the modified insulin preparations (NPH, lente, globin, protamine zinc) the blood sugar falls slowly and the onset of hypoglycemia is gradual and insidious occurring within eight to twenty-four hours after the injection. The symptoms are cerebral as manifested by headaches, visual disturbances, mental confusion, coma, and finally convulsions. The two groups of symptoms may merge when the fall in blood sugar is rapid, profound, and persistent (Table II[9]).

The symptoms of hypoglycemia may simulate numerous psychiatric and neurologic diseases. They have been erroneously diagnosed as being due to epilepsy, alcoholism, anxiety state, hysteria, psychosis, brain tumor, diabetic coma, head injury, or poisoning. Irreversible brain damage leading to mental deterioration or epilepsy may occur from prolonged hypoglycemia or repeated episodes of hypoglycemic reactions.[34-36] Transient hemiplegia and coronary insufficiency may be manifestations of hypoglycemic reactions in those with preexisting vascular disease.

One of the great hazards of excess insulin dosage is the exacerbation of the diabetes.[37] Somogyi[38] has shown that excess insulin dosage can produce hyperglycemia, and the deleterious effects may not disappear for months after the dose of insulin is reduced. Gordon[39] reviewed the hazards of excessive insulin dosage and discussed the therapeutic regimen for the highly unstable or "brittle" diabetic patient who fluctuates erratically from hypoglycemic shock to marked glycosuria with ketosis while consuming the same diet day after day and receiving the same insulin dosage. Physicians confronted by this dilemma have been uncertain about whether or not to increase the insulin dose to eliminate the hyperglycemia or decrease the dose to stop the hypoglycemic reactions. "It may be stated categorically, as a basic principle, that diabetic patients should have no insulin reactions and their insulin dosage should be adjusted accordingly."[39]

The danger of the development of hypoglycemic reactions without the usual warning symptoms of tremor, sweating, hunger, diplopia, and so forth has been stressed by Root.[40] Patients continued to work automatically, became emotional, pugnacious, or even unconscious. Retrograde amnesia for periods varying from three minutes to an hour before the reaction was common. Neuropathy involving the autonomic or higher cerebral centers due to repeated hypoglycemic reactions was considered a possible explanation.

Hypoglycemia initiates a sequence of physiologic events which results in a rebound hyperglycemia. The first response is the secretion of epinephrine due to the stimulation of the adrenal medulla.[41] This causes the sweating, pallor, nervousness, tremor, restlessness, palpitation, dilated pupils, and hunger. The epinephrine increases the conversion of hepatic glycogen to glucose thus raising the blood sugar and preventing loss of consciousness in those patients with sufficient hepatic glycogen stores. It is ineffective in the malnourished patient.

The stress of the hypoglycemia stimulates the adrenal cortex to produce hydroxycorticoids which cause gluconeogenesis from noncarbohydrate sources, resulting in the replenishment of glycogen stores and a rise in the blood sugar level.

A mild hypoglycemic reaction may occur at night. The adrenal compensatory mechanisms are stimulated so that by morning the blood sugar level may be elevated. Because of this elevated fasting blood sugar the insulin dose may be increased thus resulting in a more severe nocturnal reaction. This stimulates compensatory mechanisms to a greater degree resulting in a higher fasting blood sugar the following day. Thus the picture of "brittle" diabetes develops with the patient taking large doses of insulin to counteract the high fasting blood sugar but having frequent episodes of severe hypoglycemia in the presence of extreme fluctuations of glycosuria and ketonuria.[42]

Prevention of hypoglycemia. The prevention of hypoglycemic episodes is essential. The patient and family must know the prodromal symptoms so as to prevent a full-blown insulin reaction.

The need for a relatively constant, rather than a fluctuating diet, becomes apparent. The effect of exercise and diet on the action of insulin must be stressed to the patient. Whenever exercise is anticipated the dose of insulin should be reduced, or additional food taken. The addition of sorbitol, a polyalcohol, was reportedly of benefit in older subjects but not in younger patients.[43-45] Further studies to determine the usefulness of sorbitol and fructose over prolonged periods of time are indicated.

Changes in the type of insulin used and in the frequency and size of doses may be necessary. When the hypoglycemic reactions occur in the mid-morning, the dose of regular insulin should be reduced. When they occur in the afternoon, evening, or overnight, the dose of intermediate insulin should be reduced. Nocturnal or early morning reactions may be a reflection of an excessive dose of long-acting insulin.

The replacement of a single dose by divided doses of insulin may prove helpful. The reduction in size of a single, before breakfast dose of a mixture of an intermediate insulin with regular insulin may be effected by giving a second dose before dinner or bedtime. At times multiple small doses of regular insulin may be required. The prevention of hypoglycemia is essential for achieving satisfactory diabetic control.

Treatment of hypoglycemia. Glucose administration is the basic treatment for the acute hypoglycemic reaction. If the patient is awake the use of orange juice, candy, or sugar should not be delayed. If the patient is unconscious, 25 cc. of 50 per cent dextrose given intravenously may result in an immediate return to consciousness. If no intravenous glucose is available, glucose may be given by a stomach tube or by a rectal tube. In addition, 0.5 cc. of a 1:1,000 solution of epinephrine may be given in an attempt to mobilize the liver glycogen sufficiently to rouse the patient so that he is able to take oral feedings. If the coma persists or deepens, large amounts of 50 per cent glucose, together with 100 mg. of intravenous hydrocortisone, are essential.

Glucagon may be used for the treatment of insulin hypoglycemia.[46-49] It mobilizes glucose from the liver, catalyzing the conversion of glycogen to glucose-1-phosphate. Glucose is then formed through the action of phosphoglucomatase and glucose-6-phosphatase. Glucagon does not release glucose from muscle glycogen nor does it inhibit the uptake of glucose by muscle. It has no sympathomimetic activity. It is supplied in a 1-mg. vial with 1 cc. of diluent (containing 1.6 per cent glycerin and 0.2 per cent phenol). The glucagon is dissolved in the diluent and injected subcutaneously, intramuscularly, or intravenously. If the patient does not awaken within twenty minutes, one or two additional doses of glucagon may be given. When the patient responds, supplemental carbohydrate is given to restore the liver glycogen and prevent secondary hypoglycemia. The repeated use of glucagon results in no untoward reaction either locally or systemically.

The advantages of glucagon are its ease of administration, enabling a member of the patient's family to give it to an unconscious or uncooperative patient; and the smooth elevation of the blood sugar obtained, often avoiding the "rebound hyperglycemia." A lack of response to glucagon may indicate an inadequate dose of glucagon, an inadequate hepatic storage of glycogen, or a faulty diagnosis. If the patient in hypoglycemia fails to respond to repeated injections of glucagon, intravenous glucose must be given.

Every diabetic patient should carry a card, obtainable from the American Diabetes Association, which states that he is a diabetic patient and that if he is found unconscious, or behaving peculiarly, he may be having an insulin reaction. The card also directs the finder to give the patient sugar, candy, or fruit juice. The card should be carried in the patient's wallet or pocketbook in an accessible place likely to be seen by people in times of need.

LOCAL COMPLICATIONS OF INSULIN THERAPY. The local complications of insulin injections, such as infections, lipodystrophy, and fat hypertrophy have been discussed in another article in this series.[50] Scrupulous care in the sterilization of the syringe and needles, cleanliness of the site of injection, and systematic variation of the sites of injection are essential but may not prevent these complications.

Allergic reactions to insulin. The over-all incidence of allergic reactions to insulin is between 5 and 10 per cent.[51,52] These reactions may be mild local, severe local, or generalized.[53] Eighty-five per cent of the reactions to insulin are of the mild local type and consist of stinging, redness, and induration at the injection site. They reach a maximum in twelve to twenty-four hours and subside within one to three days. They usually clear in spite of the continued use of insulin.

The severe local reactions consist of pain, induration, urticaria, erythema, bullae, and even purpura.

One per cent of the reactions are generalized and are manifested by cutaneous, circulatory, and/or intestinal findings. Anaphylactic shock has been reported occasionally.[54]

A detailed study of these reactions is presented in another article of this series.[55]

INSULIN PRESBYOPIA. Insulin presbyopia may occur with the rapid control of diabetes. There is a bilateral temporary loss of near vision due to a change in osmotic equilibrium between the lens and ocular fluids. It usually clears in two to four weeks. It is, of course, not due to insulin per se.

EFFECTS OF INSULIN AND ORAL HYPOGLYCEMIC AGENTS. Exogenous insulin is effective in all types of diabetes. In milder cases of diabetes, (that is postmaturity-onset type) diet alone may result in control. Sulfonylurea derivatives and biguanides also may be effective in this group.

Combined therapy with the oral hypoglycemic agents in the insulin-dependent diabetic patient has been reported favorably by several investigators.[56-61]

The beneficial results obtained with tolbutamide as an adjunct to insulin therapy in both labile and stable diabetic subjects have been noted to be ease and greater uniformity of metabolic control and a reduction in insulin dosage. It was found that good control could be obtained with a reduced amount of insulin together with a daily dose of 1 to 2 Gm. of tolbutamide.

The biguanides, when used with insulin in the treatment of the unstable, "brittle," juvenile-type diabetic patient, have, in some cases, demonstrated a stabilizing effect on the wide fluctuations between hyperglycemia and hypoglycemia.[61-63] Small doses (50 to 200 mg. per day) of the biguanide have been used. The initial dose of the biguanide may be 50 mg. daily divided into two doses. If good control is obtained a small decrease (5 to 10 units) in the amount of insulin may be attempted. If inadequate control is obtained, no change is made in the dose of insulin and the biguanide is increased up to a maximum of 200 mg. daily. Changes in dosage may be made at four- to seven-day intervals.

The danger of ketosis occurring in the presence of normoglycemia in insulin-dependent diabetic patients taking phenformin has recently been stressed.[64,65] It was suggested that, in those cases receiving supplementary insulin, the antiketotic effect of insulin is antagonized by the phenformin. Ketonuria was noted in 34 (29 per cent) of 117 patients and in 13 patients an alkali reserve of less than 20 mEq. per liter was noted. Children and young adults with growth-onset diabetes and older persons with unstable diabetes usually develop ketosis easily. Such individuals require daily insulin injections for survival. In these individuals "insulin should form the basis and mainstay of treatment, and if the physician desires to try phenformin it should be used only as a supplement to insulin."[65] The danger of ketoacidosis is serious and demands caution in the use of phenformin in all insulin-dependent cases.

INSULIN INHIBITORS AND RESISTANCE. Berson and Yalow[66] have published an excellent review of insulin inhibitors and insulin resistance. Virtually all insulin-treated subjects show the presence of insulin-binding antibodies after a few weeks of therapy. In the majority of subjects the circulating antibody is saturated by relatively small amounts of insulin, and insulin in excess is free to exert its hormonal influence. Therefore, a significant increase in insulin requirements is not found. However, in some insulin-resistant subjects, insulin-binding capacities may be much greater, ranging from 60 to 750 units of plasma per liter and higher. In such cases relatively enormous doses of insulin may be required to exceed the antibody-combining capacity and to allow for an effective concentration of free insulin.

Tyler and Beigelman[67] reported a case of diabetic coma requiring 97,740 units of insulin in a fifty-six-hour period to change the blood sugar from 1,200 to 472 mg. per 100 ml. Sera obtained from the patient during the course of insulin therapy demonstrated high levels of insulin-like activity. This insulin or insulin-like material was relatively ineffective in lowering the blood sugar. Similarly others have demonstrated the presence of insulin-like activity in patients resistant to insulin.[68-70] All of these cases demonstrated that there may be insulin-like activity in the sera of some insulin-resistant diabetic patients but this activity is not associated with the reduction of the hyperglycemia. They suggested that peripheral tissue defect or alteration may be responsible for insulin resistance in these cases. While there is abundant evidence that circulating serum or plasma factors are associated with insulin resistance, there is also strong evidence pointing to the importance of peripheral tissue factors.

To control ketosis, insulin-resistant patients may require vast doses of insulin during the acute episode. Following recovery from ketosis the patients may experience repeated hypoglycemic reactions in spite of withholding further insulin therapy. These reactions may be due to the slow release of insulin from the large amount trapped in insulin-antibody complexes.[71]

Treatment of insulin-resistant diabetes. "Insulin-resistant diabetes" is a term applied to patients whose daily insulin requirements exceed 200 units. It occurs in many conditions such as acidosis, infection, liver disease, and hyperfunction of the thyroid, adrenal, or anterior pituitary.[72]

Smelo[73] has pointed out the difficulty in evaluating the effect of any specific treatment because of the variable course of insulin resistance. The steroids have been reported to be effective in reducing the insulin requirements in insulin-resistant patients, but the mechanism of their effect is unknown.[74] It has been suggested that they influence antibody formation. Oakley and his colleagues[75] treated 6 patients with prednisone with a marked decrease in insulin requirements in those with demonstrable insulin antibodies. The 2 patients who showed no response to prednisone had negative test results for insulin antibodies. Morse[76] also showed a significant reduction in insulin requirement following treatment with adrenocortical steroids, with an accompanying decrease in insulin-antibody concentration in such cases. Field[77] found that all but one of his patients who were chronically insulin-resistant had augmented amounts of insulin bound to the fastest moving gamma globulins. This occurred only in patients who had received exogenous insulin for at least three months. Corticotrophin therapy did not benefit all patients with chronic insulin resistance, even though a circulating insulin inhibitor was detected. Sera from patients who were benefited by treatment no longer inhibited insulin but were still capable of binding large amounts of insulin.

The insulin dosage decreases in four to five days following the institution of steroid therapy and usually is less than 100 units in ten to fourteen days, when it is effective. It is difficult to explain the early fall in insulin dosage by decreased antibody synthesis since gamma globulins have a half-life of the order of fourteen days. The early decrease could be due to a direct effect on insulin-sensitive cells, an effect on capillary membrane permeability, or an alteration of the protein binding.[78] Prout and Katims[79] reported that methyl prednisolone lowered the serum-binding globulin concomitantly with insulin in an insulin-resistant patient.

Menczel and Diengott[80] reported the successful treatment with tolbutamide of an insulin-resistant diabetic patient. Others have used tolbutamide with variable success. Phenformin (DBI) has been used because of its effect on the peripheral utilization of carbohydrate. The relationship of DBI to the immune mechanism has not been defined. The hormonal substances that influence insulin sensitivity and antagonism are covered in an excellent review by De Bodo and Altszuler.[81]

Vallance-Owen and Lilley[82] recently have shown the presence of a serum albumin-bound insulin antagonist in obese diabetic patients as well as in prediabetic patients. They also found greater than normal amounts of a similar substance in the blood of depancreatized but not of depancreatized-hypophysectomized cats. The presence of the antagonist in increased amounts in depancreatized animals appears to be due to insulin deficiency. It seems probable that its presence in diabetic patients is also the result of insulin deficiency rather than the cause of it.

Summary

The characteristics of the presently available insulins have been reviewed, and the use of insulin in the routine management of diabetes mellitus has been discussed. Methods of treating the complications of insulin therapy, including insulin hypoglycemia, have been outlined. The need for the supervision and individualization of treatment, with careful attention to diet, exercise, and insulin therapy has been stressed.

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Nutrition Excerpts

Prepared with the cooperation of the faculty of the Graduate School of Nutrition, Cornell University, Ithaca, New York

R. A. NELSON, M.D., Editor

Trace Elements

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THERE ARE several trace elements which have been found to be essential or useful for the normal growth and development of various species of animals, but for which no corresponding information is available in the case of man. The marked physiologic abnormalities which result in animals from a deficiency of these trace elements, their essentiality for certain basic enzyme reactions common to all species, and the changes which have been observed in their levels in the blood, tissues, and excretory products in certain human diseases indicate that they must have some specific significance in human metabolism. This article presents a brief review of the status of present knowledge with respect to some of these elements. No discussion is given of iron, iodine, and fluorine, the nutritional importance of which is well recognized.

Copper

The human body contains 100 to 150 mg. of copper. The liver is the chief storage organ, but the element is widely distributed in other organs and tissues. According to Herring *et al.*[1] the blood plasma normally contains from 0.5 to 1.93 parts per million with a mean value of 1.03. The level is altered considerably in certain pathologic states.

Copper deficiency has been demonstrated in various experimental animals, reflected in nervous symptoms, bone abnormalities, hair and skin changes, decreased iron absorption and utilization, hypochromic microcytic anemia, and other pathologic states. Quantitative requirements have been established for farm animals. Despite considerable study a dietary need for man has not been demonstrated. Wilson and Lahey[2] recently have reported an experiment with premature infants who should be especially susceptible to copper deficiency because they are born with very low stores of this element. One group was fed a milk formula containing only 0.07 mg. of the element per quart, resulting in an intake of about 14 micrograms per kilogram of body weight, a level much below the requirement for animals. A check group was fed a formula containing several times as much copper. Over a two-month period there were no differences in the growth rate or in the hemoglobin, copper, or protein levels in the serum. Thus no dietary need for copper was demonstrated.

Although copper has not been proved essential, there are many conditions in which alterations in plasma and tissue levels have been noted. Herring *et al.*[3] have reviewed the work in these fields as well as cited findings of their own. Hypocupremia occurs in normal pregnancy, in the newborn child, and in several pathologic conditions, such as the nephrotic syndrome, Wilson's disease, kwashiorkor, and sprue. In some of these conditions, however, the body store of copper is increased. In some diseases hypercupremia occurs. The significance of these various findings cannot be interpreted at present, particularly as regards body needs. While there is evidence that copper is essential for hemoglobin synthesis in animals, it has not been found useful in treating hypochromic anemia in man.

Copper has been shown to be essential as a constituent or activator of several enzymes, including ascorbic acid oxidase, polyphenol oxidase, uricase, butyl coenzyme-A hydrogenase, liver catalase, and tyrosinase. Some of the pathologic conditions found as a result of copper deficiency in animals appear to be associated with a lessened activity of copper-containing enzyme systems. For example, a deficiency of tyrosinase activity is probably involved in the hair and skin changes noted. The fact that certain copper enzymes are essential in human metabolism indicates that the element must be required in the diet despite failures to prove its essentiality.

It has been shown that adults will remain in balance on 2 mg. of copper each day. Customary diets supply from 2 to 5 mg. The report of the Food and Nutrition Board[4] states that infants and children require about 0.05 mg. per kilogram of body weight, but the basis for this statement is not given. The role of copper in human metabolism has been reviewed by Gubler.[5]

Manganese

Manganese has been found in all the animal tissues that were examined. Most of them contain substantially lower levels of manganese than of copper. The highest concentrations (2 to 4 parts per million on a fresh basis) are found in the bones, liver, kidney, pancreas, and pituitary gland. The bones and, to a lesser extent, the liver serve as storehouses of the element, as indicated by experiments showing that their content can be influenced appreciably by the dietary intake. In animals a lack of a few parts per million of manganese has been found to result in slower growth, bone abnormalities reflecting a defective mineral structure, and depressed reproductive functions. In the female there is irregular estrus, resorptions during gestation, and the birth of weak or dead young. In the male there is a failure of spermatogenesis and, marked testicular degeneration results.

No such abnormalities in man have been associated with a manganese deficiency. Its essentiality remains unproved. Nevertheless, its role in certain enzyme systems indicates that it must be a dietary essential for man as well as for the animals studied. It is required for the decarboxylation of oxalosuccinic acid to alpha-ketoglutaric acid in the Krebs cycle through which carbohydrates and fats pass in their metabolism. In manganese deficiency, as studied with rats and rabbits, there is a reduction in liver arginase. A decrease in bone alkaline phosphatase activity also has been observed in these species on manganese-deficient diets, indicating at least one way in which manganese affects bone formation. The element also has been reported to be an activator of certain peptidases.

Several manganese balance experiments have been reported. On the basis of such a study with children an intake of 0.2 to 0.3 mg. per kilogram of body weight has been recommended. North, Leichsenring, and Norris[6] found that college women receiving intakes of 3.7 mg. of manganese daily retained 1.54 mg.

Zinc

The total amount of zinc in the human body is approximately 2.2 mg., nearly half its content of iron. The element is widely distributed, having been found in all organs and tissues thus far examined. It is relatively high in the skin, hair, and nails. Herring *et al.*[1] have reported plasma levels for different age groups. The mean values for the different groups ranged from 2.82 to 3.14 parts per million. There was a rather wide range of individual values within a group. In animal experiments it has been proved essential for normal growth and for the prevention of various pathologic conditions. In pigs a specific dermatitis, designated as parakeratosis, results from its deficiency. In chicks shortened and thickened leg bones and poor feathering are the more prominent symptoms. In mature rats testicular atrophy has been found. None of these various animal troubles have been associated with zinc deficiency in man.

Disturbances of zinc metabolism have been noted in man, however, in a variety of conditions, as reviewed by Vallee[7] who has made several studies in this field. Additional information is provided in the paper by Herring *et al.*[3] which deals particularly with hematologic diseases. The zinc level in the serum has been found to be decreased in pneumonia, bronchitis, erysipelas, untreated pernicious anemia, hepatic dysfunction, and myocardial infarction. Alterations also have been noted in other troubles. Vallee points out that, while disturbances of zinc metabolism have been noted in a variety of conditions, much more research is needed before it can be assigned a diagnostic role and that it has no known therapeutic role in systemic disease. Because the enzyme zinc dehydrogenase is involved in the oxidation of ethanol Vallee *et al.*[8] was led to study zinc metabolism in patients with postalcoholic cirrhosis and found that its concentration in liver tissue was lowered.

Zinc is a constituent of several enzymes which are essential for normal human metabolism. It is an integral part (0.3 per cent) of the molecule of carbonic anhydrase which is essential for cell respiration. It functions in four dehydrogenases and several other enzymes. These enzymic roles indicate that there must be a dietary requirement for zinc in man as well as in animals, although a human requirement has not been demonstrated positively. Balance experiments have suggested that an intake of 0.3 to 0.6 mg. per kilogram of body weight is adequate.

Other trace elements

Cobalt is contained in the vitamin B_{12} molecule and as such is a requirement for all species. In ruminants the vitamin is synthesized by bacteria in the rumen, provided the ration contains cobalt. Thus cobalt is a dietary essential for this species since their customary rations contain little or none of the vitamin. There is no evidence that cobalt has essential functions in any species other than as a constituent of vitamin B_{12}.

Despite its highly toxic properties, selenium at levels of fractions of a part per million in the diet has been found to prevent dietary liver necrosis in rats, exudative diathesis, a hemorrhagic disease in chicks, and "muscle dystrophy" in lambs and calves. Molybdenum, another highly toxic element, has been found to be a component of the xanthine oxidase molecule. There is still some question, however, as to whether or not this enzyme performs an essential role in vital functions. There are reports based on animal experiments that chromium, bromine, vanadium, barium, and strontium perform useful and perhaps essential functions, but much more study is needed to clarify the observations made. There is no evidence from studies on human beings as to the usefulness of any of the elements just mentioned. A discussion of them will be found in a report of the American Academy of Pediatrics[9] and also in the papers by Herring *et al.*[1,3]

Trace element interrelationships

One of the complicating factors in studying trace element needs is their interrelationships with each other in metabolism. The effective and even the safe levels of certain trace elements are influenced greatly by the levels of others in the diet, as shown by animal experiments. In rats an excess of zinc results in an anemia which is overcome by the feeding of more copper. High levels of zinc, nickel, and manganese have been found to decrease the storage of copper in the livers of sheep. An intake of manganese which is two and a half times the required amount for baby pigs interferes with hemoglobin synthesis. This synthesis is restored to normal by adding more iron to the diet. Molybdenum poisoning is characterized by symptoms of copper deficiency which can be alleviated by the feeding of more copper. The sulfate ion also mitigates the harmful effects of molybdenum. Excess calcium increases the requirement of zinc to prevent parakeratosis in swine. These are only a few of the many findings in this complicated field.

Comment

It is quite evident from this brief review that there is only limited specific knowledge of the needs for and the function of trace elements in man. The importance of further studies is indicated. There is no clear evidence that customary diets need supplementation by the elements here discussed. Caution in making such a supplementation is suggested by the adverse effects of relative excesses, as mentioned in discussing their interrelationships. Mineral-vitamin mixtures are being sold containing a dozen or more mineral elements, including copper, zinc, cobalt, manganese, nickel, molybdenum, and fluorine. Clearly, their use is unwise.

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Number twenty-six in a new series of Nutrition Excerpts

Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the NEW YORK STATE JOURNAL OF MEDICINE from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the JOURNAL, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

BENJAMIN J. CILIBERTI, M.D., Chairman
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Sickle-Cell Disease and Anesthesia

THE PRESENCE of sickle-cell disease increases the hazard of surgery and anesthesia. This chronic, familial, hemolytic anemia of unknown etiology is found in general in the Negro race. The incidence in the American Negro generally approaches 11 per cent.[1] There is no apparent difference in the sex incidence. The preoperative diagnosis of sickle-cell anemia is not always made, and routine laboratory methods may not disclose its presence.

An understanding of this disease is essential to both the surgeon and the anesthesiologist. The following case report illustrates the problems and seriousness of the disease.

Case report

This twenty-two-year-old female Negro patient came to surgery for an emergency exploratory laparotomy with a diagnosis of possible ovarian abscess. Her past history revealed a nephrotic syndrome of unknown etiology for which cortisone therapy had been administered. She also had an underlying hemoglobinopathy classified as a sickle-cell trait. At this time she complained of pain in the lower portion of the abdomen, severe sore throat, and a septic fever which was resistant to antibiotics. A physical examination revealed a somewhat obese, lethargic patient. Her temperature was 103 F., pulse 120 beats per minute, and respirations 26 per minute. Her blood pressure was 120/70, and her heart was enlarged with a soft blowing systolic murmur at the pulmonic area. A 3 plus ankle edema was present, and the spleen was found to be enlarged. The electrocardiogram showed nonspecific ST wave changes. Laboratory tests revealed a decline in her hemoglobin from 14 to 8 Gm. per 100 ml. of blood within a two-week period. The white blood cell count was 6,600 per cubic millimeter, and the blood urea nitrogen was 12 mg. per 100 ml. Her urinalysis showed 4 plus albumin. She received a transfusion of 1 unit of packed cells which elevated her hemoglobin to 10 Gm. per 100 ml. preoperatively.

Anesthesia was induced with 150 mg. of thiopental sodium, and cyclopropane-oxygen in a circle carbon dioxide absorption system was used for maintenance. Endotracheal intubation was accomplished with ease. Muscular relaxation during surgery was obtained by the use of a slow intravenous succinylcholine drip. Ice bags were utilized to reduce the patient's temperature to 98 F. during the procedure. An infusion of cortisone also was administered to the patient. The anesthesia was uneventful. The blood pressure varied between 100/60 and 110/70 and the pulse between 120 and 100 beats per minute.

The exploratory laparotomy revealed no surgical disease. The patient expired on the third postoperative day with a nephrotic syndrome and sickle-cell crisis.

The autopsy report revealed hemoglobinopathy, nephrotic nephrosis, hepatomegaly with congestion and fibrosis, splenomegaly, pulmonary edema and congestion, and dilatation of the right ventricle. The causes of death were stated to be sickle cell crisis and nephrotic syndrome.

Comment

Sickle cell disease can give rise to symptoms and syndromes referable to almost any

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Presented and discussed at a conference held at Bellevue Hospital, New York City, October 2, 1961. Clinical Anesthesia Conferences are held on the first Monday of each month.

organ or system of the body. The manifestations of generalized anemia, the increased blood viscosity and sludging effect from bizarrely shaped erythrocytes, and the resultant emboli and thrombi are responsible factors. The most severe manifestation of sickle-cell disease is the abdominal crisis, consisting of severe pain which is sudden in onset and recurrent. It mimics the pain of other diseases and is said to imitate syphilis. The stress of surgery and anesthesia through diagnostic error, as in this patient, complicates the picture and predicates a stormy postoperative course and poor prognosis. Operations for incorrectly diagnosed surgical conditions are not infrequent in these patients. The diagnostic problem is evidenced by the joint agreement of the medical, surgical, and gynecologic departments to perform an exploratory operation on this patient.

Sudden, unexpected death may occur at any time from (1) vascular occlusion or thrombosis as the result of sickling of erythrocytes with clumping, (2) hemorrhages in vital organs due to increased fragility of the erythrocytes, and (3) sickle-cell crisis with the sudden destruction of erythrocytes.[2] Death also may result from sickle-cell trait alone or, more commonly, when associated with other conditions, especially hypoxia. One bout of hypoxia may precipitate a crisis.[3] It becomes apparent, then, that the cells are extremely sensitive to hypoxia, and hypoxia is a condition which must be combated in every anesthetic administration. No ideal anesthetic agent or technic has been found for patients with sicklemia, but over-premedication, deep anesthesia, exaggerated surgical positions, sudden excessive blood loss, respiratory obstruction or depression, and hypotension should be avoided. The maintenance of high oxygen saturation throughout the course of anesthetic administration is an essential requirement for these patients.[4]

The cardiac enlargement found in this patient may have been the result of the anemia itself or the result of multiple thrombi in the vessels of the pulmonary circulation with a resulting cor pulmonale. This patient also had hepatomegaly and splenomegaly. The sudden increase in the size of the liver and spleen can occur during crisis. The spleen also may be found to be shrunken and atrophic following repeated infarction after a period of time.

Since this patient also had renal disease, fixed agents or drugs excreted by the kidneys should have been avoided. The use of ice bags to lower her temperature was indicated. This tended to eliminate or reduce the demand hypoxia resulting from high fevers.

At present, there is existing evidence that an increase in hydrogen ion concentration also can be responsible for precipitating an acute sickle-cell crisis. Salisbury[5] reported on a patient with sickle-cell disease who developed a hypotensive episode, coma, and focal neurologic signs following cholecystectomy. These corresponded with a decrease in arterial blood pH because of metabolic acidosis. Recovery in this patient was attributed to frequent measurements of arterial blood pH and correction of the acidemia.

It is difficult to state whether or not the patient herein reported developed an acidemia following the exploratory laparotomy. She may well have had an acidosis since she did have renal involvement.

In sickle-cell disease a detailed analysis of each case and an understanding of the pathologic processes, coupled with careful anesthetic management of these patients during surgery, is important. The avoidance of hypoxia and the assurance of a high oxygen saturation during anesthetic administration are essential. Attention to physiologic detail and the correction of any acidosis may insure a better postoperative prognosis in these patients.

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Number one hundred eighteen in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

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Suspected Barbiturate and Nonbarbiturate Sedative Intoxications with Fatal Outcome

The following incidents were reported recently to the New York City Poison Control Center.

Incident 1

Substance Ingested	*Age*	*Sex*
Dry Ice	3 years	Female

The mother reports that this child obtained a piece of dry ice which was dissolved previously in water and swallowed about 3 ounces of the solution. The mother frantically called the Poison Control Center which assured her there was no cause for alarm since the dry ice had been dissolved by the carbonating action, and the resultant product amounted to an impure soda water.

A follow-up form was sent to the home, and the father's comments on the incident are noteworthy:

> After dissolving a 1/4- by 1/4-inch piece of dry ice in water it was consumed by my three-year-old daughter. Then, calling your office and learning there was no cause to worry as long as the dry ice had dissolved completely, there was no need for a doctor. Thank you very much.
>
> Sincerely,
> A Very Grateful Father

This case is cited primarily not for the testimonial but to indicate the additional function of a Poison Control Center, that is, not only to advise on the management and treatment of poisonings but also to allay unnecessary anxiety and overtreatment in cases which are not recognized as inconsequential by the distraught parent.

It is unfortunate that the manufacturers of many harmless household products do not have the courage to indicate that these products are safe when ingested.

Incident 2

Substance Ingested	*Age*	*Sex*
Barbiturate	8 months	Female

One day prior to admission to a hospital this child was observed to be lethargic, unresponsive, and had an elevated temperature of 100 F. The child had a normal birth history but an afebrile convulsion at three months of age. An electroencephalogram done at that time showed entirely negative findings. The child's growth and development were said to be normal except for an inability to sit up.

On admission to the hospital the white count was 4,000 with a normal differential. The x-ray films of the skull and chest showed entirely negative findings. The patient had a spasticity of both lower and upper extremities with hyperactive reflexes and was unable to hear as determined by gross testing. This finding was not present the day before admission and, according to the mother, had never existed before.

The blood chemistries done soon after admission showed a potassium of 5.1, chlorides 98, and sodium normal. The calcium level was not obtained.

The patient was seen by a neurologist who did a spinal tap at the time. The spinal fluid revealed no cells, no increased pressure, and normal chemistry values. There was some suggestion of pallor of the optic disks, but it was not marked. Twelve hours following the spinal tap the patient lapsed into a comatose state. The white count shifted from 4,000 to 36,000 with a shift to the left. The temperature rose to 102 F., and the patient was put on intravenous fluids with penicillin. An x-ray film of the chest at this time revealed some increased hilar markings suggestive of a bronchopneumonic process, and therefore, she was placed on tetracycline also. At this time it was felt that the patient was pooling secretions and had a definitely diminished gag reflex. After three days in the first hospital, the patient was transferred to Long Island Jewish Hospital with nasal oxygen and an intravenous catheter during transport.

Jack Frankel, M.D., at Long Island Jewish Hospital, reported that on admission there the patient was in a critical state, comatose, slightly responsive to stimuli, and had the appearance of a decerebrate rigidity. The color was fair, and respirations were extremely shallow and rapid. The pupils reacted to light with diminished corneal reflexes. The gag reflex was sluggish but was present. The lung fields were clear with an overlay of numerous coarse rhonchi. The heart sounds were rapid but of good quality. The abdomen was soft, and there were no masses. The genitalia showed negative findings, and the extremities were held in a spastic state.

The patient was seen at this point by a neurologist and a neurosurgeon. A repeat lumbar puncture was done but produced negative findings. A pneumoencephalogram was done with no significant findings, and an arteriogram performed by injecting dye into the carotid artery also showed normal findings. Ear, nose, and throat examinations revealed that a tracheostomy was not indicated at this time because of the precarious condition of the child. The patient was under constant careful observation.

Her condition in the hospital continued to worsen. She was kept on intravenous fluids and on the second day of hospitalization developed absent respirations. The child's respirations were maintained by means of positive pressure with a resuscitator and an endotracheal tube.

An attempt to obtain any history of the ingestion of drugs or barbiturates was unsuccessful. The parents, as well as the patient's private physician, denied the administration of such drugs. Further history revealed by the pediatrician who had seen the child when she was three months of age and subsequently six and seven months of age indicated normal development except that the child was somewhat retarded in sitting up. Vision and hearing had been perfectly normal up until this time.

The patient failed to improve, developing cyanosis of the nail beds with the heart sounds becoming faint and more distant. On the last day of life, three days following admission to the second hospital, a barbiturate level was drawn on the urine, and although there was no history of ingestion of any barbiturate and no question of it being given any place, a level of 0.6 mg. per 100 ml. of barbiturate was obtained. This test was repeated and showed 0.4 mg. per 100 ml. barbiturate content in the urine and 3.1 mg. per 100 ml. in the blood.

A laboratory work-up in Long Island Jewish Hospital on admission revealed a white count of 24,600 with 47 per cent segmented neutrophils, 5 band cells, 45 lymphocytes, 2 monocytes, and a normal hematocrit and hemoglobin. Cultures of the blood and urine and spinal fluid were entirely negative. A urinalysis was negative except for a 1 plus acetone, but one day prior to expiration the patient developed a 3 plus albuminuria. The sodium, potassium, blood urea nitrogen, glucose, chlorides, and carbon dioxide-combining power all were within normal limits.

The patient expired on the third hospital day, or twelve hours following the second barbiturate determination, with a questionable diagnosis of demyelinating disease as the possible diagnosis suggestive of Schilder's disease. On the basis of the blood and urine barbiturate levels, however, the body was turned over to the medical examiner to rule out barbiturate poisoning.

The positive findings on the postmortem internal examination revealed about 10 cc. of clear, straw-colored fluid in the left pleural cavity, about 5 cc. in the right, 5 cc. in the pericardial sac, and approximately 150 cc. of liquid and clotted blood in the peritoneal cavity. The clotted blood was partially organized. There was no communication from any of the needle punctures with the body cavities.

The gastrointestinal tract presented postmortem autolytic perforation at the esophageal gastric junction and a thickened area in the duodenum through which perforation had occurred. This is the first portion of the duodenum on the anterior surface.

The heart, spleen, liver, pancreas, adrenals, and kidneys showed no abnormal findings.

The thymus was atrophic, and the larynx was unobstructed. The trachea contained a scant amount of aspirated food.

The lungs were remarkably well aerated. The tracheobronchial tree had a light pink mucosa.

The cause of death was listed as a ruptured duodenal ulcer.

Because of the manifest symptoms and the condition of the child, the barbiturate level in the blood (3.1 mg. per 100 ml.) and urine (0.4 mg. per 100 ml.), although low, was highly suggestive of barbiturate ingestion in spite of denial by the family that the child had received or accidentally ingested any barbiturate. The postmortem examination, however, contributed to the possibility of making a more definitive diagnosis of the cause of death. However, one is still puzzled concerning the presence of barbiturates in the blood and urine. The admission of patients in coma often presents a challenge to the diagnostic acumen of physicians.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
Glutethimide	47 years	Male

This patient was depressed for some time and ingested forty 500-mg. glutethimide tablets with suicidal intent. This patient had made a previous attempt at suicide several years ago. His depression at this time was attributed to his inability to find employment. It was reported that he had left a suicide note which was obtained by the police.

The patient was admitted to the hospital in a deep coma. He vomited following the ingestion, and on admission to the hospital his stomach was lavaged with sodium bicarbonate. The gastric contents contained some white sediment and mucus. Both pupils were markedly dilated, and the reflexes were absent. The lungs showed a few scattered rales in both bases; the respirations appeared labored.

The Poison Control Center was called at this time in regard to therapeutic management.

In addition to the emergency treatment, 1,000 cc. of intravenous fluids were given. Caffeine sodium benzoate was given intramuscularly, and Megimide was given intravenously. After the second administration of this stimulant the deep reflexes were obtained. However, the patient still remained comatose. The blood pressure was 140/60, pulse 82, and respirations 16. The administration of oxygen via mask was begun. The hospital considered transferring the patient to Bellevue Hospital the following morning. However, the patient was pronounced dead at 7:55 A.M., having failed to regain consciousness. The final clinical diagnosis was glutethimide poisoning.

The postmortem examination was done by the Office of the Chief Medical Examiner. The positive findings were as follows: The lungs were voluminous, boggy, and noncrepitant. The cut section was dark red. On pressure it exuded a moderate amount of thin, frothy, reddish liquid. There were some poorly defined, granular, slightly raised, reddish areas. The remainder of the lung was fairly well aerated. The tracheobronchial tree was patent. The mucosa was slightly and diffusely reddened.

The liver was normal in size and shape and weighed 1,750 Gm. The capsule was thin and smooth. The tissue was congested but otherwise normal. The gallbladder contained about 20 cc. of thin bile.

The kidneys were congested but otherwise normal. The pelves and ureters were normal.

The urinary bladder was moderately dilated with about 20 ounces of clear amber urine. The wall was of normal thickness, and the mucosa was slightly trabeculated.

The gastrointestinal tract findings showed that the stomach contained about 12 ounces of thin, cloudy, brownish-gray liquid. The small intestine contained some grayish chyme.

There was no evidence of trauma to the scalp or to the skull. There was an old laceration of the brain involving the temporal lobe and the gray matter, in which there was a loss of brain substance. This involved the middle and superior temporal gyri in their mid-portion. There was also one point of loss of gray matter on the hippocampal gyrus over an area approximately one-half cm. in diameter on the right side. The blood vessels at the base were thin-walled and patent. The cerebrospinal fluid appeared clear.

The anatomic findings showed hypostatic congestion, edema, and pneumonia of the lungs; an old superficial laceration of the right temporal lobe; and congestion of the viscera.

The causes of death were listed as an old laceration of the brain and bronchopneumonia.

A toxicologic examination of the brain and stomach produced findings negative for alcohol. Other volatiles were absent. Findings for barbiturates, carbonates, Noludar, glutethimide, and salicylates were absent. Organic bases and organic amphoterics also were absent.

This is another example of a fatality from a nonbarbiturate drug where the use of an analeptic drug was unsuccessful. It is again emphasized that the implied safety of nonbarbiturate sedatives is unfounded.

Number eighty-five in a series of Accidental Chemical Poisonings

Retrolental fibroplasia in premature infants

The incidence of eye disease associated with the administration of oxygen to premature babies has declined sharply since 1954, according to *Patterns of Disease*, a Parke, Davis & Company publication for the medical profession. Retrolental fibroplasia has dropped from an incidence of 28 per cent to 8 per cent in its mild form from 1954 to 1958, and from 8 per cent to zero in its severe form during the same period. Between these years, the average duration of oxygen therapy administered to infants was reduced from more than ninety hours to less than twenty.

Maternal Welfare

Prepared by the Subcommittee on Maternal and Child Welfare, Committee on Public Health and Education, Medical Society of the State of New York

EDWARD C. HUGHES, M.D., Syracuse, Editor

Roentgen Radiation and Female Reproductive System

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THERE SEEMS TO BE little practitioners can do about the potential genetic effects of atmospheric fallout from nuclear devices. They can, perhaps, reduce the apprehensions of their patients concerning fallout if they choose to agree with the authoritative opinion, namely, that any increase of radiation will do some harm genetically, but the practical results, in terms of increasing congenital anomalies, will be very slight. Widespread publicity has increased public interest concerning the harmful effects, both somatic and genetic, of radiation in general. It is, perhaps, appropriate to consider the potential harm of the current medical use of diagnostic x-ray procedures.

Dangers of radiation

Most expert radiologists are acutely aware of the dangers of radiation and use current knowledge to establish good x-ray hygiene principles in their work. Recent surveys suggest that some physicians may not be giving their patients maximum protection against the noxious results of diagnostic x-ray procedures. The problem seems to involve medical judgment, x-ray equipment, and technics.

One survey showed that one third of the fluoroscopes used in a particular community delivered more roentgens per minute than are recommended for patient protection by the National Committee on Radiation Protection and Measurement. Another report states that the individuals using 133 x-ray units used gonadal shielding in x-raying infants in only 15 per cent of cases. There is some opinion, which may or may not be correct, that these findings represent average conditions in the United States. There is some evidence that a tendency has developed to use diagnostic x-ray procedures as laboratory tests, much as one would use blood counts.

The subject should concern the physician who deals with female patients in the child-bearing age group primarily in two ways: (1) He should consider radiation effects on the ovaries in terms of damage that could influence future pregnancies by causing congenital anomalies and, more important, causes the production of recessive mutant characteristics possibly affecting future generations; (2) he should, also, think in terms of potential damage to the embryo in women who are in the early stages of pregnancy and potential damage to the fetus in later stages of pregnancy.

There seems to be some acceptable evidence, based on animal experimentation, that regardless of where x-radiation beams are directed, the ovaries are affected to some extent by means of scatter. A rational approach to the use of diagnostic x-ray technics would seem to involve the principle that where one cannot avoid a certain amount of necessary exposure to a noxious agent, such exposure should be kept to a minimum.

The translation of this principle into practical terms can be done by considering a few examples. There are a few physicians who apparently continue to use chest fluoroscopy rather than chest films in ordinary physical examinations. Some radiologists feel this is poor radiation hygiene because it involves a larger dosage, while the information gained is materially less.

The use of x-ray technics as diagnostic procedures depends on their potential importance in providing information weighed against any possible damage that such studies may do. This would seem especially true, for example, with intravenous pyelograms, lower gastrointestinal tract studies, and other studies that involve anatomy in proximity to the ovaries. Certainly the advantages of screening technics, wherever possible, needs ever-increasing attention in females in the age group below forty years.

The increasingly prevalent idea of delaying routine chest x-ray films of pregnant women until at least the second, and preferably the third, trimester seems to be based on good reasoning. This is true also of the use of lower dosage technics, utilizing full-size radiographs rather than the miniature film technic which used fluoroscopic principles. There seems to be considerable merit in preliminary screening with tuberculin tests, reserving chest x-ray films for the tuberculin-positive. The nontuberculous pathologic conditions that might be missed in tuberculin-negative patients deserve consideration, even to the extent of considering postpartum chest films.

No physician can be expected to deny a woman who is two months pregnant the benefits of all diagnostic technics if he suspects she may have a lower intestinal tract malignant condition. It is possible that a proctoscopic examination could establish a diagnosis, and this examination should be done before using x-ray tests.

The physician who does sterility work should evaluate the relative merit of establishing tubal patency by means of nonopaque media technics, such as the Rubin test, as against an opaque medium technic with fluoroscopic visualization of the pelvis. The latter technic may eventually be indicated, but is the physician justified in employing the opaque contrast medium technic as his "routine" method of determining tubal patency?

Summary

There seems little doubt that diagnostic radiation involves both somatic and genetic danger. Very little, if any, somatic harm should result from diagnostic procedures performed in an adequate fashion. There is reason to think that medical practice has evolved in such a manner that some of us instinctively tend to order x-ray examinations much as we would order urinalyses. We apparently must accept the fact that all types of x-ray procedures carry a potential risk of doing some minimal damage.

We can agree with those workers who feel that each case should be determined on its own merits. No individual should be deprived of the value of necessary diagnostic x-ray procedures. It is necessary, however, that the physician decide the relative gain from any diagnostic procedure and whether or not these merits outweigh the risks involved.

It makes no difference whether the physician actually does his own diagnostic x-ray work or whether he refers his patients for such tests. The principle remains that the individual doctor should accept his responsibility in practicing satisfactory radiation hygiene.

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Acknowledgment. We wish to thank Paul A. Riemenschneider, M.D., Chief, Department of Radiology, Syracuse Memorial Hospital, for advice in the preparation of this article.

Surgical Lesions of Spine and Spinal Cord Simulating Disk Syndrome

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WHILE THE SO-CALLED "classical history and physical findings of a ruptured lumbar disk" are common knowledge, these typical symptoms of disk herniation are not as pathognomonic as is believed.[1-4] One of the most important groups of cases in which the primary complaint is that of low back and sciatic pain is those of spinal cord tumors which present symptoms in this fashion; moreover, the history of trauma may be misleading in such a patient. In spite of the fact that the findings on neurologic examination are negative, an examination of the cerebrospinal fluid and myelography as well as plain x-ray films frequently are necessary to establish the correct diagnosis.

Among the lesions which have been reported to produce the disk syndrome are structural anomalies of congenital origin; inflammatory processes within the spinal canal; spondylitis; toxic metabolic changes of muscles and their associated fascia; degenerative and senescent changes in the spinal column; tumors of the spine, spinal cord, pelvis, and femur; and sciatic nerve compression in its peripheral distribution.[5-9]

The purpose of this paper is to present 3 cases, seen within one month's time, of tumors in the spine and spinal cord simulating the lumbar disk syndrome following injury, and to re-emphasize the methods which may be helpful in reaching the correct diagnosis prior to surgery.

Case reports

CASE 1. A forty-eight-year-old, left-handed white male was admitted to the hospital on July 26, 1961, with a history of a fall in June, 1961. He developed low back pain and paresthesia in the medial aspect of his left leg; the symptoms improved spontaneously in a few days. The low back pain recurred several weeks later and became constant, being worse in the supine position with pelvic traction.

In August of 1960 he developed a feeling of coldness in the buttocks. Later there was a diminution of libido which was not complete. The sphincters were normal. He also had some weight loss in spite of a good appetite. There was a past history of alcoholism ending about ten years prior to his admission.

In December, 1960, the patient was examined by a neurosurgeon who demonstrated numbness to pain, touch, and temperature over the thighs and legs bilaterally, extending to the outer border of the foot including the fourth and fifth toes on the left side. There was also a diminution of sensation over the skin of the left Achilles tendon and slightly on the dorsum and inner aspect of the left foot. There was a mild atrophy of the left anterior tibial muscles. His left patellar and right ankle reflexes were absent. The forward spine flexion was limited to 15 to 20 degrees with pain in the left calf and foot. Straight raising of the leg on the left side was limited to 65 to 70 degrees. The rest of the neurologic examination gave negative results. A lumbar puncture showed a clear spinal fluid under normal pressure with a protein of 136 mg. per 100 ml. A manometric reading revealed no block. Myelography showed a small defect of the fourth to fifth lumbar vertebrae on the left side. X-ray films of the chest and spine showed normal conditions as did the blood count and urinalysis. The sedimentation rate was 21 mm. per hour.

A left hemilaminectomy was performed, and a small bulging disk at the fourth to fifth lumbar vertebrae was removed. The histologic diagnosis was herniated nucleus pulposus. At the time of the patient's discharge on December 29, 1960, the patellar reflexes were equal and hyperactive. There were no ankle reflexes. The sensory loss was less than before surgery but followed the same pattern. The patient walked well but stiffly, guarding his gait.

Shortly after he was discharged from the hospital he developed urinary retention which required repeated catheterizations and finally the insertion of an indwelling catheter. After the removal of the catheter in a month, his bladder function improved considerably but with occasional frequency.

On July 29, 1961, the patient was admitted to the University Hospital where a general physical examination revealed a markedly emaciated white male with considerable atrophy of both legs. The positive neurologic findings were marked weakness of the legs, right greater than left; hypesthesia and hypalgesia of the fifth lumbar and first sacral vertebrae; and dermatomes bilaterally. The left perianal area was hypesthesic and hypalgesic. His deep tendon reflexes were hypoactive throughout and absent at the left knee and both ankles.

A bone survey showed multiple osteolytic lesions in both femoral shafts, large destructive lesions at the ischial tuberosity and body of the ischium, and extreme radiolucency of the body of the sacrum.

After a complete work-up, a left kidney biopsy revealed carcinoma.

Case 2. A thirty-two-year-old, right-handed salesman was admitted to the University Hospital on July 24, 1961, with the chief complaint of intermittent low back pain and a tingling sensation of the right leg.

The patient had noted a sudden onset of these symptoms approximately six years earlier when, after teeing off at golf, he developed pain across his low back. This pain persisted for two weeks, then gradually subsided. A year later he again experienced severe low back pain, this time while he was in bed. This pain subsided gradually in ten days.

The low back pain recurred about one or two years prior to his admission and had been continuous ever since. The patient noted that the pain was aggravated by walking, coughing, abdominal straining, or lying down in bed.

For the past several months prior to admission, he had been suffering from occasional urinary frequency and a tingling sensation on the posterior aspect of the right thigh.

A general physical examination on admission was unremarkable. A neurologic examination revealed a slight weakness of the right leg. A slight hypersensitivity between the tenth and twelfth dorsal vertebrae on the right was demonstrable. There was hypesthesia and hypalgesia over the right perianal area. The vibratory sense was diminished in the right ankle, but the position sense was intact in the toes. Deep tendon reflexes were hyperactive in both knees and absent in the right ankle.

X-ray films of the chest and spine were reported as showing negative findings. A lumbar puncture showed colorless fluid under a normal pressure with a protein of 113 mg. per 100 ml.; the manometric readings showed a slow rise and fall. Myelography revealed an incomplete obstruction at the twelfth dorsal and first lumbar vertebral interspace on the left side.

A laminectomy of the twelfth dorsal and first and second lumbar vertebrae was performed on July 28, 1961. At operation, a yellow, soft, cystic tumor measuring 1 by 1 by 2 cm. was found attached to the left posterolateral aspect of the conus medullaris at the level of the twelfth dorsal and first lumbar vertebrae. After the grayish cheesy content was evacuated, the cyst wall was removed, except for the portion that was attached firmly to the neural elements.

The postoperative course was uneventful, and there was immediate improvement of the paresthesia in his right leg. The urinary frequency has been improving progressively.

A histologic section of the specimen revealed an epidermoid cyst.

Case 3. In December, 1960, a forty-two-year-old, white female bookkeeper developed pain in the low back and the posterior aspect of the left thigh a few hours after she fell, landing on her back. The following morning the leg pain was relieved but the low back pain persisted for a few weeks. Following this episode the patient suffered from intermittent pain in the low back and left leg, particularly when she was walking, straining, or driving. There was no change in the character of the pain when she was lying down; however, it was relieved successfully by aspirin.

In early June, 1961, the low back pain became worse and continuous, associated with more frequent radiation into the left leg. The latter pain was shooting in character, with a tingling sensation of the sole of the left foot including the big toe. In July, 1961, she developed a slight weakness of the left leg with a progressive paresis of the foot.

A neurosurgical consultation on August 8, 1961, revealed two small fungating scalp lesions on the right occipital area. She was in much discomfort from pain on the left buttock which radiated to the posterior aspect of the left leg. The patient had a loss of the normal lumbosacral lordosis with minimal muscle spasm. There was atrophy of the left thigh and calf, with marked weakness of the dorsiflexion of the left foot. Hypalgesia was noticed over the left fifth lumbar vertebral dermatome. Deep tendon reflexes were hyperactive throughout, with unsustained ankle clonus. The left plantar response was extensor.

A lumbar puncture on the same day showed clear colorless fluid with a normal pressure and a protein content of 72 mg. per 100 ml. Manometrics were open and myelography revealed a defect on the fifth lumber vertebra on the left. X-ray films of the skull and chest showed negative findings.

On August 10, 1961, a laminectomy was performed at the fifth lumbar vertebral level. This revealed that the fifth lumbar body was involved with a tumor. Biopsy and decompression were carried out, and an excision of the scalp lesion was done at the same time.

The pathologic report on the specimens was that of metastatic carcinoma of the vertebra and scalp. A small nodule above the left breast that was biopsied on a later day was reported to be an adenocarcinoma. Postoperatively the patient has shown some improvement of the paresthesia and has regained strength in the left leg, but the foot drop has remained.

Comment

We wish to re-emphasize that many patients with spine or spinal cord tumors frequently can masquerade as suffering from herniated lumbar intervertebral disks, despite what is considered an adequate work-up. It is evident that a variety of lesions may produce this so-called disk syndrome.[1,3,7,10,11] An awareness of this problem, however, will, we believe, aid in recognizing the disease process, and the following points may lead to correct diagnosis and treatment.

1. While the history of an injury is of importance in the diagnosis of herniated intervertebral disks, many patients who have spinal cord or spine lesions develop neurologic symptoms shortly after an injury. A history of injury does not, therefore, exclude the possibility of a tumor.

2. The fact that low back pain or radiculalgia is aggravated by a recumbent position in many patients who have tumors is an important differential point in distinguishing between most pain due to tumors and that due to disk herniation.[1,2,9]

3. Careful attention to sensory, motor, sphincter, and reflex status is very important in the differential diagnosis of lesions in the spine or spinal cord. While sciatic pain with a loss of the Achilles tendon reflex is considered pathognomonic for herniated lumbar disks, many patients who have spine or spinal cord lesions show a similar neurologic picture. Additional neurologic deficits are, however, more often present in patients harboring tumors than in those suffering from disk herniations.

4. A careful evaluation of laboratory findings is always mandatory. If a rapid sedimentation rate is found and pregnancy, infection, and other causes can be excluded, a malignant condition must be considered.

In osteoblastic lesions the serum alkaline phosphatase is nearly always elevated, while in osteolytic lesions, although it may be normal, it frequently is elevated. A markedly elevated cerebrospinal fluid protein content or an abnormal cellular count should also raise one's index of suspicion.

5. X-ray films of the spine and pelvis may frequently demonstrate changes suggestive of tumor rather than of disk herniation. Negative findings, however, by no means rule out the possibility of spine or spinal cord tumors. Roentgenograms should always include the upper lumbar and lower thoracic spine as well as the lumbosacral area.[12–14]

6. Myelography in patients suspected of having a lumbar lesion or a protruded intervertebral disk should include the entire lumbar and thoracic subarachnoid space to the level of the eighth thoracic vertebra if possible.

Summary

Three cases of spinal cord tumor simulating the lumbar disk syndrome following injury, seen within one month, are presented, and the methods by which the correct diagnosis may be reached prior to surgery are emphasized.

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Dystonic reactions produced by tranquilizers

One of the side-effects of the phenothiazines is dystonia, the symptomatology of which should be recognized promptly to prevent diagnostic confusion and to facilitate treatment. A common error is explaining the dystonia either as a catatonic or conversion phenomenon. Solomon Hirsch, M.D., and Doris L. Hirsch, M.D., in an article in the May, 1961, issue of the *American Journal of Psychiatry*, present 3 case summaries in which the physicians' original impression was that the symptoms were functional or emotional in origin.

Specific clinical manifestations of dystonia include tonic contractions and myoclonic twitches of any muscle groups, unilaterally or bilaterally. Hyperextension of the neck and trunk with the spine curved backward from the hip may be noted. Spasm of the jaw muscles is common, with the mouth either tightly closed or held fixedly open with protrusion of the tongue. Speech is difficult at times. Perioral tremors, mandibular tics, and difficulty in swallowing are noted frequently. Also observed have been oculogyric spasms. Symptoms sometimes are strikingly similar to those seen in postencephalitic states. The dystonic symptoms are usually sudden in onset. They occur episodically, often are brief in duration, and occasionally under partial voluntary control. There may be pallor or flushing. Fear is usually marked, with feelings of "going crazy" or peculiar explanations for the symptoms. Usually there are no signs of Parkinsonism.

Embryonal Teratoma of Neck of Newborn Infant

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Congenital teratoma of the neck is rare. The first case was reported by Hess in 1854[1] and was later restudied histologically by Wetzel in 1895.[2] Saphir, in 1929,[3] collected and reviewed 38 cases and added 1 of his own. The last comprehensive review was reported by Bale in 1950[4] and comprised 61 cases. In 1952 McGoon[5] reported 4 cases to which Thomas[6] added 2. To date there are only 67 cases known in the literature. The rarity of this neoplasm warrants the following report.

Case reports

A full-term white female infant was born by normal spontaneous delivery in Morrisania City Hospital on January 29, 1959. The mother was a twenty-three-year-old primipara. At birth the baby weighed 6 pounds, 8 ounces. On admission to the nursery a small, movable, nontender mass of soft consistency was discovered at the left side of the infant's neck. No fluctuation or bruit was noted. The rest of the physical examination indicated essentially negative findings.

An x-ray film of the neck revealed no evidence of extrinsic pressure on the treachea or extraneous calcification. On surgical consultation a soft, nodular, freely movable mass measuring approximately 2 inches in diameter was found in the left anterior triangle. The diagnosis of either cystic hygroma or teratoma was suggested.

On February 19, 1959, an operation was performed. The cervical mass was removed under endotracheal anesthesia through a transverse skin incision. The tumor was soft, solid, well encapsulated, and somewhat adherent to the trachea. The postoperative course was uneventful, and the infant was discharged on March 4, 1959, in good condition.

At the time of the first follow-up visit to the outpatient clinic on March 12, 1959, the wound was healing well, and no edema or lymphadenopathy was noted.

Macroscopic examination. The specimen consisted of an irregularly shaped, encapsulated, reddish-brown, bosselated, and elastic soft mass measuring 6 by 2.5 by 2.5 cm. A section revealed a compact, pinkish-yellow glistening cut surface with numerous cystic spaces varying from 0.3 to 0.5 cm. in diameter. The cysts contained viscid, slightly opaque material.

Microscopic examination. Slides from the different parts of the tissue revealed a markedly varied pattern with a predominance of neural elements. These elements were composed of fibrillary structures and glial cells interspersed with occasional compact groups of mature ganglion cells (Fig. 1A). Infrequently a palisading pattern of the neuroglia elements was noted. There were scattered groups of striated muscle bundles, traversed by fibrillary nerve tissue (Fig. 1B). In some areas the neuroglial fibers could be traced to the walls of the cystic structures. Some of these cysts were lined by pseudostratified, occasionally ciliated columnar epithelium, displaying goblet cells at the luminal surface (Fig. 1C). Other cysts showed a closely-set papillary proliferation of the cuboidal lining (Fig. 1D).

In the fibrous center of one of the broad papillae a cartilage formation with scattered chondroid cells and chondromucin stroma was found (Fig. 2A). In close proximity to the cystic areas there were small groups of colloid-containing acini lined by low cuboidal epithelium (Fig. 2B). In addition to these

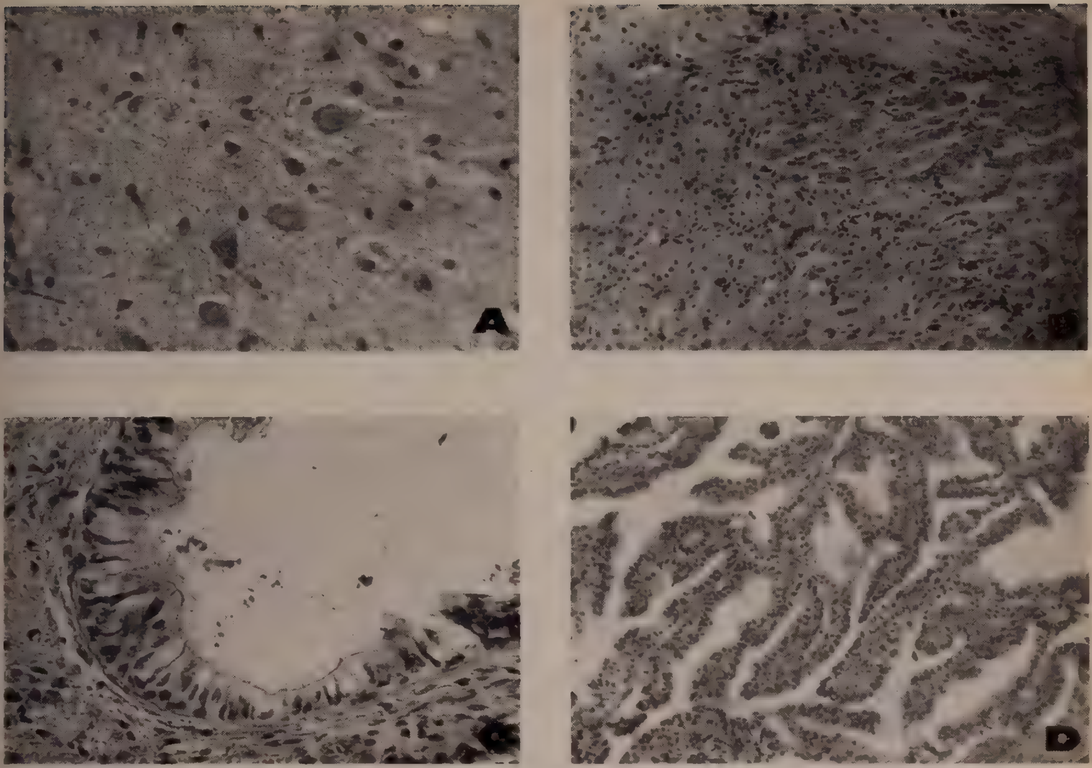

FIGURE 1. (A) Neural tissue with ganglion cells; (B) striated muscle and neural tissue; (C) cyst, lined with pseudostratified plus ciliated columnar epithelium; (D) papillary lining of cyst wall.

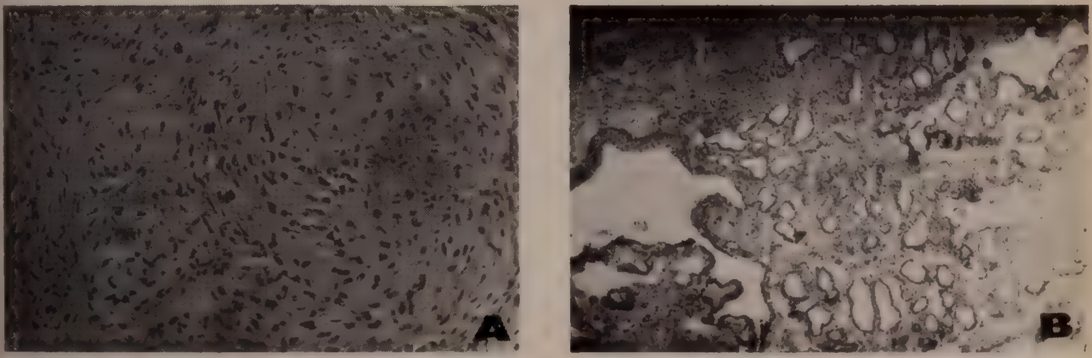

FIGURE 2. (A) Cartilage formation; (B) thyroid follicle-like groups.

structures within the glial tissue, alveolar masses of pale large cells with indistinct cytoplasm and centrally placed ovoid nuclei containing fine granules of chromatin were seen. This picture, with its abundant vascularity, resembled that of the carotid body structure (Fig. 3).

Although in our case the neural elements were predominant, tissues originating in other germinal layers were also clearly recognized. In the specimen the ectodermal layer was represented by glial cells and glial fibers and ganglion cells; the mesodermal layer was represented by clusters of cartilage cells. The presence of thyroid follicles suggested an entodermal origin.

Based on this complex pattern, the diagnosis of embryoid teratoma consisting of all

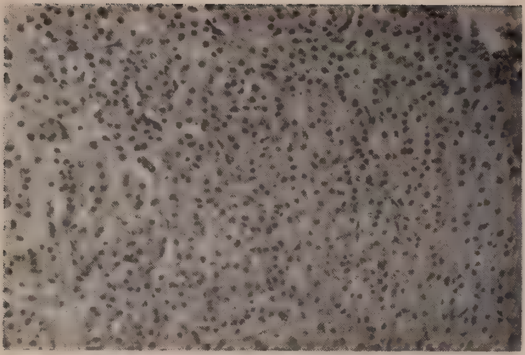

FIGURE 3. Carotid body-like structure.

three germinal elements was made.

Comment

The morphogenesis of teratomas is still a much-debated issue. Saphir,[3] quoting in his article the theory of Budde, said, "Teratomas originate from complexes of cells arising from the symmetrically fusing blastopore, the matrix of the cellular material of the three germinal layers."

Since the blastopore extends through the entire length of the "Anlage," Budde's hypothesis seems to provide an explanation for a uniform monogerminal autochthonous origin of the teratomas of the various regions.

Willis[7] believed that this problem can only be clarified by increasing our knowledge of the chemistry of early embryonic growth, including the chemistry of the "organizer" or growth hormones which determine the orderly sequence of normal development and the influence of growing blastic tissues on one another. Experimental embryology demonstrated that the blastules, deprived of their primary organizer, grew and differentiated into a variety of tissues in a chaotic manner without forming an axis or well-defined organ.

Budde's classification divides the teratomas into embryomorphous and embryoid tumors. The embryoid teratomas, which are of immediate interest to us, identify a disorderly arrangement of the structures which develop from the three germinal layers.

Bale[4] classified the cervical teratomas as (1) teratomas of the thyroid gland, a tumor which derives its blood supply from inferior and/or superior thyroid arteries; (2) teratoma of the neck in the region of the thyroid gland, a tumor which is not supplied by thyroid vessels but which displaces all or part of the thyroid gland; and (3) teratoma of the neck, probably in the region of the thyroid gland, a tumor which is not supplied by the thyroid vessels.

Thomas[6] refused to accept both Group 2 and Group 3 as separate pathologic entities since, in his opinion, they indicated only the anatomic location of the tumors. Of 67 published cases there were but 6 in which an anatomic connection between the vessels of thyroid gland and cervical tumors could be demonstrated.

McGoon[5] felt that the blood supply of the tumor could constitute no more than suggestive evidence for its origin from the thyroid gland. Although our specimen was located in the anterolateral region of the neck and contained thyroid follicles, we were unable to demonstrate any relationship between the tumor and the thyroid gland, which was not removed at the time of the operation.

The American and British literature, including our case, records 38 surgically treated patients of whom 33 survived and 5 died. These figures seem to suggest that, at the present time, a surgical removal of the tumor must be regarded as the treatment of choice. Generally these tumors are benign in nature, and there were only 3 cases in the literature which have been histologically malignant: Pupovac (1896), Lure (1908), and Fritsche (1920).[3,4]

In the differential diagnosis of an embryoid teratoma the following possibilities should be considered: cystic hygroma, congenital goiter, mixed tumor of the parotid gland, congenital lipoma, thyroglossal duct cyst, and branchial cleft cyst.

In our case the combination of tracheal, thyroidal, and carotid body-like elements in a cervical mass lead us to the conclusion that this tumor probably originated from the level of the third or fourth branchial arch; the predominance of neural tissue, however, remains unexplained.

Summary

A case of embryonal teratoma of the neck has been presented. So far, including our case, 68 cases have been reported.

This tumor was successfully removed surgically. The histologic study revealed a predominance of nervous tissue elements of ectodermal origin. Entodermal tissue was represented by the rudimentary tracheal structure, accompanied by the thyroid gland and carotid body-like tissues. Scattered areas of striated muscle and cartilage represented the mesodermal layer.

A brief review of the literature on histogenesis and a classification of cervical teratoma have been presented.

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Organic factor found in teen-age violence

An abnormal brain pattern has been found among a significant number of adolescents who commit murder and other acts of violence, according to an article by Dr. Sherwyn M. Woods in the December, 1961, issue of *Archives of General Psychiatry*. It is the author's belief that the brain abnormality "does not in itself induce violence." Rather it represents a crucial, biologic stress which enhances aggression resulting from the psychologic make-up of the individual. He theorized that both the organic and psychologic factors would have to be present to result in violence, and therefore the abnormal brain pattern could be associated with nonviolent behavior. Dr. Woods also theorized that the organic abnormality might trigger the violent acting out of conflict as a form of release from tension in much the same way that the brain abnormality of epileptic individuals triggers epileptic seizures.

The brain pattern which correlates with aggressive behavior in adolescents has been termed the "6 and 14 dysrhythmia" syndrome since the electroencephalograph of the brain waves shows distinctive peaks every sixth and fourteenth second. The causes of the syndrome are not known, but blows to the head, hereditary factors, and encephalitis have been suggested.

The author reported 2 cases of murders committed by fifteen-year-old boys who demonstrated the 6 and 14 syndrome. There have been at least 10 other such murders reported previously, and the syndrome has been associated with a wide variety of violent behavior.

He speculated that many more so-called murders without motivation by adolescents might be linked to the 6 and 14 syndrome if adequate electroencephalographic studies were made. At present there is no known effective medication for treating this disorder, and psychotherapy has not been investigated sufficiently to evaluate its benefit.

However, he said, the abnormality "tends to disappear with advancing age," and there is some evidence to suggest that the aggressive behavior associated with it may change with its disappearance.

The presence of the 6 and 14 syndrome also has legal implications, Dr. Woods pointed out. These patients "may well represent a pure-form example of a truly irresistible impulse."

Retroperitoneal Abscess Communicating with the Spinal Epidural Space

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SPINAL EPIDURAL INFECTION has been discussed extensively in the literature.[1,2] The source of epidural abscess is most commonly a distant furuncle. Staphylococcus aureus is the usual responsible organism, but pneumococci, streptococci, salmonella, brucella, pseudomonas, and actinomyces also have been isolated.[3] No report has been found of epidural infection resulting from the direct extension of a retroperitoneal abscess, and a review of the files of the Armed Forces Institute of Pathology also has failed to locate such a case.[4]

Case report

A sixty-three-year-old white female domestic was admitted to Bergstrom Air Force Base Hospital on March 8, 1960, after having fallen in the bathroom. The patient said she had been well until three days before, when she noted a dull, intermittent, nonradiating pain, unrelated to position or exertion, in the lower portion of her back. She also noted generalized weakness, especially in the legs; urinary frequency; polyuria; and a parched sensation in the mouth. On the day of admission, while she was standing in the bathroom, the patient felt so weak she was unable to support her large frame, and without losing consciousness she sank to the floor, where her family found her.

She had been obese all her life and always had become somewhat short of breath on exertion, and so she climbed stairs slowly. She had never been told of diabetes mellitus, and there was no family history of diabetes. There was no history of a preceding skin infection.

The patient was massively obese. She was garrulous, but her speech was normal otherwise. The temperature was 103 F. A faint systolic bruit was heard over the upper portion of the left carotid artery. The head showed otherwise negative findings. Papilledema was absent, and the motion of the eyes was normal. The mouth was dry, and the thyroid was not enlarged. The neck was supple. There were occasional inspiratory rales heard over the lower portion of the left lung field. The heart was not enlarged, but an apical splitting of the first sound and a soft systolic murmur were heard. The pulmonic second sound was equal to the aortic second sound. The abdomen was very obese and doughy in consistency, but no tenderness was noted. The spine was not tender. The legs were very large, and mild varicosities were present. Dorsalis pedis pulses were strong bilaterally. The patient moved her legs, but all the muscles seemed weak. No sensory or reflex changes were found.

The white blood cell count was 20,500 with 88 per cent neutrophils, and the sedimentation rate was 59 mm. in one hour. The blood glucose was 305 mg. per 100 ml., and the serum acetone was positive in a 1:4 dilution. Acetonuria and carbon dioxide of 29 volumes per cent further confirmed the impression of diabetic acidosis. Control was achieved in four hours with 275 units of regular insulin, and thereafter 40 units of NPH insulin daily provided smooth maintenance.

Cultures of the throat, cerebrospinal fluid, urine, and blood all grew out Staph. aureus which was beta hemolytic and coagulase positive. Three additional blood cultures were positive for the same organism.

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Despite penicillin (100,000,000 units daily) and tetracycline (800 mg. daily) therapy intravenously, the patient became uncooperative and disoriented. A careful neurologic examination revealed slight ptosis of the right lid and a smaller pupil in the right eye than the left. Headache was denied, and no papilledema or meningeal signs were found. An initial lumbar puncture performed on March 10 yielded deeply turbid, hemorrhagic spinal fluid. A repositioning of the needle obtained yellow, turbid spinal fluid, but no pus was encountered. Both specimens contained white cells too numerous to count, including 65 per cent polymorphonuclear leukocytes. The spinal fluid sugar was 212 mg. per 100 ml., protein 152 mg. per 100 ml., and chlorides 625 mg. per 100 ml. Gram-positive cocci were evident on direct smear, and Staph. aureus was cultured readily. A study for other pathogens was unrevealing.

The sensorium became progressively clouded, urinary and fecal incontinence developed, and by March 11 the patient was only slightly responsive, moaning and crying out at the slightest motion of any part of her body. A sensory examination still showed negative findings. Vancomycin was added to the regimen on March 11 (1 Gm. every twelve hours, intravenously). The fever subsided within twenty-four hours, but stiffness of the neck developed. In view of the large citrate content of the penicillin and the muscular irritability, calcium gluconate therapy was tried, and the stiff neck became more supple. The serum calcium remained normal.

By March 15 there was some clearing of the sensorium, and the neck was less stiff. A repeat spinal tap yielded less turbid fluid containing 900 cells per cubic millimeter, protein of 192 mg. per 100 ml., and sugar of 172 mg. per 100 ml. The fluid now was sterile although a blood culture on the same date was positive again for Staph. aureus. By March 20 the patient could recognize people and speak. The neck was supple, and the blood was sterile. The spinal fluid was only faintly turbid and contained under 400 cells per cubic millimeter, but the protein was 250 mg. per 100 ml. By March 24 the sensorium seemed clear. Back pain and headache were denied, but some abdominal tenderness was found. Physiotherapy was begun.

There was no further improvement despite continuing vancomycin therapy and sterilization of the spinal fluid and blood, and so the spinal tap was repeated on March 29, and thick, creamy pus was obtained. Two days later a tonic convulsion, unresponsive to calcium gluconate, occurred and lasted for several minutes. There were no focal neurologic signs other than the previously noted eye findings. Further deterioration of the patient's mental status occurred, and it was felt that a cerebral abscess might have ruptured into the subarachnoid space. The patient was transferred to Lackland Air Force Base Hospital where anisocoria and ptosis of the right lid again were noted. A spinal tap again produced viscid pus containing gram-positive cocci on smear. Despite the addition of kanamycin sulfate, bacitracin, intrathecal bacitracin, and penicillin, the patient became progressively more obtunded and had recurrent convulsions. Spasticity of the left side and right hemiparesis developed, the temperature rose to 103 F., pulmonary edema and shock supervened, and the patient expired on the twenty-fourth hospital day. Cultures of the nose, throat, gastric contents, spinal fluid, urine, ear, and decubiti failed to reveal the original infecting organism.

An autopsy was performed thirteen hours after death by Capt. D. A. Johnson (MC), U.S. Air Force. The neuropathologic examination was performed by Maj. Francis Kruse, Jr., (MC), U.S. Air Force.

A large retroperitoneal abscess on the right side was encountered which extended behind the kidney (not involving the immediately adjacent perinephric fat) from the level of the diaphragm down to the pelvic brim. The abscess occupied the entire posterior aspect of the right retroperitoneal space. On stripping away the paravertebral tissue prior to removing the vertebral bodies, it was discovered that abscesses were present in both the right and left paravertebral areas in the region of the fourth and fifth lumbar vertebral bodies. On removing the vertebral bodies, it was found that the right and left paravertebral abscesses were continuous with an abscess within the intervertebral disk between the fourth and fifth

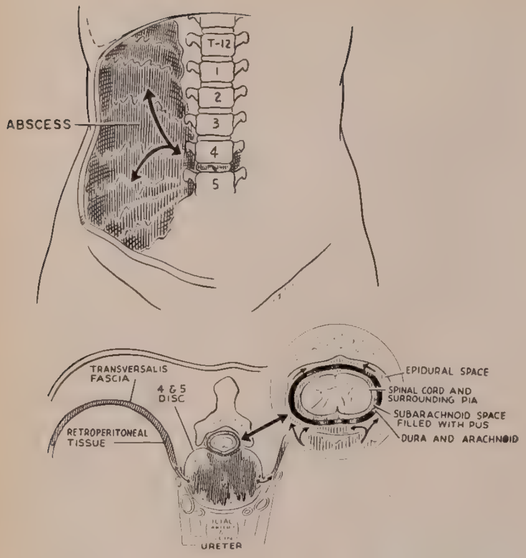

FIGURE 1. (upper portion) Abscess involving right retroperitoneal space, right and left paravertebral areas, fourth lumbar intervertebral disk, and subdural spaces in region of fourth and fifth lumbar vertebrae. (lower portion) Section through spinal cord.

lumbar vertebrae. Also, the right paravertebral abscess was continuous with the large right retroperitoneal abscess described previously. After the removal of the vertebral bodies the abscess within the intervertebral disk between the fourth and fifth lumbar vertebrae was seen to communicate directly posteriorly with the epidural space, completely surrounding the dura. When the dura was opened, the subdural space was seen to be filled almost entirely with a fibrinopurulent material similar to that seen elsewhere in the abscess. The abscesses in the epidural and subdural spaces were limited grossly to the region of the fourth and fifth lumbar vertebrae. In summary, a large continuous abscess was present which involved the right retroperitoneal space, the right and left paravertebral areas, the fourth lumbar intervertebral disk, and the epidural and subdural spaces in the region of the fourth and fifth lumbar vertebrae (Fig. 1, upper portion). That portion of the spinal cord not within the fourth and fifth lumbar vertebral region was grossly uninvolved. The brain itself also was grossly uninvolved. The appendix was normal, and no other gross primary suppurative focus was found.

Sections through the spinal cord from the area of gross abscess showed a fibrinopurulent exudate present within the pachymeninges and marked congestion of the vasculature of the meninges (Fig. 1, lower portion). The exudate contained no bacterial colonies. The substance of the spinal cord in the areas of the abscess showed severe congestion and severe, generalized swelling of all of the myelin sheaths. The sections of the grossly uninvolved portions of the spinal cord and brain showed only moderate edema and congestion without exudation or other evidence of meningitis.

Cultures taken from the meninges of the brain showed no growth. Cultures were not taken from the abscess at the time of the autopsy since it was inadvertently contaminated when it was first discovered. No cerebral lesions were discovered on gross or microscopic examination.

Other pathologic findings were bilateral pulmonary edema and congestion, moderate cardiac hypertrophy and dilatation, moderate chronic pyelonephritis, superficial hemorrhagic cystitis, fatty atrophy of the pancreas, fibrosis of the islands of Langerhans, multiple cut-down sites, and a recent tracheostomy wound.

Comment

This obese diabetic patient had a large retroperitoneal abscess which extended through the intervertebral disk between the fourth and fifth lumbar vertebrae and involved the epidural space. Pus also filled the spinal subarachnoid space. Epidural involvement and probably subarachnoidal involvement must have been present at the time of admission since the spinal fluid already was turbid and contained high protein and a leukocytic exudate. The fact that two different fluids were obtained by varying the position of the needle in the subarachnoid space suggests that an inflammatory reaction already had created areas of subarachnoid loculation. Weakness of the legs, urinary and fecal incontinence, and back pain may be attributed to the epidural component of the abscess. Ordinarily, epidural abscesses localize posteriorly because the anterior dura is adherent to the vertebrae.[5] Even with posterior localization, however, only 50 per cent of the cases of epidural abscesses have spinal tenderness.[6] In this case perhaps the abscess at first lay anterior to the cord and thus was not entered during the initial lumbar puncture. At the time of autopsy the abscess surrounded the cord.

The possibility of the dissemination of an epidural abscess into the subarachnoid space as a result of lumbar puncture was raised by Benoit in 1929,[7] and instances of this occurrence have been described.[8] Whether or not spinal taps could have aided the development of the purulent subarachnoid collection in the present case remains speculative. The location of the abscess makes this probable, but the initial presence of viable organisms and leukocytosis in the subarachnoid space makes it likely that localized subarachnoid infection was present even before instrumentation. However, it remains possible that the needle carried organisms from the abscess into the spinal fluid. Yellowish spinal fluid with high protein but few cells is thought to be typical of epidural infection.[9] In this instance, many leukocytes were found in the spinal fluid, and the cerebral symptoms directed attention away from the spine although the classical sequence of spinal ache, root pain, weakness of muscles and sphincters, and paralysis might have suggested epidural involvement with cord compression.[10]

Ghormley, Bickel, and Dickson[11] refer to a case of intervertebral disk destruction with an abscess appearing and draining through a nephrectomy scar. Taylor and Kennedy[12] describe a fifteen-year-old girl in whom an abscess along a rib extended to involve the epidural space. Studdert's[8] Case 4 suggests that a perinephric or epidural abscess may have ruptured into the subarachnoid space, but no abscess was demonstrated. Paravertebral abscesses have been reported to connect with the epidural space,[13] but no case of retroperitoneal abscess communicating with the epidural space has been found. The rarity of epidural extension of suppuration from an involved intervertebral disk also has been remarked on.[14]

The peculiar virulence of the staphylococcus has been of increasing medical concern, and much study has been devoted to the problem.[15] The elaboration of coagulase, hemolysins, leukocidins, hyaluronidase, fibrinolysin, proteases, lipase, and enterotoxin has been demonstrated, but their role in pathogenicity remains unsettled.[16]

It has been stated that the cure of an epidural abscess probably cannot be achieved without surgery.[3] A case of staphylococcal sepsis, severe back pain, and tenderness over the lumbar region responded well to vancomycin, but the presence of an abscess was not proved.[17] Had the unusual circumstances of the present case been interpreted correctly, possibly an early drainage of the retroperitoneal abscess might have led to a favorable outcome. It is hoped that an awareness of the possibility of communication of a retroperitoneal abscess with the epidural space may lead to a prompt diagnosis if future instances are encountered.

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Special Article

"Now Is the Time for All Good Men . . ."*

LEONARD W. LARSON, M.D.
Bismarck, North Dakota

President, American Medical Association

We are engaged in a historic struggle to preserve our country's unique system of medical care and our stature as a profession. Both are seriously threatened by current proposals to incorporate health care benefits into the Social Security system.

Because of this threat, I shall devote my entire time today to a discussion of the issues involved: why we fight, how our opponents are attacking, how we are answering the challenge, and the legislative outlook.

Reasons for struggle

First, why do we fight? We fight because we have dedicated our lives to providing the best medical care possible to all our patients; we fight for our patients and their well-being. We fight because the Administration's medical care proposal, if it were enacted, would certainly represent the first major, irreversible step toward the complete socialization of medical care. A proposal which places the primary responsibility for the purchase of health care on the Federal government, which is financed by compulsory payroll taxes and equivalent taxes on employers, which is administered directly by the Social Security Administration, which provides benefits without regard to financial need, and for which the Federal government has no logical responsibility certainly can properly be categorized as "socialized medicine."

The immediate objective of this legislation is to substitute compulsion for voluntarism in the financing of health care. It is to substitute decision-making by a small elite corps of Federal administrators for the independent decisions of millions of consumers of medical service. As one candid authoritarian said, "Individuals cannot be trusted to spend their medical care dollars prudently."

The compelling issue then is socialization versus voluntarism—or compulsion versus freedom of choice. As Prof. Milton Friedman of the University of Chicago said recently:

> Fundamentally there are only two ways in which the activities of a large number of people can be coordinated: by central direction, which is the technic of the army and of the totalitarian state and involves some people telling other people what to do; or by voluntary cooperation, which is the technic of the market place and of arrangements involving voluntary exchange.

We are for voluntarism. We do not believe that Americans, acting either as citizens or as patients, require central direction from the government in their choice of a doctor or hospital, in the spending of their health care dollars, or in their selection of the health services and facilities which are best suited to their own individual needs.

Only in the case of needy or medically needy persons should the government intervene. We vigorously support the Kerr-Mills Medical Aid for the Aged Act because it is tailored to help those who need help. Through Federal grants-in-aid the states are being assisted in developing medical care programs which are designed specifically to help needy old persons. Given time, and notwithstanding constant efforts by the

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* Address delivered to the House of Delegates of the American Medical Association, Denver, Colorado, November 27, 1961.

Department of Health, Education, and Welfare to sabotage and discredit the program, the Kerr-Mills Act will solve the health care needs of relatively insolvent aged persons.

Another great issue—one which merits far more emphasis than it has received—is the constitutional question of the relations between the Federal government and the states. The King bill abrogates the rights of the states since the program of health benefits is administered directly from Washington. All the rules and regulations are promulgated in Washington. All the eligibility requirements are established in Washington both for the recipients of benefits and the vendors of care.

Compared with the proposed Federal aid to education bills, the King-Anderson bill is truly extreme in its circumvention of the states and local communities. The aid to education bills did provide for local administration. Imagine the universal opposition to these bills if they, like the medical aid bill, provided for direct Federal payment of teacher's salaries. Yet this is exactly what the King bill does for hospitals, nursing homes, and thousands of physicians.

This bill is, in truth, one of the most destructive proposals affecting the Federal-state relationship ever introduced in Congress.

What do we stand for? We take our stand for voluntary cooperation, for preservation of the historic Federal-state organizational structure, for individual responsibility, and for help for those persons who need help.

We are for an improved public attitude toward older citizens. We are for their integration into the mainstream of society. We urge liberalization of the retirement policies in industry to permit the continued productivity of older employes and their employment in any capacity for which they are qualified. We are for measures which are designed to protect the earning capacity of those who can take care of themselves. We supported the bill for Federal guaranteed mortgage loans for private nursing homes and Hill-Burton Federal grants for nonproprietary nursing homes. Our sponsorship of national congresses on mental illness, quackery, voluntary health insurance, Kerr-Mills implementation, and aging is familiar.

We are for a free profession, not an enslaved one. We are for the preservation of our constitutional republic; we are opposed to a welfare state. We are for the right of our citizens to spend their own dollars in their own way, not for Washington authoritarians to spend their money for them. Our philosophy is wholly positive. It reflects the spirit that lives throughout American history—the philosophy that a dynamic, progressive society is the result of the voluntary actions of a free, responsible people.

And yet, no matter how positive our position, we must understand the tactics of our adversaries if we want to assure victory.

Tactics of opponents

What are some of these tactics?

The proponents of King-Anderson-type legislation have cleverly promoted the false idea that earmarked payroll and employer taxes would be voluntary prepayments against the cost of health care benefits which would be received subsequently in retirement. The fact is that the King bill levies a compulsory tax on young workers and their employers to pay for a Federal program of health benefits for older people, millions of whom are self-reliant and solvent. The King-Anderson program does not provide insurance or prepayment of any type, but it compels one segment of our population to underwrite a socialized program of health care for another, regardless of need.

We urge all Americans to look this gift horse in the mouth, because if we don't the consequences could be tragic. Wilbur Cohen, Assistant Secretary of the Department of Health, Education, and Welfare, made the following admission under questioning by Senator Carl Curtis of Nebraska on March 23, 1961. The Senator asked this question:

> If compulsory health insurance was extended to everybody, the total payroll tax would be up to 19 or 20 per cent. If it was a 20 per cent rate, the self-employed rate would be 15 per cent. With a $9,000 taxable wage base, the maximum tax on the employe and employer would be $900 each; and the maximum tax on a self-employed person would be $1,350, if we do what you advocated today plus what you advocated in 1946.

> Do you feel that as much of that man's earnings of $9,000 as a Federal tax source should be devoted to this one single program of social security as is available to help finance all other activities—the functions of the Government, the paying of the national debt, and the defense of our country?"

Mr. Cohen's reply was: "Yes, I do, Senator."

To sum up this historic colloquy, down the road is envisioned a Federal program of total benefits that would cost more than all other government functions and expenditures and which would be financed by a total tax of 20 per cent on all earnings up to $9,000.

The vilification of the AMA has been a principal tactic of our opponents, led by the administration and the AFL-CIO. An enormous smear campaign was launched. It is being carried out by labor's radio and television outlets, the labor press, some commentators, and certain government spokesmen.

Read the testimony of labor's witnesses before the Ways and Means Committee, July, 1961, when the major portion of their testimony was directed against the AMA. The King bill became almost a side-issue. Or look at the statements which were prepared by the Committee on Political Education (COPE) and given wide distribution purporting to prove that the AMA, on 25 selected issues from social security to smallpox vaccination, opposed every one. Every citation is false and every AMA policy distorted or maliciously misrepresented. Or, more recently, observe Secretary Ribicoff's attempt to cast the AMA as a monolithic, dictatorial organization exercising sanctions against our members who disagree with the leadership—a totally false accusation made purely for its propaganda effect. The latest story planted by an Administration spokesman is that AMA has been joined by the National Association of Manufacturers and the U.S. Chamber of Commerce in a massive 20 million-dollar campaign against the Administration's medical care program. This statement is absolutely false. It is the old technic of building up your adversary to make you appear the underdog.

We can expect even more bitter attacks in the year ahead. As Allan Drury pointed out in his great novel, *Advise and Consent,* the orchestrated chorus of the left is potent, virulent, and tireless.

The latest attempt of labor and the Administration to build pressure on Congress is the organization of the National Council of Senior Citizens for Health Care through Social Security. This is a purely political group of older people which is headed by ex-representative Aime Forand and staffed by a former undersecretary of the Department of Health, Education, and Welfare. In announcing the formation of the National Council, Mr. Forand bluntly stated:

> . . .The primary purpose. . .is to weld senior citizens, organizations, and millions of interested individuals from all over the country into one strong and effective voice in Washington. Our immediate goal is to secure legislation providing health care for the aged through Social Security . . . .

I believe, however, that the vast majority of our older citizens are self-reliant. Further, I believe that when the true objectives of this lobbying organization are made clear to them, and when they realize that they are being manipulated—cynically—as political pawns, they will make their feelings known.

Much of the crisis atmosphere created by the King-Anderson proponents derives from the carefully propagated myth that practically all persons over sixty-five are insolvent and necessarily depend on the government for their health care. Of course, there is a sizable group of such persons. Approximately 2.3 million of the 17 million persons over sixty-five are on public assistance today, and another indeterminate number, while not on public assistance, has difficulty in meeting the costs of major illness. For these groups the Kerr-Mills bill was enacted to provide more ample funds and broader health benefits. Millions of other persons over sixty-five are able to pay the total cost of health care out-of-pocket, or they have health insurance or prepayment coverage of some kind.

However, it is the dramatic change in the economic status of the aging that is most noteworthy. Today, only 14 per cent of aged persons over sixty-five are on public assistance, whereas 22 per cent were receiving public aid in 1950. Today, more than 53 per cent of all persons over sixty-five have some kind of health insurance as contrasted with only 26 per cent in 1952. In many respects, the aged group is better off than any other group in the nation. Their liquid assets are higher and have risen faster than any age group; a much higher percentage own their homes free of mortgages; their financial obligations are significantly less; and they enjoy tax advantages which are not available to younger citizens. Hospitals report they have less difficulty obtaining payment from patients over sixty-five than from younger patients. The growth of annuity plans, company purchase of health insurance benefits for retired employes, life insurance accumulation, and many other factors have led to a significantly more favorable economic situation for our older citizens than has ever been true previously. Competent economists predict that this improvement will continue at an accelerating pace. We are dealing, then, with a diminishing problem which belies the crisis propaganda of our opponents.

It is no secret that within the hospital and Blue Cross groups there are some individuals who, at this time, are leaning toward a Federal program directed from Washington which would use the Blue Cross plans as fiscal agents. We have requested medical societies and, where appropriate, individual staff physicians to contact hospital administrators and trustees to acquaint them with our position and to explain the reasons for it. We have urged our medical representatives not to impugn their motives but to recognize their thorny fiscal problems and to discuss with them these controversial issues in an atmosphere of mutual trust.

We hope these conversations will have two results: to strengthen the majority of American Hospital Association and Blue Cross members in their opposition to the King-Anderson approach and, even more, to lead to constructive joint actions to meet the admittedly difficult financial problems of some hospitals and the Blue Cross plans especially.

Medicine's campaign

I have sketched in broad outline the chief tactics of those who favor the King-Anderson bill. Now, what is the nature of our own campaign?

In December, 1960, we made it clear that, notwithstanding the election of an Administration dedicated to the King-Anderson program, we intended to fight this proposed government takeover of medicine to the limit of our ability. As physicians we knew what this legislation would mean not only to our freedom as a profession but more important to the long-range welfare of our patients.

We knew that when physicians are forced to become pawns of Federal administrators and politicians, rather than responsible to their patients, it affects adversely the quality of care.

Only now reports to this effect are beginning to come from distinguished economists in England.

Prof. D. S. Lees concludes:

> The fundamental weaknesses of National Health Service are the dominance of political decisions, the absence of built-in forces making for improvement, and the removal of the test of the market. These defects bring dangers for the quality of medical care that cannot be removed without far-reaching reform. We should aim to diminish the role of political decisions and to enlarge the influence of consumer choice. Governments should move away from taxation and free services to private insurance and fees by allowing tax concessions to those who can provide for themselves and direct assistance to the dwindling minority who cannot. To those in England who object that the clock is being put back, we must reply that it is desirable to put the clock back if it is telling the wrong time.

We have achieved our initial objective of arousing physicians and alerting Congress to the soundness of the Kerr-Mills approach and the dangers inherent in the radical King-Anderson proposal. We are now engaged in stimulating effective action by state and county medical societies, individual physicians, women's auxiliaries, and others.

We are telling our story as widely and forcefully as possible, and through as many avenues as we can devise, to the public and the members of Congress.

Special efforts are being made to correct the falsehoods disseminated by the proponents of King-Anderson legislation.

In our fight we do not stand alone. Many other great national organizations, as well as millions of individual citizens, are firm in their opposition to socialized medicine. When we are under heavy attack, we should remember that in our ranks are the American Farm Bureau Federation; the insurance industry; the Blue Shield Plans; the pharmaceutical associations; manufacturing, wholesale and retail; the American Dental Association; the Federation of Business and Professional Women; the young men of the Junior Chambers of Commerce and Young Americans for Freedom; the U.S. Chamber of Commerce; and many more organizations. No, Mr. Ribicoff does not speak for all 180 million Americans as he has repeatedly declared. Every state and county medical society, every physician and his wife, should work closely with these organizations, dedicated as we all are to a free society.

Primary attention will continue to be given to implementing the Kerr-Mills Act, promoting voluntary health insurance and prepayment plans designed for aged individuals, and upgrading nursing homes.

We will strive to create a new climate of hope, pride, and self reliance for the aged.

Legislative outlook

What outcome do I predict in this titanic struggle facing us? Predictions are always difficult because, as Roger Fleming of the Farm Bureau says, "I am not a bookie, I'm a jockey!" We need to ride hard, with courage and determination and the will to win. If we do, I predict the King-Anderson bill will be defeated in Congress in 1962.

I cannot close with more appropriate remarks than those made recently by Senator Kerr in a talk before a group of physicians when he said:

> I would not discourage you, because the task is not hopeless—but it's not self-executed. You have probably the greatest opportunity of any generation of your profession that has ever lived, and all future generations of your profession are going to know whether or not you did your part in keeping the environment for them that has been such a blessing to you. If you do what you are capable of doing and the rank and file of those identified with you across the nation join you, you can tell your children that you made the fight that kept for you the environment which has been your blessing—and passed it on, unimpaired and unsullied, to those that you love even more than you do yourself.

Husband and wife develop simultaneous baldness

The rare occurrence of simultaneous bald spots in a husband and wife was reported in an article by Sheldon Swift, M.D., in the December, 1961, issue of *Archives of Dermatology*. Emotional factors appeared to be at least partly responsible. The couple developed a type of baldness, known as alopecia areata, which left a sharply defined bare spot in almost the identical part of the scalp of both patients. The husband also had bare spots on his face and chin.

Studies have shown that a high proportion of patients with this form of baldness have psychoneurotic tendencies or psychoses, and there were a number of emotional factors involved in the present case.

A psychiatric evaluation of the forty-six-year-old husband and forty-year-old wife revealed that each was emotionally dependent on the other, each admired the qualities of the other, and there seemed to be a strong cross identification. The author speculated that the loss of hair in the woman might symbolize a loss of feminine traits and the loss of facial hair in the man might symbolize the loss of masculine traits. He concluded that the simultaneous appearance of baldness might be "in part due to strong counter-identification." The wife's bald spot disappeared in six months, but the husband developed a new area of baldness on the scalp.

Questions and Answers on Health Insurance

Prepared by the New York State Professional Relations Committee of the Health Insurance Council, New York City

FRANCIS T. CRAWLEY, Editor

Has the Medical Society of the State of New York taken a position with respect to a doctor being paid for filling out claim forms?

Yes, it has. Action taken by their Council on December 11, 1958, left no doubt as to how the society looked on this much discussed problem. At this meeting the Council adopted and later ran in editorial form the following*:

> The House of Delegates on May 13, 1958, adopted a resolution as follows: "Resolved that this House of Delegates of the Medical Society of the State of New York recognizes that the completion of insurance company forms is a task for which a fee should be paid."
>
> An editorial in the August 1, 1958, issue, of the NEW YORK STATE JOURNAL OF MEDICINE comments, "Many companies, of course, have established the practice of paying for these services. In the case of those who do not, the doctor is well within his rights to require it."
>
> Further clarification of this problem still seems desirable. Forms relating to applications for life insurance, forms requested by the insurance company, with a proper release from the patient, pertaining to a past illness in relation to current insurability—these constitute compensable work on the part of the doctor. However, the completion of forms to establish a period of disability and such forms as are minimally necessary to record continuation and/or termination of said disability or furnish routine information for payment of hospital, surgical, or medical benefits constitute a service to the patient and therefore do not carry a fee for the physician.
>
> In the event that the insurance company demands an excessive number of forms or requires forms to be filled out with an unjustifiable frequency, the physician may well request the company to pay for such extra service. Each physician must settle such problems directly with the insurance company on an individual basis. More widespread use of the standard forms as advocated by the Health Insurance Council should minimize unnecessary forms to establish and terminate a period of disability.

What might a physician do when he has been informed previously that the fees will be taken care of by insurance only to learn later that only part of the fees are taken care of because of a deductible and coinsurance and the patient expects the doctor to accept the amount paid by the insurance company as full payment?

The doctor who finds himself in this situation might simply explain to the patient that he has charged his usual and customary fee without regard to the existence of insurance and any difference between what the insurance allows and the balance owed to him he expects to receive from the patient. A cardinal thought here embraces an underlying principle that the insurance industry does not set the doctor's fees nor does it wish to. However, it does urge the doctor to charge his usual and customary fee without regard to the existence of insurance.

Doctors reading this column are encouraged to send in their questions to the Health Insurance Council, 750 Third Avenue, New York 17, New York.

Number four in a series of Questions and Answers on Health Insurance

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* Editorial: Payment for completion of insurance forms, NEW YORK STATE J. MED. 59: 226 (Jan. 15) 1959.

Abstracts

Herter, F. P., Malm, J. R., Markowitz, A. M., Demetz, A., and Evans, S.: Cancer chemotherapy by regional perfusion, New York State J. Med. **62:** 465 (Feb. 15) 1962.

Experience with 50 perfusions in 48 patients, all of whom exhibited an advanced stage of cancer, is described. Almost all had undergone unsuccessful conventional therapy. The overall results were disappointing in terms of prolonged tumor regression or palliation. Of the total series 42 patients were followed long enough to determine accurately the effects of perfusion therapy in terms of tumor response. Of these, 9 (4 genitourinary carcinomas, 1 parotid carcinoma, 1 liposarcoma, and 3 melanomas) demonstrated tumor regression. This was transient in 8 and only "permanent" in 1. However, 9 of 11 patients with intractable pelvic pain were benefited, and where pain was a major factor in tumors of other areas, perfusion achieved similar relief. The 7 complications (1 fatal, 2 serious, and 4 minor) occurred during the first few months of clinical trial when the drug dosages were not firmly established and the methods of vascular isolation were experimental. There are two principal values of perfusion: (1) the possibility of delivering to the area in question concentrations of drug which would be lethal if given systemically; and (2) the symptomatic relief afforded many of the patients. Limitations to perfusion stem from difficulty in achieving adequate vascular isolation in most areas of the body, deficiencies inherent in the drugs themselves, and danger of chemotherapeutic stimulation of tumor growth. Perfusion technics have not been standardized, and there is need for technical improvements, methods to minimize the systemic toxicity of the available chemotherapeutic agents, and a means for long-term exposure of tumor to drug. Tentative criteria for selection of patients for perfusion are proposed.

Hyman, Y. K., and Orkin, L. R.: Triflupromazine and fluphenazine as adjuncts in anesthetic management, New York State J. Med. **62:** 480 (Feb. 15) 1962.

A study was undertaken to evaluate the sedative, hypnotic, and antiemetic properties of triflupromazine hydrochloride (Vesprin) and fluphenazine dihydrochloride (Prolixin). Trials were made on 24 patients scheduled for electroconvulsive therapy with thiopental sodium alone and in combination with triflupromazine or fluphenazine. It appears that 6 mg. of triflupromazine and 6 mg. of fluphenazine have approximately the same sedative potency as 50 mg. of pentobarbital sodium. In a group of 160 patients, triflupromazine used alone or with scopolamine hydrochloride as preoperative medication produced well-sedated patients. Fluphenazine proved to be a tranquilizer in doses of 4 to 6 mg. with little sedative effect. Triflupromazine was very useful in relieving apprehension and quieting 28 patients scheduled for bronchospirometry or bronchoscopy under topical anesthesia. In a group of patients under spinal or peridural anesthesia, marked hypotension was frequently seen with small doses of triflupromazine. As an antiemetic, fluphenazine appeared to be more effective than triflupromazine, and a smaller dose was needed. Both drugs were effective in treating emergence delirium, although fluphenazine is preferred because it does not prolong the anesthesia time. Triflupromazine potentiated the general anesthetic effect, but fluphenazine did not. Both drugs are contraindicated in spinal anesthesia. Side-effects were not noted, but the discussant warns against potential side-effects and points out the need for further research on the subject.

McKnight, W. K., Yoder, C., and Beckett, T.: Treatment of emotionally ill children; nature and management of initial resistance factors, New York State J. Med. **62:** 486 (Feb. 15) 1962.

In general the causes of emotional illness in a child are found in a disturbance in the equilibrium between the hereditary and constitutional characteristics of the child and present or past adverse environmental influences. Abnormal behavior indicates that the child is inwardly disturbed because of a pathogenic relationship with someone near him. The pathogenic attitudes most likely to cause emotional disturbance in the child are parental rejection, excessive parental demands, and parental overprotection. The general pathologic reaction patterns are submission, withdrawal, rebellion, and substitutive reactions. However, therapy must be directed to a modification of the pathogenic relationship rather than toward treating the behavior symptom itself. As a result, the concept of family-centered treatment has replaced the child-centered concept of child guidance. Initial resistance in parents who come to a child guidance clinic for help is normal. Proper handling of referral and greater understanding of the parents can help to overcome this resistance. Resistance to introspection occurs frequently, and the child patient displays resistance symptoms also. Overcoming resistance in parents and children is one of the major tasks of the child guidance clinic.

Stoll, H. L., Jr., and Crissey, J. T.: Epithelioma from single trauma, New York State J. Med. **62:** 496 (Feb. 15) 1962.

The question of the role of trauma in the appearance of cancer is a controversial one which is particularly important in workmen's compensation cases. In 1901 the following criteria were established for evaluating the factor of trauma as a cause of skin cancer: previous integrity of the traumatized part; adequate and authenticated trauma; positive diagnosis of a nonmetastatic carcinoma; origin of the carcinoma at the exact point of injury; reasonable time interval between trauma and the appearance of the carcinoma; and continuity of signs from trauma to the appearance of the carcinoma. Satisfactory proof for or against the proposition that single trauma can cause cancer is lacking, but the use of the preceding criteria is recommended, and further research using animal experiments and clinical studies is suggested.

Redway Medal

The first Laurance David Redway Medal will be awarded at the Annual Meeting of the Medical Society of the State of New York which will be held in New York City, May 14 to 18, 1962.

A gold medal and cash prize of $500 in memory of the late editor of the New York State Journal of Medicine will be awarded annually for the article judged to be the most outstanding of those which appeared in the Journal during the previous year.

Every Journal subscriber is invited to send his nomination to the editor of the Journal for the best article which appeared in the Journal in 1961, giving brief reasons for the choice.

Nominations must reach the editor by March 31, 1962. They should be addressed to William Hammond, M.D., Editor, New York State Journal of Medicine, 750 Third Avenue, New York 17, New York.

Month in Washington

Reports by the American Medical Association and the Health, Education, and Welfare Department showed that 38 states have taken advantage of the Kerr-Mills law providing medical care for the aged with a total expenditure of $121 million in the first fifteen months of the program.

Citing the program's wide acceptance, Leonard W. Larson, M.D., president of the A.M.A., said that 27 states had enacted Kerr-Mills Medical Assistance to the Aged (MAA) programs, and 11 other states had expanded Old Age Assistance (O.A.A.) medical benefits under the new law.

In addition, he said, nine states already had O.A.A. medical programs on the books, and in most instances they are considered to be adequate to provide the necessary health care for those over age sixty-five.

Two of the three remaining states—Arizona and Delaware—have excellent assistance programs at the local level which include medical care, Dr. Larson said. "These figures certainly contradict statements by Kerr-Mills critics who say that the program can't and won't work."

"In just fifteen short months Kerr-Mills has been widely accepted across the land and with each passing day is proving that it can and, if given the fullest opportunity, will do the job. Kerr-Mills is being implemented by the states as fast, if not faster, than any previous Federal-state matching program.

"Such rapid acceptance of this principle makes any compulsory health program through the Social Security mechanism totally unnecessary."

A variety of new approaches to better care for the chronically ill and aged will be made possible through the Community Services and Facilities Act of 1961, the Health, Education, and Welfare Department said. The Act authorizes grants to community agencies to develop new and improved home nursing, home care, and other out-of-hospital services. The Act also raises the ceiling for grants to the states for the construction of nursing homes from $10 million to $20 million annually.

Under the Hill-Burton program, 535 hospitals, nursing homes, rehabilitation centers, and other facilities were awarded $146,330,000 in Federal funds toward $468,661,000 of construction in 1961.

* * *

Manufacturers accepted a congressional proposal for further government controls over the efficacy of prescription drugs, but stood pat in opposing patent provisions of the controversial drug legislation sponsored by Sen. Estes Kefauver (D., Tenn.).

Eugene N. Beesley, chairman of the board of the Pharmaceutical Manufacturers Association, said that the PMA "fully endorses the principle that a drug should be effective for the uses that a manufacturer claims for it; and, second, that the Food and Drug Administration, in passing on new drug applications to determine the safety of the new product, already evaluates, in many cases, the evidence of its effectiveness for the uses claimed."

"Since the F.D.A. has expressed a desire to have its authority clarified with respect to its consideration of the effectiveness as well as the safety of new drugs, we wish to support the proposal as we understand it," he added.

Beesley said such F.D.A. clearance "would assure physicians that a drug effectively produces certain physiological actions; but the physician, not the F.D.A., would determine whether these specific physiological effects would be useful or beneficial with respect to particular patients."

Beesley said the patent restrictions proposed in the bill "would virtually destroy the patent system with respect to medicines. This proposal obviously strikes directly and crucially at the industry's capacity and incentive for discovery of new and improved medicines, and we vigorously oppose it."

Sen. Kefauver indicated he might compromise on the patent provision, saying that he was "not irrevocably wedded to the precise approach" of his legislation.

Kefauver endorsed A.M.A.'s expanded drug information program which will put the data directly in the hands of prescribing physicians in contrast to new F.D.A. regulations which place the emphasis on distribution of new drug information to pharmacists.

"The P.M.A. is supporting and, I trust, will continue to support the new and broadened program it has established with the American Medical Association of disseminating to physicians better and more accurate information concerning the bad as well as the good features of drugs," Kefauver said.

"And it is supporting, and again I trust will continue to support, the new program of the U.S. Pharmacopoeia and the A.M.A. in establishing simpler and more usable generic names for drugs. These are important steps forward."

Prepared by the Washington office of the American Medical Association, Washington, D.C.

Necrology

Earl E. Babcock, M.D., of Adams Center, retired, died on December 24, 1961, at the age of seventy-five. Dr. Babcock graduated in 1908 from Albany Medical College. A former health officer for the town of Adams, he was one of the original members of the board of managers of the former Jefferson County sanatorium and in 1945 was elected president, serving for several terms. Dr. Babcock was a member of the American Academy of General Practice, the Jefferson County Medical Society (a past-president), the Medical Society of the State of New York, and the American Medical Association.

Reuben Morris Dicker, M.D., of Long Island City, died on December 29, 1961, in San Juan, Puerto Rico, at the age of sixty-two. Dr. Dicker graduated in 1924 from New York University and Bellevue Hospital Medical College and interned at Greenpoint Hospital. He was president of the American College of Legal Medicine and chief consultant to the National Casualty and Health Association and to the New York State Insurance Fund. Dr. Dicker was a member of the American Board of Legal Medicine, the Society of Medical Jurisprudence of New York City, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Gerald Payne Fincke, M.D., of Salem, died on December 19, 1961, at the age of fifty-eight. Dr. Fincke graduated in 1931 from Hahnemann Medical College of Philadelphia. A major in World War II, he served in Germany and worked with displaced persons and was the recipient of the Bronze Star. Dr. Fincke was a member of the Washington County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Isidore Frank Fishman, M.D., of the Bronx, died on January 3 at the age of fifty-eight. Dr. Fishman graduated in 1928 from New York Homeopathic Medical College and Flower Hospital. He was an associate clinical professor at New York Medical College, an attending physician in ophthalmology at Metropolitan Hospital and the Bird S. Coler Memorial Hospital and Home, and an associate physician in ophthalmology at Flower and Fifth Avenue Hospitals. Dr. Fishman was a Diplomate of the American Board of Ophthalmology, a Fellow of the International College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the New York Society for Clinical Ophthalmology, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Darwin Nagel, M.D., of Byram, Connecticut, died on August 12, 1961, at the age of ninety-four. Dr. Nagel graduated in 1889 from Columbia University College of Physicians and Surgeons. He was a consulting physician at French Hospital. Dr. Nagel was a member of the American Academy of General Practice, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Virgilio Occhiuzzi, M.D., of New York City, died on December 31, 1961, at Columbia Hospital at the age of sixty-three. Dr. Occhiuzzi received his medical degree from the University of Naples in 1923. He was an attending physician in gynecology at the Italian Hospital. Dr. Occhiuzzi was a member of the New York County Medical Society and the Medical Society of the State of New York.

Samuel Schmerzler, M.D., of Brooklyn, died on January 3 at Lefferts General Hospital at the age of sixty-eight. Dr. Schmerzler graduated in 1917 from Long Island College Hospital Medical School and interned at Harlem Hospital. He was an assistant attending physician in obstetrics and gynecology at University Hospital and an associate attending physician in obstetrics and gynecology at Swedish Hospital in Brooklyn and an attending physician in gynecology at the Menorah Home and Hospital for the Aged and Infirm. Dr. Schmerzler was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Carmelo Teresi, M.D., of Rochester, died on December 13, 1961, at Genesee Hospital at the age of sixty-seven. Dr. Teresi graduated in 1917 from the University of Buffalo School of Medicine. He was the owner of Lake Avenue Hospital. Dr. Teresi was an Associate Fellow of the American College of Gastroenterology and a member of the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Jack Francis Warshaw, M.D., of Brooklyn, died on January 10 in his office at the age of sixty-six. Dr. Warshaw graduated in 1919 from Long Island College Hospital Medical School and interned at Jewish Hospital of Brooklyn. He was an adjunct physician at the Brooklyn Hebrew Home and Hospital for the Aged. Dr. Warshaw was a member of the American Academy of General Practice, the American Geriatrics Society, the Kings County Medical Society, and the Medical Society of the State of New York.

Medical Meetings

New York State Society of Internal Medicine

The New York State Society of Internal Medicine will hold its third annual internists' day at the Savoy Hilton Hotel in New York City, on Saturday, March 3. The subject of the meeting will be a symposium on "Diseases of the Thyroid Gland: Current Concepts."

The program is as follows: Opening remarks by Herbert Berger, M.D., F.A.C.P., president, New York State Society of Internal Medicine; "Iodine Metabolism," Solomon Berson, M.D., chief, Radioisotope Service, Bronx Veterans Administration Hospital; "Chemistry and Physiology of the Thyroid Hormones," Rosalind Pitt-Rivers, F.R.S., National Institute for Medical Research, London, England; "The Thyroid Pituitary Relationship," T. S. Danowski, M.D., Renziehausen Professor of Research Medicine, University of Pittsburgh School of Medicine; "Autoimmunity and Its Relation to Thyroid Disease," Ernest Witebsky, M.D., professor and head, Department of Bacteriology and Immunology, University of Buffalo School of Medicine; "Diagnostic Methods in Thyroid Disease," A. Stone Freedberg, M.D., associate professor of medicine, Harvard Medical School; "Thyroid Scans Interpretation," Millard Croll, M.D., associate professor of radiology and director of the Clinical Isotope Section, Hahnemann Medical College, Philadelphia.

Also, "Myopathies in Relation to Thyroid Disease," David Grob, M.D., professor of medicine, State University of New York Downstate Medical Center; Introduction to luncheon speaker, Charles Donegan, M.D., St. Petersburg, Florida; Luncheon address, Hon. Abraham Ribicoff, Secretary, Department of Health, Education, and Welfare; Physiologic Concepts in the Diagnosis and Therapy of Hyperthyroidism," Solomon Silver, M.D., associate clinical professor of medicine, Columbia University; "Genesis and Treatment of Nontoxic Nodular Goiter," Martin Perlmutter, M.D., clinical associate professor of medicine, State University of New York Downstate Medical Center; "Genesis and Therapy of Thyroid Carcinoma," George Crile, Jr., M.D., chief, Department of General Surgery, Cleveland Clinic; "Genesis and Management of Thyroiditis," Penn G. Skillern, M.D., Endocrinology Department, Cleveland Clinic; "Physiology and Therapy of Hypothyroidism (Myxedema)," Jacob Lerman, M.D., Harvard Medical School. A panel discussion on the topic "Various Forms of Thyroid Disease" will also be a part of the program. Rulon W. Rawson, M.D., professor of medicine, Cornell University Medical College, and chairman, Department of Medicine, Memorial Sloane-Kettering Cancer Center, will be the moderator.

Herbert Berger, M.D., Maxwell Spring, M.D., and Robert E. Westlake, M.D., will preside at the morning, luncheon, and afternoon sessions respectively.

For further information contact: Maxwell Spring, M.D., F.A.C.P., Program Chairman, 800 Grand Concourse, Bronx 51, New York.

Symposium on nutrition

A symposium on "Recent Advances in the Appraisal of the Nutrient Intake and the Nutritional Status of Man" will be presented on March 6 and 7 at the Massachusetts Institute of Technology, Cambridge, Massachusetts.

The symposium has been organized by the Department of Nutrition, Food Science, and Technology of the Massachusetts Institute of Technology and is supported by The National Vitamin Foundation. The themes of the four sessions will relate to recent advances in the appraisal of food intake, knowledge of food composition and availability of food nutrients, clinical appraisal of nutritional status, and biochemical estimation of nutrient intake and nutritional status.

For further information write to: Professor Robert S. Harris, Room 16–337, Massachusetts Institute of Technology, Cambridge 39, Massachusetts.

Society of Medical Psychoanalysts

The Society of Medical Psychoanalysts will hold a symposium on "The Etiology of the Neuroses" on March 17 and 18 at the Hotel Commodore, New York City.

For information contact: David B. Friedman, M.D., Committee on Arrangements, Society of Medical Psychoanalysts, Fifth Avenue and 106th Street, New York 29, New York.

Division of Dermatology, Downstate Medical Center

The Division of Dermatology of the Department of Medicine, State University of New York Downstate Medical Center, will present a discussion on "Cutaneous Manifestations of Endocrine Diseases" on April 6, from 10:00 to 11:30 A.M., in the E Building Auditorium, Kings County Hospital, 451 Clarkson Avenue, Brooklyn.

J. Lester Gabrilove, M.D., F.A.C.P., clinical associate professor of medicine, State University of New York Downstate Medical Center and associate chief of endocrinology, Mount Sinai Hospital, will be the speaker and Lawrence Frank, M.D., professor of dermatology, State University of New York Downstate Medical Center, will be the moderator.

Conference on tuberculosis

The New York Tuberculosis and Health Association has announced its annual conference on tuberculosis and other respiratory diseases to be held on Monday, April 16, at the Hotel Statler Hilton, New York City. The conference is sponsored by the Brooklyn Tuberculosis and Health Association, the New York State Committee on Tuberculosis and Public Health, the New York Trudeau Society, the New York Tuberculosis and Health Association, and the Queensboro Tuberculosis and Health Association.

For further information contact: New York Tuberculosis and Health Association, 260 Park Avenue South, New York 10, New York.

Third international congress for hygiene and preventive medicine

The third international congress for hygiene and preventive medicine, organized by the Austrian Scientific Society for Preventive and Social Medicine, will be held in Vienna, Austria, May 27 through 30.

German, English, and French will be the official languages of the congress. Simultaneous translation into these languages will be provided for the papers presented at the principal sessions. The subject of the congress is "Public Health and Protection Against Radiation."

For information write to: Secretariat, Third International Congress for Hygiene and Preventive Medicine, Vienna IX, Alserstrasse 4, Wiener Medizinische Akademie.

San Diego symposium on biomedical engineering

Announcement has been made of the San Diego symposium on biomedical engineering to be held June 19 through 21 at San Diego, California. The symposium will be sponsored by Inter-Science, Inc., and will be cosponsored by the American Institute of Electrical Engineers, Committee on Electrical Techniques in Medicine and Biology; Simulation Councils, Inc.; the U. S. Naval Hospital, San Diego; and the University of California at San Diego.

The technical program will cover: medicine and biology, where advances have been made possible by technics or equipment of the physical sciences and engineering; and those aspects of the physical sciences and engineering which are applicable or closely related to medicine and biology, for instance the simulation of biologic functions, neural models, "intelligent" machines, and bionics.

Papers are solicited which describe significant progress, or real potential in the aforementioned areas which has not been reported elsewhere. Titles and summaries of papers should be sent to: Program Committee, 8484 La Jolla Shores Drive, La Jolla, California. Authors of selected papers will be notified by April 23.

Abstracts in Interlingua

Herter, F. P., Malm, J. R., Markowitz, A. M., Demetz, A., e Evans, S.: Chimotherapia anti cancere per perfusion regional, New York State J. Med. **62:** 465 (15 de feb.) 1962.

Es describite le experientias colligite in 50 perfusiones in 48 patientes qui omnes exhibiva un stadio avantiate de cancere. Quasi omnes habeva essite subjicite, sin successo, a therapia conventional. Le resultatos general del therapia conventional habeva essite disappunctante con respecto al regression del tumores a longe vista e con respecto al effectos palliatori. Quaranta-duo del 48 remaneva sub observation satis longo pro determinar accuratemente le effectos del therapia perfusional con respecto al responsa del tumores. Novem de illos, i.e. 4 carcinomas genitourinari, 1 carcinoma parotidic, 1 liposarcoma, e 3 melanomas, monstrava regression. Isto esseva transiente in 8 e "permanente" in solmente 1. Tamen, 9 de 11 patientes con intractabile dolores pelvic experientiava un effecto benefic, e in le caso de tumores de altere areas—in tanto que dolores esseva un factor importante in illos—le perfusion resultava in un simile alleviamento. Occurreva 7 complicationes, incluse 1 letal, 2 serie, e 4 minor, omnes durante le prime menses del essayos clinic quando le dosages de droga esseva non ancora firmemente establite e quando le methodos del isolation vascular esseva ancora experimental. Le methodo del perfusion ha duo major avantages: (1) Le possibilitate de applicar al area in question un concentration de droga que esserea mortal si illo esseva administrate systemicamente e (2) le alleviamento symptomatic effectuate pro multes del patientes. Le limitationes del methodo resulta del difficultate de effectuar un adequate isolation vascular in multe areas del corpore, de imperfectiones inherente in le drogas mesme, e del periculo de un stimulation chimotherapeutic del crescentia neoplastic. Le technicas del perfusion es non ancora standardisate. Il etiam existe le desideratos de meliorationes technic, de methodos pro reducer o eliminar le toxicitate systemic del disponibile agentes chimotherapeutic, e de un procedimento que permitterea le perdurative exposition del tumor al effecto del droga. Es proponite, a base tentative, criterios pro le selection de patientes pro le therapia perfusional.

Hyman, Y. K., e Orkin, L. R.: Triflupromazina e fluphenazina como adjunctos in le practica del anesthesia, New York State J. Med. **62:** 480 (15 de feb.) 1962.

Esseva interprendite un studio visante a evalutar le proprietates sedative, hypnotic, e antiemetic de hydrochloruro de triflupromazina (Vesprin) e de dihydrochloruro de fluphenazina (Prolixin). Essayos esseva facite in 24 patientes, ante lor subjection a therapia electroconvulsive, con thiopental a natrium sol e con thiopental a natrium in combination con triflupromazina o fluphenazina. Il pare que 6 mg de triflupromazina e 6 mg de fluphenazina ha approximativemente le mesme potentia sedative como 50 mg de pentobarbital a natrium. In un gruppo de 160 patientes, le uso de triflupromazina sol o in combination con hydrochloruro de scopolamina como medication pre-operatori produceva un bon grado de sedation. Fluphenazina in doses de 4 a 6 mg se provava un tranquillisante con pauc effecto sedatori. Triflupromazina esseva multo utile in alleviar le anxietate e promover le quietessa de 28 patientes durante lor preparation a bronchospirometria o bronchoscopia sub anesthesia topic. In un gruppo de patientes sub anesthesia spinal o peridural, marcate grados de hypotension esseva notate frequentemente post micre doses de triflupromazina. Como agente antiemetic, fluphenazina pareva esser plus efficace que triflupromazina. Un plus micre dose de illo esseva requirite. Ambe drogas esseva efficace in le tractamento de delirios de emergentia, sed fluphenazina es preferite proque illo non prolonga le tempore del anesthesia. Triflupromazina potentiava le effecto anesthetic general. Isto non vale pro fluphenazina. Ni le un ni le altere del duo drogas es indicate in anesthesia spinal. Adverse effectos lateral non esseva notate. Nonobstante, le possibilitate potential de tales demanda attention. Recercas additional es un desiderato.

McKnight, W. K., Yoder, C., e Beckett, T.: Le tractamento de emotionalmente malade juveniles; le natura e le manipulation de factores de resistentia initial, New York State J. Med. **62:** 486 (15 de feb.) 1962.

A generalmente parlar, le causas de maladias emotional in juveniles se trova in un disturbation del equilibrio inter (1) le characteristicas hereditari e constitutional del individuo mesme e (2) adverse influentias presente o passate per factores de milieu. Anormalitates de comportamento in juveniles indica que illes es disturbate in lor vita interne como effecto de un relation pathogene con le un o le altere persona in le milieu. Le causas potential de un disturbation emotional in juveniles include un attitude de rejection del parte del parentes, excessive demandas parental, e hyperprotectivitate. Le formas general in que le reaction pathologic se manifesta es submission, retrahimento, rebellion, e varie reactiones substitutive. Le therapia debe occupar se de modificar le relation pathogene mesme plus tosto que solmente le symptoma de comportamento per se. Per consequente, conceptos de therapia a orientation familial ha reimplaciate le previe conceptos de puericultura a orientation verso le puero o puera sol. Resistentia initial del parte de parentes consultante un clinica de puericultura es normal. Le appropriate manipulation del referage de casos e plus empathia verso le parentes pote esser de adjuta in vincer iste resistentia. Es etiam frequente un attitude de resistentia contra le desiderato de introspection, e etiam le patiente juvenil exhibi symptomas de resistentia.

Vincer le resistentia del parte de parentes e del parte de juveniles es un major mission del clinica puericultural.

Stoll, H. L., Jr., e Crissey, J. T.: Epithelioma ab trauma solitari, New York State J. Med. **62:** 496 (15 de feb.) 1962.

Le question del rolo de trauma in le apparition de cancere es controverse. Illo es particularmente importante in casos de indemnification pro accidentes de travalio. In 1901 le sequente criterios esseva establite pro le evalutation de trauma como factor causal in cancere cutanee: Le previe integritate del parte traumatisate; adequatia e autenticitate del trauma; diagnose positive de un carcinoma nonmetastatic; origine del carcinoma al sito precise del vulneration; lapso de un plausibile intervallo de tempore inter le trauma e le apparition del carcinoma; e continuitate de signos ab le momento del trauma usque ad le apparition del carcinoma. Un prova satisfacente pro o contra le these que trauma solitari pote causar cancere non existe, sed le uso del supra-listate criterios es recommendate. Recercas additional—a base de experimentos animal e studios clinic—es recommendate.

Brain can be alarm clock

One can "set one's mind" to waking up at a certain hour, according to an article by Dr. Jack Arbit in the December 30, 1961, issue of the *Journal of the American Medical Association.* The ability is based on certain learned cues. Beginning in infancy and continuing throughout a person's life, a number of cues are associated with various times of the day and the sleeping and waking cycles. One cue which is highly correlated with the depth of sleep is body temperature. Wakefulness appears to depend on brain centers which can be aroused not only by external means but also by the activity of other parts of the brain. "One might hypothesize, therefore, that in going to sleep a person may 'set' the number of hours he might like to sleep, and when such a stimulus such as body temperature associated with this number of hours or depth of sleep occurs, there is a downward firing from the cortex to the wakefulness center."

Medical News

Myelogenous leukemia patients sought

The cooperation of physicians is requested in a study of chronic myelogenous leukemia being conducted by the Chemotherapy Service of the National Cancer Institute at the Clinical Center, National Institutes of Health, Bethesda, Maryland.

Referrals of patients with chronic myelogenous leukemia are needed, including some treatment refractory patients with high platelet and white blood cell counts, for studies of newer chemotherapeutic agents and as a source of white cells and platelets for in vitro and in vivo study. Accepted patients will be hospitalized for approximately eight to twelve weeks.

Interested physicians may write or phone: Paul P. Carbone, M.D., Chemotherapy Service, Medicine Branch, National Cancer Institute, Bethesda 14, Maryland. Telephone: 496–4251.

Course in pediatric oncology

The Pediatric Department of Memorial Sloan-Kettering Cancer Center, New York City, announces its annual comprehensive three-day course in pediatric oncology for pediatricians, general practitioners, and health officers to be held April 25 through 27.

Current developments and established methods in diagnosis, differential diagnosis, and management of benign and malignant tumors, Hodgkin's disease, leukemia, and reticuloendothelioses in childhood, are included.

Twenty members of the attending staffs of Memorial Hospital for Cancer and Allied Diseases and the Memorial Sloan-Kettering Cancer Center will be on the faculty.

For information write to: Chairman, Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, 444 East 68th Street, New York 21, New York.

Apparatus measures radiation

Cornell University has put into operation an apparatus which will aid scientists in determining the effects of nuclear radiation on living things. It is a specially constructed 30-ton inverted scintillation counter, or whole body counter, which measures the amount of radiation in a subject.

The apparatus will be useful in discovering the radioactive accumulation by humans, animals, and foodstuffs, such as milk, as a result of fallout or other sources of radiation.

Amputees will get better care

Leona Baumgartner, M.D., Commissioner of the City of New York Department of Health and chairman of the Interdepartmental Health Council, has announced that the 250 amputees who each year get artificial limbs through the Department of Health, the Department of Welfare, or the Department of Hospitals will receive better care and treatment under a new program worked out by the Interdepartmental Health Council.

Formerly "medically indigent" persons who required prosthetic devices could obtain them at any hospital. In many instances, this proved unsatisfactory since the skill in fitting artificial limbs and in training amputees in their use varied widely. So far 13 hospitals have been designated as having approved amputee service by the Advisory Committee on Amputee Services of the Interdepartmental Health Council (which is made up of the Departments of Health, Hospitals, and Welfare, and the Community Mental Health Board).

Under the new program any medically indigent amputee requiring an artificial limb whose care is being paid for by a City agency will be sent to one of the 13 approved hospitals. There the amputation will be cared for, the prosthetic device will be fitted, and the amputee will be given training in the use of the device.

Hospitals which have been approved for the new program are: *Bronx:* Bronx Municipal Hospital Center and Montefiore Hospital; *Brooklyn:* Jewish Chronic Disease Hospital and Kings County Hospital Center; *Queens:* City Hospital at Elmhurst; *New York City:* Bellevue Hospital Center, Hospital for Joint Diseases, Hospital for Special Surgery, Institute of Physical Medicine and Rehabilitation, Metropolitan Hospital, Mount Sinai Hospital, Presbyterian Hospital, and St. Vincent's Hospital.

New York City gives grants

Grants totaling $10,194,789 to medical institutions and to young scientists in New York City have been announced by the Health Research Council.

In all, 130 grants were approved for the current fiscal year ending June 30. Included were 54 investigatorships amounting to $3,162,709. These are grants given for long-term support of young scientists who might otherwise be forced to give up research in favor of better paying opportunities in other fields.

The awards bring to $20,936,373 the amount allocated by the City for medical and health research in the three-year history of the council.

Empire State Award for Medical Reporting

Nominations are now being accepted for the third annual Empire State Award for Excellence in Medical Reporting. The $500 award is sponsored by the Medical Society of the State of New York and Annual Health Conference Inc., on behalf of the New York State Department of Health.

The award was established to encourage the further development of sound medical reporting in New York State and to recognize the significant contributions to public knowledge and understanding of health and medicine that are made by reporters and newspapers in New York State.

Any member of the editorial staff of any newspaper published five or more times a week in the State of New York may be nominated for the award. The reporter may be nominated for a single article or for a series of articles. However, the judges will also consider the general science and health stories written by each nominee during the year. In addition, any newspaper published in the State may be nominated for a public service award in the field of medical reporting.

Nominations for the award can be made by the newspaper employing the reporter, the county medical society in the area served by the nominee's newspaper, or the county, city, or district health officer in the area served by the nominee's newspaper.

Nominations should be sent to: Secretary, Empire State Medical Reporting Award Committee, Office of Public Health Education, New York State Department of Health, 84 Holland Avenue, Albany 8, New York.

Morgagni Society of Brooklyn

The Morgagni Society of Brooklyn has announced the election of the following officers for 1962: Joseph J. Ricca, M.D., president; John J. Ippolito, M.D., president-elect; Frank Sconzo, M.D., vice-president; Thomas J. Sinatra, M.D., secretary; Ernest Buffone, M.D., treasurer; and Marcello Petraroja, M.D., corresponding secretary.

Society of Certified Internists of the County of New York

The Society of Certified Internists of the County of New York, a chapter of the New York State Society of Internal Medicine, has announced the election of the following officers for 1962: Seymour L. Halpern, M.D., president; Arthur M. Master, M.D., president-elect; William B. Rawls, M.D., vice-president; Clifford L. Spingarn, M.D., secretary; and Charles Ressler, M.D., treasurer.

Elected to the board of directors of the society were the following: For the term ending in December, 1962: Asa L. Lincoln, M.D., Alfonso A. Lombardi, M.D., and Harry A. Solomon, M.D.; for the term ending in December, 1963: Constance Friess, M.D., Bernard J. Handler, M.D., and Henry B. Kirkland, M.D.; and for the term ending in December, 1964: William J. Grace, M.D., Carl Muschenheim, M.D., and Robert Wallach, M.D.

Course on allergy to be held in Pittsburgh

The Section on Allergy of the Montefiore Hospital, Pittsburgh, Pennsylvania, will present a seven-day course in allergy May 20 through 26. The course is intended to orient the internist and the general physician in the various phases of allergic diseases. Sessions will be held daily from 8:30 A.M. to 5:00 P.M. with dinner conferences scheduled in the evenings.

For information write to: Leo H. Criep, M.D., Bigelow Apartments, Pittsburgh 19, Pennsylvania.

Heart research fellowship program

A fellowship program aimed at stimulating research in medical education has been established by the American Heart Association. Undertaken in an effort to meet the need for specialists to guide and evaluate professional education activities at both the undergraduate and postgraduate level, the new program will seek to encourage clinical and/or basic scientists to study educational principles and methods of educational research.

Candidates selected will be given an opportunity to receive training at one of the three medical schools that have established departments of research in medical education. They will also take part in the investigative programs in which these groups are engaged and in the experimental pilot projects in continuing education now being established by the American Heart Association.

In order to meet the needs of candidates drawn from varied background and experience, no fixed fellowship stipend has been established. An appropriate level of support can be provided for candidates who have just completed residency training, or those who have already achieved the level of independent investigation.

For information write to: Frederick J. Lewy, M.D., Associate Medical Director, American Heart Association, 44 East 23rd Street, New York 10, New York.

Statistics on tuberculosis

Tuberculosis in New York City—1960, an annual statistical yearbook, has been published by the New York Tuberculosis and Health Association. The report contains factual data with interpretations concerning cases of newly diagnosed disease and deaths from tuberculosis. The data were derived mainly from hospitals and public health and welfare agencies of the city and were compiled and reviewed by the Association's statistician, Anthony M. Lowell.

Distribution of the book is being made to individuals and agencies actively engaged in the campaign against tuberculosis or with a serious interest in the problem. For information write to: New York Tuberculosis and Health Association, Inc., 260 Park Avenue South, New York 10, New York.

Alcoholism panel named

Governor Nelson A. Rockefeller has announced the appointment of a twelve-member advisory council on alcoholism. John L. Norris, M.D., Rochester, has been designated as chairman and Arthur N. Seiff, New York City, as vice-chairman.

Members of the advisory council will serve without compensation. It will be their duty to advise the Division of Alcoholism within the Department of Mental Hygiene.

In addition to Dr. Norris and Mr. Seiff other members of the council are: Harold Riegelman, Chappaqua; James H. Wall, M.D., White Plains; Rev. Ace L. Tubbs, Yonkers; R. Brinkley Smithers, Locust Valley; Ruth Fox, M.D., New York City; Rev. Raymond Kennedy S.J., Syracuse; Eleanor H. McHugh, Schenectady; Emerson Laughland, Watertown; S. Mouchly Small, M.D., Buffalo; and Marvin A. Block, M.D., Buffalo.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that the next scheduled examinations (part II, oral and clinical) will be conducted at the Edgewater Beach Hotel, Chicago, April 9 through 14. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates.

Candidates who participated in the part I examination will be notified of their eligibility for the part II examinations as soon as possible.

Current bulletins outlining the requirements for application may be obtained by writing to: Robert L. Faulkner, M.D., American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Tobacco industry gives grants

Timothy V. Hartnett, chairman of the Tobacco Industry Research Committee, has announced that the tobacco industry has given 30 research grants, totaling more than $296,000, to independent scientists in 14 states for studies relating to tobacco use and health.

The new grants make a total of 154 initial grants and 172 renewals awarded to scientists in some 75 institutions. All grants-in-aid are made by a scientific advisory board comprised of independent doctors and scientists which direct the Tobacco Industry Research Council's program.

Postgraduate course at Medical College of Georgia

Early recognition and proper management of problems arising in the pre- and postsurgical states will be featured in the continuing education course scheduled for March 20 through 22 at the Medical College of Georgia.

Case analysis clinics will be held with active participation by registrants and the presentation of problem cases will be encouraged.

For information write to: Claude-Starr Wright, M.D., Director, Department of Continuing Education, Medical College of Georgia, Augusta, Georgia.

St. Luke's Hospital elects officers

St. Luke's Hospital, New York City, has announced the election of Harold A. Zintel, M.D., as president of its medical board. William S. Norton, 2nd, M.D., has been elected vice-president, and Herbert Parsons, M.D., was named secretary.

The Hospital also announced the appointment of John F. Bertles, M.D., as director of the Hematology Unit of the Medical Service and chief of the Hematology Clinic.

Computer as an aid in cancer treatment

Announcement has been made by the Memorial Hospital for Cancer and Allied Diseases of what is thought to be the first computer installation in a center for the diagnosis and treatment of cancer.

Richard D. Vanderwarker, vice-president and general manager of Memorial Hospital for Cancer and Allied Diseases, said hospital scientists are programming a Bendix G-15 computer system for use in applying data processing technics to the study of radiation in diagnosing and treating cancer patients. The Hospital is the treatment unit of the Memorial Sloan-Kettering Cancer Center.

Fellowships in field of handicapped

Fifteen fellowships of $400 each and a number of scholarships to help further the skills of professional persons working with the crippled are available from the National Society for Crippled Children and Adults, the Easter Seal Society has announced.

Deadline for filing applications for these awards is March 15 for fellowships and April 1 for scholarships. For information write to: Personnel and Reporting Service of the National Society for Crippled Children and Adults, 2023 West Ogden Avenue, Chicago 12, Illinois.

Rehabilitation seminar

The Burke Foundation Rehabilitation Center, located on Mamaroneck Avenue in White Plains, announces its second seminar in rehabilitation to be held March 5 through May 7. The seminar will be held under the direction of Edward J. Lorenze, M.D., medical director of the Center. An integrated multidisciplinary approach to the rehabilitation of children and adults with physical disabilities will be presented.

For information write to: Mr. Anthony J. DeRosa, Coordinator of Rehabilitation and Educational Services, Burke Foundation Rehabilitation Center, White Plains, New York.

Personalities

Speakers. Henry I. Fineberg, M.D., Jamaica, on January 3, before the Queens County Grand Jurors' Association on the subject "Quacks and Quackery and Their Cost to the American People" . . . Harold Jacobziner, M.D., New York City, on January 18, at the Lutheran Medical Center in Brooklyn on the topic "Causation, Epidemiology, Control, and Prevention of Accidental Chemical Poisonings" . . . Stanley Lesse, M.D., New York City, before the one hundred and eighty-sixth scientific meeting of the Association for the Advancement of Psychotherapy on January 26.

Awarded. Paul Klemperer, M.D., New York City, the medal of the New York Academy of Medicine in recognition of his "outstanding contributions to progress in medical science" . . . Robert L. Levy, M.D., New York City, the New York Academy of Medicine's plaque in recognition of "extraordinary service" to the Academy . . . Colin M. MacLeod, M.D., New York City, for his contributions to research in the field of immunologic and infectious processes and on genetic transformation of bacteria, and George E. Moore, M.D., Buffalo, for his contributions in the field of cancer surgery and research, Distinguished Achievement Awards from *Modern Medicine* . . . Thomas D. Rees, M.D., New York City, the distinguished service award of the Young Men's Board of Trade in recognition of his work in Africa in the field of plastic surgery.

Medical Schools

Albany Medical College

Grant. The National Institute of Allergy and Infectious Diseases awarded a grant of $221,928 for fundamental research into the mechanisms of fever, for a four-year period. Fairfield Goodale, M.D., associate professor of pathology, is the senior investigator, and he will be assisted by Hideshige Imai, M.D., instructor in pathology, George W. Gander, M.D., research associate in pathology, and Joseph A. Sisson, M.D., fellow in pathology.

Postgraduate Course. A course on the problems of mental illness was held at the College from January 11 through February 8. The course was designed to aid the general practitioner in the recognition and treatment of psychiatric problems encountered in the everyday practice of medicine and was presented by the members of the Psychiatry Department. The demand to attend the course was such that it will be repeated next fall. The content of the course was determined by the College's Psychiatry Department in conjunction with the district branch of the American Psychiatric Association and the mental health committee of the Albany County Medical Society. The New York State Department of Mental Hygiene provided funds to partially defray the cost of the course.

Appointed. Dr. Frank L. Husted has been appointed a director of research in medical education. The appointment was effective January 15. Dr. Husted will make a thorough study of the educational program and will implement and evaluate curriculum changes recommended by faculty delegates to the College's teaching institutes which were held annually the last four years. Dr. Husted also will observe teaching at other medical schools.

New York University School of Medicine

Howard Fox Memorial Lecture. Dr. Gustav Asboe-Hansen, professor of dermatology and director of the Connective Tissue Research Laboratory, University of Copenhagen, Denmark, will speak on "Dermatologic Aspects of Mast Cell Activity," on May 8. The lecture will begin at 4 P.M. in Alumni Hall, 550 First Avenue, New York City.

State University of New York Downstate Medical Center

Faculty appointments and promotions. Dr. Leo Srole, sociologist, has been appointed professor in the Department of Psychiatry. Dr. Srole is the first sociologist to be appointed to the psychiatry staff at the Center and his appointment is sponsored by the Foundation's Fund for Research in Psychiatry, New Haven, Connecticut. Stephen N. Steen, M.D., has been named assistant professor of anesthesiology. George H. Roberts, M.D., and Harold Merwarth, M.D., have been named clinical professor emeritus of medicine and neurology, respectively. Promoted from lecturer to associate professor of psychiatry is Jan Frank, M.D., and promoted from clinical instructor to clinical assistant professor, Abbott Lippman, M.D. Laurence S. Maynard, M.D., who has been a research associate in the Department of Psychiatry since 1960, has been named assistant professor of psychiatry. Benjamin C. Berliner, M.D., has been named clinical assistant professor of pediatrics.

Postgraduate courses. A series of "Postgraduate Lectures in Psychiatry" for accredited psychiatrists and for psychiatrists in training which began on October 3, 1961, and will run through April 3, 1962, is sponsored jointly by the Department of Psychiatry and the Brooklyn Psychiatric Society. A symposium on "Pathogenesis and Management of Connective Tissue Diseases," sponsored by the Department of Medicine, the Arthritis and Rheumatism Foundation, and the Kings County Chapter of the American Academy of General Practice, was held on November 15, 1961. During February and March a course in dermatology is being held on Wednesday afternoons in the first floor lecture hall of the Basic Sciences Building, 450 Clarkson Avenue. The course is sponsored by the Division of Dermatology of the Department of Medicine and one hour Category I credit will be granted by the American Academy of General Practice for each hour and one-half session. Doctors interested in registering for the course should write to the Office of Postgraduate Education, State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

Symposia. A two-day symposium reviewing the psychiatric problems related to asthma in children was held on December 6 and 7, 1961. A symposium on "Heart Disease in Infancy," sponsored by the Department of Pediatrics, will be held on March 14 in the sixth floor lecture hall of the Basic Sciences Building. Inquiries should be addressed to the Office of Postgraduate Education, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York. Advanced registrants will receive seating priority.

Visiting professors. Dr. Donald L. Wilhelm, Foundation Professor of Pathology at the University of New South Wales, Sydney, Australia, is serving as visiting professor in the Department of Microbiology and Immunology for the month of February. Dr. Percy Olaf Lindgren, docent, Department of Pharmacology, Karolinska Institute, Stockholm, Sweden, has been named visiting associate professor in the Department of Pharmacology for one year.

Speaker. Arthur Shapiro, M.D., associate professor of medicine, spoke on "Recent Research in Dreaming" at a meeting of the Center's Parents' Association on January 18.

Grants. Received during November and December, 1961, were 14 research grants totaling $273,931. Three grants were to support new projects and the remaining 11 were renewals of research projects already under way. The allocations are from the National Institutes of Health, the Office of Naval Research, and A. H. Robins Company.

State University of New York Upstate Medical Center

Interim editor. Dr. Justus F. Mueller, professor, Department of Microbiology, has been appointed interim editor of the *Journal of Parasitology*. The editorship will continue to January 1, 1964. Dr. Mueller is a charter member of the American Society of Parasitologists which was established in 1924. He served on the editorial board of the *Journal* from 1940 to 1944.

Books Received

The following books were received during the month of November, 1961

The American Academy of Orthopaedic Surgeons. Instructional Course Lectures. Volume XVIII, 1961. Edited by Fred C. Reynolds, M.D. Quarto of 310 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $17.

Eye Symptoms in Brain Tumors. By Alfred Huber, M.D. Octavo of 329 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $16.

Progress in Liver Diseases. Volume I. Edited by Hans Popper, M.D., and Fenton Schaffner, M.D. Quarto of 363 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $13.75.

Histopathology of the Skin. By Walter F. Lever, M.D. Third edition. Octavo of 653 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $16.50.

Textbook of Gynecology. By John I. Brewer, M.D. Third edition. Octavo of 831 pages, illustrated. Baltimore, The Williams & Wilkins Company, 1961. Cloth, $15.

Gynecologic Endocrinology. By Edward A. Graber, M.D. Octavo of 218 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $7.50.

Psychiatry, Biological and Social. By Ian Gregory, M.D. Octavo of 577 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $8.50.

Unit-Step Radiography. By Gerhart S. Schwarz, M.D. Octavo of 230 pages, illustrated. Springfield, Charles C Thomas, 1961. Cloth, $8.75.

Disturbances of Heart Rate, Rhythm and Conduction. By Eliot Corday, M.D., and David W. Irving, M.D. Octavo of 357 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $8.50.

Hemodynamics of Aortic and Mitral Valve Disease. By Alvin J. Gordon, M.D., Paul A. Kirschner, M.D., and Howard L. Moscovitz, M.D. Octavo of 136 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $5.75.

The Medical Clinics of North America. Nationwide Number. November, 1961. Office Practice and Procedures. Michael G. Wohl, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bi-monthly (six numbers a year). Cloth, $18 net; Paper, $15 net.

Physical Foundations of Radiology. By Otto Glasser, Ph.D., Edith H. Quimby, Sc.D., Lauriston S. Taylor, ScD., J. L. Weatherwax, M.A., and Russell H. Morgan, M.D. Third edition, revised and enlarged. Duodecimo of 503 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $10.

Anatomy of the Coronary Arteries. By Thomas N. James, M.D. Quarto of 211 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $18.

Stapes Surgery for Otosclerosis. By Victor Goodhill, M.D. Quarto of 212 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $11.50.

Therapeutic Communication. By Jurgen Ruesch, M.D. Octavo of 480 pages. New York, W. W. Norton & Company, Inc., 1961. Cloth, $6.50.

Ciba Foundation Study Group No. 9. Progesterone and the Defence Mechanism of Pregnancy. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Margaret P. Cameron, M.A. With 22 illustrations. Duodecimo of 108 pages. Boston, Little, Brown and Company, 1961. Cloth, $2.50.

Ciba Foundation Study Group No. 10. Biological Activity of the Leucocyte. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. With 17 illustrations. Duodecimo of 120 pages. Boston, Little, Brown and Company, 1961. Cloth, $2.50.

Cerebral Vascular Diseases. Transactions of the Third Conference. Edited by Clark H. Millikan, Robert G. Siekert, and Jack P. Whisnant. Octavo of 247 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $5.75.

The Mold of Murder. By Walter Bromberg, M.D. Octavo of 230 pages. New York, Grune & Stratton, 1961. Cloth, $4.75.

How to be an Adolescent—and Survive. By John L. Schimel, M.D. Duodecimo of 158 pages. New York, Richards Rosen Press, Inc., 1961. Cloth, $2.95.

The Art of Thinking. By Dagobert D. Runes. Duodecimo of 90 pages. New York, Philosophical Library, 1961. Cloth, $2.75.

Life's Key—DNA. By Carleen Maley Hutchins. Octavo of 64 pages, illustrated. New York, Coward-McCann, Inc., 1961. Cloth, $2.50.

The Doctor Business. By Richard Carter. Revised edition. Duodecimo of 276 pages. Garden City, N.Y., Doubleday & Company, Inc., 1961. Paper, $0.95.

Books Reviewed

Chemistry of Drug Metabolism. By William H. Fishman, Ph.D. Octavo of 235 pages, illustrated. Springfield, Charles C Thomas, 1961. Cloth, $10.50.

The toxicity of drugs is conditioned by several properties and events. One of these is the inactivation of an enzyme system or a poisoning of a catalyst, an example of which is cyanide poisoning. Then there are those drugs, mercury, for example, which denature protein and which have affinities for certain tissues, for example, the kidneys. Other substances are toxic because they are excreted very slowly and build up toxic levels through small increments, such as digitalis. Some are changed into toxic metabolites, whereas others are detoxified in the course of metabolic conversions. In fact drug action, by and large, is dependent on the metabolites into which a drug is changed—and drug metabolism is essentially a study of the conversions which a drug undergoes.

This book is a relatively brief exposition of the metabolic transformations to which drugs are subject and the manner in which their pharmacologic effects are understood to be exerted. There are various mechanisms of such metabolic transformations more or less characteristic of and even specific to given drugs. One of them is the glucuronic acid conjugation which is characteristic of carbohydrates. This book is concerned largely, but not exclusively, with that type of conjugation, and the author is one of the outstanding workers in that field.

The book explores the conversions of classes of organic substances including drugs, such as substituted benzenes, aromatic amines, and so forth, and particularizes briefly in the case of specific drugs such as the barbiturates, the salicylates, morphine and its analogues, and the sulfonamides. Among the various biochemical processes that are surveyed are hydroxylation, acetylation, dehydrogenation, alkylation, deamination, and hydrolysis.

Far less extensive than Williams' *Detoxication Mechanisms* or Schueler's *Chemobiodynamics and Drug Design*, it draws into focus many of the phases in drug metabolism, which are conveyed with textual clarity, aided by good illustrative materials as tables and flow sheets showing conversion to intermediate and end metabolites. It will be of considerable interest to clinicians interested in how, and at times why, certain drugs work as they do.—ERWIN DI CYAN, PH.D.

Meaning and Methods of Diagnosis in Clinical Psychiatry. By Thomas A. Loftus, M.D. Octavo of 169 pages. Philadelphia, Lea & Febiger, 1960. Cloth, $5.00.

This handy volume is intended not only as a progressive guide to medical students and psychiatric interns and residents who seek a clear, practical examination outline for history taking, method of examination, and diagnosis, but also as a follow-through heuristic attitude which tends to make more firm and discriminating the student's understanding of psychiatric patients.

The author is associate professor of clinical psychiatry, The Jefferson Medical College, Philadelphia. The content is rooted in thoroughgoing clinical experience. There is a helpful foreword by Robert A. Mathews, M.D., professor of psychiatry, who emphasizes the usefulness of this volume for the undergraduate medical student as well as a means of sharpening the diagnostic acumen of the resident and, indeed, the general practitioner who, by and large, is our first line of defense in the recognition and management of this number one public health problem, namely, the care and treatment of mentally ill persons.

The author is to be commended for keeping the reader mindful of the fact that the psychiatrist is first and always a physician and must be well versed in all physical diagnostic aids and procedures. Moreover, he does not sell himself out to any particular psychiatric school but maintains a wholesome eclectic point of view. The contents include chapters on the meaning and method of diagnosis, history taking, comparative histories, psychiatric consultation, emergency work, the doctor-patient relationship, and the use of drugs in diagnosis. There follow synoptic psychiatric histories illustrating consultation notes and exercises.

A helpful appendix and complete index lend added value to this very welcome addition to the psychiatric armamentarium.—FREDERICK L. PATRY, M.D.

Congenital Malformations of the Heart. Volume II: Specific Malformations. By Helen B. Taussig, M.D. Quarto of 1,049 pages, illustrated. Cambridge, Mass., published for The Commonwealth Fund by Harvard University Press, 1960. Cloth, $17.50.

The long-awaited second edition of Taussig's monumental contribution to medical literature is even better than expected. Although the main general outlines of its predecessor are preserved, the text has been widely revised and augmented. A visual index, outlining the essential features of the various malformations, is a useful addition. The newer knowledge of congenital heart disease, a division of medicine which has been catapulting forward, is well set forth. A good example is Marfan's syndrome which was covered in a paragraph before and which is now deservedly given several pages. This is a worthy addition to every library.—MILTON PLOTZ, M.D.

Clinical Obstetrics and Gynecology, Volume 4 Number 1, March 1961. Obstetric Anesthesia and Analgesia. Edited by Robert A. Hingson, M.D. **Vaginal Surgery.** Edited by Abraham F. Lash, M.D. Octavo of 304 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Published quarterly (four numbers a year). Cloth, $18 per year.

As noted in the title, the subject of obstetric analgesia and anesthesia is covered in the first part of the book. Particular attention is called to the role of analgesia and anesthesia in the mortality and morbidity of mothers and infants. Various technics and drugs used are discussed, and such allied subjects as uterine dynamics, psychorelaxation management for labor and delivery, and resuscitation of the newborn infant are included. In a chapter on special problems in obstetric anesthesia, women in three extremes of reproductive life—the unmarried mother, the "grande multipara," and the mother giving birth to multiple fetuses—are noted to present special problems in obstetric anesthesia.

The second part of the book is devoted to vaginal surgery. The author of this portion is an accomplished vaginal surgeon, who describes the technic of vaginal hysterectomy with particular reference to the removal of abnormally large uteri. Various other vaginal operative procedures are described and discussed by experts in their use. The book also includes a special article on the medicolegal aspects of psychogenic abortion.—ALEXANDER H. ROSENTHAL, M.D.

A Manual of Cutaneous Medicine. By Donald M. Pillsbury, M.D., Walter B. Shelley, M.D., and Albert M. Kligman, M.D. Octavo of 430 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $9.50.

This book was written for the purpose of covering the field of cutaneous medicine by a manual of handbook size. The essentials are retained, but the uncommon diseases have been eliminated.

It is really a thoroughly edited and rewritten book based generally on the larger textbook by the same authors which appeared in 1956. Changes in dermatologic thought both as to etiology and treatment are brought up to date.

All three authors hold the title of professor of dermatology at the University of Pennsylvania and are perfectly competent to accomplish the purpose of this book. As in the earlier book, the numerous names and synonyms for various skin diseases, which have appeared in the dermatologic literature, have been thoroughly edited and simplified. Each disease is designated by the more commonly accepted title.

The authors are to be commended for stating without equivocation that for certain diseases of the skin there is no treatment which is presently of value. The authors have succeeded remarkably well by producing a book which

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GENERAL SESSIONS SCHEDULE

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Monday Through Friday

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3:00–5:00	Albert Einstein College of Medicine of Yeshiva University

TUESDAY, MAY 15

1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Mecicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
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3:30–5:00	New York University School of Medicine

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1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
3:30–5:00	New York Medical College

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Pathology of Tumours. By R. A. Willis, M.D. Third edition. Octavo of 1,002 pages, illustrated. Washington, D.C., Butterworth Inc., 1960. Cloth, $21.

This is an excellent, refreshing, well-planned treatise on the structural characteristics of tumors. A goodly portion of this tome gives the broad fundamental principles of pathology by a single modest, elder scholar for pathologists, research workers, and senior students as well as clinicians. Since the second edition of 1953, all the chapters have been revised and the text changed in the discussion of the experimental production of tumors, tumors of animals, carcinosarcoma, epithelial tumors of long bones, congenital epulides, bronchial carcinoma, pancreatic islet tumors, arrhenoblastoma, dysgerminoma, infantile testicular carcinoma, hemangiopericytoma, chemodectomas, embryonic hepatic tumors, and vascular lesions of malignant tumors.

Shear's finding that 0.0004 mg. of dibenzanthracene can initiate tissue malignancy is mentioned. Willis stresses the diagnostic unreliability of sputum smears. He thinks that the value of the smear examination in early carcinomas of the cervix has been overestimated. Also touched on are the perplexities of determining the natural course of tumors.—BERNARD SELIGMAN, M.D.

Clinicopathological Conferences of the Massachusetts General Hospital. Edited by Benjamin Castleman, M.D., and H. Robert Dudley, Jr., M.D. Quarto of 295 pages, illustrated. Boston, Little, Brown and Company, 1960. Cloth, $12.50.

These case records originally appeared in the *New England Journal of Medicine*. They span a period of twenty-five years. Dr. Dudley and Dr. Castleman, the editors, have chosen fifty of the most interesting for this volume.

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Neuroradiology Workshop. Volume I: Scalp, Skull and Meninges. By Leo M. Davidoff, M.D., Harold G. Jacobson, M.D., and Harry M. Zimmerman, M.D. Quarto of 256 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $16.50.

This first volume of a projected series on neuroradiology is an interesting departure from the usual textbook on the subject but should be considered as an adjunct and not as a substitute for the classic method of presentation. The informal presentation of case studies of neurologic interest, with particular reference to radiographic abnormalities, branching off (but not too far off) into discussions of etiology, therapy, and prognosis, makes for easy and profitable reading. It is to be recommended for students in neurology and radiology at all levels.

The participants in the discussions are eminent in their fields of neurology, neurosurgery, pathology, and radiology, and the opinions expressed, although not always concurring, certainly carry the authority of experience.

The excellence of the reproduction of radiologic material, particularly the large format of the illustrations, is especially to be commended. However, because of the manner of presentation, the organization is rather too loose for use as a systematic review of the field.—HOWARD FREEDMAN, M.D.

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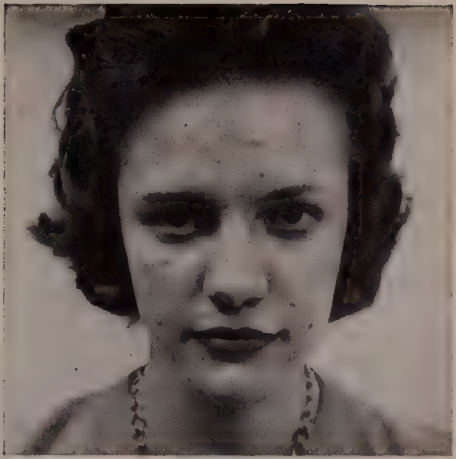

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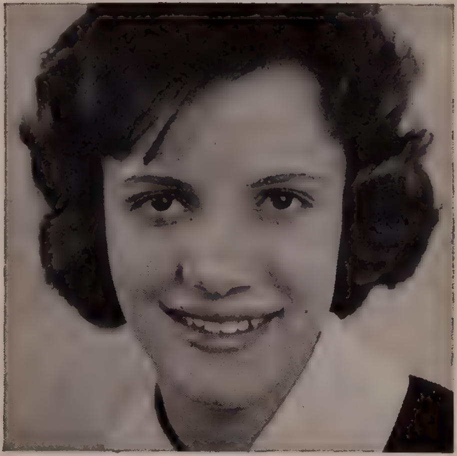

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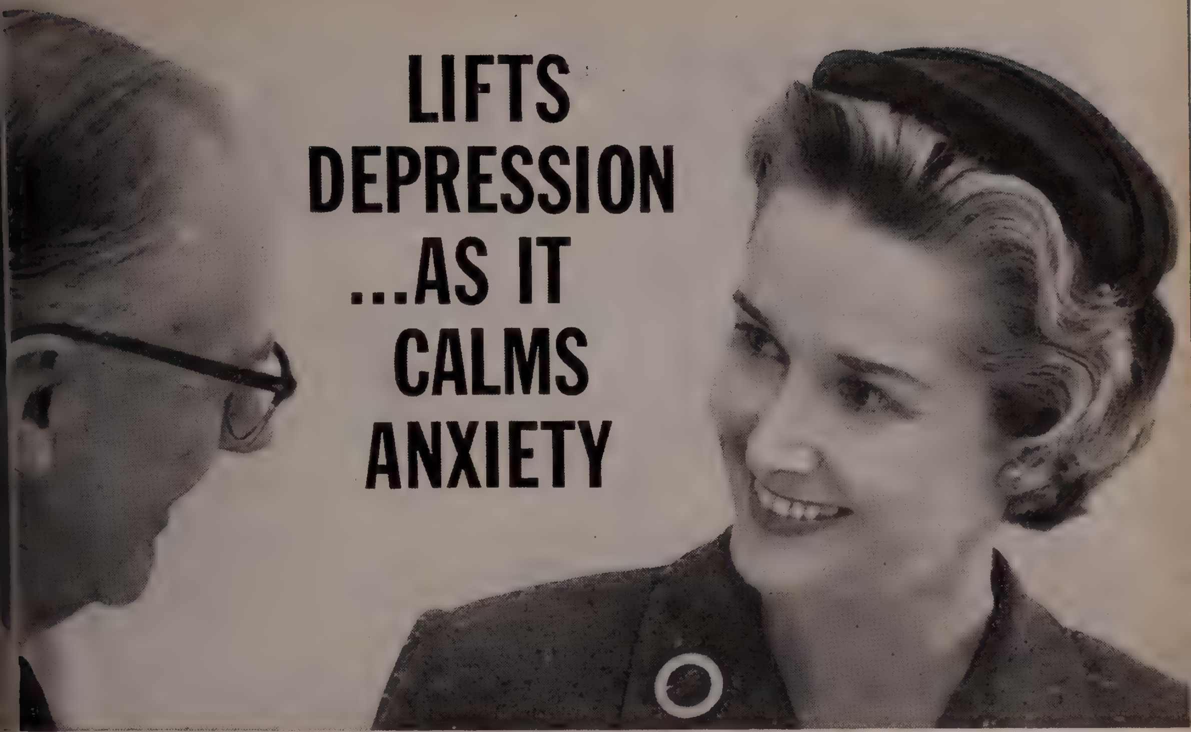

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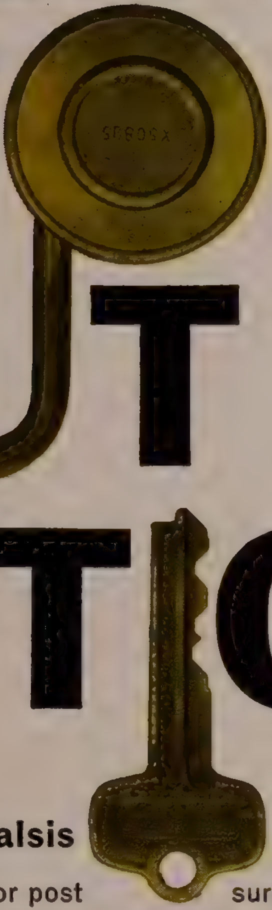

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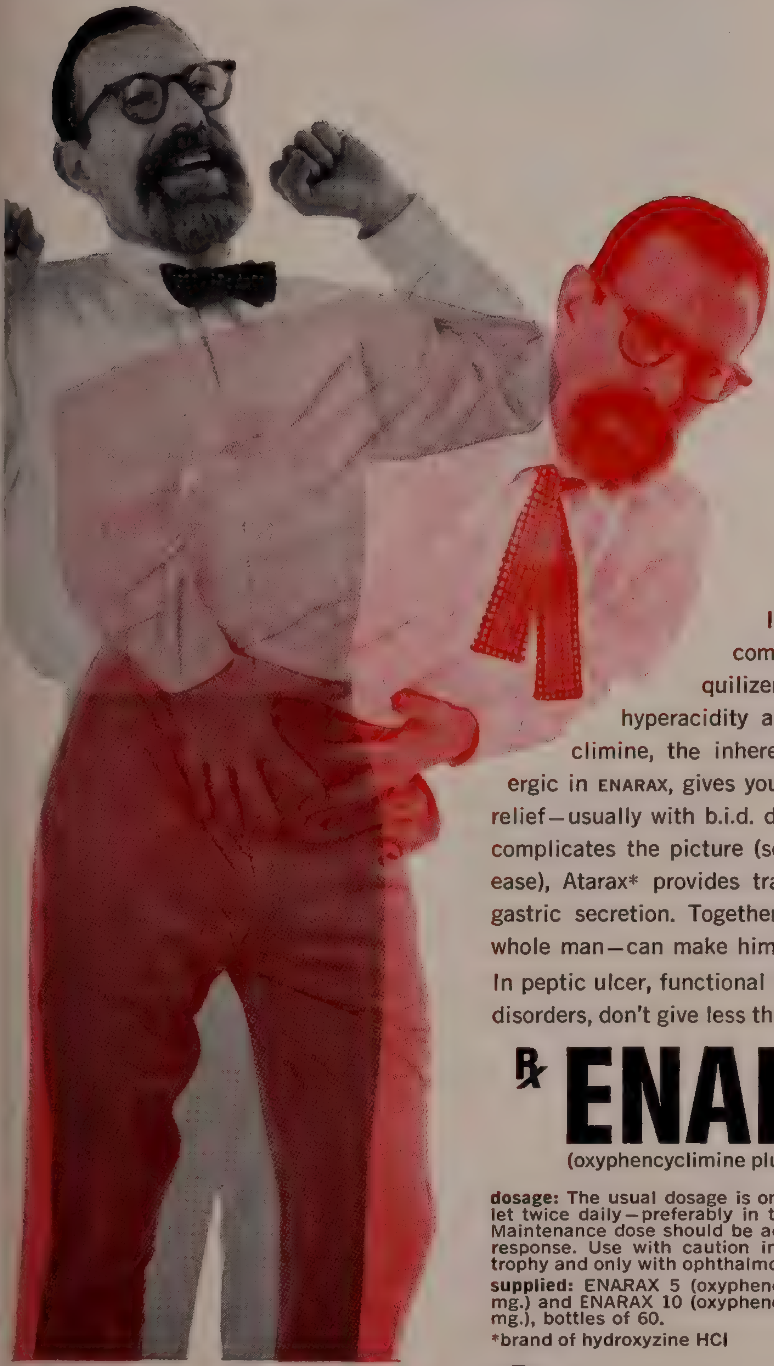

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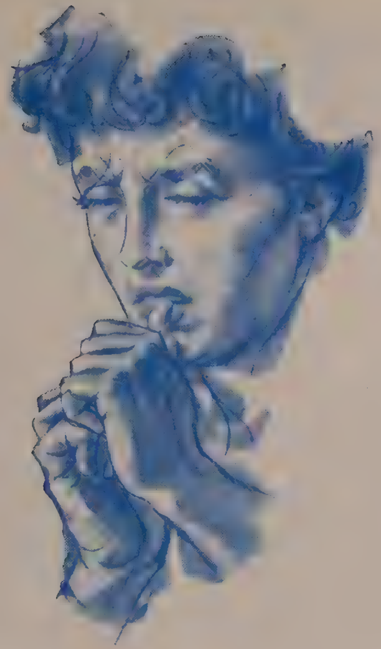

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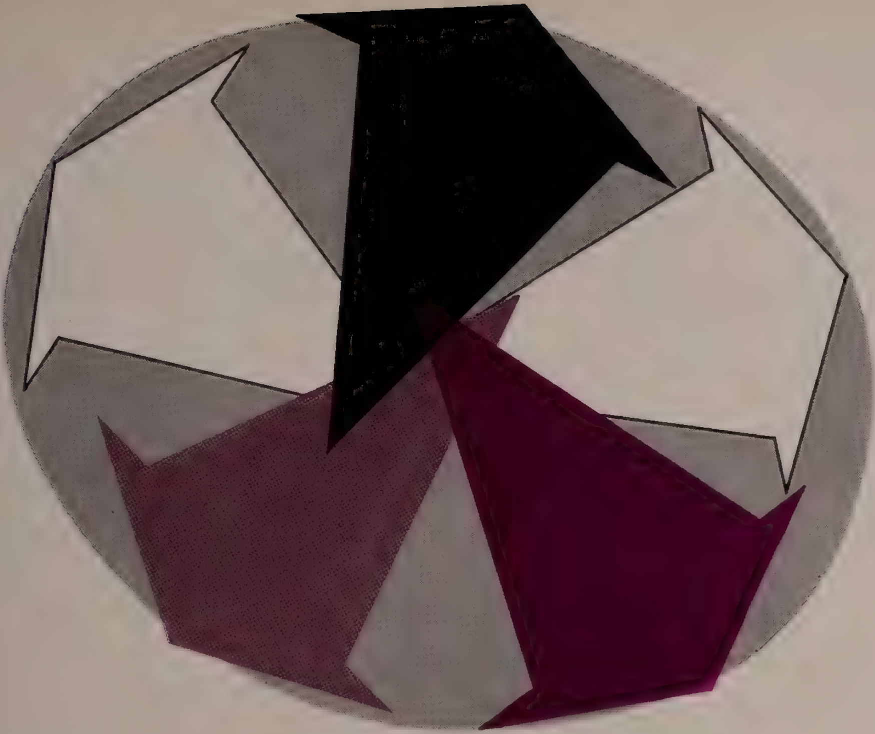

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Clinical and Pharmacological Reports **1.** Berger, F.M., Douglas, J.F., Kletzkin, M., Ludwig, B.J. and Margolin, S.: The Pharmacological Properties of 2-methyl-2-*sec*-butyl-1,3-propanediol dicarbamate (mebutamate, W-583) a New Centrally Acting Blood Pressure Lowering Agent. J. Pharmacology. *134:*356 (Dec.) 1961. **2.** Berger, F. M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W 583) Fed. Proc. *20:* 113 (March) 1961. **3.** Bohensky, F. S.: Mebutamate, a New Drug for the Treatment of Hypertension. N.Y. State J. Med. In press, 1962. **4.** Diamond, S., and Schwartz, M.: Blood Volume in Uncomplicated Essential Hypertension. Mod. Med. In press, 1962. **5.** Douglas, J.F., Ludwig, B.J., Ginsberg, T., and Berger, F.M.: Studies on W-583 metabolism. Fed. Proc. *20:*113 (March) 1961. **6.** Duarte, C., Brest, A.N., Kodama, R., Naso, F. and Moyer, J.H.: Observation on the Antihypertensive Effectiveness of a new Propanediol Dicarbamate (W-583) Curr. Therap. Res. *2:*148-52 (May) 1960. 7. DuChez, J.W.: Scientific Exhibit, American Medical Association, New York, 1961. **8.** Holloman, J.S.L., Jr.: Treatment of Hypertensive Patients with Mebutamate, a New Antihypertensive Drug—a Preliminary Report. J. Nat. Med, Assoc. In press, 1962. **9.** Kletzkin, M., and Berger, F.M.: A Centrally Acting Antipressor Agent. Fed. Proc. *20:*113 (March) 1961. **10.** Leslie, C.H.: The Efficacy of Mebutamate, a New Antihypertensive Drug, in Treatment of Refractory Geriatric Hypertensive Patients—a Preliminary Report. J. Am. Ger. Soc., *10:*85 (Jan.) 1962. **11.** Mulinos, M.G.: Scientific Exhibit, Amer. College of Cardiology, New York, May, 1961. **12.** Mulinos, M.G., Saltefors, S., Boyd, L.S. and Cronk, G.A.: Human Pharmacology Studies with W-583. Fed. Proc. *20:*113 (March) 1961. **13.** Shubin, H.: Scientific Exhibit, Amer. College of Cardiology, New York, 1961. **14.** Turek, L.: Clinical Evaluation of Mebutamate, an Antihypertensive Agent. Preliminary Report. Clin. Med. *8:*1335-39 (July) 1961.

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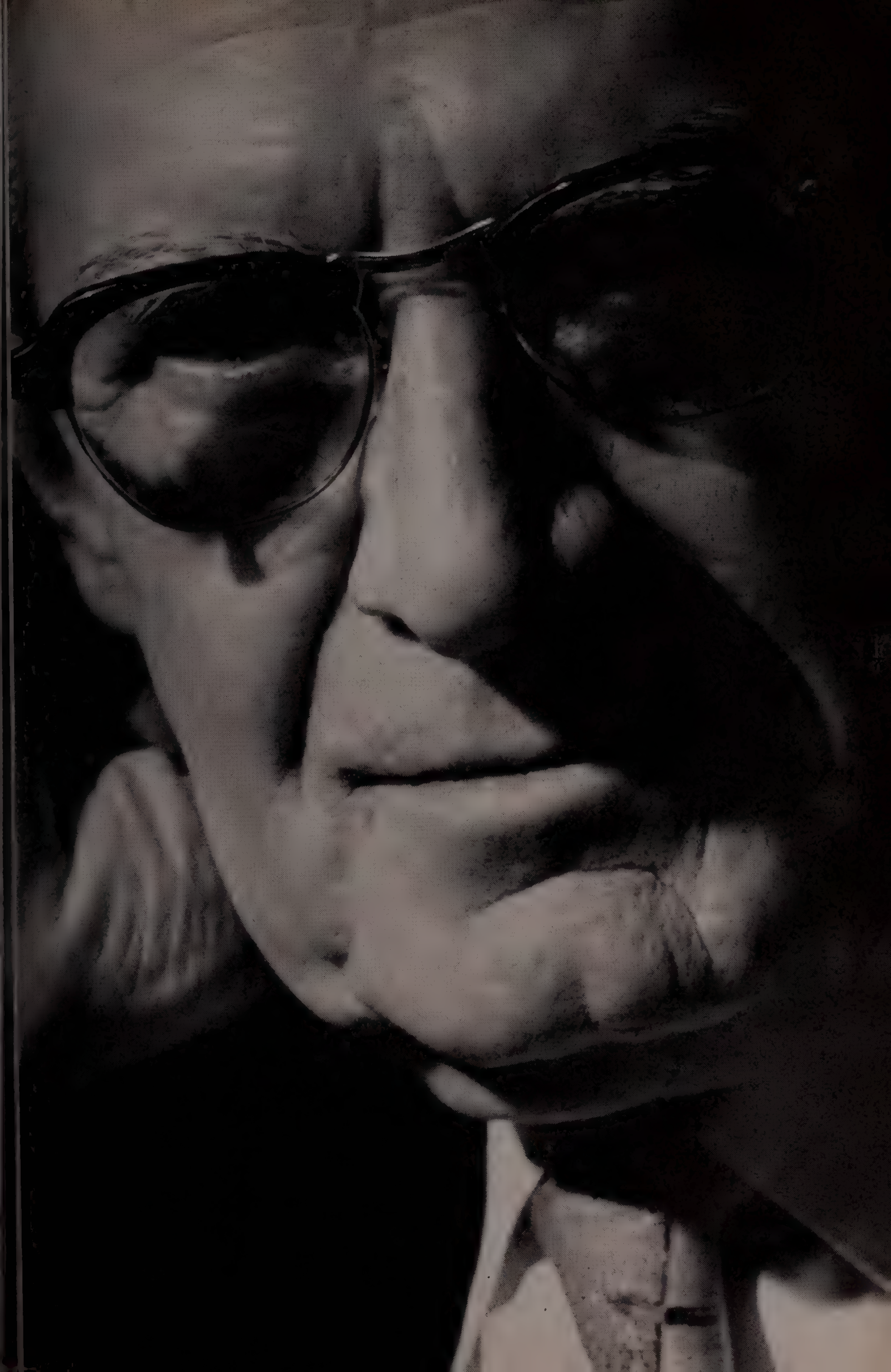
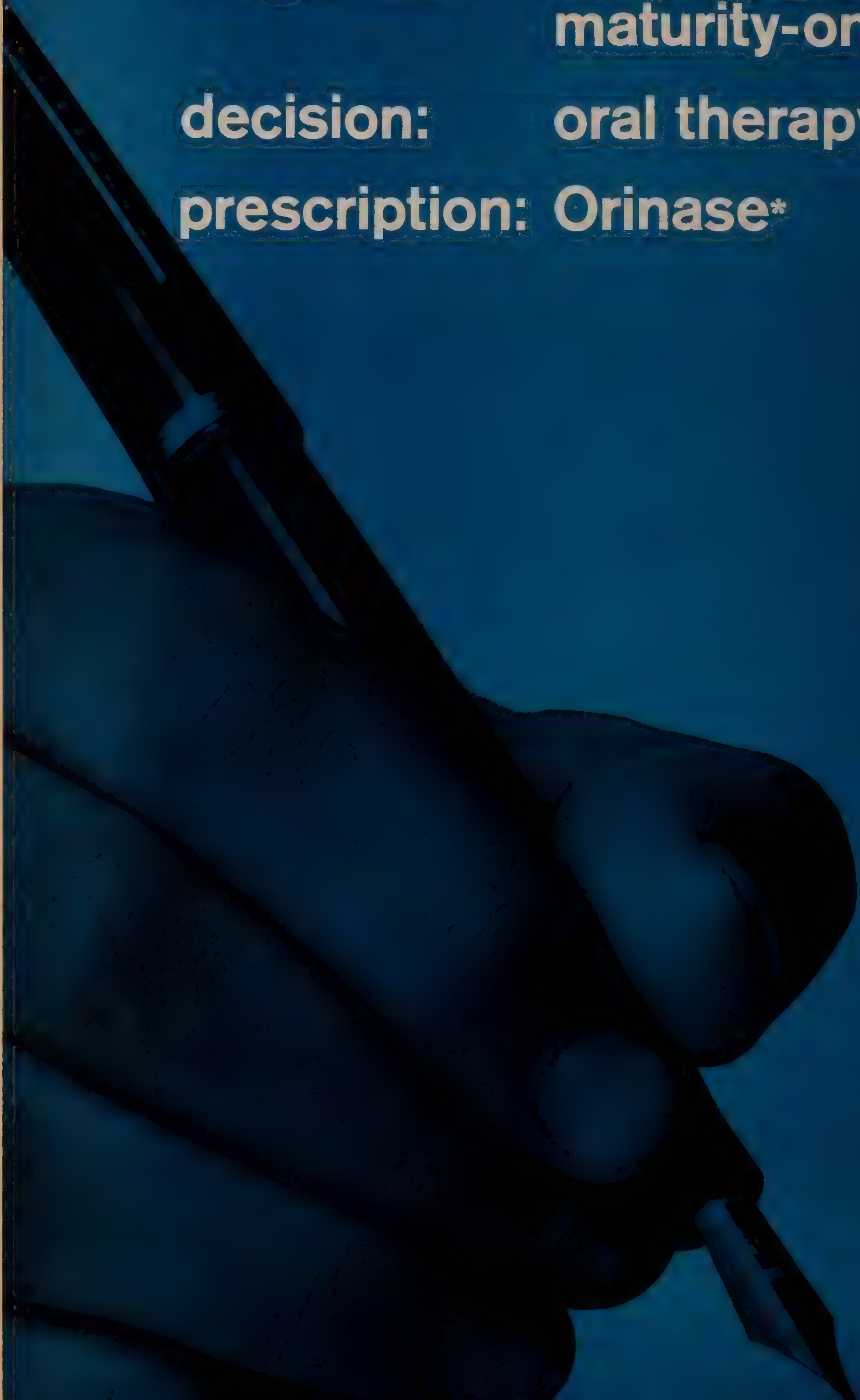


diagnosis: diabetes, maturity-onset

decision: oral therapy

prescription: Orinase*



"It is our practice in those patients in whom oral therapy is indicated to use tolbutamide [Orinase] first."[1]

And when you adopt this approach in newly-discovered, non-ketotic adult diabetics, you provide optimal control in the great majority of instances.

More than 700,000 diabetics are now controlled on Orinase.

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[1] Miller, E. D., Jr., and Roller, G. W.: M. Times 89:196 (Feb.) 1961.

Indications and effects: The clinical indication for Orinase is stable diabetes mellitus. Its use brings about the lowering of blood sugar; glycosuria diminishes, and such symptoms as pruritus, polyuria, and polyphagia are alleviated.

Dosage: There is no fixed regimen for initiating Orinase therapy. A simple and effective method is as follows: **First day** – 6 tablets; **second day** – 4 tablets; **third day** – 2 tablets. The daily dose is then adjusted – raised, lowered or maintained at the two-tablet level, whichever is necessary to maintain optimum control.

Patients receiving insulin (less than 20 units) – discontinue insulin and institute Orinase; (20 to 40 units) – initiate Orinase with a concurrent 30 to 50% reduction in insulin dose with a further careful reduction as response to Orinase is observed; (more than 40 units) – reduce insulin by 20% and initiate Orinase with a further careful reduction in insulin dosage as response to Orinase is observed. In candidates for combined Orinase-insulin therapy, an individualized schedule is usually obtainable during a trial course of two or more weeks.

Contraindications and side effects: Orinase is contraindicated in patients having juvenile or growth-onset, unstable or brittle types of diabetes mellitus; history of diabetic coma, fever, severe trauma or gangrene.

Side effects are mild, transient and limited to approximately 3% of patients. Hypoglycemia and toxic reactions are extremely rare. Hypoglycemia is most likely to occur during the period of transition from insulin to Orinase. Other untoward reactions to Orinase are usually not of a serious nature and consist principally of gastrointestinal disturbances, headache, and variable allergic skin manifestations. The gastrointestinal disturbances (nausea, epigastric fullness, heartburn) and headache appear to be related to the size of the dose, and they frequently disappear when dosage is reduced to maintenance levels or the total daily dose is administered in divided portions after meals. The allergic skin manifestations (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) are transient reactions, which frequently disappear with continued drug administration. However, if the skin reactions persist, Orinase should be discontinued.

Clinical toxicity: Orinase appears to be remarkably free from gross clinical toxicity on the basis of experience accumulated during more than four years of clinical use. Crystalluria or other untoward effects on renal function have not been observed. Long-term studies of hepatic function in humans and experience in over 700,000 diabetics have shown Orinase to be remarkably free of hepatic toxicity. There has been reported only one case of cholestatic jaundice related to Orinase administration, which occurred in a patient with pre-existing liver disease and which rapidly reversed upon discontinuance of the drug.

Each tablet contains:

Tolbutamide .... 0.5 Gm.

Supplied: In bottles of 50 and 200.

Orinase

Upjohn

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January 1962

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MONDAY, MAY 14

1:00–3:00	Albany Medical College of Union University
3:00–5:00	Albert Einstein College of Medicine of Yeshiva University

TUESDAY, MAY 15

1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

FRIDAY, MAY 18

1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
3:30–5:00	New York Medical College

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Vitamin B_2 (Riboflavin)	10 m
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Vitamin C (Ascorbic Acid)	300 m
Vitamin B_6 (Pyridoxine HCl)	2 m
Vitamin B_{12} Crystalline	4 mcgr
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Recommended intake: Adults, 1 capsule dai or as directed by physician, for the treatme of vitamin deficiencies.

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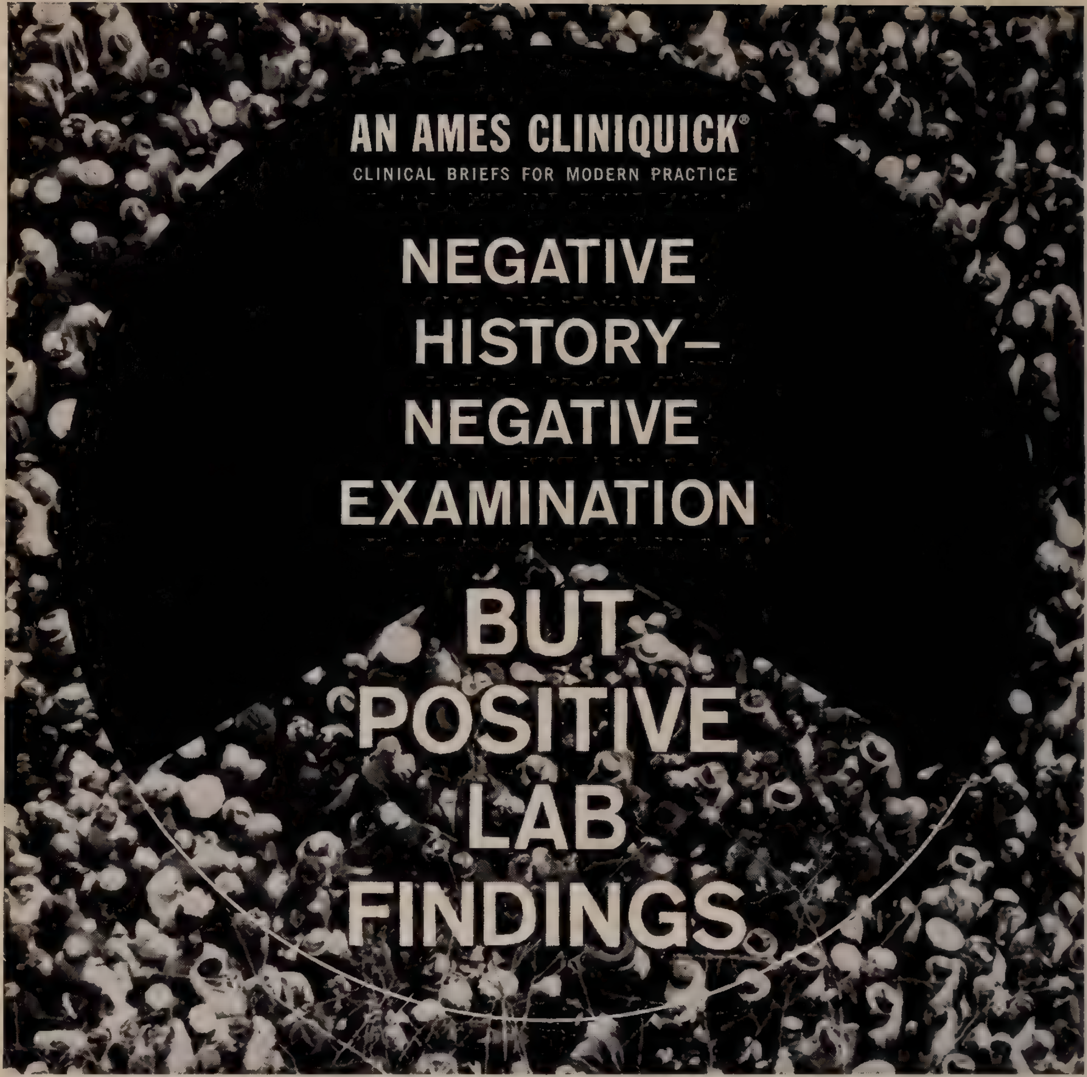
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The value of laboratory tests as an adjunct to the diagnosis is well expressed in the following health survey. Out of 10,709 apparently well and asymptomatic adults, significant findings were noted by urinalysis in 33.2 per cent.*

*Schenthal, J. E.: J.A.M.A. *172*:1 (Jan. 2) 1960.

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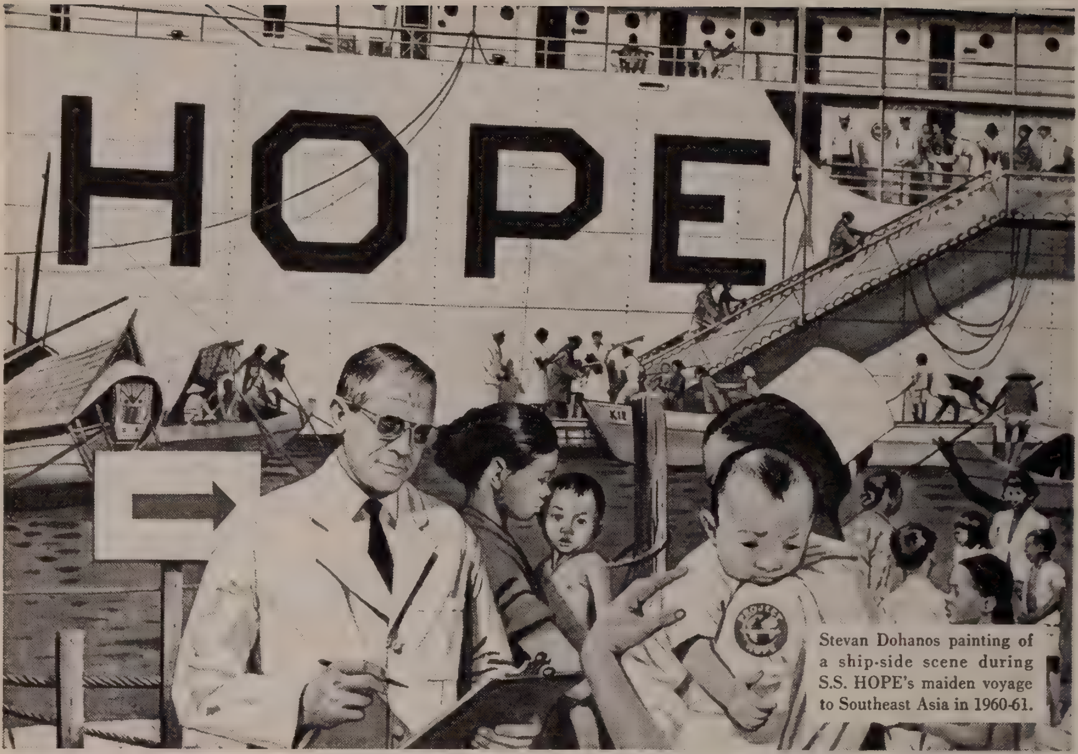

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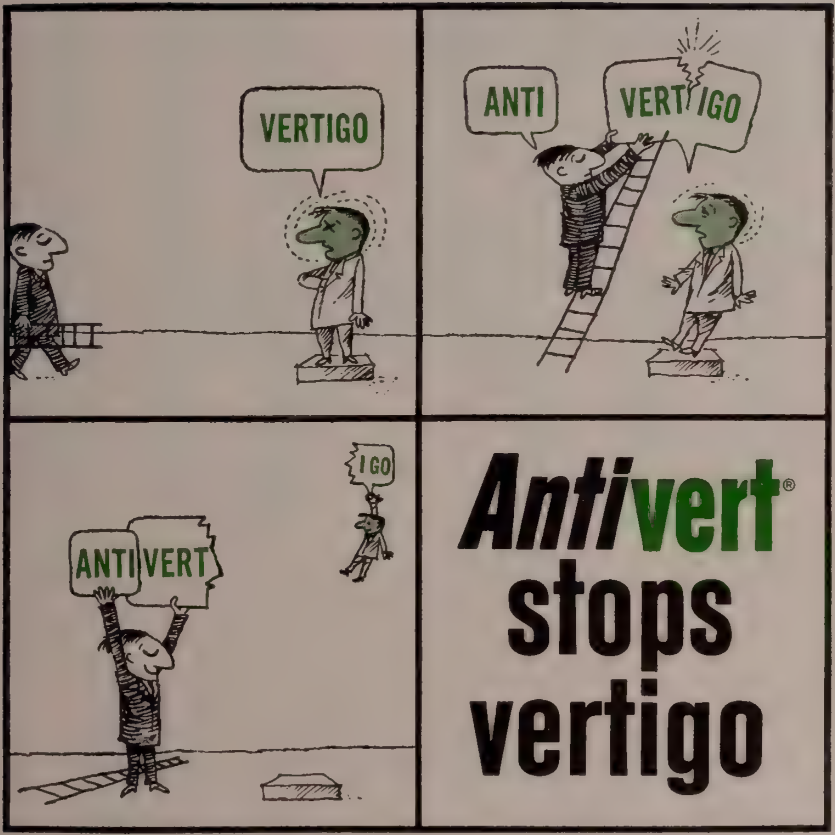

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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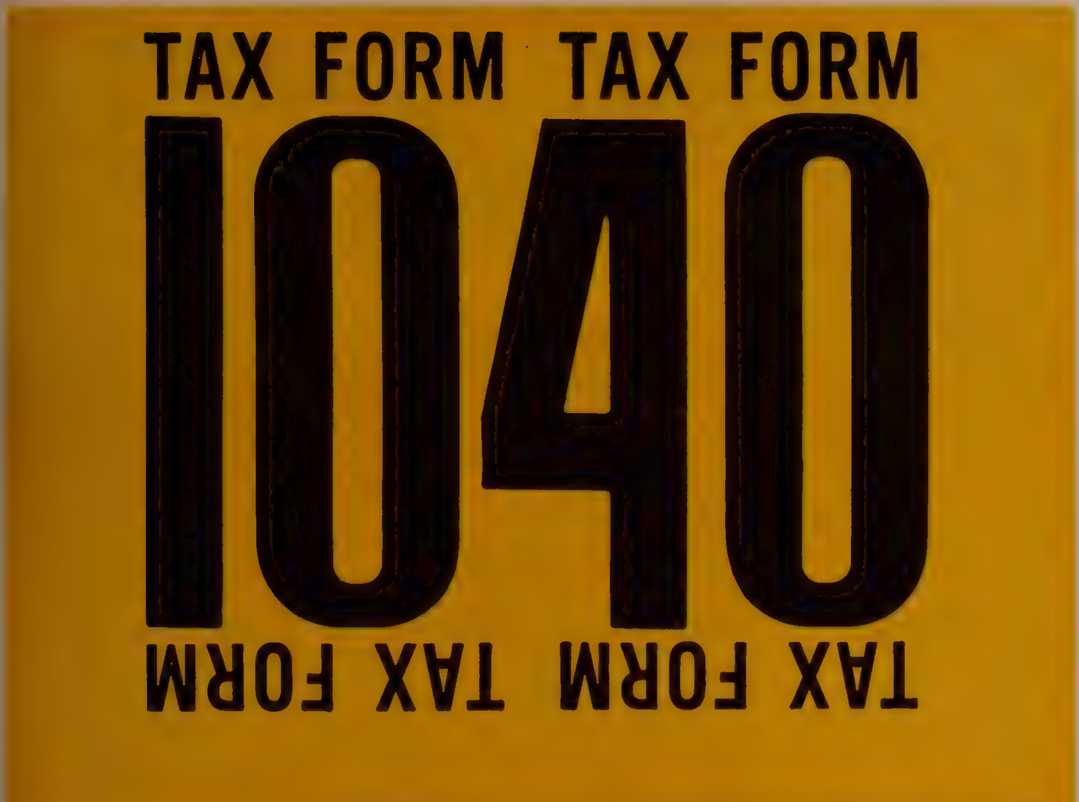

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[1] Taub, S. J.: Management of Anxiety in Allergic Disorders—New Approach. To be published in Psychosomatics; [2] Cahn, B.: Experience with a New Tranquilizing Agent (Hydroxyphenamate). Ibid; [3] Bergal, M., Beck, C., Davis, O. F., and Sloan, N.: On Use of Hydroxyphenamate in Anxiety Associated with Somatic Disease. To be published; [4] Alexander, L.: Effect of Hydroxyphenamate on Conditional Psychogalvanic Reflex in Man. Supplement to Diseases of the Nervous System, Sept., 1961: [5] Cahn, B.: Effect of Hydroxyphenamate in Treatment of Mild and Moderate Anxiety States. Ibid; [6] Cahn, M. M., and Levy, E. J.: Use of Hydroxyphenamate (Listica) in Dermatological Therapy. Ibid; [7] Eisenberg, B. C.: Amelioration of Allergic Symptoms with a New Tranquilizer Drug (Listica). Ibid; [8] Friedman, A. P.: Pharmacological Approach to Treatment of Headache. Ibid; [9] Greenspan, E. B.: Use of Hydroxyphenamate in Some Forms of Cardiovascular Disease. Ibid; [10] Gouldman, C., Lunde, F., and Davis, J.: Clinical Trial of Hydroxyphenamate in Alcoholic Patients. Ibid; [11] Personal Communications to Medical Department, Armour Pharmaceutical Company.

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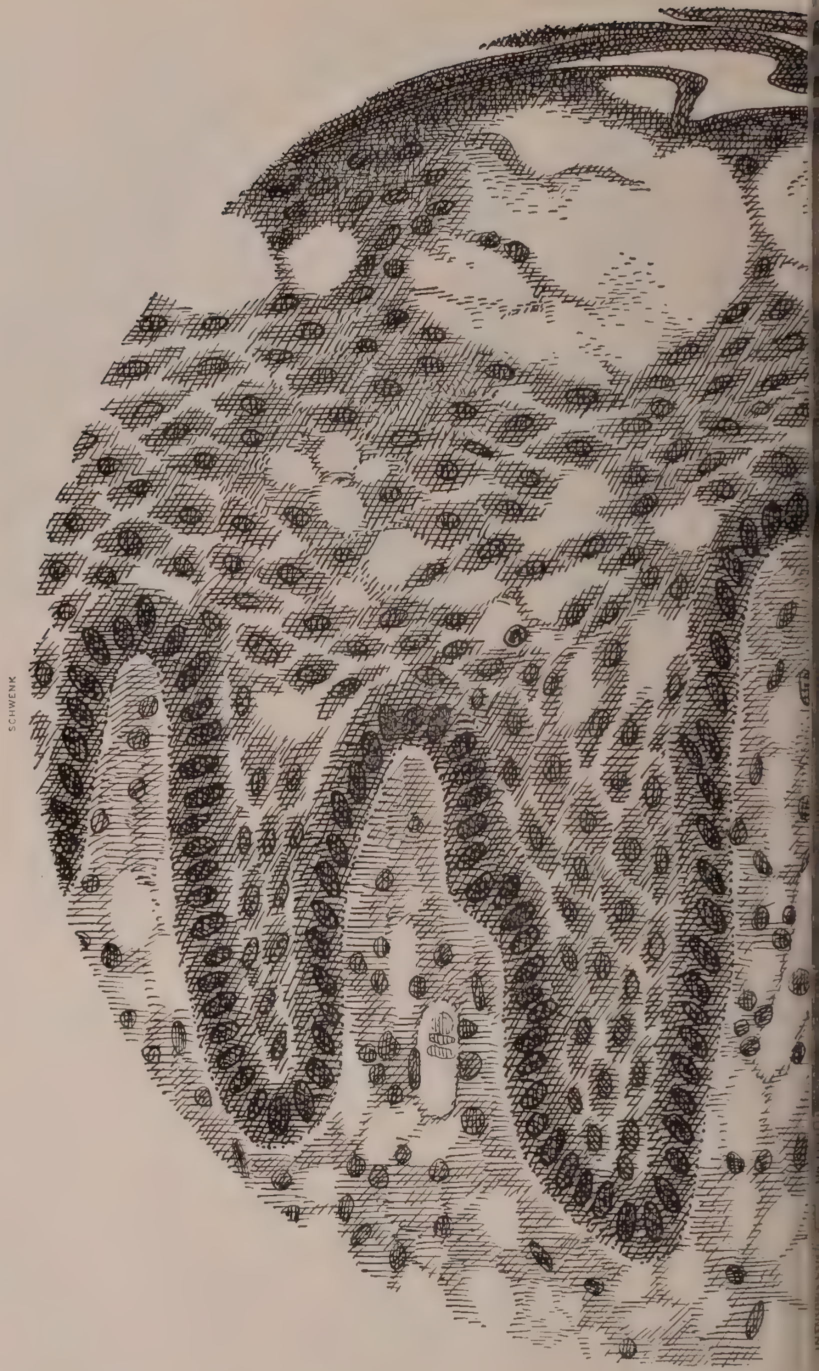
ARMOUR PHARMACEUTICAL COMPANY, KANKAKEE, ILLINOIS



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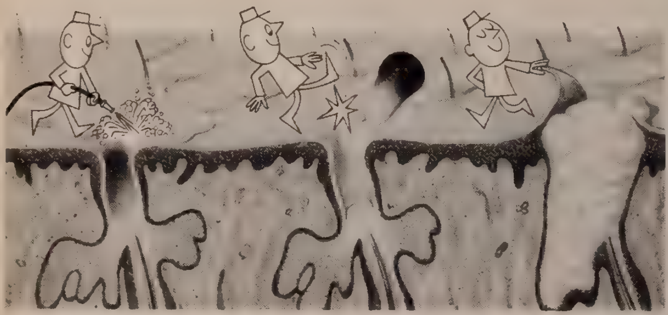

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presented by:

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3:00–5:00	Albert Einstein College of Medicine of Yeshiva University
TUESDAY, MAY 15	
1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine
WEDNESDAY, MAY 16	
1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College
THURSDAY, MAY 17	
1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine
FRIDAY, MAY 18	
1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
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caffeine	30 mg.
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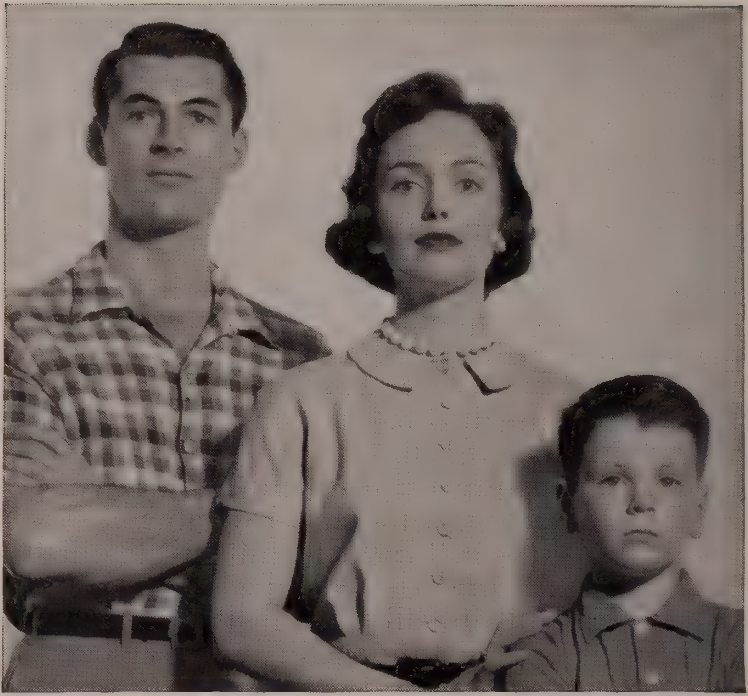

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OR PSORIASIS—ESPECIALLY IN INTERTRIGINOUS AREAS

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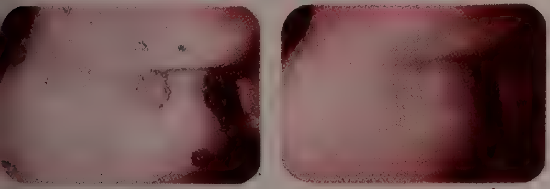
EMOVES SCALES! REDUCES ERYTHEMA! RELIEVES IRRITATION!

Now! The Clinically Proven LPHOSYL Formula in a New Cream Base that Simulates Natural Skin Lipids!

Marked success in treating psoriasis—especially in intertriginous areas—is reported with new Alphosyl Lubricating Cream.[1] In a study of 96 psoriatics, 73 patients experienced 75% to 100% clearing—15 showed 50% to 75% clearing.[1] Alphosyl Lubricating Cream not only helps remove scales and reduce erythema, but a new cream base affords added lubrication between the skin folds.



Patient E. C. Treatment started Jan. 14. On Feb. 18 clearing is almost complete.

Thus, it prevents the painful irritation that results from the rubbing of lesion against lesion. The base enhances moisture retention and, containing squalane, dissolves a cement substance in psoriatic scale.

Active Ingredients: Allantoin 2% and special coal tar extract (Tarbonis®) 5%.
Supplied: In tubes of 60 Gm.
Important Therapeutic Note: Instruct patient to rub Alphosyl vigorously into the skin.
Reference: 1. Bleiberg, J.: Clin. Med. 8:1724 (Sept.) 1961.

For generalized and scalp psoriasis
ALPHOSYL LOTION
For psoriasis—with acute inflammation
ALPHOSYL HC
LOTION WITH 0.25% HYDROCORTISONE

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"The first prescription I ever wrote was for 'Empirin' with Codeine...

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as been well-known since the influenza epidemic of 1918). Satisfaction through
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ability of addiction is negligible.

lease accept our thanks for continuing to place your trust in a product that has
een used more widely in medicine each year for the past four decades.

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cetophenetidin, gr. 2½
cetylsalicylic Acid, gr. 3½
affeine, gr. ½

Remember there are now four strengths available...

**Warning—May be habit-forming. Subject to Federal Narcotic Regulations.*

No. 1 – gr. ⅛
No. 2 – gr. ¼
No. 3 – gr. ½
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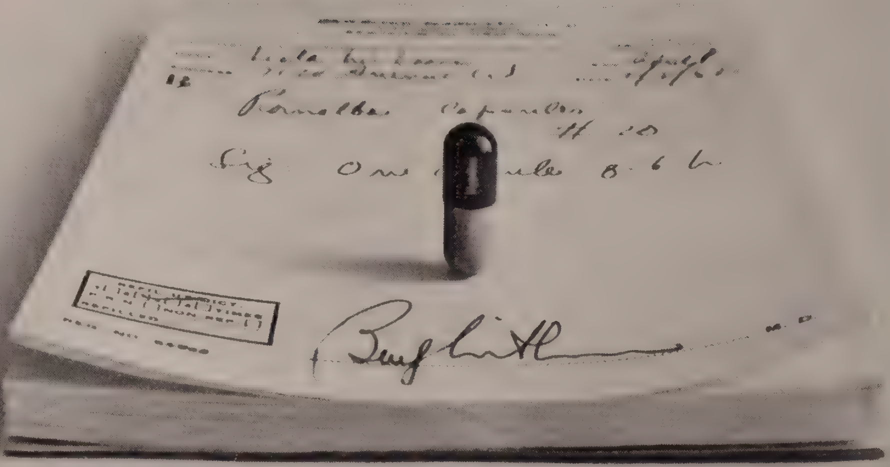

Launching Pad

In infections of unknown etiology, prescribe Panalba. From the outset, pending laboratory determinations, your treatment is broadened in antibacterial coverage because of the simultaneous administration of two antibiotics that complement each other. They were carefully chosen for this purpose.

Panalba combines tetracycline (selected for its breadth of coverage) and novobiocin (selected for its unique effectiveness against staph). That is why, in most infections of unknown etiology, Panalba offers excellent chances for therapeutic success—and why it should be your antibiotic of first resort.

Upjohn

The Upjohn Company
Kalamazoo, Michigan

Panalba* product information

Supplied: Capsules, each containing Panmycin* Phosphate (tetracycline phosphate complex), equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin,* as novobiocin sodium, in bottles of 16 and 100.

Usual Adult Dosage: 1 or 2 capsules three or four times a day.

Side Effects: Panmycin Phosphate is well tolerated clinically and has a very low order of toxicity comparable to that of the other tetracyclines. Side reactions are infrequent and consist principally of mild nausea and abdominal cramps.

Leukopenia has occurred occasionally in patients receiving novobiocin. Rarely, other blood dyscrasias including anemia, pancytopenia, agranulocytosis and thrombocytopenia have been reported. In a recent report it was observed that three times as many newborn infants receiving novobiocin developed jaundice as control infants. For this reason, administration of novobiocin to newborn and young infants is not recommended, unless indication is extremely urgent because of serious infections not susceptible to other antibacterial agents.

The development of jaundice has also been reported in older individuals receiving Albamycin. Serious liver damage has developed in a few patients, which was more likely related to the underlying disease than to therapy with novobiocin. Although reports such as the above are rare, discontinuance of novobiocin is indicated if jaundice develops. If continued therapy appears essential because of a serious infection due to microorganisms resistant to other antibacterial agents, liver function tests and blood studies should be performed frequently, and therapy with novobiocin stopped if necessary.

In a certain few patients treated with this agent, a yellow pigment has been found in the plasma. The nature of this pigment has not been defined. There is evidence that it may be a metabolic by-product of novobiocin, since it has been reported to be extractable from the plasma (pH 7 to 8.1) with chloroform while bilirubin is not. These properties have been employed to differentiate the yellow pigment due to the metabolic by-product of novobiocin and bilirubin. However, recent reports indicate that this method of differentiation may be unreliable.

Urticaria and maculopapular dermatitis have been reported in a significant percentage of patients treated with Albamycin. Upon discontinuance of the drug, these skin reactions rapidly disappeared.

Warning: Since Albamycin possesses a significant index of sensitization, appropriate precautions should be taken in administering the drug. If allergic reactions develop during treatment and are not readily controlled by antihistaminic agents, use of the product should be discontinued.

Total and differential blood cell counts should be made routinely during the administration of Albamycin. If new infections appear during therapy, appropriate measures should be taken; constant observation of the patient is essential. If a yellow pigment appears in the plasma, administration of the drug should be continued only in urgent cases, and the patient's condition closely followed by frequent liver function tests. In case of the development of liver dysfunction, therapy with this agent should be stopped.

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a look
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CORDRAN™
(flurandrenolone, Lilly)

an excellent drug

“Based both on laboratory studies and clinical impressions, it [Cordran] appears to be an excellent drug for the relief of cutaneous inflammation, possibly more effective than any steroid we have hitherto used.”

—Rostenberg, A., Jr.: Clinical Evaluation of Flurandrenolone, a New Steroid, in Dermatological Practice, J. New Drugs, 1:118, 1961.

A look at the products

Cordran cream and ointment are new corticosteroid preparations especially formulated for the skin. Each Gm. contains 0.5 mg. Cordran.

Cordran™-N cream and ointment combine Cordran and the wide-spectrum antibiotic, neomycin. Each Gm. contains 0.5 mg. Cordran and 5 mg. neomycin sulfate (equivalent to 3.5 mg. base). Cordran-N is particularly useful in steroid-responsive dermatoses complicated by potential or actual skin infections.

All forms are supplied in 7.5 and 15-Gm. tubes.

Cordran™-N (flurandrenolone with neomycin sulfate, Lilly)

Product brochure available; write Eli Lilly and Company, Indianapolis 6, Indiana.

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New York State Journal of Medicine

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Editorials

The aura of quality

The headlong flight into informality and togetherness which characterizes our age has brought with it a consequent tarnish to that patina of quality, good manners. Deplorable when encountered in streets and shops, this slippage is particularly regrettable when displayed about our hospitals.

Time is not so far distant when the attending staff set a high tone of dignity to our institutions, one that rubbed off successively on everyone. One need not go back to Osler, Pepper, or Peabody to find that pleasing virtue—it lies beneath the surface of us all.

Should our hurried and harried lives rob the seriousness of our work of its aura of quality? We think not, but some lifting by the bootstraps is in order. Look closely about on your next hospital visit, and make some comparisons.

Is the nurses' station a business-like place or has it deteriorated into a gossip center, a first-name-based smoking room, a home away from home? Are personal telephone calls being made from the desk? This station is often a point of contact with patients' relatives and friends, and an impression made here is lasting.

The patient in room 10 is not "that gallbladder"—his name is Mr. Antrobus, and criticism of his food tray or his nursing care is not to be made in his presence or in the presence of others. A decent respect for the feelings of others is basic. Curtain lectures are given behind drawn curtains.

Are we so weary that we must sit on the patient's bed?

Irritability, like a lady's slip, should never show. It is a fault in self-discipline, easily corrected. The place for the latest story is in the cloakroom. Good manners will have a rebirth when we regard everyone involved in the patient's care and comfort as a respected and trusted colleague but not as a bosom pal.

The practice of medicine is a serious calling. We must not permit it to be vulgarized.

Waiver of the physician-patient privilege

The Appellate Division, Fourth Department, of the Supreme Court of the State of New York on November 30, 1961, in a clear statement of the law, held that the privilege of confidential communication between a doctor and a patient can be waived by the personal representative of a deceased patient or other "party in interest" and that an attorney for a party in interest can make the waiver.

The decision grew out of a will contest proceeding in which the appellant, a brother of the deceased, sought to prove the latter's mental incapacity to make a valid will. He attempted to question two doctors who had treated the deceased and also tried to introduce certain hospital records in evidence. The attorney for the proponent of the will objected, claiming privilege under section 352 of the Civil Practice Act. The trial judge in the lower court proceeding sustained the objection on the ground that under section 354 of the Civil Practice Act the privilege could be waived only by the appellant-brother himself in open court. He was not in court, but he had previously executed a written power of attorney expressly authorizing his attorney to waive the privilege afforded by section 352.

Section 352 of the Civil Practice Act defines the privilege of confidential communication between a doctor and a patient, while section 354 of the same act specifies the manner in which the privilege may be waived. The pertinent provisions of section 354 are as follows:

> The last four sections apply to any examination of a person or witness unless the provisions thereof are expressly waived upon the trial or examination by. . .the patient. . . . But a physician or surgeon. . .upon the trial or examination may disclose any information as to the mental or physical condition of a patient who is deceased, which he acquired in attending such patient professionally, except such confidential communications as would tend to disgrace the memory of the patient and such facts as would tend to disgrace his memory, when the provisions of section three hundred and fifty-two have been expressly waived on such trial or examination by the personal representatives of the deceased patient. . .or if the validity of the last will and testament of such deceased patient is in question, by the executor or executors named in said will, or the surviving husband, widow or any heir-at-law or any of the next of kin of such deceased, or any other *party in interest*. . . . In a judicial action or proceeding the waivers herein provided for must be made in open court, on the trial of the action or proceeding, *and a paper executed by a party prior to the trial providing for such waiver shall be insufficient as such a waiver.* But the attorneys for the respective parties prior to the trial of the judicial action or proceeding, may stipulate for such waiver, and the same shall be sufficient therefor.

It was not disputed, nor was there any doubt, that the appellant-brother was a "party in interest" who had the right to waive under this section alone and without joinder by other interested parties. There was also no claim by anyone that the testimony offered by the appellant would tend to disgrace the patient's memory. The only question raised was the manner in which the waiver must be made in order to comply with the provisions of section 354.

The Appellate Court pointed out that the lower court had erred in sustaining the objection to the admission of the testimony offered by the appellant apparently because of confusion over the power of attorney signed by the appellant in view of the above quoted portion of the section which provides that a written waiver executed by a party prior to the trial shall be insufficient. It showed that this prohibition had been enacted to overcome the prejudicial effect of some life insurance contracts which provided for the written waiver long before the death of the insured and in advance of a trial or any real prospect of a judicial controversy.

The court pointed out that the language in question did not prevent the admission of the testimony for two reasons: First, the power of attorney was not a waiver, but an authorization to trial counsel to waive, and second, it was not used as the basis for counsel's waiver. Counsel for the appellant in open court had waived on the basis of his general authority as the legal representative of his client rather than by virtue of the document. The effect of the document was merely to fortify, if fortification were necessary, the authority of the attorney to waive.

It stated the principle that "merely calling the physician to the stand and questioning him will suffice to establish a waiver. Trial counsel need not specifically state his intention to waive."

The court in reversing the lower court said:

> . . .the very language of the statute negates the construction placed upon it by the Trial Justice. The statute simply states that the waiver must be made in open court and then goes on to provide that a paper executed by a party prior to the trial, purporting to waive, shall be insufficient. There is no inconsistency between those two phrases. The waiver must be in open court or in the trial of the action or in a proceeding preliminary to the trial of the action. Merely because a power of attorney had been executed in advance which authorized *the attorney* to waive the privilege in relation to specific testimony should not be held to abridge or annul the general authority of the attorney to conduct litigation for his client in accordance with his own judgment, whether the client is present in court or not. The ruling of the Trial Justice thwarted the purposed and intent of the section. It should be so construed as to preserve its beneficial aspects. (In the Matter of the Probate of the Will of Luigi Frangeline, Deceased; Appellate Division, Fourth Department, November 30, 1961.)

First operational storage and retrieval system

The communication of scientific information took a forward step on January 8, 1962, with the institution of Mediphone.

This is a central repository in Washington, D.C., which has filed automatically complete information on all of the 8,500 drugs and chemicals in use at the present time. In some cases there may be 20 or more names for the same drug.

A subscriber to Mediphone needs only to call this service, and in a matter of seconds he will receive whatever information on a drug that he desires.

This systematic organization of material and the pinpoint retrieval of any designated facet is one of the miracles of our age. The machines that do this work can work faster than the human brain.

Mediphone at present is a distant early warning system for drugs. If has filed all the published information of the past fifteen years on how each drug reacts on the human body, dosages, methods of administration, side-effects, contraindications, and antidotes.

The future of storage and retrieval makes exciting speculation. When doctors start to feed back to Mediphone their own individual experiences with drugs and an analysis of the questions is made, the usable information will become truly comprehensive, and statistics will actively serve the practicing physician and all those interested in the field of pharmacology.

The robot of course will never replace the doctor's judgment, but it can act as a multivolumed library instantly available on the other end of the telephone.

It is not recorded what question Leonard W. Larson, M.D., President of the American Medical Association, put to Mediphone on the first ceremonial call on January 8, but it might very well have been, "What hath God wrought?"

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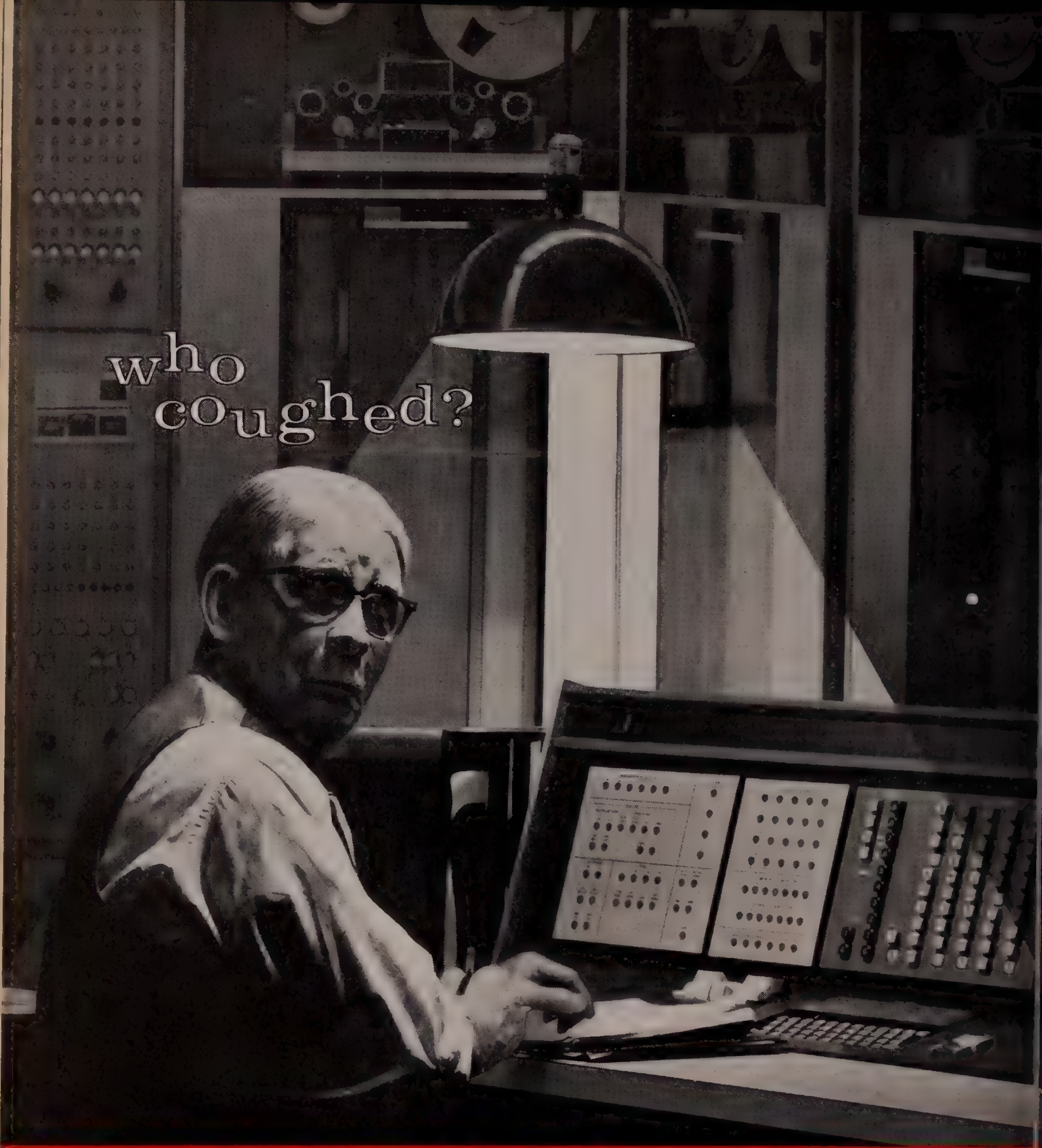
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Hemoglobin A_2 Analysis in Hypochromic Anemias

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HYPOCHROMIC ANEMIAS that do not respond to adequate treatment with iron may be difficult to diagnose. Most persons who inherit the gene for thalassemia from only one parent grow and develop normally. Heterozygous thalassemia, however, may have a variety of clinical symptoms and hemoglobin levels ranging from near-normal to moderate anemia. The finding of an increased red cell hemolysate fraction (A_2) in heterozygous thalassemia has made the diagnosis easier. In 96 patients with hypochromic anemias due to causes other than thalassemia, a range of 3 to 9 per cent of the total hemoglobin as A_2 was found, using paper electrophoresis with thick paper, a large sample of hemoglobin, and a buffer containing Tris-EDTA-boric acid. In 23 patients with heterozygous thalassemia the values ranged from 8.6 to 15.5 per cent. The disease is most common in persons of Mediterranean descent, particularly Italians.

HYPOCHROMIC ANEMIAS that do not respond to adequate treatment with iron may present difficulty in regard to cause and clinical differential diagnosis. Most persons who inherit the gene for thalassemia from one parent and the corresponding normal gene from the other parent grow and develop normally. They may have mild anemia only, and sometimes they have no morphologic abnormalities of the erythrocytes other than hypochromia. Because of generally good health, some of these persons never have a blood examination until their admission to the hospital for an unrelated problem or because of some trauma for which a blood count is done with regard to an evaluation of the patient's injury.[1,2] Heterozygous thalassemia (AA^T) shows more clinical and hematologic variability than the heterozygous ("trait") forms of the hemoglobin variants when these forms occur in association with a gene for normal adult hemoglobin. These forms are usually asymptomatic clinically and have normal laboratory findings except for the hemoglobin pattern. In contrast, thalassemia heterozygotes may have a variety of clinical symptoms and hemoglobin levels ranging from near-normal to moderate anemia. This has been attributed to the variable penetrance of the thalassemia gene and its variable expression.[3-7] If the disorder is present in its more severe form, there is usually no difficulty in making the diagnosis. However, such commonly employed criteria as the morphologic variations of the erythrocytes (target cells, oval cells, and basophilic stippling) and a resistance to hemolysis by hypotonic saline solutions may be seen in hypochromic anemias other than thalassemia (for instance, the hypochromic anemia associated with chronic infection or heavy metal intoxication).[3] Many patients with heterozygous thalassemia have normal serum bilirubin levels and normal reticulocyte counts. They usually do not have spleno-

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megaly. In addition, the problem frequently arises of a patient with suspected heterozygous thalassemia who may have chronic blood loss and in whom the anemia will respond to iron therapy up to a certain level and then show no further improvement.

In 1955 Kunkel and Wallenius[8] observed that a fraction of red cell hemolysate (A_2) was increased in the blood of patients with heterozygous thalassemia. This had been previously noted as an additional hemoglobin component in electrophoresis patterns prepared from the blood of thalassemia heterozygotes by other workers,[9-11] but its significance was not appreciated. The finding of an increased hemoglobin A_2 level in heterozygous thalassemia now made the diagnosis much easier in the majority of patients with this disorder.

In our laboratory we have used the technic of Cradock-Watson, Fenton, and Lehmann[12] to demonstrate the increased A_2 hemoglobin by paper electrophoresis rather than by the laborious technics in which a starch block or starch-agar gel is used as the supporting medium. Using a thicker filter paper, a larger amount of hemoglobin applied to the paper, and a buffer containing Tris-EDTA-boric acid, it is possible to perform this analysis in as easy a manner as routine hemoglobin electrophoretic fractionation. Previous difficulty in demonstrating this hemoglobin component by paper electrophoresis may well have been due to the failure to apply a large enough amount of hemoglobin solution to the paper to demonstrate this small minor component. After electrophoresis, the paper strips are scanned and quantitated without staining. With this technic, we have found a range from 3 to 9 per cent of the total hemoglobin as A_2 in 96 patients who had hypochromic anemias of causes other than thalassemia. The majority of these fell between 5 and 8.5 per cent. In 23 patients in whom the diagnosis of heterozygous thalassemia had been established by hematologic and chemical testing and by family history the values ranged from 8.6 to 15.5 per cent, with the majority falling between 10 and 15.5 per cent. The area of overlapping between high normal values and low thalassemia values (8.5 to 10 per cent) should be expected and has been noted by Hilgartner *et al.*[13] Their actual values for normal and thalassemia patients were somewhat higher than ours, but their technic included staining of the paper strips and automatic electronic analysis. The quantities, as determined by paper electrophoresis in both laboratories, are higher than those previously determined by starch or starch-gel electrophoresis.[14-16]

The use of such studies can be shown best by brief clinical summaries of several patients in whom the cause of anemia was unexplained or the presence of heterozygous thalassemia was not suspected.

Case reports

CASE 1. A forty-year-old female was hospitalized following an automobile accident and was found to have a moderately severe anemia. She did not sustain a significant blood loss at the time of the accident and was not aware of a previous history of anemia. Treatment with blood tranfusions and iron improved her anemia somewhat in direct relation to the blood transfusions. After discharge from the hospital, her hemoglobin fell again, and she consulted a gynecologist because of long-standing hypermenorrhea. Despite improvement in her hypermenorrhea, the hemoglobin level rose only slightly following an adequate oral administration of iron. A hematologic investigation was carried out because of her persistent anemia and revealed 9.1 Gm. per 100 ml. hemoglobin and 4 per cent reticulocytes. Her fetal hemoglobin, as determined by the method of alkali denaturation,[17] was 9.6 per cent (normal less than 3 per cent). Electrophoresis of hemoglobin solutions prepared from the patient's red cells revealed an A_2 hemoglobin level of 8.7 per cent. Because of these findings and the morphologic changes noted in her erythrocytes (target cells, hypochromia, oval erythrocytes, and basophilic stippling), 2 daughters whose ages were twenty and thirteen years were examined. Both girls had shown normal growth and development and had not been known to be anemic previously. The older daughter had a hemoglobin of 9.5 Gm. per 100 ml., a hematocrit of 33.5, and an erythrocyte count of 4,440,000 per cubic millimeter. Her fetal hemoglobin was 6.9 per cent and the A_2 hemoglobin was 15.5 per cent. The younger girl had a hemoglobin of 11.5 Gm. per 100 ml., a hematocrit of 325, erythrocytes of 4,460,000 per cubic millimeter, a fetal hemoglobin of 6.5 per cent, and an A_2 hemoglobin of 13.5 per cent. Thus, the presence of the thalassemia gene was demonstrated in the mother and in both daughters.

CASE 2. A forty-two-year-old man had been healthy enough to fulfill military service obligations but had been told on several occasions that he could make only "a certain number of red blood cells and no more." He was referred for a hematologic examination and had a 12 Gm. per 100 ml. hemoglobin, a 40.5 hematocrit, a 4.1 per cent fetal hemoglobin and a 15.2 per cent hemoglobin A_2. Blood samples from the patient's wife were examined and found completely normal. However, studies made on 2 of his children, aged fifteen and ten years, showed hypochromic anemia with a 10.5 Gm. per 100 ml. hemoglobin and a 36 hematocrit. Both children had fetal hemoglobin levels of only 2.2 per cent, but they had A_2 hemoglobin levels of 9 and 12.2 per cent.

CASE 3. A twenty-seven-year-old man was admitted to the hospital with a diagnosis of hepatitis because of clinically visible jaundice that occurred intermittently. His serum bilirubin level was 4.4 mg. per 100 ml. on admission to the hospital and dropped to 1.6 mg. per 100 ml. during his stay. All liver function tests were normal. The hemoglobin concentration was 11.5 Gm. per 100 ml. and his hematocrit was 37. Reticulocytes numbered 3.6 per cent, and he had a 7.8 per cent fetal hemoglobin and a 15 per cent hemoglobin A_2.

CASE 4. A fifteen-year-old girl was seen in consultation by David K. Miller, M.D., who made a diagnosis of infectious mononucleosis. An unusual feature of her illness was a moderate hypochromic anemia for which she had been transfused several times. Although the girl's last name was of German rather than Mediterranean origin, an inquiry by Dr. Miller disclosed that the mother of this girl was Italian. Blood samples made available to us by Dr. Miller revealed that the patient had a 10.3 Gm. per 100 ml. hemoglobin and a 35 hematocrit. Her fetal hemoglobin was 7.2 per cent, and her A_2 hemoglobin was 14.2 per cent.

CASE 5. A twenty-five-year-old woman in the second trimester of pregnancy was referred for hematologic consultation because of moderate anemia. She was the niece of a patient with heterozygous thalassemia whom we had previously examined and whose diagnosis had been established with these studies. The blood had a hemoglobin concentration of 9.8 Gm. per 100 ml., the hematocrit was 30.5, and the erythrocytes were 4,170,000 per cubic millimeter. Her fetal hemoglobin was only 2.6 per cent, but her A_2 hemoglobin was 11.3 per cent

Comment

Utilizing the A_2 hemoglobin analysis, we have been able to demonstrate heterozygous thalassemia in 2 Negro women whose anemia was otherwise unexplained and in several other patients with heterozygous thalassemia whose fetal hemoglobin levels were within the normal range.

It is not expected that this method will be helpful in diagnosing patients with heterozygous thalassemia in whom the gene is thought to involve the alpha chain of the hemoglobin molecule.[18,19] However, the majority of heterozygous thalassemia patients are apparently those who have the genetic abnormality located in the beta chain.

It is well known that thalassemia may be present in persons other than those of Mediterranean descent.[3, 5, 20–22] However, in New York State, especially along the eastern seaboard and following the path of the Erie Canal to the Niagara Frontier, we may expect to find a significant number of Italian patients in whom the demonstration of this hemoglobin anomaly may be of great importance. Smith[23] has superimposed the Italian population, according to the 1940 census, on the map of the United States. It suggests the frequency with which we may expect to see this hematologic disorder in New York State, since Neel and Valentine[24] have estimated that 4 per cent of the Italian population of Rochester, New York, may have heterozygous thalassemia.

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Health record of Americans favorable in 1961

The health record of the American people was exceptionally favorable in 1961, according to the statisticians of the Metropolitan Life Insurance Company, who report that the mortality rate fell to the lowest level in six years.

The national death rate in 1961 was about 9.3 per 1,000 population, down from 9.5 in 1960 and only slightly above the all-time low recorded in 1954.

The reduction of about one sixth in the death rate from pneumonia and influenza contributed to the good record. These diseases took an unusually heavy toll of life in the years 1957 through 1960; in the latter year the death rate from pneumonia and influenza rose to 36.6 per 100,000 population, the highest in more than a decade.

There was also a small decrease in the mortality from the diseases of the heart and arteries, which now account for more than half the total mortality in the United States. The death rate from the cardiovascular diseases was about 2 per cent lower in 1961 than in the year before; this was probably a consequence of the decreased incidence of the respiratory diseases.

There was an appreciable reduction in the mortality rate from diabetes. However, the death rate from cancer, which ranks second only to heart disease, remained close to the 1960 level.

Some progress was made in reducing the mortality from accidents. Suicide was also relatively less frequent in the year just ended than in 1960.

Tuberculosis mortality continued its long-term downward trend, the rate falling to an all-time low of about 5 per 100,000 in 1961. The death rate from this disease dropped about a third in the past five years and nearly three fourths in the past decade.

Infant mortality likewise established a new minimum, with a rate of little more than 25 per 1,000 live births. Last year was the third in succession to show a decrease in mortality among infants. Maternal mortality continued at the very low rate of 3 per 10,000 live births, which is less than half that of a decade ago.

The incidence of poliomyelitis decreased sharply in 1961. Only about 1,300 cases of the disease were reported in the United States during the year, or 60 per cent below the number in 1960 and at least 95 per cent below the number reported in 1954, just before the Salk vaccine was introduced.

In sharp contrast, the incidence of infectious hepatitis reached an all-time high in 1961. Nearly 75,000 cases of the disease were reported, or almost twice the number reported in 1960.

Gastrointestinal Physiology

Gluten-Induced Enteropathy and Protein-Losing Enteropathy

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IT APPEARS THAT *celiac disease and nontropical sprue, or gluten-induced enteropathy, and idiopathic hypercatabolic hypoproteinemia, or protein-losing enteropathy, are etiologically and pathologically distinct, although physiologically they overlap considerably. A gluten-free diet produces excellent responses in the majority of children with celiac disease and adults with nontropical sprue; however, despite clinical remission, changes in the small-bowel mucosa persist without observable improvement. This suggests that the anatomic alteration of the mucosa may be a secondary effect rather than the cause of these disorders, and that the underlying defect is biochemical rather than anatomic. The mechanism of the noxious activity of gluten is not known, but it appears to depend on the presence of glutamine in combination with one or more of the peptide components of gluten. The occurrence of hypoproteinemia, when it is not a complication of disorders resulting in malnutrition, defective protein synthesis, or excessive protein loss, has not been explained adequately. Recent evidence suggests that most of such patients suffer excessive loss of serum protein into the gastrointestinal tract and excessively rapid destruction of serum albumin. Studies with* I^{131}*-labeled PVP* (*polyvinylpyrrolidine*) *have shown that patients with hypercatabolic hypoproteinemia excrete excessive amounts of the PVP intravenous test dose in the feces. The present hypothesis is that the protein-losing enteropathies represent a group of disorders in which there is an increased passive loss of protein into the gut and that, although the products of digestion of this protein are largely reabsorbed, the maximal rate at which albumin can be synthesized is insufficient to keep up with the losses.*

IN THE PAST TEN YEARS a significant advance has been made in the understanding and management of celiac disease, nontropical sprue, and idiopathic hypercatabolic hypoproteinemia. The first two of these disorders, celiac disease and nontropical sprue, are now referred to as gluten-induced enteropathy; the last idiopathic hypercatabolic hypoproteinemia, is referred to as protein-losing enteropathy. In this review the first group will be considered separately from the second group, for at present they appear to represent distinct entities or at least easily distinguishable groups of disorders. Evidence is now beginning to appear which indicates that, on one hand, excessive intestinal protein losses occur in gluten-induced enteropathy, and, on the other hand, that malabsorption comparable clinically and by absorption testing to that seen in sprue may often be a feature of protein-losing enteropathy.[1] In the light of our present knowledge, it appears that these disorders are etiologically and pathologically distinct. Physiologically, however, there is considerable overlap between them.

Gluten-induced enteropathy

A new era in the treatment of celiac disease and nontropical sprue opened in 1950 with Dicke's[2] observations on the

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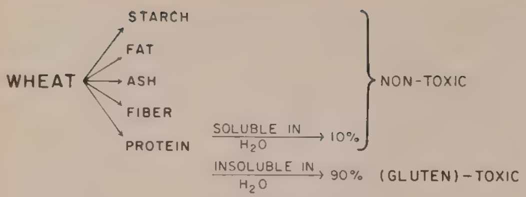

FIGURE 1. Fractionation of wheat.[4]

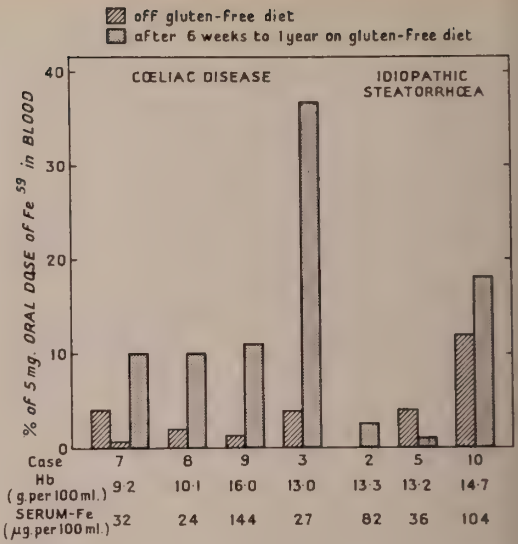

FIGURE 2. Effect of gluten-free diet on absorption from 5 mg. Fe^{59} in patients with steatorrhea.[10]

harmful effects of certain cereals on celiac disease and the striking benefits obtained by restriction of dietary wheat. By 1952 it became apparent that this dietary restriction produced similar beneficial effects in nontropical sprue in the adult.[3] Not only did this finding profoundly alter the life and outlook of these patients, but a potent tool for research became available. Subsequent investigations into the nature and mode of action of the offending dietary agent have opened the way for advances in understanding several aspects of these diseases and may eventually prove to be the key to disclosing the basic defect involved. Furthermore, the responsiveness of the patient to such dietary restriction has served as a means of reclassification of several subgroups of the sprue syndrome.

Effect of gluten. The presence of a toxic dietary component in celiac disease and the possibility that this component might be the crucial factor in determining the course of the celiac child was by no means a new idea. It was thought for some time that starch was the offending dietary agent, but when wheat (or rye or oats) are split into the fractions shown in Figure 1,[4] starch is found to be innocuous. The toxicity resides primarily within the water-insoluble protein fraction.[5] This toxic fraction, gluten, makes up 90 per cent of the proteins in wheat and is the principal group of proteins in rye and oats.

When gluten is eliminated from the diet of children with celiac disease, a remarkable and rapid symptomatic response occurs with considerable regularity. Anorexia, vomiting, abdominal pain, and irritability disappear. The onset of hematologic improvement is also surprisingly rapid. The steatorrhea subsides somewhat more slowly, and fecal fat losses often return to normal or almost normal within six weeks. Except for 7 per cent of celiac children who fail to respond, all others make a clinical recovery with return of normal growth and weight gain.[6]

The time required for a full clinical response to occur in adult nontropical sprue may be more prolonged, but with the continuation of therapy for as long as six months some patients who at first appear to be refractory to treatment later show excellent clinical responses.[7] Not only does the steatorrhea disappear and the tests of absorption improve, but the characteristic x-ray film changes in the small bowel may revert to normal. Careful metabolic balance studies indicate that the high fecal losses of sodium, potassium, phosphorus, and magnesium diminish, and calcium and nitrogen balance results become positive;[8] also, vitamin B_{12}[9] and iron absorption improve (Fig. 2).[10] The reintroduction of gluten into the diet leads to prompt and often violent exacerbation of the entire clinical picture. On the basis of these observations, many workers have come to consider the term "gluten-induced enteropathy" as synonymous with celiac disease or nontropical sprue, and they believe that those patients who fail to respond to a gluten-free diet most likely have some other disorder of absorption.

It has long been taught that celiac disease of childhood could be expected to subside with maturation, provided the patient survived. Many students in the field had pointed out, from the earliest days, that there were some striking similarities between celiac disease and its adult counterpart, nontropical sprue. Also, many adult cases were known to have begun as childhood disease. Additional evidence favoring the identity of these diseases is afforded by the remarkable responses of both groups to the gluten-free diet and by the identical histologic lesion in the small-bowel mucosa in both.[11,12]

This histologic abnormality may not be specific in these disorders, but this point is still controversial.[13] The mucosal changes consist of the flattening, broadening, and coalescence of villi, and often the complete loss of villi. The crypts tend to become elongated, so that the over-all thickness of the mucosa may not be altered. There is an increase in the submucosal inflammatory cells, and these are often seen to invade the mucosa itself. The epithelial cells of the villi become flattened, assuming a cuboidal shape, and their nuclei fail to maintain a regular basal orientation and seem irregular and denser than normal. The brush border may be abnormal. As seen by electron microscopy, this border normally consists of closely-packed, tiny, cylindrical microvilli. In celiac disease and nontropical sprue these microvilli become markedly shortened or stunted.[14]

Most available evidence indicates that these changes persist without observable improvement despite prolonged clinical remission in response to the gluten-free diet.[15–17] If histologic improvement does take place, this happens long after the clinical remission has occurred.[18] Some observers have pointed out that the tremendous loss of absorbing mucosal surface, present as a result of villus and microvillus atrophy, may play a role in the limitation of absorption.[14] Although the extent to which this is true is not clear, the return of normal absorption on the gluten-free diet becomes all the more startling despite the persistence of this severe mucosal abnormality. This observation implies that the anatomic alteration of the mucosa may be a secondary effect rather than the cause of these disorders, and that the underlying defect is biochemical rather than anatomic in nature. This point of view is strengthened by the observation that the severity of the histologic lesion cannot be correlated with the severity of the absorptive defect[19,20] and by the occasionally normal mucosal biopsies in patients with what otherwise seems to be nontropical sprue.[12,20]

MECHANISM OF GLUTEN. The mechanism of the noxious activity of gluten is unknown. The digestion of wheat gluten by juices obtained from patients with celiac disease is not demonstrably different from that obtained with the intestinal juice of normal subjects, and furthermore, the product of peptic and tryptic digestion of gluten retains its toxic properties. Incubation with hog intestinal mucosa, however, renders the gluten innocuous.[21] These findings suggest that the basic defect in the handling of gluten lies within the mucosal cells.

Gluten itself is a mixture of proteins which have not been completely separated and characterized. The chemical treatment of wheat flour in refining processes is not a factor in rendering gluten toxic.[22,23] On the contrary, the chlorine dioxide treatment of wheat in its commercial preparation, if anything, renders it less toxic.[24]

If gluten is treated with 45 per cent ethanol, the portion which goes into solution, gliadin, is highly active in the induction of symptoms in celiac patients.[5] Diarrhea is produced when as little as 3 Gm. per day are fed to patients with celiac disease in remission. One quality of this protein is its high glutamine content of 43 per cent. By contrast, the amido group containing amino acids account for only 11 per cent of the amino acid residues in the protein of such foods as meat, fish, potato, rice, corn, and dairy products, whereas the glutamine content of oats is 13 per cent, barley 14 per cent, rye flour 17 per cent, wheat flour 23 per cent, and gluten 27 per cent.[25] The toxicity of these foods seems to increase in direct proportion to their glutamine content. The next logical step in this story is the administration of glutamine itself. This produces no ill-effects, and so glutamine alone is not the offending agent. However, glutamine in combination with some other gliadin component is apparently needed to produce symptoms, since a partial hydrolysis of gliadin, converting glutamine to glutamic acid without altering the remainder of the protein, renders the gliadin innocuous.[25]

Evidence has been obtained which indicates that glutamine must be linked to one or more of the peptide components of gluten to show activity in the production of steatorrhea. The water-soluble peptide fraction obtained after peptic and tryptic digestion of gluten is highly toxic. This is a complex mixture of polypeptides and peptides which is not identical with gluten but contains all the amino acids of gluten. When this mixture is autoclaved at 120 F. for twenty minutes, its antigenic properties are so changed that it no longer reacts with guinea pig intestine previously sensitized to wheat gluten. It continues, however, to retain its enteropathic activity. The ultrafiltrate of a peptic-tryptic gluten digest is similarly toxic.[22] The feeding of gliadin itself (350 mg. per kilogram) to celiac children results in an abnormally high rise in blood glutamine, with values ranging from 55 to 193 per cent above fasting values, whereas in normal subjects the change in blood glutamine ranges from minus 13 to plus 40 per cent.[24] By comparing blood glutamine plus peptide time curves alone, it is seen that the rise in blood glutamine following gliadin loading does not result from free glutamine, but rather from bound glutamine, which appears in the blood in the form of a peptide.

These studies have been supported to some extent by subsequent observations but were less clear-cut, and considerable overlap was noted between the celiac and the normal subjects.[26-28] The inference of these findings is clearly that a glutamine-containing polypeptide or peptide is the elusive offending agent in gluten, and that a defect in the intracellular (small-bowel mucosal?) metabolic processes involved in the breakdown or change of this peptide may be present in celiac disease and nontropical sprue.

Just how the presence of such a toxic polypeptide in the blood might produce the characteristic clinical picture is not clear. The possibility of such a substance acting systemically as a toxic or blocking agent is supported by the clinical observation that the omission of gluten from the diet produces remarkably rapid improvement, which occurs in advance of what one might expect on the basis of improved absorption alone. The possibility that this toxic glutamine peptide is interfering with folic acid or tryptophane metabolism is currently being studied in several laboratories. Cooke[29] has pointed out that the abnormal excretion of folic acid in celiac disease following parenteral administration may represent malutilization of folic acid. This abnormality persists for prolonged periods of observation despite clinical remission on a gluten-free diet and the presence of normal hematologic findings. He therefore suggests that the fundamental defect may be in folic acid metabolism and that the toxic polypeptide fraction of gluten might act by accentuating this defect.

Excessive amounts of 5-hydroxyindoleacetic acid and indole-3-acetic acid appear in the urine of about 90 per cent of celiac or nontropical sprue patients when the diet includes gluten.[30-32] Although the specificity of this finding in celiac disease and nontropical sprue is controversial, its occurrence in these disorders is clear and well established. The pathogenetic implications of such findings are obvious when one considers the physiologic effects of serotonin or other tryptophane metabolites on the gut. To take this one step further several observers have reported elevated serotonin levels in the blood of these patients during the activity of their disease.[33,34] The urinary indolacetic acid excretion returns to normal after from six weeks to two months on the gluten-free diet.[31] Kowlessar *et al.*[35] have recently demonstrated excessive urinary excretion of a group of indolic derivatives in gluten enteropathy including kynurenin, xanthurenic acid, and indican. These migrate very closely with indolacetic acid on paper electrophoresis, and there is evidence that these additional abnormalities of indole excretion are related to a deficiency of vitamin B_6. Although some of the abnormal indolacetic acid excretion results from bacterial activity within the bowel, about 40 per cent of the excess

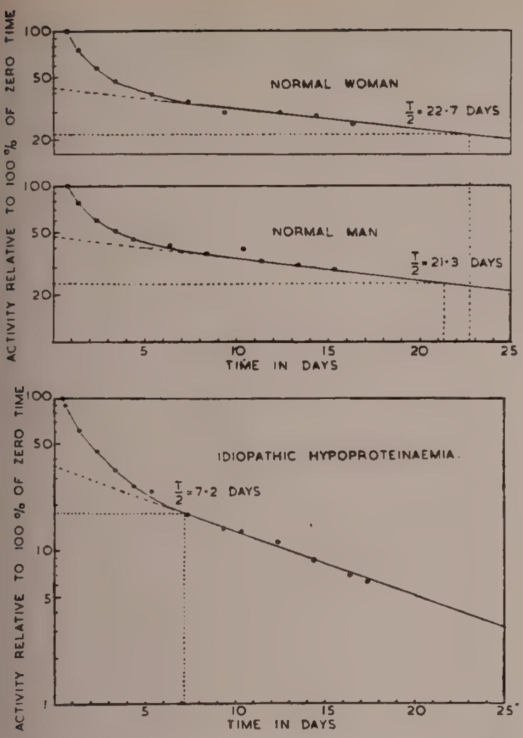

FIGURE 3. Plasma disappearance curve of I^{131}-labeled albumin in normal subjects and in patients with idiopathic hypoproteinemia.[37]

persists after antibiotic therapy, indicating that a disorder of tryptophane metabolism may be induced by dietary gluten.[32]

Protein-losing enteropathy

A reduction in the level of serum proteins may occur as a complication of disorders resulting in malnutrition, defective protein synthesis, or excessive protein loss. The group of patients who have hypoproteinemia without any of these apparent causes has long been a clinical puzzle. At various times they have been thought to suffer from inadequate protein synthesis or from excessive protein catabolism.

Studies of serum albumin. Recent evidence indicates that most of these patients suffer excessive loss of serum protein into the gastrointestinal tract. Often the patient's only symptom is edema; however, a considerable number of patients (up to 50 per cent) complain of minor digestive disturbances, particularly moderate and intermittent diarrhea. Usually there are diminished levels of serum albumin and gamma globulin with normal or low-normal total serum globulins. In contrast to nephrotic syndrome and to congenital hypoalbuminemia resulting from failure of albumin synthesis, the serum cholesterol is either normal or low.

TABLE I. Albumin degradation in patients with idiopathic hypoalbuminemia and in control subjects[38]

Degradation	Controls (N = 17)	Hypo-albuminemia (N = 11)
Albumin concentration (Gm. per 100 ml. serum)	3.9	1.8
Total exchangeable albumin (Gm. per kilogram)	4.2	2.0
RISA T* $^1/_2$ (days)	16.0	4.1
Albumin "turnover" (Gm. per kilogram per day)	0.17	0.30

* Radioiodine-serum albumin.

In 1949 Albright, Bartter, and Forbes[36] reported a metabolic balance study conducted in a patient with hypoalbuminemia in which they administered serum albumin intravenously and calculated the proportion of this albumin which was broken down and the amount which was converted to body protoplasm. The expectation was that in an individual depleted of albumin the "burned" aliquot would be small, and the amount of the administered albumin retained unchanged would be high. Just the opposite occurred. More than 65 per cent of the albumin was calculated to be "burned," as compared with the normal individual in whom less than half the albumin given was "burned" during the twelve days of administration. In this way a hypoalbuminemic patient was shown to be destroying serum albumin at an excessive rate. Where and how this destruction took place was not known.

This rapid disappearance of intravenous serum albumin was then clearly demonstrated in studies using I^{131}-labeled serum albumin (Fig. 3).[37] In subjects with idiopathic hypoproteinemia of this type the labeled albumin disappears from the plasma at rates from two to three times greater

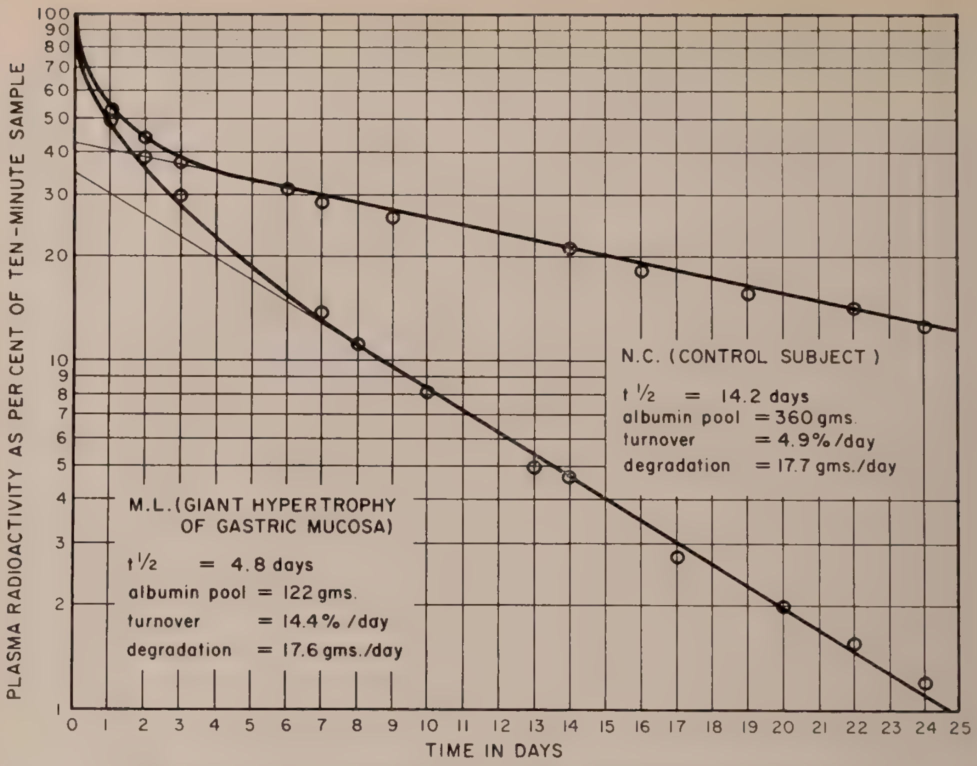

FIGURE 4. Plasma disappearance curves of I^{131}-labeled albumin.[39]

than in normal controls. Whereas normal subjects break down about 4 per cent of the total exchangeable albumin pool each day, the hypoproteinemic patients break down an average of 15 per cent. Table I is part of the data presented by Waldmann and illustrates the shortened I^{131} (radioactive iodine)-albumin half-life, the increased daily albumin turnover, and the diminished exchangeable albumin pool seen in these patients in comparison with a group of control subjects.[38] These findings in the absence of an obvious external source of albumin loss were considered as evidence favoring the hypercatabolism of protein. However, it was noted that except for the absence of proteinuria the picture was similar to that found by the same technic in the nephrotic syndrome.[38] As calculated from these studies the rate of albumin synthesis in "hypercatabolic" patients is only slightly greater than normal. This is also similar to findings in nephrosis where the maximal rate of albumin synthesis at best may reach levels of only twice normal.

GASTROINTESTINAL PROTEIN LOSSES. Citrin, Sterling, and Halsted[39] studied a patient with the already well-known association of giant hypertrophy of the gastric rugae and hypoproteinemia and demonstrated for the first time that such a patient suffered the loss of large amounts of serum albumin into the gastric contents. In this case they identified I^{131}-labeled albumin in the gastric contents and calculated that about 8 Gm. of albumin were lost into the stomach daily, accounting for almost half of the patient's total daily albumin degradation. Since insignificant amounts of radioactivity were recovered in the feces, it was assumed that the gastric losses of albumin I^{131} were digested and reabsorbed as amino acids, the tagged fraction, monoiodotyrosine, being subsequently deiodinated and I^{131} excreted in the urine.

Citrin, Sterling, and Halsted[39] pointed out that digestion in the gastrointestinal tract results in the loss of intact albumin which exceeds the capacity of the liver to reconstitute albumin despite the avail-

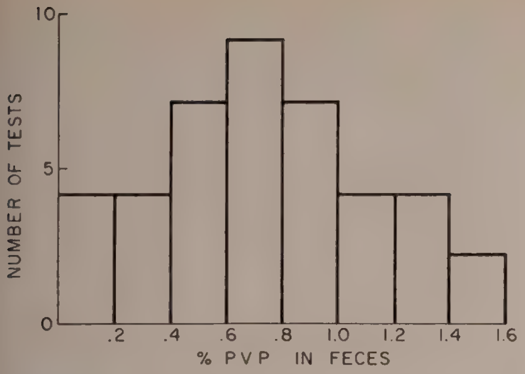

FIGURE 5. Percentage of intravenous dose of I^{131} PVP found in feces of control subjects.[40]

ability of the constituent amino acids through reabsorption. Although this fundamental contribution was thought to explain the hypoproteinemia of giant hypertrophy of gastric rugae, it was not then related to the group still classified as having idiopathic or hypercatabolic hypoalbuminemia.

Gordon[40] pointed out that the plasma decay curves and I^{131}-labeled serum albumin turnover studies in hypercatabolic hypoproteinemia were indistinguishable from those in this patient with excessive albumin losses into the stomach (Fig. 4). Because of the breakdown of the labeled albumin by the normal digestive juices, technics of direct measurement do not permit quantitation of gastrointestinal protein losses. Gordon[40] therefore attempted to measure the gastrointestinal protein losses indirectly. This was accomplished through the use of PVP (polyvinylpyrrolidine), a macromolecular substance with a somewhat variable molecular weight averaging 40,000 and an initial distribution in the body similar to that of serum albumin. When labeled with I^{131}, this material is stable and easily identifiable. If administered by mouth to normal subjects, about 90 per cent of it appears in the feces and only a small fraction of the radioactivity is put out in the urine. When I^{131} PVP was given intravenously to subjects with normal gastrointestinal tracts and normal serum proteins, up to 1.5 per cent of this substance appeared in a four-day stool collection. Figure 5 demonstrates the percentage of PVP appearing in the stools of these control subjects. Test subjects with hypoproteinemia resulting from the nephrotic syndrome, liver disease, and agammaglobulinemia fall into the normal range of fecal PVP excretion. Patients with "hypercatabolic hypoproteinemia" were found to excrete excessive amounts of the PVP intravenous test dose in the feces. The fraction of administered PVP appearing in the stool ranged from 2 to nearly 15 times the upper limit of normal. The question as to how accurate a measure fecal PVP is of gastrointestinal protein loss is not fully answered, but a rough correlation exists between the percentage of PVP appearing in the feces and the plasma decay rate of intravenously administered I^{131} albumin. Furthermore, the relationship between the fraction of intravenous PVP which appears in the stool and the serum albumin level is essentially the same as that expected if one assumes that PVP loss in the feces is a linear measure of protein loss in the feces (in the presence of unimpaired, but rate-limited albumin synthesis).

OTHER FINDINGS. Holman, Nickel, and Sleisenger[41] have shown that not only do these patients have an accelerated loss of I^{131} albumin, but in addition I^{131} gamma globulin disappears from the serum with excessive rapidity, and serum levels of gamma globulin are low. A portion of a labeled protein test dose which had been given intravenously was found in intestinal juices collected by a long tube. Utilizing the gel-diffusion immunologic technic of Ouchterlony,[42] the albumin and gamma globulin which appeared within the lumen of the gastrointestinal tract were identified as serum proteins. These serum proteins were also found in the intestinal juices of normal and control subjects; however, it was not possible to quantitate losses by this method. In this regard it has been demonstrated electrophoretically that serum albumin is a normal component of the mixed secretions of the isolated canine gastric pouch.[43]

In 3 of the 6 patients studied by Holman, Nickel, and Sleisenger,[41] intestinal lesions became apparent at some time after the appearance of the hypoproteinemia. Two of these patients had nonspecific small intestinal lesions which could not be classified, but dilatation of the mesenteric lymphatics was pronounced. In one of these there was a return of the serum proteins to normal after resection of the diseased bowel. In a report of excessive "fecal PVP excretion" in 4 hypoproteinemic subjects, Schwartz and Jarnum[44] noted in 1 patient marked pigmentation of the intestinal wall (as seen in a variety of small-bowel disorders)[45] with edema of the bowel and mesentery, an unusually distinct lymphatic pattern, and mesenteric lymph node enlargement. Two patients had giant hypertrophic gastric rugae, and 1 patient had no discernible gastrointestinal lesion. A subtotal gastrectomy was performed on the 2 patients with giant rugal folds. In 1 of these patients the edema disappeared, the serum albumin rose, and the PVP excretion became normal. The other patient died in the immediate postoperative period.

Approximately 70 per cent of patients with sprue seen in this country have total serum proteins of less than 6 Gm. per 100 ml., and 60 per cent have serum albumin levels of less than 3.5 Gm. per 100 ml.[46] Although much of this protein depletion results from malabsorption, it has been suspected that some of the fecal nitrogen losses derive from endogenous sources. Schwartz and Jarnum[44] noted increased fecal PVP losses in a patient with sprue and hypoproteinemia. Parkins[47] studied 11 patients with sprue syndrome (celiac disease and tropical and nontropical sprue), and found that 4 patients showed increased losses of I^{131} PVP into the gut.

Crane and Neuberger[48] also studied this problem by administering N^{15}-labeled yeast protein and protein hydrolysate to adults with nontropical sprue and measuring the subsequent elimination of isotope in the urine and feces. The great increase in fecal nitrogen found in these patients appears to be largely of endogenous origin, although the absorption of nitrogenous material is also deficient.

Conclusion. The mechanism of these excessive gastrointestinal protein losses is not yet understood. Since PVP is an inert substance and its distribution results for the most part from osmotic and hydrostatic gradients, there is indirect evidence that the protein loss itself is not the result of a secretory process. The roles played by disordered absorption and possibly by disordered protein synthesis remain to be evaluated. The loss of protein into the gastrointestinal tract of normal subjects suggests that the excessive losses described may represent the exaggeration of a normal process and that destruction of serum proteins within the gastrointestinal tract constitutes part of the normal catabolism of serum protein. The present hypothesis is that the protein-losing enteropathies represent a group of disorders in which there is an increased passive loss of protein into the gut, and that, although the products of digestion of this protein are largely reabsorbed, the maximal rate at which albumin can be synthesized is insufficient to keep up with the losses. The demonstration of excessive loss of endogenous protein in sprue may indicate an increased permeability of a disordered small-bowel mucosa. Whether this is related to a primary mucosal defect itself or is a secondary effect of sprue remains to be seen.

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Egg's cholesterol unchanging

The method of cooking an egg does not alter its cholesterol content, according to an article by Philip L. White, Sc.D., in the January, 1962, issue of *Today's Health.* He said: "The length of time than an egg is boiled in no way affects its cholesterol content. There are approximately 340 mg. of cholesterol per egg, and once the egg has been laid the cholesterol value remains essentially the same."

Modern Treatment of Common Bullous Dermatoses

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PROBABLY THE MOST DIFFICULT cutaneous eruptions to diagnose correctly are the bullous dermatoses. However, because the prognosis varies greatly from one bullous eruption to another, the correct diagnosis becomes extremely important. For example, the diagnosis of pemphigus vulgaris connotes a much graver prognosis as to life than does that of pemphigus foliaceus.

Generally speaking, the bullous dermatoses consist of three large groups of diseases, namely pemphigus, dermatitis herpetiformis, and erythema multiforme. Each of these bullous dermatoses has subdivisions. For example, in the classification of pemphigus itself, there are two types. One is pemphigus vulgaris, the variations of which include pemphigus erythematosus (Senear-Usher syndrome) and pemphigus vegetans. The other type, pemphigus foliaceus (fogo selvagem), stands alone, with a better prognosis as to life (the patient may live several decades) but a poor outlook because of prolonged, incapacitating suffering and complete social dependence.[1]

The divisions of dermatitis herpetiformis include herpes gestationis and subcorneal pustular dermatosis of Sneddon-Wilkinson.[2] There are two main divisions of erythema multiforme: those forms associated with a known causal agent and those with an unknown etiology.

Certainly, the number of diseases that are accompanied by bullae is great. Although these groups of bullous diseases have attracted most attention and interest, they have been least studied and understood etiologically and have been most difficult to manage.

However, it is not the purpose of this paper to discuss the various clinical differences between these eruptions. Rather, the most recent treatment of these diseases, together with the complications that may arise from such treatment, will be discussed.

Treatment of pemphigus vulgaris

ADRENOCORTICOIDS AND/OR ACTH. Before the introduction of the adrenocorticoids and ACTH in the treatment of pemphigus vulgaris, the disease was almost uniformly fatal.[3] Today, with the use of the adrenocorticoids and/or ACTH, about two thirds of the patients with this eruption survive.[1] In fact, of the approximate one third that die with pemphigus vulgaris, probably one half of these patients die as a result of complications arising from the use of the adrenocorticoids and/or ACTH.

There are two schools of thought concerning the dose of adrenocorticoid and/or ACTH to be administered initially. There are those who believe that initially one should employ massive doses of the adrenocorticoids, achieve some degree of clinical stability, and then reduce the dose slowly as the patient shows continued clinical improvement. On the other hand, there are those who feel that cautious but steady in-

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crease in the dosage should be attempted in a systematic, stepwise fashion. We favor a modification of the former mode of therapy but are less prone to use the massive doses suggested by some.

Naturally each patient with pemphigus vulgaris is an individual treatment problem. One would not treat the elderly female having a few recurrent, somewhat painful bullae of the mouth with massive adrenocorticoid therapy, but one would certainly entertain the use of such a regime in a rapidly spreading, severely debilitating type of pemphigus vulgaris. In any case, it must be emphasized that the earlier the diagnosis is made in pemphigus vulgaris and the earlier the hormonal treatment is instituted, the more favorable will be the prognosis.[4]

In addition to the adrenocorticoids, aqueous ACTH (corticotropin) given intravenously in 5 per cent dextrose solution or by intramuscular injection has been employed (as either a repository gel or aqueous solution).

COURSE OF TREATMENT. The treatment of a moderately severe case of pemphigus vulgaris consists in the administration of 8 to 10 tablets of adrenocorticoid initially. If considerable improvement is not noted within four days, then the dose is doubled immediately. Generally, this latter increase in medication produces eventual control in the majority of cases of pemphigus vulgaris. Once the suppression of new bullae formation is attained, the dose of adrenocorticoid is reduced slowly. For initial maintenance, we have found that 4, 6, or 8 tablets of adrenocorticoid are required for several weeks or longer. Following this regime, the majority of patients are soon free of active lesions and are maintained on 3 or 4 tablets daily. There are those who believe that it is advantageous to augment this routine with 40 units of repository corticotropin injections administered intramuscularly once or twice a week. If the urgency is great, 25 to 40 units of aqueous corticotropin dissolved in 500 to 1,000 cc. of 5 per cent dextrose may be administered daily, intravenously over a six-to-eight-hour period in the hospital, or 40 units of repository corticotropin injection may be administered twice daily in the hospital, office, or clinic.[4] Occasionally, patients become sensitive to the ACTH produced from pork. In this instance, a beef extract may be substituted.[5]

In treating patients with pemphigus vulgaris it is unwise to try to rid the patient of every "last" lesion by continuing the treatment on even a moderate dosage schedule. If a lesion or two remain and the patient is not inconvenienced by their presence, the dose should not be increased, because such therapy may lead to serious complications.

We use prednisone in the treatment of pemphigus vulgaris because it is less expensive and as effective and has fewer side-effects when compared with the other oral adrenocorticoids. Whether or not injections of ACTH should accompany the administration of the adrenocorticoids is debatable, but most authorities agree that there is little or no clinical or experimental evidence to support such use of ACTH. Physiologically, adrenocorticoid depression by cortisone is a consequence of suppression of the output of adrenotrophic hormone by the anterior pituitary rather than a direct effect of cortisone on the adrenal glands themselves. Administrations of ACTH cannot be expected to lessen the suppression of pituitary function by cortisone and may indeed aggravate it. However, the administration of ACTH may be employed advantageously when one anticipates the imminent withdrawal of the adrenocorticoids.

THERE ARE THREE GROUPS *of bullous dermatoses: pemphigus, dermatitis herpetiformis, and erythema multiforme. Adrenocorticoids and/or ACTH are used in the treatment of pemphigus until the suppression of new bullae but may cause complications such as peptic ulcer, pulmonary or musculoskeletal complications, electrolyte disturbance, diabetes, elevation in weight, and hypotension. Topical therapy consists of potassium permanganate tub baths and, when possible, a heat-regulated cradle. Dermatitis herpetiformis is treated by sulfoxone sodium (Diasone) or acetosulfone (Promacetin). The former may produce methemoglobinemia or hemolytic anemia, and the blood should be studied continuously. Sulfapyridine is used also but may produce renal damage or agranulocytosis. The treatment of erythema multiforme is similar to that of pemphigus, together with local use of antibiotics.*

Complications produced by adrenocorticoid therapy

Because the adrenocorticoids are employed for long periods of time and often at high doses, the management of pemphigus today revolves around the complications induced by these agents.

Peptic ulcers. One of the ever-present dangers of oral adrenocorticoid administration is the possible production, or activation, of peptic ulcers. Although some physicians tend to minimize this hazard, it is our opinion that the hazard exists whenever the adrenocorticoids are administered for a long enough period and in high enough doses. In fact, the patient who develops complications and difficulty when he is treated for his pemphigus vulgaris has usually been treated with excessive doses of the adrenocorticoids for prolonged periods of time. Because of this potential danger, all patients with a previous or present history of a peptic ulcer should be maintained on a full ulcer regimen when they are receiving the adrenocorticoids.

In addition to repeated blood counts and hematocrit determinations all patients who are potential "ulcer bleeders" should have repeated stool guaiac tests and should have their blood typed on admission.

The diet of the patient with pemphigus vulgaris should be fortified with supplemental panvitamin preparations. In addition, a high protein, high caloric, low salt, and low carbohydrate diet should be routine.

A preparation of value in the relief of pain associated with the oral ulcerations seen in pemphigus vulgaris is lidocaine (Xylocaine viscous).[6]

Pulmonary complications. One should always be on guard for the development of bronchopneumonia or a staphylococcic abscess of the lung as a result of the lowered resistance of patients with pemphigus vulgaris. A frequent cause of death occurring as a result of the debility associated with pemphigus vulgaris was, and still is, pulmonary complications.

Musculoskeletal complications. Often it is in the musculoskeletal system that many of the complications of adrenocorticoid therapy occur. There is no doubt that long-term adrenocorticoid therapy predisposes to osteoporosis and vertebral fractures, especially in patients past middle age. Unfortunately it is only before one third of the skeleton is lost that x-ray examination will reveal osteoporosis. Theoretically, the administration of a sex hormone, such as 6 to 10 mg. of testosterone propionate daily, should prevent this osteoporosis,[7, 8] but in our experience all such preparations are of limited value. However, a polyvitamin preparation should be administered. High calcium diets may be not only ineffective but actually harmful. The use of corsets in patients with osteoporosis should be employed to encourage ambulation, and a mattress board is imperative. Muscle wasting and weakness of the muscle groups of an extreme degree is frequently seen with long-term triamcinolone therapy for pemphigus.[9]

Electrolyte disturbances. Undoubtedly, the most profound and severe body alterations occur in the electrolytes of the blood. Because the patient with pemphigus vulgaris usually has various areas of denudation with exudation of serum, electrolyte disturbances are compounded when the adrenocorticoids are administered. Frequent electrolyte determinations, especially for sodium and potassium, should be done. In view of the fact that adrenocorticoid therapy lowers the serum potassium level and elevates the serum sodium level, supplemental potassium salts have been advocated. Unfortunately, all too often these enteric-coated potassium chloride tablets are not absorbed from the intestines but are found intact in the feces. It is for this reason that we advocate liquid potassium preparations of either potassium chloride or potassium gluconate (Kaon, Potassium Triplex). A table salt, containing potassium chloride rather than sodium chloride, is marketed under the trade name of Neocurtasal and may be used.

It should be noted that, with the frequent use today of chlorothiazide (Diuril) and hydrochlorothiazide (HydroDiuril), caution should be employed when combining these agents with the adrenocorticoids since both tend to deplete potassium stores throughout the body.

Blood cultures should be drawn whenever patients are receiving high doses of the adrenocorticoids for prolonged periods of time.

Septicemia occurring in patients receiving adrenocorticoid therapy is usually unattended by the usual signs of infection—fever, headache, chills, and so forth.

Nonspecific, randomly administered, prophylactic antibiotic therapy may often be harmful, whereas specific massive antibiotic therapy employed for a specific indication may be life-saving.

DIABETES MELLITUS. Diabetes mellitus "induced" by the adrenocorticoids is an ever-present hazard, especially when high doses of the adrenocorticoids are employed, as in the treatment of pemphigus vulgaris. One may uncover "latent" diabetes in this manner, but unfortunately patients with pemphigus vulgaris who become diabetic do not fare well. Although the diabetes in these patients is generally mild, we have been forced to rely on insulin by injection, rather than using the newer oral antihyperglycemic agents in controlling their diabetes.

ELEVATIONS IN WEIGHT. All patients with pemphigus vulgaris should be weighed daily. Elevations in weight should alert the physician to altered electrolyte physiology first, altered cardiac function second, and pathologic conditions of the kidney third. Therefore, in addition to the daily determination of body weight patients should have daily urinalyses. If septicemia occurs (most frequently staphylococcal), as it occasionally does, the organism is most prone to form abscesses in the lungs, heart, or kidney.

The vital signs should be recorded daily.

INTERCURRENT INFECTIONS. A point of controversy exists regarding the problem of an intercurrent infection occurring in a patient with pemphigus vulgaris who is receiving adrenocorticoids. Should the dose of adrenocorticoids be maintained, elevated, or reduced? It has been our experience that an increase in dose (often doubling the dose) is generally indicated under these circumstances.

In regard to the latter point, when patients are discharged from the hospital environment on maintenance adrenocorticoids, it is the duty of the physician to notify the patient that should a subsequent injury or infection occur or operation be required, the physician should be notified immediately, for it is under just these stressful situations that an increase in adrenocorticoid dosage is mandatory. In addition, it is advisable to give the patient a printed, wallet-sized card noting the fact that the patient is receiving adrenocorticoids.

HYPOTENSION. From the standpoint of the surgeon, the most prominent sign of previous long-term adrenocorticoid therapy is persistent hypotension which cannot be explained by blood loss or coronary disease. This hypotension does not respond to adequate blood replacement.[10]

Topical therapy

The most effective form of topical therapy that can be administered to the patient with pemphigus vulgaris is the bath. We prefer potassium permanganate tub baths (1:80,000 or $^3/_4$ teaspoon of the crystals completely dissolved in an average tub of water). The potassium permanganate bath is stimulating, mildly astringent, drying, antiseptic, and deodorizing. It is unwise to allow debilitated patients with pemphigus vulgaris to take a tub bath unattended. A nurse should be present to aid the patient in and out of the tub. She should be in attendance during the entire bath period. Elderly patients may go into syncope if they are removed from a recumbent bathing position to a standing position too quickly. The patient may bathe for fifteen-minute periods once a day if the baths are not enervating.

Ointments and oily lotions should be applied to the body after the bath, while the skin is still wet. We prefer Lubriderm, Nivea Skin Oil, or peanut oil. Bacitracin ointment may be applied to infected areas.

Optimum topical therapy for the patient with pemphigus vulgaris includes a heat-regulated cradle. However, this form of therapy requires a great deal of nursing care that is rarely available. Gauze dressings, no matter how well saturated with ointment, are unsatisfactory, because over denuded areas the gauze is too coarse. Linen or Telfa pads should be substituted for gauze. The patient may be grateful for a change to dry therapy, which can be accomplished by the use of talcum powder dusted on the patient's body and sheets after the bath. In the treatment of these serious dermatoses, one must not forget that experienced nursing care is of utmost importance.

Other forms of pemphigus

Another variety of pemphigus is pemphigus foliaceus. This rare disease, which resembles dermatitis exfoliativa clinically, is also treated with the adrenocorticoids. What has been said for pemphigus vulgaris is applicable to the treatment of pemphigus foliaceus, but larger doses of the adrenocorticoids and/or ACTH must be employed. Complete remission is not accomplished, but improvement with large doses of the adrenocorticoids or ACTH may be anticipated.

On occasion, the antimalarial drugs, particularly quinacrine hydrochloride (Atabrine) may improve this type of pemphigus.

Pemphigus vulgaris and pemphigus erythematosus respond best to the administration of the adrenocorticoids, whereas pemphigus vegetans and pemphigus foliaceus respond not so well (in that order).

Fundamentally, however, the topical and systemic treatment of pemphigus vulgaris is almost identical to the treatment advised for other forms and variants of this disease.

Dermatitis herpetiformis

Dermatitis herpetiformis (Duhring's disease) is a rare bullous dermatosis which is chronic and continuous in its course. It practically never affects the mucous membranes. It is associated with frequent exacerbations. It is one of the most pruritic diseases known to man and may persist for many years (in 1 case for over thirty years). Dermatitis herpetiformis has challenged the therapeutic ingenuity of physicians since it was first described by Duhring in 1884.[11]

Drugs. Today the most effective treatment for dermatitis herpetiformis is sulfoxone sodium (Diasone), one tablet (0.333 Gm.) four times a day. The daily dosage should be reduced gradually until a therapeutic maintenance level is achieved. This may be one tablet three times a day or less. A few of our patients with dermatitis herpetiformis have been controlled on one tablet every other day. Unfortunately this drug almost invariably produces methemoglobinemia with subsequent alterations in the color of the skin to a slate blue. The depth of this blue color is dependent on the color of the patient's normal skin and the degree of methemoglobinemia. For instance, the skin assumes a greenish color in the Oriental. Sulfoxone sodium is a potentially dangerous drug. It has been frequently reported to produce hemolytic anemia, often of sudden onset. However, large doses of this drug have been administered to patients with Hansen's disease without a high incidence of untoward reactions.

Despite the fact that sulfoxone sodium is the most effective therapy for dermatitis herpetiformis, it is our practice to administer acetosulfone (Promacetin) as the initial drug, because of the paucity of major toxic reactions compared with sulfoxone sodium. The minor reactions consist of a mild secondary anemia and a morbilliform or scarlatiniform dermatitis medicamentosa.

The initial dose of acetosulfone is 1 Gm. or two tablets three times a day. In the majority of patients, the dosage can be reduced to one tablet three or four times a day. However, approximately 20 per cent of the patients with this disease require eight to ten tablets a day to control their eruption. Frequently, the effect of this drug has been augmented by the concurrent administration of 1 Gm. or two tablets of sulfapyridine daily.

In the winter of 1938 to 1939, sulfapyridine first became available in the United States. The senior author first used the drug successfully in the treatment of dermatitis herpetiformis.[12,13] It is potentially toxic; renal damage and agranulocytosis are two of the more frequently occurring toxic manifestations. The dosage of sulfapyridine is two tablets (1 Gm.) administered three times a day. The dose should be reduced gradually until the therapeutic maintenance level is attained. For obvious reasons, it is unwise to administer more than 3 Gm. in any twenty-four-hour period.

Precautions. Since all of the previously mentioned drugs are potentially toxic, it is necessary to have a complete blood count and urinalysis performed at the beginning of therapy. These tests should be repeated at weekly intervals for the first month and at monthly intervals thereafter. It is a matter of judgment as to the frequency of subsequent laboratory tests.

It is our impression that, if a patient takes these drugs with no untoward side-effects occurring in the first month, then he may be able to tolerate them indefinitely. This is attested by the fact that the great majority of our patients have completely controlled dermatitis herpetiformis for years without any untoward effects occurring from medication. When sulfapyridine is administered, it is necessary to force fluids and alkalinize the urine.

We believe that the previously mentioned sulfa drugs are so specific in the control, but not in the cure, of dermatitis herpetiformis that the response to their administration may serve as a therapeutic test.

In our experience the adrenocorticoids, Roniacol, para-aminobenzoic acid, nicotinic acid, and the antihistamines are of no value in the treatment of this disease.

There have been several reported instances where patients with dermatitis herpetiformis have been cured permanently of their disease after the removal of a focus of infection, such as a bronchiectatic lung.[14,15] In our experience, several of our patients with dermatitis herpetiformis died of carcinoma of the colon in early middle life.

VARIANTS OF DERMATITIS HERPETIFORMIS. Herpes gestationis is a variant of dermatitis herpetiformis which occurs in pregnant women. Patients with this disease do not tolerate the sulfa drugs well. They are prone to develop hemolytic anemia which at times can take on serious proportions. We have been impressed by the efficacy of the adrenocorticoids in the treatment of this form of Duhring's disease, compared with the relative ineffectiveness of the sulfa drugs.

Subcorneal pustular dermatosis of Sneddon-Wilkinson is a variant of dermatitis herpetiformis. We believe it is a superficial, polymorphous, pustular form because it also responds so well to sulfa therapy in addition to other similarities. It should therefore be treated as dermatitis herpetiformis.

Finally, one should note that infants and children suffering from dermatitis herpetiformis respond well to acetosulfone. The dose administered should be regulated according to the weight of the child.

Erythema multiforme

Erythema multiforme, which in some of its types may be bullous, is essentially a systemic disease involving mainly the skin and mucous membranes. Yet, the involvement of these tissues is as variable as the constitutional reactions associated with the disease.[16] The mucous membranes of the mouth, nose, eyes, genitalia, and anus are most frequently involved.

The following list shows the classification of erythema multiforme that we prefer. It should be noted that the term pemphigoid has been used to describe eruptions of a bullous nature occuring in older people, usually consisting of severe, extensive, recalcitrant bullous lesions, sparing the mucous membranes and not associated with severe systemic reaction. However, we feel it is best to reserve this term for erythema multiforme of unknown causation (erythema multiforme pemphigoides).

Classification of erythema multiforme

ETIOLOGY UNKNOWN
- Hebra type
    1. Mild
    2. Moderate
    3. Severe (erythema multiforme pemphigoides)
- Stevens-Johnson type
    1. Mild
    2. Moderate
    3. Severe
    4. Malignant (erythema bullosum malignans, pluriorificial type)

ETIOLOGY KNOWN
- Type accompanying known infectious or neoplastic diseases
- Osler type accompanying visceral diseases
- Drug causation type

All forms of erythema multiforme, whether the Hebra or the Stevens-Johnson type, are treated in a manner somewhat similar to that described for pemphigus vulgaris.[1] The adrenocorticoids and ACTH are of considerable value in the mild, moderate, and severe Hebra types. Intravenous injections of ACTH are of lifesaving value in the severe Stevens-Johnson type of the disease if they are administered early. The adrenocorticoids are of considerable value in shortening the attack of the Hebra type of erythema multiforme and in relieving the discomfort of the patient.

The malignant form of the Stevens-Johnson type of erythema multiforme (erythema bullosum malignans) offers a serious problem in immediate effective treatment. The over-all mortality rate in all types of Stevens-Johnson disease is 18 per cent. It was much higher in the malignant type (50 per cent) but has been greatly reduced by the administration of the adrenocorticoids, ACTH, and the antibiotics.

In those forms of erythema multiforme associated with infectious and visceral diseases, and those caused by hypersensitivity to medications, the treatment of the eruptions is the treatment of the conditions producing them, in addition to the administration of the adrenocorticoids.

The local treatment of this group of diseases applies mainly to erythema multiforme pemphigoides and the Stevens-Johnson type of erythema multiforme.

Baths of potassium permanganate (1:80,000), starch (Linit), and oatmeal (Aveeno) will relieve pruritus and are cleansing when the patient is afebrile and ambulatory.

The antibiotic ointments are helpful in preventing and controlling infection when they are applied locally.

Partial or complete, temporary or permanent blindness is a serious complication of the malignant form of Stevens-Johnson type of erythema multiforme. An ophthalmologist should be consulted in regard to eye complications.

Summary

The adrenocorticoids are often lifesaving drugs when they are employed in the treatment of pemphigus. However, they are double-edged swords, for the treatment of pemphigus today also revolves around the therapy of the complications induced by the adrenocorticoids.

We believe that initially a comparatively vigorous adrenocorticoid dosage scheme should be employed when treating pemphigus.

Our therapy for erythema multiforme corresponds in general to that employed for pemphigus.

Dermatitis herpetiformis is probably best treated today with sulfoxone sodium, although acetosulfone and sulfapyridine have been used on occasion with success. Acetosulfone is to be recommended in the beginning because of the paucity of reactions from its administration.

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Photocoagulation

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PHOTOCOAGULATION *is a surgical procedure which derives its effect from the destruction of tissue by heat as distinct from the medical or physical therapeutic use of heat to improve the state of a tissue. The photocoagulator is used prophylactically in the retinal detachment field. It may be used as a supplement to conventional diathermy and to halt giant cysts or retinoscheisis. It is effective in the treatment of retinal and choroidal angiomas. In the treatment of retinal neovascularization and intraocular malignant conditions its use is still of questionable value. The instrument is effective in the destruction of anterior chamber cysts but must be handled with care. Experience has tempered early enthusiasm for its use in optical iridectomies. There are physical factors to be considered in its use: The media must be clear; the pupil must be dilated widely and strongly; and the presence of choroidal scars presents an obstacle. The photocoagulator is a valuable instrument whose greatest use is in supplementing older methods of treatment, but it must be used with great skill and caution, for while it offers help in one hand, it offers danger in the other.*

So NEW AND UNEXPLORED is photocoagulation and so great is the enthusiasm engendered by the vistas of its potential that a nearly continuous reporting of experience as to its capabilities and hazards will be necessary for some time if we are to keep this new therapeutic tool in perspective and use it wisely. This, therefore, is not a repeat report on the subject but rather a continuation of an earlier report presented to the American Academy of Ophthalmology and Otolaryngology, arising from further experimental work and clinical observation and from the enthusiastic and often ill-founded claims that have been made at various meetings.

The photocoagulator is an instrument which releases more power in one half-second burst of light than it takes to light one's home during a long winter evening. It has fired the imagination and hopes of the laity who, it may be said to our credit, welcome new power placed in medical hands even as they fear new power placed in the hands of the military. But their enthusiastic anticipation must not be allowed to infect those of us who use or prescribe the use of the instrument, for the intemperate use of this powerful device would brand us quite properly as "hot-rod surgeons," and such opinion, held by the public, is often reflected in court decisions.

First, a word of classification should be given. Photocoagulation is a surgical procedure which derives its effect from the destruction of tissue by heat as distinct from the medical or physical therapeutic use of heat to improve the state of a tissue. Second, it is not "radiation therapy," as ionization is not the mode of its action. Last, there is a caution against the term "light coagulation." The word light is both a noun and an adjective. We are all aware of the hazards of ambiguity which are inherent already in the insurance forms, and we should not compound them.

Recently the popular press has published various articles on this new instrument, and in most of these either it has been stated or at least implied that the photocoagulator is used to cure retinal detachments. While the instrument has been found to be a valuable tool in this field, its use is almost completely prophylactic. When the retina becomes separated from the pigmented layers the elevated retinal membrane diffuses the light beam and prevents its focus at a point in sufficient intensity to produce the desired burn, and the layer of subretinal fluid prevents the formation of an adhesive bond even if sufficient heat is created by the beam

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to produce an exudative reaction in the underlying layers. So it can be stated that the photocoagulator is not useful in treating detached retinas.

Prophylactic use

The light beam does find an important role in the detachment field, however, in sealing off retinal holes where a detachment is threatened but has not yet taken place and as a supplement to conventional diathermy in areas where the treatment seems to be too light and postoperative leaks are threatened.

In the prophylactic use not only can the photocoagulator seal holes to prevent detachment, but also, in an eye in which a frank detachment has been treated by the conventional method, it may be used to treat threatening degenerative areas which are not involved in the detachment process of that eye or in the fellow eye. Also, in eyes with extensive peripheral degeneration and early cataractus lens changes, the retinal lesions may be walled off and the eventual cataract extraction made safer. This is particularly efficacious in the case of nuclear cataracts where the periphery remains clearly visible. Here care must be exercised lest the heating of the retina, which accompanies the cauterization of the pigment layers, cause retinal shrinkage and the tearing of new holes. One such case was seen in which a line of coagulation was laid down completely around the equator with a resulting evulsion of the retina from the ora serrata over the entire 360 degrees.

Also under prophylaxis come the so-called "macular holes." These lesions are so easy to treat as to be almost irresistible. Unless one is familiar with their appearance, these macular cysts can easily be mistaken for a retinal hole, as the surrounding gray area of cystic change resembles closely an area of detachment, and when the large central cyst loses its inner wall the effect of looking down into the resulting crater heightens this deception. Actually, these cysts rarely cause detachments but may rupture through secondarily when the retina is detached by a primary hole in the peripheral retina. Some of these cysts have been sent in for photocoagulation with vision as good as 20/50. The treatment of these is obviously contraindicated for not only will the cyst not cause a detachment but also the treatment will destroy the macular area and drop the vision to 20/200 or less.

As a supplement to diathermy

The use of photocoagulation as a supplement to conventional diathermy is most gratifying when it works. It may be used immediately after the original operation to reinforce areas where the diathermy reaction seems inadequate, or it may prevent a redetachment later in the healing stage when the tissue contraction pulls loose a part of the retina within or adjacent to the treatment area. However, it should never be counted on to remedy careless surgery or inadequate preoperative examination. Such use is almost certain to be disappointing.

The final use of photocoagulation in the retinal detachment field is that which was described in the symposium of the American Academy of Ophthalmology and Otolaryngology meeting in 1960. This is a two-stage procedure in which a choroidal ridge is created around the equator by implanting an encircling, silicone rubber filament beneath the sclera, then draining the subretinal fluid and forcing the retina into place over the ridge by injecting vitreous or saline fluid. The retina is then sealed to the ridge by the use of the photocoagulator beam. This operation may be used in eyes which have suffered widespread disease either in the detachment process or from previous diathermy, but its value is extremely limited.

Treatment of giant cysts

An associated field in which the coagulating beam is useful is that of the domelike, giant, retinal cysts and the flatter, more rapidly progressing retinoscheisis. A delimiting boundary of photocoagulation will halt both of these effectively but may not be needed in the former for many of these giant cysts progress slowly or not at all.

In general, a word of caution is in order when prophylactic treatment with photocoagulation is contemplated. This is a powerful instrument beset by hazards and undesirable side-effects and should be used only when there is definite evidence of a progressive pathologic condition and a real threat of detachment, for adding a thermal burn to an area which is already taxed by degenerative changes may well precipitate a latent disease. This is particularly true in the younger-age groups. Several surgeons have now learned to their sorrow that lattice degeneration in a young person should never be touched by coagulation for in these children and young adults the formed vitreous is usually adherent in such areas and the heat of coagulation will cause a disastrous contraction.

Treatment of angiomas and neovascularization

One of the most gratifying uses found for the photocoagulator is in the treatment of angiomatous lesions of the retina and choroid. Blood vessels, because of the dark, light-absorbent, blood column that they contain and their extremely heat-sensitive lining cells, are easily destroyed with very small doses of the light beam. Choroidal hemangiomas can be destroyed by several applications of so little intensity that there is no visible reaction at the time of treatment and little or no damage to the overlying retinal elements. When the procedure is done properly, these lesions can be destroyed without the formation of a scotoma.

Retinal angiomas as seen in the Lindau-von Hipple disease, which used to be difficult or impossible to handle, can be completely destroyed with only scarring in their own area resulting. Early observers reported that total retinal detachments, due to vessel transudates, followed the first treatment, but the use of far lighter initial doses now has eliminated this. The early treatments sought to destroy the vessels by coagulation. The present concept is to irritate the vessels and let them destroy themselves.

In retinal neovascularization (Eales's disease) the photocoagulator is still of questionable value; it is best used in obliterating the vessels by scarring the perivascular tissues. In the neovascularization of diabetes and sickle-cell disease, its use is contraindicated.

Treatment of intraocular malignant conditions

In the treatment of malignant intraocular tumors there is great and, as yet, unresolved controversy to which time alone will give us the answer. Many believe that the malignant melanoma of the choroid can be safely treated, and the follow-ups from the clinics at Bonn and Essen would indicate that this is so, but in this country we have largely reserved its use for extreme cases.

The retinoblastoma, particularly those of small size and in the posterior half of the globe, can be destroyed, probably by the destruction of their blood supply. It must be remembered, however, that the tumor is but a single manifestation of the disease, and the more general treatment by radiation and chemical agents should be used as the primary treatment. In that these tumors have been shown to be radiosensitive in inverse proportion to the amount of oxygen present in the tissues, the photocoagulation, which diminishes the blood supply, should be used after the radiation therapy has been completed.

Melanomas of the iris have been obliterated by photocoagulation, but the current opinion holds that surgical excision is best with photocoagulation of the edges of the iris wound used afterward to destroy any vagrant cells. In this way a pathologic specimen is obtained for use in prognosis or court as the case may demand.

Tumors of the conjunctiva or lids are probably best treated by excision or cauterization by an agent whose destructive force can be better controlled.

Destruction of anterior chamber cysts

The destruction of implantation cysts in the anterior chamber, in the manner described by Cibis, in the symposium mentioned previously, is most effective but must be done with great care and by one thoroughly versed in handling the instrument. Its success is based on heating the fluid within the cyst by successive short bursts of light and allowing this heat to be carried around the lining of the cyst by the resulting convection currents. Overtreatment causes severe corneal and iris damage.

Creation of optical iridectomies

The creation of optical iridectomies in cases of updrawn pupil following cataract extraction received much early enthusiasm, but experience has tempered this enthusiasm in most hands and has completely chilled it in others. The technic is not easy to master, and the successes are met and often outweighed by the corneal opacifications which occur too often to allow this to be classified as a safe procedure.

Physical requirements

In addition to what has just been briefly reviewed as to the tissue indications and limits for the use of the photocoagulator, there are certain physical factors which must be considered in its use. In that the therapeutic effect results from the heat created by the interruption of a focused light beam by the pigmented layers of the eye, certain requirements must be met before the use of this instrument can be considered for use in treatment:

1. The media must be clear. Corneal, lens, or vitreous haze not only diffuses the intensity of the beam and prevents its concentration at a point to create a burn, but they also impair the visibility of the lesion which the operator must have to direct the beam safely.

2. The pupil must be dilated widely and strongly so that the beam of light can enter the eye. In this connection we must remember that, as we vary from any axis save that perpendicular to the plane of the pupil, the pupillary opening becomes first an oval, then an ellipse, and finally a narrow slit. Thus the treatment of lesions in the peripheral fundus becomes increasingly difficult. Added to the optical impediment thus offered is the hazard of burning the pupillary border of the iris and thereby causing the immediate constriction of the pupil and, later, iris atrophy.

3. The presence of choroidal scars presents both an obstacle and a hazard. First, the absence of pigment in the area of scarring greatly reduces the ability to create a point of heat, and, second, the retina overlying these scars is atrophic and friable and may easily be torn by the contraction at the point of heating.

4. The presence of high degrees of refractive error must be met by the use of an appropriate contact lens which, while correcting the refractive error, imposes further optical impediment so that under the powers of plus or minus 10 D., they have been found to impair the effect more than they aid it.

Summary

In conclusion, then, we may say that the photocoagulator is a valuable addition to our armamentarium but one which is still in the stage of clinical experimentation. Its greatest use lies in supplementing older methods of treatment, save alone in treating intraocular angiomas. It is a tool which, because of its great power, offers help in one hand and danger in the other. In the hands of the temperate and careful surgeon, it is an awkward but powerful assistant. In the hands of the overly enthusiastic surgeon, it may be a dangerous weapon.

635 West 165th Street, New York 32

Discussion

William F. Regan, Jr., M.D., *New Rochelle, New York.* To all that Dr. Clark has said, I can only add "Amen." I certainly agree that there has been far too much discussed about the pros of photocoagulation. It is too early to discuss what photocoagulation can do. It is not too early to discuss the dangers and complications and what photocoagulation cannot do.

In our hands at Manhattan Eye, Ear and Throat Hospital, the largest use for the photocoagulator is in retinal tears without detachment. These are frequently found in the other eye of a patient with detachment. These fellow eyes must be fully examined for retinal breaks.

In the fellow eye of a patient with a retinal detachment that was not cured there was a retinal tear without detachment in the upper outer quadrant. The eye was aphakic. The vision was 20/20. After coagulation through a pupil that could not be dilated adequately, a photocoagulation was done. This was followed by a bullous keratopathy, a secondary glaucoma, and vision down to light perception. After four months the cornea was clearing. There was a great deal of iris atrophy, and the vision was 16/200.

Therefore, even in this area of its greatest use, it still can be a dangerous instrument. In an eye that cannot be dilated, the photocoagulator should not be used, even for posterior segment work.

Most of the ophthalmologists using this machine now are retinal specialists, the same retinal specialists who over the past ten years have urged ophthalmologists to do nothing but diathermy, nothing but scleral resections, nothing but vitreous implants, and nothing but encircling 360-degree corsets. We have found a place for each of these procedures. We are in the process of finding the place for photocoagulation.

In 1958 I was extremely enthusiastic about the photocoagulator. Now, in 1961 I am still extremely enthusiastic about the photocoagulator, but my enthusiasm has been tempered with a great deal of caution.

Effect of diaper-roll support on well-being of premature infants

According to *Behavior Patterns of Premature Infants, A Nursing Study*, by Eileen Hasselmeyer, R.N., published by the United States Public Health Service, premature infants appear to sleep more, cry less, and move about less when they are provided with diaper-roll support, but the support did not result in greater weight gain for premature infants.

The research was carried out in the premature unit of Bellevue Hospital Center in New York City. All 59 subjects weighed under $4^1/_2$ pounds at birth. Thirty of them had a rolled diaper placed at the lower back or side for support, the remaining 29 served as controls. Using measurement methods developed for this study, observers checked the infants every ten minutes around the clock for from three to six weeks and kept records of their sleeping, crying, moving, eating, and other behavior patterns.

Other tentative findings of the study were: Premature infants sleep 80 per cent of the time during the first week of life and 75 per cent by the sixth week; they exhibit vocal behavior only 10 per cent of the time during the first week and are even quieter during the second week; and their amount of bodily activity is fairly constant during the first six weeks of life, with no evidence of movement about 70 per cent of the time.

Histoplasmin Sensitivity in Niagara County

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THE RELATIVELY RECENT INCREASE in the incidence of histoplasmosis in the State of New York has stimulated our further interest in evaluating the evidence of this condition in the active and inactive forms in a representative portion of Niagara County. Cronk's* work constituted the first published paper on this topic arising from the western region of the State.

Materials and methods

Our study consisted of patients in the Lockport and Niagara Falls areas on whom skin tests were performed; they represented a well-balanced segment of Niagara County. The investigation extended over a three-and-one-half-year period. The patients who were selected had symptoms referable to the respiratory system or had abnormal chest x-ray findings which necessitated further investigation. Approximately 7 patients with positive skin reactions had originally resided out of the State, and these patients were excluded from the final statistical analysis. All the patients had skin tests for both histoplasmosis and tuberculosis, and readings were made at twenty-four and forty-eight hours respectively. The total number of patients who were tested are recorded in Table I, and comparative studies from the Lockport and Niagara Falls hospitals (both Niagara Falls Memorial Hospital and Mt. St. Mary's Hospital) with corresponding results are shown.

Table II includes the breakdown of the patients with positive reactions to histoplasmin according to age groups and sex. Of the total of 247 patients who were tested, 10.5 per cent had positive results.

Comment

Asymptomatic inactive histoplasmosis manifested by histoplasmin sensitivity accounts for the most common variety of this condition. None of the patients in this study had signs or symptoms of active disease. One patient demonstrated calcifications in the spleen and lung but never exhibited clinical activity.

Although another patient had a complement fixation test reaction of 1:4 at the time of the initial examination, no stigmas of active disease were found. This patient had an influenza-like picture five months previous to skin testing and was symptom-

TABLE I. Skin test reactions

Hospital(s)	Number of Patients	Histoplasmin Positive Reactions	Histoplasmin Negative Reactions	Tuberculin Positive Reactions	Tuberculin Negative Reactions
Mount View	99	16	83	99	0
Mt. St. Mary's and Niagara Falls Memorial	148	10	138	12	136
TOTALS	247	26	221	111	136

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* Cronk, G. A.: Pulmonary calcification and histoplasmin sensitivity in New York State, NEW YORK STATE J. MED. 51: 1919 (Aug. 15) 1951.

TABLE II. Age and sex of patients with positive reactions to histoplasmin

Age (Years)	Mount View Hospital		Niagara Falls Hospitals	
	Male	Female	Male	Female
0 to 14	0	0	0	0
15 to 24	0	0	0	0
25 to 34	0	2	2	0
35 to 44	0	1	2	1
45 to 55	6	1	0	0
Over 55	3	3	4	1

free at the time of the x-ray examination. Another patient with a mediastinal nodular lesion also had a positive skin test reaction but at no time exhibited any signs or symptoms of active histoplasmosis. His complement fixation test also showed normal findings. Several other patients had complement fixation tests performed at the Albany State Laboratories, and the results were entirely negative.

Those patients who were admitted to Mount View Hospital had x-ray findings suggestive of pulmonary tuberculosis with the predominant lesion being either cavitary or exudative. Diffuse nodular or linear areas of opacification were found in a smaller number of individuals.

Cough, hemoptysis, and dyspnea constituted the initial symptoms in most of those patients who were admitted for suspected tuberculosis. A great majority of these patients had post-tussive rales, and a few had sibilant rales.

No cases of miliary tuberculosis were seen in our study, but one patient had concomitant active laryngeal and pulmonary tuberculous infection.

Summary

We have found that inactive asymptomatic histoplasmosis exists in Niagara County. The high yield of 10.5 per cent of positive reactors is unexplained, although almost one half of the patients in the group tested were admitted to the county sanitorium for suspected active tuberculosis. Although the presence of active tuberculosis and histoplasmin sensitivity in the same patient is uncommon, it is far from rare. In the entire series of 247 patients, 16 showed positive reactions to both tuberculin and histoplasmin.

Implanted jack corrects spine curvature

An operation in which a permanently placed jack is used to straighten curvature of the spine was described in an article by H. L. Wenger, M.D., in the December, 1961, issue of *Archives of Surgery*. Thirty-six patients have undergone the operation since 1954. Most of the patients left the hospital within two weeks with no external support necessary. However, the operation is reserved for persons with a crippling curve creating a great disability. The operation cannot help persons with a very rigid curvature.

The operation requires an incision in the chest and the back, and usually seven ribs are removed. An especially designed screw is placed at the upper and lower ends of the lateral curve. Then the turnbuckle jack, which can be elongated with a wrench, is attached to the screws on the concave side of the curve. As the spine jack is lengthened, the curved spine is straightened. The jack in its final position lies near the straightened spine and is locked in place. X-ray films are taken during the operation to visualize the spine.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
October 25, 1961

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by MAXWELL L. GELFAND, M.D.

Asthma, Arrhythmias, and Congestive Heart Failure

Case history

J. HIGBY FARTHINGTROUT, M.D.: A sixty-seven-year-old woman was hospitalized for the first time on May 25, 1959. For seventeen years she had suffered from attacks of dyspnea unrelated to the season or the time of day. She was considered to have bronchial asthma and was relieved by epinephrine. Four years before admission she first experienced palpitations independent of the asthma and lasting up to several hours. Two years later she noticed dyspnea on exertion and fatigability followed shortly by orthopnea and peripheral edema. All her symptoms were slowly progressive. Four months prior to admission digitalization was attempted but was stopped because of anorexia, nausea, and sharp epigastric pain which was unrelieved by food of antacids. During this latter period she lost 30 pounds.

Her first hospital admission was for paroxysmal atrial fibrillation with a ventricular rate of 180 beats per minute. The blood pressure was 135/90. The cardiac impulse was in the sixth intercostal space in the anterior axillary line. No murmurs were audible. The neck veins were distended and the liver enlarged, but there was no peripheral edema.

The laboratory studies revealed normal hemogram findings, slight albuminuria and pyuria, and normal liver function test findings. The nonprotein nitrogen was 30 mg. per 100 ml., and the total protein was 5.8 Gm. per 100 ml., with 3.2 Gm. albumin and 2.6 Gm. globulin. The serum sodium varied between 128 and 137 mEq. per liter and chlorides between 89 and 100 mEq. Serum potassium and bicarbonate were normal. A chest x-ray film showed a heart enlarged in the transverse diameter with slight fullness of the pulmonary conus and congestion of both lung fields. A roentgenographic study of the gallbladder and upper gastrointestinal tract was unrevealing.

The initial electrocardiograms confirmed the clinical impression of rapid atrial fibrillation. There was high voltage S-T segment depression in the left ventricular leads that was ascribed either to the rapid rate or to left ventricular hypertrophy. She was digitalized rapidly over a twenty-four-hour period and then was maintained on oral digoxin. The ventricular rate slowed, although paroxysms of rapid ventricular rate often occurred for no apparent reason. Subsequent electrocardiograms showed only minor increases in the S-T segment depression.

Although venous distention, hepatomegaly, and atrial fibrillation persisted, she felt well for several months, when nausea and epigastric pain recurred, and the ventricular rate increased. These signs and symptoms were not affected by changes in the dosage of digoxin. When digoxin was withdrawn, the ventricular rate increased to 180 beats per minute, and she was readmitted.

The physical examination showed findings essentially unaltered from those found on her previous admission except that crackling rales were now present at the lung bases since there was slight peripheral edema. The blood pressure was 135/95. The venous pressure at the antecubital fossa was 192 mm. water, and the circulation time with sodium dehydrocholate was 25 seconds. The nonprotein nitrogen had risen to 66 mg. per 100 ml. The serum sodium was 128 mEq., potassium 3.8 mEq., chlorides 95 mEq., and bicarbonate 19 mEq. per liter. The chest x-ray films showed no change in cardiac size or configuration. Septal lymphatic lines, the so-called B lines of Kerley, had appeared in the lower fields of both lungs, but the lungs were otherwise unchanged. Oblique and lateral projections confirmed the impression of fullness of the pulmonary conus but demonstrated no enlargement of the left auricle.

The cardiac rhythm varied between atrial fibrillation and atrial flutter with a 2:1 auriculoventricular block. There were no other electrocardiographic changes. She was redigitalized cautiously, and the ventricular rate slowed, but atrial fibrillation persisted.

The hospital course was relentlessly downhill. Edema progressed to anasarca despite salt restriction, mercurial diuretics, and chlorothiazide. The serum sodium fell to 118 mEq. per liter and was restored to 135 mEq. by water restriction and small amounts of oral salt. Icterus appeared, and the serum bilirubin rose to 4.5 mg. per 100 ml. The blood urea nitrogen rose to 96 mg. per 100 ml. The SGOT (serum glutamic oxaloacetic transaminase) was 65 units, but other liver function tests produced normal results. The total protein was 4.4 Gm. per 100 ml. with 3.3 Gm. albumin and 1.1. Gm. globulin. A loud apical systolic murmur appeared as did a pericardial friction rub. At one time the cardiac rhythm reverted spontaneously to a sinus rhythm, and high peaked P waves were noted in the electrocardiogram. There were no other significant changes. The patient died suddenly on September 15, 1959.

Discussion

Maxwell L. Gelfand, M.D.: This patient was apparently well until her fiftieth year, seventeen years prior to her rather untimely death, when she first developed so-called asthma. This continued episodically but nonetheless was progressively more severe for fifteen years before unmistakable signs of pulmonary insufficiency first became manifest. At this point signs and symptoms of congestive heart failure also developed. For a two-year period prior to her death symptoms related to heart failure progressed slowly. Four months prior to her admission to the hospital digitalization became necessary. The episode which first brought the patient into the hospital was paroxysmal atrial fibrillation. This event heralded the terminal phase of her illness which lasted only a few months.

It is clear from the protocol that the patient had long-standing bronchial asthma, most probably associated with emphysema. Two years before her entry to the hospital, signs of right-sided heart failure developed. It has been known since the eighteenth century that chronic lung disease ultimately can embarrass cardiac function, but it remained for Cournand and his coworkers in the past two decades to fill in the details of this process. Chronic cor pulmonale is more common than statistical studies indicate, but inasmuch as it occurs at an age when both coronary arteriosclerosis and hypertension appear, it is frequently unrecognized. Long-standing bronchial asthma almost invariably leads to emphysema, and emphysema in turn leads to pulmonary hypertension.[1] Precisely how the increased pulmonary vascular resistance leads to hypertrophy of the right ventricle is a matter of debate, but changes in the pulmonary vasculature certainly are associated commonly with the process.

The physical signs and symptoms of chronic cor pulmonale may be divided into two phases: (1) an early pulmonary, or precardiac phase, and (2) a later cardiac phase. Cough, expectoration, dyspnea, cyanosis, clubbing of the fingers, polycythemia, flaring of the ribs, and fixation of the diaphragms are characteristic of the first phase. Engorged veins, a large tender liver, and peripheral edema are characteristic of the second phase. Further corroboration of right ventricular strain is to be noted by the x-ray finding of fullness of

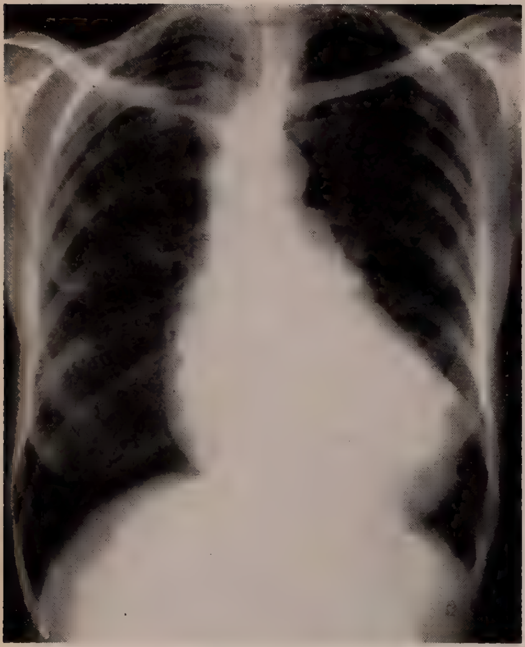

FIGURE 1. Roentgenogram of chest at time of first admission showing generalized cardiac enlargement. The apex is displaced downward, to the left, and posteriorly.

the pulmonary conus. In some patients with cor pulmonale the electrocardiographic changes are helpful, but not in this instance. In fact, the electrocardiogram findings suggested left ventricular hypertrophy in addition to atrial fibrillation. At one time it was believed that atrial fibrillation did not occur in chronic cor pulmonale, but recently it has been shown to develop with some frequency.[2] It is also of some interest to note that patients with cor pulmonale, when developing manifestations of congestive heart failure is of another cause. There is also a greater degree of digitalis intoxication in this condition. These latter features are exemplified by our patient.

The second admission was characterized by signs of biventricular failure, still predominantly right-sided, plus the added feature of azotemia. At this point we might look at the x-ray films.

Joseph M. Moynahan, M.D.: A radiographic examination of the chest revealed moderate generalized cardiac enlargement. The posteroanterior (Fig. 1) and left anterior oblique projections revealed displacement of the apex downward, to the left, and posteriorly, suggesting left ventricular enlargement. The right anterior oblique view revealed prominence of the pulmonary conus, and a lateral view showed encroachment on the retrosternal space, both observations suggesting right ventricular enlargement. The esophagus was displaced posteriorly due to the generalized enlargement of the heart, but there was no disproportionate enlargement of the left atrium. There was a moderate increase in the pulmonary markings, especially on the initial study, consistent with mild congestive changes.

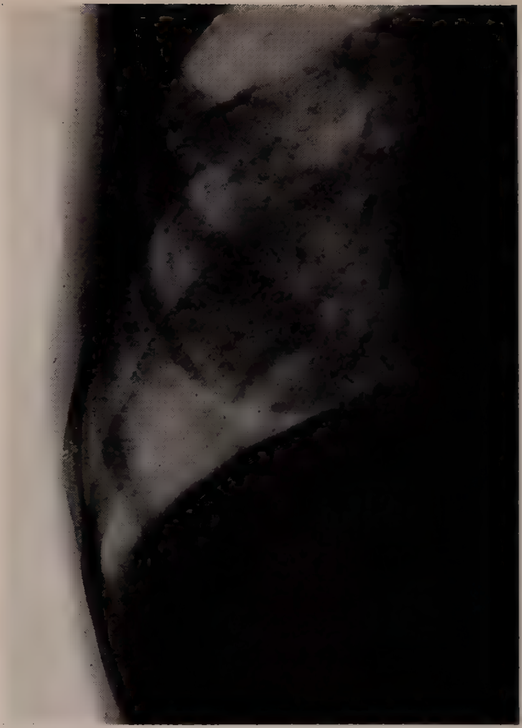

FIGURE 2. Detail of chest roentgenogram during the second admission showing the B lines of Kerley, short straight linear densities above the costophrenic angle running perpendicular to the pleura.

A few scattered fine, short, straight, relatively dense lines were noted in the pulmonary parenchyma just above both costophrenic angles, extending perpendicular to the pleura. These are the so-called B lines of Kerley (Fig. 2). They are of importance since they indicate interstitial edema of the lungs and a critically high pulmonary venous pressure.

Dr. Gelfand: If these are B lines of Kerley, what are A lines of Kerley?

Dr. Moynahan: The A lines are similar in character and are seen in the central lung fields, but they are observed much less frequently than the B lines. They tend to be longer and are frequently curved or sharply angulated and may even simulate the picture of cystic disease of the lungs. However, they have the same pathophysiologic significance as the B lines, namely, pulmonary edema and critically high pulmonary venous pressure.

Hirsch Kirsch, M.D.: Are these lines seen in any condition other than heart disease?

Dr. Moynahan: They are most common in chronic passive congestion of the lungs with a high pulmonary venous pressure. A typical situation would be mitral stenosis with right-sided heart failure. However, they also may be seen in cases with lymphatic obstruction caused by mediastinal node involvement in carcinoma, lymphoma, or other conditions.

Kim Shane, M.D.: Was there any x-ray evidence of pulmonary emphysema?

Dr. Moynahan: There were no bullae, and there was no "brightness" in the upper lung fields, nothing really to make a diagnosis of emphysema radiologically valid. However, we all know that a patient can have extensive emphysema and an unimpressive chest film.

Dr. Gelfand: Well, there seems to be no doubt about the increased pulmonary tension. Before I attempt to discuss its etiology, let me consider the patient's rising azotemia. It may represent decreased cardiac output and an inadequate glomerular filtration pressure. The observation that pyuria and mild albuminuria were present makes me suspect intrinsic renal disease, possibly pyelonephritis, which is so common in females. Precisely why this patient did not have the hypertension that is so common in chronic nonobstructive pyelonephritis is obscure. Also, I do not know whether to attribute the friction rub heard terminally to her azotemia or to some intrathoracic disturbance, but I shall bet on the former.

The terminal phase of the patient's illness was characterized by transient improvement, then a rapid downhill course followed by sudden death, or at least unexpected death. There are several reasons why patients with heart trouble die suddenly: (1) improper diagnosis, (2) inadequate or excessive treatment, (3) electrolyte imbalance with renal failure, (4) associated systemic infection, (5) superimposed cardiac infection, such as endocarditis or myocarditis, (6) myocardial infarction, and (7) pulmonary or systemic embolization. From this list and from the data in the protocol it appears that our patient may have had several of these factors operating in concert. The electrolyte imbalance apparently was corrected, but that is no guarantee against further cryptic renal damage. However, the presence of an elevated SGOT and an elevated serum bilirubin in close proximity to sudden death makes me focus my attention on either a myocardial infarct or a pulmonary embolus. The absence of chest pain does not exclude either possibility. In favor of a myocardial infarct are the elevated SGOT, the pericardial friction rub, and the sudden death. If so, we must explain the elevated serum bilirubin by chronic passive congestion of the liver, possibly to the point of cardiac cirrhosis, and the systolic murmur on the basis of dilatation of the mitral valve ring. Recently, Wacker *et al.*[3] have proposed a triad purporting to be diagnostic of pulmonary embolism. The triad consists of elevated LDH (serum lactic acid dehydrogenase), elevated serum bilirubin, and a normal SGOT. Since an LDH determination was not done, we cannot fit this patient into this triad. Also, I can explain the elevated SGOT and elevated serum bilirubin on the basis of right ventricular failure and central congestion and necrosis of the liver. Actually, I think this triad can be misleading. In the long run pulmonary emboli with infarction are more likely to be silent than is myocardial infarction, even when there are multiple pulmonary emboli over a long period of time. A patient with chronic cor pulmonale and an atrial arrhythmia is very likely to have a thrombus in the right atrium which is a very suitable source for multiple pulmonary emboli.

As long ago as 1935, McGinn and White[4] emphasized a number of physical signs of pulmonary embolus and infarction over and above the "classical triad" of dyspnea, chest pain, and hemoptysis. These are: (1) pulsation in the second left intercostal space, (2) an accentuated pulmonic second sound, (3) a pleuropericardial friction rub, (4) distended jugular veins, (5) increased cardiac dullness to the right of the sternum, (6) gallop rhythm heard best at the pulmonic area, and (7) an enlarged liver. I can see little in the protocol that is inconsistent with this possibility, and my suspicion of multiple pulmonary emboli is strengthened by the patient's failure to respond to digitalis.

Owen *et al.*[5] described the syndrome of chronic cor pulmonale due to multiple unrecognized emboli to the lungs. In their group of 12 patients collected from twenty years of autopsy experience there were 7 women and 5 men ranging in age from thirty-two to seventy-two years. The duration of the episodes of embolization ranged from a few weeks to seventeen years. The major symptoms were cough, dyspnea, and cyanosis. Polycythemia was present in only a few patients. X-ray films of the chest showed right ventricular hypertrophy with prominent hilar vessels but clear lung fields. Most of the cases were not diagnosed clinically, an observation that should make one versed in the art of CPC-manship highly suspicious.

In any event, I shall make this my primary diagnosis. What other conditions could mimic this picture? Primary pulmonary hypertension should be considered, but when there is such a likely source of emboli as the right auricle in cor pulmonale, I must avoid the pitfall of "essential hypertension of the lesser circuit."

Persistent cardiac failure and a complex pattern of arrhythmias which do not respond well to the usual measures might be due to some of the less common forms of heart disease, such as amyloidosis, any one of a variety of myocarditides, or some form of collagen disease. However, there is very little positive evidence in the protocol to implicate any of these, and I shall dismiss them.

Michael S. Bruno, M.D.: Dr. Gelfand mentions the diagnosis of emphysema as the underlying cause of pulmonary hypertension and eventually the development of chronic cor pulmonale. How does one relate this diagnosis to the radiographic findings?

Dr. Moynahan: One cannot make the diagnosis of emphysema by x-ray in this case, but one cannot exclude it.

Dr. Bruno: While we all accept the fact that there are tremendous pitfalls in making the diagnosis of emphysema radiographically, I am still disturbed by the almost total lack of other manifestations of this condition. What were the auscultatory findings during the latter part of this patient's hospital course?

Perry Berg, M.D.: The breath sounds were not remarkable. There certainly was no clear-cut evidence of pulmonary emphysema at physical examination.

Dr. Bruno: If that be the case, the very diagnosis of pulmonary emphysema could be questioned seriously and, as a corollary, the diagnosis of chronic cor pulmonale as well.

Marcel Tuchman, M.D.: Dr. Gelfand, would you consider any other source other than the right side of the heart for the pulmonary emboli that this patient ostensibly had?

Dr. Gelfand: From a purely statistical point of view the leg veins and those of the pelvis more commonly would be the source of emboli, but in this particular case we have no reason to localize our thrombosis in these sites. The right side of the heart seems to be the most logical source for pulmonary emboli if that is what she had.

Dr. Bruno: When do you postulate that this patient started to embolize?

Dr. Gelfand: Possibly many years before her final admission. Her attacks of so-called asthma might well have represented instances of bronchospasm secondary to repeated small pulmonary emboli. I would suspect that this process had been going on over a period of years.

Vincent Vinci, M.D.: What is the mechanism for the development of arrhythmias in chronic cor pulmonale?

Dr. Gelfand: The most prevalent view is that the arrhythmias are due to the presence of anoxia and pulmonary hypertension.

Ren´ Silva, M.D.: Are you not disturbed by a lack of electrocardiographic evidence of right ventricular hypertrophy in view of

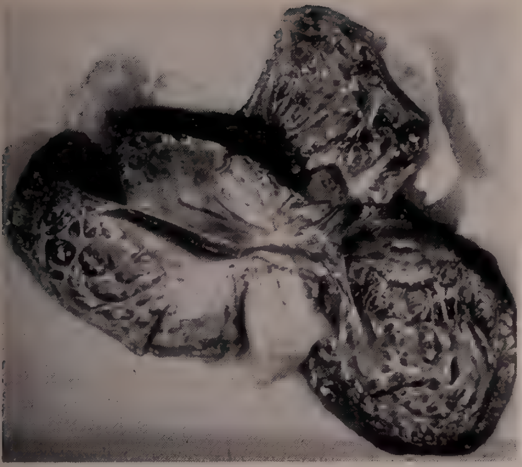

FIGURE 3. At autopsy the heart weighed 340 Gm. and was greatly dilated. There was diffuse thickening and opacity of the endocardial surface of the left ventricle, maximal in the posteroseptal region, and of the right ventricle, also in the posteroseptal region. Valvular lesions were not present.

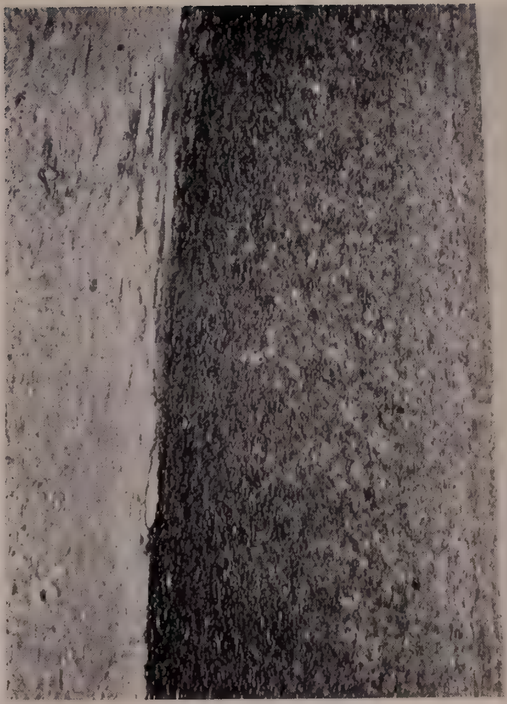

FIGURE 4. The mural endocardium of the left ventricle shows a severe degree of thickening, the consequence of proliferation of collagen and elastic fibers. Verhoeff-van Gieson stain.

your proposed diagnoses?

Dr. Gelfand: This is a disturbing point, but during the latter part of her hospital stay she did have prominent P waves, an indication of pulmonary hypertension.

Clinical diagnoses

1. *Rheumatic heart disease with mitral insufficiency*
2. *? Heart disease of unknown etiology*

Dr. Gelfand's diagnoses

1. *Chronic cor pulmonale secondary to multiple pulmonary emboli*
2. *Mural thrombus, right side of heart*
3. *? Pulmonary emphysema*

Pathologic report

William B. Ober, M.D.: The lungs did contain multiple pulmonary infarcts, both old and recent, in all lobes. There was even a fresh antemortem thrombus coiled in one of the dissectible branches of the right pulmonary artery. However, this is not quite the picture described by Owen *et al.*[5] and Castleman and Bland[6] of multiple emboli to tertiary branches of the pulmonary artery tree with subsequent organization. medial hypertrophy of large segments of the pulmonary arterial bed, and the stigmata of pulmonary hypertension. As Dr. Gelfand pointed out, this picture mimics closely primary pulmonary hypertension, and there is still debate whether some of the peculiar configurations seen in the small pulmonary arteries represent congenital arteriovenous anastomoses or organizing emboli. The picture seen in this case more closely resembles the type of situation not uncommonly seen in rheumatic heart disease when somewhat larger embolic thrombi gain access to the lesser circulation over a period of time. These usually are derived from an auricular thrombus, and they produce large infarcts, such as the ones we encountered in this patient. In such patients there is usually pulmonary hypertension, but the congeries of pulmonary arterial changes seen in the Castleman-Bland type of case is not present.

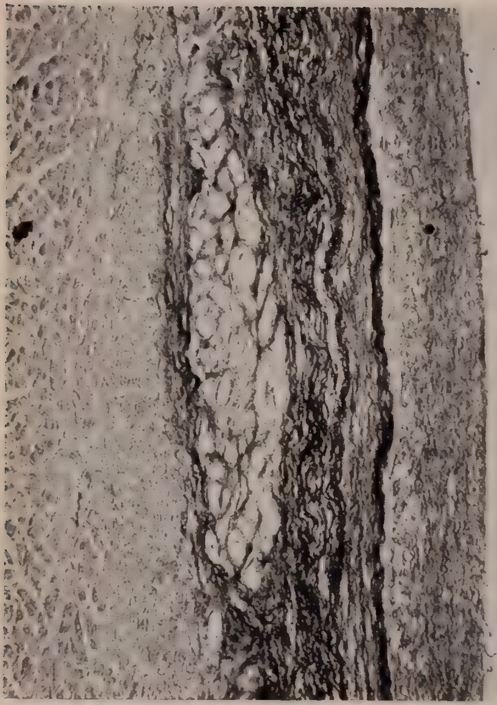

FIGURE 5. Similar proliferation of connective tissue fibers involves Purkinje tissue at the base of the interventricular septum. Verhoeff-van Gieson stain.

The source for emboli in the present case was a large mural thrombus impacted in the right auricle, presumably the consequence of the cardiac arrhythmias. Indeed, the heart is the central feature of the case. It weighed 340 Gm. and was markedly dilated but not conspicuously hypertrophied. There were no lesions in the myocardium or the valves. The principle lesion consisted of a diffuse endocardial thickening, maximal over the left ventricular aspect of the interventricular septum and posterior wall of the left ventricle, but present to some degree diffusely in the lining of that chamber (Fig. 3). Endocardial thickening also was present on the right ventricular aspect of the interventricular septum and portions of the posterior wall of the right ventricle. Elsewhere, the right ventricular endocardium was normally thin and translucent. A few small, scattered patches of endocardial thickening were seen in the lining of the left auricle. Microscopically, the lesion was that of endocardial fibroelastosis (Fig. 4), and sections through the base of the interventricular septum showed infiltration of Purkinje tissue by the proliferation of collagen and elastic fibers (Fig. 5). The left coronary artery tree was normal in size and distribution; only at one point about 5 to 6 cm. from its origin was there significant narrowing of the lumen by arteriosclerosis. However, the right coronary artery was markedly hypoplastic, and there was moderate fibrous thickening of its intima. At its origin the right coronary artery measured barely 1 mm. in total diameter, and its lumen was about half that size. Its visible branches were small in proportion to the main artery.

Endocardial fibroelastosis is a well recognized albeit uncommon congenital cardiac lesion. When found in older children or young adults, it is considered an instance of late survival of the congenital form of the disease. A majority of the reported congenital cases are associated with valvular deformities. However, when the lesion is found in an adult who was in good health until the age of fifty, one must consider it an acquired lesion. A review of the literature indicates that valvular lesions are not present in the adult form of the disease, and in only 1 case was there a significant myocardial malformation.[7] Many theories have been advanced to explain the pathogenesis of endocardial fibroelastosis.[8] In the present case hypoplasia of the right coronary artery lends some degree of support to theories involving continuous low-grade hypoxia to the endocardium. This support is reinforced by the observation that in the present case the endocardial thickening was maximal in areas normally supplied by the right coronary artery. However, the fact that this hypoplasia of the right coronary artery must be construed as a congenital malformation blurs somewhat the distinction between congenital and acquired forms of the disease.

In addition to the cardiac and pulmonary lesions, this patient also had a large peptic ulcer of the duodenum which had penetrated the posteromedial wall and which was lying in apposition to the pancreas. So far as I can tell it was completely asymptomatic. She also had a large adenomatous polyp of the endometrium and a medium-sized adenomatous polyp of the endocervix, neither of which had produced any symptoms. The kidneys showed a moderate degree of banal benign nephrosclerosis, entirely appropriate in a sexagenarian and insufficient to explain the rising azotemia.

Anatomic diagnoses

1. *Endocardial fibroelastosis, adult type*
2. *Cardiac dilatation*
3. *Hypoplasia, right coronary artery tree*
4. *Mural thrombus, right auricle*
5. *Pulmonary emboli and infarcts, old and recent*
6. *Peptic ulcer, duodenum, large, penetrating to pancreas*
7. *Adenomatous polypi, endometrium, endocervix*
8. *Benign nephrosclerosis*

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Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the New York State Journal of Medicine from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the Journal, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

Sponsored by the
Clinical Society of the
New York Diabetes Association

Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Diabetes and Infection

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IT IS GENERALLY accepted among physicians that diabetic patients are more susceptible to infection than are nondiabetic patients of equivalent age, sex, race, or economic status, and furthermore that when infection occurs in such patients it is apt to be more severe and fulminating. This impression is attributable to a number of older statistical surveys wherein a significantly higher incidence of staphylococcal, tuberculous, and genitourinary tract infections had been reported in diabetic than in nondiabetic individuals. Despite this presumed hypersusceptibility to infection, when the causes of death of 307 diabetic patients over the age of twelve were compared with those of 2,800 consecutive nondiabetic cases in 1944,[1] the relative incidence of pulmonary and other infections found at autopsy was approximately the same in both groups. The only exceptions to this were acute pyelonephritis and infections of the extremities, both of which were observed more frequently among diabetic patients. With regard to these latter infections, however, other factors might have been operative. Patients with diabetes are subjected to more frequent catheterization, and this procedure is undoubtedly associated with an increased risk of urinary tract infection. They also are more prone to vascular degenerative disease which in turn may alter kidney function and lead to neurologic disturbances affecting bladder function and stasis, an important contributory factor in the pathogenesis of urinary tract infection. In the same way, a diminished blood supply to the extremities resulting from vascular involvement probably renders diabetic individuals more liable to peripheral infections.

In view of the current availability of improved methods for the management of the basic disease as well as of effective prophylactic and therapeutic anti-infective agents, it is doubtful that the earlier observations with respect to diminished resistance on the part of diabetic patients to infection still pertain. More up-to-date studies directed toward this problem would be of great value in providing more definitive information in this regard. This is especially important since the question as to whether or not diabetic individuals are inherently more susceptible than normal individuals to infection has never been resolved satisfactorily. Many complex factors are involved in susceptibility or resistance to infection, and much of the experimental evidence is conflicting and far from conclusive.

There is little reason to believe that hyperglycemia per se increases susceptibility to infection. The addition of up to 1 per cent glucose to blood does not enhance the rate of growth of staphylococci in culture,[2] nor does the inclusion in the culture medium of plasma with increased sugar content obtained from rabbits with alloxan diabetes enhance the growth of pneumococci in vitro as compared with plasma obtained from normal control rabbits.[3] Cruickshank[4] found no clear-cut or significant deviation in the survival rate or course of bacteremia following intravenous injection of pneumococci, staphylococci, and tubercle bacilli in rabbits rendered diabetic with alloxan as compared with normal control animals. With respect to specific immune mechanisms, some evidence of decreased antibody production on the part of diabetic subjects as compared with normal subjects had been noted. Thus, Bates and Weiss[5] found antibody development to staphylococcus toxin to be delayed as well as lower in titer in diabetic children than in a similar group of normal children. These authors found, however, that the antibody production of the diabetic children whose disease was under control was equivalent to that of normal children in contrast with those poorly controlled who demonstrated a definitely retarded and diminished production of antistaphylolysin. Similarly, Richardson[6] observed a lower antibody titer in the sera of 40 diabetic patients than in the sera of a similar number of controls following the administration of typhoid vaccine as an antigen. Considering antibody production in general, the major part of the antibody content of serum is contained in the gamma globulin fraction, and diabetic individuals have never been shown to be hypogammaglobulinemic as a group. Diabetic whole blood regardless of its blood sugar level, possesses a weaker bactericidal activity against a variety of pathogenic organisms than does blood obtained from normal individuals.[6] However, two thirds of the diabetic patients included in this series failed to demonstrate a decreased blood bactericidal activity. With regard to serum complement, no decrease in the blood complement titer was found in a series of diabetic patients, irrespective of their blood sugar levels or whether or not insulin was being administered.[6] In dogs rendered diabetic by pancreatectomy, however, a marked decrease in the serum complement titer has been claimed to prevail.[2]

No measurable defect in the properdin system, which is intimately concerned with resistance to infection, has been observed among diabetic subjects.[7,8] In fact, a mean properdin level of 10.57 units was found among the diabetic patients studied as compared with 5.24 for a series of patients with a variety of other illnesses, and 6.35 for normal subjects in the latter report. That the patient's nutritional state may play a role in his susceptibility to infection is evidenced by the fact that underfed rabbits with depleted liver glycogen produce definitely lower agglutinin titers to typhoid vaccine than do well-fed controls with high liver glycogen[9] and that there is a significant correlation between the amount of glycogen in the liver of normal rabbits and depancreatized dogs and the survival time after the intravenous inoculation of staphylococci.[10] Finally, some observations by Dubos[11] and by Perillie, Nolan, and Finch[12] offer interesting explanations that might account for the assumed increased susceptibility of diabetic patients to infection in the light of the metabolic disturbance associated with ketosis existing in this disease. Staphylococci and tubercle bacilli were found by Dubos to die very rapidly at acid reactions in media containing 0.01 M. or smaller concentrations of lactic acid, which is known to accumulate in inflammatory areas and be produced by normal leukocytes in vivo. Nevertheless the organisms mentioned survived longer under the same conditions in the presence in the fluid suspension of some acids but more particularly of certain ketone bodies. Perillie and his associates,[12] for their part, have shown that the early granulocytic phase of the local cellular response is significantly delayed and diminished in patients with diabetic acidosis as compared with normal subjects and nonacidotic diabetic patients. The latter observations as well as some previously cited serve to emphasize the fact, which is well borne out in clinical experience, that it is the diabetic patient in ketosis rather than the well-controlled patient who is susceptible to microbiologic infection.

Infectious processes associated with diabetes

A number of infectious processes often associated with the diabetic state have aroused considerable interest within the past two decades particularly among physicians concerned with the management of this disease. These include mucormycosis, bacteremia with gram-negative bacilli, and nonclostridial gas infection.

Mucormycosis. With regard to mucormycosis, all three genera of the family Mucoraceae, namely, rhizopus, mucor, and absidia, may be the etiologic agent for this mycotic infection. It was first reported in the United States by Gregory, Golden, and Haymaker in 1943,[13] and it is noteworthy that 2 of the 3 cases included in this report were known to have diabetes and both were in acidosis and coma at the time of admission. Since then further attention has been directed toward its characteristic association with uncontrolled diabetes, although other diseases and other factors such as leukemia, debilitating disease, and the administration of certain therapeutic agents, as for example steroids, antileukemic agents, and antibiotics, also play a contributory role.[14,15]

Rhizopus, the genus most often involved, a ubiquitous mold often found on bread and fruits, ordinarily is considered to be saprophytic and to date no satisfactory explanation has been forthcoming to account for its enhanced invasiveness and pathogenicity. The route of infection is usually by way of the nose, paranasal sinuses, or orbit, following which rapid intracranial involvement with thrombosis and infarction ensues. Pulmonary, ocular, intestinal, as well as disseminated forms also occur, and diabetes is similarly associated with these forms as well in a considerable proportion of cases.

Unlike other systemic fungal infections the onset and clinical course of which are usually chronic in nature, mucormycosis is characterized by a sudden onset and a short duration, fatal cases lasting only from one day to a month with but rare exception. Most of the cerebral cases succumb rapidly. The important aspect of this mycosis is its association not with diabetes per se but with uncontrolled and acidotic diabetes. Experimentally, no difference has been noted in the susceptibility of normal rabbits and rabbits in the chronic phase of alloxan diabetes to induced infection with rhizopus. However, fulminating mucormycosis closely resembling the fulminating lesions found in human mucormycosis, was readily producible in rabbits in the acute state of alloxan diabetes.[16] Although the toxic factor responsible for the pathogenesis of this disease has not been established definitely, it is pertinent that rabbits in the chronic phase of alloxan diabetes ordinarily do not exhibit ketosis whereas rabbits in the acute toxic phase do.[16]

Because of the etiologic association of uncontrolled diabetes with this fungal disease, a most important step in its treatment consists of the institution of prompt measures to control both the basic disease and the acidosis. Because of their possible etiologic role, the use of steroids and antibiotics should be discontinued whenever possible. Although the true therapeutic effectiveness of such antifungal agents as nystatin and amphotericin B against mucormycosis has not been established, no alternative remains but to institute treatment with either of these compounds, preferably the latter.

BACTEREMIA DUE TO GRAM-NEGATIVE BACILLI. A significant proportion of diabetic patients, from 10 to 18 per cent, have been among the cases of bacteremia due to gram-negative bacilli included in a series of reports on this disease state.[17-21] The high incidence among diabetic patients, however, does not in itself necessarily indicate a decreased resistance on the part of these patients to infection with the organisms involved, namely, Escherichia coli, Aerobacter aerogenes, Pseudomonas aeruginosa, and the Proteus species. Rather this may be a reflection of the greater frequency of urinary tract infections in diabetes in view of the fact that the portal of entry of the infective microorganism into the blood was the genitourinary tract in a high percentage of these cases. In addition, diabetic individuals are subjected more often to catheterization, a procedure not infrequently followed by blood-stream invasion. Blood cultures should be performed on all diabetic patients with unexplained fever, especially those with a history of obstruction or recent manipulation or surgery of the urinary tract. A culture positive for gram-negative bacilli provides the diagnosis as well as the material for determining the antibiotic sensitivity of the offending microorganism or microorganisms. These infections may pursue a rapidly fatal course, and treatment should be started promptly and empirically with a broad-spectrum antimicrobial agent known to include gram-negative bacilli within its spectrum of activity, as for example chloramphenicol, tetracycline, streptomycin, neomycin, polymyxin, and so forth. If such therapy fails to elicit a satisfactory response, other chemotherapeutic agents to which the etiologic organisms are maximally sensitive by laboratory tests should be substituted when the latter become available. Bacteremia with gram-negative bacilli not infrequently results in the production of "septic shock" which may present a problem in differential diagnosis since shock can develop in diabetic patients from other causes related to the existing metabolic disturbance. Frequent blood pressure determinations should be made to detect impending bacteremic shock, and when indicated, vigorous measures to combat this potentially serious complication should be instituted.

NONCLOSTRIDIAL GAS INFECTIONS. Nonclostridial gas infections usually involve the extremities and are characterized by a rapidly spreading course.[22,23] Gas in varying amounts is produced in the tissue so that the process may simulate closely that observed in clostridial gas gangrene. The microorganism most often involved is Escherichia coli, either alone or in association with other bacteria, both aerobic and anaerobic. Escherichia coli readily produces gas on media containing carbohydrate in culture, and the increased glucose content of the tissue in diabetes, acting as a substrate, may well be responsible for the production of greater amounts of gas which may then become clinically crepitant. The impaired circulation resulting from the vascular involvement often associated with diabetes may provide favorable conditions for enhanced metabolism and growth of these organisms with a resultant increase in gas production and may similarly interfere with the absorption of the gas formed. Roentgenograms are of value in recognizing the presence of gas as well as in determining the limits of its spread. A smear and culture of the lesion should be performed promptly to identify the organism or organisms involved and to exclude a possible clostridial causation wherein treatment with specific clostridial antiserum would be indicated. In addition to the management of the basic diabetic condition, early and adequate surgery, general supportive measures, and the prompt, adequate administration of appropriate broad-spectrum antimicrobial agents are indicated to treat this condition.

Diabetic patients have not been reported as being singularly disposed to viral infections, and such infections in patients with this disease are not necessarily more severe or fulminating than in other individuals. An elevated mortality rate from influenza has been reported in certain population groups attributable chiefly to secondary bacterial infection. Because of their presumed hypersusceptibility to staphylococcal infection, diabetic patients have been included with pregnant women, normal persons over the age of sixty-five, and patients with chronic debilitating disease, rheumatic heart disease, cardiovascular disorders, and Addison's disease among those recommended by the Surgeon General of the United States Public Health Service to receive prophylactic immunization with polyvalent influenza vaccine. However, evidence for an elevated mortality rate from influenza among diabetic individuals is far from conclusive.

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Number thirty-four in a series of articles on Current Concepts in Diabetes Mellitus

Flashlight used to find brain defects in babies

An ordinary flashlight is being used routinely to find brain defects in infants examined at Massachusetts General Hospital, according to an article by Philip R. Dodge, M.D., and Philip Porter, M.D., in the December, 1961, issue of *Archives of Neurology*, published by the American Medical Association.

The flashlight which illuminates the cranial cavity has aided the diagnosis of a variety of cerebral abnormalities. The authors urged wider application of the method, which is termed transillumination and was employed as early as 1831 by Richard Bright with sunlight and candle.

In the newborn or very young infant, transillumination may be the only definite way to find whether or not anything is amiss. The technic can be useful in following the course of a brain condition. A two-battery flashlight with the glass lens removed and a soft rubber cup attached for contact with the baby's head was used. The examinations were done in a dark room, and color photographs of the illuminated brain were taken with flashbulbs. The technic was generally successful in all infants up to one year old although the color of the hair and the complexion of the skin influenced the results.

Clinical Rehabilitation Conference

Prepared by the Department of Rehabilitation Medicine,
The Albert Einstein College of Medicine,
Bronx Municipal Hospital Center, New York City

EDWARD F. DELAGI, M.D., and
HEINZ I. LIPPMANN, M.D., Editors

Patellectomy

EDWARD F. DELAGI, M.D.: Today we have a problem of rehabilitation after a knee injury and orthopedic operation. Will the student please present the case.

Case history

This is the first Bronx Municipal Hospital Center admission, on August 18, 1961, of a sixty-one-year-old previously healthy Negro female who was seen shortly after sustaining a fall on her right knee. A physical examination revealed a painful swollen right knee with an effusion. A roentgenographic examination showed what looked like a transverse fracture of the right patella. Three days after admission the patella was found to be comminuted and was removed in toto, and the quadriceps mechanism was repaired. The postoperative course was uneventful, and the patient began to ambulate on crutches with partial weight-bearing six days postoperatively. She was discharged one month postoperatively on September 19, on partial weight-bearing, on crutches with a long snug plaster cylinder to her right lower extremity. The plan was to follow her in the outpatient clinic.

When the cylinder was removed four weeks later on October 18, the quadriceps was found to be markedly atrophied, and only 5 degrees of active or passive knee flexion were possible. There was much knee swelling and effusion, and the joint was hot and painful. The patient was readmitted to Jacobi Hospital, Department of Rehabilitation Medicine. After one week's treatment consisting of active exercise in a whirlpool at 110 F., the range of passive knee flexion increased to 20 degrees. She was placed in a Thomas suspension to favor flexion, and exercises were continued for another few days. Thereafter she received active and active-assistive exercises progressing to active-resistive exercises in a Hubbard tank. However, very little increased flexion resulted from this procedure. Therefore, manipulation under general anesthesia was carried out by the orthopedists on November 8, 1961, twenty-one days after the second admission. Eighty degrees of flexion (from 0 to 80 with the anatomic position considered zero) were obtained. Immediately after the operation knee extension was complete, but flexion remained limited to 60 degrees. Presently the patient is receiving physical therapy and other modalities of rehabilitation medicine. Today, that is, one week after the lysing of the adhesion, much of the inflammation of the knee and the effusion has regressed, but the range of motion outside of the Hubbard tank has remained unchanged at 60 degrees (180 through 120 degrees, with the anatomic position considered 180).

DR. DELAGI: Thank you. May we see the x-ray films?

JEROME GRISTINA, M.D.: On the preoperative roentgenograms a transverse fracture of the patella was diagnosed. However, on operation it was found that the patella was fractured in 8 pieces, and it was removed.

Dr. Delagi: May we see the patient? (The patient is wheeled into the conference room, and an examination shows a warm right knee joint with some effusion. There is conspicuous wasting of the right thigh musculature. Knee flexion is limited from normal extension to maximum 60 degrees of passive flexion [range 180 to 120]). As far as can be judged by manual testing, the knee muscles have fair to good strength. The patient appears to guard her knee during these motions because of some pain. (The patient is wheeled out of the conference room).

Dr. Delagi: Dr. Gristina, will you kindly comment on the operative management of patella fractures.

Operative management of patella fractures

Dr. Gristina: There are two types of patella fractures. One is the comminuted fracture resulting from a fall on the patella itself, and the other is the transverse fracture said to be caused by a vehement contraction of the quadriceps with the knee in partial flexion. The typical history leading to the former is that of a fall which causes the knee to hit on hard ground. The typical history of the latter is that of a nonconditioned individual who trips while descending stairs and violently contracts the quadriceps muscle in an attempt to avoid falling; he may feel a snap in the knee which buckles without control. If a transverse fracture involves the lower end of the patella which does not articulate with the knee joint, it may be treated with the removal of this lower fragment only. If the transverse fracture is a little higher than the center which forms part of the anterior aspect of the knee joint, wiring of the fragments is usually done. These wired fragments have to withstand considerable force during the physiologic contraction of the quadriceps while the patient walks up a hill or stairs. In a comminuted fracture, it may be difficult to obtain complete healing of the patella. Some orthopedists prefer to remove the patella entirely under these circumstances.

Medical Student: Can the patella be removed without disturbing knee function?

Heinz I. Lippmann, M.D.: The patella contributes to the efficiency of knee function by increasing the angle at which the patellar tendon inserts into the tibia and thereby insures the mechanical advantage of extension in the knee. The power of the quadriceps to extend the knee grows gradually with the degree of knee extension and is most effective in the fully extended position. Contrariwise, the more the knee is bent, the less effectively is the quadriceps pull transmitted to the tibia.[1] The effectiveness of quadriceps extension power is diminished at all angles if the patella is removed. Not too long ago it was believed erroneously that the patella was a sesamoid bone and a phylogenetic remnant with no useful function.[2] After patellectomy, not much disturbance in function of the knee may actually be noticeable, but some weakening of the normal reserve strength of the knee extensor mechanism can be demonstrated. We have seen patients develop quadriceps atrophy after patellectomy in spite of little visible limitation of function. Incidentally, the changed silhouette of the knee without patella may be unsatisfactory cosmetically, especially to women. Among the patellar fractures not mentioned before are those rather disabling ones which involve the joint surface only. These "osteochondral" fractures may give rise to loose joint bodies and may interfere with the normal functioning of the knee joint.

Visiting Physician: This patient wore a cylindrical cast for more than six weeks. Is immobilization usually extended that long? Does the prolonged casting account for the extreme quadriceps atrophy in this patient?

Alfred Ebel, M.D.: This patient probably had so much knee synovitis initially that immobilization had to be prolonged. In our hospital, in similar cases the knee is usually immobilized no more than from two to three weeks, and then we find atrophy and limitation of knee motion as well, but perhaps not to such an extreme degree. It may be that the initial pathologic condition made it necessary to prolong the immobilization here.

Medical Student: While the patient has a plaster cylinder immobilizing the knee, what can be done to maintain the musculature?

Quadriceps-setting exercises

Resident: We usually prescribe quadriceps-setting exercises in such cases. This literally means isometric exercises, contracting the muscle strongly without significant motion, for instance by lifting the whole casted leg to a point where the heel just touches the bed and not further, with or without resistance effected by a therapist or by a weight. In practice, however, we often have the patient lift his whole leg through as much hip flexion as possible with the plaster cast on.

Dr. Delagi: With the knee in plaster do you contract the entire quadriceps femoris by this maneuver?

Resident: No, only the rectus femoris portion of the quadriceps and of course the iliopsoas and abdominal muscles.

Medical Student: When I saw the patient some weeks ago in the orthopedic ward she did not exercise effectively. It looked as though she had not learned how to do it.

Nicholas Panin, M.D.: Your question raises an important point. We believe that, when possible, the patient should be taught quadriceps-setting exercises before an operation so that the exercise is familiar before the pain arising from arthrotomy makes learning this procedure more difficult. The patient should be urged to continue quadriceps setting just the way he learned it before the operation, as soon as possible after the operation, and as often as 10 times every waking hour until the cast comes off weeks later. We believe that this procedure shortens the total period of recovery to full function. We have often not been satisfied with the results if the patient had to be taught only after the operation, because somehow he does not learn it effectively. Of course this does not apply here since we are discussing a traumatic injury.

Dr. Delagi: I might add that it is difficult to teach this kind of exercise at a time when the plaster cast does not permit inspection of the contracting muscle. Dr. Ebel, would you comment on the technic of muscle maintenance, based on the so-called cross exercise effect?

Dr. Ebel: It is said that vigorous exercise of the contralateral identical muscle, in this case the contralateral quadriceps, will provide training by some sort of reflex participation. We have investigated this problem electromyographically and have found that if any activity takes place it is minimal in quantity. In fact, we found that the antagonist, in our case the hamstring, would contract strongly if the contralateral quadriceps contracted. We could demonstrate that this represented the patient's attempt to stabilize his body, and it does not indicate any "reflex activity." The actual muscle strengthened by this technic would depend on the patient's position and gravitational need to stabilize his body. Contralateral muscle exercises are therefore without merit in our opinion in maintaining the strength in a muscle under a cast.

Electric stimulation

Dr. Lippmann: To what extent can electric stimulation maintain muscle strength while the knee is in a plaster cylinder?

Herbert L. Thornhill, M.D.: The muscles in question, of course, are normally innervated and will respond to faradic stimulation. Good contractions can be obtained by tetanizing currents. Unfortunately, in practice this technic cannot be applied very easily, because it is quite painful. We have had good experience with the Batrow stimulator which employs extremely high voltages (up to 60,000 volts), weak currents (about 0.025 milliampere), and short discharge times (about 7 milliseconds). The discharge rate may be increased to 50 per second, which produces a good tetanizing effect without causing pain. The disadvantage is that contractions of not more than 20 to 30 per cent of the total muscle strength can be obtained. We believe that the method has an application in occasional cases but is not really very effective in preventing muscle atrophy.

Dr. Lippmann: I think we would agree that volitional contraction against resistance is the most effective method of maintaining muscle strength and is the preferred tool in rehabilitation management from every point of view, physically and psychologically, as long as there is sufficient innervation. Actually, the maintenance of muscle function in patients with knee operations is of great concern to us, and I wonder whether some explanatory statement is in order.

Chief Resident: The quadriceps apparatus with its four muscles (the rectus femoris and vastus intermedius, lateralis, and medialis) represents a formidable mechanism to stabilize the knee. The last 15 degrees of extension, which "screw" the tibia into the tight position of the knee in full extension, which secures lateral stability, are brought about by the action of the vastus medialis. In painful knee conditions marked quadriceps atrophy may develop rapidly. Two of the responsible mechansims are "guarding" of the knee, which represents a form of constant muscular inhibition which can be demonstrated electromyographically, and disuse atrophy due to plaster immobilization. In our patient, probably both mechanisms played a role. Ambulation does not help redevelop this muscle since walking on a level surface requires little active participation of the quadriceps,[3] and in an acutely inflamed knee weight-bearing may be harmful, leading to more effusion and subsequent stretch of capsule and ligaments. Thus, a vicious cycle may be established which leads to more instability and muscle atrophy and which must be broken by effective strengthening of the muscle without weight-bearing.

Dr. Delagi: We would like to consider now what can be done for the patient after the cylinder has been removed, which in our case happened several weeks ago.

Resident: We found, as previously noted, that the patient had a considerable amount of swelling of the knee and a small amount of effusion. There were only 5 degrees of flexion possible from the anatomic 0 position, and there was extreme quadriceps atrophy.

Dr. Delagi: What was the therapeutic approach for each of these problems?

Underwater exercises

Resident: We have utilized the Hubbard tank and three weeks ago started active assisted range of motion to the knee under water. This has been continued to date.

Dr. Ebel: It is my impression from today's examination that this patient now has a fair to good quadriceps muscle, since by definition, a fair muscle is one which can move the joint through the full range that this patient is capable of at the time, against gravity. Under these circumstances I don't see any need for availing ourselves of the buoyancy of the water to move the joint to the possible full range since the muscle is capable of doing it without the water. I do not question the need for underwater exercises three weeks ago.

Dr. Delagi: Was the Hubbard tank used because of the patient's muscular weakness?

Resident: No. We use exercise in warm water when dealing with a painful joint because we feel that it is less painful to the patient. In this patient we actually saw her stretch her knee more readily under water.

Dr. Delagi: It might be added that exercises under water may be considered active-assistive or active-resistive, depending on the speed of motion under water and the mass of the segment moved. It is also an established fact, although not completely explained, that range-of-motion exercises induce less pain when they are performed in warm water than without this modality.

Visiting Physician: Could the whirlpool bath be used instead of the Hubbard tank for the same purpose?

Dr. Ebel: That is perfectly reasonable, but the shape of the Hubbard tank makes it possible to position the patient with her hips extended.

Other physical modalities

Dr. Delagi: Does this conference feel that other physical modalities could be employed to increase the range of motion of the knee?

Resident: Deep mild heating with short wave diathermy is available, and we have occasionally used it in similar cases with alleviation of the pain. In other cases we have used a paraffin cast applied to the knee overnight which provides heat over many hours and serves to splint the knee at the same time. This overnight immobilization may be indicated in the face of an acute or subacute synovitis.

Dr. Ebel: Ultrasonics could be used here with some benefit. This modality of heat application is claimed to have some effect on the lysis of adhesions which in our case may be in the joint or in the structures surrounding it. In our hands, ultrasound under similar circumstances has proved beneficial and gratifying to the patient.

Dr. Delagi: I would like to ask the chief resident how she would prescribe ultrasonics for this patient.

Chief Resident: I would use 1 to 2 watts per square centimeter for from five to seven minutes, once daily under water, immersing the sound generator head with a handle and applying it so that the sound head is in proximity with the various parts of the knee joint.

Dr. Ebel: In addition to this modality, we have a simple way of utilizing gravity to produce an increase of range of knee flexion. I like to place the thigh of such a patient, who is lying supine, slightly elevated by a pillow while the leg is hanging free at the end of the bed, couch, or table. Flexion will slowly increase through the action of gravity. Such a procedure should always be supervised by a therapist; when the patient develops pain, it should be interrupted immediately.

Dr. Delagi: Most of these modalities are used to re-establish range of motion of the knee and some to strengthen the extensor muscle mechanism. I would like to defer a full discussion of available methods to maintain and strengthen these muscles to another occasion. I would only like to know, once the patient has had her plaster cylinder removed, what method of muscle strengthening has been used?

Muscle strengthening

Resident: We have given her progressive resistive exercises[4] to knee extension and flexion once daily, except for weekends and hospital holidays. She has recently lifted 10 pounds through full range of motion 10 times, which is three quarters of her maximum strength as measured on the uninvolved side. Weights are added to the shoe at the rate of 1 pound or more every week. She has made progress with this regimen from a poor quadriceps (unable to move the joint through the range of 20 degrees against gravity) to a good-minus-one (able to move the joint through its increased range of 60 degrees against some resistance). Similar progress was made in hamstring function (flexion).

Dr. Delagi: We heard that adhesions were freed under anesthesia. I want to point out that this orthopedic procedure has helped significantly to increase the range of motion.

Resident: We found one day after operation that the range of motion had increased by about 30 degrees, although even more increase than that had been obtained during operation. This gain has been maintained, and we hope to improve it while the synovitis is abating and the quadriceps and hamstrings are gaining in strength.

Dr. Lippmann: Since synovitis is still a problem here, I presume, weight-bearing is not permitted. When do you think weight-bearing will be safe?

Weight bearing

Matei Roussan, M.D.: I think there is no disagreement among us that during an active synovitis the patient should not bear weight. At the rate our patient's synovitis has been subsiding in the past few weeks, we would anticipate that in three to four weeks we can allow a gradual increase of weight-bearing. As of now, she bears some weight for short periods only. That is when she transfers from her bed to a wheel chair, to the toilet, and so forth. The effect of increased weight-bearing on her knee will guide us as to how fast she can return to normal ambulation. We may elect to have her use a cane in her left hand when she becomes ambulatory. In the meantime, her almost-no-weight-bearing does not preclude range-of-motion and active-resistive exercises designed to maintain or increase muscle strength, as was outlined before. Without elaborating too much I would like to add that we have experience in several cases that progressive quadriceps exercises contributed to the disappearance of effusion of the knee and of other clinical signs of traumatic synovitis. Abramson[3] has published such cases in detail.

Of course, we avoid trauma to the inflamed knee at present in planning our therapeutic program, since this may lead to the vicious cycle previously discussed and to long severe disability. Only recently we treated such a patient in our outpatient department: a middle-aged man whose traumatized knee had to be ankylosed several years ago, which caused some considerable disability and difficulty in ambulation so that he injured his second knee.

Range-of-motion goals

Dr. Delagi: I wonder what your goals are in the patient, as far as the range of motion of the knee is concerned? To what point should we continue range-of-motion exercises and increase flexion?

Dr. Roussan: It would be ideal to restore the range of motion to normal in every patient. If this is not possible, one might perhaps consider surgery to reach such a point. I believe this is rarely necessary and that the actual desirable degree of range of motion depends on the needs of the individual patient. The restoration of range of motion to 90 degrees might be a reasonable aim here, since it would enable the patient to negotiate stairs with safety. If we are dealing with a younger person or with one who has to scrub floors or do other chores on her knees, flexion of the knee to 90 degrees is insufficient, and flexion to 120 degrees is necessary, which is still 30 degrees short of normal maximal flexion. However, in our patient who is elderly and retired this would hardly be warranted. A restoration of her knee flexion to 90 degrees, namely, 30 degrees more flexion than has been presently obtained, will be a satisfactory compromise.

Conclusion

Dr. Delagi: This patient has given us the opportunity to review some of the physical modalities in the management of traumatic disorders of the knee. This case also demonstrates the importance of the recognition of limitations to be placed on the activity of such patients in the presence of synovitis. It goes without saying that every patient presents individual problems of disability and our goals and methods of treatment must be formulated accordingly. We look forward to further restoration of function in this patient. We trust she will be able to resume her duties as a housewife without difficulty within the next few weeks, about four and one-half months or so after her injury and patellectomy.

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Number six in a series of Clinical Rehabilitation Conferences

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Working days lost because of peptic ulcer

According to *Patterns of Disease*, a Parke, Davis & Company publication, on the average working day 49,000 working persons with peptic ulcer were absent from their jobs because of this illness. The disease causes temporary disability totaling about 47 million days of restricted activity annually, about 13 million days of bed disability, and some 12 million lost working days.

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Injudicious Use of Analgesics

THE PRESCRIPTION of drugs is usually based on the therapeutic response desired. It requires familiarity with the drug's mode of action, side-effects, indications, contraindications, and dosage. A disregard of the patient's age, physical status, and disease entities may lead to the injudicious use of potent drugs. Awareness and improvement as to the proper dosage of narcotics both preoperatively and postoperatively has resulted through the constant efforts of most anesthesiologists. Small community hospitals may escape these efforts. The following case report is from such a hospital in which undesirable effects and almost fatal complications were invited by an overdose of potent analgesics in the postoperative period. The favorable outcome in this case can be attributed to the recommendations and therapy initiated by a consultant anesthesiologist.

Case report

This eighty-three-year-old white male, speaking only Italian, was admitted for diagnosis and therapy for urinary retention. He had been on Rauwolfia aklaloid therapy for many years. Because of a language barrier and his uncooperative nature, further history was unobtainable. He did have generalized arteriosclerosis and emphysema. The chest x-ray film revealed left ventricular enlargement and tortuosity and dilatation of the aorta. The electrocardiogram showed a sinus arrhythmia and inverted T waves in V_5 and V_6 leads. His usual blood pressure was 200/110. One week prior to the present episode he had a saddle block anesthetic for cystoscopy without any untoward reactions. A recommendation was made to discontinue reserpine for fourteen days before proceeding with an elective suprapubic prostatectomy.

Five days later, the patient was scheduled for a suprapubic prostatectomy. The reserpine medication was discontinued the night before surgery. His laboratory data revealed 2 plus albumin in the urine, hemoglobin 92 Gm. per 100 ml., white blood cell count 14,300 per cubic millimeter, blood urea nitrogen 12 mg. per 100 ml., fasting blood sugar 78 mg. per 100 ml., and acid phosphatase 2.8 Gutman units (normal 0.5 to 3.5).

The patient's preoperative blood pressure was 180/90, and occasional premature ventricular contractions were noted. A subarachnoid block with tetracaine hydrochloride 12 mg. was employed for a one-stage suprapubic prostatectomy. Prophylactic ephedrine 50 mg. was given intramuscularly. The anesthetic level was T9, and the blood pressure dropped to 120/70. Nitrous oxide-oxygen was used intermittently because of pain on bladder retraction.

The patient complained of pain postoperatively and received two doses of meperidine hydrochloride 100 mg. two and one-half hours apart. This was followed by morphine sulfate

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15 mg. Six hours following surgery questionable coffee-ground vomitus was reported. The patient's blood pressure had fallen to 106/54. An intravenous drip of norepinephrine was started because the patient's blood pressure continued to fall. His blood pressure rose to 230/100 but fell immediately to 130 systolic. Two doses of methantheline bromide (Banthīne) also were administered due to reported coffee-ground emesis.

Seven hours postoperatively the patient's condition became critical. The patient was digitalized, and one dose of mercuhydrin was given because of evidence of cardiac failure. The electrocardiogram revealed upright T waves in V_5 and V_6 and a sinus arrhythmia. His hemoglobin at this time was 88 Gm. per 100 ml. There was no improvement for the next two and one-half days while he was on a medical regime.

A consultant anesthesiologist observed the patient lying flat in bed in an oxygen tent with restraints because of restlessness. A physical examination gave evidence of early pulmonary edema and the presence of a markedly tympanitic abdomen. A repeat electrocardiogram, chest x-ray film, carbon dioxide-combining power, blood urea nitrogen, and electrolyte studies were requested.

The immediate management consisted of the insertion of a Levin tube and aspiration of gastric contents which were negative for gross blood, the insertion of a rectal tube, removal of restraints, semi-Fowler position, and nasal catheter oxygen therapy. The norepinephrine infusion was discontinued, and intramuscular metaraminol bitartrate was given when necessary to maintain the blood pressure. Intensive corticosteroid therapy also was instituted after guaiac tests of gastric contents were reported showing negative findings. The patient began to manifest signs of recovery after eight hours. His electrocardiogram returned to a normal sinus rhythm, and his systolic blood pressure was maintained at 140 to 160. The patient was less restless and manifested an improvement in strength as well as a return to rationality. Within twenty-four hours the patient fully recovered from his state of shock. The laboratory studies had reverted to normal at this time.

Comment

Perhaps one of the most striking features in this case report is the large quantity of narcotics that this patient received in approximately two and one-half hours for postoperative pain. Although the respiratory effects were not mentioned, one can appreciate the respiratory results following their administration to this eighty-three-year-old patient with pulmonary emphysema. One could predict a decrease in minute volume, rate, and respiratory response to carbon dioxide from the dosages administered to this elderly patient. Narcotics, when employed for such patients, should be minimal. Perhaps some regional nerve-blocking procedure might have been considered for pain relief in this case. The restlessness and the restraints used justify the assumption of respiratory depression and existing hypoxia. The repeated narcotic doses were given to overcome restlessness due to hypoxia which further aggravated the condition. The ensuing circulating depression also could be based on the large doses of narcotics. They may have exerted a direct depressant effect on the myocardium itself.

The total extent of the role of Rauwolfia therapy on postoperative circulatory collapse is difficult to evaluate but cannot be disregarded. The present pharmacologic knowledge of Rauwolfia alkaloids is sufficient to cause concern by the anesthesiologist and surgeon. Although the recommendation was made to discontinue such therapy for two weeks prior to surgery, this was not done. In all probability the patient was deprived of his natural mechanism of homeostasis. Spinal anesthesia for this procedure may not have been the best choice under such circumstances.

The gastrointestinal symptoms could well have been the product of large doses of narcotics. The ensuing emesis and distended abdomen are well-known side-effects of these drugs. Methantheline bromide was employed to overcome these symptoms without results. Decompression of the abdomen not only improved the gastrointestinal symptoms but in all probability aided ventilation in this patient.

The overdose of narcotic drugs was responsible for the chain of events in the postoperative period. This led to the administration of norepinephrine, methantheline bromide, digitalis, mercuhydrin, and oxygen in an attempt to counteract the effects of the injudicious use of potent analgesics.

Number one hundred nineteen in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
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Boric Acid and Rodenticide Poisonings and Use of Ipecac

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Boric Acid	4 weeks	Male

This four-week-old infant mistakenly was given 1/2 ounce of a solution which contained 1 teaspoon of boric acid to 1 pint of water. The godmother fed this infant the solution at 9:30 P.M. The child vomited at noon the following day and was taken to a hospital where he was admitted to the inpatient service although the patient was entirely asymptomatic.

During his four-day hospital stay all chemistries and renal function tests showed normal findings, and four stools showed negative guaiac test results.

Hospitalization always is indicated in cases of boric acid ingestion in young infants even though the patient may be entirely symptom-free.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
J-O Paste	30 years	Male

This patient ingested an unknown amount of roach poison with suicidal intent. About an hour and a half following the ingestion he began to vomit. He then was taken to St. Luke's Hospital where his stomach was lavaged with saline, copper sulfate, and potassium permanganate. This was repeated three hours later. The symptoms on admission were nausea, vomiting, abdominal pains, dyspnea, burning in the mouth and throat, stupor, and tachycardia.

The laboratory findings showed a potassium of 6.1 mEq. and sodium of 128 mEq. per liter. The gastric contents were found to show positive guaiac test findings. During his hospital stay the patient became progressively worse, lapsed into a deep coma, and became hypotensive with acute abdominal pain. Fibrillation began, and the hypotension became more marked and was refractory to vasopressors. The patient expired on the day following his admission.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
J-O Paste	27 years	Male

This case was reported by Barbara Parker, M.D., of Bellevue Hospital.

A twenty-seven-year-old Puerto Rican man mixed three-quarters of a can of J-O Paste in milk and drank it. He was taken at once to Knickerbocker Hospital where he was given mineral oil and ipecac. He began to vomit about two hours after the ingestion. A gastric lavage was done with potassium permanganate at Bellevue about five hours postingestion; at this time he passed a large "fuming" stool which had a strong garlic odor. The gastric lavage was not odiferous. On the fourth hospital day the patient began to vomit and have epigastric tenderness. The liver became palpable, and chemical studies showed an elevation of serum transaminase levels and serum bilirubin concentration. On the eighth hospital day the patient felt improved, began to eat without vomiting, and went on to an uneventful recovery. He was discharged on the seventeenth day to be followed in the medical clinic. On clinic visits he has felt well and is able to work at his usual occupation.

The final diagnosis was acute, accidental phosphorus intoxication with liver damage.

It is possible that the large dose of mineral oil administered to this patient caused the elimination of a large proportion of the ingested phosphorus in the stool, thereby preventing more severe intoxication.

In view of the absence of a specific therapeutic agent for phosphorus poisoning, evidence would appear to favor the widespread use of mineral oil in such poisonings.

TABLE I. Poisonings about which information was requested over a recent weekend

	Patient	
Product	Age (Years)	Sex
Ant trap	1	F
Aspirin	$2^{1}/_{2}$	M
Barcolene, pine oil and Oxydol	2	M
Benzene	3	F
Bleach	2	F
Boric acid	4	F
Boric acid	3	F
Carbon paper	$1^{1}/_{6}$	F
Chlordane	5	F
Chlortrimeton	2	M
Cleanser	$^{3}/_{4}$	M
Clorox	34	F
Clorox	5	M
Clorox	2	M
Clorox	$^{3}/_{4}$	M
Clorox	10	M
Cologne	39	F
Cologne	$3^{1}/_{2}$	M
Compazine	2	F
Compazine	19	M
Crayon	2	M
Deodorant	2	M
Detergent	2	Unknown
Detergent	30	M
Detergent	30	F
Diuril	2	F
Easy-Off	30	F
Fiorinal	20	F
Floor wax	$2^{1}/_{2}$	M
Fluorescent bulb	24	F
Gantrisin	2	M
Gasoline	Unknown	Unknown
Haze-It (crab grass treatment)	2	M
Hibiscus plant	$6^{1}/_{2}$	F
Hydrogen peroxide	3	F
Insect spray	5	F
Insect spray	3	M
Lighter fluid	$2^{1}/_{2}$	M
Lysol	$2^{1}/_{2}$	F
Lysol	24	F
Matches	1	M
Matches	1	M
Matches	$1^{3}/_{4}$	F
Metaldehyde	11	F
Mercury (from thermometer)	4	F
Mercury (from thermometer)	3	F
Miltown	43	F
Moth ball	1	M
Mushroom (wild)	2	F
Nytol	30	F
Oil of citronella	4	F
Oil of wintergreen	72	F
Paint	$1^{1}/_{6}$	M
Paint	40	M
Paint	$2^{1}/_{2}$	M
Phenobarbital	32	F
pHisoHex	55	M
Plant (stem of marigold)	8	F
Pine oil	3	M
Powder	$1^{1}/_{6}$	F
Privine	2	M
Rat and mouse seed	2	M
Rat and mouse seed	2	M
Rolaids	4	M
Soap cake	$1^{5}/_{12}$	M
Soma tabs	14	F
Stelazine	Unknown	Unknown
Toilet water	2	M
Vermifuge (insecticide)	$1^{1}/_{2}$	F
Vermifuge	5	F
Vermifuge	$1^{1}/_{2}$	F
Wall plaster	4	M
Unknown	22	M

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Creosote	22 months	Female

This case was reported by a parent from out of town. The mother relates as follows:

> The child, twenty-two months old, put her hands in creosote in the presence of two other children, one about five years of age and the other about four years of age. According to the younger child, my daughter put her hands in her mouth. The older child said that she did not put her hands in her mouth. On the advice of our family physician we administered ipecac to our child. After giving her about $4^1/_2$ teaspoonfuls in about forty minutes we discontinued the treatment. Vomiting did not occur, nor did any effects from the possible consumption of the creosote occur.

We believe that the mother exercised good judgment in not continuing the medication since it was not effective as an emetic. In view of the known hazards of ipecac as an emetic and of the known hazards of overdosage, the discontinuance of the drug was medically sound. This case exemplifies the frequent ineffectiveness of ipecac although the exact reason for its failure is yet obscure.

The accurate and complete reporting of health information by parents is noteworthy and salutary.

A fatal case of acute ipecac poisoning was reported by Smith and Smith[1] in a recent issue of the *New England Journal of Medicine*. This occurred in a four-year-old boy who received the fluid extract of ipecac because he ingested 36 antacid tablets. Because of the difficulty encountered in the removal of the tablets by lavage, 30 cc. of fluid extract of ipecac with two glasses of water were given. Since vomiting did not occur after fifteen minutes, the dose was repeated. The outstanding symptoms were persistent vomiting and diarrhea which terminated in shock, collapse, and death. The pertinent autopsy findings were dehydration, moderate esophagitis, and erosions of the stomach and duodenum, as well as kidney and liver damage, gastrointestinal inflammation, and epicardial hemorrhage.

The present status of ipecac as an emetic has been discussed previously by us[2] in the *Archives of Pediatrics* and also reviewed by the National Clearinghouse for Poison Control Centers.[3] Considerable investigative work is needed to develop a safe and effective emetic. The danger of stricture formation following the overdosage of the present-day "emetics" is worth re-emphasizing. Although admittedly not an optimal agent, syrup of ipecac is at the present time the only advisable emetic to be used for home or emergency room therapy.[4]

Table I lists incidents reported to the New York City Poison Control Center over a recent weekend.

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Number eighty-seven in a series of Accidental Chemical Poisonings

Medical Care Insurance

A series of articles on health insurance prepared by the Associated Blue Shield Plans of New York State

LEONARD J. RAIDER, M.D., Editor

Developing New Opportunities for Growth and Progress in Blue Shield Locally and Nationally*

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THERE IS AN EPIC QUALITY suggested in the very title of the subject I am privileged to consider: "Developing New Opportunities for Growth and Progress in Blue Shield Locally and Nationally." These words indicate to me that at this moment we stand poised between the great Blue Shield developments of the past and the potential of the future. Years ago, when the freedom of medical practice was being challenged on a broad front and efforts were being made to replace it with a governmental system, men of wisdom, with enthusiasm and dedication, came forth with new ideas to adjust to changing needs. They struggled hard—hard enough and long enough to have produced the results we see today: a nation-wide Blue Shield program serving the people of our country. We owe a great debt to these men and to the cause for which they worked. Many of them have left the scene. Those who remain with us still hope for greater fulfilment of their dream. Certainly, the record of their achievements is here before us. Starting from a dream, a concept, they pressed forward so that now one quarter of the people of the United States are participating in Blue Shield programs.

Yet, along with success, reverses were suffered. Some of the original principles and goals of Blue Shield are yet to be realized. What are these principles and goals? They are community coverage through Blue Shield, a means through which medical care could be financed for all or most of our people, and a way for individual doctors and the medical profession as a whole to use Blue Shield as the method through which the public and the profession could adjust to changing and pressing needs for the financing of medical care.

Today as we contemplate and prepare for the future, we are aware of the need for a continuity of theme and purpose. On us falls full responsibility for continuation and progress. We are being challenged by the future. For some years now we have been striving, modifying, and improving. And we have achieved a remarkable degree of success. But we have not attained all our goals. Rather, we are at an interim period, a plateau, a time for review and planning. We would seriously misjudge our challenges if we were to feel even close to a final expression of the goals Blue Shield must accomplish in the interest of the public and the medical profession.

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* Adapted from a speech presented at the Annual Program Conference of Blue Shield Plans, Chicago, Illinois, October 23 and 24, 1961.

It seems to me that among some physicians there is a degree of overconfidence as to the survival of our private practice system. Such an attitude is just not consistent with present environmental pressures. We must learn to examine and judge. Only through knowledge can we reach wise decisions. If only all doctors throughout the country had full knowledge of events bearing on medical economics and social forces in special areas of our country, such as Michigan, New York, and California, what a valuable tool for judgment each of us would have. Each of us is an individual, practicing in a local community. But collectively we are called on to make decisions relating to medical practice and medical economics on a national basis. Our greatest danger is arriving at judgments based solely on our own local environment rather than on the national picture.

But there is a need to be specific, and in doing so I would like to emphasize that the ideas and recommendations I present are expressions of my personal attitude. Since the activities of the Blue Shield Study Commission encompass the range of my remarks, I wish to point out that my associates in the study group bear no responsibility for what I say.

Need for national accounts

Of foremost concern to the contniued success of Blue Shield on both a local and national basis is the current and pressing problem of national accounts. Blue Shield is sponsored and supported by physicians, nation-wide. More and more nation-wide corporations and national organizations are becoming interested in purchasing health insurance coverage on a uniform, nation-wide basis. But Blue Shield, at this moment, is not sufficiently equipped as a national movement to supply and service their need for nation-wide health insurance coverage. That we have the potential has been proved when, at a critical time, we were able to develop and present, along with Blue Cross, a program for Federal employes. The response was most gratifying and I think this response demonstrated the public's preference for a Service Benefit program. Then what holds us back today? Why aren't we strengthening our position in the great national account market? In talking to physicians from many parts of the country I have found they all agree we ought to get together on this problem, that without further delay we ought to create national contracts with enough uniformity to satisfy the national need, and that under our national account offering there should be sufficient flexibility in service levels and scope of benefits to supply the needs of the national market. Why then have we not developed a proper national presentation? At present we have 69 Blue Shield Plans in the United States. Their programs have been planned and developed only through great effort and with the active participation of hundreds of county medical societies and the many state medical societies.

Parenthood is a proud and sensitive state. We must acknowledge, however, that the children—our Plans—vary considerably in detail. And therein lies our problem. Too often, after Plans agree to the need for national programs and after expressing willingness to participate and cooperate, there is insufficient effort to follow through. Each Plan thinks its approach to the problem is best and allows for little give and take. And we are sometimes told: "If you violate this or that principle of our Plan, you will destroy Blue Shield." The principle that concerns me is that Blue Shield serve as a major mechanism to preserve for the public and the medical profession the freedom of the voluntary system of medical practice in this country.

If we do not cooperate and combine to present adequate national programs, with a sufficient degree of uniformity and flexibility to serve nation-wide needs, then we fail in our duty to support fully our system of medical practice. We must come to a meeting of minds and agree on specific national contracts. There is an adjustment and a cooperative effort to be made in the interest of all the Plans and all physicians interested in Blue Shield. Because a national program may in some way vary from our own local Plan, we must not consider it a violation of our Plan's principles or program. A national offering should be regarded for what it is—a necessary response to a different need. It would be regrettable indeed if the philosophy of the physicians backing Blue Shield Plans varied so widely that they could find no common meeting ground. Even those in indemnity areas might consider the feasibility of experimenting with Service Benefits within the framework of a national contract. I would like to point out, however, that accommodation to indemnity areas is included in the proposed national programs. We must all remember our major purposes as we encounter obstacles. Bear in mind that the movement toward national coverage can and will have an impact on each local Plan. Branch offices of industries we now serve on a local basis may shift to a national program. We must hold them in Blue Shield by creating a good national Blue Shield contract.

Community coverage

Also of considerable importance to us is Blue Shield's goal of community coverage. One of Blue Shield's major objectives has been to achieve a sufficiently broad distribution of coverage so that a common subscription rate can be established for high- and low-cost users of medical service. Thereby we have been able to include in Blue Shield coverage and retain as private patients many people who otherwise would have been medically indigent—patients who could not have afforded any measure of health insurance protection. Remember that this was the medical profession's mandate to Blue Shield. Blue Shield responded and has served the public and the medical profession well in this regard. But unfortunately, there are some doctors who do not appreciate and who, perhaps, are not even aware of the valuable service Blue Shield has performed. They take it for granted.

It must be emphasized that wherever health insurance leaves gaps in coverage in segments of the population—be it farmers, migratory workers, self-employed individuals, senior citizens, or unemployed persons—therein lies an open invitation for government intervention. Piecemeal socialization can result in over-all socialization. The medical profession particularly must maintain an alert, informed attitude on this subject. There remains with us the basic problem of providing Blue Shield protection to all economic levels of the population, not just those with low incomes. Even though Blue Shield is designed to help most those with low or moderate incomes, it should not be limited to these groups. Blue Shield must be a program for the vast majority of people. It must not be allowed to become a "poor man's plan." Today, too much health insurance is sold without regard to over-all community need. Health insurance programs that may be good in quality but which are not available to large segments of the population are not enough. The continuation of this approach will not maintain our system of freedom of medical practice.

What has happened over the course of time to our high hopes of community coverage? In the early days, concern over "cost impact" and insurance underwriting rules resulted in a partial disregard of the community concept and persons over sixty-five years of age were overlooked. This omission certainly has come home to roost. Fortunately, most of our Plans have retained subscribers who have reached sixty-five, and we can be justly proud of the large number of senior citizens now enjoying Blue Shield protection.

The major problem impairing the Blue Shield and Blue Cross community concept is the competition of other insurers who have been offering reduced rates to selected, low-impact cost groups. Thereby these groups are removed from the community group. A continuation of this practice will require what remains of the community group to pay a higher rate for health insurance coverage. This process, carried to its ultimate, could price health insurance out of the range of those who need it most.

Surely we agree that access to medical care should be available to all. Should we not, then, favor equal access to medical care through health insurance without financial discrimination as to premium rates? Certainly not under a system of higher rates for higher risk groups. Certainly not under state laws governing, as they do today, the sale of voluntary health insurance. I suggest that a change in law, with a shift in the responsibility of insurers, is needed. In broad terms, a new law or regulation could operate in the following manner: Any insurer offering a specific scope of coverage for health care expenses to any individual or group would be required to supply that same scope of coverage to any other individual or group at the identical premium charge. This may be considered a rather unusual idea, and I may be asked if such a law could be passed. I don't know. But I would ask, "Is this concept fair and right?" Should government programs to equalize the spread of costs by taxation be discouraged while no efforts are made to promote such equalization under a voluntary system? It is my view that our broad-based community approach to voluntary health insurance could thus be really strengthened. In this manner cost problems, which create gaps of coverage among segments of our population, could be lessened. I firmly believe that present population gaps in coverage make our whole voluntary system vulnerable to government intervention.

This proposal may well be opposed by those who consider prepaid health care financing simply an insurance mechanism. But because I feel there is social justice in this concept, I consider it my responsibility to give it exposure.

Service Benefits reciprocity by participating physicians

There is an interesting aspect of Blue Shield's national position that I would like to present for consideration also. As physicians we have a common sense of purpose and, I am sure, are anxious to aid and support each other in attaining desirable aims and goals. Can we not direct this community of interest toward the concept of Service Benefits? It is an accepted fact that Americans travel more today than ever before. We have become a mobile people. Consequently, a physician will treat on occasion a traveler who is a Blue Shield member of a Plan in another area. Would we not greatly strengthen the public image of the physician and Blue Shield, if as participating physicians in our local Blue Shield Plan, we gave "courtesy" Service Benefits to these out-of-area patients. The Medical Society of the State of New York has recommended that physicians do this for members of the seven Blue Shield Plans in New York State. Should we not strive for such reciprocal participation on a national basis? The actual impact of this effort might be limited as far as the individual physician is concerned, but the value to the individual patient, to the medical profession generally, and to Blue Shield's national image would be significant. I believe the public at large, and particularly Blue Shield subscribers, would be pleased if a resolution embodying such a recommendation were presented to and passed by the House of Delegates of the American Medical Association.

Measurement of performance of Blue Shield Plans

Another matter I would like to discuss briefly is the measurement of performance of the individual Plans. With the passing of time and the gaining of experience, Blue Shield has reached a maturity that should now enable us to examine and judge our performance as individual Plans. The public considers Blue Shield to be national in scope. The public attitude toward one Blue Shield Plan has an impact on other Blue Shield Plans. Therefore, the performance of any one Plan is of importance to all. There is today a real need to evaluate the effectiveness of each individual Plan—to review their achievements and, if necessary, to offer advice and assistance in improving their performance both qualitatively and quantitatively. I feel that our national organization should be assigned this responsibility.

Today our established standards relate mainly to the soundness of financial operations. To itemize all the factors of Blue Shield operations that are necessary for good Plan function and establish these as minimal requirements would seem to me to be a rather rigid approach at this time. Instead, I would like to suggest some standards by which satisfactory performance could be measured: (1) local public acceptance; (2) the proportion of area population covered; (3) the proportion of subscribers' medical costs paid by the Plan; (4) the degree of protection afforded by Service Benefits; (5) the percentage of physicians in the Plan area who participate; (6) the degree of cooperation between physicians and the Plan; (7) the adequacy of coverage in scope of service, for example, the availability of supplemental coverage; and (8) administrative costs.

If we are to make such an evaluation of each Plan, I believe our judgment must be arrived at in terms of these multiple considerations. Further, such evaluation must be related to and modified by the social and economic environment in each local Plan area. I would suggest further that we use a point scoring system to arrive at an estimate or evaluation of a Plan's performance. Where Plan weakness is demonstrable, advice and assistance should be supplied by our national organization. In this way we may achieve increasing public satisfaction throughout the country.

Structure of our national organization

In planning for the future we must also turn our attention to the structure of Blue Shield as a national organization and to consider this structure in terms of future needs. Surely we are acutely aware of our interdependence. And I expect this interdependence will increase. As a nation-wide movement there are responsibilities which the National Association of Blue Shield Plans must assume in progressively increasing degree. As I have already mentioned, there is need for measuring Plan performance and the availability of advice and guidance when necessary. Assistance and participation in the resolution of problems arising in local areas is surely a present need. And too, there must be an increase in statistical research as applied to utilization patterns, administrative costs, and other factors. The need for our Plans to act in unity is becoming increasingly apparent. To achieve a national attitude that can be presented with authority we must correlate the views and opinions of all areas. This is another of our needs. I want to suggest that we examine our national structure with a view to increasing its responsibility and authority. It may be that we should move toward a more federated type of structure rather than retain our present loose arrangement. It is my hope that in the very near future consideration will be given to this matter.

Political or legislative activity

In conclusion, I wish to draw attention to the deep interest that doctors and Blue Shield have in social legislation. While at times it is necessary to oppose proposed legislation, we should also, in a constructive and positive manner, strive to advance our beliefs and principles through legislation. In this connection I have some thoughts that I would like to propose.

First, I suggest that the individual as a purchaser of health insurance be afforded tax relief corresponding to that enjoyed by group purchasers. In effect, he should be able to subtract directly from his income the cost of his health insurance. At present, business organizations are permitted to do just that. I propose that a degree of equity be restored to the individual purchaser.

Second, the Kerr-Mills Law is in the process of being implemented by the states. I believe we should strive for legislation to permit the medically indigent covered by that law to receive state financial aid toward the purchase of voluntary health insurance. We should not stand by while medical care of these otherwise self-supporting people is shifted from the physician in private practice to the welfare department.

Third, I have previously indicated a proposal whereby we might restore the community concept to health insurance coverage. Briefly, it is to establish by law the right of all individuals to purchase at the same cost or premium any specific scope of coverage offered by any insurer.

Space does not permit me to go into details on any of these proposals. Some of the ideas I have presented require expert committee study. It is my hope, however, that some of these thoughts and suggestions will be of interest. Inherent in these several suggestions is a basic goal that should be of serious concern to every one of us.

It is obvious then that there is much to be done. But our tasks are of a highly constructive and valuable nature. They will bring highly rewarding results, I am sure, because in improving the quality and performance of each Blue Shield Plan and the leadership of our national organization, we strengthen not only traditional medicine but also the entire system of free enterprise. We have to prove that Blue Shield has maintained the verve and drive it possessed at its inception. Blue Shield's purpose is to serve the prepaid medical care needs of the people of this country under the guidance of and with the support of the medical profession. Blue Shield is the best mechanism by which the medical profession, under its traditional freedoms and responsibilities, can provide the American people with a universally acceptable system of prepayment for physicians' services.

Although we have good reason to be proud of our past accomplishments, we cannot rest on our laurels. The future of Blue Shield, and with it the future of medical practice in this country, is in our hands. I hope that we shall move ahead in partnership and in service to the people across the nation.

Number sixteen in a series of special articles on Medical Care Insurance

Air-purifying apparatus

In a comparative study of pollen, mold, and bacterial counts in hospital rooms variously equipped, performance of the so-called air-purifying apparatus did not live up to its advance billing. Jay Spiegelman, M.D., George I. Blumstein, M.D., and Herman Friedman, Ph.D., in an article in the June, 1961, issue of *Annals of Allergy*, reported that they were unable to note any significant drop in the pollen or other counts in rooms with the air purifier as compared with those without it; in fact, over 50 per cent of the counts were slightly higher in rooms which were purifier-equipped. However, there was an obvious difference in rooms equipped with air conditioners, and it appeared to be of little or no consequence whether or not their filters were in place or whether or not the room also was equipped with the air-purifying apparatus. There was a marked fluctuation in bacterial counts from day to day, but there was a constant reduction in the number of airborne organisms in the air-conditioned rooms as compared with the counts in the rooms with the windows open, whether the latter were equipped with an air purifier or not.

Use of X-Ray Equipment By Chiropractors Forbidden

Summary of Decision by Hon. Albert Conway

On November 15, 1961, Hon. Albert Conway, the former Chief Judge of the Court of Appeals of the State of New York, now retired, sitting as an official referee of the Court of Appeals, handed down a decision of tremendous significance to the well-being and health of the people of this State.

In a most well-reasoned and exhaustive opinion he ruled that chiropractors are not entitled to an injunction restraining the State Commissioner of Health from enforcing the provisions of the State Sanitary Code which prohibits the application of radiation to human beings except by persons licensed to practice specified professions or under the direction of such persons and which thus prohibits the use of x-ray equipment by chiropractors. His ruling was by stipulation equally determinative of another proceeding in the City of New York by which chiropractors attempted to enjoin a similar prohibition contained in the Sanitary Code of the City of New York.

The particular section of the State Sanitary Code involved is found in Chapter XVI entitled "Ionizing Radiation" and designated as Regulation 19. It reads as follows:

> 19. Limitations on application of radiation to humans.
>
> No person shall apply radiation to a human being unless such person is licensed or otherwise authorized to practice medicine, dentistry, podiatry or osteopathy under the provisions of the Education Law of the State of New York. Radiation shall be applied by a licensed or otherwise authorized person to only those parts of the human body specified in the law under which such person is licensed or authorized to diagnose and treat.
>
> This regulation shall not prohibit the use of radiation by a technician, nurse or other person if such use is directed or ordered by a person licensed or authorized to practice medicine, dentistry, podiatry, or osteopathy under the provisions of the Education Law of the State of New York.
>
> The sale, lease, transfer or loan of x-ray or fluoroscopic equipment or the supplies appertaining thereto, except to persons engaged in an occupation where such use is permitted and except to hospitals, infirmaries, and medical and dental schools, institutions and clinics, is prohibited. However, this restriction shall not apply to persons intending to use such equipment and supplies solely for the application of radiation to other than human beings, nor to the acquisition of such equipment or supplies by wholesalers, distributors or retailers, in the regular course of their trade or business.

One of the significant comments made by Judge Conway in his opinion includes the following:

> Chiropractors are not licensed in the State of New York to practice any of the healing arts or, indeed, to do anything in our State.
>
> They are not regulated by any statute or supervised in their acts by any State agency. For at least each of the last eighteen years chiropractors have sought from the legislature of this State professional recognition. In each year such recognition has been denied.
>
> For many, many years past, partial professional status has been sought by chiropractors in the courts and in each case it has been withheld.

Chiropractic Association of New York, Inc. on behalf of itself and its individual members, and *Ernest E. Quatro* v. *Herman E. Hilleboe, M.D.*, as Commissioner of Health of the State of New York, November 15, 1961.

He then quoted from Section 6501, subdivision 4 of the Education Law which defines the practice of medicine:

> A person practices medicine within the meaning of this article, except as hereinafter stated, who holds himself out as being able to diagnose, treat, operate or prescribe for any human disease, pain, injury, *deformity or physical condition*, and who shall either offer or undertake by any means or method to diagnose, treat, operate or prescribe for any human disease, pain, injury, *deformity or physical condition.* (Emphasis supplied by Judge Conway.)

And then observed:

> When in this State a man, whether he calls himself a chiropractor or something else, diagnoses the case of one who comes to him for help as requiring an x-ray and either takes the x-ray himself or sends the one seeking help to some one else to take the x-ray, he is practicing medicine within the meaning of Section 6501, subd. 4 just quoted.
>
> In our case Quatro testified that when "a new patient" came to him, the patient would have complaints; that he made a patient's history card for "each new patient"; that he put on it the date the "patient" consults him, his name, address, occupation and the "comments he makes about his condition that he is coming in for" (S.M. 219); the complaints the patient has then and is making to him; that he has treated children; their ages would not make any difference; he would "treat" a seven year old child but he is "not sure" whether he ever "treated a six year old child." (S.M. 220) Quatro's guilt of a violation of Section 6501 is clear and by his own words.

Of particular interest are the answers given by the individual plaintiff chiropractor Quatro to a series of questions concerning his methods of "treatment" and about whom Judge Conway observed: "I am assuming that Quatro was thought by the corporate plaintiff to be the best it had to offer as the individual plaintiff."

The following is an excerpt from the questions and answers quoted in the decision:

Q. In the course of your practice when you adjust the vertebrae, the cervical vertebra at C-2, why are you doing it?
A. To correct a malpositioning of C-2.

* * *

Q. Let us take all the levels or places there is interference. Tell us all the levels and all the places of interference.
A. It doesn't matter, they all go some place.

* * *

Q. Let us go down from C-2 to C-3. You treat the subluxation at C-2 because it is doing what—now tell me.
A. I adjust the subluxation at C-2 because it is a subluxation that is creating nerve interference. That is the only way.

* * *

Q. Whereabouts?
A. At the nerve trunk where the nerve emits from the intervertebral foramen. That is what I am trying to correct.

* * *

Q. Out to what organs of the human body from C-2?
A. I am not familiar with all of them, I don't know where what fibers go.

* * *

Q. You find the subluxation at C-3, so you adjust that, but why do you adjust it?
A. Because it is creating nerve pressure at the "C-3" level.

* * *

Q. At the C-3 level it is creating nerve pressure and is interfering with the flow of nerves going out to what organs in the human body?
A. Several organs.

* * *

Q. What are some of them? Give me one of them from C-3.
A. I don't remember.

* * *

Q. Give me one of them in the human body being affected or allegedly affected. Give me one of them from C-2.
A. I would have to check to find out exactly.

* * *

Q. Do you know what—assuming you found a misalignment or subluxation in between C-7 and T-1, and you wanted to correct the nerve interference there, do you know what organs are fed by that nerve line that will, according to your theory, be interfered with? Would you know now?
A. No, I would have to check.

* * *

Q. By checking you would have to look it up in the anatomy?
A. Yes.

* * *

Q. Would your answer be the same as to T-10, T-11, and T-12, that you would have to look it up; that you do not know?
A. I think you just went through these.
Q. Apparently I hadn't, but would your answer, as of that date, have been the same?
A. Yes, sir.
THE REFEREE: Namely, that you would have to look it up in the anatomy?
THE WITNESS: To find a complete distribution in each one of those nerves, yes, sir
THE OFFICIAL REFEREE: You added the word "complete"; you didn't use that word when you were being examined
THE WITNESS: He asked for all of the organs supplied by the particular nerves.
THE REFEREE: I didn't hear him do that. I say—if you will answer my question, you have added the word "complete" now, but you didn't add it when you were being examined on June 18, 1959?
THE WITNESS: He asked the question, and wanted to know the distribution of each one of those nerves, and I wasn't able to tell him, your Honor.
THE REFEREE: You didn't know?
THE WITNESS: No, I didn't.
THE REFEREE: Aren't you supposed to know when you are treating patients?
THE WITNESS: The complete—
THE REFEREE: No. Aren't you supposed to know?
THE WITNESS: No, your Honor.
THE REFEREE: How old are you?
THE WITNESS: Thirty-one, your Honor.
THE REFEREE: Go ahead.

The witness then testified that in the period between January of 1957 and June of 1959 he had taken 119 full spine x-rays and 11 cervical x-rays using a 1932 model of a Fischer machine which he had purchased from the widow of a chiropractor in 1954, and on which, as of August, 1958, he was not using a cone.

The Assistant Attorney General then read into the record the following questions and answers taken at a pretrial hearing:

BY ASSISTANT ATTORNEY GENERAL:
Q. Were you aware as of the time you were radiating the lumbar and sacral region along with the rest of it that I have referred to and radiating the gonads; were you aware of the very great danger that is attached to any kind of radiation of the direct primary beam or scatter that hits the gonads of either the man or the woman?
BY ASSISTANT ATTORNEY GENERAL: Now follows colloquy of counsel.
BY ATTORNEY FOR PLAINTIFFS: I think it should be read, your Honor. I objected to that question and it was left to the Court to determine whether that was a proper question.
THE REFEREE: Did you receive an answer to it?
ASSISTANT ATTORNEY GENERAL: Yes, I did, Judge.
THE REFEREE: Read the answer.
ASSISTANT ATTORNEY GENERAL: "I was not aware at that time of the very great danger."

Judge Conway then asked the chiropractor witness if he used a lead apron to protect himself and the latter admitted that he stood behind a lead shield when taking the x-ray. The following questions and answers then ensued:

THE REFEREE: So, you must have known there was some danger in taking x-rays, danger to the patient?
THE WITNESS: Yes, sir, your Honor.
BY ASSISTANT ATTORNEY GENERAL:
Q. And that danger or potential danger would be one of the reasons you, yourself, would get behind that lead screen so that you wouldn't even be hit by any of the matter; isn't that so?
A. Yes, sir.
Q. To say nothing of being hit by the primary beam?
A. Yes, sir.

The judge, after further reference to the chiropractor Quatro's testimony concerning his use of a stethoscope and a sphygmomanometer or blood pressure machine and his training at chiropractic school, made the following significant observation: "I have quoted enough of the individual plaintiff's testimony to indicate why I think he is and has been unlawfully practicing medicine . . ."

The referee then referred to the testimony of one O'Neill, a chiropractor and former secretary and president of the plaintiff chiropractic association, who testified in part as follows:

Q. Mr. O'Neill, tell us the qualifications of membership of the plaintiff.

* * *

THE WITNESS: Article 8, Section 1, shows that the membership is divided into four classes: active membership, associate membership, student membership, and honorary membership.

* * *

A candidate for active membership must be a resident course graduate of a chiropractic school or college *and in active practice in the State of New York.* He shall be of good moral character and *a resident practitioner of recognized standing and ability in the State of New York.*

The Official Referee: Read that last part again—May I look at that?

The Witness: Yes, sir. (The witness hands document to the Referee.)

The Referee: In active practice in the State of New York. I didn't think you were admitted to practice in the State of New York.

The Witness: I think the mere fact that we are *conducting our activities is a form of practice.*

The Referee: You are not *licensed to practice* in the State?

The Witness: We are *conducting our affairs.*

The Referee: You may be doing it illegally; but active practice I didn't think you were permitted in the State of New York.

The Witness: Sir, I am at a loss as *to what you call this,* then.

* * *

By Attorney for Plaintiffs:

Q. *In the course of your practice is it necessary that you use x-ray,* Mr. O'Neill?

* * *

A. I believe that it is necessary, yes, sir, in the majority of cases.

The Referee: To do what? To accomplish what?

The Witness: The *purpose of taking x-rays is to be able to determine the structural situation,* the *posture,* the type of *curvature,* the *spinal subluxations,* the *misalignments,* or *distortions* that might be *present in the vertebral column.* This gives us a great deal of information on how to proceed with the patient, and it also shows us whether or not there may be any contraindications to our type of therapy. (The *American College Dictionary* and the *New Century Dictionary* define therapy as the treatment of disease, as by some remedial or curative process.)

By Attorney for Plaintiffs:

Q. In what percentage of your practice has it been your experience that it is essential to have x-rays?

A. I would say *about 80 to 90 per cent of my practice* requires it.

The Referee: That is for the purpose of determining what the man is suffering from?

The Witness: No, sir; it is more for the purpose of determining the structural postural situation of the individual.

The Referee: That has nothing to do with the determination of what he may be suffering from?

The Witness: *Not necessarily.* It does from the *standpoint of manipulated therapy,* but not necessarily does it show a specific symptomatology that *the other healing arts* use more predominantly in arriving at a decision.

The Referee: Symptomatology—

The Witness: —would be the *complaints* of the *patient.*

The Referee: What was the word you used after symptomatology?" would you check it?

(the reporter read from the record as requested)

The Referee: What do you mean by "Not necessarily?"

The Witness: For instance—let me see. If a person complained of a headache the x-ray wouldn't show that he had a symptom of the headache. We are concerned primarily with—

The Referee: We are now talking about "not necessarily." You said it did not necessarily show anything from which he suffered.

The Witness: What I say, the *symptomatology that the other healing arts* might place more on—for instance, spinal distortion wouldn't necessarily show that the patient possibly had a temperature or a headache, or that he might be suffering with an acute pain in his belly at the moment; but *it does give us structural information to enable us to proceed with our type of manipulation.*

The Referee: And that is what you meant by "not necessarily?"

The Witness: Yes, sir.

By Attorney For Plaintiffs:

Q. Did you tell us the percentage of cases in which the x-rays are necessary?

The Witness: I think 80 to 90 per cent.

Q. And *this x-ray used by you in your occupation is for detection purposes,* Mr. O'Neill?

A. Yes, *for analysis and also detection,* to determine, perhaps, if there might be some situation that should not be handled under manipulated *therapy* and should be referred to one of the *other* healing arts.

* * *

By Assistant Attorney General:

Q. Do you happen to know what percentage, approximately, of that 563 do the same as you do, send their patients out to an x-ray laboratory to be x-rayed?

A. I would say a hundred per cent of them.

Q. *So that all of those 1,000 members are either applying x-ray radiation themselves in their offices, or sending their patients out to a laboratory to have x-ray radiation applied?*

A. I think that would be correct.

* * *

Q. As one of the officers, secretary, et cetera, and finally president for two years of the plaintiff association did you come to know approximately how many chiropractors there are practicing in the State of New York, approximately?

A. We had an unofficial survey made, I believe it was 1954, the first year that I took over as secretary, where we requested the yellow pages of telephone books from all over the state to be sent to us so we could make a compilation and try to get an idea of the total number of chiropractors, and as of that time— I can't give you an accurate figure, but it was somewhere in the vicinity of 23 to 24 hundred.

Q. Twenty-three to 24 hundred plus or minus, we'll leave it.

A. Yes, sir.

THE REFEREE: As a matter of fact, a man can put out a sign "Chiropractor" on his door no matter what his education is and your association has no power to stop him from so doing?

THE WITNESS: That's correct, sir. The regulatory status belongs with the State, not with us.

THE REFEREE: You mean the State of New York?

THE WITNESS: Yes, sir.

THE REFEREE: The State of New York does not regulate chiropractors at all?

THE WITNESS: If they regulate any of the healing arts—

THE REFEREE: *Chiropractic under the State Law is not a healing art.*

THE WITNESS: *I understand that.*

THE REFEREE: *That is correct,* isn't it?

THE WITNESS: Yes.

THE REFEREE: *So anybody can put out a sign and say he is a chiropractor and there is no control over them in the State of New York;* that is correct, isn't it Mr. O'Neill?

THE WITNESS: I think it is *essentially correct,* your Honor.

* * *

Q. Of the six or seven that you sent down to the Joseph Maynard Lab to be x-rayed per month in the year 1960 how many of those six or seven would the records of the Maynard Lab show were full spinographs?

A. May I say that *in the majority of cases I do ask for the full spinograph.*

THE REFEREE: Do you ever ask for anything else?

THE WITNESS: Yes, sir, sometimes I ask for cervical plates, neck plates.

THE REFEREE: Before you do that you must have treated the patient?

THE WITNESS: No, sir. This is when I start with the patient that I request these things.

THE REFEREE: Before you give the *patient any treatment?*

THE WITNESS: *In many instances, yes, Judge.*

THE REFEREE: In some instances—

THE WITNESS: In some instances I don't.

THE REFEREE: *In some instances you do give the patient* the treatment and then go down and ask for a cervical plate?

THE WITNESS: In some instances, in a few instances I might do that, yes, sir.

THE REFEREE: It isn't what you might do. Let us understand. If a man comes in to you, such as I, you can go down and say "Let me have a full spinograph." Now, in the case where a man comes in to you, or a woman, and in the first instance *do you ever go down and ask for a cervicalgraph without ever touching the patient?*

THE WITNESS: Oh, no, *I have palpated the patient* and I have a *pretty fair idea of what I want to start with.* I don't just make it a promiscuous thing, that they walk in and I immediately send them down. *I check with manual manipulation. I do check the areas that are concerned.*

Judge Conway, after quoting further from O'Neill's testimony concerning his use of x-ray in treating persons coming to him, concluded:

> The witness apparently lawlessly has disregarded Education Law 6501, subd. 4 (See *People* v. *Vandecarr,* 288 N. Y. 640; *People* v. *Devinny,* 227 N. Y. 397, 401).

He then went on to say:

> There were other witnesses who testified for plaintiff. Of those, two were doctors of chiropractic; another was a Doctor of Philosophy as well as a Doctor of Chiropractic; another was a chiropractor from Chicago who was admitted to practice there under Illinois law; another was a teacher of physics "and in particular of radiation physics." Each, except the ones from Chicago and the teacher of physics, established to my satisfaction that he was practicing medicine in the State of New York where our Legislature has refused permission to do so, despite the efforts of chiropractors, in session after session of the Legislature, to obtain such permission. Each of them in testifying used words which might be termed "doctors' or osteopaths' words" since they were words involving terms used by medical men admitted in New York State to the practice of one of the healing arts as permitted by our Legislature. They surely were words which would cause the persons whom they described as "patients" and who came to them with "complaints" to believe that these men had competent medical knowledge. After talking with those patients either before treating them or after laying hands upon them to give so-called chiropractic adjustment or treatment, most of those

people who claimed to be sick were sent off to another chiropractor, or a laboratory operated by a chiropractor, to have a complete spinograph from nearly the upper part of the cranium to the end of the spinal column with the consequent results depicted by Dr. Morgan and Dr. Glass. If the chiropractor consulted by such patient had his own x-ray machine capable of so doing, he took a complete spinograph himself. The spinographs were generally on a 14 by 36 (3 feet) plate. In some instances an x-ray of a portion or portions of the spinal column were taken generally, but not always, in addition to the spinograph.

Those other witnesses do not impress me as frank, truth-telling witnesses, with the exception of the chiropractor from Chicago. I shall digest the testimony of the teacher of physics, Grisewood, and make but brief references to that of Clarence W. Weiant, Sol Goldschmidt, and Charles Krasner.

The witness Weiant testified that he lived and practiced chiropractic in Peekskill, New York. He had not been licensed in any of the healing arts in New York State or City. He did have a degree of Doctor of Philosophy. He was Dean of the Chiropractic Institute of New York, located on East 38th Street, New York City. He has his own x-ray equipment at his office in Peekskill which has a value of approximately $2,500.

He said that he took full spine A-P pictures and lateral cervical and lumbar views, but took the pictures in sections only because he did not have the equipment to take a full spinal x-ray.

Doctor of Philosophy Weiant was a difficult witness. He did not impress me as being frank. Certainly he was illegally practicing medicine in our State (S.M. pp. 172–176).

Mr. Goldschmidt, who lives and has an office in Manhattan, testified that he was chairman of the X-ray Committee of the Chiropractic Association of New York; that certain questionnaires were sent out to the members of the corporate plaintiff and statistical information received in reply. The questionnaires, replies, and the subsequent compilation of information based thereon were offered and received in evidence.

The witness said that about half of the chiropractors, practicing in New York State, do not belong to the corporate plaintiff.

Mr. Goldschmidt testified that after he sent a patient out to be x-rayed and the x-ray came back, he read it and interpreted it and in part those readings and interpretations of that film so returned, entered into his deliberations and determinations "as to what manipulation to do on the patient." Patients are x-rayed in a substantial part of his practice. He said that in the majority of cases he sent the patient out to have an x-ray taken before he put his hands on him. He said he palpates his new patients. He also takes blood pressure and uses in his practice a sphygmomanometer, a stethoscope, and an otoscope. However, he said he made no record of the data of what he observed upon his examinations on the patients' history cards.

The operation of this witness' mind may be deduced from the following questions to him and his replies:

Q. Do you recognize that the sphygmomanometer and the otoscope and the stethoscope are instrumentalities for the practice of medicine?

A. No, not exclusively, Mr. Murphy.

Q. You claim the chiropractors have the right to use them, also?

A. I believe *any member of the healing arts* has a right to use them.

THE OFFICIAL REFEREE: Chiropractic is not recognized as one of the healing arts in New York State, is it?

THE WITNESS: That is correct, from a Legislative standpoint, sir.

Apparently this witness does not know our theory of government with its division of powers and responsibilities or else is boldly lawless. Whether it be ignorance or lawlessness, we may well be grateful to our Legislators for protecting us and not licensing these men. Again, we must assume that the witnesses produced by the plaintiffs were the most learned, law-abiding and truthful men in the plaintiff Association. (Emphasis added.)

Charles Krasner testified that he was a licensed chiropractor in the State of Vermont and in Puerto Rico. That before graduating from the Chiropractic Institute of New York, he was a graduate of Abraham Lincoln High School and attended Brooklyn College for two years; and that he has been a chiropractor for twelve years. That he owns x-ray equipment which he purchased in 1952 and which he described. That he usually takes a 14 by 36 inch full spine x-ray with a lateral plate in 75 per cent of his cases.

He said that he used an otoscope to look into the ear and on occasion looked into the nose with it; that he used an ophthalmoscope to observe the eyegrounds, the eye disk, the retinal arteries; that he does not put down the results of his findings and observations from the use of the ophthalmoscope nor of the otoscope; that he listens to the heart with the stethoscope but not on all new patients; that he reads and interprets the x-ray which he takes; that his teacher of x-ray was another chiropractor and not an M.D.

Certainly he was "holding himself out" as a medical practitioner.

* * *

The judge made the following significant observation:

> Certainly the members of the corporate plaintiff and Quatro were holding themselves out as competent to cure disease within the meaning of Education Law 6501, subd. 4. Not only that, but the members of the corporate plaintiff and Quatro also violated the first and second paragraphs of Regulation 19 of Chapter XVI of the New York State Sanitary Code.

Judge Conway reviewed in detail the testimony of a witness, Edgar N. Grisewood, called by the plaintiffs as a nonchiropractor radiation expert. Grisewood testified that he had been a teacher of physics since 1923 at a university; that he had no doctorate degree; that he lectured in radiation physics and that part of his work entailed the calibration of x-ray machines. The testimony disclosed that he, at the request of the chiropractors' counsel had gone to the offices of various individuals, including the chiropractor witness, Krasner, to make tests of the radiation received by persons subject to x-ray examination. The judge stated after reviewing the witness's testimony concerning his use of "*Victoreen manometer chambers*" to determine "*the amount of radiation received close to the genital organs or the gonads*" that:

> The testimony of Grisewood, as we have noted, was given on two occasions three months apart. On the first occasion, he talked of one manometer only. This was placed in the groin of the patient. When he was recalled three months later he testified to having two manometers. They were shown to him by counsel for the plaintiffs, and they were marked at least for identification. Those two manometers were not capable of enabling the witness to determine the amount of x-ray "*directed at the patient.*" The witness said so in his answer: "Your Honor, I agree, that's right, your Honor. The chamber will not read that high." The truth was that the two manometers shown to the witness and marked for identification could measure only scatter. They were not strong enough to measure the direct beam directed at the patient. As the witness said on his second appearance, that would be made with a Victoreen r-meter, and as he said "that required, of course higher levels." It will be noted that on the second examination the witness for the first time spoke of a Victoreen r-meter. On his original examination he mentioned only "a Victoreen manometer placed in the groin or crotch of the patient." He also testified as I have pointed out heretofore: "This is the standard Victoreen 200 milliroentgen chamber, whose length is approximately 3 inches," and "whose internal diameter is approximately one-quarter inch." The truth was, as the witness said on his first appearance, "I put a Victoreen manometer in the groin of the patient during the exposure, and then measured the amount of scatter, the amount of radiation recorded by that chamber." *The truth appeared on this witness' second examination. He never tested for anything but scatter. He never tested for the direct radiation from the beam directed toward the patient.*

The judge then observed that the reason for the second appearance of the chiropractor's witness, Grisewood, was the testimony of Russell H. Morgan, M.D., of Baltimore, Maryland, a witness for the defendant Commissioner of Health of the State of New York. Dr. Morgan testified that he was a physician specializing in radiology; that he was Professor of Radiology at Johns Hopkins University and Radiologist-in-Chief at the Johns Hopkins Hospital. He testified to his experience in medicine prior to becoming Professor of Radiology and Radiologist-in-Chief at the Hospital in 1946. He is responsible for a substantial radiobiologic program, where among other subjects, genetics is an area in which he is engaged. He is a member of the American Medical Association, the American Roentgen Ray Society, the Radiological Society of North America, the American College of Radiology, the American Physicians Society, and the Radiation Research Society.

Dr. Morgan had testified:

> A. The testimony that I presented this morning was an anteroposterior spine film taken with conventional x-ray apparatus under recognized good technics of today and with films and screens and other conditions also optimum in character and lead to an exposure dose of the patient of something of one roentgen or a thousand milliroentgens. Now, in some notes that I took yesterday Professor Grisewood reported that with some studies which he made the exposure doses were of the order of one-tenth of these values. I, of course, was not present when Professor Grisewood made his measurements and hence can only wonder about the reasons why his testimony of actual measurements might be different from my testimony which also is based upon the actual measurements

in practice and which, incidentally, is supported by tables of exposure dose values under conditions identical to those which Professor Grisewood cited, in the handbooks prepared by the National Committee on Radiation Protection and published by the National Bureau of Standards. Now, one thing that the witness said yesterday was of interest to me because he said that he used a device called a Victoreen manometer, and it has been my experience in the use of such an instrument that at the relatively high radiation intensity levels characteristic of those intensities used in the diagnostic x-ray field that the instrument tends to be unreliable and unreliable in the direction of yielding values which are less than proper values, than actual values. Now, it is speculation on my part that this may be the reason for the discrepancy, but in view of Mr. Murphy's question I feel it proper to report my experience in this field, particularly where the experience not only of myself, but also of the scientists who prepared the material for the handbooks of the National Committee on Radiation Protection, was also at some variance to that of the witness yesterday.

By Assistant Attorney General:

Q. At any rate, Doctor Morgan, it has been your experience and observation and you have found that the Victoreen manometer is unreliable for the purpose of measuring accurately x-ray exposure, under the proper technics, of one milliroentgen or up to ten?

A. Yes, I can. The answer is yes. I think my testimony a moment ago stated that.

Judge Conway in his opinion reviewed the increase in knowledge as to ionizing radiation beginning with the year 1930 as follows:

> In the year 1930 Herman Joseph Muller discovered "that x-ray will produce mutations in the hereditary material." (SM 574) Muller was later awarded the Nobel prize for his discoveries. Then in 1945, on August 6th and August 9th, atomic bombs were dropped on Hiroshima and Nagasaki in Japan. Later, experimental prototypes of the hydrogen bomb were detonated in 1951 and 1952 by our National Government. In 1954 the hydrogen bomb advanced from the experimental stage to the status of a usable weapon, and our National Government exploded three hydrogen bombs during that year at its Pacific proving ground in the Marshall Islands. (*Encyclopedia Britannica Book of the Year 1955.*) The taking of x-ray, the dropping of bombs over Hiroshima and Nagasaki, and the explosion of hydrogen bombs, all produce ionizing radiation with similar effects upon the human body.
>
> These various events, beginning with Muller's discovery in 1930, which I have listed in the preceeding paragraph, all involving ionizing radiation, alerted the National Academy of Sciences, and our health statutes affecting both our city and our state have been amended and our research has continued unabated.

He then quoted from Dr. Morgan's testimony in part as follows:

Q. Doctor, in any anterior-posterior x-ray film of the spine, including the lumbar and sacral area, the gonads are going to be of necessity in the direct primary beam, are they not?

A. Yes. In the case of a female this is certainly true. In the case of a male it is also almost certain.

The Referee: Almost certainly true?

The Witness: Yes.

Q. And for the production of a clear and adequate lateral view of the full spine, including the lumbar and sacral and coccyx area, the gonads of the male and female are in the direct primary beam of the x-ray?

A. This is true.

The Referee: Did you ever hear of x-ray machines being made differently for chiropractors than for medical doctors?

The Witness: The x-ray generating equipment is, to my understanding, identical. There is no special characteristic concerning the x-ray generating apparatus.

Dr. Morgan then testified in detail as to the technical nature of x-rays and the purpose and function of male and female gonads. In response to a series of questions put to him by the Assistant Attorney General, he testified in part as follows:

Q. In those gonads of the male and the female are contained the hereditary material from which the human beings in existence came, and from which the generations yet unborn are to come?

A. That's correct.

Q. Doctor, do you agree that the hereditary material of the human race is one of the most precious trusts that we have in our care, and that it should be handed down from generation to generation in the best possible condition?

By Attorneys for Plaintiffs: I object to that as improper and prejudicial.

The Referee: Overruled. I will allow him to answer.

The Witness: Yes, I do. This is an expression used by many people, particularly the geneticists who are primarily concerned with this important problem.

BY ASSISTANT ATTORNEY GENERAL:

Q. Doctor, do you have an opinion which you can express with a reasonable degree of radiological-genetic certainty as to whether or not x-rays passing through the gonadal organs of the male and female damage that hereditary material?

A. I do.

Q. Will you state what that opinion is?

A. The effect of x-rays is destructive upon biological materials, and this is true whether the biological materials are cancer tissues, with which I do deal in my daily practice, or whether the material is normal cells composing the various tissues of the body, including the gonads. Now, of the various parts of the cell, regardless of gonadal tissue, cancer tissue, or the like, the most sensitive part of ionizing radiation, and the part most likely to undergo destructive change, is the nucleus which contains the chromosome material which determines in the case of the reproductive cells the characteristics of future generations, and radiation produces within these cells, thereby, by its destructive action, changes in this chromosome material which may materially affect the characteristics of future generations.

The changes are almost always deleterious ones. The chances of the changes being deleterious, indeed, are so great that one can essentially neglect the possibility of the changes being beneficial, and hence, radiation exposure of gonadal tissue has to be a serious business whenever such exposure is carried on, and the damage created must be considered in relationship to the benefits to be achieved by that exposure.

Q. What is your opinion as to whether or not x-ray exposure to the gonads of the order of 1,000 milliroentgens is damaging and deleterious, in part, at least?

THE WITNESS: Well, the genetic information on this point I think is sufficiently clear to give an estimate of the damage which such a dose might produce. It is a fact of nature, as you perhaps know, that mutations are continually taking place in the genetic material of the human being, and that geneticists have stated that the number of mutations which are spontaneously taking place in nature are of something of the order of two per cent fertilizations.

* * *

THE WITNESS: This, therefore, leads us to the point, what do a thousand milliroentgens do as far as the creation of additional mutations within the genetic material, and here the genetic evidence is that an exposure dose of about 40 roentgens to the reproductive organs will double the spontaneous mutation rate.

In other words, a dose of 40 roentgens would cause the percentage of mutations existing within the population to change from approximately 2 per cent to the 4 per cent level; and, proportionately, 1 roentgen, or 1,000 milliroentgens exposure doses, which are identical, would proportionately create an effect in changing the mutation rate upward.

He went on to state that "*as additional exposures take place from time to time throughout the reproductive life of the individual these additional exposure doses are cumulative in the effect.*" And that "*the amount of damage to the reproductive cells from all of the scientific evidence at hand today is that the amount of damage is proportional to the quantity of radiation absorbed by the reproductive cells, and also not only is there a proportionality here, but that the relationship between the biological effect and dose begins from zero dose upward. In other words, there is no dose below which one is completely safe; there is no so-called safe dose. The effects produced by a small dose qualitatively are exactly the same as the effects produced by a large dose. The only difference here is a quantitative one; the relationship being one of proportionality.*"

The Assistant Attorney General asked Dr. Morgan:

Q. Based upon your background in the subject, whether from reading or observation, or otherwise, can you state what some of these resultant abnormalities from the situation that I have described in my previous question and your previous answer, could be?

A. Well, there are a wide variety of abnormalities which might result from such a mutation in the reproductive cell, and these abnormalities involve almost every system of the body: the cardiovascular system, the nervous system, bone and joint system, and so on, just to cite a few of some of these; the abnormalities of congenital heart disease, of which, as I said, there are many, abnormalities of the blood-forming tissues in which one or more of the chemical and cellular constituents of the blood may be absent; abnormalities of the bony system with multiplication of an absence of certain of the normal parts of the body—almost every system can show abnormalities, and where these abnormalities will develop is a straight random process which might result in the abnormality appearing in one state in one individual and the abnormality taking another form in another individual.

Q. These abnormalities are all harmful, are they not?

A. Yes.

Later in his testimony, Dr. Morgan was asked:

Q. Doctor, do you have an opinion which you can express with a reasonable degree of medical and radiological certainty as to whether or not an exposure, an x-ray exposure of 1,000 milliroentgens needed or necessary to produce a satisfactory film such as shown in Defendant's Exhibit A (a full spinograph reproduction of an x-ray in an anterior-posterior projection) increases the probability of the person receiving that dosage of acquiring leukemia?

A. I do.

Q. Will you state what that opinion is?

* * *

A. As I recall, the question is what is that opinion. The effect of radiation on biological tissues is one which not only affects the genetic elements of the reproductive organs, but also the other cells of the body, including the cells which are involved in the process of forming blood.

Now, scientific evidences are perhaps not as extensive in this area as in the genetic field; yet, I think the evidence is rather conclusive on one or two points. Number 1: That radiation of the blood-forming tissues can produce leukemia. There is no question about this point in other mammals, including the mouse. In the experimental observations made of the populations of Nagasaki and Hiroshima following the atomic bombs of World War II there has been an increased incidence of leukemia, an incidence of leukemia over and above that which might have been expected if there were no bombings, and that this increase in leukemia is sufficiently substantial that it has been possible for one or two scientists to have calculated what the relationship is quantitatively between radiation dose and the probability of one developing leukemia. I cite here the reports of Dr. Lewis of the California Institute of Technology and Science a few years ago who studied this problem thoroughly and who found that the probability of one's developing leukemia was one to two parts per million per roentgen of whole body dose per year of survival after the exposure was over. And from this, one can calculate what the probabilities might be of developing leukemia after a given x-ray exposure of the whole body or substantially of the whole body if one assumes that the person will live from a number of years equal to the normal life span.

For example, if the normal life span extends to seventy years and the individual has received his exposure at twenty, this means that normally he would live another fifty years, and if one roentgen were delivered to the whole body, on the basis of Lewis' data, this would indicate that the probability of that individual developing leukemia would be one or two parts per million multiplied by 50, and although my mental arithmetic is not necessarily good here, I think this works out to be something of the order of one part in 10 to 20 thousand. Now, this in itself, of course, is not very great, but here again it appears prudent to assume that the effects of radiation on the blood-forming tissues are cumulative, and hence a number of exposures will add to the probabilities. One can calculate from them what the increased probabilities are, and one should probably also from a public health standpoint assume one more thing from the standpoint of prudence, something which is not absolutely proven, but which seems entirely possible and perhaps likely, namely that the result of an exposure to radiation will be proportional to it, not only proportional to the dose given, but that there is here also no threshold dose below which no effect can be detected.

As I said, the scientific evidence on this threshold proposition is incomplete, but, again, looking at the problem from a public health standpoint, it is necessary to exercise prudence, and prudence requires that one assume a similar relationship, namely that there is no threshold as was the case and is the case in the genetic field. This is the answer, I think, to your question, Mr. Murphy.

THE REFEREE: And these bombs over the two cities you mentioned had the effect of affecting the total bodies with x-rays of those who were within the reach of the bomb?

THE WITNESS: That is right. Technically speaking, these are not x-rays, but are similar in their effects to x-rays. X-rays, technically, are rays produced in a particular type of interaction of electrons with matter, and the radiation involved in the

Hiroshima and the Nagasaki bombings were not produced in precisely that way, but the radiations which were involved in Nagasaki and Hiroshima have the same effect. They were ionizing radiation, high energy radiation of the sort identical in characteristic, qualitatively perhaps a little bit different, biologically identical.

BY ASSISTANT ATTORNEY GENERAL:

Q. Coming back to the final question, without reference to Exhibit A, an x-ray exposure of the full spine, including all those bones that I had referred to, will increase the probability of that person acquiring leukemia?

A. That is correct.

He then testified that in the year ending June 30, 1960, in excess of 80,000 diagnostic x-ray examinations were done at Johns Hopkins; that a few over 1,500 were examinations of the cervical spine, a few over 800 of the thoracic spine and a few under 2,300 of the lumbar spine. He was then asked by the Assistant Attorney General:

Q. Doctor, before the examination was made of the cervical spine, the thoracic spine, or the lumbar spine, had a physical and medical examination been made of that patient for the purpose of determining the existence of possible pathology in the cervical, thoracic, or lumbar area?

A. That is correct. No examinations are taken unless a thorough work-up of the patient has taken place beforehand.

Q. No x-ray examinations?

A. No x-ray examinations.

Q. Without a thorough work-up of the patient beforehand?

A. That is right. A work-up includes a regular taking of a history and the performing of a physical examination by one of the members of the clinical staff of the hospital.

Q. And that pre-existing clinical examination had been made of all of these patients and the observation that there was a possible actual pathology in the cervical, thoracic, or lumbar spine before they were x-rayed?

A. That is correct. The thesis on which we operate is radiation is undesirable and hence the clinical indications for the taking of a film or series of films must be established beforehand.

He was then asked:

Q. What proportion—withdrawn. In what proportion of those films where the cervical, thoracic, or lumbar spine was x-rayed was there a subluxation found?

A. I can't give you a quantitative answer on this, but I would estimate that the number, that the incidence of this is quite rare—that is a real subluxation proven by a sufficient number of films to rule out the possibility that what might have been a subluxation is not merely a matter of the posture of the patient or the positioning of the patient by the x-ray technician.

THE REFEREE: Would you amplify that answer, please.

THE WITNESS: Well, your Honor—

THE REFEREE: Not amplify it—you mean—I am not going to ask you what you mean; you tell me.

THE WITNESS: The mobility of the joints is quite large in order that an individual can perform the many things that he does, the normal work and life, and hence, in the positioning of a patient there may be a sufficient movement in setting a patient up, of the spine let us say, so that the appearance of the spine may give the impression that one joint relative to another is not in its exact normal alignment. On the other hand, a patient may have a real subluxation which will look very much like the normal situation, and then one can be certain of this situation only by taking several films in various stages of flexion and extension to see whether or not the joint is actually abnormal. If the situation is fixed into a position which is abnormal and during the stages of flexion and extension normalcy is not approached, then one can be reasonably certain that a pathological state exists. But actually under our experience subluxation, except under rather limited circumstances, is something that we are not greatly concerned about.

THE REFEREE: Would you be good enough to define subluxation?

THE WITNESS: A joint may completely dislocate in which the articular surfaces of the two bones involved in the joint are completely deranged one to the other, and in the case of a subluxation the changes in the joint and the bones associated with the joint are somewhat less than this to the extent that the relationships extend all the way from normalcy on one side to that approaching dislocation on the other side.

The next witness called on behalf of the Commissioner of Health was Dr. H. Bentley Glass. He testified that he was a professor of biology in Johns Hopkins University and in particular a human geneticist; that he is engaged in the study and research of the effect of ionizing radiation for x-ray exposure on genetic cells and somatic cells. Judge Conway noted that in 1955 he was appointed secretary of the National Academy of Sciences' committee on genetic effects of radiation, having begun the use of x-rays in the study of mutations in 1929.

He testified that in an *anterior-posterior* exposure of the full spine including the pelvis and gonadal areas, the gonads in either a male or female would be in the direct primary beam of the x-ray and would be irradiated. He also stated that a *lateral* exposure of the full spine including the lumbar spine would send the direct primary beam of the x-ray through the gonads of either the male or female depending on which would be irradiated. He further said that to obtain the satisfactory x-ray film shown in Exhibit A an x-ray dose of approximately 1,000 milliroentgens would be needed. Also that to obtain a satisfactory x-ray film of the area shown in Exhibit D—a *lateral* view of the full spine—an x-ray dose of approximately up to 10 roentgens (that is, 10,000 milliroentgens) would be needed.

Judge Conway noted in his opinion that:

> Dr. Glass further testified that the hereditary material of the reproductive cells, as of all cells, is located in the threadlike chromosomes of those cells, and these can be either fractured by ionizing radiations, as Dr. Morgan had described on the preceding day, or they can be made to alter in their chemical nature so as to produce permanent chemical changes in the nature of the genes, and consequently in the characterization of the offspring and descendants of any individual, arising from those mutated cells. That in addition, all of the evidence which geneticists have obtained over the past more than thirty years in working with ionizing radiations, indicates that the frequency of chromosome breakage and the frequency of chemical mutations of the genes is directly proportionate to the size of the dose. Dr. Glass further said that in his laboratory recent experiments showed that that held down to doses as low as 5 roentgens.
>
> He further testified that the frequency of the mutations is directly proportionate to the dose; that that simply means that a dose of 5,000 milliroentgens would produce five times as many mutations as one of 1,000 milliroentgens and that could be carried up or down the scale of magnitudes, as one may wish; that there is no evidence that there is any dose so low that it does not produce a proportionate number of mutations and the scientific evidence is that it does.

Dr. Glass further testified as follows:

Q. Do you have an opinion as to whether or not the genetic and somatic cellular damage from x-ray is cumulative and additive?

A. I do.

Q. What is that opinion?

A. It is both cumulative and additive. All of the experiments that I have conducted personally and that other geneticists have conducted, according to my knowledge, have indicated that all of the radiation, the ionizing radiation received by the reproductive cells during the course of a generation up to the termination of the productive period is additive and cumulative.

Q. That is, that the x-ray exposure taken today must be added to the one taken next month plus the one three months later, plus the one a year later, plus the one five years later, and so on?

A. Exactly.

Q. And prescinding, for the purpose of this question, away from the hereditary material, would your opinion be the same as to the additive and the cumulative effect of x-ray exposure on the somatic cells in all the rest of the body?

A. So long as that is referred to the chromosomes, the hereditary material of the other cells, it does so apply.

Q. Do you have an opinion as to whether or not, as far as the total general population is concerned—in the State of New York it is roughly sixteen million, plus or minus—in the long run a little radiation to a lot of people is as harmful as a lot of radiation to a lesser number, do you have such an opinion?

The Witness: I wrote that sentence, myself, in the report to the National Academy of Sciences Committee. It is my opinion.

He also said in response to questioning by the Assistant Attorney General:

Q. You have testified that when the reproductive cells are damaged by irradiation, mutated genes result?

A. That is correct.

Q. Is it your opinion that once that gene mutates it remains permanently altered?

A. It remains permanently altered, barring the extremely rare possibility of its mutating back again. This is—this reverse mutation is an event that occurs with extreme rarity.

Q. Doctor, what happens then, if in the master plan a male sperm cell that has been damaged by mutation from x-ray exposure unites with a female ovum in the reproduction process?

A. Theoretically all mutations, an overwhelming majority of them, produce damage. This damage may be evident in the immediate offspring or only in subsequent generations even to the fortieth, or later, generation. The types of damage which may arise can affect virtually any part or system of the body. These might include:

Mental or nervous defects and disorders, such as epilepsy, for example;

Neuromuscular disorders;

Defects of vision or hearing, such as deafness;

Defects in the growth of the skeletal system, such as dwarfness;

Defects of a hematological kind, such as inability of the blood to clot properly;

Or endocrine disorders, such as diabetes, or modifications;

Congenital deformities and defects of the heart, of the digestive tract, or of the urinary and genital organs.

Everything can be covered. This is because the genes control the pattern of normal development—the master plan, as you called it, of development is in the gene.

When a gene is mutated it is unable to perform its normal function either entirely or partly.

* * *

Q. One more question, Doctor: Do you have an opinion which you can express with a reasonable degree of certainty as to whether or not an x-ray exposure of approximately 1,000 milliroentgens to the human body, to the full spine and lumbar area, increases the probability of the person receiving that dosage of getting leukemia—increases the probability?

A. I do.

Q. Will you state what that opinion is?

* * *

BY ASSISTANT ATTORNEY GENERAL:

Q. Just state whether the opinion is that it can or cannot.

A. It can increase the probability.

Judge Conway then observed that:

Dr. Herman E. Hilleboe is the Health Commissioner of the State of New York. He testified at length. He is the defendant herein and his testimony was in accord with that of Dr. Morgan and Dr. Glass. I shall rest upon that without digesting Dr. Hilleboe's testimony since this opinion is already quite lengthy. I shall merely add that Dr. Hilleboe testified that the stethoscope, the sphygmomanometer, the ophthalmoscope and the otoscope "are instruments of medical practice" and that an x-ray machine is "an instrumentality of medical practice." (SM 847-850). I find as facts those statements of Dr. Hilleboe as to the instruments mentioned.

The Judge then ruled that the case of *Matter of Sausser* v. *The Department of Health* (242 N.Y. 66, 69) decided in 1926, on which the plaintiff chiropractors relied heavily, was not in point since (1) it was obsolete, applying only to a regulation of the Board of Health of the City of New York accompanying Section 107 of the Sanitary Code of the City of New York only as it existed in 1926, and (2) it was never applicable to the Sanitary Code of the State of New York, Chapter 16, Regulation 1 or Regulation 19.

He observed that "the case was decided in 1926 and was applicable to the City of New York only. . . . It was a different world in which we were living in 1926 from the one in which we lived in 1950. We had learned of mutation of the genes by x-ray, beginning in 1930. We had learned of atom bombs by 1945. . . . Chiropractors have never been licensed under the laws of this State to diagnose and treat disease either in the City of New York, to which Section 107 of the Sanitary Code and the accompanying Regulation applied, or in the State of New York.

Judge Conway concluded his comprehensive and far-reaching decision by dismissing the complaint of the chiropractors in its entirety. The chiropractors have appealed his decision, and the ruling of the Appellate Court is awaited with eager interest by all those concerned with the health and well being of the people of New York.

Chiropractic Association of New York, Inc. on behalf of itself and its individual members, and *Ernest E. Quatro* v. *Herman E. Hilleboe, M.D.*, as Commissioner of Health of the State of New York, *N.Y. Law Journal*, Dec. 14, 1961, p. 1, col. 7.)

Guidelines for Tuberculin Testing

From the Ad Hoc Committee of the State Department of Health and the State Committee on Tuberculosis and Public Health of the State Charities Aid Association

Early in 1960 there was formed a joint Ad Hoc Committee of the State Department of Health and the State Committee on Tuberculosis and Public Health of the State Charities Aid Association. Its purpose was to develop joint policies for official and for voluntary agencies in tuberculosis control activities.

At the first meeting of this committee in April, 1960, two subjects were discussed: changes in case-finding policies, and the Arden House Conference recommendations. At this meeting it was decided to confer on the subject of tuberculin testing, and two discussion meetings were subsequently held in June and in September. This statement is based on these discussions.

As stated in the *Tuberculin Testing Handbook* of the National Tuberculosis Association in 1958:

> Case-finding, using the tuberculin testing or chest x-ray as an initial screening method, continues to be the responsibility of the health department . . . . If the Tuberculosis Association undertakes a tuberculin testing demonstration, the entire plan should be in complete conformity with health department policies.

The following, information is supplied to supplement that of the handbook.

Uses of tuberculin testing

Selective tuberculin testing is only a part of an adequate tuberculosis case-finding program, and case finding itself is only a part of a total community tuberculosis control program.

It is necessary to distinguish between the clinical testing of individuals and mass tuberculin testing.

TESTING OF INDIVIDUAL PERSONS. *As a diagnostic procedure.* The tuberculin test is a valuable procedure for differential diagnosis in private physicians' offices, in clinics, nursing homes, infirmaries, and hospitals.

Contact examination. The examination of contacts of persons with active tuberculosis is still the most efficient and economical way to find new cases of tuberculosis. When a person with active tuberculosis is discovered, all household contacts and other close associates should receive a tuberculin test, and reactors should be x-rayed. Nonreactors should be retested within six months and at intervals thereafter, as determined by a physician. Those who change from nonreactors to reactors, especially children under five years of age, should be considered as candidates for chemotherapy.

Preliminary to BCG vaccination. The tuberculin test is, of course, a necessary step prior to BCG vaccination.

MASS TUBERCULIN TESTING. Elementary and high school students comprise a group frequently approached for tuberculin testing. The following suggestions relate to the basic purposes of the test and supply a guide to its employment.

On the occurrence of active tuberculosis in a school. When active tuberculosis is found either in a student or in an employe of a school, it is recommended that those students in direct contact with the active case be tuberculin tested, followed by chest x-raying of the reactors. In instances where the first exposure to the active case has occurred quite recently, for example less than six weeks before the discovery of that case, the testing could be deferred at the discretion of the physician for several weeks. It is often wise to repeat the test on nonreacting contacts within three to six months after the initial test. The employes could be either tuberculin tested and the reactors x-rayed or have a chest x-ray only.

As a case-finding procedure. Case finding has been the primary purpose of most mass tuberculin testing programs among school children. However, an analysis of the results of a large number of such projects in New York and other states has given evidence that active tuberculosis seldom has been found by routine tuberculin testing among school children or among the household contacts of those children found to be positive reactors. The often negligible yields must be measured against the considerable expense of the program in terms of time and efforts of health officers, school physicians, nurses, teachers, volunteers, and the children themselves.

It is true that a properly done tuberculin test does detect those children who have been infected in the past, although lacking in any evidence of active disease at the time of the testing. Some school authorities may wish to have the tuberculin test included to make the school examination complete; certainly there would seem to be other aspects of the school examination that would have higher priority when funds are limited.

In support of this opinion, an editorial in the *Bulletin of the National Tuberculosis Association* (October, 1959) states: "Experience indicates that testing programs are frequently costly and time consuming and produce little new active tuberculosis contrasted with more selective programs."

An exception to these policies is justified in schools located in low socioeconomic areas or in geographic areas where the prevalence of tuberculosis is high.

Thus, as a general principle, mass tuberculin testing of school children in those areas of New York State where morbidity and mortality rates are low is an expensive and relatively unproductive way to find children with active tuberculosis. This does not contraindicate the utilization of tuberculin testing for the determination of prevalence and trends, which is done on a restricted sampling basis at intervals of several years.

Likewise, mass tuberculin testing for the purpose of detecting active tuberculosis among the contacts of school children who are positive reactors is also expensive and unproductive for routine use in New York State.

Where mass tuberculin testing is to be done, particular attention should be given to the material used, the dosage, the definition of a reactor, the time interval for reading tests, the follow-up of household associates of reactors, and the criteria for diagnosis and classification of new "cases" found among reactors and contacts. One should keep records on cost data to determine what value is received in new active cases per dollars spent.

For educational purposes. A tuberculin testing program among school children should not be done solely for educational purposes about tuberculosis, since there are available more effective methods of the health education of school children, teachers, and parents.

In sampling surveys among school children to determine the prevalence of tuberculous infection in certain age groups in the community, concurrent health educational efforts are beneficial. The same is true of special surveys following the discovery of an active case of tuberculosis among school employes or students.

There is a need for scientific studies to measure what health education values derive from selective tuberculin testing surveys among school children and other special groups. The social scientists could team up with health educators to provide some new data on this subject about which too little is known at the present time.

To determine the prevalence of tuberculous infection. The tuberculin test employed on a sampling basis is useful to determine the prevalence of tuberculous infection in groups of persons or in a whole community. Testing and retesting random samples of the same population at appropriate intervals, such as every three years, will indicate trends in the levels of infection and can serve as a measure of the effectiveness of control activities. A reasonable approach is to test samples of the school population on their entrance to school and again during adolescence or on leaving school.

The sampling for determining the prevalence of tuberculous infection should be scheduled on a periodic basis for regional areas of New York State. This will measure the degree to which the state and its communities are making progress in tuberculosis control, in accordance with the intermediate goal proposed by an Ad Hoc Committee as a follow-up of the Arden House Conference on tuberculosis. This goal is as follows: "For the community, control of the spread of infection to the point where not more than 1 per cent of the fourteen-year-olds react to tuberculin."

IMPORTANCE OF FOLLOW-UP. When mass tuberculin testing is done either for case finding or for prevalence studies, particular attention should be given to the follow-up of those individuals who show reactions of 10 mm. or over. Studies have indicated that there is a strong correlation between the size of the tuberculin reaction (particularly those of 10 mm. and over) and the risk of the development of active tuberculosis in subsequent years.

Tuberculin test material and dosage

The patch test is not recommended for mass testing because of the variability of results among different age groups. The Mantoux test is much preferred for individual and mass testing, but some physicians like to use the Heaf test, so both tests are included here.

For Mantoux or intradermal tests, PPD (purified protein derivative) is recommended; the dosage is 5 toxic units (0.0001 mg.) when a single test is used.

The standard concentrated solution of tuberculin (protoderm or PPD-Connaught) should be used in doing the "Heaf" or multiple puncture test.

Interpretation of tests

It is desirable to have at least 2 persons make independent interpretations of the tuberculin test because of variations in the interpretation.

MANTOUX OR INTRADERMAL TEST. The largest transverse diameter of induration (not the area of redness) should be measured in millimeters and classified in the following groups: 0 to 4 mm., 5 to 9 mm., 10 to 19 mm., and 20 mm. or over.

The Mantoux test should be read at from forty-eight to seventy-two hours after the test. A positive test reaction is usually 5 mm. or more. Recording the actual size of the reaction and grouping into the previously mentioned categories makes it possible for others to compare their results or to use different sizes of reactions as positive.

HEAF OR MULTIPLE PUNCTURE TEST. Four or more indurated points are considered to show a positive reaction. The test should be interpreted in from five to seven days after the test.

Records and reports

It is recommended that the suggestions contained in the *Tuberculin Testing Handbook* published in 1958 by the National Tuberculosis Association be used as a guide in the design of records and reports.

Evaluation methods

The periodic evaluation of case-finding activities is essential to determine whether or not the number of new cases of tuberculosis found is sufficient to justify the cost of such activities. This applies to tuberculin testing for this purpose as well as other case-finding activities.

A guide for conducting such evaluations was prepared by the Ad Hoc Committee and has been published.* Its use is recommended for evaluating tuberculin testing projects.

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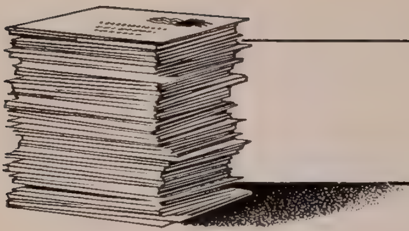
* Evaluation of Case Detection Surveys of Population Groups: Bull. Nat. Tuberc. A. 47: 3 (Mar.) 1961.



Letters to the Editor

Footnote on tricuspid insufficiency

To the Editor: With the advent of surgery for mitral stenosis, there has occurred a resurgence of interest in tricuspid insufficiency as a clinical entity. This interest has focused around the differentiation of tricuspid insufficiency from mitral insufficiency, for generally the latter is a contraindication to mitral commissurotomy while the former is not. In 1837[1] Thomas King of Guys Hospital published his classic essay on the physiology of the tricuspid valve. Contained in a rather lengthy footnote on page 132 of this essay are observations on the clinical findings and bedside diagnosis of tricuspid incompetence which deserve quotation:

> If any one were inclined to infer that whatever reflux occurs by the tricuspid or safety valve should be manifest by the pulsation of the jugular veins, I would observe that such is not to be expected as a common result, and for the following reasons: The overdistended ventricle has lost something of its power—the accumulation within it is a material source of resistance—the imperfect systole is partly expended in sending blood to the lungs—and the refluent overplus is driven into the capacious auricle, and scarcely less capacious cavae: in which, when any diastole is produced, it should not be very remarkable, and, of course, the dilatation of the superficial jugulars would be less forcible; these vessels being still more remote, and much assisted in transmitting their contents by the forces of gravity and inspiration, and by the play of considerable valves. All these circumstances tend to preserve the circulation of the brain and senses, etc. Most physiologists must be aware how mysteriously the older vivisectors regarded the pulses of the abdominal cava. It is not very difficult to understand, that when distention has subverted the action of the jugular valves, the refluent pulse becomes so exaggerated as to be both seen and felt. It scarcely needs to be explained, that when, from an increased distention, the jugular valves cease to act, the refluent pulse in the neck is manifest enough. It should, however, be remembered, that a reclining posture and the intervals of inspiration render the pulsation more remarkable.[1]

As King clearly recognized almost one hundred and twenty-five years ago, it is only the severest cases of tricuspid insufficiency that present the characteristic manifestations of a pulsating liver and neck veins. Recently, Korner and Shillingford[2] have quantitated this observation and shown that a pulsating liver usually signifies a regurgitant flow of at least 3.5 L. per minute. This means that many of the milder cases of tricuspid insufficiency may masquerade as mitral insufficiency[3,4] and that patients with mitral stenosis and an apical systolic murmur should not be denied surgery without more definitive attempts to clarify the diagnosis.

Tricuspid insufficiency can be diagnosed by a number of sophisticated specialized technics: cardiac catheterization, angiocardiography, and indicator dye dilation studies.[5-8] However, as King points out, the diagnosis can be suspected on the initial physical examination simply by noting the effect of respiration on the intensity of the murmur. Inspiration increases right ventricular output and decreases left ventricular output. During inspiration, then, the murmur of tricuspid insufficiency is accentuated while that of mitral insufficiency is diminished.

It should also be recognized that tricuspid insufficiency can be precipitated by atrial fibrillation. Little[9] has shown in dogs that atrial systole is essential for complete closure of the tricuspid valve. Müller and Shillingford[10] have reported a patient with chronic rheumatic heart disease and mitral stenosis in whom tricuspid incompetence could not be demonstrated when he was in sinus rhythm, but who developed gross tricuspid insufficiency on a change of rhythm to atrial fibrillation; a subsequent reversion to sinus rhythm was accompanied by the disappearance of the tricuspid regurgitation. Such experiences suggest that a vigorous attempt should be made to convert all cases of tricuspid insufficiency with atrial fibrillation to a normal sinus rhythm.

MYRON R. SCHOENFELD, M.D.

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[1] King, T. W.: An essay on the safety valve function in the right ventricle of the human heart and on the gradations of this function in the circulation of warm blooded animals, Guys Hosp. Rep. **2:** 104 (1837).

[2] Korner, P., and Shillingford, J.: Tricuspid incompetence and right ventricular output in congestive heart failure, Brit. Heart J. **19:** 1 (Jan.) 1957.

[3] Uricchio, J. F., Bentivoglio, L., Gilman, R., and Likoff, W.: Tricuspid regurgitation masquerading as mitral regurgi-

tation in patients with pure mitral stenosis, Am. J. Med. **25**: 224 (Aug.) 1958.

[4] Schilder, D. P., and Harvey, W. P.: Confusion of tricuspid incompetence with mitral insufficiency—a pitfall in the selection of patients for mitral surgery, Am. Heart J. **54**: 352 (Sept.) 1957.

[5] Sepulveda, G., and Lukas, D. S.: The diagnosis of tricuspid insufficiency; clinical features in 60 cases with associated mitral valve disease, Circulation **11**: 552 (Apr.) 1955.

[6] Lukas, D. S., and Dotter, C. T.: Modifications of the pulmonary circulation in mitral stenosis, Am. J. Med. **12**: 639 (June) 1952.

[7] Dotter, C. T., Lukas, D. S., and Steinberg, I.: Tricuspid insufficiency; observations based on angiocardiography and cardiac catheterization in twelve patients, Am. J. Roentgenol. **70**: 786 (Oct.) 1953.

[8] Collins, N. P., Braunwald, E., and Morrow, A. G.: Detection of pulmonic and tricuspid valvular regurgitation by means of indicator solutions, Circulation **20**: 561 (Oct.) 1959.

[9] Little, R. C.: Effect of atrial systole on ventricular pressure and closure of the A-V valves, Am. J. Physiol. **166**: 289 (July) 1951.

[10] Müller, O., and Shillingford, J.: Tricuspid incompetence, Brit. Heart J. **16**: 195 (Apr.) 1954.

Work required of foreign medical graduates

To the Editor: I am not personally interested in writing you this letter, which is meant purely to be pleasant to you.

I passed the ECFMG exam last year, and in the near future I will be back in my home, where my family waits for me.

In leaving America I would like to make my good suggestion.

I would like to draw your kind attention to a tragic situation, apparently created by shortage but sometimes wanted or neglected by the hospitals.

I would like to tell you about some poor exchange visitors who have not yet passed the exam, and they will never pass if you don't take care of this problem promptly.

In one hospital of 450 beds in New York City, where I have been for a while, one unqualified doctor serves as a whole staff of house in internal medicine. There are only one or two interns in surgery (probably unqualified). You can realize now how a foreign physician works ten to twelve hours only in the operating room, having in his charge 8 to 13 new admissions; he has to prepare a history and physical examination and any technical needs such as infusion, catheter, and so forth. A bleeding ulcer occurs as an emergency, and he is easily called to scrub, assisting until 3 A.M.

This does not affect in any way his regular schedule of starting at 8 A.M. And who starts infusions? The same person must do all! You can realize now how such a person has no time for sleeping, eating, or urination. Such a person has no time to read or to study. How do you expect him to pass ECFMG?

Such heavy work could be found only in the history of slavery—this is not human.

Such a foreign doctor will not be a good ambassador of America in his country.

Please, believe me as a sincere friend, the present writing is to help an ideal exchange program, to earn more prestige for the free world!

I suggest fixing logical limited work hours for a trainee who is not qualified, enabling him to pass his exam and achieve his stay abroad.

I suggest that qualified doctors help more, not being satisfied to order as a big boss, proud to have passed the exam.

Gentlemen, as a human being, anxious for others, here ends my duty, where yours begins!

Waiting to hear of your prompt intervention, I thank you for your kind attention.

NASSEHE AMIN, M.D.

Right eye perhaps more efficient than left

Although a person has normal vision, his right eye may be more efficient than his left, according to an article by Dr. Maria Wyke and Dr. G. Ettlinger in the December, 1961, issue of *Archives of Neurology*. Experiments to test the ability of normal persons to identify meaningful drawings on the right and left sides of the visual field were described. The study involved 18 persons. All except 1 were right-handed. The outline drawings of familiar objects were flashed on a screen, first successively in the left and right field, then simultaneously in both fields. "These experiments indicate that with normal subjects visual recognition of familiar objects . . . is significantly more efficient on the right side than on the left. The phenomenon apparently is not due to attentional factors. It was found that even though a subject had identified a picture presented on his right, he remained unable to identify a picture presented simultaneously on his left, in spite of repeated exposures. This was true even when his attention was concentrated on his left visual field.

Abstracts

Fisher, B.: Hemoglobin A_2 analysis in hypochromic anemias, New York State J. Med. **62:** 641 (Mar. 1) 1962.

Hypochromic anemias that do not respond to adequate treatment with iron may be difficult to diagnose. Most persons who inherit the gene for thalassemia from only one parent grow and develop normally. Heterozygous thalassemia, however, may have a variety of clinical symptoms and hemoglobin levels ranging from near-normal to moderate anemia. The finding of an increased red cell hemolysate fraction (A_2) in heterozygous thalassemia has made the diagnosis easier. In 96 patients with hypochromic anemias due to causes other than thalassemia, a range of 3 to 9 per cent of the total hemoglobin as A_2 was found, using paper electrophoresis with thick paper, a large sample of hemoglobin, and a buffer containing Tris-EDTA-boric acid. In 23 patients with heterozygous thalassemia the values ranged from 8.6 to 15.5 per cent. The disease is most common in persons of Mediterranean descent, particularly Italians.

Werther, J. L.: Gastrointestinal physiology; gluten-induced enteropathy and protein-losing enteropathy, New York State J. Med. **62:** 645 (Mar. 1) 1962.

It appears that celiac disease and nontropical sprue, or gluten-induced enteropathy, and idiopathic hypercatabolic hypoproteinemia, or protein-losing enteropathy, are etiologically and pathologically distinct, although physiologically they overlap considerably. A gluten-free diet produces excellent responses in the majority of children with celiac disease and adults with nontropical sprue; however, despite clinical remission, changes in the small-bowel mucosa persist without observable improvement. This suggests that the anatomic alteration of the mucosa may be a secondary effect rather than the cause of these disorders, and that the underlying defect is biochemical rather than anatomic. The mechanism of the noxious activity of gluten is not known, but it appears to depend on the presence of glutamine in combination with one or more of the peptide components of gluten. The occurrence of hypoproteinemia, when it is not a complication of disorders resulting in malnutrition, defective protein synthesis, or excessive protein loss, has not been explained adequately. Recent evidence suggests that most of such patients suffer excessive loss of serum protein into the gastrointestinal tract and excessively rapid destruction of serum albumin. Studies with I^{131}-labeled PVP (polyvinylpyrrolidine) have shown that patients with hypercatabolic hypoproteinemia excrete excessive amounts of the PVP intravenous test dose in the feces. The present hypothesis is that the protein-losing enteropathies represent a group of disorders in which there is an increased passive loss of protein into the gut and that, although the products of digestion of this protein are largely reabsorbed, the maximal rate at which albumin can be synthesized is insufficient to keep up with the losses.

Costello, M. J., and Gibbs, R. C.: Modern treatment of common bullous dermatoses, New York State J. Med. **62:** 654 (Mar. 1) 1962.

There are three groups of bullous dermatoses: pemphigus, dermatitis herpetiformis, and erythema multiforme. Adrenocorticoids and/or ACTH are used in the treatment of pemphigus until the suppression of new bullae but may cause complications such as peptic ulcer, pulmonary or musculoskeletal complications, electrolyte disturbance, diabetes, elevation in weight, and hypotension. Topical therapy consists of potassium permanganate tub baths and, when possible, a heat-regulated cradle. Dermatitis herpetiformis is treated by sulfoxone sodium (Diasone) or acetosulfone (Promacetin). The former may produce methemoglobinemia or hemolytic anemia, and the blood should be studied continuously. Sulfapyridine is used also but may produce renal damage or agranulocytosis. The treatment of erythema multiforme is similar to that of pemphigus, together with local use of antibiotics.

Clark, G.: Photocoagulation, New York State J. Med. **62:** 661 (Mar. 1) 1962.

Photocoagulation is a surgical procedure which derives its effect from the destruction of tissue by heat as distinct from the medical or physical therapeutic use of heat to improve the state of a tissue. The photocoagulator is used prophylactically in the retinal detachment field. It may be used as a supplement to conventional diathermy and to halt giant cysts or retinoscheisis. It is effective in the treatment of retinal and choroidal angiomas. In the treatment of retinal neovascularization and intraocular malignant conditions its use is still of questionable value. The instrument is effective in the destruction of anterior chamber cysts but must be handled with care. Experience has tempered early enthusiasm for its use in optical iridectomies. There are physical factors to be considered in its use: The media must be clear; the pupil must be dilated widely and strongly; and the presence of choroidal scars presents an obstacle. The photocoagulator is a valuable instrument whose greatest use is in supplementing older methods of treatment, but it must be used with great skill and caution, for while it offers help in one hand, it offers danger in the other.

Medical Meetings

New York State Society of Internal Medicine

The New York State Society of Internal Medicine will hold its third annual internists' day at the Savoy Hilton Hotel, New York City, on Saturday, March 3. The subject of the meeting will be a symposium on "Diseases of the Thyroid Gland: Current Concepts." For a more detailed program see Medical Meetings of February 15.

Further information can be obtained from: Maxwell Spring, M.D., 800 Grand Concourse, Bronx 51, New York.

Buffalo Academy of Medicine

The Buffalo Academy of Medicine will hold its regular monthly meeting at 8:30 P.M. on Wednesday, March 7, at the University of Buffalo School of Medicine. The meeting will be preceded by cocktails at 6:00 P.M. at the University of Buffalo Faculty Club and dinner at 7:15 P.M. at the University's Norton Hall.

Guest speakers will be Maxwell Finland, M.D., Boston, and Jack A. Pritchard, M.D., Dallas. Robert Collins, M.D., Buffalo, will be the moderator.

For information contact: H. Paul Longstreth, M.D., Secretary, Buffalo Academy of Medicine, 193 Mt. Vernon Road, Buffalo 26, New York.

College of Physicians and Surgeons, Columbia University

The College of Physicians and Surgeons of Columbia University will hold a scientific program on basic problems in cancer March 12 through 14 to commemorate the fiftieth anniversary of the Institute of Cancer Research at Columbia and the tenth anniversary of the Francis Delafield Hospital.

All interested physicians, scientists, and students are invited to attend. There will be no fee for any of the sessions.

Kings County Pediatric Section

The Pediatric Section of the Medical Society of the County of Kings and the Academy of Medicine of Brooklyn will meet in the Basic Science Building of the State University of New York Downstate Medical Center, Clarkson and New York Avenue, Brooklyn, on Wednesday, March 14, at 8:30 P.M.

The topic for discussion will be "Diseases of the Chest in the Neonatal Period." Edward B. D. Neuhauser, M.D., clinical professor of radiology, Harvard Medical School, will be the discussant.

Symposium on diabetes

The State of New Jersey Department of Health in cooperation with the New Jersey Chiropodists Society will present a symposium on "Diabetes and the Lower Extremity" in Murdock Hall, Jersey City Medical Center, Jersey City, New Jersey, on Wednesday, March 28, from 1:00 to 5:00 P.M.

For further information contact: Arthur Krosnick, M.D., Coordinator, Diabetes Control Program, Division of Chronic Illness Control, State of New Jersey Department of Health, Trenton 25, New Jersey.

George Tartikoff Memorial Lecture

The board of trustees and the Department of Obstetrics and Gynecology of Maimonides Hospital of Brooklyn announce the third annual George Tartikoff Memorial Lecture to be delivered by Dr. Gregory Pincus, research director, The Worcester Foundation for Experimental Biology, on Wednesday, March 28 at 4:30 P.M., in the Kronish Solarium of the Hospital. The subject of the lecture will be "Conception and Senescence."

American Academy of General Practice

The American Academy of General Practice will hold its fourteenth annual scientific assembly April 9 through 12 in Las Vegas, Nevada. The assembly will be the first national medical meeting to be held in the new Las Vegas Convention Center.

American Academy of Pediatrics

The American Academy of Pediatrics will hold its spring session at the Statler Hilton Hotel, New York City, April 30 through May 2. For further information write to the executive office of the Academy at 1801 Hinman Avenue, Evanston, Illinois.

Forum on syphilis

A world forum on syphilis and other treponematoses will be held at the Sheraton Park Hotel, Washington, D.C., September 4 through 8.

Sponsors of the forum are the American Venereal Disease Association, the American Social Health Association, and the United States Public Health Service. The World Health Organization and the International Union Against the Venereal Diseases and the Treponematoses will participate.

For information write to: William J. Brown, M.D., Venereal Disease Branch, Communicable Disease Center, U. S. Public Health Service, Atlanta 22, Georgia.

Twelfth international congress of dermatology

The twelfth international congress of dermatology will take place in Washington, D.C., September 9 through 15. Sponsor of the congress is the American Academy of Dermatology. Cosponsors are the American Dermatological Association, the A.M.A. Section on Dermatology, the Society for Investigative Dermatology, and the Canadian Dermatological Association.

For information write to: Mr. Stephen T. Donohue, Director of Public Relations, Twelfth International Congress of Dermatology, 420 Lexington Avenue, New York 17, New York.

Symposium on human and animal diseases

An international symposium on comparative medicine, bringing together outstanding investigators in the human and veterinary medical fields from this country and abroad, will be held under the auspices of The Animal Medical Center, at the Waldorf-Astoria Hotel, New York City, October 10 through 12.

The symposium is being supported by a grant from the Eaton Laboratories Division of The Norwich Pharmacal Company. For further information contact: Mr. Jere Daniel, Fuller, Miele, Inc., 30 East 42nd Street, New York 17, New York.

American Cancer Society

The American Cancer Society will hold its 1962 scientific session at the Biltmore Hotel, New York City, October 22 and 23. The theme of the meeting will be "The Clinical Impact of a Quarter Century of Cancer Research."

For further information write to: Director of Professional Education, American Cancer Society, 521 West 57th Street, New York 19, New York.

American Heart Association

The 1962 annual meeting and scientific sessions of the American Heart Association will be held in Cleveland, Ohio, October 26 through 30.

May 15 is the deadline for submitting abstracts of papers for presentation at the scientific sessions. Papers must be based on original investigations in, or related to, the cardiovascular field. Official forms for submitting abstracts or applications for scientific exhibit space are available from: Richard E. Hurley, M.D., Medical Associate, American Heart Association, 44 East 23rd Street, New York 10, New York. For general information concerning the meeting address inquiries to Mr. H. Douglas Chisholm, Associate Director, American Heart Association, at the above address.

Pan American Medical Association

The Pan American Medical Association plans to celebrate its thirty-eighth anniversary with a fifteen-day cruise February 16 through March 3, 1963. Papers are to be read at sea and at a two-day medical meeting in San Juan, Puerto Rico, a one-day meeting in Caracas, Venezuela, and a one-day meeting in Port-au-Prince, Haiti. Other ports tentatively scheduled are the Barbados, Curacao, and Jamaica. Members will be notified when final arrangements have been completed.

Pan-Pacific Surgical Association

The ninth congress of the Pan-Pacific Surgical Association will be held November 5 through 13, 1963, in Honolulu, Hawaii, and the first Pan-Pacific Mobile Educational Lecture Seminar will be held November 13 through December 10, 1963, in New Zealand, Australia, Thailand, the Philippines, Hong Kong, and Japan.

For further information write to: F. J. Pinkerton, M.D., Director General, Pan-Pacific Surgical Association, Suite 570, Alexander Young Building, Honolulu 13, Hawaii.

Necrology

Leo Alfonse Amorosi, M.D., of Brooklyn, retired, died on December 17, 1961, in his home at the age of sixty-three. Dr. Amorosi graduated in 1925 from the University of Colorado School of Medicine. He was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Gregory Aronowitz, M.D., of Rochester, retired, died on December 30, 1961, at the age of seventy-three. Dr. Aronowitz graduated in 1912 from Columbia University College of Physicians and Surgeons and interned at Beth Israel Hospital. He was a member of the Kings County Medical Society and the Medical Society of the State of New York.

Walter Edkins, M.D., of Forest Hills and Jamaica, died on August 31, 1961, at the age of sixty-one. Dr. Edkins received his medical degree from the University of Cologne in 1925. He was a Fellow of the International College of Surgeons and a member of the American Geriatrics Society, the Rudolf Virchow Medical Society, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Rosary J. Ferrara, M.D., of New York City, died on September 22, 1961, at the age of sixty-seven. Dr. Ferrara graduated in 1920 from Fordham University School of Medicine.

Edward Peter Forrestel, M.D., of Buffalo, died on August 21, 1961, at Our Lady of Victory Hospital at the age of seventy-three. Dr. Forrestel graduated in 1911 from the University of Buffalo School of Medicine. He was an honorary attending obstetrician at Our Lady of Victory Hospital, a consulting physician in obstetrics at Mercy Hospital, and an honorary member of the staff at the Sisters of Charity Hospital of Buffalo. Dr. Forrestel was a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter Clayton Fox, M.D., of Fort Plain, died on January 5 at his home at the age of seventy-four. Retired, Dr. Fox graduated in 1911 from Albany Medical College and interned at Albany Hospital. He was a member of the Montgomery County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Cornell Herger, M.D., of Buffalo, retired, died on January 2 at the Sisters of Charity Hospital of Buffalo at the age of sixty-seven. Dr. Herger graduated in 1920 from the University of Buffalo School of Medicine. He was an honorary attending urologist at the Sisters of Charity Hospital of Buffalo. Dr. Herger was a Diplomate of the American Board of Urology and a member of the American Radium Society and the Buffalo Academy of Medicine.

Julius Jacob Hertz, M.D., of New York City, died on January 14 at Beth Israel Hospital at the age of seventy-five. Dr. Hertz graduated in 1903 from Cornell University Medical College and interned at The Mount Sinai Hospital. He was a consulting physician at Beth Israel Hospital. Dr. Hertz was a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Anthony Thomas Jurasz, M.D., of Margaretville, died on September 19, 1961, at St. Clare's Hospital at the age of seventy-nine. Dr. Jurasz received his medical degree from the University of Heidelberg in 1907. He was an attending in surgery at Margaretville Hospital and a consultant in surgery at St. Clare's Hospital, New York City. A native of Poland, from 1920 to 1939 he was director of the surgical department at the University of Poznan, where in 1925 he became dean of the medical faculty, and vice-chancellor in 1930. During World War II he served as colonel in the Polish campaign and in 1941 following his escape as a prisoner of war he organized a Polish medical faculty within the University of Edinburgh and also the Paderewski Hospital, a training school for physicians and surgeons chosen from the Polish forces serving in England and Scotland, for which he was director and chief surgeon until its closing in 1947. From 1928 to 1939 he was president of the Red Cross of Western Poland and founder and president from 1925 to 1939 of the Society of Surgery and Orthopedics of Western Poland. Dr. Jurasz was a Fellow of the American College of Surgeons and a member of the Delaware County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Kenneth Keill, M.D., of Willard, died on January 7 at his home at the age of sixty-five. Dr. Keill graduated in 1922 from Queen's University Faculty of Medicine (Ontario, Canada). He was director of Willard State Hospital. Dr. Keill was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Life Fellow of the American Psychiatric Association, and a member of the Finger Lakes Neuropsychiatric Society, the Seneca County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Morris Lattman, M.D., of New York City, retired, died on January 23 at Doctors Hospital at the age of sixty-five. Dr. Lattman graduated in 1931 from Georgetown University School of Medicine. He was former chief cardiologist with the Veterans Administration Regional Office. Dr. Lattman was a Diplomate of the American Board of Internal Medicine and a Fellow of the American College of Physicians.

Abram Lichtyger, M.D., of the Bronx, died on June 24, 1961, at the age of fifty. Dr. Lichtyger received his medical degree from the University of Geneva in 1935. He was a clinical assistant attending physician at The Mount Sinai Hospital, an assistant attending physician at Harlem Hospital, and an assistant hematologist at the Harlem Hospital Outpatient Department. Dr. Lichtyger was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Jacob Lister, M.D., of the Bronx, died on September 6, 1961, at the age of seventy-one. Dr. Lister received his medical degree from the University of Jena in 1919. He was an assistant attending physician at Flower and Fifth Avenue Hospitals and an assistant physician (affiliate) at the Metropolitan Hospital. Dr. Lister was an Associate Fellow of the American College of Gastroenterology and a member of the Rudolf Virchow Medical Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harry Loeb, M.D., of Brooklyn, died on September 12, 1961, at the age of sixty-eight. Dr. Loeb graduated in 1916 from Long Island College Hospital Medical School and interned at Beth Israel Hospital. Dr. Loeb was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James Erwin Lovell, M.D., of Trumansburg, died on August 21, 1961, at the age of eighty-six. Dr. Lovell graduated in 1898 from the University of Vermont College of Medicine. He was a member of the Tompkins County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Livingston MacDowell, M.D., of Delmar, died on December 26, 1961, at the age of forty-eight. Dr. MacDowell graduated in 1939 from Columbia University College of Physicians and Surgeons. He was a clinical assistant attending physician at Albany Hospital and an associate attending physician at the Albany Hospital Outpatient Department. Dr. MacDowell was a member of the American Academy of General Practice, the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry Fancher Mace, M.D., of Menands, died on January 9 at the age of eighty-six. Dr. Mace graduated in 1899 from Jefferson Medical College of Philadelphia. Since 1925 he had been police doctor for Menands and was a former state medical inspector for the New York State Education Department, retiring from this post in 1945. Dr. Mace was a member of the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Marton, M.D., of New York City, died on August 16, 1961, at the age of sixty-one. Dr. Marton graduated in 1924 from the University of Maryland School of Medicine and College of Physicians and Surgeons and interned at City Hospital in Newark, New Jersey. He was physician-in-charge of the Allergy Department at Fordham Hospital and an associate in allergy and chief of the Allergy Clinic at Jewish Memorial Hospital. Dr. Marton was a Fellow of the American College of Allergists, a Fellow of the American Academy of Allergy, and a member of the New York Allergy Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Moitrier, Jr., M.D., of Brooklyn, died on September 23, 1961, at his home at the age of seventy-four. Dr. Moitrier graduated in 1913 from Columbia University College of Physicians and Surgeons. He was director of pathology at St. Mary's Hospital. Former secretary of the Section on Pathology of the Kings County Medical Society, Dr. Moitrier was a Diplomate of the American Board of Pathology and a member of the American Society of Clinical Pathologists, the New York State Society of Pathologists, the Kings County Medical Society, the Medical Society of the State of New York and the American Medical Association.

William Elmer Munroe, M.D., of Rochester, died on September 29, 1961, at the age of seventy-six. Dr. Munroe graduated in 1910 from the University of Pennsylvania School of Medicine. He was a member of the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Rowland V. O'Malley, M.D., of Lockport, died on January 6 at Lockport Memorial Hospital at the age of sixty-nine. Retired, Dr. O'Malley graduated in 1922 from the University of Buffalo School of Medicine. He was an honorary surgeon at Lockport Memorial Hospital. Dr. O'Malley was a member of the Lockport Academy of Medicine, the Niagara County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Ezra Rubin, M.D., of the Bronx, died on October 2, 1961, at the age of twenty-eight. Dr. Rubin graduated in 1958 from New York University College of Medicine and interned at Washington Hospital Center. He was a resident physician at Lincoln Hospital. Dr. Rubin was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Howard J. Schneckenburger, M.D., of Nunda, died on January 7 at his home at the age of fifty-nine. Dr. Schneckenburger graduated in 1927 from the University of Buffalo School of Medicine. He was health officer for the village and town of Nunda, Portage, and Grove. Dr. Schneckenburger was a member of the Livingston County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis James Sokol, M.D., of the Bronx, died on August 20, 1961, at the age of sixty-eight. Dr. Sokol graduated in 1914 from Fordham University School of Medicine and interned at Fordham Hospital. He was a consulting physician at Fordham Hospital. Dr. Sokol was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Arthur Stein, M.D., of New York City, died on January 17 at the age of eighty-four. Dr. Stein received his medical degree from the University of Strassburg in 1901. He was a consultant in obstetrics and gynecology at Lenox Hill Hospital. Dr. Stein was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, and a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Paul Stein, M.D., of Los Angeles, formerly of Sunnyside, died on January 12 in Los Angeles at the age of sixty-four. A native of Austria, Dr. Stein received his medical degree from the University of Vienna in 1922. Retired, Dr. Stein was an associate attending physician at Gouverneur Hospital and an adjunct physician at Montefiore Hospital. Dr. Stein was a Fellow of the American College of Cardiology and a member of the New York Cardiological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George William Tong, M.D., of Libertyville, Illinois, formerly of Great Neck, died on June 1, 1961, at the age of eighty-three. Dr. Tong graduated in 1903 from Long Island College Hospital School of Medicine. Retired he was a consultant in anesthesiology at Brooklyn Hospital and the House of St. Giles the Cripple and senior staff anesthetist at St. Mary's Hospital. Dr. Tong was a member of the American Society of Anesthesiologists, Inc., the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Abstracts in Interlingua

Fisher, B.: Analyse de hemoglobina A_2 in anemias hypochromic (*anglese*), New York State J. Med. **62:** 641 (1 de martio) 1962.

Anemias hypochromic que non responde a adequate formas de tractamento con ferro es a vices difficile a diagnosticar. Le majoritate del subjectos a qui le gen pro thalassemia es transmittite per un del parentes solmente, cresce e se disveloppa normalmente. Tamen, thalassemia heterozygotic pote haber un varietate de symptomas clinic, e le nivellos de hemoglobina pote variar inter quasi normal e le valores characteristic de moderate anemia. Le diagnose ha devenite plus facile per le constatation de un augmentate fraction (A_2) in hemolysatos erythrocytic. In 96 patientes con anemias hypochromic con causas altere que thalassemia, il esseva constatate que inter 3 e 9 pro cento del hemoglobina total esseva A_2. In isto, electrophorese a papiro (con spisse papiro) esseva usate. Le specimen de hemoglobina esseva grande, e le tampon contineva tris-EDTA acido boric. In 23 patientes con thalassemia heterozygotic le valores variava inter 8,6 e 15,5 pro cento. Le morbo es le plus commun in individuos de lineage mediterranee, particularmente italian.

Werther, J. L.: Physiologia gastrointestinal; enteropathia a induction per glutine e enteropathia a perditade proteina (*anglese*), New York State J. Med. **62:** 645 (1 de martio) 1962.

Il pare que morbo celiac e sprue nontropic (o enteropathia a induction per glutine) e idiopathic hypoproteinemia hypercatabolic (o enteropathia a perdita de proteina) es etiologicamente e pathologicamente distincte, ben que physiologicamente illos ha multo in commun. Un dieta libere de glutine produce excellente resultatos in le majoritate del juveniles con morbo celiac e del adultos con sprue nontropic, sed—in despecto del remission clinic—le alterationes in le mucosa del intestino tenue persiste sin observabile formas de melioration. Isto suggere que le alteration anatomic del mucosa es possibilemente un effecto secundari plus tosto que le causa de iste disordines e que le subjacente defecto es biochimic plus tosto que anatomic. Le mechanismo del activitate nocive de glutine non es cognoscite, sed il pare que illo depende del presentia de glutamina in combination con un o plures del peptidos componente de glutine. Le occurrentia de hypoproteinemia—quando illo non es un complication de disordines resultante in malnutrition, defectos del synthese de proteina, o excessive perditas de proteina—ha non ancora trovate un adequate explication. Recente constatationes suggere que le majoritate de tal patientes suffre perditas excessive de proteina seral ad in le vias gastrointestinal e un excessivemente rapide destruction de albumina seral. Studios con polyvinylpyrrolidina marcate con I^{131} ha demonstrate que patientes con hypoproteinemia hypercatabolic excerne in lor feces un excessive procentage de doses experimental de polyvinylpyrrolidina intravenose. Le presente hypothese assere que le enteropathias a perdita de proteina representa un gruppo de disordines in que il occurre un augmentate perdita passive de proteina ad in le intestinos e que—ben que le productos del digestion de ille proteina es reabsorbite in grande mesura—le productivitate maximal del organismo in le synthese de albumina non es sufficiente pro restituer le perditas.

Costello, M. J., e Gibbs, R. C.: Le moderne tractamento de commun dermatoses bullose (*anglese*), New York State J. Med. **62:** 654 (1 de martio) 1962.

Il existe tres gruppos de dermatoses bullose: pemphigo, dermatitis herpetiforme, e erythema multiforme. Adrenocorticoides e/o ACTH es usate in le tractamento de pemphigo usque al suppression de nove bullas, sed iste regime pote causar complicationes como, per exemplo, ulcere peptic, etiam complicationes pulmonar o musculoskeletic, disturbation electrolytic, diabete, augmento de peso, e hypotension. Le therapia topic consiste del uso de balneos a permanganato de kalium e, in tanto que possibile, de un cuna thermo-regulabile. Dermatitis herpetiforme es tractate con sulfoxon a natrium (Diasone) o acetosulfon (Promacetin). Le prime de iste duo agentes produce a vices methemoglobinemia o anemia hemolytic, e le sanguine debe esser studiate continuemente. Sulfapyridina es etiam usate, sed illo pote producer lesiones renal o agranulocytosis. Le tractamento de erythema multiforme es simile a illo de pemphigo, in combination con le uso local de antibioticos.

Clark, G.: Photocoagulation (*anglese*), New York State J. Med. **62:** 661 (1 de martio) 1962.

Photocoagulation es un technica chirurgic que utilisa calor in le destruction de tissu, per contrasto con le uso therapeutic de calor, medical o physic, in meliorar le stato del tissu. Le photocoagulator es usate prophylacticamente in le campo del distachamento retinal. Illo pote

esser usate como supplemento a diathermia conventional e pro arrestar cystes gigante o retinoscheisis. Illo es efficace in le tractamento de angiomas retinal e choroidic. In le tractamento de neovascularisation retinal e de maligne conditiones intraocular, le valor de su uso remane questionabile. Le instrumento es efficace in le destruction de cystes del camera anterior, sed su empleo require circumspection. Le enthusiasmo initial pro su uso in iridectomia optic ha devenite plus temperate in le curso del subsequente experientias. Certe factores physic debe esser prendite in consideration in su uso: Le media debe esser clar, e le pupilla debe esser dilatate large-e fortemente. Le presentia de cicatrices choroidic presenta un obstaculo. Le photocoagulator es un instrumento de alte valor. Su uso primari es in le supplementation de methodos de tractamento plus conventional. Su application require habilitate e circumspection, proque illo promitte assistentia de un latere e alberga periculos del altere.

Medical News

New York Society of Colon and Rectal Surgeons

The New York Society of Colon and Rectal Surgeons has announced that the following officers were elected for 1962: Con Amore V. Burt, M.D., New York City, president; Norman L. Freund, M.D., Brooklyn, vice-president; and Jack W. McElwain, M.D., Bethpage, secretary-treasurer.

Elected to the society's council were: *Brooklyn:* A. W. Martin Marino, M.D., and Saul Schapiro, M.D.; *New York City*: Michael R. Deddish, M.D., Meyer H. Freund, M.D., Harry Goldman, M.D., Rudolph V. Gorsch, M.D., Irving Schoenfeld, M.D., Maus W. Stearns, Jr., M.D., and Sydney D. Weston, M.D.; *Paterson, New Jersey:* George L. Becker, M.D.

Pediatric refresher courses

Intensive refresher courses in pediatrics are being offered at the University of Buffalo School of Medicine under the sponsorship of the Medical Society of the State of New York and the Bureau of Maternal and Child Health, State of New York Department of Health. The courses, designed especially to meet the needs of general practitioners, will be held May 14 through 18 and June 6 through 10.

The courses will be a review of principles and recent developments in diagnosis and treatment of pediatric disorders and in the care of the well child. All teaching will be done by the faculty of the University of Buffalo School of Medicine under the supervision of Mitchell I. Rubin, M.D., chairman of the Department of Pediatrics.

Application for enrollment in either of the courses must be made prior to May 1 through the offices of county or city departments of health, or to district health officers.

Course in radiation therapy in dermatology

A two-months course in basic physics and the practical uses of radiation therapy in dermatology will be offered at the Queens Hospital Center by the Radiation Medicine and Dermatology Departments. The course will be held on Wednesdays from 5:30 to 7:30 P.M., April 4 through May 23.

For information and application write to: Philip J. Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York.

FIGURE 1. From left to right: Student nurse Helena Wolf, Ray E. Trussell, M.D., Commissioner of Hospitals, New York City, and student nurse Carla Mae Schlegel.

Surgeon speeds x-ray developing

A new technic for developing x-ray films without a darkroom will reduce to the minimum the extra time a patient must spend waiting on the operating table for the results of such films. Credit for the perfection of the new technic goes to David R. Telson, M.D., a Brooklyn orthopedic surgeon.

In Dr. Telson's method the film is placed in an opaque, polyethylene envelope. After the picture is taken, the envelope containing the film is dunked in the tanks containing the developer, water, and fixer. This can be done in the lighted operating room. The plastic envelope keeps out the light but allows the liquid to enter through a slit at one edge. The negative can then be taken out of the folder, dried with a sponge, and be ready for viewing. The great advantage in Dr. Telson's method lies in its low cost—only twenty cents extra for the plastic envelope.

Papers on cardiology invited

Abstracts of papers to be presented by residents of the United States at the fourth world congress of cardiology in Mexico City, October 7 through 13, must be submitted through the American Heart Association for screening not later than March 15.

The organizing committee of the congress requests that presentations be addressed to the clinical cardiologist in keeping with its purpose to integrate cardiology as far as possible with technical progress in individual related fields.

Abstracts should consist of a maximum of 200 words and should include the paper's purpose, the technics used in the studies, and the results obtained. Forms for submitting abstracts may be obtained from: Frederick J. Lewy, M.D., Associate Medical Director, American Heart Association, 44 East 23rd Street, New York 10, New York.

For information concerning the congress write to: Dr. I. Costero, Secretary General, Instituto Nacional de Cardiologia, Avenida Cuauhtemoc 300, Mexico 7, D.F.

Commissioner receives stamps

Ray E. Trussell, M.D., Commissioner of Hospitals of New York City, was the recipient recently of a framed sheet of the new United States postage stamps honoring the nursing profession. The stamps were presented to Dr. Trussell by student nurses Helena Wolf, of Hunter College and Carla Mae Schlegal, of Plattsburgh College (Fig. 1).

Summer School of Alcohol Studies

The Summer School of Alcohol Studies which in the past has been held at Yale University will open its twentieth session this year at the new Rutgers Center of Alcohol Studies in New Brunswick, New Jersey. The administration, curriculum, and over-all educational philosophy will remain substantially the same as in the past.

For information write to: Mrs. Esther W. Henderson, Registrar, Summer School of Alcohol Studies, Rutgers, The State University, 35 College Avenue, New Brunswick, New Jersey.

Gift to Lenox Hill Hospital

The Lenox Hill Hospital has announced that it has received a gift of one million dollars from Mr. Charles R. Lachman, one of the founders of Revlon, Inc. The gift is to be used to aid in the construction of the Hospital's new Community Health Center.

The new 12-story structure, which will be named in honor of Mr. Lachman, will double the capacity of the Hospital's 39 outpatient clinics now located in a fifty-four-year-old building at 76th Street and Park Avenue. It also will provide additional private maternity facilities, greatly needed modernized and expanded quarters for the Hospital's 50 interns and residents, improved emergency room facilities, and a larger and more up-to-date pharmacy.

Course in internal medicine

A postgraduate course designed to review recent developments in internal medicine and allied fields is being scheduled for practicing physicians at Maimonides Hospital of Brooklyn, 4802 Tenth Avenue, Brooklyn 19, New York.

The course, "Review of Current Progress in Internal Medicine" is cosponsored by the Hospital's Department of Medical Services and the State University of New York Downstate Medical Center. It will be under the direction of David Grob, M.D., and will consist of 20 biweekly sessions held from 3:30 to 5:30 P.M. on Tuesdays and Fridays from April 3 through June 8.

Scholarships for medical students

The Allergy Foundation of America has announced that it will again award student research scholarships. Outstanding students who have completed their second or third year in medical school will be considered as candidates.

The scholarships are to be for a minimum of eight weeks during which the student will receive training and experience in clinical and research allergy in approved American and Canadian medical schools.

The Allergy Foundation of America has its headquarters at 801 Second Avenue, New York 17, New York.

Treatment of alcoholism

Paul H. Hoch, M.D., New York State Commissioner of Mental Hygiene, has announced the opening of two new units for the treatment and rehabilitation of individuals suffering from alcoholism.

A 75-bed inpatient unit has been set up at Central Islip State Hospital on Long Island, and a 20-bed inpatient unit will be located at Rochester State Hospital, Rochester. These will be pilot projects aimed at demonstrating the operation of a local, comprehensive treatment program for alcoholic patients.

Chest physicians plan postgraduate courses

The Council on Postgraduate Medical Education of the American College of Chest Physicians, under the chairmanship of J. Winthrop Peabody, Sr., M.D., Washington, D.C., has planned five postgraduate courses to be held in New York, Philadelphia, Chicago, and Detroit during 1962.

The courses are as follows: "Cardiopulmonary Problems in Children," Chicago, Edgewater Beach Hotel, July 23 through 27; "Recent Advances in the Diagnosis and Treatment of Diseases of the Heart and Lungs," Philadelphia, Warwick Hotel, September 17 through 21; "Occupational Diseases of the Heart and Lung," Detroit, Sheraton-Cadillac Hotel, October 1 through 5; "Clinical Cardiopulmonary Physiology," Chicago, Knickerbocker Hotel, October 22 through 26; and "Recent Advances in the Diagnosis and Treatment of Diseases of the Heart and Lungs," New York, Barbizon-Plaza Hotel, November 12 through 16.

For information write to: Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Gill Memorial Eye, Ear and Throat Hospital

The thirty-fifth annual spring congress in ophthalmology, otology, rhinology, laryngoscopy, maxillofacial surgery, bronchoscopy, and esophagoscopy of the Gill Memorial Eye, Ear and Throat Hospital and the Elbyrne G. Gill Eye and Ear Foundation will be held at the hospital in Roanoke, Virginia, April 2 through 6.

For further information write to: Gill Memorial Eye, Ear and Throat Hospital, 711 South Jefferson Street, Roanoke, Virginia.

Medical specialties recognized by the A.M.A.

The following is a list of the medical specialties now recognized in the American Medical Association's historical-biographical records: A-Allergy; ADM-Administrative Medicine; ALR-Otolaryngology; AM-Aviation Medicine; ANES - Anesthesiology; C - Cardiovascular Disease; D-Dermatology; GE-Gastroenterology; GP-General Practice; I-Internal Medicine; N-Neurology; NS-Neurological Surgery; OBG - Obstetrics, Gynecology; OM - Occupational Medicine; OPH-Ophthalmology; OR-Orthopedic Surgery; P-Psychiatry; PATH-Pathology; PD-Pediatrics; PH-Public Health; PL-Plastic Surgery; PM-Physical Medicine and Rehabilitation; PR-Proctology; PREV-Preventive Medicine; PUL-Pulmonary Diseases; R-Radiology; S-General Surgery; TS-Thoracic Surgery; and U-Urology.

The following medical specialties are no longer listed in the physicians' records of the American Medical Association: BACT-Bacteriology; CP-Clinical Pathology; FP-Family Practice; G-Gynecology; HAD-Hospital Administration; LM-Legal Medicine; MAD-Medical Administration; OALR-Ophthalmology, Otology, Laryngology, Rhinology; OB-Obstetrics; PN-Psychiatry and Neurology; PACP-Pathology, Pathologic-Anatomy, Clinical Pathology; and R-Roentgenology.

Medical vocabulary ills

An invitation to membership in The National Association on Standard Medical Vocabulary has been extended to all persons interested in improving the medical vocabulary.

The area of improvement in which the Association is most interested is the elimination of polysemia (multiplicity of meanings attributed to one word), excessive synonymy, inconsistent spelling, antitheses (the condition in which a word has nearly opposite meanings), and polyepy (The condition in which a word has several pronunciations).

For information write to: Erwin Di Cyan, Ph.D., Director, National Association on Standard Medical Vocabulary, 12 East 41st Street, New York 17, New York.

Hospital administrators development program

The Sloan Institute of Hospital Administration at Cornell University will offer its fifth annual hospital administrators development program from June 24 through July 20. The program is an intensive course of lectures, readings, and discussions and is divided into three seminars dealing with medical care programs, the administrative process, and trends in hospital administration.

For information write to: Hospital Administrators Development Program, Sloan Institute of Hospital Administration, Rand Hall, Cornell University, Ithaca, New York.

Course on surgery of the nasal septum

An introductory course on expanded surgery of the nasal septum and closely related structures will be presented at the St. Michael Hospital, Milwaukee, May 16 through 19 with the cooperation of the American Rhinologic Society. Maurice H. Cottle, M.D., Chicago, professor of otorhinolaryngology at the Chicago Medical School, will be the guest director.

For further information write to: Educational Committee, American Rhinologic Society, 530 Hawthorne Place, Chicago 13, Illinois.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that the next scheduled examinations (part II), oral and clinical, for all candidates will be conducted at the Edgewater Beach Hotel, Chicago, April 9 through 14. Formal notice of the exact time of each candidate's examination will be sent to him in advance of the examination dates.

Candidates who participated in the part I examinations will be notified of their eligibility for the part II examinations as soon as possible.

The deadline for the receipt of new and reopened applications for the 1963 examinations has been advanced to July 1, 1962. For information write to: Robert L. Faulkner, M.D., Secretary, American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Library dedicated to Dr. Rhoads

The library of the Sloan-Kettering Institute for Cancer Research was dedicated on January 19 in honor of the late Cornelius P. Rhoads' M.D. Dr. Rhoads was director of the Institute in New York City from 1945 until his death in 1959. The library is located at the Institute's Donald S. Walker Laboratory on the Boston Post Road, Rye, New York.

Students to use research facilities

In the interest of the advancement of research in the area of chronic illnesses the Isaac Albert Research Institute of the Jewish Chronic Disease Hospital in Brooklyn will permit graduate students now attending Brooklyn College to use its laboratory facilities as well as the services of its staff. The affiliation of the Institute and College took effect on February 8 with the beginning of the spring semester.

Influenza vaccine

The influenza vaccine shortage has occasioned a number of questions about vaccination procedure. Many physicians would like to know if it is feasible to extend the vaccination schedule since the completion date of January 1 is already past. The City of New York Department of Health assures physicans that there is no reason why the schedule cannot be extended even in communities where influenza infection is present. The Department of Health advises physicians to limit the vaccination to one dose of vaccine and to give the second dose at a later date when vaccine becomes more plentiful. In this way twice as many persons can be protected with the available vaccine. A subcutaneous dose of 1.0 ml. of vaccine for adults is preferable to a 0.1 ml. dose administered intradermally.

Personalities

Awarded. Joseph S. Diasio, M.D., Oakfield, the New York State Civil Defense Commission's Award of Merit in recognition of his outstanding work in the civil defense program of Genesee County.

Appointed. John Henry Beckley, M.D., New York City, as director of medical research services of Colgate-Palmolive Company . . . Leo Wollman, M.D., Brooklyn, as editor of the news letter of the American Society of Clinical Hypnosis.

Elected. Milton Berger, M.D., New York City, as president of the American Group Psychotherapy Association . . . Howard A. Rusk, M.D., New York City, as a term trustee of the University of Pennsylvania.

Month in Washington

The American Medical Association again endorsed a legislative proposal that the Federal Government help finance the construction of new medical schools and the expansion and modernization of existing ones.

Gerald D. Dorman, M.D., of New York City, a member of the A.M.A. Board of Trustees, told the House Interstate and Foreign Commerce Committee: "We believe that there is need for assistance in the expansion, construction, and remodeling of the physical facilities of medical schools, and, therefore, a one-time expenditure of Federal funds on a matching basis is justified where maximum freedom of the school from Federal control is assured."

Dr. Dorman was presenting the A.M.A. position on the Kennedy Administration's ten-year, $932 million program (H.R. 4999) for Federal aid to medical education. The legislation also proposed scholarships for medical and dental students.

"If the high standards of medical education are to be maintained, increased attention must be given to the adequacy of physical facilities, the availability of qualified instructors, and the availability of teaching material and patients for the clincial phases of medical education," Dr. Dorman said. "Any attempt to increase the number of medical students without regard to these conditions will result in a lowering of the standard of medical education. At this time, priority should be given to an increase in the physical facilities available for medical education."

Dr. Dorman said the A.M.A. had not taken a position on the other sections of H.R. 4999. However, he reviewed related A.M.A. programs.

"For some time, the American Medical Association has been aware of the decline in the number of eligible college students seeking admission to medical schools," he said. "This apparent shift away from medicine is due, in part, we believe, to the high cost in time and money of securing a medical education. This trend has been accentuated by a dramatic emphasis on careers in science and engineering. . . .

"The House of Delegates of the American Medical Association in November, 1960, established two programs, the objectives of which are complementary and interrelated.

"First, the House authorized a student honors and scholarship program designed to focus attention on careers in medicine to attract a substantial group of able students to prepare for admission to medical schools and to assist financially a limited number of outstanding students who, for financial reasons, are unable to pursue a career in medicine.

"Second, the A.M.A. House of Delegates has adopted a student loan program designed to alleviate the financial difficulties of medical students and to encourage career decisions in favor of medicine."

Dr. Dorman also pointed out that the A.M.A. in the past ten years, in collaboration with the Association of American Medical Colleges, had aided interested organizations in the establishment of six new medical schools. "Currently, commitments have been obtained for another five schools and we are in consultation with sixteen institutions or organizations presently contemplating the establishment of new medical schools," he added.

* * *

The A.M.A. said it would be irresponsible to combine the King-Anderson bill with legislation that would permit physicians and other self-employed persons to defer Federal income tax on income placed in specified private retirement funds.

Sen. Clinton P. Anderson (D., N. M.), co-author of the King-Anderson bill which would provide limited health care for aged persons under Social Security, suggested the combining tactic during a televised debate on the medical care issue with Sen. John Tower (R., Tex.).

The private retirement legislation—H.R. 10, the Keogh bill—would extend to an estimated 11 million self-employed persons and their employes the same tax benefits now provided to about 20 million wage earners covered by 66,000 company pension plans.

"This 'doubling-up' proposal of Sen. Anderson certainly proves the insincerity of the King-Anderson bill," F. J. L. Blasingame, M.D., executive vice-president of the A.M.A., said. "It lays bare the fact that this is wholly a political issue and not a sincere attempt to grant meaningful medical care for the aged.

"It would be an irresponsible bit of legislative slight of hand to combine Sen. Anderson's proposed compulsory medical care program with a bill to eliminate tax inequities inflicted on the self-employed.

"Such unwarranted action could only serve Sen. Anderson's own political ambitions at the expense of millions of Americans.

"The bills have nothing in common. There is no reason whatsoever for combining them except that Sen. Anderson is attempting to

Prepared by the Washington office of the American Medical Association, Washington, D.C.

harass critics of his bill into silence. He even calls the Keogh bill the 'doctors' special pension program, ignoring the fact that doctors make up only about 2.6 per cent of those self-employed who would be getting tax equity."

The Keogh bill has received widespread bipartisan support in both houses of Congress. It was passed by an overwhelming vote in the House last summer and cleared the Senate Finance Committee by a 13-3 vote.

Books Received

The following books were received during the month of December, 1961

Problems in Surgery. By Frank Glenn, M.D. Edited by George E. Wantz, Jr., M.D. Octavo of 512 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $16.50.

Tumours of the Oesophagus. Edited by Norman C. Tanner, M.D., and D. W. Smithers, M.D. Octavo of 352 pages, illustrated. Edinburgh, E. & S. Livingstone, (Baltimore, The Williams & Wilkins Co.), 1961. Cloth, $13.

Strong Medicine. By Blake F. Donaldson, M.D. Octavo of 245 pages, illustrated. Garden City, N. Y., Doubleday & Company, Inc., 1962. Cloth, $3.95.

Einfache Psychotherapie fur den Hausarzt. By H. K. Knoepfel. Octavo of 222 pages. Berne, Switzerland, Hans Huber, 1961. Cloth, Fr./DM 18.50.

The Layman's Guide to Psychiatry. By James A. Brussel, M.D. Duodecimo of 235 pages. New York, Barnes & Noble, Inc., 1961. Paper, $1.50.

Books Reviewed

Management of Obstetric Difficulties. Revised by J. Robert Willson, M.D. Sixth edition. Octavo of 687 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $16.50.

The author of this sixth revision is a prominent teacher who, as in previous editions, has designed his text to be a ready reference for the practicing obstetrician rather than for the medical student.

Sections of the book are devoted to infertility, diagnosis of pregnancy and prenatal care, complications of pregnancy, labor and the puerperium, obstetric operations, special therapy, and the care of the newborn infant. In this revision, obsolete or outmoded methods of therapy have been deleted, and the recent advances in the diagnosis and therapy of habitual abortion with particular reference to the incompetent internal cervical os, septic abortion, carcinoma of the cervix during pregnancy, diabetes, anemia, heart disease, hypertension, and preeclampsia are included. Some of the newer diagnostic procedures such as fetal electrocardiography are described also. The chapter on the care of the newborn infant has been revised. The 323 illustrations include 66 new illustrations which supplement the text. The book is recommended to the profession.—ALEXANDER H. ROSENTHAL, M.D.

A Functional Approach to Neuroanatomy. By Earl Lawrence House, Ph.D., and Ben Pansky, Ph.D. Quarto of 494 pages, illustrated. New York, The Blakiston Division, McGraw-Hill Book Company, Inc., 1960. Cloth, $12.50.

The authors of this volume are nonmedical anatomists who have attempted to offer the medical student a systematically organized functional approach to the study of neuroanatomy. To strengthen the motivation for learning, some clinical correlations by means of the presentation of short case histories and clinical neurotopical technics are described. The clinical presentations, although not interwoven with the anatomic descriptions and appearing apart under a separate chapter heading, serve to emphasize the structural and functional significance of the central nervous system. The authors, however, make no claim to presentation of a study of clinical neuroanatomy, an approach to study, which in recent years, would seem to have many advocates for a more meaningful method of undergraduate teaching.

The text is succinctly presented with a minimum of conjectural discussion and with clear and functional correlations with the structure of the nervous system. The diagrams are sharply and boldly drawn and suffer minimally from obfuscation by the labeling process, but often inevitably become quite complex, despite the authors' avowed intention of presenting simple diagrams designed to illustrate a single fact of anatomic knowledge.

The value of the summary charts at the conclusion of each chapter is questionable, since the student would do best to prepare his own device for review. The atlas of routine brain sections is satisfactory and requires no comment, since it is ample for the undergraduate's purpose.

The text is easy to read and accessible for quick reference because of the boldface labeling of the paragraphs, the clear lettering, and the nonglare paper.—MORTON H. HAND, M.D.

Cardiovascular Dynamics. By Robert F. Rushmer, M.D. Second edition. Quarto of 502 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $12.50.

To clear up some confusion, it should be noted that this is a more accurately titled second edition of Rushmer's *Cardiac Diagnosis: A Physiologic Approach.* It should be said at once, too, that no one can practice cardiology in 1961 without a working knowledge of the dynamics of the circulatory system as set forth in this book, nor is this material as well organized and elucidated in any other single volume, as far as this reviewer knows. The author, professor of physiology and biophysics at the University of Washington, has depended heavily on figures and illustrations to visualize concepts, concepts which are not always easy to understand from the text alone. He has sensibly avoided graphs and tables which so often are tedious and even misleading.

Cardiovascular Dynamics will be useful as a supplementary text for every student, undergraduate and postgraduate. It will be especially valuable for the practicing physician now over forty who may have been educated in the now largely outdated morphologic approach to cardiology. Unless he has been especially alert in following recent advances in the physiologic and metabolic approach to heart function and disease, he will have much to learn from Rushmer.—MILTON PLOTZ, M.D.

Essays on the First Hundred Years of Anaesthesia. Volume 1. By W. Stanley Sykes, M.B. Octavo of 171 pages, illustrated. Edinburgh, E. & S. Livingstone Ltd. (Baltimore, The Williams & Wilkins Company), 1960. Cloth, $7.00.

Essays on the First Hundred Years of Anaesthesia by W. Stanley Sykes deserves to be in the library of all physicians. The author's reason for including the word "essays" in the title is obviously that he presents a variety of incidents in the history of anesthesia, but includes circumstances that describe the practice of medicine in general. It rambles from the general picture of poor sanitation and animal-like existence to the indifference and isolation of the aristocracy and the wealthy. It is interesting how the author ties the two together by the death of Prince Albert.

The poor regard that is accorded the physician in the early nineteenth century and the inability of the sick to pay the physician his almost starvation fees make one stop and think of the importance of organization and public relations in medicine.

Dr. Sykes delves deeply and minutely into the backgrounds of fame and credit-seeking doctors who gave this world anesthesia. The many illustrations of equipment both ingenious and ridiculous add to the entertainment. A laughable example is the description of a machine which requires that the unconscious patient provide his own foot power for resuscitation.

His high regard of serendipity may be a cliche, but it serves to substantiate his philosophy.

This book bears the aura of authenticity and provides an evening of pleasant reading.—IRVING M. PALLIN, M.D.

Medical Department, United States Army. Preventive Medicine in World War II. Volume V. Communicable Diseases Transmitted Through Contact or by Unknown Means. Editor-in-chief, Colonel John Boyd Coates, Jr., MC. Editor for Preventive Medicine, Ebbe Curtis Hoff, M.D. Assistant Editor, Phebe M. Hoff, M.A. Octavo of 530 pages, illustrated. Washington, D.C., Office of the Surgeon General, Department of the Army, 1960. Cloth, $5.75.

This is part of a comprehensive record of wartime experience with medical problems. It gives the basis for the prevention and control of disease in peace as well as in future wars (perish the ignoble thought). Other books in this series relate to environmental hygiene, personal health measures and immunization, and communicable diseases transmitted chiefly through respiratory and alimentary tracts. The "steady erosion" of manpower, namely, morbidity and mortality, is described. The book is for the Archives of the Medical Division of the Army.

The evolution of an effective form of treatment and of prophylaxis of fungus infections, epidemic keratoconjunctivitis, pretibial (Fort Bragg) fever, Bullis fever, scabies, schistosomiasis, hepatitis, and of course syphilis, among many others, are elucidated. It is well written with numerous instructive illustrations. The "bombshell" of viral heptatitis and the separation of the types of hepatitis is fascinating. The extent of coverage makes it a valuable addition to the library of any medical student, physician, epidemiologist, immunologist, venereal disease control officer, entomologist, parasitologist, malariologist health officer and nurse, as well as any sanitarian.—BERNARD SELIGMAN, M.D.

Recent Advances in Biological Psychiatry. Volume III. Edited by Joseph Wortis, M.D. Octavo of 241 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $9.75.

The questions in biologic psychiatry concern what metabolic changes are associated with, are prodromal to, precipitate, or may be of prognostic importance in psychiatric treatment, or, in psychopharmacology, what exogenous materials may influence favorably the course of a mentally aberrated state. The psychodynamic view and the biologic view are not antithetical; the recognition of the biologic component does not prevent the realization that psychodynamic forces are integrally involved in a psychosis, nor does the recognition of the psychodynamic view preclude the existence of a metabolic anomaly. The nature of the trigger does not necessarily determine the cure. In other words, affective sterility requiring verbal psychotherapy does not exclude the existence of an enzymatic or other physiologic aberration which eventually may be favorably influenced by drugs.

Biologic psychiatry encompasses more than the perfunctory administration of tranquilizers or psychic energizers. Depressions and manic states must be indeed treated expeditiously. The interdisciplinary nature of therapy is apparent, for the correction of the biologic anomaly still leaves the need to treat the psychic disturbance present. But an increasing understanding of the role for example, of the coenzymes, adenosine triphosphate, the psychogens, the indole alkaloids, is slowly adding pieces to the jigsaw puzzle although the greater part of the picture has not yet been constructed. Moreover, as the horizon has been expanded because reasonably well-related and well-functioning people have sought treatment, an investigation of a physical basis will probably become routine.

Parallel with the rise of the study of the biologic aspect of mental disease, the classification of psychiatric states themselves has undergone a change. This is not an idle play at nosology, but a reflection of a better, or at least a different understanding of the psychoses. For that reason among others, the biologic aspect cannot be ignored merely because a dependable relationship regarding ceruloplasmin or taraxein, for example, has not been found or because no substance has yet been described to be present in a psychotic state but not present in a nonpsychotic one. The biologic orientation presents additional hypotheses for investigation—one, for example, that an inactivating substance may be lacking, which lack may prevent the metabolic conversion which would otherwise take place. To investigate the relationships in the ill-defined division between the predominantly physical cause and the predominantly mental is not limited to severe psychotic patients—parameters for the minor conditions probably will be developed. However, there is a capacious pitfall ready for those who believe that emotions can be measured by the scientific method (which is frequently merely a specious exercise in scientism) and that unless a parent-child relationship, love, or other affects are measured by the double-blind method they are not valid. One cannot espouse a method as if one is hawking a commodity.

The present text, volume 3, is much smaller and less broad in scope than volume 2 and especially volume 1. It is nonetheless worthy of study for developments in the field.

Among the contributions are animal studies of drugs, biochemical as well as clinical, traits and their interrelationship, evaluation of psychotherapeutic agents, proposal of possible mechanism and how they are influenced, and behavioral changes induced by a variety of agents. There is a creditable chapter on catecholamines in psychophysiologic states, showing findings and limitations. There is a chapter on mental and social rehabilitation with tranquilizers. One chapter describes certain biochemical measures in comprehensive psychiatric treatment, especially in schizophrenia; although recounting nothing particularly new, it is an informative review of results.

A well-integrated chapter, "Theoretical Implications of Chemotherapy of Depressions," details experimental work with monoaminooxidase inhibitors. And two other well-organized and informative chapters deal with the effect of 5-hydroxytryptamine and serotonin on the relationship between condition reflexes and certain somatic functions and on neurochemical factors in behavior. Also, Hoch's presidential address on achievements in biologic psychiatry is worth reading. It is of a caliber comparable to Mackay's, Wickler's, or Masserman's contributions in earlier volumes of this series. One wishes however that a lower price would make this book more accessible.—Erwin Di Cyan, Ph.D.

Adolescents: Psychoanalytic Approach to Problems and Therapy. Edited by Sandor Lorand, M.D., and Henry I. Schneer, M.D. Octavo of 378 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $8.50.

This book concerning adolescents is written by nineteen specialists who have a common philosophic background through their psychoanalytic orientation. It is based on a series of lectures given at the Downstate Medical Center, Brooklyn, New York. The papers offer the therapeutic applications of psychoanalytic knowledge to the management of adolescent difficulties. One of the excellent features is the use of carefully prepared case studies to illustrate hypotheses and therapeutic effects. Some of the chapter headings include character formation, the menarche, delinquency, psychosomatic disorders, adolescence and schizophrenia, treatment of adolescents, and the role of the parents.

This book will be of greatest use to psychiatrists who are actively involved in the therapy of adolescent problems. To other physicians it offers background information toward the understanding of the teen-ager.—Stanley S. Lamm, M.D.

An Atlas of Acquired Diseases of the Heart and Great Vessels. Volume I, Diseases of the Valves and Pericardium. Volume II, Coronary Arterial Disease, Systemic Hypertension, Myocardiopathies, the Heart in Systemic Disease, and Cor Pulmonale, Acute and Chronic. Volume III, Diseases of the Great Vessels. By Jesse E. Edwards, M.D. Quarto of 1,401 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $70, set of 3 volumes.

This *Atlas of Acquired Diseases of the Heart and Great Vessels* represents the experience of Jesse E. Edwards, M.D., consultant pathologist at the Mayo Clinic, who in the past fourteen years has concerned himself with detailed studies of cardiac pathology. The atlas is a detailed presentation of the pathologic anatomy of acquired heart disease. The anatomic changes are described accurately and concisely and are illustrated by many well-reproduced photographs of gross and microscopic specimens. Wherever applicable, physiologic, electrocardiographic, and roentgenologic data are presented. This is particularly emphasized in the section on valvular heart disease where the orientation has clearly been influenced by advances in cardiac catheterization and surgical correction of valvular deformities. In the section on coronary disease, electrocardiographic changes are correlated with the extent and distribution of areas of infarction, as illustrated in cross section diagrams of the heart. Rare entities, such as the myocardiopathies of viral or unknown origin, are presented as complete case reports with a discussion of clinical, electrocardiographic, and physiologic data.

The three volumes are primarily a reference atlas with much information for the cardiologist, the cardiac surgeon, and the pathologist. Medical students will find this atlas useful also because the author has accomplished

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his purpose of presenting each entity as a correlation of the pathologic anatomy with clinical, physiologic, electrocardiographic, and roentgenographic abnormalities.—IRVING G. KROOP, M.D.

Key and Conwell's Management of Fractures, Dislocations, and Sprains. By H. Earle Conwell, M.D., and Fred C. Reynolds, M.D. Seventh edition. Octavo of 1,153 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $27.

The popularity of this fine work is attested by the fact that it is now in its seventh edition. New material has been added. For example, the use of the medullary nail is discussed; there is an excellent chapter on anesthesia in patients with injuries of the extremities.

As stated by the authors in the preface, they have found "little reason to depart from the basic concepts of conservatism." This sound judgment is reflected throughout the entire volume.

The photographs are excellent and have been clearly reproduced. This adds greatly to the value of the book.—MAYER E. ROSS, M.D.

Modern Drug Encyclopedia and Therapeutic Index. Edited by Harry D. Fein, M.D. Eighth edition. Octavo of 1,649 pages. New York, The Reuben H. Donnelley Corporation, 1961. Cloth, $17.50.

This publication is a listing of most of the products of about 200 pharmaceutical manufacturers in the United States. It occupies the position in this country of an unofficial publication of ethical drugs, an analogue to the German Gehe's *Codex*, the *Repertorium*, or Bernouli's *Rote Liste*, or the French Vidal's *Dictionnaire de Spécialitiés Pharmaceutiques*.

Each of the entries is supplied by the manufacturer. The products are classified alphabetically by the trade name—a designation by which a drug is best known. There is also given the generic name, the chemical name or formula of components, actions and uses, dosage, and precautions in use or contra-indications. The uniformity of the entries and the reasonably informative presentation make this useful to the physician when he requires quickly available data on a drug. Monthly supplements (called *Modern Drugs*) list new drugs which have become available during the preceding month, and in many instances lengthy package inserts for a drug are reprinted therein. Though this compilation is published every two years, it is kept in a current state by the monthly supplements.

The *Modern Drug Encyclopedia* (MDE) differs from the *Physicians' Desk Reference* (PDR) in a number of respects, though each has its own valid place. The entries in MDE are free to the manufacturer, and the publisher therefore charges for the book, whereas PDR is supplied to the physician without charge as the manufacturer pays for the space he buys to list his products. The PDR entries tend to be shorter and more to the point; PDR lists many products of firms not found in MDE—and the reverse is also the case. The choice of what product to list in PDR is primarily the manufacturer's, for he buys the space, whereas the selection of listings in MDE is an editorial function although largely the well-known products, and those not so well known, are listed. Both MDE and PDR have comprehensive indexes—the latter has perhaps more elaborate ones—which enable the location of a product if only one or two elements about it are known.

Neither publication is pharmacologically oriented—these publications show what is available, and they are sources of recall or retrieval of information, but they are never guides to therapy. Each publication in its own way performs an excellent service for it opens to the physician a concise list of available preparations and gives information about the preparations it lists so that he may choose the articles supplying the therapy he wishes to prescribe.—ERWIN DI CYAN, PH.D.

Coronary Vasodilators. By R. Charlier. Octavo of 208 pages, illustrated. New York, Pergamon Press, 1961. (International Series of Monographs on Pure and Applied Biology) Cloth, $8.50.

Coronary Vasodilators by R. Charlier is a studious quest for much needed medication to alleviate and control coronary artery disease. In 1923, while taking a postgraduate course in Vienna, I heard Professor Wenkebach pronounce angina pectoris as the great American disease. As a result of its growing incidence, the medical profession has been bombarded by an avalanche of preparations purporting to desensitize the cardiac nerves, to provide for an increased coronary blood flow, and to promote the oxygenation and repair of the cardiac muscle. Of all these therapeutic agents, nitroglycerin has stood the test of time, followed by the derivatives of papaverine as a close second. The volume is a courageous attempt for the solution of a world-wide problem.—SIMON FRUCHT, M.D.

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   Constantine D. J. Generales, M.D., New York
   Assistant Professor of Space Medicine and Co-ordinator of Space Medicine Program, New York Medical College

2. **The United States Government's Role in Current Space Exploration**

   Hon. Victor L. Anfuso, Brooklyn (By invitation)
   House of Representatives, Committee on Science and Astronautics

3. **Unusual Earthly Forms of Life and Extraterrestrial Implications**

   John Palister, New York (By invitation)
   President Explorers Club; Research Associate, Department of Entomology, New York Museum of Natural History

4. **The Significance of the Magnetosphere to Man**

   Alistair G. W. Cameron, Ph.D., New York (By invitation
   Institute for Space Studies, National Aeronautics and Space Administration

5. **Biomedical Engineering as a Physician's Aid**

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   Director, New England Institute of Medical Research

8. **Electromagnetism and its Effect on Human Behavior**

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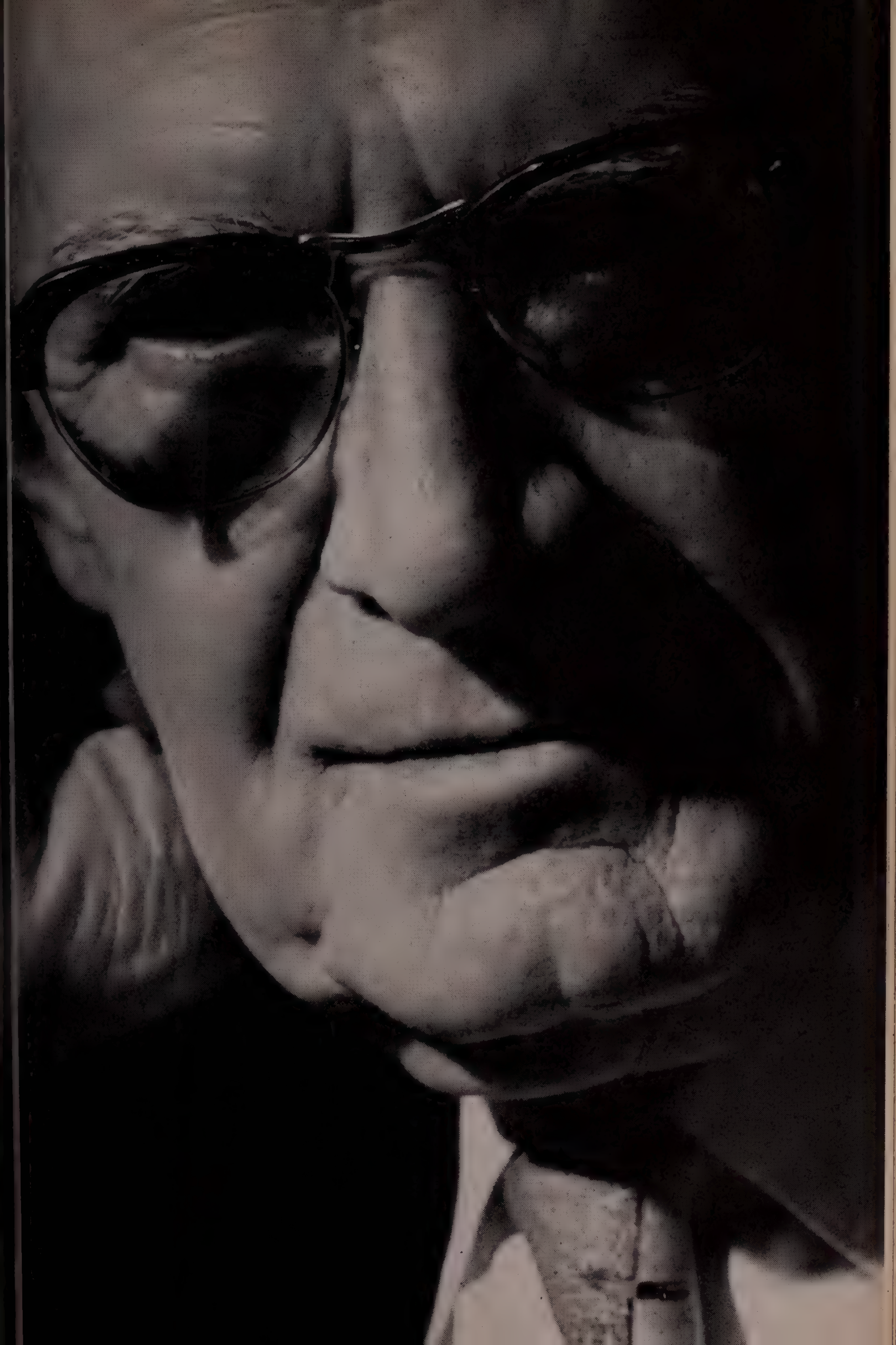

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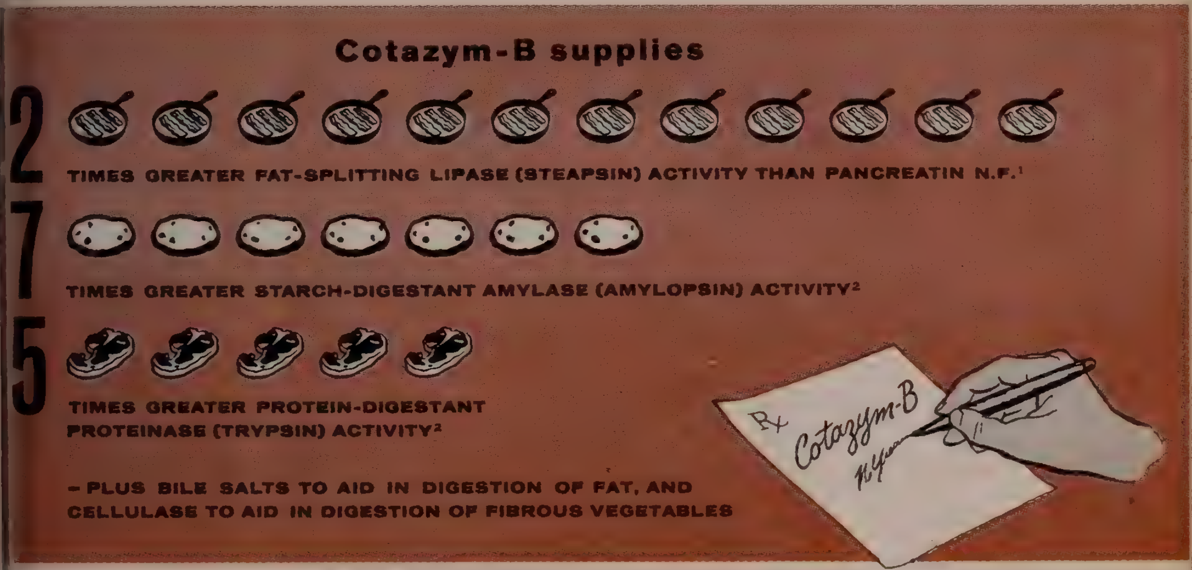

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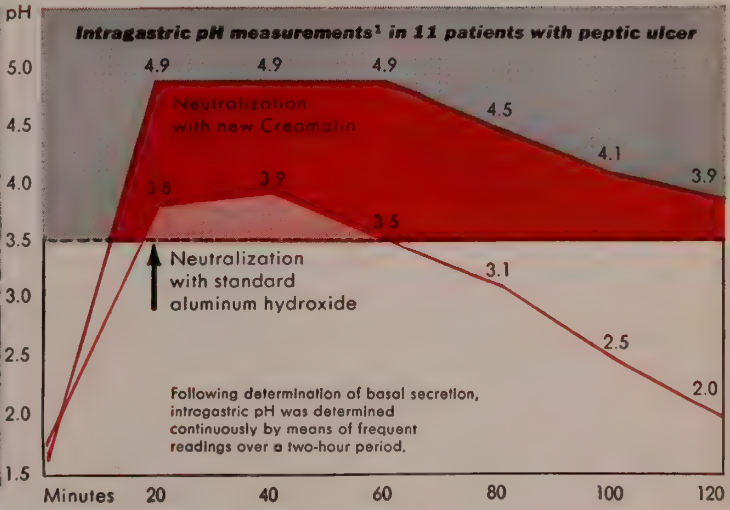
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5.0
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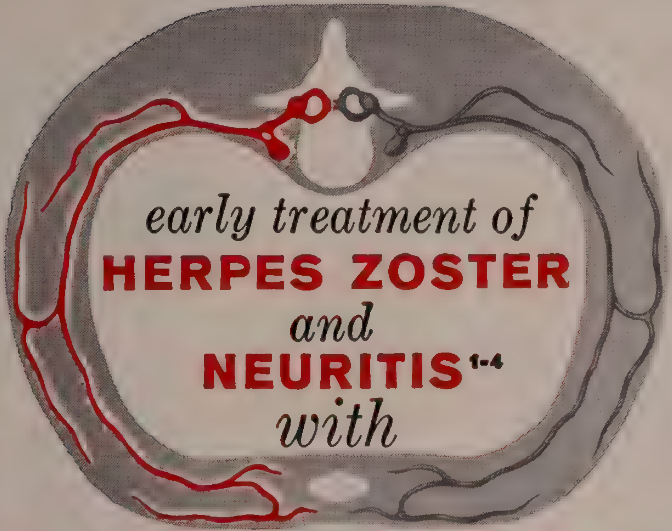

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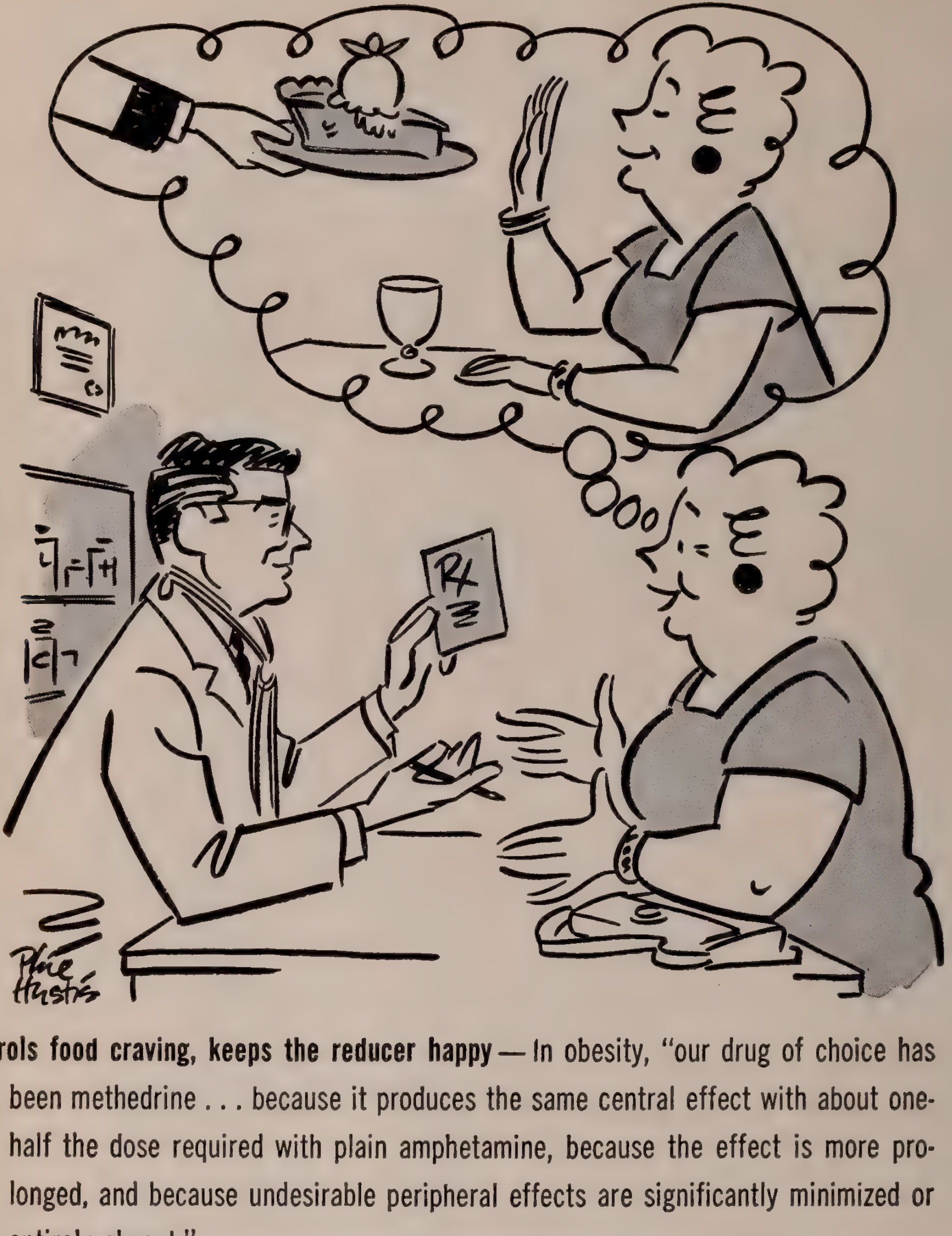

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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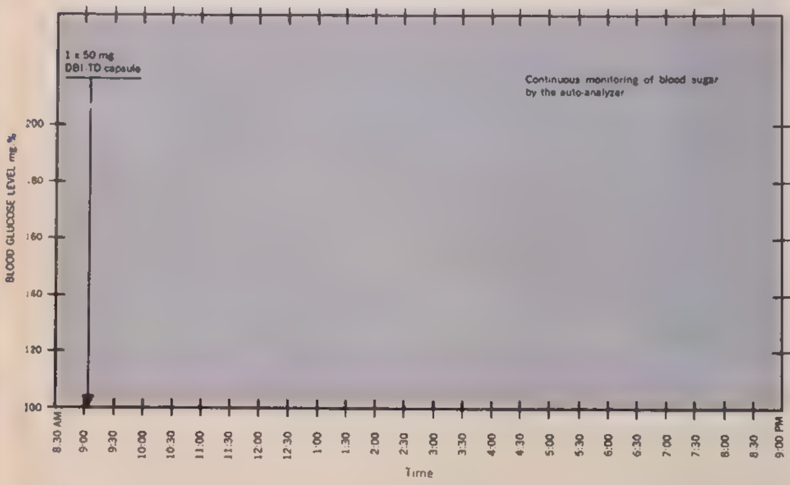

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1. Walker, R. S.: Brit. M. J. 2:405, 1959. 2. Hamel, J. F.: Applied Therapeutics 2:137, 1960. 3. Moss, J. M., DeLawter, D. E., Tyroler, S. A., and Field, J. B.: Med. Times 89:561, 1961. 4. Krall, L. P.: Applied Therapeutics 2:137, 1960. 5. Craig, J. W.: Personal communication. 6. White, P. and Krall, L. P.: Personal communication. 7. Miller, E. C., and Roller, G. W.: Med. Times 89:196, 1961. 8. Pomeranze, J.: Clinical Medicine 8:1155, 1961. 9. Barclay, P. L.: J.A.M.A. 174:474, 1960. 10. Krall, L. P.: Med. Clinics N.A. In press. 11. Radding, R. S., and Zimmerman, S. J.: Metabolism 10:238, 1961. 12. Beaser, S. B.: Personal communication. 13. Gurol, F.: Personal communication. 14. Pearlman, W.: Phenformin Symposium, Houston, Feb. 1959. 15. Weller, C., and Linder, M.: Metabolism 10:699, 1961. 16. Fabrycant, M. and Ashe, B. I.: Metabolism 10:684, 1961. 17. Radding, R. S., McHenry, J. I., Neely, W. B., and Lummis, F. [illegible]: Presented at Fourth Congress of Internat. Diabetes Fed., Geneva, June 1961.

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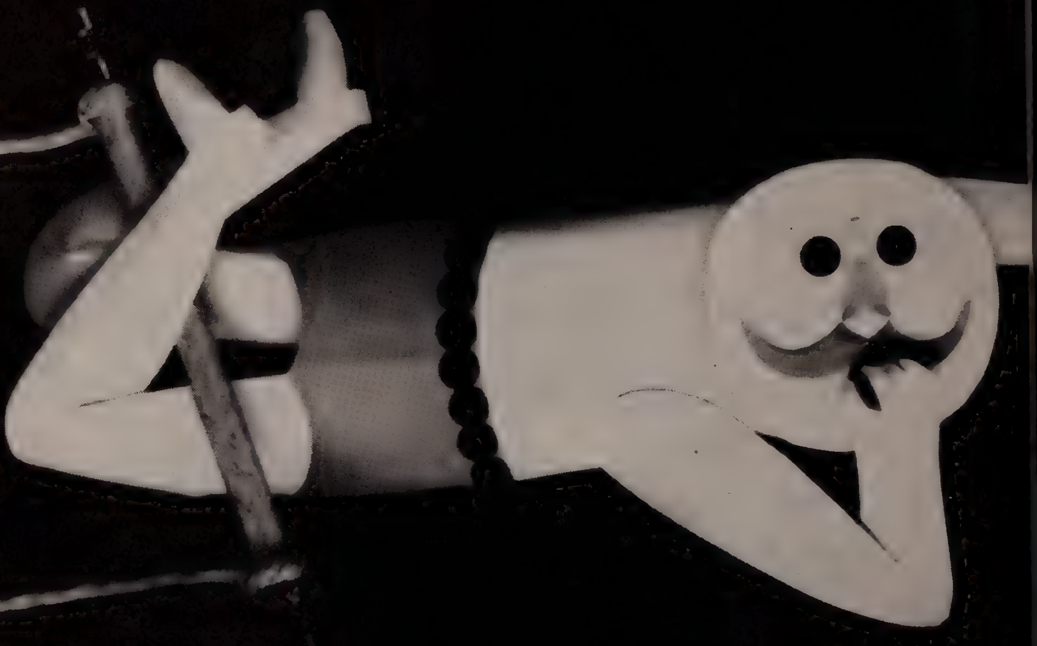
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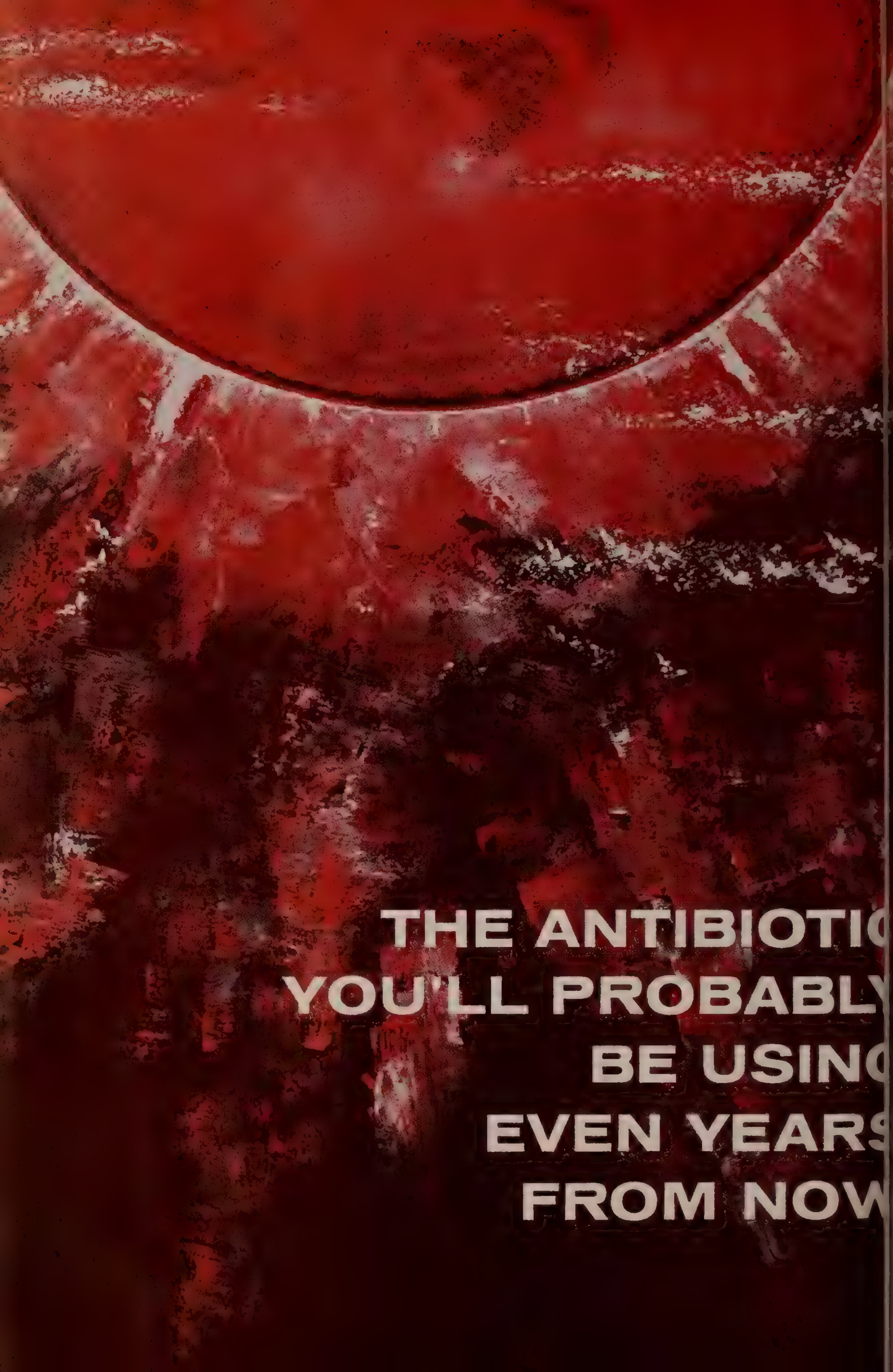
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2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

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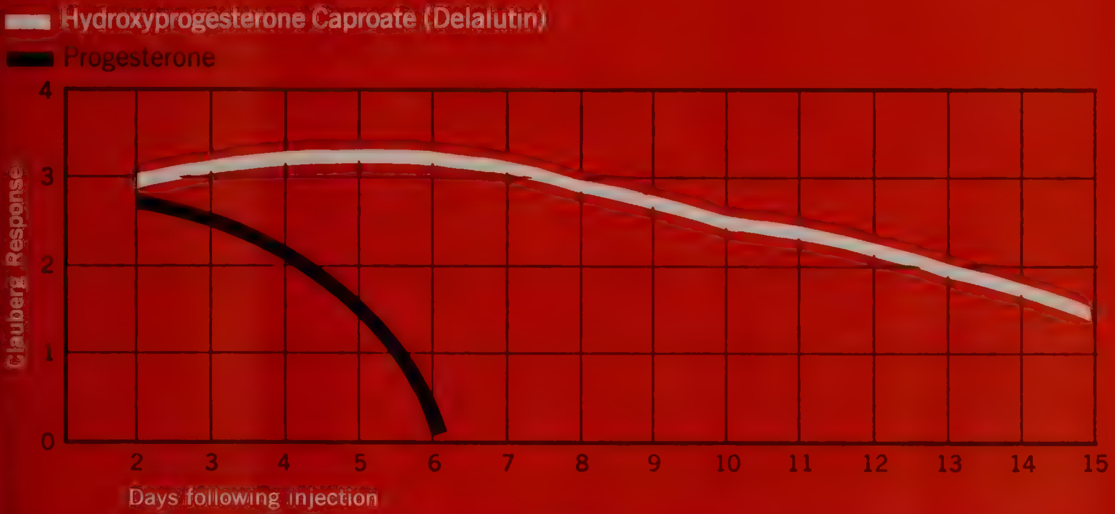
Comparative effect of single subcutaneous injection of Delalutin and progesterone on the progestational changes [Clauberg Test] in the rabbit uterus.

Borman, A.: Laboratory Report on the Duration of Action of 17-Alpha-Hydroxy-progesterone-n-Caproate (Delalutin). The Squibb Institute for Medical Research, May 17, 1955.



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Complete information on administration and dosage is supplied in the package insert and in your Squibb Product Reference and Product Brief.

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—Rostenberg, A., Jr.: Clinical Evaluation of Flurandrenolone, a New Steroid, in Dermatological Practice, J. New Drugs, 1:118, 1961.

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Editorials

The lift in the shoe

The frequency with which a simple procedure alleviates an aggravating symptom is known to all of us. In one area particularly, that of low back pain, the trial of a simple shoe lift is often overlooked. When this is recommended by an irregular practitioner its success is a source of embarrassment to the qualified practitioner.

Perhaps we do not use shoe lifts as much as we should because of the element of quackery which has grown up about this. Often enough cases of back pain and even frank disk protrusions are helped by heel elevations on the asymptomatic side which divert the superincumbent weight, taking pressure off the constricted nerve root.

Certain conditions about the legs and feet are very definitely helped. These include such things as tenosynovitis or irritation of the bursa in the region of attachment of the tendo achillis. It is also helpful in relief of symptoms following partial ruptures of gastrocnemious or soleus muscles or entire rupture of the plantaris tendon. A heel lift in such a situation will take tension off the tendon and provide definite relief.

A shoe lift is far from a panacea and is all too frequently disappointing. Despite careful theoretic reasoning many cases are not helped by the lift. On the other hand, it seems certain that many favorable responses are more than psychologically induced.

We are less empirically minded than we used to be—we must know exactly why a thing works before we use it. This is scientifically commendable. The impatience of the lay person is understandable—he wants relief and quick relief. If a simple procedure will do this while we study the problem, well and good.

The patient need not drift from his doctor's office to that of the unlawful practitioner if we focus on the obvious as well as the obscure.

Survey with the Guthrie test

Phenylketonuria (PKU) occurs only once in every 20,000 to 40,000 live births. If the underlying metabolic fault remains undetected, severe mental retardation requiring lifelong institutionalization ensues.

Heretofore the most widely used test has been the simple ferric chloride test of the urine, known as the diaper test, which cannot be made effectively until several weeks after birth. It has been used on only 10 per cent of all babies born in the United States.

A new test devised by Robert Guthrie, M.D., associate professor of pediatrics at the University of Buffalo, gives promise of being of value as early as the first few days of life. This test uses blood drawn from the baby's heel and is based on the fact that certain organisms require phenylalanine for growth. The organism and the infant's blood are brought together on a nutrient plate and incubated, and the presence or absence of bacterial growth is determined.

The Children's Bureau of the Department of Health, Education, and Welfare proposes a nation-wide test of this method on newborn infants to begin July 1. Some 400,000 babies will be tested. Laboratory technicians are to be trained under Dr. Guthrie's guidance, and the over-all direction will be by the state health departments.

It is expected that early detection of

phenylketonuria by this method and the early institution of a phenylalanine-free diet will prevent at least this form of mental retardation from developing.

Narcotic don'ts

The 1961–1962 edition of the *Pharmacists' Compendium*, published by the Pharmaceutical Society of the State of New York, is just off the press.

The 24-page booklet contains the code of ethics for pharmacists; a compilation of Federal and New York State narcotics laws and barbiturate law; Food, Drug and Cosmetic Act; excerpts from the Pharmacy Law; and rules and regulations of the New York State Board of Pharmacy.

This booklet enables physicians to inform themselves on the often overlapping and conflicting provisions of Federal and State laws which relate to narcotics, barbiturates, and the general handling of drugs.

Of particular interest to physicians is an important section described as "Narcotic Don'ts for the Pharmacist," which discusses subterfuges used by addicts to obtain narcotics from pharmacists. Many of these have as their point of origin the physician's office or the hospital, and we should be aware of them. Appended here is the entire list for underscoring as may apply.

Don't leave prescription pads lying around.

Addicts want them for effecting narcotic forgeries.

Don't leave narcotics exposed near your dispensing counter.

Drugs disappear this way. Check receipts on your order forms.

Don't accept a narcotic prescription written in pencil.

It is not a valid order even when written by a physician.

Don't fail to scrutinize prescriptions when written thus: Morphine HT $^{1}/_{2}$ #X or Morphine HT $^{1}/_{4}$ #10.

Several X's or zeros can be added to raise amounts. Use brackets or spelling.

Don't carry a large stock of narcotics.

Only a three months supply or less is good practice. Addicts are breaking into pharmacies and hospitals to get their drug needs.

Don't leave the key inserted in the lock of your narcotic cabinet.

Keep cabinet locked. Make it hard to effect robberies. Keep stock in a safe if possible.

Don't place your narcotic stock where it is accessible to others.

Avoid storage near sink or toilet. Patrons may ask to use these.

Don't leave anyone alone near the prescription room of your pharmacy if you can help it.

Cabinets have been pilfered this way. Addicts pose as salesmen or ask admittance to your prescription room on some pretext.

Don't become rattled by a rush request to fill a narcotic prescription.

Claim for emergency use may be made to create confusion and pass a forgery.

Don't be taken in by a person wearing a white uniform presenting a narcotic prescription.

Addicts have posed as nurses to mislead pharmacists and put them off guard.

Don't fill a telephone order for narcotics unless you are assured that a prescription will be available on delivery.

Bogus doctors calls are made to effect delivery to addicts. Watch change of package racket along with this method.

Don't fill prescriptions for unusual quantities of narcotics unless checked with physician.

Diversion to addicts is a profitable business, M.S. $^{1}/_{4}$ gr. tablets going for as much as a dollar each.

Don't hesitate to call the physician about a narcotic prescription you may question.

The pharmacist is held responsible for filling forgeries. The doctor's cooperation should be sought.

Don't supply a doctor with his office narcotic needs (except certain solutions).

The law requires him to use an official

order form filled by a wholesale druggist and to submit an official order form to the pharmacist for office stock solutions.

Don't dispense any narcotics without keeping record.

You must account for the distribution of your purchases.

Don't break the law to accommodate others or for professional expediency.

Explain the regulations. The patron or physician will cooperate if he sees the point.

Don't hesitate to call on the U.S. Bureau of Narcotics or the State Bureau of Narcotic Control to get or give information.

It will be held strictly confidential.

Don't use the telephone number on the prescription when you are calling the physician to clarify a doubt as to validity of the prescription.

Addicts have been known to have prescription blanks printed with the name of an actual physician, but with a false phone number.

Copies of the compendium are available from the Pharmaceutical Society of the State of New York, 117 East 69th Street, New York 21, New York.

Redway Medal

The first Laurance David Redway Medal will be awarded at the Annual Meeting of the Medical Society of the State of New York which will be held in New York City, May 14 to 18, 1962.

A gold medal and cash prize of $500 in memory of the late editor of the NEW YORK STATE JOURNAL OF MEDICINE will be awarded annually for the article judged to be the most outstanding of those which appeared in the JOURNAL during the previous year.

Every JOURNAL subscriber is invited to send his nomination to the editor of the JOURNAL for the best article which appeared in the JOURNAL in 1961, giving brief reasons for the choice.

Nominations must reach the editor by March 31, 1962. They should be addressed to WILLIAM HAMMOND, M.D., Editor, New York State Journal of Medicine, 750 Third Avenue, New York 17, New York.

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The Basic Action. Enovid (1) induces and maintains a pseudodecidual endometrium, preventing uterine bleeding, (2) inhibits pituitary gonadotropin, preventing ovulation.

When Enovid is withdrawn, bleeding occurs in about three days and usually resembles a normal menstrual period in duration and volume of flow.

***Cyclic* Enovid Therapy.** When Enovid is prescribed for 20 days of each cycle, commencing on day 5, the menstrual cycle will adjust to about 28 days regardless of menstrual timing prior to Enovid therapy. A few cycles of therapy will frequently restore a normal pattern to women with irregularities as menorrhagia, metrorrhagia or secondary amenorrhea.

Since ovulation is inhibited, Enovid may be prescribed *cyclically* over prolonged periods to suspend fertility. During Enovid therapy the ovary remains in a state of physiologic rest. After discontinuance of the drug the normal ovulatory pattern returns. Indeed, subsequent pregnancy appears to be enhanced through a probable "rebound" phenomenon. Thus, *cyclic* Enovid administration has been successful in treating endocrine infertility.

***Continuous* Enovid Therapy.** When Enovid is given on a *continuous* dosage basis, menstruation as well as ovulation is completely suspended. In endometriosis, *continuous* Enovid therapy produces a pseudodecidual reaction with subsequent absorption of aberrant endometrial tissue. This often eliminates the need for radical surgery. When surgery is indicated, Enovid is an effective adjunct preoperatively, as well as postoperatively, to prevent recurrence.

Continuous administration of Enovid is also utilized in habitual abortion, providing balanced hormonal support of the endometrium and permitting continuation of pregnancy.

***Emergency* Enovid Therapy.** In high doses, Enovid has a prompt hemostatic effect and will usually control severe dysfunctional uterine bleeding within 6 to 24 hours. Prompt, high-dosage administration of Enovid is also a rational recourse in threatened abortion.

A Note on Safety. The effects of Enovid have been studied in more than 3,500 women during more than 49,500 menstrual cycles, representing 3,800 woman-years of experience. Enovid has been administered *cyclically* to the same patients for as long as five and one-half years for ovulation inhibition without serious complication. For the present, however, Enovid is not recommended for more than two years, although it is expected that this period will be lengthened as experience continues to accumulate. There has been no impairment of subsequent fertility and no effect on children born to women who conceived after discontinuing Enovid therapy.

The basic dosage of Enovid is 5 mg. daily in *cyclic* therapy, beginning on day 5 through day 24 (20 daily doses). Higher doses may be used to prevent or to control occasional "spotting" or breakthrough bleeding during Enovid therapy, or for rapid effect in the emergency treatment of dysfunctional uterine bleeding or threatened abortion.

Enovid is available in tablets of 5 mg. and of 10 mg. Available on request: literature and references covering more than six years of intensive clinical study.

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Some physicians and laymen believe that medical journal advertising is contrived to persuade physicians to prescribe drugs needlessly, thoughtlessly and indiscriminately. The truth is that "*advertising of drugs is intended to arouse the doctor's curiosity, to acquaint him with new products or dosage or uses, and to encourage him to ask questions. It is not intended to urge the physician to act without adequate knowledge.*"[1]

True, advertisers gain from it, but *medical journal advertising also serves the medical profession.* Without interfering with traditional editorial independence, advertising provides income to publishers enabling them to distribute scientific information.

Proposed legislation aimed at classifying medical journal advertising as "labeling" could so increase advertising costs as to make much of it economically unjustifiable. And while it is improbable that enactment of these controls would abolish medical journal advertising, it is highly possible that it would lead to severe curtailment of advertising revenues for medical publishers and these deplorable consequences:

Many popular journals, covering news, management, the humanities and medical abstracts, now sent without charge to physicians, would disappear.

Your medical association journals and subscription journals would face several choices: to cut editorial content, and decrease the number of photos and charts; to cease publication; or to raise dues or subscription rates.

Most important of all, the lag in publishing scientific papers which now delays their appearance from 6 to over 18 months might well lengthen to 2 to 5 years. Obviously, the communication of vital medical news would suffer immeasurably.

We ask you, therefore, when critics denounce medical advertising, to remember and commend its many contributions to medical progress.

(1) "The Pharmaceutical Industry"/Searle, et al. The Journal of Medical Education, January, 1961.

Scientific Articles

Lucien Howe Prize Essay

The Lens in Human and Experimental Galactosemia

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CONGENITAL GALACTOSEMIA is a rare hereditary disease caused by an inborn error of galactose metabolism, the severity of which depends on the degree of the metabolic block present in the red cells, liver, and lens of the individual patient. The main clinical features of the disease are: early nutritional failure, hepatic and splenic enlargement, jaundice, lethargy, osteoporosis, mental retardation, and cataract formation. Cataracts are present in about 75 per cent of the cases. Most dietary galactose comes from lactose, a combination of glucose and galactose. In the red blood cells, lens, and liver in galactosemia there is an absolute or relative lack of the enzyme galactose-1-phosphate uridyl transferase which is necessary to complete metabolism. Although the liver is probably the major site for converting galactose to glucose, both the red blood cells and the lens are capable of performing this function. In the milk-fed infant the lens is probably called on to handle galactose to a much greater extent than in later life. In a series of studies on rats, comparing a group maintained on a high galactose diet with a control group, the carbohydrate and protein metabolism were shown to be the main areas affected in the development of experimental galactose cataract, while ribonucleic acid metabolism remained virtually unimpaired. From the results it may be assumed that the normal rapidly developing lens of the young rat contains an active direct oxidative pathway of glucose metabolism and that the monophosphate shunt plays only a relatively important role in the metabolic economy of the lens.

CONGENITAL GALACTOSEMIA is now well established as an hereditary disease caused by an inborn error of galactose metabolism. The clinical features of this rare condition usually become manifest shortly after birth, although the severity of this syndrome bears some relationship to the degree of the metabolic block present in the red cells, liver, and lens of the individual patient. Thus, some individuals with a relative deficiency of the specific enzyme necessary for the proper metabolism of galactose by the liver and lens may survive long enough to enable them to develop a more active alternative pathway of galactose metabolism within these organs. The presence of such an accessory pathway of galactose metabolism recently has been demonstrated in the liver[1,2] and lens.[3]

The main clinical features of congenital galactosemia consist of early nutritional failure, hepatic and splenic enlargement, jaundice, lethargy, osteoporosis, mental retardation, and cataract formation. The relationship between the development and

This study and the experiments reported in this study were supported in part by research funds granted by the Rochester Eye Bank and Research Society, Inc., and by the United States Public Health Service Grant B-3081.

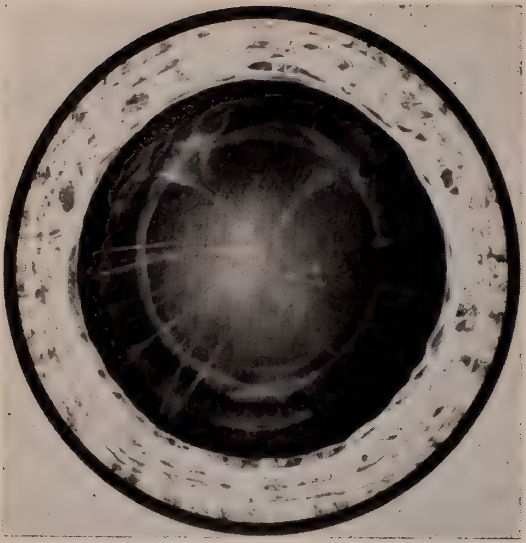


FIGURE 1. Zonular cataract in congenital galactosemia.[15]

the progression of these clinical signs and the continued ingestion of galactose has been documented amply.[4-14]

Cataracts

Cataracts, which are present in about 75 per cent of the cases,[15] may become manifest within the first few days or weeks of life,[16] and in some cases the only clinical sign of this disease is the presence of a congenital cataract.[17] The lentricular changes that have been noted and described in the literature have varied in appearance from a ringlike lamellar opacity with or without vacuoles in the anterior cortex to zonular (Fig. 1) and nuclear opacities.[3,8,11-13,15-28] This varied picture is probably related to the severity and the duration of the galactosemia and the age of the patient when the diagnosis is first established.

Mitchell and Dodge[29,30] first reported on the occurrence of cataracts in rats maintained on lactose diets, and galactose soon was incriminated as the cause of these experimental cataracts.[31,32] These observations have been confirmed since by many investigators.[33-37] The earliest histologic changes in such lenses consist of hydropic degeneration of a few subcapsular fibers located at the equator.[38] As opacification proceeds an increasing number of fibers undergo vacuolation, and this process extends anteriorly to involve the anterior subcapsular cortex, later extending deeper into the cortex.[38,39] Figures 2 and 3 demonstrate some of these changes in lenses derived from young rats maintained on a cataractogenic galactose diet. Many of the cataracts in the human galactosemic patients have a similar slit lamp and histologic appearance. Since galactose has been shown to accumulate in the red cells and liver of the galactosemic individual[40,41] and in the lens of the experimental animal,[42] it is probably safe to assume that cataract formation in both the human and in the experimental animal is initially due to an accumulation of this ester within the lens.

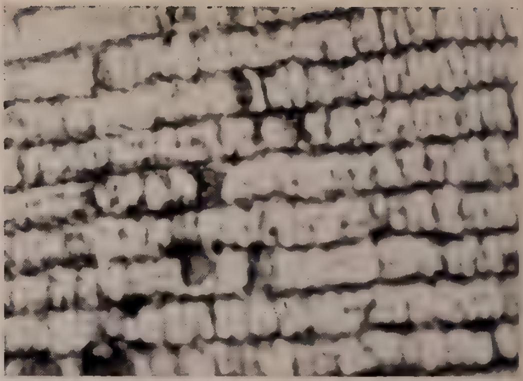


FIGURE 2. Early state of experimental galactose cataract showing hydropic changes on a few lens fibers at the equator.[38]

Galactose

Galactose is a six-carbon monosaccharide that differs from glucose only by virtue of the orientation of the hydroxyl group attached to the number 4 carbon atom (Fig. 4).

Most of our dietary galactose is ingested in the form of lactose, which is a disaccharide present in milk. It consists of glucose and galactose joined together in a 1, 4-glucose-β-galactoside linkage (Fig. 5).

In the intestine lactose is split into glucose and galactose. Galactose then can be utilized by the body in at least three ways. First, galactose is required for the synthesis of the galactolipids which constitute the great bulk of brain matter. This is not an absolute requirement since these cerebrosides

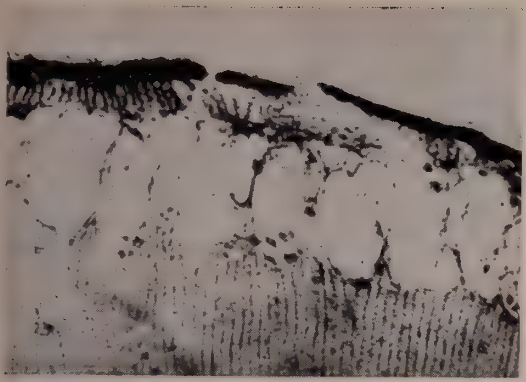


FIGURE 3. Advanced galactose cataract showing large vacuoles in subcapsular cortex of rat lens.

also can be synthesized from dietary glucose in the absence of galactose. Second, galactose is incorporated into chondroitin sulfate which, in conjugation with certain proteins, constitutes the glycoproteins found mainly in the ground substance (matrix) of cartilage and bone and in the cornea and sclera of the eye. Third, most of the ingested galactose is converted into glucose and its derivatives and is thereby utilized by the body as an important source of energy. It is in this pathway of galactose metabolism that the metabolic block occurs that leads to an accumulation of galactose-1-phosphate in certain body tissues.

Studies by Leloir,[43,44] Paladine and Leloir,[45] Leloir and Trucco,[46] Maxwell,[47] and Kalckar and his associates[40,41,48,49] have elucidated the manner whereby galactose is converted to glucose. The following scheme of galactose metabolism is based on these investigations.

Reaction 1 involves the phosphorylation of galactose to galactose-1-phosphate (gal-1-P):

$$\text{galactose} + \text{ATP} \xrightarrow{\text{galactokinase}} \text{gal-1-P} + \text{ADP}$$

Reactions 2 and 3 involve two specific nucleotides, UDPG (uridine diphosphoglucose) and UDPgal (uridine diphophosphogalactose) and two specific enzymes:

Reaction 2:

$$\text{gal-1-P} + \text{UDPG} \xrightleftharpoons{\text{gal-1-P-uridyl transferase}} \text{UDP gal} + \text{G-1-P}$$

Reaction 3:

$$\text{UDPgal} \xrightleftharpoons{\text{UDPgal-4-epimerase}} \text{UDPG}$$

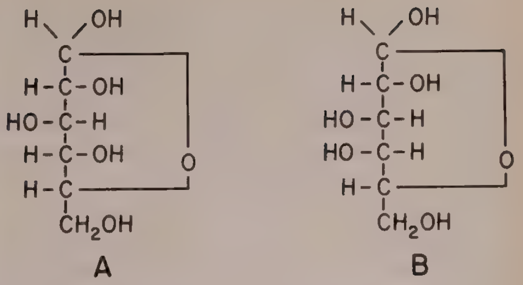


FIGURE 4. Structural formula of (A) glucose and (B) galactose.

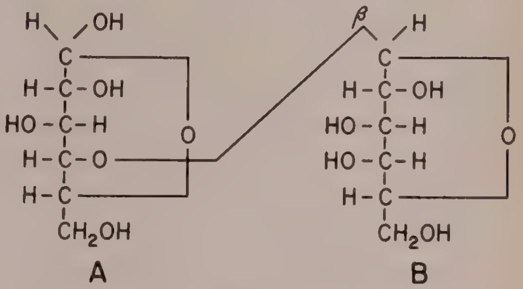


FIGURE 5. Structural formula of lactose.

Reaction 4:

$$\text{UDPG} + \text{PP} \xrightleftharpoons[\text{DPN}]{\text{UDPG pyrophosphorylase}} \text{UTP} + \text{G-1-P}$$

In the red blood cells, lens, and liver in galactosemia there is an absolute or relative lack of the enzyme galactose-1-phosphate uridyl transferase which is necessary in reaction 2.[3,48-52] This results in the marked accumulation of gal-1-P in these tissues with the subsequent development of the clinical signs and symptoms characteristic of this disease.[40,41,53] In the experimental animal fed on a high galactose diet there is a similar tenfold accumulation of gal-1-P in the lens.[42]

The hereditary nature of this metabolic block in the red cells, liver, and lens of galactosemic patients has long been appreciated. It has been suggested that galactosemia is inherited as a simple recessive, and this concept apparently has been substantiated recently.[3,54,55] In some individuals this block may be an incomplete one, and thus the severity of this syndrome may be decreased markedly, or the condition may be present only in a clinically latent form. Furthermore, an alternate pathway has been demonstrated to exist in the liver[1] and probably in the lens.[3] If there is only a relative rather than an absolute lack of the enzyme gal-1-P uridyl transferase, some individuals may be capable of tolerating this decreased efficiency in galactose metabolism for a sufficient period of time until the activity of this accessory pathway increases with age. This pathway occurs via a pyrophosphorylase reaction similar to reaction 4 and involves the enzyme UDPgal pyrophosphorylase:

$$\text{gal-1-P} + \text{UTP} \xrightleftharpoons{\text{UDPgal-pyrophosphorylase}} \text{UDPgal} + \text{PP}$$

Kalckar, Braganca, and Munch-Petersen[56] had suggested originally that such a reaction was present in yeast, and Neufeld *et al.*[57] recently have found such an enzyme in plants. Another possibility is suggested by a report from Topper and Pesch[58] in which they found, with in vitro studies, that the steroids progesterone, methyltestosterone, hydrocortisone, and cortisone all exert a profound stimulatory effect on galactose oxidation. This effect occurs somewhere between cell entry and conversion to glucose-6-phosphate.

Although the liver is probably the major site for converting galactose to glucose, both the red blood cells and the lens also are capable of performing this function. It seems unlikely that in the normal person galactose would be an important constituent in lens metabolism, since the ingested galactose probably is quickly converted to glucose by the liver before it can rise to any significant level in the lens. In the milk-fed infant the lens probably is called on to handle galactose to a much greater extent than in later life. The absence of gal-1-P uridyl transferase in such a lens therefore can result in a very rapid accumulation of galactose-1-phosphate. The effect of a high-galactose diet on the lens of the post-weanling rat, twenty-eight to thirty-two days old, is probably analagous to what occurs in the milk-fed infant with a partial or complete lack of the enzyme gal-1-P uridyl transferase. In both of these situations galactose-1-phosphate accumulates rapidly to at least a tenfold excess. Since the metabolism of glucose provides the lens with its main source of energy, it seems likely that an accumulation of this ester may be the precipitating factor in the development of both the human and experimental galactose. Gal-1-P thus would exert its cataractogenic action by means of inhibiting the metabolism of glucose in this organ.

The ease with which cataracts can be produced in the rat lens definitely is related to the concentration of galactose in the diet and also to the level of the blood galactose concentration. Diets containing 25 to 70 per cent galactose are all cataractogenic, but the amount of time required for cataract formation increases with the lower galactose concentrations.[29,30,59] The age of the animal is also an important factor in the experimental production of galactose cataract.[60–62] As the animal ages, the lens becomes increasingly more resistant to the cataractogenic action of this sugar.[61,62] Furthermore, different strains of rats vary quite considerably with respect to their degree of susceptibility to galactose. This latter phenomenon may be due in part to differences in the level of gal-1-P uridyl transferase in the lenses of various strains[63] as assayed by the method of Anderson *et al.*[51]

There are several possible loci where galactose theoretically could interfere with glucose metabolism in the ocular lens. Hormann[64] has suggested that this ester may exert its cataractogenic influence by interfering with the pyruvate-lactate equilibrium. However, Pirie and Van Heyningen[65] were unable to observe any change in lactic acid formation by cattle lenses incubated with a 5:1 ratio of galactose to glucose. In the rat the concentration of lactate in lenses derived from animals maintained on a high galactose diet did not differ significantly from the normal values.[66] Similarly, in studying the effect of carbohydrates on the extent and duration of the production of pyruvate, Helmreich *et al.*[67] were unable to find any significant difference when glucose or galactose were employed as substrates. These findings, together with other evidence to be presented later, also would tend to refute the possibility that galactose may exert its deleterious effects by inhibiting the phosphorylation of glucose to glucose-6-phosphate as suggested by some investigators.[68,69]

Although Sidbury[70] recently has demonstrated an in vitro inhibition of phosphoglucomutase by high concentrations of galactose, he has been unable to reproduce this effect in the liver or lens derived from rats maintained on a high galactose diet.[71] Furthermore, it is difficult to see how an inhibition at this locus could have any marked effect on lenticular metabolism since glycogenolysis is of little consequence within this organ.

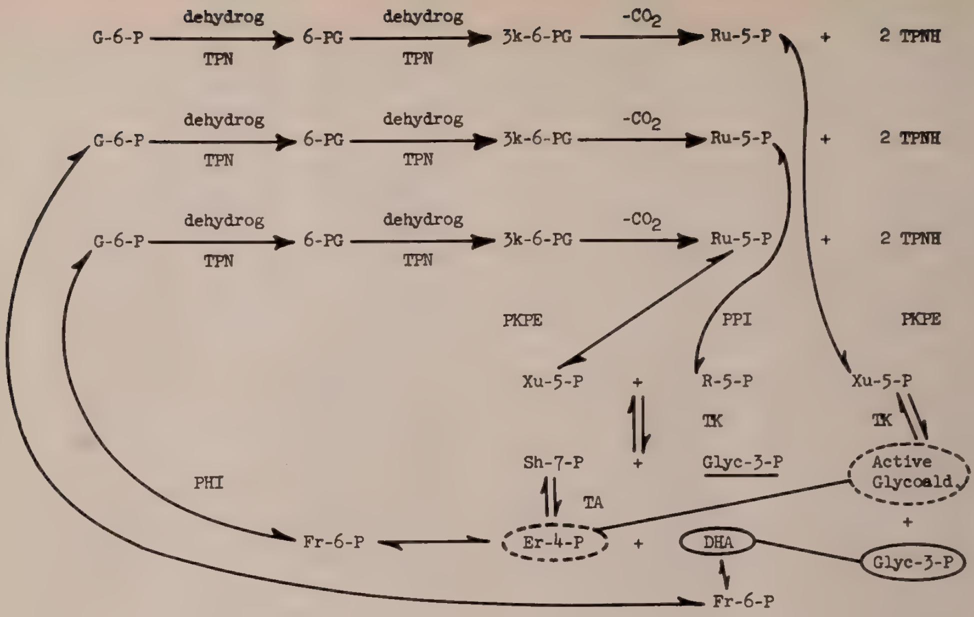
Hexose monophosphate shunt

Kinoshita and Wachtl[72] recently have shown that the hexose monophosphate shunt is an active pathway in the combustion of glucose to carbon dioxide in the bovine, rabbit, and cat lens. A similar situation also exists in the rapidly developing lens of the young rat[61,62] as well as in other tissues and organs during periods of marked growth, and in many types of tumor tissues.[73-91] These experiments all are based on determining the fate of C^{14}-labeled glucose (in the C_1 and C_6 position) incubated with various tissue slices or in whole-animal experiments. The relative importance of each pathway usually is determined by calculating the yields of $C^{14}O_2$ from glucose-6-C^{14} and glucose-1-C^{14}. With only the Embden-Meyerhoff pathway operating, the ratio of $C_1:C_6$ yield of $C^{14}O_2$ from G-6-C^{14} and G-1-C^{14} should be equal to unity. With the hexose monophosphate shunt the ratio would be considerably more than one. To avoid the effect of dilution from endogenous carbon compounds similar experiments could be done employing uniformly labeled glucose, thereby obtaining a factor to correct for such a dilution.

Wood[92] recently has reviewed and analyzed many of the experiments relating to the hexose monophosphate shunt which have appeared in the literature during the past decade. As he pointed out, these experiments are based on several assumptions which may turn out to be invalid. One of these assumptions is that the hexose monophosphate shunt begins with the oxidative decarboxylation of the C_1 atom from glucose resulting in the formation of pentose phosphates and is followed by the transketolase and transaldolase series of reactions on these phosphates. But as was shown by Racker, de la Haba, and Leder[93] and Horecker, Smyrniotis, and Klenow,[94] fructose-6-phosphate can participate directly in the transketolase-transaldolase reaction to form xylulose and ribose phosphates. These pentose phosphates then can re-enter the hexose monophosphate shunt to be transformed to hexose phosphates. The over-all result of this mixing of the hexose and pentose pools would be a rapid redistribution of the carbon atoms in glucose, and eventually a $C_1:C_6$ ratio of unity could be accounted for by the combined hexose monophosphate shunt pentose phosphate cycle as well as by the Embden-Meyerhoff pathway. A further source of error was indicated by the report of Beevers and Gibbs[95] and others[96] who showed that the $C_1:C_6$ ratio of $C^{14}O_2$ recovered from glucose-1-C^{14} and glucose-6-C^{14} decreased with time (that is, approached unity) in such tissues as mouse lymphosarcoma. Therefore, the calculation of such ratios to determine the relative activity of the hexose monophosphate shunt or the glycolytic pathway based on a single experimental period is open to some doubt with respect to its validity.

However, there is a good deal of evidence based on other experiments, such as the determination of the levels of TPN (triphosphopyridine nucleotide) which tend to confirm the impression that rapidly growing tissue contains an active shunt pathway of glucose metabolism.[88,91] There are also some data which indicate that rapidly growing tissue requires an active hexose monophosphate shunt[61,62] and Krahl,[86] who studied glucose oxidation in the Arbacia egg (sea urchin), concluded that during the early stages of cleavage glucose is oxidized predominantly via the hexose monophosphate shunt while the glycolytic pathway becomes quantitatively more important as development proceeds. The recent report by Glock, McLean, and Whitehead[85] is also of interest since they showed that there was a marked increase in the activity of the hexose monophosphate shunt during lactation, while the glycolytic pathway remained relatively constant.

Since the mechanisms involved in this direct oxidative cycle have been subject to a great deal of investigation and study during the last decade and many steps have been



Net:

$$\text{G-6-P} \longrightarrow 3\ CO_2 + \text{Glyc-3-P}$$

$$6\ \text{TPNH} + 3\ O_2 \longrightarrow 6\ \text{TPN} + 3\ H_2O$$

$$\text{G-6-P} \longrightarrow 3\ CO_2 + 3\ H_2O + \text{Glyc-3-P}$$

FIGURE 6. Schematic representation of the hexose monophosphate shunt.

clarified only recently, a brief description of this pathway will be presented prior to considering the manner in which it may be affected by galactose.

The net result of the hexose monophosphate shunt can be schematically pictured as shown in Figure 6.

Since 6 mols of reduced triphosphopyridine nucleotide are produced, 3 mols of oxygen are required for oxidation in the previously mentioned cycle. The net effect is the combustion of one triose unit to form 3 CO_2 + 3 H_2O. The remaining Glyc-3-P mol can be used for the synthesis of hexose phosphate.

An opportunity to study galactose metabolism in the human lens occurred early in 1958 when a male infant, four weeks old, was admitted to Strong Memorial Hospital showing the typical picture of congenital galactosemia. This diagnosis was confirmed subsequently by laboratory studies. His lenses showed a slight degree of opacification localized to the anterior cortical region and extending toward the equator. These lenses were removed within one hour after death and assayed for gal-1-P uridyl transferase and UDPG pyrophosphorylase. Similar assays were carried out on several lenses obtained from one premature infant and one eight-week-old baby.

Table I shows the results obtained from assaying two galactosemic lenses (obtained from 1 patient) and two normal lenses. Table II shows the level of these two enzymes in the red cell hemolysate from 5 normal persons. It is also of interest to note that the mother of the affected infant and his only sibling, a seven-year-old male, both showed a marked depression of erythrocyte transferase activity. The level in the mother's red blood cell was 0.8 units, and the brother showed an enzyme activity of 0.75 units. The mother also showed

TABLE I. Enzyme activity in galactosemic and normal lenses

Lens	Units of Gal-1-P-Uridyl Transferase Activity*	Units of UDPG Pyrophosphorylase Activity*
Galactosemic; number 1	−0.68 (−0.34)†	391.73 (19.59)
Galactosemic; number 2	−0.47 (−0.024)	380.01 (19.00)
Normal; A	46.13 (2.36)	241.49 (12.06)
Normal; B	25.05 (1.25)	146.93 (7.35)

* The enzyme activity is expressed in micromols of UDPG consumed per hour per gram of soluble lens protein per milliliter of homogenate.

† The values in parentheses are obtained by dividing the original value by 20 to arrive at a figure comparable for enzyme activity in the red blood cell.

TABLE II. Enzyme activity in red cell hemolysate

Subject	Age	Units of Gal-1-P-Uridyl Transferase Activity*
A	4 weeks	2.45
B	10 months	2.06
C	28 years	5.84
D	30 years	4.82
E	22 years	3.20

* The enzyme activity is expressed in micromols of UDPG consumed per hour per gram of hemoglobin per milliliter of hemolysate.

minimal lenticular opacities situated in the deeper layers of the anterior cortex. She had been aware of this condition since childhood, but her visual acuity was affected only slightly. The mother and brother were otherwise in good health, and their galactose-tolerance curves were normal.

To investigate the biochemical effects of a cataractogenic galactose diet on the ocular lens of the rat, the following series of experiments was performed. These studies will be considered in two sections, the first one pertaining to the role of the hexose monophosphate shunt and carbohydrate metabolism in these lenses and the second section discussing protein and nucleic acid metabolism in this organ. The materials and methods employed in all these experiments have been or shall be reported in other communications.[3,61,62,97–104]

Carbohydrate metabolism

THE RECOVERY OF $C^{14}O_2$ FROM LENSES INCUBATED WITH GLUCOSE-1-C^{14} AND GLUCOSE-6-C^{14}. In the normal rat lens the average recovery of $C^{14}O_2$ from glucose-1-C^{14} (as shown in Figure 7) was 4,660 counts per minute per gram wet weight per twenty-one hours (range from 3,550 to 6,320 counts per minute),* while the amount of $C^{14}O_2$ recovered from glucose-6-C^{14} was 312 counts per minute per gram wet weight per twenty-one hours (range from 75 to 500 counts per minute), resulting in a $C_1:C_6$ ratio of approximately 15. Although this value is considerably lower than the results reported by Kinoshita[105] for the cat and bovine lens and Kinoshita and Wachtl[72] for the rabbit lens, it is in agreement with their observations that the hexose monophosphate shunt is largely responsible for the production of carbon dioxide from glucose in the animal lens.

In the animals maintained on the high galactose diet, the recovery of $C^{14}O_2$ from glucose-1-C^{14} began to fall rapidly after two and one-half days on the diet. At this time, the amount of $C^{14}O_2$ recovered was 2,440 counts per minute, or 65 per cent of the average normal value. The recovery of $C^{14}O_2$ continued to decline proportionately with the length of time the animals were maintained on the diet, and by eight and one-half

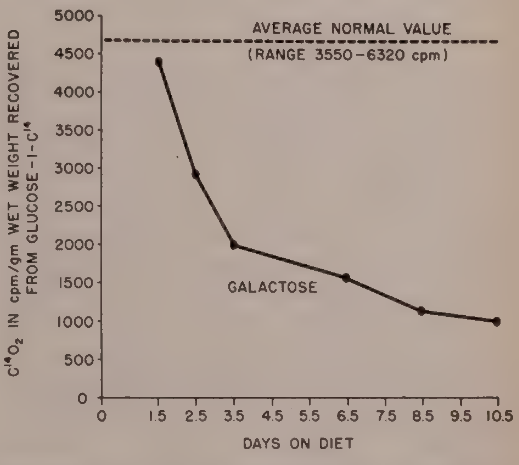


FIGURE 7. The recovery of $C^{14}O_2$ from normal and galactose-fed rat lenses incubated with glucose-1-C^{14}.

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* These figures (in contrast to the published reports) have been corrected for self-absorption. Since infinitely thick layers were counted, the calculated self-absorption of $BaCO_3$ at this weight range was 75 to 80 per cent.

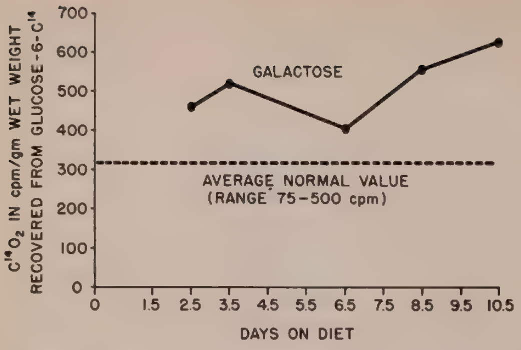
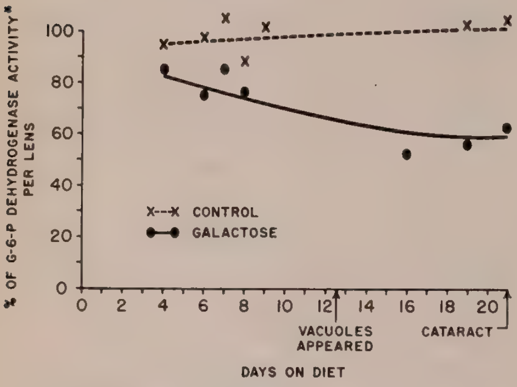


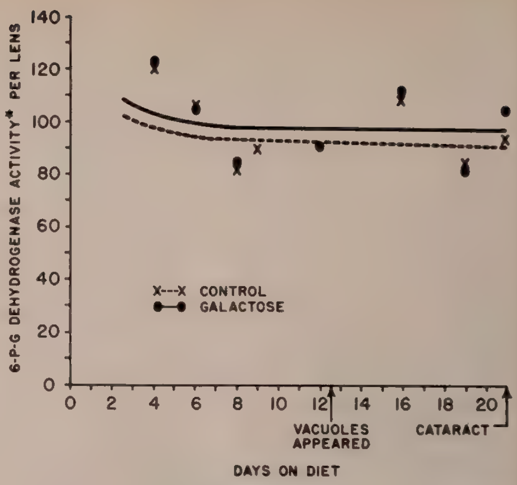
FIGURE 8. The recovery of $C^{14}O_2$ from normal and galactose-fed rat lenses incubated with glucose-6-C^{14}.



* THE ENZYME ACTIVITY (ASSAYED AT pH 7.4) IS EXPRESSED AS μgrams TPN⁺ REDUCED PER HOUR PER mgm. OF SOLUBLE LENS PROTEIN.

100 % G-6-P DEHYDROGENASE ACTIVITY = 21.93 UNITS

FIGURE 9. The activity of G-6-P dehydrogenase in the lenses from the normal and galactose-fed rat.



* THE ENZYME ACTIVITY (ASSAYED AT pH 7.4) IS EXPRESSED AS μgrams TPN⁺ REDUCED PER HOUR PER mgm. OF SOLUBLE LENS PROTEIN.

100 % 6-P-G DEHYDROGENASE ACTIVITY = 6.9 UNITS

FIGURE 10. The activity of 6-PG dehydrogenase in the lenses from the normal and galactose-fed rat.

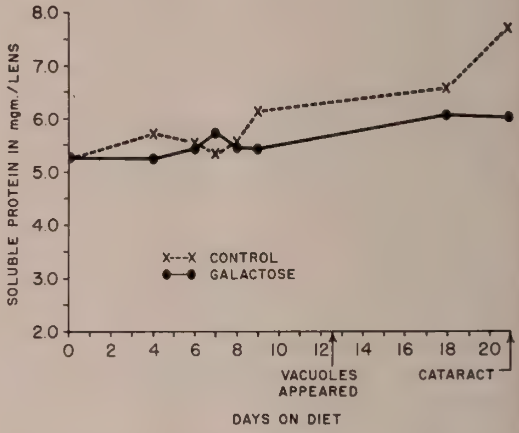


FIGURE 11. The level of soluble lens protein in the normal and galactose-fed rat.

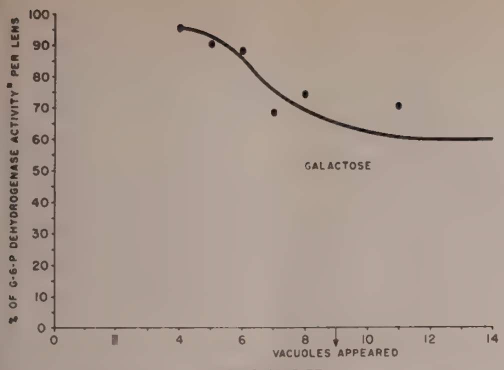
days it reached a level approximately 25 per cent of normal (Fig. 7). Lens vacuoles became apparent after nine days on the diet.

The results of the incubation experiment in which the second lens from each galactose-fed rat was incubated with glucose-6-C^{14} as the substrate are shown in Figure 8. The amount of $C^{14}O_2$ recovered in this experiment (as total counts per minute per gram wet weight) was somewhat higher than the corresponding values obtained from the control lenses although this was not statistically significant.

ACTIVITY OF G-6-P DEHYDROGENASE AND 6-PG DEHYDROGENASE IN VIVO AND IN VITRO. The results of the serial enzyme and protein studies on the Rochester Colony rats are shown in Figures 9 through 11.

The activity of G-6-P dehydrogenase showed a significant reduction on the fourth day of galactose feeding. The inhibition of this enzyme increased until the fourteenth day, and then it leveled off at about 60 per cent of normal (Fig. 9).

There was no change in the activity of 6-PG dehydrogenase (Fig. 10), even at the twenty-first day when cataracts were fully developed.



THE ENZYME ACTIVITY (ASSAYED AT pH 7.4) IS EXPRESSED AS μgrams TPN REDUCED PER HOUR PER mgm. OF SOLUBLE LENS PROTEIN

100 % G-6-P DEHYDROGENASE ACTIVITY = 23.9 UNITS

(HOLTZMAN STRAIN OF RATS)

FIGURE 12. The activity of G-6-P dehydrogenase in the lenses of a second strain of galactose-fed rats.

The level of soluble protein in the galactose lenses showed a very slight increase over the twenty-one-day period under study, while in the control animals the soluble protein level increased approximately 50 per cent (Fig. 11). These results are in agreement with the findings of Dische, Zelmenis, and Youlus,[106] although the apparent inhibition of protein synthesis in our studies did not occur until the eighth day of galactose feeding.

The results of the serial enzyme studies on the Holtzman strain of animals were in close agreement with those observed in the Rochester Colony rats (Fig. 12). The inhibition of G-6-P dehydrogenase occurred after four days on the galactose diet and fell to 50 per cent of normal by the fourteenth day. In these animals lens vacuoles appeared on the ninth day in contrast to the previous group where vacuolization did not become manifest until the twelfth day of the diet.

TABLE III. In vitro inhibition of combined glucose-6-phosphate and 6-phosphogluconate dehydrogenase activity

Animal Number	Animal Weight (Gm.)	Wet Weight of 2 Lenses (Mg.)	Inhibition (Per Cent)*
1	45.5	43.4	34.3
2	51.0	32.6	17.1
3	70.0	38.9	17.7
4	61.9	49.9	15.6
5	69.7	36.6	23.7

* Mean inhibition = 21.7 per cent.

TABLE IV. TPNH:TPN and DPNH:DPN ratios in the lens from the control and galactose-fed rat

Days on Diet	Control		Galactose	
	TPNH: TPN	DPNH: DPN	TPNH: TPN	DPNH: DPN
$2^1/_2$	7.94	1.10	3.11	1.18
$5^1/_2$	3.60	0.96	1.39	0.88
$7^1/_2$	3.30	0.81	1.11	1.65
$9^1/_2$	Lost	Lost	1.19	1.27
$10^1/_2$	2.80	0.84	1.35	0.93
$12^1/_2$	6.47	1.20	0.52	0.64
$14^1/_2$	3.60	1.30	1.31	0.85
Mean	4.62	1.04	...	...

The results of the in vitro experiments showed a mean inhibition of the combined G-6-P and 6-PG dehydrogenase activity of 21 per cent (Table III). The assay for G-6-P dehydrogenase activity alone revealed a similar degree of inhibition of 20 per cent (15 to 34 per cent range).

Concentration of oxidized and reduced di- and triphosphopyridine nucleotides. The results of these experiments are shown in Tables IV and V. The DPNH (reduced diphosphopyridine nucleotide):DPN (diphosphopyridine nucleotide) ratio in the control lens was 1.04 (range from 0.81 to 1.30) while the TPNH (reduced triphosphopyridine nucleotide):TPN ratio was 4.62 (range from 2.80 to 7.94). In the lenses from the galactose-fed rats the DPNH:DPN ratio remained relatively unchanged during the first nine and one-half to ten and one-half days on the diet, and then a slight decline became apparent. The TPNH:TPN ratio fell markedly after two or three days on the diet and remained close to unity thereafter. The decrease in this ratio was mainly due to the fall in TPNH concentration in these lenses (Table V).

Concentration of ATP (adenosine triphosphate). The results of the ATP assay are shown in Figure 13. In the control lenses the mean value of ATP was 52.14 micrograms per lens (range 42.50 to 57.50; significant difference ±5.22). After one and one-half days on the galactose diet, there was no change in the ATP level, but the concentration of high-energy phosphate rapidly decreased beyond this date, and after three and one-half days the level had

TABLE V. Concentration* of reduced and oxidized pyridine nucleotides in the lens of the control and galactose-fed rat

Days on Diet	Control				Galactose			
	TPNH	TPN	DPNH	DPN	TPNH	TPN	DPNH	DPN
2½	147.0	18.4	125	113.5	50.4	16.2	140.0	118.4
5½	113.0	31.0	93	97.5	35.7	25.6	100.3	114.0
7½	72.6	21.9	80	99.0	15.2	13.7	81.9	49.7
9½	Lost	Lost	Lost	Lost	54.2	45.6	146.2	115.5
10½	97.5	34.8	92	110.0	45.8	34.0	93.5	100.8
12½	213.7	33.0	170	141.3	10.6	20.4	57.8	90.0
14½	129.3	36.0	190	146.0	48.5	37.0	97.5	115.3

* The concentrations are expressed as micrograms per gram wet weight.

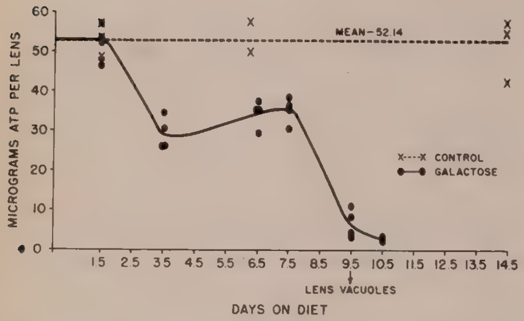


FIGURE 13. The level of ATP in the lenses from the normal and galactose-fed rat.

TABLE VI. DPNH and TPNH cytochrome c reductase in the control lens

Number of Lenses	Average Wet Weight Per Lens (Mg.)	Cytochrome c Reductase Activity	
		TPNH*	DPNH
4	19.10	14.40	6.91
4	19.20	17.75	14.40
4	19.02	19.72	14.79
4	19.60	19.72	14.79
Mean		17.90	12.72

* The enzyme activity is expressed as the change in extinction of 0.001 at 550 millimicrons per minute per lens at 24 C.

fallen to approximately 30 micrograms per lens. The ATP values remained at this level until seven and one-half days and then declined rapidly to 6.88 micrograms per lens at nine and one-half days, and after ten and one-half days on the galactose diet there was practically no measureable amount of ATP remaining (2 to 3 micrograms per lens).

Assays for pyridine nucleotide transhydrogenase, DPNH and TPNH lactic dehydrogenase and DPNH and TPNH cytochrome c reductase. The assay for pyridine nucleotide transhydrogenase activity failed to reveal any evidence of such a system within the lens. A total of 18 lenses pooled in groups of two, four, and six were employed in these experiments.

The results of the determinations of TPNH and DPNH lactic dehydrogenase revealed the presence of a very active DPNH lactic dehydrogenase in the lens. While TPNH lactic dehydrogenase also is present in the lens, its activity (at pH 7.4) is at least one-fifteenth that of DPNH lactic dehydrogenase.

Both TPNH and DPNH cytochrome c reductase are present in the rat lens. TPNH cytochrome c reductase was approximately 30 per cent more active than DPNH cytochrome c reductase (Table VI). There was no change in the activity of either TPNH or DPNH cytochrome c reductase in the lenses derived from the animals maintained on the galactose diet.

Protein and RNA (ribonucleic acid) metabolism

The level of soluble and insoluble lens protein. There was no change in the concentration of insoluble lens protein in the lenses derived from the galactose-fed rats as compared with the control lenses during the experimental period.

The concentration of soluble lens protein remained relatively constant in the experimental lens while this fraction increased by approximately 40 to 50 per cent in the control lens during this period of active lenticular development (Fig. 11). These results are essentially in agreement with the observations reported by Dische, Zelmenis, and Youlus.[106]

The level of total RNA. The results of the RNA determinations are shown in

TABLE VII. RNA levels in control lenses

Rat Lens	Days on Glucose Diet	Micrograms of RNA in Lens*
1A	1	50.00
1B	1	49.17
2A	3	45.00
2B	3	42.50
3A	6	67.50
3B	6	57.50
4A	10	37.50
4B	10	50.00

* Mean = 49.90. Significant difference ± 9.26.

TABLE VIII. RNA levels in galactose lenses

Rat Lens	Days on Galactose Diet	Micrograms of RNA in Lens*
1A	1	80.83
1B	1	74.17
2A	1	65.00
2B	1	50.00
3A	$3\frac{1}{2}$	45.00
3B	$3\frac{1}{2}$	Sample lost
4A	$3\frac{1}{2}$	25.00
4B	$3\frac{1}{2}$	25.83
5A	$5\frac{1}{2}$	55.83
5B	$5\frac{1}{2}$	51.58
6A	$5\frac{1}{2}$	Sample lost
6B	$5\frac{1}{2}$	Sample lost
7A	$6\frac{1}{2}$	40.00
7B	$6\frac{1}{2}$	47.50
8A	$6\frac{1}{2}$	51.67
8B	$6\frac{1}{2}$	55.83
9A	$9\frac{1}{2}$	50.00
9B	$9\frac{1}{2}$	55.00
10A	$9\frac{1}{2}$	51.67
10B	$9\frac{1}{2}$	Sample lost

* Mean = 51.56. Significant difference ±15.04.

Tables VII and VIII. There was no significant difference between the amount of RNA present in the control lenses (mean value 49.90 micrograms per lens; range 37.50 to 67.50) and the amount of RNA present in the lenses derived from the rats maintained on the high galactose diet. Although the lenses from one experimental animal sacrificed at three and one-half days showed a very low level of RNA (25 and 25.83 micrograms, respectively), the remaining RNA values were all in the same range as the RNA levels in the control group. There was no statistically significant difference between the mean RNA value in the experimental group (51.56 micrograms per lens; significant difference ± 9.26).

TABLE IX. The in vivo incorporation of C^{14} leucine, valine, and histidine into lens protein of the normal and galactose-fed rat; three-hour and twenty-four-hour study. The values are expressed as c.p.m. per mg. protein recovered in each planchet

Amino	—Control—		Galactose	
	3-hour	24-hour	3-hour	24-hour
Leucine	11.6	4.3	6.0	4.3
	10.9	. . .	8.3	. . .
Valine	10.6	4.4	6.7	1.5
	8.4	. . .	6.8	. . .
Histidine	9.3	7.2	7.2	2.8
	11.1	. . .	7.3	. . .

TABLE X. The in vivo, three-hour incorporation of C^{14} leucine, valine, and histidine into the soluble lens protein fraction from normal and galactose-fed rats. The values are expressed as c.p.m. per mg. protein recovered in each planchet*

Amino Acid	Control	Galactose
Leucine	14.09	7.35
	9.31	8.62
	11.91	7.67
	8.93	7.08
	12.04	8.21
	9.53	8.28
Mean	10.97	7.87
Significant difference	±1.91	+0.189
Valine	12.57	5.71
	12.90	6.57
	9.82	5.00
	8.36	7.61
	8.93	6.52
	10.38	8.15
Mean	10.49	6.59
Significant difference	±1.71	±1.08
Histidine	14.40	6.10
	13.34	8.79
	12.04	9.31
	12.70	6.82
	12.70	7.44
	12.60	8.18
Mean	12.96	7.77
Significant difference	±0.87	±1.11

* $P < 0.01$.

THE INCORPORATION OF C^{14} LEUCINE, VALINE, AND HISTIDINE INTO THE RNA-PROTEIN COMPLEX; IN VIVO AND IN VITRO EXPERIMENTS. The results of the in vivo experiment in which the degree of incorporation of C^{14} leucine, valine, and histidine into lens protein was studied are shown in Table IX. In the galactose-fed rat the three-hour incorporation of C^{14} leucine, valine, and histidine into the protein of the rat lens was approximately 30 per cent lower as compared

TABLE XI. The in vitro, three-hour incorporation of C^{14} leucine, valine, and histidine into lens protein of the normal and galactose-fed rat. The values are expressed as c.p.m. per mg. protein recovered in each planchet

Amino Acid	Control	Galactose
Leucine	21.4	26.3
	33.9	26.0
	25.2	23.3
Mean	26.8	25.2
Valine	16.6	15.2
	18.6	13.5
	17.3	15.3
Mean	17.5	14.6
Histidine	22.5	20.7
	22.5	22.8
	21.6	23.1
Mean	22.2	22.2

TABLE XII. The effect of Co++ on the in vitro, three-hour incorporation of C^{14} leucine, valine, and histidine into lens protein of the normal and galactose-fed rat. The values are expressed as c.p.m. per mg. protein recovered in each planchet

Amino Acid	Control	Galactose
Leucine	207.7	158.2
	199.3	191.6
	195.4	164.1
Mean	200.8	171.9
Valine	142.0	140.0
	138.1	153.6
	148.2	165.3
Mean	142.8	154.3
Histidine	595.5	635.1
	590.6	594.5
	672.6	749.2
Mean	622.9	659.6

TABLE XIII. Protein-RNA complex expressed as c.p.m. per mg. of protein

Species	Age	Leucine u-C^{14}	Valine u-C^{14}	Histidine u-C^{14}
Rat	5 to 6 weeks	540	440	1,300
Rabbit	6 months	474	506	1,322

with the control animal. However, there are insufficient data for a statistical analysis of the results expressed in Table IX, and these data can be interpreted only as indicating a decrease in the incorporation of C^{14} leucine, valine, and histidine into the protein of the lens from the galactose-fed animal.

The results of the twenty-four-hour studies show a considerable decline in the retained activity with the control and galactose-fed rat lenses. Although only single experiments were done with each amino acid, the data indicate that in the lenses from these two groups of rats there is no marked difference in the turnover of the three amino acids employed.

A more significant evaluation can be derived from Table X which shows the results obtained from a similar study in which the lens protein was separated into the soluble and insoluble fractions. In the galactose-fed rat, there was a significant decline in the incorporation of all three amino acids into the soluble lens protein fraction ($P < 0.01$ in each) as compared with the results obtained with the control animal. With respect to the insoluble lens protein fraction, there was no significant difference in the degree of incorporation of C^{14} leucine, valine, or histidine into this fraction from the control and galactose-fed rat lens.

The results of the in vitro studies are shown in Tables XI and XII. In the experiments in which the reaction mixture contained Mg++ rather than cobalt, there was no change in the in vitro incorporation of C^{14} leucine, valine, and histidine into the lens protein of the galactose-fed rat as compared with the control animal (Table XI).

Similarly, when Co++ replaced Mg++ in the reaction mixture, there was no change in the degree of incorporation of the three

TABLE XIV. Lens RNA and protein in concentration in various species

Species	Total RNA Micrograms per 100 Mg. Wet Weight	Soluble RNA Micrograms per 100 Mg. Wet Weight	Ratio of Total to Soluble RNA	Total Protein Mg. per 100 Mg. Wet Weight
Rat	285.0	26.50	10.8	34.5
Rabbit	147.3	24.00	6.1	33.5

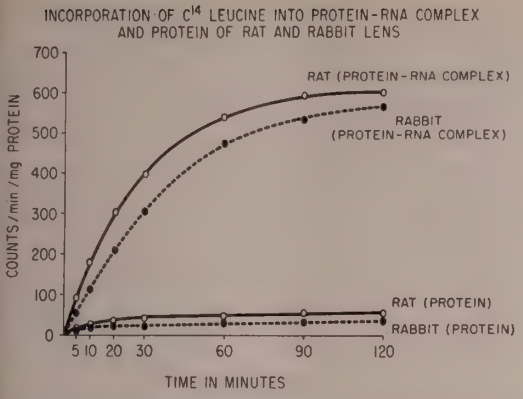


FIGURE 14. The incorporation of C^{14} leucine into the RNA-protein complex and the protein fraction of the rat and rabbit lens.

amino acids into the lens protein of the galactose-fed rats as compared with the control group (Table XII). The marked increase in the degree of amino acid incorporation effected by Co++ was evident in all three groups of lenses.

The RNA content and the amino acid-RNA incorporating system in the rabbit and rat lens, in vitro studies. The results of the in vitro incorporation of the three amino acids are shown in Table XIII, and Table XIV shows the total RNA and protein content and soluble ribonucleic acid content in these lenses.

Figure 14 represents the degree and rate of incorporation of C^{14} leucine into the ribonucleic acid-protein complex of the rabbit and rat lens and the amount of incorporation that actually occurred in the protein fraction only. The difference between these two values represents the degree and rate of incorporation of this amino acid into the ribonucleic acid fraction of these lenses. Well over 80 per cent of the amino acid is taken up by ribonucleic acid in both the rabbit and rat lens, and the maximum rate of incorporation occurs within the first hour.

The results of the chromatographic analysis of several samples of ribonucleic acid extracted at the completion of one hour's incubation revealed that 85 to 90 per cent of the activity was retained at the origin; the remaining activity was present in the spot which had the same RF value as a standard leucine sample run concurrently.

Comment

The results of the foregoing series of experiments indicate that carbohydrate and protein metabolism are the main areas affected in the development of experimental galactose cataract in the rat, while RNA metabolism remains virtually unimpaired. Furthermore, from the time sequence of the occurrence of these biochemical changes within such lenses, it would appear that the earliest changes observed in these experiments become manifest as an impairment of the metabolism of glucose by this organ, followed by a marked decrease of available high energy phosphate and consequently an inhibition of soluble protein synthesis. Since the normal lens is almost entirely dependent on glucose as its major source of energy, it is not surprising that the sequence of events which apparently occurs in the pathogenesis of galactose cataract should begin with a rapid and marked derangement of this metabolic pathway.

From experiments based on the $C_1:C_6$ ratio of $C^{14}O_2$ recovered from lenses incubated with glucose-1-C^{14} and glucose-6-C^{14}, it became apparent that the lens of the rabbit, cow, and cat contained an active hexose monophosphate shunt pathway of glucose oxidation.[72,105] This observation was confirmed also in the rat lens on the basis of similar experiments.[61,62,98,99] However, in view of the questions raised by Wood[92] regarding the validity of such an experimental technic as a basis for determining the presence and degree of activity of the hexose monophosphate shunt and the Embden-Meyerhoff pathway of glucose metabolism in various tissues and organs, an attempt was made in the studies on the rat lens to circumvent one of the possible sources of error. This was done by incubating these lenses for twenty-one hours compared with the usual two to four hours employed by other investigators. Furthermore, the resultant $C_1:C_6$ data, although indicative of the presence of an active shunt pathway in the rapidly developing rat lens, should not be considered as conclusive evidence. Thus, other experiments were performed which consisted of determining the degree of activity of G-6-P dehydrogenase and 6-PG dehydrogenase in this organ.

The high level of activity subsequently found in the lens of the young rat served as corroboratory evidence favoring the presence of an active shunt in this organ. Similarly, the TPNH:TPN ratio in such lenses was approximately 4.5 to 1, while the DPNH:DPN ratio was near unity. A high level of TPNH also should be indicative of an active hexose monophosphate shunt since the first two steps in the combustion of glucose by this pathway leads to the formation of a considerable amount of TPNH.

From these results, it is probably safe to assume that the normal rapidly developing lens of the young rat (twenty-eight to thirty-two days of age) contains an active direct oxidative pathway of glucose metabolism. The degree of importance that can be assigned to this pathway in such an organ has not as yet been definitely established. However, it is probably valid to assume an important role for this pathway in the lens of the young rat in view of the following observations:

1. One specific and marked effect of a cataractogenic galactose diet on the rapidly growing lens of the young rat is the rapid and severe impairment of the hexose monophosphate shunt in this organ as evidenced by the sharp and concurrent decrease in both the $C_1:C_6$ and TPNH:TPN ratios and the associated specific inhibition of the enzyme G-6-P dehydrogenase.

2. The activity of the hexose monophosphate shunt apparently decreases as the rat ages as indicated by the decline in the $C_1:C_6$ and TPNH:TPN ratios in the lens of the eighty-five to one hundred-day-old rat.[61,62]

3. The effectiveness of a cataractogenic galactose diet is related directly to the age of the rat.[60-62] As the animal grows older the lens apparently becomes increasingly more resistant to the deleterious action of this sugar as evidenced by the increasing length of time required for cataract formation. In such lenses the inhibition of G-6-P dehydrogenase becomes evident at about the same time that it occurs in the young lens (two to three days), but it takes many more weeks for lenticular changes to become apparent.

The foregoing observations thus tend to corroborate the assumption that the hexose monophosphate shunt plays a relatively important role in the metabolic economy of the young and rapidly developing lens of the post-weanling rat.

When such an animal is placed on the cataractogenic galactose diet, galactose-1-phosphate accumulates to at least a tenfold excess within the lens.[42] A rapid and marked inhibition of G-6-P dehydrogenase has been shown to develop both in vitro and in vivo (Figs. 9 and 12, Table III); the in vitro inhibition becomes manifest after two and one-half to three days on the diet. There is a concurrent sharp decline in the $C_1:C_6$ ratio, and this fall is due to a marked decrease in the recovery of $C^{14}O_2$ from glucose-1-C^{14}; the recovery of $C^{14}O_2$ from glucose-6-C^{14} remains relatively unchanged. Furthermore, there is no significant difference in lactate production by these lenses as compared with control lenses,[66] and in vitro experiments with rabbit lenses revealed no change in the ratio of lactate produced to carbohydrate consumed when a large excess of galactose was present in the incubation media.[107] A similar study by Pirie and Van Heyningen,[108] in which the formation of lactate by cattle lens was investigated, failed to reveal any change in lactate formation when galactose rather than glucose was present in the incubation media in high concentration.

If an inhibition of glucose metabolism is an important factor in the pathogenesis of experimental galactosemic cataract, then the evidence available at this time would indicate that the hexose monophosphate rather than the Embden-Meyerhoff pathway of glucose metabolism is the one that is most severely affected.

Since glucose oxidation is believed to provide the lens with its major source of energy, an important consequence of an inhibition of glucose metabolism in this organ should be reflected by a change in the concentration of high-energy phosphates. The results of assaying the level of ATP in the lens of the normal and galactose-fed rats were shown in Figure 13. The initial decrease in ATP concentration (in the experimental lenses) occurred at about the same time that the changes in the $C_1:C_6$ and TPNH:TPN ratios became evident. That is, with the apparent inhibition of the hexose monophosphate shunt there was a concurrent fall in ATP concentration of about 30 per cent. The secondary marked decline in the ATP level became manifest after the animals had been on the cataractogenic galactose diet for nine or ten days, at which time lenticular opacification was grossly evident, and a marked derangement in carbohydrate and protein metabolism already had occurred.

In an attempt to correlate the initial decline of ATP with the marked inhibition of the hexose monophosphate shunt in these lenses, the possibility that the reoxidation of the relatively large amounts of TPNH generated by the shunt could result in the production of a significant amount of ATP was investigated. The present conception of terminal respiration is the transport of electrons from DPNH → flavoprotein → cytochrome b → cytochromes a + a_3 → oxygen with the concomitant yield of a considerable amount of ATP. Kaplan *et al.*[109,110] also have presented evidence that the oxidation of TPNH could be mediated via the previously mentioned pathway through the intervention of transhydrogenase enzymes. Such a mechanism also would give rise to efficient phosphorylation. The presence of a pyridine transhydrogenase system in various tissues has been confirmed by several investigators.[111-114] Navazio, Ernster, and Ernster[115] also have suggested that TPNH-linked oxidations might be regulated by the DPN and TPN lactic dehydrogenases. They attempted to account for the oxidation of TPNH in rat liver by the action of lactic dehydrogenase, which eventually would transfer hydrogen from TPNH to DPN with the mediation of the specific substrate of LDH. The formed DPNH then could be oxidized via the mitochondrial cytochrome system with the production of ATP. Wenner[116] recently has reported on the oxidation of TPNH by ascites tumor cells, and he concluded that the principal electron acceptor for in vitro TPNH oxidation was pyruvate and that this reaction was catalyzed by LDH. These data were in agreement with the observation that ascites tumor cell homogenates contain very low activities of TPN cytochrome c reductase or transhydrogenase.[117] Another possible mechanism for the oxidation of TPNH is the enzyme TPN-cytochrome c reductase. Such an enzyme was first purified and characterized from pig liver mitochondria by Horecker[118] as a flavin adenine dinucleotide enzyme highly specific for TPNH. More recently, Lang and Nason[119] have described a TPN cytochrome c reductase from heart muscle which differed from Horecker's enzyme in that it could be extracted in soluble form from heart homogenates. These authors also suggested that this enzyme might function independently from the associated respiratory enzymes, such as DPN and succinate-cytochrome c reductase.

In the rat lens, two assay procedures for the transhydrogenase system failed to reveal the presence of such a mechanism for TPNH oxidation. While both DPN and TPN lactic dehydrogenase were found in this organ, the former was at least 15 times as active as TPNH-LDH. An active TPN-cytochrome c reductase also was found in the rat lens, and this enzyme was shown to be approximately 30 per cent more active than DPN-cytochrome c reductase in this organ (Table VI). Furthermore, the activity of all these enzymes present in the normal lens was not changed when the rat was placed on the cataractogenic galactose diet.

Thus the oxidation of the relatively large amounts of TPNH present in the lens of the young (postweanling) rat could be accounted for by the presence of the aforementioned enzyme systems. In view of the relative rates of activity of these enzymes it is not unreasonable to speculate that TPNH cytochrome c reductase would be of greater importance than TPNH lactic dehydrogenase in this organ. Since the rate of phosphogluconate decarboxylation is probably limited by the oxidation of TPNH the fact that the activity of these enzymes remains unchanged in the lens of the galactose-fed rat obviates the possibility that the observed inhibition of the hexose monophosphate shunt in this organ could be due to a decrease in available TPN.[117]

Although TPNH oxidation by the aforementioned enzyme systems had not as yet been shown to yield ATP directly, it is possible that such a mechanism may be operative in the rat lens. Thus the inhibition of the hexose monophosphate shunt in the galactosemic rat lens, which is paralleled by a decline in TPNH concentration, may be the basis for the concurrent initial decrease in the concentration of ATP (Fig. 13).

One consequence of a decrease in available high-energy phosphates in the lens is a marked impairment of protein synthesis. The observations of Dische, Zelmenis, and Youlus[106] that there is an apparent inhibition of soluble protein synthesis in the lens of the galactose-fed rat was confirmed in the in vivo studies on the concentration of soluble lens protein (Fig. 11) and on the degree of amino acid incorporation in such lenses (Tables IX through XI). The results of the in vitro experiments (Tables XI and XII) indicate that the incorporating system in the galactosemic lens is capable of proceeding at a rate and degree that is similar to that in the normal lens. Apparently galactose does not directly affect this system in the rat lens (at least for the first six to seven days on the diet), and the addition of exogenous ATP enables the lens to incorporate the amino acids at a normal rate.

Summary

These experiments have demonstrated that in the lens of the postweanling rat maintained on a cataractogenic galactose diet, galactose-1-phosphate, which accumulates to a tenfold excess in this organ, may act as or give rise to a specific inhibitor of the enzyme G-6-P dehydrogenase. Since this enzyme catalyzes the first step of glucose oxidation via the hexose monophosphate shunt, a concurrent and rapid decline in the activity of this pathway soon becomes apparent (as measured by the $C_1:C_6$ and TPNH:TPN ratios). Since the fall in the TPNH:TPN ratio is due to the decrease in TPNH concentration, this may be an important factor in accounting for the initial decline in available high-energy phosphates.

At present, the only known mechanisms in the lens which could reoxidize the relatively large amounts of TPNH in this organ are the TPNH cytochrome c reductase and TPNH lactic dehydrogenase systems. Although the oxidation of TPNH by these enzymes has not as yet been shown to yield ATP directly, it is possible that such a mechanism may be operative. Thus a fall in TPNH content could be paralleled by a fall in ATP concentration. It is further postulated that this decline in available ATP is to some extent responsible for the apparent inhibition of soluble protein synthesis which occurs in such lenses after the animal has been maintained on the cataractogenic galactose diet for from six to eight days.

The role that these biochemical changes play in the development of experimental galactose cataract is still a speculative one, but it is not unlikely that they may prove to be important factors in the pathogenesis of this condition.

Due to the difficulty of obtaining sufficient human lenses in a fresh state for adequate experimentation, as well as the extreme rarity with which one can obtain lenses from a human being suffering from congenital galactosemia, practically nothing is known about the biochemical changes which occur in such lenses. At present the only experimental evidence available is the observation that the enzyme galactose-1-phosphate uridyl transferase is lacking in the lens as well as the red blood cells and liver in such individuals. There is also some evidence that galactose-1-phosphate accumulates to a tenfold excess in the red blood cells of the galactosemic patient. Bearing in mind the dangers inherent in extrapolating experimental observations based on animal experimentation to human diseases, one may speculate that the biochemical changes observed in the experimental galactosemic rat lens also may occur to a varying degree in the lens of the human galactosemic patient.

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Discussion

HERBERT R. REITZ, M.D., *Buffalo, New York.* All of us have had the opportunity to read many fine papers by Dr. Lerman in various publications, especially the *Archives of Ophthalmology*, on the subject of galactosemia. It is a real pleasure to hear him present the subject so completely and so thoroughly. I think we all share in the good feeling that there is an ophthalmologist among us so conversant with basic science. This is such a lively subject of interest among pediatricians, internists, biochemists, geneticists, and ophthalmologists that I believe we shall look to Dr. Lerman for many years to come for the newest concepts.

The older reports are very interesting. The first reported case in 1908 correctly described the etiologic role of milk. However, the cirrhosis of the liver found at autopsy was ascribed to alcoholism since the baby had been fed a tablespoonful of cognac daily since birth. During the past ten years much has been learned about galactose metabolism. Still, as a clinician one reads published reports on changing attitudes toward cholesterol, for example, and one cannot help but be both intrigued and frustrated by the complexity of body reactions. I am informed that if one were able to eliminate cholesterol completely from the diet, our body would learn to produce it from other ingested foods.

The accumulation of galactose in the blood causes an accumulation of this sugar in the tissues and its loss through the urine, as well as a decrease in blood glucose. Galactose in the tissues may lead to cirrhosis of the liver, kidney failure with amino aciduria, and cataracts. The decrease of blood glucose is very serious since it can cause convulsions and finally even mental deficiency.

Much emphasis is being placed on the role of galactosemia as a genetic mechanism. Hugh-Jones, Manfield, and Brewer,[a] writing in the *Archives of Disease in Childhood* in 1960, feel that it is definitely transmitted by a Mendelian autosomal recessive gene. This is because of its frequent occurrence among siblings, equal distribution in both sexes, and the increased incidence of consanguinous matings among the parents of these children. For those interested there is a fine paper elaborating on the hereditary defects in galactose metabolism in man and microorganisms by Kalckar[b] of Baltimore in the December, 1960, *Federation Proceedings of the American Societies for Experimental Biology*.

The Children's Hospital of Buffalo has 4 reported cases, the first in 1952 and the last in 1959. The clinical signs and symptoms seemed to be quite uniform. In no case was the admission diagnosis correct, but in two or three days it was found that the blood and urine sugars were unfermentable. Galactosemia was then quickly diagnosed. All 4 cases appeared to do well except 1 child who was readmitted two more times because of failure to stay on the milk-free diet. Easily assimilated protein was the principle food in therapy. Cataracts were described in 2 of the cases. In 1 case the involvement was not great since the ocular fundi were described as normal. In the other, nuclear cataracts cleared almost entirely except for slight residue in the left eye.

The therapy is disarmingly simple.

I would like to refer you to a paper by Donnell, Bergren, and Cleland[c] published in 1960 in the *Pediatrics Clinics of North America*. Its illustrations show findings in 22 cases of galactosemia and show the galactose tolerance test. Normals and carriers are compared. It is noted that the galactose index is higher in parents and siblings.

Also presented is the intelligence quotient in galactosemic families, with a before and after picture—before treatment and after ten years on a galactose-free diet.

Since the morphology of the galactosemic cataract is variable and hence probably depends on the severity of the condition, one wonders whether we are failing to diagnose many mild cases of galactosemia. This paper seems to provide an impetus to study all patients with congenital cataracts and their relatives more thoroughly than I am sure is commonly done today.

[a] Hugh-Jones, K., Manfield, P. A., and Brewer, H. F.: Congenital thrombocytopenic purpura, Arch. Dis. Childhood **35:** 146 (Apr.) 1960.

[b] Kalckar, H. M.: Hereditary defects in galactose metabolism in man and microorganisms, Fed. Proc. **19:** 984 (Dec.) 1960.

[c] Donnell, G. N., Bergren, W. R., and Cleland, R. S.: Galactosemia, Pediat. Clin. North America **7:** 315 (May) 1960.

Acute Thrombosis of Large Arteries

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THE SUBJECT of acute thrombosis of the large arteries has been of interest to me because in my limited experience in vascular matters I am slowly beginning to learn that some of the concepts that we had in past years might possibly not be quite as valid as we had thought. I am not referring to our ideas of anatomy or even of pathogenesis but to the frequency and the natural history of the disease.

In exploring the history of acute thrombosis of the large arteries, I went through the last twenty years of the *Index Medicus* and the current periodicals and tried to get some idea as to the frequency of occurrence of thrombosis of the large arteries in the greater circulation to compare it with my own limited experience.

Interestingly enough, when I went back over Leriche's[1] famous monograph of fifteen years ago on arterial thrombosis, I was amused to discover that the distribution approximated what I thought to be the incidence of this condition and, roughly, it was similar to the material presented in the accompanying illustrations.

Sudden thrombotic occlusion of certain vital arteries is an understandable occurrence in terms of the factors generally associated with the pathogenesis of this process. An acute occlusion of a coronary, retinal, or cerebral artery is not a strange phenomenon since previous degenerative disease further narrowing the small lumen leaves a passageway liable to instant closure as a result of insult either in the wall of the vessel or outside it or due to changes in the normal clotting mechanisms of the blood. By contrast, a sudden closure of a large vessel in the greater circulation, either the aorta or one of its direct branches, is actually not as common and not as easily explained. To complicate an analysis further, experience indicates a distribution of sites of acute thrombosis that does not lend itself readily to the usual explanation.

First we should like to review the factors generally considered involved in the mechanism of arterial thrombosis and then to consider the actual sites of this occurrence in terms of our own experience and that of others.

Factors in mechanism of arterial thrombosis

First, an interruption of the continuity of the intima is of prime importance and is generally due to subintimal disease or to trauma of the entire vessel wall. A loss of continuity of the intima initiates the clotting mechanism at the site of erosion, the deposition of platelets, fibrin, and clot formation.

Second, a narrowing of the lumen of a vessel occurs either by encroachment due to a subintimal process or by a distortion of the lumen by outside pressure.

Third, the loss of elasticity of the vessel wall leads to functional distortion and eddy formation, with resultant increased stress on the weakened intima. Changes in the intraluminal pressure due to systemic hypertension and increased peripheral pressure are also manifest.

Fifth, changes in the clotting elements of the blood take place as the result of chronic disease or as part of the body response to a state of stress.

Currently it is felt that a great preponderance of nontraumatic arterial thrombosis is

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atherosclerotic in nature, and there is a fairly long chapter on Buerger's disease as a factor in arterial thrombosis in Leriche's book. The status of thromboangiitis is now in doubt as a pathologic entity. Whatever role syphilis played in the past is almost nonexistent now.

The other vascular diseases generally manifest themselves in the arteriolas and the capillary bed. Therefore, in our review of large vessel sites of thrombosis the pathogenesis will be found to be either atherosclerotic or traumatic.

Common sites of thrombosis

In Figure 1 we have marked the more common sites of thrombosis. Before discussing specific examples, I should like to offer my own point of view about the incidence of trouble in these particular areas.

Let us start first with thrombosis in the common and internal carotid artery. We know that the characteristic site here is the carotid bifurcation which is the most usual place for occlusive or occluding disease. I think the work of Charles Rob, M.D., of Rochester, is classical, and the whole concept could be considered to have been inititated by J. Ramsay Hunt, M.D., fifty years ago. But the actual incidence of occlusion of these large vessels, the common carotid and the internal carotid, is not easy to determine, and it will not be accurately determined until it becomes the habit of the pathologist when he opens the skull after a so-called cerebrovascular accident to do a dissection of the carotid vessels. It is my impression that despite all that is being done in surgery today and all that is being written about it, in many excellent institutions this dissection is still not performed.

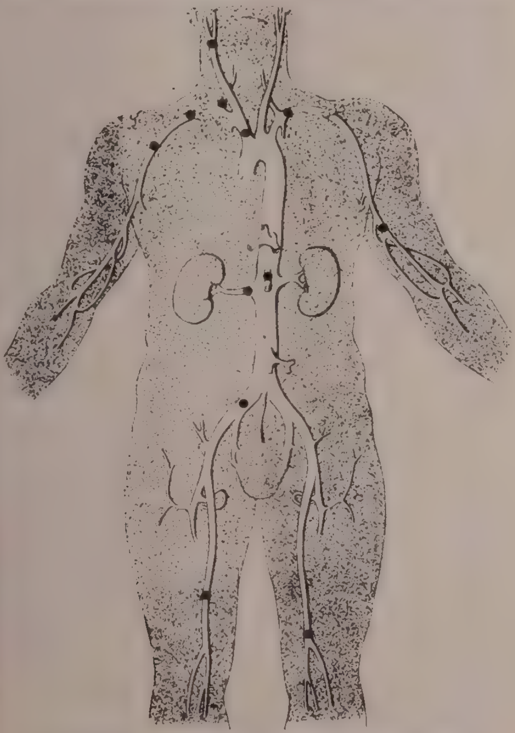
FIGURE 1. Common sites of thrombosis.

I therefore feel that the actual incidence of acute thrombotic occlusion at these sites and the entire picture of acute ischemia of the brain is probably not known. I personally suspect that acute thrombotic occlusion of the large vessel is as common as it is in many other sites which heretofore have been considered rather frequent areas for this manifestation. The vertebral vessel which has probably become infamous because it narrows the lumen, particularly at its origin from the subclavian, is included as one of these sites. I suspect by a parallel with vessels of similar diameter elsewhere that complete occlusions of the vertebral artery are probably considerably more common than acute occlusions in the carotid system.

There are rare cases of sudden acute thrombosis of the innominate artery. Acute

ACUTE OCCLUSION *of a coronary, retinal, or cerebral artery is not a strange phenomenon considering underlying degenerative disease. This narrows the small lumen and leaves a passageway liable to instant closure as a result of insult either in the wall of the vessel or outside it. Changes in the normal clotting mechanisms of the blood are an added element. On the other hand, sudden closure of a large vessel in the greater circulation, either the aorta or one of its direct branches is not as common and not as easily explained. Acute thrombosis results from thrombotic occlusion superimposed on existing disease. The importance of the stress phenomenon in acute thrombosis in relation to surgical judgment is emphasized.*

thrombosis of the subclavian artery is not common. It has been described in conjunction with the recognized cervical rib.

An occlusion of the subclavian artery under the clavicle has been described. I have 1 or 2 cases of this condition that I will describe later. As a matter of fact, the proponents of the narrow outlet theory between the clavicle and the first rib are suggesting that trauma is the cause of this thrombosis. In the brachial artery, as we shall see shortly and as Leriche commented, the most common cause of acute thrombosis is trauma.

As we go down the arterial tree, I think it can be stated with some assurance that acute thrombosis of the aorta is truly a rarity, and you have to go into the pediatric literature to find this condition described. It usually occurs in a normal aorta, and there the term "stress phenomenon" can be used properly. Acute thrombosis of the aorta was described accurately by Rothstein[2] thirty years ago in toxic infants at a time when dehydration and infection could not be controlled. Gross[3] reviewed the subject in 1945 in his thorough consideration of embolism and thrombosis in children. In the adult thrombosis of the aorta is a rarity, and the contrast between gradual thrombotic occlusion of the aorta and acute thrombosis is, of course, well known.

The visceral vessels are a law unto themselves. I think the anatomist must tell us the answer there. I strongly suspect that even with the encroachment on the lumina of such vessels as the renal, acute thrombosis is a rarity, and it is only in the more intensive cases of narrowing with changes in the blood that thrombosis occurs.

Thrombosis of the common iliac artery has been of interest to me because I think that it is something of a syndrome of its own. It seems to be a caliber of vessel approaching that seen in the extremities where acute thrombosis is more likely to occur; where it is due to its position and function, the results of acute thrombosis are not immediately lethal but are associated with a high morbidity and a high mortality.

I am sure that many readers will agree with me that femoral artery thrombosis between the bifurcation of the iliac and Hunter's canal is actually a rare occurrence when one considers how extensively diseased this area is, as a rule, in the sixth, seventh, and eighth decades of life. The differential between thrombosis and embolus, aside from the other important differential points, can be made generally if the site of the occlusion is in this area. As time goes on, I find the ruling out of thrombosis an easier and easier diagnostic matter.

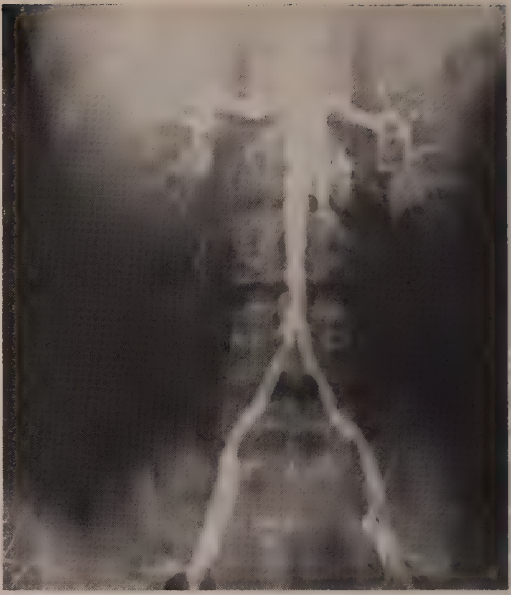

FIGURE 2. X-ray film of patient with atherosclerosis.

We all know about thrombosis in Hunter's canal. It is probably the most common site of thrombosis in a vessel of that caliber in the body. I do not think that acute thrombosis there is to be associated with the patient who comes to us with a severe ischemia, threatening impending and finally actual gangrene of the extremity. I think that the capacity of the collateral is so great that the first insult in the main channel does not lead to gangrene.

Finally, popliteal artery thrombosis is a very unfortunate occurrence from the point of view of morbidity, in contrast to the more common embolism of the popliteal artery which is a relatively benign condition. Popliteal artery thrombosis, which can occur in the absence of organic disease in the artery, is a condition that is not well taken care of by the body and is even less well taken care of by the surgeon.

NARROWING OF LUMEN. Figure 2 is an

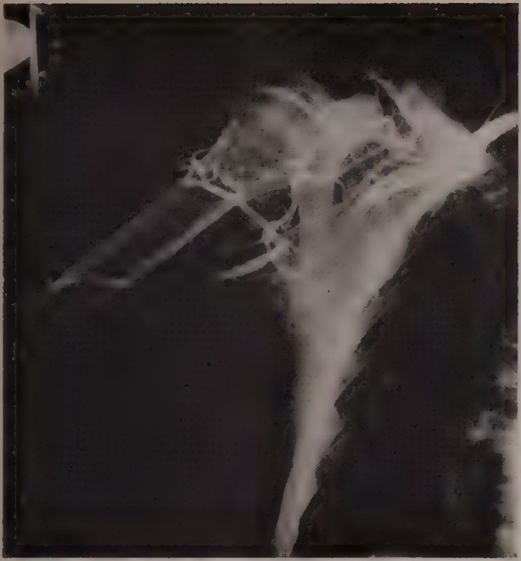

FIGURE 3. X-ray film of patient with acute thrombosis of subclavian artery.

x-ray film of a man who was unfortunate enough to have inherited a disposition to atherosclerosis. Since both renal arteries were pinched off by atheroma, he had good reason for his hypertension. Finally, it is a good demonstration of what happened to the left common carotid vessel. This is the type of disease in which acute occlusion does occur in the main branches coming off the aorta, and the predisposing cause, of course, is the narrowing of the lumen so that a small vessel is present and thrombosis can occur. This is the situation in which there is a collateral response from the body so that the extent of the disease seen at autopsy is not manifested by visceral and extremity symptoms, as one would expect, even if there is evidence of acute occlusion as one of the final steps.

Subclavian artery. Figure 3 shows an example of a subclavian artery in acute thrombosis in a male patient, initiated by trauma. This man had an unusual type of trauma. He worked in a shipyard with a percussion hammer which was used to knock bolts into a ship. The men worked in teams, and the patient's partner weighed 240 pounds. One man worked with this trip hammer against his right clavicle because he was right-handed, and the patient, smoking a cigaret, leaned against his back to steady him so that he would not move as the trip hammer punched a hole in the steel. He had a sudden acute occlusion which occurred between the subclavian artery and the first rib. After exploration, we discovered that the patient had managed to obliterate his peripheral vessels, and we put a graft in from the subclavian artery and tunneled it under the clavicle to an open area of the brachial artery, hoping to reverse the circulation. We accomplished this, and after about six months the patient kept on smoking and again experienced a thrombosis. It should be mentioned that in pictures that demonstrate the difference in color of the affected extremities one can see a return of pallor of the extremity following the thrombosis of the graft. Later we did a dorsal preganglionic sympathectomy, and this was 1 patient who responded very well.

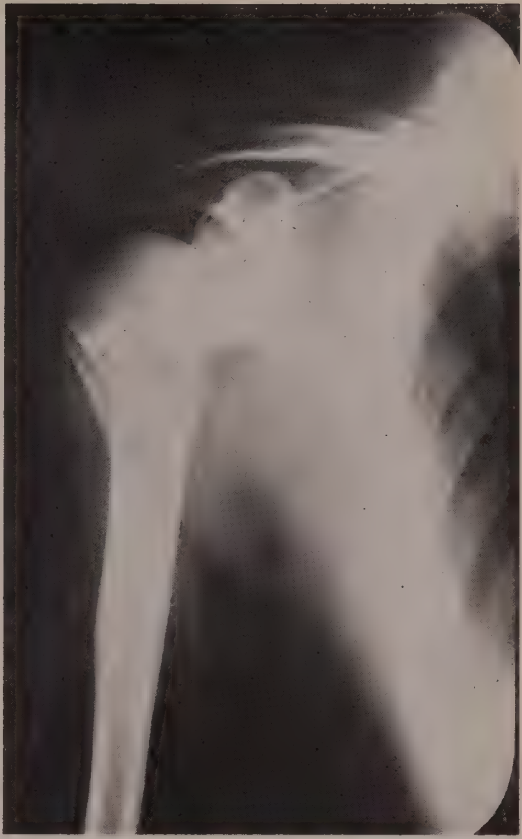

FIGURE 4. X-ray film of patient with involvement of lumen of axillary artery.

Brachial artery. As Leriche pointed out, trauma causes thrombosis in the bra-

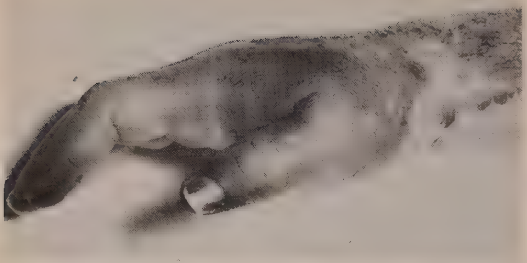

FIGURE 5. Amputated portion of arm.

chial artery. We have had cases in which with this fracture there was first the usual laceration which is associated with thrombosis in this vessel.

Axillary artery. Figure 4 shows the involvement of the lumen of the axillary artery. We managed to lever the kink over the displaced bone free, and, to our great surprise, the patency of this artery was restored, the spastic effect was released, and the patient's pulse became audible. I did not think that this would happen.

Mechanical-chemical trauma. A mixture of the mechanical and the chemical is a most serious type of trauma and one with which the surgeon is concerned. During catheterization in children and the utilization of contrast medium accidents have occurred, which result in such radical measures as the amputation of an elbow.

Another patient was a man in the throes of an unhappy emotional experience. Without knowing why, he went back to his childhood home and became acutely alcoholic. An injection of sparine was given, supposedly intravenously; unfortunately, it was injected into the radial artery, and an amputation was necessary. Ultimately, we did not lose any more of the arm than is seen in Figure 5.

I have recorded 2 other cases of accidental injection of a chemical into an artery, and this depicts a form of acute arterial thrombosis that is on the increase. It is most harrowing in its effects because what happens apparently is that the thrombosis extends against the flow of blood upstream and there is extensive necrosis.

In 2 other cases upper-arm amputations followed injections. One was the injection of Nembutal into what was supposedly the vein but proved to be the brachial artery. Of course, distally, there was thrombosis too. These chemicals, the drugs, and the solvents are most harrowing in their effects, and we are bound to see more of these unfortunate mishaps in the literature.

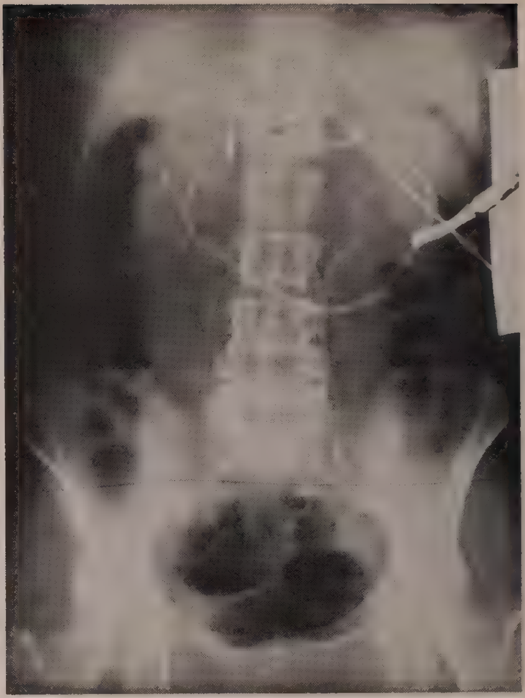

FIGURE 6. X-ray film of patient at operation, showing size of aorta.

Vessel size. The size of the vessel is one factor that I am convinced exists in a condition of thrombosis. I have had about 4 or 5 cases that tend to prove the point.

Aorta. A female patient was operated on, and in her case the aortal femoral bypasses worked very nicely. Her aorta ended in the renal arteries as terminal arteries, but the size of the aorta at operation was precisely what you would expect (Fig. 6). With difficulty we managed to use a dacron graft which was big even for this particular aorta.

The relationship of renal artery thrombosis to ascending aortic thrombosis is a mystery to me. I do not know how often it occurs. I do not know how valid are our ideas that the indication for operation in this case is the threat of involvement of the renal arteries. I know that on one occasion, performing the usual procedure, I

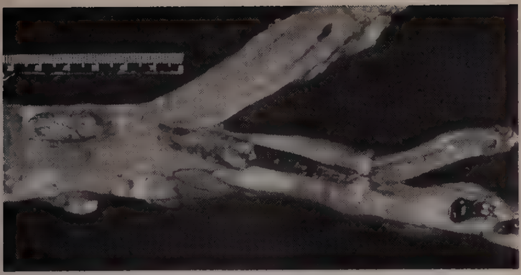

FIGURE 7. Acute thrombosis of common iliac artery superimposed on atherosclerotic disease.

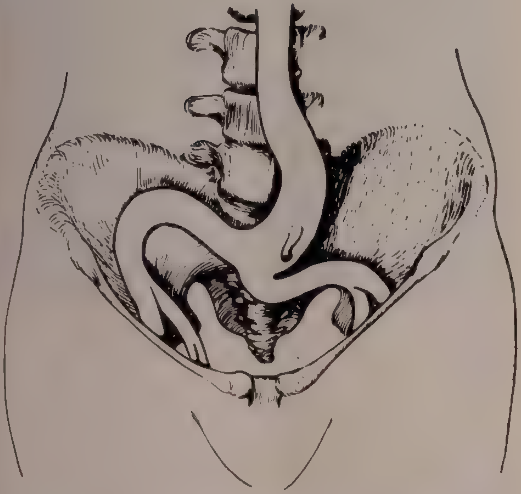

FIGURE 8. Acute thrombosis of large artery.

was guilty of thrombosing the renal artery with a too effective curettage.

Iliac artery. In the last two years I have seen 5 cases in which, following an operation or in conjunction with coronary artery thrombosis, an acute thrombotic occlusion (a condition that is uncommon in large vessels) has occurred in the common iliac artery which, of course, resulted in a loss of the extremity, and in 3 of the 5 instances death occurred due to the combination of this insult and the original lesion (Fig. 7). I suggest that this probably is the working of a true stress phenomenon. Under the stress of the operative procedure, whether it be cholecystectomy or gastrectomy, or under the stress of coincidental or immediately preceding disease, such as coronary artery thrombosis, these patients experience changes in the body chemistry that lead to this phenomenon in an already diseased person.

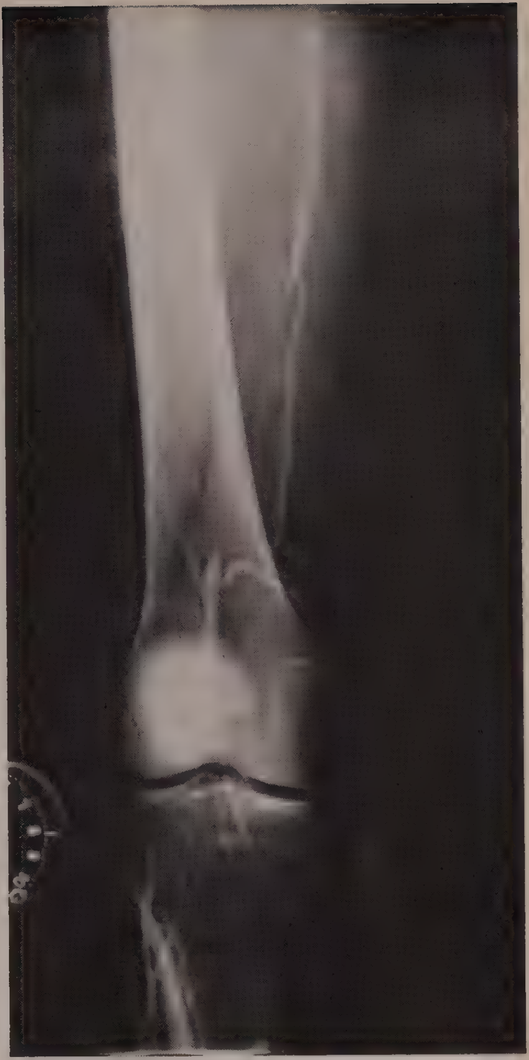

FIGURE 9. Acute arterial thrombosis of thigh.

I think the important thing to practice in stress phenomenon is conservatism. I was not conservative in 3 out of 5 cases, and I think I did the patients considerable harm. I think the thing to try to do is to get your patient to survive the insult and settle for the amputation.

I think an important factor in the production of acute thrombosis in a common iliac artery, among other things, is the distortion of the vessel characteristic of atherosclerotic disease. In 4 of the 5 cases the lesion was on the left, and of all the cases 1 case was not autopsied. One case was autopsied and 3 cases were operated on. I think that the distortion that was disclosed, which was well known to all of us, was an important factor in the acute thrombosis at this site. Together with all the other factors, there was an acute turn, and as the elongated aorta twisted, there was a looped common iliac artery on the right which is commonly mistaken for an aneurysm because it is so easily felt. The thrombosis also occurs on this same side, and this is one type of acute thrombosis of a large artery that I think can be considered a stress phenomenon (Fig. 8). It is a condition that surgeons, undoubtedly, have seen and will see more of.

Hunter's canal. Finally, I should like to mention acute arterial thrombosis in the most common of all sites, Hunter's canal, which is in the thigh (Fig. 9).

In the first place, I strongly suspect that since such a large proportion of our male population in the sixth and seventh decades of life walk lithely along without palpable pulses, they really have rather mild symptoms of thrombosis following the original interruption of the continuity of their femoral arteries. This condition may have been due to the gradual narrowing of the arteries, but certainly at some time there is an acute occlusion.

There are, of course, a fair percentage of patients who come to us with the first insult and who are in acute occlusion, and they have varying degrees of response, depending on the collateral and depending on what we do or do not do for them. But it seems to me that here again the ability of the collaterals as long as we do not interfere with them, is truly amazing. Without going into the subject of grafts, for treatment of this particular condition I merely suggest that the natural history of the first insult in the common area of this canal in the absence of previous insult is not one of tragedy or great morbidity.

Popliteal artery. One of my cases was a popliteal artery thrombosis in a young man of thirty years. A sympathectomy and blood flow studies were done. The collateral had been broken off. The patient did fairly well but suffered from claudication. Ten years after the occurrence, he has not had any other manifestation of ischemia. But it is a fact that popliteal artery thrombosis not only has a severe morbidity, but also there is little that we can do about it. Probably the best thing we can do is to perform a sympathectomy.

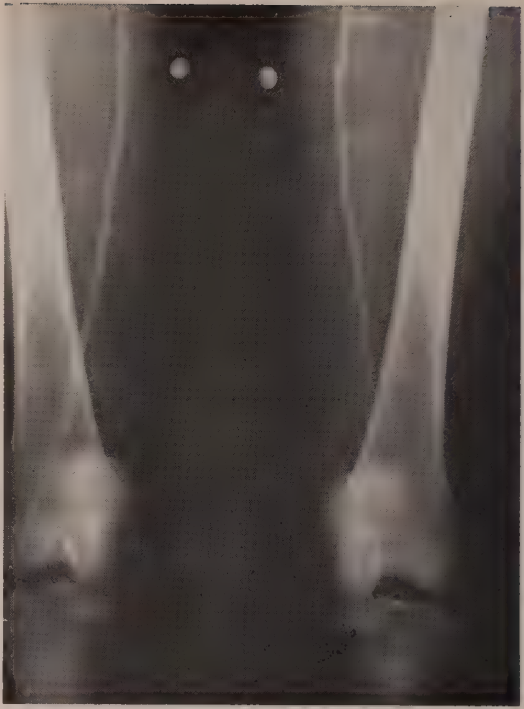
FIGURE 10. X-ray film of patient with popliteal thrombosis.

A young man at the age of twelve years first noticed that he was sensitive to cold. He never developed Raynaud's syndrome. He was much better at basketball indoors than at baseball, and he did very badly in football because he was cold all the time. When he was seventeen years of age, he was crossing a field one day near his home and he noticed that his right foot was numb. The numbness became worse and despite a year in bed with various conservative measures, the numbness and severe claudication persisted.

After a sympathectomy was done, the patient was turned over and the popliteal artery was explored. It was a normal-looking artery, except that it was completely occluded with a fairly well-organized thrombus. A large piece of the artery was cut out and sent to the pathologist. We were all set for a real diagnosis of thromboangiitis obliterans, but the section showed an artery that was indistinguishable from a perfectly normal vessel (Fig. 10). You can draw your own conclusions. Although I grant you that the vessel is not quite normal on the right side and that the patient may have patches that we would call atherosclerotic disease, I am not satisfied that we know exactly why this thrombosis took place. But it adds more fuel to the fire of fear in regard to popliteal artery thrombosis. This is a serious condition.

Comment

The whole point of this report is simply this, that it is my belief that we are almost ready to write an equation for an acute thrombosis of the artery. We are not all very talented mathematically, but the factors involved in acute thrombosis of an artery are pretty well known, and the only difficulty in writing the equation would be the weight given to all the factors. We would have no trouble in having the factors on each side of the equation identified.

I suggest that acute thrombosis of the larger vessels of the greater circulation is in itself a comparatively rare disease. I think we must agree that what we call acute thrombosis is an acute thrombotic occlusion superimposed on an existing disease.

We must recognize the importance of the stress phenomenon with which Selye's name is so closely associated, but which was so beautifully described by Cannon and Gray[4] in the early part of this century. We have to realize that acute thrombosis of a large vessel can occur as a result of systemic disease elsewhere.

Finally, I would like to suggest that the surgeon who is called in to examine a lower extremity that is massively ischemic and in which, on the physical signs, he would like to make a diagnosis of acute common iliac artery occlusion, should be wary of a stress situation. He should beware of an unrecognized impending or slowly progressing occult arterial condition going on elsewhere, and he should recognize that this patient can in the next few hours develop a coronary thrombosis or a cerebral hemorrhage.

A differential diagnosis, of course, is dissecting aneurysm. If the patient is unfortunate enough to have episodes of arrhythmia, you have to make a differential diagnosis of embolism. But where you can with reasonable certainty diagnose a common iliac artery thrombotic occlusion, I recommend conservatism.[5]

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Mortality rate of newborn infants

The first twenty-four hours of life are the most dangerous, according to a special report on the newborn infant by *Patterns of Disease*, a monthly Parke, Davis & Company publication for physicians. During the first day the mortality rate is 10.3 per 1,000 live births, dropping to 2.8 at one day, 1.8 the second day, and 0.9 the third day.

The mortality rate of infants under twenty-eight days of age is greater than the rate for infants twenty-eight days to eleven months of age according to records for the ten-year period from 1951 to 1960.

Fate of Circulating Hemoglobin in Man

Preliminary Clinical Study*

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THE CLASSIC experimental studies of Whipple's group, using dogs, showed that intravenously administered hemoglobin is retained in the body provided the plasma level remains low.[1-4] Very large "doses" of hemoglobin will be partially retained and partially excreted by the kidneys. Therefore, it was possible to postulate a "renal threshold" mechanism. Only when this threshold was exceeded did hemoglobin appear in the urine. Moreover, the renal threshold appeared to be a function of the glomeruli, since mercury poisoning fails to affect it. The renal threshold concept later was studied in human beings and found to be somewhat variable but not in contradiction with Whipple's "glomerular threshold" theory.[5]

A new concept was developed recently from the stimulating observations of French investigators who found a specific plasma protein having a great avidity for hemoglobin. This glycoprotein, called "haptoglobin" by Polonovski and Jayle,[6] forms a complex with hemoglobin, the biochemical sequelae of which have been recognized only recently.[7] Whereas "free" hemoglobin apparently is eliminated rapidly via the kidney, the hemoglobin-haptoglobin complex remains within the body. Apparently the hemovascular portion of the reticuloendothelial system is responsible for the clearance of this complex and for its catabolism.[8] These recent discoveries shed new light on the earlier work of Whipple and his associates, and the concept of a "glomerular threshold" has been replaced by that of the hemoglobin-binding ability of the plasma haptoglobin.

During the past few years haptoglobin has been studied extensively, both chemically and clinically. Recently Nyman[7] published a comprehensive review of the diagnostic significance and clinical interpretation of this complex. Little is known, however, about the mechanism involved in the clearance of the circulating hemoglobin-haptoglobin complex from the body. Only a few sketchy observations and rather contradictory reports could be found in the available literature.

Laurell and Nyman[9] injected hemoglobin into 2 subjects. In both there was a steady, parallel decrease of hemoglobin and haptoglobin, indicating that the two are removed not only simultaneously but also as a complex. In 1 subject the hemoglobin removal occurred at the rate of 13 mg. per 100 ml. of plasma per hour; in the other the rate fluctuated around 11 mg. per 100 ml. of plasma per hour. Garby and Noyes,[10] on the other hand, employing Fe^{59}-tagged hemoglobin, described a concentration-dependent removal rate. They maintain that a constant rate of elimination is found at high plasma hemoglobin levels, but at low levels the transfer rate of the hemoglobin-haptoglobin complex is an exponential function. Lathem and Worley,[11] however, found both linear and exponential removal rates occurring with equal frequency in 13 healthy subjects injected with a rather large dose (14 to 16 Gm.) of hemoglobin.

Since the pertinent literature on blood clearance of the hemoglobin-haptoglobin

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complex is inconclusive, extensive studies were undertaken in this laboratory in an attempt to ascertain the factors involved. The findings obtained in rats, using I^{131}-tagged hemoglobin, have been reported elsewhere.[12] The preliminary results when the study was repeated in human beings are reported here.

Technic

A number 18 needle with a three-way stopcock was inserted into a cubital vein, a blood aliquot was collected, and the plasma haptoglobin content was determined according to the method of Jayle as outlined by Nyman.[7] Another sample of blood (10 ml.) was collected in a sterile vial containing 20 ml. of sterile, pyrogen-free distilled water. When hemolysis was completed, this solution was adjusted to isotonicity with a 50 per cent dextrose solution.

The estimated blood volume of the subject and his plasma haptoglobin level were used in computing the maximum "dose" of hemoglobin to be injected, which was kept to at least 5 to 10 mg. per 100 ml. of plasma below his hemoglobin-binding capacity. The calculated amount of hemoglobin then was injected, and the level of hemoglobinemia was determined in eight subsequent blood samples collected at ten-minute intervals. The needle was kept open between the collection of samples by the slow infusion of a physiologic saline solution. The plasma hemoglobin level was determined by a modification of the method of Fielding and Langley.[13] The possible presence and degree of peroxidase inhibitors were established previously for each subject's plasma by adding, in vitro, three different graded amounts of hemoglobin and determining the peroxidase activity. The deviation from the expected values indicated the degree of inhibition.

Findings

A group of 20 apparently healthy volunteers between the ages of twenty-five and seventy-five years was tested in this pilot study. The quantity of hemoglobin injected varied between 176 and 386 mg.

A STUDY TO DETERMINE *the factors involved in blood clearance of the hemoglobin-haptoglobin complex was undertaken on 20 apparently healthy volunteers. Between 176 and 386 mg. of hemoglobin were injected, the dose being kept to at least 5 to 10 mg. per 100 ml. of plasma below the hemoglobin-binding capacity of the individual. The plasma hemoglobin level decreased uniformly at a constant rate as a linear function of time. The clearance rates were within a remarkably narrow range, suggesting a clearing mechanism of low efficiency independent of the plasma hemoglobin level and indicating saturation of a metabolic pathway. The average clearance rate was found to be 122 mg. of hemoglobin per hour, but if the combined weights of the entire hemoglobin-haptoglobin complex are calculated the correct value is more than doubled. In open-heart surgery the patient's plasma haptoglobin level is a limiting factor on the amount of hemoglobin hemolysis the pump can be permitted to cause. In pilot studies the rate of removal of the circulating plasma hemoglobin has been shown to be increased in several diseases involving the reticuloendothelial system.*

In this relatively small series the plasma hemoglobin level decreased uniformly at a constant rate as a linear function of time. The clearance rates obtained also were within a remarkably narrow range, suggesting a biologic constant (Table I). No sex difference was apparent immediately. In the older-age group there seemed to be a slight tendency toward faster removal, but because of the small number of observations no significance can be attached to this pending the results of a larger study now under way.

Comment

PHYSIOLOGIC IMPLICATIONS. In this series a uniformly constant rate of clearance of hemoglobin from the blood was noted. This would indicate a clearing mechanism independent of the plasma hemoglobin level. It also would indicate the saturation of a metabolic pathway; apparently the actual rate reflects the maximal efficiency of a limiting step. One may speculate that this limiting step represents the intracellular splitting of hemoglobin into smaller components. Nevertheless, whatever this

TABLE I. Clearance rate of intravenously injected hemoglobin

Age	Sex	Weight (Pounds)	Hemoglobin Dose (Mg.)	Hbc.*
26	F	100	176	3.2
31	F	125	303	4.0
33	M	133	267	4.3
35	M	190	386	5.25
35	F	128	195	4.95
36	M	136	255	3.1
39	F	135	238	4.5
39	F	135	250	4.3
40	M	196	282	4.8
41	F	140	242	5.75
48	F	145	295	4.0
48	M	180	258	4.0
52	F	118	199	3.0
54	F	115	231	5.8
54	M	175	332	3.45
62	M	186	290	4.3
62	F	145	242	3.3
68	M	178	199	5.6
74	F	132	226	4.5
78	F	120	218	4.5

* Hbc. is the clearance rate expressed as the decrease of milligrams of hemoglobin per 100 ml. of plasma per hour.

limitation may be, it is apparent that the capacity of the system responsible for removing the circulating hemoglobin-haptoglobin complex is of a low order of magnitude. Our findings do not necessarily conflict with those of Garby and Noyes,[10] since it is conceivable that we did not follow the hemoglobin clearance long enough to find the exponential removal rate at low plasma hemoglobin levels. Our interest was focused on the initial removal rate during the first eighty minutes. Within this period the pathway apparently was overloaded; therefore, the removal rate was independent of the plasma level.

From the data obtained the maximum total capacity of the hemoglobin-removing mechanism may be estimated. In healthy subjects, the average clearance rate was found to be 4.3 mg. of hemoglobin per 100 ml. of plasma per hour. Considering the average total plasma volume to be 2,600 ml., the hourly net clearance of hemoglobin would be approximately 112 mg. However, if the combined weights of the entire hemoglobin-haptoglobin complex are calculated, the correct value would be more than doubled. In other words, about 230 mg. of protein are removed in one hour by the clearing mechanism.

With these values in mind one may speculate further. The normal daily hemoglobin turnover due to the renewal of aged erythrocytes is 6 or 7 Gm. The average daily plasma hemoglobin-clearing capacity as found in our studies is about 2.7 Gm. If the liberation of hemoglobin due to physiologic red-cell lysis occurred entirely within the vascular tree, the hemoglobin release would exceed the capacity of the normal clearing mechanism. Although several of our observations differ from those reported by Garby and Noyes,[10] we certainly agree that the intravascular lysis of old red cells and the subsequent clearance of hemoglobin-haptoglobin complex "is a relatively unimportant pathway in normal hemoglobin metabolism and that a few red cells die intravascularly." The physiologic graveyard of aging erythrocytes must be in extravascular sites.

Our studies also indicate the need for further data on the efficiency of the various metabolic pathways in the human reticuloendothelial system, especially that of lipid macromolecules. By extrapolating the animal experimental data, one might be led to believe that the reticuloendothelial system's phagocytic capacity and its post-phagocytic recovery are too fast and nearly inexhaustible properties of this system.[14] However, the fallacy of such a conclusion is demonstrated clearly in the present report. In human beings the reticuloendothelial capacity as tested with hemoglobin loadings is rather small. Strikingly different results were noted in laboratory animals; for example, we found that the hemoglobin-clearing mechanism is many times more efficient in the rat than in the human being.[12]

CLINICAL IMPLICATIONS. The clearance of plasma hemoglobin presents a problem in open-heart surgery. The traumatic effect of the oxygenator-pump system results in erythrocyte lysis and hemoglobin liberation. It is important, therefore, to bear in mind that the hemoglobin liberated will combine with haptoglobin and that the patient's plasma haptoglobin level is a limiting factor on the amount of hemolysis the pump can be permitted to cause.

Also in progress are pilot studies on

patients with various diseases to determine the role played by the reticuloendothelial system. Of particular interest are the findings on 5 patients with different types of carcinoma. The rate of removal of the circulating plasma hemoglobin was found to be greatly accelerated in 4 of these patients. This is in complete agreement with an investigation on the response of the reticuloendothelial system of rats and mice following tumor grafting.[15] During the early phase of tumor growth a maximal reticuloendothelial hyperplasia was found, whereas with progressive deterioration of the tumor-bearing host, a return to normal or even below normal level occurred.

The fifth patient had an advanced prostatic carcinoma with multiple metastases. The clearance rate was 5.6 mg. per hour. The patient died fourteen days after the clearance study was made.

Further investigations on a larger group of patients are needed to ascertain whether the reticuloendothelial hyperplasia found associated with malignant growths is a cause or a consequence of the lesion. Additional studies are now being undertaken in an effort to determine whether the accelerated rate of hemoglobin clearance in the presence of malignant growths is due to proliferation of the reticuloendothelial system or to an increased efficiency of the system without proliferation. In certain other diseases which probably involve the reticuloendothelial system, such as Hodgkin's disease, accelerated clearance was found, while in some patients with a disease probably not affecting the reticuloendothelial system, such as osteoarthritis and duodenal ulcer, the plasma hemoglobin clearance rate was unchanged. In a case of chronic glomerulonephritis and mild uremia, a clearance rate of 1 mg. per 100 ml. per hour was found. Much further work is needed before these clinical findings can be interpreted properly.

Summary

Hemoglobin, when injected intravenously, forms a complex with plasma haptoglobin. This combination results in a selective transport and clearance different from the renal pathway of "free" hemoglobin. In healthy human beings the mechanism which removes this circulating hemoglobin-haptoglobin complex (presumably the reticuloendothelial system) is of low efficiency and can easily become overloaded. The pilot study reported indicates a total clearance rate of approximately 110 mg. of hemoglobin complex per hour. The rate seems to be increased in several diseases involving the reticuloendothelial system.

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The Common Cold and Humidity Imbalance

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STATISTICS GATHERED by the Common Cold Foundation show that the cold costs the nation $5 billion annually in lost wages, production, and medical expenses, which makes it the most costly ailment in the United States.[1] John R. Steelman, M.D., Director of the United States Conciliation Services, is the authority for the statement that "Industry has lost five times as much time by the common cold as by strikes." The work force loss is over 150 million days per year in the United States. In this country the North Central States have the highest cold incidence. The United States Public Health Service reports 500 million colds annually. On any given winter day 20 million people are suffering from colds.

The report of the American Institute for Public Opinion "Gallup Poll," as of February 3, 1956, for the week of January 12, which had low temperatures, was $28^1/_2$ million persons with colds which the Institute considered the normal prevalence and much below the record of 35 million with colds during January, 1953. In a study of respiratory infections in families, Dingle *et al.* found in 1949,[2] and this was confirmed by a later study,[3] that the common respiratory diseases composed the largest group of illnesses (94.85 per cent of the total) of which the common cold accounted for about 60 per cent or about 40 per cent of all illnesses. Their findings were: "The annual and seasonal occurrence of illnesses, plotted by months showed the total illness rate was high during the first quarter, fell abruptly during April and May and remained low until September when a sharp rise occurred which persisted throughout the remainder of the year."

Other surveys of minor respiratory illnesses, particularly the common cold, generally have demonstrated three or four winter peaks between the months of September and May, the usual months of the heating season in temperate climates.

Causes

More theories and old wives' tales have been advanced as to the cause of the common cold than is the case with any other disease. Seneca, 41 A.D., points out the worthlessness of these theories as well as one could do today with this passage: "The man who has always had glazed windows to shield him from a draught, whose feet have been kept warm by hot applications renewed from time to time, whose dining halls have been tempered by hot air passing beneath the floor and circulating round the walls—this man will run great risk if he is brushed by a gentle breeze." Few new principles have been developed since ancient times, and a cure for the common cold seems as far away as ever.

Since 1946, large numbers of volunteers have submitted to extensive investigations at the Common Cold Research Unit in Salisbury, England. Much information was obtained at this center by Andrewes[4] concerning the transmission of colds from man to man by means of an exciting agent which can be filtered out of the nasal secretions of a person with an active cold. He found, however, that only 50 per cent of the volunteers developed experimental colds after nasal washings from patients with natural colds were instilled into their nasal passages. It also was found that some of the Salisbury volunteers showed no symptoms themselves but were capable of infecting others. Colds, apparently, can be transmitted by "immune" carriers to susceptible persons. It is thought that the cold-producing agent usually is spread from person to person by airborne droplets, but attempts at causing contact infection under carefully controlled conditions, surprisingly enough, failed.

The science of virology dates from 1892 when Iwanowski found the agent responsible for the tobacco-mosaic disease. It was not, however, until 1935 that Wendell M. Stanley, M.D., was able to isolate the tobacco virus in the form of a crystalline material. Using similar methods it soon was possible to isolate over a dozen viruses in highly purified, and in some instances, crystalline form including many of the cold-producing group. On the basis of numerous experiments it is believed that colds are caused by a large number of viruses, some of which have been cultivated, most of which have not. The fact that the virus does not disappear during the summer months is explained as being due to latent virus harbored by the nasal mucosa during this period which later, under favorable circumstances, multiply and produce a cold. However, efforts at developing a vaccine against the common cold have met with serious obstacles because the makeup of the virus appears to change from year to year. As a result, Christopher H. Andrewes, M.D., director of the Research Council's Common Cold Unit in England, after years of labor in this field predicts that the cold will "always be with us." Dr. Andrewes reports that early results of immunologic tests at the English Unit are "quite disappointing."[5]

Prevention

Although a direct approach to the conquest of the common cold is not possible at present, there is ample evidence that along with temperature control the regulation of the humidity of the living quarters will go a long way toward creating an indoor climate much less favorable for the activity of the cold-inciting agent. It is significant that coincidental with the institution of furnace heat in the fall, patients complain of smarting and burning in the pharynx, and the usual seasonal infections begin to make their appearance. These are popularly attributed to the inclement weather, but the actual cause of the coughs and colds is a dry nose and throat caused by artificial heating. An examination of the nose and throat of these individuals will show the characteristic dry spots, incriminating evidence against the low humidity. The irritations of the nose and throat usually will persist until the air in the individual's apartment, especially the sleeping quarters, is properly humidified. Among the many sins committed in the name of air conditioning, the worst offenses are those against humidity.

EFFORTS AT DEVELOPING *a vaccine against the common cold have met with serious obstacles because the makeup of the virus appears to change from year to year. A dry nose and throat caused by artificial heating creates an indoor climate favorable to the cold-inciting agent. Dry nasal mucus is an excellent culture for the infective agent. Adequate moisture is necessary also for the proper function of the cilia, pharynx, larynx, trachea, and lungs. During the heating season the best method of prevention of colds is maintenance of a proper balance of humidity by means of such devices as a mechanical humidifier. In summer, regulation of the humidity in air-conditioning is necessary to prevent summer colds.*

A relative humidity of about 45 per cent is generally regarded as optimal. By relative humidity is meant the vapor content expressed as a fraction or percentage of the concentration required to saturate the air at a given temperature. Cold air can hold less moisture than warm air. The absolute humidity of air is the percentage by weight of water vapor in the composition of the air at a given temperature. It was understood as early as 1886 that the air reaches the larynx practically saturated. This places a great work load on the nasal passages. The quantity of water required to saturate the inspired air in the course of twenty-four hours varies with the temperature and the state of saturation of the atmospheric air. According to Proetz,[6] the human adult under ordinary conditions requires approximately 500 cu. feet of air in twenty-four hours, and the daily intake of dry air at 37 C. requires about 680 cc. for saturation. Nevertheless, the nose has been shown to secrete about a liter (1,000 cc.) in twenty-four hours, the balance being applied to the cleansing process and eventually swallowed.

Mechanism

The lining of the upper respiratory tract is equipped with cilia, hairlike structures of microscopic size with a wavelike motility, which carry a blanket of mucus with which they are covered toward the posterior pharynx where it is swallowed. The cilia thus constitute a veritable conveyor belt for ridding the nasal passages of dust and other irritating foreign matter which they filter from the air. The nasal mucus, which has a 97 per cent water content, is more viscous than mucus elsewhere in the body, and even slight drying increases the viscosity enough to interfere with the work of the cilia. The restriction or absence of moisture, even for a matter of minutes, may destroy the cilia which then must be regenerated. In the meantime there is a piling up and thickening of the mucous blanket due to a lack of ciliary action. In this gelatinous state the mucus affords an excellent culture medium where the infective agent can flourish and is able to penetrate the lining membrane, with the resultant respiratory infection.

The wiping action of the palate which completes the cleansing process at the pharyngeal end of the respiratory tract likewise depends on the proper amount of moisture covering the opposing surfaces of the soft palate and the posterior pharyngeal wall. The saliva is not sufficient since it evaporates quickly. Not only does a person suffering from a dry throat have some difficulty in swallowing, but also he has a constant desire to do so, partly because of throat irritation but also because of the accumulation of dried mucus beyond the reach of the swallowing mechanism.

Below the level of the throat is the larynx which, if improperly moistened is first burdened with dried secretions which cause constant clearing of the throat. Later the lining membrane of the larynx becomes thickened, because of the irritation of the inspissated mucus, with chronic hoarseness and after a period of time a possible predisposition to a cancerous growth of the larynx.

Below the larynx, the trachea, under the conditions of insufficient atmospheric humidity, is likewise unable to rid itself of the dust-laden mucus which accumulates on its surface. The irritation from the presence of this material results in violent coughing. At first this occurs only on arising, in conjunction with abundant expectoration, but later it will occur at intervals throughout the day as well. This condition is most frequent at the end of the winter after the respiratory system has been subjected to furnace heat for months with a consequent prolonged drying of the respiratory mucous membranes and superimposed inflammatory reaction to such drying. It often is seen in the old and infirm.

The proper humidification of the inspired air is extremely important to the proper function of the lungs. The lining membrane of the alveoli of the lungs is a delicate structure whose walls are only a single cell in thickness and must be protected from drying and injury. In fact, the essential function of respiration, the exchange of carbon dioxide and oxygen, requires a moist surface.

Comment

In winter the absolute humidity of the atmosphere will be much less than the absolute humidity on a summer day, even though the relative humidity remains the same. This is so because the water saturation point of air is a function of temperature. The cold winter air, already low in moisture, is brought indoors and heated with the result that the relative humidity is reduced still further, usually down to 10 or 15 per cent. Opening the window for a part of the winter day to let the moisture in does not solve the problem even when there is plenty of snow and rain and moisture, because cold air can hold only a small amount of moisture, while the heated indoor air can hold a large amount of moisture. If the moisture is not supplied to the heated air, it will absorb moisture from the mucous film which lines the respiratory mucous membranes. When one considers that even the Sahara Desert averages 23 per cent humidity, it appears quite evident how important a problem humidity imbalance can become.

The respiratory system is unable to compensate for the dryness of heated air, and it becomes necessary to add moisture to the air for comfort and health.

Summer colds and similar respiratory difficulties often are thought to be caused by air conditioning. Here again most of the difficulty is due to improperly regulated humidity. The relative humidity of outdoor summer air is high in many areas. The relative humidity becomes even higher when the air is drawn indoors and chilled. Under these circumstances perspiration does not evaporate readily from the skin, and one experiences the usual symptoms following chilling, with an awareness of damp, clammy cold. It becomes necessary to reduce the relative humidity to 45 per cent because at this point the evaporation of perspiration can take place. Indeed, because of the cooling effect on the skin brought about by the evaporation of perspiration, there is less reduction of room temperature necessary for the same sensation of coolness. It is quite evident that successful air conditioning depends as much on relative humidity as on temperature. Indeed, perhaps more so, since one can dress in accordance with the temperature, but there is no such protection against improper humidity.

During the heating season proper humidity should be maintained. Contrivances depending on evaporation, such as open pans, are incapable of supplying even a small fraction of the needed moisture. Steam vapor, preferably divided into fine droplets by a mechanical humidifier, must be added to the air. An apparatus that can perform this function is on the market at present. In colder climates it is necessary to install double glass sash to prevent the loss of moisture through condensation on cold windows, or this loss of moisture must be compensated for.

Summary

The common cold has been with us for as long as man can remember. It has been and continues to be the greatest single cause of illness. Colds are a constant drain on the economy of a nation both in terms of medical expenses and lost wages and production. Once started, any upper respiratory infection tends to produce edema, increase secretion, and further reduce the ciliary activity of the nasal mucous membrane. Under these conditions the abnormally dry air becomes an additional aggravating factor.

In spite of the remarkable progress made in medicine in conquering most other diseases, there is as yet no cure for the common cold. A virus etiology has been established, but an effective vaccine cannot be obtained because of the large number of viruses capable of producing colds, each having the ability to "mutate" or change its characteristics, resulting in an infinite variety of strains producing their own types of disease. Prevention at present is our nearest approach to a cure. The most important preventive measure would appear to be the proper regulation of the humidity, especially during the heating season with its distressing drying of the air in living quarters, especially the sleeping quarters, and the prevention of an environment favorable to the cold-inciting agent. It is of importance to note here that the chemobiotics are of no value against the cold virus. Once it takes hold the virus causes lowered resistance and prepares the ground for the secondary bacterial invaders and complications that may follow.

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Interlobar Pleural Effusion in Congestive Heart Failure

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IN 1928,[1] STEWART reported a case of chronic congestive heart failure in which a loculated pleural effusion occurred on the right side in the horizontal fissure. The patient was admitted three times in congestive heart failure, and with each bout of failure the shadow reappeared and, after treatment for failure, disappeared. On the fourth and last admission for heart failure, the shadow again reappeared, and the patient died. A postmortem examination disclosed complete obliteration of the right pleural cavity with the exception of a small space between the upper and middle lobes (horizontal fissure), which was filled with fluid. This original description established the clinical profile for the condition, which has come to be known by the various names of interlobar pleural effusion, loculated pleural effusion, vanishing tumor, and phantom tumor.

During the period of 1928 through 1956, a total of 45 additional cases were reported in the literature.[1−28] An additional case was reported by Sanghvi in 1958,[29] in which chronic malaria with severe anemia and congestive heart failure was the background for a loculated paramediastinal effusion. This case was of additional interest because the absence of pleural symphysis was demonstrated by successful artificial pneumothorax three months after the disappearance of the loculated effusion. The relatively small number of total cases which have been reported since 1928 would suggest that this condition is rare, but this may be more apparent than real, considering that congestive heart failure is a very common situation. It might indicate also that neither radiologists nor internists are as familiar with the situation as they might be, as illustrated by the fact that patients with interlobar pleural effusion are often admitted with a diagnosis of lung tumor. The following 3 cases are reported by the author and illustrate some of the important features of this condition.

Case reports

CASE 1. A sixty-four-year-old housewife was admitted to the Albany Hospital on August 7, 1955. Her illness had begun approximately six months before admission, with dyspnea and fatigue on exertion which gradually increased. She had complained also of nervousness and insomnia, suggesting the probability of paroxysmal nocturnal dyspnea. Roentgenograms, which were taken prior to admission, disclosed the presence of opacities in the right lung field, which raised the suspicion of tumor, and admission to the hospital was arranged for evaluation. Her past history indicated growing pains in childhood and empyema at age six, which was drained through thoracotomy incision. Hypertension had been present for approximately twenty-five years, but no symptoms referable to this were described. A heart murmur had been heard about one year before.

A physical examination revealed: temperature 99.2 F., pulse 90 and regular, respirations 22, weight 132 pounds, and blood pressure 196/80. The patient was well developed and nourished but appeared somewhat ill. There was no lymphadenopathy in the cervical or supraclavicular regions. The thyroid was not enlarged, and the trachea was in the midline. The neck veins were distended in the upright position. The heart was enlarged to the left, with the point of maximal impulse slightly beyond the midclavicular line. The apical impulse was diffuse and heaving. A Grade II harsh systolic murmur was audible in the second right interspace, near the sternal border, and was transmitted into the carotid arteries. A

Grade II to III diastolic murmur was audible to the right of the sternum, in the second interspace and also was transmitted along the left sternal border. The lung fields disclosed no abnormality of percussion or auscultation. A diastolic gallop was audible near the apex. The liver was enlarged 2 fingerbreadths below the costal margin. The spleen was not felt. There was no dependent edema. The venous pressure was 210 mm. of saline. The circulation time was 10 seconds arm to lung and 22 seconds arm to tongue. The electrocardiogram was abnormal, displaying the pattern of left heart strain.

An x-ray film of the chest, which was taken on August 8, 1955, disclosed enlargement of the heart, primarily due to left ventricular hypertrophy (Fig. 1). There was moderate widening and tortuosity of the thoracic aorta, with calcification in the aortic arch. The posteroanterior and right lateral films disclosed the presence of a fairly well circumscribed density in the upper portion of the right lung which, on the lateral view, was seen to lie in the upper end of the long fissure. The short or transverse fissure apparently was normal. Tissue which was obtained at bronchoscopy disclosed an inflamed bronchial wall without evidence of tuberculosis or tumor. A cytologic examination of bronchial secretions revealed no malignant cells. It was felt that the lesion represented encapsulated pleural effusion secondary to congestive heart failure. The patient was treated with sodium restriction, mercurial diuretics, and digitalis, with good diuretic response. A repeat chest x-ray film on August 16, 1955, disclosed that the encapsulated effusion had been completely absorbed (Fig. 1). The final diagnosis was rheumatic heart disease with aortic stenosis and incompetence, left ventricular hypertrophy, and congestive heart failure with encapsulated interlobar pleural effusion.

CASE 2. A seventy-six-year-old male was admitted to the Albany Hospital on June 25, 1960, for evaluation of a lung tumor which had been disclosed on a routine fluoroscopic examination. His illness had begun approximately two years before admission, with acute myocardial infarction, for which he was treated in another hospital. That episode had been complicated by right-sided pneumonia and congestive heart failure. Following recovery from the infarction and its complications, he was maintained on a low-salt diet, digitalis, and oral diuretics. Hypertension had preceded the attack for many years. At the time, the opacities in the lung field had been noted, and there was no other overt evidence of visceral congestion.

On physical examination, there was no cyanosis, dyspnea, or orthopnea. The blood pressure was 210/100. The thyroid was not enlarged. The trachea was in the midline. The neck veins were not distended in the upright position. The lung fields were normal to percussion and auscultation. The heart was slightly enlarged, with the point of maximum impulse slightly beyond the midclavicular line. The rhythm was regular, the rate was 80 per minute, and a gallop was not heard. There was a Grade II systolic murmur in the mitral area, transmitted into the axilla. The abdomen disclosed no enlargement of the liver or spleen. The genitalia were normal. A rectal examination showed normal findings. There was no dependent edema. Laboratory data showed that urinalysis, blood count, fasting blood sugar, blood urea nitrogen, alkaline phosphatase, serum protein, serum bilirubin, and transaminase were within normal limits. An electrocardiogram displayed the pattern of old anterior wall infarction and digitalis effect. A teleoroentgenogram taken on June 26, 1960, disclosed enlargement of the heart (Fig. 2). There were two, irregularly large, rounded densities in the region of the horizontal fissure on the right. There were two similar, but smaller, linear densities in the region of the right oblique fissure. These were interpreted by the radiologist as interlobar effusions. The patient was treated with salt restriction, digitalis, and mercurial diuretics. A repeat chest film on June 29, 1960, three days after the first one, disclosed complete resolution of the effusions described previously (Fig. 2). The final diagnosis was arteriosclerotic heart disease, manifested by old myocardial infarction, and congestive heart failure, with interlobar pleural effusion.

THE SMALL NUMBER *of reported cases of interlobar pleural effusion in congestive heart failure would seem to indicate that the condition is rare, but the common occurrence of congestive heart failure itself and the fact that patients with interlobar pleural effusion are often admitted with a diagnosis of lung tumor suggest that the condition may be more frequent than is commonly thought. Three cases are reported, illustrating the etiologic cardiac diagnoses most commonly encountered: hypertension, coronary atherosclerosis, and rheumatic valvular disease. With appropriate therapy there is prompt disappearance of the loculated effusion. The majority of loculated effusions reported occurred on the right side with 75 per cent in the transverse fissure. Adhesive pleuritis is not a prerequisite to interlobar effusion. Careful fluoroscopic and roentgenographic examination of patients in congestive heart failure would probably uncover many more cases of interlobar pleural effusion.*

CASE 3. A seventy-two-year-old man was admitted to the Albany Hospital on July 30,

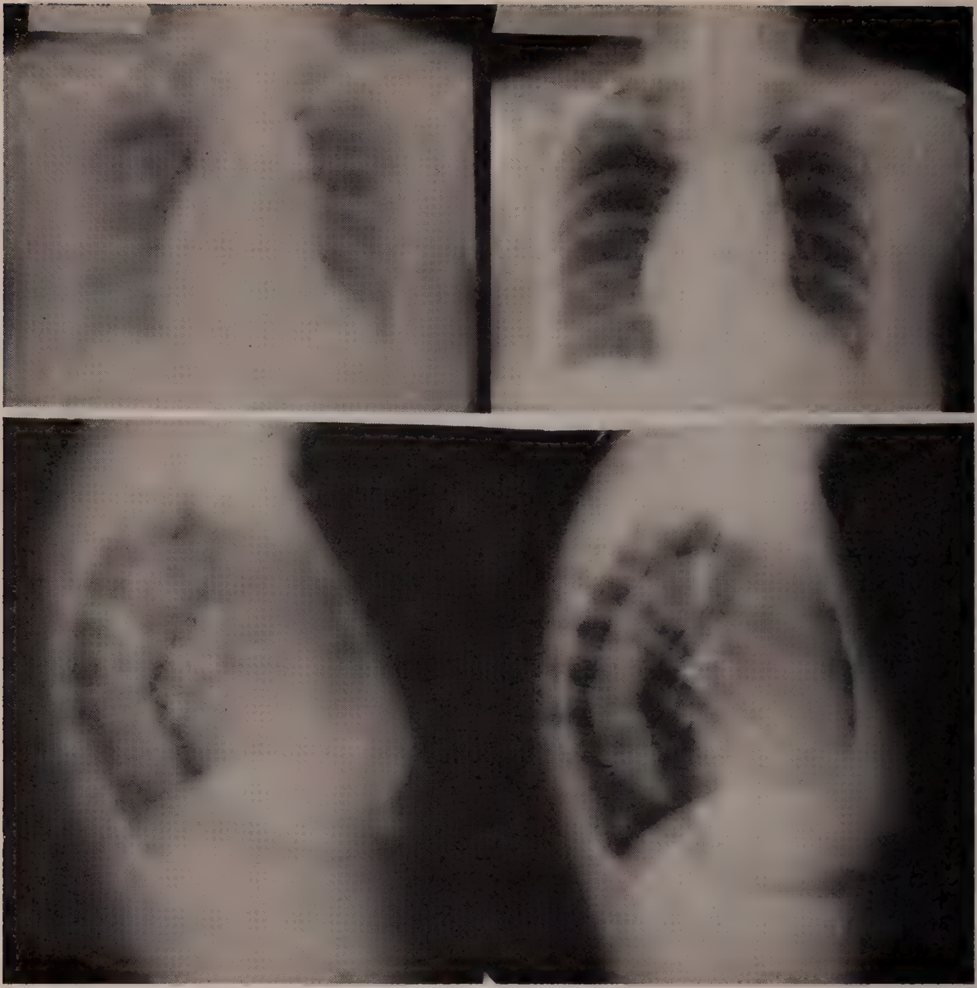

FIGURE 1. Case 1. Left panels show roentgenograms taken on August 8, 1955, right panels roentgenograms taken on August 16, 1955.

1960, with the presumptive diagnosis of bronchogenic carcinoma. In January, 1960, he had been treated for right-sided pneumonitis and pleuritis, from which he recovered, but with a residual nonproductive cough. In addition, he complained of increasing exertional dyspnea, occasional wheezing, and for a short while, prior to admission, paroxysmal dyspnea occurring during the night. Studies in another hospital had disclosed the presence of a shadow in the right lung, which raised the suspicion of a neoplasm. On the review of systems, the presence of diabetes mellitus was disclosed, which had been controlled with diet and insulin.

A physical examination revealed: temperature 98.4 F., pulse 94 and regular, respirations 20, weight 136 pounds, and blood pressure 200/120 mm. Hg. The patient was slightly dyspneic on phonation. The trachea was in the midline, and the thyroid was not enlarged. There were no nodes palpable in the supraclavicular or axillary regions. Moist rales were heard at both lung bases. The heart was not grossly enlarged, and no murmurs were audible, but a diastolic gallop was easily heard. The liver was not enlarged, and no dependent edema was noted. An electrocardiogram was abnormal, owing to the pattern of left heart strain, without infarction.

An x-ray film of the chest on August 1, 1960, indicated the presence of encapsulated pleural effusion on the right, in both the horizontal and oblique fissures (Fig. 3). Following treatment with digitalis and mercurial diuretics, there was brisk diuresis, with rapid disappearance of respiratory symptoms. Chest films, three days later, on August 4, 1960, indicated almost complete resolution of pleural effusions (Fig. 3). The final diagnosis was hypertensive heart disease, manifested by left ventricular hypertrophy,

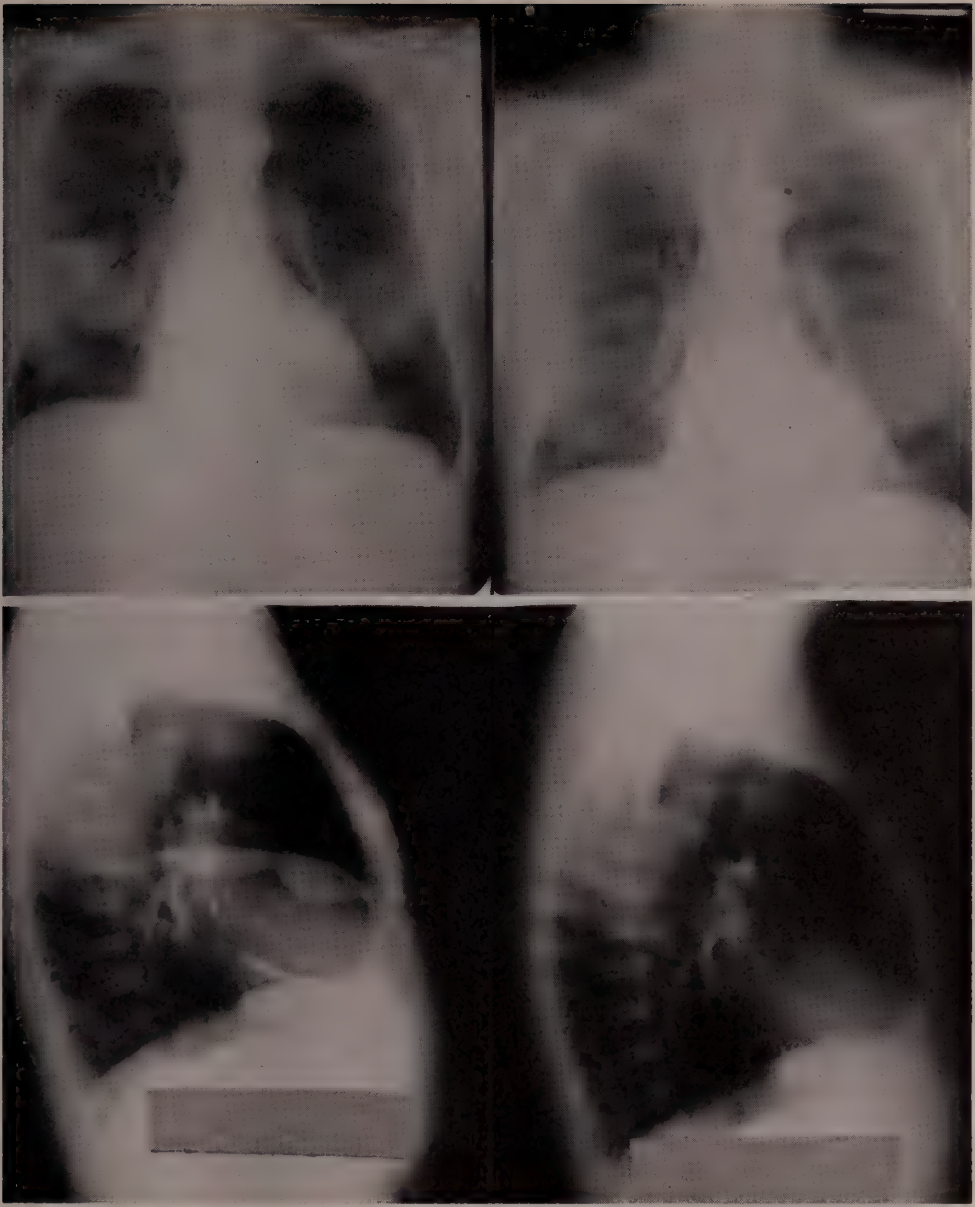

FIGURE 2. Case 2. Left panels show roentgenograms taken on June 26, 1960, right panels roentgenograms taken on June 29, 1960.

congestive heart failure, and encapsulated pleural effusions involving the right oblique and horizontal fissures.

Comment

The 3 cases reported by the author contain the main diagnostic features considered necessary for the diagnosis of interlobar effusion, or so-called phantom tumor or vanishing tumor of the lung. All 3 patients, as others in the literature, presented unequivocal clinical and laboratory evidence of congestive heart failure. These 3 cases also illustrate that the etiologic cardiac diagnoses which are most commonly encountered are hypertension, coronary atherosclerosis, and rheumatic valvular disease. These same 3 diagnoses are commonly

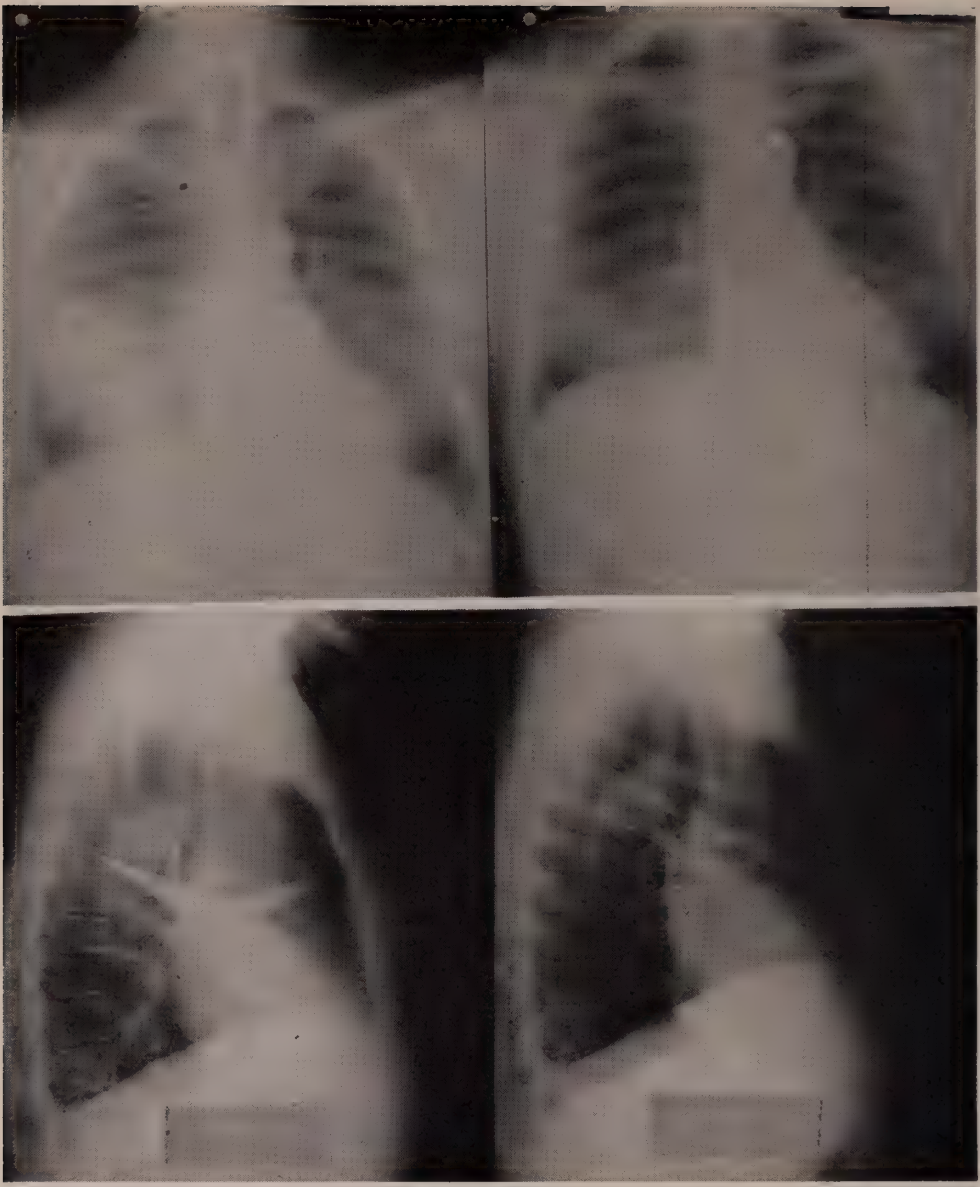

FIGURE 3. Case 3. Left panels show roentgenograms taken on August 1, 1960, right panels roentgenograms taken on August 4, 1960.

encountered in some of the larger series reported[12,19,25,27]; the diagnosis is rarely syphilitic and thyrotoxic heart disease.[19,27] With appropriate therapy the prompt disappearance of the loculated effusion is invariably observed, and this may occur in a relatively few days, as illustrated in Cases 2 and 3, in which only three days elapsed between the two comparative films. Apparently, however, effusion can collect again in the same place with each bout of failure, as illustrated in the case reported by Stewart[1] and that reported by Steele.[3] All loculated effusions were located on the right, with the exception of the 2 reported by Bedford and Lovibond.[12] In the majority of cases, over 75 per cent, the transverse or short fissure was involved.[27] The apparent reason is that loculated effusions located in the short or horizontal fissures are seen more readily on routine posteroanterior roentgenograms, because the x-rays pass through the longest diameter of the fluid mass. Effusions in the oblique or long fissure, on either left or right, are best seen on lateral views and may well be overlooked.

Great emphasis has been placed repeatedly on the presence of adhesive pleuritis as a prerequisite to the accumulation of interlobar effusion. In the author's cases, 2 had a history of pleuritis and 1 of empyema. Much more impressive is the autopsy evidence in the 8 cases reported in the literature[1,3,5,10,25,27,28] in which obliterative pleuritis was demonstrated. There is considerable evidence, however, that adhesive pleuritis is not necessary for the appearance of interlobar effusion. Stein and Schwedel[7] reported 7 cases, Bedford and Lovibond[12] 5 cases, and Newman[22] and Weiss[25] each 1 case, in which interlobar effusion was associated with free fluid in the main pleural cavity. In addition, Sanghvi[29] reported a case of loculated paramediastinal effusion, in which the absence of pleural symphysis was demonstrated by successful artificial pneumothorax three months after the disappearance of the loculated effusion. Therefore one must conclude that loculated and interlobar effusions can form either with or without symphysis or obliteration of the main pleural cavity.

The radiologic shadows have been described as being band-shaped, wedge-shaped, elliptic, round, or ovoid, depending on the amount of distention and the area of pleural surfaces involved.[7] In the differential diagnosis must be included all causes of interlobar effusion, such as pneumonia, tuberculosis, neoplasm, pulmonary infarction, empyema, abscess, cyst, and atelectasis of the right middle lobe. The dramatic disappearance of the shadow by diuresis would tend to exclude the preceding conditions.

The great preponderance of right-sided interlobar effusions, as compared with the left, is in keeping with the common concept that hydrothorax in congestive heart failure is also predominantly right-sided.[30] There is evidence in the literature, however, that in left ventricular failure hydrothorax may appear as frequently, if not more frequently, on the left. Bedford in 1939[11] described 154 cases of left heart failure, of which 38 presented hydrothorax, divided into 18 left-sided, 9 right-sided, and 11 bilateral. It is of interest that he also observed the appearance of hydrothorax after attacks of pulmonary edema, in the absence of other signs of systemic congestion. Also, in 3 of his cases there was an interlobar effusion on the right side. This is somewhat at variance with the generally accepted view that hydrothorax is usually associated with the clinical picture of failure of the right side of the heart. These differing views have been reconciled by some observers[12,31] with the assumption that pleural sacs have both systemic and pulmonary venous drainage. The parietal pleura is drained by the systemic and the visceral pleura, which lines the interlobar spaces, by the pulmonary venous systems. The parietal pleural veins are systemic and drain into the superior vena cava, or its tributaries, namely, the azygos veins, which are also connected with the tributaries of the inferior vena cava via the lumbar veins. The capillary network of the visceral pleura drains almost entirely to the pulmonary veins.[31] Therefore hydrothorax must be considered in relation to both systemic and pulmonary venous engorgement. It was pointed out by Bedford and Lovibond[12] that situations which presented symptoms of predominant failure in the right side of the heart, with massive edema and ascites, were not always associated with hydrothorax, as in tricuspid disease. They postulated that the only satisfactory explanation of hydrothorax without edema, excluding pulmonary infarction, was the presence of hypertension in the pulmonary venous circuit, due to failure of the left side of the heart, and it was concluded that hydrothorax was found in the same conditions as pulmonary edema, namely, failure of the left side of the heart. It follows, therefore, that increased pressure in the pulmonary venous system, brought about by failure of the left ventricle, is more likely to produce interlobar effusion than failure of the right ventricle, which would raise the systemic venous pressure and impair the drainage of fluid from the free pleural spaces. However, as might be expected, the coexistence of failure of both right and left sides of the heart is common in the cases reported.

In view of the fact that congestive heart failure is a very common clinical condition, the relatively small number of cases of interlobar effusion reported since 1928 would suggest that this is a rare finding. Indeed, some of the reports in the literature would support the view that it is extremely rare. For example, in some 250,000 photofluorograms, which were taken at the Philadelphia Tuberculosis and Health Association over a five-year-period, only 1 proved case of vanishing tumor was encountered.[19] Consider also that among 33,084 individuals who were x-rayed at the Philadelphia General Hospital in 1951, only 5 cases of interlobar effusion were recognized.[25] These, of course, were individuals who were ill enough to be admitted into the hospital. The same report stated that of 96,554 food handlers who were x-rayed, not one vanishing tumor was found, despite the fact that one of the observers was on the alert for this possibility. It was suggested, therefore, that the condition was very uncommon.

However, when vanishing tumor is considered within the framework of congestive heart failure and as a manifestation thereof, it is not so uncommon as suggested previously. From 1930 to 1934 Stein and Schwedel[7] found 18 patients with interlobar effusions, who had been on the wards of the Montefiore Hospital. It was pointed out that the patients were studied by combined fluoroscopic and roentgenographic technics which they felt were superior in taking films alone for the purpose of detecting effusions. One of the interesting features of their survey was the finding of linear shadows or scars, in the interlobar regions, of more than 75 per cent of several hundred cardiac patients who were examined. It is conceivable that many of these linear scars represented small accumulations of fluid. In 1939[11] Bedford described a series of 154 cases of left ventricular failure, of which 3 displayed interlobar effusion. Bedford and Lovibond[12] over a five-year period reviewed 356 consecutive cases of heart failure and 109 consecutive cases of heart failure, examined at postmortem, and found 11 cases of interlobar pleural effusion. Therefore, one cannot escape the conclusion that against the background of congestive heart failure, this condition is not uncommon. It also follows that more careful fluoroscopic and roentgenographic technics, as suggested by Stein and Schwedel,[7] would uncover many more cases. Lateral chest films will facilitate recognition and help to determine whether a fluid collection is in the plane of a fissure, as in the oblique fissure it tends to be hazier and less well demarcated than a collection in the transverse or horizontal fissure on the posteroanterior view. In the oblique fissure, fluid is spread out on a plane which is not parellel to the direction of the x-rays as they pass through the chest, and the shadow cast is less dense than that of fluid collected in the transverse fissure.

Summary

The author reports 3 additional cases of interlobar effusion in congestive heart failure and describes the clinical profile. The literature on the subject is reviewed from 1928. The 3 common etiologic forms of heart disease found were hypertension, coronary atherosclerosis, and rheumatic valvular disease. The preponderance of effusions on the right side, with over 75 per cent, in the horizontal or tranverse fissure, was noted, as was the rapid disappearance of the shadows with appropriate therapy. It was found further that adhesive pleuritis, obliterating the main pleural cavity, is not a prerequisite for the formation of transudative fluid in the interlobar pleural spaces. The rarity of the condition is more apparent than real, and it is suggested that careful fluoroscopic and roentgenographic examinations of patients in congestive heart failure will disclose that the condition is not uncommon.

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Survey of physicians on subject of adoption

Physicans, in general, believe that adoption should be handled by recognized adoption agencies, according to the results of a special survey conducted by *Patterns of Disease*, a Parke, Davis & Company publication for the medical profession.

The physicians think that the emotional stability of the adoptive parents and the stability of their marriage are more important considerations in adoption than are education, economic, or religious factors. Almost 70 per cent of the physicians think that couples forty to fifty years of age are too old to adopt a child less than one year old, although some physicians believe that this applies only to the upper-age range. According to the majority of the physicians, an adopted child should be told he is adopted, but opinions differ as to when the child should be told. Almost one half think that the child should be told before he is six years of age, but some of the physicians think that this depends on when the child asks and on his maturity.

Phenothiazine Tranquilizers in Anesthesia

Review, with Report on Fluphenazine

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A NEW CLASS of drugs that has entered the medical world in the last few years consists of the ataraxtics or the so-called tranquilizers. Their consumption has reached tremendous proportions, and more and more of them are being marketed constantly.[1] There are four major groups of tranquilizers: the Rauwolfias, diphenylmethane, glycerol, and the phenothiazines. The phenothiazines themselves constitute almost 50 per cent of all the tranquilizers on the market.[2]

As anesthesiologists, we must be familiar with these drugs for several reasons. Patients undergoing anesthesia may already be receiving these drugs, and their effect in conjunction with anesthetic agents is important for us to know. As with all drugs, some of the phenothiazines can be of greater value to us than others. Only by possessing a thorough knowledge of these drugs will we be able to choose and select those which will promote better anesthesia.

A chart has been prepared describing most of the phenothiazines popularly used today (Fig. 1). By noticing the chemical compositions of these derivatives, you will be able to deduce several interesting factors. For example, as the halogenation increases, there is a corresponding increase in the potency of the drug.[3] Notice that the derivatives in the fluoride column are more potent than those in the chloride column which, in turn, are stronger than those in the hydrogen column. Inclusion of the piperazine ring, which is found in many of the newer derivatives, increases potency while it is reputed to cause less hypotension and tachycardia.[3] The derivatives listed under the sulphur column (Fig. 1) are of less interest to us as anesthesiologists, since they can only be given orally and have minimal antiemetic effects.[4]

Indications for phenothiazines in anesthesia

In anesthesia the phenothiazines may be used for several purposes. Preoperative tranquilization of the overly apprehensive patient may be attained successfully with these drugs. However, your selection, generally speaking, should be made from among those derivatives incorporating the piperazine ring or promethazine hydrochloride.

The asthmatic patient can best be premedicated with promethazine hydrochloride, since it incorporates the basic antihistaminic structure in its side chain. It still retains its excellent sedative effect and has minimal effects on blood pressure and pulse. Since promethazine hydrochloride can accomplish sedation independently of barbiturates, it negates the possibility of initiating a barbiturate-caused asthmatic attack. A new derivative, propiomazine hydrochloride (Largon) has the same number 10 side chain as promethazine hydrochloride. Its antihistaminic effect is somewhat less than that of promethazine hydrochloride, however,[5] and

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it has not been as extensively tested.

One of the most valuable attributes of some of the phenothiazines is their antiemetic effect, as has been brought out by numerous and well-controlled studies.[6-8] This is not only an anesthetic problem, but wound dehiscence and acute electrolyte imbalance are the serious potential end results of severe nausea and vomiting. In an independent double-blind study we undertook with fluphenazine dihydrochloride this antiemetic effect was confirmed in more than 200 patients. We administered the drug intravenously only at the conclusion of surgery, so that in case of any operative or anesthetic complications it could be withheld completely. Of course the drug should be given judiciously and administered primarily to those patients in whom attacks of nausea and vomiting would invalidate the surgical benefits. Incidentally, when the phenothiazine is given in this connection, the dose administered is only a fraction of that given for tranquilization.[9]

Phenothiazines aid in producing hypothermia. Here chlorpromazine is the agent of choice. It was an original member of the Lytic Cocktail which, you will recall, was

IN ANESTHESIA *the phenothiazines may be used in preoperative tranquilization of the overly apprehensive patient, preoperative medication of the asthmatic patient to prevent a barbiturate-caused asthmatic attack, as an antiemetic, as an aid in producing hypothermia, in pediatric cardiac catheterization, in postpartum hypertension, and in combating singultus. The anesthetic requirement is only a fraction of that necessary for psychiatric use. Hypotension and tachycardia are possible complications, but the newer derivatives with the piperazine nucleus pose no real threat if used judiciously. Blood dyscrasias, jaundice, weight gain, and photosensitivity may be caused by the phenothiazines but only after prolonged dosage. Extrapyramidal symptoms do not occur when the drug is given while the patient is still subject to an anesthetic. A double-blind study on more than 200 females scheduled for dilation and curettage was undertaken to determine the effects of fluphenazine dihydrochloride given postoperatively. The results showed a 5 per cent incidence of retching and vomiting with fluphenazine and a 14 per cent incidence with the placebo. The mode of recovery was more serene when the drug was administered, and there was no noticeable difference in blood pressure and pulse.*

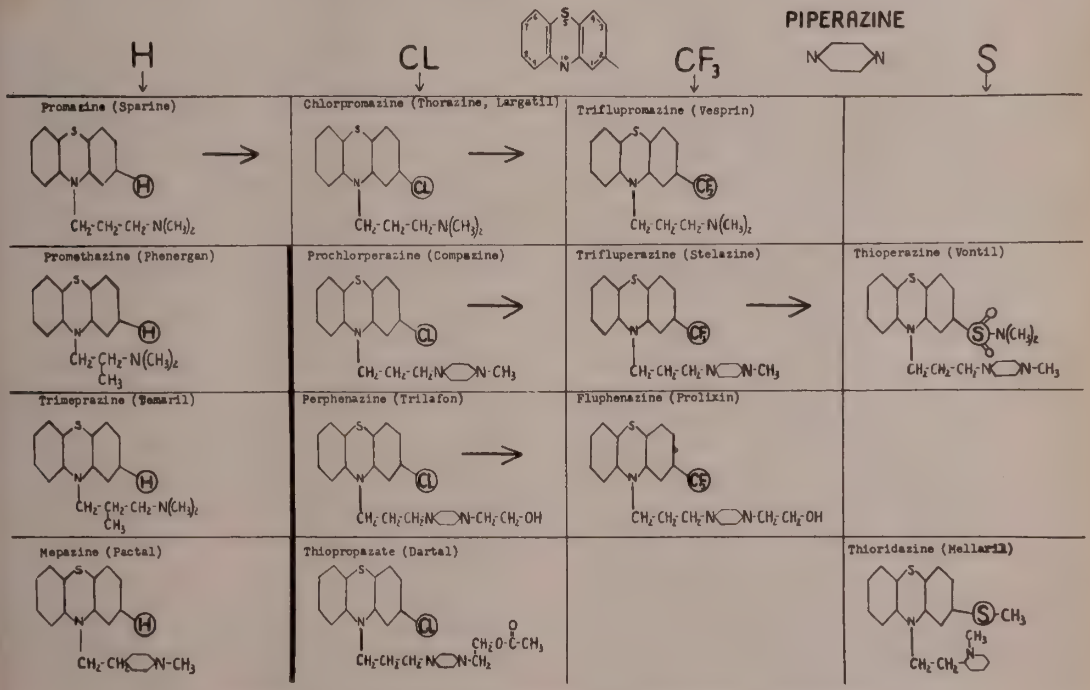
H
CL
CF3
PIPERAZINE
S
Promazine (Sparine)
Chlorpromazine (Thorazine, Largatil)
Triflupromazine (Vesprin)
Promethazine (Phenergan)
Prochlorperazine (Compazine)
Trifluperazine (Stelazine)
Thioperazine (Vontil)
Trimeprazine (Temaril)
Perphenazine (Trilafon)
Fluphenazine (Prolixin)
Mepazine (Pactal)
Thiopropazate (Dartal)
Thioridazine (Mellaril)

FIGURE 1. Chemical compositions of phenothiazine derivatives.

comprised of chlorpromazine hydrochloride, promethazine hydrochloride, and meperidine hydrochloride (Demerol hydrochloride). Chlorpromazine hydrochloride, due to its vasodilation effect, will accelerate the production of hypothermia when given intramuscularly prior to the administration of anesthesia or when given in minute amounts (1 to 2 mg.) intravenously during anesthesia.[10]

When using the phenothiazines in conjunction with anesthesia, it is well to note that those phenothiazines incorporating the piperidine or piperazine nucleus have no noticeable effect in prolonging the sedative employed preoperatively; or, if a case is being conducted with thiopental sodium (Pentothal sodium) as an anesthetic component, a drug such as fluphenazine dihydrochloride would not prolong the postoperative sleeping time. Consideration of such a factor would help to alleviate any unnecessary strain on the recovery room. Promethazine hydrochloride, which lacks the piperazine nucleus, will greatly increase the postoperative sleeping time.[11]

Although popular opinion has perpetuated the dogma that phenothiazines potentiate narcotics, recent studies with promethazine hydrochloride in this country and in England take exception to this.[12,13] In England, in fact, the experience has been that when promethazine hydrochloride was administered with meperidine hydrochloride, the pain threshold in some patients was lowered. However, since narcotics and some phenothiazines each independently tend to lower the blood pressure, their dosage quantities, when used concurrently, must be reduced.

In conducting pediatric cardiac catheterizations, phenothiazines are often employed. A frequently used mixture consists of the combination of promethazine, chlorpromazine, and meperidine hydrochlorides.[14]

A new use for the phenothiazine derivatives is in connection with postpartum hypertension. When vasopressors and oxytocics are used simultaneously, the end result is often a sharp increase in blood pressure, leading even to cerebrovascular accidents. This can be combated effectively and rapidly by the judicious use of small amounts of chlorpromazine hydrochloride ($2^1/_2$ mg. at a time until the blood pressure drops or a total of 15 mg. is employed).[15]

Phenothiazines are also useful in connection with anesthesia in combating singultus (often encountered during anesthesia or postoperatively).[16] There is experimental evidence that phenothiazines are of assistance in preventing cardiac arrhythmias[17,18] and in inhibiting the shock syndrome.[19] There is also some evidence that these drugs may enhance the action of muscle relaxants.[20] Their antisialogogue effect is only minimal, and a therapeutic dose of scopolamine or atropine must be given to insure a proper drying effect.[21] In cases of tetanus with spasms large doses of chlorpromazine hydrochloride are administered to reduce the incidence and severity of the attacks.[22]

Complications of phenothiazines

Among the side-effects caused by the phenothiazines which are of particular interest to anesthesiologists are hypotension and tachycardia. Numerous articles, cautioning against the use of the phenothiazines, have mostly cited chlorpromazine hydrochloride as the causal agent.[23,24] It is important to remember that newer derivatives contain the piperazine nucleus. In these drugs hypotension and tachycardia pose no real threat when they are used judiciously.[3,25] However, none of these newer derivatives have received the "tilt-table" test which established that promethazine hydrochloride, hailed as having minimal cardiovascular effects actually caused these side-effects when the patient was subjected to more dynamic testing.[26] Actually, the tilt-table test should be routine in the investigation of all phenothiazines.[7]

Another facet to the problem mentioned is that when epinephrine was used to correct hypotension caused by the phenothiazines, there was a further reduction in the blood pressure known as the "epinephrine reversal effect." The vasopressors of choice with the phenothiazines are norepinephrine or neo-synephrine hydrochloride, never epinephrine.[27]

Symptoms such as blood dyscrasias, jaundice, weight gain, and photosensitization may be caused by the phenothiazines, but only after prolonged dosage.[28] Extrapyramidal symptoms, a frequent complica-

TABLE I. Premedication dosage for fluphenazine dihydrochloride study

Weight		Preoperative Medication (Mg.)*		Postoperative Medication (Mg.)†
Pounds	Kilograms	Meperidine Hydrochloride	Atropine	Fluphenazine Dihydrochloride
Below 100	45	30	0.3	1.0
Up to 130	60	40	0.4	1.75
Up to 160	75	50	0.4	2.5

* Given intramuscularly for forty-five minutes.
† Given intravenously.

tion with the phenothiazines, do not occur when given while the patient is still subject to the anesthetic agents. However, the newer phenothiazines are long-acting drugs, and it has been reported that a single dosage, given intramuscularly but independently of anesthesia, caused extrapyramidal effects after twenty hours.[29] Caution should be exercised in the parental usage of the phenothiazines. If an artery is injected inadvertently, gangrene of the extremities may be caused.[30]

Results of study

Now I would like to offer the results of a study with a new phenothiazine derivative, fluphenazine dihydrochloride, which we conducted at St. Vincent's Hospital. The problem in this study was to determine if the intravenous administration of this drug given immediately postoperatively, would have any effect on the blood pressure, pulse, retching and vomiting, and mode of the patients' recovery in regard to tranquility. To accomplish this, we conducted a double-blind study on more than 200 patients who were scheduled for dilation and curettage and who were premedicated identically according to weight (Table I). The subjects were females, aged from twenty to forty-five years and not weighing over 160 pounds (75 kilograms). Their physical status was number 1, that is, the hemoglobin had to be at least 10 Gm. per 100 ml. In each instance the case involved nitrous oxide and thiopental sodium. The method of anesthesia consisted of intravenous infusion of 0.4 per cent of thiopental sodium, nitrous oxide, and oxygen (6 : 2 L. per minute); inhalation was done with a semiclosed circle with carbon dioxide (absorption).

Subsequent to surgery, these patients were watched carefully for one hour after receiving either a drug or a placebo. The blood pressure and pulse were taken frequently. Retching and vomiting, if present, were noticed, as was the general mode of recovery regarding agitation or serenity.

In brief, our results showed a 5 per cent incidence of retching and vomiting with fluphenazine dihydrochloride and a 14 per cent incidence with the placebo (Table II). In general, the mode of recovery was much more serene when the drug was administered, and there was no noticeable difference in the blood pressure and pulse caused by it. Our results correspond to those obtained by other investigators with fluphenazine dihydrochloride.[7]

Summary

In conclusion, we believe that phenothiazines do have a role in the armamentarium of the anesthesiologist. However, they must be used intelligently, the physician must know the particular derivative well, and he must use the minimal amount possible in each instance, since the anesthetic requirement is only a fraction of that necessary for psychiatric use. Bearing these cautions in mind, the best possible use of the drug can be made with the least adverse effects.

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TABLE II. Effects on patients treated with placebo and with fluphenazine dihydrochloride

	Placebo Group (100 Patients)		Group Treated with Fluphenazine Dihydrochloride (100 Patients)	
Effects	Patients (Per Cent)	Variations (Per Cent)	Patients (Per Cent)	Variations (Per Cent)
Blood pressure				
Increase	18	...	8	...
Decrease	66	0 to 10	77	0 to 10
	15	11 to 20	14	11 to 20
	1	Over 20	1	Over 20
Pulse	34	...	40	...
Decrease	46	0 to 10	40	0 to 10
Increase*	12	11 to 20	16	11 to 20
	8	20 to 30	4	20 to 30

* There was no incidence of a pulse increase of more than 30 per cent.

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Discussion

IRVING M. PALLIN, M.D., *Brooklyn, New York.* It is a pleasure to discuss this report. I recommend to you, as a ready reference, the chart (Fig. 1) which summarizes the phenothiazine drugs by their chemistry and the portion which gives a thumbnail pharmacologic sketch of each drug.

Interest in the phenothiazines increased with the synthesis of chlorpromazine hydrochloride and its use as a tranquilizer and as a supplement in preanesthetic medication. Here chlorpromazine hydrochloride was noted to[a-c] enhance both the analgesic and sedative properties of narcotics. A high incidence of hypotension was associated with chlorpromazine hydrochloride which led to its being limited in use. The antihistamine promethazine hydrochloride was then substituted in premedication because it did not produce the severe hypotension noted with chlorpromazine hydrochloride. Several studies implied that promethazine hydrochloride approached closely the ideal premedicant and to this drug were assigned all the desirable attributes of chlorpromazine hydrochloride. One of these attributes was the ability to potentiate narcotics. Let us reexamine this "potentiation."

The majority of preoperative narcotic doses are administered to pain-free patients in an attempt to allay apprehension and anxiety. It is this narcotic action that is commonly alluded to in discussions of potentiation by phenothiazines. However, it has been shown that tranquilizers such as chlorpromazine hydrochloride and triflupromazine hydrochloride are capable also of potentiating analgesia by modifying the subjective responses to pain. It is now generally agreed that promethazine hydrochloride is not a tranquilizer, nor is it able to enhance the analgesic action of narcotics.

Of the phenothiazine antihistamines currently available, trimeprazine and propiomazine hydrochloride are the most effective as adjuncts to premedication.[d,e]

Returning to the tranquilizers, however, one encounters compounds whose specific action is the reduction of anxiety and tension. Investigative studies in which these drugs were used preoperatively revealed that excellent preoperative sedation could be achieved, while at the same time postoperative vomiting was reduced to 5 per cent from control levels of 24 per cent.[f]

The two most effective agents in this regard, as determined by blind studies, are fluphenazine dihydrochloride and perphenazine. The latter compound was associated with a high degree of preoperative sedation and minimal blood pressure disturbance.

The comment that the tilt-table test should be routine in the investigation of all phenothiazines is not valid. Current studies, carried out independently by reliable investigators, have challenged the reliability of this phenomenon in evaluating the effects of new drugs on the cardiovascular system. The results of this evaluation are due in print in the very near future.

It seems to me that we have hardly scratched the surface of the phenothiazines. This report is another good milestone on the road to full knowledge about these amazing drugs.

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Frequency of duodenal ulcer in men and women

Duodenal ulcer occurs three to four times more often among men than women, and gastric ulcer about twice as often, according to *Patterns of Disease*, a Parke, Davis & Company publication for physicians. The disparity decreases in older groups, especially after age forty-five, although in no age group is the incidence among men less than twice that among females. At ages twenty-five to thirty-four, for every woman with a peptic ulcer there are about 4 men with a peptic ulcer. The ratio of males to females drops to 3.1:1 at ages thirty-five to forty-five; 2.3:1 at ages forty-five to fifty-four; 2.7:1 at ages fifty-five to sixty-four; and 2.5:1 at ages sixty-five and older.

Mechanism of Griseofulvin Failure

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A NEW ERA in the treatment of superficial fungus diseases began with the introduction of griseofulvin in 1959. The success of this agent was verified by hundreds of reports. Now, with the passage of time and the natural decrease of some of the early enthusiasm, attention must be directed to the proper evaluation of the place of griseofulvin in therapy. One definition of failure is "a thing which does not fulfill expectations." It is now known that failures sometimes occur with griseofulvin, and we have therefore evaluated our cases in an attempt to shed light on this problem.

Case report

Our first therapeutic frustration occurred in 1959 when a three-year-old Negro boy, weighing 25 pounds, with tinea capitis due to Microsporum audouini failed to improve after twelve weeks of therapy with griseofulvin. The cumulative dosage was 60.25 Gm., including 0.75 Gm. daily for three weeks and 1 Gm. daily for one week. Roentgen-ray epilation eventually produced a cure. The child's sister was also infected and was cured with a much lower dosage. Both siblings have the sickle-cell trait and a history of anemia. Except for sinus tachycardia and an enlarged heart, there were no other abnormalities.

The organisms were cultured and examined by W. H. Spencer, Ph.D., biologist at Millard Fillmore Hospital, and were found to be equally sensitive to griseofulvin in vitro. Cultures were treated with various concentrations of griseofulvin, and the effects on growth are shown in Table I.

Since then we have evaluated all of our patients treated with griseofulvin.* More than 60 cases have been omitted from this series. A few appeared to be fungus diseases clinically, but laboratory confirmation was not obtained. The others were referred patients, incorrectly diagnosed as having fungus diseases. The conditions which clinically mimicked fungus diseases were psoriasis of the scalp and feet, impetigo contagiosa, herpes zoster, herpes simplex, nummular eczema, dyshidrosis, seborrheic dermatitis, pityriasis rosea, and dermatitis venenata.

Attempts were made to treat moniliasis and tinea versicolor with griseofulvin. This treatment was ineffectual because of misapplication rather than actual failure of the drug. The organisms (Candida albicans and Malassezia furfur respectively) which cause these diseases have been shown to be unresponsive to griseofulvin. The organisms which respond to griseofulvin are species of Epidermophyton, Microsporum, and Trichophyton. Laboratory identification of the responsible organism will prevent similar mistakes in the future. The other cases were eliminated from this series because the patients could not be followed adequately. Many patients with tinea capitis showed evidence of infection at the last visit, but subsequently normal-appearing scalps were reported by telephone.

Methods and materials

The series presented here includes only the 94 patients who were followed closely for as long as twenty months and for whom repeated cultures were performed. Thus, they can be considered valid for evaluation. Results were considered successful in 71

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* Griseofulvin (Fulvicin) was provided by G. K. Hawkins, M.D., Medical Research Division, Schering Corporation, Bloomfield, New Jersey.

patients and unsuccessful in 23. One additional patient is now free from infection but is being continued on griseofulvin because of a previous relapse. There were 22 recurrences or relapses in this group. Some of these patients are now cured, and others are classified as failures. Most of the recorded failures were in patients who actually responded to the drug initially but who had recurrences after therapy was discontinued. With 2 exceptions, all of these relatively unsuccessful results were among patients with lesions on the nails or skin of the hands or feet. The infecting organisms in these latter 21 patients were trichomycosis rubra in 15, Trichophyton mentagrophytes in 5, and Epidermophyton floccosum in 1. The series is summarized in Table II.

Analyses of 18 patients including 5 with true failure and 13 with recurrence or relapse are shown in Table III.

Ten of the patients with tinea pedis weighed between 170 and 210 pounds. Overweight patients require daily doses of from 1.5 to 2 Gm. daily for cure, and a relapse probably will occur if they are treated with doses below this level. One patient could not tolerate more than 1.25 Gm. daily, and this was inadequate for cure despite one hundred and ninety-six days of treatment.

In t. pedis the last positive and first recurrence cultures were made from heavily keratinized sites. The heavy keratin must be reduced if cure is to occur. We used 10 per cent chrysarobin in chloroform, Whitfield's ointment, and recently, as suggested by Newcomer,[1] 40 per cent salicylic acid plaster molded to the affected areas and left in place for from twelve to twenty-four hours. The presence of infected nails also decreases the likelihood of cure. The areas of the foot most likely to harbor fungus infections are shown in Figure 1.

Murrell *et al.*[2] reported that 17.8 per cent of patients with t. rubra infections of the palms were cured, as compared with a 47.5 per cent rate of cure in patients with similar

NINETY-FOUR PATIENTS *with superficial fungus disease who were treated with griseofulvin were followed closely for as long as twenty months. Results were considered successful in 71 patients and unsuccessful in 23. Some of the failures were actually recurrences or reinfections. All but 2 of the failures occurred in patients with lesions on the nails or skin of the hands or feet. Sixty patients were omitted from the series because of incorrect diagnosis of fungus disease or diagnosis of moniliasis or tinea versicolor, which do not respond to treatment with griseofulvin. Organisms which respond to griseofulvin are species of Epidermophyton, Microsporum, and Trichophyton. The dose of griseofulvin and duration of treatment required for cure vary between a single dose of 1 Gm. and a cumulative dose of more than 500 Gm. during four hundred days. In at least 7 patients unsuccessful results might have been due to inadequate daily and cumulative dosage; relatively large dosage is required if there is heavy callus formation.*

TABLE I. Effect of griseofulvin on growth of cultures of M. audouini*

Concentration of Griseofulvin (Micrograms per Milliliter)	Macroscopic Appearance on Plate	Microscopic Appearance After Six Days	Result of Subculture
10.0	No growth	Filaments with short side branches	No growth
5.0	No growth	Filaments with short side branches	No growth
2.5	Fair growth	Normal branching filaments	Good growth
1.25	Fair growth	Normal branching filaments	Good growth
0.625	Fair growth	Normal branching filaments	Good growth
0.31	Fair growth	Normal branching filaments	Good growth
0.16	Good growth	Normal branching filaments	Good growth
0.08	Good growth	Normal branching filaments	Good growth
0.04	Enhanced growth	Normal branching filaments	Good growth
0.02	Enhanced growth	Normal branching filaments	Good growth
None	Good growth	Normal branching filaments	Good growth

* Three cultures were used for each concentration: A: resistant M. audouini infection; B: M. audouini infection from sibling of A; C: culture of t. rubra. The response of the three cultures was the same, as shown.

TABLE II.—Clinical results with griseofulvin

Location	Organism	Treated	Cured	Relapse	Failure
Scalp	M. audouini	21	20	1	1
	Microsporum canis	3	3	0	0
Trunk and extremities excluding hands and feet	T. rubra	4	3	2	1
	Tinea tonsurans	1	1	1	0
	T. mentagrophytes	1	1	0	0
Groin	T. rubra*	5	5	1	0
	Trichophyton violaceum	1	1	0	0
	E. floccosum	3	3	0	0
Hands	T. rubra	5	3	2	2
	T. mentagrophytes	1	0	1	1
Feet	T. rubra	25	17	9	8
	T. violaceum	1	1	0	0
	T. mentagrophytes	12	8	3	4
	E. floccosum	1	0	0	1
Fingers	T. rubra	5	3	1	2
Nails	T. rubra	5	2	1	3
TOTALS		94	71	22	23

* One patient also had T. tonsurans.

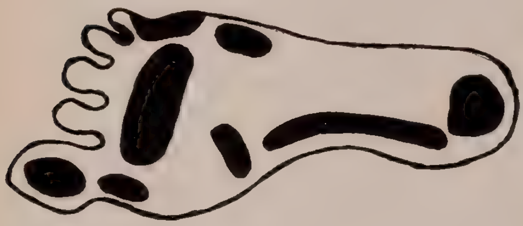

FIGURE 1. Sites most likely to harbor fungi (rubra strain).

infections of the fingernails. Their dosage, 1 Gm. daily, may have been inadequate for all but the most superficial infections. They believe, as we do, that t. pedis will not be cured in the presence of infected toenails, and only 8.8 per cent of their patients with these latter infections were cured. These investigators reported that 94 per cent of their 430 patients with t. capitis were cured after 3 Gm. of griseofulvin in three doses during one day. This supports the opinion that intensive therapy of t. capitis with griseofulvin might be efficacious.

Hargreaves[3] reported that avulsion of the nail is unnecessary in fingernail infections but provides quicker and more certain cures of infections of the toenail. Avulsion was performed in 17 patients of whom 14 were cured, but only 7 of 15 patients treated with griseofulvin alone were cured. Moniliasis was a factor in some poor responses.

Desai[4] reported that the higher incidence of t. rubra infections in adults, as compared with the incidence in children, probably is due to the transformation of the smooth skin of childhood into the more heavily keratinized skin of adulthood. Desai and Bhat[5] have also shown, by experimental inoculation, that prior treatment with griseofulvin does not protect against t. rubra reinfection, often from contacts with asymptomatic family members.

Follicular nodules with deep involvement were relatively resistant to therapy, but superficial lesions healed rapidly. Desai and Bhat[5] pointed out that viable hyphas and spores might be found in clinically healed areas sixty days after the termination of treatment.

We also observed this condition in 1 patient. A second relapse occurred eight weeks after the discontinuance of therapy. Treatment had been stopped despite the presence of heavily keratinized plaques because the patient stated these were normal for him. The recurrences or reinfections occurred at these sites and were confirmed by cultures and a microscopic examination of scrapings stained with potassium hydroxide. Originally this patient's cultures indicated T. mentagrophytes, but at present the cultures show t. rubra. This patient apparently is very susceptible to infection. Since the first course of treat-

TABLE III. Analysis of failures

Location and Organism	Age	Weight (Pounds)	Daily Dosage (Gm.)	Cumulative Dosage (Gm.)	Duration of Treatment (Days)	Comment
Right foot; t. rubra.	Adult	175	One raised to 1.25 or 1.5 occasionally	76.25	74	Cleared slowly; relapsed twice; drug caused loose stools so retreatment only if symptomatic relief desired; relapse occurred first on pressure areas with heavy callus.
Feet; T. mentagrophytes.	Adult	120	One for 6 weeks; 1.25 for 15 days.	60.75	57	Cleared; relapsed; patient prefers control with socks and powder only.
Groin, feet, toenails; t. rubra, t. tonsurans.	Adult	170	0.75 to 1.25; variable.	38.25, then to another physician.	Approximately 100	Cleared; relapsed; cleared with second course except one nail; duration and daily dosage inadequate for cure.
Hands, feet, fingernails, toenails; T. mentagrophytes, then t. rubra.	Adult	190	1 to 1.5	Over 500	410; intermittent to date.	Cleared twice with second recurrence; only right hand, both feet and toenails involved now; presently under treatment; T. mentagrophytes only for one year; now t. rubra only for over 18 months.
Hands, feet, one fingernail; t. rubra.	Adult	210	1.5	63	42	Clearing but treatment discontinued by patient; failure due to inadequate treatment.
Feet; E. floccosum	Adult	190	1	15	15	Clearing but treatment discontinued by patient; relapsed; failure due to inadequate treatment.
Feet; T. mentagrophytes.	Adult	200	1	112	112	Cleared; recurrence after 2 months; patient refused further treatment; probable reinfection.
Feet; t. rubra.	Adult	180	0.5 to 1.5	247.75	238 (3 courses)	Cleared and relapsed twice; now only mild scaling; patient prefers powders only; dosage below 1 Gm. inadequate; dosage of 1.5 Gm. 1 week only.
Feet; t. rubra.	Adult	105	0.25 to 0.75	152.25	Over 280	Cleared twice; minimal recurrence after 6 months; pruritus controlled with 0.25 Gm.; dosage inadequate for cure.
Feet; t. rubra.	Adult	205	One for 20 weeks; 1.5 for 1 week; 2 for 1 week.	166.5	154	Good response to higher dosage but never clear; maximal dosage required because of weight.

TABLE III. (continued)

Location and Organism	Age	Weight (Pounds)	Daily Dosage (Gm.)	Cumulative Dosage (Gm.)	Duration of Treatment (Days)	Comment
Feet; T. mentagrophytes.	Adult	200	0.5 to 1.25	94.75	196	Dosage inadequate for weight; patient could not tolerate more than 1.25 Gm. and discontinued treatment.
Feet; t. rubra.	Adult	140	One for 23 weeks; 1.5 for 2 weeks; 2 for 7 weeks.	259	224	Cleared; relapsed after 14 weeks; no further treatment; possible reinfection.
Feet; t. rubra.	Adult	170	One for 8 months; 2 for 3 months.	448 to date	Approximately 390	Cleared; recurrence with positive culture; clearing again under treatment.
Fingernail; t. rubra.	7 years	60	0.25 to 1	73	126	Only slightly improved after 18 weeks.
Feet; t. rubra.	Adult	140	0.75 to 1 for 9 months; 1.5 for 3 weeks; 2 for 2 weeks.	330	287	Mild scaling when treatment stopped; increasing scaling 8 months after discontinuance.
Scalp; M. audouini.	3 years	25	0.75 for 3 weeks; 1 for 1 week; 0.5 for 8 weeks.	60.25	84	Complete failure in child with sickle cell trait; organism sensitive in vitro; epilation required for cure; sibling cured easily.
Trunk; t. rubra.	Adult	105	0.5 for 4 weeks; 0.75 for 4 weeks; 1 for 22 weeks.	205	210	Improved but relapsed after 10 days; daily dosage inadequate.
Groin, feet, right palm; t. rubra.	Adult	160	One for 23 days; 0.75 for 20 days.	38	43	Cleared; relapsed after 6 months; dosage inadequate.

TABLE IV. Dosage and duration of treatment

Location	Organism	Optimal Daily Dosage (Gm.)	Duration of Treatment	Response (Per Cent)	Comment
Scalp	M. audouini Microsporum canis t. tonsurans	0.5 to 0.75*	3 to 4 weeks	96 Excellent; failures rare.	Most important contribution of griseofulvin.

Trunk and extremities excluding hands and feet	M. audouini t. rubra T. tonsurans	0.5 to 0.75;* 1 to 1.25	3 weeks to over 1 year	83 Highly variable; usually excellent.	Responds readily but will recur if palms or soles are infected.
Groin	t. rubra T. tonsurans T. violaceum E. floccosum	1 to 1.25	2 to 4 weeks; E. floccosum 2 to 3 weeks.	100 Excellent	Readily cleared; recurrence only if feet exacerbate.
Hands	t. rubra T. mentagrophytes	1 to 2	6 weeks to over 18 months	50 Fair to good if feet and nails uninfected	Best results with minimal callus; high relapse rate if nails or feet are infected.
Feet	t. rubra T. violaceum T. mentagrophytes E. floccosum	1 to 2	4 weeks to over 18 months	69 Poor to fair; many failures, many relapses.	T. rubra relapses frequent; intermittent therapy required; T. mentagrophytes variable.
Nails	t. rubra	1 to 2	3 to 18 months	46 Fingernail, fair; toenail, poor.	Long treatment needed; high relapse rate; can spread to skin.

* In children, according to weight.

ment, the fingernails and one hand have remained free from infection.

The dose of griseofulvin and duration of treatment required for cure varies between a single dose of 1 Gm. in some cases of t. capitis to a cumulative dose of more than 500 Gm. during four hundred days in resistant tinea of the feet and toenails. The smaller doses are effective when they are absorbed and when the hair or skin is rapidly replaced, as in the scalp and groin.

Crounse[6] demonstrated wide variations in griseofulvin absorption, as reflected by blood levels of the drug. Two of 3 patients with t. capitis in our series remained free from infection after single doses of 1 Gm. of griseofulvin. The third patient relapsed after four weeks; retreatment with three 1 Gm. doses produced cure.

In at least 7 patients unsuccessful results might have been due to inadequate daily and cumulative dosage. Prolonged therapy will not compensate for daily doses which are too low. Very rarely a patient will be unable to tolerate the necessary higher doses because of diarrhea and dizziness.

Callaway[7] treated a seven-year-old girl with tinea corporis due to t. rubra. She did not improve on 1 Gm. daily for several months, but there was 80 per cent improvement when the dosage was raised to 2 Gm. daily. Costello[8] reported a patient with onychomycosis who did not improve after surgical removal of the nails and after the administration of 3 Gm. of griseofulvin daily.

According to Wilson,[9] griseofulvin can be used effectively despite the presence of anemia, leukemia, tuberculosis, lupus erythematosus, sarcoidosis, and many other diseases. However, Mandel[10] reports that diabetes, if uncontrolled, can block cure.

Comment

Our present experience and opinion with respect to dosage and duration of treatment with griseofulvin is summarized in Table IV. Some apparent failures are actually recurrences or reinfections; far fewer are true therapeutic failures which at present cannot be explained. Many failures actually are due to misapplication or to inadequate dosage. Relatively large doses and ancillary treatment are required if the infected areas have heavy callus. Some apparently cured patients have relapses or reinfections weeks or months after treatment is discontinued.

Acknowledgment. The assistance of W. H. Spencer, Ph.D., bacteriologist, Millard Fillmore Hospital, is gratefully acknowledged.

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Optimum radiotherapy of cancer

Four points might well be borne in mind by the nonradiologist faced with a request for optimum radiotherapy of cancer: (1) The clinical cure rate of cancers suitable for radical radiotherapy has not been improved with megavoltage or supervoltage. (2) The clinical palliation rate of most cancers suitable for palliative radiotherapy has not been improved with supervoltage. (3) While megavoltage or supervoltage spares the skin of some patients, as compared with orthovoltage (200 kv.) therapy, it causes relatively greater insult to the subcutaneous tissues. As a result of this, serious damage to the subcutaneous tissues is more apt to occur with the higher voltage radiation. (4) The expense to the average patient is approximately three times as great for megavoltage as for orthovoltage.—*L. Henry Garland, M.D., Current Medical Digest, October, 1961*

Mebutamate, a New Drug for the Treatment of Hypertension

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A STUDY WAS UNDERTAKEN *on 51 ambulatory hypertensive patients to determine the effects of therapy with mebutamate. On the basis of blood pressure readings, 46 (90 per cent) of the patients responded favorably to mebutamate therapy. In 26 patients with systolic hypertension, the average reduction in systolic pressure was 31 mm. Hg, and the normotensive diastolic pressures were not decreased below normotensive levels. In 25 patients with diastolic hypertension, the average reduction in systolic pressure was 31 mm. Hg, and in diastolic pressure 20 mm. Hg. The amount of reduction attained was proportional to the height of the initial systolic and diastolic pressures. Drowsiness occurred in 21 patients and light-headedness in 14, possibly owing to overlapping of previous therapy or overdosage. These side-effects were eliminated spontaneously or by decreased dosage. All 20 patients who had improved on previous therapy obtained further improvement on mebutamate; of 22 who had failed to respond to previous therapy, 19 improved on mebutamate, 1 was unchanged, and 2 became worse. Two of 3 patients who had become worse on previous therapy improved on mebutamate, and 1 was unchanged. Of 6 who had not received previous therapy, 5 were improved, and 1 became worse.*

TEN YEARS AGO, in 1952, there were a few ganglionic blocking agents available for use in the treatment of hypertension. However, the drug most frequently prescribed for hypertension at that time was phenobarbital. Dissatisfaction with the drugs then available led to the development of newer and more potent agents, such as the Rauwolfia preparations in 1953, the thiazides in 1958, and combinations thereof in 1959. Today, as ten years ago, dissatisfaction still exists, not with the potency of currently available drugs, but with the severe side-effects associated with the increased potency.

Continued research to develop better pharmacologic agents for the treatment of hypertensive disease led to the introduction of a number of new antihypertensive agents, among them, mebutamate.*

Mebutamate (2-methyl-2 sec-butyl-1, 3-propanediol dicarbamate), a compound of a new type, reduces blood pressure by producing vasodilation.[1] This is mediated through the central nervous system by acting on certain areas of the hypothalamus and medulla. There is no direct action on the blood vessels or ganglia.[2] Mebutamate also has the ability to lower the blood pressure without decreasing the cardiac output.[3] In clinical studies it was demonstrated to be nontoxic and free from severe side-effects.[4,5]

Because of its reported lack of severe side-effects and because of the failure of previously prescribed medication to produce the desired results, it was decided to evaluate the usefulness of mebutamate in the treatment of hypertensive patients seen in private practice.

Clinical study

Fifty-one ambulatory hypertensive patients, 36 women and 15 men, ranging in age from forty-six to eighty-three years (average age, 65.8 years) were included in this study.

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* The mebutamate used in this study was supplied in the form of Capla through the courtesy of Wallace Laboratories, Cranbury, New Jersey.

TABLE I. Pathologic conditions in 51 patients

Pathologic Condition	Number of Patients
Essential hypertension (including neurogenic hypertension)	7
Hypertensive heart disease	18
Arteriosclerotic heart disease	19
Both arteriosclerotic and hypertensive heart disease	1
Rheumatic heart disease	3
Luetic heart disease	1
Chronic renal disease	1
Pheochromocytoma*	1
TOTAL	51

* Patient refused surgical treatment, therefore was continued on medical treatment and was included in the study to determine the effects of mebutamate therapy.

Forty-two of the 51 patients had symptoms attributable to hypertension which had led them to seek medical advice. In this group 24 complained of headache, 14 of dyspnea, 13 of vertigo, 3 of tinnitus, and 2 of insomnia. Nine patients were asymptomatic, and their hypertensive states had been discovered during routine physical examinations. The primary pathologic conditions represented in these patients are presented in Table I. Eleven patients had other disorders in addition to hypertension: 3 were obese, and 8 had diabetes mellitus which was complicated by obesity in 3 patients.

More than half of this group of 51 patients had received antihypertensive agents, including Rauwolfia aklaloids, thiazide compounds, hydralazine hydrochloride, Veratrum preparations, or mecamylamine hydrochloride. The duration of previous antihypertensive therapy ranged from five months to twelve years.

Method

Although it would have been desirable from a research viewpoint to discontinue all antihypertensive therapy in this group for at least a week before beginning an evaluation of a new drug, it was deemed unwise to risk the blood pressure elevations which might have occurred in at least half of this ambulatory and essentially geriatric group of patients.

It is of the utmost importance, therefore, to bear in mind that an extra burden was placed on mebutamate even before the drug was administered. The pretreatment blood pressures to be reported later represent, in most instances (45 of 51 patients), the minimum blood pressure achieved on all previous therapies and not the higher pressures of untreated hypertension.

After the initial examination all previous antihypertensive therapy was discontinued except for chlorothiazide for 8 patients, and mebutamate therapy was started. The patients were seen every two weeks for a period of six weeks. Forty-nine of the 51 patients initially received one tablet of mebutamate (300 mg.) three times daily. The remaining 2 patients received one-half tablet (150 mg.) three times daily. One patient received a reduced amount because the hypertension was mild; for the other, a new patient, a lower dose was deemed advisable because of the pretreatment complaint of dizziness. Other therapeutic agents administered concomitantly included digitalis for 13 patients, pentaerythritol tetranitrate for 3, d-amphetamine and dl-amphetamine combination for 6, conjugated estrogens for 1, and insulin, tolbutamide, or chlorpropamide for 6. The diabetic condition was controlled by diet alone in 2 patients.

On the basis of blood pressure readings taken just prior to transferring these patients to mebutamate therapy, the patients were classified into two groups. Group A included 26 patients who had systolic hypertension (systolic pressure greater than 140 mm. Hg; diastolic pressure within normal range, 90 mm. Hg or less). Group B included 25 patients who had diastolic hypertension (diastolic pressure greater than 90 mm. Hg, accompanied as a rule by a marked increase in systolic pressure).

The systolic pressure was greater than 170 mm. of mercury in all 51 patients before mebutamate therapy. In Group A the systolic pressures ranged from 170 to 199 mm. of mercury for 17 patients (65 per cent) and from 200 to 235 mm. of mercury for 9 (34 per cent). In Group B the systolic pressures ranged from 170 to 199 mm. of mercury for 11 patients (44 per cent) and

TABLE II. Results of mebutamate therapy

	—Blood Pressure (mm. Hg)—		Decrease or Increase in Blood Pressure (mm. Hg)		Change in Mean Arterial Pressure**
Age (Years)	Pretherapy*	Post-therapy	Systolic	Diastolic	
Group A 57	180/80	180/80	0	0	0
46	230/75†	200/75	−30	0	0
58	185/90	150/85	−35	− 5	−15
78	180/80	162/80	−18	0	− 6
67	220/80	180/90	−40	+10	− 7
59	190/70	155/70	−35	0	−12
56	185/90	180/90	− 5	0	− 2
76	175/80†	182/80	+ 7	0	+ 2
51	170/90	145/80	−25	−10	−15
66	235/90	180/90	−55	0	−16
62	185/80†	150/80	−35	0	−12
63	210/90	160/80	−50	−10	−23
77	184/88	155/75	−29	−13	−18
74	178/75	150/70	−28	− 5	−12
77	200/90	176/84	−24	− 6	−12
67	200/90†	155/75	−45	−15	−15
75	175/90	145/80	−30	−10	−16
57	175/82	150/75	−25	− 7	−13
75	200/80	155/75	−45	− 5	−15
75	175/85	150/75	−25	−10	−18
55	180/90	145/75	−35	−15	−22
58	170/80	150/65	−20	−15	−17
63	210/70	170/70	−40	0	−14
71	220/90†	155/90	−65	0	−16
67	180/90	150/80	−30	−10	−17
52	180/80†	160/70	−20	−10	−13
Group B 71	195/100†	160/80	−35	−20	−25
56	180/110	175/100	− 5	−10	− 8
68	210/110	170/90	−40	−20	−26
73	190/110	165/90	−25	−20	−20
59	220/120	170/100	−50	−20	−30
63	230/125	180/100	−50	−25	−33
60	200/110	160/80	−40	−30	−33
75	200/140	180/120	−20	−20	−20
64	200/100	150/70	−50	−30	−36
71	220/140	180/100	−40	−40	−40
62	190/100	155/80	−35	−20	−20
71	210/115	170/95	−40	−20	−27
69	190/95	160/95	−30	0	−10
64	184/100	160/90	−24	−10	−15
69	190/100	205/100	+15	0	+ 5
70	185/100	170/90	−15	−10	−11
71	180/105	160/80	−20	−25	−23
66	245/122	190/90	−55	−32	−40
70	195/105	160/90	−35	−15	−22
61	210/110	180/75	−30	−35	−33
64	260/120	210/110	−50	−10	−20
83	200/115	165/85	−35	−30	−31
61	180/100	190/100	+10	0	+ 3
67	205/105	175/80	−30	−25	−26
65	245/120	190/90	−55	−30	−39

* Pretherapy blood pressure represents minimum pressure achieved on previous therapy.
† No previous therapy—initial blood pressure used.
** Mean arterial pressure = diastolic pressure + one-third pulse pressure.

from 200 to 260 mm. of mercury for 14 (56 per cent).

In Group A the diastolic pressures were normotensive and ranged from 70 to 90 mm. of mercury; in Group B the diastolic pressures ranged from 95 to 140 mm. of mercury.

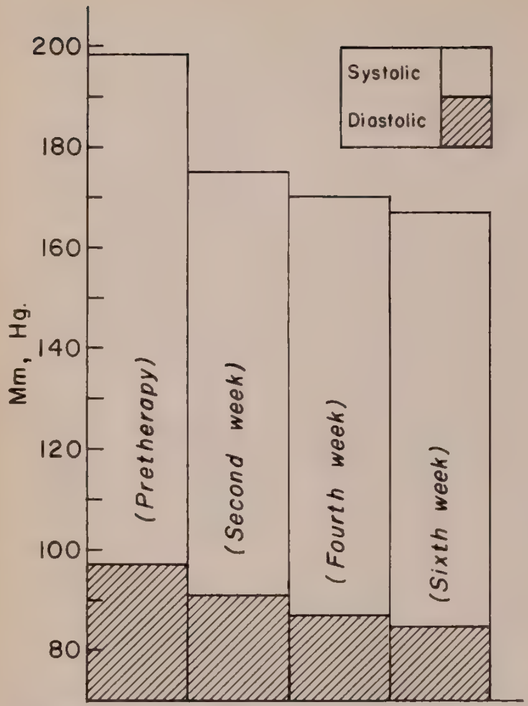

FIGURE 1. Average decrease in systolic and diastolic blood pressure over period of therapy.

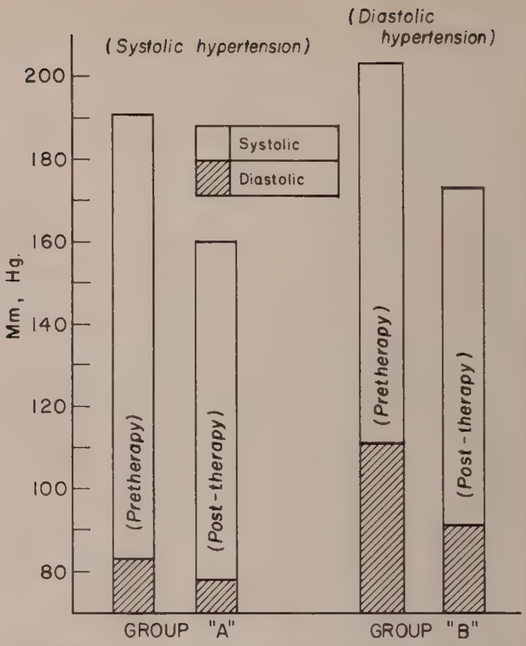

FIGURE 2. Average blood pressure decrease by groups.

Results

On the basis of blood pressure readings, 46 (90 per cent) of the 51 patients in this study responded favorably to mebutamate therapy. Presented in Table II are the systolic and diastolic pressures before and after mebutamate therapy, the reduction in millimeters of mercury, and the decrease in the mean arterial pressure for each patient.

The average reduction in systolic and diastolic pressure for the 51 patients from the onset of mebutamate therapy to the completion of the study is shown graphically in Figure 1. There was a gradual reduction in blood pressure with the greatest rate of reduction occurring during the first two weeks of therapy.

In Group A (26 patients with systolic hypertension) the average reduction in systolic pressure was 31 mm. of mercury (Fig. 2). Eighty-five per cent (22 patients) obtained reductions of 20 mm. of mercury or more (range from 20 to 65 mm. Hg). The reduction in normotensive diastolic pressure for the patients in Group A averaged 5 mm. of mercury (range from 0 to 15 mm. Hg), but none was decreased to less than 65 mm. of mercury. The fact that the normotensive diastolic pressures in this group were not decreased below normotensive levels was particularly significant inasmuch as it demonstrates that mebutamate can be administered safely to patients who have diastolic pressures within normotensive levels without fear of disturbing the physiologic regulation of the blood pressure. Postural hypotension, which so frequently occurs with the use of some antihypertensive drugs, did not occur with the use of mebutamate.

In Group B (25 patients with diastolic hypertension) the average reduction in systolic pressure was 31 mm. of mercury (Fig. 2). Eighty-four per cent (21 patients) obtained reductions of 20 mm. of mercury or more (range from 20 to 55 mm. Hg). The average reduction in diastolic pressure for the patients in Group B was 20 mm. of mercury (range from 0 to 40 mm. Hg). Eighty-eight per cent of the patients obtained reductions in diastolic pressure of 10 mm. of mercury or more.

In both groups it was demonstrated that the amount of reduction attained on mebutamate was, in general, proportional to the

TABLE III. Results for groups A and B according to type of hypertensive disease

	Diagnoses	Number of Cases	Improved	No Change	Worse
Group A (systolic hypertension)					
	Essential hypertension	5	4	1	. . .
	Hypertensive heart disease	7	7	. . .	. . .
	Arteriosclerotic heart disease	10	8	1	1
	Rheumatic heart disease	3	3	. . .	. . .
	Luetic heart disease	1	1	. . .	. . .
	TOTALS	26	23	2	1
Group B (diastolic hypertension)					
	Essential hypertension	2	2	. . .	. . .
	Hypertensive heart disease	11	11	. . .	. . .
	Arteriosclerotic heart disease	9	7	. . .	2
	Hypertensive and arteriosclerotic heart disease	1	1	. . .	. . .
	Chronic renal	1	1	. . .	. . .
	Pheochromocytoma	1	1	. . .	. . .
	TOTALS	25	23	0	2

height of the initial systolic and diastolic blood pressure levels; that is, the higher the initial systolic and diastolic pressures, the greater the reduction obtained. The results obtained by the patients in each group are presented in Table III.

It was not necessary to increase the dosage of mebutamate for any patient. For 16 patients the initial dose of medication was continued throughout the study; for 33 patients the dose was decreased. In no case did the reduction in the amount of medication prescribed alter the favorable antihypertensive action of mebutamate.

The blood counts done for 49 patients before and after therapy showed no significant change. The urinalyses performed for 38 patients showed no change for 36. In 2 diabetic patients the urinalyses showed an increase in sugar from 1 to 2 plus for 1 and an increase in albumin to 2 plus for the other. Mebutamate was compatible with other drugs used concomitantly (digitalis, pentaerythritol tetranitrate, d-amphetamine and dl-amphetamine combined, conjugated estrogens, and insulin, tolbutamide, or chlorpropamide) and did not interfere with the antidiabetic or antiobesity treatment of several patients.

Side-effects

Side-effects occurred in 35 patients: drowsiness in 21 and light-headedness in 14. No side-effects other than the two mentioned were experienced by the patients or observed by the investigator. None was sufficiently severe to warrant the discontinuation of the medication.

Since, in most instances, these side-effects occurred during the first two weeks of therapy, it was difficult to determine whether they were related to dose levels of mebutamate, to the carry-over effect of previous treatment, or to a combination thereof. Nevertheless, it was deemed advisable to reduce the amount of medication for 33 patients. In some instances in which the dose was not decreased the side-effects abated spontaneously with the continuation of the medication at the same dose level. However, when the dose was decreased, the side-effects were eliminated promptly. No acquired tolerance to the drug was noted.

Comparison with previous therapy

Of the 45 patients who had received some form of therapy previously, 91 per cent obtained definite improvement on mebutamate therapy, 4.5 per cent were unchanged, and 4.5 per cent became worse. All 20 patients who had improved on previous therapy obtained further improvement on mebutamate.

Very striking results were obtained in the 22 patients who had failed to respond to previous therapy; 19 of these (86 per cent) improved on mebutamate, 1 was unchanged, and 2 became worse. Two of 3 patients who had become worse on previous therapy improved on mebutamate; 1 was unchanged.

Of the remaining 6 patients who had not received any form of therapy previously, 5 were improved, and 1 became worse.

Conclusions

The results obtained in this study were excellent, especially in view of the fact that for 45 of the 51 patients the blood pressure recorded before the onset of mebutamate therapy represented the minimum pressure achieved on previous therapy.

Mebutamate was effective in reducing the blood pressure in 46 (90 per cent) of the 51 patients. Included in the 46 patients who obtained a reduction in blood pressure were 20 patients who had improved on previous therapy, 19 who had not improved on previous therapy, 2 who had become worse on previous therapy, and 5 who had not received previous therapy.

The reduction in both systolic and diastolic pressure was steady and gradual. The maximum effect was attained during the first two weeks of therapy, and thereafter the reductions were maintained as long as the drug was administered. In addition, the amount of reduction attained was proportional to the height of the initial systolic and diastolic pressures; that is, the higher the blood pressure, the greater the reduction.

The fact that the normotensive diastolic pressures in those patients who had systolic hypertension were not decreased below normotensive levels demonstrated that mebutamate could be prescribed for patients who had diastolic pressures within normotensive levels without fear of disturbing the physiologic regulation of the blood pressure. There was no evidence of postural hypotension; thus, mebutamate can be used with safety in elderly or debilitated patients as well as in younger-age groups. Also, mebutamate did not interfere with the treatment of obese patients or of those who had diabetes mellitus.

The side-effects of drowsiness and lightheadedness, which may have been attributable either to the overlapping effects of previous and present therapy or to overdosage, were abated with continued medication at the same dose level or were eliminated by reducing the amount of medication prescribed. No acquired tolerance to the drug was noted. It was not necessary to discontinue medication because of these side-effects, and no other side-effects were observed.

Mebutamate is a valuable antihypertensive agent which is effective in lowering the blood pressure and which lacks the severe side-effects associated with the use of the available antihypertensive drugs.

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Acknowledgment. The author wishes to express his appreciation to Samuel Pollack, M.D., and Henry Schlesinger, M.D., of Brooklyn for their assistance with the clinical data.

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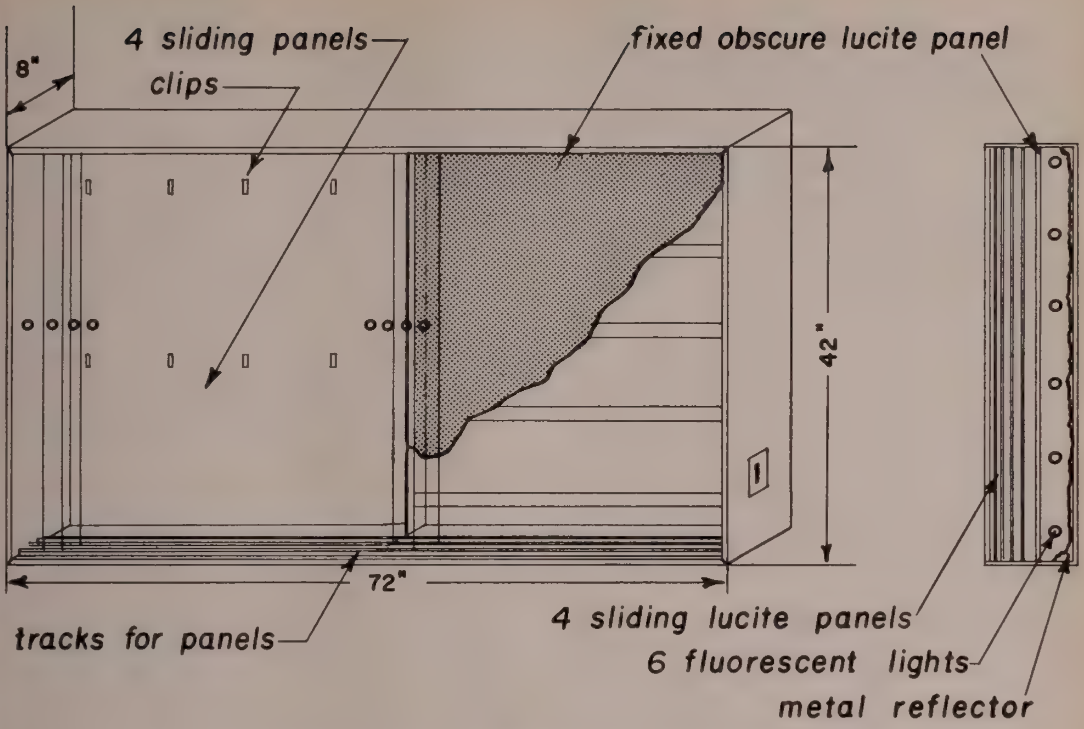
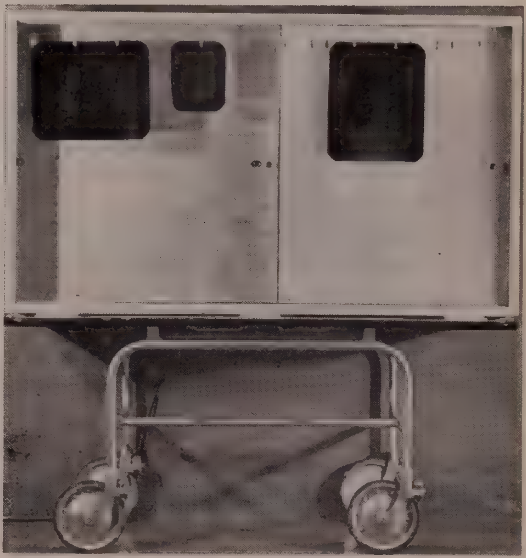

8"
4 sliding panels
clips
fixed obscure lucite panel
42"
72"
tracks for panels
4 sliding lucite panels
6 fluorescent lights
metal reflector

Specifications for a Mobile X-Ray Film Viewer

ALAN A. KANE, M.D., Brooklyn, New York

From the Department of Surgery, Coney Island Hospital Research Institute, Inc.

The use of x-ray films in the presentation of case reports is routine. Often, several different cases are presented in a series. To expedite the presentation we have devised a shadow box with sliding panels. The x-ray films are put up for view on each panel before the lecture. As the case is completed, the panel can be slid back and a new case presented. The doors are of plastic to avoid breakage.



The materials required include $^1/_2$-inch plywood, two pieces 8 by 42 inches for the sides, two pieces 8 by 72 inches for the top and bottom, and one piece 42 by 72 inches for the back. Also needed are tracks and runners for the top and bottom and fluorescent lights, wire, a switch, and sliding panels. We have mounted the shadow box on an old stretcher to make it mobile.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
November 29, 1961

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by BENJAMIN E. KRENTZ, M.D.

Toxemia of Pregnancy—Progressing to Uremia?

Case history

SALVATORE BALDINO, M.D.: A twenty-two-year-old Negro female was admitted to Knickerbocker Hospital on September 12, 1961, complaining of nausea, vomiting, headache, and frequency and burning on urination, all of about one week's duration. Two months previously she had been a patient at another hospital for two weeks with nausea, vomiting, and abdominal and flank pain. She was found to be hypertensive with a blood pressure of 220/120 on admission. On bed rest this fell to 170/110. No other abnormal physical findings were reported. Her blood urea nitrogen was found to be 24 mg. per 100 ml. She was discharged without specific treatment and advised to stay on a low-salt diet. During the interval from July to early September she felt improved, took no medication, and did not seek medical attention. She did not adhere to a low-salt diet, nor did she return to the outpatient clinic of this hospital.

The patient dated the onset of her illness to her last pregnancy which had terminated August, 1960. It was her third pregnancy, and during the last trimester she developed swollen ankles, blurred vision, and headaches. A urinalysis revealed 3 plus albumin, 3 to 4 red blood cells, and 16 to 18 white blood cells, as well as occasional casts. The blood urea nitrogen was 9 mg., uric acid 4.8 mg., creatinine 0.7 mg., and glucose 63 mg. per 100 ml. However, she had a normal pelvic delivery. She was advised to stay in the hospital for further study because of persistent albuminuria; however, she refused. She stated that she was told during this pregnancy that she had high blood pressure and that this persisted after the pregnancy. However, recorded blood pressures on the antenatal clinic chart and on the hospital chart show only pressures ranging from 110/60 to 120/80.

Her first pregnancy had terminated normally in August, 1957, following an uncomplicated prenatal course; her antepartum blood pressure was never above 130/90, and it remained at about this level during and after parturition. Albuminuria was not detected during this gestation.

Her second pregnancy had terminated in August, 1958. During this pregnancy she had no prenatal care. When admitted for delivery at thirty-eight weeks, her blood pressure was 125/80 and remained at about this level. She had a mild degree of ankle edema but no subjective symptoms. Urinalysis on admission showed 2 plus albumin, no red blood cells, and 2 to 5 white blood cells. All three of her pregnancies went to term and were delivered spontaneously from below.

She denied any episode of hematuria, periorbital edema, or a known episode of renal disease. Her father was known to have had high blood pressure for many years, and one of his brothers also was hypertensive and had suffered a stroke.

The present episode in her illness began approximately one week before her entry to the hospital with recurrent nausea, vomiting, and flank pain. The vomiting was not related to food intake, and the vomitus did not contain blood or dark material. Headache developed and became severe and almost constant. Urinary frequency and burning developed concomitantly; there was no gross hematuria and no chills or fever.

On admission the temperature was 98.4 F., pulse 88, respirations 20, and blood pressure 210/135. The ocular fundi showed blurred disk margins and bilateral fresh hemorrhages and exudates. The lungs were clear. The heart was not enlarged; the sounds were of good quality, and no murmur or friction rub was heard. The abdomen was soft, and no organs or masses were felt. There was no costovertebral angle tenderness. There was 2 plus pitting edema of the ankles. The deep tendon reflexes were hypoactive.

The urine had a specific gravity of 1.007, was alkaline, and contained 2 plus albumin, no sugar or acetone, and 3 to 6 red blood cells and 2 to 5 white blood cells per high power field. The red blood cells were hypochromic, and there was anisocytosis and poikilocytosis. The white cell count was 8,600 with a normal differential count. The reticulocyte count was 4.8 per cent. The sedimentation rate was 130 mm. per hour. The stool guaiac test showed positive results. The nonprotein nitrogen was 109 mg., creatinine 9.2 mg., calcium 8 mg., phosphorus 8.2 mg., and cholesterol 174 mg. per 100 ml. The serum sodium was 137 mEq., potassium 4.4 mEq., chlorides 96 mEq., and carbon dioxide 11.5 millimols per liter. The total protein was 4.8 Gm. per 100 ml. with 2.4 Gm. albumin and 2.4 Gm. globulin. Several lupus erythematosus preparations showed negative results. The bleeding time was three minutes, the clotting time five and one-half minutes, and the prothrombin time sixteen seconds (control fourteen seconds). The serology gave negative results. An electrocardiogram showed normal findings. A chest x-ray film showed mild generalized cardiac enlargement with prominence of the hilar markings suggesting early congestive changes.

She was treated with 2 units of packed red blood cells, and her hemoglobin rose to 8.8 Gm. per 100 ml. She was placed on a salt-deficient diet and given intravenous calcium gluconate. The day following admission a Fishberg urinary concentration test was done; all specimens concentrated to 1.010. The following day a twenty-four-hour urine specimen with a volume of 550 ml. contained sodium 53 mEq., potassium 19.4 mEq., and chlorides 55 mEq. per liter. A urine culture taken on the day after admission grew out Aerobacter aerogenes. A second urine culture taken on the tenth hospital day showed no growth. Repeated urinalyses showed albumin up to 4 plus, 10 to 20 red cells, and 10 to 30 white cells.

She was treated symptomatically with Compazine for nausea, aluminum hydroxide, analgesics, and mild sedatives. Her blood pressure remained in the range of 200/120. She felt subjectively improved, and her ankle edema disappeared. However, on the eighth hospital day the nonprotein nitrogen was 159 mg., creatinine 11.1 mg., calcium 6.8 mg., and phosphorus 10.2 mg. per 100 ml. The serum sodium was 133 mEq., potassium 4.9 mEq., chlorides 92 mEq., and carbon dioxide 17 millimols per liter. On the tenth hospital day an operation was performed.

Discussion

Benjamin E. Krentz, M.D.: It is my surmise that this twenty-two-year-old Negress, the subject of this conference, who was found in mid-September to be suffering from uremia and malignant hypertension, proved on needle biopsy of the kidney to have the picture of chronic pyelonephritis with an acute phase superimposed and also a marked degree of arteriolar nephrosclerosis with some necrotizing component. There is no necessity to belabor the well-known fact that clinically the end states of renal disease resemble each other closely. The uremias of systemic lupus erythematosus, polyarteritis nodosa, diabetic glomerulosclerosis, glomerulonephritis, and pyelonephritis are indistinguishable without a proper evaluation of the case history, and sometimes not even then.

The protocol assures us of an innocent first eighteen years of life but strikes two portentous chords; a family history of hypertension and a blood pressure of 130/90 for a while after the first pregnancy. At the age of nineteen the patient, pregnant for the second time, was found to have slight fluid retention, albuminuria, and slight pyuria. Her blood pressure was normal at that time. Two years later, at the age of twenty-one, progression of her renal disease may be inferred, because persistent albuminuria, microscopic hematuria, and a greater degree of pyuria as well as cylindruria were recorded. The pre-eclamptic syndrome of blurred vision, headache, and ankle edema necessitated hospitalization, but she was neither azotemic nor hypertensive at the time.

One year after her third spontaneous term delivery and two months before being admitted to Knickerbocker Hospital, she sought medical aid for the first time, pregnancy excluded, because of symptoms presumably related to her hypertension. Her blood pressure had leaped to 220/120 within a year, and she bordered on azotemia. Eight weeks later she was admitted here with malignant hypertension and uremia with its spectrum of anemia, acidosis, hyponatremia, hypocalcemia, and hyperphosphatemia; but she was fully conscious at the time.

The various laboratory data shed little light on etiology or pathogenesis. However, if we assume that her illness began as an interstitial pyelonephritis either in her early youth or during her second pregnancy at the age of nineteen and was exacerbated from time to time, especially by her pregnancies, then a final recurrence of renal infection with little left in the way of renal reserve finds support in the urinalysis showing 4 plus albumin, hematuria, pyuria, and A. aerogenes on culture.

The sudden appearance of hypertension and/or uremia may be due to vascular catastrophes. Bilateral renal vein thrombosis may give rise to sudden uremia, but it is not usually accompanied by an increase in blood pressure. Unilateral occlusion of a renal artery may raise the blood pressure, but if the other kidney is normal, uremia is unlikely.

Pyelonephritis, acute or chronic, is considered one of the greatest problems in infectious disease today, and it appears to be increasing in frequency. A carefully documented study from the Cincinnati General Hospital found that pyelonephritis outranks glomerulonephritis as a cause of chronic uremia by a ratio of 5 to 1.[1] McManus[2] has reported that pyelonephritis is more frequent in women than in men and in Negroes than in white persons; many other studies corroborate this observation.

Few differences in opinion exist about the bacterial etiology of acute pyelonephritis. Organisms presumably find their way to the kidney via the blood stream, the lymphatics, direct ascent up the column of urine in the ureters, or through the subepithelial layer of the ureter. Infection is more prone to engraft on a kidney with a congenital anomaly or on one in which there is obstruction to the excretory pathway. Some 93 per cent of the causative organisms are Escherichia coli, Streptococcus fecalis, Pseudomonas aeruginosa, Bacillus proteus, the omnipresent Staphylococcus, and A. aerogenes. It has been postulated that repeated infection destroys renal architecture and produces scarring. Minute colonies of microorganisms may be sequestrated in scars, becoming active from time to time and producing more destruction and more scarring. A more speculative hypothesis is that renal tissue, once damaged by any means, may initiate a series of autoimmunizing events and hasten its own destruction by self-induced antibody formation in the absence of overt infection. Such a mechanism has been invoked to explain chronic thyroiditis and sympathetic ophthalmia, and it has been seen in kidney transplants.

In the chronic and quiescent phases of pyelonephritis the symptoms are far more subtle than in the florid, acute phase, and in fact may present symptoms as unobtrusively as in the present case. Hypotonia of the ureters with impaired peristalsis has been described in early pregnancy, while pressure on the ureters by the enlarging uterus of the third trimester has been blamed for relative urinary stasis and for what is termed "physiologic hydroureter." Some 2 per cent of pregnant women develop pyelonephritis, and renal infection has been incriminated as a major factor in the production of toxemia of pregnancy. The number of patients with pure toxemia of pregnancy, that is, those without antecedent renal disease or essential hypertension, is dwindling as we recognize forms of renal disease and hypertensive disease imposed on and perhaps modified by the gravid state.

We now have reached the point in our discussion where the dramatic appearance of severe hypertension should be explained. Was it really sudden in its appearance? We have no information about the patient for an entire year; could not the blood pressure have been climbing steadily during this period to the point where it became symptomatic? The causal relationship between pyelonephritis and hypertension, including malignant hypertension, has been the subject of many studies. Interstitial infection of the kidney is supposed to destroy vessels and lead to local, even segmental areas of renal ischemia which, as Goldblatt[3] has demonstrated, can give rise to sustained hypertension. At any point in the indolent progression of chronic pyelonephritis, an acute attack may precipitate accelerated hypertension. This patient, in addition, may have had some constitutional or hereditary factor which predisposed her to develop nephrosclerosis or "essential" hypertension at an early age. At least this idea is suggested by the family history of hypertensive disease and by the blood pressure of 130/90 after her first pregnancy.

I have little doubt that the development of uremia was the result of the progressive destruction of nephrons to the point where they were quantitatively insufficient to maintain chemical homeostasis. There is no evidence that this is a salt-losing form of nephritis, but the other chemical derangements are typical. I am somewhat at a loss to explain the severe depression of the bicarbonate ion in the absence of other chemical or even clinical manifestations of acidosis. Perhaps sulfates and organic acids were retained as well as phosphates. Possibly tachypnea and hyperpnea were present but not recorded.

I have no real explanation for the elevation of the sedimentation rate to 130 mm. per hour. However, it is a nonspecific test which depends partly on increased serum globulins for accelerated values. It is easy to explain the serum albumin of 2.4 Gm. in terms of continuing proteinuria. However, the serum globulin of 2.4 Gm. is both relatively and absolutely increased. Does it reflect some auto-immune mechanism? And is it responsible for the elevated sedimentation rate? Possibly, but one can only speculate.

Last, I must ask myself whether or not the patient could have had a diffuse glomerulonephritis. Certainly she could. However, she was a woman; she was a Negress; she had had three pregnancies; she harbored A. aerogenes in her urine. The chances that the renal lesion was pyelonephritis are much greater.

JIM HARRIS, M.D.: When the patient first was seen on the ward, we felt that she was in definite but mild congestive failure. Also, minimal periorbital edema was present on admission, but this disappeared spontaneously within the first two days. The service diagnosis was chronic glomerulonephritis.

MARDOQUEO I. SALOMON, M.D.: Kimmelstiel *et al.*[4] recently have challenged the idea that pyelonephritis is as common as many observers have reported. They feel that in autopsy material many of the cases so diagnosed represent nonspecific foci of scarring indistinguishable from ischemic changes and that there is no substantive evidence to support a bacterial etiology in a large number of these cases. Be that as it may, in my experience the elevated blood pressure values seen in chronic pyelonephritis rarely approach those seen in hypertension secondary to other forms of chronic renal disease.

PERRY BERG, M.D.: In August, 1960, the blood urea nitrogen and creatinine values indicated very good renal function. It is difficult to believe that chronic pyelonephritis could progress so rapidly in little over a year to compromise renal function so severely. I would think that there must be some acute process involved, probably acute glomerulonephritis.

DR. KRENTZ: According to the protocol the patient had significant urinary abnormalities dating back at least to 1958. Even considering that she was pregnant at the time, I cannot disregard these findings in view of the subsequent course.

MICHAEL S. BRUNO, M.D.: I am impressed by the patient's family history and would like to mention malignant hypertension as an etiologic factor.

MAXWELL L. GELFAND, M.D.: Because

of her age I think malignant hypertension a bit unlikely. It should be mentioned that many patients with toxemia of pregnancy have underlying renal disease.

Dr. Bruno: I agree that she was very young to have malignant hypertension as we usually see it, but we have seen this disease, albeit rarely, in patients under the age of thirty. I wonder if it is possible that her three pregnancies in rapid succession may have accelerated the appearance of hypertensive disease and whether indeed the toxemia in her last pregnancy may not have accelerated its course.

Marcel Tuchman, M.D.: A point against the diagnosis of chronic glomerulonephritis is that the patient had oliguria rather than polyuria which is seen so commonly in end-stage renal disease. Also, it is not necessary to have chronic renal disease to have an increased serum phosphorus; this can happen in acute renal failure as well.

Clinical diagnosis

Chronic glomerulonephritis

Dr. Krentz's diagnosis

Chronic pyelonephritis with necrotizing arteriolitis

Pathologic report

William B. Ober, M.D.: Needless to say, the operation performed was a needle biopsy of the kidney. It revealed a subacute to chronic glomerulonephritis (Fig. 1). Many of the glomeruli were hypercellular and showed synechiae and epithelial crescents (Fig. 2). A smaller number showed collapse of the capillary loop and early fibrosis. There was a superimposed necrotizing arteriolitis consistent with the accelerated course of the patient's hypertension. Almost all the arterioles showed either smudgy necrosis or concentric hyperplasia with some hyalinization (Fig. 3).

The patient died on the second day after the biopsy. An autopsy disclosed pale, swollen kidneys weighing 175 Gm. each. The capsular surfaces were smooth, and there were no petechiae. The corticomedullary junction was indistinct, but the cortices were not reduced in width. The microscopic features were identical with those seen in the bioptic material. There was nothing to suggest chronic pyelonephritis except for an occasional accumulation of lymphocytes beneath the epithelium of the renal pelvis. I would interpret this as something distinct from the glomerulonephritis, a low-grade chronic pyelitis, probably an ascending infection, consistent with the occasional recovery of A. aerogenes from the urine. Also at autopsy there was a moderate degree of cardiac hypertrophy, chiefly of the left ventricle, and a certain degree of pulmonary congestion but no frank edema.

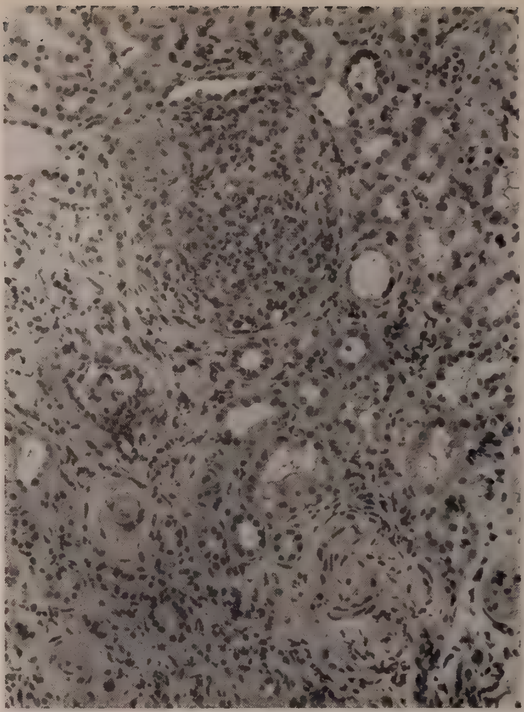


FIGURE 1. Medium-power view of kidney biopsy showing relatively well preserved architecture. There is no scarring, and the interstitial infiltrate is minimal. The glomerulus in the upper half of the field is hypercellular, and the arterioles in the lower half are hyperplastic.

For many years there has been much speculation about the nature of the glomerular lesion in severe toxemia of pregnancy, and it has been an open question whether the renal lesion of eclampsia resolves after delivery or progresses to chronic renal disease. When kidneys from patients dying

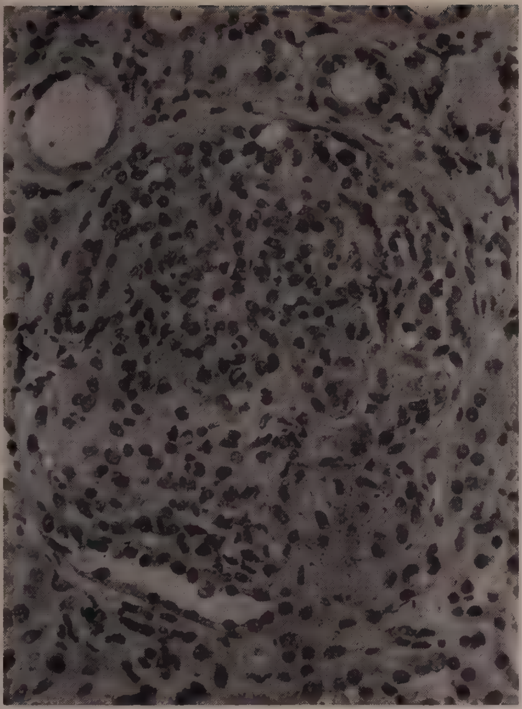


FIGURE 2. High-power view of the glomerulus in Figure 1. The visceral and parietal layers of Bowman's capsule are fused, and there is a characteristic crescent of proliferated glomerular epithelium.

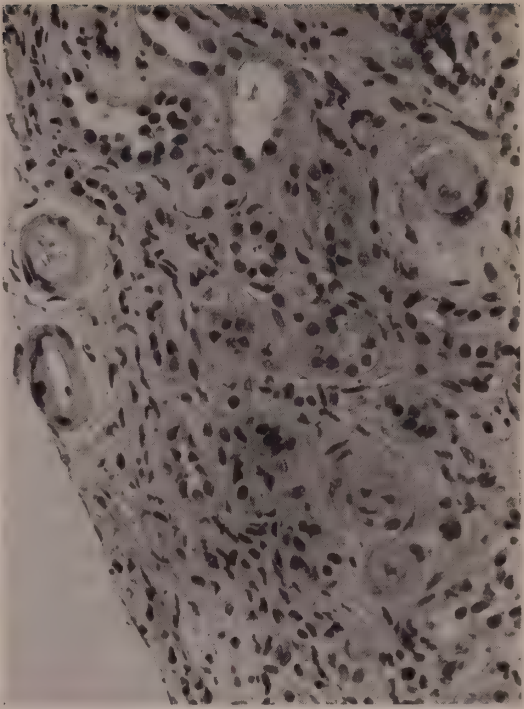


FIGURE 3. High-power view of the margin of the kidney biopsy showing several cross sections of arterioles, some showing concentric hyperplasia, some showing smudgy necrosis of the wall.

with pre-eclampsia or eclampsia are viewed under the light microscope, routine hematoxylin and eosin preparations afford little information beyond the fact that the glomeruli are swollen and relatively bloodless. A careful measurement of many glomeruli yielded the statistic that the glomeruli were 1.2 times larger than those in control kidneys, scarcely an impressive degree of swelling. Sections stained to demonstrate the glomerular basement membrane have yielded conflicting observations. Some observers have found occasional thickening of the basement membrane; others have failed to find substantive thickening.[5] A recent study by Altcheck,[6] using electron microscopy, has revealed the nature of the glomerular lesion in severe pre-eclampsia. The lesion is identified by a pronounced swelling of the cytoplasm of endothelial cells to the point of virtual obliteration of the capillary lumen. Not infrequently there is a dark-staining deposit within the cytoplasm of the endothelial cell. Occasionally such a deposit may appear to lie between the endothelial cell and the basement membrane, but the basement membrane itself is not thickened. There is also an inconstant increase in the number of intercapillary cells. Some observers have termed the intracytoplasmic deposit as "fibrinoid," but it is not the same as fibrinoid commonly seen in collagen diseases. Some observers have called the intercapillary cells "the mesangium," and this term has a traditional status in renal microanatomy. It is not difficult to visualize how this sort of lesion results in the reduction of glomerular filtration so characteristic of the pre-eclamptic state; however, the explanation for proteinuria remains to be found. Similar lesions were not found in control patients including those with essential hypertension and superimposed pre-eclampsia.

In general, the glomerular lesion of pre-eclampsia does regress after the evacuation of the uterine contents. However, Hopper *et al.*[7] have found some degree of persistence of the lesion in 1 patient on whom a rebiopsy was performed at five weeks postpartum. Further documentation is needed to determine how completely the lesion resolves and at what rate this process takes place. Also, whether it invariably resolves or whether it may persist and make some morphologic transition to a chronic glomerular lesion requires the study of a larger number of patients in a number of different clinics over a longer period of time.

To me, the interesting clinical feature of this case appears in retrospect. Utilizing the history the patient gave, one would conclude that she developed hypertension and albuminuria during her third pregnancy, that these features persisted, and that they terminated in chronic renal disease with renal failure, just about as good an example as one would want of pre-eclampsia progressing to chronic renal disease. However, a careful scrutiny of her charts at other hospitals indicates that this sequence of events is false. She first had albumin and cells in her urine during her second pregnancy. She was not hypertensive at that time, and she was asymptomatic. She may well have incurred some form of renal insult during this gestation or even prior to it, but after her first delivery. In any case, she entered her third pregnancy with antecedent renal disease, albeit it was not severe. Nonetheless, she did develop pre-eclampsia. By definition, this was not an "unprovoked toxemia"; it was toxemia secondary to underlying renal disease. Despite this, she did not really become hypertensive until after the delivery of her third child. Ergo, the hypertension was superimposed on the antecedent renal disease, and its morphologic correlative is the necrotizing arteriolitis. It is very important in this sort of case to have as precise chronologic data as possible, otherwise one may be led astray. If the precise sequence of events is not determinable even in retrospect, one cannot come to a rational conclusion.

Anatomic diagnoses

Subacute to chronic glomerulonephritis with necrotizing arteriolitis

Chronic pyelitis, slight

Cardiac hypertrophy, moderate

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Death rate of newborn premature infants

The death rate of newborn premature babies whose weight at birth was less than 2,501 Gm. was almost 30 times greater than for those of higher weight at birth and comprised more than 70 per cent of the deaths of newborn infants of known weight in New York City last year, according to *Patterns of Disease*, a monthly Parke, Davis & Company publication. Premature infants weighing less than 1,001 Gm. at birth have the least chance of survival, 88.2 per cent of these infants dying within twenty-eight days after birth.

Sponsored by the
Clinical Society of the
New York Diabetes Association

Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Lipoatrophic Diabetes

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IN 1946 LAWRENCE[1] described the syndrome of lipoatrophic diabetes as being characterized by: (1) a complete absence of subcutaneous, intra-abdominal, and perinephric fat; (2) insulin-resistant diabetes with little, if any, tendency to develop ketosis on the omission of administered insulin; (3) hepatomegaly with cirrhosis and splenomegaly; (4) hyperlipemia with cutaneous xanthomas; and (5) a greatly elevated basal metabolic rate without other evidence of hyperthyroidism. In addition the case Lawrence reported had generalized lymphadenopathy. He also discussed 2 cases reported previously[2,3] which appeared to be lipoatrophic diabetes. Since then 13 additional cases have been described making a total of 16 reported thus far (Table I).

This generalized lipoatrophy with its associated metabolic aberrations is to be distinguished from progressive lipodystrophy (Barraquer-Simons disease)[4] in which there is a symmetrical and slowly progressive loss of subcutaneous fat from the face and in more severe cases from the neck, arms, thorax, and abdominal wall, with a preservation or even an increase in the fat of the lower portions of the body. This disease is most common in young females, the etiology is unknown, and there are generally no significant related metabolic derangements. Some cases have been recorded, however, with elevation of the basal metabolic rate as well as disturbances of fat and carbohydrate metabolism.[1,2,5] The localized loss of subcutaneous fat often noted at the sites of insulin injections is unrelated to the syndrome of lipoatrophic diabetes.

Lipoatrophic diabetes generally has appeared by the age of fifteen but has been described as occurring from age three to age fifty. Twelve patients have been female and 4 male, while 14 have been white and 2 Negro. Its occurrence in 2 sisters has been the only instance in which a family history of the syndrome has been obtained. The afflicted females have had a rather masculine appearance due to the better definition of superficial muscles resulting from the disappearance of overlying subcutaneous fat.

The carbohydrate abnormality has been variable in severity as measured by the insulin requirements. In 6 patients 125 or more units of insulin were required daily, while in others a glucose tolerance test was necessary to make the diagnosis. Despite the excessive daily insulin requirements in the patient described by Schwartz, Schafer, and Renold,[6] the patient's plasma did not contain significant quantities of insulin-neutralizing factors or "antilipogenic" factors. Berson and Yalow[7] recently have demonstrated low levels of circulating insulin antibodies in this syndrome. Schwartz and associates[6] demonstrated persistent plasma insulin activity five months after discontinuing the administration of exogenous insulin as well as a diminished rate of degradation of insulin-I^{131} and a normal capacity to metabolize lipid loads.

TABLE I. Lipoatrophic diabetes*

Case	Investigator	Race	Sex	Age at Last Report (Years)	Age at Onset (Years)		Daily Insulin (Units)	Keto-nuria	Hyper-lipemia	Hepato-megaly	Spleno-megaly	Basal Metabolic Rate (Per Cent)
					Lipoatrophy	Diabetes Mellitus						
1	Lawrence[1] and Ziegler[2]	. . .	F	38 (died)	11	24	0	0	0	+	+	+57
2	Hansen and McQuarrie[3] Lawrence[1]	White	M	9 (died)	3	4	284	0	+	+†	+	Normal
3	Lawrence[1]	White	F	34 (died)	26	26	2,160	±	+	+†	+	+170
4	Berardinelli[9]	White	M	7 1/2 (died)	2 1/2	6 or less	0	0	+	+†	+	. . .
5	Berardinelli[9]	White	M	3	1/2	3	0	0	+	+†	+	. . .
6	Corner[13]	White	F	22	<14	15	125	0	+	+†	. . .	+45
7**	Craig and Miller[5]	Negro	F	21	<13	13	2,000	±	+	+	. . .	+40
8**	Craig and Miller[5]	Negro	F	17	<12	12	70	0	+	0	. . .	+45
9	Schwartz, Schafer, and Renold[6]	White	F	14	4 months	12	200	±	+	+†	0	+20
10	Hood[5]	White	F	55	42 or less	41	24	±	+	+	. . .	+95
11	Aarseth[5]	White	F	58	29 or less	50	68	0	+	+	. . .	+44
12	Conn[5]	White	M	12	7	8	360	0	+	+	. . .	+27
13	Conn[5]	White	F	28	6	21	0	0	+	+	. . .	Normal
14	Witzgall[5]	. . .	F	41	40 or less	40	80	0	+	+	. . .	+64
15	Davis[6]	. . .	F	9	<2	. . .	. . .	0	+	+	. . .	+44
16	Fontan *et al.*[6]	. . .	F	10 1/2	14 months	. . .	. . .	. . .	0	+	. . .	Normal

* Modified from Craig and Miller[5] and Schwartz, Schafer, and Renold.[6] † Cirrhosis demonstrated histologically. ** Sisters.

Studies with carbon^{14} glucose by Craig and Miller[5] indicated that the rate of oxidation of glucose to carbon dioxide was similar to that observed in normal and stable diabetic subjects. The rate of carbon dioxide production, however, was found to be abnormally high with the percentage of expired carbon dioxide derived from glucose less than normal, suggesting an abnormally large carbon dioxide production from nonglucose sources, perhaps fat. Hennes and Shreeve[8] found an abnormally large and rapid incorporation of carbon^{14} from acetate into triglyceride and cholesterol with a significantly diminished rate of disappearance of carbon^{14} activity from these lipids, indicating a slow turnover of these fractions. These findings suggest that the striking loss of adipose tissue in this condition is not due to an increased utilization of fat, since a more rapid disappearance of radioactivity than is normal should have been noted if such were the case, but rather to an inability to store and perhaps to synthesize fat in adipose tissue.

Ketonuria has been absent characteristically even with extreme hyperglycemia and glycosuria. Mild and easily reversible ketosis has been noted in response to a prolonged cessation of insulin administration, carbohydrate starvation, infections, and emotional trauma.[1,5,6] Ketoacidosis and coma have not been observed. The absence of ketosis has been noteworthy particularly in juvenile patients with this syndrome, since these are the patients who would be expected to develop ketosis and ketoacidosis in response to minor provocation or the withdrawal of administered insulin.

Hepatomegaly has been described in all but 1 of the reported cases and has been associated frequently with cirrhosis and splenomegaly but not with esophageal varices or increased abdominal veins.

Hyperlipemia and hypercholesterolemia of sufficient magnitude to render the serum milky have been common but not invariable findings. The reduction of blood glucose by insulin therapy has been accompanied by a decrease in lipemia, while the omission of insulin therapy with a rise in blood glucose has prompted an increase in lipemia,[1] suggesting a meaningful correlation between the control of the diabetes mellitus, as measured by blood glucose, and the level of blood lipids.

The basal metabolic rate has varied from normal to plus 170 per cent. No other evidence of hyperthyroidism has been noted. The results of protein-bound iodine and radioactive iodine uptake studies have been normal when performed.[6] In 2 cases subtotal thyroidectomy did not reduce the basal metabolic rate to normal. In Lawrence's patient[1] a subtotal thyroidectomy reduced the basal metabolic rate from plus 170 to plus 38 per cent at which level clinical stigmata of myxedema appeared. To abolish the myxedema completely it was necessary to administer 3 grains of thyroid daily, which raised the basal metabolic rate to plus 100 per cent.

There has been considerable interest in the pituitary and adrenal activity in this syndrome, but there is no definite evidence of hyperfunction of these endocrine glands. An increased rate of growth has been noted in at least 5 patients with this syndrome,[6] and hyperactivity of the pituitary gland has been suggested as a contributing factor.[6,9] A diminished rise in the plasma and urinary 17-hydroxycorticosteroids in response to corticotropin stimulation has been observed. A failure to suppress the excretion of urinary 17-hydroxycorticosteroids after ten days of therapy with 9-alpha-fluorohydrocortisone also has been noted.[6]

Etiology and pathogenesis

Lipoatrophic diabetes is a rare and most interesting syndrome. Its etiology and pathogenesis are understood no better than are the tantalizing interrelationships of its various facets. Several authors[5,6,9] have discussed the role of anterior pituitary hormone in the etiology of this syndrome. The ability of anterior pituitary extracts in animals to produce both diabetes mellitus and a mobilization of fat from adipose tissue to the liver is compatible with this syndrome.[10,11] In addition, many patients with lipoatrophic diabetes have manifested increased growth rates.[6] Coexisting lipoatrophic diabetes and acromegaly or gigantism has not been described.

The pathogenesis of the lipoatrophy is still a matter of speculation. Lawrence[1] hypothesized that since fat could not be stored in the normal fat depots it circulated in excess, and since there was little fat that could be mobilized ketosis did not occur. He considered the inability of insulin to convert glucose into stored fat to be the basis for the hyperglycemia and the insulin resistance. The work of Hennes and Shreeve[8] appears to substantiate this hypothesis. It could be postulated further that the increased growth rate noted in this syndrome might be due to a persistently increased insulin secretion in response to continuous hyperglycemia in the absence of increased amounts of growth hormone.[6,12] The increased secretion of insulin and the hyperlipemia might be responsible for the deposition of fat in other storage sites such as the liver, with resultant steatosis and ultimate cirrhosis.[6]

Pathology

Autopsy studies of 2 patients and tissue biopsies from 4 others have provided the details of pathologic changes in this syndrome. A complete absence of subcutaneous, intra-abdominal, and perinephric neutral fat was observed in one of the autopsied patients, while in the other neutral fat was noted to be absent from the skin as well as from the subcutaneous and perinephric sites. The netural fat content of the livers studied has been normal or increased in all cases except 1 in which the neutral fat was decreased while the cholesterol and phospholipids were normal. The histologic changes in the liver have been fatty infiltration, portal cirrhosis, and hypertrophic cirrhosis. Enlarged stone-hard parotid glands in 1 patient showed extensive lymphocytic infiltration and almost complete replacement of secreting acini by proliferated ducts. The pancreas was described as normal in 1 case and fibrotic in another; special studies of the islet cells were not performed in either instance. Subtotal thyroidectomies were performed in 2 cases: one gland showed many nodular areas of hyperplasia with small and irregular acini lined by columnar epithelium often forming papillary projections and containing reduced quantities of colloid; while the pathologist's report of the other was "colloid and foetal thyroid with extensive interacinar hyalinisation."[1]

The other endocrine glands of the 2 autopsied patients were considered normal. The lymph nodes often have been enlarged, and specimens obtained at autopsy or by means of biopsy have shown fibrosis, inflammatory changes, or dilatation of lymph sinuses with vacuolated esoinophilic material. On postmortem examination the two spleens were found to be greatly enlarged with chronic fibrosis noted in one and little abnormality on sections reported in the other. The heart and kindeys were found to be enlarged in 1 patient but were essentially normal histologically. There was no evidence of diabetic microangiopathy.

Course, prognosis, and therapy

The lipoatrophy has preceded the appearance of diabetes mellitus in most reported cases by one or more years. Occasionally the two conditions have appeared simultaneously. Four patients are known to have died. Death has occurred from five to twenty-seven years after the appearance of lipoatrophy and one and a half to fourteen years after the diagnosis of diabetes mellitus; death in 2 of the 4 cases has been secondary to hepatic disease and portal hypertension. The ultimate prognosis for those patients still living must be guarded, since they may suffer the consequences of progressive hepatic disease as well as the complications of diabetes mellitus.

There is no treatment for lipoatrophic diabetes other than effective control of the diabetes mellitus. The management of hyperglycemia and glycosuria is essentially the same as for other diabetic patients who do not have this syndrome. Insulin is required by most of the patients. The satisfactory control of the hyperglycemia decreases the hyperlipemia, with regression of the cutaneous xanthomas. Drastic alterations in dietary fat are not warranted since the lipemia cannot be reduced with a low-fat diet, and the body fat cannot be restored with a high-fat diet.[1,6] Experience with oral hypoglycemic drugs is limited in patients with lipoatrophic diabetes, but these drugs may have a place in the treatment of this syndrome.[5,6]

Summary

Lipoatrophic diabetes is a syndrome consisting of generalized lipoatrophy, insulin-resistant diabetes without ketosis, hepatomegaly with cirrhosis, hyperlipemia with cutaneous xanthomas, and an elevated basal metabolic rate without hyperthyroidism. The etiology and pathogenesis are not known but seem to be related to the inability of insulin to convert glucose into stored fat. There is no treatment at present other than control of the diabetes mellitus.

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Number thirty-five in a series of articles on Current Concepts in Diabetes Mellitus

Nutrition Excerpts

Prepared with the cooperation of the faculty of the Graduate School of Nutrition, Cornell University, Ithaca, New York

R. A. NELSON, M.D., Editor

Antihypercholesterolemic Agents

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IF IT BE ACCEPTED that hypercholesterolemia is one of the predisposing factors contributing to the genesis of atherosclerosis, then there is considerable rationale in the search for compounds with hypocholesterolemic action. Actually the search for such compounds, especially with respect to compounds that induce hypocholesterolemia by the inhibition of cholesterol synthesis, has been pursued actively for several years in a number of laboratories both in this country and abroad. While the "ideal" compound has not been found, a number of compounds with some utility as hypocholesterolemic agents have been encountered. This review is concerned with the pros and cons of a number of these compounds.

In recent years the individual biochemical reactions involved in the biosynthesis of cholesterol have been nearly completely worked out.[1] The biochemical sequence is essentially as follows: acetyl coenzyme A → acetoacetyl coenzyme A → hydroxymethyl glutaryl coenzyme A → mevalonic acid → mevalonic acid phosphate → mevalonic acid pyrophosphate → equilibrium mixture of isopentenyl pyrophosphate and dimethylallyl pyrophosphate → geranyl pyrophosphate → equilibrium mixture of farnesyl pyrophosphate and nerolidol pyrophosphate → squalene → lanosterol → other unknown sterols → desmosterol → cholesterol. Most individuals concerned with a search for hypocholesterolemic agents feel that an ideal inhibitor of cholesterol biosynthesis should be a compound that inhibits some reaction in the biochemical sequence between acetoacetyl coenzyme A and lanosterol. A compound that inhibits the activation of acetate to acetyl coenzyme A or the condensation of acetyl coenzyme A units to acetoacetyl coenzyme A would be expected to inhibit fatty acid biosynthesis as well as cholesterol biosynthesis. A compound that inhibits the conversion of one sterol to another might permit concentrations of various intermediary sterols to be built up in the tissue which would be as undesirable as the accumulation of cholesterol.

Nicotinic acid

The hypocholesterolemic effect of nicotinic acid when administered orally to human beings was first reported by Altschul, Hoffer, and Stephen[2] and has been confirmed widely. Relatively large amounts of nicotinic acid are required for a hypocholesterolemic effect, the daily dose being in the order of 3 to 6 Gm. Nicotinic acid causes peripheral vascular dilatation which may be troublesome, but the effect gradually wears off after one or two weeks. Nicotinamide (the amide of nicotinic acid) has no activity as a hypocholesterolemic agent. The mechanism of action of nicotinic acid is not entirely clear. Nicotinic acid inhibits the biosynthesis of cholesterol from acetate but not from mevalonate in rat liver homogenates.[3] Presumably, therefore, nicotinic acid inhibits reactions between acetate and mevalonate in the biosynthesis of cholesterol. On the other hand, Gaylor and de Villafranca[4] have shown in rats that large amounts of dietary nicotinic acid depress the incorporation of an injected dose of labeled cholesterol into serum lipoproteins. Sera from control and nicotinic acid-fed rats "bind" added cholesterol to the same extent in vitro. Apparently then the effect of nicotinic acid is not due to an altered structure of the lipoprotein molecule, but in some way nicotinic acid affects the physiologic incorporation of cholesterol into the lipoprotein molecule in the intact animal. Blood levels of cholesterol return to pretreatment levels following the discontinuance of nicotinic acid therapy. There is a certain amount of synergism between nicotinic acid and triparanol (MER/29) in lowering blood levels of cholesterol.[5]

Triparanol

Triparanol probably has received more study than any other antihypercholesterolemic drug since it was first shown that it lowers blood levels and tissue concentrations of cholesterol in experimental animals.[6] The locus of action of this compound in the biosynthetic sequence leading to cholesterol is between 24-dehydrocholesterol (desmosterol) and cholesterol itself.[7] Since desmosterol is present in the tissues of subjects treated with triparanol in lieu of cholesterol, it has been suggested that caution be exercised in the use of triparanol until more is known about the biologic properties of desmosterol. Triparanol is not without a certain amount of toxicity. In a small percentage of cases treated with triparanol, cataracts, hair changes, ichthyosis and other skin changes, depression of adrenocortic function, and other effects are seen.

Thyroid hormones and related compounds

It has been known for some time that the administration of thyroxin or triiodothyronine leads to an increase in the basal metabolic rate and a reduction in the blood level of serum cholesterol. Apparently the reduction of serum levels of cholesterol is not a consequence of the increase in the basal metabolic rate since 2,4-dinitrophenol causes an increase in the basal metabolic rate without an effect on serum cholesterol. Thyroid-stimulating compounds do not cause a decrease in the absorption of cholesterol and apparently cause an increase in the biosynthesis of cholesterol. It is likely that thyroid-stimulating compounds cause an increased elimination of cholesterol resulting in some hypocholesterolemic action.[8] Many synthetic compounds related in structure to thyroxin have been synthesized and shown experimentally to have hypocholesterolemic activity.[9] These compounds are not without undesirable effects since anginal attacks sometimes occur in patients with coronary heart disease.

A number of other compounds have been suggested as hypocholesterolemic agents but have not been satisfactory for one reason or another and therefore have not received a trial.

Farnesinic acid (farnesoic acid) a compound related in structure to farnesyl pyrophosphate, an intermediate in cholesterol biosynthesis, was shown early to be an inhibitor of cholesterol biosynthesis in rat liver homogenates.[10] It is known now that farnesinic acid inhibits mevalonic acid kinase, the enzyme that converts mevalonic acid to mevalonic acid phosphate.[11]

A level of 1 per cent of Δ-4-cholestenone in the diet of rats depresses the incorporation of acetate into the nonsaponifiable lipid fraction by about 70 per cent over a five-week period and lowers the serum cholesterol by approximately 50 per cent.[12] As a practical drug Δ-4-cholestenone is unsatisfactory because it leads to a marked inhibition of adrenocortic steroid production and because it causes an accumulation of dihydrocholesterol in the tissues.

Benzmalecene, N-[1-methyl-2,3-bis(p-chlorophenyl)-propyl] maleamic acid, has been shown to be a potent inhibitor of the incorporation of mevalonic acid into cholesterol by rat liver homogenates.[13] Unfortunately benzmalecene causes pyrosis or dysphagia, diarrhea, and transient vomiting so that the compound probably has no clinical utility.[14]

Alpha-phenylbutyrate has been reported

to be clinically effective in the treatment of hypercholesterolemia, but there is considerable controversy on this point.[15] It is known, however, that the compound inhibits cholesterol biosynthesis by interfering with the activation of acetate.[16] Since free acetate in contrast to acetyl coenzyme A is not an obligatory intermediate in cholesterol biosynthesis, it is apparent that alpha-phenylbutyrate in spite of its activity in vitro as an inhibitor of the incorporation of free acetate into cholesterol is not a suitable compound.

Many compounds related in structure to the sterol precursor mevalonic acid have been synthesized, tested, and found active as inhibitors of cholesterol biosynthesis in various in vitro systems.[1] For a number of reasons some of which are obvious and some of which are not obvious, these compounds apparently have not been tested further in experimental animals or in the clinic.

A text has recently become available which is a comprehensive but very readable storehouse of information on factors influencing cholesterol biosynthesis.[17] This text can be highly recommended for those having a further interest in the subject of this review.

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Number twenty-seven in a new series of Nutrition Excerpts

Miracle drugs . . . household words

Over the past twenty or thirty years medical contributions to the health and welfare of our people through careful research have been magnificent. That this is true is clearly evidenced by the fact that miracle drugs, lifesaving vaccines, and new types of equipment have become household words even for the man on the street.—*Charles S. Rhyne, former president, American Bar Association*

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
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Mixture of Tranquilizers, Lighter Fluid, Paint Thinner, And Iodine Poisonings

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Trifluoperazine, Meprobamate, Imipramine Hydrochloride, Promazine Hydrochloride, Codeine	34 years	Female

This incident was reported from out of town. The patient's physician called the Poison Control Center to inquire about the management of such a poisoning. We are indebted to Marshall F. Driggs, M.D., of Englewood, New Jersey, for the complete summary which he forwarded to us and which follows:

> This thirty-four-year-old woman was under psychiatric care for the past seven years for manic-depressive psychosis. There was a suicidal attempt in 1954 (gas and pentobarbital sodium) successfully treated at Englewood Hospital. She has been under tranquilizer therapy and during the past few months has been a patient at the Payne-Whitney Psychiatric Clinic. She was signed out from there by her husband one week prior to her entry here (Englewood Hospital).
>
> Three days prior to emergency room therapy at this hospital the patient was given 40 trifluoperazine, 40 imipramine hydrochloride, and 40 meprobamate tablets by her psychiatrist which, plus 25 promazine hydrochloride and 10 to 15 codeine sulfate tablets, all were seen by the patient's husband to be present in the bathroom prior to the present episode.
>
> The husband left at 8:30 A.M. and returned at 9:00 A.M. to find the patient stuporous. She was brought to the emergency room at 9:30 A.M. in a deep stupor.
>
> An examination on admission showed some reaction to painful stimuli plus small, spontaneous motions of the extremities. The pulse was 80, blood pressure 110/70, and respirations 30. The pupils were equal, responding poorly to light. There were weak knee and ankle jerks, and no conjunctival reflex was obtained at this time. The lungs were clear, and the heart sounds were of good quality. An examination of the ears, nose, throat, and abdomen produced negative findings.
>
> The admission diagnosis was cerebral depression from trifluoperazine, imipramine hydrochloride, meprobamate, promazine hydrochloride, and codeine overdosage, and depressive psychosis.
>
> Over the next twenty-two hours the patient was treated in the emergency room for the previously described diagnosis. She was given a stomach aspiration with the production of a fair amount of brownish, turbid fluid with some small, formed elements, but with-

out any demonstrable capsules or pills. Over the first two hours in the emergency room, the stupor became Grade III coma, that is, the pupillary reflexes were barely present. The knee, ankle, and biceps jerks were not obtained.

> Shortly after admission the patient was started on a continuous infusion of 5 per cent glucose in saline, with the addition of metaraminol bitartrate (Aramine bitartrate) when the blood pressure dropped to 75/60. The following laboratory data were obtained: The blood sugar was 178 mg. per 100 ml., urea nitrogen 15 mg. per 100 ml., and carbon dioxide 26, sodium 145, potassium 3.6, and chlorides 107.7 mEq. per liter. An airway was placed during the whole hospital stay. A Foley catheter was inserted. No therapy with analeptics was given. However, the patient was put on metaraminol bitartrate in the infusion. At 2:00 A.M. she was awake but drowsy, and at 2:45 A.M. she was awake and alert. At 7:00 A.M. she was up in a chair and was quite lucid. At 8:00 A.M. she was examined thoroughly, and at 9:00 A.M. she was transferred from the Englewood Hospital Emergency Room to the Gracie Square Hospital via car with her husband and a police officer for further psychiatric care.
>
> The patient was admitted to Gracie Square Hospital on April 14 and was discharged on May 19. While in the hospital, she received eight electroshock treatments and concomitant psychotherapy, with resultant continued improvement. The diagnosis made at Gracie Square Hospital was schizophrenic reaction, schizo-affective type. As of the date of her last visit with the psychiatrist in July, 1961, the patient was able to carry on her activities.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Charcoal Lighter Fluid	21 months	Male

The Poison Control Center was contacted by the pediatrician, Alvah M. Weiss, M.D., relating to the management of this patient who was practically in a moribund condition. The physician inquired whether corticosteroids would be of value. Since we have had information in which favorable outcomes with the use of corticosteroids were recorded, we suggested that such therapy might be used in this case.

The following report from the physician about the course of the illness may be of interest:

> The patient ingested charcoal lighter fluid. He vomited on the way to the hospital and was cyanotic on admission. After recovery from the initial episode he seemed in good condition. About thirty-two hours after the ingestion he went into a semicoma with pulmonary edema. Hydrocortisone was given intramuscularly, and intravenous cut-down was started with glucose solution. The response was dramatic with a temperature drop from 106.6 to 99.4 F. within twelve hours. The lungs gradually cleared with classic lobar pneumonic signs on the right lung posteriorly.
>
> This was an interesting outcome and I am sure that the cortisone medication was life saving. I wonder if it should not have been given IM from the start and not orally as we did. Do you have others where the cortisone was given IM with lessening of intense febrile response? It is difficult, I realize, to quantitate these cases.
>
> I want to thank you for your kindness and help in talking to me about this patient. It was a real service and I want to wish you well in your extremely helpful work.

In reply to Dr. Weiss we indicated that the content of the charcoal lighter fluid is chiefly colored refined kerosene. We do recall another case where in addition to pulmonary involvement, the child developed a temperature of 105 F., and after the administration of steroids intramuscularly there was a dramatic improvement in the general condition as well as a drop in the temperature.

In the NEW YORK STATE JOURNAL OF MEDICINE* I reported a case which was told to me by a physician from Texas where similar dramatic results also were obtained. I believe that the child's temperature was also very high and it dropped following the administration of steroids.

Although we are extremely conservative with the use of steroid therapy and firmly believe that it should be used only when it is the sole effective measure or when other therapeutic agents fail, we believe that in such cases as have been described the use of steroids is justified. It has been reported recently that corticosteroids have been used in the treatment of aspiration pneumonitis in Canada for over four years with uniformly good results.

The serious illnesses resulting from the ingestion of petroleum fractions present in barbecue fluids, cigaret lighter fluids, insecticides, and so forth throw an interesting light on the definition of poisons. Normally, these materials are not poisons, but when ingested, because of their physical properties, these products represent a "mechanical" type of poisoning rather than a systemic toxic effect. The term poisoning therefore must be broadened to include the additional varieties which may exert a deleterious effect on cells and organs and on the entire body functions. In the light of the broader definition, anoxia also should be included as an example of poisoning.

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* Jacobziner, H., and Raybin, H. W.: Quinine, aspirin, kerosene, and analgesic intoxication, NEW YORK STATE J. MED. 60: 3461 (Nov. 1) 1960.

Incident 3

Substance Ingested	*Age*	*Sex*
Paint Thinner	2 years	Male

This case was reported by a physician from New Jersey. The patient's father was cleaning paint brushes when the telephone rang. He left the child alone with the brushes and paint thinner for only a few minutes. When he returned, he found that the boy had drunk a small amount of the paint thinner and was choking and coughing. About five minutes following the ingestion the patient vomited spontaneously. He was taken to a hospital emergency room where his stomach was lavaged with water twenty minutes following the ingestion.

The symptoms on admission were vomiting, dyspnea, cyanosis, and coughing. An examination of the patient revealed rales in the lower lobe of the right lung, and x-ray films showed evidence of infiltration at the right mid-base in a very small area which cleared prior to discharge.

The patient was treated with antibiotics and supportive therapy as well as oxygen. After fourteen days all symptoms, including the x-ray findings, subsided, and the patient was discharged as cured.

The physician reported that the label on the product does not list the ingredients and that no mention is made relating to the danger that may be associated with the use of such a product. As a matter of fact, the label stresses that it is "safe." The physician himself called the president of the manufacturing company because the composition of this particular brand was not available from other sources.

The new Federal Hazardous Substances Labeling Act will be of great assistance in eliminating this important gap in information since all such products will be required to indicate ingredients and also will give some guide as to their toxicity.

Incident 4

Substance Ingested	*Age*	*Sex*
Iodine	11 years	Female

The medication was used as a throat gargle by the household. The patient used iodine in water as a gargle and suddenly became panicky and almost hysterical since the mixture was very pungent. The family did not realize what had happened and called their doctor who advised hospitalization. The parents immediately administered as a first aid measure the white of an egg, milk, and black coffee. Since no stomach tube was available in the first hospital to which the patient was taken, she was transferred to another hospital for indicated treatment. The stomach was lavaged with saline one hour following the ingestion, and after a short period of observation the patient became symptom-free and was sent home.

It would appear that physicians are still conditioned by the older concepts concerning iodine ingestion. For many years now, the USP iodine has been reduced from $7^1/_2$ to about 3 per cent. This alone has resulted in a great decrease in the incidence of iodine poisoning. The so-called "tamed" iodine solutions, of which the present case is an instance, represent still weaker solutions, mostly about 1 per cent. The case reported would appear to be a good example of over-treatment which, at times, can be just as harmful as under-treatment.

In addition, since there is a specific relatively safe chemical neutralizer for iodine, that is, sodium thiosulfate, it would appear that the administration of the latter actually should be the treatment of choice for all present-day iodine poisonings. Although the sodium tetrathionate produced is claimed to be toxic, the amounts involved in the therapeutic procedure are within the safe range and should not be a deterrent to its use.

Number eighty-six in a series of Accidental Chemical Poisonings

Maternal Welfare

Prepared by the Subcommittee on Maternal and Child Welfare, Committee on Public Health and Education, Medical Society of the State of New York

EDWARD C. HUGHES, M.D., Syracuse, Editor

Stage of Pregnancy at which Patients Start Prenatal Care

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State University of New York Upstate Medical Center

THE CENTRAL NEW YORK Maternal and Perinatal Mortality Study† recently completed a study to ascertain the time of pregnancy at which patients start prenatal care. The survey was made as a "spot check" of the metropolitan Syracuse area during May, June, and July, 1961. Data on 711 patients are presented.

Evaluation of data

It should be made clear that the data presented do not represent a true cross-section of the average pregnant population of the Syracuse area. Data were obtained on all clinic patients in the six prenatal clinics conducted, but the private patients represented only a relatively small number of all the private patients. An attempt was made to obtain a reasonably accurate distribution between patients under the care of general practitioners and obstetric specialists, but the effort was not accomplished. The private patient material is based on data submitted by 2 physicians who include obstetrics in their general practice and 12 physicians who are classified as obstetric specialists. The data are also influenced by the fact that one local hospital admits a disproportionately large number of patients who have had no prenatal care. This hospital, for many years, has conducted a large service for out-of-wedlock mothers.

Data were collected on a current basis and included the weeks of gestation at the first prenatal visit (based on the estimated date of conception), the number of previous pregnancies, and the circumstances under which the patient made the first prenatal visit. The circumstances were subdivided to include the following: a routine examination—patient who came to the physician or to the clinic for routine prenatal care; a differential diagnosis—patient who came to find out if she was pregnant; and an examination because of symptoms and/or signs—patient who came in because she had vaginal bleeding, nausea, and/or vomiting, and because of "other" signs or symptoms.

The data were desired only on patients who in the current pregnancy sought prenatal care of their own volition, and the following patient categories were excluded: (1) patients currently under care, that is, sterility cases, chronic aborters, gynecologic disorders, and those under care for any medical or surgical condition; and (2) "transfer cases," that is, patients who previously had been under care by another physician or clinic for the present pregnancy.

Patients in labor who had had no prenatal care and who entered any of the five Syracuse

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* Secretary of the Subcommittee on Maternal and Child Welfare.

† Supported by the Health Department of the State of New York through a grant from the Empire State Medical, Scientific and Educational Foundation, Inc.

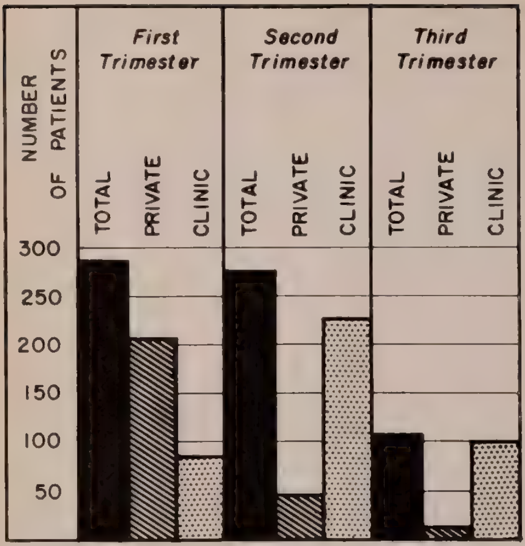

FIGURE 1. Stage of pregnancy at which 666 patients started prenatal care.

hospitals which have active obstetric services were recorded for the study by the hospitals. The data on 711 patients are presented. The time of pregnancy, by trimesters (Fig. 1), when patients started prenatal care is presented in Table I.

It is gratifying that this spot check reveals that over 78 per cent of the private patients began prenatal care before the fourteenth week of pregnancy. This is in contrast to about 21 per cent for the clinic cases. The difference, of course, comes as no surprise and re-emphasizes the amount of attention that the clinic group needs. This need is also apparent from the data on patients who had no prenatal care. These 45 patients represent approximately 1.5 per cent of the total deliveries in Syracuse during the period of the survey: 2,857 live and 50 stillbirths for a total of 2,907 deliveries during May, June, and July, 1961.

The week of gestation during which the patients first sought medical care is tabulated in Table II. It would be more accurate to use the term "estimated week of gestation." The time element was determined on the basis of menstrual history and, in most instances, it was supplemented by a pelvic examination. The series was not limited to patients with regular menstrual cycles. Public health nurses were responsible for recording the data in the clinics. Data on the private patients were recorded according to the physicians' discretion. Nurses were carefully briefed and physicians received an explanatory letter on the method of recording of data on prepared forms. Detailed data were obtained for all weeks of gestation, but it seems practical to limit the breakdown of details to the first trimester.

Table III presents the time of beginning prenatal care for 288 patients in the first trimester, according to gravidity.

The circumstances that prompted the patients to seek prenatal care in the first trimester are recorded in Table IV. It was anticipated that some patients could not be categorized specifically, since there might be an overlapping of the groupings of "routine," "differential diagnosis," and "because of symptoms." Explanatory instructions requested that the patients be placed in the various categories according to the judgment of the physician. It seems encouraging that 65 per cent of the patients apparently started prenatal care in the first trimester, principally because they felt it was a good idea. Approximately three quarters of the women (72 per cent) who

TABLE I. Data of prenatal care of 711 patients by trimesters

Prenatal Care	Total Patients Number	Total Patients Per Cent	Private Patients Number	Private Patients Per Cent	Clinic Patients Number	Clinic Patients Per Cent
Started						
First trimester	288	43.2	204	78.2	84	20.7
Second trimester	273	41.0	46	17.6	227	56.1
Third trimester	105	15.8	11	4.2	94	23.2
Total patients	666		261		405	
Patients with no prenatal care (entered hospital in labor)	45	—	9	—	36	—

TABLE II. Weeks of gestation at which patients started prenatal care*

Weeks of Gestation	Patients Total	Patients Private	Patients Clinic
3	2	2	0
4	5	5	0
5	15	11	4
6	21	15	6
7	26	22	4
8	65	48	17
9	22	14	8
10	47	37	10
11	15	12	3
12	59	31	28
13	11	7	4
14	20	12	8
15	7	3	4
16	47	9	38
17	7	2	5
18	17	4	13
19	4	0	4
20	58	6	52
21	20	2	18
22	13	3	10
23	12	2	10
24	43	1	42
25	12	0	12
26	13	2	11
27	8	1	7
28	27	1	26
29	3	0	3
30	7	0	7
31	3	2	1
32	20	2	18
33	8	2	6
34	8	0	8
35	8	1	7
36	6	1	5
37	1	0	1
38	1	0	1
39	2	1	1
40	3	0	3
TOTALS	666	261	405

* These figures do not represent a population relationship, since all clinic prenatal patients who met the requirements of the survey (during May, June, and July, 1961) are included, but only a relatively small number of private patients in the Metropolitan Syracuse area are included.

TABLE III. Patients reporting in first trimester according to gravidity

Gestation (Weeks)	Number of Patients	Gravidities 1	2	3	4	5+
3	2	0	0	1	1	0
4	5	0	2	0	2	1
5	15	5	3	4	2	1
6	21	3	4	7	3	4
7	26	5	7	4	7	3
8	65	13	19	15	8	10
9	22	1	5	8	3	5
10	47	6	12	12	7	10
11	15	2	4	2	3	4
12	59	14	7	15	10	13
13	11	5	3	1	0	2
TOTALS	288	54	66	69	46	53

TABLE IV. Reasons 288 patients first sought prenatal care in first trimester

Reason for Care	Number of Patients	Per Cent
Routine	187	64.9
Differential diagnosis	45	15.7
Signs and/or symptoms	56	19.4
TOTAL	288	

TABLE V. Signs and/or symptoms showing why 57 patients first reported for prenatal care in first trimester

Signs and/or Symptoms	Number of Patients	Per Cent
Vaginal bleeding	27	47.4
Nausea and/or vomiting	23	40.3
Other	7	12.3
TOTAL	57	

started prenatal care in the first trimester were private patients.

The signs and symptoms which were responsible for 57 patients seeking care in the first trimester are analyzed in Table V. Of these, 47.4 per cent reported because of vaginal bleeding, 40.3 per cent reported because of nausea or vomiting, and 12.3 per cent reported for various other reasons. The vast majority of this category of patients were under the care of private physicians. Only 5 clinic patients registered because of signs or symptoms. Perhaps fewer signs and symptoms occur among the prenatal clinic clientele, but it is more likely that clinic patients simply do not interpret the abnormalities as being of sufficient significance to indicate their seeking medical care. The pattern reversed in the middle and last trimester, with more clinic patients registering because of signs or symptoms than private patients.

Comment

One of the reasons for this spot survey was to obtain background information from the viewpoint of faulty first trimester physiology. There is current interest in the "hazards of the first trimester" in terms of the consideration of postconceptional environmental causes in relation to congenital anomalies. Faulty physiology involves some aspects of fetal wastage and, perhaps, other facets of perinatal mortality and morbidity.

The Committee on Maternal and Child Care of the Council on Medical Care of the American Medical Association recommends that "An adequate history during the nine months of pregnancy should be recorded on the clinical record with particular attention paid to infection and chemical stresses early in pregnancy."[1] There seems to be a feeling that accurate mass clinical data are needed for evaluating the role of environmental factors during pregnancy in relation to fetal abnormalities. Such data seem of importance, since they could contribute to various approaches of a preventive nature.

The relatively selected data in this spot survey show that a considerable number of private patients start prenatal care in the first trimester. The number starting care from the third to the eighth week is not large. The anticipated findings in the prenatal clinic group demonstrate that, regardless of first trimester hazards, much effort is needed in terms of the over-all need for better prenatal care in this group.

There are many conflicting reports on the incidence of congenital anomalies due to maternal German measles infections. Evidence presented by Lock *et al.*[2] that the highest incidence of serious malformations (50 per cent) results when German measles infection occurs in the first four weeks of the first trimester seems sufficiently well documented to be accurate. We feel justified in pointing out that a clinical observation of patients very early in gestation is important, since there may be parallels to the German measle situation. This statement is made with full knowledge of the many practical problems involved, including the establishment of a diagnosis of pregnancy in the very early weeks of pregnancy. The concept needs to be accepted even with our present feeling that the perinatal problem concerns primarily what might be called "the hazards of late pregnancy complications and the stress of labor and delivery to the fetus."

There is little doubt that prematurity presents a major obstacle to progress in solving perinatal problems. The question arises as to whether or not real progress in this area will be made unless breakthroughs are made which will afford preventive technics concerning the many etiologic factors involved in premature labor.

One facet of the over-all approach to the perinatal problem seems to involve how much would be accomplished by a clinical acceptance of the idea of starting prenatal care shortly after conception and if such a concept of prenatal care could be translated into practical usage. The vast majority of pregnancies involve normal physiology, and meticulous data would be useful in terms of fetal wastage and perinatal problems in relatively few cases.

The preventive approach to the perinatal problem is deserving of consideration. A most important approach to the perinatal mortality and morbidity problem, which is currently practical, consists of the careful recording of clinical data and of making this information available for the efficient functioning of hospital perinatal mortality committees.

766 IRVING AVENUE,
SYRACUSE 10

ACKNOWLEDGMENT. Acknowledgment is made to the private physicians and to the Syracuse Department of Health for their active cooperation in the survey.

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Case Report

Toxic Epidermal Necrolysis (Lyell)

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In 1956 Lyell[1] gave the name "toxic epidermal necrolysis" to an extraordinary skin disease in which the skin appeared extensively scalded. He indicated that Lang and Walker[2] had described a similar case in 1956, and Soltermann,[3] in a subsequent case report, culled an assortment of isolated cases of an apparently similar nature from the earlier literature. Potter, Auerbach, and Lorincz[4] were the first to use this name in the American medical literature when they described a child with the disease.

It seems worth-while to report the following 2 instances of the disease to increase awareness of it and to point up the possible ineffectiveness of steroid therapy in its treatment.

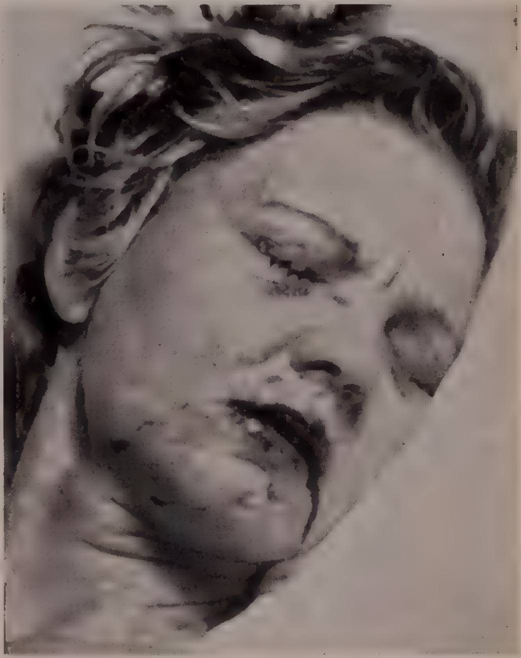

FIGURE 1. Case 1. Hemorrhagic lesions of lips, exudative, crusting lesions of eyelids, and erythematous eruption of face and neck.

Case reports

Case 1. A thirty-seven-year-old white woman entered Meadowbrook Hospital on April 11, 1960, because of a generalized skin eruption of two days duration.

Three weeks before admission her family doctor had given her vitamin B_{12}, ACTH, and a preparation containing phenylbutazone for pain in her right knee. This symptom had subsided quickly, but two weeks later she developed an upper respiratory infection with a cough productive of mucoid sputum. She received proprietary preparations containing thenylpyramine, dihydrostreptomycin, and penicillin G, but continued to feel ill and to complain of occasional nausea and vomiting.

Two days before admission her eyes began to burn and itch, her lips blistered and became swollen, and swallowing became painful. Within the next few hours a nonpruritic, macular rash appeared on her trunk and became almost generalized during the next two days. During this time her face became puffy, a fever developed, and she complained of increasing malaise, burning of the soles of her feet, mild dyspnea, and burning and frequency of urination. Streptomycin, tetracycline, and penicillin G, given after the onset of the rash, had no apparent effect.

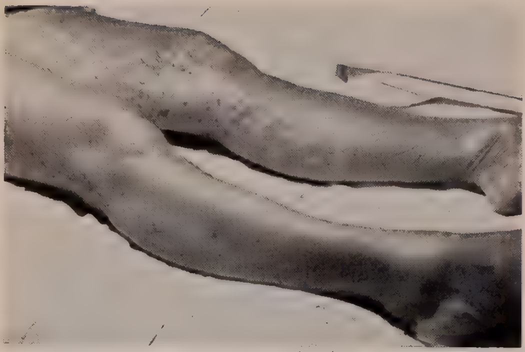

FIGURE 2. Case 1. Nonblanching macular lesions, both discrete and confluent, of extremities. Wrinkling above left knee and linear creases of the skin of the left leg are signs of epidermolysis.

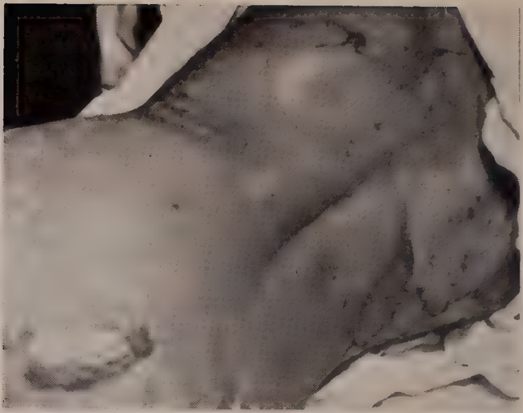

FIGURE 3. Case 1. Extensive denudation of back, superimposed on widespread purpuric erythema. The dissociation between erythema and epidermolysis is seen clearly in the large denuded area of the right posterior aspect of the thorax. Note epidermolytic wrinkling of the skin in the right lumbar area.

On admission the patient appeared acutely ill, but was mentally clear and cooperative. Her temperature was 104.6 F., and her blood pressure was 95/60. She had a purulent conjunctivitis, and there was a clear discharge from her nose. Her lips were swollen and covered with hemorrhagic crusts (Fig. 1), and her oral mucosa had largely desquamated.

Her face, neck, trunk, and extremities showed a widespread eruption (Fig. 2). The elementary lesion appeared to be a dark red, nonblanching macule of about $^1/_2$ cm. in diameter and surrounded by a zone of lighter erythema. The lesions had become confluent over extensive areas, and there were a few bullae which expanded laterally when pressed. The Nikolsky's sign was universally positive, and the skin on her soles was elevated into massive bullae.

The results of the remainder of the physical examination were within normal limits except for rales and wheezing over the left lower lobe of her lung and scattered soft rhonchi and wheezes throughout both lungs.

In the belief that the patient had a drug eruption, she was given prednisone orally, 80 mg. a day. During the next few days her fever abated and her general condition improved somewhat, but broad areas of skin sloughed off her back and extremities (Fig. 3). Nursing care was difficult, since even the slightest manipulation removed more skin.

At the end of the first week of hospitalization the skin remained in a static state of extensive, inflamed denudation, and her fever began to rise again. There was no response to erythromycin and chloramphenicol, supportive intravenous fluids, continued high doses of soluble cortisone sodium succinate, and blood transfusion. Her fever gradually became higher, and her general condition worsened. She died on April 21, 1960, ten days after admission, with no essential change in her dermatologic condition.

Laboratory findings. A postmortem examination cited acute purulent staphylococcal bronchopneumonia (Staphylococcus aureus, coagulase positive) as the immediate cause of death. There were no abnormal findings on the chest x-ray films at the time of admission, but her sputum showed clusters of cocci within leukocytes twice during the course of her illness (April 9 and 20), and a coagulase positive Staph. aureus was recovered from the second specimen. Cultures from the eyes, nose, and throat on admission had shown hemolytic Staph. albus, coagulase negative. Three blood cultures done on April 8, 18, and 20 were sterile.

The blood cell count on admission was 15,200 white cells with 57 per cent polymorphonuclear leukocytes, 42 per cent lymphocytes, and 1 per cent monocytes. At the end of the first week the white blood cell count was 9,750 with 77 per cent polymorphonuclear leukocytes, many of which showed toxic granulation, and 23 per cent lymphocytes. The white blood cell count rose to 27,450 on the day before the patient's death. The initial hematocrit value of 33 was maintained well throughout the illness.

The patient had persistent albuminuria (2 to 3 plus), glucosuria (trace to 4 plus terminally), hematuria (a few erythrocytes), and pyuria (8 or 12 white blood cells with occasional clumps). Her fasting blood sugar and urea nitrogen were normal. A urine culture done on April 9 was negative, but on April 21 a nonhemolytic, coagulase positive Staph. aureus was recovered. At autopsy the kidneys showed only simple congestion.

The sodium, chloride, potassium, and carbon dioxide-combining power were within essentially normal range during the entire course, but there was a gradual decrease in serum albumin. On admission the albumin was 4.7 Gm. per 100 ml. and the globulin 1.7 Gm. per 100 ml. On the day before death these values were 2.6 and 2.4 Gm. per 100 ml. respectively.

The blood serologic studies were negative for syphilis, cold agglutinins, and the lupus erythematosus phenomenon. Agglutinins for typhoid, paratyphoid, and brucellosis were absent, but proteus OX-19 agglutination was positive 1:40. A blood specimen drawn on April 11 was reported as showing no influenza A, influenza B, Q fever, psittacosis, mumps, or measles; the herpes simplex titer was 14.

Case 2. A two-year-old white girl entered Meadowbrook Hospital on September 1, 1960, because of fever and a skin eruption of three days duration.

She had been well until one week before admission when her parents noticed "many mosquito bites" on her body. These lesions had apparently subsided spontaneously.

Three days before admission her eyes became puffy. Later in the day she developed salivation, a discharge from her eyes and nose, and a red eruption of the skin on the lower aspect of her trunk. During the next two days the eruption spread to the rest of her trunk and to the proximal portions of her extremities. At the same time blistering and exudative lesions appeared on her face and neck, and she became progressively anorectic, constipated, and febrile.

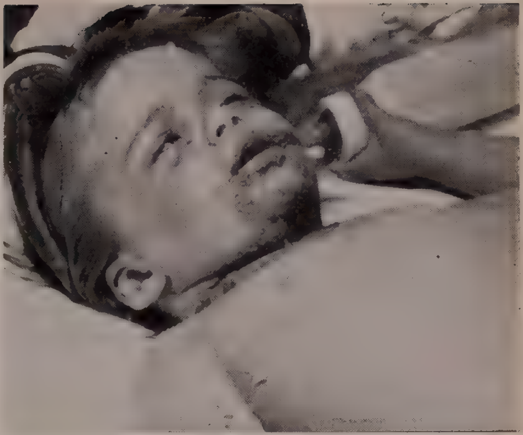

FIGURE 4. Case 2. Exudative and crusty lesions about mouth and neck; eyes and ears are less involved. Early epidermolysis present on right side of thorax and on the right side of the forehead. The associated diffuse erythema does not show up well in the photograph.

On admission the child appeared acutely ill. Her temperature was 104.6 F., pulse 130, respirations 24. She slept constantly except when being examined. When awake she was irritable and her skin seemed tender. There were purulent discharges from her eyes, ears, nose, and throat. Her tonsils were enlarged and reddened and her pharyngeal and vaginal mucous membranes showed patchy inflammation. Her neck and circumoral areas showed sharply demarcated, crusted, impetiginous lesions (Fig. 4); her trunk and extremities had a diffuse erythema. A few bullae, which extended laterally when pressed, were noted on her neck and axillas, and the Nikolsky sign was positive on all of her glabrous skin.

The patient was placed in an oxygen tent and given intravenous fluids, penicillin, and chloramphenicol. ACTH was given both intramuscularly and intravenously. Within forty-eight hours there was a remarkable improvement: the impetiginous lesions of her face and neck had dried and the desquamation was beginning to heal. Both antibiotic and corticosteroid therapy were gradually decreased, and she was discharged essentially well at the end of a week.

Laboratory findings. On admission the

white blood cell count was 15,000 with 4 stabs, 72 segmented cells, and 24 lymphocytes. Two days before discharge it was 22,800 with 47 polymorphonuclear leukocytes, 48 lymphocytes, and 4 eosinophils.

When the patient entered the hospital, the blood glucose, blood urea nitrogen, sodium, potassium, and chloride were of normal value. The bicarbonate radical was 14 mEq. per liter, and the urine showed 1 to 3 red blood cells, 10 to 15 leukocytes, and 1 plus acetone. The result of a chest x-ray was negative, and the antistreptolysin titer was 12 Todd units.

Cultures from the crusted neck and chin lesions grew a coagulase positive Staph. aureus, but a blood culture taken on admission was sterile.

Comment

The diagnostic feature of toxic epidermal necrolysis is the generalized Nikolsky phenomenon. The tendency for the epidermis to slide off under the slightest pressure soon leads to the large denuded areas which are so prominent in most of the photographs of published cases. Soltermann[3] aptly described his patient as "slipping away from the fingers" when grasped and, as Lyell[1] pointed out, the blebs so often seen appear to be "almost incidental" to this widespread epidermolysis.

A second element in the picture is erythema. It usually is diffuse, but sometimes is spotty and occasionally purpuric. In conjunction with the peeling, it tends to produce the scalded appearance described by Lyell. In the first case reported here, the consultant ophthalmologist, J. T. Calaviere, M.D., noted that the eyelids appeared recently severely burned.

The precise relationship between the epidermolysis and the erythema, however, is not clear because both of my patients had a positive Nikolsky sign in areas of unreddened skin. This was also noted by Rook.[5] It seems possible that these two major manifestations of the disease may be independent, or dissociable, phenomena.

Etiology. Most observers have been inclined to view toxic epidermal necrolysis as an allergic or toxic response of some sort. In a number of patients there has seemed to be a significant relationship to drug ingestion, and Soltermann[3] has argued cogently in favor of considering the disease a manifestation of drug allergy. In our era, in which an abundance of therapeutic chemicals is so often and so indiscriminately applied, one cannot categorically refute this possibility.

In the second case, however, no significant drug history could be obtained and it is possible that the real culprit was actually lurking further back in the sequence of causality. Most of the reported cases had a precedent illness, often of a systemic nature, such as Hodgkin's disease,[6] diarrhea,[5] or impetigo.[7,8] In my first patient the negligible response to adrenal corticosteroid therapy was suggestive, though hardly conclusive, evidence than an allergic drug eruption was not involved. The previous, and possibly continuously progressive, respiratory infection may well have been a significant etiologic factor.

Of all of the conventional bullous diseases, toxic epidermal necrolysis seems to parallel erythema multiforme most closely. Both diseases are relatively short-lived reactions, and both, when causes can be suggested, tend to be associated with drugs or specific diseases. In my first patient the resemblance to erythema multiforme was striking, and this was also Lang and Walker's impression in both their reports.[2,9] On the other hand, the histologic picture, which usually displays little or no dermal inflammation and a variable plane of cleavage in the epidermis, does not fit any defensible stretching of the present concept of erythema multiforme.

Potter, Auerbach, and Lorincz[4] suggest that toxic epidermal necrolysis may be the disease described in the past as acute, or butcher's, pemphigus. Soltermann[3] explicitly denied this relationship, and the negative blood cultures in both of my cases would seem to reinforce his position.

In 1960 Asboe-Hansen[10] described a sign which he considered to be diagnostic of pemphigus vulgaris. This sign, in which the bulla spreads laterally through the acantholytic epidermis when pressed, was elicited in both my patients. Since toxic epidermal necrolysis has not been considered to be a form of pemphigus vulgaris, it seems probable that this sign, like Nikolsky's sign, is not entirely specific.

TREATMENT. There is no real evidence that any particular treatment has been either specific or effective in the small number of patients recorded to date. In some cases recovery was spontaneous; in others it followed antibiotic, or combined antibiotic and corticosteroid, therapy. But one may ask whether they might not have recovered without medical intervention.

In my first patient, at first treated by steroids alone, there was a slight temporary improvement in the patient's general condition, but at no time was there any sign of epidermal regeneration. In view of her death from infection, despite subsequent antibiotic therapy, it seems likely that the prolonged steroid therapy was deleterious.

In the child in Case 2 the course of the disease was the same as in the 3 children reported previously in the literature: short and benign. The patient appeared so critically ill on admission, however, that it was not felt safe to withhold treatment.

Summary

Toxic epidermal necrolysis is a singular disease entity in which a combination of epidermolysis and erythema produces a generalized Nikolsky sign and makes the patient appear scalded. It is probably a toxic or allergic skin response unrelated to the orthodox bullous diseases, but its precise nature and etiology are unknown.

Two female patients with the disease are reported. The first patient, an adult, had no appreciable response to corticosteroid therapy and died of a lung infection. The second, a child treated with antibiotics and ACTH, recovered promptly.

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Diet link causing safflower boom

A growing preoccupation with diet is causing a boom in an industry based on a small yellow flower. It is a thistle-like plant known as the safflower, whose seeds are rich in polyunsaturated vegetable oil. Therein lies the secret of its popularity.

The oil, according to many dietary experts, is an effective weapon against cholesterol. Some authorities say the oil is also effective in weight control. A book that recommends the use of safflower oil in dieting recently has appeared on best-seller lists.

Food products made with safflower oil, once found only in health stores, are now appearing on West Coast grocery shelves. They are expected to go into national distribution this year.

Salad oils, cooking oils, mayonnaise, French dressing, bakery goods, and other products made with safflower oil will be marketed.—*The New York Times, January 8, 1962*

Industrial Health and Workmen's Compensation

ROBERT KATZ, M.D., Director,
Bureau of Industrial Health and Workmen's Compensation
PETER J. DINATALE, M.D., Chairman,
Council Committee on Industrial Health
CARL F. FREESE, M.D., Chairman,
Council Committee on Workmen's Compensation

Medical Society of the State of New York

Workmen's Compensation Law

The Practicing Physician and the Medical Society

A REVIEW OF THE history of Workmen's Compensation legislation shows that most laws are intended to cover these fundamental points:

1. Provide certain prompt and reasonable compensation to victims of work accidents and their dependents.
2. Free the courts from delay, cost, and the tremendous work load of the mass of personal injury litigation.
3. Relieve public and private charities of the financial drain caused by uncompensated industrial accidents.
4. Eliminate economic waste in the payment of fees to lawyers and witnesses and save the time consumed by trials and appeals.
5. Supplant the concealment of fault in accidents by a spirit of frank study of causes, thereby eliminating accidents that are preventable and reducing cost and suffering.

Aside from cash benefits to replace lost income, the legislation provides for medical and rehabilitation care to restore the employe to his previous earning capacity as closely and as soon as possible. Thus the medical care which the injured employe receives is of the utmost importance for the handling of his entire case.

The Workmen's Compensation Law of the State of New York and the Rules and Regulations promulgated thereunder are updated from time to time to allow for the inclusion of modern concepts of medical care and rehabilitation, to streamline the administrative procedure, and to safeguard and clarify the right of the involved parties.

Authorization

To care for compensation patients a physician must be licensed in the State of New York and must be currently registered with the New York State Education Department (renewed every two years on application and on payment of a registration fee). Furthermore, he must be especially authorized by the chairman of the

Workmen's Compensation Board. Such authorization can be obtained on filing the prescribed application form with the local county medical society for review and recommendation. Then the chairman of the Workmen's Compensation Board will issue an authorization number and a code letter to indicate the type of practice of the applicant. Applicants have a right to appeal from this rating and can apply for a rerating, should the nature of their practice change at any time (such as specialization). A physician's authorization to treat compensation cases can be revoked by the chairman for cause (see Section 13-d of the Workmen's Compensation Law) and after due process. There is no application fee, and the authorization and rating remain in force until they are changed or revoked. Forms may be obtained on request from the county medical society.

This authorization from the chairman of the Workmen's Compensation Board is also required to certifying patients for benefits under Article 9 of the Workmen's Compensation Law dealing with disability benefits for nonoccupational disorders. It is therefore recommended that physicians apply for such authorization, even if they do not treat Workmen's Compensation cases.

Except for emergency cases, special authorization must be requested from the employer or insurance carrier for physical therapy in excess of $25, for consultations and surgical operations in excess of $25, and for x-ray and laboratory examinations in excess of $10. A physician whose request for authorization of medical services has been denied or has not been acted on within five working days after a written request was made may apply to the Workmen's Compensation Board to have the necessity for the requested medical services determined

In cases falling under Section 25-a of the Workmen's Compensation Law and where payment is to be made from the Special Fund, such as cases in which seven years have elapsed from the date of injury and in which three years have elapsed from the date of the last payment, authorization for any treatment or examination must be obtained in advance.

Reports

The necessity for complete and detailed records cannot be overstressed in compensation cases. Filling out the required forms completely and answering all the questions to the best of one's ability without omissions, question marks, dashes, blanks, and so forth will avoid much unnecessary correspondence and delay in adjudication and will serve in the best interest of the patient. It may also avoid the need for personal testimony before a referee of the Workmen's Compensation Board in disputed cases. A narrative report may be appended to the prescribed form if it is felt that there is insufficient room to give all the pertinent information in the space provided.

The law requires physicians to file with the chairman of the Workmen's Compensation Board and also with the employer or carrier the following medical reports within the times stated: (1) within forty-eight hours after the first treatment, a forty-eight-hour preliminary report; (2) within fifteen days after filing the forty-eight-hour preliminary report and in no event later than seventeen days after the first treatment, a fifteen-day report giving the complete report of injury and treatment; (3) thereafter at intervals of not more than twenty-two days a progress report, if treatment is continued; and (4) immediately on termination of treatment, a final report.

These medical reports must be made on combined form C-4 prescribed by the chairman of the Workmen's Compensation Board and must contain the authorization number and code letters of the physician. This form, as revised in February, 1961, requires the physician to complete the history portion of the report (items 12 to 15) only once. It need not be repeated on subsequent progress reports. In the event of an eye injury, the medical reports mentioned must be made on the prescribed form C-5.

If, following the submission of a final form C-4 or C-5, a resumption of treatment is indicated and the compensation claim has not been closed, and up-to-date C-4 or C-5 report should be submitted. If the claim has been closed, form C-27, duly verified, should be submitted to the Board in support of an application for reopening of the claim.

If the worker is discharged from treatment within forty-eight hours after the first treatment, only a complete report on board form C-4 should be filed, marked "Final."

In case of a herniotomy, the operating surgeon must file a form C-24 report immediately following the final examination of the injured person, made not less than eight weeks after the operation in case of a single hernia and not less than twelve weeks in case of a double hernia. Report forms, other than form C-27, do not require the verification by the physician before a notary public.

A physician who files his report late should submit a signed statement verified before a notary public, giving the reasons for which he requests excuse for late filing.

The attending physician is required to transmit copies of medical reports to the claimant's licensed representative or attorney on written request, accompanied by a notice of retainer and the claimant's consent to such a transmittal.

The failure to report on time or in sufficient detail may result in failure of the claimant to receive vitally needed compensation. The physician also may be required to appear at hearings, possibly at inconvenient times and at a distance from his office. All of this may be avoided by proper and timely reporting.

Treatment

An injured worker who is entitled to Workmen's Compensation benefits may choose his own physician with the limitation that the choice, other than for emergency treatment, is to be made from the roster of physicians authorized by the chairman of the Workmen's Compensation Board to render medical care or treatment under the Workmen's Compensation Law.

The employer is liable for all necessary medical, surgical, or other treatment; nurse and hospital service or other attendance; medicine; and crutches and apparatus during such period of time as the nature of the worker's injury or process of recovery may require.

The employer is required to provide for the medical rehabilitation of his injured employes. The prompt recognition of a proper case for Workmen's Compensation and the prompt initiation of rehabilitative procedures are all important to achieve the maximum benefit.

Insurance carriers shall not participate in the treatment of injured workers, but may employ medical inspectors to examine compensation cases periodically and may maintain rehabilitation bureaus operated by qualified physicians if authorized by the chairman in accordance with Section 13-c. When a patient is to be examined by a physician designated by the employer or his carrier, the attending physician and the patient may designate the place for such an examination, and the attending physician may be present if he feels that it is necessary or if the employe desires his presence.

A physician should always inquire whether or not the patient has been under the care of another physician and must communicate promptly with such a physician to ascertain the history of the case, together with any laboratory or x-ray reports, and advise the prior physician as to the reasons for the transfer. Care should be taken before rendering further treatment in cases which have been discharged by other physicians. If in doubt, the insurance carrier or self-insured employer may be consulted for further information as to prior treatment and its sufficiency.

Where a physician is in doubt as to the compensability of the claim, he should render medical care, especially in an emergent case, and ascertain the facts concerning the injury from the employer or carrier as soon as possible. If the employer denies that the injury was received during employment or as the result of employment and the patient persists in his story of a compensation injury, the physician should file the necessary forms.

A physician is required to look to the employer or insurance carrier for the payment of all medical bills in compensation cases. He may not accept a fee from the claimant. If under unusual circumstances a fee is paid or accepted and the case is declared compensable subsequently, the physician is required to reimburse the claimant and bill the employer or insurance carrier.

The liability of an employer or insurance carrier for medical treatment as provided by the Workmen's Compensation Law shall not be affected by the fact that his employe was injured through the fault or negligence of a third party, not in the same employ. Procedures and action against the third party by the employe and the employer or his insurance carrier are covered by Section 29 of the Workmen's Compensation Law and by Board Rule 20.

Fees

A fee schedule has been set up representing minimum fees for general practitioners and specialists for services rendered to injured workers. No employer or carrier may pay less than the minimum, and no physician may bill for less than the minimum. An employer or carrier may, on request, pay more than the minimum if, in the attending physician's opinion, the services warrant a higher fee or the patient's social or economic status justifies such a greater fee. If such a request is refused, the value of the physician's services may be determined by arbitration as provided in the law.

The fee schedule is promulgated by the chairman of the Workmen's Compensation Board after consideration of the views of the Medical Society and other interested parties. Its provisions are under constant review by the Advisory Committee on Medical Fees and Allied Problems of the Workmen's Compensation Board.

Disputed bills

An employer or insurance carrier who receives a bill for medical care has thirty days to object to the value of the services rendered and the fees charged. Since July, 1961, the Form A-1 ("Objection to Medical Bill for Treatment") simultaneously requests an impartial examination of the bill and submits the dispute to arbitration, as provided by the Workmen's Compensation Law. Unless objection is made within the stipulated thirty-day period, the bill rendered by an authorized physician is deemed to be the fair and reasonable value of the services rendered.

Technical, nonmedical issues and a determination of compensability require the decision of a referee prior to arbitration. When these issues have been removed, the Medical Registration Section of the Workmen's Compensation Board forwards to the physician Form A-5 ("A Letter of Inquiry to the Physician") to ascertain whether or not the physician agrees to submit the disputed bill for arbitration. This new form, which does not require notarization, replaces the old Form A-2.

Physicians who agree to arbitration should complete within thirty days both sides of the form and return it with a check of $2 to cover the minimum assessment fee. If the physician does not wish to arbitrate, he should complete only the bottom of page 1 and return the forms to the Workmen's Compensation Board.

In order for the arbitrators to get a clearer concept of the issues involved, the physician should complete the reverse side of Form A-5 very carefully. This will also assist the State Medical Society representative at the hearing to speak for the physician, in the event that he is unable to appear in person and has made his wish for representation known.

Beginning in July, 1961, arbitration committees have been made up of three physicians, one each selected by the chairman of the Workmen's Compensation Board, the county medical society where the hearings take place, and by the Compensation Insurance Rating Board. The Workmen's Compensation Board physician acts as chairman and casts the deciding vote in case of a tie. Both parties to the dispute have an opportunity to make brief remarks. No stenographic record is kept of the hearings, and decisions are made in an executive session. The parties are notified of the decision by mail. An assessment of 5 per cent of the award or a minimum of $2 is levied on each party. Hearing notices are mailed about thirty days in advance. Attempts at settlement are permitted but are subject to the assessment as outlined previously if agreed on within ten days of the hearing date. Settlements negotiated earlier should be reported promptly to the Workmen's Compensation Board and a Form A-3 "Withdrawal of Objection" should be filed.

Since the abolition of the Medical Practice Committee in May, 1960, this procedure is uniform in all counties of this State, regardless of the number of inhabitants. Arbitration hearings are held as soon as a sufficient number of cases have accumulated to warrant a calendar. At times it may become necessary to hold one calendar for several counties to avoid unnecessary delay for physicians practicing in sparsely industrialized areas. In that case the county medical society representative from the county in which the hearings are held is appointed with full agreement of the surrounding county medical societies.

Functions of medical societies

County society. It is recommended that each county have a Workmen's Compensation Committee to review applications of physicians for authorization and rating under the Workmen's Compensation Law and to make appropriate recommendations to the chairman of the Workmen's Compensation Board. Whenever there appears to be reason for changes in the fee schedule or of any of the provisions of the Workmen's Compensation Law, the county should transmit those changes together with appropriate recommendations to the Council Committee on Workmen's Compensation of the State Medical Society. The county committee may also function in the matter of alleged cases of violation of the Workmen's Compensation Law by a physician practicing in the area and has the power to subpoena witnesses, conduct hearings, and submit recommendations to the chairman of the Workmen's Compensation Board for action and implementation.

It is hoped that each county committee will conduct educational programs for its members to promote greater understanding and easier compliance with the many aspects of compensation affecting the practicing physician.

State society. All matters dealing with compensation are referred for consideration to the Council Committee on Workmen's Compensation. The recommendations of the Committee are subject to approval by the governing body of the Society, the House of Delegates, or the Council when the House is not in session. On approval, the Committee, through certain of its members, acts as a liaison with the Workmen's Compensation Board and the representatives of other interested groups (Compensation Insurance Rating Board, self-insurers associations, labor and management representatives, and so forth) and has membership on several important advisory committees appointed by the chairman of the Workmen's Compensation Board dealing with problems of medical care, rehabilitation, ratings, fee schedules, and others.

Through its Bureau of Industrial Health and Workmen's Compensation, the State Society helps in the arrangements of arbitration calendars and advises county representatives sitting as arbitrators. Attempts at settlement with carriers prior to the scheduled arbitration hearing are frequently successful in saving the physician time, inconvenience, and money and permitting him to devote more time to patient care. The Bureau may also represent physicians before arbitration committees, should such physicians be unable to attend in person for cause and on their specific request.

Assistance is offered to county societies in planning programs on Workmen's Compensation for stated or special meetings, and physicians and/or lay speakers can be supplied to cover numerous topics dealing with compensation.

A constant vigilance is maintained over proposals to our Legislature dealing with workmen's compensation. Proposals from county medical societies are studied carefully and evaluated for possible action and recommendations to improve the Workmen's Compensation system.

The Bureau studies and reviews problems arising in the handling of compensation at any phase and makes recommendations to the Council Committee. Suggestions are welcome from individuals or groups and will be given prompt consideration.

Woman's Auxiliary

The Auxiliary and legislation

The Auxiliary, as the name implies, aids the Medical Society of the State of New York and the county societies in a program to advance medicine and better public health. The activities of each auxiliary are confined to directives and policies as prescribed by its respective medical group, through close cooperation with advisory councils appointed by each medical group for this specific purpose.

The Legislation Committee is one of the many standing committees of the Auxiliary. Its purposes are: (1) to keep the membership informed concerning proposed Federal and State legislation in fields of public health, medical care, and other related programs; (2) to assist the State and county medical societies in promoting interest among physicians' families in health legislation, and (3) to encourage the members and their families to exercise the privileges of American citizenship.

We have the privilege of being doctors' wives. With that privilege goes the responsibility of defending that which we know to be right and good.

Our members are aware that there has been and will continue to be a definite campaign to create a "climate" of public opinion favorable to Social Security care of the aged. We also know that, if we allow this to go unchallenged, we are simply shirking our civic responsibility, both as individuals who value a certain way of American life and as an organization which has a unique insight into the quality of current medical practice in this country.

In April, 1961, the American Medical Association provided for the exclusive use of the Auxiliary a record made by the actor Ronald Reagan and asked that we sponsor a project called "Operation Coffee Cup." We have played this record in our homes and at meetings, and to our relatives, friends, and members of other community organizations. These people were then asked to write to their congressmen expressing their viewpoints regarding the King-Anderson Bill.

The current deluge of poor medical information is a challenge to every physician's wife, and we feel that the member who carries accurate, timely information about medical legislation or health problems into the programs of civic groups serves her community well. In assuming this responsibility, we recognize at the same time the need for programs with teaching and guidance value. Members are advised to call on their local medical societies and the State Medical Society for speakers and material.

There may have been times in years past when we had a choice of goals and a choice of direction of effort. We do not feel that in the year that lies ahead this can be true, because Federal planners continue to propose schemes out of tune with the ideals of freedom as we conceive them. Our ultimate goal must be the defeat of any projects of this type.

Mrs. Henry I. Fineberg, *Chairman*
Legislation
82-68 164th Street
Jamaica, New York

Why we have staff meetings

I do not know, nor can I conceive, any human contrivance that can more effectually and irresistibly oblige the physician to study carefully the case of his patient; to attend to every symptom or change of symptom; to exert himself to the utmost for his patient's relief; and at the same time to be as cautious as possible in the remedies that he employs; than to find himself under the necessity of giving a minute account of everything he has done, in a very public manner, and before a number of competent judges.—*Dr. James Gregory, of Edinburgh, 1862, cited in Bulletin of the Joint Commission on Accreditation of Hospitals, December, 1961*

Necrology

Amos Trevallee Baker, M.D., of Briarcliff Manor, died on January 19 at the age of eighty-eight. Dr. Baker graduated in 1897 from the University of Buffalo School of Medicine. A former psychiatrist at Sing Sing Prison, Dr. Baker was a Life Fellow of the American Psychiatric Association and a member of the New York Society for Clinical Psychiatry, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Alfred Melchisedech Barone, M.D., of Brooklyn and Stamford, Connecticut, died on November 10, 1961, at the age of sixty-eight. Dr. Barone graduated in 1918 from Columbia University College of Physicians and Surgeons.

Louis Joseph Benton, M.D., of Ogdensburg, died on December 27, 1961, at the A. Barton Hepburn Hospital at the age of fifty-five. Dr. Benton graduated in 1933 from the University of Pennsylvania School of Medicine. He was an attending physician at the A. Barton Hepburn Hospital and city health officer for Ogdensburg. Dr. Benton was a member of the St. Lawrence County Medical Society and the Medical Society of the State of New York.

Edmund Bergler, M.D., of New York City, died on February 6 at The Mount Sinai Hospital at the age of sixty-two. Dr. Bergler received his medical degree from the University of Vienna in 1926. He was a member of the American Psychoanalytic Association, the American Association for Research in Psychosomatic Problems, the Society for Psychopathology and Psychotherapy—"Schilder Society," the New York Psychoanalytic Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Bernhard, M.D., of the Bronx, died on January 1 at the age of fifty-nine. Dr. Bernhard graduated in 1929 from the University of Maryland School of Medicine and College of Physicians and Surgeons. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Matteo Carasso, M.D., of Northport, died on January 11 at the age of fifty-nine. Dr. Carasso received his medical degree in 1925 from the University of Paris Medical School. He was an attending in psychiatry at the Veterans Administration Hospital in Northport. Dr. Carasso was a member of the New York County Medical Society and the Medical Society of the State of New York.

Mark Cohn, M.D., of the Bronx, died on November 22, 1961, at the age of seventy-five. Dr. Cohn graduated in 1908 from Cornell University Medical College.

Charles Wilson Collins, M.D., of Saratoga Springs, died on January 13 at Saratoga Hospital at the age of forty-eight. Dr. Collins graduated in 1939 from Cornell University Medical College and interned at Memorial Hospital, Worcester, Massachusetts. He was an attending physician and a junior in obstetrics at Saratoga Hospital as well as president of the staff. Dr. Collins was a member of the American Academy of General Practice, the Association of Military Surgeons of the United States, the Aerospace Medical Association, the Saratoga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Leonard Elihu Field, M.D., of New York City, died on February 6 at The Mount Sinai Hospital at the age of fifty-one. Dr. Field graduated in 1936 from the University of Pennsylvania School of Medicine. He was a research assistant in cardiology and a senior clinical assistant attending physician in the Cardiac Department at The Mount Sinai Hospital and an associate attending physician at the Hospital for Joint Diseases. Dr. Field was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, a Fellow of the American College of Cardiology, and a member of the American Society of Clinical Pathologists, the American Federation for Clinical Research, the New York Academy of Medicine, the New York Pathological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Richard William Finn, M.D., of New York City, died on January 26 at his home at the age of sixty-four. Dr. Finn graduated in 1922 from Tufts College Medical School. He was a member of the William H. Luckett Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Rudolf R. Freudenberger, M.D., of New York City, died on October 10, 1961, at the age of sixty-eight. Dr. Freudenberger received his medical degree from the University of Wurzburg in 1920. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Sidney T. Friedman, M.D., of New York City, died on January 26 at his home at the age of sixty-two. Dr. Friedman graduated in 1922 from Cornell University Medical College and interned at The Mount Sinai Hospital. A former president of the medical board at Jewish Memorial Hospital he was an attending in surgery there. Dr. Friedman was a Fellow of the American College of Surgeons and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Aaron Edward Greenberg, M.D., of Brooklyn, died on January 24 at the age of fifty-nine. Dr. Greenberg graduated in 1925 from New York University and Bellevue Hospital Medical School. He was an attending in gynecology at the Jewish Chronic Disease Hospital Dispensary, an attending in obstetrics and gynecology at Madison Park Hospital of Adelphi College, and an associate attending in obstetrics and gynecology at Maimonides Hospital of Brooklyn. Dr Greenberg was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Obstetricians and Gynecologists, and a member of the Brooklyn Gynecological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Alphonsus Leo Grohowski, M.D., of Rochester, died on November 13, 1961, at the age of fifty-five. Dr. Grohowski graduated in 1934 from the University of Rochester School of Medicine and Dentistry. He was an attending in radiology at the Rochester General Hospital. Dr. Grohowski was a Diplomate of the American Board of Radiology, a Fellow of the American College of Radiology, and a member of the Radiological Society of North America, Inc., the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Crawford Avery Hart, M.D., of New York City, retired, died on January 27 at the age of sixty-eight. Dr. Hart graduated in 1918 from the University of Maryland School of Medicine and College of Physicians and Surgeons. He was an affiliate associate in obstetrics at City Hospital at Elmhurst, an assistant attending obstetrician and gynecologist at St. Vincent's Hospital, and assistant house physician at the Waldorf-Astoria Hotel. Dr. Hart was a member of the New York County Medical Society and the Medical Society of the State of New York.

William M. Hughes, M.D., of Albany, died on December 16, 1961, at the age of sixty-five. Dr. Hughes graduated in 1920 from Columbia University College of Physicians and Surgeons. He was an assistant attending physician in general practice at St. Peter's Hospital, an examining physician for the Workmen's Compensation Board, and an Albany School physician. Dr. Hughes was a member of the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Wilfred C. Hulse, M.D., of New York City, died on January 9 at Roosevelt Hospital at the age of sixty-one. Dr. Hulse received his medical degree from the University of Breslau in 1924. He was an associate in child psychiatry at The Mount Sinai Hospital, a clinical professor of psychiatry at Albert Einstein College of Medicine, chief psychiatrist at the Sheltering Arms Children's Service, and supervising psychiatrist for the Jewish Family Service. Dr. Hulse was a Diplomate of the American Board of Psychiatry and Neurology (Child Psychiatry), a Diplomate of the American Board of Pediatrics, a Fellow of the American Psychiatric Association, and a member of the American Academy of Child Psychiatry, the Association for the Advancement of Psychotherapy, the American Group Psychotherapy Association, the American Orthopsychiatric Association, the Association of Military Surgeons of the United States, the New York Academy of Medicine, the New York Society for Clinical Psychiatry, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frederick Conrad Keller, M.D., of New York City, died on November 24, 1961, at the age of ninety-three. Dr. Keller graduated in 1894 from Columbia University College of Physicians and Surgeons. He was a consultant in surgery at St. John's Long Island City Hospital. Dr. Keller was a Fellow of the American College of Surgeons and a member of the New York Academy of Medicine, the New York Pathological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry J. Kuhlmeyer, M.D., of Woodhaven, died on January 15 at the age of sixty-six. Dr. Kuhlmeyer received his medical degree from the University of Heidelberg in 1921. He was an assistant attending surgeon in general practice at Evangelical Deaconess Hospital, Brooklyn. Dr. Kuhlmeyer was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Elton Gardiner Littell, M.D., of Yonkers, died on February 3 at St. John's Riverside Hospital at the age of eighty-three. Dr. Littell graduated in 1904 from Columbia University College of Physicians and Surgeons and interned at St. Luke's Hospital and Lying-In Hospital. He was an emeritus pediatrician at St. John's Riverside Hospital. Dr. Littell was a member of the Yonkers Academy of Medicine, the New York Academy of Medicine, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Coloman Lowenkopf, M.D., of the Bronx, died on December 30, 1961, at the age of seventy. Dr. Lowenkopf received his medical degree from the University of Budapest in 1923. He was an assistant attending in ophthalmologic surgery at the Bronx Eye and Ear Infirmary and an associate attending ophthalmologist at Lincoln Hospital. Dr. Lowenkopf was a Diplomate of the American Board of Ophthalmology and a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Aron Mozes Martin, M.D., of Ridgewood, died on November 6, 1961, at the age of fifty-eight. Dr. Martin received his medical degree from the University of Vienna in 1930. He was an assistant attending physician at Greenpoint Hospital. Dr. Martin was a member of the Queens County Medical Society and the Medical Society of the State of New York.

Ohannes H. Mowsessian, M.D., of Forest Hills, died on October 18, 1961, at the age of seventy-five. Dr. Mowsessian received his medical degree from the Faculte Francaise de Medecine de l'University de St. Joseph, Beyrouth, Lebanon, in 1912. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Anthony Philip Nicosia, M.D., of Long Island City, died on January 1 at the age of sixty-one. Dr. Nicosia received his medical degree from the University of Rome in 1934. He was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Cornelius O'Hare, M.D., of the Bronx, was shot and killed in his office on January 26 at the age of fifty-eight. Dr. O'Hare graduated in 1932 from Boston University School of Medicine. He was an associate attending physician at St. Francis Hospital. Dr. O'Hare was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ewald Olsson, M.D., of Baldwin, died on January 21 at the age of seventy-five. Dr. Olsson graduated in 1916 from the University of Vermont College of Medicine. He was a consultant in orthopedics at the Swedish Hospital in Brooklyn.

David Edward Overton, M.D., of Riverhead, died on January 26 at Mather Memorial Hospital, Port Jefferson, at the age of fifty-eight. Dr. Overton graduated in 1927 from Yale University School of Medicine, in 1942 received his Master of Public Health from Johns Hopkins University School of Medicine, and interned at Kings County and Long Island College Hospitals. He was Suffolk County Health Commissioner. Dr. Overton was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the American Public Health Association, the Suffolk County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Perlman, M.D., of Brooklyn, died on November 25, 1961, at the age of seventy. Dr. Perlman graduated in 1913 from New York University and Bellevue Hospital Medical School. He was a physician in the Department of Health Tuberculosis Clinic. Dr. Perlman was a member of the American Trudeau Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Prince, M.D., of Brooklyn, died on April 9, 1961, at the age of sixty-two. Dr. Prince graduated in 1924 from General Medical College, Chicago. He was an adjunct in general practice at Prospect Heights Hospital.

Solomon Joseph Sambur, M.D., of Brooklyn, died on December 4, 1961, at Miami, Florida, at the age of seventy-six. Dr. Sambur graduated in 1916 from Long Island College Hospital Medical School. He was a member of the Kings county Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Shalet, M.D., of the Bronx, died on January 16 at the age of seventy. Dr. Shalet graduated in 1930 from Marquette University School of Medicine. He was a member of the Bronx County Medical Society, the Medical

Society of the State of New York, and the American Medical Association.

Bernard Joseph Sisson, M.D., of Syracuse, died on January 11 at St. Joseph's Hospital at the age of forty-five. Dr. Sisson graduated in 1941 from Syracuse University School of Medicine. An assistant professor of plastic surgery at the State University College of Medicine at Syracuse, he was also an assistant attending in plastic surgery at University and Syracuse Memorial Hospitals, and an associate attending in plastic surgery at St. Joseph's Hospital. Dr. Sisson was a member of the American Society of Plastic and Reconstructive Surgery, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Harry Francis Tashman, M.D., of New York City, died on November 5, 1961, at the age of sixty-one. Dr. Tashman graduated in 1924 from Tufts College Medical School. He was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Member of the American Psychiatric Association, and belonged also to the Society of Medical Psychoanalysts, the New York Society for Clinical Psychiatry, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David Tropauer, M.D., of the Bronx, died on January 25 at the Bronx Veterans Hospital at the age of sixty-eight. Dr. Tropauer graduated in 1917 from New York University and Bellevue Hospital Medical School.

Alfred Jean Vignec, M.D., of New York City, died on February 4 at St. Vincent's Hospital at the age of fifty-six. Dr. Vignec graduated in 1934 from Yale University School of Medicine. He was director of pediatrics at St. Vincent's Hospital, medical director at the New York Foundling Hospital, a consultant in pediatrics at St. Joseph's Hospital (Yonkers), St Agnes Hospital (White Plains), New York State Rehabilitation Hospital (West Haverstraw), and St. Clare's and Misericordia Hospitals, and an associate attending in pediatrics at University Hospital. He was a former instructor in pediatrics at the Long Island College of Medicine, Cornell Medical College, and a medical director of the Kennedy Child Study Center, and an adviser to the New York City Departments of Health and Welfare. Dr. Vignec was a Diplomate of the American Board of Pediatrics and a member of the New York Academy of Medicine, the American Academy of Pediatrics, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Herbert Northrup Wallace, M.D., of Poland, died on December 25, 1961, at St. Luke's-Memorial Hospital Center, Utica, at the age of sixty-four. Dr. Wallace graduated in 1925 from the University of Michigan Medical School. He was an associate member of the staff of St. Luke's-Memorial Hospital Center, Utica. Dr. Wallace was a member of the Utica Academy of Medicine, the Oneida County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Announcement

Because of the interest in the recent series of 12 articles on "The Physician in Civil Defense" prepared by Solomon Garb, M.D., and published in the NEW YORK STATE JOURNAL OF MEDICINE from August 1, 1960, through January 15, 1961, reprints of the series are now available.

The 12 articles on "Survival in a Thermonuclear War" have been reprinted in a 56-page pamphlet and may be ordered from the JOURNAL, 750 Third Avenue, New York 17, New York, at a charge of fifty cents per pamphlet to cover costs.

Abstracts

Lerman, S.: The lens in human and experimental galactosemia, NEW YORK STATE J. MED. **62:** 785 (Mar. 15) 1962.

Congenital galactosemia is a rare hereditary disease caused by an inborn error of galactose metabolism, the severity of which depends on the degree of the metabolic block present in the red cells, liver, and lens of the individual patient. The main clinical features of the disease are: early nutritional failure, hepatic and splenic enlargement, jaundice, lethargy, osteoporosis, mental retardation, and cataract formation. Cataracts are present in about 75 per cent of the cases. Most dietary galactose comes from lactose, a combination of glucose and galactose. In the red blood cells, lens, and liver in galactosemia there is an absolute or relative lack of the enzyme galactose-l-phosphate uridyl transferase which is necessary to complete metabolism. Although the liver is probably the major site for converting galactose to glucose, both the red blood cells and the lens are capable of performing this function. In the milk-fed infant the lens is probably called on to handle galactose to a much greater extent than in later life. In a series of studies on rats, comparing a group maintained on a high galactose diet with a control group, the carbohydrate and protein metabolism were shown to be the main areas affected in the development of experimental galactose cataract, while ribonucleic acid metabolism remained virtually unimpaired. From the results it may be assumed that the normal rapidly developing lens of the young rat contains an active direct oxidative pathway of glucose metabolism and that the monophosphate shunt plays only a relatively important role in the metabolic economy of the lens.

Blum, L.: Acute thrombosis of large arteries, NEW YORK STATE J. MED. **62:** 804 (Mar. 15) 1962.

Acute occlusion of a coronary, retinal, or cerebral artery is not a strange phenomenon considering underlying degenerative disease. This narrows the small lumen and leaves a passageway liable to instant closure as a result of insult either in the wall of the vessel or outside it. Changes in the normal clotting mechanisms of the blood are an added element. On the other hand, sudden closure of a large vessel in the greater circulation, either the aorta or one of its direct branches is not as common and not as easily explained. Acute thrombosis results from thrombotic occlusion superimposed on existing disease. The importance of the stress phenomenon in acute thrombosis in relation to surgical judgment is emphasized.

Gabrieli, E. R., and Wypych, J. I.: Fate of circulating hemoglobin in man; preliminary clinical study, NEW YORK STATE J. MED. **62:** 812 (Mar. 15) 1962.

A study to determine the factors involved in blood clearance of the hemoglobin-haptoglobin complex was undertaken on 20 apparently healthy volunteers. Between 176 and 386 mg. of hemoglobin were injected, the dose being kept to at least 5 to 10 mg. per 100 ml. of plasma below the hemoglobin-binding capacity of the individual. The plasma hemoglobin level decreased uniformly at a constant rate as a linear function of time. The clearance rates were within a remarkably narrow range, suggesting a clearing mechanism of low efficiency independent of the plasma hemoglobin level and indicating saturation of a metabolic pathway. The average clearance rate was found to be 122 mg. of hemoglobin per hour, but if the combined weights of the entire hemoglobin-haptoglobin complex are calculated the correct value is more than doubled. In open-heart surgery the patient's plasma haptoglobin level is a limiting factor on the amount of hemoglobin hemolysis the pump can be permitted to cause. In pilot studies the rate of removal of the circulating plasma hemoglobin has been shown to be increased in several diseases involving the reticuloendothelial system.

Lubart, J.: The common cold and humidity imbalance, NEW YORK STATE J. MED. **62:** 816 (Mar. 15) 1962.

Efforts at developing a vaccine against the common cold have met with serious obstacles because the makeup of the virus appears to change from year to year. A dry nose and throat caused by artificial heating creates an indoor climate favorable to the cold-inciting agent. Dry nasal mucus is an excellent culture for the infective agent. Adequate moisture is necessary also for the proper function of the cilia, pharynx, larynx, trachea, and lungs. During the heating season the best method of prevention of colds is maintenance of a proper balance of humidity by means of such devices as a mechanical humidifier. In summer, regulation of the humidity in air-conditioning is necessary to prevent summer colds.

Filippone, J. F.: Interlobar pleural effusion in congestive heart failure, New York State J. Med. **62:** 820 (Mar. 15) 1962.

The small number of reported cases of interlobar pleural effusion in congestive heart failure would seem to indicate that the condition is rare, but the common occurrence of congestive heart failure itself and the fact that patients with interlobar pleural effusion are often admitted with a diagnosis of lung tumor suggest that the condition may be more frequent than is commonly thought. Three cases are reported, illustrating the etiologic cardiac diagnoses most commonly encountered: hypertension, coronary atherosclerosis, and rheumatic valvular disease. With appropriate therapy there is prompt disappearance of the loculated effusion. The majority of loculated effusions reported occurred on the right side with 75 per cent in the transverse fissure. Adhesive pleuritis is not a prerequisite to interlobar effusion. Careful fluoroscopic and roentgenographic examination of patients in congestive heart failure would probably uncover many more cases of interlobar pleural effusion.

Archer, J. S., Smessaert, A. A., and Hicks, R. G.: Phenothiazine tranquilizers in anesthesia; review, with report on fluphenazine, New York State J. Med. **62:** 828 (Mar. 15) 1962.

In anesthesia the phenothiazines may be used in preoperative tranquilization of the overly apprehensive patient, preoperative medication of the asthmatic patient to prevent a barbiturate-caused asthmatic attack, as an antiemetic, as an aid in producing hypothermia, in pediatric cardiac catheterization, in postpartum hypertension, and in combating singultus. The anesthetic requirement is only a fraction of that necessary for psychiatric use. Hypotension and tachycardia are possible complications, but the newer derivatives with the piperazine nucleus pose no real threat if used judiciously. Blood dyscrasias, jaundice, weight gain, and photosensitivity may be caused by the phenothiazines but only after prolonged dosage. Extrapyramidal symptoms do not occur when the drug is given while the patient is still subject to an anesthetic. A double-blind study on more than 200 females scheduled for dilation and curettage was undertaken to determine the effects of fluphenazine dihydrochloride given postoperatively. The results showed a 5 per cent incidence of retching and vomiting with fluphenazine and a 14 per cent incidence with the placebo. The mode of recovery was more serene when the drug was administered, and there was no noticeable difference in blood pressure and pulse.

Gudgel, E. F., and Winer, M.: Mechanism of griseofulvin failure, New York State J. Med. **62:** 834 (Mar. 15) 1962.

Ninety-four patients with superficial fungus disease who were treated with griseofulvin were followed closely for as long as twenty months. Results were considered successful in 71 patients and unsuccessful in 23. Some of the failures were actually recurrences or reinfections. All but 2 of the failures occurred in patients with lesions on the nails or skin of the hands or feet. Sixty patients were omitted from the series because of incorrect diagnosis of fungus disease or diagnosis of moniliasis or tinea versicolor, which do not respond to treatment with griseofulvin. Organisms which respond to griseofulvin are species of Epidermophyton, Microsporum, and Trichophyton. The dose of griseofulvin and duration of treatment required for cure vary between a single dose of 1 Gm. and a cumulative dose of more than 500 Gm. during four hundred days. In at least 7 patients unsuccessful results might have been due to inadequate daily and cumulative dosage; relatively large dosage is required if there is heavy callus formation.

Bohensky, F. B.: Mebutamate, a new drug for the treatment of hypertension, New York State J. Med. **62:** 841 (Mar. 15) 1962.

A study was undertaken on 51 ambulatory hypertensive patients to determine the effects of therapy with mebutamate. On the basis of blood pressure readings, 46 (90 per cent) of the patients responded favorably to mebutamate therapy. In 26 patients with systolic hypertension, the average reduction in systolic pressure was 31 mm. Hg, and the normotensive diastolic pressures were not decreased below normotensive levels. In 25 patients with diastolic hypertension, the average reduction in systolic pressure was 31 mm. Hg, and in diastolic pressure 20 mm. Hg. The amount of reduction attained was proportional to the height of the initial systolic and diastolic pressures. Drowsiness occurred in 21 patients and light-headedness in 14, possibly owing to overlapping of previous therapy or overdosage. These side-effects were eliminated spontaneously or by decreased dosage. All 20 patients who had improved on previous therapy obtained further improvement on mebutamate; of 22 who had failed to respond to previous therapy, 19 improved on mebutamate, 1 was unchanged, and 2 became worse. Two of 3 patients who had become worse on previous therapy improved on mebutamate, and 1 was unchanged. Of 6 who had not received previous therapy, 5 were improved, and 1 became worse.

Medical News

Rochester Roentgen Ray Society

The Rochester Roentgen Ray Society has announced the election of the following officers: Raymond Gramiak, M.D., president; Peter G. Gleason, M.D., vice-president; and Harry J. Pinsky, M.D., secretary-treasurer.

The society meets on the last Monday of each month, September through May.

Physician gives art show for charity

A Brooklyn cardiologist, Nathaniel E. Reich, M.D., is holding a one-man art show at the Greer Gallery, 35 West 53rd Street, New York City, March 11 through 30, for the benefit of the Heart Fund.

Medical bibliography available

The National Library of Medicine announces the publication of the *Bibliography of Medical Reviews, volume 6, Cumulation, 1955–1961.* This volume supersedes the annual volumes published during the past five years and lists 3,300 additional review articles from the 1960 literature not previously indexed in the *Bibliography of Medical Reviews.* The *Cumulation,* containing some 21,000 subject entries for approximately 13,500 review articles collected from 1,949 journal titles over a six-year period, has been edited to conform to the subject headings listed in *National Library of Medicine Medical Subject Headings* (*1960*). The entries are in the style used in the *Index Medicus.*

The volume is available from the Superintendent of Documents, United States Government Printing Office, Washington 25, D.C., at $3.50 a copy.

Symposium on the newborn

A symposium on the newborn child will be held at The Hospital of St. Raphael, New Haven, Connecticut, on Wednesday, April 11. The scientific program will be as follows:

"Maternal Factors in Perinatal Morbidity," by Robert E. L. Nesbitt, Jr., M.D., Syracuse, New York; "Prematurity," by Harry H. Gordon, M.D., Baltimore, Maryland; "Respiratory Disorders," by Herbert C. Miller, M.D., Kansas City, Kansas; Radiological Diagnosis," by Edward B. D. Neuhauser, M.D., Boston, Massachusetts; "Significance of Jaundice," by Sidney S. Gellis, M.D., Boston, Massachusetts; "Early Diagnosis of Congenital and Genetic Defects," by Alexander J. Schaffer, M.D., Baltimore, Maryland; "Problem of Infections," by Louis Gluck, M.D., New Haven, Connecticut; and Surgical Emergencies," by H. William Clatworthy, Jr., M.D., Columbus, Ohio.

For information write to: Paul F. McAlenney, M.D., Chairman, Department of Pediatrics, The Hospital of St. Raphael, New Haven, Connecticut.

Prevention of blindness research grants

The Committee on Basic and Clinical Research of the National Society for the Prevention of Blindness invites requests for research grants in 1962. Funds are available for projects that may contribute to basic understanding of eye function and pathology, or that may improve methods of diagnosis, treatment, or prevention of blinding eye diseases. Grants will be made this spring for requests submitted prior to April 1, 1962.

For information write to: Committee on Basic and Clinical Research, National Society for the Prevention of Blindness, 16 East 40th Street, New York 16, New York.

Standardization of hypodermic syringes

To facilitate interchangeability of hypodermic syringes and needles in time of emergency or disaster, the six per cent conical taper may soon be universally accepted throughout the world. A technical committee of the International Organization for Standardization has drafted a proposal providing for such standardization which is expected to be voted on by all 44 member nations soon.

United States representation on the international standards project was provided through the U.S.A. Committee, an arm of the American Standards Association. Committee chairman is E. W. Bednarz of Decton, Dickenson and Company, Rutherford, New Jersey.

Sports medicine newsletter

Medicine in Sports, a newsletter devoted exclusively to reporting the latest information on the care and prevention of athletic injuries, is now being distributed to all physicians interested in the subject as a professional service by the Rystan Company, Mount Vernon, New York.

Physicians interested in receiving the publication should write to: Charles Stanton, Editor, Medicine in Sports, Rystan Company, 7 North MacQuesten Parkway, Mount Vernon, New York.

United Nations narcotics control

American pharmaceutical manufacturers have urged that the United States not ratify, in its present form, a United Nations proposal to replace all individual international agreements on the control of narcotics with a single document.

The U.S. producers contend that the proposed "Single Convention on Narcotics" would permit countries that now produce no opium to do so, thus compounding existing problems of international narcotics control.

In a resolution sent by the Pharmaceutical Manufacturers Association (PMA) to Secretary of State Dean Rusk, the drug makers urged the U.S. instead to encourage complete ratification of the stronger 1953 United Nations Opium Protocol. This agreement would effectively limit opium production to countries that traditionally have produced it.

Mammalian heart bank available to investigators

A collection of more than 11,500 hearts from several hundred kinds of North American wild mammals is available at the University of Kansas for study by qualified investigators.

The collection was assembled during the last four years by Professor E. Raymond Hall, Director, Museum of Natural History, University of Kansas, for a comparative study of cardiovascular disease in free-living mammals, other than man, as correlated with habits, habitat, and heritage. The assembled hearts belong to the mammalian orders Marsupialia, Insectivora, Chiroptera, Rodentia, Lagomorpha, Carnivora, and Artiodactyla.

Qualified investigators interested in working with the collection should write to: Dr. E. Raymond Hall, Director, Museum of Natural History, University of Kansas, Lawrence, Kansas.

Arthritis Foundation research awards

The Arthritis and Rheumatism Foundation has announced that during the ten years following the start of its program of advanced training in rheumatic disease research in July, 1951, with 6 fellows, the Foundation has spent $1,414,655 to support the studies of 117 scientists for a total of 240 fellowship years. This year the Foundation's medical and scientific committee has approved $395,000 to support 49 fellows.

The Foundation's national medical director, Ronald W. Lamont-Havers, M.D., said a survey of the 88 scientists who completed their training in the program's first ten years shows that 80 per cent have remained in research and teaching. Six are full professors, 10 associate professors, and 34 assistant professors.

Postgraduate courses at sea

The University of Southern California Postgraduate School of Medicine will present a refresher course in the Royal Hawaiian Hotel in Honolulu in July and aboard the *S.S. Matsonia* sailing from Honolulu August 9 for Los Angeles.

The course is designed for practicing physicians and features advancements in diagnosis, drugs, and medical management.

For information write to: Postgraduate Division, University of Southern California School of Medicine, 2025 Zonal Avenue, Los Angeles 33, California.

Otolaryngologic assembly

The University of Illinois College of Medicine Department of Otolaryngology will offer an intensive postgraduate basic and clinical program under the direction of Emanuel M. Skolnik, M.D. This assembly for practicing otolaryngologists offers a condensed program of one week of daytime and evening sessions. It is designed to bring to specialists a wide variety of current advances in management, therapy, and philosophies. A review of basic morphologic features under the direction of Maurice F. Snitman, M.D., and Frederic J. Pollock, M.D., is also included. The review will feature laboratory demonstrations and prosection, all augmented by visual aids.

For information write to: Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

Resolution on food faddists

At the December, 1961, annual meeting of the American Medical Women's Association in Cleveland, Branch 18, New York State, introduced and had passed a resolution that the A.M.W.A. support existing agencies investigating the erroneous and misleading information on health and nutrition which is being presented on radio and television stations. The resolution also provided for the establishment of a service to provide qualified speakers and information on nutrition and health to such stations.

Course in pediatric oncology

The Pediatric Department of Memorial Sloan-Kettering Cancer Center, New York City, announces its annual comprehensive three-day course in pediatric oncology for pediatricians, general practitioners, and health officers to be held April 25 through 27.

Current developments and established methods in diagnosis, differential diagnosis, and management of benign and malignant tumors, Hodgkin's disease, leukemia, and reticuloendothelioses in childhood are included.

Twenty members of the attending staffs of

Memorial Hospital for Cancer and Allied Diseases and the Memorial Sloan-Kettering Cancer Center will be on the faculty.

For information write to: Chairman, Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, 444 East 68th Street, New York 21, New York.

Personalities

Awarded. Ludwik Gross, M.D., the Lucy Wortham James Award of $500 from the James Ewing Society for his research work in preclinical aspects of cancer . . . George T. Pack, M.D., New York City, the honorary degree of "Doctor Honoris Causa" from the University of Rio Grande do Sul, Porto Alegre, Brazil . . . Marion B. Sulzberger, M.D., Washington, D.C., the title "knight" by the French Legion of Honor . . . James B. Wray, M.D., Syracuse, the Kappa Delta national award for original research in orthopedic surgery.

Appointed. Maxwell L. Littman, M.D., New York City, as chief mycologist of the City of New York Department of Health . . . H. Houston Merritt, M.D., New York City, reappointed as chairman of the colleges and universities division of the New York City Cancer Committee's 1962 April Cancer Crusade . . . Lawrence P. Roberts, M.D., Orangeburg, as director of Harlem Valley State Hospital, Wingdale . . . Arthur Purdy Stout, M.D., New York City, as chairman of the doctor's division of the New York City Cancer Committee's 1962 April Cancer Crusade . . . Anthony R. Tortora, M.D., Brooklyn, to the publication committee of the journal *Psychosomatics*, official organ of the Academy of Psychosomatic Medicine.

Speakers. George Kayman, M.D., Brooklyn, a series of six lectures on the topic "Psychiatry and the Law" before the residents in psychiatry at the Kings County Hospital . . . Stanley Lesse, M.D., and D. Keith McElroy, M.D., New York City, on the subject "Psychosomatic Aspects of Orthopedic Medicine" before the Association for the Advancement of Psychotherapy . . . Frederick Reiss, M.D., New York City, in February before the fourth All-India Congress of Dermatologists and Syphilologists in Bombay on the subject "Dermatologic Clues in the Detection of Internal Diseases" and at the University of Colombo and Teheran on the subject "Diagnosis and Treatment of Fungus Diseases of the Skin, Hair, and Nails" . . . Morton L. Rosenthal, M.D., Brooklyn, before the Eastern New York Eye, Ear, Nose and Throat Association on February 1 on the topic "Some Interesting Retinal Detachment Syndromes" . . . Joseph Wilder, M.D., New York City, on the subject "Psychosomatic Aspects of Orthopedic Medicine" on February 23 before the Association for the Advancement of Psychotherapy.

Medical Meetings

American College of Obstetricians and Gynecologists

The American College of Obstetricians and Gynecologists will hold its tenth annual clinical meeting at the Palmer House in Chicago, April 2 through 4. President-elect, Edward C. Hughes, M.D., of the State University of New York Upstate Medical Center, will deliver the inaugural address.

The meeting will be preceded March 31 through April 1 by five postgraduate courses offered to interested physicians whose training in certain subjects may have been deficient or who wish to bring their knowledge up to date.

For further information write to: The American College of Obstetricians and Gynecologists, 79 West Monroe Street, Chicago 3, Illinois.

West Virginia Academy of Ophthalmology and Otolaryngology

The West Virginia Academy of Ophthalmology and Otolaryngology will hold its fifteenth annual meeting at the Greenbriar Hotel, April 23 through 25. For further information write to: Worthy W. McKinney, M.D., Secretary-Treasurer, Professional Park, Beckley, West Virginia.

Symposium on headache

A symposium on "Headache: Its Mechanism, Diagnosis, and Management" will be presented at the fourteenth annual meeting of the American Academy of Neurology, at the Statler-Hilton Hotel, New York City, at 2:00 P.M., on April 28.

The program is as follows: "Introduction," by H. Houston Merritt, M.D., professor of neurology, College of Physicians and Surgeons, Columbia University, and director, Service of Neurology, Neurological Institute, Presbyterian Hospital, New York City; "Classification of Headache," by E. Charles Kunkle, M.D., professor of neurology, Duke University School of Medicine, Durham, North Carolina; "Recent Experimental Studies on Headache," by Harold G. Wolff, M.D., Anne Parrish Titzell, Professor of Medicine (neurology), Cornell University Medical College, New York City; "The Natural History and Epidemiology of Migraine and Muscle Contraction Headache," by Adrian M. Ostfeld, M.D., associate professor of preventive medicine, University of Illinois, College of Medicine, Chicago; "Six Common Headache Profiles," by John R. Graham, M.D., instructor in medicine, Harvard Medical School, Boston; "Comments on Certain Clinical Features of Headache," by Dr. Kunkle; "The Diagnosis of Headache," Francis L. McNaughton, M.D., professor of neurology, McGill University, Montreal, Canada; "Studies in the Pharmacotherapy of Headache," by Arnold P. Friedman, M.D., associate professor of clinical neurology, College of Physicians and Surgeons, Columbia University, New York City; "Psychiatric Aspects of Treatment of Headache," by Lawrence C. Kolb, M.D., professor of psychiatry, College of Physicians and Surgeons, Columbia University; and "Summary," by Dr. Merritt.

For further information write to: Arnold P. Friedman, M.D., Symposium Coordinator, Headache Unit, Montefiore Hospital, 210th Street and Bainbridge Avenue, New York 67, New York.

Division of Dermatology, State University Downstate Medical Center

The Division of Dermatology of the Department of Medicine, State University of New York Downstate Medical Center, will present a discussion on "Depression in Dermatology" on May 4 from 10:00 to 11:30 A.M., in the E Building Auditorium, Kings County Hospital, 451 Clarkson Avenue, Brooklyn 3, New York. Samuel Greenberg, M.D., clinical instructor of psychiatry, State University of New York Downstate Medical Center, will be the speaker. Lawrence Frank, M.D., will be the moderator.

Food and Nutrition Council of Greater New York

The Food and Nutrition Council of Greater New York will present an institute of nutrition services for Puerto Ricans on May 16 from 1:00 to 5:00 P.M., in the Horace Mann Auditorium, Teachers College, Columbia University, 120th Street and Broadway, New York City.

For information contact the chairman: Morton B. Glenn, M.D., 131 East 61st Street, New York 21, New York.

Medical Library Association conference

The sixty-first annual meeting of the Medical Library Association will be held in Chicago, June 4 through 8, at the Sheraton-Chicago Hotel.

For information write to: Medical Library Association, 919 North Michigan Avenue, Chicago 11, Illinois.

American Physical Therapy Association

The American Physical Therapy Association will hold its thirty-ninth annual conference at The Jack Tar Hotel in San Francisco, California, June 17 through 22. The theme of the scientific program will be "Dynamics of Human Motion."

For further information write to: American Physical Therapy Association, 1790 Broadway, New York 19, New York.

No drug breakthroughs in Russia

A couple of years ago I spent a good deal of time with a Russian mission representing the drug industry, including a Mr. Natradze who, I understand, is or was the head of the whole Russian pharmaceutical operation. From him I learned about the Soviet system, and it does supply medicine for the sick. But in the forty-odd years of its existence the Soviet Union—despite its achievements in space—has not produced a single important pharmaceutical breakthrough.—*Francis Boyer, Chairman of the Board, Smith Kline & French Laboratories, The Generic Fallacy*

Abstracts in Interlingua

Lerman, S.: Le crystallino in galactosemia human e experimental (*anglese*), New York State J. Med. **62:** 785 (15 de martio) 1962.

Galactosemia congenite es un morbo hereditari rar que es causate per un innate error del metabolismo de galactosa. Su severitate depende del grado de completessa del bloco presente in le erythrocytos, le hepate, e le crystallino del patiente individual. Le major aspectos clinic del morbo es: precoce disfallimento nutritional, allargamento hepatic e splenic, jalnessa, lethargia, osteoporosis, retardation mental e formation de cataractas. Cataractas es presente in circa 75 pro cento del casos. Le plus grande parte del galactosa dietari es fornite per lactosa, le qual es un combination de glucosa e galactosa. In le erythrocytos, le crystallino, e le hepate in galactosemia il existe un manco absolute o relative del enzyma galactosa-1-phosphato-uridyl-transferase, le qual es necessari pro le metabolismo complete. Ben que le hepate es probabilemente le sito principal pro le conversion de galactosa in glucosa, tanto le erythrocytos como etiam le crystallino es capace a exercer iste function. In le infante nutrite con lacte, il es probabile que le crystallino debe occupar se del conversion de galactosa multo plus extensemente que plus tarde in le vita. In un serie de studios in rattos, gruppos mantenite con dietas ric in galactosa esseva comparate con gruppos de controlo, e il esseva trovate que le metabolismo de hydrato de carbon e de proteina esseva le principal areas afficite in le disveloppamento experimental de cataracta de galactosa, durante que le metabolismo de acido ribonucleic remaneva virtualmente intacte. A base del resultatos il pote esser concludite que le crystallino normal que se disveloppa rapidemente in le juvene ratto contine un active circuito directe de oxydation in le metabolismo de glucosa e que le shunt a monophosphato ha un relativemente minus importante rolo in le economia metabolic del crystallino.

Blum, L.: Thrombose acute in arterias major (*anglese*), New York State J. Med. **62:** 804 (15 de martio) 1962.

Acute occlusion del arteria coronari, retinal, o cerebral non es un phenomeno estranie si on considera le subjacente morbo degeneratori. Isto restringe le micre lumine e resulta in un passage apte a suffrer un clausura instantanee como resultato de insulta del pariete del vaso o al extero de illo. Alterationes in le mechanismo normal del coagulation del sanguine es un elemento additional. Del altere latere, un clausura subitanee de un vaso major in le circulation major—i.e. le aorta o un de su brancas directe—es minus commun e minus facile a explicar. Thrombosis acute resulta ab occlusion thrombotic superimponite a preexistente morbiditate. Es sublineate le importantia del phenomeno de stress in thrombosis acute in relation al judicamento chirurgic.

Gabrieli, E. R., e Wypych, J. I.: Le destino de hemoglobina circulante in le homine; studio clinic preliminari (*anglese*), New York State J. Med. **62:** 812 (15 de martio) 1962.

Esseva interprendite in 20 apparentemente normal voluntarios un studio visante a determinar le factores interessate in le clearance del complexo hemoglobina-haptoglobina ab le sanguine. Le subjectos recipeva injectiones de inter 176 e 386 mg de hemoglobina, con le dose in omne caso individual seligite de maniera que illo remaneva infra le capacitate de ligar hemoglobina per al minus 5 a 10 mg per 100 ml de plasma. Le nivello de hemoglobina del plasma declinava uniformemente como function lineari del tempore. Le valores absolute del clearance variava remarcabilemente pauco in varie subjectos. Isto suggere que le mechanismo del clearance de hemoglobina, characterisate per basse grados de efficacia, esseva independente del nivello de hemoglobina del plasma e indica un stato de saturation pro un circuito metabolic. Le magnitude medie del clearance esseva 122 mg de hemoglobina per hora, sed si le combinate pesos del complete complexo de hemoglobina-haptoglobina es calculate, le correcte valor es plus que duplate. In operationes chirurgic a corde aperte, le nivello de haptoglobina in le plasma del patiente es un factor limitatori pro le permissibile grado de hemolyse hemoglobinic per le pumpa. In studios pilota il ha essite demonstrate que le circulante hemoglobina del plasma es augmentate in plure morbos que affice le systema reticuloendothelial.

Lubart, J.: Le catarrho commun e le factor de disbalancia del humiditate atmospheric (*anglese*), New York State J. Med. **62:** 816 (15 de martio) 1962.

Le effortios de disveloppar un vaccino contra le catarrho commun ha incontrate serie difficultates in consequentia del facto que le character del virus responsabile pare variar ab anno in anno. Siccitate in naso e gurgite, causate per calefaction artificial, crea un climate de interior que es favorabile pro le agente catarrhogene. Desiccate muco nasal es un excellente medio cultural pro le agente infective. Adequate grados de molliatura es etiam necessari pro le efficace function del cilios, del pharynge, del larynge, del trachea, e del pulmones. Durante le saison de calefaction le melior methodo pro prevenir catarrhos es mantener un bon balancia del humiditate per medio de dispositivos mechanic de humidification. Durante le estate, regulation del humiditate in interiores climatisate es necessari pro prevenir catarrhos de estate.

Filippone, J. F.: Effusion interlobar pleural in congestive disfallimento cardiac (*anglese*), NEW YORK STATE J. MED. **62:** 820 (15 de martio) 1962.

Le micre numero de reportate casos de effusion interlobar pleural in congestive disfallimento cardiac poterea esser prendite como indication que iste condition es rar, sed le occurrentia commun de congestive disfallimento cardiac per se e le facto que patientes con effusion interlobar pleural es frequentemente hospitalisate con un diagnose de tumor pulmonar suggere que le condition es forsan plus frequente que lo que es generalmente supponite. Es reportate tres casos que illustra le bases etiologic del diagnoses cardiac incontrate le plus communmente. Illos es hypertension, atherosclerosis coronari, e rheumatic morbo valvular. Un appropriate therapia produce le prompte disparition del loculate effusion. Le majoritate del loculate effusiones reportate in le litteratura occurreva al latere dextere, 75 pro cento de illos in le fissura transverse. Pleuritis adhesive non es un precondition absolute de effusion interlobular. Plus meticulose examines fluoroscopic e roentgenographic de patientes in congestive disfallimento cardiac resultarea probabilemente in le discoperta de numerose casos additional de effusion interlobar pleural.

Archer, J. S., Smessaert, A. A., e Hicks, R. G.: Tranquillisantes phenothiazinic in le anesthesia; revista, con un reporto in re fluphenazina (*anglese*), NEW YORK STATE J. MED. **62:** 828 (15 de martio)1962.

In le anesthesia, le phenothiazinas pote esser usate in le tranquillisation pre-operatori del excessivemente apprehensive patiente, in le medication pre-operatori del patiente asthmatic pro prevenir attaccos asthmatic de causation barbituratogene, como agente antiemetic, como adjuta in le production de hypothermia, in pediatric catheterismo cardiac, in casos de hypertension post parto, e in combatter singulto. Le requirimento de dosage in anesthesia es solmente un fraction de lo que es necessari in uso psychiatric. Hypotension e tachycardia es complicationes possibile, sed le recentemente disveloppate derivatos a nucleo piperazinic non representa un ver menacia si illos es usate judiciosemente. Dyscrasias de sanguine, jalnessa, ganio de peso, e photosensibilitate pote esser causate per phenothiazinas, sed isto occurre solmente post cursos prolongate. Symptomas extrapyramidal non se declara si le droga es administrate durante que le patiente es ancora subjecte al effecto de un anesthetico. Un studio a duple anonymato esseva interprendite in plus que 200 femininas destinate a dilatation e curettage, con le objectivo de determinar le effectos de dihydrochloruro de fluphenazina in administration post-operatori. Le resultatos monstrava un augmento del incidentia de vomituration e vomito amontante a 5 pro cento in le gruppo a fluphenazina e a 14 pro cento in le gruppo a placebo. Le modo de recuperation esseva plus seren quando le droga esseva administrate, e le duo gruppos non differeva notabilemente in tension de sanguine e pulso.

Gudgel, E. F., e Winer, M.: Le mechanismo del non-successo in le uso de griseofulvina (*anglese*), NEW YORK STATE J. MED. **62:** 834 (15 de martio) 1962.

Novanta-quatro patientes con morbos fungose superficial esseva tractate con griseofulvina e tenite sub observation durante periodos de usque a vinti menses. Le resultatos esseva considerate como successose in 71 del patientes e como non-successose in 23. Un certe numero del non-successos esseva de facto casos de recurrentia o de re-infection. Omne le non-successos—con 2 exceptiones—occurreva in patientes con lesiones del ungulas o del pelle in mano o pede. Sexanta patientes esseva excludite ab le serie a causa de un incorrecte diagnose de morbo fungose o a causa del diagnose de moniliasis o de tinea versicolor (le quales non responde al tractamento con griseofulvina). Le organismos que responde a griseofulvina include species de Epidermophyton, Microsporum, e Trichophyton. Le dose de griseofulvina e le duration del curso de su uso que esseva requirite pro effectuar le curation varia inter 1 g in un sol dosage e un total de 500 g usate in le curso de quatro centos dies. In al minus 7 del patientes, le non-successose resultatos esseva possibilemente causate per un inadequate dosage diurne e cumulative. Un relativemente massive dosage es requirite in le presentia de forte formationes callose.

Bohensky, F. B.: Mebutamato, un nove droga pro le tractamento de hypertension (*anglese*), NEW YORK STATE J. MED. **62:** 841 (15 de martio) 1962.

Esseva interprendite un studio in 51 ambulante patientes hypertensive pro determinar le effectos del therapia con mebutamato.

In terminos del lecturas del tensiones de sanguine, 46 del patientes (90 pro cento) respondeva favorabilemente al therapia a mebutamato. Le serie includeva 26 patientes con hypertension systolic. In illes, le reduction medie del tension systolic esseva 31 mm de Hg, durante que le normotensive valores del tension diastolic non declinava a nivellos infra illos del normotensivitate. In 25 patientes con hypertension diastolic, le reduction medie del tension systolic esseva 31 mm de Hg; e le reduction medie del tension diastolic esseva 20 mm de Hg. Le magnitude del reduction obtenite esseva proportional al nivellos initial del tensiones systolic e diastolic. Somnolentia occurreva in 21 patientes. Un sensation de vacuitate de capite esseva reportate in 14 casos, possibilemente in consequentia de superimposition a previe therapias o in consequentia de un excesso de dosage. Iste effectos lateral esseva eliminate spontaneemente o per un reduction del dosage. Omne le 20 patientes qui habeva beneficiate ab altere therapias obteneva meliorationes additional con mebutamato. Vinti-duo non habeva respondite a previe therapias, e 19 de illes se meliorava con mebutamato, durante que 1 monstrava nulle alteration e duo se pejorava. Duo del tres patientes pejorate sub previe therapias se meliorava con mebutamato el le tertie monstrava nulle effecto. Inter le 6 non previemente tractate, 5 se meliorava e 1 se pejorava.

Major catastrophes in 1961

Catastrophes (accidents which kill five or more persons) were responsible for about 1,250 deaths in the continental United States during 1961, Metropolitan Life Insurance Company statisticians report. The toll was about 250 less than in 1960.

The principal factor in the decrease was the smaller number of fatal injuries in major catastrophes (accidents in which at least 25 persons are killed).

About 260 lives were lost last year in major catastrophes, whereas approximately 450 lives were taken in comparable accidents during 1960.

Of the 5 major catastrophes in 1961, 3 involved civil aviation. One of them—the worst of the year—killed 78 persons when a scheduled plane plunged into a field near Chicago on September 1. Another claimed 77 lives on November 8 when a chartered aircraft crashed near Richmond, Virginia. In the third aviation catastrophe a scheduled plane crashed in Chicago on September 17, taking 37 lives.

The remaining 2 major catastrophes of the year were natural disasters. Hurricane Carla caused nearly 50 deaths in the Southwest and Midwest in September, and floods which struck the Midwest last May claimed 25 lives.

Thirty per cent of the deaths in accidents taking 5 or more lives last year resulted from motor vehicle accidents. Fires and explosions—many of them in the home—ranked second with about one fourth of the catastrophe death toll. And civil aviation was responsible for one fifth of the fatal injuries sustained in catastrophes in 1961.

Civil aviation catastrophes, those involving motor vehicles, and fires and explosions were responsible for an appreciably smaller death toll in 1961 than in 1960. Natural catastrophes contributed a considerably greater number of fatalities than in the year before.

Medical Schools

Albany Medical College

Three-year study. The National Institute of Arthritis and Metabolic Diseases has granted $36,712 to the College for a three-year study that seeks to prove how the adrenal glands of birds are able to respond to stressful stimuli even though the pituitary gland has been removed. The research will be done by Dr. Richard A. Miller, professor of anatomy. If Dr. Miller's research establishes that the adrenals of birds respond to stressful stimuli via a pathway that does not involve pituitary cells, he will investigate whether stressful stimuli affect the adrenals through something in the bloodstream or through nerves. Discovery of this pathway might have an important bearing on the treatment of various endocrine disorders in humans.

Albert Einstein College of Medicine

Grants. A grant from the National Foundation-March of Dimes for $31,204 has been received for basic studies of the structure and chemistry of joints. Dr. Alex B. Novikoff, research professor, Department of Pathology, is directing the project which is being done by David Hamerman, M.D., associate professor of medicine, and Peter Barland, a postdoctoral fellow in the Pathology Department, now in the Department of Medicine.

The National Institutes of Health recently awarded the following grants: Dr. Harry Eagle, chairman, Department of Cell Biology, $37,500 for a "Training Program in Cell Biology"; Sanford Edberg, M.D., Alfred A. Angrist, M.D., chairman, and Robert Terry, M.D., Department of Pathology, $36,685 for the study of "Physical Vascular and Electron Microscopy Studies in Head Trauma"; Leonard Greenburg, M.D., chairman, Department of Preventive and Environmental Medicine, $59,616 for the study of "Air Pollution, Meteorology, Morbidity and Mortality"; Dr. Murray E. Jarvik, Department of Pharmacology, $19,538 for the study of "Effects of Drugs Upon Memory in Rodents"; and Dr. Josiah Macy, Jr., Department of Physiology, $217,895 for the study of "Physiological Data Processing and Analysis Facility."

Appointments. Dr. Everett W. Bovard, associate professor, and Dr. Johannes Moll, visiting associate professor, Department of Anatomy; M. Jack Frumin, M.D., clinical professor, Department of Anesthesiology; Dr. Christian DeDuve, visiting professor, and Dr. Nobus Motohashi, visiting assistant professor, Department of Biochemistry; Dr. Jacob V. Maizel, assistant professor, Department of Cell Biology; Julian Ivor E. Hoffman, M.D., assistant professor (joint appointment), Departments of Medicine and Pediatrics; Richard J. Lebowich, M.D., assistant professor, Department of Pathology; Harry H. Gordon, M.D (joint appointment), Departments of Pediatrics and Obstetrics, as professor of pediatrics and research professor of obstetrics (maternal and child health); Paul Worthen Dale, M.D., assistant clinical professor, Department of Psychiatry.

Promotions. From instructor to research associate, Nechama Sternchuss Kosower, M.D., Department of Medicine; from assistant to associate professor, Herbert Weiner, M.D., Department of Psychiatry; from assistant clinical to associate professor, John R. Herman, M.D., Department of Surgery.

Visiting lecturers. During February and March the following visiting lecturers were at the College: Elena Ottolenghi, M.D., Department of Medicine, New York University School of Medicine; Robert Freiberge, M.D., Hospital for Special Surgery; Orlando Miller, M.D., Columbia University College of Physicians and Surgeons, Dr. David Perkins, Stanford University; and Dr. M. S. Fox, Rockefeller Institute.

Center for research in maternal and child health. A Center for Research in Maternal and Child Health and Human Development is being established at the College. Harry H. Gordon, M.D., has been appointed to the faculty as professor of pediatrics and research professor of obstetrics (Maternal and Child Health) and will be the scientific director of the program. Dr. Gordon's appointment will inaugurate an interdisciplinary program of research and teaching linking the Departments of Obstetrics, Pediatrics, and Child Psychology and Psychiatry.

Columbia University College of Physicians and Surgeons

Ceremony. A ground-breaking ceremony was held on February 5 signalizing the start of the construction of a new medical research building. The structure will be known as the "William Black Medical Research Building." Principal speaker at the ceremony was Robert F. Loeb, M.D., Bard Professor Emeritus of Medicine at the College. H. Houston Merritt, M.D., dean, presided.

New York University Medical Center

University Hospital. A grant of $110,700 from the John A. Hartford Foundation, Inc., for a three-year program to further existing studies of pancreatitis in all its phases has been received. Robert B. Pfeffer, M.D., assistant professor of clinical surgery, is the principal investigator under John H. Mulholland, M.D., chairman, Department of Surgery.

Irvington House Institute. Jonathan W. Uhr, M.D., has been appointed the first director of the Irvington House Institute for Rheumatic Fever and Allied Diseases. The Institute will be housed in University Hospital at 32nd Street between First Avenue and the East River Drive and occupancy will take place in the early fall of 1962.

State University of New York Downstate Medical Center

Visiting professor. Lucie Jessner, M.D., professor of psychiatry and director of child psychiatry, University of North Carolina Medical School, was visiting professor of psychiatry for the month of February.

Appointment. Abraham G. White, M.D., has been appointed director of medical education and attending physician at The Brooklyn Hospital and associate professor of medicine at the Medical Center. In his new post, Dr. White will coordinate The Brooklyn Hospital's educational activities, which include the teaching of third- and fourth-year students assigned for clinical clerkships at the Hospital as well as the educational program for interns and residents.

New prize in obstetrics. The Board of Trustees has accepted a bequest of $5,000 from the estate of the late Abraham G. Rongy, M.D., to establish a prize in obstetrics. The award will be known as "the Rongy Prize," and will be made each year to the member of the graduating class who excels in obstetrics.

Special lectures. Dr. Gerald Oster, professor of chemistry, Polytechnic Institute of Brooklyn, delivered a special lecture in February on "Photochemistry of Chlorophyll and Its Relation to the Problem of Photosynthesis." The lecture was sponsored by the Sigma Xi Club. Dr. Donald L. Wilhelm, visiting professor of microbiology, delivered two special lectures, one in February and one in March. The February lecture was on "The Vascular Events of Inflammation" and the March lecture was on "The Australian Aborigine."

Promotions. Philip N. Sawyer, M.D., from assistant professor to associate professor of surgery; from clinical instructors to clinical assistant professors in medicine, Philip J. Cantor M.D., and David Friedman, M.D.

New appointments. Department of Surgery: Peter Kottmeier, M.D., and William Nelson, M.D.; Departments of Medicine and Psychiatry, respectively, Constantin Teodoru, M.D., and Ferruccio di Cori, M.D., as clinical assistant professors.

State University of New York Upstate Medical Center

The Hutchings Society. The Hutchings Society sponsored a lecture on "Alkaloids and Yogic Enstasis" in January. Professor Agehananda Bharati, Syracuse University anthropologist, discussed the relationship between certain yogic experiences and states by specific induced alkaloid drugs.

MEND. Frederik B. Bang, M.D., professor of pathobiology, Johns Hopkins School of Hygiene and Public Health, was the Medical Education for National Defense speaker in January. Dr. Bang lectured on "The Hepatitis Problem in Light of Newer Virus Studies." Before the MEND lecture, Dr. Bang addressed the second year class in microbiology and the epidemiology seminar group.

Visitor. Dr. J. K. Steward, pediatrician-pathologist, from Manchester, England, visited the Center. Dr. Steward discussed "Spontaneous Regression of Retinoblastoma" at Pediatric Grand Rounds and then visited members of the Pediatric Department. This year Dr. Steward is doing research at the Connaught Medical Research Laboratories at the University of Toronto, Canada. In England he is associated with the Manchester Royal Infirmary and has been in charge of the Manchester Children's Tumor Registry since 1953.

Faculty changes. John J. Sullivan, M.D., from clinical instructor to clinical assistant professor, Department of Ophthalmology; Carlos Mendez, M.D., former senior investigator at the Masonic Medical Research Laboratory, Utica, as research associate professor, Department of Pharmacology.

Grants. New grants amounting to $119,266 have been received by: J. A. Abildskov, M.D., associate professor, Department of Medicine, from the Heart Association of Onondaga County, Inc.; Herbert D. Gullick, M.D., assistant professor, Department of Surgery; Charles W. Lloyd, M.D., professor, Department of Obstetrics-Gynecology, from Organon, Inc.; Richard H. Lyons, M.D., professor and chairman, and William Faloon, M.D., associate

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professor, Department of Medicine; Julius B. Richmond, M.D., professor and chairman, Department of Pediatrics, from the Commonwealth Fund; Dr. Kenneth A. Trayser, instructor, Department of Biochemistry, from the U.S. Public Health Service; Mary L. Voorhess, M.D., assistant professor, Department of Pediatrics, from the U.S. Public Health Service; Dr. Chester L. Yntema, professor, Department of Anatomy, from the U.S. Public Health Service (this grant was awarded to Dr. Mattheus Jan Toerien, from South Africa, who is under the supervision of Dr. Yntema).

Renewal grants received are: Dr. Myron Brin, associate professor, Departments of Biochemistry and Medicine, from the U.S. Public Health Service; Francis S. Caliva, M.D., assistant professor, Department of Medicine, from the Heart Association of Onondaga County, Inc.; Dr. Henry S. DiStefano, associate professor, Department of Anatomy, from the U.S. Public Health Service; Robert H. Eich, M.D., associate professor, and Harold Smulyan, M.D., assistant professor, Department of Medicine, from the U.S. Public Health Service; Dr. Carlyle Jacobsen, dean, from the U.S. Atomic Energy Commission; Thomas W. Mou, M.D., associate professor, and Harry A. Feldman, M.D., professor and chairman, Department of Preventive Medicine, from the U.S. Public Health Service; Dr. Justus F. Mueller professor, Department of Microbiology, Dr. James B. Preston, professor and chairman, Department of Physiology, Dr. David G. Whitlock, professor, Department of Anatomy, and Dr. Peter N. Witt, associate professor, Department of Pharmacology, all from the U.S. Public Health Service.

University of Rochester School of Medicine and Dentistry

Appointment. Isidore Levine, M.D., assistant professor of medicine and of preventive medicine and community health, has been appointed associate medical director of the Strong Memorial Hospital and an associate professor in the new Department of Health Services. Dr. Levine has also been promoted to associate professor of preventive medicine and community health.

Higher death rate among foreign-born persons

Foreign-born persons in the United States have always experienced a higher death rate than native-born Americans, but the disparity in the mortality rates has diminished appreciably since 1900, according to statisticians of the Metropolitan Life Insurance Company.

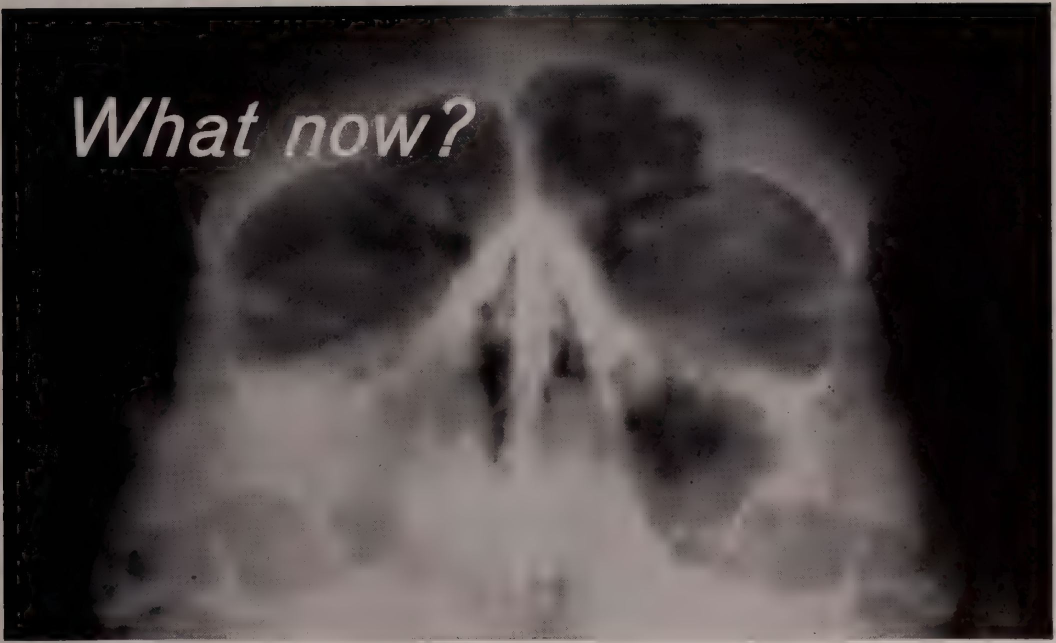
In a review of the death rates from 1900 to 1950 it was reported that by midcentury the mortality rate for native-born white males was 11.0 per 1,000, compared with 11.7 for foreign-born males. For native-born females, the rate in 1950 was 7.2 per 1,000 and 8.6 for foreign-born females.

Under age forty-five the death rate for native males in 1950 was 2.8 per 1,000, while the rate for foreign-born males was 2.9. A comparison of the female death rate shows a slightly greater difference. The mortality rate for native women in 1950 was 1.8 per 1,000 in the same age group, and 2.3 per 1,000 for the foreign-born females.

In the group at ages forty-five and over, the death rate in 1950 for native-born males was 31.7 per 1,000, compared with 33.7 for foreign-born males. For women, the respective rates were 20.9 and 24.5.

The higher mortality of the foreign-born persons, particularly in the early decades of the century, has been attributable largely to such environmental factors as living and working under unhealthful conditions, nutritional imbalances, and ignorance of available medical and public health facilities.

But as time went on, many of the handicaps diminished, and immigrants have shared increasingly in the spectacular reductions in mortality.



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1. Parsons, D. J.: Asthma, bronchitis, rhinitis and sinusitis: Adjunctive treatment with intramuscular chymotrypsin, Clin. Med. 5:11, 1958. 2. Teitel, L. H., *et al.:* Clinical observations with chymotrypsin, Indust. Med. *29:*150, 1960. 3. Taub, S. J.: Chymotrypsin therapy of bronchial asthma, Clin. Med. 7:2575, 1960.

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1. The Composition of Milks, Publication 254, National Academy of Sciences and National Research Council, Revised 1953. 2. Brown, G. W.; Tuholski, J. M.; Sauer, L. W.; Minsk, L. D., and Rosenstern, I.: J. Pediat. *56*:391 (Mar.) 1960.

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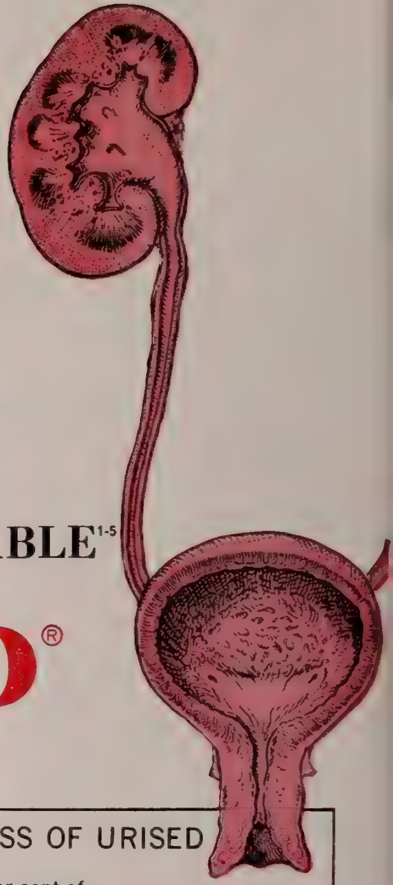

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Renner,[3] et al. (Common Urinary Infections)	50	96	None
Marshall[4] (Cystitis)	100	80	None
Strauss[5] (Urinary Infections in the Aged)	50	72	None
Total Cases	333		

References: (1) Sands, R. X.: Trigonitis during Pregnancy: A Method of Treatment. New York St. J. Med. 61: 2598-2602, 1961; (2) Haas, Jr., J., and Kay, L. L.: Management of Urinary Tract Infections. Southwest. Med. 42:30-32, 1961; (3) Renner, M. J., et al.: Urinary Tract Infections: Treatment with Antiseptic-Antispasmodic Agent. Hosp. Topics 39:71-73, 1961; (4) Marshall, W.: Treatment of Cystitis in General Practice. Clin. Med. 7:499-502, 1960; (5) Strauss, B.: Treatment of Urinary Tract Infections in the Elderly. Clin. Med. 4:307-310, 1957.

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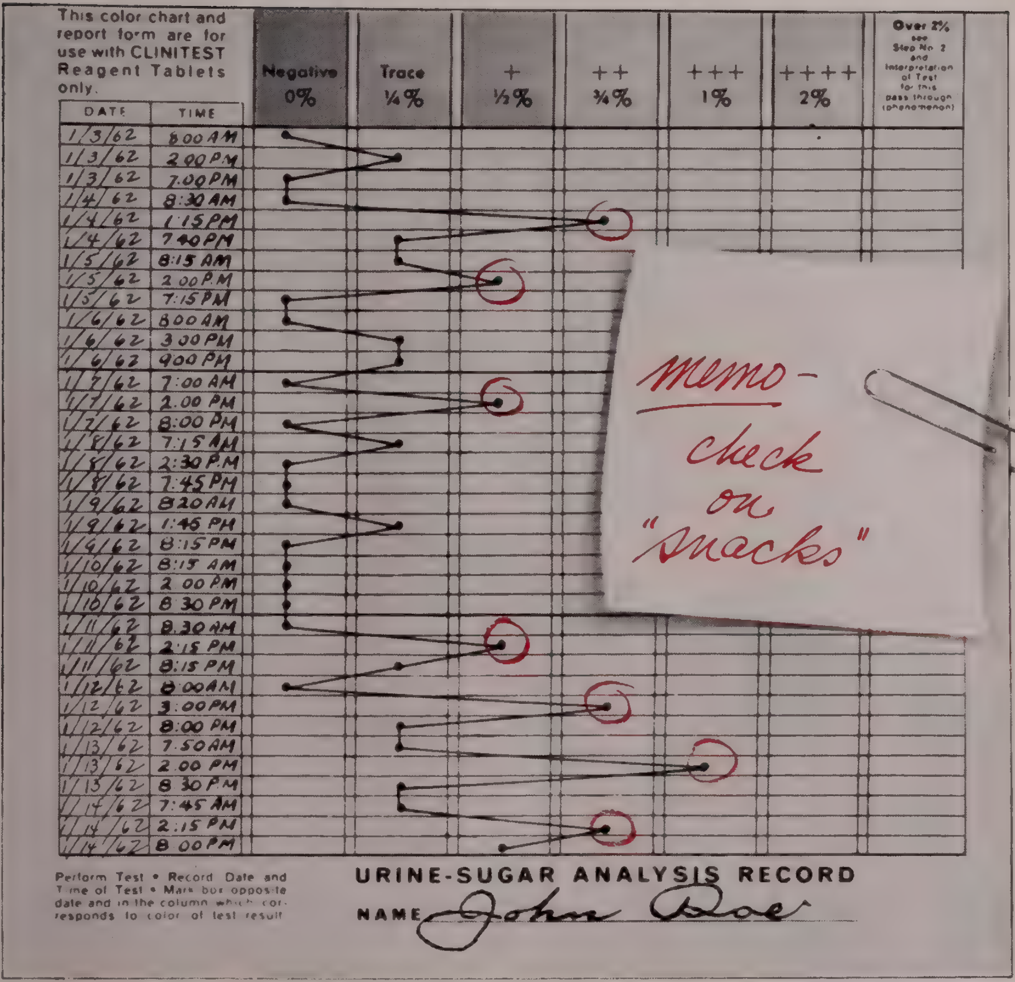

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NVENTION ISSUE

Medical Society of the State of New York

156th Annual Convention, May 14 to 18, 1962

The Statler Hilton, New York City

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the margin of success

in asthma therapy, it's the expectorant in Bronkotabs

In Bronkotabs, the efficacy of the classic ephedrine, theophylline and phenobarbital compound for the treatment of bronchial asthma has been improved—with the addition of the expectorant agent glyceryl guaiacolate.

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Spielman[1] found that "The combination of drugs used in . . . [Bronkotabs] . . . gave greater relief in these patients than the conventionally used tablet [ephedrine, theophylline and phenobarbital] . . ."

[1] Spielman, A. D.: Evaluation of a Combination Tablet of Theophylline, Ephedrine Sulphate, Phenobarbital, Thenyldiamine and Glyceryl Guaiacolate in the Treatment of Chronic Asthma, Ann. Allergy 18:281 (Mar.) 1960.

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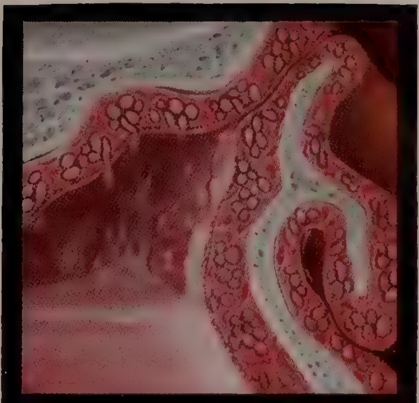
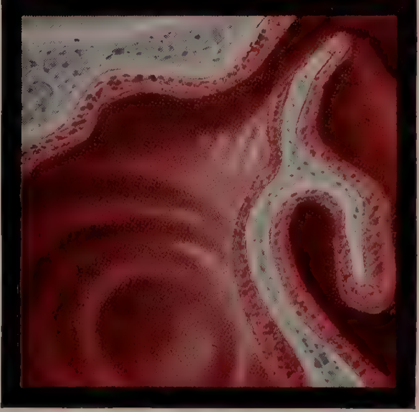


The clogged sinus
In sinusitis, the mucous membrane becomes hyperemic and edematous, lymph glands and goblet cells hyperactive. Ostium is closed by edema and secretions cannot drain freely.



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1. Grant, L. E.: Coryza and nasal sinus infections, **Clin. Med. & Surg.** 42:121, March, 1935. 2. Putney, F. J.: Sinus infection, in Conn, H. F. (Ed.): Current Therapy 1952, Philadelphia, W. B. Saunders Company, 1952, p. 110. 3. Simonton, K. M.: Current treatment of sinusitis, **Journal-Lancet** 79:535, Dec., 1959.

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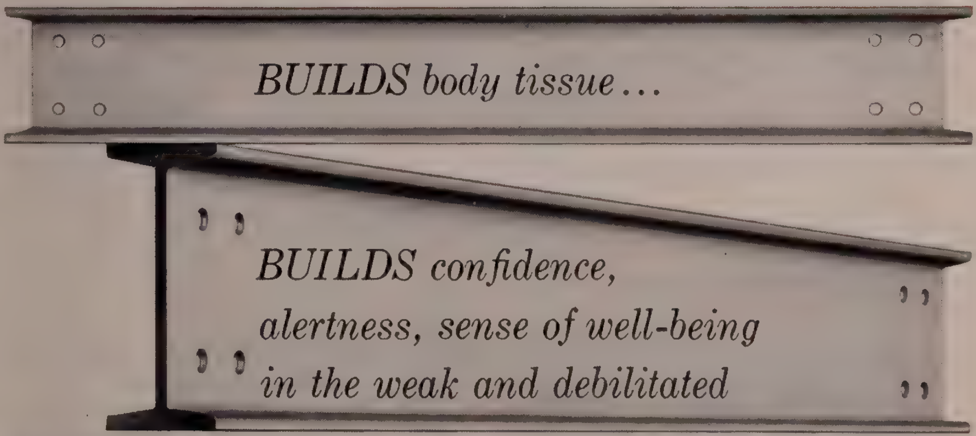
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*Ayd, Frank J., Jr.: Drug-induced Extrapyramidal Reactions: Their Clinical Manifestations and Treatment with Akineton. Psychosomatics 1:143 (May-June) 1960.

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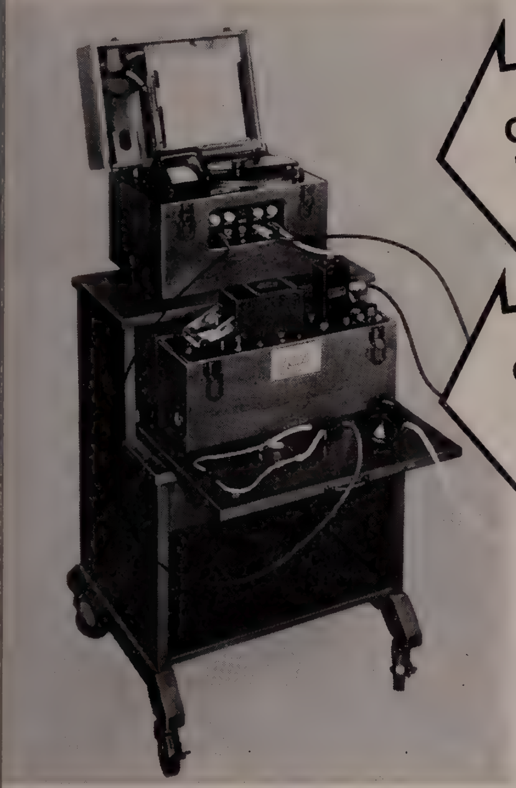

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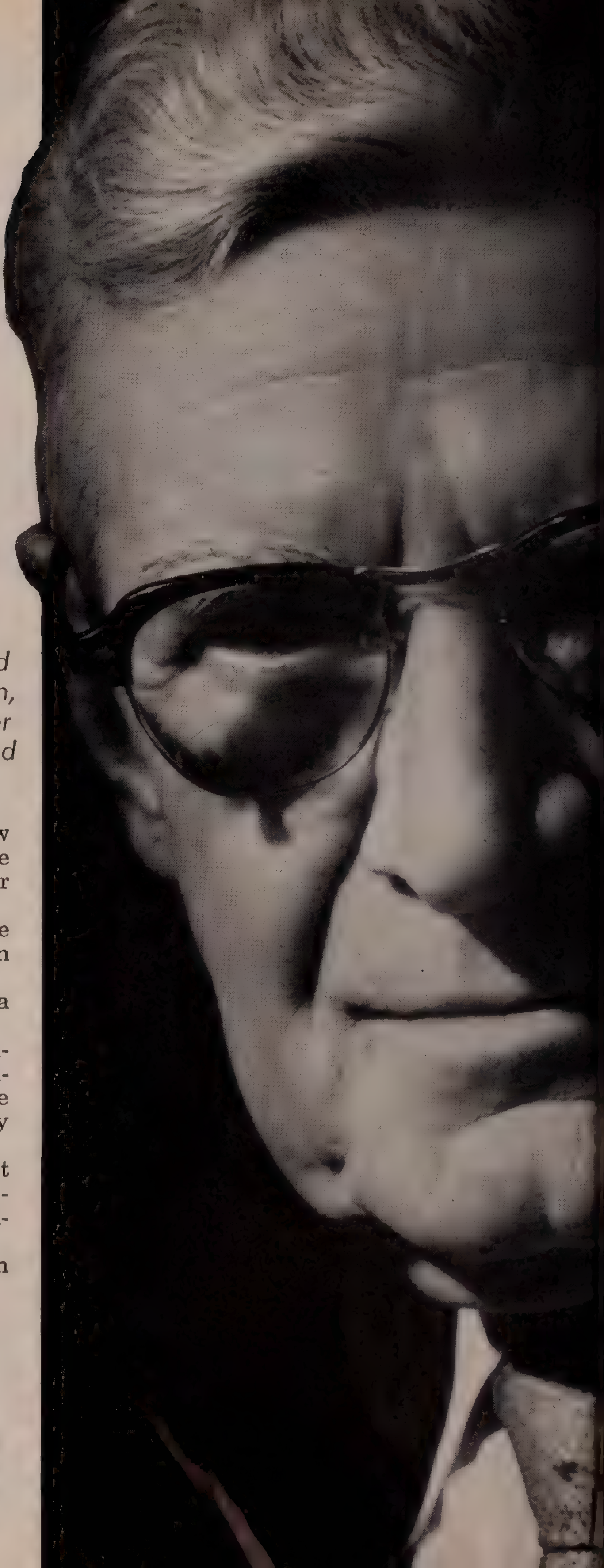

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[1] Taub, S. J.: Management of Anxiety in Allergic Disorders—New Approach. To be published in Psychosomatics; [2] Cahn, B.: Experience with a New Tranquilizing Agent (Hydroxyphenamate). Ibid; [3] Bergal, M., Beck, C., Davis, O. F., and Sloan, N.: On Use of Hydroxyphenamate in Anxiety Associated with Somatic Disease. To be published; [4] Alexander, L.: Effect of Hydroxyphenamate on Conditional Psychogalvanic Reflex in Man, Supplement to Diseases of the Nervous System, Sept., 1961: [5] Cahn, B.: Effect of Hydroxyphenamate in Treatment of Mild and Moderate Anxiety States. Ibid; [6] Cahn, M. M., and Levy, E. J.: Use of Hydroxyphenamate (Listica) in Dermatological Therapy. Ibid; [7] Eisenberg, B. C.: Amelioration of Allergic Symptoms with a New Tranquilizer Drug (Listica). Ibid; [8] Friedman, A. P.: Pharmacological Approach to Treatment of Headache. Ibid; [9] Greenspan, E. B.: Use of Hydroxyphenamate in Some Forms of Cardiovascular Disease. Ibid; [10] Gouldman, C., Lunde, F., and Davis, J.: Clinical Trial of Hydroxyphenamate in Alcoholic Patients. Ibid; [11] Personal Communications to Medical Department, Armour Pharmaceutical Company.

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TUESDAY, MAY 15

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2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

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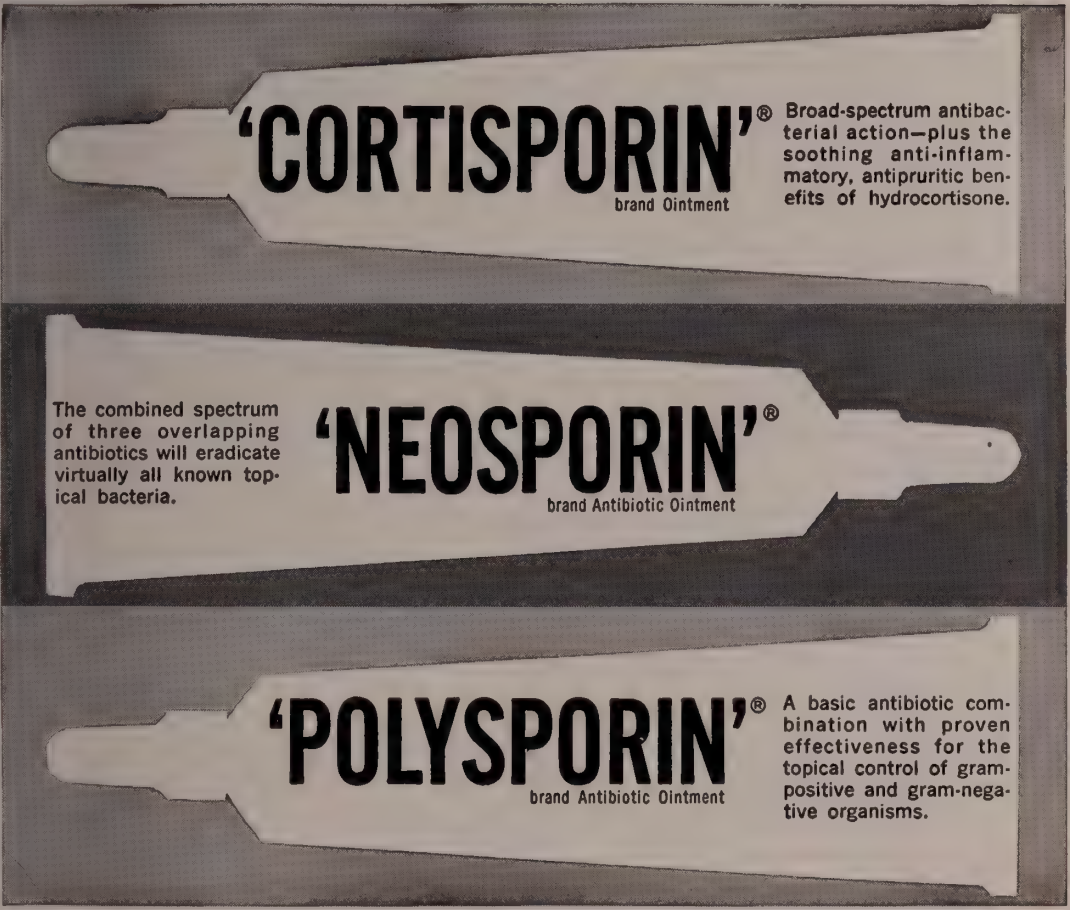
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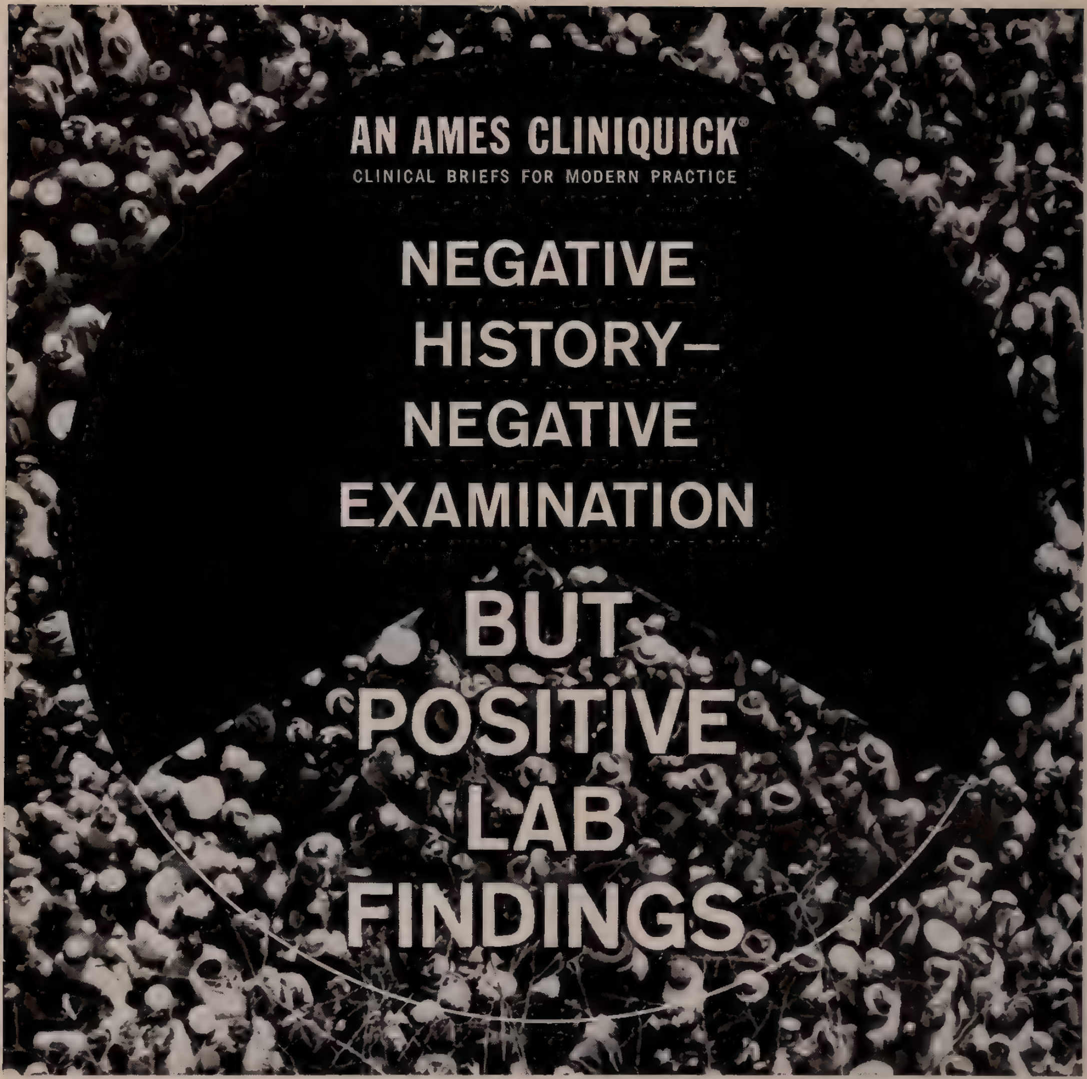
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*Schenthal, J. E.: J.A.M.A. *172*:1 (Jan. 2) 1960.

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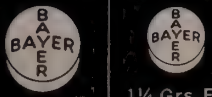

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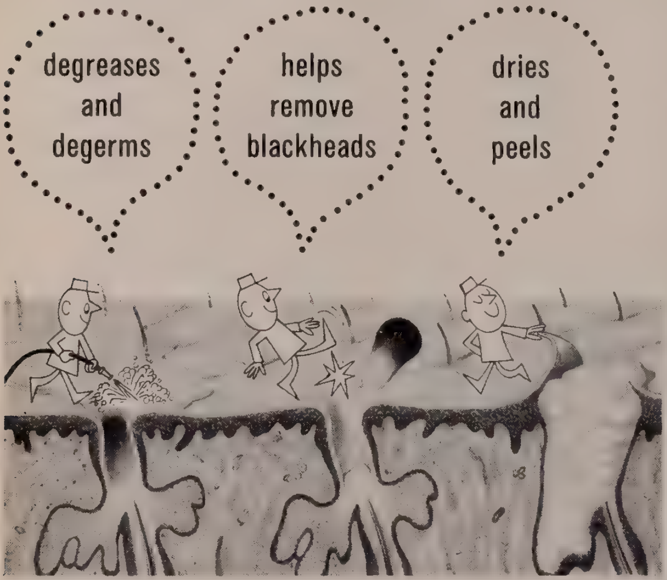

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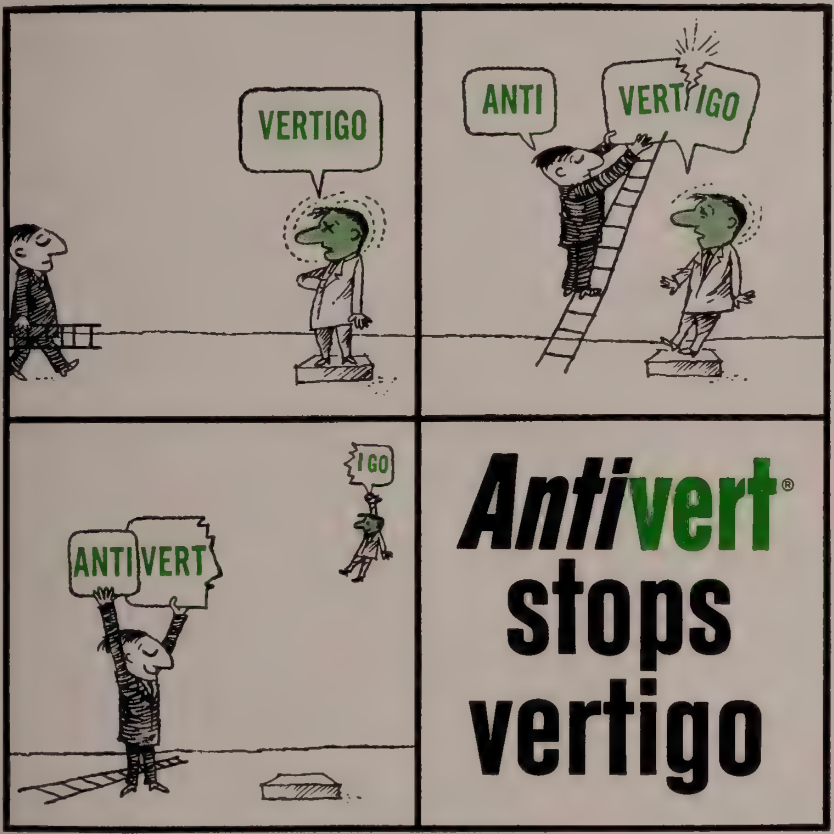

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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1. *Chairman's address:* **The Dynamics of Space Medicine**

   CONSTANTINE D. J. GENERALES, M.D., New York
   Assistant Professor of Space Medicine and Co-ordinator of Space Medicine Program, New York Medical College

2. **The United States Government's Role in Current Space Exploration**

   HON. VICTOR L. ANFUSO, Brooklyn (By invitation)
   House of Representatives, Committee on Science and Astronautics

3. **Unusual Earthly Forms of Life and Extraterrestrial Implications**

   JOHN PALISTER, New York (By invitation)
   President Explorers Club; Research Associate, Department of Entomology, New York Museum of Natural History

4. **The Significance of the Magnetosphere to Man**

   ALISTAIR G. W. CAMERON, PH.D., New York (By invitation
   Institute for Space Studies, National Aeronautics and Space Administration

5. **Biomedical Engineering as a Physician's Aid**

   LEE B. LUSTED, M.D., Rochester
   Associate Professor of Radiology and Biomedical Engineering, The University of Rochester School of Medicine and Dentistry

6. **Fossil Life in Meteoric Carbonaceous Matter**

   BARTHOLOMEW NAGY, PH.D., Bronx (By invitation)
   Associate Professor of Chemistry, Fordham University

7. **Electromagnetism and Its Effect on the Organism**

   JOHN H. HELLER, PH.D., Ridgefield, Conn. (By invitation)
   Director, New England Institute of Medical Research

8. **Electromagnetism and its Effect on Human Behavior**

   ROBERT O. BECKER, M.D., Syracuse
   Chief of Orthopedic Section, Veterans Administration Hospital

9. **Selected Topics on Space Medicine in the USSR**

   V. J. YAZDOVSKY, Moscow, USSR (By invitation)
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3:00–5:00	Albert Einstein College of Medicine of Yeshiva University

TUESDAY, MAY 15

1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

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1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

FRIDAY, MAY 18

1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
3:30–5:00	New York Medical College

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5

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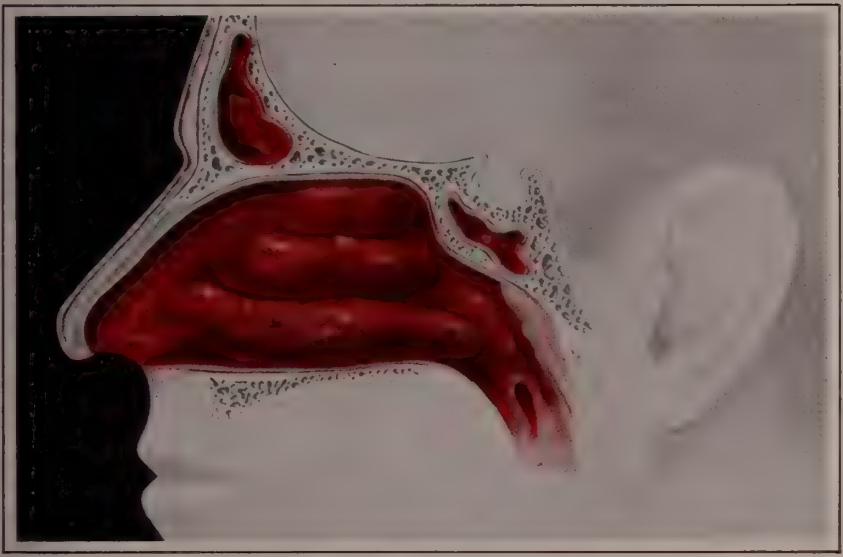

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[1] Accumulated reports from thirty-six clinical investigators: Lilly Research Laboratories.

New York State Journal of Medicine

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April 1, 1962 Volume 62 Number 7

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Preparation of Manuscript: Manuscripts should be face copy typed double-spaced with adequate margins on firm paper. Carbon copy flimsy cannot be used. The first page should list the title, the name of the author (or authors), degrees, and any institutional or other credits. Pages should be numbered consecutively. Tables should be typed and numbered and should have a brief descriptive title. Quotations must include full credit to both author and source. Periodical references should include in order: author's name with initials, title, periodical abbreviation, volume, pages, and year. References should be numbered consecutively in the order in which they appear in the text. Drawings and charts should always be made in black. For half tones, glossy photographs should be submitted. Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration.

General Information

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Editorials

The Annual Convention—1962

By custom of long standing this issue of the JOURNAL is devoted entirely to matters related to the Annual Meeting of the Medical Society of the State of New York which will take place in the succeeding month. The Society has met in convention each year since its founding in 1807. This year's gathering will mark the 156th meeting of the Society and its House of Delegates. In addition there was a special meeting of the House on February 10, 1962.

The special meeting of the House of Delegates was called to express unequivocally the convictions of the members of the Medical Society of the State of New York relating to proposed legislation at both the State and Federal level which would affect the practice of medicine. It was urgent that this expression take place while the two legislative bodies were in session.

Four resolutions were passed unanimously. The first pledged the physicians of this State to provide the best medical care to everyone regardless of any and all circumstances. The second reaffirmed the doctors' unalterable opposition to any nibbling away at the Medical Practice Act which would permit scientifically unqualified persons to diagnose and treat human disease. The third called for revision of the enabling act of the Kerr-Mills legislation known as the Metcalf-McCloskey Act in this State to the end that it provide medical aid to the aged through insurance coverage and obviate the creation of another welfare category. The fourth resolution stated that if the Kerr-Mills Act is implemented to its full intention, there is no need for the wide open door of the proposed King-Anderson approach at the Federal level.

The most important part of this issue is taken up by the reports of your officers and working committees of the Society. This is a true report to the stockholders and represents a tremendous amount of work on the part of those you have entrusted with your leadership. Read these reports critically of course but with respect for the considered judgment of your representatives which was arrived at through careful study, often of many months duration.

All members may attend the sessions of the House of Delegates as spectators, and they may attend all sessions of the reference committees as full participants. We urge you to attend, if only to get a close-up view of your democratic medical organization at work.

The theme of the scientific session this year will be "Medical Centers on Parade." The 10 medical teaching centers in this State, which include the University of Buffalo School of Medicine, the University of Rochester School of Medicine and Dentistry, the State University of New York Upstate Medical Center, the Albany Medical College (Union University), the Albert Einstein College of Medicine (Yeshiva University), the College of Physicians and Surgeons (Columbia University), Cornell University Medical College, New York University College of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, and the State University of New York Downstate Medical Center, will furnish interesting programs covering teaching and research. This presents an opportunity to learn what is going on in the medical schools and to meet and discourse with key members of the faculties. The scientific exhibits will be of the usual high order, and prizes will be awarded to those of particular interest.

The date of the annual meeting is May 14 to 18. The place is the Statler Hilton in New York City. We urge you to reserve this time and to arrange for hotel accommodations early.

Announcement

It is called to our attention for the information of our subscribers that the New York City Excise Tax on Gross Receipts imposed pursuant to the General Business and Financial Tax Law is due May 15, 1962. The tax applies to persons conducting any trade, business, profession, vocation, or commercial activity within the City of New York for gain or profit. In general, the tax is based on the gross receipts for the entire calendar year 1961. However, if the taxpayer has reported in a return for a prior period his gross receipts for a portion of such calendar year, the tax is measured by his gross receipts during the balance of the year.

In filing General Business Tax returns on Form B, doctors are required to report thereon as Item 4 the gross receipts (gross fees) from the practice of their profession. Dividends and interest received from investments and profits derived from stock and bond transactions should not be included in the measure of the tax when filing General Business Tax returns if such transactions are occasional transactions of a nature extraneous to the taxpayer's regular activities. In reporting gross receipts, no deduction may be taken for salaries, rent, and other office expenses.

Where a doctor is also a member of a medical group associated with the Health Insurance Plan of Greater New York, the distributive share of the income he receives from the group is not to be included in his gross receipts, since the various medical groups associated with H.I.P. are generally regarded as partnerships and are required to file returns on the basis of their total gross receipts.

In computing gross receipts subject to tax, the taxpayer may take a specific deduction of $10,000.00 from his gross receipts. Tax at the rate of $^{2}/_{5}$ of 1 per cent is to be paid on his gross receipts in excess of $10,000.00. No tax is imposed when the gross receipts do not exceed $10,000.00, and no return need be filed in such case.

The return must be filed on or before May 15, 1962, with the City Collector in the borough in which the taxpayer maintains his office. A remittance for the total amount of tax due, drawn to the order of the City Collector, must accompany the return when filed. Form B for filing this return will be mailed to all taxpayers who have filed returns in prior years. The office of the Comptroller of the City of New York will be pleased to furnish further information or assistance in the preparation of returns.

Redway Medal

The first Laurance David Redway Medal will be awarded at the Annual Meeting of the Medical Society of the State of New York which will be held in New York City, May 14 to 18, 1962.

A gold medal and cash prize of $500 in memory of the late editor of the New York State Journal of Medicine will be awarded annually for the article judged to be the most outstanding of those which appeared in the Journal during the previous year.

Every Journal subscriber is invited to send his nomination to the editor of the Journal for the best article which appeared in the Journal in 1961, giving brief reasons for the choice.

Nominations must reach the editor by March 31, 1962. They should be addressed to William Hammond, M.D., Editor, New York State Journal of Medicine, 750 Third Avenue, New York 17, New York.

Do You Have Your Hotel Reservation for the Annual Convention?

If you do not now have a confirmed hotel reservation in New York City for the Annual Convention of the Medical Society of the State of New York, May 13 to May 18, 1962, at the Statler Hilton Hotel, please fill out and mail the form at the bottom of this page and send it directly to the Statler Hilton.

Should your request be received after the five hundred rooms set aside for the Society at the Statler Hilton have been assigned, your reservation will be turned over to one of the hotels in the neighborhood. Confirmation will come to you direct from the hotel making the accommodation.

If you do not use the form below, please be sure to identify yourself as a physician when writing regarding reservations. This will insure proper attention to your request.

William L. Wheeler, Jr., M.D., *Secretary*

All Reservations Must be Received by April 30

156th Annual Convention of the Medical Society of the State of New York, May 13 to 18, 1962

Front Office Manager
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Please reserve accommodations as checked (√) below):

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Address . . . .

City . . . . Zone . . . . State . . . .

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Date arriving . . . . Hour . . . . A.M. . . . . . . P.M. . . . .

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Double-Bed Room with Bath for two—per day	11.00 ☐ 13.50 ☐ 14.00 ☐	14.50 ☐ 15.00 ☐ 15.50 ☐	16.00 ☐ 16.50 ☐ 17.00 ☐	17.50 ☐ 18.00 ☐ 18.50 ☐
Twin-Bed Room with Bath for two—per day	15.00 ☐ 16.00 ☐ 16.50 ☐	18.00 ☐ 18.50 ☐ 19.50 ☐	20.50 ☐ 21.50 ☐ 22.00 ☐	22.50 ☐ 24.00 ☐ 25.00 ☐
Suite—Living Room, Bed Room and Bath			36.50 ☐ 41.00 ☐	40.00 ☐ 45.00 ☐

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We're looking to you for the money. Not a lot—just enough to put one kid one day closer to walking. That's about $5.

"Fight with them—against crippling"

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Convention Schedule

156th Annual Convention

MEDICAL SOCIETY OF THE
STATE OF NEW YORK

May 14 through 18, 1962

Statler Hilton
New York City

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House of Delegates

The annual meeting of the House of Delegates of the Medical Society of the State of New York will be called to order at 10:00 A.M. on Monday, May 14, 1962, in the Georgian Room of the Statler Hilton, New York City.

In accordance with Chapter II, Section 3 of the Bylaws, the House will assemble according to the following schedule:

Monday, May 14, 1962, 10:00 A.M.
Wednesday, May 16, 1962, 9:00 A.M. and 2:00 P.M.
Thursday, May 17, 1962, 9:00 A.M.

At the last adjourned session (Thursday, May 17, 9:00 A.M.) the election of officers, councillors, trustees, and delegates to the American Medical Association will take place in accordance with Chapter III, Section 1 of the Bylaws.

FREDERICK A. WURZBACH, JR., M.D.,
Speaker
WILLIAM L. WHEELER, JR., M.D.,
Secretary

156th Annual Meeting

The 156th Annual Meeting of the Medical Society of the State of New York will be held on Wednesday, May 16, 1962, at 8:00 P.M. in the Terrace Ballroom of the Statler Hilton, New York City.

JOHN M. GALBRAITH, M.D.,
President
WILLIAM L. WHEELER, JR., M.D.,
Secretary

Registration

Registration for *delegates* will be held in the foyer of the Georgian Room, Ballroom floor of the Statler Hilton, on Sunday, May 13, from 3:00 P.M. to 7:00 P.M., and on Monday, May 14, after 9:00 A.M.

General registration for *State Society members and guests* will be held on the west mezzanine, Monday through Thursday, May 14 through 17, from 8:30 A.M. to 5:30 P.M., and Friday, May 18, from 8:30 A.M. to 12:00 NOON.

Exhibits

Scientific Exhibits will be located in the Exhibit Hall on the mezzanine.

Scientific Motion Pictures will be shown in the Motion Picture Theatre in the Exhibit Hall.

Technical Exhibits will be located in the Ballroom and in the Exhibit Hall.

Exhibits will be open as follows:

Monday through Thursday, May 14 through 17, 9:00 A.M. to 5:30 P.M.; Friday, May 18, 9:00 A.M. to 12:00 NOON.

Scientific Program

"MEDICAL CENTERS ON PARADE"

General Sessions will be held every afternoon, Monday through Thursday, May 14 through 17, at 1:00 P.M. in the Gold Ballroom, Ballroom balcony, and Friday, May 18, at 1:00 P.M. in the Georgian Room.

Section and Session Meetings will be held Monday through Friday, May 14 through 18, at 9:00 A.M.

See page 943 for program of meetings.

Dinner Dance

The Dinner Dance will be held in the Terrace Ballroom, main floor of the Statler Hilton, at 8:00 P.M., preceded by the President's Reception at 7:00 P.M., Wednesday, May 16.

Tickets should be ordered in advance from the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York, or from your county medical society. Subscription is $17.50 per person.

Woman's Auxiliary

See page 970 for program.

1962 ANNUAL CONVENTION

Scientific Program

Chairman — ALFRED P. INGEGNO, Kings
Associate Chairmen — WILLIAM F. LIPP, M.D., Erie
BERNARD J. PISANI, M.D., New York
CHAIRMEN OF SECTIONS AND SESSION

GENERAL SESSIONS
"Medical Centers on Parade"

The General Sessions programs were arranged with the cooperation of the ten medical centers in New York State. Each center has an alloted time and a liaison officer who worked with the State Medical Society to prepare the programs.

Monday
May 14
Gold Ballroom
Ballroom Balcony
1:00 p.m.

ALBANY MEDICAL COLLEGE OF UNION UNIVERSITY

FRANK M. WOOLSEY, JR., M.D., Albany
Associate Dean; Professor and Chairman, Department of Postgraduate Medicine

Medical Center Responsibilities to Practicing Physicians

FRANK M. WOOLSEY, JR., M.D., Albany

Explanation and On-the-Air Demonstration of the Albany Medical College Two-Way Radio Conference Network

WILLIAM P. NELSON, III, M.D., Albany
Assistant Dean, Associate Professor of Postgraduate Medicine

Two-Way Radio Conference Seminar Between the Albany Medical College and the General Session

Four Albany Medical Center research projects will be discussed and there will be an opportunity for the physicians in attendance at the General Session to question the discussers via two-way radio.

Risk Factors in Coronary Heart Disease
JOSEPH T. DOYLE, M.D., Albany
Professor of Medicine, Head of the Subdepartment of Cardiovascular Medicine

Geographic Pathology of Arteriosclerosis
WILBUR A. THOMAS, M.D., Loudonville
Professor and Chairman, Department of Pathology

Experiment in Medical Center-Community Hospital Collaboration
WILLIAM P. NELSON, III, M.D., Albany
Assistant Dean, Associate Professor of Postgraduate Medicine

Post-Traumatic Acute Renal Failure
SAMUEL R. POWERS, JR., M.D., Albany
Professor of Experimental Surgery

3:00 p.m. **ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY**

QUENTIN B. DEMING, M.D., Bronx
Associate Professor of Medicine

1. **A Human Heredity Research Unit**
2. **Art in the Teaching of Medicine**
3. **Surgery for Dissecting Aneurysm**
4. **Psychiatry Teaching and Community Service**
5. **Physiology of the Ureter**

Tuesday
May 15
Gold Ballroom
Ballroom Balcony
1:00 p.m.

COLUMBIA-PRESBYTERIAN MEDICAL CENTER

GEORGE A. PERERA, M.D., New York City
Assistant Dean, College of Physicians and Surgeons

PANEL DISCUSSION: **Chronic Pulmonary Disease—Physiology, Diagnosis, and Management as Taught to Students and House Staff**

ANDRÉ F. COURNAND, M.D., New York City
Professor of Medicine
DICKINSON W. RICHARDS, M.D., New York City
Professor of Medicine
ALFRED P. FISHMAN, M.D., New York City
Associate Professor of Medicine
HARRY W. FRITTS, JR., M.D., New York City
Associate Professor of Medicine

2:30 p.m. **Public Relations Session**

3:30 p.m. **UNIVERSITY OF BUFFALO SCHOOL OF MEDICINE**

ROSWELL K. BROWN, M.D., Buffalo
Acting Dean

SYMPOSIUM AND PANEL DISCUSSION: **Recently Acquired Knowledge of Blood Flow**

IVAN L. BUNNELL, M.D., Buffalo, *Moderator*

Electronic Flow Meter
WORTHINGTON G. SCHENK, JR., M.D., Buffalo
Associate Professor of Surgery
KHLAR E. MCDONALD, M.D., Cheektowaga
Resident in Surgery, Edward J. Meyer Memorial Hospital

Implanted Cardiac Pace Maker
WILLIAM M. CHARDACK, M.D., Buffalo
Associate Professor of Surgery
ANDREW A. GAGE, M.D., Buffalo
Clinical Associate in Surgery

Inaudible Heart Sounds (Undergraduate Research)
D. JACKSON COLEMAN, M.D., Washington, D.C.
U.S. Public Health Service

Blood Flow and Endocarditis
Simon Rodbard, M.D., Buffalo
Professor of Experimental Medicine

Ultrafiltration Treatment of Heart Failure
Sidney Anthone, M.D., Buffalo
Assistant Clinical Professor of Surgery
Roland Anthone, M.D., Buffalo
Assistant Clinical Professor of Surgery

Questions and Answers

Wednesday
May 16
Gold Ballroom
Ballroom Balcony
1:00 p.m.

STATE UNIVERSITY OF NEW YORK UPSTATE MEDICAL CENTER IN SYRACUSE

William A. Harris, M.D., Syracuse
Assistant Dean for Postgraduate and Graduate Medical Education

Symposium and Panel Discussion: **Diabetic Retinopathy**

Arthur H. Dube, M.D., Syracuse, *Moderator*
Clinical Assistant Professor of Medicine

Introduction
Arthur H. Dube, M.D., Syracuse

Defects in Fat Metabolism
Clint Elwood, Ph.D., Syracuse
Instructor in Biochemistry

Diagnosis and Pathology
John J. Sullivan, M.D., Syracuse
Clinical Instructor in Ophthalmology

Neurosurgical Therapy
Herbert Lourie, M.D., Syracuse
Assistant Professor of Neurosurgery

Questions and Answers

2:30 p.m.

DEANS' PANEL

Panel Discussion: **Medical Education**
Robert A. Moore, M.D., Brooklyn, *Moderator*
Dean, State University of New York Downstate Medical Center

Problems in medical education vital to the understanding of the practicing physician will be discussed, followed by a question and answer period.

3:30 p.m.

NEW YORK HOSPITAL—CORNELL MEDICAL CENTER

Richard A. Saunders, M.D., New York City
Associate Dean

1. **Modern Concepts in Anesthesia**
   Joseph F. Artusio, Jr., M.D., New York City
   Anesthesiologist-in-Chief; Professor of Anesthesiology in Surgery
2. **Use of Thermal Dilution for Evaluation of Vascularity of Various Organs**
   Edward I. Goldsmith, M.D., New York City
   Assistant Attending Surgeon; Assistant Professor of Clinical Surgery

3. **Aortic Stenosis—Medical and Surgical Aspects**

Thomas Killip, III, M.D., New York City
Assistant Attending Physician; Assistant Professor of Medicine

Lucian I. Arditi, M.D., New York City
Assistant Attending Physician; Clinical Instructor in Medicine

George R. Holswade, M.D., New York City
Associate Attending Surgeon; Clinical Associate Professor of Surgery

Thursday May 17
Gold Ballroom
Ballroom Balcony
1:00 p.m.

STATE UNIVERSITY OF NEW YORK DOWNSTATE MEDICAL CENTER

Robert A. Moore, M.D., Brooklyn
President and Dean

Panel Discussion: **The Role of Chemotherapy in the Treatment of Cancer**

John G. Masterson, M.D., Brooklyn, *Moderator*
Associate Professor of Obstetrics and Gynecology; Director, State University Gynecologic Tumor Service, Kings County Hospital

Irving Enquist, M.D., Brooklyn
Professor of Surgery; Attending in Surgery, Kings County Hospital

Herbert C. Lichtman, M.D., Brooklyn
Associate Professor of Medicine; Attending in Medicine, Kings County Hospital

2:30 p.m. **The Albert F. R. Andresen Memorial Lecture: Problems and Approaches in the Clinical Management of Intra- and Extrahepatic Obstructive Jaundice**

Alfred P. Ingegno, M.D., Brooklyn
Attending Physician, Long Island College Hospital; Clinical Associate Professor of Medicine, State University of New York Downstate Medical Center

3:30 p.m. **NEW YORK UNIVERSITY MEDICAL CENTER**

William A. Frosch, M.D., New York City
Assistant Dean, New York University School of Medicine

Friday May 18
Georgian Room
Ballroom Floor
1:00 p.m. to 3:30 p.m.

UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE AND DENTISTRY

Donald G. Anderson, M.D., Rochester
Dean

A Multidisciplinary Approach to the Problem of Arthritis

Ralph F. Jacox, M.D., Rochester
Associate Professor of Medicine; Director of Arthritis Program

2:30 p.m. **A. Walter Suiter Lecture**

3:30 p.m. **NEW YORK MEDICAL COLLEGE, FLOWER AND FIFTH AVENUE HOSPITALS**

David Lehr, M.D., New York City
Professor and Chairman, Department of Physiology and Pharmacology

SECTIONS

All papers read before the Society by members become the property of the Society. The original copy of each paper shall be left with the Secretary of the Section or Session.

Discussers should have their remarks typed and should hand them to the Secretary.

Section and Session meetings shall begin promptly at the hour specified.

Executive Session—The first order of business, election of officers.

"To participate in the election of any section, a member must register with such section."—Bylaws, Chapter XII, Section 3.

SECTION ON

Allergy

Chairman......FRANCIS E. EHRET, M.D., Erie
Vice-Chairman...HARRY LEIBOWITZ, M.D., Kings
Secretary...ALEXANDER CHESTER, M.D., Kings

Monday, May 14/9:00 A.M./East Room, Ballroom Floor

1. **The Present Status of Foods in the Etiology of Allergic Diseases**

A. IRWIN KLEINMAN, M.D., Brooklyn
Attending in Allergy, Beth-El Hospital
HARRY MARKOW, M.D., Brooklyn
Chief of Allergy, Beth-El Hospital

2. **Drug Allergy—Immunologic and Clinical Aspects**

JOHN H. VAUGHAN, M.D., Rochester
Associate Professor of Medicine and Assistant Professor of Bacteriology (Immunology), University of Rochester School of Medicine and Dentistry

3. **The Pulmonary and Allergic Manifestations of Cystic Fibrosis of the Pancreas**

PAUL A. DI SANT'AGNESE, M.D., Bethesda, Maryland (*by invitation*)
Chief, Pediatric Metabolism Branch, National Institute of Arthritis and Metabolic Diseases

4. **The Present Status of Steroid Therapy with a Discussion of the Newer Steroids**

THOMAS F. FRAWLEY, M.D., Albany
Professor of Medicine and Head of Department of Endocrinology and Metabolism, Albany Medical College of Union University

5. **The Problem of Urticaria—Present Concepts of Etiology and Management**

JOHN M. SHELDON, M.D., Ann Arbor, Michigan (*by invitation*)
Professor of Medicine, University of Michigan Medical School

SECTION ON

Anesthesiology

Chairman.......................................WILLIAM S. HOWLAND, M.D., New York
Vice-Chairman.......................................JACOB S. ISRAEL, M.D., Onondaga
Secretary.......................................SOLOMON G. HERSHEY, M.D., New York

Tuesday, May 15/9:00 A.M./East Room, Ballroom Floor

1. **Prophylactic Aspects of Post-Traumatic Renal Insufficiency**

ANTONIO BOBA, M.D., Albany
Associate Professor of Anesthesiology, Albany Medical College of Union University
CHARLES M. LANDMESSER, M.D., Loudonville
Professor of Anesthesiology, Albany Medical College of Union University
Discussion: V. D. B. MAZZIA, M.D., New York
Professor and Chairman, Department of Anesthesiology, New York University School of Medicine

2. **General Anesthesia with Minimal Equipment**

C. PAUL BOYAN, M.D., New York City
Associate Attending Anesthesiologist, Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases
Discussion: ERNEST SALANITRE, M.D., New York City
Assistant Professor of Anesthesiology, Col-

lege of Physicians and Surgeons of Columbia University

3. **Respiratory Management of the Crushed Chest**

ALISTAIR J. GILLIES, M.D., Rochester
Professor of Anesthesiology, University of Rochester School of Medicine and Dentistry

Discussion: WILLIAM S. HOWLAND, M.D., New York City
Attending Anesthesiologist, Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases

4. **A Universal Anesthesia Vaporizer for Use in Disasters**

ALLEN B. DOBKIN, M.D., Syracuse
Professor of Anesthesiology, State University of New York Upstate Medical Center in Syracuse

Discussion: RAPHAEL W. ROBERTAZZI, M.D., New York City
Professor of Clinical Anesthesiology, New York University Post-Graduate Medical School

5. **Effect of Radiation on Anesthetic Agents**

LOUIS R. ORKIN, M.D., New York City
Professor and Chairman, Department of Anesthesiology, Albert Einstein College of Medicine of Yeshiva University

HOWARD L. ZAUDER, M.D., Hartsdale
Assistant Professor of Anesthesiology, Albert Einstein College of Medicine of Yeshiva University

Discussion: SHIH-HSUN NGAI, M.D., New York City
Associate Professor of Anesthesiology, College of Physicians and Surgeons of Columbia University

6. **Intravenous and Intramuscular Hydroxyzine Hydrochloride Given as Preanesthetic Medication**

DANTE BIZZARRI, M.D., New York City
Associate in Anesthesiology, New York Medical College, Flower and Fifth Avenue Hospitals

Discussion: ERWIN LEAR, M.D., Williston Park
Assistant Clinical Professor of Anesthesiology, State University of New York Downstate Medical Center

SECTION ON

Chest Diseases

Chairman . . HENRY W. LEETCH, M.D., Franklin
Vice-Chairman . . . . WILLARD J. DAVIES, M.D., Nassau
Secretary . . . . . HARRY GOLEMBE, M.D., Sullivan

Wednesday, May 16/9:00 A.M./East Room, Ballroom Floor

1. **Chronic Cough In Children: Diagnosis and Treatment**

DANIEL C. BAKER, JR., M.D., New York City
Clinical Professor of Otolaryngology, College of Physicians and Surgeons of Columbia University; Attending Otolaryngologist, Presbyterian and Babies Hospitals

2. **Advances in Treatment of Carcinoma of the Esophagus**

DAVID P. BOYD, M.D., Boston, Massachusetts (*by invitation*)
Associate Director, Department of Thoracic Surgery, Lahey Clinic; Attending Surgeon, Deaconess Hospital

Discussion: GEORGE T. PACK, M.D., New York City
Director, Pack Clinic; Attending Surgeon, James Ewing Hospital, Flower and Fifth Avenue Hospitals

3. **The Medical Management of Some Common Esophageal Disorders**

HERMAN J. MOERSCH, M.D., Rochester, Minnesota (*by invitation*)
Professor of Medicine, University of Minnesota School of Medicine; Chairman, Section of Internal Medicine, Mayo Clinic

Discussion: ARTHUR Q. PENTA, M.D., Schenectady
Director, Department of Broncho-Esophagology, St. Clare's and Ellis Hospitals; Visiting Lecturer, Department of Medicine, Temple University Medical School

SECTION ON

Dermatology and Syphilology

Chairman . . . . ROYAL M. MONTGOMERY, M.D., New York
Vice-Chairman . JOSEPH J. RUSSO, M.D., Albany
Secretary . . . . ALEX W. YOUNG, JR., M.D., New York

Thursday, May 17/9:00 A.M./East Room, Ballroom Floor

Symposium and Panel Discussion—**Skin Diseases of the Lower Extremities**

VICTOR H. WITTEN, M.D., New York City, *Moderator*
Associate Clinical Professor of Dermatology, New York University Post-Graduate Medical School

1. *Chairman's Address*—**Corns, Calluses, and Warts—Their Differential Diagnosis**

ROYAL M. MONTGOMERY, M.D., New York City
Attending in Medicine (Dermatology),

Roosevelt Hospital; Consulting Dermatologist, Hospital for Special Surgery

2. **For Papillomas and Cancer: Are Viruses the Answer?**

FRED RAPP, PH.D., New York City (*by invitation*)
Assistant Professor of Microbiology and Immunology, Cornell University Medical College; Virologist to Philip D. Wilson Research Foundation, Hospital for Special Surgery

3. **Plantar Warts—Newer Treatments**

DANIEL HYMAN, M.D., Suffern
Associate Attending in Medicine (Dermatology), Roosevelt Hospital

4. **Common Mycotic Infections of the Lower Extremity**

FRED REISS, M.D., New York City
Chief of Dermatology Service, Montefiore Hospital

5. **Surgical Management of Stasis Ulcer and Dermatitis of the Leg**

RICHARD W. KESSLER, M.D., New York City
Attending Surgeon, St. Clare's Hospital

6. **Inflammatory Dermatoses of the Lower Extremity**

JOSEPH J. HALLETT, M.D., Rochester
Clinical Senior Instructor in Dermatology, University of Rochester School of Medicine and Dentistry; Chief of Dermatology, Rochester General Hospital

7. **Tumors of the Lower Extremity**

PERRY M. SACHS, M.D., New York City
Assistant Attending Dermatologist, The Mt. Sinai Hospital; Consultant Dermatopathologist, St. Luke's Hospital

SECTION ON

Gastroenterology and Proctology

Chairman.... VICTOR W. LOGAN, M.D., Monroe
Vice-Chairman............................
...........I. RICHARD SCHWARTZ, M.D., Kings
Secretary..................................
.....MAUS W. STEARNS, JR., M.D., New York

Friday, May 18/9:00 A.M./East Room, Ballroom Floor

1. **Complications and Course of Chronic Ulcerative Colitis at a Medical Center in Western New York State**

MAURICE L. KELLEY, JR., M.D., Rochester
Assistant Professor of Medicine, University of Rochester School of Medicine and Dentistry; Associate Physician, Strong Memorial Hospital

2. **Sphincter Preserving Operations in Cancer of Rectum and Rectosigmoid**

MICHAEL R. DEDDISH, M.D., New York City
Associate Professor of Clinical Surgery, Cornell University Medical College; Attending Surgeon, Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases

3. **Serum Nonspecific Alkaline Phosphatase, 5-Nucleotidase and Leucine Aminopeptidase in Bone and Liver Disease**

O. DHODANAND KOWLESSAR, M.D., New York City (*by invitation*)
Assistant Professor of Medicine, Cornell University Medical College

4. **Gastrointestinal Polyvinylpyrrolidone-I^{131} (PVP) Loss During Neomycin-Induced and Other Malabsorptive States**

GEORGE E. OWEN, M.D., Syracuse (*by invitation*)
Assistant Instructor in Medicine, State University of New York Upstate Medical Center in Syracuse
KATHLEEN DUGGAN, Syracuse (*by invitation*)
Research Assistant, State University of New York Upstate Medical Center in Syracuse
MARY W. RUBERT, Syracuse (*by invitation*)
Research Assistant, State University of New York Upstate Medical Center in Syracuse
ROBERT B. CHODOS, M.D., Syracuse (*by invitation*)
Associate Professor of Medicine, State University of New York Upstate Medical Center in Syracuse; Assistant Director, Professional Services for Research, Veterans Hospital
WILLIAM W. FALOON, M.D., Syracuse
Associate Professor of Medicine, State University of New York Upstate Medical Center in Syracuse

Symposium and Panel Discussion—**Schistosomiasis Mansoni in New York State**

HAROLD W. BROWN, M.D., New York City, *Moderator*
Professor of Parisitology, College of Physicians and Surgeons of Columbia University

Life Cycle and Epidemiology

B. H. KEAN, M.D., New York City
Clinical Associate Professor of Tropical Medicine, Cornell University Medical College

Clinical Picture and Diagnosis

HARRY MOST, M.D., New York City
Professor of Preventive Medicine, New York University School of Medicine

Chemotherapy

HOWARD B. SHOOKOFF, M.D., New York City
Chief, Division of Tropical Diseases, Bureau of Preventable Diseases, City of New York Department of Health

Discussion

SECTION ON

General Practice

Chairman .... LAWRENCE AMES, M.D., Kings
Vice-Chairman .... CHARLES R. HARRIS, M.D., Monroe
Secretary .... RUDOLF H. STEINHARTER, M.D., Nassau

Joint Meeting of Section on General Practice and Section on Physical Medicine

Monday, May 14/9:00 A.M./West Room, Ballroom Floor

1. **Rehabilitation Problems in Children**

GEORGE DEAVER, M.D., New York City
Clinical Professor of Physical Medicine and Rehabilitation, New York University School of Medicine

Discussion: JOSEPH J. KAUFMAN, M.D., Newark
Attending Surgeon, Newark-Wayne Community Hospital

2. **Rehabilitation Procedures in Geriatrics and the Aging Patient**

HEINZ I. LIPPMANN, M.D., Teaneck, New Jersey (*by invitation*)
Associate Professor of Rehabilitation Medicine, Albert Einstein College of Medicine of Yeshiva University; Visiting Physician, Bronx Municipal Hospital Center

Discussion: SAMUEL WAGREICH, M.D., Bronx
Adjunct Obstetrician, Bronx Hospital

3. **The Prescription in Physiatric Medicine**

JOSEPH G. BENTON, M.D., Brooklyn
Professor and Chairman, Department of Rehabilitation Medicine, State University of New York Downstate Medical Center; Director, Department of Physical Medicine and Rehabilitation, Kings County Hospital Center

Discussion: MILTON B. SPIEGEL, M.D., Brooklyn
Assistant in Physical Medicine and Rehabilitation, Kings County Hospital Center

SECTION ON

Industrial Medicine and Surgery

Chairman . RAYMOND J. MURRAY, M.D., Nassau
Vice-Chairman . . MARVIN L. AMDUR, M.D., Erie
Secretary . . MARCUS B. BOND, M.D., New York

Tuesday, May 15/9:00 A.M./West Room, Ballroom Floor

1. *Symposium and Panel Discussion*—**Pitfalls in Diagnosis of Occupational Disabilities**

Skin Lesions Frequently Missed

ARTHUR W. GLICK, M.D., New York City
Associate Attending Dermatologist, The Mount Sinai Hospital

Post-Traumatic Syndromes of Skull Injuries

I. MELBOURNE GREENBERG, M.D., Freeport
Attending Neurosurgeon, Mercy Hospital, Rockville Centre; Consulting Neurosurgeon, U. S. Naval Hospital, St. Albans

STEPHEN R. FROMM, M.D., Freeport
Assistant Neurosurgeon, Mercy Hospital; Neurosurgeon, Meadowbrook Hospital

Upper-Extremity Injuries

OTHO C. HUDSON, M.D., Hempstead
Associate Professor of Clinical Orthopedic Surgery, New York University School of Medicine; Director of Orthopedic Surgery, Meadowbrook Hospital

2. *Symposium and Panel Discussion*—**Automotive Safety**

Medical Factors

HAROLD BRANDALEONE, M.D., New York City
Associate Clinical Professor of Medicine, New York University School of Medicine; Associate Visiting Physician, Bellevue Hospital

The Impaired Driver

JAMES MALFETTI, PH.D., New York City (*by invitation*)
Professor of Education; Director of Safety Research Project, Columbia University

Engineering Factors in Safe Driving

JOHN MOORE, New York City (*by invitation*)
Director of Research and Development, American Safety Equipment Corporation

SECTION ON

Medicine

Chairman.....WALTER T. ZIMDAHL, M.D., Erie
Vice-Chairman....AARON FEDER, M.D., Queens
Secretary..........ROBERT BLUM, M.D., Erie

Thursday, May 17/9:00 A.M./West Room, Ballroom Floor

1. *Chairman's Address*—**The Use of Methoxamine in the Treatment of Paroxysmal Supraventricular Tachycardia**

WALTER T. ZIMDAHL, M.D., Buffalo
Associate in Medicine, University of Buffalo School of Medicine

2. **ACTH in Human Plasma**

VERNON K. VANCE, M.D., Buffalo
Assistant Professor of Medicine, University of Buffalo School of Medicine; Director, Endocrinology Clinic and Laboratory, Buffalo General Hospital

3. **Headache and Hypertension**

MARVIN MOSER, M.D., White Plains
Adjunct Attending Physician in Cardiology, In Charge of Hypertension Clinic, Montefiore Hospital
HELEN WISH, M.D., Bayside
Adjunct Attending Physician in Medicine, Montefiore Hospital
ARNOLD P. FRIEDMAN, M.D., New York City
Physician-in-Charge of Headache Unit, Montefiore Hospital

4. **Acute Mycordial Infarction: Follow-Up Studies**

BENJAMIN A. ROSENBERG, M.D., Brooklyn
Co-Chief, Special Cardiac Clinic, and Associate Attending Physician, Kings County Hospital Center
MONTE MALACK, M.D., Brooklyn
Clinical Assistant Professor of Medicine, State University of New York Downstate Medical Center

5. **Blood Pressure Levels which Constitute Hypertension and Indicate Use of Antihypertensive Therapy**

ARTHUR M. MASTER, M.D., New York City
Consulting Cardiologist, The Mount Sinai Hospital
RICHARD P. LASSER, M.D., New York City
Assistant Attending Cardiologist, The Mount Sinai Hospital
MANNING FEINLIEB, M.D., New York City (*by invitation*)
Intern, The Mount Sinai Hospital

6. **The Modern Use of Diuretics and the Low-Sodium Diet: Some Complications and Fallacies**

MILTON PLOTZ, M.D., Brooklyn
Clinical Professor of Medicine, State University of New York Downstate Medical Center

Discussion: ALBERT N. BREST, M.D., Philadelphia, Pennsylvania (*by invitation*)
Director, Hypertension, Renal Unit, Hahnemann Medical College and Hospital

7. **Newer Acidifying Agents and Mercurial Diuretics in the Treatment of Refractory Edema**

RICHARD P. LASSER, M.D., New York City
Assistant Attending Physician for Cardiology, The Mount Sinai Hospital
CHARLES K. FRIEDBERG, M.D., New York City
Director of Cardiology and Attending Physician, The Mount Sinai Hospital; Associate Clinical Professor of Medicine, College of Physicians and Surgeons of Columbia University

Discussion: Albert N. Brest, M.D., Philadelphia, Pennsylvania (*by invitation*)

8. **Recent Advances in the Application of a Dialyzer**

ROLAND ANTHONE, M.D., Buffalo
Assistant Clinical Professor of Surgery, University of Buffalo School of Medicine
SIDNEY ANTHONE, M.D., Buffalo
Assistant Clinical Professor of Surgery, University of Buffalo School of Medicine; Clinical Assistant in Surgery, Buffalo General Hospital

Discussion: JOHN E. KILEY, M.D., Albany
Associate Professor of Medicine, Albany Medical College of Union University

9. **A Long-Term Study of Phenformin Capsules (DBI-TD) in Combination with Insulin in Management of Insulin-Dependent Diabetes**

MAXIMILIAN FABRYKANT, M.D., New York City
Assistant Professor of Clinical Medicine, New York University Post-Graduate Medical School
BENJAMIN I. ASHE, M.D., New York City
Associate Professor of Clinical Medicine, New York University Post-Graduate Medical School

Discussion: ROBERT BLUM, M.D., Buffalo
Associate in Medicine, University of Buffalo School of Medicine; Clinical Assistant Physician, Buffalo General Hospital

10. **Studies in Idiopathic Edema**

DAVID H. STREETEN, M.D., Syracuse
Associate Professor of Medicine, State University of New York Upstate Medical Center in Syracuse

11. **The Use of Triiodothyroproprionic Acid (Triopron) in the Treatment of Hyperthyroidism**

Maxwell Spring, M.D., New York City
Assistant Professor of Clinical Medicine, New York Medical College, Flower and Fifth Avenue Hospitals

12. *Panel Discussion*—**Evaluation of Present-Day Diagnostic Tests for Congenital and Acquired Heart Disease**

Paul N. Yu, M.D., Rochester, *Moderator*
Associate Professor of Medicine, University of Rochester School of Medicine and Dentistry
David G. Greene, M.D., Buffalo
Harry M. Dent Professor of Clinical Research in Cardiovascular Diseases, University of Buffalo School of Medicine
Daniel S. Lukas, M.D., New York City
Associate Professor of Medicine, Cornell University Medical College

SECTION ON

Medical-Legal and Workmen's Compensation Matters

Chairman.......Herbert Lansky, M.D., Erie
Vice-Chairman.............................
.........Sidney B. Weinberg, M.D., Suffolk
Secretary.......Milton J. Schulz, M.D., Erie

Wednesday, May 16/9:00 A.M./West Room, Ballroom Floor

1. **Medical Investigation of Rape**

Herbert Lansky, M.D., Buffalo
Director of Pathology, Edward J. Meyer Memorial Hospital; Assistant Professor of Pathology and Clinical Associate in Legal Medicine, University of Buffalo, School of Medicine
Vincent J. Capraro, M.D., Buffalo
Attending in Obstetrics and Gynecology, Edward J. Meyer Memorial Hospital; Assistant Clinical Professor of Obstetrics and Gynecology, University of Buffalo, School of Medicine

Discussion: Alexander S. Wiener, M.D., Brooklyn
Attending Immunohematologist, Adelphi and Jewish Hospitals; Research Associate, Jewish Chronic Disease Hospital

2. **The Physician—His Testimony, Including the Hypothetical Question**

Irvin Klein, M.D., New York City
Medical Director, Workmen's Compensation Board; Assistant Clinical Professor of Industrial Medicine, New York University School of Medicine

3. *Panel Discussion*—**Cardiac in Industry**

Robert Katz, M.D., New York City, *Moderator*
Director, Bureau of Industrial Health and Workmen's Compensation, Medical Society of the State of New York
J. G. Fred Hiss, M.D., Syracuse
Senior Consultant in Medicine, University Hospital of the Good Shepherd; Senior Attending in Medicine, Syracuse Hospital and St. Joseph's Hospital
Herman K. Hellerstein, M.D., Cleveland, Ohio (*by invitation*)
Assistant Professor of Medicine, Western Reserve University School of Medicine; Assistant Physician, University Hospitals
Leland Hill, Esq., New York City (*by invitation*)
Principal Attorney, Workmen's Compensation Board
John V. Thornton, Esq., New York City (*by invitation*)
Adjunct Professor of Law, New York University School of Law; Lecturer on Ethics and Jurisprudence, New York University College of Dentistry
Barnett S. Fox, New York City (*by invitation*)
Lecturer on Industrial Medicine, New York University Post-Graduate Medical School

SECTION ON

Neurology and Psychiatry

Chairman.................................
.........Murray E. Margulies, M.D., Kings
Secretary.......Bernard H. Smith, M.D., Erie

Friday, May 18/9:00 A.M./Washington Room, Mezzanine

1. *Chairman's Address*—**Future of Neurology**

Murray E. Margulies, M.D., Brooklyn
Chief of Neurology, Veterans Administration Hospital, Clinical Assistant Professor of Neurology, State University of New York Downstate Medical Center

2. **An Evaluation of Aging as a Modifying Factor in the Pathogenesis of Brain Tumors**

Stanley M. Aronson, M.D., Brooklyn
Professor of Pathology, State University of New York Downstate Medical Center

Discussion: Albert W. Cook, M.D., Brooklyn
Visiting Neurosurgeon, Kings County Hospital; Associate Professor of Neurosurgery, State University of New York Downstate Medical Center

3. Recent Advances in the Surgical Therapy of Intracranial Aneurysms and Arteriovenous Malformations

JOSEPH RANSOHOFF, M.D., New York City
Professor and Chairman, Department of Neurosurgery, New York University School of Medicine

Discussion: HARRY A. KAPLAN, M.D., Brooklyn
Attending Neurosurgeon, Kings County Hospital; Clinical Associate Professor of Neurosurgery, State University of New York Downstate Medical Center

BERNARD H. SMITH, M.D., Buffalo
Chief Neurologist, Edward J. Meyer Memorial Hospital; Neuropsychiatrist, Millard Fillmore Hospital

4. Some Neurologic Complications of Diabetes Mellitus

RICHARD A. CHAMBERS, M.D., Jersey City, New Jersey (*by invitation*)
Professor of Neurology, Seton Hall College of Medicine and Dentistry

Discussion: ABRAHAM M. RABINER, M.D., Brooklyn
Consulting Neurologist, Kings County Hospital; Emeritus Professor of Neurology, State University of New York Downstate Medical Center

5. Present Status of Chemotherapy in Psychiatric Disorders

PAUL H. HOCH, M.D., New York City
Commissioner, New York State Department of Mental Hygiene; Professor of Clinical Psychiatry, College of Physicians and Surgeons of Columbia University

Discussion: JOHN G. ROBINSON, M.D., Buffalo
Psychiatrist, Edward J. Meyer Memorial Hospital

MORTON H. HAND, M.D., Brooklyn
Attending Neurologist, Kings County Hospital Center; Clinical Assistant Professor of Neurology, State University of New York Downstate Medical Center

SECTION ON

Obstetrics and Gynecology

Chairman . . . ROBERT E. L. NESBITT, JR., M.D., Onondaga
Vice-Chairman . . . ROBERT S. MILLEN, M.D., Nassau
Secretary . CHARLES A. GWYNN, M.D., Onondaga

Friday, May 18/9:00 A.M./Hartford Room, Mezzanine

1. Genetic Basis for Sexual Development

THOMAS F. SHELLEY, M.D., Syracuse (*by invitation*)
Assistant Professor of Obstetrics and Gynecology, State University of New York Upstate Medical Center in Syracuse

2. Clinical Entities and Differential Diagnosis

HERBERT S. KUPPERMAN, M.D., New York City
Associate Professor of Medicine, New York University School of Medicine; Consultant, Gynecologic Endocrinology, Community Hospital, Glen Cove

3. Medical Therapy: Endocrinologic and Psychologic Aspects

JOHN MONEY, PH.D., Baltimore, Maryland (*by invitation*)
Associate Professor of Medicine, Psychology, and Pediatrics, Johns Hopkins University School of Medicine

4. Surgical Therapy

ALBERT ALTCHEK, M.D., New York City
Instructor in Obstetrics and Gynecology, Albert Einstein College of Medicine of Yeshiva University

General Discussion

SECTION ON

Orthopedic Surgery

Chairman . . . CRAWFORD J. CAMPBELL, M.D., Albany
Vice-Chairman . . . JAMES A. NICHOLAS, M.D., New York
Secretary . . . HUDSON J. WILSON, JR., M.D., New York

Thursday, May 17/9:00 A.M./Washington Room, Mezzanine

1. End Result Study of the Treatment of Club Feet

RUDOLPH DANGELMAJER, M.D., New York City (*by invitation*)
Resident, Hospital For Special Surgery

Discussion: ALEXANDER HERSH, M.D., New York City
Chief of Club Foot Outpatient Department, Hospital for Special surgery

2. Current Concepts of Bone Grafting

C. ANDREW L. BASSETT, M.D., New York City
Associate Professor of Orthopedic Surgery, College of Physicians and Surgeons of Columbia University

Discussion: ROBERT S. SIFFERT, M.D., New York City
Associate Attending in Orthopedic Surgery, The Mount Sinai Hospital

3. **The Rationale For Primary Grafting in Open Reduction of Fractures**

J. P. JONES, JR., M.D., New York City (*by invitation*)
Orthopedic Resident, Columbia-Presbyterian Medical Center

Discussion: CHARLES S. NEER, II, M.D., New York City
Associate Attending in Orthopedic Surgery, Columbia-Presbyterian Medical Center

4. **Streamlining Degenerative Arthritis of the Hip by Osteotomy**

ALBERT B. FERGUSON, JR., M.D., Pittsburgh, Pennsylvania (*by invitation*)
Silver Professor of Orthopedics, Chairman, Department of Orthopedic Surgery, University of Pittsburgh School of Medicine

Discussion: JOHN H. DOHERTY, M.D., New York City
Chief of Orthopedic Service, Bronx Veterans Administration Hospital

5. **Causes and Treatment of Osteoarthritis of the Hip Joint**

HERBERT KNODT, M.D., Columbus, Ohio (*by invitation*)

Discussion: JOHN H. DOHERTY, M.D., New York City
Chief of Orthopedic Service, Bronx Veterans Administration Hospital

6. **The "Broken Pin" as a Complication in Hip Surgery and Removal**

EDWARD R. KAMEN, M.D., Albany
Assistant Clinical Professor of Orthopedic Surgery, Albany Medical College of Union University; Attending Orthopedic Surgeon, Memorial Hospital for Cancer and Allied Diseases

Discussion: EDWARD M. WINANT, M.D., New York City
Attending Orthopedic Surgeon, St. Luke's Hospital

SECTION ON
Ophthalmology

Chairman . . . . BERNARD KRONENBERG, M.D., New York
Vice-Chairman . JOHN A. CETNER, M.D., Albany
Secretary . . . . . GRAHAM CLARK, M.D., New York

Tuesday, May 15/9:00 A.M./Washington Room, Mezzanine

Symposium—**Recent Advances in Ophthalmology**

1. *Chairman's Address*—**Ocular Therapeutics**

BERNARD KRONENBERG, M.D., New York City
Assistant Surgeon, New York Eye and Ear Infirmary; Associate Clinical Professor of Ophthalmology, New York University School of Medicine

2. **Medical Glaucoma Therapy**

ADOLPH POSNER, M.D., New York City
Attending Surgeon, Manhattan Eye and Ear Hospital; Associate Clinical Professor of Ophthalmology, Albert Einstein College of Medicine of Yeshiva University

3. **Glaucoma Surgery**

JOSEPH HOFFMANN KRUG, M.D., New York City
Surgeon, New York Eye and Ear Infirmary; Associate Ophthalmologist, Lenox Hill Hospital

4. **Cataract Surgery**

WALTER CHARLES MOTT, M.D., Albany
Attending Ophthalmologist, Albany Hospital; Associate Clinical Professor Emeritus and Head, Department of Ophthalmology, Albany Medical College of Union University

5. **Surgery of Congenital Cataracts**

JOHN F. GIPNER, M.D., Rochester
Professor Emeritus of Ophthalmology, University of Rochester School of Medicine and Dentistry

6. **Corneal Surgery**

A. BENEDICT RIZZUTI, M.D., Brooklyn
Physician-in-Charge, Corneal Clinic, Brooklyn Eye and Ear Hospital; Attending Ophthalmologist, Holy Family Hospital

7. **Muscle Surgery**

HUNTER ROMAINE, M.D., New York City
Surgeon, New York Eye and Ear Infirmary; Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School

8. **Management of Optic Nerve Diseases**

FRANK D. CARROLL, M.D., New York City
Assistant Clinical Professor of Ophthalmology, College of Physicians and Surgeons of Columbia University; Associate Attending Ophthalmologist, Presbyterian Hospital

SECTION ON
Otolaryngology

Chairman . . . . . JOHN F. DALY, M.D., New York
Vice-Chairman . . . . MARSHALL Y. SOLDINEER, M.D., Erie
Secretary . . . . ARTHUR J. CRACOVANER, M.D., New York

Monday, May 14/9:00 A.M./Washington Room, Mezzanine

1. **The Treatment of Sudden Deafness, Ménière's Disease, and Bell's Palsy**

David O. Zenker, M.D., Morristown, New Jersey (*by invitation*)
Assistant Otolaryngologist, Columbia-Presbyterian Medical Center

Edmund P. Fowler, Jr., M.D., New York City
Director of Otolaryngology, Columbia-Presbyterian Medical Center; Professor and Chairman, Department of Otolaryngology, College of Physicians and Surgeons of Columbia University

Discussion: Wesley H. Bradley, M.D., Syracuse
Assistant Clinical Professor of Otolaryngology, State University of New York Upstate Medical Center in Syracuse

2. **Modern Trends in Intranasal Surgery**

Joseph L. Goldman, M.D., New York City
Clinical Professor of Otolaryngology, College of Physicians and Surgeons of Columbia University; Director, Department of Otolaryngology, The Mount Sinai Hospital

Discussion: Benjamin M. Volk, M.D., Albany
Associate Clinical Professor of Otolaryngology, Albany Medical College of Union University; Head of Department of Otolaryngology, Albany Medical Center

3. **Audiometry and Recruitment in Acoustic Neurinomas: Aids in Early Diagnosis**

Raymond B. Strauss, M.D., New York City
Assistant Resident in Otolaryngology, Columbia-Presbyterian Medical Center

Discussion: Miles Atkinson, M.D., New York City
Associate Professor of Clinical Otorhinolaryngology, New York University School of Medicine; Associate Attending Otolaryngologist, Bellevue Medical Center

4. *Symposium and Panel Discussion*—**Voice Problems and Laryngeal Pathology**

John F. Daly, M.D., New York City, *Moderator*
Professor and Chairman, Department of Otolaryngology, New York University School of Medicine; Director of Otolaryngology, Bellevue Medical Center

Vocal Nodules

Godfrey E. Arnold, M.D., New York City
Director of Research, New York Eye and Ear Infirmary; Director, National Hospital for Speech Disorders

Contact Ulcer

David W. Brewer, M.D., Syracuse
Clinical Associate Professor of Otolaryngology, State University of New York, Upstate Medical Center in Syracuse; Attending Otolaryngologist, Syracuse Memorial Hospital

Polypoid Vocal Cord

Daniel C. Baker, Jr., M.D., New York City
Clinical Professor of Otolaryngology, College of Physicians and Surgeons of Columbia University; Attending Otolaryngologist, Presbyterian and Babies Hospitals

Voice Therapy

Georgiana M. Peacher, Ph.D., Philadelphia, Pennsylvania (*by invitation*)
Associate Professor of Phoniatrics, Chevalier Jackson Clinic, Temple University Medical Center

SECTION ON

Pathology, Clinical Pathology, and Blood Banking

Chairman.......................................Nathanael M. Fedde, M.D., Richmond
Vice-Chairman. Silik H. Polayes, M.D., Kings
Secretary.......................................George K. Higgins, M.D., Westchester

Thursday, May 17/9:00 A.M./Hartford Room, Mezzanine

1. *Symposium and Panel Discussion*—**Cooley's Anemia**

Silik H. Polayes, M.D., Brooklyn
Clinical Associate Professor of Pathology, State University of New York Downstate Medical Center

Harold Fink, M.D., Brooklyn
Chief Hematologist, Coney Island Hospital

R. Janet Watson, M.D., Brooklyn
Associate Professor of Pediatrics, State University of New York Downstate Medical Center

2. **Enzyme Activities Characteristic of Growth and Regeneration**

Patrick J. Fitzgerald, M.D., Brooklyn
Professor and Chairman, Department of Pathology, State University of New York Downstate Medical Center

3. **Anatomic Changes Due to Serotonin Toxicity**

Alfred A. Angrist, M.D., Bronx
Professor and Chairman, Department of Pathology, Albert Einstein College of Medicine of Yeshiva University

SECTION ON

Pediatrics

Chairman. . HARRY R. LITCHFIELD, M.D., Kings
Vice-Chairman. . . . .
. . . . SAMUEL KARELITZ, M.D., Nassau
Secretary. . . . . FRANK A. DISNEY, M.D., Monroe

Tuesday, May 15/9:00 A.M./Hartford Room, Mezzanine

1. **Calcium and Phosphorus Metabolism in the Neonate During the First Week of Life**

JOSEPH B. PINCUS, M.D., Brooklyn
Director of Pediatrics, Brooklyn Jewish Hospital

Discussion: SAMUEL NATELSON, PH.D., New York City (*by invitation*)
Director of Biochemistry, Roosevelt Hospital; Consultant Research Chemist, Department of Pediatrics, Brooklyn Jewish Hospital

2. **The Diagnosis and Management of Congestive Heart Failure in Infancy**

JOSHUA LYNFIELD, M.D., Brooklyn
Director of Pediatric Cardiology, State University of New York Downstate Medical Center

Discussion: EUGENIE F. DOYLE, M.D., New York City
Associate Professor of Pediatrics, New York University School of Medicine; Chief of Children's and Adolescent Cardiac Clinics, Bellevue Hospital

3. **The Significance of Synovitis of the Hip in Children**

BERNARD JACOBS, M.D., New York City
Instructor of Orthopedic Surgery, Cornell University Medical College; Fellow in Orthopedic Research, Hospital for Special Surgery

Discussion: ROBERT SIFFERT, M.D., New York City
Chief of Orthopedic Surgery, The Mount Sinai Hospital

4. **Measles Immunity**

SAMUEL KARELITZ, M.D., New Hyde Park
Chief of Pediatrics, Long Island Jewish Hospital

Discussion: FRANCIS BLACK, M.D., New Haven, Connecticut (*by invitation*)
Assistant Professor of Epidemiology, Yale University School of Medicine

5. **Fetal and Maternal Terramycin Blood Levels After Maternal Intravenous Administration**

JOHN A. MONFORT, M.D., Brooklyn
Director of Pediatrics, Lutheran Medical Center
ISRAEL DIAMOND, M.D., Brooklyn
Director of Pathology, Lutheran Medical Center

Discussion: ARTHUR MACGREGOR, M.D., Brooklyn
Director of Obstetrics and Gynecology, Lutheran Medical Center

6. **A Study of Accidents (Nonfatal) in the School Age Child**

HAROLD JACOBZINER, M.D., New York City
Assistant Commissioner, Maternal and Child Health, City of New York Department of Health

Discussion: ROBERT W. CULBERT, M.D., New York City
Director of Bureau of School Health, City of New York Department of Health

JOINT MEETING

Section on Pediatrics and Section on Urology

Friday, May 18/10:30 A.M./Gold Ballroom, Ballroom Balcony

Problems and Advances in Diagnosis and Management of Urinary Tract Disorders in Children (*see page 959*)

SECTION ON

Physical Medicine

Chairman. . . . . JOSEPH G. BENTON, M.D., Kings
Vice-Chairman . . . .
. . . . VICTOR CUMMINGS, M.D., Bronx
Secretary. . . . . MILTON B. SPIEGEL, M.D., Kings

JOINT MEETING

Section on General Practice and Section on Physical Medicine

Monday, May 14/9:00 A.M./West Room, Ballroom Floor

Rehabilitation Problems in Children; Rehabilitation Procedures in Geriatrics and the Aging Patient; The Prescription in Physiatric Medicine (*see page 950*)

SECTION ON

Preventive Medicine and Public Health

Chairman . . . . THEODORE ROSENTHAL, M.D., New York
Vice-Chairman . . . . DAVID E. BIGWOOD, JR., M.D., Onondaga
Secretary . . . . MALCOLM A. BOUTON, M.D., Schenectady

Wednesday, May 16/9:00 A.M./Washington Room, Mezzanine

1. *Symposium*—**Public Health Aspects of Addictive Disorders**

A. **Alcoholism**

MARVIN A. BLOCK, M.D., Buffalo
Assistant Professor of Medicine, University of Buffalo School of Medicine; Chairman, American Medical Association Committee on Alcoholism

B. **Narcotics Addiction**

ALFRED FREEDMAN, M.D., New York City
Professor of Psychiatry, New York Medical College; Chairman, Department of Psychiatry, New York Medical College, Metropolitan Hospital Center

2. **The Anticoronary Club—A Report of the First Four Years**

SEYMOUR H. RINZLER, M.D., New York City
Cardiologist in Charge of Diet and Coronary Heart Disease Project, City of New York Department of Health; Chief, Adult (Day) Cardiac Clinic, Beth Israel Hospital
MORTON ARCHER, M.A., New York City (*by invitation*)
Bureau of Nutrition, City of New York Department of Health; Senior Statistician, City of New York Department of Health
JAMES H. STEPHENSON, M.D., New York City (*by invitation*)
Anticoronary Project, Kips Bay Health Center; Clinic Physician, Diet and Coronary Heart Disease Project, City of New York Department of Health
GEORGE CHRISTAKIS, M.D., New York City (*by invitation*)
Acting Director, Bureau of Nutrition, City of New York Department of Health

3. **Recent Developments in Artificial Immunization**

JAMES R. MCCARROLL, M.D., New York City
Director, Division of Epidemiologic Research, Cornell University Medical College; Assistant Attending Physician, New York Hospital

4. **Radiation Hazards from the Standpoint of the Practitioner**

HANSON BLATZ, E.E., New York City (*by invitation*)
Director, New York City Office of Radiation Control; Associate Professor of Industrial Medicine, New York University School of Medicine

SECTION ON

Radiology

Chairman . . . . WILLIAM B. SEAMAN, M.D., New York
Vice-Chairman . . . . CHARLES E. SHERWOOD, M.D., Monroe
Secretary . . . . MILTON ELKIN, M.D., Westchester

Monday, May 14/9:00 A.M./Hartford Room, Mezzanine

1. **Physiologic Aspects of Pulmonary Emphysema**

HAROLD LYONS, M.D., Brooklyn
Professor of Medicine, State University of New York Downstate Medical Center

2. **Pathologic-Roentgenographic Correlation Studies of the Emphysematous Lung**

CHARLES ODERR, M.D., New Orleans, Louisiana (*by invitation*)
Chief of Radiology, New Orleans Veterans Administration Hospital

3. **The Role of the Diaphragm in Pulmonary Emphysema**

ALVAN L. BARACH, M.D., New York City
Consultant in Medicine, Columbia-Presbyterian Medical Center

SECTION ON

Space Medicine

Chairman . . . . CONSTANTINE D. J. GENERALES, M.D., New York
Vice-Chairman . . . . HANS H. ZINSSER, M.D., New York
Secretary . . . . CORTEZ F. ENLOE, JR., M.D., New York

Friday, May 18/9:00 A.M./Georgian Room, Ballroom Floor

Space Medicine Spectra: Anno V of Space Exploration

1. *Chairman's Address*—**The Dynamics of Space Medicine**

CONSTANTINE D. J. GENERALES, M.D., New York City
Assistant Professor of Space Medicine

and Coordinator of Space Medicine Program, New York Medical College, Flower and Fifth Avenue Hospitals

2. **The United States Government's Role in Current Space Exploration**
   HON. VICTOR L. ANFUSO, Brooklyn (*by invitation*)
   House of Representatives, Committee on Science and Astronautics

3. **Unusual Earthly Forms of Life and Extraterrestrial Implications**
   JOHN PALISTER, New York City (*by invitation*)
   President, Explorers Club; Research Associate, Department of Entomology, New York Museum of Natural History

4. **The Significance of the Magnetosphere to Man**
   ALASTAIR G. W. CAMERON, PH.D., New York City (*by invitation*)
   Institute for Space Studies, National Aeronautics and Space Administration

5. **Biomedical Engineering as a Physician's Aid**
   LEE B. LUSTED, M.D., Rochester
   Associate Professor of Radiology and Biomedical Engineering, The University of Rochester School of Medicine and Dentistry

6. **Fossil Life in Meteoric Carbonaceous Matter**
   BARTHOLOMEW NAGY, PH.D., Bronx (*by invitation*)
   Associate Professor of Chemistry, Fordham University

7. **Electromagnetism and Its Effect on the Organism**
   JOHN H. HELLER, PH.D., Ridgefield, Connecticut (*by invitation*)
   Director, New England Institute of Medical Research

8. **Geomagnetic Environment and Its Relationship to Human Biology**
   ROBERT O. BECKER, M.D., Syracuse
   Chief of Orthopedic Section, Veterans Administration Hospital

9. **Selected Topics on Space Medicine in the USSR**
   V. J. YAZDOVSKY, Moscow, USSR (*by invitation*)
   Professor, Academy of Sciences of the USSR

10. **The Saturn Program**
   WERNHER VON BRAUN, PH.D., Huntsville, Alabama (*by invitation*)
   Director, George Marshall Space Flight Center

Again to the Stars
ACADEMY OF SCIENCES, USSR

Colored film of Titov's orbital flight, shown in Motion Picture Theatre, Exhibit Hall (First New York showing, *see page 968*)

SECTION ON
Surgery

Chairman .... HAROLD G. BARKER, M.D., New York
Vice-Chairman . . CHARLES E. WILES, M.D., Erie
Secretary .... SEYMOUR I. SCHWARTZ, M.D., Monroe

Wednesday, May 16/9:00 A.M./Hartford Room, Mezzanine

Symposium and Panel Discussion—**Frontiers of Surgery**

PHILIP N. SAWYER, M.D., Brooklyn
Assistant Professor of Surgery, State University of New York Downstate Medical Center

CHARLES G. ROB, M.D., Rochester
Professor and Chairman, Department of Surgery, University of Rochester School of Medicine and Dentistry

ADRIAN KANTROWITZ, M.D., Brooklyn
Associate Professor of Surgery, State University of New York Downstate Medical Center

IRVING M. ARIEL, M.D., New York City
Associate Professor of Surgery, New York Medical College, Flower and Fifth Avenue Hospitals

PAUL S. RUSSELL, M.D., New York City
Associate Professor of Surgery, College of Physicians and Surgeons of Columbia University

SECTION ON
Urology

Chairman .... GUSTAVUS A. HUMPHREYS, M.D., New York
Vice-Chairman .... DONALD F. MCDONALD, M.D., Monroe
Secretary . GEORGE A. FIEDLER, M.D., New York

Friday, May 18/9:00 A.M./Gold Ballroom, Ballroom Balcony

1. **Studies of Hyperadrenocorticism—Past and Present**
   J. HARTWELL HARRISON, M.D., Boston, Massachusetts (*by invitation*)
   Clinical Professor of Urology, Harvard Medical School
   Discussion: FRANK GLENN, M.D., New York City

Professor and Chairman, Department of Surgery, Cornell University Medical College

10:30 A.M.: Joint Meeting of Section on Pediatrics and Section on Urology

2. *Symposium*—**Problems and Advances in Diagnosis and Management of Urinary Tract Disorders in Children**

Albert J. Paquin, M.D., Charlottesville, Virginia, *Moderator* (*by invitation*)
Professor of Urology, University of Virginia School of Medicine

Urinary Infection

Current Problem: The Significance of Urinary Infection in Childhood

Calvin M. Kunin, M.D., Charlottesville, Virginia (*by invitation*)
Assistant Professor, Department of Preventive Medicine, University of Virginia School of Medicine

Recent Advances: The Management of the Child with Urinary Infection

Victor F. Marshall, M.D., New York City
Professor of Surgery (Urology), Cornell University Medical College

Disorders of the Vesical Neck

Current Problem: The Diagnosis of Disorders of the Vesical Neck in Girls

John K. Lattimer, M.D., New York City
Professor of Urology, College of Physicians and Surgeons of Columbia University

Recent Advances: The Treatment of the Vesical Neck Disorders in Childhood

R. Keith Waterhouse, M.D., Brooklyn
Assistant Professor of Surgery (Urology), State University of New York Downstate Medical Center

Disorders of the Ureterovesical Junction

Current Problem: The Diagnosis of Disorders of the Ureterovesical Junction

William L. Parry, M.D., Syracuse
Associate Professor of Urology, University of Rochester School of Medicine and Dentistry

Recent Advances: The Treatment of Disorders of the Ureterovesical Junction

John H. McGovern, M.D., New York City
Assistant Professor of Surgery (Urology), Cornell University Medical College

SESSION

SESSION ON

History of Medicine

Chairman. . .John A. Benjamin, M.D., Monroe

Wednesday, May 16/9:00 A.M./Pennsylvania Room, Ballroom Floor

1. **The Story of the A. N. Brady Maternity Hospital in Albany, New York**

William J. Fitzgerald, M.D., Albany
Clinical Instructor in Obstetrics and Gynecology, Albany Medical College of Union University

2. **The History of Goiter in the State of Michigan**

Isidor Greenwald, Ph.D., New York City (*by invitation*)
Professor Emeritus, Department of Biochemistry, New York University School of Medicine

3. **The Pest House**

Howard B. Slavin, M.D., Rochester
Associate Professor of Medicine and Bacteriology, University of Rochester School of Medicine and Dentistry

4. **Hindu Medicine: Ayur Veda**

Robert A. Gutstein, B.A., New York City (*by invitation*)
Medical Student, College of Physicians and Surgeons of Columbia University

5. **Prosper Ménière: The Story of the Famous Four Papers**

Miles Atkinson, M.D., New York City
Associate Professor of Clinical Otorhinolaryngology, New York University Post-Graduate Medical School; Associate Attending Otolaryngologist, Bellevue Medical Center

6. **Selected Events Leading to the Development of Space Medicine**

Constantine D.J. Generales, M.D., New York City
Assistant Professor of Space Medicine and Coordinator of Space Medicine Program, New York Medical College, Flower and Fifth Avenue Hospitals

1962 ANNUAL CONVENTION

Scientific Exhibits

Statler Hilton, New York City
Monday, May 14 through Friday, May 18, 1962
Exhibit Hall, Mezzanine

Chairman	WILLIAM L. WATSON, M.D., New York
Cochairman	BEVERLY C. SMITH, M.D., New York
	FRANCIS P. BILELLO, M.D., Nassau
	FRED W. BUSH, M.D., Monroe
	ALBERT H. DOUGLAS, M.D., Queens
	FREDERICK LEE LIEBOLT, M.D., New York
	GUSTAVE PHILIP MILKEY, M.D., Erie
	ARTHUR R. WILSEY, M.D., Fulton

Visualization and Perfusion of Bronchial Arteries: Application in the Treatment of Lung Carcinoma

D. Raj Mahajan, M.D.
Eugene E. Cliffton, M.D.
William L. Watson, M.D.
Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases, New York City

Regional perfusion of the pulmonary artery has recently been advocated by various authors for unresectable carcinoma of the lung. However, it is probable that the major blood supply of the bronchogenic tumors is derived from the bronchial arteries and their perfusion appears more logical. A technic showing how the segment of the descending thoracic aorta from which the bronchial arteries arise is isolated, using a specially made double balloon, double lumen, woven cardiac catheter inserted through the superficial femoral artery, under local anesthesia with fluoroscopic control, is presented. The flow in this segment is stopped temporarily by balloon occlusion and bronchial arteries perfused with nitrogen mustard after bronchial arteriograms are obtained by injecting a small amount of contrast medium. A demonstration of the technic is part of the exhibit. Clinical and experimental data are provided **(Booth 201).**

Mammography, An Examination of Technics

Robert S. Sherman, M.D.
Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases, and Cornell University Medical College, New York City

Quantitative measurements have been made of those quantities of interest to the radiologist engaged in mammography, including skin dose, contrast, resolution, and so forth. Films have been taken using special-purpose phantoms, radical mastectomy specimens, and patients. Using these data, the effects of varying technical factors such as kilovolt peak filtration, target-skin-distance, and film type have been evaluated to aid the radiologist in determining an optimum technic for his purpose and equipment **(Booth 202).**

Survival Rations for Fallout Shelters

Herman E. Hilleboe, M.D., Commissioner of Health
New York State Department of Health, Albany

This exhibit is intended to inform persons about food requirements for survival in a fallout shelter during a two-week period **(Booth 203).**

Hydroxyzine Premedication: A Double-Blind Intravenous Study

F. E. Fierro, M.D.
F. S. Latteri, M.D.
D. Bizzarri, M.D.
New York Medical College, Metropolitan Medical Center, New York City

The double-blind technic is used in obtaining objective data in the evaluation of this drug. The study was conducted in three phases: (1) a pilot study to determine dosage and concentration of drug, (2) an uncontrolled efficacy study with intravenous hydroxyzine, and (3) a double-blind study with intravenous hydroxyzine to check on the validity of the previous results **(Booth 204).**

Anorectal Anesthesia for Anorectal Surgery

ROBERT S. DONNENFELD, M.D.
Mid-Island Hospital, Bethpage

A simple procedure for providing anesthesia of the anus and rectum is presented. If desired, this technic may be combined with various methods of basal anesthesia to provide complete amnesia and analgesia for anorectal surgery. The method of anesthesia provides excellent patient comfort plus improved operating conditions **(Booth 205).**

Management of Severe Respiratory Depression

ALLEN B. DOBKIN, M.D.
JACOB S. ISRAEL, M.D.
AUGUSTO L. SAMONTE, M.D.
State University of New York Upstate Medical Center in Syracuse

The etiology, signs and symptoms, and appropriate treatment of severe respiratory depression are tabulated below a central human figure which alternately turns cyanotic and pink. Standard supportive therapy required for all comatose patients is described, as well as special conjunctive therapy in the management of critical symptoms **(Booth 206).**

Management of Ocular Emergencies

DAN M. GORDON, M.D.
New York Hospital-Cornell Medical Center, New York City

The general practitioner can handle many ocular injuries with a minimum of equipment. Basic guideposts for evaluation of the type and degree of injury, as well as for emergency and follow-up management, are pointed out. Many of these patients, once properly evaluated, can be handled easily. Others require more specialized care. Here, too, the important diagnostic criteria are highlighted. Rules for the management of all types of ocular emergencies are stressed **(Booth 207).**

The Use of Radioactive Phosphorus (P^{32}) in the Diagnosis of Ocular Tumors

BERNARD GOLDBERG, M.D.
GERALD B. KARA, M.D.
DAVID TABOWITZ, A.B.
New York Eye and Ear Infirmary, New York City

Basic considerations, technics, and criteria for the P^{32} test in ophthalmology are presented. The external approach for anterior segment lesions (iris, ciliary body, and anterior choroid) is compared and contrasted with the transconjunctival approach for posterior segment lesions (choroidal lesions posterior to the equator). The indications for each approach are considered **(Booth 208).**

Low-Vision Corrections

ELEANOR E. FAYE, M.D.
GERALD FONDA, M.D.
CHARLES P. KOEHLER
New York Association for the Blind, New York City

Methods of correcting low-vision patients with special glasses and aids are shown, as well as representative samples of spectacles and aids **(Booth 209).**

The Margaret Sanger Research Bureau

New York City

The services of the Sanger Bureau and its educational and research programs are described **(Booth 210).**

The Birth Canal (Reconstruction): Practical Applications

JOSHUA WILLIAM DAVIES, M.D.
Grasslands Hospital, Valhalla
ELISE L. RENNING, M.D.
St. Luke's Hospital, New York City

To assist in the comprehension of the shape and direction of the birth canal a cast of the true pelvis has been made, and from this a transparent hollow cage has been reconstructed. Close scrutiny of the cage reveals two separate shapes whose functions differ. The first segment is a horizontal cylinder which acts as the fourchet to the distal curving elbow-shaped portion. By means of a molded rubber child's head, engagement and descent are analyzed and suggestions are made which facilitate engagement and descent of the child's head **(Booth 211).**

Abdominal Wall Hernias

ALFRED H. IASON, M.D.
BEN PANSKY, PH.D.
New York University School of Medicine, New York City

The complete anatomy of various types of hernia enumerated as follows, together with detailed illustrations of surgical procedures, are demonstrated in detail. The types of hernias shown are: epigastric, umbilical, spigelian, Petit's triangle, inguinal, sliding, femoral, obturator, sciatic, perineal and intra-abdominal hernias near the ligament of Treitz, and transmesocolic. A résumé of statistics is included **(Booth 212).**

The Aging Skin

COMMITTEE ON COSMETICS
American Medical Association, Chicago, Illinois

The changes and factors involved in normal aging of the skin and available methods of management are described and illustrated **(Booth 213).**

Skeletal Abnormalities Associated with Gonadal Dysgenesis

NATHANIEL FINBY, M.D.
REGINALD M. ARCHIBALD, M.D.
St. Luke's Hospital and The Rockefeller Institute, New York City

Gonadal dysgenesis is a genetic syndrome usually associated with an absent sex chromosome and a resultant XO pattern. Few of these patients have the classical Turner's syndrome, but most do show skeletal abnormalities which are helpful in diagnosis. These abnormalities include dwarfism, slight retardation of skeletal maturation, metacarpal or carpal abnormalities with a positive metacarpal sign, cubitus valgus, and a tibia vara-like deformity of the knees. The very young patient may show soft-tissue edema, and the older patient may show osteoporosis **(Booth 214).**

Charcot Joints

Sidney N. Eichenholtz, M.D.
Veterans Administration Hospital and Hospital for Special Surgery, New York City

Histopathologic findings in Charcot joints are described and comparison made with other joints. A mechanism of formation of Charcot joints is suggested. An original concept of three stages of development and progression of Charcot joints is proposed. A comparison with osteoarthritic joints and paraplegic joints indicates the differentiation. Examples of various Charcot joints are included. Results of surgery on Charcot joints and fractures of long bones adjacent to Charcot joints also are described. Examples include neuropathic foot, Charcot spine, and extremity Charcot joints **(Booth 215).**

Medical Procedure in Workmen's Compensation

Irvin Klein, M.D.
New York State Workmen's Compensation Board, New York City

The importance of educating the medical profession in Workmen's Compensation procedures, thus bringing about better cooperation between those treating claimants and the Workmen's Compensation Board, is emphasized. The benefits of proper care and the application of rehabilitation are stressed **(Booth 216).**

Progressive Muscular Dystrophy

Herbert T. Wagner, M.D.
Muscular Dystrophy Associations of America, Inc., New York City

Progressive wasting and weakness as noted first in proximal muscle groups and later in nearly all striated body muscle are presented. Gross changes in advanced cases are illustrated. The manifestations of muscular dystrophy are shown. Postural changes which occur in various stages of the condition are indicated. A concise statement is made on the common forms of dystrophy—their onset, course, and duration in persons of varying ages. A differential diagnosis is outlined **(Booth 217).**

The Prescription For Physical Medicine

Lewis Dickar, M.D.
State University of New York Downstate Medical Center, Brooklyn

The importance of an adequate, accurate prescription for physical medicine is presented. The ethical and legal aspects are indicated. The reasons for and the information on a satisfactory prescription are shown. The specific details of the prescription are presented, so that this phase of treatment, in addition to other therapy, is carried out according to directions, and no part of prescribing is delegated to the physical therapist. Sample prescriptions are included to demonstrate how treatment is ordered, together with changes made necessary by the progress of the patient **(Booth 218).**

Objective Measurement of Muscle Extensibility

Harold T. Hansen, M.D.
Earl F. Hoerner, M.D.
F. Ray Finley, Ph.D.
Hospital Center, Orange, New Jersey

After many and various unsuccessful attempts to appraise subjectively the effectiveness of pharmaceutical agents for skeletal muscle relaxation in various pathologic syndromes, an objective means was developed. By utilizing an electrogoniometer, an electronic force transducer, and electromyographic recordings, the pounds of pressure required and the degrees of movement in passive dorsiflexion of the foot were recorded graphically using a polygraph recorder. By this method, the relaxation of the triceps surae group was appraised and evaluated in several pathologic conditions: the arthritides, muscle disease, and increased muscle tone conditions. The instrumentation and test procedure are demonstrated and results shown. Data are given for test validity and reliability **(Booth 219).**

Hemophilic Arthropathies and Myopathies

Henry H. Jordan, M.D.
Lenox Hill Hospital, New York City

The main features of hemophilic arthropathies and myopathies are illustrated with series of x-ray films and clinical photographs. Rehabilitation technics and appliances are presented. Several case histories are shown in detail. The exhibit demonstrates that apparently hopeless bedridden cases can be returned to ambulatory useful life **(Booth 220).**

Radiation Medicine at Queens Hospital Center

Leonard B. Goldman, M.D.
Murray Schulman, Ph.D.
Gerald Shapiro, M.S.
Queens Hospital Center, Jamaica

The principles and technics of typical diagnostic and therapeutic applications of radioactive isotopes are described, demonstrated, and discussed with special emphasis on routine office rocedures. Nuclear instrumentation, radioharmaceuticals, technical literature, and guides o courses of instruction are available for xamination. Participants will have an opporunity to carry out the basic technic for assessng thyroid function with the use of radioiodine. ther diagnostic isotope tests exhibited include ssessment of blood volume, pernicious anemia, d cell survival time, fat digestion and absorpon, placental localization, and thyroid scaning. Therapeutic applications will reflect the se of isotopes in treating hyperthyroidism, olycythemia vera, angina pectoris, effusions, nd malignant conditions **(Booth 221).**

ignificant Abdominal Gas Patterns

THEODORE COHEN, M.D.
ROBERT CHRISTMAN, M.D.
ALLAN R. ARONSON, M.D.
New York University Medical Center, New York City

When faced with a gastrointestinal problem, a mple preliminary film of the abdomen without e utilization of contrast media or special techics may prove to be the most rapid, inexpenve, and readily available method of establishg a specific diagnosis. At times this proceure may prove to be lifesaving.

The different gas patterns which may be oberved on an ordinary "scout" film of the abdoen are exhibited. The location, distribution, nd contour of the gaseous accumulates are ften suggestive or diagnostic of various gastrotestinal pathologic states. The presentation onsists of: (1) a group of films demonstrating a umber of clinical entities including intestinal bstruction, acute pancreatitis, mesenteric arery thrombosis, perforated viscus, and so forth; 2) a suggested approach to the interpretation of hadows; and (3) an outline of various condiions producing the abnormal patterns **(Booth 22).**

n In Vivo Dosimetry System for Clinical nd Experimental Radiation Therapy

BERNARD ROSWIT, M.D.
STANLEY J. MALSKY, M.S.
CYPRIAN B. REID, B.S.
Veterans Administration Hospital, The Bronx

We have developed a practicable and reliable icrodosimeter system for accurate in vivo uman dosimetry in radiation therapy. The etectors consist of tiny photoluminescent glass ylinders enclosed in miniature gold cartridges hich can be easily and quickly fabricated. his system is immediately adaptable to routine linical use and experimental studies. It has een employed successfully in nearly all body issues and spaces in cancer patients receiving nizing radiation **(Booth 223).**

Vide-Angle Radiography

SOL M. UNGER, M.D.
HERBERT S. BERLIN, M.D.
LEON CORBIN, M.D.
Veterans Administration Hospital, The Bronx

Wide-angle radiography is a new radiographic procedure. With one radiographic exposure and using conventional chest technic two radiographs of excellent diagnostic quality are obtained. These two radiographs are at right angles to each other and present a panoramic appearance of the entire thorax. The shoulder girdle, soft tissues of the axillas, periphery of the bony thorax, and lung parenchyma are vividly demonstrated. In addition, the hilar densities are projected in such a manner that differentiation can be made between the normal hilar vascular and abnormal hilar nodes. Several cases are shown illustrating axillary soft-tissue masses, traumatic and neoplastic rib fractures, as well as peripheral lung and hilar pathologic conditions **(Booth 224).**

The Radioactive (I^{131}-Tagged) Rose Bengal Hepatoscan

SIDNEY RUBENFELD, M.D.
FRIEDA FELDMAN, M.D.
CARL COLLICA, B.S.
New York University School of Medicine, New York City

Experience with the radioactive rose bengal hepatoscan in over 200 cases has enabled us to associate particular radioactive spatial distributions with certain hepatic diseases. A "literature of patterns" has been evolved. Clinical examples and graphic illustrations of some of the representative and most frequently occurring entities are presented **(Booth 225).**

Perigastric Adhesions Simulating Carcinoma of the Stomach

ABRAHAM GEFFEN, M.D.
FRIEDA FELDMAN, M.D.
Beth Israel Hospital, New York City

Perigastric adhesions may produce antral deformity simulating cancer of the stomach. Biliary tract surgery was found to be the cause in 6 of 10 cases cited. Clinical history of previous surgery is therefore very significant in differential diagnosis. Specific radiologic criteria are also suggested to differentiate a benign extrinsic from a malignant intrinsic deformity **(Booth 226).**

A New Blood-Screening Test to Prevent Mental Retardation

ROBERT GUTHRIE, M.D.
Children's Hospital, Buffalo

Phenylketonuria (PKU) was first detected in 1935 with the simple ferric chloride test for phenylketone, universally used since to detect the disease. However, in the very young infant the only chemical abnormality is increased phenylalanine in blood and urine. This has not allowed the early detection necessary to initiate the low-phenylalanine diet treatment before irreversible brain damage occurs. The "inhibition assay" for phenylalanine, described in this exhibit for the first time, permits detection of PKU in the newborn baby, as a simple hospital routine. Detection, followed by the use of a low-phenylalanine diet, makes possible complete eradication of this form of mental retardation **(Booth 228)**.

The Modified Jones Criteria Used to Verify a History of Rheumatic Fever

Norman S. Blackman, M.D.
Cardiac Consultation Service, Bureau For Handicapped Children, Department of Health, New York City

The modified Jones criteria were used to verify a history of rheumatic fever. The parents, private physicians, and hospitals were used as sources of information concerning the Jones "major and minor manifestations of rheumatic fever" as observed during the initial illness. In 100 children referred for consultation with a diagnosis of a history of rheumatic fever and/or rheumatic heart disease, it was found that only 65 per cent could satisfy the modified Jones criteria after a maximal effort was made to obtain historical information. The type of manifestation and its observed frequency as reported by parents, physicians, and hospital chart summaries are presented individually. A presentation of the modified Jones criteria is included **(Booth 229)**.

Physical Diagnosis of Chest Disease—Fifteen New or Neglected Signs

Coleman B. Rabin, M.D.
Alvin S. Teirstein, M.D.
The Mount Sinai Hospital, New York City

Fifteen new or neglected physical signs which are important in the diagnosis of chest disease are described. They are classified under four general headings: (1) pulmonary periosteopathy and clubbing—the absence of arthropathy is emphasized; (2) signs of bronchial obstruction—the bagpipe sign, pendular motion of the trachea, and palpable inaudible rhonchus; (3) tracheal signs—fixation of the trachea, the tracheosternomastoid space, the depth of the jugular notch, fluctuation of the trachea, and anterior d'Espine's sign; and (4) signs relating to the neck—auscultatory crepitus, ecchymosis of the neck, palpation of cervical nodes with cough or straining, and the Valsalva and Mueller maneuvers in carcinoma of the apex **(Booth 230)**.

X-Ray Manifestations of the Lungs in Congestive Heart Failure

Maxwell L. Gelfand, M.D.
Robert Christman, M.D.
Lambros Costopoulos, M.D.
New York University Medical Center, New York City

The lungs are a mirror of the hemodynamics of the circulation and frequently indicate the presence of cardiac decompensation early. The typical hilar engorgement and butterfly-shaped symmetrical densities involving both lung fields are well known. However, there are often many atypical pulmonary x-ray findings that are generally mistaken for those characteristic of a different disease, such as lobar pneumonia, bronchopneumonia, tumor of the lung, pulmonary infarct, atelectasis, bronchiectasis, unilateral miliary lesion, and mediastinal lesion such as neoplasm.

The purpose of this exhibit is to call attention to those patterns that may be misleading and emphasize the fact that response to therapy for congestive heart failure establishes the diagnosis of heart failure as the cause of these pulmonary roentgenographic changes **(Booth 231)**.

Accompaniments of Endemic Goiter in Different Regions and at Different Times

Isidor Greenwald, Ph.D.
New York University School of Medicine, New York City

Cretinism, deaf-mutism, hyperthyroidism, congenital goiter, and goiter in farm animals may accompany endemic goiter, but the proportions vary widely. Cretinism was the classic accompaniment in the Alpine regions of Europe. In South America it was deaf-mutism; in the United States, Japan, and in England, it was hyperthyroidism. Congenital goiter seems to have been much more frequent in Europe than in the United States. The reverse relation was true of hairlessness in pigs. This appeared recently in southern Germany. It seems that none of these conditions had been common in any of the goiter regions of Africa until recently **(Booth 232)**.

The Obesity-Diabetes Clinic

S. K. Fineberg, M.D.
Harlem Hospital, New York City

The first clinic solely for the treatment of obesity in diabetic patients (85 per cent of the total) was organized in October, 1960. It was founded on the axiom, "Treat the obesity before the diabetes." Patients are treated with diets, diet education, and group psychotherapy, and last, for their diabetes. After one year 86 per cent are still attending, 77.8 per cent have lost more than one pound per month. The average weight loss per patient is 22.7 pounds. Eighty per cent of those taking insulin or hypoglycemic drugs at the start have been able to discontinue them entirely. None of these had lost weight in the regular diabetic clinic on diet restriction **(Booth 233)**.

Phenformin (DBI-TD) Capsules in Combination with Insulin in Insulin-Dependent Diabetes

Maximilian Fabrykant, M.D.
Benjamin I. Ashe, M.D.
New York University Post-Graduate Medical School, New York City

Phenformin timed-disintegration capsules were used with insulin in 80 insulin-dependent diabetic patients for two and one-half years. There were 21 patients with labile and 29 with stable diabetes previously treated with tolbutamide and insulin for one to four years. Beneficial results were obtained in all but 3 patients who were intolerant to the drug. They consisted in stabilization of diabetes in labile patients, greater ease and uniformity of metabolic control, and a sense of general stability and well-being in both groups. Case histories are presented to illustrate the achieved results with this therapy **(Booth 234).**

Cystic Fibrosis of the Pancreas (Mucoviscidosis)

Paul A. di Sant'Agnese, M.D.
Kenneth S. Landauer, M.D.
National Institutes of Health, Bethesda, Maryland

This is a comprehensive exhibit covering all significant aspects of this congenital inherited disease of childhood and adolescence. After a general introduction which characterizes the clinical picture, incidence, and epidemiology of muscoviscidosis, the exhibit elaborates on the following individual facets: pathogenesis, respiratory involvement and complications, bacteriology, electrolyte disturbances, heat casualties, genetics and the heterozygous state, diagnostic criteria, diagnosis, sweat-test procedure, treatment, and prognosis. Original observations and studies are featured for each of the above-mentioned aspects of the disease. In order to facilitate leisurely study of the exhibit at the meeting and to supply viewing physicians with information of practical importance, two mimeographed brochures of five pages each have been prepared to accompany the exhibit and will be available to those interested. One brochure covers the iontophoretic sweat test, the main diagnostic test for cystic fibrosis; the other brochure gives a detailed outline of treatment of cystic fibrosis as used at the National Institute of Arthritis and Metabolic Diseases in Bethesda **(Booth 235).**

Evaluation of Long-Term Triamcinolone in Allergic Diseases

Henry Sherwood, M.D.
Joseph I. Epstein, M.D.
Harry Kaplan, M.D.
Roosevelt Hospital, New York City

Five hundred and fifty patients treated for various allergic diseases were maintained for up to five years on daily doses of triamcinolone. A comparison was made with 40 patients on prednisone. One hundred patients on triamcinolone for from fourteen to forty-eight months have had x-ray gastrointestinal series prior to therapy, many during therapy, and all at the end of the treatment to determine the incidence of ulcers **(Booth 236).**

The Medical Letter—New Drug Appraisals

Harold Aaron, M.D.
The Mount Sinai Hospital, New York City

This display represents the method of operation of *The Medical Letter* in arriving at unbiased and timely appraisals of drugs promoted to physicians. It indicates the procedure in selecting drugs to be investigated and shows how consultants chosen for their special knowledge review the manufacturers' claims against a background of published and unpublished studies and clinical experience. The consultants submit their reports in terms of effectiveness, toxic effects, and comparisons with other drugs already in use. These reports, after extended study and review by its editorial and advisory boards and consultation with other investigators, appear in *The Medical Letter* **(Booth 237).**

Survey of Deaths Related to Diagnostic and Therapeutic Procedures

Dominick J. Di Maio, M.D.
State University of New York Downstate Medical Center, Brooklyn

A survey of deaths related to diagnostic and therapeutic procedures investigated by the Office of the Chief Medical Examiner, New York City, from 1946 through 1955 is presented. The exhibit is divided into four parts: statistics, fatalities from air procedures, instrumentation, and physical and chemical agents. The statistics illustrate the percentage of deaths during or following diagnostic and therapeutic procedures. Air procedures result in death from air embolism or shock. Instrumentation results in perforation, with sepsis, hemorrhage, and shock. Physical and chemical agents can cause death by inducing blood dyscrasias, nephrosis, hepatitis, encephalopathy, sepsis, and anaphylactic shock **(Booth 238).**

Differential Diagnosis and Treatment of Hypertension

Albert N. Brest, M.D.
John H. Moyer, M.D.
Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

The known causes of diastolic hypertension include three major categories: renal, vascular, and adrenal. Approximately 10 per cent of the hypertensive population fall into this category. In 90 per cent the diastolic blood pressure elevation is essential in origin. The differential diagnosis of renal, adrenal, vascular, and essential hypertension is presented. All of the currently employed diagnostic procedures are discussed. In addition, medical and surgical management is described. Effective therapeutic measures are now available in the overwhelming majority of instances **(Booth 239).**

Treatment of Thromboembolic Disease with Human Fibrinolysin

Eugene E. Cliffton, M.D.

Carlo E. Grossi, M.D.
Cornell University Medical College and Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases, New York City

Fibrin formation and dissolution is an important homeostatic mechanism. Thrombosis is a serious distortion in this process. Blood contains an inactive enzyme precursor which can be activated by many means to produce a fibrinolytic enzyme. Some means of activation plus experimental and clinical evidence for the effectiveness of this enzyme are demonstrated **(Booth 240).**

Bleeding Peptic Ulcer and Heart Disease

William J. Grace, M.D.
William F. Mitty, Jr., M.D.
New York University School of Medicine, New York City

A study of bleeding ulcers in 72 patients with severe cardiac disease with a 23.6 per cent mortality is compared with a mortality rate of 4.6 per cent in 498 noncardiac patients with bleeding ulcers. The mortalities are compared in both groups in relation to the amount of blood required in twenty-four hours to stabilize the patient. The mortalities by decades in both groups are compared. An outline for the management of patients with bleeding ulcer is detailed **(Booth 241).**

Renal Biopsy

Mardoqueo I. Salomon, M.D.
Michael S. Bruno, M.D.
William B. Ober, M.D.
Knickerbocker Hospital, New York City

The indications for percutaneous renal biopsy and the technic for performing this relatively simple procedure are discussed and illustrated. Photomicrographs (light and electron) depict pathologic findings in several renal conditions. Patients with essential hypertension are followed up in an attempt to correlate renal biopsy with cardiac, vascular, and funduscopic observations and to see whether or not successful blood pressure control affects renal biopsies. The diagnostic and prognostic value in various nephropathies are illustrated **(Booth 242).**

Two-Way Radio Conferences—Postgraduate Medicine in a 50,000-Square Mile Classroom

Frank M. Woolsey, Jr., M.D.
William P. Nelson, III, M.D.
Henry S. M. Uhl, M.D.
Albany Medical College of Union University, Albany

The Department of Postgraduate Medicine of Albany Medical College has had seven years of experience utilizing two-way radio facilities for postgraduate medical education. There are 36 hospitals in which radio conference rooms have been established. The staff physicians not only listen to the presenting faculty but through special transmitting equipment are able to ask questions or enter the discussion **(Booth S 51, 52).**

Medical Society of the State of New York Exhibits

New York State Journal of Medicine

MEDICAL SOCIETY OF THE STATE OF NEW YORK
New York City

The NEW YORK STATE JOURNAL OF MEDICINE will have its exhibit on display in Booth A in the Ballroom. Members of the Editorial and Circulation Departments will be present at all times to talk "JOURNAL" with you and to hear what you think of the JOURNAL's new look. Interesting suggestions on implementing JOURNAL contents will be welcomed.

Medical Directory of New York State

MEDICAL SOCIETY OF THE STATE OF NEW YORK
New York City

A representative of the *Medical Directory of New York State* will be on hand in Booth B in the Ballroom to answer any questions you may have about the *Directory* and YOUR OWN LISTING IN IT. The next *Directory* will not be published until 1963 which means that the 1961 edition is still current. However, you may have ideas about next year's book which you will want to discuss at the *Directory* exhibit.

Voluntary Prepaid Blue Shield Plans
Medicare—New York State Division
Bureau of Medical Care Insurance

MEDICAL SOCIETY OF THE STATE OF NEW YORK
New York City

Material describing the various benefits offered by the seven Blue Shield plans in New York State is available.

Information regarding medical benefits paid to servicemen's dependents under Public Law 569 (Medicare), as well as changes in the Law beginning January 1, 1960, is also available.

What Goes On Bulletin

COMMITTEE ON PUBLIC HEALTH AND EDUCATION
MEDICAL SOCIETY OF THE STATE OF NEW YORK
ACADEMY OF MEDICINE OF NEW JERSEY
New York City

The *What Goes On Bulletin*, published monthly and distributed to the physicians of New York and New Jersey, serves the doctors by bringing postgraduate medical meetings to their attention and aiding them in planning their busy schedules. Reader reactions and suggestions are appreciated.

1962 ANNUAL CONVENTION

Scientific Motion Pictures

Monday, May 14, through Friday Noon, May 18
Motion Picture Theatre, Exhibit Hall

Chairman WILLIAM J. SULLIVAN, M.D., Westchester
Cochairman KENNETH B. OLSON, M.D., Albany
E. DEAN BABBAGE, M.D., Erie
LESTER COLEMAN, M.D., New York
COLGATE PHILLIPS, M.D., Warren

Highlights of 1962 Program

1. Three or four premiere showings, including a presentation by the U.S.S.R. Academy of Sciences.
2. A variety of subjects of general interest.
3. Continuation of our policy of having many of our films narrated or discussed by their authors.

Monday, May 14

9:00 A.M. Presentation by the Medical Film Guild, Ltd., New York City

Medical Society Presentation

10:00 A.M. **No Real Pathology**
Edwin Dunlop, M.D., Attleboro, Massachusetts

10:22 A.M. **Intrathoracic Aneurysm of the Vertebral Artery Associated with Coarctation of the Aorta**
Elliott S. Hurwitt, M.D., New York City

10:28 A.M. **Surgical Management of Extracranial Obstructions to Cerebral Blood Flow**
Elliott S. Hurwitt, M.D., New York City

10:42 A.M. **The Family Physician and Cancer**
Cancer Cytology Foundation, New York City

11:04 A.M. **50,000 Lives**
Johnson & Johnson, New Brunswick, New Jersey

11:19 A.M. **Frontiers of Allergy**
Leo Criep, M.D., Pittsburgh, Pennsylvania

11:46 A.M. **The Larynx**
Wayne State University Audiovisual Utilization Center, Detroit, Michigan

2:00 P.M. **Prolapse of Uterine Cervix and Inversion of the Vagina Following Removal of the Cervix**
Joshua Davies, M.D., St. Luke's Hospital, New York City

2:21 P.M. **Intermittent Positive Pressure Breathing (IPPB/I), Its Clinical Indications and Application**
Theodore H. Noehren, M.D., Buffalo

2:53 P.M. **Forty Causes of Acute Abdominal Pain**
Hilger P. Jenkins, M.D., Chicago, Illinois

3:28 P.M. **Gait and Musculoskeletal Disorders**
Wayne State University Audiovisual Utilization Center, Detroit, Michigan

4:00 P.M. Presentation by the Medical Film Guild, Ltd., New York City

Tuesday, May 15

9:00 A.M. Presentation by the Medical Film Guild, Ltd., New York City

Medical Society Presentation

10:00 A.M. **Active Management of Disability in the Aged**
Pfizer Laboratories, New York City

10:42 A.M. **Diagnosis and Surgical Repair of Atrial Septal Defect**
Hugh F. Fitzpatrick, M.D., New York City

10:59 A.M. **Medical Genetics—Part I**
Victor McKusick, M.D., Johns Hopkins University School of Medicine, Baltimore, Maryland

11:35 A.M. **Life Story**
American Cancer Society, Purchase

11:51 A.M. **Endoscopy of the Major Bile Ducts**
Clarence J. Schein, M.D., Montefiore Hospital, Bronx

2:00 P.M. **Chronic Ulcerative Colitis**
R. J. Jackman, M.D., J. A. Bargen, M.D., Mayo Clinic, Rochester, Minnesota

2:15 P.M. **Treatment of Incurable Breast Cancer**
Lederle Laboratories, Pearl River

3:02 P.M. **Fibrosarcoma of the Lower Extremity—Hemipelvectomy**
Richard D. Brasfield, M.D., New York City

3:19 P.M. **Cerebral Vascular Diseases: The Challenge of Diagnosis**
American Heart Association, New York City

4:00 P.M. Presentation by the Medical Film Guild, Ltd., New York City

Wednesday, May 16

9:00 A.M. Presentation by the Medical Film Guild, Ltd., New York City

Medical Society Presentation

10:00 A.M. **The Diagnosis and Treatment of Depressions in General Practice**
S. Bernard Wortis, M.D., New York City

10:23 A.M. **The Ear and Hearing**
Wayne State University Audio-visual Utilization Center, Detroit, Michigan

10:47 A.M. **Tracheotomy and Cricothyrotomy**
David S. Ruhe, M.D., Gene V. Williams, M.D., University of Kansas School of Medicine, Kansas City, Kansas

11:12 A.M. **Emergency Airway**
David S. Ruhe, M.D., Gene V. Williams, M.D., University of Kansas School of Medicine, Kansas City, Kansas

11:35 A.M. **The Management of Disabling Pain of Nonarticular Rheumatic Origin**
Symposium conducted and narrated by Howard A. Rusk, M.D., New York City

12:00 NOON **Again to the Stars**
U.S.S.R. Academy of Sciences

2:00 P.M. **Anatomy of the Cell**
E. R. Squibb & Sons, New York City

2:22 P.M. **Disorders of Motility**
Wayne State University Audio-visual Utilization Center, Detroit, Michigan

2:59 P.M. **Introduction to Speech Problems**
Wayne State University Audio-visual Utilization Center, Detroit, Michigan

3:31 P.M. **The Silent Witness**
William S. Merrell Company, Cincinnati, Ohio

4:00 P.M. Presentation by the Medical Film Guild, Ltd., New York City

Thursday, May 17

9:00 A.M. Presentation by the Medical Film Guild, Ltd., New York City

Medical Society Presentation

10:00 A.M. **The Family Physician and Cancer**
Cancer Cytology Foundation, New York City

10:22 A.M. **Endoscopy of the Major Bile Ducts**
Clarence J. Schein, M.D., Montefiore Hospital, Bronx

10:34 A.M. **Treatment of Incurable Breast Cancer**
Lederle Laboratories, Pearl River

11:21 A.M. **The Diagnosis and Treatment of Depression in General Practice**
S. Bernard Wortis, M.D., New York City

11:44 A.M. **The Recurrent Laryngeal Nerve in Thyroid Surgery**

Max M. Simon, M.D., Poughkeepsie

Questions and Answers

2:00 P.M. **Forty Causes of Acute Abdominal Pain**

Hilger P. Jenkins, M.D., Chicago, Illinois

2:35 P.M. **Life Story**

American Cancer Society, Purchase

2:51 P.M. **Carcinoma of the Thyroid—Thyroidectomy and Radical Neck Dissection**

Richard D. Brasfield, M.D., New York City

3:04 P.M. **Fibrosarcoma of the Lower Extremity—Hemipelvectomy**

Richard D. Brasfield, M.D., New York City

3:21 P.M. **Cerebral Vascular Diseases: The Challenge of Diagnosis**

American Heart Association, New York City

4:00 P.M. Presentation by the Medical Film Guild, Ltd., New York City

Friday, May 18

9:00 A.M. Presentation by the Medical Film Guild, Ltd., New York City

Medical Society Presentation

10:00 A.M. **Chronic Ulcerative Colitis**

R. J. Jackman, M.D., J. A. Bargen, M.D., Mayo Clinic, Rochester, Minnesota

10:15 A.M. **Tracheotomy and Cricothyrotomy**

David S. Ruhe, M.D., Gene V. Williams, M.D., University of Kansas School of Medicine, Kansas City, Kansas

10:40 A.M. **Emergency Airway**

David S. Ruhe, M.D., Gene V. Williams, M.D., University of Kansas School of Medicine, Kansas City, Kansas

11:03 A.M. **The Silent Witness**

William S. Merrell Company, Cincinnati, Ohio

11:35 A.M. **Intermittent Positive Pressure Breathing (IPPB/I), Its Clinical Indications and Application**

Theodore H. Noehren, M.D., Buffalo

12:00 NOON **Again to the Stars**

U.S.S.R. Academy of Sciences

The Committee is most grateful for the cooperation of the Medical Film Guild, Ltd., and of its president, Mr. Joseph P. Hackel, who will handle all our films on the Convention program.

Mr. Hackel will present his own films before 10:00 A.M. and after 4:00 P.M. The State Society program will be scheduled from 10:00 A.M. to 4:00 P.M.

Woman's Auxiliary

26th Annual Convention
Statler Hilton, New York City
Sunday, May 13, through Wednesday, May 16, 1962

Our president, Mrs. Eugene F. Wolff, the officers, and the Convention Committee cordially invite you to attend all sessions and social activities.

All doctors' wives, not only Auxiliary members, are invited and urged to register.

Sunday, May 13

3:00 P.M.–5:00 P.M.	Registration, *Skytop Foyer*
3:00 P.M.	Board of Directors meeting, *Schuyler Room*
6:00 P.M.–8:00 P.M.	Reception, honoring past-presidents of the State Auxiliary. Doctors and their wives cordially invited, *Cafe Rouge*

Monday, May 14

8:30 A.M.–4:30 P.M.	Registration, *Skytop Foyer*
9:00 A.M.–12:00 NOON	House of Delegates, *Skytop* Dr. Ethel J. Alpenfels, Professor of Educational Anthropology, New York University, *Guest Speaker*
1:30 P.M.–4:30 P.M.	House of Delegates, *Skytop*

Tuesday, May 15

8:30 A.M.–12:30 P.M.	Registration, *Skytop Foyer*
9:00 A.M.–12:00 NOON	House of Delegates, *Skytop*
1:30 P.M.	Luncheon honoring Mrs. Eugene F. Wolff, President, Woman's Auxiliary to the Medical Society of the State of New York, *Waldorf-Astoria Hotel, Starlight Roof;* Mrs. Harlan English, President American Medical Association Auxiliary, *Guest Speaker*

Wednesday, May 16

8:30 A.M.–10:30 A.M.	Registration, *Skytop Foyer*
9:00 A.M.–12:00 NOON	House of Delegates, *Skytop;* Installation of Officers
12:00 NOON	Postconvention meeting; *Skytop*
2:30 P.M.	Board of Directors meeting, *Presidents' Suite*
6:30 P.M.	Social Hour and Reception; Dinner Dance honoring John M. Galbraith, M.D., President, Medical Society of the State of New York, *Terrace Ballroom*

Officers

President	Mrs. Eugene F. Wolff, Newburgh
President-Elect	Mrs. Herbert J. Ulrich, Buffalo
First Vice-President	Mrs. Dominic R. Pitaro, Troy
Second Vice-President	Mrs. Henry I. Fineberg, Jamaica
Recording Secretary	Mrs. Edward W. Briggs, Jr., Wellsville
Corresponding Secretary	Mrs. David E. Block, Tivoli
Treasurer	Mrs. Irwin Alper, Utica

Convention Committee

Chairman	Mrs. Walter Heldmann, Staten Island
Cochairman	Mrs. John J. Scalzo, Brooklyn

1962 ANNUAL CONVENTION

Technical Exhibits

THE TECHNICAL BOOTHS *at the Annual Convention of the Medical Society of the State of New York will be located in the Statler Hilton's new Exhibit Hall as well as in the Ballroom and the Ballroom Foyer. The 1962 displays will have greater than usual variety. Many new physicians' services will be on view.*

Exhibitors, particularly those from the pharmaceutical industry, will make every effort to coordinate their showing with the over-all convention program.

Members of the Society and their guests are cordially invited to come and browse and see the many new items that will be available at the largest array of technical exhibits to be found at any medical meeting in the East this year.

Abbott Laboratories, North Chicago, Illinois (Booths B–124, B–125), invites you to visit our exhibit. Our representatives will be happy to answer any questions you may have concerning our leading products and new developments.

Albert-Acan X-Ray Solutions, Inc., Woodside, New York (Booth E-59).

The Alkalol Company, Taunton, Massachusetts (Booth B–146), will feature Alkalol, the balanced alkaline-saline solution for the treatment of mucous membranes and irritated tissues. It is bland, nontoxic, and effective and has been a favorite for many years. We are also showing Irrigol, a powder which in solution makes an aseptic, slightly astringent vaginal douche. It also is used widely for colonic irrigations and as an effective rectal enema.

American Sterilizer Company, Professional Division, Erie, Pennsylvania (Booths E–20, 21), will exhibit a new physician's table known as Dynapoise. The table is recognized as the most versatile and efficient physician table ever produced. Also on display will be Amsco's highly efficient office-type, pressure-steam sterilizers, Models 8816M and 613–R. A floor model pressure-steam sterilizer, Model 1022 "Aristocrat," and a nonpressure, portable, office-type sanitizer, Model A–416S, will be exhibited. An efficient one-gallon per hour water still will represent Amsco's complete still line.

Ames Company, Inc., Elkhart, Indiana (Booth B–151). Ames diagnostic products which facilitate your "diabetic program" will be presented from the standpoint of their relation to each other in office and patient management. Your attention will be called particularly to the new improved Clinistix for the patient and to the new Dextrotest Kit, a rapid blood sugar test, for your office use.

Amfre-Grant, Inc., Brooklyn, New York (Booth E–27), cordially invites you to visit their booth where representatives will demonstrate our many prescription specialties for use in the fields of cardiology, urology, and obstetrics and gynecology. On display will be Corovas and Neo-Corovas Tymcaps, Dicorvin tablets, Azolate tablets, desPlex tablets, Baculin tablets, and Causalin tablets.

Armour Pharmaceutical Company, Chicago, Illinois (Booth B-127).

Astra Pharmaceutical Products, Inc., Worcester, Massachusetts (Booth E–45). Descriptive literature pertaining to preparations of Xylocaine Hydrochloride (Astra) for infiltration, regional block, peridural, spinal, and topical anesthesia; Xylocaine Ointment, Xylocaine Jelly, and Xylocaine Viscous for topical application; as well as Astrafer I.V. for iron-deficiency states will be available at the Astra booth presided over by Mr. Arnold G. Everson.

Aveeno Corporation, New York City (Booth B–133). "Safety in skin therapy" is our motto, and all our products have been developed with this in mind. For the latest in the treatment of acute inflammations, chronic dermatoses, acne, and dry skin, please visit our booth.

Ayerst Laboratories, Little Falls, New Jersey (Booth F-72). Visit the Ayerst booth where Grisactin, Dermoplast, and Riopan will be displayed. An Ayerst representative will be most happy to answer your questions.

Constance Bannister Enterprises, Inc., Syosset, Long Island, New York (Booth E-32), will feature the Bannister Babies, now available to doctors, directly from Bannister. These are not just "baby pictures," but have an ability to change one's outlook from "low to high," bring an element every doctor needs in his reception room. There's something for hospitals too.

Barrows Biochemical Products Corporation, New York City (Booth E-14). Physicians are cordially invited to visit this booth where the Barrows representatives are on hand to welcome you and to discuss our product, Coenzyme-B. Coenzyme-B (cocarboxylase) is the key coenzyme in biochemical decarboxylation. Information concerning the use of Coenzyme-B in diabetes, herpes zoster, multiple sclerosis, cardiac conditions, malnutrition, and so forth is available.

Baxter Laboratories, Inc., Morton Grove, Illinois (Booth E-57), will display its latest developments in parenteral fluid therapy. The Travenol Division will feature Perfuso-Pac and Cozyme. The regional perfusion oxygenerator, Perfuso-Pac, serves as a small "heart-lung" for the portion of the body undergoing treatment for certain cancers and permits administration of huge doses of cancer-fighting drugs previously not used in such quantity because of possible damage to vital organs. Cozyme physiologically corrects and prevents intestinal atony and abdominal distention and safely and effectively restores normal peristaltic activity.

Beech-Nut Life Savers, Inc., New York City (Booth B-111). Beech-Nut nutritionists welcome you to the Babyland booth to discuss the nutritive values and the uses of Beech-Nut Baby Foods in infant and modified diets. Educational and technical literature is available, and the newest Beech-Nut strained foods will be introduced: Orange Banana Juice; Rice and Hi-Protein cereals in jars with fruit; and Apricots with Tapioca.

Birtcher Medical Distributors of New York, Brooklyn, New York (Booth E-34), manufactures hyfrecator, electrocardiograph (portable and hospital units), external and internal defibrillators, heart pacer, electrosurgical units, diathermies, ultrasonic, myosynchron muscle stimulator, and phonatrace.

Blakiston Division, McGraw-Hill Book Company, New York City (Booth E-22). Among the many new books to be featured at the Blakiston booth will be the American Public Health Association's *Accident Prevention;* Pettit's *Gynecologic Diagnosis and Treatment;* Harrison, *et al.*: *Principles of Internal Medicine, 4th Edition;* Brown-Pearson's *Clinical Uses of Adrenal Steroids;* Maxwell-Kleeman's *Clinical Disorders of Fluid and Electrolyte Metabolism;* Lippman's *Treatment of the Child in Emotional Conflict, 2nd Edition;* Reich-Nechtow's *Pitfalls in Gynecologic Diagnosis and Surgery;* and Ryan's *Medical Care of the Athlete.*

Borcherdt Company, Chicago, Illinois (Booth F-67), will feature the following: Maltsupex (Malt Soup Extract), liquid and powder, a laxative modifier of milk for constipated babies, also useful for geriatric constipation and pruritus ani; Urolitia, for chronic urinary tract infections in older patients, that quickly relieves burning urination and is especially useful for use over a long period of time; and Ferromalt Tablets, nonconstipating ferrous sulfate tablets, which gave good clinical response without the usual side-effects of oral iron. Ferromalt Tablets are inexpensive and well tolerated. Stop in for recently published papers and samples.

The Borden Company, New York City (Booth B-87). Extending the Metha principle to a wider area of topical dermatologic usefulness, new Methatar, new Methaphor, and new Methaseptic are being introduced at the Borden exhibit. A concise guide to the treatment of skin disorders with Metha topicals is available. Also on display are the well-established infant nutritionals, Bremil and Mull-Soy.

Brewer & Company, Inc., Worcester, Massachusetts (Booth E-9), is presenting their well-known specialties: Theosodate, Luasmin, Enkide, Amchlor, Asteric, and Quinidine (both injectable and oral forms). Also featured are two new specialty products developed by Brewer research: Sus-Phrine, aqueous suspension of epinephrine 1:200 for subcutaneous administration; and Nabcon, a complete natural B-complex liquid concentrate, each teaspoonful of which is equivalent in potency to 35 tablets of brewer's yeast.

Bristol Laboratories, New York City (Booth F-77), will feature information on a new oral penicillin, Prostaphlin, orally effective against penicillin-G staphylococci. Now for the first time treatment in the office and home as well as in the hospital becomes practical and reasonable with this new special purpose penicillin, all the antistaphylococcal activity of Staphcillin, orally.

Burdick Equipment Company, Inc., New York City (Booth B–129). Qualified representatives will be in attendance to demonstrate the famous Burdick EK–111 direct writer electrocardiograph, cardiac monitoring equipment, as well as physical medicine equipment. The photomotograph (Achilles tendon reflex time measurement equipment) will also be demonstrated.

Burroughs Wellcome & Co. (U.S.A.) Inc., Tuckahoe, New York (Booth F–69), cordially invites you to visit their booth for the latest information on our products and the newest developments from the extensive research facilities of Burroughs Wellcome & Co. Of particular interest at this meeting will be our new topical and ophthalmic antibiotic products, as well as our Actifed-C Expectorant. Our informed staff welcomes this opportunity to show you these new products.

Cambridge Instrument Company, Inc., New York City (Booth F–78). The Cambridge Versa-Scribe, the versatile portable electrocardiograph; the Cambridge Simpli-Scribe, model direct-writing portable electrocardiograph, and the Cambridge standard string galvanometer-type electrocardiograph will be displayed at this booth; also other important Cambridge instruments, including the audiovisual heart sound recorder, operating room cardioscope, educational cardioscope, multichannel physiologic recorder, electrokymograph, plethysmograph, pH meters, and pulmonary function tester.

Cameron Surgical Instruments Company, Chicago, Illinois (Booth B–130). See the new 1962 models of the Cameron instruments, especially the "last word" in electrosurgical units for office, clinic, and operating room. See the first electrified biopsy forcep. The Cameron Headlite has now been approved by both the United States government and the City of New York for operating room use.

S. H. Camp and Company, Jackson, Michigan (Booth B–143). An entirely new concept in surgical garments will be on display, consisting of a new treatment for low back pain by pressurized therapy. Based on the principle of the space suit used by jet pilots, it has an inflated pad covering the entire lumbar area. This pressurized support is used for conditions of low back pain such as osteoarthritis of the lumbar spine, rheumatoid spondylitis, sciatica, sacroiliac strain, herniated intervertebral disk, wear and tear of the lower back muscles, angina, and arteriosclerosis of the arteries in the pelvis which can produce pain in the buttocks as well as in the lower back. You will be surprised by the simplicity of operation, and when it is worn the garment is not discernible on the patient. Do not miss seeing this new innovation for low back syndrome. Also see the other new Camp supports and appliances.

Carnation Company, Los Angeles, California (Booth E–61), cordially invites you to visit their booth where medical representatives will be pleased to welcome members and guests of the Medical Society of the State of New York. Recent literature and information regarding Carnation Evaporated, Carnation Instant Non-Fat, and Carnalac are available. Any questions pertaining to our physician-researched material for use in your practice or hospital will be cheerfully discussed.

Carnrick Laboratories, Summit, New Jersey (Booth E–28), welcomes you to our booth which will feature Midrin capsules, the new product which relieves migraine, migraine variants, and tension headaches by reducing intracranial pressure and throbbing, emotional stress and cephalic pain; Bontril Timed, the triple-layer, triple-release tablet that provides maximum anorectic activity at the hunger peaks; Nolamine tablets, elixir and expectorant, for rapid and more prolonged relief of nasal congestion; and Penite Sustained capsules, the more effective coronary vasodilator.

Chicago Pharmacal Company, Chicago, Illinois (Booth E–46), will feature the following products: Urised, clinically proved tablet for both comfortable sedation and thorough antisepsis in genitourinary affections; Estrosed, a tablet containing reserpine and ethinyl estradiol for treatment of the menopausal syndrome; Anameba, a new and potent amebacide in tablet form which has proved 90 per cent effective in clinical trials; and Dicasan, an excellent tablet for the relief of chronic constipation, particularly effective in the treatment of fecal impaction in the chronically ill and aged.

The Chloraseptic Company, Washington, D.C. (Booth B–158). Chloraseptic is a nontoxic, pleasant-tasting mouthwash and gargle specifically designed to destroy infectious bacteria while relieving soreness and pain of the oral and pharyngeal tissues. It possesses profound bactericidal and fungicidal properties and is an effective topical anesthetic. Chloraseptic is indicated in the treatment of pharyngitis, tonsillitis, post-tonsillectomy soreness, smoker's throat, aphthous ulcers, infectious stomatitis, moniliasis (thrust), and Vincent's infection.

Ciba Pharmaceutical Products, Inc., Summit, New Jersey (Booth B–138), will feature Forhistal, a new low-dosage antiallergic and antipruritic agent. Clinically, Forhistal has proved highly effective in a wide range of allergic and pruritic disorders. It is well tolerated by patients of all ages. Forhistal is available in four forms of issue: Lontabs, tablets, syrup, and pediatric drops.

Circulator Therapeutics, Inc., Freeport, New York (Booth B–135). The Circulator is an automatic unit for the reduction of lymphedema and for general use in the treatment of venous arterial and lymphatic insufficiencies of the extremities. The 'milking' action is directionally controlled, and application is extremely simple, no complicated procedure being involved. Treatment may be in the doctor's office or at the home of patient.

The Coca-Cola Company, Atlanta, Georgia (Booth B–161). Ice-cold Coca-Cola will be served through the courtesy and cooperation of The Coca-Cola Company Bottling Company of New York, Inc., and The Coca-Cola Company.

The Combined Book Exhibit, Inc., New York City (Booth E–1). A collection of books (from many publishers) in the area of medicine and allied sciences are arranged by subject for easy access to the fields of knowledge represented. A subject-arranged bibliography is available free.

Contour Chair Lounge Corporation, New York City (Booth B–104). The Contour chair that will be on exhibit is made in five different sizes to give body-conforming comfort. Your body is properly supported at 6 points head-to-foot. As often recommended, legs and feet are always supported and elevated in any of Contour's adjustable positions. A trial sitting in a Contour will give you a new experience and a new gift idea, for giving or getting.

Dannon Milk Products, Inc., Long Island City, New York (Booth E–29), will feature information on Dannon yogurt in various applications to daily practice, including certain gastrointestinal disturbances and help in controlling obesity. Of particular interest is literature on a study of the effectiveness of prune whip in chronic constipation, a study of the control of antibiotic-induced gastrointestinal symptoms with yogurt, and a booklet on weight control, "Dieting to Reduce." Free, cool, refreshing samples of Dannon yogurt in eight appealing varieties will be served.

Davies, Rose & Company, Limited, Boston, Massachusetts (B–157). We cordially invite the members of the Medical Society of the State of New York to visit our booth. Although most physicians need no introduction to our outstanding cardiac therapies, Pil. Digitalis and Tablets Quinidine Sulfate (Natural), our representatives will be on hand to greet you and to explain the dependability of our laboratory productions.

F. A. Davis Company, Philadelphia, Pennsylvania (Booth E–6). A broad selection of new books and new editions will be featured. Among these will be Morse's *Congenital Heart Disease*, Sadove and Wallace's *Halothane*, Dilling's *Clinical Pharmacology*, Cantor's *Traumatic Medicine and Surgery*, Cooper and Ross' *Hypothermia*, and many others on the F. A. Davis reference list.

Desitin Chemical Company, Providence, Rhode Island (Booth E–19). Desitin ointment, for the treatment of burns, ulcers, diaper rash, abrasions, and so forth is presented: Desitin powder relieves chafing, sunburn, diaper rash, and so forth; Desitin Suppositories and Rectal Ointment, for relief of pain and itching in uncomplicated hemorrhoids and fissures; Desitin Baby Lotion, protective, antiseptic; Desitin Acne Cream, a nonstaining, flesh-tinted "Medicream" for the treatment of acne vulgaris; Desitin Cosmetic and Nursery Soap, supermild; Desitin Suppositories with Hydrocortisone, for prompt response to inflammatory conditions in proctitis, severe pruritus, and edema; Desitin Ointment with Hydrocortisone, provides hydrocortisone 1 per cent (as the alcohol) added to the well-known Desitin formula of Norwegian cod liver oil; and Desitin Hydrocortisone Cream, nonstaining, washable hydrophilic base with sol. al. acetate. An elegant cosmetic preparation with hydrocortisone 1 per cent, Desitin Cor-D-Tar cream is a nonstaining, hydrophilic base with a special solution coal tar 3 per cent and nonstaining diiodohydroxyquin 2 per cent, for bacterial fungal infectious eczematous discomfort.

The Dietene Company, Minneapolis, Minnesota (Booth E–26). Have you tasted Meritene? Meritene is the good-tasting protein vitamin mineral food supplement prescribed to provide concentrated nutrition for patients with poor appetite or tolerance for ordinary food. Visit our booth and let us serve you a cool, refreshing Meritene nourishment. While there, review also our Dietene reducing plan, designed to get better cooperation from overweight patients. The Dietene plan provides optimum nutrition and maximum satiety without the use of drugs. Meritene and Dietene are advertised only to the medical profession.

Dome Chemicals, Inc., New York City (Booth B-91), world leader in dermatologicals, will feature dermatologic specialties that are of general interest to the members of the Medical Society of the State of New York. Topical steroid products including Cort-Dome, Neo-Cort-Dome, Neo-Domeform-HC, and Neo-

Lida-Mantle-HC will be featured. Newer products, such as Vi-Dome-A Capsules and Domol Bath Emollient will be introduced. The recently published "Common Sense Facts About Steroid Therapy" will be available.

Dorsey Laboratories, Lincoln, Nebraska (Booth B–101). We are pleased to have a part in making your meeting a success. If you haven't yet had the opportunity to use the Triaminic family of products in your practice, won't you visit with us? Dorsey representatives will be happy to provide you with Kanulase, Kanumodic, Triaminic, and Nebralin for your personal use during the convention.

Eastern School for Physicians' Aides, Inc., New York City (Booth B–95). Meet our physician-director or placement representatives. Entering its second quarter century, Eastern School for Physicians' Aides formalizes "training by physicians for physicians" of the doctor's assistant, medical secretary, clinical, or x-ray laboratory personnel. Founded by H. F. Wolf, M.D., and S. E. Bilik, M.D., members of the Medical Society of the State of New York, Eastern is licensed by the State of New York.

Eaton Laboratories, Div. of The Norwich Pharmacal Company, Norwich, New York (Booth B–93), will feature new Furacin (brand of nitrofurazone)-HC Cream, which combines the dependable antibacterial action of Furacin, the most widely prescribed single topical antibacterial, with the anti-inflammatory, antipruritic, effects of hydrocortisone in a fine vanishing cream base. Furacin-HC Cream is effective in infected and potentially infected dermatoses, pyodermas, ulcers, burns, after minor office surgery, and following anorectal or other operative procedures. Our representatives will supply you with complete information at our booth.

Encyclopaedia Britannica, New York City (Booth E–11), will feature the 1962 edition of *Encyclopaedia Britannica.* This leading reference work with its almost 200-year history has been completely revised in an intensive effort over the last thirteen years, representing an investment of over $5,000,000. Illustrated in color, it contains 38,984,125 words, 26,268 illustrations, by 6,871 contributors from 75 countries, and is easily handled through 539,138 index references. The 1961 edition features 7,942,125 word changes, 11,689 page revisions, 12,112 new articles, and 2,774 new illustrations.

C. B. Fleet Company, Inc., Lynchburg, Virginia (Booth B–131). Patients are happier when physicians choose Phospho-Soda, a laxative that fits into any busy schedule. Patients are happier when physicians choose Fleet Enema, because it's easier and more effective than soapsuds. Booth attendants will present interesting clinical data on both products.

E. Fougera and Company, Inc., Hicksville, New York (Booth B–132). A visit to Fougera's booth will prove interesting and helpful. Well-informed attendants are prepared to discuss both older established products and newer items in many areas of medicine. Product information and clinical literature pertaining to products of both general interest and specialty use are available for your inspection. All physicians are cordially invited to stop by our booth.

Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, Ardsley, New York (Booth E–49), cordially invites members and guests of the Medical Society of the State of New York to visit its exhibit. The exhibit features important new therapeutic developments in the management of inflammation, as well as current concepts in the control of hypertension and edema, depression, obesity, and other disorders, which may be discussed with physicians and representatives in attendance.

Geriatric Pharmaceutical Corporation, Bellerose, New York (Booth B–123), pioneers in geriatric research, will exhibit Ger-O-Foam, an anesthetic analgesic in aerosol form which, when massaged into muscular-skeletal conditions, will relieve pain in minutes and last for hours. We will also exhibit the first break-through in gastrointestinal enzymes, Gustase and Bilezyme.

The Grolier Society, Inc., Bronxville, New York (Booth B–141). This exhibit will be devoted to the following publications: The Golden Anniversary edition of the famous *Book of Knowledge* in 20 volumes and *The Book of Popular Science* in 10 volumes, considered indispensable in the A.A.A.S. Science Book List, compiled by the American Association for the Advancement of Science and the National Science Foundation.

Grune & Stratton, Inc., New York City (Booth B–144). Our Mr. Kurzer will be on hand to show you some of our important new volumes of interest to the specialist and the general physician, such as: Allen's *The Kidney, Second Revised Edition;* Bannerman's *Some Aspects of Thalassemia;* Bigsby and Muniz's *Practical Management of the Obese Patient;* Criep's *Clinical Immunology and Allergy;* Friedberg's *Heart, Kidney and Electrolytes;* Galetti and Brecher's *Heart-Lung Bypass;* Lazarus and Volk's *The Pancreas in Human and Experimental Diabetes;* Stefanini and Dameshek's *The Hemorrhagic Disorders, Second Revised and Enlarged Edition;* Tocantins' *Progress in Hematology, Volume III;* Thannhauser-Estren's *Metabolism and Metabolic Disorders;*

Zucker-Franklin and Braunsteiner's *Physiology and Pathology of Leukocytes;* as well as many other important works which you are invited to inspect.

Health Insurance Council, New York (Booth F–68). This exhibit is designed to provide general information on health insurance as underwritten by insurance companies. In addition, it also makes available information on uniform claim forms for use by doctors and hospitals in support of health insurance claims.

H. J. Heinz Company, Pittsburgh, Pennsylvania (Booth E–41). Heinz Baby Foods are now made by a revolutionary new process. Important results are: superior nutrition, flavor, color, and consistency. Taste some of these varieties at the Heinz booth. Newest varieties are: Apple-Cherry Juice, Strained and Junior Vegetable and Dumplings with Beef and Bacon; Junior Meat Sticks; and Junior Apricots and Oatmeal. Literature is available for office and for patients' use.

Holland-Rantos Company, Inc., New York (Booth E–44), will feature: Hyva Gentian Violet Vaginal Tablets, a simple antimycotic treatment for antibiotic moniliasis, diabetic vulvitis, and mixed infections; improved Nylmerate Jelly and Nylmerate Antiseptic Solution Concentrate for trichomoniasis, leukorrheas, and mixed infections; Hollandex, a skin ointment for dermal disorders, diaper rash, chafing skin dryness, prickly heat, and sunburn; Koromex Vaginal Jelly for conception control when jelly alone is advised; Koro-Flex Contouring Diaphragms and Sets; and Koromex Contouring Diaphragms and Sets.

International Latex Corporation, Dover, Delaware (Booth F–86), is introducing the new Playtex Nurser which duplicates many of the principles of breast feeding. Many features are: The soft pliable container permits air to be expelled before feeding so that baby takes in nourishing formula instead of "swallowed air" which can cause distress, crying, spitting up, and colic; the natural-shaped and natural-action nipple promotes proper sucking action; and the bottle is presterilized and disposable.

Jacuzzi Research, Inc., Berkeley, California (Booth B–106). The Jacuzzi Whirlpool Bath is the first portable hydrotherapy equipment that can be used in any bathtub, swimming pool, or therapy tank. It weighs only 24 pounds, needs no special installation. Jacuzzi also makes lightweight fiberglas hip and foot tanks.

Johnson & Johnson, New Brunswick, New Jersey (Booth B–109), will display the latest improvements in surgical dressings, as developed by the Johnson & Johnson Research Laboratories. Of a special interest is Surgicel Absorbable Hemostat, a major advance in the control of hemorrhage which does not depend on the normal clotting mechanism. Dermicel Surgical Tape, a special-purpose dressing tape for patients with unusual adhesive tape sensitivity, is also of particular interest. Other products, designed for your office, hospital, or patient use, are also displayed. You will find well-informed representatives pleased to discuss these products or provide information on any other items made available by the world's largest manufacturer of surgical dressings and baby products.

Kenwood Laboratories, Brooklyn, New York (Booth B–113). Featured in our display is Papavatral L.A. Capsules, the continuous controlled release combination of a vasodilator and smooth muscle relaxant for the treatment of angina pectoris and peripherovascular diseases. Promoms, the potent prenatal containing a fecal softener, is also presented.

Kirsch Beverages, Inc., Brooklyn, New York (Booth B–126). No-Cal is the original and leading nonfattening soft drink. It contains no sugar, no salt, no fats, carbohydrates, or proteins, with no available calories to be derived therefrom. No-Cal comes in nine flavors, plus salt-free Club Soda. The latest addition to the line is absolutely nonfattening No-Cal Quinine Water. No-Cal is safe for diabetics and those on salt-free, sugar-free, and other reducing diets. (An attractive key case will be distributed to all doctors registering at the No-Cal booth.)

Knoll Pharmaceutical Company, Orange, New Jersey (Booth E–39). You may now prescribe fruit-flavored, taste-appealing Quadrinal suspensions for asthma patients who prefer a liquid to the time-proved Quandrinal tablet. Dilaudid is for pain that synthetic analgesics frequently fail to relieve; also for the cough that must be controlled. Metrazol, Vita-Metrazol, and Nico-Metrazol elixir and tablets are for the geriatric and convalescent patient. Akineton is the new antiparkinsonism agent.

Lakeside Laboratories, Inc., Milwaukee, Wisconsin (Booth B–103), will feature Imferon, Dactilase, and Cantilyn. Complete descriptive information and clinical references will be available. In addition, Lakeside's family of diuretics, including Mercuhydrin and Metahydrin, will be on display. You are cordially invited to visit our exhibit. Professional service representatives will be in attendance, and registration forms for requesting clinical samples will be available.

Fred Landauer Company, Rockville Centre, New York (Booth E–36), is showing Teca electromyographs and Chronaxie Meters for electrodiagnosis of neuromuscular diseases. Apparatus for performing nerve conduction velocity tests, chronaxie determinations, strength duration curves, and other procedures will be demonstrated. Also shown will be a complete line of Teca low-volt generators and muscle stimulators, in addition to other electronic specialties for the medical profession.

Lederle Laboratories, Division of American Cyanamid Company, Pearl River, New York (Booth E–5). Your Lederle representative will be on hand to serve you. He can furnish information on any Lederle product and is prepared to bring to bear on any of your medical problems the knowledge of the world-wide Lederle research organization.

Eli Lilly & Company, Indianapolis, Indiana (Booths E-17 and E–30), cordially invites you to visit its booths. The Lilly sales people in attendance welcome your questions about Lilly products and recent therapeutic developments.

J. B. Lippincott Company, Philadelphia, Pennsylvania (Booth B–90), presents for your approval a display of professional books and journals geared to the latest and most important trends in current medicine and surgery. These publications, written and edited by men active in clinical fields and teaching, are a continuation of more than one hundred years of traditionally significant publishing.

Lloyd Brothers, Inc., Cincinnati, Ohio (Booth E–42). Welcome to the Lloyd Brothers exhibit. Our professionally trained sales representatives will be pleased to greet you and discuss the merits of our products in your practice. Of particular interest will be a new booklet on erythropoitin, the erythropoietic hormone.

Loma Linda Food Company, Arlington, California (Booth B–112). With the background of years of experience in perfecting a hypoallergenic milk powder and also a newly developed concentrated liquid milk, the protein of which is fully derived from the soy bean and formulated with other essential additives to care for the needs of babies, growing children, and adults, the Loma Linda Food Company will be happy to welcome you to their exhibit. Attendants will be pleased to discuss the values of Soyalac powder and concentrated liquid. Samples of this flavorful product will be served at the exhibit.

The Lorvic Corporation, St. Louis, Missouri (Booth B–105), will feature the following products: Karidium, sodium fluoride sodium chloride tablets and drops for the systemic control of dental caries; Vapor Phase, rust inhibitor for autoclaving of surgical instruments; Decalcifier, scale and rust remover for autoclaving and sterilizers; and Rinse, antirust agent for the wash cycle of surgical instruments for use in hot water sterilizers.

Luke Pharmaceutical, Inc., New Castle, Delaware (Booth B–89). The following products will be displayed. Dione, a new approach to therapy for collagen diseases, helps reduce inflammation and rebuild new collagenous fibers; Enisyl with iron, the aminogram approach to anemia, treats the entire hemoglobin molecule, not just the 6 per cent heme portion; and Enisyl V, the complete lysine-fortified prenatal supplement fulfilling the increased need of vitamins and amino acids during pregnancy.

The S. E. Massengill Company, Inc., New York City (Booth B-94). Best wishes to the Medical Society of the State of New York for a very successful 1962 meeting. Massengill representatives will be glad to discuss any products which interest you. Exhibited will be Trimagill, the logical therapy for vaginal infections, and Livitamin, the hematinic with built-in nutritional support.

Materna-Line, Inc., and Dora Miles Co., New York City (Booth B–88). Vulvar varicosities need no longer be a problem with Materna-Line's improved combination of foundation garment with pad. Also featured is a range of undergarments especially adaptable to all forms of ptosis as well as postpartum conditions.

Mayflower Surgical Supply Company, Brooklyn, New York (Booth E–40), distributors for The Birtcher Corporation, Liebel-Flarsheim, American and Castle Autoclaves, Ritter Company, and Continental X-Ray, is the largest medical distributor of physicians' consultation and reception room furniture, such as desks, swivel chairs, lamps, and bookcases. All equipment is financed on a low-interest plan.

Mead Johnson Laboratories, Evansville, Indiana (Booth B–145). This exhibit has been arranged to give you the optimum in quick service and product information. To make your visit productive, especially trained representatives will be on duty to tell you about their products.

Medco Products Company, Inc., Tulsa, Oklahoma (Booth E–2), is presenting the Medco-Sonlator which provides a new concept in therapy by combining muscle stimulation and ultrasound simultaneously through a single three-way sound applicator. The Medco-Sonlator is a distinct advance in the effectiveness of physical therapy in your office or hospital. A few minutes spent in our booth should prove of value to your practice.

Medical Film Guild, Ltd., New York City (Booth B–97). What's new in educational aides in medicine? New motion pictures, new slide films on diagnosis, new audiovisual equipment for lecturers, and all brand new thought-stimulating devices and teaching material. New motion picture films include: "Diabetes and Its Long Range Control," sponsored by the New Jersey State Department of Health; and "Blood Flow, Newer Technics for Measurement in Various Vascular Beds"; collaborators include research teams at seven universities including New York University Research Division, Goldwater Memorial Hospital, and Albany Medical College. New slide films in diagnosis, a complete new approach to medical teaching, applies to postgraduate and undergraduate groups; equipment is unique, simple to operate, and low in cost. Vu-Graph Projection, the new way to lecture with mural-size images, allows pointing to vital areas while maintaining eye-to-eye contact with an audience. Sten-O-Tape dictating and transcribing machines, a variety of models, simplify and expedite correspondence, conference notes, case histories, records, and so forth. Model TR–711 is transistorized, battery powered; model G256/60 is $6^{1}/_{2}$ pounds, two-hour play; and model G3/10 has ten-hour play.

Merck Sharp & Dohme, Philadelphia, Pennsylvania (Booths E–24, E–25). The theme of the Merck Sharp & Dohme exhibit is "Service to Medicine." One phase features the details of the Merck Sharp & Dohme postgraduate program. Another feature includes information on teaching films for use by the profession, and also lay films that can be utilized to portray the story of medicine to the lay public. The exhibit is concluded with a display of fingertip files on selected Merck Sharp & Dohme products.

The Wm. S. Merrell Company, Cincinnati, Ohio (Booth F-73).

Milex of New York, Long Island City, New York (Booth B–96). Gynecologic products will be featured. Trimo-San for trichomonas, monilia, and mixed leukorrheas will be introduced. Amino-Cerv Creme will be demonstrated as the treatment of choice for cervicitis and post-cervical surgery. Samples of "A Doctor Discusses the Menopause," "A Doctor's Marital Guide for Patients," "What Teenagers Want to Know," and a "Rhythm Calculator," are available on request.

National Dairy Council, New York City (Booth E–7). "Your Food Today Shapes Your Figure Tomorrow," a National Dairy Council exhibit, tells the weight-control story as developed at Michigan State University by Dr. Margaret A. Ohlson. Featured are the 1,400- and 1,800-calorie diets set up in attractive, nutritious meals. Education materials related to weight control will be on display. The exhibit will be staffed by Dairy Council nutritionists.

The National Drug Company, Philadelphia, Pennsylvania (Booth B–122). Tepanil, Tepanil Ten-tab, and Orenzyme are being featured at our exhibit. Tepanil is a completely new compound that curbs the appetite with little or no central nervous system stimulation. Orenzyme is the first oral anti-inflammatory enzyme tablet on the market. Orenzyme is indicated for the treatment of any acute inflammatory process when swelling slows recovery.

New York Medical Exchange, New York City (Booth F–63). Once again Patricia Edgerly of the New York Medical Exchange will be at the Annual Convention of the Medical Society of the State of New York. Stop by her booth and discuss with her any personnel needs you may have. She can suggest office assistants, nurses, secretaries, technicians, or interesting opportunities that may appeal to you.

New York Telephone Company, New York City (Booths B–139, B–140). This exhibit will demonstrate how medical data electrocardiograms in particular can be transmitted from one point to another over regular telephone lines with Data-Phone service. The transmission of x-ray pictures over telephone lines also will be shown.

Organon, Inc., West Orange, New Jersey (Booth E–60). Physicians are cordially invited to visit the Organon booth for information on useful therapeutic specialties. Included among these will be: Cortrophin-Zinc, the long-acting aqueous ACTH indicated for the relief of allergic and inflammatory disorders; Durabolin, a totally new anabolic stimulant offering prolonged tissue-building action; Wigraine; Nugestoral; and Cotazym and Cotazym-B. Organon representatives will gladly discuss these specialties with all interested physicians.

Ortho Pharmaceutical Corporation, Raritan, New Jersey (Booth B–136). Of especial interest to physicians, Ortho is presenting new data on Actase Fibrinolysin (human) in a new potency, facilitating the lysis of intravenous clots in an extended therapeutic range. Your questions will be welcomed.

Parke, Davis & Company, Detroit, Michigan (Booth E–23). Medical service members of our staff will be in attendance at our booth to discuss important Parke-Davis specialties which will be on display.

Pfizer Laboratories, Division, Chas. Pfizer & Co., Inc., New York City (Booth F–70). Professional service representatives from Pfizer Laboratories will be pleased to have you in attendance at their booth to discuss the latest products of Pfizer research.

Pharmacia Laboratories, Inc., Rochester, Minnesota (Booth 76), will exhibit its product, Azulfidine, a new sulfa compound for the treatment of ulcerative colitis and regional enteritis. Also, Pharmacia will exhibit Pharmalax, the suppository with enema-like action. The quick action of Pharmalax causes defecation through mechanical stimulation of the intestinal musculature by carbon dioxide released from the suppository. Skopyl, a new concept in the medical treatment of infant colic, will also be displayed. Literature and important reprints will be available on request.

Plough Laboratories, Inc., Memphis, Tennessee (Booth B–128). This display includes two demonstrations of the unique pharmacologic activity of Silain, a gastrointestinal defrothicant. In vitro, Silain by breaking the foam which holds much gas aids in its elimination. In vivo, gastroscopic photographs show Silain's effect on foam in the stomach.

Procter & Gamble Company, Cincinnati, Ohio (Booth B–115). Ivory Soap offers a series of time-saving leaflet pads for doctors, each pad containing 50 identical tear-out sheets. These sheets, which may be given to patients, contain routine instructions covering six different topics. There are also samples of other free, helpful material prepared especially for physicians.

Procter & Gamble Company, Cincinnati, Ohio (Booths 107–108). The Procter & Gamble "Facts on Fat" exhibit, through its illuminated panels and scientific personnel manning the booth, is designed to answer important questions on dietary fats. New Crisco, the highly unsaturated vegetable shortening with double the linoleic content, will be featured. Cookies made with New Crisco will be distributed.

The Purdue Frederick Company, New York (Booth F–65), will feature these products at their booth: Senokot Granules and Senokot Tablets, standardized concentrate of total senna pod principles used in the management of constipation. The correction of constipation is physiologically gentle and neurogenically persuasive. Senokot Granules are pleasantly cocoa-flavored. Full product disclosure is available on request at the Purdue Frederick Company's booth. Also, Paremycin Elixir, an exempt narcotic containing per teaspoonful 50 mg. neomycin sulfate and 0.03 ml. tincture of opium in a palatable banana-flavored vehicle, is indicated in infectious and noninfectious diarrheas, dysenteries, and infantile gastroenteritis. The recommended dosage for infants under two years of age is $^1/_2$ to 1 teaspoonful four times daily; for children over two, 1 to 2 teaspoonfuls four times daily; and for adults, 1 to 2 tablespoons four times daily. Full product disclosure may be obtained on request at the Purdue Frederick Company's booth.

Reed & Carnrick, Kenilworth, New Jersey (Booth B–154). Featured will be the following products: Phazyme Tablets, indicated for the relief of all the discomforts of gastrointestinal gas distress, pain and bloating associated with belching borborygmus, and flatulence resulting from aerophagia, faulty digestion, and food intolerance, as well as many other functional or organic conditions; Trichotine, the modern vaginal irrigant used for routine feminine hygiene and as adjunctive cleansing therapy in the treatment of cervicovaginitis; and Alphosyl Cream and Lotion, indicated for psoriatic skin conditions associated with scales, itching, and redness, which aids in the removal of scales, suppresses the formation of scales, and helps maintain the normal appearance and condition of the skin.

Reid Laboratories, Inc., Atlanta, Georgia (Booth B–134). Products featured by our exhibit will be Amurex Capsules, dl-methionine, used for the treatment of diaper rash due to ammoniacal urine; Ferisorb Tablets, a chewable hematinic tablet containing ferrous fumarate, ascorbic acid, and pyridoxine hydrochloride; and Kapigam, Reid's diarrhea preparation, the third product to be featured.

Riker Laboratories, Inc., Northridge, California (Booth F–79). Representatives of Riker Laboratories will be happy to have you visit their booth and discuss the latest information about their products.

Ritter Company, Inc., Rochester, New York (Booth F–74). Tired of bending and stooping, doctor? Qualified representatives can show you the effortless operation of the Ritter Universal and Specialist Tables. The popular Speedclave and Model 999 Autoclave as well as the new Castle #8 Diagnostic Light will be displayed. The Liebel-Flarsheim Bovie and Self-Calculating BasalMeteR can be demonstrated at your request.

A. H. Robins Company, Inc., Richmond, Virginia (Booth E–16). When too much food causes your patient's complaint, prescribe

Ambar Extentabs (No. 1 or No. 2) to curb appetite without jitters. When too much water is his problem, prescribe the unsurpassed diuretic, Naclex. It gets water out fast! Also featured: Dimetane Extentabs; just one provides antihistaminic relief for from ten to twelve hours. Donnazyme combines Donnatal and Entozyme for nervous indigestion.

Roche Laboratories, Division of Hoffmann-LaRoche, Inc., Nutley, New Jersey (Booth B–102), will feature the following products: Librium, a therapeutic agent for superior, safer, faster control of nervousness, anxiety, tension, and other common emotional disturbances without the dulling effect or depressant action of the tranquilizers; also, Gantanol, a single sulfonamide for the common bacterial infections encountered in daily practice.

J. B. Roerig & Company, New York City (Booth E–43), will welcome members of the medical profession at the company's exhibit of leading specialties and new products. Representatives will be in attendance to answer any questions you may have. Roerig recently introduced a number of new products which representatives at the exhibit will describe and give information on the results of clinical reports.

William H. Rorer, Inc., Philadelphia, Pennsylvania (Booth E–4), features Ananase Tablets, a new oral, fibrin depolymerizing (proteolytic) enzyme from vegetable origin. Also, Maalox, a pleasant-tasting, nonconstipating antacid in suspension, Tablets No. 1 and Tablets No. 2. Representatives will gladly answer questions concerning Rorer products.

Rystan Company, Mount Vernon, New York (Booth B–114), introduces a new anti-inflammatory enzyme, Buclamase, for the management of swelling and pain of sprains, fractures, bruises, and other orthopedic or postoperative conditions. A development of original Rystan research, Buclamase is a buccal tablet containing the amylolytic enzyme, alpha amylase. Safe, inexpensive, and convenient, Buclamase is particularly suited to routine, on-the-spot administration for injuries sustained in organized sports programs.

Sanborn Company, Waltham, Massachusetts (Booth E–56). New electrocardiographs of advanced design and function, as well as the latest models of other instruments for diagnostic use, will be displayed and demonstrated at the Sanborn booth. Demonstrations and/or data will also be available on Sanborn instruments for biophysical research, single and multichannel recording systems, monitoring oscilloscopes, and physiologic transducers. Qualified Sanborn representatives will be pleased to answer questions and assist you with technical problems.

Sandoz Pharmaceuticals, Division of Sandoz, Inc., Hanover, New Jersey (Booth E–35), cordially invites you to visit our display, where we are featuring Mellaril, Cafergot P-B, and our new product, Sansert. Any of our representatives in attendance will gladly answer questions about these and other Sandoz products.

Saratoga Springs Commission, Saratoga Springs, New York (Booth B–120). The exhibit portrays the physical attractions and natural beauty of the Saratoga Springs Reservation, home of The Saratoga Spa; the naturally carbonated, mineralized bottled waters; the research laboratories; the Gideon Putnam Hotel; plus golfing, swimming, picnicking, cycling, and other forms of recreation. Physical medicine procedures involved in the baths and the general atmosphere of the Spa are depicted in a series of colored slides and large blow-ups. The Reservation is directed by a doctor of medicine.

W. B. Saunders Company, Philadelphia, Pennsylvania (Booth E–10). New Saunders books of especial clinical interest include: *Current Therapy 1962;* Davidson and Wells: *Todd and Sanford Clinical Diagnosis by Laboratory Methods;* Green and Richmond: *Pediatric Diagnosis;* Huffman: *Gynecology and Obstetrics;* Lore: *Atlas of Head and Neck Surgery;* Owen: *Hospital Administration;* Reid: *Obstetrics;* and Williams: *Endocrinology*.

Schering Corporation, Bloomfield, New Jersey (Booth E–18). You are cordially invited to visit the Schering technical exhibit where the following products will be featured: Fulvicin and Advicin, the first combination to meet the requirements for successful athlete's foot therapy; Celestone, a new magnitude in anti-inflammatory corticosteroid short-term therapy; and Chlor-Trimeton, the unsurpassed antihistamine.

Schieffelin & Company, New York City (Booth F–85), is exhibiting several products of importance and interest to the physician. Among these products are the Resulin products for acne and Neo-Resulin-F, a dermatological that offers four-pronged action for acne therapy. Another efficacious dermatological being exhibited is Hydro-Tar, which offers the patient a therapeutic combination of crude coal tar and hydrocortisone. Also of interest to the attending physician is Estivin, the ophthalmic preparation suggested for hay fever and other minor ocular allergic irritations. The Almay hypoallergenic cosmetic division will also exhibit a complete line of fashion-oriented cosmetic products.

Julius Schmid, Inc., New York City (Booth E–15). An interesting and informative exhibit will feature Immolin Vaginal Cream Jel for use without a diaphragm; Ramses Flexible Cushioned and Bendex Diaphragms; Ramses Vaginal Jelly; Vagisec Jelly and liquid for vaginal trichomoniasis therapy; and XXXX (Fourex) Skin Condoms, Ramses, Sheik, and Esquire Rubber Condoms for the control of trichomonal reinfection.

The Scholl Mfg. Company, Inc., Chicago, Illinois (Booth E–62). Registered nurses will be available to demonstrate the latest technics and innovations of bandaging with Tubegauz, the seamless tubular gauze dressing. In addition, on display will be other new surgical dressings that will be demonstrated by registered nurses and other qualified personnel.

G. D. Searle & Company, Chicago, Illinois (Booth F–71). You are cordially invited to visit the Searle booth where our representatives will be happy to answer any questions regarding Searle products of research.

Seven-Up Developers of New York State, New York City (B–142). Seven-Up is the all-family drink. On the back of every bottle of Seven-Up are listed all the ingredients of this sparkling crystal-clear drink. Such listing is not required, but Seven-Up is proud to do it, proud to let you see what a pure and wholesome drink it is. Seven-Up is so pure and wholesome folks of all ages may have it. Seven-Up is truly an all-family drink. Come visit us at our booth for a sample of the all-family drink.

Sherman Laboratories, Detroit, Michigan (Booth E–33), will feature the following products: Elixophyllin; severe asthmatic attacks are not merely relieved, but terminated in ten to twenty minutes by Elixophyllin, given orally. In milder attacks, its speed has been described as instantaneous. Persistin is a long-acting non-narcotic analgesic. Prescribed as a single dose, Persistin provides therapeutic salicylate levels up to eight hours and permits avoidance of narcotics and hypnotics for many patients.

Smith Kline & French Laboratories, Philadelphia, Pennsylvania (Booth F–84). Our representatives welcome the opportunity to discuss SKF products with you and are always ready to be of help in any way they can. Products featured are: Parnate Tablets, Eskatrol Spansule capsules, and Ornade Spansule capsules.

Smith, Miller & Patch, Inc., New York City (Booth B–98). Featured are Tempotriad, a new psychokinetic activator designed to give a lift to the lethargic, elevate mood, counteract sleepiness, relieve depression, and produce a sense of well-being, in liquid and tablet dosage. Vitron-C, a potent oral hematinic, ferrous fumarate with ascorbic acid, has been clinically proved to be effective in treating iron-deficiency anemia with a high degree of toleration in patients with gastrointestinal irritability or ulcerative disease; a chewable, pleasantly flavored sugar-free tablet that offers iron with maximum toleration. Bistrimate is a safe, effective, and economical therapeutic to combat subacute, chronic, or recurrent sore throat. Preliminary tissue studies indicate Bistrimate has an antiviral effect on adenovirus type 3 and adenovirus type 7. No serious reactions to Bistrimate have been noted in over fifteen years use. Trulase, the only digestive aid designed to help prevent postprandial pain and discomfort due to inadequate digestion, acts physiologically without delay and contains three essential enzymes standardized to assure dependable activity.

Spencer, Incorporated, New Haven, Connecticut (Booth B–160). Every Spencer support is individually designed, cut, and manufactured according to prescription needs, for men, women, or children, to assist in corrective and rehabilitative treatment. You are cordially invited to visit the Spencer booth to see samples of our supports or to inquire about supports for the specific requirements of patients. Ask about our Spencer emergency service for patients requiring immediate support. You may register for a Posture Manikin and a Simulated Vertebrae model.

E. R. Squibb & Sons, New York (Booth E–50), has long been a leader in the development of new therapeutic agents for the prevention and treatment of disease. The results of our diligent research are available to the medical profession in new products or improvements in products already marketed. We are pleased to present up-to-date information on these advances for your consideration.

The Stuart Company, Pasadena, California (Booth F–66). A cordial invitation is extended to all members and guests attending this meeting to visit the Stuart Company booth. Especially trained representatives will be in attendance to answer your questions on new products developed in our new and modern laboratories which have received international acclaim.

M. R. Thompson, Inc., Subsidiary of The J. B. Williams Company, Inc., New York City (Booth B–121), will feature the following products: Quinidate capsules, a special formulation of quinidine sulfate in edible oil which minimizes gastrointestinal irritation in the treatment of the ectopic arrhythmias; Quinidate injectable, solution quinidine sulfate in propylene glycol, minimizing tissue irritation and pain at the site of injection whenever rapid quinidinization is necessary; Verwolfia tablets, which combine the peripheral vasodilating action of standardized whole root veratrum viride with the control action of standardized Rauwolfia serpentina for the therapy of moderately severe hypertension; Rauwistan tablets, standardized whole root extract of Rauwolfia serpentina for the therapy of mild hypertension; and Margel tablets and suspension, pleasant-tasting formulations of long- and short-acting antacids for the treatment of hyperacidity with a minimum of constipation.

United Medical Service, Inc., New York City (Booth B–99). Blue Shield, the community service plan designed and guided by the medical societies to meet the public health care needs, is the theme of the display. Through photographs, art, and graphs, the broad community enrollment and coverage aspects of Blue Shield are depicted, and literature presenting further information about UMS, New York's Blue Shield, is available.

The Upjohn Company, Kalamazoo, Michigan (Booth E–37). Professional representatives of The Upjohn Company are eager to contribute to the success of your meeting. We are here to discuss with you products of Upjohn research that are designed to assist you in the practice of your profession. We solicit your inquiries and comments.

U.S. Vitamin & Pharmaceutical Corporation, New York City (Booth B–92), will feature DBI, the new full-range oral hypoglycemic agent. DBI, a brand of phenformin (Nl-B-phenethylbiguanide HCl) is distinctly different in chemical structure and physiologic action from the oral hypoglycemic sulfonylureas. It effectively lowers blood sugar and eliminates glycosuria in mild, moderate, and severe diabetes. DBI, in combination with insulin, improves the regulation of brittle adult and juvenile diabetes. In juvenile diabetes, DBI often permits up to 50 per cent reduction in insulin requirement; is also effective in the insulin-resistant patient and in primary and secondary tolbutamide and chlorpropamide failures. Full details are available.

Vaponefrin Company, New York City (Booth B–118) will exhibit Vaponefrin Solution, the 2.25 per cent solution of racemic epinephrine, as hydrochloride, equivalent in potency to 1.25 per cent U.S.P. Reference standard epinephrine by bioassay produces prompt bronchodilation for effective relief of bronchial asthma, emphysema, chronic bronchitis, or other respiratory diseases; is notably free of side-effects. The Vaponefrin nebulizer is especially constructed to deliver particles in the desirable range of 0.5 to 3 microns for disposition in the bronchi and bronchioles.

Walker Laboratories, Inc., Mount Vernon, New York (Booth F–64), will feature Nicalex for safe, effective reduction of serum and tissue cholesterol as well as phospholipid and triglyceride levels. Also featured will be new clinical information regarding the effect of Hedulin and other anticoagulants on lipid metabolism.

Wallace Laboratories, Cranbury, New Jersey (Booths B–116–117), features information on Capla, a new kind of drug for the treatment of hypertension. Capla acts specifically on the brain centers that control blood pressure, rather than indirectly or peripherally like older antihypertensives. It has proved nontoxic in clinical use, and side-effects are limited to occasional cases of drowsiness, usually transient in nature.

Wampole Laboratories, Stamford, Connecticut (Booth E–47), will feature the following products: Avazyme Tablets, the first all-chymotrypsin preparation for oral use. Stability studies in human intestinal juice show that after twenty minutes only 8 per cent of active trypsin is left whereas over 60 per cent of chymotrypsin is still active; Alvinine Shampoo, a new agent for the treatment of seborrhea capitis; VoSol/VoSol HC, VoSol Otic Solution, and VoSol-HC Otic Solution, for the treatment of otitis externa without antibiotics or sulfas. VoSol Otic Solution is bactericidal and fungicidal and may also be used for otitis prevention. The hydrocortisone in VoSol-HC helps reduce inflammatory swelling and relieve symptoms such as itching and pain.

Warner-Chilcott Laboratories, Morris Plains, New Jersey (Booth B–137), will feature the following products: Gelusil, the physician's antacid for the relief of gastric hyperacidity and management of peptic ulcer, provides two protective coating gels for prompt, prolonged relief of pain. Gelusil is all antacid in action, is nonconstipating, and contains no laxative. Also, Peritrate, a long-acting coronary vasodilator for patients with coronary artery disease, whether angina pectoris or coronary occlusion, improves coronary blood flow, thereby increasing collateral circulation, with no significant change in blood pressure or pulse rate. A smooth onset of action virtually eliminates nitrate headache.

The Warren-Teed Products Company, Columbus, Ohio (Booth B–159), will feature the following pharmaceutical specialty products at their exhibit: Ilopan, an injectable d-pantothenyl alcohol for the treatment and prevention of flatulent gastrointestinal distention; also, Chymolase, an aqueous sterile solution of chymotrypsin (5,000 W-T units per cc. and 50 mg. gelatin per cc.) for the relief of local inflammation and/or edema. Warren-Teed representatives cordially welcome all registrants to visit their display.

Westwood Pharmaceuticals, Division of Foster-Milburn Company, Buffalo, New York (Booth E–48), invites physicians to stop by their booth to discuss their unique dermatologic products: Fostex Cream, Fostex Cake, Lowila Cake, Lowila Emollient, Sebulex, Fostril, and Alpha-Keri. These products are particularly suitable for personal use by physicians and their families who may be plagued with dandruff, acne, dry and itchy skin, and sensitivities to soap. Register, so that we may send prescription units to your home.

White Laboratories, Inc., Kenilworth, New Jersey (Booth B–100), will feature A and D Ointment and Aspergum. Healing is rapid and dramatic when A and D Ointment is applied during each diaper change in the treatment of diaper rash. A and D Ointment stimulates wound healing and promotes healthy granulation and rapid epithelization in a wide variety of other skin conditions including burns, minor skin irritations, indolent ulcers, sunburn, postoperative dressings, and fissured nipples. Aspergum, aspirin in flavored chewing gum form, provides immediate local relief from oropharyngeal pain and discomfort following tonsillectomy. Chewing and swallowing also help prevent local muscular stiffness so common after tonsil removal.

Winthrop Laboratories, New York City (Booth E–31), cordially invites you to visit their booth at which they are planning to feature the following product: Winstrol, the new complete "physiotonic" for the underweight, the weak, and debilitated. It builds body tissue, confidence, and alertness. Winstrol is highly active orally, simple to administer, and suitable for prolonged therapy in most cases.

W. T. S. Pharmaceuticals, Division of Wallace & Tiernan, Inc., Rochester, New York (Booth E–53), features the following products: Desenex, the most widely prescribed fungicide used in the prevention and treatment of athlete's foot and other superficial fungus infections of the skin; also, Caldesene, which provides a lubricating and emollient film which is effective in the prevention or treatment of diaper rash and minor skin irritations.

Wynn Pharmacal Corporation, Philadelphia, Pennsylvania (Booth B–119), will feature the following products: Quinaglute Dura-Tabs, the only sustained medication quinidine gluconate tablets, for control of cardiac arrhythmias, which maintain effective plasma levels with convenient twice daily dosage, are well tolerated; Aminophylline Dura-Tabs, sustained medication aminophylline tablets, $4^1/_2$ grains, twice daily, with virtually no gastric distress; and Dexaline Dura-Tabs and Dexatal Dura-Tabs, for appetite control all day with one morning dose.

F. E. Young and Company, Chicago, Illinois (Booth E–8), will exhibit Young's Dilators, PSP Test Set, Young's Albumin Test and Jen-i-sol. Young's Dilators are used in the treatment and prevention of contracted anus, particularly following hemorrhoidectomy, constipation, congenital stricture, prolapse, dysmenorrhea, dyspareunia, perineal dissection, and repair following delivery.

Syntex Laboratories, Inc., New York City (Booth B–110).

MEDICAL SOCIETY
OF THE STATE
OF NEW YORK

WEDNESDAY
MAY 16, 1962

TERRACE BALLROOM
STATLER HILTON

32nd Street &
Seventh Avenue
New York City

Annual Dinner Dance

in honor of

JOHN M. GALBRAITH, M.D.
President

Reception at 7 p.m.

Gourmet Dinner

Music by Ben Cutler

Dress Optional

Subscription $17.50 Per Person

RESERVATION BLANK

make checks payable to:
Medical Society of the State of New York
750 Third Avenue
New York 17, New York

Please send me———tickets for the Annual Dinner Dance on May 16.

Enclosed please find my check for————.

NAME

ADDRESS

Please attach guest list

MEDICAL SOCIETY OF THE STATE OF NEW YORK

House of Delegates

May 14 through 17, 1962
Statler Hilton, New York City

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Schedule of Sessions

Monday, May 14, 1962

Opening Session	10:00 A.M.
Reference Committees	2:00 P.M.

Tuesday, May 15, 1962

Reference Committees	10:00 A.M.
Reference Committees	2:00 P.M.

Wednesday, May 16, 1962

Second Session	9:00 A.M.
Third Session	2:00 P.M.

Thursday, May 17, 1962

Fourth Session	9:00 A.M.

According to the Bylaws, Chapter II, Section 7, the following shall be the order of business at the sessions of the House of Delegates:

Order of Business

1. Calling the meeting to order.
2. Invocation.
3. National Anthem.
4. Report of Reference Committee on Credentials.
5. Report by the secretary as to the presence or absence of a quorum.
6. Remarks by the speaker.
7. Reading the minutes of the previous meeting by title.
8. Report of the president.
9. Address of the president-elect.
10. Report of the Judicial Council.
11. Report of the Council.
12. Report of the secretary.
13. Report of the treasurer.
14. Report of the Board of Trustees.
15. Reports of district branches by district delegates.
16. Reports of special committees.
17. Reports of reference committees.
18. Unfinished business.
19. New business.
20. Adjournment.

Members

The following pages contain a complete list of the members of the 1962 House of Delegates of the Medical Society of the State of New York.

Officers, 1961–1962

President—John M. Galbraith, Nassau
President-Elect—Joseph A. Lane, Monroe
Vice-President—Reid R. Heffner, Westchester
Secretary—William L. Wheeler, Jr., New York
Assistant Secretary—Ezra A. Wolff, Queens
Treasurer—Maurice J. Dattelbaum, Kings
Assistant Treasurer—Samuel Z. Freedman, New York
Speaker—Frederick A. Wurzbach, Jr., Bronx
Vice-Speaker—E. Dean Babbage, Erie

Councillors

Term Expires 1962

James M. Blake, Schenectady
Peter J. DiNatale, Genesee
George J. Lawrence, Jr., Queens
Waring Willis, Westchester

Term Expires 1963

Gerald D. Dorman, New York
Edward C. Hughes, Onondaga
Alfred P. Ingegno, Kings
Raymond S. McKeeby, Broome

Term Expires 1964

Harold F. Brown, Erie
John C. McClintock, Albany
George A. Burgin, Herkimer
Joseph G. Zimring, Nassau

Trustees

John J. Masterson, Kings
Frederic W. Holcomb, Ulster
J. Stanley Kenney, New York
Leo E. Gibson, Onondaga
Thurman B. Givan, Kings
Norman S. Moore, Tompkins
Renato J. Azzari, Bronx

Ex-Presidents

1923–1924—Orrin Sage Wightman, New York
1932–1933—Chas. Gordon Heyd, New York
1934–1935—Arthur J. Bedell, Albany
1944–1945—Herbert H. Bauckus, Erie
1947–1948—Louis H. Bauer, Nassau
1949–1950—John J. Masterson, Kings
1950–1951—Carlton E. Wertz, Erie
1951–1952—J. Stanley Kenney, New York
1952–1953—Edward T. Wentworth, Monroe
1953–1954—Andrew A. Eggston, Westchester
1955–1956—Renato J. Azzari, Bronx
1956–1957—James Greenough, Otsego
1957–1958—Thurman B. Givan, Kings
1958–1959—Leo E. Gibson, Onondaga
1959–1960—Henry I. Fineberg, Queens
1960–1961—Norman S. Moore, Tompkins

Commissioner, New York State Department of Health

Herman E. Hilleboe, Albany

District Delegates

(*Elected Delegates of District Branches*)

First—Joseph F. Shanaphy, Richmond
Second—Albert M. Biglan, Suffolk
Third—Lee R. Tompkins, Sullivan
Fourth—Milton J. Greenberg, Washington
Fifth—Arthur F. Gaffney, Oneida
Sixth—Norman C. Lyster, Chenango
Seventh—Milton Tully, Steuben
Eighth—Wilfrid M. Anna, Niagara
Ninth—Maxwell Gosse, Dutchess

Section Delegates

(*Delegates from Scientific Sections*)

Allergy—Richard D. Wiseman, Onondaga
Anesthesiology—Victor J. Tofany, Monroe
Chest Diseases—Arthur Q. Penta, Schenectady
Dermatology and Syphilology—Richard L. Saunders, Niagara
Gastroenterology and Proctology—Michael R. Deddish, New York
General Practice—Royal S. Davis, Westchester
Industrial Medicine and Surgery—Norman Plummer, New York
Medical-Legal and Workmen's Compensation Matters—Reuben M. Dicker, Queens
Medicine—Arthur Gordon, Queens
Neurology and Psychiatry—Frederick H. Hesser, Albany
Obstetrics and Gynecology—Michael J. Jordon, New York
Ophthalmology—James I. Farrell, Oneida
Orthopedic Surgery—Frederick Lee Liebolt, New York
Otolaryngology—George M. Trainor, Monroe
Pathology, Clinical Pathology, and Blood Banking—John J. Clemmer, Albany
Pediatrics—Richard A. Downey, Erie
Physical Medicine—Henry Fleck, Bronx

Preventive Medicine and Public Health—William E. Mosher, Erie
Radiology—Frank J. Borrelli, New York
Space Medicine—William Hall Lewis, Jr., New York
Surgery—Vernon Weinstein, New York
Urology—E. Craig Coats, New York

Delegates From Component County Societies

ALBANY (4)
H. John Mellen, Albany
James A. Moore, Albany
Joseph J. Russo, Albany
Francis A. Stephens, Albany

ALLEGENY (1)
Irwin Felsen, Wellsville

BRONX (12)
Carl R. Ackerman, Bronx
Henry J. Barrow, Bronx
Herbert G. Cohen, Bronx
Walter Einhorn, Bronx
Jerome B. Flynn, Bronx
Leonard L. Heimoff, Bronx
George Howley, Bronx
Frank LaGattuta, Bronx
Samuel Leo, Bronx
Samuel Lieberman, Bronx
Thomas F. McCarthy, Bronx
Samuel Wagreich, Bronx

BROOME (3)
George C. Hamilton, Binghamton
John A. Kalb, Endicott
Jason K. Moyer, Binghamton

CATTARAUGUS (1)
Joseph A. Wintermantel, Allegany

CAYUGA (1)
Bernard J. Hartnett, Auburn

CHAUTAUQUA (2)
Herbert A. Laughlin, Westfield
Garra L. Lester, Chautauqua

CHEMUNG (2)
William T. Boland, Elmira
Swen L. Larson, Elmira

CHENANGO (1)
Thomas M. Flanagan, Norwich

CLINTON (1)
Edward Siegel, Plattsburgh

COLUMBIA (1)
Carl G. Whitbeck, Hudson

CORTLAND (1)
George Nevin, Cortland

DELAWARE (1)
Philip J. Hust, Sidney

DUTCHESS (3)
Robert Barbieri, Poughkeepsie
Irving Cohen, Poughkeepsie
Raymond Koloski, Poughkeepsie

ERIE (8)
Antonio F. Bellanca, Buffalo
John C. Brady, Buffalo
Thomas S. Bumbalo, Buffalo
Max Cheplove, Buffalo
Kenneth H. Eckhert, Buffalo
Martin L. Gerstner, Buffalo
Eugene J. Hanavan, Buffalo
John D. Naples, Buffalo

ESSEX (1)
James Glavin, Port Henry

FRANKLIN (1)
Alfred A. Hartmann, Malone

FULTON (1)
Joseph J. Thompson, Gloversville

GENESEE (1)
Alfred L. George, Batavia

GREENE (1)
Edwin Mulbury, Windham

HERKIMER (1)
Harold T. Golden, Herkimer

JEFFERSON (1)
James L. Harrington, Watertown

KINGS (21)
George E. Anderson, Brooklyn
Louis Berger, Brooklyn
Matthew Brody, Brooklyn
Leo S. Drexler, Brooklyn
David Farber, Brooklyn
John J. Flynn, Brooklyn
S. Louis Hornstein, Brooklyn
David Kershner, Brooklyn
Arthur E. Lamb, Brooklyn
Warren A. Lapp, Brooklyn
Harry S. Lichtman, Brooklyn
Charles H. Loughran, Brooklyn
John G. Masterson, Brooklyn
Charles F. McCarty, Brooklyn
Irving M. Pallin, Brooklyn
Louis Pellman, Brooklyn
Solomon Schussheim, Brooklyn
Abraham D. Segal, Brooklyn
Milton B. Spiegel, Brooklyn
Vincent J. Tesoriero, Brooklyn
Leslie H. Tisdall, Brooklyn

LEWIS (1)

Livingston (1)
Melville A. Hare, Caledonia

MADISON (1)
Felix Ottaviano, Oneida

MONROE (6)
Hobart L. Boyd, Rochester
Michael J. Crino, Rochester
Merle D. Evans, Rochester
Donovan M. Jenkins, Webster
Maurice M. Maltinsky, Rochester
Charles R. Mathews, Rochester

MONTGOMERY (1)
Roman R. Violyn, Amsterdam

NASSAU (8)
Jeff J. Coletti, Old Westbury
Ralph S. Emerson, Roslyn Heights
Gerard V. Farinola, Roosevelt
Leo T. Flood, Hempstead
A. W. Freireich, Malverne
E. Kenneth Horton, Rockville Centre
Harvey L. Myers, Cedarhurst
Paul H. Sullivan, Great Neck

NEW YORK (25)
Philip D. Allen, New York City
Michael C. Armao, New York City
Norton S. Brown, New York City
Samuel B. Burk, New York City
William A. Cooper, New York City
C. Joseph Delaney, New York City
James H. Ewing, New York City
George W. Fish, New York City
Carl Goldmark, Jr., New York City
August H. Groeschel, New York City
Keith O. Guthrie, Jr., New York City
Milton Helpern, New York City
George Himler, New York City
Ely Elliott Lazarus, New York City
Julia V. Lichtenstein, New York City
David Lyall, New York City
Ira A. McCown, New York City
George W. Melcher, New York City
Bernard J. Pisani, New York City
Henry T. Randall, New York City
William B. Rawls, New York City
Guy F. Robbins, New York City
Adelaide Romaine, New York City
Theodore Rosenthal, New York City
Maus W. Stearns, Jr., New York City

NIAGARA (3)
Joseph A. D'Errico, Niagara Falls
H. Braden Fitz-Gerald, Lockport
Victor L. Pellicano, Niagara Falls

ONEIDA (3)
Irwin Alper, Utica
Anthony G. Jarosewicz, Utica
John F. Kelley, Utica

ONONDAGA (5)
Richard D. Eberle, Syracuse
Irving Ershler, Syracuse
Robert F. McMahon, Syracuse
William E. Pelow, Syracuse
W. Walter Street, Syracuse

ONTARIO (2)
Robert E. Doran, Geneva
Philip M. Standish, Canandaigua

ORANGE (3)

ORLEANS (1)
Angelo F. Leone, Medina

OSWEGO (1)
Kent Wood Jarvis, Oswego

OTSEGO (1)

PUTNAM (1)
Garrett W. Vink, Carmel

QUEENS (13)
Alfred A. Angrist, Beechhurst
Sol Axelrad, Woodhaven
William Benenson, Flushing
Monroe M. Broad, Jamaica
Thomas M. d'Angelo, Jackson Heights
Albert H. Douglas, Jamaica
Harry H. Epstein, Jamaica
Frank W. Farrell, Flushing
Jerome L. Leon, Forest Hills
John Edward Lowry, Flushing
Charles C. Mangi, Woodhaven
Louis J. Morse, Kew Gardens
Kurt Rosenberg, Long Island City

RENSSELAER (2)
Allen Gifford, Troy
John J. Pohl, Troy

RICHMOND (3)
Walter T. Heldmann, Staten Island
Frederic D. Regan, Staten Island
Edward H. Robitzek, Staten Island

ROCKLAND (3)
James Alva Dingman, New City
George Gordon Knight, Piermont
Michael P. Lefkowitz, Pearl River

ST. LAWRENCE (1)
William R. Carson, Potsdam

SARATOGA (1)
Webster M. Moriarta, Saratoga Springs

SCHENECTADY (3)
Raymond J. Byron, Schenectady
John L. Clowe, Schenectady
Philip Parillo, Schenectady

SCHOHARIE (1)

SCHUYLER (1)
Fritz Landsberg, Watkins Glen

SENECA (1)
Stanley B. Folts, Interlaken

STEUBEN (2)
Thomas S. Cotton, Hornell
Maynard W. Gurnsey, Corning

SUFFOLK (5)
Earl W. Douglas, West Islip
Jesse W. Mahoney, Patchogue
John L. Sengstack, Huntington
Charles W. Shlimbaum, Bay Shore
Sol Shlimbaum, Bay Shore

SULLIVAN (1)
Sirkka Elisabeth Vuornos, Liberty

TIOGA (1)
John Hans Jakes, Candor

TOMPKINS (1)
C. Stewart Wallace, Ithaca

ULSTER (2)
Eugene F. Galvin, Rosendale
Edward F. Shea, Kingston

WARREN (1)
Morris Maslon, Glens Falls

WASHINGTON (1)
Walter S. Bennett, Granville

WAYNE (1)

WESTCHESTER (8)
Charles M. Brane, Yonkers
Arthur H. Diedrick, Port Chester
John N. Dill, Yonkers
Harold J. Dunlap, New Rochelle
James Q. Haralambie, Larchmont
Thomas C. Jaleski, New Rochelle
James M. Jones, Bronxville
Wallace M. Sheridan, White Plains

WYOMING (1)

YATES (1)
John A. Hatch, Penn Yan

1962 HOUSE OF DELEGATES

Reference Committees

Credentials

Garra Lester, Chautauqua, *Chairman*
Michael C. Armao, New York
Henry J. Barrow, Bronx
John L. Clowe, Schenectady
John H. Jakes, Tioga
Charles F. McCarty, Kings, *Adviser*

Reports of Officers

PRESIDENT
PRESIDENT-ELECT
SECRETARY
TREASURER
BOARD OF TRUSTEES
EXECUTIVE VICE-PRESIDENT
WAR MEMORIAL
BUDGET

Arthur H. Diedrick, Westchester, *Chairman*
William R. Carson, St. Lawrence
Kenneth H. Eckhert, Erie
Edward H. Robitzek, Richmond
Solomon Schussheim, Kings

Commission on Medical Services—A

ECONOMICS
LIAISON WITH U.S. VETERANS ADMINISTRATION
PUBLIC MEDICAL CARE
MEDICAL CARE INSURANCE
MEDICARE

Jason K. Moyer, Broome, *Chairman*
Walter Einhorn, Bronx
Irving Ershler, Onondaga
Louis J. Morse, Queens
Bernard J. Pisani, New York

Commission on Medical Services—B

WORKMEN'S COMPENSATION
INDUSTRIAL HEALTH
HOSPITAL AND PROFESSIONAL RELATIONS
QUESTIONS OF ETHICS
MEDICAL SERVICE (RURAL)

C. Joseph Delaney, New York, *Chairman*
Philip D. Allen, New York
David Kershner, Kings
Joseph J. Thompson, Fulton
Victor J. Tofany, Monroe, Section on Anesthesiology

Public Health and Education

PUBLIC HEALTH AND EDUCATION
ACCIDENT PREVENTION
ADDICTION TO ALCOHOL AND NARCOTICS
AGING AND NURSING HOMES
CANCER
CHILD ACCIDENTS
DIABETES
GENERAL PRACTICE
GLAUCOMA AND OTHER DISEASES OF THE EYE

HARD OF HEARING AND THE DEAF
HEALTH ASPECTS OF IONIZING RADIATION
HEART DISEASE
MATERNAL AND CHILD WELFARE
MEDICAL FILM REVIEW
MENTAL HYGIENE
OPERATING ROOM DEATHS
PHYSICAL MEDICINE AND REHABILITATION
SCHOOL HEALTH

Thomas S. Bumbalo, Erie, *Chairman*
Abraham W. Freireich, Nassau
Samuel Leo, Bronx
Edward F. Shea, Ulster
Edward Siegel, Clinton

Legislation and Legal Matters

MALPRACTICE INSURANCE AND DEFENSE BOARD
LEGAL COUNSEL
LEGISLATION
LICENSURE OF CLINICAL LABORATORIES
FEDERAL LEGISLATION
AUTOPSY AND THE DEAD HUMAN BODY
CULTS
JUDICIAL COUNCIL

Milton Helpern, New York, *Chairman*
Joseph A. D'Errico, Niagara
Harold T. Golden, Herkimer
George Himler, New York
Milton B. Spiegel, Kings

Medical Communication

PUBLICATION
PUBLIC RELATIONS
COOPERATION WITH MEDIA OF INFORMATION
AMERICAN MEDICAL ASSOCIATION EDUCATION AND RESEARCH FOUNDATION
CONVENTION

Merle D. Evans, Monroe, *Chairman*
William Benenson, Queens
Earl W. Douglas, Suffolk
John F. Kelley, Oneida
David Lyall, New York

Organization and Policies

PLANNING
OSTEOPATHIC SOCIETY, AD HOC JOINT COMMITTEE WITH
DISTRICT BRANCHES
OFFICE ADMINISTRATION AND POLICIES
CONSTITUTION AND BYLAWS
CONFERENCE OF COUNTY MEDICAL SOCIETY OFFICERS
MEMBERSHIP

Charles C. Mangi, Queens, *Chairman*
Charles M. Brane, Westchester
Thomas M. Flanagan, Chenango
Frank LaGattuta, Bronx
Angelo F. Leone, Orleans

Medical Care

DISABILITY DETERMINATIONS, ADVISORY TO BUREAU
DISASTER MEDICAL CARE
COLUMBIA UNIVERSITY STUDY, ADVISORY

Irving M. Pallin, Kings, *Chairman*
James M. Jones, Westchester
William B. Rawls, New York
Philip M. Standish, Ontario
Sirkka Elisabeth Vuornos, Sullivan

Ancillary Groups

WOMAN'S AUXILIARY
NURSING EDUCATION
BAR ASSOCIATION
EMPIRE STATE MEDICAL, EDUCATIONAL AND SCIENTIFIC FOUNDATION
NEW YORK STATE ASSOCIATION OF PROFESSIONS

Samuel Lieberman, Bronx, *Chairman*
William Hall Lewis, Jr., New York, Section on Space Medicine
Morris Maslon, Warren
Robert McMahon, Onondaga
H. John Mellen, Albany

Miscellaneous Business

AMERICAN MEDICAL ASSOCIATION

Walter S. Bennett, Washington, *Chairman*
Maxwell Gosse, Dutchess, Ninth District Branch
John A. Hatch, Yates
Michael Lefkowitz, Rockland
John Edward Lowry, Queens

Sergeant-at-Arms

Carl Goldmark, Jr., New York, *Chairman*
Raymond J. Byron, Schenectady
Herbert G. Cohen, Bronx
Alfred L. George, Genesee
Joseph Shanaphy, First District Branch

Instructions from 1961 House

A résumé of instructions of the 1961 House of Delegates and actions thereon by the Council, Board of Trustees, and Officers are listed below.

Coinsurance Provision in Hospital Insurance Plans (Section 195).—The House of Delegates adopted the recommendation of the reference committee that resolution 61–21 be referred to the Council for further study. The resolution provides that this Society "endorse the initiation of a deductible and/or coinsurance provision in all hospital insurance plans, whereby the patient is charged a moderate lump sum as a deductible amount for a hospital stay or a modest but significant sum for each hospital day as coinsurance," and "that a copy of this resolution be forwarded to the State Commissioner of Insurance, urging that he consult with whomever necessary on the feasibility of and the method for implementation of the resolution."

The Council referred this to the Committee on Economics. At the October 20 Council meeting the Committee recommended that the last "resolved" be amended to read "That a copy of this resolution be forwarded to the State Commissioner of Insurance, calling attention to this proposal as a practical means of reducing hospitalization insurance premiums," and that the amended resolution be forwarded to the State Commissioner of Insurance. The Council voted approval. The amended resolution was transmitted by the Economics Committee to the State Insurance Department and acknowledged by them. (*See Annual Reports, Council Committee on Economics*)

Payments to Physicians in Insurance Cases (Section 201).—The House referred resolution 61–16 to the Council for further study. The resolution provides that the Society (1) "take immediate steps to obtain an agreement from all carriers concerned with medical and surgical coverage that they protect the physician from unscrupulous patients by joining the physician's and patient's names as payees on any check paid for medical and surgical services; (2) through its liaison with the State Bar Association, obtain a similar agreement from the legal profession that will make it mandatory for attorneys to protect the physician by joining the name of the physician and the client as payees on his check for medical services rendered in the case; and (3) assure the Bar Association and the carriers of the cooperation of the medical profession in submitting prompt reports and statements when requested in these cases, and the use of county society level grievance machinery in those cases where the amount of a bill may be in dispute, in return for their cooperation in providing protection to the physician by adding his name as copayee with the claimant on checks issued to pay for medical and surgical services."

The Council referred this to the Committee on Economics. At the October Council meeting, the Committee recommended that this resolution be referred to the Committee on Liaison with the Bar Association and that the Committee on Economics confer with them and, if favorable opinion is obtained, that legislation be introduced at the next session of the Legislature to change the lien law to protect the doctors. The Council approved this recommendation. The Committee on Economics reported this action to the chairman of the Medical Society representatives on the Joint Committee with the New York State Bar Association. (*See Annual Reports, Council Committee on Economics and Joint Committee with New York State Bar Association*)

Workmen's Compensation Fee Schedule (Section 208).—The House amended and adopted resolution 61–51 that this Society study means whereby payment in all compensation cases, regardless of date of origin, shall be made in accordance with the fee schedule in effect not longer than two years prior to the date of any particular treatment.

The Council referred this to the Committee on Workmen's Compensation. At the October Council meeting the Committee reported as follows: "Following through with the suggestions of the September 14 meeting (of the Workmen's Compensation Board's Advisory Committee on Medical Fees and Allied Problems) at which in accordance with the mandate of the House of Delegates, a request was submitted to study the applicability of the current workmen's compensation fee schedule to old cases, a list of states with official fee schedules was forwarded to the secretary of the committee to enable him to gather information from other

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Sections referred to are from the Minutes of the House of Delegates of the 1961 Annual Meeting, as published in the New York State Journal of Medicine, September 1, 1961, Part II.

state authorities on how this problem is handled outside of New York. (*Sec Annual Reports, Council Committee on Workmen's Compensation*)

Medical Service Committee (Section 210).—The House voted that the word "rural" be deleted from the name of the Council Committee on Rural Medical Service but that the name *not* be changed to "Community Medical Health Service Committee," as suggested, because this might be confused with the Community Service Society in this city. No objection was made to the suggestion of the committee that it be enlarged to include members from each district branch.

This action was reported to the Council in June; all committee lists and report headings have been changed accordingly.

Telephone Prescription of Narcotics (Sections 155 and 156).—The House adopted resolution 61–24 that the Society (1) "go on record as favoring the oral prescription of said Class B drugs provided a written prescription is in the hands of the pharmacist not later than seventy-two hours after the said drugs are dispensed" and (2) "confer with other interested parties to the end that legislation be introduced effectuating the intent of this resolution."

The Council referred this to the Subcommittee on Addiction to Alcohol and Narcotics of the Public Health and Education Committee and to the Committee on Legislation. The Public Health and Education Committee reported in September that the Advisory Council on Narcotics to the State Department of Health advocated the same approach as the resolution, that is, "a written prescription must be in the hands of the pharmacist not later than seventy-two hours after the drugs are dispensed."

At the October meeting of the Council the Committee on Legislation reported that "this resolution, or a similar resolution covering the subject, is being introduced into the Legislature by the New York State Department of Health as a department bill. Inasmuch as it is being introduced in this respect, the committee voted to support the bill accordingly." (*See Annual Reports, Council Committee on Legislation and Council Committee on Public Health and Education*)

Establishment of Departments of General Practice in Medical Schools (Section 162).—The House adopted resolution 61–19 "that the deans of all medical schools in New York State be contacted by a committee designated by the Council. . .with the purpose of requesting that departments of general practice be instituted in these schools and that a definite effort be made to promote the graduation of physicians who will become dedicated 'family physicians.' "

The Council referred this to the General Practice Subcommittee of the Committee on Public Health and Education. The Committee on Public Health and Education reported to the Council in September that, at a meeting of the committee members and subcommittee chairmen, the Subcommittee on General Practice had been requested to prepare some suggestions for the curriculum of a general practice department. (*See Annual Reports, Council Committee on Public Health and Education*)

Difficulties in Obtaining Enactment of Physicians' Lien (Section 229).—The House voted to amend and adopt resolution 61–17, "Difficulties in Obtaining Enactment of Physicians' Lien Law," as rewritten by the reference committee.

The Council referred this to the Joint Committee with the New York State Bar Association. In October the Committee on Legislation reported to the Council that "this has been introduced in the Legislature for a number of years, but to no avail. Consideration will again be given to it this year and if it seems desirable and the possibility of passage of the law favorable, it will again be reintroduced. This was previously referred to the Joint Committee of the Medical Society of the State of New York and the New York Bar Association, and we are awaiting a report of this committee, which will determine our possible action." (*See Annual Reports, Joint Committee with the New York State Bar Association and Council Committee on Legislation*)

Metcalf-McCloskey Program (Section 222).—The House voted that this Society encourage its component medical societies to establish committees for the purpose of surveying the application of the Metcalf-McCloskey program in their counties, to work closely with their local welfare agencies, and to submit regular reports to a suitable body of the State Society as a basis for recommendations by the State Society to the State Welfare agency or the Governor and the further recommendation of the reference committee that "the State Society continue to explore other means and programs for providing this aid more adequately."

In October the Committee on Legislation reported to the Council: "Your chairman called to your attention last month the apparent dissatisfaction which had arisen with reference to the implementation of the Metcalf-McCloskey legislation. This dissatisfaction has continued and during the month Senator George Metcalf, who sponsored the original legislation, publicly called attention to this, stating that the Department of Social Welfare of the State of New York had "thwarted the intent of the legislation." It is therefore anticipated that some amendments to this legislation can be expected. I would again call your attention to the question of whether or not the Medical Society of the State of New York should express itself as being dissatisfied with the implementation of this legislation as a 'welfare measure.' " (*See Annual Reports, Council Committee on Legislation*)

Keogh-Simpson Bill (Section 222).—The House voted to approve the recommendation of the reference committee that the Subcommittee on Federal Legislation make suitable representations at the proper time for the purpose of ensuring passage of the Keogh-Simpson Bill. This was referred by the Council to the Subcommittee on Federal Legislation.

At the September Council meeting, the Subcommittee reported: "Action also was taken on another important bill—H.R. 10, the Keogh Bill. Upon receiving notice that public hearings were to be held by the Senate Finance Committee on the proposed law, your chairman sent letters to all county medical societies urging them to express support of the bill to the members of the committee. Your chairman is not happy to report that the Senate Finance Committee by a vote of 14 to 3 on August 25 ordered that a modified version be reported out of committee. This version is a very much watered-down version of the original bill, and your chairman questions whether medicine should vigorously support the watered-down version. . . . Chances for further action on H.R. 10 this year are slight. . . . The Administration opposes it, and the plan would face a stiff fight on the Senate floor."

Medical Practitioners to Organize as an Association for Tax Purposes (Section 232).—The House referred to the Council for "further study and implementation" resolution 61–28 approving a study by this Society "exploring the possibility of an amendment to the laws of the State of New York for introduction into the 1962 session of the New York State Legislature, for the purpose of permitting groups of medical practitioners so to organize themselves as to be qualified as an association taxable as a corporation within the criteria established by the regulations of the Internal Revenue Service." The Council referred this to the Committee on Legislation. At the October Council meeting, the Committee reported: "The Committee requested Mr. Foy, our legislation counsel, to contact Raymond Harris, M.D., chairman of the legislation committee of Albany County, who prepared the resolution, also Mr. Spencer L. McCarty, managing director of the New York State Association of Life Underwriters, who are specifically interested in such. Mr. Foy is to submit information at the next meeting of the committee and action will be taken based on results of these conferences." (*See Annual Reports, Council Committee on Legislation*)

Only Doctors of Medicine to Practice Psychiatry (Section 238).—The House approved and referred to the Council for appropriate action a resolution, substituted by the reference committee for resolution 61–57, that failure to enforce the laws limiting the diagnosis and treatment of nervous and mental disorders to trained and duly licensed physicians be called to the attention of the Governor and the Attorney General. The Council referred this to the Committee on Legislation. The Committee reported to the Council in October that they were referring this matter to the Governor and the Attorney General. (*See Annual Reports, Council Committee on Legislation*)

Ophthalmology and Optometry (Section 243).—The House requested the Council to undertake a study of the relationship between ophthalmologists and optometrists regarded as a problem pertaining to the permissible limits of practice of optometrists (resolution 61–72). The Council referred this request to the Committee on Public Health and Education. The Public Health and Education Committee reported in September the recommendation of its Subcommittee on Ophthalmology that the Council await some decision of the commission recently appointed by the American Medical Association to work on the subject. (*See Annual Reports, Council Committee on Public Health and Education*)

Permanent Convention Committee (Section 120).—The House approved the recommendation of its reference committee that a permanent Convention Committee of the House of Delegates be established. The Council referred this recommendation to the Planning Committee for Medical Policies. (*See Annual Reports, Planning Committee for Medical Policies*)

Medical Directory of New York State (Section 122).—The House voted to approve a reference committee recommendation that resolutions 61–5, "Listing of All Accredited Hospitals in the *Medical Directory of New York State*," 61–29, "Listing of Previous Hospital and Research Affiliations in *Medical Directory*," and 61–40, "Listing of Accredited Proprietary Hospitals in *Directory*," be referred to "the committee now revising the *Medical Directory of New York State*." The Council referred these recommendations to the Publication Committee. (*See Annual Reports, Council Committee on Publication*)

Cuban Refugee Physicians (Section 114).—House of Delegates resolution 61–67, requesting the Council "to give immediate and critical consideration to legal and humanitarian measures calculated to be of assistance" to Cuban refugee physicians, was referred by the Council to the president, the secretary, and the executive vice-president.

At its June meeting the Council adopted a recommendation of the Executive Committee that Dr. Hilleboe be encouraged to reactivate for this particular group the program of courses provided earlier in the year for foreign medical graduates and that appropriate hospitals in the area be urged to employ them as soon as they pass the ECFMG examination. In September, 1961, the Executive Committee received as information a letter from Dr. Hilleboe stating that the Health Department could not provide such courses but that the New York Polyclinic Medical School and Hospital was doing so.

Membership Increase (Section 134).—The House voted that a concerted effort be organized in New York State to secure as members full-time men in medical schools, hospitals, and research centers and that the A.M.A. be requested to exert its influence towards this end. The Council referred these instructions to the Membership Committee. (*See Annual Reports, Council Committee on Membership*)

Section on Medical-Legal and Workmen's Compensation Matters (Section 136).—The House directed (resolution 61-45) that the name of the Section on Legal Medicine be changed to "Section on Medical-Legal and Workmen's Compensation Matters" and that the scope of its activities be broadened accordingly. The Council referred this to the Scientific Program Subcommittee of the Convention Committee. This resolution has been implemented by the Subcommittee. (*See Scientific Program, Section on Medical-Legal and Workmen's Compensation Matters*)

Tenure of Committee and Officer Positions (Section 136).—The House recommended that the Council attempt to study the length of tenure of members on committees and in officer positions as soon as possible. The Council referred this assignment to the Planning Committee for Medical Policies. (*See Annual Reports, Planning Committee for Medical Policies*)

Disability Determinations Bureau Examinations: Reimbursement and Reports (Section 178).—The House referred to the Council, for study by the Committee on Economics, the problem created by inadequate reimbursement of physicians for examinations undertaken for the Bureau of Disability Determinations and by the extensive and detailed reports required by the Bureau. This was referred by the Council to the Committee on Economics. (*See Annual Reports, Council Committee on Economics*)

Generic Names of Drugs (Section 181).—The House approved in principle and referred to the Council resolution 61–2, "The Use of Generic Names in Prescribing Drugs." The resolution provides that the Society (1) urge its members to use generic names in prescribing "where the prescribing physician or the licensed pharmacist can be assured of the quality of the drugs," (2) maintain a continuing educational program to facilitate the use of generic names in prescribing, (3) "join with pharmacy and ancillary professions in working out a system of controls on the generic drugs which may be prescribed," (4) "petition the Council on Drugs of the A.M.A. and the United States Pharmacopeia to devise meaningful and pronounceable nonproprietary or generic names for new drugs promptly upon their initial introduction into commerce and for use in any and all advance promotional literature," and (5) "recommended that generic prescribing be urged on physicians under conditions whereby the manufacturing and quality control of these products can be assured."

The Publication Committee reported as follows to the Council in June: "The suggestion of the Committee was that it defer action in implementing this resolution because of the many facets of the problem and because we must first be assured, as it states in the resolution, that the physician is satisfied, as well as the pharmacist, with the quality of the drug prescribed under generic prescribing, and certainly under present circumstances there is no such assurance." In discussion of this report of the Publication Committee, Mr. Baldwin suggested that we confer regarding this program with representatives of the pharmaceutical industry.

The Council voted to approve the suggestion of the Publication Committee and to refer Mr. Baldwin's suggestion to the Subcommittee on Federal Legislation "for whatever action it deems advisable with respect to the Kefauver Bill and any contacts with industry." (*See Annual Reports, Council Committee on Publication and Council Committee on Legislation*)

Woman's Auxiliary (Section 147).—The House recommended that the Woman's Auxiliary be highly commended on its 25th anniversary and be more actively encouraged, possibly by closer liaison at county and State Medical Society levels. The reference committee suggested county society liaison committees "to further aid the Auxiliary." (*See Annual Reports, Special Advisory Committee to the Woman's Auxiliary*)

Obligations of Operating Surgeons (Sections 152 and 211).—The House recommended that the 1961 Annual Report of the Joint Committee with the Bar Association, containing a statement by the A.M.A. Law Department on the obligations of operating surgeons to their patients, be read by every member of this Society and of the New York State Bar Association, that copies be distributed to all senior medical and law students in the State, and that the statement be drawn to the attention of all physicians working in hospitals wherein resident training programs exist. The Council referred these recommendations to the Joint Committee with the Bar Association and to the Publication Committee. (*See Annual Reports, Joint Committee with the Bar Association and Council Committee on Publication*)

Quality of Medical School Students (Section 144).—The House referred to the Council for study resolution 61–35 that this Society "request the American Medical Association to encourage medical schools to have a six-year combined course, as is being done in three schools already, so that Grade A college students may be encouraged once more to apply for entrance to medical schools." The Council referred this to the president and the executive vice-president to study. (*See Annual Reports, Report of the President and Report of the Executive Vice-President*)

Secretary's Disposition of Instructions of the 1961 House of Delegates.—*A. Recommendations of Officers, Committees, and Reference Committees Adopted by the House:*

1. The House adopted a resolution prepared by the Reference Committee on Commission on Medical Services—A as a substitute for resolutions 61–3, 61–7, 61–23, and 61–68. The resolution reaffirms the support of the State Society for Social Security for physicians and instructs the Society's delegates to the A.M.A. House of Delegates to introduce a resolution favoring Social Security benefits for physicians. This was referred to the New York State delegation to the American Medical Association.

2. Several recommendations of the Reference Committee on Public Health and Education were called to the attention of the chairman of the Film Review and School Health Subcommittees of the Public Health and Education Committee and the chairman of the Motion Picture Subcommittee of the Convention Committee.

3. The House approved the statement of the Reference Committee on Legislation and Legal Matters that legislation providing for review and revision of the Medical Practice Act should be energetically sought. This was called to the attention of the chairman of the Council Committee on Legislation.

4. The Reference Committee on Medical Communication combined resolutions 61–31 and 61–41. The resulting resolution, recommending to the Board of Trustees that they appropriate $25,000 for the use of the Federal Legislation Subcommittee for the period July 1, 1961, to July 1, 1962, was transmitted to the chairman of the Board of Trustees.

B. Resolutions Adopted by the House:

61–6, "County Medical Society Assistance in Accreditation of Hospitals," as amended by the Reference Committee on Commission on Medical Services—B, was transmitted to the Joint Commission on Accreditation of Hospitals.

61–8, "Membership of Planning Committee," was called to the attention of the President.

61–10, "Determination of Relationship Between Doctors of Medicine and Doctors of Osteopathy," was referred to our delegation to the American Medical Association.

61–12, "Nonservice-connected Cases in Veterans Administration Hospital," was transmitted to Mr. Sumner G. Whittier, Administrator of Veterans Affairs, Washington 25, D.C.

61–13, "Food and Drug Administration Control of New Drugs," as amended by the reference committee and by the House, was referred to our delegation to the A.M.A. and was transmitted to Senators Javits and Keating.

61–15, "Improved Procedures for School Physical Examinations," as amended by the reference committee and the House of Delegates, was transmitted to the chairman of the Public Health and Education Committee and the chairman of the Legislation Committee.

61–18, "Medical School Scholarships," as amended by the reference committee, was referred to the Council Committee on Legislation.

61–22, "Prescriptions for Welfare Patients," was transmitted to Dr. Raymond W. Houston, Commissioner of Social Welfare of the State of New York, Albany.

61–27, "Essay Contest on the Advantages of Private Medical Care or on Advantages of the American Free Enterprise System Over Communism," was transmitted to the secretary of each county medical society and to the chairman of the Advisory Committee to the Woman's Auxiliary.

61–30, "Discontinuing of Educational Council for Foreign Medical Graduates Examination for Physicians Licensed in Any State," was referred to the delegation to the American Medical Association and was transmitted to the Advisory Board of Medical Specialties.

61–32, "Use of General Practitioners as Assistants at Operations," as amended by the House of Delegates, was transmitted to the medical boards of all voluntary and proprietary hospitals in the State and to our delegation to the American Medical Association.

61–34, "Inequities in Workmen's Compensation Law," as amended by the reference committee and adopted by the House, was transmitted to the chairman of the Council Committee on Workmen's Compensation.

61–43, "Legislation to Provide Tax-Deductions for Medical School Tuition," was referred to the Committee on Legislation.

61–44, "Legal Responsibility in Performance of Postmortem Cesarean Section," as amended by the reference committee, was referred to the Committee on Legislation. The chairman of the Committee on Autopsy and the Dead Human Body was notified of this action.

61–50, "Publication of a List of Participating Physicians in United Medical Service," amended by the reference committee, with approval of the House of Delegates, to request publication of lists of participating physicians of all New York State Blue Shield Plans, was transmitted to the Associated Blue Shield Plans of New York State.

61–56, "Elimination of the Examination of the Educational Council for Foreign Medical Graduates," as amended by the reference committee to request a change in the type of examination given by the council rather than its elimination, was referred to our A.M.A. delegation and was transmitted to the Educational Council for Foreign Medical Graduates.

61–58, "Uniform Identification Method for Citizens with Certain Diseases," as reworded by the reference committee, has been transmitted to the Council Committee on Public Relations.

61–62, "Hospital Review and Planning Council," as amended by the reference committee, was transmitted to the New York State Hospital Review and Planning Council and to the secretary of each district branch.

61–70, "Endorsement of H.R. 5222," was referred to our delegation to the American Medical Association.

61–74, "Creation of Commission to Study Problems of Patient Care," as amended by the House, was referred to the New York State delegation to the American Medical Association.

A.M.A. Resolutions.—The following resolutions were adopted by the House of Delegates for presentation to the A.M.A. House of Delegates:

1. "Social Secretary for Self-Employed Doctors of Medicine," substituted for resolutions 61–3, 61–7, 61–23, and 61–68 (*Sections 40, 44, 60, 106, and 198*);
2. "Determination of Relationship Between Doctors of Medicine and Doctors of Osteopathy," resolution 61–10 (*Sections 47 and 142*);
3. "Food and Drug Administration Control of New Drugs," resolution 61–13 (*Sections 50 and 228*);
4. "Discontinuing of Educational Council for Foreign Medical Graduates Examination for Physicians Licensed in Any State," resolution 61–30 (*Sections 67 and 175*);
5. "Use of General Practitioners as Assistants at Operations," resolution 61–32 (*Section 216*);
6. "Change in the Educational Council for Foreign Medical Graduates Examination," resolution 61–56 (*Sections 93 and 175*);
7. "Endorsement of H.R. 5222," resolution 61–70 (*Sections 108 and 241*);
8. "Creation of Planning Commission to Study Problems of Medical Education, Hospital Practice, and Patient Care," resolution 61–74 (*Sections 111 and 214.*) (*See Annual Reports, American Medical Association Delegates*)

Nominating Committee

To the House of Delegates, Gentlemen:

In accordance with Chapter XI, Section 4 of the Bylaws of the Medical Society of the State of New York, the Nominating Committee met at the Cornell Club, 107 East 48th Street, New York City, on Tuesday, December 19, 1961, at 5:00 p.m.

Present were the following:

Sixth District—Norman S. Moore, M.D., *Chairman*, Tompkins

First District—Warren A. Lapp, M.D., Kings

Second District—John L. Sengstack, M.D., Suffolk

Third District—Albert Vander Veer, II, M.D., Albany

Fourth District—Herbert J. Wright, Jr., M.D., Schenectady

Fifth District—W. Walter Street, M.D., Onondaga

Seventh District—Philip M. Standish, M.D., Ontario

Eighth District—E. Dean Babbage, M.D., Erie

Ninth District—Waring Willis, M.D., Westchester

Member-at-large—Frederick A. Wurzbach, Jr., M.D., Bronx

Member-at-large—Philip D. Allen, M.D., New York

Ex officio—John M. Galbraith, M.D., Nassau

Ex officio—William L. Wheeler, Jr., M.D., New York

Ex officio—Henry I. Fineberg, M.D., Queens

Your Committee reviewed suggestions of names for those to be nominated as received from the following counties: Bronx, Chemung, Dutchess, Erie, Kings, Monroe, New York, Queens, Suffolk; also the Co-ordinating Council of the First District Branch and the Seventh and Eighth District Advisory Councils in response to a memorandum of November 3, 1961. The communication from Oneida, Herkimer and Madison Counties arrived after the Nominating Committee had met.

Your Nominating Committee submits the following nominations for vacancies for the Society year commencing May 16, 1962:

President	Joseph A. Lane, M.D., Monroe
President-Elect	William L. Wheeler, Jr., M.D., New York
Vice-President	John F. Kelley, M.D., Oneida
Secretary	Waring Willis, M.D., Westchester
Assistant Secretary	Ezra A. Wolff, M.D., Queens
Treasurer	Maurice J. Dattelbaum, M.D., Kings
Assistant Treasurer	Samuel Z. Freedman, M.D., New York
Speaker	Frederick A. Wurzbach, Jr., M.D., Bronx
Vice-Speaker	E. Dean Babbage, M.D., Erie
Councillors (three years)	James M. Blake, M.D., Schenectady Charles M. Brane, M.D., Westchester Peter J. DiNatale, M.D., Genesee George J. Lawrence, Jr., M.D., Queens
Trustee (five years)	John J. Masterson, M.D., Kings
Trustee (two years, unexpired term)	John M. Galbraith, M.D., Nassau

Delegates to the American Medical Association (two years commencing January 1, 1963):

Philip D. Allen, M.D., New York
William T. Boland, M.D., Chemung
Harold F. Brown, M.D., Erie
Peter J. DiNatale, M.D., Genesee
Ralph S. Emerson, M.D., Nassau
Irving L. Ershler, M.D., Onondaga
Merle D. Evans, M.D., Monroe
Henry I. Fineberg, M.D., Queens
John M. Galbraith, M.D., Nassau
Thurman B. Givan, M.D., Kings
Carl Goldmark, Jr., M.D., New York
Alfred P. Ingegno, M.D., Kings
John F. Kelley, M.D., Oneida
Joseph A. Lane, M.D., Monroe
Warren A. Lapp, M.D., Kings
Charles R. Mathews, M.D., Monroe
John C. McClintock, M.D., Albany
Irving M. Pallin, M.D., Kings
Robert F. Warren, M.D., Kings
Carlton E. Wertz, M.D., Erie
William L. Wheeler, Jr., M.D., New York
Ezra A. Wolff, M.D., Queens
Waring Willis, M.D., Westchester
Frederick A. Wurzbach, Jr., M.D., Bronx

The twelve receiving the largest number of votes will be delegates, and the second twelve will be alternates. We are allowed one delegate for each thousand A.M.A. members or part thereof.

Respectfully submitted,
Norman S. Moore, M.D., *Chairman*

Special Committee on Constitution and Bylaws

To the House of Delegates, Gentlemen:

Your Special Committee on Constitution and Bylaws consists of the following:

George A. Burgin, M.D., *Chairman*	Herkimer
Philip D. Allen, M.D.	New York
Alfred A. Hartmann, M.D.	Franklin
Robert F. Warren, M.D.	Kings
Ezra A. Wolff, M.D.	Queens

The following amendments to the Constitution and Bylaws of the Medical Society of the State of New York, submitted as resolutions at the annual meeting of the House of Delegates in 1961, were studied carefully at a meeting of the committee on December 15, 1961. Representative of the legal counsel was also present.

The proposed amendments and the committee's recommendations follow.

Resolution 61–75—Amendment to the Bylaws Regarding Membership of Planning Committee; Introduced by Louis H. Bauer, M.D., Past-President.

This amendment provides that the Planning Committee, which now consists of the five most recent past-presidents of the Medical Society of the State of New York and two others appointed by the president, be changed so that the two members-at-large shall be nominated by the Nominating Committee and elected by the House of Delegates at its annual meeting.

The resolution reads as follows:

> WHEREAS, The Planning Committee at present is composed of the five most recent past-presidents and two members-at-large appointed by the president for a term of one year with the advice and consent of the Council; and
>
> WHEREAS, The Planning Committee is a committee of the House and it has by its past actions elected the past-presidents to their office and it is desirable that the House should have the ultimate responsibility for determining the composition of the entire committee, including the members-at-large; now therefore be it hereby
>
> *Resolved,* That Chapter III, Section 1, of the Bylaws be amended to add the words "and one member-at-large of the Planning Committee" following the words "Board of Trustees" in the first sentence of said section; and be it further
>
> *Resolved,* that Chapter III, Section 2, of the Bylaws be amended to add the following new paragraph after the paragraph beginning "Four members of the Council. . . ."
>
> "In the year 1962 the Nominating Committee shall nominate two members-at-large for terms of two years and one year, respectively. Thereafter, one member-at-large shall be nominated and elected annually for a term of two years."

The committee unanimously approves the resolution.

Resolution 61–64—Amendment to Constitution and Bylaws to Change Title of Executive Director to Executive Vice-President; Introduced by George A. Burgin, M.D., Councillor.

The resolution follows:

> WHEREAS, The American Medical Association and many state medical societies designate their chief administrator as "executive vice-president" rather than "executive director"; and
>
> WHEREAS, It is desirable for purposes of clarity and uniformity that the chief administrator of the Medical Society of the State of New York bear a similar title; now therefore be it hereby
>
> *Resolved,* That the title of the chief administrator be changed from "executive director" to "executive vice-president"; and be it further
>
> *Resolved,* That the Constitution and Bylaws of the Medical Society of the State of New York be amended as follows:
>
> Amend the Constitution, Article IV (Council), first sentence of the second paragraph, to substitute the words "vice-president" for the word "director"; and amend the Bylaws, Chapter IV (Council), Section 1 (a), last sentence, to substitute the words "vice-president" for the word "director."

Your committee unanimously approves this resolution.

Resolution 61–46—New Sections of the Society; Introduced by Ezra A. Wolff, M.D., Assistant Secretary.

The resolution follows:

> WHEREAS, Sections of the Medical Society of the State of New York should be of sufficient interest to attract a sizeable number of members in order to justify their costs and usefulness to the Society; and
>
> WHEREAS, The creation of sections without first demonstrating a demand for them by having had their subject matter presented in the form of one or more annual sessions is inadvisable; now therefore be it hereby
>
> *Resolved,* That the Bylaws of the Medical Society of the State of New York be amended by adding to Chapter XII a new section (Section 6) to read as follows:
>
> "*Section 6.* No new section shall be created unless a session devoted to its subject matter or specialty shall have been held at at least two successive previous annual meetings."

This resolution is approved unanimously by your committee.

Your chairman wishes to thank the members of his committee for their sound advice. We are sincerely indebted to Miss Doris K. Dougherty for her patient interest and advice.

Respectfully submitted,
George A. Burgin, M.D., *Chairman*

Convention paging system

We hope that physicians attending the 156th Annual Convention of the Medical Society of the State of New York will be able to devote all their attention to the interesting program, exciting exhibits, and other features of the meeting. However, if it is necessary, physicians can always be in touch with their offices, their patients, or whoever else may wish to contact them, through the SherPage System. They may be reached by television anywhere at the convention.

This service is provided through the courtesy of Sherman Laboratories, Detroit, Michigan.

Reports of Officers

President

To the House of Delegates, Gentlemen:

It has been approximately ten months since I had the privilege of addressing this House of Delegates as your president-elect. This report, therefore, will not be a complete survey of my entire term. A supplementary report, of necessity, will be presented to the House in May.

JOHN M. GALBRAITH, M.D.

At the very outset, allow me to state that a great deal of progress has been made during the period that I have served as your president. On the other hand, there have been many things that have been left undone because of varying factors which I shall not detail at this time. Let me stress, however, that the progress we have made was not a solo job on my part but was the result of the teamwork of our Society officials and staff. It is impossible to recount for you the numberless hours of dedicated work that has been given by the officers of this Society, members of the Council, members of the Board of Trustees, members of the various committees, and our personnel. I am indeed grateful to all of them for what has been accomplished and request that they and their successors continue the great work so well begun.

It is not my intention to cover the whole gamut of operations of our State Society. The details of the various committees will be outlined by the various chairmen in their reports to this body. I will concentrate on commenting on the more important projects and on certain observations which I believe will be of interest to this House.

You will recall that our immediate past-president, Norman S. Moore, M.D., in addressing this House in person last May, concluded his excellent remarks by stating, "It will be during Dr. Galbraith's administration that the answer to the question concerning medicine's continued freedom in this country will unfold. If we can learn from some of our mistakes and take positive action where we have been negative or neutral, become informed instead of remaining uninformed, restore through individual example the former image of the physician with the public, we will win the present challenge to freedom."

In my remarks to this House immediately following Dr. Moore's presentation, I echoed the sentiments expressed by him. I also stated, "This year my primary target will be to awaken every physician, every county medical society, every allied health group, and every individual and organization concerned with the preservation of our free enterprise system to the crisis facing all interested in the health and welfare of our people."

Our predictions concerning the major issue of my term of office have been completely fulfilled. As you know, during the past ten months we have been engaged in an all-out fight to preserve the free enterprise system of medicine. In accordance with my promise, I, with the help of my colleagues, did everything possible to awaken every segment of our Society and allied groups, including individual physicians and other interested persons, to the necessity not only for being opposed to Federal intervention into medicine but for also taking positive action.

How well we succeeded in our efforts in awakening everybody it is impossible to tell. We know, however, that a great deal has been done and that we are making progress in our fight to preserve medicine's freedom. One of the great instruments in this fight has been the work of our Federal Legislation Subcommittee, headed by George J. Lawrence, Jr., M.D. Since the last annual session of the House there has been constant positive action in the fight against the enactment of the King-Anderson bill. Details of what has been done will be found in the report of that group.

The climax, to date, of our efforts in this major issue before us was the calling of the special session of the House on February 10 to discuss primarily this issue and that of chiropractic licensure. Incidentally, the House will be interested to know, according to the best source of our information, that this special session was the first called at the request of the Council in our one hundred fifty-five years of existence. There was another session which was scheduled by the House itself which took place in 1932.

The actions of the House at this special session are well known to all of you. They strengthened our hand in our negotiations with the State officials and with our Federal representatives. I am pleased to report that within a few days after this report is being compiled a delegation of about 25 physicians will visit Washington in our second trip in two years to confer with our United States Representatives and our two United States Senators. There will be visitations in the various offices as well as a formal conference with Senators Keating and Javits and a reception for all during our visit. A report on this project will be given to the House in May.

Council Meetings. As presiding officer of the Council during the past ten months I am pleased to report to the House that this group has been most active and most diligent in attendance at meetings. In an effort to streamline the procedure of the Council, your president suggested that the meetings be held every two months instead of every month as has been customary in the past. The Council voted to accept this suggestion so that for the past several months we have had a meeting every two months, although the Board of Trustees and the Executive Committee have met every month. This procedure is a big improvement and has resulted in saving the time of our councillors as well as in saving a great deal of expense to our State Society.

In our reports to the last annual session of the House, Dr. Moore and I made several suggestions for approval and implementation. I should like, at this time, to review briefly some of these important projects.

Planning Committees. One of the items which was discussed at great length by Dr. Moore was the proposal that the Planning Committee for Medical Policies be revised. He suggested that it be along the lines of the Management Survey Committee report concerning the reorganization of our State Society. He suggested that the name of the Planning Committee for Medical Policies be retained and that the group be composed of the five immediate past-presidents and that the senior past-president whose term on the committee next expires should be chairman for that year. In addition, he suggested that the new committee should have two members nominated by the Nominating Committee and elected by the House. He made a further suggestion that the committee should have as ex-officio members the Speaker of the House, the President-Elect, the President, the Secretary, and the Treasurer.

This plan, basically, has been put into operation. Your president appointed the two members which the House will elect in the future, provided it approves the necessary amendments to the Constitution and Bylaws which will be presented at this session.

Committee Tenure. Another plan proposed was that the tenure of office of members of our committees be studied carefully and evaluated with a view to changing the current procedure. Under the present system a member of a committee or an officer of the Society may be in various positions for an unlimited period of time. This plan has resulted in stifling the activities of younger men who find that they have to wait a great number of years before they can become a member of the Council, an officer, or a member of a committee. One suggestion that was made was that the terms on committees might be limited to three years and on expiration of the term the individual would be ineligible for reappointment to the same committee but would be eligible for a term on another committee.

The Planning Committee will submit suggestions along these lines at this session of the House. I hope that due consideration will be given to the committee's ideas and that a practical, up-to-date method of committee operation will be ultimately evolved.

Foundation. One of our comparatively new projects is the Empire State Medical, Scientific, and Educational Foundation. The purpose of this project is well known to all of you. Basically the idea is to permit the Society to solicit funds from outside the organization and to expend these funds in the profession's and general public's behalf for better postgraduate programs for the profession and better health programs for the public, such as rural health programs or promotion of public health departments where they do not exist and are needed. The first grant came from the State Health Department which was earmarked by the directors, acting as a project committee as a whole, for a maternal mortality study with Edward C. Hughes, M.D., as project director.

Professional Associations. I would like to announce that a new organization, the New York State Association of the Professions, Inc., has been formed. Our Society is one of the organizing members. The other participating members are: the Dental Society of the State of New York, the New York State Association of Architects, the Pharmaceutical Society of the State of New York, the New York State Society of Professional Engineers, and the New York State Veterinary Medical Society. I am gratified that this Association was organized during my term in office. A campaign for individual memberships is about to be undertaken and I heartily recommend that you take advantage of the opportunity to join this Association. This Association will be a vital force in assembling and consolidating the opinions of the several learned professions, which are participating members of the organization, on matters of general public interest in this State.

Meetings. One of the problems that has confronted us for years and probably will be with us for years to come is the question of attendance at meetings. From all indications there has not been too much progress in the improvement of attendance at meetings of county medical societies throughout the State. We must continue to work on this problem and try to find a solution to it. Perhaps one method may be the curtailment of the number of meetings which we as members of the medical profession have to attend. A change in the format of the programs at meetings is another method. Many county medical societies are now stressing medical economic and public relations projects in place of the scientific programs which are readily available in most parts of the State through hospitals and other institutions.

Full-Time Men. Another matter that was discussed before this House last year was the relationship of the full-time man with the private practitioner of medicine. Every possible attempt should be made to have very able full-time men participate actively in this Society's activities.

Society's Name. One of the progressive steps that should be taken by our organization is the consideration of the change of our name. You will recall that it was pointed out last year that this is a cumbersome title. It is outmoded in this present generation and it is very often misinterpreted as meaning a part of the New York State government. Certainly in these trying times when we are battling governmental intervention we should clarify our name so as not to be mistaken for a governmental agency. I urge that this matter be given immediate and serious attention.

Physical Fitness. Much emphasis was placed, in my remarks last year, on the importance of a physical fitness program for our people, such as that sponsored by the President of the United States. This matter is being pursued by the Public Health and Education Committee. The A.M.A. has stressed this program for many years and is performing the major part of this important activity.

Air Pollution. The specific problem of ionizing radiation is being studied by the Subcommittee on Health Aspects of Ionizing Radiation in cooperation with the State Health Department, headed by our good friend, Herman E. Hilleboe, M.D.

Reorganization. Turning now to some of our internal matters, the reorganization of our Society continued to go forward. Our executive vice-president, Henry I. Fineberg, M.D., has made great strides in carrying out this plan. The Willers Report, which was made at the request of the State Society concerning the positions of the personnel, was implemented. This meant clarification of job positions as well as salary implementations where needed. A brochure which will explain the various staff jobs at the headquarters of our Society is now in the process of being prepared and is expected to come off the press in the very near future. This publication will be a great help in improving the morale and the working of our staff.

Communications. The problem of public relations is still with us and will be with us throughout our future days. Through our Department of Communications we have been advancing in our efforts to improve the functions of our public relations arm and to better the public relations of the medical profession in general. There are two points in this connection that I should like to make.

The first point is that we must come to realize that our Department of Communications is not involved solely in public relations. The work of public relations is only one small segment of all the activities of this department. As a matter of fact the department functions more in the field of administration insofar as it is intimately connected with every group within our Society. It does work for committees. It does work for departments. It does work in regard to special meetings. It does work for the officers and other projects too numerous to mention. If we were to break down the amount of money spent on public relations out of the entire budget we would be amazed to find that it is a very small part of the total allotment.

The second point which I should like to make is that we must expand rather than curtail our activities in the realm of the Communications Department. There is much work to be done, particularly in the field of public relations, and this can be accomplished only by expanded personnel and expanded funds. I strongly recommend to you the report of the Public Relations Committee on its activities during the year and the plans for the future.

Legislation. I have already mentioned the fact that we have been very active in the field of Federal legislation because of its continuing importance. I would be remiss, however, if I did not call to your attention the tremendous amount of work being carried on by the parent Council Committee on Legislation, directed by our able James M. Blake, M.D. Dr. Blake and his committee have been most active not only during the Legislature session which is now going on in Albany but throughout the entire twelve months of the year. The bulletin entitled *Capital News* goes out periodically to key people in our Society, particularly the chairmen of county medical society committees. More activity has been going on in regard to personal contact with State legislators on the scene in Albany.

Incidentally, the Department of Communications is very directly involved in this whole legislation scene, both on the Federal and State levels. A great deal of the time of the staff is devoted to these activities. Your attention is called to the fact that a detailed account of the excellent work being done in Albany by your committee will be found in Dr. Blake's report. I particularly call to your attention the part concerning our perennial problem—licensure of chiropractors—which was one of the important matters on the agenda at the special session of the House in February.

On this matter of legislation much thought should be given to the proposition which has already been suggested that the activities of the Legislation Committee and the Public Relations Committee be combined. This might be done under another commission similar to the Commission on Medical Services which is functioning very well.

Journal. You already have noticed the change in the format of our NEW YORK STATE JOURNAL OF MEDICINE. This was done so that the style of the publication could be modernized and thereby attract more readers and consequently increase the circulation of the JOURNAL and its revenue. We are hopeful that the present plan will advance the JOURNAL.

Directory. Plans are under way for streamlining the next issue of the *Directory* which will be published in 1963. Dr. Fineberg is actively engaged in trying to streamline this publication so as to weed out a lot of the information that has nothing to do with the professional qualifications of a doctor of medicine. I am certain that this is a step in the right direction and will improve the appearance and the value of the *Directory*.

Woman's Auxiliary. Your president would be very remiss if he did not extol the adjunct to our basic organization, namely, the Woman's Auxiliary. Its members are ready, willing, and able to carry out any project proposed by the State Medical Society and the component county medical societies to advance the art and science of medicine. During the past year they have done a terrific job in various areas about which I will not go into detail. I recommend to you the report of the liaison member of our Society with the Woman's Auxiliary.

I wish to thank the Auxiliary personally and on behalf of our State Medical Society for the work they have done and for the plans they have for the future. During the past year the Woman's Auxiliary has been very ably directed by Mrs. Eugene F. Wolff, and this work, I am certain, will be continued by the very capable president-elect, Mrs. Herbert J. Ulrich.

I wish to reiterate my statement made to the House last year concerning wider utilization of the members of the Auxiliary. It would be an excellent idea if members of the Auxiliary were appointed to committees of our State Medical Society for the activities in which they could play an effective part. I recommend that this be given further consideration and implemented wherever possible and feasible.

Medical Education. Early in this report I referred to the Foundation we have established which we hope will play a great part in the future of postgraduate medical education. Allow me now for a few moments to discuss the problem of basic medical education in the United States and particularly as it concerns our own State of New York.

There is a marked disparagement between the number of graduates from medical schools in the United States and the number of approved internships. A few years ago it was estimated that the figure for approved internships in this country was approximately 12,000 and that the number of American graduates was not quite 7,000.

In 1959, the Surgeon General's Consulting Group on Medical Education published a report, "Physicians for A Growing America." They estimated that by 1975 the number of physicians must increase from 7,400 to 11,000, an increase of 3,600 graduates, in order to maintain the minimum essentials to protect the health of the population of the United States. They estimated also that this would require at least 25 new medical schools in the United States. When the figures were broken down by states it was found that New York State would need at least two and probably three new medical schools.

Since I am familiar with the situation I should like to address my remarks to one portion of the State where this problem is now being discussed. I refer to the area of Nassau County where I am pleased to reside and practice and the adjoining county of Suffolk. With its rapidly expanding population, this area has had a tremendous lag in the number of physicians per capita. Plans therefore are now being discussed for the possibility of having a medical school in that area.

Among other factors which should be considered in consideration of a school on Eastern Long Island is that, according to a sales management survey, Nassau County has been ranked as the country's tenth largest community entity. Also, it is the only one of the 20 largest community entities in the United States that does not have a medical school or for which funds have not already been appropriated for the construction of a medical school. Allow me to add that a medical school in Nassau County would be an institution available for all of Long

Island, including Nassau, Suffolk, and probably Queens County.

I recommend to this House that the matter of additional medical schools for the State of New York be carefully studied and that specific recommendations in regard to this matter be made to the proper authorities.

Conclusion. In closing my remarks to the 1961 House I stated: "During the next twelve months, in which I hope there will be a definite awakening to the problems that I have mentioned and to many others, can you, can I, can our fellow members of our profession cope with the changes that will occur and meet the challenges we will encounter? Will we be caught asleep in a blanket of indifference or will we be found wide awake, keeping abreast of the times and truly advancing the art and science of medicine and the health and welfare of our people? These questions I ask today. Only tomorrow can supply the answers."

The tomorrow I spoke about in May, 1961, is the today of February, 1962.

What about the answers to these two questions?

First, did we cope with changes and meet the challenges? In my humble opinion, through the concerted efforts of the officers, Council, Board of Trustees, staff, and other countless interested members, we did. The millenium of perfection was not attained but great strides were made.

Second, were we caught asleep? My answer on the part of the Society in regard to its official representatives is a categorical no! My answer concerning the rank and file of our members is that many awoke but that too many are still asleep.

To win the short-term skirmishes and the long-range battles in the war to preserve the freedom of American medicine there must be a constant alertness on the part of the State Society and its members. There must be a further awakening by all of us to the challenges and changes ahead. There must be positive specific action by the Society as an organization and by its members as individuals to meet these challenges and changes. If this is done, there will be no radical changes in American medicine and the challenges to its future will be adequately met. The end result will be that the people of our country will continue to have the best medical care in the world under the voluntary way of life.

Respectfully submitted,

John M. Galbraith MD

John M. Galbraith, M.D., *President*

Secretary

To the House of Delegates, Gentlemen:

The Secretary submits the following report.

Routine Duties. As required by the Constitution and Bylaws, the Secretary has kept minutes of the regular and special meetings of the House of Delegates, the Council, the Executive Committee, the Board of Trustees, and the Judicial Council. He has edited the minutes of the annual and special sessions of the House of Delegates and has transmitted them to the JOURNAL Editorial Department for publication. He has transmitted instructions of the House of Delegates, the Council, and the Executive Committee to committee chairmen, has carried out instructions of those bodies to the Secretary, and has prepared an amended edition of the Constitution and Bylaws in accordance with the instructions of the House of Delegates.

With the cooperation of the Executive Vice-President he has notified officers, councillors, and trustees of their election, has prepared programs for the annual meetings of the Society and of the district branches, has notified Council, Board of Trustees, and committee members of meetings, and has conducted other official correspondence of the Society. He has notified committee members of their appointments and life members of their election, has provided for the registration of delegates at the annual and special sessions of the House, and has kept membership records as noted below.

Membership. The following figures have been compiled by the Membership Department under the direction of our Controller.

1960	Membership	25,250	
1961	New members	804	
1961	Reinstated members	105	26,159
1961	Deaths	316	
1961	Resignations	280	
1961	License revoked	7	
1961	License suspended	3	606
			25,553
1961	Delinquent members		202
1961	TOTAL MEMBERSHIP		25,351

Honor counties, those having no 1961 delinquents, are: Chenango, Clinton, Cortland, Franklin, Fulton, Genesee, Greene, Livingston, Monroe, Orleans, Richmond, Schoharie, Schuyler, Steuben, Tioga, and Wyoming.

Comparative totals of membership since 1950 follow:

1950	21,861	1956	24,031
1951	22,124	1957	24,182
1952	22,637	1958	24,370
1953	23,145	1959	24,689
1954	23,545	1960	25,250
1955	23,838	1961	25,351

Remission of 1961 dues were voted for 157 members as follows: Illness 96, Temporary Service in the Armed Forces or United States Public Health Service 50, and Financial Hardship 11.

The Controller states that the number of dues-paying members will be reported at the time of the House of Delegates meeting.

Physicians' Placement Bureau. The Physicians' Placement Bureau has been active in 1961 in trying to place doctors and to assist communities and individuals seeking physicians by (1) placing localities in need of doctors on our list of opportunities which are sent out constantly to interested parties; (2) sending out lists of physicians' names to communities and individuals who have expressed the need of a doctor; (3) informing physicians that certain openings have come to our attention; (4) sending out follow-up letters to communities and individuals who, in the past, have been seeking the services of a physician, to ascertain if their opportunities have been filled. This enables us as far as is possible to keep our files up to date.

Although our list of opportunities did not carry so great a number of openings during 1961 as in some previous years, we had a greater number of associations, groups, industrial opportunities, and others. This information was channeled to interested parties and for various reasons was not contained on our list.

We heard, through A.M.A. referral, individual mail, telephone calls, and personal office visits, from a total of 409 doctors interested in locating in the following types of practice: anesthesiology 9, dermatology 4, general practice 85, industry 7, internal medicine 80, obstetrics and gynecology 34, ophthalmology 7, orthopedics 8, pathology 4, pediatrics 36, psychiatry 2, radiology 20, surgery 60, urology 15, and miscellaneous 38.

Practically every one of the 409 physicians was written to individually. As far as we know, 12 physicians with whom we had dealings found locations in which to settle. Since we are seldom informed in this regard, we are unable to be accurate in our figures.

Our lists of opportunities have a "new look," and changes and improvements can and will continue to be made. The forms for our questionnaires have also been improved and are more detailed. An interesting occurrence took place on August 27, 1961, when the need for a physician in the village of Narrowsburg was shown on the "Editor's Choice" program on ABC television. We completed a questionnaire concerning the workings of our Placement Bureau for a publication entitled "R.I.S.S." (for residents, interns, and senior students) which is put out by Medical Economics, Oradell, New Jersey.

Miss Doris K. Dougherty, with the assistance of Mrs. Beatrice Moosa, conducts this bureau.

Representatives. Members have been designated to represent the Society at meetings of other state medical societies as follows:

Connecticut, May, 1962, Henry I. Fineberg, M.D.

Maine, June, 1962, Samuel Z. Freedman, M.D.

Massachusetts, May, 1962, Joseph A. Lane, M.D.

New Jersey, May, 1962, James Greenough, M.D.

Pennsylvania, October, 1961, John M. Galbraith, M.D., and Henry I. Fineberg, M.D.

Vermont, September, 1961, Renato J. Azzari, M.D.

Appointments. The following appointments were made as proposed by this Society:

By the Education Department to the Nurse Advisory Council—George A. Burgin, M.D.

By the Education Department to the Medical Grievance Committee—Francis M. Benedetto, M.D., Saul Heller, M.D., John F. Kelley, M.D., Charles H. Loughran, M.D., Solomon Schussheim, M.D., and Frederick A. Wurzbach, Jr., M.D.

By Mr. Victor Borella, as advisor to the Governor's Workmen's Compensation Review Committee—Carl F. Freese, M.D.

Meetings. The Secretary has attended all meetings of the Council, the Board of Trustees, and the Executive Committee throughout the year as well as meetings of the A.M.A. Delegation and many committee meetings. He served as a delegate from this Society at meetings of the A.M.A. House of Delegates in June and November, attended the Saturday sessions of the Annual Fall Conference of Officers and Committee Chairmen of County Medical Societies in September, accompanied the other representatives of this Society to the Congress on Medical Quackery in Washington, D.C., October 6 and 7, 1961, and plans to attend the President's Conference on Occupational Safety, March 6 to 8, 1962. He also took part in the Special Session of the House of Delegates in February, 1962.

General. The most important occurrences of the year so far as the internal life of the Society is concerned are (1) the inauguration of required A.M.A. membership for all members of this Society; (2) the addition of Dr. Greenough to the staff as full-time chairman of the Public Health and Education Committee; (3) the assumption of responsibility for the publication of *What Goes on Bulletin;* (4) the reduction of the number of Council meetings, and (5) the special meeting of the House of Delegates, the first special meeting which the House has held since January 14, 1932.

Acknowledgments. It has been customary to close the Secretary's annual report with a statement commending the work of officers and staff members. It would be inappropriate to close without applauding the energy and effectiveness with which the affairs of the Society have been conducted throughout the year by our new executive vice-president, Dr. Fineberg. The Secretary quite obviously depends to a great extent on the friendly cooperation of the other officers and the efficiency, tact, and industry of many staff members. He wishes to thank all of them but especially the three with whom he has worked most closely, Miss Doris K. Dougherty, Mr. Thomas E. Alexander, and Mr. George W. Forrest, Jr.

Respectfully submitted,

WILLIAM L. WHEELER, JR., M.D., *Secretary*

Board of Trustees

To the House of Delegates, Gentlemen:

The Board of Trustees consists of the following members:

John J. Masterson, M.D., *Chairman*	Kings
Frederic W. Holcomb, M.D.	Ulster
J. Stanley Kenney, M.D.	New York
Leo E. Gibson, M.D.	Onondaga
Thurman B. Givan, M.D.	Kings
Norman S. Moore, M.D.	Tompkins
Renato J. Azzari, M.D.	Bronx

The Board of Trustees met in June, September, October, and November, 1961, and January, February, and March, 1962.

At the September meeting of the Council, Dr. Holcomb presented a resolution which was approved that no motion calling for expenditure of money be adopted unless the motion stated where the money was to come from if not already in the budget. This is an official action of the Council and should be implemented and enforced by Henry I. Fineberg, M.D., our executive vice-president, and by Mr. Thos. E. Alexander, our controller. It should be an effective measure in controlling overexpenditures which are not in the budget.

The Trustees have been greatly disturbed at the deficits which have been taking place in the last three years, notwithstanding an increase of ten dollars in dues during that time. The deficit in 1959 was $99,144; in 1960, $117,622; in 1961, $54,956, totalling $271,722.

The budget submitted to the Council by the Budget Committee at its January meeting has a projected income of $1,290,000 and expenses of $1,429,000, resulting in a deficit of $139,000. There is no way of telling at this time what effect the required membership in the American Medical Association will have on our membership. If there is an increase in the number of physicians who drop their membership or an increase in the number applying for retired membership, then our deficit for 1962 will be increased. Increases in postal rates will also add to our deficit.

Building Fund. At the September, 1961, meeting of the Board, Dr. Fineberg stated that if increased space requested by some of our departments were obtained, our rent would be approaching $100,000 a year. He suggested we should consider the possibility of our building suitable quarters in an area contiguous to New York City.

With this in mind, the Board of Trustees at its November, 1961, meeting approved the transfer of $500,000 of securities at market value from our Investment Fund to a Building Fund, the income from these securities to accrue to the Building Fund. It was left to the discretion of the Investment Committee as to just what bonds or stocks in the portfolio of the Investment Fund should be allocated to the Building Fund.

Personnel Survey. The personnel survey referred to in last year's report was completed in 1961. The recommendations in the report regarding job classifications and other procedures were approved and adopted, resulting in greatly improved staff morale.

Executive Vice-President. Henry I. Fineberg, M.D., assumed his duties in May, 1961. Dr. Fineberg has had considerable administrative experience and as a former president and trustee of our Society is well acquainted with our problems. We were most fortunate in obtaining for this important position someone with the ability and experience of Dr. Fineberg. Some one or two people are usually vital for the success of a business or organization and our executive vice-president should be given full authority for the administration of our headquarters in a business-like manner and for implementing mandates of the House of Delegates and Council.

The Council, Trustees, and House of Delegates will welcome any suggestions or recommendations from him regarding our policies, expenditures, or any other matters affecting the good and welfare of our Society, its members, and the public.

War Memorial Committee. A report of this committee will be submitted in a separate report by the chairman of the committee, Dr. Azzari.

Resignation of James Greenough, M.D. Dr. Greenough resigned as trustee after being appointed full-time chairman of the Public Health and Education Committee. His resignation was accepted by the Board at its January, 1962, meeting and Thurman B. Givan, M.D., of Kings, was appointed to complete the term of Dr. Greenough until the next meeting of the House of Delegates.

Dues. Only three state societies have lower dues than our Society—Virginia $25, Ohio $30, and Connecticut $33. Six states have dues of $35, the same as New York. Seven states have dues from $42 to $45 and 33 states have dues from $50 to $100.

It is our duty and fiscal responsibility to live within our income. If our dues are not increased in an amount to meet our expenditures, then it will be the duty of the House of Delegates to tell us which of our activities should be curtailed if we are to live within our income. We urgently recommend that the House of Delegates go on record as being heartily in favor of living within our income and that the Board of Trustees be urged to proceed immediately to follow through on this action.

Auditor's Report. Our auditors have not completed their audit at the time this report was submitted in March for publication in the convention issue of our STATE JOURNAL. A supplementary report will be made to the House of Delegates giving more details of our receipts and expenses for the past several years.

Acknowledgments. The Board of Trustees expresses sincere thanks to the members of the Budget Committee of which Dr. Holcomb is chairman. The chairman of the Board also thanks the other two members of the Investment Committee, Dr. Kenney and Dr. Holcomb.

Our treasurer, Dr. Dattelbaum, and our secretary, William L. Wheeler, Jr., M.D., attended all meetings of the Board, and our thanks are due them for their valuable assistance.

Our legal counsel, Mr. William F. Martin, is present at our meetings and his advice and experience is most helpful.

We are also grateful for the assistance of our executive assistant, Miss Doris K. Dougherty, and for the valuable contribution of our controller, Mr. Thos. E. Alexander.

Finally, in behalf of the Trustees, I wish to express our appreciation to Mrs. William Grimm for the accuracy and promptness in reporting of the minutes of the Board of Trustees.

Respectfully submitted,
JOHN J. MASTERSON, M.D., *Chairman*

Executive Vice-President

To the House of Delegates, Gentlemen:

Since this communication is being compiled during the early part of February, it can be only a report of progress, a preliminary report. An attempt will be made to be brief, since many of the Society activities in which your executive vice-president has participated undoubtedly will be discussed in considerable detail in the various annual messages submitted to this House by our president and other officers, by the chairmen of committees, and by the Board of Trustees. We will try to avoid duplication of the observations of these gentlemen, and in the main we will confine our remarks to matters of personnel management, staff functions, and other subjects related to administration. However, we will stay away from describing the ordinary routines of everyday Society business. On the other hand, we may stray somewhat and present here in summary form a number of items, divorced from the administrative field, which we consider interesting or important.

It should be understood clearly that policy determinations are not the responsibility of the executive vice-president. These belong in the realms of the House of Delegates and the Council, although it is the duty of the executive officer to enter into the deliberations of these two bodies and to make recommendations whenever the proper occasions arise. Once decisions have been reached, it is the function of the administrator to have them implemented expeditiously.

Your executive vice-president is grateful to have been given the opportunity to serve a great organization. Since he assumed his position on May 1, 1961, he has been evaluating and reviewing continually the situation at headquarters. Various problems have been discussed, and he has been the recipient of much information. The old rule still holds—we can learn something new every day of our lives. Most of the staff have been very cooperative and pleasant.

Contrary to the usually accepted concept, the summer months were not dull or idle. There was considerable hustle and bustle, brought on mainly by an attempt to create a "new look" at 750 Third Avenue and by an abnormally large number of meetings and conferences.

Headquarters Administration. In any undertaking such as ours, shortcomings creep into the system and become precedential or traditional, and we have been no exception. One of our prime objectives has been to eliminate certain abuses. Towards this end, a number of administrative changes have been effected. Poor office "habits," which have developed over a number of years, have been re-evaluated and either eliminated entirely or limited to a great degree. A few fundamental regulations have been established. Before taking action, the changes have been discussed with the chairman of the Committee on Office Administration and Policies.

Additional measures will be taken as time goes on to assure better efficiency and improve cohesiveness among the members of our staff. We know that we can depend upon most of our people to enter into the spirit of creating a wholesome atmosphere. It has been pointed out to the staff that, although we work for a dedicated and benevolent profession, our office must be operated on a business basis, governed by sound and practical procedures. Here as in any calling the executives must have the full cooperation of the men and women who work with them. One cannot exist and function properly without the other.

Working conditions in the office have been improved, and in the opinion of many folks the morale of our staff is higher than it has been.

Using a job analysis prepared by Mr. Dietrich K. Willers of Cornell University as the basis for our study, we evaluated every position in our office. Each position was reclassified according to function and responsibility. A Table of Organization (T.O.) of the staff was prepared, showing diagrammatically the title, duties, and office location of each employe. Equitable salaries were determined and the scales brought up to date as of October 1. Our recommendations were approved by the Committee on Office Administration and Policies, the Council, and the Board of Trustees.

The job evaluation program will be a continuous one. At regular intervals the positions will be re-examined and future increases will be determined, based on merit and years of service.

Soon after his arrival, your executive vice-president discovered that, despite our immediate past-president's fine emergency program during his term of office, inadequacies existed in our Membership Department. The records appeared to be hopelessly behind. Since membership is closely related to the financial aspect of our Society (the collection of dues), the department was placed under the supervision of the controller with instructions that this important division must be brought back to normalcy as quickly as possible. Our controller was directed to visit a number of agencies in order to review the routines in those places where modern systems operate properly, such as the American Medical Association, the International Business Machine Corporation, and others.

In the near future, we plan to develop new procedures in submitting budget estimates. It is the feeling of your executive vice-president that these should be prepared sometime during the summer months, after due consultation with chairmen of committees and department heads. By early fall, all budget estimates should be presented to the Budget Committee for study and approval. Only in this way can proposals be examined properly and judged equitably. Of course our suggestions and recommendations for a new system of "budgeteering" will be transmitted to the Budget Committee and to the Council for approval.

Your executive vice-president is happy to announce that the first issue of the staff paper, or house organ, called the "preview issue," appeared just before the Christmas holidays. It represents the realization of a dream first brought to our attention by Alvina Rich Lewis, its supervising editor. A great deal of planning and toil have gone into the implementation of this grand idea. Miss Lewis and her group should be congratulated for making it possible for our staff to be kept informed of what is going on at our headquarters and elsewhere. Are there any people better equipped to spread the gospel of what the medical profession is trying to do in the area of health than the folks who labor with us to achieve our lofty aims?

A staff handbook or manual is now in process of preparation and should be completed within the next few months. There has been a need for such a brochure for quite sometime. We have been told that some of the shortcomings encountered in our office may be due to the fact that we have never developed definite statements of policy in a form in which they can be understood readily and referred to when the occasion arises.

The handbook will contain detailed information about office procedures, rules governing the staff, descriptions of the valuable fringe benefits which we provide, and other pertinent matters. Staff department heads and certain members of our official body will be consulted before it is released in its final form.

During the month of September, a past-presidents gallery was established at central office. The pictures of these men, who have served our Society with distinction, are on display throughout the halls leading to the Council Chamber. We invite all the members of our Society to visit our headquarters to see what has been done in this direction.

At the request of the Department of Communications, your executive vice-president will write a column for the *Newsletter*. It will be called "Facing Facts" and will be used as a medium to bring messages of interest and importance to the members of the Medical Society of the State of New York and to the medical profession as a whole. The policies of our Society, as determined by the House of Delegates and the Council, will be transmitted to the doctors of medicine in all areas. From time to time the way in which these policies have been implemented will be described.

Also, our colleagues have been invited to get in touch with us concerning subjects in which they may be interested. It is contemplated that the members of the Council will participate in this new undertaking. The first column appeared in the October issue.

Annual Convention. Following the last annual convention in Rochester, we held what has come to be known as a "postmortem" conference. Present were those members of the staff who had participated in the program. The purpose of the meeting was to review the activities, to discuss the inadequacies, and to project ideas for improvement. In general, it was agreed that we can and should do a much better job.

These deliberations resulted in certain recommendations, which have been transmitted to the chairman of the Convention Committee and to the Speaker of the House of Delegates for their considerations. These include the following:

1. (*a*) that registration start on Sunday evening; (*b*) that a separate table be set up on Monday morning for the distribution of the handbooks to the delegates. (We discovered that many delegates appeared behind the registration desk in search of handbooks, and this created considerable confusion. In the future, the registration area will be so arranged as to prevent this occurrence.); (*c*) that the registration lines be split up on an alphabetic basis. This system is in effect at American Medical Association meetings and has worked very well; (*d*) that more handbooks be ordered, so that there will be a sufficient number of copies for representatives of out-of-state societies and others; (*e*) that an "information desk" be established. (We found that members of the staff working in the House of Delegates were being asked constantly about hospitality suites, meetings, and other things. Not only did they not have this information, but at the registration desk and the press table they were unable to take the time to answer questions. In the future, we will request the county societies to provide us with this pertinent material about their organizations.)

2. We expect to conduct preconvention briefing sessions for the staff. The speaker and vice-speaker and the chairman of the Convention Committee and the Dinner Subcommittee will be invited to these conferences.

3. That a sergeant-at-arms committee be appointed, similar to that at the House of Delegates of the American Medical Association.

4. That a steering committee of the staff be organized to work with the executive vice-president towards the creation of better coordination at House of Delegates meetings.

5. That the Guest Reception Subcommittee play a more active role. It should be on hand to receive visitors, a very important function.

6. That night sessions of the House of Delegates be eliminated.

Meetings. During the past ten months your executive vice-president has attended a number of significant meetings and conferences, in addition to the usual committee and Society meetings. We will only mention the important ones:

1. A meeting of the American Medical Association Council on Medical Education and Hospitals, in New York City, on June 24. Besides New York, the states represented were Delaware, Maryland, New Jersey, Pennsylvania, Virginia, West Virginia, and the District of Columbia.

The following topics were discussed: continuing education (postgraduate training), increasing the supply of physicians, the future of graduate education, and medical school affairs.

2. The chairman of the Subcommittee on Federal Legislation and your executive vice-president appeared before the House Ways and Means Committee, in Washington, on July 27, in order to discuss H.R. 4222, the "Health Insurance Benefits Act of 1961." Hearings were held from July 24 through August 4. People from all walks of life testified. Judging from the communications from a number of the members of the Ways and Means Committee and the American Medical Association, our short fifteen-minute presentation was well received.

3. In August there was an informal reception and conference with a group of over 20 Italian doctors of medicine. Previously these ladies and gentlemen had been entertained by the American Medical Association and the Medical Society of the County of New York. Present from this area were your president, the president and executive secretary of the Medical Society of the County of New York, the chairman of the board of United Medical Service, and your executive vice-president. With the help of an interpreter, all of us participated in a discussion of American methods of medical

organization, voluntary health insurance, and other topics.

4. Opening of the Health Exposition at the Coliseum in New York City on August 18. Your president and executive vice-president accompanied Mayor Wagner and Health Commissioner Baumgartner on a tour of the entire project. Among the exhibits was the Medical Society of the State of New York's display on medicine's role in "putting man into outer space."

5. On August 24 at the request of the Department of Communications your executive vice-president visited Station WEVD and appeared on a taped program of the Jewish Home Show. He was asked to discuss an article in the September issue of *Redbook*, "What Your Doctor Thinks of You—Forty doctors turn the tables and talk about the faults and foibles of their patients."

6. Meeting of the New York State Polio Advisory Committee to the Commissioner of Health, in Albany, on August 25. The chairman of the Committee on Public Health and Education and your executive vice-president were asked to serve with this group. Careful consideration was given to various questions regarding the use of oral polio vaccine and particularly to the situation in Syracuse. Dr. Hilleboe has reported to us that, with the full cooperation of public health personnel and private physicians, they proceeded rapidly with the job of immunizing 350,000 persons in the tricounty area around Syracuse.

7. American Medical Association Institute, at the Drake Hotel in Chicago, on August 31 and September 1. The theme was "Medicine in Action." Directors of American Medical Association bureaus and divisions and others talked about: "AMA's Greatest Challenge," "Are We Fighting A Battle We Can Win?", "The Case Against Socialized Medicine," "What's Right and What's Wrong with AMA's Image," "AMA Today and Tomorrow," and other subjects.

8. Public hearing conducted by the State of New York Joint Legislative Committee on Health Insurance Plans, in New York City, on September 22. The purpose of this conference was to study suggestions for improvement in the administration of the State's program of Medical Aid to the Aged (MAA), now being carried out to implement the Metcalf-McCloskey Act.

A variety of agencies were represented. The main speakers for government were James R. Dumpson, Commissioner of Welfare of the City of New York, and Raymond W. Houston, Commissioner of Social Wefare of the State of New York. Our president and the chairman of the Subcommittee on Federal Legislation presented the case of the doctor of medicine. Members of a few county medical societies were also present.

Chief criticisms directed at the implementation of the act, cited by speakers at the hearing, were: . . . Although 92,000 persons were supposed to receive aid under the program, the figure for New York City (where approximately half of the State's population is located) has so far been only 600. . . . Many elderly people hesitate to apply because the program is administered by local public welfare offices and they do not wish to be "stigmatized" in this manner. . . . Many elderly people hesitate to apply because they are reluctant to compel sons and daughters, who may have their own families to support, to contribute to the parents' medical bills. . . . The program is unnecessarily duplicative of personnel, procedures, and paper work.

9. The 70th annual meeting of the New York State Veterinary Medical Society at Saranac Lake October 4 and 5. Your executive vice-president was the guest speaker at the dinner. He discussed the role of the veterinarian in public health and the New York State Association of the Professions (NYSAP). It was gratifying to meet a gracious and hospitable group of practitioners of veterinary medicine who are anxious to help us in our fight against the governmental control of the "learned" professions.

10. National Congress on Medical Quackery, sponsored by the American Medical Association and the Food and Drug Administration, in Washington, D.C., on October 6 and 7. This was one of the finest meetings on quackery that we have ever attended, and it was covered adequately by the press. Addresses of welcome were delivered by the Honorable Abraham A. Ribicoff, secretary of the Department of Health, Education, and Welfare, and Leonard W. Larson, M.D., president of the American Medical Association.

Many governmental and voluntary agencies were represented, including the Department of Justice, the Federal Trade Commission, the Post Office Department, the American Cancer Society, the Arthritis and Rheumatism Foundation, the National Better Business Bureau, the Association of Food and Drug Officials of the United States, the Federation of State Medical Boards of the United States, and science writers and editors. We came away from this conference convinced that medical quackery is one of the great problems that confront America today.

11. Meeting of the Nurse Advisory Council of the State Education Department (representing the president of our Society) in Albany, on October 23.

12. The Golden Anniversary Dinner of the Committee on Public Health of the New York Academy of Medicine, in New York City on November 6.

13. The staff Christmas party at the Summit Hotel, New York City, on December 21. This was a very fine affair.

14. Appearance at the WEVD radio station, in New York City, on December 21 to discuss

the recent American Medical Association meeting and the "Future of Medicine."

15. Testimonial dinner for Miss Doris K. Dougherty and Miss Alice E. Wheeler, in New York City, on January 15, to honor these two very wonderful ladies for more than twenty-five years of dedicated and devoted service to our Society and the medical profession of our State.

16. A meeting called by Senator Metcalf in Albany on January 18 to discuss the problems of hospital care insurance.

17. Meeting of the Advisory Committee to the Columbia University Study of Prepaid Medical Care Insurance Plans, in New York City on January 23. A draft of the long-awaited Trussell Report was reviewed.

18. The Eighth Annual Conference of Mental Health Representatives of State Medical Associations, sponsored by the American Medical Association's Council on Mental Health, in Chicago on February 2 and 3. This was an extraordinarily fine meeting. Your president and the chairman of the Council Subcommittee on Mental Hygiene also were present. All of us participated in the group discussions on: medical education, communicating mental health knowledge, mental health services in the community, hospital programs, personnel problems, and research.

We left this grand conference more convinced than ever that we of the medical profession—and our country as a whole—are confronted with a problem of great magnitude where mental health is concerned. Also, what is significant is that the psychiatrists look to the state and local medical societies for guidance and help. In a recent communication, Leo H. Bartemeier, M.D., former chairman of the American Medical Association Council on Mental Health, had this to say: "The success of our mental health program will depend primarily and ultimately on its implementation by physicians at state and local levels and through action of state and local medical organizations in cooperation with state and local mental health agencies, social and welfare agencies, individual physicians, lay organizations and interested nonmedical individuals."

The Conway Decision. A short time ago your executive vice-president received a copy of an opinion, dated November 15, 1961, which is of tremendous significance to the well-being and health of the people of this State. It was handed down by the Hon. Albert Conway, the former Chief Justice of the Court of Appeals of the State of New York, now retired and sitting as an official referee of the Court of Appeals. This document has been summarized by a member of our counsel's legal staff. A copy is being transmitted to every member of the Legislature, and it will appear in the JOURNAL.

Quoting from the abstract—"In a most well-reasoned and exhaustive opinion he ruled that chiropractors are not entitled to an injunction restraining the State Commissioner of Health from enforcing the provisions of the State Sanitary Code which prohibits the application of radiation to human beings except by persons licensed to practice specified professions or under the direction of such persons and which thus prohibits the use of x-ray equipment by chiropractors. His ruling was by stipulation equally determinative of another proceeding in the City of New York by which chiropractors attempted to enjoin a similar prohibition contained in the Sanitary Code of the City of New York."

Mr. Conway's decision also contains much interesting evidence by experts and a number of comments which should warm the hearts of every doctor of medicine and well-informed intelligent lay people.

Medical Directory. At the request of the Publication Committee and the Council, your executive vice-president is in the process of "streamlining" the *Medical Directory*, the next edition of which will appear in 1963. Some research has revealed that certain definite changes are indicated if the *Directory* is to be entirely factual and serve its purpose as an important reservoir of much needed medical information concerning doctors of medicine. In general, the data in the *Directory* should include only those qualifications and other facts which determine the standing of a physician. The present *Directory* has been compiled by an efficient staff, but it requires a number of modifications more in keeping with modern times.

Thus far the Publication Committee has agreed that the hospital listings in the 1963 *Directory* will be broken down into three groups: (1) voluntary hospitals, (2) governmental (federal, state, county, and municipal) and (3) proprietary hospitals approved by the Joint Commission on Accreditation of Hospitals. This has been ratified by the Council.

National Chamber of Commerce. Your executive vice-president is happy to report that the Medical Society of the State of New York is now a member of the Chamber of Commerce of the United States. This enrollment was approved by the Council in October.

The national Chamber works through voluntary organized action to do these things: (1) protect, strengthen, and improve the private business system; (2) keep the economy dynamic and expanding, keep the American standard of living increasingly high, create new jobs and new opportunities, keep the country productive and strong against the threat of war; and (3) safeguard and preserve our representative form of government.

The national Chamber promotes the concepts of a free-market economy, limited government control, and the dignity and self-reliance of the individual. The national Chamber represents all business and industry, large and small, and every section of the country. It is composed of more than 3,600 organization members—local, state, and regional chambers of commerce and trade and professional associations. We are in very good company, along with men who fight for the principles in which we believe. They will join us in our battle to protect the free enterprise system.

Medical Specialties. Recently we have been informed that the American Medical Association has revised the list of medical specialties, as follows:

Medical Specialty Services Recognized by American Medical Association

A—Allergy
ADM—Administrative Medicine
ALR—Otolaryngology
AM—Aviation Medicine
ANES—Anesthesiology
C—Cardiovascular Disease
D—Dermatology
GE—Gastroenterology
GP—General Practice
I—Internal Medicine
N—Neurology
NS—Neurological Surgery
OBG—Obstetrics, Gynecology
OM—Occupational Medicine
OPH—Ophthalmology
OR—Orthopedic Surgery
P—Psychiatry
PATH—Pathology
PD—Pediatrics
PH—Public Health
PL—Plastic Surgery
PM—Physical Medicine and Rehabilitation
PR—Proctology
PREV—Preventive Medicine
PUL—Pulmonary Diseases
R—Radiology
S—General Surgery
TS—Thoracic Surgery
U—Urology

The following medical specialties are no longer listed in the physicians' records of the American Medical Association:

BACT—Bacteriology
CP—Clinical Pathology
FP—Family Practice
G—Gynecology
HAD—Hospital Administration
LM—Legal Medicine
MAD—Medical Administration
OALR—Ophthalmology, Otology, Laryngology, Rhinology
OB—Obstetrics
PN—Psychiatry and Neurology
PACP—Pathology, Pathologic-Anatomy, Clinical Pathology
R—Roentgenology

Miscellaneous. As most of you know, for quite sometime it has been the strong feeling of your executive vice-president that there should be a very close and wholesome relationship between the State Society, the district branches, and the county medical societies. He has attempted to keep the district branches and county medical societies informed of important developments. Wherever possible, inquiries from these constituents have been answered promptly. Questions demanding legal interpretation have been referred to our legal counsel without delay.

At the same time your executive vice-president has tried to keep in close touch with the executive secretaries of the various county medical societies. The first meeting with this group was held in conjunction with the third annual conference with County Medical Society Officers and Committee Chairmen, in New York City on September 29. A second conference of this type is scheduled for February 9, at which time we will discuss those problems of greatest concern to us. We believe that these meetings are of great import.

Your executive vice-president has been very fortunate to have been invited to county society and district branch meetings throughout the State. These visits have given him the opportunity to renew old friendships and to establish new ones. He will always remember the warm hospitality and the many kindnesses he has received in the various sections of the State. It brings back sweet memories of the days when, as president of the Society, he toured the highways and byways of New York.

Mere words are not adequate to describe my gratitude to those who have contributed much to make my stay at 750 Third Avenue stimulating and enjoyable. Without their devotion, personal loyalty, and great assistance, very little would have been accomplished. I am indebted to our officers, the Board of Trustees, the councillors, the chairmen and members of committees, and, as I have mentioned previously, the folks throughout the State. I am grateful to the members of our staff, many of whom I now know intimately. Our relationship has been heartwarming. Having been an administrator in other areas, I know the tremendous value of an able staff.

It is a privilege to serve with people of dedication.

Respectfully submitted,
HENRY I. FINEBERG, M.D.,
Executive Vice-President

War Memorial

To the House of Delegates, Gentlemen:

The War Memorial Committee consists of the following members of the Board of Trustees:

Renato J. Azzari, M.D., *Chairman*....Bronx
Leo E. Gibson, M.D..............Onondaga
Maurice J. Dattelbaum, M.D., *ex officio*.....
..................................Kings
Henry I. Fineberg, M.D., *ex officio*,...Queens

At this time, when the public image of the doctor seems to have deteriorated and when our many acts of generosity and kindness are hidden under a barrage of accusations of self-interest and self-aggrandizement, I bring to your attention our War Memorial Fund.

In 1948, our House of Delegates brought into being the War Memorial Fund. The members of the State Society, by a voluntary assessment of $12 each, contributed $248,000, which was invested wisely in a special fund and all accrued interest added to it. The cost of administering the Fund is absorbed by the State Medical Society. The Fund is an active, beneficent memorial to our colleagues who died in the service of our country, for the college education of their children. At present, when the education of our young people is so important to them and to our country, the War Memorial Committee takes justifiable pride in the impressive contribution the Fund has made to date and will continue to make for some years to come.

We have already helped 62 children, from 1948 to the present academic year, with their graduate and postgraduate education in diverse fields of interest. These include, among others, medicine, nursing, dentistry, teaching, law, art, and social work. For the 1961–1962 school year, we have 25 beneficiaries, five in college for their freshman year. Twelve hundred dollars per year for each student is the stipend paid the guardians of our children to help toward their education.

The letters of gratitude from the students and their mothers are a heartwarming substantiation, if such is needed, of the wisdom of our House of Delegates in establishing the War Memorial Fund, and the interest of our profession in the welfare of these young people.

Following are excerpts from just a few letters in our files:

> *Mother of two sons:* " . . . Thank you very much for the checks for my sons. The money is so much appreciated, as it makes their college education possible. Words cannot express how very generous and wonderful are the members of your Society."
>
> *Mother of five children whom we have helped over the years:* " . . . My oldest son, C., is now practicing urology. May I thank you again for the wonderful help you have been to me through the years, in the task of educating my children. I am so deeply grateful."
>
> *Mrs. R., mother of two daughters:* " . . . I am returning the signed receipts and wish to express my deep appreciation for this wonderful aid to my children. N. is doing very well at New York University and enjoys so much the opportunity of going full time. B. is working hard at Oneonta. The work is not easy but she has determination of purpose which I hope will sustain her to her goal. Thank you again for this much appreciated assistance."
>
> *Mrs. F., mother of three, oldest son a freshman:* " . . . to let you know that T. is doing well. He completed his exams about two weeks ago and missed the dean's list by one point. He feels badly over this and will keep trying. To say 'thank you' to your marvelous group seems very inadequate, but T. would not be able to pursue his career without your help. I am proud that my late husband was a member of your wonderful organization."
>
> *Mrs. S.:* " . . . You asked about the progress J. is making in school. He is in the last semester of his senior year at Loyola University School of Law and will graduate in June. He is student bar president and was recently enrolled as a member of Alpha Sigma Nu, the national Jesuit honor society. I know he ranks high scholastically in his class. Once more, may I express my gratitude to you and all the members of the Medical Society of the State of New York for the wonderful financial assistance you have given me through the years."
>
> *Mrs. B.:* " . . . My son, J., has completed his first semester at the College of Medicine at the State University of New York at Syracuse. His work has been at least satisfactory to the professors, since I understand that the students are not given numerical grades at this school. I do know that J. is most enthusiastic about the study of medicine and his future contribution to humanity."

Following is the financial report as of December 31, 1961:

Total assessments received*	$248,618
Total interest received*	65,937
Total paid out in benefits*	160,500
Assets of Fund, December 31, 1961	147,617
Year ended December 31, 1961	
Assessments received	0
Interest received	5,313
Payment to beneficiaries	28,800

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* Since inception of Fund.

At the present time it is estimated that the last payment to any beneficiary will be made in

TABLE I. Projection of War Memorial Fund financial status through 1978

Year	Assets Beginning of Year*	Interest Earned During Year	Estimated Payments to Beneficiaries	Surplus End of Year
1962	171,104	4,959	29,260	146,793
1963	146,793	3,469	25,740	124,522
1964	124,522	3,069	22,440	105,151
1965	105,151	2,594	20,020	87,725
1966	87,725	2,184	18,040	71,869
1967	71,869	1,787	16,060	57,596
1968	57,596	1,332	9,460	49,468
1969	49,468	1,072	5,720	44,820
1970	44,820	910	5,280	40,450
1971	40,450	780	5,060	36,170
1972	36,170	650	4,180	32,640
1973	32,640	520	3,300	29,860
1974	29,860	422	2,860	27,422
1975	27,422	357	1,980	25,799
1976	25,799	292	1,980	24,111
1977	24,111	260	1,540	22,831
1978	22,831	195	440	22,586

* Securities at par value plus cash.

1978. It is possible that funds may be needed beyond that date but this is not anticipated at this time.

A projection is appended (Table I) which shows that approximately $23,000 cash will remain in the Fund in 1978. It is pointed out, however, that this is obviously a guess. Should demands upon the Fund increase, the remaining balance will be less.

A report of investments is included in the report of our certified public accountants.

The chairman wishes to thank the members of his committee for their sage advice and assistance and Mr. Thomas E. Alexander for his painstaking efforts in preparing the projection. The committee extends to Miss Mollie Pesikoff sincere thanks for her devoted and enthusiastic work in carrying out the administrative duties of the Fund and for her friendly interest in our beneficiaries.

Respectfully submitted,
Renato J. Azzari, M.D., *Chairman*

Budget

To the House of Delegates, Gentlemen:

The Budget Committee consists of the following:

Frederic W. Holcomb, M.D., *Chairman*	Ulster
Maurice J. Dattelbaum, M.D.	Kings
Samuel Z. Freedman, M.D.	New York
John J. Masterson, M.D.	Kings
Reid R. Heffner, M.D.	Westchester

For several years the Budget Committee has onsisted of Maurice J. Dattelbaum, M.D., treasurer; Samuel Z. Freedman, M.D., assistant treasurer; and Frederic W. Holcomb, M.D., trustee. In order to increase the effectiveness of the Budget Committee, our president, John M. Galbraith, M.D., added two additional persons, John J. Masterson, M.D., chairman of the Board of Trustees, and Reid R. Heffner, M.D., vice-president.

To further strengthen the control of the Society's expenditures a resolution was passed by the Council at its September meeting. This resolution was prepared with the assistance of Norman S. Moore, M.D., past-president, and Thos. E. Alexander, controller, and reads as follows:

Whereas, The House of Delegates mandated the Council and the Board of Trustees to manage efficiently the fiscal affairs of the Medical Society of the State of New York; and

Whereas, Inflation has caused the fiscal costs of carrying on traditional activities of the Society to increase greatly; and

Whereas, Expansion of activities and continuation of traditional activities have threatened large annual deficits even in the face of increased revenue from dues increase; and

Whereas, There is a general feeling among the officers of the Society that savings would accrue from more orderly processes of carrying on the business of the Society than is now provided for; now therefore be it hereby

Resolved, That the Council vest the Budget Committee with authority to prepare an annual budget on a line item basis; and be it further

Resolved, That the chairman of the Budget Committee and the Controller set up accounting procedures to call attention automatically to depleted item accounts before they are overdrawn; and be it further

Resolved, That the present policy of a purchase order procedure is to be adhered to, such orders being prepared upon the ordering of the material or service; and be it further

Resolved, That all budgetary changes shall be referred to the Budget Committee through the Controller before being presented to the Council and Board of Trustees. The Controller shall be empowered to obtain all necessary information regarding such items being presented to the Budget Committee; and be it further

Resolved, That the Executive Vice-President be provided with a fund not to exceed $2,000 from which he can make minor adjustments in personnel salaries within the range set up by the Office Management and Policies Committee not to exceed $300 per item, without specific permission of the latter committee; the Executive Vice-President, however, is to report his actions at the next regular meeting of the Budget Committee; and be it further

Resolved, That this action be reported to the House of Delegates in the annual report of the Council with the recommendation that when the House of Delegates votes a large expenditure for a certain specific activity that it be understood that unless the resolution carries the source of funds that the implementation of the mandated expenditure of the funds be at the discretion and judgment of the Budget Committee and the Board of Trustees.

Four meetings have been held since last May. These meetings were also attended by John M. Galbraith, M.D., president; Joseph A. Lane, M.D., president-elect; Henry I. Fineberg, M.D., executive vice-president, and Mr. Thos. E. Alexander, controller. About twenty-five hours of these meetings were devoted to our 1962 budget. The departmental budgets for Administration, JOURNAL, Communications, Legislation Bureau, Workmen's Compensation and Bureau of Industrial Health, Bureau of Medical Care Insurance, Scientific Activities, Woman's Auxiliary, Travel, Annual Meeting, *Medical Directory*, as well as various single items, were studied on a line basis. There were a total of 425 different items. Conferences were held with Council committee chairmen and staff officers and attempts were made to control expenditures without detracting from the efficient management of these various departments and activities in our Society.

At the last meeting of the House of Delegates it was voted to recommend to the Board of Trustees that $25,000 be budgeted for the work of the Federal Legislation Subcommittee. This passed the House by a vote of 140 to 52. The Board of Trustees referred this item to the Budget Committee. After review and discussion by this committee, the matter was presented to the Council with the recommendation that $5,000, instead of $25,000, be appropriated. No details were presented to justify the higher amount. From a budgetary standpoint, the committee felt that the $5,000 recommended would be sufficient for the time being. Furthermore, should more than $5,000 be required, the appropriation could be increased. Both the Council and Board of Trustees approved the Budget Committee's recommendation.

Our membership consists of approximately 25,000 physicians. Our House of Delegates must be reminded that our income is derived primarily from dues. It must be pointed out that our dues of $35 per year rank among the lowest of any state medical society in the country. Of the dues of 48 states (except Alaska and Hawaii) and including the District of Columbia, the lowest annual dues are $25 and the highest are $200. The following is a breakdown of these states showing the number in each dollar group:

1	$ 25	
1	30	
1	33	
7	35	
3	40	
1	42	
2	45	(Texas)
13	50	
4	55	
2	60	(Pennsylvania)
1	$ 65	
1	70	
3	75	(Michigan)
2	80	(California)
1	83	
1	85	
1	90	
2	95	
1	150	
1	200	

During the past three years ending December 31, 1961, our total deficit for operations amounted to approximately $272,000. During this three-year period we had a dues increase of $10 per annum. If we had not had an increase in dues, our deficit would have been over a half million dollars for the three-year period. The Board of Trustees has found it necessary, beginning in August, 1961, to borrow a total of $250,000 from commercial banks to carry on the activities of our State Society. Only because we have enough collateral in our Investment Fund have we been able to effect such borrowing.

TABLE I. Budget for the year ended December 31, 1962

INCOME	
Dues income	$698,800
JOURNAL (net)	−22,698
TOTAL INCOME	$676,102
EXPENDITURES	
Administration	$285,955
Department of Communications	150,000
Legislation Bureau	16,500
Workmen's Compensation Bureau and Bureau of Industrial Health	34,061
Bureau of Medical Care Insurance	22,704
Scientific Activities	33,011
Woman's Auxiliary	10,004
Travel	66,250
Annual Meeting	21,478
District Branches	6,100
Planning Committee for Medical Policies	2,000
Malpractice Insurance and Defense Board	2,500
Malpractice audit	2,000
Legal counsel	40,540
A.M.A. Delegates expense fund	8,000
Conference of Presidents	75
Empire State Health Council	100
New York State Society for Medical Research	100
World Medical Association	1,000
Salary and overtime contingency fund	5,000
Relative Values Study for the State of New York	1,000
New York State Association of Professions	5,000
Contribution to Empire State Medical, Scientific and Educational Foundation, Inc.	8,000
Federal Legislation Subcommittee	5,000
Special Meeting, House of Delegates	5,000
Medical Directory	85,456
TOTAL EXPENDITURES	$816,834
Excess of Income over Expenditures	−140,732
Interest earned	1,800
NET EXCESS OF INCOME OVER EXPENDITURES	$−138,932

There are those who would look beyond our General Fund and include income from those funds segregated from the General Fund by the Board of Trustees. If the income from the special funds was to be added to our 1961 General Fund deficit, our net operating loss for the year would have been approximately $27,423. Our proposed budget for the year 1962 (Table I) includes an anticipated gross income of approximately $1,290,000 and anticipated gross expenditures of $1,429,000. This anticipates a net General Fund operating deficit amounting to approximately $139,000.

If the Medical Society of the State of New York is to develop an expanding and progressive program directed toward our participation in the influencing of our membership to take a more active interest in the preservation of the private practice of medicine in this country; if we are to keep abreast in the program of medical education, legislation, medical economics, scientific activities, and other vital fields which are being carried on in the larger states, such as California, Texas, Pennsylvania, and Michigan, then our members must realize that these expanded programs can be developed only by more generous funds from our members.

It is difficult to say at this time just what the impact of required membership in the A.M.A. will have on our revenue from members, but some of the committee feel that there will be an increase in applications for retired membership as a result of this action. Some of the counties have reported a marked delay in payment of dues. This will result in a delay in payment of our bank loans and increase interest payments. We are hopeful our membership loss will be very little, if any.

The chairman of the Budget Committee is of the opinion that the House of Delegates must consider one of two solutions. These are: (1) a request by the House of Delegates to the Council that future programs be effectively limited to result in greater economy in operating expenses, or (2) an increase in our present annual dues. Either of these actions would help to balance our budget.

Your chairman wishes to take this opportunity to express his appreciation of the time and advice received from each member of the committee and of our ex officio members, Drs. Galbraith, Lane, and Fineberg, and Mr. Alexander.

Respectfully submitted,

FREDERIC W. HOLCOMB, M.D., *Chairman*

Commission on Medical Services—A

COMMISSION ON MEDICAL SERVICES

To the House of Delegates, Gentlemen:

The Commission on Medical Services consists of the following committees and committee chairmen: Economics under Waring Willis, M.D., with subcommittees on Public Medical Care under Marcelle T. Bernard, M.D., and on Liaison with the U.S. Veterans Administration under Herbert H. Bauckus, M.D.; Questions of Ethics under Harold F. Brown, M.D.; Industrial Health under Peter J. DiNatale, M.D.; Medical Care Insurance under Melvin S. Martin, M.D.; Medical Service (formerly Rural Medical Service) under Edward C. Hughes, M.D.; and Workmen's Compensation under Carl F. Freese, M.D.

The Commission has attempted to coordinate the work of its component committees and to see that the reports of committee chairmen who are not members of the Council are presented for consideration at Council meetings.

On behalf of the Committee on Economics, the chairman of the Commission has recently been able to negotiate with Walker W. Evans, contracting officer of the Dependents Medical Program, a more favorable contract than originally proposed by them.

Respectfully submitted,

GERALD D. DORMAN, M.D., *Chairman*
EDWARD C. HUGHES, M.D., *Vice-Chairman*

Economics

To the House of Delegates, Gentlemen:

The Economics Committee is composed of the following:

Waring Willis, M.D., *Chairman*	Westchester
George Rehmi Denton, M.D.	Albany
Ralph Stanton Emerson, M.D.	Nassau
Merle D. Evans, M.D.	Monroe
Frank W. Farrell, M.D.	Queens
Samuel Lieberman, M.D.	Bronx
Milton B. Spiegel, M.D.	Kings

The committee has held four meetings: June 8, 1961, September 28, 1961, October 25, 1961, and February 13, 1962. The committee has met, as required, for the review and adjudication of Medicare claims.

The following matters were considered and acted upon by your committee.

1. **Relative Value Study.** Program regarding the establishment of a Relative Value Study in the State of New York: On May 8, 1961, the September, 1960, Relative Value Study of California and work sheets on surgery, medicine, pathology, and radiology were sent to the president of each county medical society for the insertion of relative value units. The work sheets were identified according to code procedure, thus enabling each county to insert the relative value unit desired, by procedure. The covering letter sent with this material emphasized that this study was not intended in any way to establish or set anyone's fees but to establish a relationship and values between medical and/or surgical procedures each to the other. The committee asked the cooperation of the county societies in returning the completed work sheets by September 1, 1961.

As of that date, responses were few; therefore on January 29, 1962, a follow-up letter with a brief questionnaire asking if the matter had been referred to a committee and if so, when the completed sheets might be returned, was sent to the presidents of each county medical society who had not responded, calling attention to the original mailing and requesting return of the work sheets by February 20, 1962.

As a result of the follow-up 26 responses have been received; among the 26, the completed work sheets have been returned, with 34 counties still to be heard from. Your committee will continue its efforts in this matter and is looking toward a completion of the study. Your committee wishes to point out at this time that a project of this type cannot be accomplished within a stated time, as the committee has thus far spent more than a year in working toward its completion.

2. **Commercial Insurance.** Consideration was given to a request made by Mr. Robert R. Decormier, president of the New York State Retired Teachers' Association, regarding the

possible approval by the State Society of a commercial insurance program in effect for this group. In reviewing the coverage, the committee felt that possibly a program with better benefits could be made available by Blue Cross and Blue Shield at possibly less premium for this group. Accordingly, the matter was referred to the Associated Blue Shield Plans of New York State for their consideration. The committee reviewed a communication from the secretary of the Associated Blue Shield Plans which indicated their interest in coming up with a program for this group and before a proposal could be made certain information was required of the retired teachers. This information was transmitted to Mr. Decormier and at the time of this report the response from Mr. Decormier did not contain the information asked for; therefore, the matter is being held in abeyance awaiting further word from the president of the Retired Teachers' Association.

3. **Hospital Utilization Studies.** Your committee with representatives of the Health Insurance Council discussed a proposed survey of hospital utilization in New York State in an effort to determine the causes of increased hospital and medical care costs. The committee was advised that a representative of the School of Business Administration, University of Michigan, had been in contact with the Nassau County Society encouraging a survey in New York State comparable to a study made by them in the State of Michigan. The committee recommended that a survey on hospital utilization be conducted in the counties of Nassau, Monroe, and Wyoming; that the area of survey be determined and a further meeting be held to consider the area of exploration with a view to having a study made, following the three-county survey, in the State of New York by the Michigan group.

At a subsequent meeting of the committee, representatives of the three counties and the Health Insurance Council met, and on invitation, Mr. Thomas Fitzpatrick, research associate of the School of Business Administration, University of Michigan, attended to present a proposal for a survey applicable to the State of New York but similar in areas to the Michigan survey. It was pointed out by Mr. Fitzpatrick that if such a survey was decided on by the State Society, there would be little or no difficulty in obtaining a grant from some foundation to pay for the survey.

In connection with this problem of hospital overutilization and other matters relative to health care costs, the committee felt that utilization committees in hospitals and grievance committees in county societies would be helpful in receiving and resolving complaints from insurance carriers on overcharging abuses which are one of the factors influencing the increased costs of medical and hospital care.

At the February 13, 1962, meeting the matter of a survey was again discussed and it was felt that a survey similar to that conducted in the State of Michigan would not bring out all the phases incident to increased health care costs, and further that an outline of areas for the survey should include not only hospital utilization but a time element involved between the patient's illness and return to work, also abuses of diagnostic procedures, and other areas which committee members might wish to include in the survey. This information is to be sent to members of the committee with a request that they add any other area which would help to determine a broad survey, and upon receipt of this information, the committee will determine the final areas to be explored. The committee was of the opinion that a survey of this type could be conducted by one of the New York State universities equipped for this type of research studies, that it did not seem feasible to utilize the Michigan University. Further exploration of this matter will continue.

4. **A.M.A. Sickness Benefits Program.** The committee considered a resolution from the Seventh and Eighth District Branches voicing opposition to a proposed plan sponsored by the A.M.A. for lifetime sickness benefits for its members. The district branches felt this plan to be actuarily unsound and would imperil the stability of those group disability plans now in existence in New York State. A letter addressed by Eugene J. Hanavan, M.D., president of the Medical Society of the County of Erie, to Hugh Hussey, M.D., chairman of the A.M.A. Board of Trustees, was read outlining the disadvantages of initiating such a plan in the State of New York. It was the opinion of your committee that the Medical Society of the State of New York should recommend disapproval of this program to the Board of Trustees of the A.M.A. prior to November 9, 1961, when the Board would meet, and that other state medical societies be informed of this action. A letter was sent by Henry I. Fineberg, M.D., executive vice-president, to the members of the Board of Trustees, November 1, 1961, informing them of the Council's action at its October 26, 1961, meeting, disapproving the program. Your chairman opposed the unrealistic offering of a lifetime sickness benefit program when presented to the A.M.A. House of Delegates at the December, 1961, meeting in Denver because of the adverse effect on local plans. It is the understanding of your chairman that the program has not been implemented.

5. **Resolution 61-21.** Your committee considered resolution 61-21, introduced by the Medical Society of the County of Richmond, and referred by the Council, requesting that the State Society endorse the initiation of a deductible and/or coinsurance provision in all hospital insurance plans whereby the patient is charged a moderate sum as a deductible amount for a hospital stay, or a moderate amount for each hospital day as coinsurance. The com-

mittee recommended that this resolution with the last resolve which read "that a copy of this resolution be forwarded to the State Commissioner of Insurance urging that he consult with whomever necessary on the feasibility of and a method for implementation of this resolution" be changed to read "that a copy of this resolution be forwarded to the State Commissioner of Insurance calling attention to this proposal as a practical means of reducing hospitalization insurance premiums" and be forwarded to the commissioner.

6. **Resolution 61–16.** Your committee reviewed resolution 61–16, introduced by the Medical Society of the County of Oneida, and referred by the Council, regarding payments to physicians in insurance cases, requesting that the Medical Society take immediate steps to obtain an agreement from all insurance carriers concerned with medical and surgical coverage by joining the physician's and patient's names as payees on any check paid for medical and surgical services, and that the State Society through its liaison with the State Bar Association obtain an agreement from the legal profession that will make it mandatory for attorneys to protect physicians by joining the name of the physician and the client as payees on their checks for medical services rendered in a case.

Your committee recommended that this resolution be referred to the Committee on Liaison with the Bar Association and this committee confer with them, and if favorable opinion is obtained that legislation be introduced at the 1962 session of the State Legislature to change the Lien Law to protect the doctors. The committee felt it necessary to have the backing of the Bar Association and that the Committee on Liaison with the Bar Association should take the first step and carry out discussions.

7. **Examinations for Disability Claimants.** Your committee considered the matter referred by the Council on the dissatisfaction of some physicians regarding the fees for examination of claimants for disability benefits and completion of the report filed by the claimant with the Bureau of Disability Determinations under the Social Security Act. At the February 13, 1962, meeting, representatives from the Bureau were present to clarify the rules and regulations under the Social Security Act. The Act places the responsibility for payment of the initial examination and completion of report by the physician on the claimant. If the initial evidence of disability is insufficient the Bureau will contact the physician for possible information omitted from his report. However, if additional evidence is required from another source, the Bureau at its expense purchases a consultative examination of its own choosing. The Bureau has nothing to do with the fee charged the claimant for the initial examination and report; this is a matter between the doctor and the claimant. Representatives from the Bureau felt that this problem had arisen because of lack of understanding on the part of the claimant and the physician as to the claimant's responsibility under the Act, and they offered any assistance possible in an endeavor to correct this problem.

8. **Group Disability Insurance.** A report was presented by Mr. Farrell at the February 13, 1962, meeting regarding the committee's efforts to resolve the problem facing physicians who enroll in a county society or district branch group insurance disability insurance program and on leaving that county possibly lose their insurance protection.

The committee sent a questionnaire to each county medical society to determine if basic accident and health, supplemental accident and health, and group life coverage was available to the members and requesting the name of the agency through whom the insurance was obtained. Practically all counties replied and with the information obtained a letter was sent to each agency for a statement regarding the subscriber's privileges in retaining his coverage or being permitted to transfer, in the event he moved to another locality where there was no program in effect, or if one was in effect, the privilege to transfer. The replies from the agencies indicated in most instances that transfer or conversion privileges were not available to the insured. If the insured maintained membership in the county society where he originally enrolled his coverage would continue in effect.

It was the committee's recommendation that each county society be informed of the information obtained from the agencies, pointing out the variations in coverage between one county and another, and that the county be advised to pursue the matter further from the county source. One agency pointed out that if the State Society endorsed a State program there would be no loss of benefits or cancellations of coverage if the insured moved to another county within the State.

The members of the committee wish to recognize the conscientious and efficient assistance provided by Mr. George P. Farrell and the members of his staff.

Respectfully submitted,
WARING WILLIS, M.D., *Chairman*

Liaison with Veterans Administration

To the House of Delegates, Gentlemen:

The Subcommittee on Liaison with Veterans Administration, of the Economics Committee, consists of the following:

Herbert H. Bauckus, M.D., *Chairman*	Erie
James L. Palmer, M.D.	Broome
Philip R. Roen, M.D.	New York

Since the last report of the Subcommittee on Liaison with Veterans Administration, all matters have been cleared by your chairman and it was not necessary to call a meeting of the entire subcommittee.

The subcommittee wishes to call to the attention of the Council of the Medical Society of the State of New York that the agreement with the Veterans Administration is subject to negotiations for the period from June 30, 1962, to July 1, 1963. Any change in fee schedules or implementation of the program should be reviewed prior to renegotiation.

Resolution 61–12, introduced by the Medical Society of the County of Cayuga, regarding nonservice-connected cases in Veterans Administration hospitals and adopted by the House of Delegates at its 1961 meeting, was transmitted to Mr. Sumner G. Whittier, Administrator of Veterans Affairs, Washington, D.C.

New York State is now under the Boston, Massachusetts, Area Medical Office, Francis B. Carroll, M.D., Medical Director.

We are indebted to the support of the chairman of the Commission on Medical Services, Gerald D. Dorman, M.D., and to Waring Willis, M.D., chairman of the Committee on Economics.

The committee expresses its appreciation to Mr. Farrell and his secretary, Mrs. Alice Arana, for their assistance.

Respectfully submitted,

HERBERT H. BAUCKUS, M.D., *Chairman*

Bureau of Medical Care Insurance

The Bureau of Medical Care Insurance, Mr. George P. Farrell, director and administrative officer of Medicare, reports through your Economics Committee to the Council. The Bureau operates under the direction of the Economics Committee and the Medical Care Insurance Committee.

In addition to his duties as director of the Bureau of Medical Care Insurance and administrative officer of the Medicare Program, Mr. Farrell's other activities were as follows:

Meetings. February 16, 1961—Hobart L. Boyd, M.D., president of the Medical Society of the County of Monroe, and representatives of the Health Insurance Council regarding survey among hospitals in Monroe County on "Conserving the Health Dollar."

February 19, 1961—Associated Blue Shield Plans of New York State subsequent to a meeting of the Medical Care Insurance Committee, February 18, 1961, in Buffalo.

March 1, 1961—Hearing at Albany called by Senator George R. Metcalf regarding hospital and medical care costs.

March 10, 1961—On invitation of John C. Kinzly, M.D., president of Western New York Medical Plan, with Superintendent of Insurance Thomas Thacher regarding payment by Blue Shield Plans for the so-called "Keller Procedure" performed by podiatrists.

February 23, 1961—Meeting with Mr. Robert R. Decormier, president of New York State Retired Teachers' Association, regarding the cooperation of organized medicine in relation to health problems of the aging. This conference was prior to Mr. Decormier's attendance at a meeting of the Economics Committee and will be reported by that committee.

March 23, 1961—Conference with Mr. Raymond W. Houston, Commissioner of Welfare, on administrative procedure to implement the Metcalf-McCloskey bill.

March 24, 1961—Sixth Regional Conference, Statler Hilton Hotel, Boston, sponsored by the A.M.A. Council on Medical Service, the subject being "The Future of Voluntary Health Insurance Prepayment Plans."

April 9, 1961—Public Relations Committee, Statler Hilton, New York City.

April 12, 1961—Spoke before office assistants group of Broome County Medical Society, Binghamton.

March 15, 1961—Economics Committee.

May 8 to 12, 1961—Annual meeting, Medical Society of the State of New York. A booth on medical care insurance and Medicare was staffed.

June 8, 1961—Economics Committee.

June 24, 1961—Medical Society Executives Conference.

June 25, 1961—A.M.A. House of Delegates.

August 3, 1961—On invitation of Clyde L. Wilson, M.D., president of the Eighth District Branch, attended a joint meeting of the advisory councils of the Eighth and Seventh District Branches regarding the transferring of group disability insurance on the members of these two branches to the America Fore Loyalty Group, this transfer having been accepted by the advisory councils becoming effective September 15, 1961.

August 7, 1961—On Dr. Fineberg's invitation attended a special meeting where Senator George R. Metcalf and Assemblyman McCloskey discussed the intent of their bill to provide hospital and medical services for the medically indigent.

August 9, 1961—Conference with Mr. Louis Orsini and Mr. Francis T. Crawley of the Health Insurance Council, Mr. Thomas Fitzpatrick,

TABLE I. Membership in Blue Shield and Blue Cross Plans in New York State

Location	Membership		Increase (Decrease)	
	Blue Shield	Blue Cross	Blue Shield	Blue Cross
New York	5,037,764	7,198,338	(67,461)	(63,014)
Buffalo	689,158	754,257	(1,778)	(10,490)
Rochester	542,699	583,127	13,639	13,905
Syracuse	277,647	410,761	8,294	(3,978)
Utica	234,408	225,145	2,264	714
Albany	307,244	356,441	9,215	4,348
Jamestown	30,052	50,155	11	(3,564)
Watertown*	...	30,219	...	(922)
TOTALS	7,118,972	9,608,443	(35,816)	(63,001)

* Utica Plan serves Watertown area for Blue Shield members.

research associate, School of Business Administration, University of Michigan, and Walter Cane, M.D., of Nassau County, to discuss the functions of utilization committees or grievance committees to handle complaints from health insurance carriers and a more acceptable method for conducting hospital utilization studies. This matter was taken up at a later meeting of the Economics Committee and will be reported in more detail in that committee's report.

September 7, 1961—Meeting of Joint Legislative Committee on Health Insurance Plans, called by Senator George R. Metcalf, to discuss a proposal made by Group Health Insurance, Inc., to the Joint Legislative Committee, to provide health insurance coverage during a period of unemployment, perhaps by a rider to existing health insurance group contracts which would prepay continuation of coverage during unemployment with possible guarantee of payment by a pooled fund contributed to by the insurance carriers and underwritten by New York State. The following groups were represented at this meeting: Group Health Insurance, Inc., Associated Hospital Service of New York, United Medical Service, Greater New York Hospital Association, Health Insurance Plan of Greater New York, Equitable Life Insurance Company, Metropolitan Life Insurance Company, Empire State Chamber of Commerce, Associated Industries, New York Academy of Medicine, Medical Society of the State of New York, legal counsels from the Office of the Governor, New York State AFL-CIO, Office Employees Industrial Union, New York City Hotel Trades Council, and others.

Representatives from the Governor's office felt the problem should be explored further and a liaison established between their staff and the Joint Legislative Committee.

September 8 to 10, 1961—Fifth District Branch.

October 11, 1961—Sixth District Branch.

September 12, 1961—Meeting with John C. Kinzly, M.D., president of Western New York Medical Plan, and Mr. Joseph Kerrigan, executive director, in the offices of Mr. William C. Gould of the State of New York Insurance Department.

September 29 and 30, 1961—Third Annual County Society Officers Conference of the Medical Society of the State of New York.

September 30, 1961—Conference of New York State Blue Shield Plans at the Biltmore Hotel, New York City.

October 2 to 4, 1961—Symposium by Group Health Insurance, Inc., held at Barbizon Plaza Hotel, New York City, on "Health Care Issues of the Nineteen Sixties."

October 13 to 15, 1961—Annual Congress of Prepaid Plans sponsored by the A.M.A.

October 22 to 24, 1961—Annual Conference of Blue Shield Plans held in Chicago.

January 22, 1962, and March 9, 1962—Meetings of the Public Medical Care Subcommittee.

March 8, 1962—Meeting of the Medical Care Insurance Committee.

Annual Progress Report. The Bureau has compiled its fifteenth Annual Progress Report on the New York State Blue Shield Plans, showing detailed analysis of each plan in regard to membership, incurred and paid claims, claim incidence, operating expenses, premium income, and surplus, for the information of the House of Delegates and members of the Society. This report will be available for distribution at the Annual Meeting exhibit booth of the Bureau.

Quarterly progress reports on the plans have been prepared and mailed to county medical society secretaries and operating offices and to a selected list of interested groups.

Table I is a statement showing membership and increases as of December 31, 1961, in Blue Shield and Blue Cross Plans in New York State.

Progress of the Blue Shield Plans in New York State shows that as of December 31, 1961, total membership (subscribers and dependents) was 7,118,972, a decrease of 35,816 for the year.

Earned premium income during the year amounted to $105,028,490 as compared to $99,342,769 during 1960, an increase of $5,685,721.

Incurred claim expense during 1961 amounted to $97,293,691 as compared to $91,537,984 in 1960, an increase of $5,755,707. Incurred claim expense was 92.64 per cent of earned premium income in 1961, as compared to 92.14 per cent in 1960.

Medicare

During the year 1961 there were few changes in the benefits of the Medicare Program, the most important being that after November 1, 1961, the attending physician will be reimbursed for his cost of poliomyelitis and/or influenza vaccine administered by injection to a dependent eligible to receive care from civilian sources under the Dependents' Medical Care Program when he determines that such immunizations are necessary for proper management of the maternity case.

Effective as of January 1, 1962, a new claim form DA 1863–2 (buff) went into effect. This form is for the use of physicians and/or dentists only, unlike the previous form DA 1863 (white) also used for hospital services. The new forms were distributed to all county medical societies for the use of their members.

During the period ending December 31, 1961, 11,800 claims were processed and $873,353 was paid to doctors for services rendered.

For the five-year period (1957 through 1961) that Medicare has been in effect, a total of 68,597 claims have been paid in the amount of $5,181,152 to 8,957 individual physicians.

The Physicians' Review Committee met on at least nine occasions to review claims which required consideration due to special reports accompanying the claim where exceptional service was rendered by the physician. Approximately 115 claims were reviewed by the committee, Waring Willis, M.D., chairman.

On Wednesday, February 28, 1962, Lieutenant Colonel Gordan A. Jones, Inspector General from the Office of The Surgeon General, Department of the Army, visited our offices, and the visit was mutually beneficial.

The doctors in the State have been advised of all changes by your committee through the State Society's *Newsletter*, a service which is appreciated, and by direct correspondence.

We wish to commend Mr. George P. Farrell, administrative officer, and also Mrs. Nan Boynton and the members of her staff for their sincere and conscientious efforts during the past year.

Convention paging system

We hope that physicians attending the 156th Annual Convention of the Medical Society of the State of New York will be able to devote all their attention to the interesting program, exciting exhibits, and other features of the meeting. However, if it is necessary, physicians can always be in touch with their offices, their patients, or whoever else may wish to contact them through the SherPage System. They may be reached by television anywhere at the convention.

This service is provided through the courtesy of Sherman Laboratories, Detroit, Michigan.

Commission on Medical Services—B

Workmen's Compensation

To the House of Delegates, Gentlemen:

The following is the report of the Committee on Workmen's Compensation and of the Bureau of Workmen's Compensation.

The committee consists of the following members:

Carl F. Freese, M.D., *Chairman*	Nassau
Monroe M. Broad, M.D., *Vice-Chairman*	Queens
Peter A. Casagrande, M.D.	Erie
Robert P. Coolidge, M.D.	Schenectady
George E. Froehlich, M.D.	Westchester
Joseph P. Henry, M.D.	Monroe
John W. Hirshfeld, M.D.	Tompkins
David Kershner, M.D.	Kings
Robert F. McMahon, M.D.	Onondaga
Isidore Sternlieb, M.D.	Bronx
Lee R. Tompkins, M.D.	Sullivan
Robert Young, M.D.	New York
Robert Katz, M.D., *Director*	Kings

The Council Committee on Workmen's Compensation met six times during the year 1961, giving serious considerations to suggested changes in the fee schedule, the interpretation of certain provisions, and to legislative amendments.

Medical Fee Schedule. A series of recommendations were drawn up by the committee and transmitted to the Workmen's Compensation Board's Advisory Committee for the Medical Fee Schedule and Allied Problems. Recommendations dealing with the upgrading of fees for services rendered or for appearances as witnesses at hearings were strongly opposed by the representatives of industry and of the insurance carriers. Matters dealing with ratings of physicians under the Workmen's Compensation Law were generally accepted. Some difficulty was encountered in the consideration of scope and qualifications for a new rating to be added in the future dealing with physical medicine and rehabilitation.

The committee also recommended the elimination of certain ratings from the present list in future revisions of the fee schedule. These recommendations were acceptable to the Advisory Committee. Clarification of several provisions of the fee schedule (for instance, fee for preoperative examination by operating surgeon, fees for injuries if the services of a specialist are not indicated or required) have been issued or are under current consideration.

In accordance with the mandate of the House of Delegates convened in Rochester, May 8 to 10, 1961, the members reviewed the Workmen's Compensation Law—specifically sections dealing with medical care.

It was also strongly urged in a communication to the Workmen's Compensation Board that the current fee schedule become applicable in all cases two years after its promulgation regardless of date of accident.

Legislation. Several proposals for legislative changes were made and are pending action at this time. One deals with the provision for payment of bills for medical services to which the carrier did not object during the statutory thirty-day period. At present such medical bill is considered only to be the fair value of the services rendered with no provisions made for its settlement.

Legislative change was also advocated to avoid harrassment, censure, inconvenience, and undue criticism for failure to file timely reports with the Workmen's Compensation Board in accordance with the provisions of the Law, a situation which may be caused from the failure of patients to admit to or deliberately conceal from the attending physician any causal relationship to their employment. Steps are under way to lift current restrictions on x-ray diagnosis by general practitioners and to eliminate certain discrepancies in the schedule relating to fees for osteopaths.

Education and Liaison. The committee reviewed recommendations sent to county medical societies regarding initial and reratings for physicians. Although the committee generally reaffirmed its previous stand, objections from two counties have caused reconsideration without any definitive conclusions to date. Since the Workmen's Compensation Law has Statewide applicability, it is desirable to have a uniform policy followed in the various counties. Negotiations along these lines are continuing and aimed at unanimous acceptance by all counties.

The committee also prepared a listing of major and subspecialty ratings for clarification and a statement on the scope of practice for certain specialists dealing with public health and industrial diseases.

To provide for better cooperation with interested parties in workmen's compensation, the Bureau through its director reached various groups (Compensation Claims Managers Council, Association of Physiotherapists, Medical Assistants). In an effort to arrive at a mutually satisfactory point of view, individual conferences were held with representatives of certain carriers whose interpretation of provisions of the Workmen's Compensation Law repeatedly conflicted with that of the Medical Society on similar issues. The assistance of other agencies (Workmen's Compensation Board, New York Compensation Insurance Rating Board) was solicited successfully on several occasions. Several cases were discussed with the New York State Department of Insurance when direct negotiations with insurance carriers had become impossible.

Assistance was offered in the consideration of various changes in the handling of disputed hospital bills in conference with the Hospital Association of New York State and with representatives of the Workmen's Compensation Board.

Arbitrations. A total of 73 arbitration sessions were held throughout the State, 55 of them in the New York City area; 1,959 cases were scheduled for hearing involving disputed medical bills adding up to $217,465.53; 1,210 cases were decided by arbitration, 362 cases were settled without hearing, and 387 were postponed; 51 cases were settled by direct negotiations between the Bureau and the parties in interest.

General. On the recommendation of the president of the Medical Society of the State of New York, the chairman of the committee was appointed a consultant to the Governor's Workmen's Compensation Review Committee.

The chairman and director of the Bureau and the chairman of the Commission on Medical Services attended 10 meetings of the Workmen's Compensation Board's Advisory Committee for the Medical Fee Schedule and Allied Problems.

The director was guest speaker at the White Plains Claims Examiners Association and lectured to two classes for Medical Assistants at the Rockland County Community College. He was also invited to speak to the New York State Society of Physiotherapists, Inc.

Your director attended the American Medical Association Legal Symposium on April 28 and 29, 1961, in New York City; the annual meeting of the Medical Society of the State of New York in Rochester, New York, May 8 to 12, 1961; the American Medical Association convention in New York City, June 26 to 30, 1961; the meeting of County Society Officers, September 29 and 30, 1961; the meeting of the American Heart Association in Miami Beach, Florida; the public hearings of the Joint Legislative Committee on Industrial and Labor Conditions held on November 30, 1961, in New York City.

Respectfully submitted,

CARL F. FREESE, M.D., *Chairman*

Industrial Health

To the House of Delegates, Gentlemen:

The following is the report of the Committee on Industrial Health and the Bureau of Industrial Health.

The committee members are as follows:

Peter J. DiNatale, M.D., *Chairman*	Genesee
George Rehmi Denton, M.D.	Albany
Ira Fink, M.D.	New York
F. W. Holcomb, Jr., M.D.	Ulster
Joseph C. Lane, M.D.	Nassau
Thomas F. McCarthy, M.D.	Bronx
Raymond J. Murray, M.D.	Nassau
Joseph M. Pisani, M.D.	New York
Harry E. Tebrock, M.D.	Queens
Robert Katz, M.D., *Director*	Kings
William P. Shepard, M.D., *Adviser*	New York

The Council Committee on Industrial Health met three times during 1961 for the consideration of projects aimed at improving or expanding industrial health services in this State.

Small Plant Health Services. The committee reviewed a plan of the industrial health committee of the Medical Society of the County of New York to establish a nonprofit voluntary organization to provide industrial health services to small plants on a fee-for-service basis. The committee after careful consideration did not hold the endorsement of such a plan in its present state of development to be within its province.

A proposal to aid the Queens County Medical Society's industrial health committee in the promotion of small plant industrial health services did not result in a generally acceptable program and is currently under consideration by the county society.

Education. The proposed project of orientation in occupational health for graduate students in business administration is progressing satisfactorily. An outline of the subject matter to be covered in the course has been prepared and will be submitted to university officials.

The committee displayed an exhibit entitled "Occupational Health Programs—In-Plant Medical Services" during the New York City Health

Exhibit at the Coliseum in August, 1961. Material for the exhibit was secured through the cooperation of several industrial medical directors in the City with the Bureau of Industrial Health and its director.

The Bureau was host to a group of physicians from West Germany who were touring the United States under the auspices of the Council for International Progress in Management. Many members of the group were interested in occupational medicine and in the similarities in as well as differences between our problems and theirs.

The director participated as leader of a study group in a speech training course conducted by the Medical Society of the State of New York.

Liaison. Attempts to relate the workings of our committee with other groups interested in occupational health were continued. A meeting was held with representatives of the New York State Society of Industrial Medicine, Inc., and the Industrial Medical Association of Upstate New York to explore outlines for cooperative efforts. As a result of this meeting it was suggested that more definitive plans be developed and discussed in the future.

Several members of our Industrial Health Committee are on the slate of newly elected officials of the New York State Society of Industrial Medicine, Inc.

Management and Union Health Centers. The committee reviewed very carefully the Guides for Management of Union Health Centers released by a Joint Committee on Medical Services and Industrial Health of the American Medical Association. The following guides have been adapted with minor modifications only.

GUIDES

I. Adherence to Ethical Principles

The organization of health centers, forms of medical practice, and types of remuneration acceptable to both the physician and the sponsors of the program should be in accordance with existing laws and should be in keeping with the Principles of Medical Ethics of the American Medical Association.

II. Establishment of Fee Schedule

Since so many variables may affect fee schedules in different sections of the country, no attempt has been made here to be specific in suggestions for formulating a schedule, except that it should be acceptable to the local county medical societies, to unions, to management, and to administrators of health and welfare funds.

III. Supplementary Benefits

It is desirable that each health center program shall include insurance or other coverage for hospital service and for medical and surgical care. Such coverage may depend upon funds available to the individual plan and may be administered separately or by the health center organization.

IV. Physical Facility

If a health center is to be established, an adequate medical facility is essential for competent medical and surgical work. Completeness and adequacy of the physical plant must be determined for specific categories, dependent on prospective case load and location.

V. Governing Body

It is desirable that the governing body shall be composed not only of representatives of the lay group which furnishes the funds, representatives of the medical staff, and the medical administrator, but may also include representatives of the community. Its composition may be subject to the laws of the respective states.

VI. The Medical Staff

A. The center should have a full-time or part-time medical director who is a qualified doctor of medicine. He should have charge of the medical administration and participate, ex officio, in the deliberations of the governing board.

B. All phases of medical work should be under medical control. The medical director and medical staff have the responsibility for seeing that the traditional personal confidential relationships between the physician and the patient are preserved and for interpreting other criteria of ethics.

C. Further, members of the medical staff should have their duties and responsibilities clearly defined by the medical director. A medical board of the medical staff should be established in accordance with the recommendations of the Joint Commission on Accreditation of Hospitals. The medical staff should have a voice in general medical policymaking through its own representatives. The usual medical board functions, including the choice of officers, the acceptance of bylaws, and the organization of specific committees on program, formulary, grievance, and other matters, should be followed.

D. Periodic staff meetings should be held to consider policies, staff functions, and appointments. Review of cases, especially problems peculiar to the industry involved, should be an integral part of staff meetings.

E. Standards for departmentalization and appointments, including procedure, qualifications, and tenure, are to be arranged insofar as practicable.

F. A plan of arbitration of disputes or grievances between members of the medical staff and/or the medical director and/or the lay administrator or lay board should be provided through a joint conference committee. This mechanism should be set in advance. The local county medical society should be ready to appoint committees to assist in settling unresolved disputes.

G. An adequate auxiliary staff is essential for the proper functioning of the program. Administrators, accountants, and clerical staff should be adequate for the maintenance of records and other administrative and clerical duties. The medical ancillary staff should include properly registered or qualified technicians in physical therapy, x-ray, laboratory, and other technical diagnostic fields; graduate registered nurses, practical nurses, and nurses aides sufficient to cover the needs of the medical service; nutritionists; social workers; and a registered pharmacist where a pharmacy is maintained in connection with the facility. The composition of the auxiliary staff will depend on the extent to which service can be offered and shall be under the direction of the medical director.

VII. Medical Records and Reports

The maintenance of accurate and complete records on every patient examined and treated is a basic principle. Patients may consult another physician for an additional opinion, or for some other germane reason.

In such instances, physicians requesting data on previous tests, medical history, x-ray examination, and the like should have these made available to them, provided the health center has the written authorization of the patient for access to his file. Reports of progress and evaluation should be maintained to serve as a basis of measuring results.

VIII. Publication Activities

A. *General Publicity.* Basic to any promotional activities are three specific aspects: (1) the complete honesty of all statements and publications, with no possibility of misleading content; (2) the avoidance of the use of the names of medical members of the staff for publicity or promotional purposes, in keeping with the Principles of Medical Ethics; (3) public advertising should not take advantage of the practicing physician in the community or be in conflict with medical ethics.

B. *Health Education.* Where publications are used as a part of health education, there should be no attempt to exaggerate or unduly feature personnel or facilities. Emphasis should be placed on preventive medicine and early diagnosis such as routine chest x-rays and periodic health examinations—those aspects which will lead to the center's greatest utilization by its members. A primary purpose of a health maintenance program for workers is health education. The medical organization has accomplished this purpose when its members seek medical service from physicians, whether or not they are connected with its organization.

C. *Scientific Publications and Other Required Reports.* Scientific reports and publications by members of the health center staff to the medical profession, to unions where required under union rules, and to state agencies where required by law shall be governed by established principles and practices.

IX. Professional Relations

The inherent strength of a medical service plan will be in direct ratio to the degree of satisfactory relationships that prevail between the administrators and medical staff of its organization and the local physicians in the community.

A. *Relationship with Medical Society.* Since all physicians serving a medical group should be members of the local medical society or eligible for such membership on application, it can be a joint responsibility for the group physicians and the members of the society to have direct information and reports on the structure and activities of the health center. The committees and meetings of the society, as well as the bulletins and reports of the center and of the society, should be effective mediums in this respect.

B. *Availability of Facilities.* It is desirable that a health center make its facilities available, insofar as reasonable and possible, to local physicians and their patients of the employee group, even when such physicians are not affiliated with the health center.

C. *Cooperation of Staff and Local Physicians.* A spirit of cooperation between the medical staff of the health center and other doctors of medicine should prevail if the best interests of the subscribers and patients, and of medicine as a whole, are to be served effectively.

D. *Medical Policy.* Because local situations vary in different parts of the country and in various types of communities, modifications of medical policy may have to be accepted by health centers organizing in specific areas. Usually, medical policies are developed and accepted by physicians to meet local needs. The newcomer will exercise good judgment if he considers established customs and facilities, assuming of course that such do not conflict with effective medical care and the Principles of Medical Ethics.

E. *Participation.* In the selection of doctors of medicine to participate in management of union-sponsored programs, it is urged that the counsel of the local medical society be sought. The nature of counsel will depend on the size of the community, the total population, specific medical and surgical needs, and other factors.

F. *Complaints.* Plans should be made for judicious consideration of complaints stemming from health center personnel, patients, or local practicing physicians. If such complaints cannot be satisfied within the institution, the cooperation of the local medical society may be sought. If a local medical society believes that a health center program is in conflict with the Principles of Medical Ethics or that a poor quality of medical service is being supplied or that a member or members of the medical staff indulge in illegal or other objectionable practices, every effort should be made to hear, record, and resolve differences. Experience has shown that a joint committee may be helpful. The cooperation of the county, state, and national bodies may be sought in order to maintain the high standards of ethical conduct physicians have established before the general public. Proper action on the local level would often expedite settlement and thus avoid additional action through state and national bodies. In the event of a question of policy between the medical plan and organized medicine or physicians in the community, the matter may be directed to the Judicial Council, the Council on Medical Service, or the Council on Industrial Health of the American Medical Association. (See A.M.A. Guides for Conduct of Physicians in Relationships with Institutions, 1951—Reaffirmed, 1954.) These bodies may then place the matter before the proper committee for adjustment or arbitration of the dispute. The procedures for adjustment or decision in policy should follow the channels of the local society, to the state society, and to the national society by process of recommendation or by process of appeal.

X. Public and Community Relations

There are many social, public health, and welfare agencies, both public and voluntary, concerned with the health and well-being of local citizens. It is the responsibility of health center personnel to maintain good and effective relations with the staffs of such organizations.

As one aspect of this responsibility the health center is urged to provide a free choice of medical service to the patient it serves. When service outside a specific center facility cannot be paid for under the terms of the plan, patients should be informed that they are privileged to obtain such services as they wish outside the center at their own expense.

Finally, to the extent that these guides are observed, the medical profession will improve the quality of medical care accorded the patient and the community.

These guides are just that and nothing more. They are not policy that has been established by the Council Committee on Industrial Health.

We believe that each county medical society can use these guides to formulate its own policy in regard to the formulation and operation of union and management health centers. We believe that the local county medical society knows best the local needs for the formulation and operation of these centers. The Council Committee on Industrial Health is available to local county medical societies in their discussions with proponents of these centers.

The Bureau studied several union health centers in the Greater New York area followed by informal discussion with union officials. The survey attempted to study the services offered by selected union health centers and to correlate them to the objectives and functions of occupational health programs established by management.

Nine union health centers, serving a total of about 180,000 members and 550,000 dependents, were surveyed. Membership in union health centers ranged from 2,000 to 50,000. None of the centers rendered care for compensable disorders. Only two are utilized for preplacement physical examinations, such services constituting only a small portion of the total services rendered. It may be noteworthy that the centers that did such services were directed by physicians trained and experienced in preventive and occupational medicine and had medical experience in the industry served by the union membership. The background of the other directors varied from general practice to surgery, orthopedics, internal medicine, and obstetrics and gynecology.

Four of the centers established by unions with a membership of less than 10,000 limited their services to diagnostic procedures only. The remaining five union health centers rendered diagnostic as well as therapeutic care to ambulatory patients. The services of an industrial engineer were available at one center only and were utilized as required to make inspection tours in cooperation with the medical director.

The rate of utilization varied from one half to one third of those eligible. Only one center offered services during hours which did not interfere with regular working hours. Although few unions had retired members at the inception of their union health center, the number of retired members is steadily increasing and the number of services rendered to such members is on the rise.

The physical layout of most of the large centers is quite impressive, and many are operated with a fair degree of efficiency. Several facilities are equipped with modalities for which there is very little need or use and for which there is a lack of skilled personnel to effect their operation. Although staffing with medical personnel rarely presents a problem, there is at times a shortage of ancillary medical personnel. Combined with underutilization of equipment this can create an impression of inefficient planning and management. Under these circumstances, the merging of several facilities into one unit may provide a way towards better utilization of personnel and equipment, but may lead to insurmountable organizational difficulties.

It would be interesting to compare the general health and the improvement of health status of people cared for in the union health center with a similar population group which does not have the benefit of union health care. The task of evaluation of this aspect of union health center care is difficult and time-consuming and was not pursued in this study.

Few patients can appreciate the quality of medical care received or the skill, training, and knowledge of those who minister to them. Although the care received by many participants may not measure up to expectations, it seems to fill a need of many who, through sheer apathy and ignorance of available community facilities, might go without adequate medical care.

From the information gathered in this survey it was concluded that the services offered in most union health centers neither duplicate nor interfere with in-plant occupational health programs. The centers could be utilized to supplement such programs but generally do not stress the preventive health aspect which is one of the major responsibilities of any good in-plant health service.

It is planned to have a formal evaluation of the results in the near future, including participation of labor, management, and hospital officials.

General. The director of the Bureau attended the 4th Annual Institute for Physicians in Industry at the Columbia University School of Public Health and Administrative Medicine. He also attended the National Health Forum; the meetings of the New York State Society of Industrial Medicine, Inc., the American Medical Association Medical Legal Symposium held in New York City in April; the annual meeting of the Medical Society of the State of New York in Rochester, and the American Medical Association convention in New York City in June.

He was present also at the inaugural session of the Section on Occupational Medicine of the New York Academy of Medicine and at the meeting of County Medical Society Officers. He attended the 21st Annual Conference on Occupational Health in Denver, October 2 to 4, 1961; the meeting of the American Public Health Association in Detroit, November 13 to 17, 1961, and the public hearings of the Joint Legislative Committee on Industrial and Labor Conditions on November 30, 1961, in New York City.

Respectfully submitted,
PETER J. DINATALE, M.D., *Chairman*

Hospital and Professional Relations

To the House of Delegates, Gentlemen:

The Hospital and Professional Relations Committee consists of the following:

Raymond S. McKeeby, M.D., *Chairman*	Broome
James Bordley, III, M.D.	Otsego
Harold T. Golden, M.D.	Herkimer
Joseph A. Kinnaman, M.D.	Nassau
Robert A. Moore, M.D.	Kings
John J. Murphy, M.D.	Suffolk
E. Dean Babbage, M.D.	Erie
Robert George Hicks, M.D.	New York

A joint meeting of the Medical Affairs Committee of the Hospital Association of New York State and the Hospital and Professional Relations Committee of the Medical Society of the State of New York was held on Wednesday, November 15, 1961, at the State Society Headquarters, 750 Third Avenue, New York City.

The primary purpose of the meeting was to discuss and, if possible, make recommendations concerning the problem of apparent discrimination of medical staff appointments currently under study by Health Commissioner Herman E. Hilleboe, M.D., at the direction of Governor Rockefeller. The study was prompted by the Governor in his veto of Assembly Bill Int. No. 4849—Rules Committee:

> "Amend §256 Insurance Law, to permit use of special contingent surplus fund of medical or dental expense indemnity or hospital service corporation for hospital beds and facilities required by insured entitled to comprehensive medical care in hospital or medical group practice unit under contract with medical expense indemnity corporation if superintendent finds that such beds and facilities are lacking, inadequate or so restrictive as to prevent such unit from providing in-hospital services to insured. Rules Committee"

In answer to the request that a statement be issued concerning the subject, the following general principles were arrived at after considerable discussion:

"The governing body of a hospital has the legal right to appoint the medical staff and the moral obligation to appoint only those physicians who are judged by their fellows to be worthy, of good character, qualified, and competent in their respective fields.

"Individual character, competence, experience, and judgment should be the criteria for selection.

"1. Under no circumstances should the accordance of staff membership or professional privileges in the hospital be dependent solely upon certification, fellowship, or membership in specialty board or society.

"2. The applicant's race, creed, and national origin should not influence his appointment.

"3. His hospital or medical insurance affiliation should not be a consideration in his appointment.

"4. The continuation of any physician's appointment should depend upon his fulfilling the obligations of membership on the medical staff of the hospital."

It was the intent that the action of this Joint Committee be presented to their respective bodies for their consideration.

At the meeting of the Council of the Medical Society of the State of New York on November 16, 1961, this report of the joint meeting was approved.

At the September 28, 1961, meeting of the Council of the Medical Society of the State of New York, a "Draft of Proposed Rules and Recommendations for Hospitals in New York State" put out by the New York State Department of Social Welfare was introduced. After going over these regulations and the statement in the foreword, "at the conclusion of a trial period the Department will evaluate the results, weigh the experiences of the hospitals and make final recommendations to the Board. Such recommendations as the Board adopts will become official mandatory rules with the force and effect of law," it was realized that this would present a dangerous and impractical set of regulations which hospitals and staff members would be unable to expedite.

Since there were many objections by members of the State Medical Society and various groups that had passed resolutions condemning the draft, the whole problem was turned over to the Hospital and Professional Relations Committee for further study.

At a meeting held in Albany on December 14, 1961, with representatives of the hospital group who also voiced their disapproval of the draft, Commissioner Raymond W. Houston agreed to set up an advisory committee with representatives from the New York State Hospital Association and representatives from the State Medical Society and further agreed to hold up any expedition of these rules until after a meeting of this advisory group. Drs. Reginald R. Steen, Felix Ottaviano, and Raymond S. McKeeby were representatives of the Medical Society.

A meeting was held on February 28, 1962, in the board room of the New York State Department of Social Welfare, 270 Broadway, New York City, with representatives from the Hospital Association and Medical Society and Commissioner Houston, Deputy Commissioner Robert Shulman, Miss Gertrude Binder, director of the Bureau of Adult Institutions, and Helen Lawler, senior welfare consultant for the Bureau of Adult Institutions, and we discussed the contents of the manual at some length.

After considerable discussion, the following conclusions were reached. Both the representatives of the Hospital Association and those of the Medical Society felt that the proposed rules and regulations were too much in detail and were too mandatory in their application of hospital regulations and staff conduct, despite the fact that there were a lot of very good recommendations in accepted hospital administration. It was suggested by both groups that it would be well for the Department of Social Welfare to look into the standards of the Joint Commission on Accreditation of Hospitals to serve as a basis for hospital regulations. It was pointed out that the rules and regulations of the Joint Commission have been in effect for some time, have stood the test of time, and have been revised and are now accepted widely throughout the State.

At the conclusion of this meeting, representatives from the Department of Social Welfare agreed to look into the Joint Commission standards on hospitals in regard to their needs and then again would consult with the advisory committee to get their reaction to them at a future meeting.

Also at this meeting the feasibility of incorporating the draft of proposed rules and regulations for hospitals in New York State as a guide book for the use of the Department of Social Welfare and as a reference to hospitals was discussed.

The representatives of the Medical Society and the Hospital Association felt that it could be used possibly by the Department but that there was some hesitancy as to its use in the hospitals throughout the State for reasons already given.

By the time the House of Delegates convenes, it is felt that a set of basic rules which will be acceptable to all parties concerned will be drawn up.

A supplementary report will be given at a later date.

Respectfully submitted,

RAYMOND S. MCKEEBY, M.D., *Chairman*

Medical Service

To the House of Delegates, Gentlemen:

The Committee on Medical Service is as follows:

Edward C. Hughes, M.D., *Chairman*	Onondaga
Thurston L. Keese, M.D	Onondaga
Donald C. Walker, M.D.	Schenectady
Eugene R. Duggan, M.D.	Monroe
Fritz Landsberg, M.D.	Schuyler
Robert V. Persson, M.D.	St. Lawrence
Hugh McChesney, M.D.	Oswego
Bert Ellenbogen, New York State College of Agriculture, Cornell University, *Adviser*	Tompkins
Granville W. Larimore, M.D., New York State Department of Health, *Adviser*	Albany

During the year, the committee has met many times to discuss the problem of rural health. Although the title of the committee has been changed to be designated as the Medical Service Committee, most of the work deals with medicine in areas outside of the larger cities.

The problems studied by the committee were as follows: (1) informational health forums for the public; (2) study of the shortage of physicians in rural areas; (3) preparation of a questionnaire to be sent to all physicians outside of the larger cities to obtain their point of view on the need of physicians in their localities; and (4) methods of obtaining physicians for the areas needing physicians.

During the year, another in the "Span of Life" series of informational health forums was held at the New York State Fair in Syracuse, from September 1 to 8. A copy of the program is attached. Over 2,000 people attended these forums. The movies were shown and after each session a discussion was held by a well-known physician. The committee is planning a more extensive program for the next State Fair and will be working out the plans with the local committee of the State Fair headed by Mrs. John Vandervort, Director, Women's Division, New York State Fair.

The committee will present to the Council, at its next meeting, a plan for obtaining physicians for rural areas. The plan states that the Empire State Medical, Scientific and Educational Foundation should be given the responsibility of planning the program. The program would entail seeking grants from industry and other sources to finance the program. A committee of the Foundation would survey the locality seeking a physician to discern the need, sponsor but not pay for a fund-raising campaign to construct an adequate office for the physician or physicians, and help obtain a physician who would assume the responsibility of the building either by purchasing or renting and amortizing it over a period of ten years. The plan also recommends that the State Board of Trustees of the State University of New York recommend to the medical centers operated by the State that more orientation be given the student for general practice in the rural areas.

Respectfully submitted,

EDWARD C. HUGHES, M.D., *Chairman*

The following is the program for the health forums presented at the New York State Fair in Syracuse:

SPAN OF LIFE*

September 1—Education and Youth Day: *Careers in Health Fields,* film "Helping Hand for Julie" discussed by Larry Pickett, M.D., clinical associate professor of surgery; *Facts About Birth,* film "Generation to Generation" discussed by Albert W. Van Ness, M.D., clinical professor of obstetrics; *Facts About Cancer,* films "Self Examination of Breast" and "Time and Two Women" discussed by Dr. Van Ness; *Know Your Heart,* film "Coronary Heart Disease" discussed by Donald Samson, M.D., associate professor of medicine; *Diabetes,* film "Diabetes and You Too" discussed by Dr. Samson.

September 2—Youth Day: *Facts About Birth,* film "Generation to Generation" discussed by James E. Covell, M.D., clinical assistant professor of obstetrics and gynecology; *Facts About Cancer,* films "Self Examination of Breast" and "Time and Two Women," discussed by Dr. Covell.

September 3—Family Day: *Facts About Birth,* film "Generation to Generation" discussed by Raymond Pieri, M.D., clinical professor emeritus, Department of Obstetrics; *Facts About Cancer,* films "Self Examination of Breast" and "Time and Two Women" discussed by Dr. Pieri; *Accident Prevention,* film "One Day's Poisoning" discussed by Arnold Moses, M.D., clinical instructor of medicine; *Facts About Your Heart,* film "Congenital Heart Defects" discussed by Dr. Moses; *Diabetes,* film "Diabetics Unknown" discussed by Dr. Moses.

September 4—Labor Day: *Facts About Birth,* film "Generation to Generation" discussed by Robert Zimmer, M.D., clinical instructor of obstetrics; *Facts About Cancer,* film "Time and Two Women" discussed by Dr. Zimmer; *Accident Prevention,* film "One Day's Poisoning" discussed by J. G. Fred Hiss, M.D., clinical professor emeritus of medicine; *Facts About Your Heart,* film "Coronary Heart Disease" discussed by Dr. Hiss; *Diabetes,* film "Diabetes and You Too" discussed by Dr. Hiss.

September 5—Women's Day: *Facts About Birth,* film "Generation to Generation" discussed by Vincent Hemmer, M.D., clinical professor of obstetrics; *Facts About Cancer,* film "Time and Two Women" discussed by Dr. Hemmer; *Facts About Your Heart,* film "High Blood Pressure" discussed by Murray Grossman, M.D., clinical assistant professor of medicine; *Diabetes,* film "Diabetics Unknown" discussed by Dr. Grossman.

September 6—Governor's Day: *Facts About Birth,* film "Generation to Generation" discussed by Ferdinand Schoeneck, M.D., director, Division of Maternal Welfare, Syracuse Department of Health; *Facts About Cancer,* film "Time and Two Women" discussed by Dr. Schoeneck; *Facts About Your Heart,* film "Coronary Heart Disease" discussed by David Nash, M.D., clinical instructor of medicine; *Diabetes,* film "Diabetes and You Too" discussed by Dr. Nash.

September 7—Senior Citizen's Day: *Facts About Birth,* film "Generation to Generation" discussed by Charles Gwynn, M.D., clinical professor of obstetrics; *Facts About Cancer,* films "Self Examination of Breast" and "Time and Two Women" discussed by Dr. Gwynn; *Accident Prevention,* film "One Day's Poisoning" discussed by Maynard Holmes, M.D., clinical professor emeritus of medicine; *Diabetes,* film "Diabetics Unknown" discussed by Dr. Holmes; *Facts About Your Heart,* film "Coronary Heart Disease" discussed by Dr. Holmes.

September 8—Government Day: *Facts About Birth,* film "From Generation to Generation" discussed by Merton Hatch, M.D., clinical professor of obstetrics; *Facts About Cancer,* films "Self Examination of Breast" and "Facts About Cancer" discussed by Dr. Hatch; *Accident Prevention,* film "One Day's Poisoning" discussed by Arthur Dube, M.D., clinical assistant professor of medicine; *Facts About Your Heart,* film "Stroke" discussed by Dr. Dube; *Diabetes,* film "Diabetes and You Too" discussed by Dr. Dube.

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* All speakers were from the State University of New York Upstate Medical Center at Syracuse.

Questions of Ethics

To the House of Delegates, Gentlemen:

The Committee on Questions of Ethics has the following members:

Harold F. Brown, M.D., *Chairman* . . . . . Erie
Frank LaGattuta, M.D. . . . . Bronx
David Lyall, M.D. . . . . New York
Ezra A. Wolff, M.D. . . . . Queens

The committee held a meeting on September 27, 1961, and considered the following matters which were reported to the Council on September 28:

1. A questionnaire from the American Medical Association asking our policy in regard to ownership of pharmacies or pharmaceutical companies by doctors of medicine and asking whether we had received any complaints or inquiries about such ownership.

Our reply was that we feel there is nothing inherently wrong with such ownership unless it exploits the patient but that, in the case of one inquiry which we had received, we had advised the county society concerned that it was unethical for a member to permit his name to be used in the stock promotion campaign of a company of which he was president.

2. Over the signature of a physician member of a county society, letters and other material were mailed to physicians throughout the country by a laboratory in this State, describing its diagnostic test services. The medical society of the county in which the laboratory is situated asked our advice.

We replied that Chapter I, Section 4, of the *Principles of Professional Conduct* (referring to professional advertising and self-laudation) appeared to be relevant in the case at issue. It is the opinion of the Ethics Committee that it would be the function of the board of censors of the county society to decide whether or not the physician sending out such material had violated this section of the *Principles of Professional Conduct.* It was also suggested that the specialty board of which the physician was a member might be asked whether or not they approved such circularization.

3. An inquiry from a county medical society as to whether or not a doctor of medicine ethically could recommend patients to a member of the Electrolysis Society of America.

We replied that we had no way of evaluating the competence and ethics of the membership of that society and that we would notify the county society when information was available from legal counsel as to the legal responsibility of a doctor of medicine who refers patients to an electrolysist.

The Committee was polled by letter or telephone regarding the following matters which were reported to the Council on October 26, 1961, and January 25, 1962:

4. An inquiry regarding the ethics of incorporating (for tax purposes) the phase of a member's practice concerned with supplying allergenic extracts to other doctors for patients who are being treated under the supervision of the member who supplies the extracts.

The committee replied that the procedure is not unethical provided (*a*) the product is of an intrinsically ethical character, (*b*) the patient is not exploited, and (*c*) the usual limitations are observed concerning use of the doctor's name in promoting the product.

5. We received an inquiry from a member of a county society as to the ethics of participating in the clinical trial of a pharmaceutical product. This would consist of one injection of a drug of proven efficacy, evaluation of clinical side-effects, and report to the manufacturer for a fee of $5.00 per patient.

We replied that this is ethically permissible provided the results are honestly arrived at and no unethical advertising arises therefrom.

The following inquiries were answered by the chairman and reported to the Council on June 15, 1961, November 16, 1961, and January 25, 1962:

6. Is it ethical for one physician to tell another in confidence that a third physician is incompetent?

Answer: It is highly irregular. The third physician should complain to his county society if he thinks he is being maligned.

7. Information was sought by an individual regarding (*a*) the need for a surgical assistant at his appendectomy, (*b*) the method of paying the assistant, (*c*) the right under a Blue Shield contract of choosing an anesthetist covered by his contract, (*d*) the proper fee for anesthesia, and (*e*) the manner in which he was dunned with a bill for anesthesia ninety days after the operation.

A partial explanation was sent to this gentleman, and his inquiry was forwarded to the county medical society involved, with a request that it be investigated by their board of censors and answered.

8. An inquiry from a physician in New Jersey as to whether or not it is a violation of medical ethics for a doctor's name to be used in the advertising of The Tobacco Guidance Center and as to the value of the product which they sell was presented to the Council in November. Although the doctor involved is not a member of our State Medical Society, the Council referred this inquiry to the medical society of the county in which he is located.

9. Inquiry was made as to whether or not it was ethical for a physician to cooperate with a certain clinical laboratory. This laboratory states "that is the physician will do the billing and/or collect the specimen; they will accept

75 per cent of the laboratory fee involved, thus allowing the physician 25 per cent of the total without increasing the standard charge to the patient."

They were informed that such a procedure would violate Chapter I, Section 6, of the *Principles of Professional Conduct.* The part of this section which seems applicable to the circumstances mentioned reads: "The acceptance of rebates on prescriptions or appliances or of commissions from attendants who aid in the care of patients is unethical. . . . He [an ethical doctor of medicine] should receive his remuneration for professional services rendered only in the amount of his fee specifically announced to his patient at the time the service is rendered or in the form of a subsequent statement, and he should not accept additional compensation, secretly or openly, directly or indirectly, from any other source, except as provided in Article VI, Section 3 of Chapter III," of the *Principles of Professional Conduct.*

10. Information was sought concerning the "Medic-Alert Foundation International" located in Turlock, California, as to whether that organization is entirely on the ethical and nonprofit basis which it asserts to be. This information was channeled to the A.M.A. They replied that this foundation is known to them as a nonprofit corporation which provides an engraved identification device and maintains a twenty-four-hour information service regarding the medical problems of its members for all who pay a membership fee and supply information regarding their medical needs. M. C. Collins, M.D., president of Medic-Alert Foundation International, has been named by the trustees of the American Medical Association to membership on the A.M.A. Committee on Emergency Medical Identification.

The A.M.A. committee is attempting to determine a universally applicable technic for emergency medical identification and has not as yet felt ready to report its opinion. Until the committee has completed its studies, individual medical associations will have to make decisions on emergency medical identification technics in terms of the local situation.

The committee again reminds the House that nowhere in the Constitution and Bylaws is there any mention of a Committee on Questions of Ethics and that nowhere is there delineated the scope of activities of such a committee.

Respectfully submitted,

HAROLD F. BROWN, M.D., *Chairman*

Public Health and Education

Public Health and Education

To the House of Delegates, Gentlemen:

The Council Committee on Public Health and Education has the following membership:

James Greenough, M.D., *Chairman*	Otsego
Wendell R. Ames, M.D.	Monroe
Irving L. Ershler, M.D.	Onondaga
Milton J. Goodfriend, M.D.	Bronx
Harry S. Lichtman, M.D.	Kings
Edward F. Marra, M.D.	Erie
Robert E. L. Nesbitt, Jr., M.D.	Onondaga
James Perkins, M.D.	New York
Herman E. Hilleboe, M.D., Commissioner, New York State Department of Health, *Adviser*	Albany
Leona Baumgartner, M. D., Commissioner of Health, City of New York, *Adviser*	New York
Abraham M. Rabiner, M.D., *Adviser*	Kings

The committee met with the chairmen of most of the subcommittees on July 12, 1961, and again as a committee on December 15, 1961.

Some major changes in the management of the committee and its subcommittees took place during the year. The chairman undertook to work full time for the committee as of October 1, 1961. Two new subcommittees have been approved by the Council and appointed by the president as of March 1, 1962. The first of these is a Subcommittee on Chronic Pulmonary Disease including tuberculosis; the second, a Subcommittee on Continuing Postgraduate Education. The need for special subcommittees concerned with these matters is self-evident.

A departure from previous procedure was the calling of the committee meeting July 12, 1961, in the Health Department council room with a chairman or representative from 15 of the 17 subcommittees. For the first time it became evident to the chairmen that each subcommittee was an integral part of the effort our Society is making to improve the health services for the entire State. Areas where two or more subcommittees overlapped and could work together to great advantage became apparent. As examples we have rehabilitation of the inmates of nursing homes, or diabetes or cancer detection among the aged, or education of school children regarding alcohol or narcotic addiction. The committee hopes to repeat such an orientation meeting another year.

Resolution 61–15, "Improved Procedures for School Physical Examinations," was referred to this committee and discussed with the Subcommittees on School Health and General Practice. The former subcommittee is at present arranging a meeting with members of the Education Department to urge adoption of periodic rather than annual physical examinations of school children. The subject was on the agenda of the meeting of the Subcommittee on General Practice on January 31, 1962.

Resolution 61–19, "Establishment of Departments of General Practice in Medical Schools," has been referred to the Subcommittee on General Practice and was also on the agenda for the January 31 meeting.

Resolution 61–24, "Oral Prescription of Class B Narcotic Compounds," was referred to the Subcommittee on Alcohol and Narcotic Addiction. This subcommittee is aware of the fact that the Advisory Committee on Narcotics to the State Department of Health had on May 3, 1961, approved action such as that described in the above resolution. No further action seems necessary than to promote attempts to alter the law to effect this change.

During the year the Public Health and Education Committee has reviewed the relationship between the State Society's activities and the activities of county medical societies in this field. Obviously many of the smaller counties cannot duplicate the State Society committee setup, which some of the larger counties certainly could and should. It is hoped that before the annual meeting the chairman will have had an opportunity to discuss the matter with many of the county medical society officers. Next year it is planned that each State subcommittee will have a vice-chairman as well as a chairman.

While a subcommittee directly involved with continuing postgraduate education has been appointed, it is not anticipated that this subcommittee will accomplish many changes in the immediate future. As was reported last year, the committee has for some time hoped for a study in depth on this subject. Attempts to obtain a grant for such a study were made during the year, but in July we learned that Governor Rockefeller was planning to appoint a committee to review all phases of medical education and it was suggested that our study await this action. As you know, such a committee was appointed late in 1961, consisting of Mr. Malcolm Muir, chairman, Thomas Parran, M.D., and William P. Willard, M.D. Our subcommittee hopes to study the findings of the Governor's committee closely and then attempt to improve our own continuing education program.

As you will note in the reports of the Subcommittees on Heart Disease and Mental Hygiene, the use of seminars or preceptor training is developing and increasing.

Your chairman attended three public hearings of the Joint Legislative Committee on Motor Vehicles and Traffic Safety and spoke strongly in favor of the organization of a research committee under the State Department of Health in order to ascertain, if possible, factors producing automotive deaths and injuries and methods for their prevention.

The committee approved a change made by the Health Department in the birth certificate, placing the color, race, and serology of mother and child in a different confidential portion of the certificate.

The committee also reviewed and approved the new edition of the Laboratory Manual of the State Health Department.

An exhibit by the Public Health and Education Committee or one of its subcommittees is being arranged for the Annual Health Conference in Syracuse in June, 1962.

The pamphlet, *What Goes On*, as of January 1, 1962, became a publication of the Medical Society of the State of New York. As before, the physicians in New Jersey also will receive this publication. It is now planned to extend coverage to the osteopaths of New York State.

I would urge you to examine the reports of the 17 (now 19) subcommittees to see how much these subcommittees are accomplishing. Note among other activities the start of a pamphlet to list rehabilitation facilities in the State, efforts to promote education on addiction in the schools, concerted attempts to bring training in emergency resuscitation to all the doctors of the State, work to improve the care of the aged in our State, and many, many other activities.

I wish to express my thanks to the members of these subcommittees and the members of the Committee on Public Health and Education for assistance that has made possible any progress which we have seen during the year.

To Herman E. Hilleboe, M.D., State Commissioner of Health, and his staff, to Leona Baumgartner, M.D., and her staff go my personal thanks and certainly the gratitude of the State Society for their continuing cooperation and assistance in the work of the committee. I hesitate to mention individuals since we get help from so many in the Departments, but I must pay tribute to Granville W. Larimore, M.D., for assistance in our whole program and Frank B. Amos, M.D., for help in the postgraduate education portion of the program.

May I also express thanks to our president, Dr. Galbraith, to Miss Doris K. Dougherty, Executive Assistant, to Miss Susan V. Baker, the administrative assistant to the committee, and to Miss Dorothy Kelleher, the editor of *What Goes On*. The entire staff of the Society from Dr. Fineberg down has helped me and the committee in so many ways throughout the year that I cannot possibly enumerate them.

Since submitting its annual report for 1960–1961, the committee has arranged, or has helped arrange, as of February, 1962, postgraduate instruction for 30 groups, presented as lecture series, symposia, single lectures, or teaching days. A total of 113 speakers have already participated or will participate in these meetings. We are always cognizant of the important contribution made to the program by the State Department of Health in providing the $25 honorarium to these speakers, and we again express our thanks. We should like to remind county medical society program chairmen to submit their requests as far in advance of the meetings as possible. This ensures a better selection of speaker and enables us to insert a notice in the *What Goes On* monthly bulletin.

Of the following list of postgraduate sessions, five were arranged by the Postgraduate Education Department of the State University of New York College of Medicine at Syracuse in cooperation with our committee.

County	*Organization*	*Number of Speakers*
Albany	Medical Society	2
Broome	Binghamton Academy of Medicine	1
Cayuga	Medical Society	1
Chemung	Medical Society	1
	Medical Society and AGP	1
Chenango	Medical Society	5
Cortland	Medical Society	3
Dutchess	Medical Society	4
Fulton	Medical Society	3
Herkimer	Medical Society	1
Jefferson	Medical Society	4
Niagara	Medical Society	2
Oneida	Utica Academy of Medicine	8
Ontario	Medical Society	4
	Geneva Academy of Medicine	9
Putnam	Medical Society	1
Rensselaer	Medical Society	9
St. Lawrence	Medical Society	2
Schenectady	Medical Society	1
Steuben	Medical Society	3
Suffolk	Medical Society	10
	South Side Clinical Society	4

Sullivan	Medical Society	7
Tompkins	Medical Society	2
Ulster	Medical Society	1

Regional Meetings and Teaching Days. For regional meetings and regional teaching days, invitations are sent to the members of the medical societies in counties adjacent to the one in which the instruction is given. The committee usually arranges for the speakers, has envelopes addressed for the memberships of the county societies, and reimburses the sponsoring county medical society for the cost of printing the programs and the postage.

This year the following such meetings have been held:

County	*Region*	*Subject*	*Number of Speakers*
Broome Medical Society	Broome, Chemung, Chenango, Cortland, Delaware, Otsego, Schuyler, Tioga, Tompkins	Cardiology	7
Lady of Lourdes Memorial Hospital		Cancer	4
Oneida Utica Academy of Medicine	Broome, Chenango, Herkimer, Jefferson, Lewis, Madison, Oneida, Onondaga, Oswego, Otsego, St. Lawrence	Trauma	4
Utica Academy and County Tumor Clinic		Cancer	5
St. Lawrence County Society and Mental Health Board	Clinton, Essex, Franklin, Jefferson, St. Lawrence	Psychiatry and the General Practitioner	4

Respectfully submitted,

James Greenough, M.D., *Chairman*

Reports of the subcommittees follow:

Accident Prevention

The Subcommittee on Accident Prevention has the following membership:

S. Bernard Wortis, M.D., *Chairman*	New York
Arthur S. Abramson, M.D.	Bronx
Harold Brandaleone, M.D.	New York
Goodwin M. Breinin, M.D.	New York
Edmund P. Fowler, Sr., M.D.	New York
Richard H. Freyberg, M.D.	New York
Milton Helpern, M.D.	New York
Walter D. Ludlum, M.D.	New York
Norman Plummer, M.D.	New York
John H. Powers, M.D.	Otsego
H. Houston Merritt, M.D., *Adviser*	New York
Abraham M. Rabiner, M.D., *Adviser*	Kings

There have been no meetings of the subcommittee this past year. However, again there have been numerous instances where the New York State Department of Health has sought advice in counseling the Department of Motor Vehicles regarding cases where the renewal of the operator's license was questionable because of single or multiple occasions of lapse of consciousness. Also, there have been a few instances where physicians have refused to draw blood samples from persons involved in vehicular accidents who were suspected of being drunk. The chairman of the parent committee has written each doctor, explaining his legal status in such cases and urging cooperation with the State Police in the future. At a meeting of the parent committee with chairmen of all subcommittees in Albany in July, 1961, it was agreed to investigate the possibility of determining the alcoholic content of the breath. It was recommended that the standard for drunken driving should be reduced to 0.10 per cent blood alcohol content.

It was also decided to attempt to obtain information in New York State and other states which would enable the State Society to recommend to the Motor Vehicle Commissioner physical standards for automobile drivers.

It was agreed to stress throughout the year the use of safety belts. Letters have been sent to county medical societies urging their promotion of seat belts. An article will be prepared for the New York State Journal of Medicine by Robert Korns, M.D., of the State Department of Health, on the use of seat belts. A letter was written by your chairman recommending that these be required in school buses.

Also at the July meeting there was discussion regarding penalties for moving infractions. It was felt that if the penalty was too severe it would not be enforced.

The chairman of your Council Committee attended three hearings of the Joint Legislative Committee on Motor Vehicles and Traffic Safety. Among other subjects Senator Speno stated that he wished to establish a research committee on motor vehicle safety. There was some indecision as to whether this committee should be established in the Motor Vehicle Department or the Health Department. At the third meeting, after consulting with the president, your chairman presented a statement advocating the placing of this committee in the Health Department.

The Council Committee concurred with the Health Department in the recommendation that determination of physical standards for applicants for operator's licenses should be postponed until more factual data are available.

Another suggestion made at the July meeting was that medical films might be a means of educating the physicians and the public regarding automobile safety.

Addiction to Alcohol and Narcotics

The Subcommittee on Addiction to Alcohol and Narcotics is composed of the following members:

Marvin A. Block, M.D., *Chairman*	Erie
Herbert Berger, M.D.	Richmond
Leonard L. Heimoff, M.D.	Bronx
Jerome L. Leon, M.D.	Queens
Webster M. Moriarta, M.D.	Saratoga
Henry Brill, M.D., *Adviser*	Albany
Granville W. Larimore, M.D., *Adviser*	Albany

1. A special committee of our subcommittee was appointed to look into all the activities relative to narcotic addiction and its treatment in the metropolitan New York area. Since most of the narcotic problem is limited to the New York City metropolitan area, and the rest of the State has comparatively little of this problem, it was deemed advisable that the activities in this field be in the charge of the two men residing in the area involved. A report of this committee will be submitted at our next meeting.

2. It was decided that the activities of our Medical Society emphasize the desirability of detecting and helping those narcotic addicts who evince a desire for treatment and whose motivation is good. Rather than spend a great deal of effort on that segment of the addict population which becomes involved with the law and whose motivation is directed toward outwitting the law rather than attaining recovery, physicians could do better in helping those addicts in the population who are well motivated and who seek their help. It was emphasized that practicing physicians, particularly family physicians, should be alerted to the opportunities of case-finding of such patients in their practices. Our subcommittee urges that all members be so alerted. The general tenor of these suggestions was in accordance with the views of the representative from the Department of Mental Hygiene.

3. In the matter of the attitude of the Board of Regents relative to the disciplinary action meted out to physicians who suffer from alcoholism, the subcommittee felt that it would take no action unless requested to do so by an individual physician who had been disciplined. When this occurs and such a request is made, the subcommittee agreed that this would be the appropriate time for action. Until such time this matter was tabled.

4. On December 11 the chairmen on alcoholism from all the counties in the State were invited to a meeting with our subcommittee. About 20 counties were represented. This was an excellent turnout, and the discussion was lively and enlightening. Copies of the survey of physicians made in Erie County relative to the problem of alcoholism were distributed to those present. Suggestions were made regarding the stimulating of interest of practicing physicians, in the field of alcoholism, and the chairmen were urged to have at least one meeting per year of their respective county societies devoted to the subject of alcoholism. They were further requested to attempt surveys similar to that of Erie County in an effort to ascertain the attitudes of physicians in their respective counties. Speakers on alcoholism were offered, with arrangements to be made through the State Society's Council Committee on Public Health and Education. It was also arranged that the American Medical Association's Manual on Alcoholism would be distributed to the physicians of the State by the subcommittee upon request through the county societies.

It was suggested that further meetings of this type be held and educational programs arranged for subcommittee members as well as others who are interested.

5. The subcommittee cooperated with the Departments of Health and Mental Hygiene in preparing legislation for enactment relative to the Public Health Law concerning the telephone prescription of Class B narcotics.

6. Education on alcoholism and narcotic addiction in the public school system was discussed, and recommendations were made that such education be emphasized in those areas lacking programs. The metropolitan New York area was cited as one area where such education was necessary. Correspondence has taken place with the president of the metropolitan Board of Education.

7. Advances in the field of alcoholism by the State Department of Mental Hygiene were noted and discussed. A new Division on Alcoholism is being established.

8. Promotion of Blue Cross and Blue Shield coverage for patients with alcoholism was urged by the subcommittee, such promotion to be conducted on the county society level with the various Blue Cross corporations.

9. The suggestion that the subcommittee meet with the Subcommittee on Mental Hygiene was endorsed. This should take place sometime in the spring.

Aging and Nursing Homes

The Subcommittee on Aging and Nursing Homes has the following membership:

Joseph J. Witt, M.D., *Chairman*	Oneida
Stephen A. Graczyk, M.D., *Cochairman*	Erie
Marcelle T. Bernard, M.D.	Bronx
Ben Albert Borkow, M.D.	Kings
Lawrence S. Kryle, M.D.	Nassau
Samuel R. Powers, Jr., M.D.	Albany
Charles L. Steyaart, M.D.	Wayne
George M. Warner, M.D., New York State Department of Health, *Adviser*	Albany

There have been six meetings of the Subcommittee on Aging and Nursing Homes since the House of Delegates meeting in 1961. Two of these were devoted to the matter of legislation pertaining to Medical Assistance to the Aged. In addition, two meetings of two members of the subcommittee with Charles B. F. Gibbs, M.D., chairman of the Subcommittee on Diabetes, and George M. Warner, M.D., of the State Health Department, were held.

Legislation. The conclusions of the two meetings on the Metcalf-McCloskey Act were essentially identical. The second meeting was called at the behest of the Committee on Public Health of the New York Academy of Medicine, who wished the benefit of the State Society's advice on possible amendments in order to achieve more nearly the original intent of the sponsors of the national and State legislation. The recommendations of the subcommittee were discussed with the Academy's committee and were approved in essence, as follows:

(1) to confine investigation of assets to the aging individual and spouse; (2) to provide total health care for the recipient of Medical Assistance to the Aged; (3) to ensure the recipient of free choice of physician at all times, and (4) to remove the management of the health program from the Department of Social Welfare to the Department of Health.

Joint Project with State Health Department. The subject chosen for the current year and the 1962–1963 period is diabetes. This project is being conducted in conjunction with the Subcommittee on Diabetes, the State Health Department, the New York State Chapter of the Academy of General Practice, and the American Diabetes Association. It entails an intensive postgraduate education effort in a clinical context to improve the physician's knowledge of the disease, with special emphasis on earlier detection and earlier postprandial testing. At this writing Albany, Bronx, and Oneida Counties have already embarked on active programs. Broome, Cayuga, Chenango, Erie, and Onondaga Counties are preparing similar projects. Agreements have been reached with three of the four upstate medical schools to provide speakers in their areas. Letters have gone to county medical societes, hospital staffs, and health officers.

Cortland County Survey. The subcommittee has been interested in a multiphasic screening survey conducted in Cortland County among persons over forty years of age not under the care of any physician. It was sponsored by the county health department, the county health association, and the State Health Department. The county medical society was listed as giving its approval, although this was procured with reservations on the part of the physicians as to the program's value, as they felt that those screened would be subjected to a number of tests without any clinical evaluation. The public was enthusiastic and looked on the project as a clinic where they would receive a "checkup." Some 2,000 persons were screened for seven tests. To date, for lack of clerical help, the results have not been completely tabulated. When all the records have been processed it may be possible to determine whether or not it is worth while conducting the same sort of project in other counties.

Local Activities. All the members of the subcommittee have been instrumental in pushing programs for the aging in their respective communities. These include "well oldster" clinics; health fairs; questionnaires to determine the definite health needs of the older person in the community; "extended courtesy" agreements calling for the lowering of fees for persons of small resources not only by the physicians but by pharmacists, dentists, and others; proposals for construction by hospitals of buildings for the older patient who is past the critical state of illness; lectures on preparation for retirement; pocket-sized directories of facilities available to people over sixty-five. The subcommittee hopes that eventually information centers may be set up for services to the aging, similar to the poison control centers throughout the State.

Joint Council to Improve the Health Care of the Aged. This organization of which your subcommittee chairman has just been re-elected chairman has been in existence for approximately two and one-half years. The second annual meeting (recessed from November 9, 1961, for a lack of a quorum) was held on January 18, 1962. Among matters considered by the Joint Council at that meeting and at a previous meeting on August 24, 1961, were (1) the "Trussell Report" as it concerned (*a*) possible transfer of authority now vested in hospital boards of trustees, (*b*) the impact of expanded Blue Cross coverage of outpatient care in hospitals, (*c*) the effect of recommendations on nursing homes; (2) proposed King-Anderson legislation; (3) regional conferences.

On September 21, 1962, the first Regional Conference on the Health Care of the Aged was held in Buffalo. The Western New York Regional Council of the Hospital Association of New York State assumed responsibility for the arrangements. A spokesman for each member organization discussed the role of his organization in the health care of the aged and its relationship to the three other member organizations. There were more than 100 registrants and the conference was considered a success. Your chairman was moderator, and Dr. Graczyk, a member of the subcommittee, spoke for the Medical Society.

A second regional conference will be held on March 28 in Garden City with the Long Island Regional Council of the Hospital Association again taking charge of local arrangements. Your chairman will moderate this meeting, also.

Your chairman led a discussion group in the workshop in Geriatric Dentistry held in Utica on September 9 and 10.

On November 17 the chairman attended a White House Regional Conference on the Aging held in New York City at the Commodore Hotel and had an opportunity to voice his opinions regarding payment of medical care for the aged during discussion with the panel on "Better Opportunities for Health and Welfare."

The chairman spoke on "Services for the Aged" at a public hearing of the Joint Legislative Committee on Problems of the Aging in Syracuse on December 14, and on December 15 and 16 he and Samuel Powers, Jr., M.D., a member of the subcommittee, attended the Second Annual Conference of the national Joint Council to Improve the Health Care of the Aged. The chairman spoke on "A Pound of Prevention."

Cancer

The Subcommittee on Cancer is composed of the following members:

John G. Masterson, M.D., *Chairman*	Kings
Daniel Burdick, M.D.	Onondaga
William R. Carson, M.D.	St. Lawrence
Emerson Day, M.D.	New York
Samuel Leo, M.D.	Bronx
Bernard J. Pisani, M.D.	New York
Charles D. Sherman, Jr., M.D.	Monroe
Paul R. Gerhardt, M.D., *Adviser*	Albany
Theodore Rosenthal, M.D., *Adviser*	New York
Roald N. Grant, M.D., *Adviser*	New York

During the past year, the Subcommittee on Cancer has endeavored to promote the wider use of cytologic examinations in the detection of cancer. The advantage of the routine cytology was well demonstrated in the area served by the St. Lawrence County Medical Society where 8 cases of cancer were detected on routine cytologic examinations in 600 patients. This activity in St. Lawrence County has been a direct result of last year's State-wide program of the Subcommittee on Cancer in the field of cytology. In an effort to expand further the cytologic program in the State of New York, the Subcommittee on Cancer approved a resolution recommending that the New York State Department of Health and the New York City Department of Health establish laboratory facilities for the carrying out of cytologic tests free of charge. This service would be similar to the diagnostic laboratory services currently available to all physicians in areas of communicable diseases.

The Subcommittee on Cancer approved with commendation the activities of the Bureaus of Cancer Control of both the New York State Department of Health and the New York City Department of Health. The subcommittee felt that their work should be further encouraged and expanded in the field of cancer control.

At a meeting of the subcommittee a film on the subject of proctoscopic examinations in the early detection of rectal cancer, entitled *Life Story*, was reviewed and was approved on the request of the New York State Division of the American Cancer Society. This film will be used in the educational work of the American Cancer Society.

The Subcommittee on Cancer proposes to discuss with the Joint Hospital Accreditation Commission the possibility of revising the standards on hospital admissions to include routine cytologic examinations on all female patients. The subcommittee feels that the establishment of this procedure would ultimately result in the elimination of certain genital malignancies as a cause of death in our State.

Coordination between the subcommittee, the American Cancer Society, and the State Department of Health is a problem facing the subcommittee. It was suggested at the meeting of subcommittee chairmen in Albany on July 12, 1961, that there be closer liaison between the Cancer Society and our subcommittee. A joint meeting of the New York State Division of the Cancer Society, the New York City Cancer Society, the State and City Health Departments, and the Subcommittee on Cancer, once or twice a year, was recommended. Also, the chairman of the Medical Film Review Subcommittee stated there were many good films on cancer detection and treatment which could be useful to the Subcommittee on Cancer's purposes.

Child Accidents

The Subcommittee on Child Accidents is composed of the following members:

Harold Jacobziner, M.D., *Chairman*	New York
Tyree C. Wyatt, M.D.	Onondaga
Arnold J. Capute, M.D.	Suffolk
Thurman B. Givan, M.D.	Kings

The Subcommittee on Child Accidents met on October 19, 1961. The following recommendations were made:

1. That a special committee on accident prevention which should concern itself with the control of accident mortality and morbidity be organized by every county medical society.

2. That effective liaison be established at the State and local level with representatives of the Academy of General Practice and the Academy of Pediatrics with regard to planning of accident prevention programs and postgraduate ed-

ucation relating to accident prevention in childhood.

3. That the membership of the State Medical Society and of its component units become more aware of the problem and exercise greater participation in the control of accidental mortality and morbidity.

4. That physicians and county medical societies work closely with their respective health departments with regard to accident prevention. Health departments may be helpful with providing reliable figures, statistics, health education material, and speakers on this subject.

5. That physicians during both home and office visits alert patients about any accidental hazards which may occur at a given stage of growth and development and provide to their patients appropriate anticipatory guidance about prevention.

6. That physicians display health education material on accident prevention in their offices and waiting rooms.

7. That practicing physicians guide and assist lay groups such as PTA's, Boy and Girl Scouts, and others, in organizing accident prevention campaigns.

8. That the State Medical Society vigorously recommend that "accident prevention" be included as an integral part of the medical curriculum and of the nursing curriculum at the undergraduate level.

9. That the Medical Society vigorously oppose "self-medications" and giving of "samples" to patients.

10. That the Medical Society strongly endorse the use of "locked medicine cabinets" and their routine installation in all new housing.

11. That physicians report in detail all fatalities from accidents and all accidental poisonings to the Department of Health and to their respective Poison Control Center.

12. That physicians of the Medical Society become more aware of the problem of lead poisoning in children and its prevention.

13. That the Medical Society include at its annual meeting scientific papers and exhibits on accident prevention.

14. That the Medical Society recommend a similar line of action to the A.M.A.

15. That the Medical Society together with the Academy of Pediatrics and the Academy of General Practice sponsor periodic postgraduate training courses on accident prevention for practicing physicians.

These recommendations will be cleared with the American Academy of Pediatrics.

During the year there has been considerable professional education relating to accident prevention directed to practicing physicians and the public. Talks were given at staff meetings of various municipal and voluntary hospitals and considerable literature was distributed to physicians and clinics. Attractive posters and pamphlets prepared by the Department of Health were also widely distributed to physicians and hospital emergency clinics.

The control and prevention of lead poisoning received greater attention than ever before and various new case-finding technics resulted in the identification of early cases, early referral, and prompt treatment.

In general, there has been a great awareness on the part of the profession of the importance of childhood accidents and their prevention.

Diabetes

The Subcommittee on Diabetes is composed of the following members:

Charles B. F. Gibbs, M.D., *Chairman*	Monroe
George E. Anderson, M.D.	Kings
Joseph B. Cortesi, M.D.	Schenectady
Maynard E. Holmes, M.D.	Onondaga
Henry E. Marks, M.D.	New York

The activities of this subcommittee were concerned with further development of ways to improve physician education, means of detection of unknown diabetes in as many communities as possible, cooperation with the Subcommittee on Aging and Nursing Homes which also was active in case-finding and education in nursing homes, and further coordination with the State Health Department and the American Diabetes Association in their parallel efforts.

The current articles in the NEW YORK STATE JOURNAL OF MEDICINE on "Current Concepts in Diabetes Mellitus," sponsored by the New York Diabetes Association and edited by Max Ellenberg, M.D., and Harold Rifkin, M.D., are an excellent aid in physician education and are to be published as a book in the future.

Together with Joseph J. Witt, M.D., chairman of the Subcommittee on Aging and Nursing Homes, and George M. Warner, M.D., director of Adult Health and Geriatrics at the New York State Department of Health, the chairman sent a letter to the presidents and secretaries of all county medical societes asking their cooperation in promoting an educational campaign on the subject of diabetes. The local chapters of the Academy of General Practice were advised that they could obtain aid in developing programs for credit and hospital staffs were asked to feature the subject at their meetings. Hospitals were urged again to accent the value of postprandial rather than fasting blood sugars as a means of detection. To avoid added expense and increased work by the laboratory it was revealed that the giving of glucose at 6:00 A.M. and the collection of specimens at the usual hour of 8:00 A.M. is working very satisfactorily in a number of hospitals. County society committees on aging and diabetes were asked to cooperate in a diabetes detection program in nursing homes and homes for the aged.

The Pharmaceutical Society was asked and expressed willingness to support efforts at detection and general education through the pharmacies when ways and means could be worked out at a future time.

Excellent cooperation was obtained at the several committee meetings with representatives from the New York State Health Department and the American Diabetes Association in formulating plans for detection and education. This seemed especially important since all three groups are interested in promoting these efforts in the field of diabetes.

General Practice

The Subcommittee on General Practice has the following membership:

Jeff J. Coletti, M.D., *Chairman*....Nassau
Carl B. Alden, M.D.............Jefferson
Floyd C. Bratt, M.D...............Monroe
Royal S. Davis, M.D...........Westchester
Gregory A. Galvin, M.D..........Tompkins
William L. Gould, M.D.............Albany
Arthur Howard, M.D...............Fulton
Garra L. Lester, M.D.........Chautauqua
Charles G. Mangi, M.D.............Queens
Samuel Wagreich, M.D..............Bronx

A meeting of this subcommittee is scheduled for January 31, and a supplementary report will have to be rendered.

Glaucoma and Other Diseases of the Eye

The Subcommittee on Glaucoma and Other Disease of the Eye has the following membership:

David F. Gillette, M.D., *Chairman*..........
............................Onondaga
James Leslie Boyd, M.D............Suffolk
John F. Gipner, M.D...............Monroe
Arthur Alexander Knapp, M.D...New York
George M. Warner, M.D., Director, Bureau of
Adult Health and Geriatrics, New York
State Department of Health, *Adviser*......
................................Albany

There have been two meetings of this subcommittee during the past year. The second, on February 7, was held in Albany and was attended by Selig Katz, M.D., and Ward Oliver, M.D., of the State Health Department.

At the first meeting the chairman described the active glaucoma detection program in Syracuse which was instituted in May, 1961, whereby the Onondaga County Medical Society and the Syracuse Health Department conduct a screening clinic every Monday evening for persons over forty years of age. Copies of the forms and procedures are available for other areas in the State.

Plans were made for coordinating statistics from the various glaucoma screening projects in the many metropolitan hospitals where this type of screening is done and to encourage attendance at these clinics. A letter was sent to all the hospitals in the Greater New York area and in Westchester County to this effect. A meeting is planned with the staff ophthalmologists of these clinics. The editors of the respective county medical society bulletins have been asked to publicize the project.

The meeting on February 7 was requested by the State Department of Health to advise them in formulating recommendations for the Motor Vehicle Department with regard to vision requirements for operators of motor vehicles. Conclusions were reached relative to the necessity for eye examinations, the intervals at which these should be conducted, and minimal vision requirements.

It should be noted here that the name of the subcommittee has been changed to Subcommittee on Glaucoma and Other Diseases of the Eye.

Hard of Hearing and the Deaf

The Subcommittee on Hard of Hearing and the Deaf has the following membership:

Edmund P. Fowler, Sr., M.D., *Chairman*.....
...........................New York
Frank W. Farrell, M.D.............Queens
Abraham I. Goldner, M.D.......New York
Karl W. Gruppe, M.D.............Oneida
Gordon D. Hoople, M.D.........Onondaga
Harrison M. Karp, M.D.......Schenectady
C. Stewart Nash, M.D.............Monroe
William R. Updegraff, M.D.......Dutchess
Clarence D. O'Connor, Ph.D.,.....Lexington
School for the Deaf, *Adviser*....New York
Mrs. Eleanor C. Ronnei, New York League
for the Hard of Hearing, *Adviser*.New York

There have been no meetings of this subcommittee thus far, but one will be scheduled during the annual meeting.

Unfortunately the proposal by the subcommittee that the Department of Education expand its conservation of hearing program to include a roster of consulting otologists for doubtful or complicated cases has reached an impasse. After several conferences with Leo Feichtner, M.D., chief of the Bureau of Health Services of the department, Dr. Karp of the subcommittee reports that no further efforts have been made by the department to zone the State into areas in need of the proposed service.

Health Aspects of Ionizing Radiation

The Subcommittee on Health Aspects of Ionizing Radiation has the following membership:

Irving R. Tabershaw, M.D., *Chairman*.......
...........................New York
Norman Simon, M.D............New York
John H. Wentworth, M.D..........Suffolk
James Lade, M.D., Office of Medical Defense,
New York State Department of Health,
Adviser........................Albany
Hanson Blatz, M.D., Department of Health,
City of New York, *Adviser*.....New York

A meeting of this subcommittee was held on November 10, 1961. This subcommittee is diligently investigating the various aspects of fallout and therapeutic radiation in order to provide authoritative information to the medical profession concerning possible health hazards. It is considering an educational program in radiation for the physician, the nonmedical use of x-ray equipment, the licensing and regulation of the use of isotopes, and the jurisdictional problem resulting from the relinquishing of the latter powers by the Atomic Energy Commission.

Commissioner Hilleboe presented to the Council at its September 28, 1961, meeting a detailed statement regarding the danger of fallout from the nuclear bomb testing by the U.S.S.R. The chairman of the parent committee attended a meeting in Albany where the subject was discussed at length. It appears that up to the present time the fallout has not presented any serious health hazard.

A brochure on the dangers of radiation of all types is still in the planning stage.

Heart Disease

The Subcommittee on Heart Disease has the following membership:

J. G. Fred Hiss, M.D., *Chairman*	Onondaga
A. Wilbur Duryee, M.D.	New York
John J. Finigan, M.D.	Monroe
Franklin W. Fry, M.D.	Nassau
David G. Greene, M.D.	Erie
Marjorie H. Greene, M.D.	Nassau
Norman Plummer, M.D.	New York
Willard H. Willis, M.D.	Oneida

The subcommittee had one meeting, October 2, 1961. A number of topics dealing with heart disease problems were presented, including the following:

1. The desirability of everyone carrying a health card. On this certain cardiac diagnoses and important medications might be entered. The use of anticoagulants could be recorded.

2. Topics for articles in the NEW YORK STATE JOURNAL OF MEDICINE were discussed.

3. The problem of whether or not the time was right to instruct the public at large in the closed chest cardiac massage technic was discussed at great length. It was felt that it was more important to see that hospital personnel was well informed about this procedure first.

4. The problem of continuing education for general practitioners, especially those far removed from medical centers, was discussed, and the "workshop" type of instruction was endorsed strongly as one method of carrying out such instruction.

5. School cardiologic problems were discussed, especially the apparent great difficulty in recognizing innocent murmurs. A great many parents are upset each year because they are notified by school physicians that their child has a "cardiac defect" whereas it is only an innocent murmur.

6. The difficulties in connection with cardiac rehabilitation were discussed at length and especially the impact of the frequent rulings of the Workmen's Compensation Board concerning the causal relationship of work, strain, and trauma to "heart attacks." The subcommittee felt that a half day should be given over at the next annual meeting of the State Medical Society to discussion of this problem.

Since the above meeting the chairman has taken part in several conferences involving closed chest cardiac massage, more correctly termed "emergency resuscitation" because the cardiac angle is only one part of the total problem. Other groups interested in this problem are the State Department of Health, the New York State Heart Association, and the medical schools. Of these the State Medical Society and the State Health Department are the most active at present, but they do have the cooperation of the other groups. It was felt that an intensive "crash" program involving all of the 293 upstate hospitals should be carried out at once using well-trained instructors to start this program. A supplementary report on this project may be available for the annual meeting.

The State Health Department and the State Medical Society are taking active steps to develop the workshop type of instruction for general practitioners with a promise of help from the Heart Association and the medical schools.

A half-day session on "The Cardiac in Industry" has been arranged for the morning of May 16 at the State Society's annual convention.

Maternal and Child Welfare

The Subcommittee on Maternal and Child Welfare has the following membership:

Edward C. Hughes, M.D., *Chairman*	Onondaga
Samuel Karelitz, M.D.	Queens
Frank A. Disney, M.D.	Monroe
Anne M. Drislane, M.D.	Albany
Eugene R. Duggan, M.D.	Monroe
Edwin M. Gold, M.D.	Kings
Edward S. Goodwin, M.D.	Albany
A. Wilmont Jacobsen, M.D.	Erie
Harold Jacobziner, M.D.	New York
Schuyler Kohl, M.D.	Kings
Jean Pakter, M.D.	New York
Clyde L. Randall, M.D.	Erie
Ferdinand J. Schoeneck, M.D.	Onondaga
Frederick H. Wilke, M.D.	New York
Tyree Wyatt, M.D.	Onondaga

There have been no meetings of the subcommittee this past year.

A report will be rendered to the House of Delegates in May.

Medical Film Review

The Subcommittee on Medical Film Review has the following membership:

Kenneth B. Olson, M.D., *Chairman*	Albany
Harold W. Mayberger, M.D.	Nassau
Jean D. Watkeys, M.D.	Monroe
James J. Quinlivan, M.D., Director, Office of Public Health Education, New York State Department of Health, *Adviser*	Albany

The Subcommittee on Medical Film Review had one formal meeting during 1961 and several informal meetings. The chairman and Dr. Quinlivan met with the Council Committee on

Public Health and Education on July 12, 1961, where it was pointed out that many excellent educational films for professional education were available from the Film Library of the Department of Health.

Arrangements are being made to supply professional films to be shown on the cruise following the annual meeting of the State Medical Society in May.

The following tabulation indicates the use that has been made of the films during the past year:

Category	*Individual Shipments*	*Films Used*
Medical schools	147	178
Private physicians	346	561
Pharmacy colleges	18	33
Nursing schools	4,792	8,048
Voluntary health agencies	496	887
Medical staffs of hospitals	256	381
Public health staffs	988	1,362

The following films have been added to the library:

A new series of "Physical Diagnosis" films, which include: "Communicable Diseases," "Gait and Musculoskeletal Disorders," "Ear and Hearing," "Introduction to Speech Problems," "Disorders of Motility," and "The Larynx."

Films added to the Medical Section include: "Congestive Heart Failure," "Diabetes and Its Long Range Control," "Current Applications of Culdoscopy," and "Rehabilitation Adds Life to Years."

Films added to the Nursing Section include: "RX: A Prescription for Better Hospital Procedures," "Infectious Diarrheas," "Beyond the Shadows," "Human Body: Respiratory System," and "PKU: Preventable Mental Retardation."

Mental Hygiene

The Subcommittee on Mental Hygiene has the following membership:

C. Douglas Darling, M.D., *Chairman*	Tompkins
Matthew Brody, M.D.	Kings
Ulysses Schutzer, M.D.	Broome
Edward F. Shea, M.D.	Ulster
Reginald R. Steen, M.D.	Nassau
Marvin Stern, M.D.	Kings
Duncan Whitehead, M.D.	Erie
Paul H. Hoch, M.D., Commissioner, New York State Department of Mental Hygiene, *Adviser*	Albany

There has been one meeting of the subcommittee as a whole, on December 8, 1961, and two meetings, November 5, 1961, and January 25, 1962, of a group representing the subcommittee, the Department of Health, the Department of Mental Hygiene, and the New York State Chapter of the Academy of General Practice.

The purpose of the two latter meetings was to expedite continuing education on mental health for the physicians of the State. The principal problem was to achieve communication among the organizations represented so that available facilities might be utilized properly through agreement on programming, financing, and publicizing. With the successful preceptor type of program in Kings County as a guide, similar courses have been instituted in St. Lawrence, Bronx, and Nassau Counties. At present plans are under way to promote expansion to the Syracuse and Rochester areas.

Certain subjects were discussed at the December 8 meeting, and others had arisen at the July 12 meeting of subcommittee chairmen, as follows:

1. The subcommittee had recommended that Workmen's Compensation fees for psychiatrists and neurologists be raised from $20 to $25. An unsuccessful effort was made by the Committee on Workmen's Compensation to carry this out.

2. Every effort should be made to prevent the practice of psychotherapy by psychologists. This would require changing the viewpoint and interpretation of the State Education Department. There has been introduced into the Legislature a bill to limit hypnosis to physicians, *certified psychologists*, and licensed dentists. The subcommittee is opposed to this since it implies that psychologists are entitled to practice medicine.

3. The subcommittee believes that the "open treatment" of narcotic addicts is a very dangerous procedure. More vacancies for addicts in State mental institutions are planned.

4. One of the members of the subcommittee had attended a symposium in New York City on commitment procedures, sponsored by the Women Lawyers Association. A certain judge accused the Department of Mental Hygiene of obtaining the passage of statutes to effect admission of elderly patients "without judicial scrutiny," allegedly thus depriving nonpsychotic elderly patients of their civil rights. He was referring specifically to the "One-Physician" and "Two-Physician" certificates.

After discussion the subcommittee voted to strengthen the hand of the Mental Hygiene Department by a statement as follows, to be withheld until after any potential legislation along this line may have been introduced into the Legislature:

The Medical Society of the State of New York, in view of the great progress that has been made in the field of mental health and the vast changes that have occurred in the mental hospitals in the State of New York, believes that admission to these hospitals should be considered similar to admission to any general hospital, and since this is primarily a medical function the Medical Society endorses direct, nonjudicial admission to State hospitals.

Operating Room Mortality

The Subcommittee on Operating Room Mortality is composed of the following members:

Richard Ament, M.D., *Chairman*	Erie
Charles W. Hayden, M.D.	Suffolk
Milton Helpern, M.D.	New York
Frederick M. Mitchell, M.D.	Tompkins
Henry T. Randall, M.D.	New York
Frederick Beck, M.D.	Otsego

The Subcommittee on Operating Room Mortality has continued its efforts toward establishing comparable operating room mortality studies throughout New York State. The new fifth edition of *Standard Nomenclature* has included a revised classification and coding for mortality associated with operative and anesthetic procedures which is being utilized as a national standard. We have recommended its adoption by the Anesthesia Study Committees throughout New York State.

An epidemiologic approach to the study of immediate anesthetic-surgical mortality has commenced in the New York City area under the direction of Milton Helpern, M.D., Medical Examiner, who is a member of this subcommittee. Similar efforts are planned in conjunction with the New York State Department of Health for the upstate areas as soon as the format of study being used downstate is deemed valid.

Physical Medicine and Rehabilitation

The Subcommittee on Physical Medicine and Rehabilitation is composed of the following members:

George M. Raus, M.D., *Chairman*	Onondaga
Morton Hoberman, M.D.	New York
Alfred L. Lane, M.D.	Monroe
Edward J. Lorenze, M.D.	Westchester
Leonard D. Policoff, M.D.	Albany
Jerome S. Tobis, M.D.	New York
George G. Deaver, M.D., *Adviser*	New York
Edward W. Lowman, M.D., *Adviser*	New York

The Subcommittee on Physical Medicine and Rehabilitation has not had occasion to meet during the past year. However, following a mail poll the subcommittee unanimously recommended the selection of James H. Sterner, M.D., medical director of the Eastman Kodak Company, Rochester, as the State Society's nominee for consideration by the Governor's Committee "Employ the Physically Handicapped," and by the President's Committee on Employment of the Physically Handicapped, for the Physician's Award.

Your chairman attended a meeting of representatives of the State Association of Rehabilitation Centers last spring in Syracuse where one of the principal recommendations was the compiling of a directory of rehabilitation facilities and agencies in this State. This subject was also discussed at the July 12 meeting of subcommittee chairmen in Albany, and efforts will be made to set such a project in motion.

The chairman and Dr. Greenough, together with Dr. Fineberg, met in New York City with Ralph E. DeForest, M.D., of the American Medical Association, to discuss better liaison with that organization in its activities in this field.

The chairman attended a meeting of the Governor's Council on Rehabilitation Ad Hoc Committee to explore possibilities of licensing qualified foreign physical therapists. Its recommendations appeared to be consistent and compatible with the policy and philosophy of the State Society and the American Medical Association.

The advice of the subcommittee has been sought by the Department of Medical Service of the American Medical Association relative to draft reports drawn up by that department concerning the New York State rehabilitation services as administered by the Department of Social Welfare and the Department of Education. Also, the State Education Department recently requested our comments on various statements and forms which they have drawn up for the Governor's Council on Rehabilitation pertaining to the licensure of physical therapists.

School Health

The Subcommittee on School Health is composed of the following members:

William E. Ayling, M.D., *Chairman*	Onondaga
Thomas S. Bumbalo, M.D.	Erie
Frederick A. Groff, Jr., M.D.	Schenectady
Rocco J. Martoccio, M.D.	Oneida
Edward L. Schwabe, M.D.	Chautauqua
Robert E. Vorisek, M.D.	Nassau
Anne M. Drislane, M.D., *Adviser*	Albany
Leon Roper, M.D., *Adviser*	Albany

One meeting was held on June 7, 1961, in Rochester at the time of the Annual Health Conference of the State Department of Public Health.

Resolution 61–15 of the House of Delegates was reviewed. This concerns changing the outmoded Education Law requiring annual examinations of school children to make them periodic, with special examinations of selected cases. The Madison County resolution was discussed and it was felt that the better spacing of periodic examinations would be to do them in kindergarten and/or first grade, fourth, seventh, and eleventh grades, with special examinations of new pupils and referred cases. It was agreed that payment for these examinations should be on a salary basis, rather than a per capita basis.

On July 12, Frederick A. Groff, Jr., M.D., a member of this subcommittee, attended a meeting of chairmen or their representatives of the subcommittees of the Public Health and Education Committee of the State Society in Albany. The minutes of this meeting state on page 8 "that any effort to abolish the present cursory annual health examination of school children and replace it with periodic complete examinations, as recommended in resolution 61–15, will require the strong support and effort of the Subcommittees on School Health and General Practice. The law could be interpreted differently by ruling of the Education Department and efforts to persuade these authorities of the merits of such a change must be pushed vigorously."

It is planned to have a meeting of this subcommittee with Dr. Van Kleeck and other personnel of the State Education Department in March, 1962, in a further attempt to bring about a change in the requirement for annual examinations. This action has been suggested by the reference committee. Meanwhile a member of our subcommittee is to draw up a model school health program to be used as a basis for our discussion.

Another conference on school health, in Albany, is being arranged by Paul R. Patterson, M.D., of the Albany Hospital, for Thursday, March 29, 1962. A member of our subcommittee, Anne M. Drislane, M.D., was instrumental in bringing this about. Similar conferences have been held in Syracuse and Buffalo.

Several symposiums on athletic injuries have been held during the year, in Nassau County, Binghamton, and Utica. The chairman of this subcommittee attended the one in Binghamton and reported to the Council committee.

This subcommittee has been asked for advice in regard to standards for physical examinations in connection with sports in schools. It was our opinion that each case must be considered individually and decisions based on the type of sport to be participated in. Routine electrocardiograms for this purpose, it was decided, were not necessary.

Your chairman represented the Society at the 8th National Conference on Physicians and Schools held March 9 to 11, 1961, in Chicago. Three major problems in school health were discussed: (1) child health needs and health education, (2) the future of school health programs, and (3) mental-emotional fitness of youth.

Each problem was introduced by speakers at general sessions and then discussed simultaneously by those attending in ten groups of about 20 each. The recorders of each group gave a brief report at the following general session.

A complete summary of the meetings has been published by the A.M.A. in book form and is now available. A few points of special interest were:

The State of New Jersey has discontinued annual examinations of school pupils and Connecticut has changed from annuals to examinations every three years. In one group there was forceful reaction against the New York State law which still requires annuals.

Many new schools, especially in the South, are being airconditioned. School health councils were recommended and workshops for discussion of services were suggested. Another recommendation was that teacher training institutions give their students more preparation in school health. Parents should take more responsibility in seeing that their children are examined by private physicians, and there should be better facilities for mental health, such as care of the emotionally disturbed pupils.

It is planned to hold the next meeting of our subcommittee at the annual meeting of the State Society, in May, in New York City.

Legislation and Legal Matters

Malpractice Insurance and Defense Board

To the House of Delegates, Gentlemen:

The Malpractice Insurance and Defense Board consists of the following:

Thomas M. d'Angelo, M.D., *Chairman*	Queens
J. Stanley Kenney, M.D., *Vice-Chairman*	New York
John C. Brady, M.D.	Erie
Waring Willis, M.D.	Westchester
Raymond S. McKeeby, M.D.	Broome
John F. Kelley, M.D.	Oneida
John J. Della Porta, M.D.	Monroe
William L. Wheeler, M.D., *ex officio*	New York
Maurice J. Dattelbaum, M.D., *ex officio*	Kings
William F. Martin, counsel, *ex officio*	New York
James M. Arnold, indemnity representative, *ex officio*	New York

During the past year, there have been no developments in the malpractice situation that are particularly noteworthy or alarming. The upward trend in new malpractice cases noted during 1960 did not continue with the same intensity. On the other hand, it was not reversed. In retrospect, 1961 will probably be represented by a temporary plane on a curve that for the past fifteen years has been persistently, if irregularly, rising.

New and Closed Cases. A comparison of new and closed cases during the last three years is as follows:

	1961	*1960*	*1959*
On hand at first of year	1,001	877	861
Reported during year	733	680	548
Total	1,734	1,557	1,409
Disposed of during year	611	556	532
On hand at end of year	1,123	1,001	877

The 733 new suits, claims, and incidents reported during 1961 involved 861 insured members. While the number of new cases reported represents an increase of nearly 8 per cent over 1960, this was to a large extent accounted for by an increase of about 6 per cent in the number of members insured. The number of insureds by county of membership is shown in Table I and now represents the largest number of physicians ever insured in the State Society program.

To illustrate the long delay in the reporting of malpractice cases, the 733 cases reported during 1961 grew out of and were charged to the policy years shown:

Policy Year	*Number of Cases*	*Per cent of Total*
1961	177	24
1960	343	47
1959	146	20
1958	46	6
1957	8	1
1956 and prior	13	2

Loss Experience. The report of the Society's actuarial consultant indicates that a modest rate increase would be justified on the basis of our loss experience. However, the Company has agreed to delay any change in the present rate schedule pending the results of efforts being made to improve our experience.

While a review of the losses charged to the various specialty groups indicates that some reallocation among premium classes might be in order, our actuaries recommend that a complete study and appropriate rate revision be postponed for at least another year.

Last year five counties were transferred from the upstate to the suburban rate area and one from suburban to metropolitan. The recent loss experience of some other upstate counties indicates that they also may eventually have to be transferred to a higher rate area. The Board hopes, however, that this may be avoided through the efforts of the county society malpractice committees and through stricter selection of risks by the Board.

At present the Board is authorized, after having established to its satisfaction that the practice, conduct, attitude, or loss experience of a member is such as to constitute an undue hazard, to disapprove an application for new insurance or to direct the discontinuance of insurance already in effect. Occasionally the Board has found that a member's loss experience, or potential for losses, indicates that he is more than an average risk. When this situation is due to unusual volume or to relatively hazardous procedures, resulting primarily from the physician's prominence in his specialty, the Board has felt that a member is still insurable, provided a premium commensurate with the indicated risk could be charged. The Board is

TABLE I. Insured Members, 1961, by county of membership

County	Number Insured	Increase or (Decrease)
Albany	322	14
Allegany	23	(3)
Bronx	850	75
Broome	209	(2)
Cattaraugus	63	3
Cayuga	71	. . .
Chautauqua	85	4
Chemung	92	. . .
Chenango	27	(1)
Clinton	39	9
Columbia	23	(2)
Cortland	26	4
Delaware	25	1
Dutchess	139	1
Erie	842	35
Essex	17	. . .
Franklin	35	. . .
Fulton (Hamilton)	40	(2)
Genesee	49	4
Greene	17	(4)
Herkimer	38	(7)
Jefferson	68	(1)
Kings	1,674	103
Lewis	7	(2)
Livingston	23	1
Madison	44	2
Monroe	635	27
Montgomery	32	3
Nassau	919	53
New York	4,091	326
Niagara	111	(3)
Oneida	237	3
Onondaga	448	20
Ontario	72	. . .
Orange	164	4
Orleans	19	2
Oswego	50	(2)
Otsego	40	(1)
Putnam	16	2
Queens	1,273	110
Rensselaer	126	3
Richmond	136	16
Rockland	129	14
St. Lawrence	73	1
Saratoga	40	(1)
Schenectady	178	19
Schoharie	19	1
Schuyler	7	(2)
Seneca	13	(1)
Steuben	82	2
Suffolk	363	16
Sullivan	46	3
Tioga	19	. . .
Tompkins	70	2
Ulster	87	5
Warren	52	5
Washington	27	4
Wayne	38	(5)
Westchester	908	47
Wyoming	19	2
Yates	13	1
TOTALS	15,400	908

therefore considering the possibility of submitting, at the insured's request, exceptional cases to our insurance carrier for judgment rating. If the Company were willing to write the risk at a special rate, an agreement to the special premium calculated would be signed by the physician and submitted to the New York State Insurance Department for approval as provided for under the insurance law.

Claim Prevention. As the result of conferences between Company representatives and the Indemnity Representative, a claim prevention program is being initiated. A part of this program will be based on a study of malpractice situations peculiar to different specialties and will include the dissemination to the specialists concerned of recommended preventive measures particularly applicable to them.

Expanded Coverage. In 1958, the insuring clause of the State Society master policy was again revised to afford protection on account of injury sustained as a "result of rendering or failing to render professional services." This revision was intended to give coverage broader than that provided under the standard policy wording of "malpractice, error or mistake," or variations that attempted further to define these terms. In 1960 at the request of the Board, the Company agreed to interpret the insuring clause to include participation by an insured in various State and county society committees. Although it was felt that a further extension of the policy to provide coverage for liability arising out of activities as a member of a formal accreditation or other professional board or committee of a hospital might more appropriately be provided under the hospital's professional liability policy than under a physician's individual insurance, the Board requested our carrier to interpret the master policy to include this coverage also, and the Company has agreed to do so.

Some members have referred to the fact that, in the recently revised standard malpractice policy of the National Bureau of Casualty Underwriters, the exclusions relating to criminal acts, to acts or omissions while under the influence of intoxicants or narcotics, and to contractual liability have been deleted. At the time this revision was announced, the National Bureau explained the deletions as follows: "These exclusions have been eliminated since they operate to create many questions of intent. Reliance will be placed on the insuring clause to establish whether an act is done in the practice of the insured's profession, and upon public policy to establish the scope of coverage." The Board feels that the exclusion of our policy relating to criminal acts more exactly defines the intended coverage and believes that it should remain unchanged. The Board feels that our policy with the exclusion affords as broad or broader coverage than does the National Bureau policy without the exclusion.

At the request of the Board, the Company has agreed in writing to interpret the master policy and the individual certificates of insurance as if the exclusions relating to intoxicants or narcotics and to contractual liability were deleted, and these exclusions [e (1) and f] will be deleted when the policy is again revised. Reliance will be placed on the insuring clause to establish whether an act is done in the practice of the insured's profession, and on public policy to establish the scope of coverage.

Although the Board is happy to announce the removal of the above exclusions because of the dangers they represent to members who might be unfairly charged, it wishes to state that any member found to have acted under the influence of intoxicants or narcotics or to have guaranteed a cure may expect to have his insurance in the State Society program discontinued as soon as such facts are established.

Limits of Coverage. Each year a few members of the Society find themselves in the uncomfortable position of having to contribute from their own funds to satisfy a judgment or settle a malpractice claim in excess of their insurance. For several years, the office of the Indemnity Representative has been recommending *minimum* limits of $50,000/$150,000 for nonsurgical practices and of $100,000/$300,000 for physicians doing major surgery or anesthesiology. The Board concurs in these recommendations and wishes to emphasize that they are recommended minimums. Under present-day conditions double these limits cannot be considered excessive.

It is both impossible and impracticable to try to carry insurance in excess of what a plaintiff's attorney may decide to demand as damages for alleged malpractice. In our application forms and rate schedules, premiums for limits of $200,000/$600,000 are published, and these limits have always provided a margin of safety when compared with the cost of disposing of any malpractice case. Although still higher limits cannot be recommended as necessary on the basis of our experience, they are available from our insurance carrier and rates may be obtained from the Indemnity Representative.

Conclusion. Again the Board acknowledges with thanks the valuable services rendered by the many physicians who have served on county society malpractice committees and specialty advisory committees. The several claim offices of the Company have continued to provide efficient and considerate service to those who have been unfortunate enough to become involved in malpractice actions. The executive officers of the Company have continued the cooperative and helpful attitude they have always shown in connection with our problems.

Respectfully submitted,
THOMAS M. D'ANGELO, M.D., *Chairman*

Autopsy and the Dead Human Body

To the House of Delegates, Gentlemen:

The Special Committee on Autopsy and the Dead Human Body has the following members:

Alfred A. Angrist, M.D., *Chairman*	Queens
Herbert Derman, M.D.	Ulster
Angelo M. Sala, M.D.	New York
Jacob Taub, M.D.	Bronx
John V. Connorton, Ph.D., *Adviser*	New York

The activities of the committee have been completed by letter rather than by any formal meeting during this year. The major activities dealt with the reversal of the Binghamton decision by the Court of Appeals, which drastically limited the authority of the medical examiner or coroner in the performance of an autopsy, and the committee's participation in the activities of the Law Revision Commission.

The chairman of your committee submitted a modified brief in response to a list of questions prepared by the Law Revision Commission. This material was mimeographed by the Commission and distributed at a hearing held on November 17, 1961, in Albany. The chairman of your committee attended this hearing and after a general statement responded to questions raised by the Commission for the record. The cooperation of the Medical Society of the State of New York was noted by the chairman of the Commission in remarks entered into the record.

The Law Revision Commission has prepared a report and recommendations to the Legislature in the form of an Act to amend Section I of the County Law adding to Article 17 A, Sections 670, 673, 674, 677, and 678. The chairman of your committee has studied these recommendations and finds that they do extend the authority of the medical examiner or coroner and offer pragmatic immediate solution to care for medicolegal needs of the State as a whole. It is felt that this Act should receive our approval.

The Law Revision Commission did not go into the problems of the revision of the Consent Law to require only any one of equal rank of next of kin. Nor did it go into the problem the situation created by the inclusion of "the performance of a complete or partial autopsy on a deceased person without lawful authority," in the definition of unprofessional conduct, thus threatening the pathologist with revocation of license, under item h of Section 30 of Article 2 subdivision 4 of the Regulations of the New

York State Education Department. Nor did the Commission go into the question of definition of autopsy to include the study of disease rather than determining the cause of death only.

It is the opinion of your chairman that the Medical Society of the State of New York should commend the efforts of the Law Revision Commission, and further petition the Governor that the activities of the Commission be continued to undertake the revision of all statutes dealing with the dead human body, to eliminate existing inconsistencies and ambiguities and to codify the law to meet the modern era.

It is the opinion also that a resolution again be introduced to the House of Delegates requesting change in the Autopsy Consent Law, inasmuch as this matter has not been taken care of by the Commission this year. It is felt that such a resolution might now be referred to the Commission for opinion by the Legislature and that the previous opposition to it might be overcome in this fashion.

Respectfully submitted,

ALFRED A. ANGRIST, M.D., *Chairman*

Judicial Council

To The House Of Delegates, Gentlemen:

The members of the Judicial Council are:

John F. Kelley, M.D., *Chairman*	Oneida
Norton S. Brown, M.D.	New York
James Greenough, M.D.	Otsego
Charles H. Loughran, M.D.	Kings
Edward T. Wentworth, M.D.	Monroe

As required by Section 1, Chapter VI of the Bylaws, the Judicial Council held an organizational meeting immediately at the close of the annual meeting of the State Society, May 10, 1961, in Rochester.

Mr. William F. Martin, legal counsel, and his associate, Mr. J. Richard Burns, attended the meeting. John F. Kelley, M.D., was elected chairman.

The council is happy to report that no appeals were presented during the year and therefore no further meetings were held.

Respectfully submitted,
JOHN F. KELLEY, M.D., *Chairman*

Medical Communication

Public Relations

To the House of Delegates, Gentlemen:

The members of the Public Relations Committee are:

John C. McClintock, M.D., *Chairman*	Albany
Samuel Wagreich, M.D., *Vice-Chairman*	Bronx
Marcelle T. Bernard, M.D.	Bronx
Erwin J. Boerschlein, M.D.	Monroe
George A. Burgin, M.D.	Herkimer
Reid R. Heffner, M.D.	Westchester
John W. Latcher, M.D.	Otsego
Charles C. Mangi, M.D.	Queens
John D. Naples, M.D.	Erie
Felix Ottaviano, M.D.	Madison
Irving M. Pallin, M.D.	Kings
Bernard J. Pisani, M.D.	New York
Edward Siegel, M.D.	Clinton
Charles M. Smith, M.D.	Seneca
C. Stewart Wallace, M.D.	Tompkins

Department of Communications. The numerous activities of the Department of Communications during the past year have been carried on under the supervision of Jack Pardee, director. Members of the staff are: Martin J. Tracey, associate director and editor of the *Newsletter*, John Schuyler, media relations officer; Gretchen Wunsch, media relations coordinator; Evelyn Clark, assistant editor, *Newsletter*, and secretary to Mr. Tracey; Anita Greenstein, secretary and part-time assistant to the Woman's Auxiliary and to the New York State Medical Assistants Association; Jean MacDonald, legislation secretary, and Joseph Citarella, secretary.

Mr. Tracey, in addition to editing the *Newsletter*, has coordinated the Federal legislation program, arranged the fall conference and two speech courses for physicians, has written articles, speeches, and reports for officers and chairmen and attended many meetings, as well as carried on routine duties at the office. Mrs. Clark, in addition to her work as assistant editor of the *Newsletter*, has worked closely with Mr. Tracey on Federal legislation, the fall conference, the two speech courses, handled reservations for the 13-day cruise, and worked on many other projects.

Mr. Schuyler has supervised the radio and television activities, as well as worked on projects upstate and department activities in connection with the fight against the King-Anderson Bill. Miss Wunsch has worked with radio, television, and the press, as well as writing reports, working on special projects, and coordinating the secretarial work of the department.

Miss Greenstein carried much of the secretarial work of the department as well as her special duties in connection with the Woman's Auxiliary and the New York State Medical Assistants Association. Miss MacDonald, in addition to secretarial duties, coordinates the State legislation activities and those of the New York Association of the Professions. Mr. Citarella, in addition to secretarial duties, works on special projects, exhibits, artwork, layouts, and other details.

The committee held monthly meetings during most of the year and the Communications Department carried on activities, under the committee's supervision, in the following areas:

Uniform Identification Method for Citizens with Certain Diseases. Resolution 61–58 as passed by the House of Delegates in May, 1961, was referred to the Public Relations Committee. This resolution concerns uniform identification methods for citizens with certain diseases. The department investigated the various methods for uniform identification, but learned from the A.M.A. that a national uniform identification method is being considered. The A.M.A. suggested that state societies await further word from it before setting up methods of their own.

Public Education and Welfare of People of New York State

Legislation, State. The department in close cooperation with James M. Blake, M.D., legislation chairman, handled a great deal of work for the Legislation Committee. All bills dealing with the health of the people of New York State were studied; 16 "Capitol News Bulletins" were prepared during the 1961 session. These were mailed to a list of 500 key persons throughout the State; committee and district meetings were arranged; mailings were prepared and sent to the 208 State legislators containing information on medical care for the aged and chiropractic; letters, telegrams, and telephone calls were used to alert the 61 county medical societies with regard to legislation; quantities of informational pamphlets were mailed to individuals, legislators, and county societies for distribution, and many telephone requests for information were handled.

The department has retained Robert C.

Gormley, Esq., to analyze bills dealing with health problems introduced during the current legislative session. Mr. Gormley and Miss MacDonald, under the supervision of Mr. Pardee, are preparing the current series of "Capitol News."

Close cooperation with the New York Association of the Professions and its legislation committee is maintained by the department. Several meetings of the legislation chairmen of the various professions have been held.

The first 1962 bulletin, carrying the State Society's legislative policy for 1962, has been mailed to a list of 500 key persons throughout the State, and five separate mailings, with enclosures, have gone to legislators to alert them to the dangers of chiropractic licensure.

Legislation, Federal. A tremendous amount of work was done by the department for the Subcommittee on Federal Legislation, chairmanned by George J. Lawrence, Jr., M.D. Special meetings were arranged, letters written (usually personally addressed); visits to Washington were arranged and made in February and July, 1961, by representatives of the Society; testimony for presentation before the House Ways and Means Committee in opposition to the King-Anderson Bill was prepared; staff members attended the hearings; meetings with legislators and State welfare officers, as well as national legislation meetings in Chicago; 800 letters were sent to allied organizations asking cooperation in defeating King-Anderson type of legislation; county society officers were asked to write their congressmen and to ask their membership to do so, too.

As the 1962 legislative session gets in motion, the department through Mr. Tracey is working in close cooperation with Dr. Lawrence and John Kiser, A.M.A. field representative, in carrying on the campaign to defeat HR 4222, entitled "Counter-Attack." Personal contact has been made with officers of county medical societies urging that they meet with their legislators. Mr. Schuyler visited 30 upstate counties in 16 days; outside public relations consultants in various areas have been used on this project.

Approximately 100,000 copies of pamphlets on medical care for the aged have been sent to county societies, editors of newspapers in New York State, and legislators, both State and national.

Plans are well underway for the second annual visitation of State Society representatives to Washington, D.C., to confer with our Federal legislators. The trip will take place February 27, 28, and March 1.

The staff of the department is, at the time this report is being written, concentrating on the special session of the House of Delegates, called for February 10 to discuss both State and Federal legislation.

Press, Radio and Television, Motion Pictures. Working under the Guide for Cooperation for Doctors, Hospitals, and Reporters the activities of the department in working with media representatives has expanded considerably. The annual meeting for reviewing the Guide was held in 1961 during March; no change was recommended at that time. The 1962 review of the Guide was held on January 25 (see report of Subcommittee on Cooperation with Media of Information).

The following services offered by the department have been called to the attention of some 2,000 representatives of the press, radio, TV, and magazines: (1) Interviews arranged with physicians in any specialty for aid in writing medical articles or for radio and TV appearances; (2) manuscripts checked by qualified physicians for medical accuracy; (3) Telanswer service (YUkon 6–5770) for holidays and weekend use of press, radio, and TV. Through this service a member of the communications staff can be reached at all times and the media representative can be put in touch with the appropriate officer or specialist; (4) information service. To carry out the above services, a list of 400 volunteer physicians is maintained.

Advance copies of the NEW YORK STATE JOURNAL OF MEDICINE are mailed to a special list of science editors and writers and editors are kept informed of the Society's stand on such matters as medical care for the aged and chiropractic licensure, by the mailing of pamphlets and kits.

Eighty interviews were arranged for representatives of the press with physicians in preparation of articles and special features; 10 manuscripts were received and sent to physicians for checking for medical accuracy. The department is now working with the special feature department of the *New York Daily News* on a series of eight articles. This will be the fifth series published by the *News* this year with aid from the State Society. Luncheon meetings have been held with members of the press, including Joe Martin, Phil Santors, both of the *Daily News*, Earl Ubell, science editor of the *New York Herald Tribune*; Delos Smith, science editor, United Press International.

Press conferences were held on intravenous procedures (Norman S. Moore, M.D.) and on the role physicians play in the administration of medical discipline (Henry I. Fineberg, M.D.); 13 members of the press attended the first conference and 11 the second. Five of the 10 New York City papers carried items on the first conference, while 6 carried the story of the second one. The *New York Times* carried a picture of Dr. Fineberg.

Releases were prepared and mailed to the 100 daily and 500 weekly papers, as well as the 250 radio and TV stations in New York State on: The annual meeting, district branch meetings, appointment of Dr. Fineberg as executive vice-president; appointment of William Hammond, M.D., as editor of the JOURNAL; the New York Health Exposition 1961 and the Medicine in Space exhibit, sponsored by the

State Medical Society; the Standards of Practice; athletic injuries conferences in the Sixth District Branch and the tricounty area; committee meetings on medical care for the aged; AMEF concert; Empire State Award for Excellence in Medical Reporting; Oustanding General Practitioner; and Fifty-year Doctors.

The department clips articles and items from the ten New York City daily papers and forwards clippings to interested officers, chairmen, the A.M.A., and other physicians. This allows the department to correct erroneous statements, such as the recent one in the *New York Post* when it was reported that "MD's Ask U.S. Not to Test." The article was reporting on a position taken by psychologists at a convention. The paper printed a letter from Mr. Pardee pointing out the error.

The department also has a clipping service which covers the entire State and in this way can evaluate the effectiveness of releases.

The department is cooperating with the State Society's Physician's Placement Bureau with respect to both public relations and publicity.

The department prepared and mailed 170 invitations to members of the press and key physicians in the Sixth District, inviting them to attend the Press Workshop, held recently in Binghamton; 45 members of the press attended this meeting. Mr. Schuyler worked with C. Stewart Wallace, M.D., in planning this workshop and in arranging for press coverage.

The department maintains a card file of 350 physicians who have volunteered to participate in interviews with representatives of the press, radio, and TV and also has a file of press, magazine, radio, and TV representatives.

Approximately 200 physicians appeared on radio and television programs, mainly in New York City, through arrangements made by the department. Promotion was done on and arrangements made for 13 weekly public services radio shows for Erie and Chautauqua Counties and a monthly show for Jefferson County. The local medical society has an option in each case to continue the show.

The Medical Societies of the Counties of Monroe, Broome, Oneida, Kings, and Onondaga have radio or TV series which they have initiated and the department, therefore, works in other areas.

Assistance was given to the A.M.A.'s East Coast Advisory Committee on Motion Pictures, Radio and Television in assembling a list of volunteer physicians, and interviews have been arranged for physicians to appear on programs. The debate on medical care, between Edward R. Annis, M.D., and Senator Hubert H. Humphrey on the "Nation's Future" program required a dinner meeting and other arrangements.

The Jewish Home Show continues with a physician being interviewed each week. This radio show has been on the air with a New York doctor appearing each Friday for three and one-half years.

Assistance was given to Nassau County, in early 1961, in connection with its medical information series to be presented on radio. Scripts were edited and general advice provided.

The department cooperated with the Health Insurance Institute in preparing a documentary film on the doctor-patient relationship, to be shown in schools, before lay audiences, service clubs, and others. Physicians were obtained by the department to assist in the writing of the script and to appear in the film.

The department made it possible to present documentary TV coverage of a New York State community seeking a resident general practitioner. The program, "Editor's Choice," was produced by the public affairs department of the American Broadcasting Company and presented on a national network.

As part of the campaign against chiropractic licensure attempts in the State Legislature, the department placed on radio a physician who gave medicine's reasons why chiropractors should not be licensed. This was done in a manner which precluded the possibility of the chiropractors being able to demand broadcast time for rebuttal under the Federal equal time law.

Facts supplied by the department caused a major New York City radio station and a nationally distributed daily newspaper to decide against accepting chiropractic association advertising and press releases.

Speakers Bureau. During the past year requests for speakers on medicosociologic subjects have increased; 20 speaking engagements were arranged for religious groups, fraternal societies, professional groups, service clubs, and others. Many of the speakers addressed audiences on medical care for the aged.

Although no formalized speakers program has been set up as of this report, several steps have been taken to establish an outstanding group of speakers. Two courses in public speaking were conducted by Dr. Robert Haakenson in Rochester and New York City with 175 physicians attending.

Exhibits. The department assisted in the presentation by Richmond County Medical Society of a medical exhibit at the science fair on Staten Island on the occasion of the Island's 300th anniversary and is currently arranging for a medical careers exhibit to be presented at the Rotary Club arts and science exhibit to be held in March in Glen Cove, Nassau County.

The exhibit, "A Career in Medicine," has been purchased and made available to county medical societies; this exhibit was shown at the annual conference.

The Society's annual exhibit at the Hall of Springs, Saratoga Spa, was seen by 100,000 persons.

The department arranged for publicity concerning the "Medicine in Space" exhibit at the New York Health Exposition, 1961. The

Woman's Auxiliary, under the direction of Mr. Walsh, manned the exhibit.

Annual Meeting. Publicity on the annual meeting was sent to the 600 newspapers and 250 radio and TV stations throughout the State. The *Newsletter* publicized the meeting and the March issue carried a digest of the scientific program. Posters urging attendance at the dinner dance and sessions of the House of Delegates and programs were sent to all hospitals in the Rochester area.

The department arranged the program for the Public Relations Session, a panel of newspapermen, which was highly successful.

The "Highlights of the House of Delegates" was mailed immediately following the close of the meeting to all delegates; 150 fifty-year certificates were mailed to recipients with a covering letter.

The department helped with the arrangements to have nurses and a doctor from Cape Canaveral present and arranged a press conference for them.

Two press rooms were maintained, to cover the scientific program and the House of Delegates. Twenty-five reporters including the wire service covered the meeting. The Rochester papers carried excellent coverage with three or four items appearing each day in each paper.

Awards. The department is preparing letters to announce the Albion O. Bernstein Award, a $1,500 yearly grant to the physician, surgeon, or scientist in the United States who makes the discovery that is most beneficial to the public. This will be presented at the meeting of the House of Delegates in May, 1962. This award is made possible by Mr. Morris Bernstein in memory of his son, Albion O. Bernstein, M.D., who was killed November 23, 1940.

Empire State Award for Excellence in Medical Reporting. 205 letters were sent out with an attractive flyer prepared by the department as well as the brochure and nomination blank prepared by the State Health Department, cosponsor with the State Society of the Award, asking for nominations for 1961. The award has been publicized also in the *Newsletter*.

The 1960 Empire State Award was presented at the annual meeting in May, 1961, followed by a luncheon for the winners, with excellent press coverage.

Monroe County Medical Society Plaque. A plaque was prepared for presentation to the Medical Society of the County of Monroe in recognition of the assistance given to the State Society during its annual meeting in Rochester.

President's Citations. 22 President's Citations were prepared and presented at the annual meeting. This citation is given to physicians nominated by the presidents of county medical societies and district branches for outstanding community service; 200 news items from all over the State resulted.

Fifty-year Doctors. 150 certificates were mailed to physicians who had completed fifty years of practice since the last annual meeting. These certificates are awarded each year and the department is now compiling the list for 1962.

1961 Outstanding General Practitioner. The department arranged for the selection of the Oustanding General Practitioner for 1961, by the Public Relations Committee, by letters and publicity sent to county societies asking for candidates. After selection by the committee the nominee's name is sent to the Council for confirmation. The department is at present working on the award for 1962.

Athletic Injuries Conferences. The department assisted in the arrangements for the Sixth District Branch's athletic injuries conference. Over 500 letters of invitation were sent out and approximately 250 attended. Press coverage was excellent. The tricounty organization also received assistance in presenting an athletic injuries conference.

Mailroom. The department supervised the maintenance of stencil files for special mailings, such as the list of key persons interested in legislation, a list of the 600 hospitals in New York State, list of 100 daily and 500 weekly newspapers, 250 radio and TV stations, and the special list for *Newsletter* mailings.

Information Service. The department answered many calls each day. Sample requests, other than those from the news media were: Calls from physicians asking for special articles and clippings; questions regarding licensing of physicians, osteopathy, chiropractic, how to implement the Kerr-Mills Bill, ethical standing of various organizations, foreign doctors, obtaining a family physician, medical schools, and State Society action on various subjects; requests for materials on many medical subjects, films on medical subjects for lay audiences, bills in State Legislature and Congress, information on legislation, pictures, scientific exhibits, and information about medical meetings.

Publications. The Department filled requests for 15,000 copies of its publications, such as Guide for Cooperation, Standards of Practice, Guiding Principles for Participation in Telecasts and Broadcasts, Principles of Professional Conduct, State Society Constitution and Bylaws, and publications on chiropractic.

Intraprofessional

Newsletter. A *Newsletter* has been published each month with the exception of August and September. Special features this year were: Standards of Practice, new edition in full; Foreign Interns; Social Security for Physicians; American Medical Education Foundation; Annual Meeting program; Medical Care for the Aged; AMEF Concert; Automatic A.M.A. Membership; Fall Conference program; List of Officers, Committee Chairmen, Headquarters Staff and Officers of Woman's Auxiliary; Explanation of A.M.A., State, and county membership (from *New York Medicine*).

A box in the *Newsletter* containing the revised Standards of Practice brought 121 orders for 3,087 copies of the Standards in handy pocket form. Requests have come from nearly all medical schools in New York State, lawyers, publishing houses, and free-lance writers interested in doing articles on the Standards. The *New York Times* published an article on the Standards, a copy of which was sent to all newspapers and radio and TV stations in the State.

Replies to a box in the *Newsletter* announcing a thirteen-day cruise offered to members of the State Society and to start immediately after the Annual Convention, May 18, have resulted in 44 inquiries and 8 firm reservations at this date.

A coupon in the *Newsletter* stating that the speeches given at the Annual Fall Conference were available brought orders for 700 copies of the various talks. A new column was inaugurated, "Facing Facts" by Henry I. Fineberg M.D., executive vice-president.

Conference of County Medical Society Officers and Chairmen. The department, under the direction of Waring Willis, M.D., organized and carried out the annual fall conference of county medical society officers and chairmen. The program presented 11 speakers and 3 moderators and was attended by 180 representatives of county societies and other interested persons. This conference was hailed as the best yet held. Senator Robert Kerr was the luncheon speaker.

An invitation to attend was sent to the press, radio, TV, and magazine medical editors, and both wire services, the *New York Times*, and several other publications covered the conference. Summaries of discussions and copies of papers given at the program were prepared and were made available to county societies and interested persons.

Services to Officers, Chairmen of Committees, and District Branches. The department is cooperating in preparations for the second regional conference of the New York State Joint Council to Improve the Health Care of the Aged. This work is being carried out by Mr. Schuyler, both as a department representative and as the public relations information officer of the State Joint Council.

Membership. Approximately 2,000 life membership cards were mailed by the department to all life members of the Society. New life members will receive a card each year on election.

Speeches and articles were prepared for officers and committee chairmen for district branch meetings, allied organization meetings, and others. Reports and minutes of meetings were prepared also for officers and committee chairmen.

District Branches. A member of the staff attended each district branch meeting to handle press relations. Advance releases and releases on election results were sent to the press in the appropriate district.

Soundscriber Equipment. The department announced to members of the Council that its new Soundscriber equipment is tied in with one of the telephone lines and is now available for use by officers and Council members for the dictation of requests, letters, and so forth. The service functions very well and expedites the work of the Society.

Public Relations Library. A public relations library has been started and material is available on a loan basis to all physicians. The department has books and pamphlets on public relations, health insurance, socialized medicine, chiropractic, and other subjects.

Lists of County Officers and Chairmen. The department maintained an up-to-date list of officers and committee chairmen for use in mailings. Each year a form to be filled in by each county society is sent.

Rush Digest of Minutes of Council. After each meeting of the Council, Mr. Tracey and Mrs. Clark prepared a digest of minutes, which was mailed to members of the Council.

American Medical Association. The department worked closely with the A.M.A., particularly through John Kiser, field representative. This has resulted in much closer liaison and better cooperation.

Invitations were sent to all delegates to the A.M.A. and officers and presidents of state medical societies extending an invitation to visit the New York State hospitality suite at the June A.M.A. meeting in New York City and again at the Denver meeting in November. During the New York meeting, the staff of the department helped to man the suite, and at the Denver meeting, Mr. Pardee was in charge.

The department also addressed Christmas cards to A.M.A. delegates from the New York State delegation, and to other state societies from the officers of the Society.

American Medical Education Foundation. Letters were mailed to the entire membership in a drive for funds for the AMEF. Under the guidance of Joseph G. Zimring, M.D., letters were sent to presidents of county medical societies with copies of Auxiliary AMEF chairmen, requesting presidents to remind members of the urgent need for funds by our medical schools. The *Newsletter* carried special articles on the Foundation and devoted one issue to the AMEF benefit concert. This concert was planned and carried out by the department, which also arranged for publicity in the press, radio, and TV.

Hospital Visitation Program. This program has proved to be most worthwhile. Mr. Pardee, Mr. Tracey, and Mr. Forrest attended 28 hospital staff meetings in the New York City area to acquaint physicians with the work of the State Society. An attractive display of the publications of the Society is used and pamphlets, such as the Guide for Cooperation, Standards of Practice, and Guiding Principles for Participation in Telecasts and Broadcasts, are distributed.

Telegrams to Other State Medical Societies. Telegrams of congratulations and best wishes were sent to each outgoing and incoming president of the other state medical societies during each society's annual convention. These were signed by the president of the State Society. Files were maintained so that the telegrams could be sent on the day the new president was inaugurated to the hotel where the convention was held.

Woman's Auxiliary. Assistance was given to the Woman's Auxiliary in the preparation and distribution of the *Distaff*. Circulation stencils were brought up to date; minutes of the convention, Fall Conference and other meetings, releases, and materials for the Health Poster Contest and letters for the various committee chairmen were prepared. During the latter part of the year, Miss Greenstein, under the supervision of Mr. Pardee, prepared communications, flyers, reports, and minutes for the Auxiliary and met with officers and chairmen in preparation for the annual convention.

Medical Assistants Association. The department prepared flyers, the *Reflex*, and other communications and assisted in preparations for the annual meeting. Miss Greenstein is working with the Medical Assistants under the supervision of Mr. Pardee.

Cooperation with Outside Organizations. *New York Association of the Professions*—The department assisted in the formation of this group and arranged meetings and prepared a constitution and bylaws. Mr. Pardee is secretary of the Association, which has recently held meetings of the legislation chairmen of the six professions.

Mr. Pardee is now a member of the New York Chamber of Commerce and has been named to serve on a committee. Membership in this organization has resulted in better liaison between the State Society and this important and influential business organization.

Continuing Education. Mr. Pardee and Mr. Tracey attended the Institute for Organization Management at Syracuse University in August. Purpose of the Institute, conducted by the United States Chamber of Commerce, is to help executives make the most effective use of their talents and abilities in the interest of the organizations they serve. The program is conducted by top-flight experienced men and concentrates on the latest public relations and management technics. At the end of the intensive one-week course, both men took a written examination. Certificates stating that they had passed with flying colors were awarded to both.

Mr. Pardee, Mr. Tracey, and Miss Wunsch attended the A.M.A. Institute in Chicago in September. This was an intensive program of discussions and presentations on public relations, medical economics, and legislation.

Mr. Tracey and Miss Wunsch attended the Medical Society Executives Association meeting in Chicago in September. The purpose of this meeting was to present the latest ideas in organization management, public relations, and related matters. Participants were medical society executives.

Mr. Pardee and Miss Wunsch attended the discussions and workshops during the annual meeting of the American Medical Writers Association in October in New York City.

Mrs. Clark attended a basic layout workshop given by New York University in November.

Meetings Attended by Mr. Pardee or Representative. New York State Chamber of Commerce, United States Chamber of Commerce Legislation Meetings (Tracey), Council meetings (all department executives and Mrs. Clark), Foreign Policy Association, Committees (Legislation, Convention, Constitution and Bylaws, Membership), Public Relations Society of America, Annual Health Conference, Medica Society Executives Association (Mr. Pardee, chairman, Continuing Education Committee and Arrangements Committee, New York meeting), National Health Forum, Health Poster Contest, Woman's Auxiliary Fall Conference (Mr. Pardee, speaker), House Ways and Means Committee, Coordinating Council, District Branches, A.M.A. Medicolegal Conference, Medical Assistants Convention, and hospital staffs.

Visual Aids. The department purchased during the year and has available for use at the Society or on a loan basis the following: several tape recorders, movie projector, slide projector (35 mm.), screens (large and small), and hook and loop display boards. The department also has a TV set and a radio for monitoring programs.

1962 Proposed Program

1. Continued widening of the scope of TV and radio activities: The Public Relations Committee at its meeting in January voted to continue preparation and placement of TV spots, medical interviews, and radio spots. It also approved the purchase of the California Medical Association TV series which will be adapted to New York and offered to stations here.

2. Expansion of contacts with the press through meetings with representatives and through such projects as the series of medical

interviews prepared by the department which will be offered to selected daily papers throughout the State. It will be suggested that these be run on Sundays as a supplement to whatever health column the paper carries. The series is in a question and answer form and is an interview conducted by Mr. Pardee with various specialists. The department is adapting a series of cartoons on medical facts to be reproduced on mats for mailing to all weekly papers in the State.

3. Continued expansion of services to writers in obtaining accurate medical information.

4. Assistance to county societies in establishing radio and TV programs, health conferences and forums, athletic injury conferences, career days, science fairs, health poster contests, and essay contests.

5. Assistance to county societies in preparing health exhibits for county fairs, hotel and bank lobbies, and other places. The department plans to purchase exhibits which will be available on a loan basis to county societies. It now has "A Career in Medicine" and will soon have other exhibits available.

6. The department will further expand its activities in the field of legislation, both State and Federal, as called on by the Legislation Committee and the Subcommittee on Federal Legislation, in order to build better liaison with legislators, obtain necessary and sound legislation, and prevent legislation which could be injurious to the health of the people of New York State.

Acknowledgment. Appreciation is due for faithful performance of their duties to Mr. Jack Pardee, Mr. Martin J. Tracey, Mr. John Schuyler, Miss Gretchen Wunsch, Mrs. Evelyn Clark, Miss Anita Greenstein, Miss Jean MacDonald, and Mr. Joseph Citarella.

Respectfully submitted,
John C. McClintock, M.D., *Chairman*

Cooperation with Media of Information

To the House of Delegates, Gentlemen:

The Subcommittee on Cooperation with Media of Information, of the Council Committee on Public Relations, consists of the following:

George A. Burgin, M.D., *Chairman*	Herkimer
John D. Naples, M.D.	Erie
C. Stewart Wallace, M.D.	Tompkins

The annual review of the "Guide for Cooperation for Doctors, Hospitals and Reporters" was held on January 25, 1962, at 4:00 P.M. in the offices of the State Society. The subject of the program was "Media Problems Concerning the Medical Profession in 1961." Dr. Burgin opened the meeting and appointed Dr. Naples as moderator; speakers were Stockton Helfrich, director, New York Code Office, National Association of Broadcasters, and Robert D. Potter, executive secretary, Medical Society of the County of New York.

This was the best attended meeting so far with 50 persons present, including representatives of the New York State Society of Newspaper Editors, the New York City Newspaper Reporters Association, the New York State Hospital Association, the Greater New York Hospital Association, the National Association of Broadcasters, the New York State Department of Health, the New York Better Business Bureau, the Macy chain (radio), the *Day-Jewish Journal*, *Medical Tribune*, and physicians from upstate New York and the metropolitan area.

It was the consensus of the representatives of the information media that these meetings have been most profitable, and the subcommittee intends to continue holding such meetings in the future.

No changes were recommended in the Guide for the coming year, but it was decided to call it to the attention of physicians in New York State once again. This is to be done through the *Newsletter*.

A meeting is being planned with representatives of the State Bar Association to review the Standards of Practice for Doctors and Lawyers. This meeting with C. Stewart Klopper, Esq., and his committee has been scheduled for Thursday, March 22, in the Medical Society office. A supplementary report will detail the results of this meeting.

Underway also is a meeting with representatives of the press in Albany, sometime during the Legislature session. This also will be detailed in a supplementary report available for the annual meeting of the House of Delegates.

Your chairman is grateful for the interest and valuable suggestions of Drs. Naples and Wallace. We are also deeply indebted to the Department of Communications, Jack Pardee, Martin Tracey, and particularly Miss Gretchen Wunsch, whose attention to details has made our meetings so successful.

Respectfully submitted,
George A. Burgin, M.D., *Chairman*

American Medical Association Education and Research Foundation

To the House of Delegates, Gentlemen:

Your Special Committee on American Medical Association Education and Research Foundation consists of the following members:

Joseph G. Zimring, M.D., *Chairman*	Nassau
William B. Ayers, M.D.	Nassau
I. M. Greenberg, M.D.	Nassau
Milton J. Greenberg, M.D.	Washington
Milton Helpern, M.D.	New York
Irving Weiner, M.D.	Orange
Carl G. Whitbeck, M.D.	Columbia

Effective January 1, 1962, the programs of the American Medical Education Foundation and the American Medical Research Foundation were consolidated within the framework of a single foundation—the American Medical Association Education and Research Foundation. These programs will be expanded and a concerted effort made to provide increased financial assistance to the medical schools, in addition to financing the other projects of the foundation. Among the other projects will be a medical journalism scholarship program, research grants for medical research work and study of prenatal mortality and morbidity, and financing of medical scholarships and loans to medical students, interns, and residents. The AMAERF will seek financial support from physicians, constituents in component medical societies, the Woman's Auxiliary, philanthropic organizations, business entities, and the general public. The success of the foundation's fund-raising efforts will in some measure be dependent on the voluntary cooperation and support from constituent and component medical societies and their counterpart components of the woman's auxiliaries.

Members of both the Medical Society of the State of New York and the Woman's Auxiliary have increased their contributions during the year 1961. The number of contributions has risen from 3,860 in 1960 to 4,865 in 1961, and from a total of $58,531.55 in 1960 to a total of $71,945.13 in 1961. Our committee has sent personal letters to the presidents of the component county medical societies urging them to write to their members appealing for their financial support of our medical schools. The response to these letters plus the open letter from the committee, published in the November issue of the *Newsletter*, and the wonderful work of our Woman's Auxiliary have made possible the increased contributions from our State to the AMAERF.

I would like to thank the various presidents of the component county medical societies of the State of New York for their cooperation in spreading our appeal for funds to their members. To the Woman's Auxiliary to the Medical Society of the State of New York, an orchid for their wonderful cooperation and terrific work in raising the necessary funds. I also would like to thank Mr. Jack Pardee, director of the Department of Communications, for his close cooperation with my committee, and also to thank my committee for their cooperation in the work we have done this year.

Respectfully submitted,
JOSEPH G. ZIMRING, M.D., *Chairman*

Convention

To the House of Delegates, Gentlemen:

The Convention Committees wish to submit the following reports:

1961 Convention. The committee consisted of the following:

Merle D. Evans, M.D., *Chairman*	Monroe
Maurice J. Dattelbaum, M.D.	Kings
John J. Finigan, M.D.	Monroe
Joseph A. Lane, M.D.	Monroe
George J. Lawrence, Jr., M.D.	Queens

The 1961 Convention was held in Rochester, May 8 through 12, 1961. Because there is no facility in Rochester large enough to have the entire convention under one roof, this had to be a "spread-out" meeting. The Woman's Auxiliary was housed and held all its meetings and functions at the Sheraton Hotel. The House of Delegates was housed and completely accommodated at the Manger Hotel which was also the headquarters hotel. All the exhibits and scientific meetings of the Society were at the War Memorial Auditorium. Despite the problems that naturally arise with such division of meetings, the convention was a success.

Registration was: Physicians, 1,405; guests and allied professions, 583; technical exhibitors, 240, for a total of 2,228.

The attendance, within 10 per cent of that for which we had planned, was good for an upstate meeting of the Society. Registered attendance was 5.5 per cent of the Society membership. At Buffalo in 1959 it was 5.3 per cent. The 1958 and 1960 meetings in New York City registered 16.9 per cent and 14.8 per cent of the Society membership. In upstate meetings registration shows twice as many Society members as guests and exhibitors, while at meetings held in New York City these two registrations are practically identical. The registration of Society members at the New

York City meetings is two and three-quarters to three times the number at upstate meetings. However, this numerical difference is not reflected in the audiences at either the section or session meetings. These figures prove the fact that more persons go to a convention held in a prominent city but not to attend scientific meetings. It is because of this fact that many of the smaller conventions—professional, industrial, educational, and so forth—are avoiding the larger cities as meeting sites.

Due to the fact that the Society meetings were held in the War Memorial Auditorium where the exhibits were set up, while the attendees were housed throughout the city, it was necessary to have several local committees to arrange for various facilities.

A Housing Subcommittee, chaired by Maurice M. Maltinsky, M.D., working through the Rochester Convention Bureau, met little difficulty in arranging satisfactory housing for all those attending the convention.

This subcommittee would like to submit the following suggestions regarding housing for future conventions:

1. The New York City headquarters should provide the chairman of the Housing Committee with (*a*) a list of officers and suites and rooms they would need, (*b*) a list of delegates, guests, and speakers and the rooms they would require. The remaining visitors would then be given accommodations accordingly.
2. The Housing Subcommittee chairman and his committee, working with each city's convention bureau and/or hotel registration department, should then be allowed to discharge their duties without pressure or interferences.

A Transportation Subcommittee, under the direction of George A. Hardie, M.D., arranged for regular free scheduled bus service by chartered Rochester Transit Corporation buses between the principal hotels and the War Memorial Auditorium. These facilities, through confused communications and advertising and poor bus markings, were not utilized effectively.

Since there are no eating facilities within several blocks of the War Memorial Auditorium, a special committee under the leadership of Michael J. Crino, M.D., arranged for luncheons at the Auditorium. A general quick-lunch arrangement was organized through the cooperation of the War Memorial Auditorium food concessionaire for the general needs of the physicians, staff, and exhibitors. By arrangement with the Burgundy Catering Service, special luncheons were catered for the Sections on General Practice, Orthopedic Surgery, Pathology, Clinical Pathology, and Blood Banking, and Obstetrics and Gynecology at the War Memorial Auditorium. Through confusion of communications, the Section on Orthopedic Surgery had asked for more lunches than could be utilized. The State Society has had to honor the requested obligation to the caterer for these extra luncheons.

These three subcommittees did remarkable jobs but their activity was limited because of the lack of understanding by those attending the convention.

House of Delegates, Joseph A. Lane, M.D., Speaker. The House reverted to the former custom of meeting concurrently with the general convention. It convened on Monday morning, May 8, and adjourned Wednesday afternoon, May 10, after the election of officers. Seventy-five resolutions were discussed and studied in 10 reference committees. Each delegate was supplied with an original and final copy of each resolution before action in the House. Each reference committee did an outstanding job in studying the resolutions referred to it, thus reducing the amount of discussion and controversy when the resolution reached the floor of the House.

This system of having the House of Delegates and the convention meetings running concurrently deprives the delegates of the opportunity of attending some important and interesting scientific meetings. This problem is worthy of much serious and sober study.

Scientific Program, Alfred P. Ingegno, M.D., chairman. Following last year's theme of "Horizons of Clinical Medicine" this year's scientific program theme was "Frontiers of Clinical Therapeutics." This theme, worked out in lilac color because of Rochester's lilac reputation, made attractive covers for the various Convention program booklets.

Twenty-two section meetings, one session meeting, and five general sessions were held from Monday through Friday. The Section on Space Medicine was transferred to the General Session on Tuesday afternoon. A large, enthusiastic audience attended this new, interesting, exciting, and well-timed meeting. A record was set when no audience showed up for the History of Medicine Session on Friday morning. The place of the meeting of the Public Relations Session was changed from the War Memorial Auditorium to the Manger Hotel without sufficient or effective notification. This reduced the attendance at a very important and interesting meeting and resulted in some disgruntlement and disappointment.

Following are the attendance records of the scientific meetings:

Sections	*Attendance*
Allergy	74
Anesthesiology	69
Chest Diseases	67
Dermatology and Syphilology	35
Gastroenterology and Proctology	35
General Practice	43
Industrial Medicine and Surgery	30
Legal Medicine	29
Medicine	115
Neurology and Psychiatry	54
Obstetrics and Gynecology	35
Ophthalmology	100
Orthopedic Surgery	43

Otolaryngology	55
Pathology, Clinical Pathology, and Blood Banking	37
Pediatrics	66
Physical Medicine	40
Preventive Medicine and Public Health	35
Radiology	27
Space Medicine	150
Surgery	35
Urology	28
Session	
Public Relations	30
General Sessions	
Monday	68
Tuesday (Space Medicine)	150
Wednesday	77
Thursday	50
Friday	40

The name of the Section on Legal Medicine was changed, by action of the House of Delegates, to Section on Medical-Legal and Workmen's Compensation Matters.

SCIENTIFIC EXHIBITS, William L. Watson, M.D., chairman. Forty interesting and informative scientific and clinical research exhibits were arranged this year, covering original work, new ideas, and new approaches to old problems. Closed-chest cardiac massage was demonstrated periodically. The exhibits this year included three extensive displays regarding space medicine.

Recognition of these exhibits was made by the Scientific Exhibit Awards Committee, Thurman B. Givan, M.D., chairman, who reported to the House at its closing session (see NEW YORK STATE JOURNAL OF MEDICINE, September 1, 1961, Part II, Minutes of the House of Delegates, Section 250, page 167).

Attractive certificates of award were sent to all the award winners.

SCIENTIFIC MOTION PICTURES, William J. Sullivan, M.D., chairman. Films covering topics in varied fields of medicine were shown. Four premiere showings were made, and many of the films were narrated and discussed by their originators.

TECHNICAL EXHIBITS, William B. Rawls, M.D., chairman. The exhibit hall of the War Memorial Auditorium lends itself very well to any variety of exhibits. Eighty-seven exhibits were set up along a labyrinth so that all going or coming from the meeting rooms would have to pass every booth. In spite of this arrangement and attractive and interesting booths, the exhibitors reported an unsatisfactory evidence of interest in the displays and a disappointing number of physician registrations at the booths. Explanation to some degree can be made by two factors: (1) The doctor arrived at the War Memorial Auditorium with little time before the meetings were to start and found a shortcut out of the building after the meetings were concluded, and (2) New York State is so well detailed that little of the material was really new. However, in the future, may we ask the convention attendees to spend some time visiting and discussing the various technical exhibits, for the technical exhibitor is essential to us in helping to meet the convention expenses.

ANNUAL MEETING AND DINNER DANCE, Arthur H. Walker, M.D., chairman. The 1961 Annual Meeting and Dinner Dance was held in the Ballroom of the Manger Hotel on Wednesday, May 10, at 8 P.M., preceded by the President's cocktail party at 6:30 in the Ontario Room of the same hotel. There was no speaker. Entertainment consisted of orchestral music supplemented by a short musical program by a quartet from the Eastman School of Music. The rest of the evening was spent in dancing.

This meeting and dinner dance sets a record in State Medical Society annals since its attendance of 361 represents a 16.1 per cent of the registered convention attendance, a record well ahead of any other annual meeting. The success of this meeting must be attributed to a very active committee under the leadership of Dr. Walker.

The subcommittee wishes to pass on to future dinner dance subcommittees this idea regarding the cost of the dinner dance ticket. The cost of the ticket should reflect the actual cost of the affair with no margin for partial cost of the many "free tickets" to be provided to officers, guests, and staff. The reduction in price of the ticket will be more than made up by the additional sale of tickets.

GUEST RECEPTION, Hobart L. Boyd, M.D., chairman. This subcommittee, inaugurated last year, was expanded and proved of great assistance to the meeting. Under its able chairman, a large and active subcommittee individually guided, counseled, and hosted convention guests and speakers. Hospitality rooms were set up at the War Memorial Auditorium and the Manger Hotel, with desks, writing and counseling facilities, light refreshments, and rest and relaxation facilities.

WOMAN'S AUXILIARY. The Woman's Auxiliary to the Medical Society of the State of New York held its annual convention, its silver anniversary or 25th annual convention, at the Sheraton Hotel, Sunday through Wednesday, May 7 through 10, 1961. A tour of Eastman House on Sunday evening, May 7, was enjoyed by many of those attending our convention. The reception honoring State past-presidents of the Auxiliary held on Monday evening, May 8, was cosponsored by the State Medical Society and enjoyed by many of the State Society members. It was a memorable affair.

The Auxiliary is of great assistance to the State Society during the annual conventions through the help of its committees, in cooperation with the dinner, publicity, guest reception, entertainment, and ticket selling subcommittees. Many of the Auxiliary members act as guides, attendance recorders, messengers, and attendants at the various scientific meetings during the convention. This is greatly appreciated by the State Society, and "thank you" cards were sent to all who assisted us, shortly after the convention.

WOMEN'S MEDICAL SOCIETY OF NEW YORK STATE. The Women's Medical Society of New York State held its annual meeting at the Manger Hotel on Sunday, May 7, 1961. The morning was taken over by a business meeting, followed by a luncheon at noon, and a scientific meeting in the afternoon.

MISCELLANEOUS. Printed "thank you" cards were sent to all scientific program and exhibit participants, to all committee members and chairmen, and others who assisted at the convention.

COMMENTS. The House of Delegates this year voted acceptance of our recommendation that the Convention Committee be made a permanent committee of the House rather than an annually-appointed committee. This creates some continuity of the committee and should be reflected in improved, smoother-running, and more economical future conventions.

After some lively and interesting discussion of future convention plans in the reference committee and on the floor of the House, it was decided that this problem is worthy of further study.

Therefore, to the new Convention Committee, the present committee refers the following suggestions regarding future conventions:

1. *Site of future meetings* According to action of the 1959 House of Delegates, all future meetings are to be held in New York City. As pointed out in our reports earlier this year, this throws into New York City every four years both the New York State meeting and the A.M.A. meeting.

2. *Type of meeting* Do the House of Delegates and the general sessions and section meetings convene concurrently? This deprives the members of the House the benefit of academic and scientific sessions. It means that all future conventions have to be held in New York City, the only city in the State large enough to handle the entire convention at one location.

3. *Season of the year for the meeting* A meeting in the spring of the year creates intense competition for good program material and speakers and vies for good exhibits.

4. *Divided meetings* The scientific meetings and exhibits need large facilities. This limits the sites for such a convention to New York City. The House of Delegates, meeting at a time by itself, could be accommodated in any one of several upstate locations. This would adapt itself to more representative distribution of the Society business meetings throughout the State.

5. *By dividing the meetings* in this way, the House could meet in the spring for its business sessions in conformance with the present set-up of the fiscal year of the various component county medical societies. The scientific meeting could be held in New York City in the winter when it would be possible to arrange an interesting and stimulating program. The attendance would undoubtedly be improved and increased. The cost should reflect some saving to the Society.

The committee wishes to acknowledge its indebtedness to the members and chairmen of all its subcommittees, to the State Society office staff, to the Monroe County Medical Society and staff, to the Rochester Convention and Publicity Bureau, to the personnel of the War Memorial Auditorium and the Manger Hotel, to the Woman's Auxiliary, and to the many others who have given so generously of their time and effort in the planning and accomplishment of a successful 155th Annual Convention of the Medical Society of the State of New York. Thanks to all of you.

Respectfully submitted,
MERLE D. EVANS, M.D., *Chairman*
1961 Convention Committee

1962 Convention. The committee consists of the following:

Bernard J. Pisani, M.D., *Chairman*	New York
Merle D. Evans, M.D.	Monroe
George J. Lawrence, Jr., M.D.	Queens
Harold W. Mayberger, M.D.	Nassau
Frederick A. Wurzbach, Jr., M.D.	Bronx
Joseph G. Zimring, M.D.	Nassau

The 1962 Convention of the Medical Society of the State of New York will be held at the Statler Hilton in New York City, May 14 through 18, 1962.

At this writing, all subcommittees of the Convention Committee have made plans and activated them for all of the facets of convention activity.

SCIENTIFIC PROGRAM, Alfred P. Ingegno, M.D., chairman. The theme of this year's program is "Medical Centers on Parade." In line with this, the ten medical centers in New York State have been asked to participate and assign a liaison officer. All of the centers have signified their willingness, and the liaison officers, the chairman, and associate chairmen of our Scientific Program Subcommittee are working together to arrange a program from each center. This will be presented in the General Sessions, every afternoon, from Monday through Friday.

The Section meetings will start on Monday and go through Friday, in order to effect a better distribution of scientific meetings.

SCIENTIFIC EXHIBITS, William L. Watson, M.D., chairman. The subcommittee considered 63 applications, from which they chose 45. This number is less than we have had in previous years. This may be due, in part, to the fact that the A.M.A. convention was held in New York City in June, 1961.

Scientific Motion Pictures, William J. Sullivan, M.D., chairman. We have in prospect what should be a most interesting program and look forward to a much more successful meeting for 1962 than we had in Rochester in 1961. Members of the State Society have been encouraged to produce and submit their own films for showing.

Dinner Dance, Samuel Wagreich, M.D., chairman. The annual dinner dance will be held Wednesday, May 16, 1962, in the Terrace Ballroom of the Statler Hilton, preceded by the president's reception. Tickets are $17.50 each. Plans are under way to make this a gala affair.

Reception, Sol Axelrad, M.D., chairman. This subcommittee will be an active one. Each invited guest to the convention will be contacted in advance by a member of the subcommittee who will act as his host during the guest's stay at the convention. A hospitality room has been set aside for the use of the Reception Subcommittee and guests.

House of Delegates, Frederick A. Wurzbach, Jr., M.D., Speaker. For the first time, the House of Delegates will be in operation for four days, Monday through Thursday. Tuesday will be devoted to meetings of the reference committees; voting will take place on Thursday.

Technical Exhibits, William B. Rawls, M.D., chairman. Mr. Charles L. Baldwin, exhibit manager, reports: Although most of the booths have been allotted to exhibitors it has taken more than the usual hard work to accomplish this for the 1962 meeting. In order to keep our annual convention one of the best in the country for technical exhibitors as well as physicians, increased effort and imagination must be used in working out all phases of convention organization. Program quality must be continued and improved in order to attract interested attendance for the technical exhibitors.

Respectfully submitted,

Bernard J. Pisani, M.D., *Chairman*
1962 Convention Committee

Organization and Policies

DISTRICT BRANCHES

First District Branch

To the House of Delegates, Gentlemen:

The annual meeting of the First District Branch of the Medical Society of the State of New York was held at the Manger Hotel, Rochester, on Tuesday, May 9, 1961. Gerald D. Dorman, M.D., president, presided, and there were 75 members present.

At the request of Dr. Dorman, the members rose in respect to the memory of Moses H. Krakow, M.D., former treasurer of the branch and of the Coordinating Council, who had passed away since the last meeting. The minutes of the May 8, 1960, meeting, which appear in the April 15, 1961, issue of the NEW YORK STATE JOURNAL OF MEDICINE, were approved as published. David Kershner, M.D., of Kings, was unanimously elected treasurer for a term of one year to fill the unexpired term of Dr. Krakow.

Dr. Alice Waterhouse, of the U.S. Public Health Service, was present by invitation and discussed the fact that from September 9 to October 23, 1961, the U.S. Public Health Service, as part of a National Health Survey, will examine about 322 persons in the New York City area. This health survey was authorized by Congress in 1956 as a continuing mechanism for assessing morbidity and health in the nation. It consists of a household interview and physical examination of persons predesignated by a probability sampling technic. The examinations are given in an examining center housed in a specially-designed trailer-truck combination. The findings will not be disclosed to the examinee but to his physician or dentist, if he so authorizes. This is simply a research project, and no interpretations or clinical diagnoses are made.

It was approved that this matter be referred to each of the five county medical societies for implementation.

Coordinating Council, May 9, 1961. At the meeting of the Coordinating Council held at the Manger Hotel, Rochester, on May 9, 1961, Matthew Brody, M.D., chairman of the subcommittee on mental health of the public health committee of the Medical Society of the County of Kings, was present by invitation and discussed the fact that last summer the Police Department became hesitant in offering cooperation and help to families of mentally disturbed patients requiring transfer to observation wards, giving the reason that there had been a recent order issued making it impossible for them to do otherwise. Thus, Section 81.2 of the Mental Hygiene Law was rendered ineffective. At the request of the Coordinating Council, the Mayor was asked to call a conference of representatives of the Police Department, the Department of Hospitals, and the Corporation Counsel, so that proper measures could be taken to protect potentially dangerous patients from themselves. Dr. Brody attended this meeting as the representative of the Coordinating Council. As a result, legislation was introduced in Albany legalizing what had been the custom in New York City for many years, amending the Mental Hygiene Law in relation to the removal of certain persons to a psychopathic hospital or ward established and operated by the City of New York. Dr. Brody reported that the bill has been signed by the Governor. Now any physician who feels that a patient should be admitted to the psychopathic wards of Bellevue or Kings County Hospitals can write a note and the police are obligated to render assistance.

It was approved that the Coordinating Council go on record approving the actions of the Advisory Council of the Department of Hospitals in attempting to alleviate the emergency condition arising on July 1, that is, by helping to furnish doctors to man the City hospitals and by arranging to have practices covered when absent from the City, thus helping those surviving City hospitals to function at a better level. It was also approved that this matter be referred to each county medical society for implementation in an attempt to meet the emergency.

Charles C. Mangi, M.D., reported for the economics committee as follows: "Your chairman has received a letter dated May 3, 1961, from Dr. Alonzo S. Yerby, director of the Bureau of Medical Services of the Department of Welfare of the City of New York, stating that effective July 1, 1961, the following fees are to be paid by this department to panel physicians: general practitioners home visit, $4.00; specialists home visit, $7.00. This is a long overdue answer from the Department of Welfare to a request initiated by the previous chairman of the economics committee, who had requested that the fee for home visits by panel physicians be raised from $3.00 to $6.00. Your chairman recommends that the Council immediately protect these inadequate fees."

Dr. Kershner, treasurer, reported as follows: As of May 9, 1961, income, $1,393.94; expenses, $1,380.00; net, $13.94.

Letters have been received by the county medical societies and the Coordinating Council from Leona Baumgartner, M.D., Commissioner of Health of the City of New York, regarding studies being made to protect the beaches of the city against pollution. The Council went on record endorsing the program as submitted by Dr. Baumgartner to correct pollution in the waters around New York City.

A communication was received from William L. Wheeler, Jr., M.D., secretary of the Medical Society of the State of New York, enclosing a letter from E. A. Burkhardt, M.D., chairman of the Committee on Disaster Medical Care of the State Medical Society. Dr. Burkhardt's letter was approved by the Council of the State Society on March 23. This letter states that the committee is concerned about disaster medicine preparedness in New York State and submitted the following program for the Coordinating Council's consideration:

"1. Reorganize a strong disaster medical care committee in each county society;

"2. Request the Mayor, Commissioner of Hospitals, or the Commissioner of Health to appoint representatives to sit in a joint meeting with these committees to consider: (*a*) the formation of permanent joint committees on disaster medicine at the county level; (*b*) to supply full-time executive directors and secretaries paid out of city funds to execute the plans developed by these committees; (*c*) to develop city-wide standard exercises and supervision at every hospital, emergency improvised hospital, and aid station.

"The weight of organized medicine behind the responsible governmental agencies would result in efficient preparation for any disaster. This would validate the statement that 'Defense is Everybody's Business.'"

The nominating committee offered the following nominations for 1961–1963, which were unanimously approved: *Chairman:* George J. Lawrence, Jr., M.D., Queens; *Vice-Chairman:* Solomon Schussheim, M.D., Kings.

At the suggestion of Dr. Broad a rising vote of thanks was given to Samuel Wagreich, M.D., in appreciation of his able leadership as chairman of the Coordinating Council for the past two years.

Coordinating Council, June 6, 1961. At the meeting on June 6, 1961, the following actions were taken:

It was approved that meetings should be for "members only" in addition to the Coordinating Council committee chairmen and county society executives, with the chairman having the right to invite anyone he desires to the meetings. Meetings will continue as dinner meetings for the months of September, November, January, and March and will be held at a place to be decided upon by the chairman, vice-chairman, secretary, and treasurer.

The recommendations covering disaster medical care made by Dr. Wheeler to the Coordinating Council at its meeting in Rochester were recorded in the minutes of that meeting and referred to the public health committee for report at the September meeting.

The matter of an exhibit at the 1964 New York World's Fair and of around-the-clock medical care for persons attending the Fair was referred to the public relations committee.

Dr. Wagreich was appointed as liaison between the Coordinating Council and the Boy Scouts. All county societies have agreed to send to Dr. Wagreich the names of doctors who are willing to serve as members of the medical advisory committee of the Boy Scouts.

Coordinating Council, September 14, 1961. At the meeting held at the Press Box on September 14, 1961, the following actions were taken:

Leonard L. Heimoff, M.D., chairman of the public health committee, reported progress on the matter of disaster medical care and reported that a meeting will be held in Chicago. It was voted that Dr. Heimoff be sent as representative to the Twelfth County Medical Societies Conference on Disaster Medical Care of the A.M.A. on November 4 and 5, 1961, in Chicago and that his expenses be paid by the Coordinating Council.

It was approved that the Coordinating Council write to Group Health Insurance requesting that they refer all cases in which a physician's bills or reports are questioned to the respective county medical societies for investigation by their grievance committees.

It was also approved that Standards for Approval by the Medical Society of the State of New York of New York State Medical Care Plans be reprinted in these minutes. These standards were attached to these minutes.

Coordinating Council, November 14, 1961. At the meeting on November 14, 1961, the following actions were taken:

The matter of the scarcity of influenza vaccine was discussed. Dr. Lawrence stated that the following release was sent to the newspapers on Saturday, October 28, 1961:

> Based on the probability that there might be an increase of influenza cases this winter, the Commissioner of Health and Chairman of the Coordinating Council recommend influenza immunization for persons over sixty-five, for pregnant women, diabetics, cardiac patients, and patients with chronic debilitating diseases.

Physicians are unable to carry out this recommendation because there is not sufficient influenza vaccine available in New York City. Some patients have been concerned with their inability to receive injections of influenza vaccine.

Dr. George J. Lawrence, Jr., chairman of the Coordinating Council of the counties of Bronx, Kings, New York, Queens, and Richmond, states that there is no cause for concern—"there is no reason to believe that an epidemic of influenza is imminent and chances of a significant increase of cases this winter is only a probability." He states—"there is no urgency. It is safe if persons in the high-risk category receive immunization before January 1, 1962. We have been informed that the manufacturers are working continuously to provide a sufficient amount of influenza vaccine to meet all needs."

Dr. Lawrence continues, "If your doctor does not have influenza vaccine now, call him in a few weeks, and by that time plenty of vaccine will be on hand."

The economics committee again recommended that the Department of Welfare be requested to increase the fee for house calls by general practitioners to $6.00.

Dr. Heimoff, for the public health committee, reported on his attendance at the meeting on disaster medical care in Chicago on November 4 and 5, 1961. Dr. Heimoff's complete report has been sent to the president of each of the five county medical societies.

Dr. Ray E. Trussell, Commissioner of Hospitals, discussed the resolution concerning the relationship of municipal hospitals to voluntary and university hospitals, which was passed at the September, 1961, meeting. The following was approved:

> "*Resolved*, that all future actions pertaining to municipal hospitals in their relationship to voluntary and/or university hospitals be presented to the county medical societies and the Coordinating Council for their consideration and possible approval."

Coordinating Council, January 9, 1962. At the meeting on January 9, 1962, the following matter was approved:

Dr. Alonzo Yerby, acting medical director of the Department of Welfare, discussed medical care rendered by that department. Dr. Yerby stated that the Department of Welfare had never given complete medical care, paying only for house calls and for certain drugs, appliances, and so forth, leaving the hospital care and office visits of welfare recipients to the Department of Hospitals and to the Department of Health. He stated that he was trying to outline a plan whereby recipients of aid from the Department of Welfare would receive complete medical care and that he was planning an experiment in Richmond County, to give medical care to certain persons who receive aid, through a Blue Cross-Blue Shield plan.

The Coordinating Council voted that the Department of Welfare of the City of New York be notified that the members of the council appreciate the fact that the Department of Welfare is making this study in Richmond County.

Dr. Heimoff, chairman of the public health committee, recommended that local committees on disaster medical care of each of the county medical societies contact their county chairmen for civil defense, offering to work with them.

Dr. Heimoff also reported that he and Jerome Leon, M.D., were appointed members of the committee on narcotic control of the Medical Society of the State of New York.

Dr. Wagreich, chairman of the public relations committee, reported that a letter was sent to General Sheldon S. Brownton, chief medical adviser of the 1964 World's Fair, offering our help in securing medical coverage for the Fair.

At the request of Dr. Kershner, treasurer, it was approved that each county medical society be requested to contribute $100 for the expenses of the Council for 1962.

Respectfully submitted,
CHARLES C. MCCARTY, M.D., *Secretary*

Second District Branch

To the House of Delegates, Gentlemen:

The Second District Branch held its 55th Annual Meeting at Grossinger's, October 29 through November 1, 1961. On Monday evening, October 30, the annual dinner was held. Attending were: Mrs. Eugene Wolff, president of the Woman's Auxiliary to the Medical Society of the State of New York; Mrs. John L. Neubert, councilor for Nassau-Suffolk Counties; Mrs. James L. McCartney, past-president of the Woman's Auxiliary to the Medical Society of the State of New York; Wendell Hughes, M.D., president of the Nassau County Medical Society; Anthony Kohn, M.D., president of the Suffolk County Medical Society, and John L. Sengstack, M.D., past vice-president of the Medical Society of the State of New York. Mrs. Wolff spoke a few words to the gathering, which were well received.

The highlight of this meeting was the presentation by John M. Galbraith, M.D., president of the Medical Society of the State of New York. Dr. Galbraith mentioned many things during his talk. He congratulated Suffolk County for its progress in the formation of an academy of medicine; he mentioned the problem of liaison between osteopathic physicians and M.D.'s, and spoke about the controversy on the use of generic names as against the use of brand names in prescribing medicine.

Dr. Galbraith also said that we must maintain our system of private health insurance if we intend to keep the government out of the practice of medicine and that this system of private health insurance should not be ruined because of injustices on the part of either physicians or patients. The King-Anderson Bill was mentioned, and the gathering was assured that the

State Society has been diligent in its opposition to this bill. It was pointed out that the Kerr-Mills law being implemented in this State by the Metcalf-McCloskey law providing medical care for the needy aged was also being carefully studied in order to iron out some of the difficulties involved.

There was a scientific program on Monday afternoon, October 30, when Anthony Kohn, M.D., spoke on "Radioiodine and the Thyroid." On Tuesday afternoon, October 31, Stuart T. Ross, M.D., spoke on "Common Rectal Disorders." Both lectures were well attended and apparently well received, judging by the questions asked following each.

The officers for the coming year are:

President—Charles W. Shlimbaum, M.D., Bay Shore
First Vice-President—Paul H. Sullivan, M.D., Great Neck
Second Vice-President—John P. Ruppe, Jr., M.D., Islip
Secretary—Albert M. Biglan, M.D., Central Islip
Treasurer—George C. Erickson, M.D., Hempstead
Delegate—Albert M. Biglan, M.D., Central Islip

Special mention should be given to Mrs. Neubert and Miss Mollie Pesikoff of the State Society office for their help in arranging this affair.

Respectfully submitted,
CHARLES W. SHLIMBAUM, M.D., *President*

Fourth District Branch

To the House of Delegates, Gentlemen:

The executive committee of the Fourth District Branch met at the Queensbury Hotel, Glens Falls, on October 12, 1961. Previous plans had called for a joint meeting of the Third and Fourth District Branches with each district conducting its own business session, then a combined scientific and social program. The Third District Branch failed in its responsibilities to make the necessary arrangements, and as a result neither the Third or Fourth District Branch held an annual meeting for its membership. The executive committee of the Fourth District found it too late to arrange a satisfactory program, so that a general business meeting was held in place of the annual meeting.

Officers of the Fourth District Branch are:

President—Milton J. Greenberg, M.D., Hudson Falls
First Vice-President—Arthur Q. Penta, M.D., Schenectady
Second Vice-President—Webster Moriarta, M.D., Saratoga Springs
Treasurer—August B. Korkosz, M.D., Schenectady

The following county representatives attended this meeting: George D. Anderson, M.D., and Claire K. Amyot, M.D., Saratoga; Raymond L. Rhodes, M.D., and N. H. Harvey, M.D., Warren; Robert B. Homer, M.D., W. S. Bennett, M.D., and R. Leith Skinner, M.D., Washington; James E. Glavin, M.D., Essex; Harold Singer, M.D., Clinton; Donald C. Walker, M.D., Schenectady; and W. L. Lanyon, M.D., Fulton. John H. Wadsworth, M.D., of the Albany Blue Shield Plan, was also present. We were fortunate in having Henry I. Fineberg, M.D., the executive vice-president of the State Society, with us for the meeting.

Dr. Fineberg addressed the meeting and pointed out that he favored continued district branch meetings with increased activity in each of the districts. He announced that a new planning committee had been created at the State level consisting of five past-presidents. This committee is considering limiting tenure of office of the secretary, councillors, Board of Trustees, chairmen of committees, and members of committees. County medical societies will be contacted for recommendations for State officers. He discussed intern situations relative to small hospitals and felt that for the present there was no easy solution to this situation. He suggested younger members of visiting staff to do intern work at a salary. The question of mandatory A.M.A. membership was brought up, and he stated that with few exceptions there was general acceptance.

There was considerable discussion at this meeting regarding the appointing of a nominating committee for State officers, and it was felt strongly that the president of the Medical Society of the State of New York, in appointing a nominating committee, should consult with the executive committee of each district for a recommendation as to the appointment of the individual from the district.

At the next meeting of the House of Delegates, a resolution will be introduced by the Fourth District Branch making it mandatory that the president shall consult with the executive committee of the various branches in regarding the appointment to the nominating committee.

A committee headed by Dr. Penta was appointed to investigate coverage for sickness and accident of physicians who are still in active practice after the age of seventy.

The next regularly scheduled meeting of the executive committee will be held April 19, 1962, at Glens Falls, and final plans will be drafted at that time for the annual meeting which is scheduled for September 20, 1962, at the Queensbury Hotel, in Glens Falls. A good scientific program is planned for this September meeting with a dinner and entertainment for the evening.

Respectfully submitted,
MILTON J. GREENBERG, M.D., *President*

Fifth District Branch

To the House of Delegates, Gentlemen:

Take a week end when the weather is so fine as to be not only unusual but almost unbelievable; add a group of men, who are not only thoroughly familiar with their subject material but possess the capacity to share this knowledge, and the interest to enjoy such participation; then add a group of interested, attentive seekers of knowledge willing to take an active part in discussions rather than sit in an aloof, supercilious manner, whose only apparent reason is to gather material for later "bar critiques"; mix these with a well-kept but not too difficult golf course, good food, well-served: then you have a successful medical meeting. These ingredients are self-miscible and require no master chemist to produce a palatable and intoxicating brew. All the planners have to do is avoid irritants and counterirritants.

This formula made the annual meeting of the Fifth District Branch if not its best at least one of its most enjoyable gatherings. We are particularly grateful and appreciative of the contribution made by our discussants: Granville Nickerson, M.D., F.R.C.P., pediatrician-in-charge, Royal Victoria Hospital, and member of the medical faculty of McGill, Montreal, and to our own members, Robert O. Gregg, M.D., chairman, Department of Surgery, and professor of surgery, Upstate Medical Center, Syracuse, Louis G. Fournier, M.D., faculty of Upstate Medical Center and chairman, Department of Obstetrics and Gynecology, Syracuse; John J. Duggan, M.D., associate professor of clinical medicine, Upstate Medical Center, and chairman, Department of Medicine, Community Hospital, Syracuse, and Herman Snow, M.D., director of St. Lawrence State Hospital, Ogdensburg.

We were honored also by a fine and delightful group from the State Society, not all of whom lolled in luxury but gave of their know-how and also as willing workers to keep the meeting rolling and contributed much to its success, particularly Jack Pardee and Miss Mollie Pesikoff. We only hope that our president, John M. Galbraith, M.D., his successor-to-be, Joseph A. Lane, M.D., as well as Drs. Fineberg and Hammond, and Mr. Farrell, as well as our own Dr. Gibson, enjoyed it as much as we enjoyed having them with us; and the gracious representatives from the Woman's Auxiliary renewed my faltering confidence in the judgment of the practicing physicians of New York State.

We think the new therapeutic approach of week-end meeting, sport shirt uniforms, and balanced program of pleasure and education, held in a locale devoted to pleasing the vacationing American and permitting family participation, has succeeded in reawakening the interest and whetted the desire for more of the same in an organization which over the years had become indifferent from neglect and atrophied with disuse.

So it is that come September there will be a similar annual meeting using the same formula as in '61, and we hope with equal success. This meeting will be a joint meeting with the Sixth District Branch and is planned for September 7 to 9 at Whiteface Inn, Lake Placid. All I can say is that if you have never known the Adirondacks in September after the youngster camps have closed and before the overeager hunters arrive then you don't know what hidden meanings of indescribable beauty can be contained in the prosaic word "weather." So if you want to experience what I can't describe treat yourself in one of America's great resorts.

Respectfully submitted,
WILLIAM R. CARSON, M.D., *President*

Sixth District Branch

To the House of Delegates, Gentlemen:

The year 1961 was very active and productive for the members of the Sixth District Branch. The executive committee consisting of the officers of the district branch and the nine component county societies' presidents met on a number of occasions in order to arrange the numerous activities during the year. Executive committee meetings were held on January 25 in Binghamton, February 8 in Ithaca, February 22 in Binghamton, August 16 in Ithaca, October 11 in Norwich, and October 25 in Binghamton.

Athletic Injury Conference. During the year a number of activities were undertaken on a district basis. On March 25, 1961, a district Athletic Injury Conference was held at the Sheraton Inn in Binghamton. Invited to attend were the coaches, athletic directors, trainers, and school physicians from all the high schools, prep schools, colleges, and universities in the district. In all 508 persons were invited and 280 attended this highly successful conference.

The following program was conducted: Welcome, C. Stewart Wallace, M.D., president, Sixth District Branch, Ithaca; "The Mechanism of Injury," Alexius Rachun, M.D., Ithaca; "Eye, Ear, Nose, and Throat Injuries," William E. Boland, M.D., Elmira; "Chest and Abdominal Injuries," William J. McAuliffe, M.D., Cortland; "Skin Infections, Locker Room and Personal Hygiene," Robert H. Broad, M.D., Ithaca; "Dental Injuries and Protective Mouthpiece," Robert W. Baker, D.D.S., Ithaca; "Fractures and Epiphysial Injuries," Reginald C. Farrow, M.D., Ithaca.

Also: "The Nine Lives of a Giant," Frank Gifford, sports announcer, Columbia Broadcasting System, former star of the New York Football Giants; "Muscle Injuries," Jack E. Thomas, M.D., Elmira; "Joint Injuries," Alvin R. Carpenter, M.D., Binghamton; "Responsibility of the Athletic Director," Robert J. Kane, athletic director, Cornell University, Ithaca; "Head, Neck, and Back Injuries," J. Worden Kane, M.D., Binghamton; "Medicolegal Aspects," Martin F. Holleran, Jr., Esq., Binghamton.

The luncheon for the program was sponsored by the following generous industries in the district: Adding Machine Division of the National Cash Register Company, Ithaca; Wilcox Press Inc., Ithaca; Cayuga Rock Salt Company, Myers; Hiss Pharmacal Company Inc., Utica; Wallace Steel and Supply Company, Ithaca; Cooperative Grange League Federation, Ithaca; and Eaton Laboratories, Norwich. The members of the panel with the exception of Mr. Frank Gifford were all members or residents of the Sixth District Branch.

Annual Meeting. The annual meeting of the Sixth District Branch was held at the Eaton Laboratories in Norwich on October 11, 1961. The following scientific program was presented: Panel Discussion—"The Comatose Patient: A Medical Emergency;" William W. Faloon, M.D., Syracuse, associate professor of medicine, State University of New York Upstate Medical Center in Syracuse, moderator; Everett W. Corradini, M.D., Elmira, attending neurosurgeon, Arnot-Ogden Hospital; James F. Johnson, M.D., Binghamton, associate pediatrician, Binghamton General Hospital; Mark H. Williams, M.D., Binghamton, attending thoracic surgeon, Binghamton General and Binghamton State Hospitals; Robert S. Sioussat, M.D., Cooperstown, attending physician, Mary Imogene Bassett Hospital.

The meeting was attended by 110 members of the branch. Following the scientific meeting a business meeting was held, and the following matters were discussed and decided:

1. That each of the nine component county societies contribute not more than $10 a year to the district branch treasury for the purpose of conducting the affairs of the district branch;
2. That the present district disability insurance program be increased as to limits of coverage. A sales campaign will be conducted during 1962 to enroll new members who have moved into the district since the last sales period. It was voted to continue under the same insurance carrier as the district's experience with them had been satisfactory during the past ten years;
3. To introduce a resolution into the House of Delegates of the Medical Society of the State of New York in 1962 increasing the allotment granted by the State Society from $400 to $600 for the purpose of holding district branch meetings;
4. The following officers were elected for the ensuing two years:

President—George F. Nevin, M.D., Cortland
First Vice-President—George G. MacCauley, M.D., Ithaca
Second Vice-President—Hugh D. Black, M.D., Oxford
Secretary—Charles L. Shute, M.D., Binghamton
Treasurer—Henry B. Marshall, M.D., Elmira
Delegate—Norman C. Lyster, M.D., Norwich

Following this meeting the group adjourned to the Canasawacta Country Club of Norwich where cocktails were served by the courtesy of Eaton Laboratories, Norwich. Dinner followed and we were honored to have John M. Galbraith, M.D., president of the Medical Society of the State of New York, as our guest of honor. Also present were Henry I. Fineberg, M.D., executive vice-president of the Medical Society of the State of New York; Mrs. Eugene F. Wolff, president of the Woman's Auxiliary to the Medical Society of the State of New York; Mrs. Dominic R. Pitaro, first vice-president of the Woman's Auxiliary, and Mrs. Herbert H. Ulrich, president-elect of the Woman's Auxiliary. One hundred twenty doctors and their wives attended the dinner at which the Honorable George R. Metcalf of Auburn, senator in the New York State Legislature, was the guest speaker. Senator Metcalf talked about legislation affecting the medical profession and gave special attention to the implementation of the Kerr-Mills Bill through the Metcalf-McCloskey Bill which was passed at the last State Legislature session. Senator Metcalf also covered the legislative aspects of Blue Shield and Blue Cross. Following his prepared talk he answered questions and there was a rather lively discussion. The meeting proved to be very excellent and informative.

The members of the Sixth District Branch are very much indebted to the Eaton Laboratories, who donated the use of their facilities for the meeting and sponsored the cocktails, and to Paul F. MacLeod, M.D., of the Eaton Laboratories, who handled the local details.

Press Relations Workshop. On November 15, 1961, a Press Relations Workshop was held at the Sheraton Inn in Binghamton. The purpose of the conference was to bring together representatives of the news media and representative doctors of the component county medical societies and the public relations chairmen of the county societies. Forty-five members of the media attended and represented the press, radio, and television.

The following people presented an excellent panel discussion covering problems arising from gathering and publishing medical news:

Moderator—Stuart Dunham, editor, *Binghamton Evening News; Panelists*—TV and Radio, Ed Kane, WNBF, Binghamton; press, Peggy Gallagher, *Elmira Star Gazette*, Elmira; public relations, Michael Hanna, manager, W.H.C.U. Ithaca; hospital administration, Robert T. Jones, administrator, Arnot-Odgen Hospital

Elmira; law, Leland Taylor, Esq., Cortland; medicine, William T. Boland, M.D., Elmira.

At the conclusion of the panel discussion cocktails were served followed by dinner. The guest speaker was Mr. Jim Reed, director of the Department of Communications of the American Medical Association. Mr. Reed gave an excellent paper covering many of the problems arising between the members of the news media and the medical profession. We are indebted to him for making the long trip from Chicago to attend our meeting. While Mr. Reed was in Binghamton he held a press conference during which he discussed many of the problems facing the American Medical Association and the medical profession today. His remarks were given wide local coverage both in the press and on radio and television.

The Press Relations Workshop was considered to be worthwhile for those who attended but would have been far more successful had the attendance of the doctors who were invited been greater.

Comment. As president of the Sixth District Branch I am now concluding my term of office, and I would like to take this opportunity to record my appreciation to those people who have helped make the above programs a success. First I would like to thank the officers of the district branch and the members of the executive committee who attended many meetings during the year. These men traveled many miles at their own expense of time and money and were always willing to cooperate and work in arranging our numerous projects.

Mr. John Schuyler of the State Society Department of Communications gave a lot of his time and advice in helping to arrange the Athletic Injury Conference, the annual meeting, and the Press Workshop. He also arranged the news coverage for these events, and as a result the medical profession in the district received considerable favorable publicity.

I also want to express my appreciation to the Broome County Medical Society for the use of the facilities of their office. Mr. Michael McManus, executive secretary of the Broome County Medical Society, and Mrs. Betty Hudda, his assistant, were most helpful. They spent many hours after completing their regular duties in assisting with the activities of the district branch and without remuneration.

I also want to express my thanks to Miss Mollie Pesikoff, Miss Gretchen Wunsch, Mr. Martin Tracey, and the staff of the Communications Department of the Medical Society of the State of New York. Through their efforts we were able to accomplish the numerous clerical details which involved printing and mailing of numerous communications to the membership of the district branch.

Respectfully submitted,

C. Stewart Wallace, M.D., *President*

Seventh District Branch

To the House of Delegates, Gentlemen:

The annual meeting of the Seventh District Branch was held in Rochester on Thursday, September 21, 1961. At this time Philip M. Standish, M.D., president, reported on the significant actions of the branch during the preceding year. These were as follows:

1. The formulation of hospital utilization committees was approved and recommended.
2. A resolution urging the strengthening of Blue Shield and inclusion of ambulatory diagnostic services in the Plan was approved and submitted to the State Society House of Delegates where it was also approved.
3. A joint Seventh and Eighth District Branch meeting was held at the State Society convention where mutual problems were discussed.
4. A public relations conference and speaking course was held in Rochester as regards Federal legislation.
5. A special joint meeting of the Seventh and Eighth District Branches advisory councils was held to discuss insurance proposals of the A.M.A. and to change the underwriters of the district branch plan. The district branches oppose the establishment of a health and accident program by the A.M.A. as being detrimental to local plans and not feasible.
6. A fine program was held during the afternoon which included the following:

"Closed Chest Cardiac Massage" (film), discussion by Alastair J. Gillies, M.D., Rochester, professor of anesthesiology, University of Rochester School of Medicine and Dentistry; "The A.M.A., You, and I, Your Representative," Gerald D. Dorman, M.D., New York City, trustee, A.M.A.; *Symposium:* "Health Care of the Future," Charles M. Smith, M.D., Waterloo, first vice-president, Seventh District Branch; "The Future Practice of Medicine," Charles G. Rob, M.D., Rochester, professor and chairman, Department of Surgery, University of Rochester School of Medicine and Dentistry; "The New Look in Hospital Patient Care," Howard J. Lockward, M.D., Manchester, Connecticut, consultant to Department of Health, Education, and Welfare, in progressive patient care; "Community Medicine of the Future," William H. Stewart, M.D., Washington, D.C., chief, Division of Public Health Methods, Department of Health, Education, and Welfare.

At dinner the following program was presented: Address, Joseph A. Lane, M.D., president-elect, Medical Society of the State of New York; remarks, Mrs. Eugene F. Wolff, president, Woman's Auxiliary; address, "Physician and Pastor: A Covenant of Concern," Gene E. Bartlett, D.D., Rochester, president, Colgate Rochester Divinity School.

At the regular business meeting the following new slate was elected:

President—Charles M. Smith, M.D., Waterloo
First Vice-President—Joseph J. Kaufman, M.D., Newark
Second Vice-President—Vincent I. Bonafede, M.D., Sonyea
Secretary—John L. Schultz, M.D., Penn Yan
Treasurer—Merle D. Evans, M.D., Rochester
Delegate—Milton Tully, M.D., Hornell
Past-President, Philip M. Standish, M.D., Canandaigua

Respectfully submitted,
CHARLES M. SMITH, M.D., *President*

Eighth District Branch

To the House of Delegates, Gentlemen:

The year 1961 for the Eighth District Branch of the Medical Society of the State of New York was marked by the annual scientific meeting and dinner, two dinner meetings of the advisory council of presidents and secretaries and other auxiliary agencies of the branch, and a joint cocktail party and dinner meeting of the Eighth and Seventh District Branches held in conjunction with the 1961 Annual Meeting of the State Medical Society in Rochester in May.

Eighth District Branch leaders also united with Seventh District Branch leaders at a special joint meeting on August 3 in Buffalo at which: (1) the two groups ratified the action taken by the Charles J. Sellers & Co., administrators, in transferring the sickness and accident insurance plans of the two branches from one carrier to a new one; (2) the two branches joined forces in a movement to defeat the proposal of the American Medical Association to sponsor a group plan of sickness insurance for members, providing lifetime benefits, which plan was branded unsound and unfeasible and certain to peril the stability of those professional group disability insurance plans now in existence.

The Eighth District Branch embarked on its year of programs and activities at a combined midwinter dinner meeting of Eighth and Seventh District Branch elements at Hotel Statler Hilton, Buffalo, arranged at the request of James M. Blake, M.D., chairman of the Council Committee on Legislation of the State Medical Society. This joint meeting was held on the night of February 9 for the main purpose of considering and acting on bills of interest of concern to medicine, and Dr. Blake directed the discussions. Chairmen of legislation committees for all component county societies of the two branches were invited to attend, and many did. About forty doctors and guests were present.

On the evening of the opening day of the 1961 House of Delegates in Rochester, on May 8, the Eighth and Seventh District Branches united for their sixth joint dinner meeting of branch leaders, delegates, and others at the Manger Hotel, with 53 persons present. Clyde L. Wilson, M.D., Eighth District Branch president, and Philip M. Standish, M.D., Seventh District Branch president, shared presiding duties. Four speakers addressed the meeting and resolutions introduced by constituent county societies in the opening session of the House were discussed and acted on.

The 56th annual scientific meeting of the Eighth District Branch was held in the Veterans Administration Hospital recreation building, Batavia, on Thursday, September 28, following a noon luncheon meeting of the advisory council and allied agencies in the Treadway Inn.

At the business session which followed the scientific program the following officers were elected: *President* (1962–1963)—Irwin Felsen, M.D., Wellsville; *President-elect*—John D. Naples, M.D., Buffalo; *Secretary*–Myron E. Williams, Jr., M.D., Batavia; *Treasurer*—John T. Donovan, Jr., M.D., Lockport.

A record-breaking attendance crammed the Treadway Inn for the evening dinner meeting to hear and applaud Edward R. Annis, M.D., of Miami, Florida, nationally known television personality, who attacked the Kennedy Administration's program for establishment of a program of medical care for the aged tied to the Social Security system.

The 1961 season of branch activities concluded with the annual early-winter dinner meeting of the advisory council and other auxiliary bodies at Hotel Statler Hilton, Buffalo, on the night of December 7. The Eighth District Branch voted to join with the Seventh District Branch for the conduct of their customary combined dinner meeting on the evening of Monday, May 14, the opening day of the House of Delegates of the 1962 Annual Meeting of the State Medical Society at Hotel Statler Hilton, New York City.

Speaker of the evening at the December 7 meeting was Carl M. Metzger, president of the Buffalo Area Blue Cross, who addressed the group on "The Impact of Rising Hospital Costs on the Future of Medicine." John C. Brady, M.D., Buffalo, spoke on "The Shape of Things to Come at the 1962 Session of the State Legislature." The meeting accepted the invitation of the Cattaraugus County Medical Society to hold the 1962 annual meeting of the branch on October 4 in Cattaraugus County, probably in Olean.

Respectfully submitted,
CLYDE L. WILSON, M.D., *President*

Ninth District Branch

To the House of Delegates, Gentlemen:

The annual meeting of the Ninth District Branch was held at the Manger Hotel, Rochester, on May 8, 1961. The minutes of the previous meeting were accepted as published in the NEW YORK STATE JOURNAL OF MEDICINE.

John F. Rogers, M.D., reported the death of William Kelly, M.D., of Putnam County, first vice-president of the district branch, and the executive committee expressed its sincere regrets.

The following officers were elected for a two-year period:

President—Maxwell Gosse, M.D., Poughkeepsie
First Vice-President—Frank E. Ciancimino, M.D., Nyack
Second Vice-President—Nathaniel T. Keys, M.D., Goshen
Treasurer—Arthur H. Diedrick, M.D., Port Chester

Eugene J. Lusardi, M.D., Cold Spring was elected *Secretary* by Putman County at its June, 1961, meeting.

The bylaws committee, under the chairmanship of Earl Waterbury, M.D., presented revised bylaws which were approved, and copies were forwarded to the component county societies for their approval before submitting them to the Council for final approval. At a meeting of the Council on January 25, 1962, the recommendation of the Committee on Constitution and Bylaws approving the bylaws of the Ninth District Branch was adopted.

Some letters and an informative report have been received, but it will not be necessary to call an executive meeting to discuss them since they will be taken up at the annual meeting in May.

Your president attended the special meeting of the House of Delegates on February 10, 1962, at the Summit Hotel, New York City.

Respectfully submitted,
MAXWELL GOSSE, M.D., *President*

Membership

To the House of Delegates, Gentlemen:

The Committee on Membership has the following members:

George W. McCormick, M.D., *Chairman*	Richmond
John H. P. Holden, M.D.	Albany
George A. Howley, M.D.	Bronx
James K. Keeley, M.D.	Dutchess
James E. Glavin, M.D.	Essex
Albert J. Addesa, M.D.	Erie
Solomon Yarvin, M.D.	Greene
Warren A. Lapp, M.D.	Kings
A. Gordon Ide, M.D.	Monroe
Gerard V. Farinola, M.D.	Nassau
Ralph E. Snyder, M.D.	New York
Robert F. McMahon, M.D.	Onondaga
Earl C. Waterbury, M.D.	Orange
John L. Finnegan, M.D.	Queens
Herbert L. Sperline, M.D.	Rockland
Eldred J. Stevens, M.D.	Steuben
Charles W. Shlimbaum, M.D.	Suffolk
Lester Lipson, M.D.	Sullivan
Paul A. Burgeson, M.D.	Wyoming

The only meeting of this committee was held on March 16, 1961, at the State Society headquarters. During this meeting there was a general discussion about the best methods to be used in the membership drive throughout the State of New York. It was mentioned that in front of the *Medical Directory of New York State* there is an alphabetic list of registered physicians. This list is also repeated according to counties with symbols in front of physicians' names, denoting their county, State, and A.M.A. membership.

From this an up-to-date nonmember roster could be obtained to be used as a format for a membership drive. This suggestion was approved and was to be passed on to the county membership committees along with a small informative statement on "What Does the State Medical Society Do For Me?", prepared by the Department of Communications of the Medical Society of the State of New York. It was thought that nonmembers might be particularly interested in the malpractice insurance coverage offered by the Medical Society of the State of New York, as well as protection of the rights of Medical Society members in both Albany and Washington, and also in potential financial assistance from the Physicians' Home.

It was also recommended that the Monroe County resolution on junior membership for trainees out of medical school after five years be sent to the Special Committee on Constitution and Bylaws for the study of a recognized traineeship program at reduced dues.

In order to implement the recommendations of the Membership Committee, the chairman, on December 1, 1961, sent a letter to each county society president asking his cooperation in a membership drive. A list of nonmembers in the county was requested, and the convenient method of determining nonmembership, mentioned above, was explained. To assist the membership committee of the county society, a copy of "What Does the State Society Do For Me?" was enclosed.

To date, the Membership Committee has heard from 13 counties. A follow-up letter is going to the counties who have not contacted us.

Respectfully submitted,
GEORGE W. MCCORMICK, M.D., *Chairman*

Office Administration and Policies

To the House of Delegates, Gentlemen:

The Committee on Office Administration and Policies is composed of the following:

John J. Masterson, M.D., *Chairman* . . . . Kings
Maurice J. Dattelbaum, M.D. . . . . Kings
Joseph A. Lane, M.D. . . . . Monroe
Norman S. Moore, M.D. . . . . Tompkins
John M. Galbraith, M.D., *ex officio* . . Nassau
William L. Wheeler, Jr., M.D., *ex officio*
. . . . New York

Appointments to the committee make for a well-balanced group. The Board of Trustees and officers have representation. In addition, the assistant to the executive vice-president and the controller attend all meetings. Since last May, your committee has met regularly except for the months of July, August, and December. This is in line with the practice of the Council and Board of Trustees to meet six times a year.

On May 1, 1961, Henry I. Fineberg, M.D., accepted the position of executive vice-president. In this capacity, Dr. Fineberg is in charge of the headquarters office and is responsible for the job that the office is doing. The committee was very gratified that Dr. Fineberg consented to take over this position. There were many problems in our office that needed a firm and equitable hand in their solution. We have found him to be able to handle these problems with ability and tact. It is our firm conviction that after a period of time has elapsed, our office will run more efficiently because of him.

Miss M. Adelene Briggs, who was on pension, passed away on December 31, 1961. Miss Briggs had been on pension since November, 1953. She was employed on November 11, 1924, for a total of twenty-nine years. Her employment was in the Albany office.

Job Evaluation Program. Probably one of the most important things this committee has accomplished during the year has to do with the setting up of a job evaluation program. In the report last year, this was mentioned briefly. Through the efforts of Norman S. Moore, M.D., we retained Mr. Diedrich K. Willers. Mr. Willers has had considerable experience and training in personnel work. Most members of the staff were interviewed and placed in a job category with a suggested specific salary range. Our executive vice-president, Dr. Fineberg, spent much time in studying the report and after certain minor changes which were made to fit our particular needs, the report was studied and approved by the committee and thereafter implemented.

One of the objectives of the program is to remunerate our staff members sufficiently in order that we might successfully compete with the salaries offered by commercial organizations. It is hoped that the whole program will be productive of better staff morale and satisfaction.

Actions to Improve Morale. Among other actions taken by the committee during the year which we believe will better staff morale are:

1. A revision in our pension plan benefits. Certain adjustments were made in the method of calculating pensions and in effect any employe will receive a greater pension than previously. A staff member having twenty years of accredited service will receive an additional $240 per annum in benefits.
2. A staff publication has been initiated. It will contain various items relating to staff activities and any special information which the staff needs or desires to know.
3. Our bowling league is in its second year, and a great deal of interest is shown in this activity.
4. Our usual picnic and Christmas party were held on September 12 and December 21, respectively.
5. There is now in preparation a handbook for employes which will explain the various office procedures and rules.
6. The committee is now in process of studying the possibility of initiating a major medical plan for the staff. At this time there are a number of questions which must be answered before we can proceed.

Twenty-five Year Club. Miss Doris K. Dougherty and Miss Alice E. Wheeler were "inducted" into our "Twenty-five Year Club." While we do not actually have a club, the staff held a dinner on January 15 in honor of these two ladies. The dinner was very well attended by the staff and in addition a number of our officers also were present. Both guests received gold wrist watches which were gifts from the Society. The first member of our twenty-five year club was Miss Janet Loy. We now have three members.

Tabulating Equipment. Two years ago the Society changed its membership records system from a manual procedure to tabulation. While there were many difficulties, the work is now on an even keel even though somewhat behind. One of the causes of this delay is that it is necessary for us to send our cards out of the office for tabulation of statistical material. After study, the committee felt that by having our own machine installation we would be able not only to process this work faster but also to put a number of our other work functions on tabulating cards. In the long run we believe that we will save money. This installation was recommended to the Budget Committee, Council, and Board of Trustees, all of whom approved. It is expected that this equipment will be in operation some time during the third quarter of 1962.

One of our problems is that we must find space for this equipment. It must also be pointed out that we need additional space for other departments. With this in mind, we are searching for additional office space.

It has been felt for some time that perhaps it might be more economical for the Society to erect its own building. After much discussion, the committee recommended this to the Council. The Board of Trustees in anticipation of this possibility has segregated securities for a "Building Fund." The total amount of securities, at market value, amounts to approximately $500,000.

Staff. As of the date of this report, our staff is made up of the following persons by order of employment:

1920	Miss Janet Loy
1935	Miss Alice Wheeler
1937	Miss Doris K. Dougherty
1943	Mr. Charles L. Baldwin
1944	Miss Mollie Pesikoff
	Mr. William Bonzer
1945	Mr. George Farrell
	Mrs. Alice Arana
	Mrs. Eunice Leonard
1946	Miss Frances E. Casey
	Mrs. Evelyn DeMarco
1947	Mr. Thos. E. Alexander
	Miss Alvina Rich Lewis
	Mrs. Evelyn Clark
1948	Miss Gretchen Wunsch
	Miss Dorothy Hart
	Miss Camille M. Marra
1949	Mr. Martin Tracey
	Miss Susan V. Baker
	Mr. Joseph Mullaney
1950	Miss Mary Singer
1951	Mrs. Florence Gallagher
	Miss Lieselotte Benz
1953	Mrs. Yvonne Chapman
1954	Miss Lucille Leipziger
	Mrs. Beatrice Moosa
	Mrs. Dorothy Lotosky
	Mr. Robert W. Miller
	Mrs. Joan V. Hughes
	Mr. Ackley Schuyler
1956	Mr. Charles Struzinski
1957	Miss Roslyn Feinberg
	Mrs. Nan Boynton
	Miss Nele Lape
	Mr. Eugene Dombrowski
	Mrs. Estelle Danzeisen
	Miss Anne-Marie Fanshaw
1958	William Hammond, M.D.
	Mr. Wiley Tatum, Jr.
	Mr. Jack O'Brien
	Miss Elizabeth C. Smith
1959	Mrs. Beatrice Duckfield
	Mrs. Olga Mielke
	Miss Dorothy Kelleher
	Miss Suzanne Glasberg
1960	Mr. George Forrest
	Mr. Jack Pardee
	Mr. John Puca
	Mrs. Miriam Mosonyi
	Robert Katz, M.D.
	James Greenough, M.D.
	Mrs. Arlene Gold
	Miss Anita Greenstein
	Miss Teresa Fitzgerald
	Mr. Edward Gold
	Mrs. Louise Scheidle
1961	Mrs. Cathleen Thayer
	Miss Jean MacDonald
	Mrs. Bethany Culhane
	Mrs. Sully Bogardus
	Mrs. Catherine Farrell
	Mr. Joseph Citarella
	Henry Fineberg, M.D.
	Miss Charlotte Heil
	Miss Vanessie Johnson
	Mrs. Alice Dale
	Mrs. Dorothy Murther
	Miss Helen Luttman
	Mrs. Lillian Newman
	Mr. Melvin Fine
	Mrs. Ginette Burger
	Mrs. Lillian Stekas
	Mr. Norman Bloomfield
1962	Mr. Joseph Mannix

Acknowledgments. This report would not be complete if we did not extend to the members of the staff our sincere thanks for their devotion to the interests and welfare of our Society. We are most appreciative of the work of Miss Doris K. Dougherty, executive assistant; Mr. Eugene Dombrowski, accounting department supervisor; Miss Janet Loy, *Directory* department supervisor, and Mr. William Bonzer, our mailroom supervisor.

Mr. Thos. E. Alexander, our controller, attends all our meetings and acts as secretary of the committee. The committee is most grateful to him for his cooperation, sound advice, and accounting information pertaining to the work of our committee. He has been most helpful to the members of this committee.

Dr. Henry I. Fineberg, our executive vice-president, also attends committee meetings, and his extensive administrative experience has been of great value at our meetings.

Respectfully submitted,
JOHN J. MASTERSON, M.D., *Chairman*

Conference of County Medical Society Officers

To the House of Delegates, Gentlemen:

The following members comprise the Committee to Arrange Conference of County Medical Society Officers:

Waring Willis, M.D., *Chairman*	Westchester
Samuel Z. Freedman, M.D.	New York
Edward C. Hughes, M.D.	Onondaga
Joseph A. Lane, M.D.	Monroe
George J. Lawrence, Jr., M.D.	Queens
John C. McClintock, M.D.	Albany

Your committee was appointed shortly after the beginning of the 1961–1962 year. Several meetings of the committee were held and the whole committee drew up tentative lists of speakers. Early in the planning a theme was chosen, "Voluntary Health Insurance"; a panel of experts from various parts of the United States was contacted; the dates, September 29 and 30, were selected, and the Hotel Biltmore in New York City was chosen for the place.

A record-breaking crowd of 180 persons attended, and the conference was rated one of the best of its kind. One of the highlights was an address delivered by the Honorable Robert S. Kerr, United States Senator from Oklahoma.

Other speakers included: William S. McNary, executive vice-president, Michigan Hospital Service, Detroit, Michigan; Louis A. Orsini, assistant director, Information and Research, Health Insurance Association of America; M. W. Shearer, assistant administrator, Ross-Loos Medical Group, Los Angeles, California; Frank P. Guidotti, M.D., medical director, Health Center of the New York Hotel Trades, New York City; Charles E. Thompson, M.D., medical director, Truck Drivers, Chauffers and Helpers Union of Chicago and Vicinity; Donald B. Harrington, M.D., chairman, Commission on Medical Service, California Medical Association; Leonard Raider, M.D., executive vice-president and secretary, United Medical Service, Inc., New York City; Bernard Greenbert, associate director, Insurance Pension and Unemployment Benefits Department, United Steel Workers of America, Pittsburgh, Pennsylvania; and Dean Hoskins, M.D., council member, Alameda-Contra Costa Medical Association, California.

Your chairman would like to take the opportunity in this annual report officially to thank all who participated in making the conference a great success. First, we are grateful to the experts who came from as far away as California, Detroit, and Chicago to give us the value of their vast experience. Second, we are thankful to the members of our own Society who acted as moderators and in other capacities. These men included: John M. Galbraith, M.D., president; Joseph A. Lane, M.D., president-elect; Carlton E. Wertz, M.D., past-president; Samuel Z. Freedman, M.D., assistant treasurer; John C. McClintock, M.D., public relations chairman; and Henry I. Fineberg, M.D., executive vice-president.

Last but not least, a word of praise should go to all members of the State Medical Society staff who helped to make the conference a success. Direct responsibility for the handling of details of the conference was in the hands of the Department of Communications, headed by Mr. Jack Pardee. Particular expressions of thanks should go to the secretarial staff and especially Mrs. Evelyn G. Clark, who handled all the minute details of the conference from the very beginning, and to Mr. Martin J. Tracey, who acted as the over-all coordinator of the program.

Your chairman also wishes to thank all the members of his committee, without whose cooperation the conference could not have been held. They were diligent in attending the meetings and most constructive and helpful in their suggestions for the contents and personnel of the program.

Respectfully submitted,
WARING WILLIS, M.D., *Chairman*

Constitution and Bylaws

To the House of Delegates, Gentlemen:

The Council Committee on Constitution and Bylaws consists of the following:

Ezra A. Wolff, M.D., *Chairman*	Queens
Norman C. Lyster, M.D.	Chenango
Homer L. Nelms, M.D.	Albany
William F. Martin, *ex officio*	New York

The committee has reviewed, at the request of the Council, all proposed changes in constitutions and bylaws of county societies and district branches which have been submitted since the last meeting of the House of Delegates. We have had the earnest cooperation of Mr. Richard Burns from the office of Martin, Clearwater and Bell, and of the office staff of the State Society.

The chairman is grateful for the diligent and painstaking analyses which have regularly been submitted by his fellow committee members, and hereby offers his sincere thanks to them, Mr. Burns, and the office staff.

Respectfully submitted,
EZRA A. WOLFF, M.D., *Chairman*

Medical Care

Disability Determinations, Advisory to Bureau

To the House of Delegates, Gentlemen:

The Medical Advisory Committee to the Bureau of Disability Determinations consists of the following:

George Himler, M.D., *Chairman*	New York
Lewis Dickar, M.D.	Brooklyn
Lawrence S. Kryle, M.D.	Nassau

The committee held no meeting during the current year. Meetings are generally called at the request of the Bureau to deal with specific problems regarding the relationship of the Bureau with the doctors of New York State.

The report of the Reference Committee on Medical Care, section 178, delivered at the 1961 meeting of the House of Delegates, was noted. Its substance was discussed with Mr. Roy Curtiss, the Bureau's director. It was felt that at least in part the report was based on an erroneous concept of what information was actually requested of physicians. The information required is that which the doctor already has on his chart and is not necessarily sufficient for the determination. The Bureau may request further information when it is necessary and it is believed that the patient's doctor has it available. Finally, if the available data are still insufficient, the Bureau may purchase consultative examinations from one or more of its panel of consultants.

Since this matter was referred to the Medical Economics Committee and since the specific criticisms of the methods of the Bureau were not clearly spelled out in the report, it was agreed that the director of the Bureau would offer to appear before the Economics Committee, together with members of the Advisory Committee, when the subject came up for discussion. At the time of this writing the matter has not yet been considered.

Respectfully submitted,

GEORGE HIMLER, M.D., *Chairman*

Disaster Medical Care

To the House of Delegates, Gentlemen:

The Special Committee on Disaster Medical Care consists of:

Edward A. Burkhardt, M.D., *Chairman*	New York
Irving G. Frohman, M.D.	Queens
Charles Sandler, M.D.	Bronx
Vincent C. Webb, M.D.	Nassau
James Lade, M.D., *Adviser*	Albany

The Committee on Disaster Medical Care has continued to work at State and national levels to develop greater liaison between those governmental agencies charged with civil defense and voluntary groups active in disaster medical care. There has been a marked improvement in the relationship between county medical disaster committees and State officials. Dedicated physicians are largely responsible for disaster training programs. Joseph S. Diasio, M.D., of Genesee County, has conducted realistic tests of a hospital evacuation, a flood disaster exercise, and a surprise simulated attack entitled "Operation Hurry Call!" These exercises utilized trucks and helicopters to remove the "wounded" to the hospitals.

The New York State Department of Health Bureau of Medical Defense, under the direction of James H. Lade, M.D., has been the most active State-wide agency in the over-all training for medical disaster care. During 1961 intensive training of teams to operate the improvised emergency hospital centers has been instituted. Forty-five training exercises were conducted with 76 persons in each group. To date 210 teams have conducted this exercise. Hospital consultants have assisted 46 hospitals in the past year in the development of adequate hospital disaster plans.

Stockpiling of State medical supplies continues and to date over $20,000,000 has been spent on these supplies. The location of these supplies is published yearly in the New York State Journal of Medicine.

During 1962 and 1963 the Special Committee on Disaster Medical Care will work with the State Civil Defense Commission under General T. W. Farrell and the State Board of Health under Dr. Lade to develop State-wide training of laymen in the Medical Self-Help Program developed by the U.S. Public Health Service. Your committee has developed publicity material to be used at the local level for this Self-Help Program. This has been presented to General Farrell for further implementation and for directions to the local civil defense directors. We in turn are requesting full cooperation by the public relations committee of each county medical society to teach the first round of the program. Each student then becomes eligible to teach this self-contained course. We must make this supreme effort in New York to assist in this national endeavor.

Your chairman has attended meetings in Chicago and Manhattan Beach in order to implement our disaster medical care with the A.M.A. and the U.S. Public Health Programs.

New York is well advanced in disaster medical care but we need more energetic activity in some of our county societies.

Respectfully submitted,

E. A. Burkhardt, M.D., *Chairman*

Columbia University Study of Nonprofit Medical Insurance Plans

To the House of Delegates, Gentlemen:

The Advisory Committee to the Columbia University Study of Nonprofit Medical Insurance Plans in New York State consists of:

John C. McClintock, M.D., *Chairman*	Albany
Carl R. Ackerman, M.D.	Bronx
Merle D. Evans, M.D.	Monroe
Leo E. Gibson, M.D.	Onondaga
Carlton E. Wertz, M.D.	Erie
Henry I. Fineberg, M.D., *Adviser*	Queens
E. Dean Babbage, M.D., *Adviser*	Erie

Ray E. Trussell, M.D., director, and Frank Van Dyke, associate director of the Study, called a meeting for January 23, 1962, which was held in the Gramercy Park Hotel in New York City. Your Advisory Committee reviewed the report prepared by the Study group with the exception of the final chapter containing the recommendations. The Advisory Committee made many suggestions for improving the content and wording of the report. The committee especially objected to reducing the number of doctors of medicine on the boards of directors of Blue Shield Plans.

Since the final chapter which will contain the recommendations of the Study group is not yet available, a supplementary report will be made to the meeting of the House of Delegates.

Respectfully submitted,

John C. McClintock, M.D., *Chairman*

Ancillary Groups

New York State Association of the Professions, Inc.

To the House of Delegates, Gentlemen:

The Certificate of Incorporation of the New York State Association of the Professions, Inc., was filed, with the consent of the Department of Education, in the office of the Secretary of the State of New York on January 9, 1962.

Temporary officers are as follows:

Henry I. Fineberg, M.D., *Chairman* .... New York City

John K. Pardee, *Secretary-Treasurer* .... New York City

Directors to serve until the first annual meeting of the Association in 1963 are as follows:

Henry I. Fineberg, M.D., New York City, and Leo E. Gibson, M.D., Syracuse, *Medical Society of the State of New York;*

Charles A. Wilkie, D.D.S., New York City, and Bernard Clug, D.D.S., New York City, *Dental Society of the State of New York;*

Simeon Heller, A.I.A., Flushing, and Nathan Ginsburg, A.I.A., New York City, *New York State Association of Architects;*

Mr. Nicholas S. Gesoalde, New York City, and Mr. Daniel Deodati, New York City, *Pharmaceutical Society of the State of New York;*

Leigh St. John, P.E., Binghamton, and Anatole R. Gruehr, P.E., Brooklyn, *New York State Society of Professional Engineers;*

Robert E. Clark, D.V.M., Mamaroneck, and Hadley C. Stephenson, D.V.M., Ithaca, *New York State Veterinary Medical Society.*

Purposes of Association. The purposes for which the Association was formed are as follows:

1. The encouragement of participation of the learned professions in programs having for their purpose the advancement of professional ideals and professional welfare;
2. The implementation of programs and measures designed to protect and safeguard the public and the learned professions against encroachments on professional practice by those not qualified;
3. The promotion of better understanding between and among the learned professions;
4. The promotion of a free interchange of opinion and information among its members on subjects of mutual professional interest;
5. The development of closer liaison between the leaders of the learned professions;
6. The fostering of the highest standards of professional ethics and conduct;
7. The production of educational programs designed to offer professional and preprofessional students more adequate preparation for professional life;
8. The stimulation and fostering of leadership by the learned professions in public service activities on community, state, and national levels;
9. The publishing of books, pamphlets, magazines, articles, papers, and other publications, in furtherance of, or related, or connected with, any of the purposes of the Corporation;
10. The acquisition of property, real and personal, and rights and interests therein, for the purposes of the Corporation, by grant, gift, purchase, devise, or bequest and the holding and disposition of the same, subject to such limitation as may be prescribed by law;
11. In general to do any and all acts and things, and to exercise any and all powers which may now or hereafter be lawful under and pursuant to the laws of the State of New York for the purpose of accomplishing any of the purposes of the Corporation.

Participating New York State organization members are as follows: Medical Society of the State of New York, New York State Association of Architects, Dental Society of the State of New York, New York State Society of Professional Engineers, Pharmaceutical Society of the State of New York, and New York State Veterinary Medical Society. A membership invitation has also been extended to the New York State Society of Certified Public Accountants.

Meetings. Four meetings of the temporary board of directors of the New York State Association of the Professions were held during 1961 and early 1962, on April 21 and November 17, 1961, at the Medical Society of the State of New York headquarters, New York City, and on January 9 and January 30, 1962, at the Sheraton Ten-Eyck Hotel, Albany.

At the April 21, 1961, meeting of the directors the following temporary officers were elected: Henry I. Fineberg, M.D., chairman, and John K. Pardee, secretary-treasurer. A committee composed of the following members was appointed to draft bylaws for the Association: Mr. John K. Pardee, director, Department of Communications, Medical Society of the State of New York, chairman; Mr. Albert H. Morgan, executive director, New York State Society of Professional Engineers; Mr. Joseph F. Addonizio, executive director, New York State Association of Architects; C. E. DeCamp, D.V.M., representing the New York State Veterinary Medical Society; Charles A. Wilkie, D.D.S., secretary, Dental Society of the State of New York, and Mr. Nicholas S. Gesoalde, executive director, Pharmaceutical Society of the State of New York.

This committee held two meetings on May 4 and May 31, 1961, and submitted drafts of a certificate of incorporation and bylaws to the directors of the Association at the November 17, 1961, meeting. Certain amendments to the certificate of incorporation were made and this was approved as amended. Certain changes and amendments in the bylaws were agreed on and the secretary and counsel were directed to make such changes and amendments and forward copies of the bylaws, as changed and amended, to each of the participating State organization members. After the bylaws have been approved by each of the State organization members, they will be formally adopted by the Association's board of directors.

It is anticipated that, following approval and adoption of the bylaws, permanent officers, including a president, vice-president, secretary, and treasurer, will be elected. The bylaws provide for annual election of officers. Directors are designated and elected for terms of two years each, two directors to be designated by each State organization member. Following the first annual meeting, the terms of such directors shall expire on alternate years so that at each annual meeting, each State organization member shall designate one director to serve for a term of two years.

State legislation chairmen of each State organization member of the Association were invited to attend the January 9 and January 30, 1962, meetings. At these meetings, representatives of each of the State organization members reviewed their legislation programs for 1962. It was decided that the New York State Association of the Professions would consider and take action on legislation matters in the public interest which affect two or more State organization members and should oppose legislation which tends to socialize or lower the standards of any of the professions.

At the January 30, 1962, meeting of the board of directors of the Association, the directors were informed that the Medical Society of the State of New York had appropriated funds to be used to help defray expenses incurred in connection with the organization of the New York State Association of the Professions, Inc. A resolution extending their appreciation to the Medical Society of the State of New York for its sponsorship of the Association was unanimously adopted by the directors.

At this meeting it was decided also to devote the efforts of the Association and its constituent members to State legislation amending the Education Law to authorize members of any profession to organize an association to engage in the practice of their profession in corporate form and thereby enjoy certain tax advantages accorded to corporations. At the date of the meeting, the following bills relating to this subject had been introduced in the Legislature: Assembly Intro. 2037 (Bartlett), companion bill to Senate Intro. 1375 (Brydges) and Assembly Intro. 2996 (Campbell).

It was resolved that since there were a number of features in the Brydges-Bartlett and Campbell bills which are objectionable to one or more of the professions to which they apply, any attempt to amend or consolidate them during this Legislature session would not be advisable.

Subsequent to the meeting, Assembly Intro. 3080 (Barbiero), Senate Intro. 2833 (Albert), and Senate Intro. 3452 (Anderson) which also relate to this subject were introduced. These bills fall in the same category as the Bartlett-Brydges and Campbell bills.

A committee consisting of Simeon Heller, A.I.A., New York State Association of Architects, chairman; Albert H. Morgan, P.E., New York State Society of Professional Engineers; Robert E. Clark, D.V.M., New York State Veterinary Medical Society; Charles A. Wilkie, D.D.S., Dental Society of the State of New York; Mr. John O'Brien, Pharmaceutical Society of the State of New York; and Leo E. Gibson, M.D., Medical Society of the State of New York, was appointed and instructed to study and review pending legislation and to explore all phases of possible legislation which may hereafter be introduced relating to the subject of authorizing professional persons to form corporations or associations for the carrying on of professional practice in corporate form. The committee was also instructed to work out the basic provisions of a bill which would be satisfactory in form and substance to the several State organization members and to report the results of their efforts as soon as possible to the board of directors. When such a report has been agreed on, a suitable legislative bill may be drafted and arrangements made for introducing the same in this session of the Legislature if time permits, or if not, in the 1963 session. The work of this committee is progressing according to the instructions of the board of directors.

At this meeting, the directors also elected Mr. Joseph F. Addonizio, executive director of the New York State Association of Architects, as the Association's legislative representative in Albany and Mr. Robert C. Gormley, New York attorney-at-law, as legal counsel.

The campaign for individual members will be undertaken following the approval of the bylaws and the election of permanent officers.

Classes of members and dues are as follows: State organization members, $100 per year; Individual members, $10 per year.

Other memberships may be created by the board of directors providing that the members of any class of membership so created have no voting rights nor be elected to any office in the Association. All State organization members now comprising the New York State Association of the Professions have paid their 1961 dues.

Respectfully submitted,

HENRY I. FINEBERG, M.D., *Chairman pro tem*

Miscellaneous Business

New York State Delegation to the American Medical Association

To the House of Delegates, Gentlemen:

This report of the delegation of the Medical Society of the State of New York to the American Medical Association House of Delegates is presented in two sections, that of the June, 1961, meeting in New York City and that of the November, 1961, clinical meeting in Denver.

June Meeting in New York City. The 110th annual meeting of the American Medical Association took place at the Statler Hilton Hotel in New York City, June 25 to 30, 1961. Its House of Delegates convened during the period from June 26 through the morning of June 29.

The following members of the Society and staff attended our conferences:

Delegates. Philip D. Allen, M.D., Renato J. Azzari, M.D., James M. Blake, M.D., Peter J. DiNatale, M.D., Henry I. Fineberg, M.D., John M. Galbraith, M.D., Leo E. Gibson, M.D., Thurman B. Givan, M.D., James Greenough, M.D., John F. Kelley, M.D., Joseph A. Lane, M.D., John C. McClintock, M.D., Norman S. Moore, M.D., Peter M. Murray, M.D., William B. Rawls, M.D., Carlton E. Wertz, M.D., William L. Wheeler, Jr., M.D., and Ezra A. Wolff, M.D.

Alternate Delegates. Solomon Schussheim, M.D., and Waring Willis, M.D.

Others. Louis H. Bauer, M.D., Gerald D. Dorman, M.D., William Hammond, M.D., J. Stanley Kenney, M.D., and John J. Masterson, M.D.; Mr. Thomas E. Alexander, Miss Doris K. Dougherty, Mr. George P. Farrell, Mr. George W. Forrest, Jr., and Mr. John K. Pardee.

The delegation met on the evening of June 25, and breakfast meetings were held on the mornings of June 27, 28, and 29.

Our hospitality suite (Maison D'Or) was kept open at various times of the day on June 26, 27, 28, and 29. Many visitors from all parts of the country visited our rooms, and our hospitality was received very well. The wives of the delegates and the staff played a great role in making this activity a grand success. These folks merit special mention and commendation.

MEETING, JUNE 25. The chairman stated that all arrangements for the reception and dinner to be given to the House of Delegates by the Medical Society of the State of New York and the medical societies of the counties in New York City had been completed; that there would be a New York host and hostess at each table; that there would be no seating list except for those on the dais and for the tables reserved for trustees, officers, and wives and husbands of guests on the dais; that the entertainment would be in the form of a short presentation (local talent) and there would be no speakers; that this would probably be the last time that the dinner would be subsidized by a state society since future dinners will be by subscription.

Members of the delegation were assigned to attend meetings of reference committees as follows:

Amendments to Constitution and Bylaws, Dr. Murray, chairman; Reports of Board of Trustees, Dr. Moore; Public Health and Occupational Health, Dr. DiNatale; Insurance and Medical Service, Drs. Wertz, Willis, and Wolff and Mr. Farrell; Legislation and Public Relations, Dr. McClintock and Mr. Pardee; Medical Education and Hospitals, Drs. Givan, Greenough, Rawls, and Schussheim; Medical Military Affairs, Dr. Blake, member; Miscellaneous Business, Dr. Azzari, member; Reports of Officers, Dr. Kelley, chairman; Rules and Order of Business, Dr. Gibson, member; Sections and Section Work, Dr. Lane.

The resolutions passed by the House of Delegates of the Medical Society of the State of New York to be presented to the American Medical Association House of Delegates were discussed. It was voted that they be assigned as follows to members of the delegation for presentation to the House:

61-10—"Determination of Relationship Between Doctors of Medicine and Doctors of Osteopathy," Dr. McClintock; it was decided to support the report of the Judicial Council which includes the purport of this resolution. (*A.M.A. Final Action*—A statement of policy was adopted—see Dr. Blasingame's report on actions of the House of Delegates, June 25–30, 1961.)

61-13—"Food and Drug Administration Control of New Drugs," Dr. Kelley; (*A.M.A. Final Action*—The House adopted a reference committee recommendation that this resolution be referred to the Board of Trustees for further study by the appropriate council or committee and that a report be made at the next meeting of the House of Delegates.)

61-30—"Discontinuing of Educational Council for Foreign Medical Graduates Examination for Physicians Licensed in Any State," Dr. Blake; (*A.M.A. Final Action*—The resolution was amended by the reference committee to read: "Resolved, That the Medical Specialty Boards be requested to delete the requirement of certification by the Educational Council for Foreign Medical Graduates for those graduates of foreign medical schools who are licensed by examination in any state of the union to practice medicine." This revised resolution was adopted by the House.)

61–32—"Use of General Practitioners as Assistants at Operations," Dr. Wolff; (*A.M.A. Final Action*—The House adopted a reference committee report recommending that no action be taken on this resolution and stated: "The question of whether or not a doctor may use nonmedical personnel to assist him is to be decided by each hospital staff on the basis of local needs.")

61–70—"Endorsement of H.R. 5222" (This bill is concerned with total tax exemption for all drugs and medicines for persons sixty-five years and older.), Dr. Givan; (*A.M.A. Final Action*—The House adopted a reference committee report commending the sponsors of this and a similar resolution and recommending that "the American Medical Association fully endorse these and similar proposals.")

61–74—"Creation of Planning Commission to Study Problems of Medical Education, Hospital Practice, and Patient Care," Dr. Allen; (*A.M.A. Final Action*—The reference committee commended the worthy intent of this resolution. The committee stated that most of the recommendations of the resolution are under continuing consideration by the American Medical Association and felt that consequently no formal action in regard to the resolution was necessary but that the various councils and committees might profit by reviewing the contents of the resolution. The reference committee report was adopted by the House.)

61–23—"Social Security for Self-Employed Doctors of Medicine," Dr. Lane; (*A.M.A. Final Action*—The House adopted a reference committee recommendation that it approve the principles of resolutions introduced by the Arizona Medical Association and by the Medical Association of Georgia, "which reaffirm the opposition of the American Medical Association to the compulsory inclusion of physicians under Social Security.")

The candidates for "officer" positions in the American Medical Association were discussed. The chairman announced that he had sent a letter to the president of the American Medical Association submitting the name of Dr. Azzari for appointment to the Judicial Council. He also reported that he had written to the chairman of the Board of Trustees of the American Medical Association requesting that the name of Dr. Moore be considered for nomination for membership on the Council on Medical Service to replace Dr. Wertz who was not eligible for re-election.

MEETING, JUNE 27. There was a general discussion of candidates. It was stated that Dr. Fister, of Utah, had resigned from the Board of Trustees in order to contend with Dr. Price, of South Carolina, for the office of president-elect. His resignation caused another vacancy on the Board of Trustees, making a total of three trustees to be elected: one to succeed Julian Price, M.D., for a full term, ending in 1966; one to fill the unexpired term of Cleon A. Nafe, M.D., of Indiana (deceased), ending in 1962; one to fill the unexpired term of George Fister, M.D., ending in 1962.

The candidates discussed were: (1) in place of Dr. Price—W. Linwood Ball, M.D., of Virginia, and Homer Pearson, M.D., of Florida; (2) in place of Dr. Nafe—E. S. Jones, M.D., of Indiana, and Charles L. Hudson, M.D., of Ohio; (3) in place of Dr. Fister—Wesley W. Hall, M.D., of Nevada.

Council on Medical Education and Hospitals: The following names were presented by the Board of Trustees to succeed John W. Cline, M.D., of California: Francis L. Land, M.D., of Indiana; Dwight L. Wilbur, M.D., of California, and Edwin H. Lawson, M.D., of Louisiana.

The following names were presented by the Board of Trustees to succeed Guy A. Caldwell, M.D., of Louisiana: Peter M. Murray, M.D., of New York; Kenneth C. Sawyer, M.D., of Colorado, and A. R. Shands, Jr., M.D., of Delaware.

It was decided to support Dr. Murray.

Council on Medical Services: The following names were presented by the Board of Trustees to succeed Carlton E. Wertz, M.D., of New York: Charles J. Ashworth, M.D., of Rhode Island; Charles Hayden, M.D., of Massachusetts, and Norman S. Moore, M.D., of New York.

The following were presented to succeed Charles Hudson, M.D., of Ohio: E. L. Bernhart, M.D., of Wisconsin; Burtis E. Montgomery, M.D., of Illinois, and Howard Nelson, M.D., of Mississippi.

It was decided to support and work for Dr. Moore to fill the position vacated by Dr. Wertz.

The chairman reported that the House of Delegates reception and dinner were a great success and that 550 persons were present.

MEETING, JUNE 28. The delegates appointed to appear at reference committee hearings submitted their reports.

MEETING, JUNE 29. The delegation discussed again the various openings for officers and members of councils.

President Elect: It was voted that the delegates support Dr. Fister of Utah.

It was noted that there was no contest for the offices of vice-president, speaker, and vice-speaker.

Trustees: It was voted to support Charles L. Hudson, M.D., of Ohio to fill the unexpired term of the late Dr. Nafe and that Dr. McClintock would second his nomination.

It was voted that the delegates vote as they pleased for either Linwood Ball, M.D., or Homer Pearson, M.D., to replace Dr. Price.

Council on Medical Education and Hospitals: It was voted to support Dwight L. Wilbur, M.D., of California, to succeed John W. Cline, M.D., of California.

It was voted to support Peter M. Murray, M.D., to succeed Guy A. Caldwell, M.D., of Louisiana.

Council on Medical Service: It was stated that Dr. Hayden of Massachusetts would withdraw as a candidate to succeed Dr. Wertz. It was voted to support Norman S. Moore, M.D.

It was thought that Dr. Bernhart of Wisconsin would withdraw as a candidate to succeed Dr. Hudson of Ohio. It was voted to support Burtis E. Montgomery, M.D., of Illinois.

Council on Constitution and Bylaws: It was voted to support Walter E. Vest, M.D., of West Virginia to succeed himself.

Judicial Council: It was reiterated that the New York delegation was in favor of the appointment of Renato J. Azzari, M.D.

The House of Delegates adjourned during the late morning of June 29. Again, it is very gratifying to report that, in the usual manner, our delegates attended to their duties faithfully. Our heartfelt thanks go to all of them, to their wives, and to the staff for their grand assistance and cooperation in making the New York meeting a memorable one.

Following is a "Report on the Actions of the House of Delegates, American Medical Association, 110th Annual Meeting, June 25–30, 1961, New York City," as transmitted by F. J. L. Blasingame, M.D., executive vice-president of the American Medical Association.

New York, June 30.—Osteopathy, medical discipline, communications, surgical assistants, drug legislation, general practice residencies, relations with allied health professions and services, and poliomyelitis vaccine were among the major subjects covered by 115 resolutions and 28 reports acted on by the House of Delegates at the American Medical Association's 110th Annual Meeting held June 25 to 30 in New York City.

George M. Fister, M.D., of Ogden, Utah, member of the A.M.A. Board of Trustees and previously a member of the House of Delegates, was named president-elect of the Association. Dr. Fister will become president at the June, 1962, annual meeting in Chicago, succeeding Leonard W. Larson, M.D., of Bismarck, North Dakota, who assumed office at the Tuesday night inaugural ceremony in New York.

The A.M.A. 1961 Distinguished Service Award was voted to Walter H. Judd, M.D., of Minneapolis, physician and member of Congress, for his contributions as a medical missionary, humanitarian, and statesman devoted to world peace.

Total registration through Thursday, with half a day of the meeting still remaining, had reached 56,315, including 22,681 physicians.

Osteopathy. In considering a report of the Judicial Council and three resolutions on the subject of osteopathy, the House of Delegates agreed with the intent of the report and resolutions, but instead adopted the following statement of A.M.A. policy:

"1. There can never be an ethical relationship between a doctor of medicine and a cultist, that is, one who does not practice a system of healing founded on a scientific basis.

"2. There can never be a majority party and a minority party in any science. There cannot be two distinct sciences of medicine or two different, yet equally valid systems of medical practice.

"3. Recognition should be given to the transition presently occuring in osteopathy, which is evidence of an attempt by a significant number of those practicing osteopathic medicine to give their patients scientific medical care. This transition should be encouraged so that the evolutionary process can be expedited.

"4. It is appropriate for the American Medical Association to *reappraise its application of policy* regarding relationships with doctors of osteopathy, in view of the transition of osteopathy into osteopathic medicine, in view of the fact that the colleges of osteopathy have modeled their curricula after medical schools, in view of the almost complete lack of osteopathic literature and the reliance of osteopaths on and use of medical literature, and in view of the fact that many doctors of osteopathy are no longer practicing osteopathy.

"5. Policy should now be applied individually at state level according to the facts as they exist. Heretofore, this policy has been applied collectively at national level. The test now should be: Does the individual doctor of osteopathy practice osteopathy, or does he in fact practice a method of healing founded on a scientific basis? If he practices osteopathy, he practices a cult system of healing and all voluntary professional associations with him are unethical. If he bases his practice on the same scientific principles as those adhered to by members of the American Medical Association, voluntary professional relationships with him should not be deemed unethical."

Medical Discipline. In a major move designed to strengthen the profession's disciplinary mechanisms, the House approved the conclusions and recommendations of the Medical Disciplinary Committee, with only three word changes. The House discharged the committee with thanks and commendation and directed that its functions be assumed as a continuing activity of the Judicial Council.

One recommendation suggests that "the Bylaws of the American Medical Association be changed to confer original jurisdiction on the Association to suspend or revoke the A.M.A. membership of a physician guilty of a violation of the Principles of Medical Ethics or the ethical policy of the American Medical Association regardless of whether action has been taken against him at local level."

Another "encourages and urges that each state association report annually to the American Medical Association all major disciplinary actions taken within its jurisdiction during the preceding calendar year."

The report urged state and county medical societies to utilize grievance committees as "grand juries" to initiate action against an offender so as to obviate the necessity of making an individual member of a medical society complain against a fellow member.

The House suggested that each medical school develop and present a required course in ethics and socioeconomic principles and that each state board of medical examiners include questions on ethics and proper socioeconomic practices in all examinations for license.

The report concluded with a recommendation that "American medicine at the national, state, and local level maintain an active, aggressive, and continuing interest in medical disciplinary matters so that, by a demonstration of good faith, medicine will be permitted to continue to discipline its own members when necessary."

Communications. Acting on four resolutions related to the Association's public relations program, the House adopted a substitute resolution directing the Speaker of the House of Delegates to name seven elected members of the House as a special committee "to study and continually advise the Board of Trustees on the broad planning and coordination of all phases of communications of the American Medical Association, so that the public and the members of the medical profession are properly and adequately advised of the policies and concern of the medical profession with respect to all phases and aspects of medical care for all people."

The House agreed with a reference committee opinion that "we have a very adequate Division within the A.M.A. capable of implementing any program of communications." The approved committee report also said that "the Communications Division of the A.M.A. needs the active support and cooperation of the House and of all members of the Association."

Surgical Assistants. In considering a Board report and two resolutions on the subject of surgical assistants fees the House approved the following five basic principles developed by the Judicial Council and the Council on Medical Service:

"1. Each member of the A.M.A. is expected to observe the Principles of Medical Ethics in every aspect of his professional practice.

"2. Each doctor engaged in the care of the patient is entitled to compensation commensurate with the value of the services he has personally rendered.

"3. No doctor should bill or be paid for a service which he does not perform; mere referral does not constitute a professional service for which a professional charge should be made or for which a fee may be ethically paid or received.

"4. It is ethically permissible for a surgeon to employ other physicians to assist him in the performance of a surgical procedure and to pay a reasonable amount for such assistance.

"This principle applies whether or not an assisting physician is the referring doctor and whether he is on a per case or full-time basis. The controlling factor is the status of the assisting physician. If the practice is a subterfuge to split fees or to divide an insurance benefit, or if the physician is not actually employed and used as a bona fide assistant, then the practice is contrary to ethical principles.

"5. Under all other circumstances where services are rendered by more than one physician, each physician should submit his own bill to the patient and be compensated separately."

Efficacy of Drugs. The House strongly endorsed a Board report which pointed out the problems that would result from amending the Food, Drug and Cosmetic Act to authorize the Food and Drug Administration to determine the efficacy, as well as the safety, of a prescription drug prior to the approval of a new drug application. The A.M.A. will oppose such legislation before the Kefauver Committee, the report pointed out, on the basis that "a decision with respect to the effectiveness of drugs is dependent upon extended research, experimentation and usage." The House agreed that vesting such authority in the Food and Drug Administration would operate to limit research, the marketing of drugs, and the exercise of discretion by the medical profession. "The marketing of a relatively useless drug is infinitely less serious than would be the arbitrary exclusion from the market of a drug that might have been lifesaving for many persons," the House declared.

General Practice Residencies. Eight resolutions were introduced on the subject of creating new two-year residency training programs in general practice. The House agreed that there appears to be a need for such programs for those individuals who desire more experience in obstetrics and surgery than may be available in the currently existing family practice program. It approved a substitute resolution directing the Council on Medical Education and Hospitals to consider for approval other two-year programs in general practice which incorporate experience in obstetrics and surgery. The Council will review these programs on the basis of their individual merits and conduct a long-range evaluation of the new programs as well as the previously established family practice programs.

Relations With Other Health Professions and Services. The House considered a Board report and 12 resolutions dealing with various aspects of medicine's relationships with allied health professions and services, including optometry. The Board report recommended the creation of a new A.M.A. Council to handle all the problems involved. The House, however, accepted a reference committee suggestion for establishment of a new Commission to Coordinate the Relationships of Medicine with Allied Health Professions and Services. The Commission will be composed of seven members appointed by the Speaker of the House. Subcommittees, composed of from three to five members selected by the Commission from lists of names submitted by the scientific sections, will consider problems in specific areas. The Commission will correlate and catalogue the reports of the subcommittees and will act as liaison agent between the subcommittees and those A.M.A. councils where there may be overlapping interests.

Polio Vaccine. The House approved a report by the Council on Drugs on the present status of poliomyelitis vaccination in the United States and urged that it be made available to all physicians through the most effective communications media. The report clearly outlines procedures recommended for implementation of mass vaccination with the new oral vaccine when it becomes available. The House complimented the Council on its "clear and succinct statement on the initiation of the new campaign which will be needed to promote the new vaccine." The House agreed that the report provides the practicing physician with a reliable series of answers to the many questions which will arise during the change-over from Salk vaccine to oral vaccine. The report emphasizes, however, that "physicians should encourage, support, and extend the use of Salk vaccine on the widest possible scale at least until the oral polio virus vaccines currently under development and clinical trial become available."

Miscellaneous Actions. In dealing with resolutions and reports on a wide variety of other subjects, the House also:

Approved the "Guides to Physician Relationships with Medical Care Plans," submitted by the Council on Medical Service, with these two changes: deletion of item 5 under "Responsibilities of the Medical Society," which said, "To recognize that properly qualified physicians employed by, or otherwise service, medical care plans should not be denied professional rights and privileges because of their service to such plans," and addition of a new item 1 under "Responsibilities of the Medical Care Plan," which reads: "To provide the beneficiary of the plan with free choice of qualified physicians";

Reaffirmed its support of the Kerr-Mills program for the needy and near-needy aged and its opposition to any legislation of the King-Anderson type, declaring that the medical profession "will not be a willing party to implementing any system which we believe to be detrimental to the public welfare";

Approved a markedly expanded drug information program submitted by the Board of Trustees and the Council on Drugs;

Adopted the final report on the Special Study Committee of the Council on Medical Education and Hospitals and recommended that copies be sent to all medical school deans in the United States;

Decided to hold the 1963 Clinical Meeting in Portland, Oregon, instead of Las Vegas, Nevada, as recommended by the Board;

Approved a plan by the new A.M.A. Department of International Health to cooperate in the recruitment of volunteer physicians for emergency medical service in foreign mission fields;

Agreed to an increase of $20 in the annual A.M.A. membership dues to be implemented over a period of two years: $10 on January 1, 1962, and $10 additional on January 1, 1963;

Discontinued the Association's General Practitioner of the Year award;

Opposed legislative and administrative mandates which would compel physicians to prescribe drugs, or require pharmaceuticals to be sold, by generic names only;

Reaffirmed the Association's opposition to compulsory inclusion of physicians under the Social Security system;

Urged immediate legislation that will provide strong economic motivation for the construction and maintenance of fallout shelters;

Disapproved two resolutions which would have discontinued the scientific activities at the Clinical Meeting;

Urged immunization campaigns against both tetanus and influenza; and

Asked state and county medical societies to give full support to the First National Congress on Medical Quackery to be jointly sponsored next October 6–7 in Washington, D.C., by the A.M.A. and the Food and Drug Administration.

Opening Session. At the opening session on Monday, E. Vincent Askey, M.D., of Los Angeles, retiring A.M.A. president, challenged physicians and medical organizations to re-examine their own efforts to strengthen and improve medicine, and he warned against defeatism and failure to accept personal responsibility for answering criticisms. Dr. Larson, then president-elect, called on the profession to strengthen methods of self-discipline in both the state and county societies, adding that physicians must be concerned with improper or incompetent practice and unethical actions of all kinds. The 1961 Goldberger Award in Clinical Nutrition was presented to Frederick J. Stare, M.D., chairman of the Department of Nutrition at Harvard Medical School.

Inaugural Ceremony. Dr. Larson, in his inaugural address Tuesday night, said that the really good doctor, guided by the professional spirit, will always remember that medicine exists for just one purpose—to serve humanity. When the essence of that spirit is diluted or destroyed, either in an individual physician or in a nation, he added, medicine ceases to be a profession in the highest sense of the word. Dr. Larson also presented the Distinguished Service Award medal to Representative Judd. Entertainment highlight of the inaugural program was a concert by the Montgomery County Medical Society Glee Club of Dayton, Ohio.

Election of Officers. In addition to Dr. Fister, the new president-elect, the following officers were named at the Thursday session:

Eustace A. Allen, M.D., of Atlanta, Georgia, vice-president; Norman A. Welch, M.D., of Boston, re-elected speaker of the House; and Milford O. Rouse, M.D., of Dallas, Texas, re-elected vice-speaker.

Elected to the Board of Trustees were Wesley W. Hall, M.D., of Reno, Nevada, to succeed Dr. Fister; Homer L. Pearson, Jr., M.D., of Miami, Florida, to replace Julian P. Price, M.D., of Florence, South Carolina; and Charles L. Hudson, M.D., of Cleveland, Ohio, to fill out the term of the late Cleon A. Nafe, M.D., of Indianapolis. The Board named the following officers: chairman, Hugh Hussey, M.D., of Washington, D.C.; vice-chairman, Percy Hopkins, M.D., of Chicago; and secretary, James Z. Appel, M.D., of Lancaster, Pennsylvania.

Named to the Judicial Council were Robertson Ward, M.D., of San Francisco, to succeed himself, and Elmer G. Shelley, M.D., of North East, Pennsylvania, to replace Dr. Pearson.

Re-elected to the Council on Constitution and Bylaws was Walter E. Vest, M.D., of Huntington, West Virginia.

New members of the Council on Medical Service are Charles Ashworth, M.D., of Providence, Rhode Island, succeeding Carlton E. Wertz, M.D., of Buffalo, and Burtis E. Montgomery, M.D., of Harrisburg, Illinois, to succeed Charles Hudson, M.D., of Cleveland.

For the Council on Medical Education and Hospitals, Dwight L. Wilbur, M.D., of San Francisco was elected to succeed John W. Cline, M.D., of the same city, and Kenneth C. Sawyer, M.D., of Denver, Colorado, was named to succeed Guy A. Caldwell, M.D., of New Orleans.

November Meeting in Denver, Colorado. The fifteenth clinical meeting of the American Medical Association was held at the Denver-Hilton Hotel in Denver, Colorado, November 26 to 30, 1961. The House of Delegates met on November 27, 28, and 29.

The following members of our Society and staff were present at our conferences (in addition, a former member of our Council, who is now affiliated with the Joint Commission on Accreditation of Hospitals—Denver M. Vickers, M.D.—was a welcome guest):

Delegates: Philip D. Allen, M.D., Renato J. Azzari, M.D., James M. Blake, M.D., Peter J. DiNatale, M.D., Henry I. Fineberg, M.D., John M. Galbraith, M.D., Leo E. Gibson, M.D., Thurman B. Givan, M.D., James Greenough, M.D., John F. Kelley, M.D., Joseph A. Lane, M.D., John C. McClintock, M.D., Norman S. Moore, M.D., Peter M. Murray, M.D., William B. Rawls, M.D., Carlton E. Wertz, M.D., William L. Wheeler, Jr., M.D., and Ezra A. Wolff, M.D.

Alternate Delegates: Solomon Schussheim, M.D., and Waring Willis, M.D.

Others: Gerald D. Dorman, M.D., William Hammond, M.D., Miss Doris K. Dougherty, Mr. John K. Pardee, Mr. Charles L. Baldwin, George J. Lawrence, Jr., M.D., and Maurice J. Costello, M.D., from New York City, representing the Section on Dermatology.

The delegation met on Sunday evening, November 26, and on Tuesday and Wednesday mornings, November 28 and 29.

MEETING, NOVEMBER 26. The chairman reported that the House of Delegates dinner had been arranged by the Colorado State

Medical Society for Monday, November 27, 1961, in the grand ballroom of the Denver-Hilton; that the price of the dinner was $12.50, dress was optional, and ladies were invited.

The chairman read the following special notice: "All members and alternates of the House of Delegates, Officers, Trustees, and committee members, who travel in the interests of American Medical Association business, are covered under a death and dismemberment policy issued by the Indemnity Company of North America for a maximum sum of $25,000 per person. This includes travel by auto, rail, or as a passenger on any aircraft having a valid Airworthiness Certificate, and operated by a properly licensed pilot. If you own, or operate, your own aircraft, you are not covered by this policy. This policy becomes effective when you have reached a point 25 miles beyond your place of permanent assignment."

It was announced that the hospitality room would be open on Monday and Tuesday from 11:00 A.M. to 2:00 P.M. and from 4:00 P.M. to 7:00 P.M.; that it would be open on Wednesday from 11:00 A.M. to 2:00 P.M.; and that souvenirs would be distributed to delegates who visited the room. The memento provided was a phonograph record, specially produced for the occasion.

Members of the delegation were assigned to attend meetings of reference committees, as follows:

Amendments to Constitution and Bylaws, Dr. Wolff; Reports of Board of Trustees, Dr. Galbraith and Dr. Givan; Public Health and Occupational Health, Dr. Moore and Dr. DiNatale; Insurance and Medical Service, Dr. Wertz and Dr. Willis; Legislation and Public Relations, Dr. Blake and Dr. Schussheim; Medical Education and Hospitals, Dr. Murray and Dr. Rawls; Medical Military Affairs, Dr. Gibson; Miscellaneous Business, Dr. Kelley; Reports of Officers, Dr. Azzari; Sections and Section Work, Dr. Lane.

The opinion was expressed that we should have more representation on reference committees and that it would not be amiss for the chairman to approach the Speaker of the House concerning this matter.

The chairman discussed new procedures relating to reference committees:

1. Resolutions will be procured ahead of time in order that they may be studied and evaluated before the House of Delegates convenes.
2. Members of the delegation will be assigned to meetings of reference committees, despite the fact that some of our men are members of the committees.
3. Those who appear at reference committee meetings should be given the privilege and the power to defend or talk against resolutions that have been discussed by the delegation.

The chairman read a message which Louis H. Bauer, M.D., wished to have read to the American Medical Association House of Delegates. In it, Dr. Bauer pointed out that this was the first meeting of the House of Delegates of the American Medical Association which he had missed since 1937 and that he had attended every clinical meeting before this one. He asked the House of Delegates to continue to fight for the freedom of the medical profession and not to yield to bureaucratic ideologies or control. Dr. Galbraith was requested to transmit this message to the House.

The chairman stated that 34 resolutions had been submitted to American Medical Association headquarters. They were read and preliminary actions were taken.

MEETING, NOVEMBER 28. The chairman called for progress reports of the delegates assigned to reference committee hearings.

Dr. Murray reminded the delegates that he was singing his "swan song" this year at delegation meetings and as a member of the American Medical Association House of Delegates. He presented the following list of states in which medical societies accord full membership to Negro physicians. He stated that Negro physicians now have some kind of medical society membership in every state except one.

The list includes:

Alabama—are eligible if accepted by county society;

Arkansas—grants full membership;

Florida—practically all county societies accept negro physicians;

Georgia—pretty generally accepted in county medical society;

Kentucky—are eligible if accepted by county societies;

Louisiana—does not permit any type of membership for Negro;

Maryland—grants full membership;

Mississippi—grants scientific membership;

Missouri—eligible;

North Carolina—granted scientific membership in 1956;

Oklahoma—grants full membership;

South Carolina—granted scientific membership in 1956;

Tennessee—are eligible if accepted by county societies;

Texas—grants full membership;

Virginia—since 1954 eligible if accepted by county society;

West Virginia—are eligible if accepted by county society.

MEETING, NOVEMBER 29. The delegates assigned to reference committees briefly reported the deliberations of the various groups. The following are some of the more important matters which were discussed:

Amendments to Constitution and Bylaws. After discussion of supplementary report R of the Board of Trustees as well as resolutions 27, 30, 31, and 32, the reference committee concluded that the dissatisfaction with statements made by the American College of Surgeons expressed by many members, a majority of them fellows of the American College of Surgeons, should be expressed at the meeting which the Trustees proposed holding with the Board of Regents of the American College in January, 1962, and that the trustees should report results to the delegates as soon as possible after that date.

Reports of Board of Trustees. It was stated that the reference committee would recommend that the House of Delegates approve the objectives and purposes of AMPAC and would also emphasize the facts that AMPAC is separate from the American Medical Association, that it should be organized at a local level, and that its organization will differ in different states according to local laws.

(After discussion, the delegation voted to approve this action.)

It was reported that the reference committee had also (1) noted that the Commission on Cost of Medical Care intended to complete its assignment in 1963; (2) approved the decision to combine the American Medical Education Foundation and the American Medical Research Foundation into the American Medical Association Education and Research Foundation; (3) approved extension of travel insurance coverage from $25,000 to $50,000 for persons traveling on official American Medical Association business; (4) agreed that the American Medical Association should not exhibit at the 1964–1965 International Exposition in New York City unless it appeared that the cost would be less than is anticipated at present; (5) concurred in the request of the Board of Trustees for additional time to complete the study of fund raising by voluntary health agencies undertaken in June, 1960; (6) commended the Communications Division for its excellent work; (7) prepared a substitute for resolution 8 to provide reimbursement of the expenses of section secretaries; (8) decided to recommend that resolution 9, "National Public Information Campaign," be not adopted but be referred to the Committee on Communications; (9) decided to recommend that resolution 11, "Guides for Hospital Operation," be referred to the Board of Trustees with instructions that the House of Delegates be informed at its next clinical session of the progress made toward developing a program for curbing rising hospital costs; and (10) decided to recommend that resolution 24, "Names of Drugs," be not adopted because its purposes are being achieved by the Section on Nomenclature of the American Medical Association Council on Drugs and by cooperation between the Council and the United States Pharmacopoeia.

Insurance and Medical Service. It was reported that this reference committee would: (1) recommend adoption of the recommendations of the Council on Medical Service in its supplementary report A regarding "Endorsement of Health Department Administration of Public Assistance Programs," that is, that the House of Delegates "uphold the right of individual states to decide the appropriate administrative mechanisms" but also "endorse administration of indigent medical care programs. . .as a legitimate activity of state and local health departments." (This was approved by the delegation.)

(2) approve the recommendation in supplementary report B that the National Congress on Prepaid Health Insurance "be held on an annual basis as long as it serves its objectives and that, where indicated, regional conferences be sponsored." (This was approved by the delegation.)

(3) urge that delegates assist in obtaining representation from every constituent association at the Second National Congress of the Joint Council to Improve the Health Care of the Aged, the subject of supplementary report C. (The delegation received this as information.)

(4) concur with the Council on Medical Care (supplementary report D) in recommending the elimination of all special categories among persons eligible for public assistance and the provision of all assistance through a single program. (This was approved by the delegation.)

(5) move adoption of resolution 18, "Reaffirmation of Position on Prepayment Health Insurance," and recommend that high priority be assigned to the activities of the Joint Commission for the Promotion of Voluntary Nonprofit Prepayment Health Plans. (The delegation approved this.)

(6) recommend that resolution 22, "Free Choice of Physician or Freedom of Choice of Physician," which calls for formation of a committee to study and clarify the American Medical Association policy, be not adopted because such study is deemed unnecessary. (The delegation approved the action of the reference committee.)

Medical Education and Hospitals. It was reported that the reference committee would recommend that the House of Delegates

(1) approve supplementary report B of the Council on Medical Education and Hospitals and instruct the Council to "undertake a study of the present and potential contribution of the American Board of Abdominal Surgery to the advancement of the art and science of surgery and the betterment of public health" and to "present a report of its findings and recommendations to the House of Delegates at the next annual meeting." (The delegation voted approval. It also decided that delegates should be ready to oppose accreditation of the Abdominal Surgery Board if that is proposed.)

(2) accept as information and read carefully supplementary report C of the Council, "Preliminary Report—Advisory Committee on Internships and Hospital Services." It was stated that the reference committee had reviewed and discussed supplementary report E of the Board of Trustees, "Joint Commission on Accreditation of Hospitals," that criticism at

the hearings appeared due to a lack of information regarding the activities of the Joint Commission, and that it was noted the Board of Trustees intends to include more information on the subject in its annual reports. It was reported that, after discussing resolution 6, "Community Hospitals and Postgraduate Training Programs," resolution 7, "Interns Versus Residents and Assistant Residents," and resolution 13, "Internship Program," the reference committee decided to recommend that no action be taken on them and to suggest that the Council on Medical Education and Hospitals transmit them to the Ad Hoc Committee on Internships and Hospital Services.

Medical Military Affairs. It was stated that the reference committee would recommend that no action be taken on resolution 5, "Fallout Shelters," or on resolution 23, "National Shelter Program," because the programs which they advocate were undertaken at the June, 1961, meeting of the House of Delegates and implementation of the House of Delegates' action has been initiated. Regarding resolution 21, "Benefits for Women Contract Surgeons in World War I," it was reported the reference committee would recommend disapproval on the ground that attempts to obtain such benefits had been made in the past and that nothing would result from another attempt.

Miscellaneous Business. It was stated that the reference committee had found nothing controversial in the reports referred to it, except for supplementary report P of the Board of Trustees, "A.M.A. Group Disability Insurance Program." Since opinions expressed at the hearing appeared more favorable to the report than unfavorable, the reference committee decided to recommend that the Board continue its negotiations.

Regarding resolutions, it was reported the reference committee would recommend that the *House of Delegates not approve resolution 15, "Proposed A.M.A. Disability Insurance Plan," in view of the action recommended on supplementary report P.*

Resolution 15, introduced by the New York delegation, reads as follows:

> WHEREAS, For years county and district branches of the Medical Society of the State of New York have developed and operated successfully disability insurance plans; and
>
> WHEREAS, Many of these plans have demonstrated their stability and performance to the satisfaction of the subscribers; and
>
> WHEREAS, There is reason to believe that provision for lifetime disability insurance benefits is of questionable actuarial soundness and could be used as a retirement program when disability, not necessarily total and permanent, does occur; and
>
> WHEREAS, By local supervision the doctor's interest is better protected; and
>
> WHEREAS, The American Medical Association has been basically opposed to the principle of national centralization in the administration of services; therefore be it
>
> *Resolved*, That this House of Delegates reconsider its action in entering the disability insurance field on a national level; and be it further
>
> *Resolved*, That the Board of Trustees be directed to return the question of disability insurance to the jurisdiction of the state medical societies.

The delegation voted to support the New York resolution 15, and to request the Speaker to accord Dr. Willis the privilege of discussing it from the floor of the House and also to recognize Dr. Lane during the discussion so that they might *present the facts on which our objection to the insurance plan is based.*

Sections and Section Work. It was reported that the reference committee would recommend that the House of Delegates approve the appointment of a special committee by the Board of Trustees (as reported in supplementary report J) to study the status of sections in the American Medical Association organization, the activities of the Scientific Assembly, and the procedures for establishing specialty certifying boards. It was stated that there had been a lengthy discussion of resolution 17, "Establishment of Medical Specialty Boards," and that the reference committee would recommend that, in view of the study to be undertaken by the special committee described above, no action be taken on this resolution. Similarly, the reference committee would recommend that resolution 35, "Identification of Attendance at Specialty Section Meetings," be referred to the special committee.

Dr. Givan presented a progress report on the work of the Committee to Evaluate the Organization and Functioning of the Board of Trustees. He stated that a full report would be made in June, 1962.

MISCELLANEOUS. The question of closing the hospitality suite on Monday evening before the House of Delegates dinner was discussed, and it was stated that Indiana and Illinois delegations have been doing this. Various suggestions for establishing a uniform closing hour for all hospitality suites and for having them all on one floor were made. An attempt will be made to promulgate standard regulations. It was decided that the chairman would contact the other delegations and arrange a meeting of the chairmen of all hospitality suites so that they might formulate a set of rules.

Once again we express our gratitude to the members of the delegation, the wives, and the staff, who worked to make our stay in Denver an enjoyable and profitable one. They should be congratulated for their devotion and dedication.

Following is the usual report submitted to us by F. J. L. Blasingame, M.D., executive vice-president of the American Medical Association. Actually, it is a summary of the Denver meeting.

Denver, November 30. Social Security health care, relations with the American College of Surgeons, organization of the American Medical Political Action Committee, medical discipline, and polio vaccine were among the major subjects acted upon by the House of Delegates at the American Medical Association's Fifteenth Clinical Meeting held November 26 to 30 in Denver.

Sounding the keynote for the Association's campaign to oppose enactment of the King-Anderson type of legislation in 1962, Leonard W. Larson, M.D., of Bismarck, North Dakota, A.M.A. president, told the opening session of the House that proposals to incorporate health care benefits into the Social Security system "would certainly represent the first major, irreversible step toward the complete socialization of medical care."

The compelling issue, Dr. Larson declared, is socialization versus voluntarism—or compulsion versus freedom of choice. He predicted that courage, determination, and the will to win on the part of physicians will bring the defeat of the King-Anderson bill in Congress next year.

Pointing out that "we are engaged in an historic struggle to preserve our country's unique system of medical care and our stature as a profession," Dr. Larson said: "We are *for* voluntarism. We do not believe that Americans, acting either as citizens or as patients, require central direction from government in their choice of doctor or hospital, in the spending of their health care dollars, or in their selection of the health services and facilities best suited to their own individual needs.

"We take our stand for voluntary cooperation, for preservation of the historic federal-state organizational structure, for individual responsibility, for help for those persons who *need* help." Dr. Larson emphasized that the A.M.A. will continue to give primary attention to implementing the Kerr-Mills Act in the states, promoting voluntary health insurance and prepayment plans designed for the aged, and upgrading nursing homes.

The House of Delegates gave enthusiastic approval to Dr. Larson's address and took several actions reaffirming strong support for the Kerr-Mills program to aid the needy and near-needy aged, and urging a concerted, determined fight against Social Security health care proposals in Congress.

The House advised all state and county medical societies to recognize the impending threat and to prepare now for any eventuality by continuing to oppose any scheme which tries to impose a substandard system of medical care on the American people.

"United, as well as individual, effort is essential," the House declared. "To stop short of our total effort is to invite disaster and to let loose on our beloved America irreversible forces which will ultimately destroy her. We cannot and we must not fail."

American College of Surgeons. The House agreed with the intent of five resolutions which expressed strong dissatisfaction over recent statements by a spokesman for the American College of Surgeons, and it also approved a Board of Trustees report informing the House that arrangements have been made for a January meeting with the College's Board of Regents to discuss that organization's recent statements and policy positions. The report expressed hope that the meeting "will lead to a unification of effort in behalf of American medicine."

The House instructed the Board of Trustees to take the five resolutions to the January meeting and to report to the delegates as soon as possible on the results of the meeting. In taking the action, the House approved a reference committee report which said:

"Your reference committee believes the public airing of disagreements between large segments of medicine can only confuse and shake the confidence of the public in the medical profession and distort the true image of medicine which the American people should have.

"However, in its hearings on the several resolutions relating to the recent statements of the American College of Surgeons, all those who testified were in opposition to the actions and statements of the A.C.S. The majority of those who spoke were Fellows of the American College of Surgeons.

"Your reference committee has no wish to fan the flames of controversy ignited by the statements of the American College of Surgeons. On the other hand, the committee feels the House has an obligation to its membership—which includes physicians in all types of practice—to agree with the indignation manifested by the introduction of these resolutions and in the discussions before the committee.

"This is all the more important because the position of the American College of Surgeons is based on an incorrect interpretation of the action of this House which in no sense is a retreat from its position of firm opposition to fee splitting."

American Medical Political Action Committee. The House heartily approved the purposes and goals of the recently organized American Medical Political Action Committee and urged all physicians, their wives, and interested friends to join AMPAC and other political action committees in their states and communities.

"Effective political action must be carried on at the local level and effective implementation must be done by local groups of physicians," the House said. "The formation of AMPAC recognizes the need for a national medical political action committee to coordinate the political activities of physician groups at all levels throughout the country."

The purposes of AMPAC, which is an organization separate and distinct from the American Medical Association, as required by Federal law, are:

1. To promote and strive for the improvement of government by encouraging and stimulating physicians and others to take a more active and effective part in governmental affairs.
2. To encourage physicians and others to understand the nature and actions of their government as to important political issues and as to the records and positions of political parties, officeholders, and candidates for elective office.
3. To assist physicians and others in organizing themselves for more effective political action and for carrying out their civic responsibilities.
4. To do any and all things necessary or desirable for the attainment of the purposes stated above.

Medical Discipline. The House received from the Council on Constitution and Bylaws a proposed amendment which would have made it possible to implement a recommendation by the Medical Disciplinary Committee that was approved by the House at the June, 1961, meeting. This recommendation was to change the Bylaws so as to confer original jurisdiction on the Association to suspend and/or revoke the A.M.A. membership of a physician found guilty of violating the Principles of Medical Ethics or the ethical policies of the Association, regardless of whether or not action has been taken against him at the local level. However, after considerable discussion on the floor of the House, the proposed amendment was referred back to the Council on Constitution and Bylaws.

In another action on medical discipline, the House approved the expanded activities of the Judicial Council, which has taken over permanent responsibility in that area, and said that the Council program should benefit all physicians, the public and the profession.

Polio Vaccine. The House adopted a resolution which urged that medical societies at the local, county, district, or state levels throughout the United States should encourage, stimulate, and participate in surveys to determine the percentage of individuals in each community who have undergone immunizing procedures for poliomyelitis.

The resolution stated that on the basis of the results of the surveys, the local medical society should determine the type of vaccine and the most effective type of program which will be of greatest benefit to the public.

Until such time as all three types of oral vaccine are available, the resolution concluded, the Salk vaccine should be the vaccine of choice for routine poliomyelitis immunization, with the choice of program for administering the vaccine to be determined on a local basis by each county medical society.

Miscellaneous Actions. In considering a wide variety of resolutions and annual and supplementary reports, the House also:

Disapproved of two proposals which would have required that resolutions be introduced thirty and forty-five days, respectively, before Association meetings.

Approved a statement that physicians have an ethical obligation to participate in medical society activities and express their opinions fully and freely.

Reaffirmed A.M.A. policy that it is not considered unethical for a physician to own or operate a pharmacy provided there is no exploitation of the patient.

Agreed with the Judicial Council that the physician himself is responsible for the control and custody of drug samples once they come into his possession, and in the high tradition of the medical profession he should not dispose of them in any way that could cause harm to others.

Commended those constituent medical societies which have moved forward in the area of human relations by eliminating membership restrictions based on race or color. In connection with the same subject, Peter M. Murray, M.D., of New York City, retiring after twelve years of service in the House, told the delegates in a farewell address that Negro physicians now have some kind of medical society membership in every state except one.

Approved a recommendation that a special House committee be appointed to investigate all facets of the operation of the Joint Commission on Accreditation of Hospitals.

Agreed with the Board's choice of Miami Beach, Florida, as the site for the 1964 Clinical Meeting.

Approved the combining of the American Medical Education Foundation and the American Medical Research Foundation into the American Medical Association Education and Research Foundation, effective next January 1.

Deferred action on a proposed study of fund raising by voluntary health agencies, pending the development of additional information by the A.M.A. Committee on Voluntary Health Agencies.

Reaffirmed the previous policy that physicians should have the privilege of prescribing drugs by either generic or brand name.

Approved the principle of income tax deductions for medical care of the aged.

Recommended, in reviewing the Medicare Program, that all county medical societies in the area surrounding armed forces hospitals make a serious attempt to establish formal liaison with the physicians on those hospital staffs.

Endorsed the administration of indigent medical care programs developed in cooperation with local medical organizations as a legitimate activity of state and local health departments.

Urged the elimination of all "categories" in programs of assistance to the needy at the Federal and state level, with all assistance provided through a single program.

Referred to the Council on Medical Service a resolution proposing the use of state and Federal tax funds to provide voluntary prepayment health insurance protection for the aged. In a related action the House approved of experimentation with prepayment plans under assistance programs.

Urged more vigorous promotion of voluntary non-profit prepayment health plans.

Urged every physician in the United States to use automobile seat belts.

Recommended, as a civil defense measure, a mass immunization program for the general public.

Suggested that the Board of Trustees continue its negotiations to develop a group disability insurance program for A.M.A. members.

Concurred in the Board's appointment of a special committee to study the organizational status of A.M.A. sections, the functions of the scientific assembly, and existing procedures for establishing medical certifying boards.

Instructed the Council on Medical Education and Hospitals to study the present and potential contribution of the American Board of Abdominal Surgery to the advancement of the art and science of surgery and the betterment of public health, to determine whether or not it should be approved as a recognized examining board.

Approved and commended the objectives and program submitted by the Committee for Liaison with National Nursing Organizations.

Recommended that the Secretary of Defense consider the advisability of developing a training program for reserve medical officers.

Awards and Donations. The A.M.A. Board of Trustees presented a special citation to the producers and cast of the Donna Reed Show for its "contribution to public understanding of the high ideals of the medical profession." Carl Betz, who portrays Dr. Alex Stone on the television show, received the award from Hugh H. Hussey, Jr., M.D., A.M.A. Board chairman, at the Wednesday session of the House.

Contributions totaling $435,275.93 from physicians in six states were presented to the American Medical Education Foundation during the opening session on Monday.

Registration. Final registration at the meeting reached a total of 6,138, including 2,976 physicians.

Respectfully submitted,
HENRY I. FINEBERG, M.D., *Chairman*

Medicine and the Law*

Report by
The New York Academy of Medicine,
Committee on Public Health,
New York City

For a number of years The New York Academy of Medicine has been concerned about the trend in the enactment and interpretation of laws impinging on medicine in New York State. It is particularly interested in the developments and present status of laws in three areas as they relate to the practice of the healing arts:

1. Licensure, including other forms of recognition
2. Bodies of deceased persons
3. Liability for both torts and breach of contract.

Each topic is so extensive and complex that only selected aspects can be covered in brief compass.

Licensure in the healing arts

In 1891 Boards of Medical Examiners were established by law in New York State for the examination and licensing of practitioners. In 1907 the present definition of the practice of medicine was first used and a single Board of Examiners was established.

The statutory framework for practice of the healing arts has not been examined critically in its entirety in broad perspective since its adoption seventy years ago. Obviously it is very old and was written for a very different period. Meanwhile, fundamental changes have taken place in all phases of the healing arts. Both expansion and specialization have occurred. Interrelationships between the various disciplines have become more complex.

This combination of a very old law and a greatly changed situation has led in recent years to the annual introduction of many bills into the Legislature, each covering only one small aspect of the healing arts. Both the problems and these attempts to remedy them by piecemeal legislation are becoming increasingly accentuated. Many of these bills originate from those groups of nonmedical persons who serve in a capacity accessory to the practice of medicine or independently in some limited phase. In many instances these groups are seeking certification, licensure, or some extension of the authority under which they practice their special skills.

Because of the large volume of legislative business and the exigencies under which it very often has to be considered, there is little or no opportunity to consider the mass of medical legislation from an over-all perspective. Each bill must be acted on separately and under conditions that make a broad and unbiased study impossible. Not only is there the pressure of time, but also there is pressure from interested persons. The result is a patchwork of legislation which, taken as a whole, is seen to be filled with inconsistencies, ambiguities, and ill-defined borderlines between some of the paramedical activities and the practice of medicine per se.

Today the situation in the area of the healing arts presents many perplexing questions and unresolved problems. In general, they fall into the following categories:

1. Several groups not now licensed are

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Approved by the Executive Committee of the Committee on Public Health, The New York Academy of Medicine, January 29, 1962.

seeking official recognition in the form of licensure.

There is an increasing number of unlicensed persons professing special competence in relieving human ailments and disease who are making persistent efforts to obtain legal recognition and licensure.

2. Groups now licensed for limited practice desire to widen their scope, even achieve independent status.
3. There are undefined relationships and difficulties in establishing a borderline between naturally kindred groups.

   For example, there is difficulty in establishing the relationships and defining the permissible areas of practice between the practice of psychiatry and the independent practice of psychology, between dentistry and surgery of the head and neck, between optometry and ophthalmology, and between many other licensed and unlicensed groups engaged in healing practices.

   There is need to assign medical responsibilities among registered nurses, hospital aides, and other related medical personnel on the basis of recognized training and experience under proper medical supervision and to utilize assembled trained personnel in the most effective and economical job assignments.
4. Various activities now actually performed as a part of the healing arts are not covered by present licensing laws.

   Large numbers of nonmedical persons provide ancillary service to medical practice or engage independently in the performance of services or in practice pertaining to a limited or a special aspect of a branch of medicine; for some, the nature of their status is not clearly defined by law. There are few basic principles and little uniformity governing the activities of these groups.

Individually these groups present different problems. But all have aspirations in common. In succession they seek independent recognition, expansion of their scope of authority and responsibility, and higher status. Most of them are naturally of limited function and scope, yet they may seek a major independent status in the healing arts. Such an outcome could create serious difficulties and have an adverse effect on public health. If groups providing limited service, whether testing or manipulation, exceed their professed bounds and purport to diagnose and treat, they are working beyond their qualifications and competence. In this action they are misleading the public. What these groups with limited services do not know or do not do may have serious consequences. For example, a failure to detect glaucoma or metastasis in the bone and reassurance to the patient may delay proper treatment and lull him into a false sense of well-being. All this may occur unwittingly and unintentionally but nonetheless seriously. Also to be noted is the assertion by hospitals that the conferral of higher status on the paramedical groups would add to the cost of hospital care for the public.

The ultimate objective of the law regulating the practice of the healing arts is to protect the health of the people. To achieve this protection it is necessary to maintain high standards of ability within the professions, while at the same time providing an adequate supply of trained personnel in medicine, nursing, and other fields relating to the care of body and mind.

When these aims are considered in the light of the present situation in medical care and the confused pattern of the law regulating it, the following needs are clearly evident:

1. To survey the whole field of the practice of healing arts in the light of new developments, viewing the relationship of all parts to the whole and to each other.
2. To study the licensing laws to determine whether they fulfill their objectives and, if not, how they should be altered.
3. To consider adequate means of enforcing the licensing laws.
4. To establish general principles and criteria to govern decisions as to whether or not a given technical or

professional group should be controlled by licensure.

5. To provide the Legislature with a basis of fact for future legislation.

For ten years The New York Academy of Medicine has been pointing out the critical need for this survey to bring order out of chaos.

Bodies of deceased persons

The present status of the laws concerning the bodies of deceased persons also affects the health of the living. These laws have defects similar to those for the practice of healing arts. It was many years ago that the framework of the law was set down, and times have since changed. Over the years amendments have been enacted at different times; hence, the statutes contain anachronisms, ambiguities, inconsistencies, contradictions, and conflicts. The list of them is long. But two are selected for mention because of their effect on the provision of medical care and consequently on the health of the population.

CONSENT FOR AUTOPSY. Consent for autopsy must be obtained from the person who is the legal custodian of the body and responsible for its proper disposal. The right to grant permission for autopsy rests with the husband, wife, or next of kin. Section 4210, Subdivision 3, of the Public Health Law states:

> Whenever and so far as the husband, wife, or next of kin of the deceased, being charged by law with the duty of burial, (*a*) may authorize dissection for the sole purpose of ascertaining the cause of death, or (*b*) may authorize dissection for any other purpose by written instrument which shall specify the purpose and extent of the dissection so authorized. . .

There is some difference of opinion in the interpretation of this law. Problems arise when there are more than one "next of kin." Some persons interpret "next of kin" to mean one member of a family, while others declare that all members of equal rank must be consulted.

This law was written when Americans were less addicted to migration. But in modern America on wheels, members of a family are no longer in close geographic relation; they are often scattered over the United States and even into other countries. The requirement that every member of equal rank in the family give consent is tantamount to foreclosing the possibility of obtaining a legal consent.

A regulation taken in conjunction with the foregoing statute adds to the difficulty by placing the pathologist in jeopardy. A new category of unprofessional conduct, which may lead to the revocation of his license to practice medicine, has been added (1956) to the regulations of the New York State Education Department. Article 2, Section 30, Subdivision 4, item h of the regulations states that "unprofessional conduct in the practice of medicine shall include . . . the performance of a complete or partial autopsy on a deceased person without lawful authority." This regulation compounds the present difficulties for the pathologist since it does not define "lawful authority." When there is more than one next of kin, both the law and the regulation are ambiguous. On the pathologist falls the full onus of a decision. He can lose his license if he chooses not to be conservative in meeting the ambiguous legal requirements. Heretofore the hospital shared the responsibility with the pathologist. Now the brunt is borne by him. It should be recalled that he does not obtain or even countersign the consent; this is an administrative function of the hospital. Whereas the pathologist has been in jeopardy of a civil action and financial loss in performance of his duties, he now has the threat of loss of license added to the penalties.

On the other hand, if the pathologist refuses to perform an autopsy on receiving what he construes to be an illegal consent countersigned by his superior, the hospital administrator, he is placed in an equally difficult position. His refusal means the loss of an autopsy.

This loss is more serious than the public perhaps realizes. The proportion of autopsies conducted in a hospital is one of the decisive factors in determining whether or not it will become or remain approved. As a yardstick of approval, the autopsy rate is a criterion and means of determining, maintaining, and promoting the quality of medical care. And the autopsy is a valuable source of information about diseases. This is the pathologist's choice: loss of an autopsy or loss of his license. It is a cruel dilemma created by law in which the pathologist can only lose.

It is also alleged that if every pathologist were to adhere strictly to the law and refuse to perform an autopsy unless the consent was signed by all of equal rank of kin, few hospitals in this State could obtain the required percentage of autopsies for approval of their intern and residency programs.

Since a number of factors are taken into consideration, the legal sequence of control of a body is not well defined in most states. Some have recognized the legal ambiguity as an obstacle and have revised their laws to simplify the requirements of consent while protecting the wishes and interests of survivors. New York State is not one of them.

UNCLAIMED BODIES. The present laws concerning unclaimed bodies likewise have repercussions on medical care. Cadavers are fundamental and necessary in the making of a physician; he must know the structure of the body. Most cadavers used in teaching medical students are obtained as unclaimed bodies. At present there is an extreme shortage of cadavers throughout the State. Some schools have been faced with the prospect of no cadavers with which to conduct their teaching programs. This nation already has a shortage of physicians; it is predicted that the shortage will increase over the next fifteen years. The creation of more medical schools has been the primary recommendation. But unless cadavers are provided, teaching will be hampered and impaired. For, the present supply of cadavers does not suffice for existing schools.

A combination of circumstances has led to the shortage. But prominent among the reasons in New York State is a legal conflict. Unclaimed bodies represent the major source of supply of anatomic material for medical and dental schools. Under Sections 4211 and 4212 of the Public Health Law the bodies are apportioned to the medical schools according to their needs.

Modern social welfare law now provides for the burial of unclaimed bodies. Under Article 5, Section 141 of the Social Welfare Law of the State of New York, persons dying without means and without relatives liable or willing to assume the expense of burial are provided interment by the public welfare agency. This law, a comparatively recent development expressing the current doctrine of social welfare, was enacted after the Public Health Law pertaining to unclaimed bodies. The Social Welfare provision is believed to contribute substantially to the diminution of unclaimed bodies delivered to medical schools. In considering this issue the Committee on Public Health recently recommended that a means be sought to resolve the conflict between Section 141 of the Social Welfare Law and Section 4211 of the Public Health Law over the disposition of unclaimed bodies by giving precedence to the Public Health Law.

The basic intent of the Social Welfare Law is actuated by motives of humanity, decency, and dignity to provide burial for unclaimed dead. But a strict observance of this law defeats the provisions in the Public Health Law which were designed to supply cadavers for the teaching of anatomy to medical students and thus ensure the production of a sufficient number of adequately trained physicians. It should be reiterated that unclaimed bodies constitute the major source of supply of anatomic material for medical and dental schools in New York City. The Social Welfare Law concerning burial of the dead can and is believed to cut off much of the supply of cadavers. Here the larger public interest, that is, the need for physicians to maintain public health, must be balanced against the aims of social welfare in its provisions for the burial of unclaimed dead.

After taking all considerations into account it is believed that the larger public interest should be served; that the means of maintaining the health of the public are paramount and should be safeguarded.

The magnitude and complexity of this segment of medicine, where the dead teach the living, and the chaotic state of the laws would alone warrant a survey preparatory to clarification and codification. But preferably it would be part of a larger study embracing licensure and liability.

Liability for torts and breach of contract

The practice of medicine per se is an exacting and demanding profession. But today its rigors have been increased grotesquely and unreasonably by liabilities that amount to harassment. In almost every professional situation a physician performs his duties under the constant threat of legal action either for what he says or does or what he does not say or do. It has reached the point where he is held accountable for occurrences unknown or only slightly or indirectly related to him.

In rendering medical services the physician warrants that he has the necessary learning and skill and that he will apply and exercise them with ordinary and reasonable care. The law has a standard of conduct for the physician and imposes on him the duty of conforming to it. The generally accepted legal standard for reasonable care is that exercised by similar physicians in the same or a similar locality. Obligations expressed in these legally implied warranties of skill and due care are the bases of liability for malpractice.

By far the most frequent legal jeopardy hanging over the physician is a suit for malpractice. Most commonly it is based on alleged negligence, or breach of duty. In effect, the patient asserts that the physician did not possess the requisite degree of knowledge or skill or did not exercise the requisite degree of care and diligence, and that this failure of duty led to injury.

In court the question of whether or not a physician has been negligent in his duty is usually treated as a question of fact. On the plaintiff rests the burden of proving that the physician was negligent. In many cases proof of malpractice requires medical testimony. To ascertain whether or not the defendant in his duties met the standards imposed by law, testimony from experts must be heard in court.

There is another class of cases in which proof of negligence is determined by circumstances. With proof of an injury and of the conditions in which it occurred, the results are such as to warrant the inference that there was a lack of proper care. In these cases three requirements must be met in applying the principle of res ipsa loquitur. When it is applied it is regarded as enough to make a prima facie case against the physician. In consequence, as some courts hold, the burden of proof is shifted from the plaintiff to the defendant. In any event, the application of res ipsa loquitur is an adverse development for the defendant.

During the last two decades suits for malpractice have been filed in increasing numbers. According to the American Medical Association, one out of seven physicians in this country has been sued for malpractice. From state to state the rate varies. California has the highest ratio, 1:4; Pennsylvania the lowest, 1:20. Apparently precise annual figures on the number of claims and suits for New York State are not available. But scattered data leave little doubt that the number is unreasonably large and has been steadily on the increase. For 1960 the Malpractice Insurance and Defense Board of the Medical Society of the State of New York reported an increase of 34 per cent in the number of suits in the State and 28 per cent in the number of suits and claims combined. It said: "The increase in loss experience that occurred during 1960 is cause for concern."

Recent developments. Serious as the present situation is, there is greater concern for the future. Several developments have grave forebodings for the medical profession. The first one has to do with a modification of the requirements of expert testimony. Several states have changed the rule of evidence so as to permit the use of medical textbooks and treatises as a substitute for expert testimony. This modification produces a change not only in the method of proof but also in the substantive law. For, the expert opinion from the textbook may not be applicable to the defendant's community.

Second, the principle of res ipsa loquitur has been extended. The broadening of one area in particular is adverse for the physician. For the application of res ipsa loquitur, the requirement that the defendant was in sole control of the instrumentality which caused the injury has been abolished. As a direct consequence, cases with multiple defendants have become more common, although the parties stand in different relations to the allegedly injurious act.

In effect, a physician may find himself a defendant in a lawsuit for an injury of which he had no knowledge. He is then compelled to assume the burden of showing that he was not negligent. Innocent although he may be, he may find himself a potential catch in a "fishing expedition" in the courtroom.

These developments are another step in the expansion of physicians' liability for malpractice. It is predicted that under the expanded rule many more malpractice cases will have the principle of res ipsa loquitur applied with its adverse consequences for the physician.

Indeed, some legal authorities predict that unless limits to the application of res ipsa loquitur in medical cases are established, the outlook is ominous for both the medical profession and the public. If the trend continues there is the possibility that the principle of res ipsa loquitur may turn into a "rule of sympathy." In effect, the physician may be held liable without any proof of fault on his part, other than an unfavorable result. In short, the trend in res ipsa loquitur is to go beyond the warranty of skill and due care into an implied warranty of cure. By this interpretation his performance of services is construed to carry a guaranty of success or even cure. Such an impression the physician never intended to convey. Any guaranty of cure would be totally unrealistic.

Third, in this movement in a direction that menaces the physician, three new classes of cases that may be characterized as situational should be mentioned.

Good Samaritan. Once it was customary for the physician, wherever he might be, to respond to accidents in an emergency. With increased transportation by motorcar and the large number of highway accidents, passing physicians were hailed to render first aid. As a reward for their humanitarian services, a number of these physicians later found themselves as defendants in legal actions. All the circumstances in the situation of rendering medical help on the roadside make it easy for the injured person to make the usual allegations of negligence, such as superficial, hasty, and incomplete examination; improper attention; and failure to follow standard procedures. This involvement in lawsuits became so prevalent that physicians were advised not to stop at highway accidents. Apparently they heeded the admonition so effectively that one state has felt the need of enacting laws that confer immunity on the physician who is stopped to render first aid in an emergency. This is the so-called Good Samaritan law.

In the hospital. Hospitals are no longer immune. Rather, their extent of liability has been expanded. They are now liable for medical as well as administrative acts. Their expanded liability has created a new threat for physicians. If a hospital loses in the courts, it may in turn seek recovery from its staff. Hence hospitals are now instituting cross-claims against physicians on their staff and proceedings to conjoin them in legal actions.

Informed consent. The necessity of explaining to a patient a contemplated procedure or treatment that has some risk and of obtaining a broad consent in writing from him is so generally recognized that the practice has become widely established.

But unfortunately the physician is vulnerable even with a signed consent. Now the amount of information imparted in the explanation and evidence of imparting it have come to assume considerable legal importance. A disappointed or disgruntled patient may claim that he was not fully informed about the extent of risk or the amount of discomfort involved when his permission was sought for a procedure. He may then sue his physician on the ground that consent was gained by fraud, deceit, and misrepresentation. Or he may choose to start legal action on the ground of negligence. Informed consent is a new area of malpractice liability.

The possibility of this development places the physician in a quandary when he is seeking consent from a patient. How much information is enough to fulfill his responsibility to the patient and satisfy legal requirements? How much information may be safely imparted from the standpoint of the patient's health? In short, to what extent should the physician disclose to the patient the existence and nature of the risks inherent in a contemplated procedure?

Patients vary greatly in their reaction to discussion of contemplated procedures that are unfamiliar to them. Thus the physician is confronted with deciding how much he may tell the patient without upsetting him unduly and how much he may advisedly withhold without incurring a subsequent lawsuit. Now the courts have made the decision for him.

One court in providing the legal ruling on the proper course has summarized the dilemma:

> . . . A physician violates his duty to his patient and subjects himself to liability if he withholds any facts which are necessary to form the basis of an intelligent consent by the patient to the proposed treatment. Likewise the physician may not minimize the known dangers of a procedure or operation in order to induce his patient's consent. At the same time, the physician must place the welfare of his patient above all else, and this very fact places him in a position in which he sometimes must choose between two alternative courses of action. One is to explain to the patient every risk attendant upon any surgical procedure or operation, no matter how remote; this may well result in alarming a patient who is already unduly apprehensive and who may as a result refuse to undertake surgery in which there is in fact minimal risk; it may also result in actually increasing the risks by reason of the physiological results of the apprehension itself. The other is to recognize that each patient presents a separate problem, that the patient's mental and emotional condition is important and in certain cases may be crucial, and that in discussing the element of risk a certain amount of discretion must be employed consistent with the full disclosure of facts necessary to an informed consent.

To avoid misunderstanding it is recommended that the physician explain the possible risks in a contemplated procedure and have the patient assume them. This explanation is to be made without frightening the patient. In urging full and frank disclosure of all pertinent facts, one authority points out that oral explanations will not suffice, that some written evidence is a necessary safeguard. Specifically, he advises that a physician who is about to commence a procedure attended with hazard send to the patient by certified or registered mail a letter outlining the contemplated procedure, the risks involved, and the possibilities of an unfavorable outcome.

Finally, in New York State a court decision bearing on the type of injury in which indemnity is allowed under malpractice and repeated attempts to change the statute of limitations in the Civil Practice Act by lengthening the period indicate further the trend toward widening the plaintiff's latitude while increasing the physician's jeopardy.

TYPE OF INJURY BROADENED. The range of the type of injury for which redress is being allowed is becoming more extensive and extreme, to the point of including complaints more remotely related. Recently damages were awarded to a patient for mental suffering arising from information imparted by a dermatologist whom she had consulted about a dermatitis attributed to alleged previous excessive application of x-rays by radiologists during the course of treatment for bursitis. Testimony brought out that she had a profound cancerophobia. The award was against the radiologists under the basic rule in New York State that the original wrongdoer is liable for the ultimate result.

It is worthy of note that the dissenting judges in the Court of Appeals could not accept the rule that damages based on mental anguish engendered by a physician's statement as to a possible development of another ailment may be recovered. They further pointed out that the majority decision will introduce "a new field of damages for cultivation by plantiffs and afford countless opportunities for fraudulent unverifiable claims."

STATUTE OF LIMITATIONS. Alternative bills that would alter the statute of limitations have been introduced into the Legislature for several years, both designed to prolong its period of applicability in malpractice: One would extend outright its present length from two to six years; the other would place its initially effective date on the day of recognition of the injury, with a fixed limit of four years after the commission of the malpractice, beyond which no legal action could be commenced. At present the New York State courts hold that an action for malpractice takes effect and the statutory period of two years begins to run immediately on the act of malpractice. They have rejected arguments that in respect to the commencement of an action in malpractice the statute should begin to run only when the claimant has discovered his injury.

Obviously any lengthening of the statute of limitations in malpractice would impose an additional handicap on the physician in his efforts to gather evidence for establishing his innocence. With the passage of time there is an increasing likelihood of loss of records, absence of witnesses, and inroads on memory.

All the foregoing developments are in the interest of the plaintiff and place the physician at a disadvantage either in defending himself or in winning his case.

Consequences. Surely the fantastic increase in suits for malpractice does not reflect a sudden development of inferior medical care. On the contrary, it is paradoxical that this spree in litigation coincides with what is regarded as an all-time high in the quality of medical care. The varying rate of cases from state to state indicates the reason for the enormous increase. It would seem to be the result of the work of the legislatures, the courts, and the legal profession, with consequences unintended and unforeseen. But it could not have been more devastating if it had been planned deliberately. It almost appears as though the nation has embarked on a course of medical litigation as a way of life, in the spirit of soaking the corporations, in this case the insurance companies, in a gigantic giveaway. It is interesting to contemplate what might have happened if there had been no malpractice insurance and no contingent legal fees. However, to reverse the present trend and to restore realism, order, and justice into the area of actions in torts and contracts against physicians, a logical starting point would be a survey of all the existing pertinent laws, including rules of procedure, and a formulation of necessary changes. Although some authorities ascribe the low rate of malpractice actions against physicians in Pennsylvania to special circumstances in individual communities, others attribute the record to the basic law in that state.

This phenomenal surge of malpractice suits has two serious repercussions for the public in its need and use of medical services. First, the harassment of physicians does not add to the attractiveness of medical practice as a professional career. At a time when there is an inadequate number of physicians in the country and a reduced number of applicants for medical schools, a continued increase in malpractice cases is surely not an inducement in recruiting manpower to the medical field.

Second, the growing propensity for malpractice suits has added tremendously to the cost of medical care. It is naïve to think that an exuberant proliferation of lawsuits and profligate awards do not affect the cost of medical care. They most definitely add to the soaring cost. Certainly the indemnifying carriers do not have a magic supply of funds. As the experience rate has steadily worsened, premiums on malpractice insurance have climbed. This effect reveals clearly the source of the carrier's income. But ultimately these increased rates must be passed on to the consuming public. Thus it is a question whether or not most of the people are to pay for the greed of a few.

Furthermore, it is usually said that one of the reasons for increased cost is the outstanding scientific development of new tests and methods of treatment. But the real reason may well be the unnecessary use of them. It is generally admitted that, because of the ever-present threat of a malpractice suit hanging over him, the physician orders tests and examinations that would not otherwise be needed. They are a legal not a medical necessity. As a form of evidence, the records may be his main, if not sole, protection in the event of litigation. Until the threat is brought within sensible bounds, the prospect of reduction in the cost of medical care is not bright.

Implied warranty. It has been noted that when a physician attends a patient, warranties of skill and due care are legally implied. But it is to be emphasized that there is no warranty of success of treatment. The physician contracts for services, not a cure. It is recognized as unwise for him expressly to guarantee a cure. Indeed, it is even regarded as imprudent for the physician to be too optimistic in his statements to the patient as to the outcome of a proposed treatment. Such statements may lead some patients to believe that the physician guarantees a satisfactory result and therefore may be construed as a warranty of cure, even though that was not the intent. If satisfactory improvement does not eventuate, these statements may form the basis of a suit against the physician for breach of contract, which is not covered by insurance for malpractice. Suits for breach of contract are becoming increasingly popular with plaintiffs' lawyers. These actions are governed by a longer statute of limitations—six years—than that for malpractice.

Under this legal jeopardy the physician must walk a tightrope. Part of his skill is in encouraging the patient and producing a state of mind that is conducive to recovery. But where is the line to be drawn between encouragement and optimism?

Furthermore, it has been pointed out that the application of the principle of res ipsa loquitur has been extended to the point of its becoming a rule of sympathy in which the physician is held liable for an unfavorable or disappointing result.

It has been predicted that the medical profession will be increasingly harassed by suits for implied warranty of a satisfactory result.

Conclusions and recommendations

Because of its anachronisms, ambiguities, inconsistencies, contradictions, conflicts, and inequities, the law as it relates to medicine is now a vast jungle of confusion. In consequence the public is unwittingly misled in matters of health, and the physician is both baffled and harassed. Medicine has had imposed on it an incredibly high occupational hazard; it has almost reached the point where the physician must practice with a law book in his hands.

Three areas illustrating the chaotic state of the law pertaining to medicine have been described: licensure, deceased bodies, and liability. It has been shown that the existing situation in these areas has serious consequences for both the economy and the health of the public. It has a profoundly adverse effect on the quantity of medical manpower and on the cost and quality of medical care.

The New York Academy of Medicine recommends that the New York State Legislature initiate a survey of all the laws pertaining to the practice of the healing arts, especially the three areas considered here, preparatory to clarification and codification. Each of the three areas is sufficiently important to warrant a separate project. Taken together their gravity and significance are of enormous magnitude.

So critical is the situation becoming that immediate action is urgently needed.

The cloak of socialism

Most people forget that they are government and the people must pay in taxes for every appropriation government makes. The issues are fast being drawn. One of them is, will government dominate research or will private initiative be left a significant role? Another is, will prices of health products and many other products be regulated by competitive forces as they have been in the past or by government? A third is, will medicine remain a free profession or will it be forced to put on the cloak of socialism under gradual Federal encroachment? . . . As we pass into any program which is socialistic, we sacrifice the total well-being, independence, and dignity of the individual to the average well-being of the masses, where people are leveled into mediocrity, with little independence and much sacrifice of dignity by the individual, just as has been done in Russia.—*Francis Brown, President, Schering Corporation, Profits Insure Progress*

Necrology

George R. Allen, M.D., of Champlain, died on November 5, 1961, at the age of sixty-seven. Dr. Allen graduated in 1921 from the University of Vermont College of Medicine. He was a member of the Clinton County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph John Arminio, M.D., of Ossining, died on January 17 at his home at the age of forty-nine. Dr. Arminio graduated in 1938 from Boston University School of Medicine and interned at Grasslands Hospital, Valhalla. He was an attending physician in allergy and general practice at Phelps Memorial Hospital Association, North Tarrytown. Dr. Arminio was a Fellow of the American College of Allergists, a Member of the American Academy of Allergy, and a member also of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Howard Barber, M.D., of Calverton and Richmond Hill, died on January 29 at Memorial Hospital, Sarasota, Florida, at the age of seventy-five. Dr. Barber graduated in 1911 from Columbia University College of Physicians and Surgeons. He was a consultant in surgery at Bellevue, French, Goldwater Memorial, and Jamaica Hospitals, and for many years was an associate professor of surgery at New York University Medical School, retiring in 1946. Dr. Barber was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the New York Academy of Medicine, the New York Surgical Society, the Queensboro Surgical Society, the Suffolk County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ralph J. Carotenuto, M.D., of Brooklyn, died on January 8 at his home at the age of fifty-four. Dr. Carotenuto graduated in 1931 from George Washington University School of Medicine. He was an associate attending psychiatrist at the Vanderbilt Clinic, an associate attending neuropsychiatrist at St. Peter's Hospital, an assistant attending psychiatrist at St. Vincent's Hospital, and a staff neuropsychiatrist at the Veterans Administration Regional Office in New York City. Dr. Carotenuto was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Fellow of the American Psychiatric Association, and a member of the Association for Research in Nervous and Mental Disease, the American Geriatrics Society, the Eastern Psychiatric Research Association, Inc., the Brooklyn Psychiatric Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Earl Burton Carr, M.D., of Schuyler Lake, died on January 24 at his home at the age of seventy-one. Dr. Carr graduated in 1915 from George Washington University School of Medicine. For many years he was in Civil Service work in the Panama Canal Zone and while there he started the Ancon Hospital. He was health officer for the Town of Exeter and school physician for the Schuyler Lake area of the Richfield Springs Central School system. Dr. Carr was a member of the Herkimer County Medical Society and the Medical Society of the State of New York.

Archibald Eastwood Chace, M.D., of Port Jervis, retired, died on October 19, 1961, at the age of seventy-eight. Dr. Chace graduated in 1906 from Cornell University Medical College. He was a Fellow of the American College of Surgeons.

De Witt Franklin Randolph Cline, M.D., of Warwick, died on August 15, 1961, at the age of seventy-eight. Dr. Cline graduated in 1909 from New York University and Bellevue Hospital Medical School.

Joseph Di Fede, M.D., of Brooklyn, was killed in his home on December 7, 1961, at the age of thirty-nine. Dr. Di Fede received his medical degree from the University of Palermo in 1949. He was an assistant attending physician in general practice at Evangelical Deaconess Hospital and a member of the staff of Mary Immaculate Hospital. Dr. Di Fede was a member of the Kings County Medical Society and the Medical Society of the State of New York.

Kendall Emerson, M.D., of Brookline, Massachusetts, formerly of New York City and Norwalk, Connecticut, died on February 5 at his home at the age of eighty-six. Dr. Emerson graduated in 1901 from Harvard University Medical School. From 1928 to 1947 he was managing director of the National Tuberculosis Association and in 1948 he served as president of the New York Tuberculosis and Health Association. In 1920 and 1921 he was deputy commissioner and medical director for the

American Red Cross in Europe and Siberia and was decorated by the Rumanian Government and Polish Red Cross. From 1931 to 1935 he served as executive secretary of the American Public Health Association, was a United States delegate to the Pan American Sanitary Conference in Buenos Aires in 1934, and was president of the National Health Council from 1940 to 1942. Dr. Emerson was a Fellow of the American College of Surgeons and a member of the New York Academy of Medicine and the Medical Society of the State of New York.

Samuel Sanders Fischoff, M.D., of Bayside, died on January 26, at the age of seventy-six. Dr. Fischoff graduated in 1914 from Albany Medical College. He was a member of the American Public Health Association, the Kings County Medical Society, and the Medical Society of the State of New York.

De Lisle Fitz-Gerald Gilkes, M.D., of Brooklyn, died on October 2, 1961, at the age of sixty-one. Dr. Gilkes graduated in 1932 from New York University and Bellevue Hospital Medical School. He was an assistant attending physician at Greenpoint Hospital. Dr. Gilkes was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas Francis Hassett, M.D., of Elmira, died on January 28 at St. Joseph's Hospital at the age of eighty-six. Dr. Hassett graduated in 1904 from Ohio State University College of Medicine. He was a member of the Chemung County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Edward Laban Hazeltine, M.D., of Jamestown, died on December 24, 1961, at the age of seventy-five. Dr. Hazeltine graduated in 1909 from Denver and Gross College of Medicine. He was an honorary staff member of the Jamestown General Hospital and an attending physician and surgeon at the Woman's Christian Association Hospital. Dr. Hazeltine was a member of the Chautauqua County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Harry Hillman, M.D., of the Bronx, died on October 8, 1961, at the age of fifty-six. Dr. Hillman graduated in 1930 from New York University and Bellevue Hospital Medical School and interned at Bronx Hospital. He was a member of the American Academy of General Practice, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Sophie Alexander Kappel, M.D., of Pine Plains, retired, died on October 23, 1961, at the age of seventy-eight. Dr. Kappel received her medical degree from the University of Bern in 1912.

Henry Franklin Kreckman, M.D., of Poughkeepsie, died on February 16 at the age of fifty-four. Dr. Kreckman graduated in 1934 from Albany Medical College and interned at the New Jersey Orthopedic Hospital and Wyckoff Heights and St. Charles (Brooklyn) Hospitals. He was an attending orthopedic surgeon at the Vassar Brothers Hospital. Dr. Kreckman was a Diplomate of the American Board of Orthopedic Surgery and a member of the Mid-Hudson Surgical Society, the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Bernard Lauterstein, M.D., of Wurtsboro, died on November 6, 1961, in Vienna, Austria, at the age of fifty. Dr. Lauterstein received his medical degree from the University of Vienna in 1926. He was an assistant attending physician at the Elizabeth A. Horton Memorial Hospital (Middletown), a member of the staff of the Monticello Hospital (Bronx), and acting coroner of Sullivan County. Dr. Lauterstein was a member of the Sullivan County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Nathaniel Edward Meyer, M.D., of the Bronx, died on January 28 at the age of fifty-seven. Dr. Meyer graduated in 1929 from Boston University School of Medicine and interned at Lincoln Hospital. He was an associate attending surgeon at Lebanon Hospital and an attending in surgery at Lincoln Hospital. Dr. Meyer was a Diplomate of the American Board of Surgery, a Fellow of the International College of Surgeons, and a member of the Bronx Surgical Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter V. Moore, M.D., of Brooklyn, died on February 19 at Brooklyn Hospital at the age of sixty-nine. Dr. Moore graduated in 1917 from Columbia University College of Physicians and Surgeons and interned at Brooklyn Hospital. He was senior attending eye surgeon at the Brooklyn Eye and Ear Hospital, senior attending ophthalmologist at the Brooklyn Hospital, and a consultant in ophthalmologic surgery at St. John's Hospital. Dr. Moore was an honorary surgeon with the New York City Police Department and had been commanding officer of the Seventy-Ninth General Hospital which was organized in 1942 by the members of the medical staff of the Brooklyn Eye and Ear Hospital under the sponsorship of the Long Island College of Medicine. During World

War I he served as first lieutenant in the Medical Corps of the Regular Army and had also been assistant camp surgeon at Camp Upton. Dr. Moore was a Diplomate of the American Board of Ophthalmology, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the New York Ophthalmology Society, the Brooklyn Ophthalmological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Peter Alfred Narath, M.D., of Yorktown Heights, died on January 3 while walking on East Fifth-Eighth Street, New York City, at the age of seventy. Dr. Narath received his medical degree from the University of Heidelberg in 1915 and interned at Lenox Hill and New York Polyclinic Hospitals. He was an adjunct consultant in urology at New York Polyclinic Hospital and director of urology at Northern Westchester Hospital (Mount Kisco). He was a founder and former editor of the *International Journal of Urology* and an honorary member of the Asociacion Espanola de Cirujanos as well as a corresponding member of the German Urological Association and the Italian Urological Association. Dr. Narath was a Fellow of the International College of Surgeons and a member of the Rudolf Virchow Medical Society, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ludwig Popp, M.D., of New York City, died on January 18 at the age of sixty-nine. Dr. Popp received his medical degree from the University of Tubingen in 1920. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

D. Edward Rowan, M.D., of Rensselaer, died on November 7, 1961, at Albany Medical Center at the age of sixty-three. Dr. Rowan graduated in 1926 from Albany Medical College. He was an attending physician in roentgenology at Cohoes Memorial Hospital. Dr. Rowan was a member of the Radiological Society of New York State, the Rensselaer County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Saul S. Samuels, M.D., of New York City and Atlantic Beach, died on October 30, 1961, at St. Joseph's Hospital, Far Rockaway, at the age of sixty-six. Dr. Samuels graduated in 1920 from Columbia University College of Physicians and Surgeons and interned at The Mount Sinai Hospital. He was chief of arterial diseases and director of experimental angiology at Stuyvesant Polyclinic, attending angiologist and director of angiology at Swedish Hospital in Brooklyn, a consultant in vascular surgery at Long Beach Memorial Hospital, and a consultant in angiology at Brooklyn Hebrew Home and Hospital for the Aged. A founder and first president of the Angiology Research Foundation, Dr. Samuels was a Fellow of the American College of Cardiology, a Fellow of the American College of Angiology, and a member of the American Urological Association, the American Geriatrics Society, the New York Academy of Medicine, the New York Cardiological Society, the Rudolf Virchow Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter Steinberg, M.D., of Astoria, died on October 12, 1961, at the age of seventy-eight. Dr. Steinberg received his medical degree from the University of Munich in 1909. He was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Adolf Wisocki, M.D., of Jamaica, died on December 31, 1961, at Queens General Hospital at the age of sixty-nine. Dr. Wisocki received his medical degree from the University of Berlin in 1919. He was a member of the Queens County Medical Society and the Medical Society of the State of New York.

Gerhard Wodtke, M.D., of New York City, died on October 18, 1961, at the age of seventy-one. Dr. Wodtke received his medical degree from the University of Jena in 1914. He was a consulting physician at Lenox Hill Hospital.

Harold G. Wolff, M.D., of New York City, died on February 21 at the Clinical Center of the National Institutes of Health at the age of sixty-three. Dr. Wolff graduated in 1923 from Harvard University Medical School. He was an attending physician and psychiatrist at New York Hospital, a consultant in neurology at New York Hospital, Westchester Division, and at Veterans Administration Hospitals in New York City and Montrose, and professor of medicine and neurology at Cornell Medical College. In 1952 City College awarded him its Townsend Harris Medal for "outstanding postgraduate achievement." He was editor in chief of the American Medical Association's *Archives of Neurology* and also had served as editor of the *Journal of Psychosomatic Research* and *Psychosomatic Medicine*, editor for "Diseases of the Nervous System," in the Cecil-Loeb *Textbook of Medicine*, consultant in research and development to the Department of Defense, and chairman of the Veterans Administration Division of Medical Sciences National Research Committees. During 1960 to 1961 he was president of the American Neurological Association.

Dr. Wolff, director of the study program in human health and the ecology of man at the New York Hospital-Cornell Medical Center, was also the recipient of many awards, including the Louis Livingston Seaman Award of the Association of Military Surgeons in 1960 and an Oxford (England) Honorary Lectureship at the Symposium on Mental Health in 1959. In 1942 to 1943 as well as 1949 to 1950 he was president of the Association for Research in Nervous and Mental Disease and editor of the *Proceedings on Pain*.

Dr. Wolf was a Fellow of the American College of Physicians, a Fellow of the American Psychiatric Association, and a member of the American Neurological Association, the American Society for Clinical Investigation, the Association for Research in Nervous and Mental Disease, the American Physiological Society, the Society for Experimental Biology and Medicine, the Association of American Physicians, the New York Academy of Medicine, the New York Neurological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

Chest physicians establish resident loan fund

The American College of Chest Physicians has established a fund providing for loans to resident physicians to stimulate interest in the postgraduate study of chest diseases and to assist postgraduate students in the continuation of studies in diseases of the chest (including diseases of the heart and lungs).

Distribution of the funds is under the jurisdiction of the Committee on Resident Loan Fund of the College. M. Jay Flipse, M.D., Miami, Florida, is chairman of the committee. Other committee members are: David A. Cooper, M.D., Philadelphia, Pennsylvania, and Philip H. Narodick, M.D., Seattle, Washington.

Any physician who has completed an internship of one year or more in an acceptable hospital may apply for a loan to continue in the specialty of chest diseases. Loans are made only to physicians serving residencies in chest medicine and cannot be made to physicians engaged in practice.

Application forms may be secured by writing to: Committee on Resident Loan Fund, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Literature on syphilis

According to William J. Brown, M.D., chief, Venereal Disease Branch, Department of Health, Education, and Welfare, infectious syphilis has been increasing since 1957 at an alarming rate in all races, sexes, ages, social groups, and geographic areas. Concurrent with this resurgence is a paucity of venereal disease literature and information available to the private physician.

To alleviate partially this situation, the Venereal Disease Program of the Public Health Service routinely abstracts current articles on venereal diseases from almost 1,000 journals both domestic and foreign. A publication entitled *Current Literature on Venereal Disease* including these abstracts is printed three or four times a year and indexed annually. It is distributed free of charge to physicians on their personal request.

Physicians who wish to be added to the mailing list for this publication should write to: William J. Brown, M.D., Chief, Venereal Disease Branch, Communicable Disease Center, Atlanta 22, Georgia.

Hospital treatment of alcoholism

February 5 marked the start at Trafalgar Hospital, New York City, of a six-month study of a new approach to the treatment of alcoholism. The study, which is based on a medical-social approach, will bear the name, Trafalgar Hospital Demonstration on Alcoholism.

The Trafalgar Demonstration will bring several new procedures to the subject of alcholism: First, it will not accept a patient unless he is diagnosed openly as suffering from alcoholism; second it insists on a complete physical and psychiatric examination; and finally, it insists on a close association with either a community case worker or a member of Alcoholics Anonymous subsequent to treatment.

Recognition of alcoholism as a disease is achieved by the diagnosis of the physician referring the patient to the Demonstration or by the diagnosis of the medical members of the Demonstration committee. During the course of his hospital stay, the alcoholic patient will be given a complete physical examination, and a medical history will be taken to discover any other disease or pathologic condition which has been overlooked in the past. This will be followed by a psychiatric examination of the patient and consultation with the close kin of the patient. When the results of these examinations are collated by the Demonstration committee, the committee's coordinator will alert the Information Center of the National Council of Alcoholism and Alcoholics Anonymous, and a worker will be assigned to the patient for close cooperation after discharge from the Demonstration.

In addition to the medical-psychiatric benefits and the contact with the patient for months, and perhaps years subsequent to hospitalization, two additional factors will be demonstrated: the feasibility of such a program medically and financially for even the smallest institution, and the great value inherent in such a program for the community, if it will cooperate with the hospitals.

Blue Cross has agreed that persons insured under its plans will receive hospital benefits for a twenty-one-day period of hospitalization provided there is a diagnosis of alcoholism.

American College of Physicians postgraduate courses

The American College of Physicians has announced a schedule of four postgraduate courses to be presented throughout the country.

The courses are as follows: "Current Concepts of the Physiology of the Endocrines, Electrolytes, and the Kidney," Philadelphia, April 5 through 7, The Bellevue Stratford Hotel; "Fundamental and Applied Aspects of Cardiology," Detroit, May 14 through 16, Wayne State University College of Medicine; "The Neurology of Diseases of Internal Medicine," Boston, May 21 through 25, Harvard Medical School; and "Psychiatry for the Internist," Baltimore, the Psychiatric Institute, University of Maryland School of Medicine.

For further information write to: The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pennsylvania.

Health Information Foundation moves

In order to enhance and broaden its program, the Health Information Foundation will move to the University of Chicago. The twelve-year-old Foundation, known for its research and education projects in the social and economic aspects of medical care, will move officially to the University campus on about April 30. It has been located in New York City since 1950 when it was organized as a nonprofit corporation by leaders in the drug industry. The Foundation is supported by annual contributions from manufacturers, wholesalers, and retailers in the drug industry. It has conducted many studies and sponsored others through grants to universities and research agencies.

Course on arthritis

The University of Buffalo School of Medicine will present a postgraduate course on arthritis on April 4 and 5. Recent advances in the therapy of arthritis, including evaluation of the newer drugs and the use of physical therapeutic and rehabilitation technics will be emphasized.

For information contact: Mary A. Lorenz, Department of Postgraduate Education, University of Buffalo School of Medicine, 3435 Main Street, Buffalo 14, New York.

Health planning experts meet

Experts from Brazil, Chile, Colombia, Mexico, Venezuela, and the United States, including observers from the Pan American Union, the Inter American Development Bank, the U.S. Agency for International Development and the U.S. Public Health Service met at the Pan American Health Organization's headquarters recently to discuss health planning.

The Charter of Punta del Este calls for each Latin American Government to prepare a national health plan covering the next ten years. The Pan American Health Organization advisory group's job is to work out guidelines as to how this can best be accomplished and to list the measures that should be taken by the various governments.

Scheduled to attend the meeting was Herman E. Hilleboe, M.D., Commissioner, New York State Department of Health.

Courses for chest physicians

The Council on Postgraduate Medical Education of the American College of Chest Physicians has planned five postgraduate courses to be held in New York, Philadelphia, Chicago, and Detroit during 1962.

The courses are as follows: "Cardiopulmonary Problems in Children," Chicago, July 23 through 27, Edgewater Beach Hotel; "Recent Advances in the Diagnosis and Treatment of Diseases of the Heart and Lungs, "Philadelphia, September 17 through 21, Warwick Hotel; "Clinical Cardiopulmonary Physiology," Chicago, October 22 through 26, Knickerbocker Hotel; "Recent Advances in the Diagnosis and Treatment of Diseases of the Heart and Lungs," New York, November 12 through 16, Barbizon-Plaza Hotel; "Occupational Diseases of the Heart and Lungs," Detroit, December 3 through 7, Statler-Hilton Hotel.

For information write to: Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Enlarged quarters for pediatricians

The American Academy of Pediatrics has opened a new wing which adds 80 per cent more space to the international headquarters office located in Evanston, Illinois. The central office of the society serves pediatricians in North and South America.

Jobs for handicapped

Placement in jobs of workers with physical and emotional disabilities by the New York State Employment Service exceeded 40,000 in 1961 according to Alfred L. Green, executive director of the State Labor Department's Division of Employment.

Activities of the Selective Placement Program, a special service to promote the employment of handicapped workers, resulted in 40,382 job placements throughout the State, as compared to 38,865 in 1960. This increase was achieved despite a decrease in the number of new applicants in 1961, a total of 28,114 as against 33,332 during the preceding year.

Section on Ophthalmology, Nassau Academy of Medicine

The regular meeting of the Section on Ophthalmology, Nassau Academy of Medicine, was held at the Academy on January 22. Robert S. Coles, M.D., New York City, presented a paper on "The Uveitis Problem." A question and answer period followed.

The next meeting of the Section will be held on May 28. Gilbert Baum, M.D., Port Chester, will be the guest speaker.

For information contact: Arthur E. Merz, M.D., F.A.C.S., Secretary-Treasurer, Section on Ophthalmology, Nassau Academy of Medicine, 520 Franklin Avenue, Garden City, New York.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that the next oral and clinical examinations (part 2) for all scheduled candidates will be held at the Edgewater Beach Hotel, Chicago, April 9 through 14.

New and reopened applications and requests for re-examination in 1963 will be accepted in the office of the executive secretary until July 1, 1962. A duplicate list of hospital dismissals for the preceding twelve months should be submitted prior to July 1.

For information write to: Robert L. Faulkner, M.D., Executive Secretary, American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Recreation facilities for older people

The continuing growth of recreation facilities to meet the needs of senior citizens is pointed up in the *Directory of Recreation Facilities for Older People* just published by the Community Council of Greater New York, the planning and coordinating organization for the City's health and welfare agencies.

Compiled as a guide to individuals and agencies looking for a suitable club for an older person, the *Directory* lists the centers and clubs found in each borough alphabetically. In addition, a special index locates the clubs by postal zones to aid in identification of those nearest the aged person's home. Still another index identifies the centers by their sponsoring organization or organizations.

For information on how to obtain a copy of the *Directory* write to: Publications Department, Community Council of Greater New York, 345 East 45th Street, New York 17, New York.

Judges named for Empire State Award

The panel of judges for the third annual Empire State Award for Excellence in Medical Reporting has been announced by Herman E. Hilleboe, M.D., Commissioner, New York State Department of Health, and John M. Galbraith, M.D., president of the Medical Society of the State of New York.

The judges are as follows: Mr. Daniel E. Button, executive editor, *Albany Times-Union*, representing the New York State Society of Newspaper Editors; Henry I. Fineberg, M.D., executive vice-president, Medical Society of the State of New York, representing the State Medical Society; Professor Hillier Krieghbaum, chairman, Department of Journalism, New York University, representing the National Association of Science Writers (Professor Krieghbaum is chairman of the awards jury); Granville W. Larimore, M.D., Deputy Commissioner, New York State Department of Health, representing the State Health Department; and James J. Quinlivan, M.D., assistant secretary, Annual Health Conference, representing Annual Health Conference Inc.

Secretary to the judging committee is Mr. Harvey I. Cobert of the State Health Department's Publications Section.

The $500 annual award is sponsored by the Medical Society of the State of New York and Annual Health Conference Inc., on behalf of the New York State Department of Health. The award was established to encourage the further development of sound medical reporting in New York State. Any member of the editorial staff of any newspaper published five or more times a week in New York State may be nominated to receive the award.

Personalities

Appointed. Vincent J. Fontana, M.D., New York City, as medical director of the New York Foundling Hospital and director of pediatrics at St. Vincent's Hospital, New York City . . . George A. Jervis, M.D., Thiells, as director of the New York State Research Institute in Mental Retardation to be located on Staten

Island . . . Sidney M. Samis, M.D., Great Neck, as director of nursing homes and home care service in the Department of Hospitals, New York City.

Elected. James H. Barnard, M.D., New York City, re-elected as treasurer of the American Academy of Allergy . . . Bernard Brill, M.D., Brooklyn, as president of the medical board of the Samaritan Hospital of Brooklyn . . . Murray Dworetzky, M.D., New York City, to the executive committee of the American Academy of Allergy.

Speakers. Irving Baras, M.D., New York City, at the March meeting of the Eastern New York Eye, Ear, Nose and Throat Association on the topic "Clinical Application of the Perilimbal Suction Cup" . . . Harold Whaley Brown, M.D., New York City, on February 26 before the Long Island Ophthalmological Society on the topic "Diagnostic Aids in Strabismus" . . . Arthur J. Cracovaner, M.D., New York City, at the March meeting of the Eastern New York Eye, Ear, Nose and Throat Association on the topic "Management of Carcinoma of the Larynx" . . . Howard Davidman, M.D., New York City, before the American Psychopathological Association on February 24 . . . George Friedman, M.D., before the members of the staff of the Veterans Administration Hospital, Northport, Long Island, on the subject "Psychiatry and the Law" . . . Abram Kanof, M.D., Brooklyn, on April 2 at the seventieth anniversary convention of the American Jewish Historical Society in Philadelphia . . . Joost A. M. Meerloo, M.D., New York City, at the New School for Social Research on the topic "Psychology of the Administrative Mind" on March 7 . . . Howard A. Rusk, M.D., New York City, at the Waldorf-Astoria Hotel on March 29 at a dinner in support of the goodwill hospital ship *Hope* . . . Jerome M. Schneck, M.D., New York City, before the Institute for Research in Hypnosis, February 7, on the topic "Hypnotherapy and Hypnoanalysis" . . . Marie Pichel Warner, M.D., New York City, on February 15 before the residents of the Department of Obstetrics and Gynecology at Beth Israel Hospital, New York City, on the subject "Contraceptive Methods, Technics, and Indications."

Medical Meetings

Symposium on oral and systemic disease

The New Jersey State Department of Health in cooperation with the New Jersey State Dental Society will present a symposium on "The Interrelationship of Oral and Systemic Disease" at Voorhees Hall, Rutgers University, New Brunswick, New Jersey, on Wednesday, April 11, from 1:00 to 5:00 P.M.

Topics for discussion will be: "Growth and Development and Its Relation to the Dentist"; "Oral Manifestations of Endocrinopathy"; "Congenital and Metabolic Disorders and Pediatric Dentistry"; and "Oral Manifestations of Endocrine-Metabolic Problems and Disorders of Growth and Development" (a panel discussion).

For information contact: Arthur Krosnick, M.D., Coordinator, Diabetes Control Program, Division of Chronic Illness Control, State of New Jersey Department of Health, Trenton 25, New Jersey.

Catholic Hospital Association

The Catholic Hospital Association will hold a three-day institute on "Psychiatry in Hospitals" April 12 through 14 at the Conrad Hilton Hotel, Chicago, Illinois.

Paul H. Hoch, M.D., Commissioner, New York State Department of Mental Hygiene, and Harvey J. Tompkins, M.D., director, Mental Health Department, St. Vincent's Hospital, New York City, will speak at the meeting.

American Congress of Physical Medicine and Rehabilitation

The American Congress of Physical Medicine and Rehabilitation will hold the annual meeting of its eastern section on Saturday, April 14, from 9:00 A.M. to 9:00 P.M. at the State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

Professional Group on Bio-Medical Electronics

The Professional Group on Bio-Medical Electronics will hold a meeting on April 24 at 8:00 P.M. at the Rockefeller Institute, Welch Hall, 67th Street and York Avenue, New York

City. Edward H. Bloch, M.D., Ph.D., Department of Anatomy, Western Reserve University, Cleveland, Ohio, will be the guest speaker. Dr. Bloch's topic will be "Instrumentation for the Microscopic Study of Dynamic Events in the Organs of Living Animals."

A pre-meeting dinner will be held at the Sutton Restaurant, 1063 First Avenue, New York City, at 6:15 P.M.

Emanuel B. Schoenbach Memorial Lecture

The board of trustees and the medical staff of Maimonides Hospital of Brooklyn will present the tenth annual Emanuel B. Schoenbach Memorial Lecture to be delivered by W. Barry Wood, Jr., M.D., professor of microbiology, Johns Hopkins University School of Medicine, on Wednesday, April 25, at 4:00 P.M. in the solarium. Dr. Wood's topic will be "The Pathogenesis of Fever."

For information contact: Maimonides Hospital of Brooklyn, 4802 Tenth Avenue, Brooklyn 19, New York. Telephone ULster 3–1200.

International Conference on Medical Motion Pictures and TV

The International Television Committee (CIT) in cooperation with the Mercato Internationale TV-Film and Documentario (MIFED) will present a conference on "The Present Status and Future Prospects of Television and Motion Pictures as Media for Medical Education" as part of the second international meeting of the CIT in Milan, Italy, April 25 through 27.

For further information contact: Leo L. Leveridge, M.D., Coordinator, Medical Television Unit, New York University Medical Center, 550 First Avenue, New York 16, New York.

Israel Strauss Lecture

Milton Greenblatt, M.D., assistant superintendent and director of Research and Laboratories, Massachusetts Mental Health Center, will give the annual Israel Strauss Lecture at Hillside Hospital, Glen Oaks, on Sunday, April 29, at 10:30 A.M. Dr. Greenblatt will discuss the problems involved in the integration of hospital and community care, with emphasis on posthospitalization planning for the psychiatric patient in an address entitled "Beyond the Therapeutic Community."

The Academy of Psychoanalysis

The Academy of Psychoanalysis will hold its annual meeting at the Park Plaza Hotel, Toronto, Canada, on May 5 and 6.

Among those scheduled to participate in the program are the following physicians from the New York area: *Glen Oaks:* Max Fink, M.D.; *New York City:* Richard G. Abell, M.D., Walter Bonime, M.D., Charles C. Dahlberg, M.D., Howard Davidman, M.D., Marvin G. Drellich, M.D., Paul H. Hoch, M.D., Joseph Jaffe, M.D., Claude H. Miller, M.D., John A. P. Millert, M.D., Simon H. Nagler, M.D., Henry B. Richardson, M.D., Janet MacK. Rioch, M.D., Nathan Roth, M.D., Jack L. Rubins, M.D., Herbert Spiegel, M.D., Rose Spiegel, M.D., James M. Toolan, M.D., and Frederick A. Weiss, M.D.; *North Caldwell, New Jersey:* Irving Markowitz, M.D.

For further information write to: Joseph H. Merin, M.D., Secretary, The Academy of Psychoanalysis, 125 East 65th Street, New York 21, New York.

Medical Society of New Jersey

The Medical Society of New Jersey will hold its one hundred ninety-sixth annual meeting May 12 through 16 at Haddon Hall, Atlantic City, New Jersey. New York State physicians are invited to attend the scientific sessions of the meeting. There is no registration fee for out-of-state nonmember physicians.

Canadian Academy of Allergy

The Canadian Academy of Allergy will hold its annual meeting June 8 through 10 at the Thousand Islands Club, Alexandria Bay, New York.

For information write to: H. L. Bacal, M.D., Secretary-Treasurer, Canadian Academy of Allergy, 4640 Stanley Weir Street, Montreal 29, Quebec, Canada. There will be no registration fee.

New York State Nutrition Institute at Cornell

Current developments and research in nutrition will be discussed at the New York State Nutrition Institute at Cornell, July 12 and 13, at the Alice Statler Auditorium, Cornell University, Ithaca, New York.

The two-day institute is sponsored by the Graduate School of Nutrition in cooperation with the New York State Colleges of Home Economics and Agriculture, Cornell University, and the New York State Nutrition Council.

Grace A. Goldsmith, M.D., Tulane University, New Orleans, will discuss the development and use of recommended dietary allowances; Dr. Bernice Watt, United States Department of Agriculture, will speak on the development of tables of nutritive value of foods; and John Browe, M.D., director of the Bureau of Nutrition of the New York State Department of Health, will discuss fallout shelter rations.

For information contact: Dr. Catherine Personius, New York State College of Home Economics, Cornell University, Ithaca, New York.

Books Received

The following books were received during the month of January, 1962

The Spine. A Radiological Text and Atlas. By Bernard S. Epstein, M.D. Second edition. Quarto of 616 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $16.50.

Measurements of Exocrine and Endocrine Functions of the Pancreas. Edited by F. William Sunderman, M.D., and F. William Sunderman, Jr., M.D. Quarto of 203 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $11.

Medical Genetics 1958–1960. By Victor A. McKusick, M.D., and contributors. Quarto of 534 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $14.50.

Electrodiagnosis and Electromyography. Edited by Sidney Licht, M.D. Second edition. Octavo of 470 pages, illustrated. New Haven, Elizabeth Licht, Publisher, 1961. Cloth, $12.

Logan Turner's Diseases of the Nose, Throat, and Ear. Edited by John P. Stewart, assisted by R. B. Lumsden. Sixth edition. Octavo of 524 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1961. Cloth, $11.

Symptoms and Signs in Clinical Medicine. By E. Noble Chamberlain, M.D. Seventh edition. Octavo of 569 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1961. Cloth, $9.00.

Ophthalmic Pathology. An Atlas and Textbook. Edited by Michael J. Hogan, M.D., and Lorenz E. Zimmerman, M.D. Second edition. Quarto of 797 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $30.

Carcinoma of the Cervix. By John B. Graham, M.D., Luciano S. J. Sotto, M.D., and Frank P. Paloucek, M.D. Octavo of 487 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $14.

Diagnosis and Therapy of the Glaucomas. By Bernard Becker, M.D., and Robert N. Shaffer, M.D. Octavo of 360 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $18.

Postpartum Psychiatric Problems. By James Alexander Hamilton, M.D. Octavo of 156 pages. St. Louis, The C. V. Mosby Company, 1962. Cloth, $6.85.

Hypertension, Recent Advances. The Second Hahnemann Symposium on Hypertensive Disease. Edited by Albert N. Brest, M.D., and John H. Moyer, M.D. Octavo of 660 pages, illustrated. Philadelphia, Lea & Febiger, 1961. Cloth.

The Medical Clinics of North America. Chicago Number. January, 1962. Spleen and Blood. Louis Limarzi, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1962. Published bi-monthly (six numbers a year). Cloth, $18 net; paper, $15 net.

Clinical Obstetrics and Gynecology, Volume 4 Number 4. December, 1961. Shock and Shocklike States. Edited by Keith P. Russell, M.D. **Exfoliative Cytology.** Edited by A. E. Rakoff, M.D. Octavo. New York, Paul B. Hoeber, Inc., 1961. Published quarterly (four numbers a year). Cloth, $18 per year.

Irritation and Counterirritation. A Hypothesis about the Autoamputative Property of the Nervous System. By Adolphe D. Jonas, M.D. Octavo of 368 pages. New York, Vantage Press, 1962. Cloth, $7.50.

Ariel. Essays on the Arts and the History and Philosophy of Medicine. By Felix Marti-Ibañez, M.D. Octavo of 292 pages, illustrated. New York, M.D. Publications, Inc., 1962. Cloth, $6.50.

Thalassemia. A Survey of Some Aspects. By Robin M. Bannerman, D.M. Octavo of 138 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $6.50. (Modern Medical Monographs, 23)

The Dynasty. By Charles H. Knickerbocker. Octavo of 416 pages. Garden City, N.Y., Doubleday & Company, Inc., 1962. Cloth, $4.50.

Common Sense about Psychoanalysis. By Rudolph Wittenberg. Octavo of 216 pages. Garden City, N.Y., Doubleday & Company, Inc., 1962. Cloth, $3.95.

Diet Manual. Compiled by the Dietary Staff of Vanderbilt University Hospital. Octavo of 157 pages. Nashville, Vanderbilt University Press, 1961. Paper, $4.00.

Annotated Bibliography of Vitamin E 1958–1960. Volume V. Compiled by David C. Herting, Wilma F. Kujawski, Marion I. Ludwig, and Philip L. Harris. Quarto of 180 pages. Rochester, N.Y., Distillation Products Industries, 1961. Paper, $3.00.

Drugs in Current Use 1962. Edited by Walter Modell, M.D. Octavo of 152 pages. New York, Springer Publishing Company, Inc., 1962. Paper, $2.25.

Women and Fatigue. By Marion Hilliard, M.D. Sextodecimo of 148 pages. New York, Pocket Books, Inc., 1962. Paper, $0.50.

The Best in Sight. By Ward L. Mould, M.D. Octavo of 52 pages, illustrated. Garden City, N.Y., the author, 1960. Paper, $0.25.

What You Ought To Know About Crossed Eyes. By Ward L. Mould, M.D. Octavo of 40 pages. Garden City, N.Y., the author, 1961. Paper, $0.25.

What You Ought To Know If You Have Glaucoma. By Ward L. Mould, M.D. Octavo of 35 pages, illustrated. Garden City, N.Y., the author, 1959. Paper, $0.25.

Books Reviewed

Developmental Genetics and Lethal Factors. By Ernst Hadorn. Translated by Ursula Mittwoch. Octavo of 355 pages, illustrated. London, Methuen & Co., Ltd. (New York, John Wiley & Sons, Inc.), 1961. Cloth, $8.50.

This is a translation into English of a volume first published in German in 1955. Ursula Mittwoch, of University College, London, has performed a great service by making this very readable English version of an invaluable book available to scientists.

This 355-page well-illustrated volume is a systematic review of all aspects of the hereditary transmission and actions of lethal genes in man as well as animals which closes with a useful glossary of terms, a comprehensive alphabetical listing of the scientific literature, a helpful author index, and a detailed subject index. It is difficult to do justice in a brief review to such a fine book which is destined to survive for a long time as a classic text and reference source on this subject.

Some idea of its scope can be gleaned from a listing of the chapter headings: systematic survey, concepts and terms, methods of demonstrating lethal factors, permanent culture of lethal factors; balanced systems; origin by mutation; chromosomal bases; dominant lethal factors; polygenic lethality; maternal influence and cytoplasmic effects; degrees of penetrance and expressivity; dominance and recessivity of action; phase specificity; cell specific and organ specific action; and so forth.

This excellent book is a bargain that no one interested in genetics can afford to let pass by. —A. S. Wiener, M.D.

Clinical Disturbances of Renal Function. By Abraham G. White, M.D. Octavo of 468 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $10.50.

The many functions of the kidney occurring simultaneously are indeed complex, as evidenced by the enormity of the literature that has elucidated the modern theories of renal physiology. To those untrained in the field this material is complex and difficult to understand. Being both a renal physiologist and a clinician, Dr. White has been able to present these current concepts and their practical application to the clinician in a readable and direct manner. The chapters of the text explain the mechanics of renal dysfunction, as well as specific disturbances caused by the nephritides and the difficulties involved when hypertension, cardiac dysfunction, liver dysfunction, and electrolyte imbalance or genetically induced disorders affect the kidney. Also there is an excellent chapter on the therapeutic use of fluids and electrolytes.

Throughout the text there are many excellent illustrations and diagrams. The tone of the text is informal, readable, and not stilted, and there are many explanatory similes. In my opinion this text will achieve a lasting place in the literature of the subject.—Sidney R. Weinberg, M.D.

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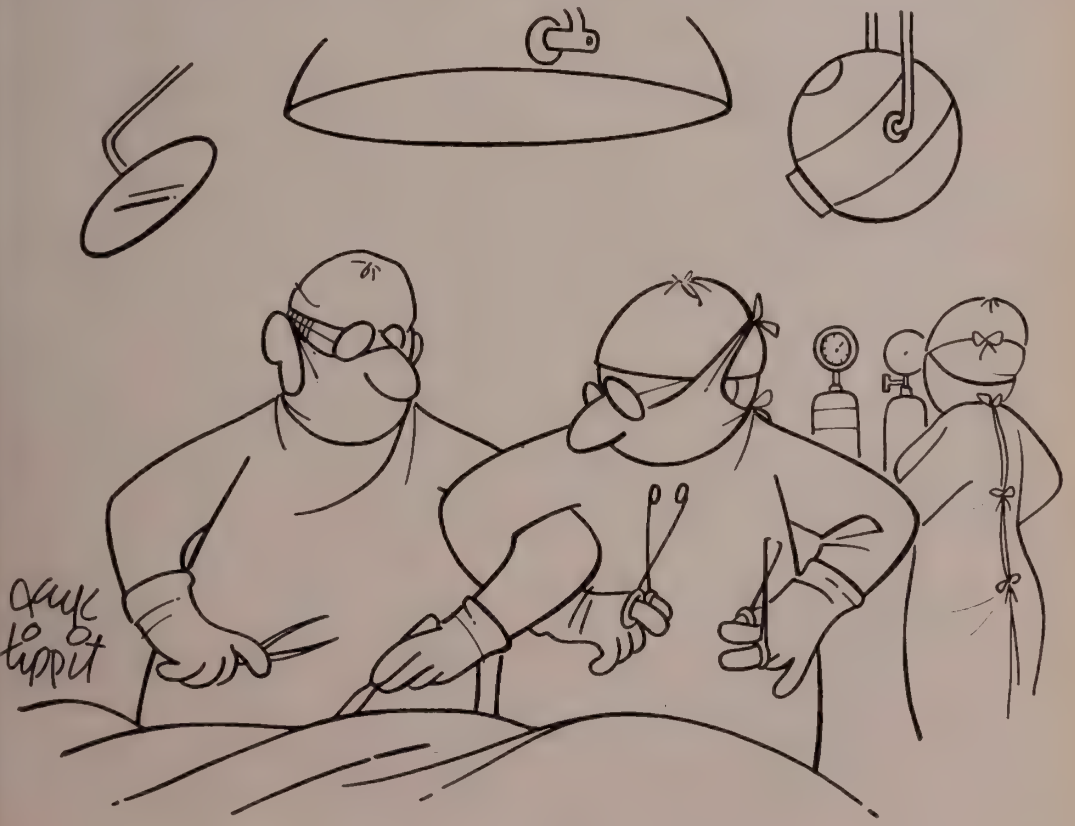

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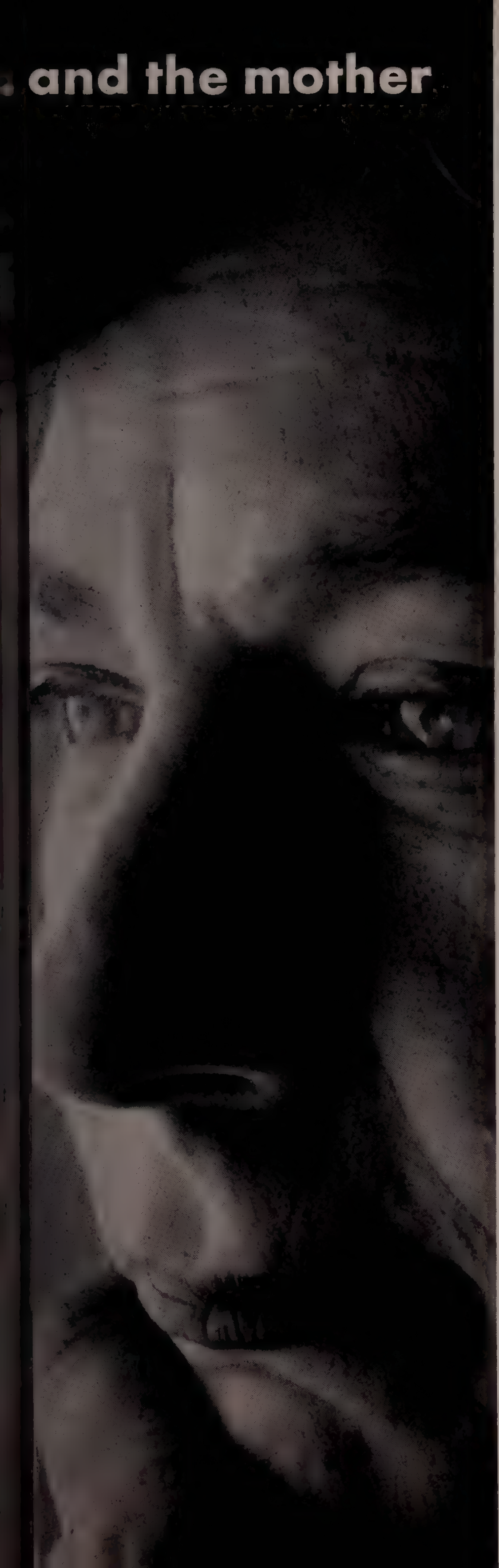

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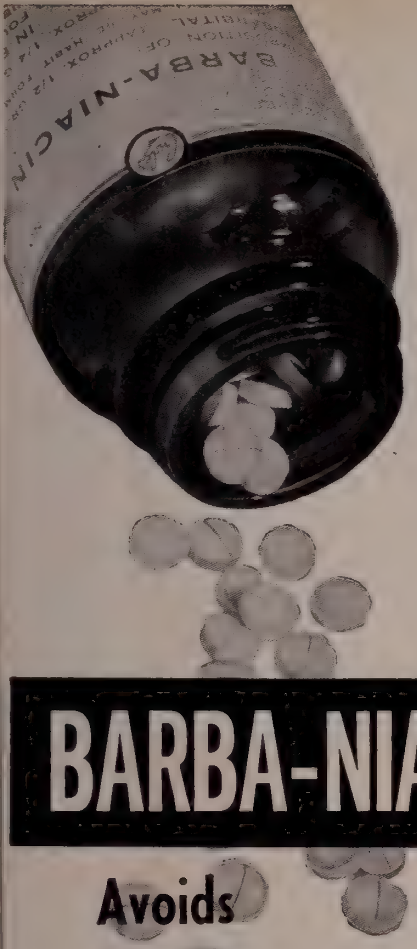

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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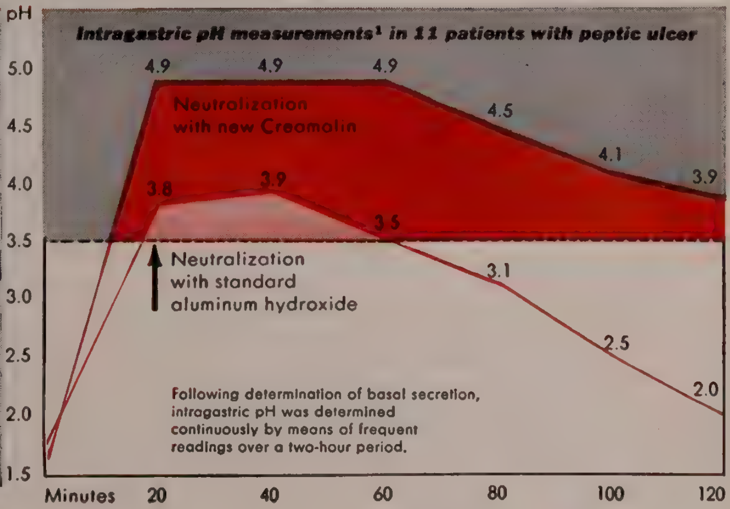
pH
Intragastric pH measurements¹ in 11 patients with peptic ulcer
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
4.9
4.9
4.9
4.5
4.1
3.9
Neutralization with new Creamalin
3.8
3.9
3.5
3.1
2.5
2.0
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Minutes
20
40
60
80
100
120

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References: **1.** Schwartz, I. R.: *Current Therap. Res.* 3:29, Feb., 1961. **2.** Beekman, S. M.: *J. Am. Pharm. A.* (Scient. Ed.) 49:191, April, 1960. **3.** Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A.* (Scient. Ed.) 48:381, July, 1959. **4.** Data in the files of the Department of Medical Research, Winthrop Laboratories. **5.** Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A.* (Scient. Ed.) 48:384, July, 1959.

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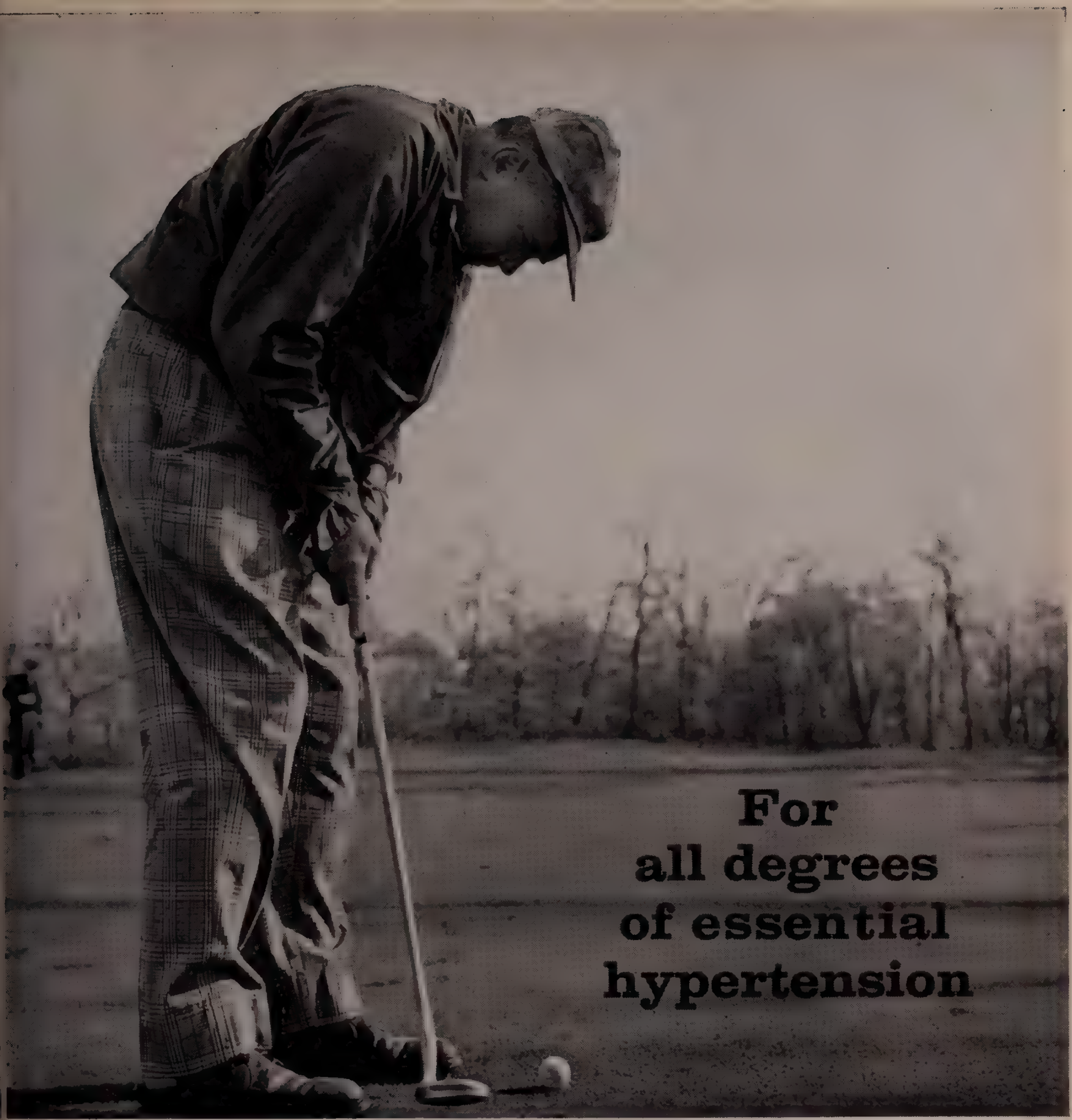

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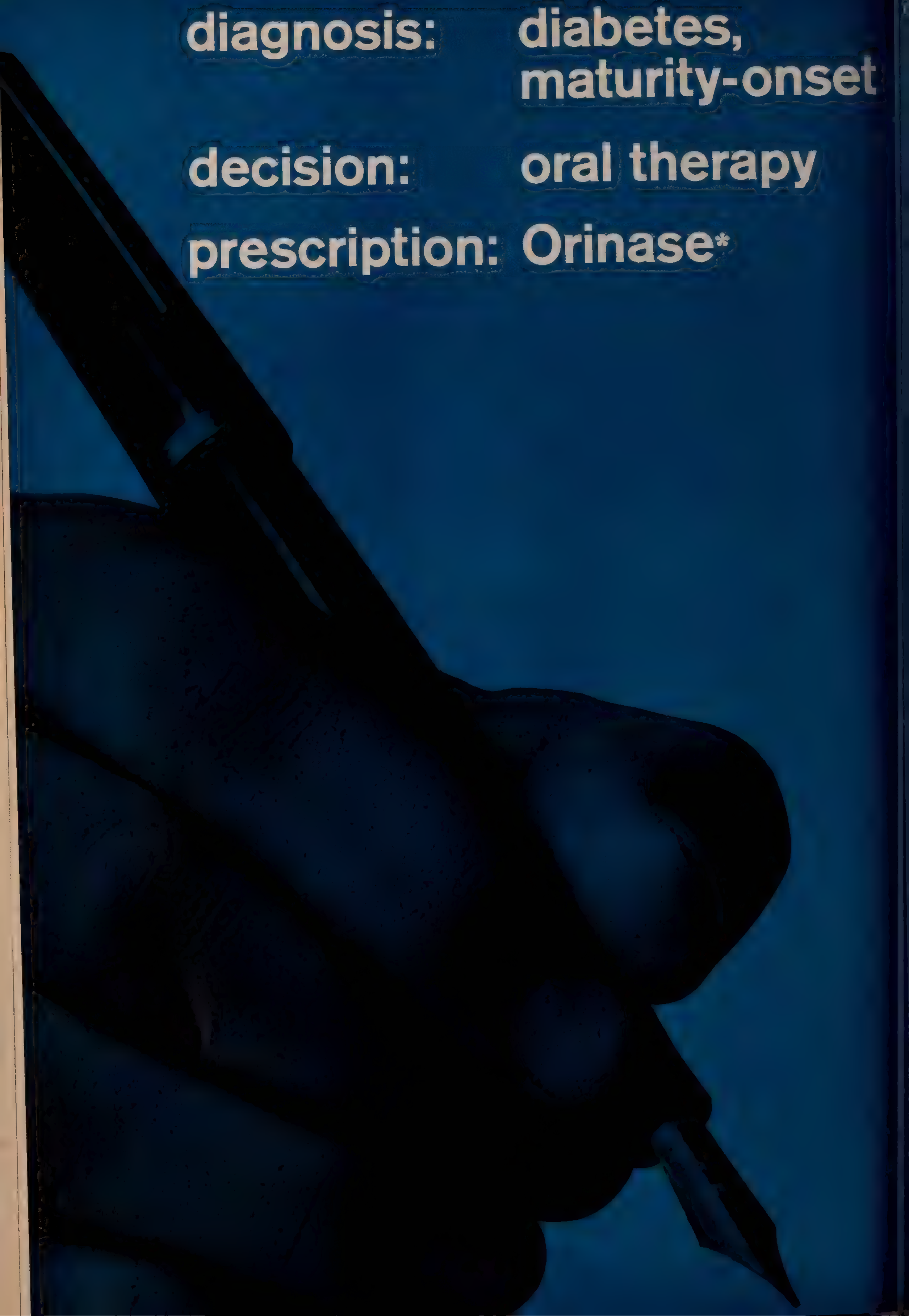
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	2:30–3:30	Public Relations Session
	3:30–5:00	University of Buffalo School of Medicine
WEDNESDAY, MAY 16		
	1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
	2:30–3:30	Deans' Panel
	3:30–5:00	Cornell University Medical College
THURSDAY, MAY 17		
	1:00–2:30	State University of New York, Downstate Medical Center
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	3:30–5:00	New York University School of Medicine
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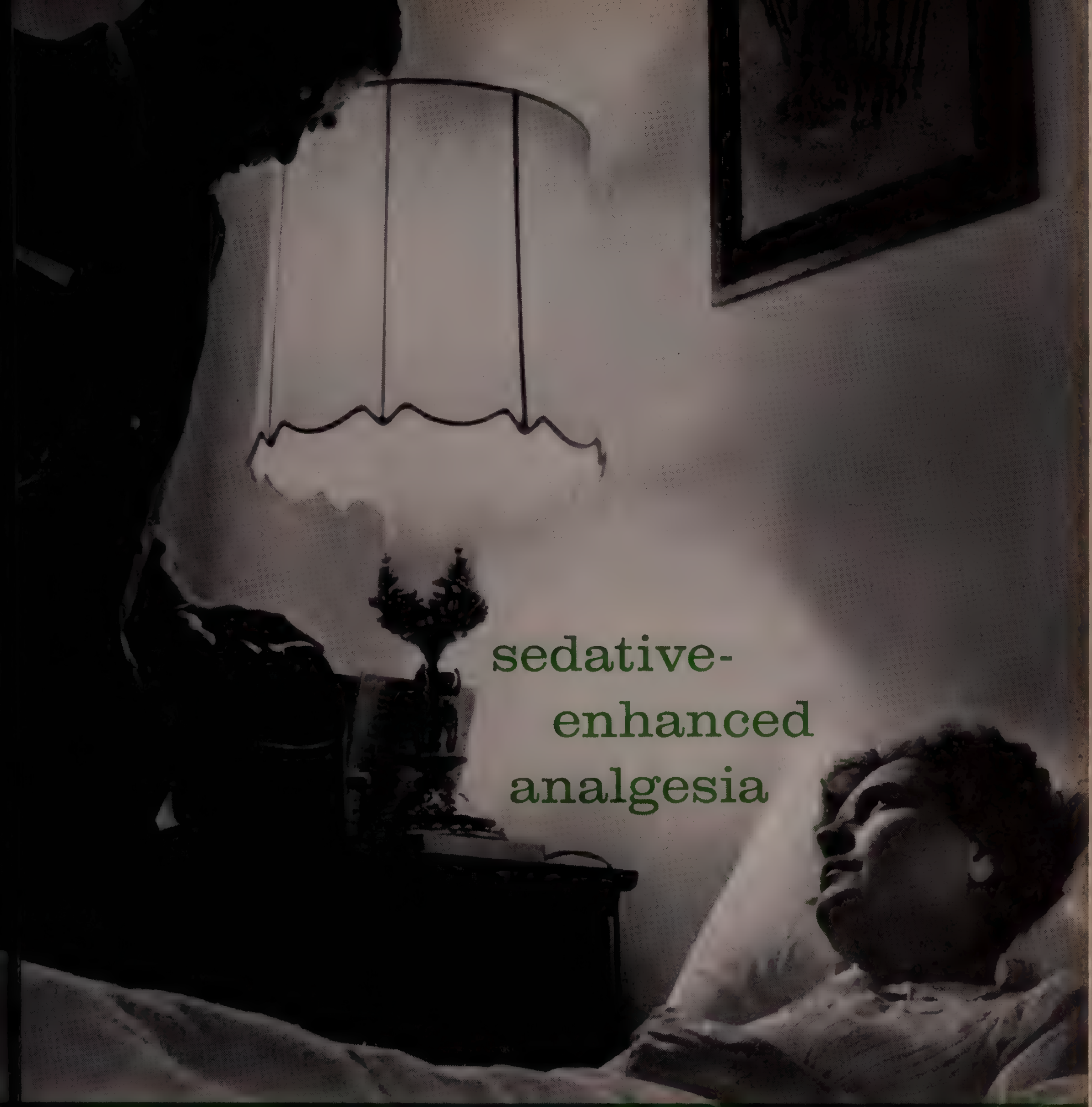

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1. Meyers, G. B.: Ind. Med. & Surg. 26:3, 1957. 2. Murray, R. J.: N. Y. St. J. Med. 53:1867, 1953.

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[1] Berger, R.A., Clinical Medicine, Sept. 1961.

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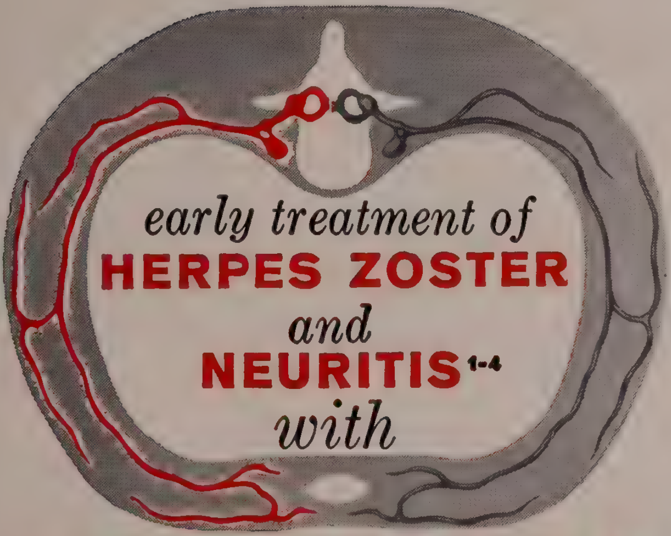

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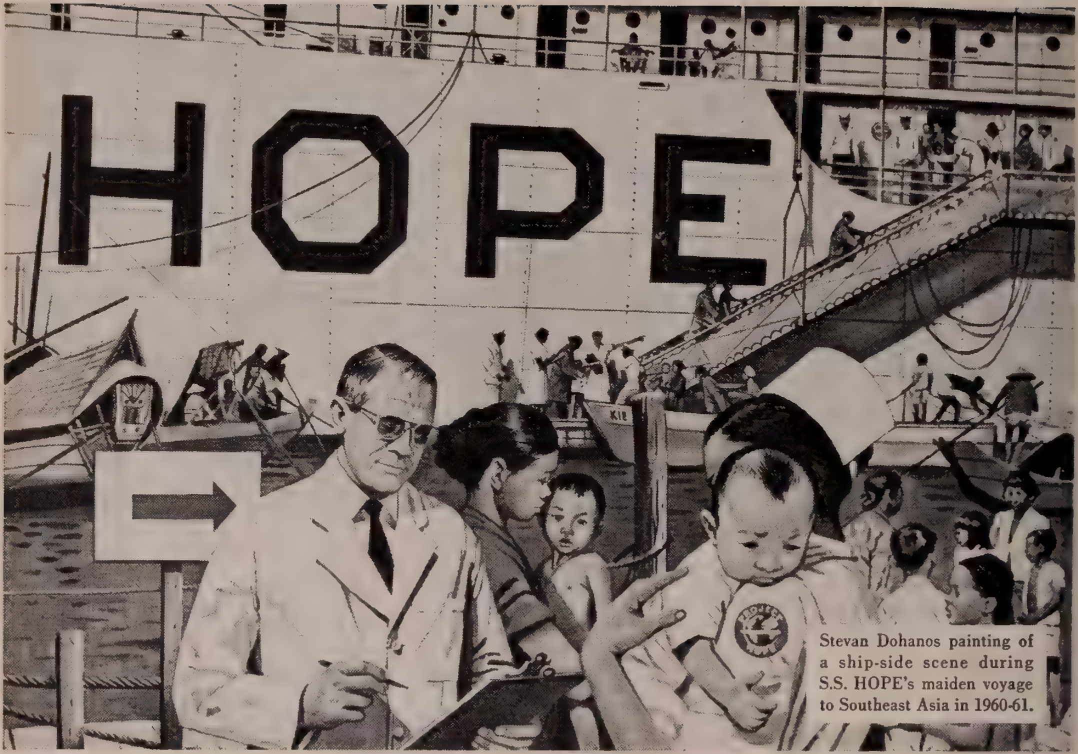

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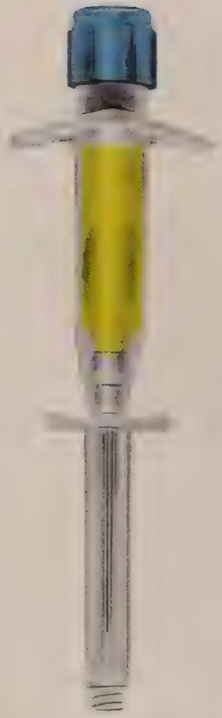

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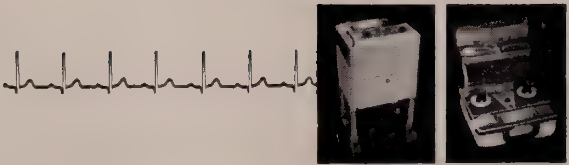

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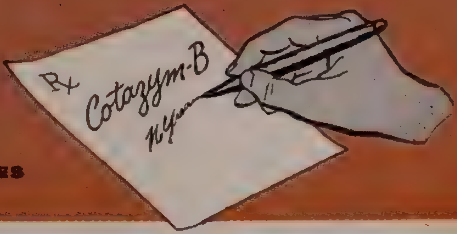

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*Schaefer, L. E.: Clin. Med. 8:1343, 1961.

S-963

SECTION ON SPACE MEDICINE at the 1962 Annual Convention, MSSNY

Friday, May 18, 9:00 A.M.
Georgian Room, Statler Hilton, New York City

* * *

SPACE MEDICINE SPECTRA: ANNO V OF SPACE EXPLORATION

1. *Chairman's address:* **The Dynamics of Space Medicine**

   Constantine D. J. Generales, M.D., New York
   Assistant Professor of Space Medicine and Co-ordinator of Space Medicine Program, New York Medical College

2. **The United States Government's Role in Current Space Exploration**

   Hon. Victor L. Anfuso, Brooklyn (By invitation)
   House of Representatives, Committee on Science and Astronautics

3. **Unusual Earthly Forms of Life and Extraterrestrial Implications**

   John Pallister, New York (By invitation)
   President Explorers Club; Research Associate, Department of Entomology, New York Museum of Natural History

4. **The Significance of the Magnetosphere to Man**

   Alastair G. W. Cameron, Ph.D., New York (By invitation
   Institute for Space Studies, National Aeronautics and Space Administration

5. **Biomedical Engineering as a Physician's Aid**

   Lee B. Lusted, M.D., Rochester
   Associate Professor of Radiology and Biomedical Engineering, The University of Rochester School of Medicine and Dentistry

6. **Life Like Forms in Carbonaceous Meteorites**

   Bartholomew Nagy, Ph.D., Bronx (By invitation)
   Associate Professor of Chemistry, Fordham University

7. **Electromagnetism and Its Effect on the Organism**

   John H. Heller, Ph.D., Ridgefield, Conn. (By invitation)
   Director, New England Institute of Medical Research

8. **Geomagnetic Environment and its Relationship to Human Biology**

   Robert O. Becker, M.D., Syracuse
   Chief of Orthopedic Section, Veterans Administration Hospital

9. **Selected Topics on Space Medicine in the USSR**

   V. J. Yazdovsky, Moscow, USSR (By invitation)
   Professor, Academy of Sciences of the USSR

10. **The Saturn Program**

    Oswald Lange, Ph.D., Huntsville, Alabama (By invitation)
    Director, Saturn Systems Office, George C. Marshall Space Flight Center

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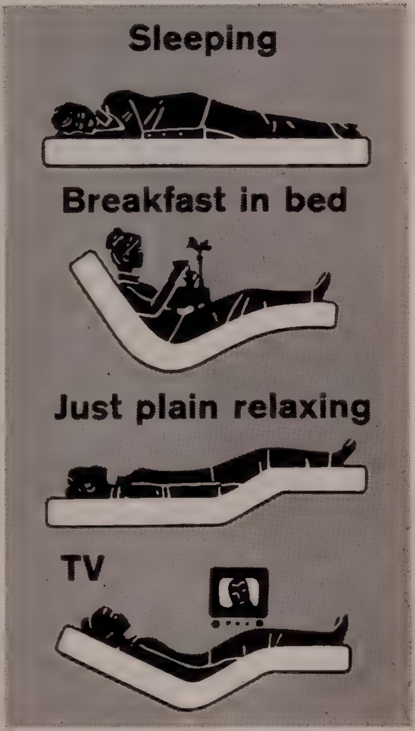

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April 15, 1962 Volume 62 Number 8

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General Information

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Editorials

The tide in the affairs of men

We are privileged to report in this issue a short review of some original research which was presented recently at the second annual Bionics Symposium at Cornell University by Robert O. Becker, M.D., Assistant Professor of Orthopedics, Howard Friedman, Ph.D., Clinical Assistant Professor of Psychology, both of the State University of New York Upstate Medical Center, and Charles H. Bachman, Ph.D., Professor of Physics, Syracuse University.

This preliminary research indicates that an electrical charge in human beings may affect their mental health and general wellbeing.

Behavior may be influenced more than we realize by environmental factors which we cannot see, hear, or smell—the magnetic fields around us and our electrical interaction with them.

The phenomena of sleep, hypnosis, response to force fields, and cyclic patterns of behavior cannot be explained adequately on the basis of present knowledge of nerve system function. The action potential of the nerve is now considered to be the way in which the nerve works.

This action potential is basically a traveling wave in the nerve fiber membrane and is not the actual transmission of electrical charges along the nerve fiber.

New evidence was presented for the existence of a second type of nerve activity which is more primitive than the action potential system. It has been discovered that all nerve cells are electrically polarized—that is, one end is positive and the other negative—and that there is a constant electrical current flowing within the nerve and its fibers.

This current is thought to be produced by the flow of electrons moving within the molecular structure of the nerve in the same fashion as within transistors or other similar solid-state devices. Changes in the amount of current or the polarization potential change the way in which the nerve fiber functions. For example, dropping the current to zero or reversing the polarization produces a state of inactivity in the nerve fiber.

This system of direct currents flowing within the nervous system has been found to be closely related to sleep, anesthesia, and hypnosis in the human being. Preliminary studies also show a difference between the direct current system of normal human beings and that of mentally ill persons.

Some relationship has been shown in animals between growth and healing processes and the direct current system.

Preliminary research shows that the electrical charge in human beings varies in a twenty-four-hour period and a longer period of about twenty-eight days. The mentally ill person shows the same pattern but with greatly exaggerated variations and in an opposite direction. This cyclic variation is similar to such cycles in nature as that of the mussel, which opens and closes with the tides even when it is not near the shore, and may have applications to the adjustment of astronauts to space travel, where the biologic clock will be affected.

Research shows that the electrical charge of a person's body changes drastically when he is under hypnosis or anesthesia. The Soviet Union is already using this principle for anesthesia in surgery. Any injury or abnormality affects the normal pattern of charges, a phenomenon which may have applications in the treatment of wounds, tumors, cancers, and mental illness, in the regrowth of limbs, in the use of hypnosis in medicine, and in many other areas of life.

Perhaps the most dramatic possibility is that our behavior and moods are influenced in part by the electromagnetism of our environment. Using data available from International Geophysical Year studies, Dr. Becker and his associates have found that the number of patients admitted to hospitals for psychiatric disturbances correlates with the magnetic index of the environment the previous day and with solar flares three days before.

The relation of our microcosm to the macrocosm bodes fair to be further illuminated by the new science of bionics.

Present recommendations regarding poliomyelitis immunization

The modified resolution on poliomyelitis vaccines adopted by the House of Delegates of the American Medical Association at its interim meeting in Denver, November 27 to 29, 1961, establishes the present policy of the Association in regard to immunization against poliomyelitis. It places considerable responsibility on local medical societies to make sound decisions based on factual surveys. The county medical societies and their appropriate committees are alerted to this by reprinting here resolution 2, "Polio Vaccines," from the Proceedings of the A.M.A. House of Delegates, Denver, November 27 to 29, 1961.

> WHEREAS, the trivalent formalin killed polio vaccine (Salk vaccine) has proved effective in preventing paralytic polio; and
>
> WHEREAS, the oral polio vaccine (Sabin type) currently is available for only Type I and Type II, with Type III expected to be licensed in the future; and
>
> WHEREAS, Types I and II oral vaccine can immunize only against Types I and II polio, respectively, and are recommended only for use in epidemic type specific situations; they are not available for widespread use in the absence of an actual or threatened epidemic; and
>
> WHEREAS, until all three types are available in oral form, continued use of the Salk vaccine is urged; and
>
> WHEREAS, when all three types of the oral vaccine are available, the question of how and when to use them must be answered; and
>
> WHEREAS, there is little evidence to indicate that community-wide use of oral vaccine will reach a significant portion of those persons who have refused or failed to take the Salk vaccine; there is considerable question as to whether or not the use of the oral vaccine in a community with a fairly high level of immunization could be expected to further reduce the actual number of paralytic cases or deaths solely because of a switch in the type of vaccine offered; there are many factors involved in the use and ability of the oral vaccine in a community with a low immunization level to produce a higher immunization level; therefore be it
>
> *Resolved*, that medical societies at the local, county, district, or state levels throughout the United States should encourage, stimulate, and participate in surveys to determine the percentage of individuals in each community who have undergone immunizing procedures; and be it further
>
> *Resolved*, that on the basis of the results of the surveys, the local medical society should determine the type of vaccine and the most effective type of program which will be of greatest benefit to the public; and be it further
>
> *Resolved*, until such time as all three types of oral vaccine are available, the Salk vaccine should be the vaccine of choice for routine poliomyelitis immunization, with the choice of program for for administering the vaccine to be determined on a local basis by each county medical society.

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William L. Wheeler, Jr., M.D., *Secretary*

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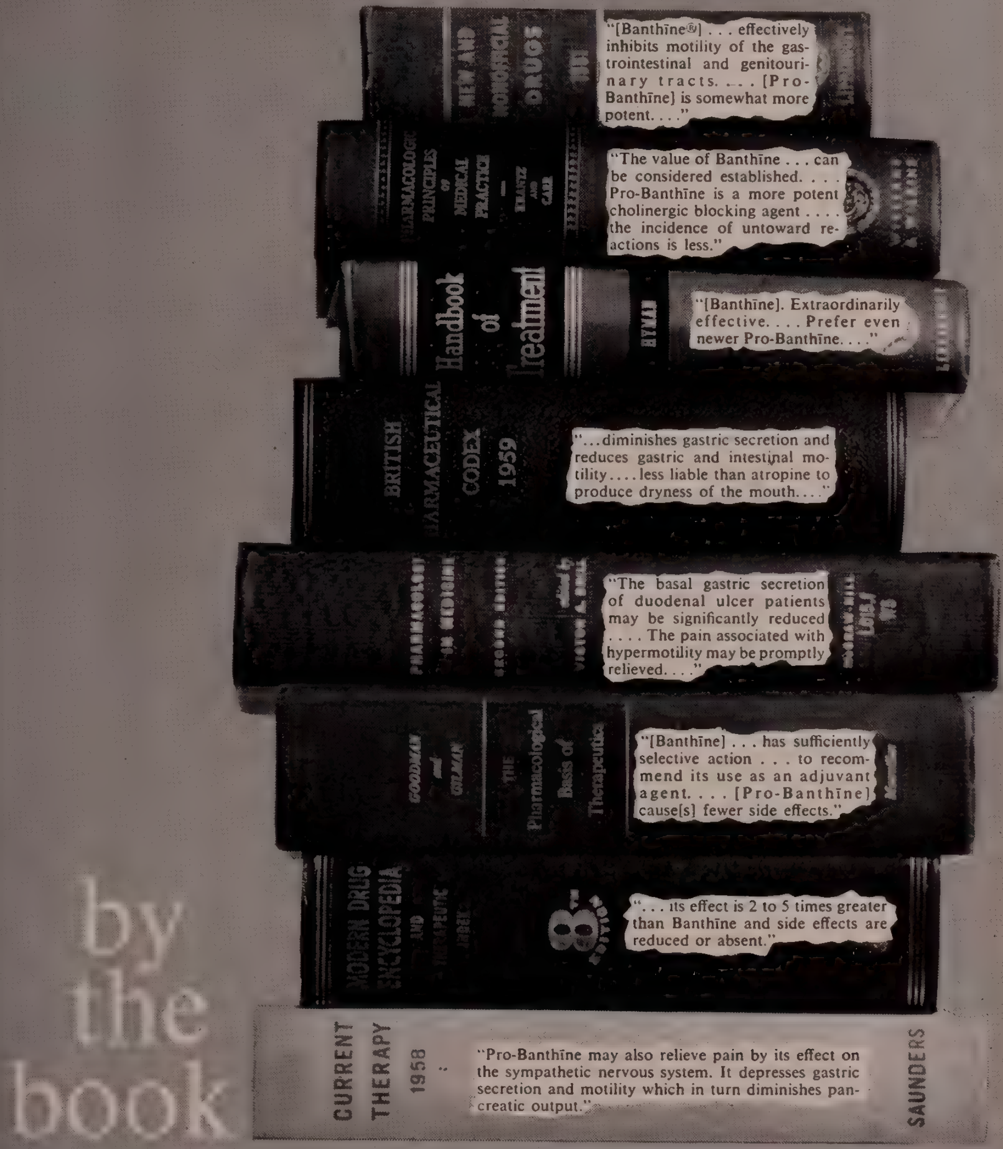
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Scientific Articles

Achilles Tendon Reflex Test (Photomotogram) as a Measure of Thyroid Function

RICHARD L. FOGEL, M.D.
New York City
JEANNE A. EPSTEIN, M.D.
New York City
JACK H. STOPAK, M.D., PH.D.
The Bronx, New York
HERBERT S. KUPPERMAN, M.D., PH.D.
New York City

From the Departments of Medicine and Therapeutics, New York University Medical Center, New York City

THYROID FUNCTION *may be evaluated accurately by the use of the Achilles tendon reflex. The duration is measured by a cell attached to a direct-writing electrocardiograph (photomotogram) and is related to the thyroid state of the patient. The principle involved is that the muscle contraction phase of the reflex occurs promptly regardless of the thyroid state of the individual, while relaxation is retarded in hypothyroidism and accelerated in hyperthyroidism. The test requires no special skills. It is not influenced by the emotional status of the patient, nonthyroid metabolic or pulmonary disease, or medication other than thyroid derivatives, nor is it affected by iodine contamination. Pregnancy does not alter the response of the Achilles tendon reflex. There is no discomfort or stress associated with the performance of the technic; hence it is readily accepted by children. The only condition nullifying the value of the test is neuromuscular disease associated with absence of deep tendon reflex. The hyper- and hypothyroid patient's response to therapy may be evaluated by the use of the photomotogram. If the physician is able to use only one test to evaluate thyroid function, the photomotogram would be the one of choice.*

A RELIABLE and rapid method for evaluating the functional state of the thyroid gland that can be done in an office practice or at the bedside would be a welcome addition to the armamentarium of the clinician. One approach to the solution of this needed diagnostic technic has been an attempt to correlate the duration of the Achilles tendon reflex with the level of thyroid function and to test the validity and reliability of any such correlations that might be observed.

History

Chaney, in 1924,[1] confirmed the observation previously reported by Woltman that the duration of the Achilles deep tendon reflex was prolonged in patients with hypothyroidism. The apparatus used by Chaney was cumbersome and involved the use of a platform on which the foot rested. The duration of the reflex was measured by noting the duration of pressure changes exerted on the platform by the ball of the foot during reflex contraction of the calf muscle. In 1951, Lambert *et al.*[2] supplied additional data supporting the usefulness of this measurement by using a strain-gauge transducer and an electro-optical system to measure the reflex duration. More recently, Lawson[3] investigated essentially the same principle of the duration of reflex contraction as a param-

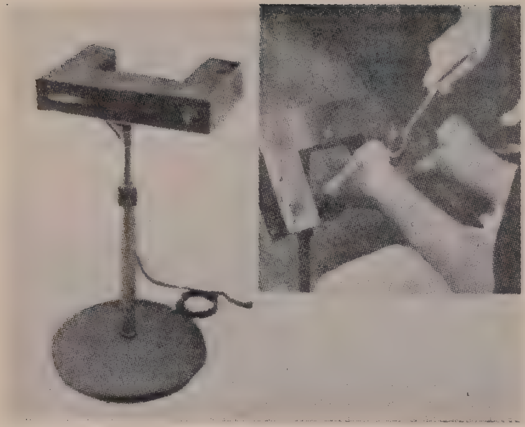

FIGURE 1. Photograph of apparatus and proper position of patient.

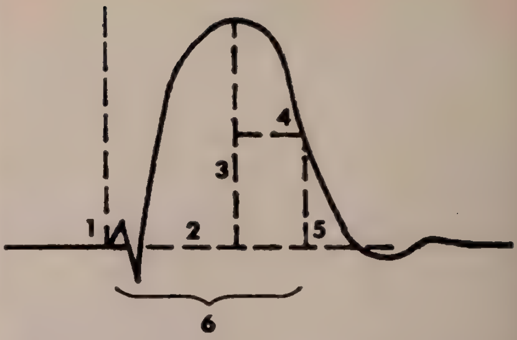

FIGURE 2. Method of calculating duration of reflex. (1) Starting point is beginning of small peak caused by mechanical effect of hammer hitting tendon. (2) Extension of baseline across base of reflex peak. (3) Perpendicular dropped from highest point on reflex curve to baseline. (4) Shows (3) bisected and perpendicular drawn to point on descending limb of reflex spike. (5) Line dropped from (4) to baseline. (6) Final measurement is duration from point (1) to point (5).

eter of thyroid function, using an electromagnetic device. Finally, Gilson[4] developed an instrument containing a photoelectric cell attached to an electrocardiograph, which recorded the displacement of the foot caused by the contraction of the calf muscles and which could be used in timing the free Achilles tendon reflex. Gilson, however, did not evaluate the test clinically. The present study reports the clinical correlation of this photoelectric cell technic with disorders of thyroid function and analyzes the specificity of the procedure. The results obtained are compared with the clinical state as well as with the other standard laboratory parameters of thyroid function.

Materials and methods

PHOTOMOTOGRAPH. This instrument employs a photoelectric device to measure displacement of the foot in timing the free Achilles tendon reflex. A lamp and condensing lens in one arm of the U-shaped housing directs a beam of light onto a photoelectric cell on the other arm of the housing. With the patient kneeling on a cushioned chair in a comfortable position, the unit is positioned so that the light beam is partially intercepted by the plantar arch of the foot. A tap on the Achilles tendon with a percussion hammer causes the foot to move in the light beam, and this movement generates a corresponding change in photocell voltage. The output of the photocell is connected to a direct-writing electrocardiograph, which records the changing voltage on standard electrocardiograph paper. A measurement is obtained from this recording (Fig.1).

MEASUREMENT. To obtain a consistent measurement of the duration of the reflex response, the criteria suggested by Lambert were adopted. Consequently the time elapsing between the stimulus of the tap on the tendon and one-half the relaxation phase is used in this report as the duration of the ankle jerk (Fig. 2).

CLINICAL MATERIAL. Three hundred and twenty-six tracings were obtained from 270 subjects. The protein-bound iodine and serum cholesterol were determined on all patients; on most patients with thyroid dysfunction, I^{131} (radioactive iodine) studies also were done. Neither the clinical diagnosis nor other laboratory results were known to the examiner when the test was interpreted, except in the instances of a few hospitalized patients.

Age, sex, race. Information concerning the age, sex, and race of 242 patients was noted when the test was performed. Such data were not available on the remaining 33 patients at the time of the evaluation. Of the 242 subjects, 205 were of the white race, 31 were Negros, and 3 were Orientals.

TABLE I. Correlation of Achilles tendon reflex time with thyroid function

State of Thyroid Function	Duration of Achilles Tendon Reflex	
	Average in Seconds	Range in Seconds
Euthyroid	0.30	0.23 to 0.40
Hyperthyroid	0.20	0.14 to 0.24
Hypothyroid	0.49	0.41 to 0.64

There were 176 females and 66 males. The youngest subject was five years old, the oldest seventy-five years of age. Seventeen patients were in the youngest age group ranging from five to fifteen years, and 6 were sixty-five years or older.

Achilles tendon reflexes were recorded at least once on 16 untreated patients who proved to be hypothyroid by other parameters. Their ages ranged from nineteen to seventy years.

There were 16 hyperthyroid subjects who also had at least one tracing done before therapy was instituted. Their age range varied from nine to fifty-six years; 10 patients were female, and 6 were male.

Statistical parameters. Two hundred and seventy-four tracings were done on subjects who were shown to be euthyroid by other standard laboratory tests of thyroid function. The duration of the Achilles tendon reflex was obtained 28 times on the hyperthyroid subjects, and 23 tracings were recorded on hypothyroid subjects.

The reflex times of all patients tested varied between 0.14 and 0.64 second. The euthyroid subjects' reflex durations varied from 0.23 to 0.40 second, with a mean and median of 0.30 second. The standard deviation of the euthyroid group was 0.037 second, so that the euthyroid range produced by 2 standard deviations from the mean is 0.23 to 0.37 second.

The hyperthyroid range was from 0.14 to 0.24 second, with a mean and median of 0.20 second, while the hypothyroids varied from 0.41 to 0.64 second, with a mean of 0.49 and a median of 0.50 second (Table I).

Validity. A valid measure of thyroid function is one that correlates well with the functional state of the thyroid as measured by standard laboratory parameters, plus the clinical state of the patient. That the Achilles tendon reflex duration, as measured by the photoelectric device, meets these criteria is borne out by observation of the

TABLE II Range of duration of Achilles tendon reflex in patients with and without thyroid disease

Reflex Duration in Seconds	Number of Subjects			Reflex Duration in Seconds	Number of Subjects		
	Normal	Hypo-thyroid	Hyper-thyroid		Normal	Hypo-thyroid	Hyper-thyroid
0.14	...	...	1	0.36	14	...	...
0.15	...	...	...	0.37	6	...	...
0.16	...	...	...	0.38	5	...	...
0.17	...	...	1	0.39	4	...	...
0.18	...	...	1	0.40	3	...	...
0.19	...	...	1	0.41	1	1	...
0.20	...	...	12	0.42	...	...	...
0.21	...	...	2	0.43	...	...	...
0.22	...	...	7	0.44	...	2	...
0.23	1	...	1	0.45	...	...	...
0.24	15	...	2	0.46	...	4	...
0.25	15	...	...	0.47	...	2	...
0.26	32	...	...	0.48	...	1	...
0.27	12	...	...	0.49	...	4	...
0.28	41	...	...	0.50	...	...	...
0.29	14	...	...	0.51	...	...	...
0.30	41	...	...	0.52	...	3	...
0.31	17	...	...	0.53	...	2	...
0.32	26	...	...	0.54	...	...	...
0.33	6	...	...	0.55	...	...	...
0.34	11	...	...	0.56	...	3	...
0.35	10	...	...	0.57	...	...	...
				0.64	...	1	...

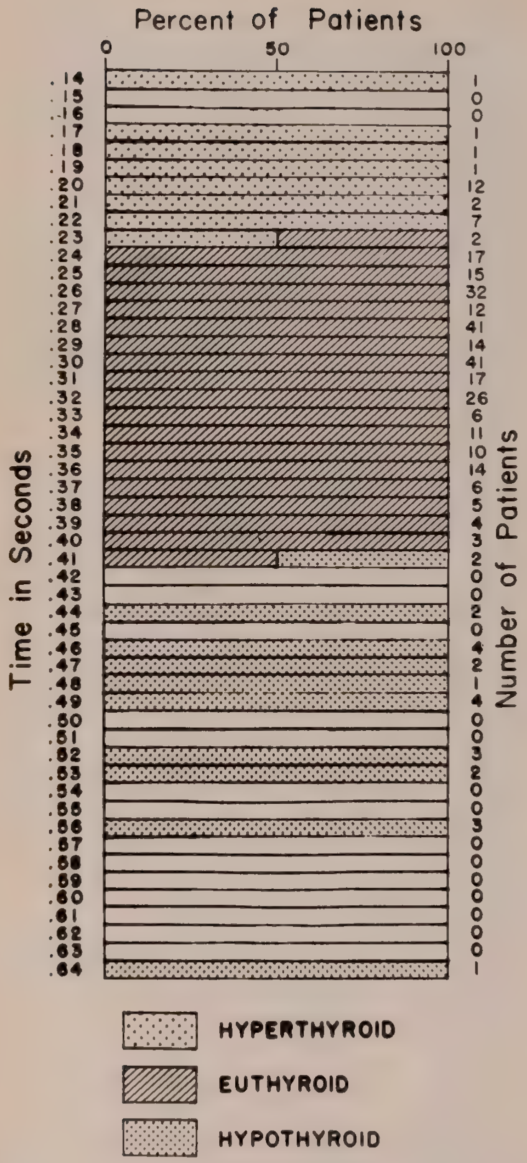

FIGURE 3. Range of duration of Achilles tendon reflex in patients with and without thyroid disease.

distribution curve (Table II, Fig. 3). It should be emphasized that all values charted in the hyper- and hypothyroid ranges represent reflex measurements from patients proved to have abnormal thyroid function by the various standard laboratory tests (protein-bound iodine, cholesterol, and radioiodine studies) as well as by clinical parameters. The degree of overlap is minimal. Where overlap did occur, the values remained in the general area expected for the functional state of the thyroid. There were no gross deviations from this observation.

Reliability. To determine the reliability and consistency of the Achilles tendon reflex measurement as a test of thyroid function, tracings were obtained at various intervals on euthyroid subjects, as well as on untreated hyper- and hypothyroid patients. In addition, reproducible values were obtained on patients with thyroid dysfunction whose therapy had not changed over the period of repeated observations.

Twenty-two euthyroid subjects were tested two to four times during a nine-month period. In no case did the reflex duration vary by more than 0.02 second. None of the hyper- or hypothyroid patients, who were tested several times before therapy, had reflex durations that varied by more than 0.04 second. The patient with thyroid dysfunction on treatment had reflex durations that did not vary by more than 0.02 second, while the patient was receiving the same therapy at the time of each test.

Response to therapy

L-TRIIODOTHYRONINE OR T_3 SUPPRESSION TEST. The T_3 suppression test[5] has been utilized to differentiate the hyperthyroid from the euthyroid subject, where that distinction cannot clearly be made by other means. Theoretically, the suppression of endogenous thyroid hormone production by replacement with an equivalent amount of exogenous hormone (in this case, L-triiodothyronine or T_3) should not affect the duration of the Achilles tendon reflex in the euthyroid individual, even though the protein-bound iodine and I^{131} values will be suppressed. Similarly, no significant alteration in the duration of the Achilles tendon reflex should occur with the administration of T_3 to the hyperthyroid individual, since the exogenous hormone will not suppress the function of the hyperactive gland. Moreover, the dose of T_3 used is insignificant relative to the excessive amounts of hormone being produced by the thyroid gland, and hence this dose will contribute nothing to making the patient "more hyperthyroid." Conversely, the administration of even

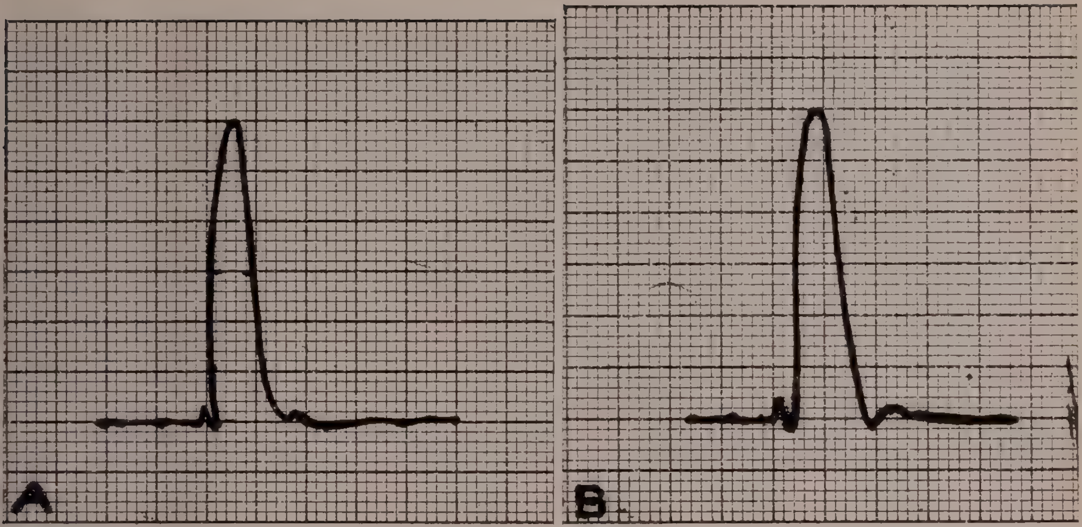

FIGURE 4. (A) Hyperthyroid fifty-six-year-old Negro male with protein-bound iodine of 14 gamma per 100 ml. and I^{131} uptake of 91 per cent in twenty-four hours. Photomotogram equal to 0.18 second. (B) Same patient on therapy with 40 mg. of methimazole daily. Photomotogram equals 0.26 second; protein-bound iodine, 6.6 micrograms per 100 ml.

smaller doses of L-triiodothyronine could be expected to shorten the prolonged reflex duration of the patient with the "hypometabolic syndrome" or with frank hypothyroidism.

Eleven euthyroid subjects received 100 micrograms of L-triiodothyronine per day for five days, the Achilles tendon reflex test being performed before and again on the fifth day of medication. In 5 cases, a third reflex test was performed some time after the cessation of medication. In no case was the variation between the pretreatment and the treatment values more than 0.02 second. This indicates that the administration of L-triiodothyronine to euthyroid patients in this dosage does not affect the duration of the Achilles tendon reflex. Four hyperthyroid patients were tested similarly and, as anticipated, showed no difference before or during T_3 administration greater than the 0.02-second variation found in the euthyroid group.

Hyperthyroidism. The duration of the Achilles tendon reflex was obtained periodically on 12 hyperthyroid subjects who were receiving antithyroid medication. A prolongation of the reflex duration to the normal range occurred in all patients as therapy was continued (Fig. 4). This change was well correlated with improvement in the clinical status of the patient. In 6 cases hyperthyroidism again ensued when therapy was stopped prematurely by the patients, and the duration of the Achilles tendon reflex reverted to the original hyperthyroid range in all.

Hypothyroidism. Eight patients in the hypothyroid category were followed with repeat Achilles tendon reflex tests while they were on thyroid replacement therapy. In all cases the reflex duration shortened toward the normal range as the optimum therapeutic dose was achieved, and there was a definite correlation between the more normal reflex time and the patient's clinical status (Fig. 5).

Note should be made of 1 patient, whose complaints and clinical signs were those of decreased thyroid activity, but who had a normal protein-bound iodine. This patient had a pretreatment reflex duration of 0.43 second. While receiving one of the thyroid analogues (T_3 alanine, 0.05 mg. every day) no change was noted in the duration of the ankle jerk. The reflex duration remained similarly prolonged while the patient was receiving placebo therapy. However, when the patient was placed on L-triiodothyronine, 100 gamma per day, there was a

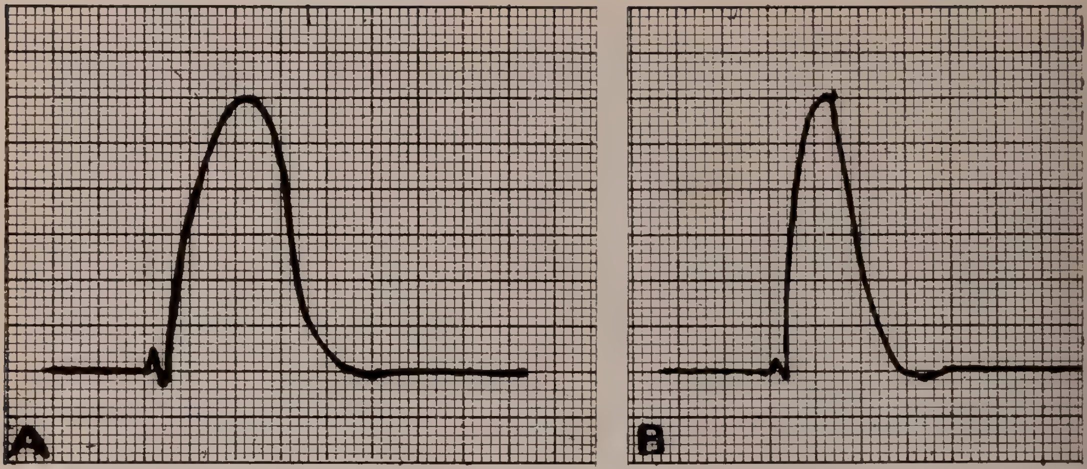

FIGURE 5. (A) Sixty-four-year-old white female with clinical myxedema, a protein-bound iodine of 0.2 gamma per 100 ml., an I^{131} uptake of 0 per cent in twenty-four hours, and a photomotogram of 0.64 second. (B) Same patient after two and one-half weeks of treatment with 37.5 micrograms of triiodothyronine daily. Photomotogram equals 0.38 second.

remarkable shortening of the duration to 0.25 second, along with concomitant clinical improvement. This case may represent an example of the so-called hypometabolic syndrome,[6] in which it has been theorized that there is a normal production of thyroid hormone, but this hormone is inactive at the cellular level because of an enzymatic defect preventing deiodination of thyroxine (T_4) to T_3.[7] Evidence supporting the concept that thyroxine is normally converted to another compound before becoming active at the cellular level, and that deiodination is a part of this process, recently has been reported by Larson and Albright.[8]

Emphasis should be placed on the fact that with the institution of thyroid replacement therapy, the standard tests of thyroid function such as the protein-bound iodine or I^{131} studies may no longer be accurate measures of the metabolic state of the individual, since both of these laboratory measures are influenced by various thyroid medications independent of their clinical effectiveness. For example, the iodine content in thyroid extract, U.S.P., which is the basis of its biologic potency, may elevate the protein-bound iodine as a contaminant and at the same time may suppress the I^{131} uptake via thyrotropin suppression. Thus, neither of these tests will necessarily give a true index of the adequacy of thyroid replacement therapy. In addition, the hypothyroid patient being treated with T_3 will have either a decrease or no increase in the basal protein-bound iodine, since the administered T_3, although efficient in metabolic activity, is not bound to protein to any degree,[9,10] and therefore will not influence the protein-bound iodine determination, nor will T_3 therapy in the hypothyroid increase I^{131} studies toward normal. These observations give added significance to the Achilles tendon reflex duration as a technic offering an excellent, reliable, and simple way of following patients under treatment for thyroid disorders. In this sense, the photomotograph replaces the notoriously inaccurate basal metabolic rate as a clinical tool for the evaluation of thyroid activity.

Hypermetabolic and hypometabolic states not associated with thyroid disease

HYPERMETABOLIC STATES. *Pregnancy.* Since the standard thyroid tests may not accurately depict the functional state of the thyroid in pregnancy,[11] it was especially important to evaluate the validity of the duration of the Achilles tendon reflex as a specific test of thyroid activity in this hypermetabolic condition. Twelve subjects were tested: 10 were in the third trimester and

2 in the second trimester. None had symptoms or signs of hyperthyroidism. Three were considered to be mildly to moderately toxemic, as characterized by blood pressure elevation and albuminuria. In all cases, the reflex duration was within normal limits, the range being from 0.26 to 0.40 second. The mean duration was 0.32 second, not significantly different from the mean duration of the nonpregnant euthyroid group.

The Achilles tendon reflex duration would seem, therefore, to be a valid measure of thyroid function in pregnancy.

Agitated states. Six patients were tested who were diagnosed as being psychotic or severely neurotic. All had marked emotional agitation at the time the reflex test was performed, yet all had reflex durations within normal limits, the range being 0.24 to 0.36 second. In several cases, hyperthyroidism was suspected strongly on clinical grounds. The result of the reflex test was the first indication, later substantiated by protein-bound iodine, cholesterol, and I^{131} tests, that the patients were euthyroid.

Agitated states apparently do not interfere with the accuracy of the reflex test as a measure of thyroid function.

Fever. Three patients with temperatures ranging from 100 to 103 F. as well as an associated actively metabolizing malignant condition were subjected to the Achilles tendon test. The Achilles tendon reflex durations were within normal limits in 2 cases, with values of 0.30 and 0.39 second. Interestingly, the patient with the latter value had a temperature of 103 F. at the time of the test. The third patient, who had an additional finding of rapid auricular fibrillation, not well controlled with the use of digitalis therapy, had a shortened reflex duration of 0.20 second. The protein-bound iodine, reported several days later, was 15 gamma per 100 ml.; the I^{131} uptake was 72 per cent, confirming the diagnosis of hyperthyroidism. This patient had metastatic disease, the primary site of which was probably pulmonary. He expired a short time thereafter, and no further tests were obtained.

HYPOMETABOLIC STATES. *Obesity.* Thirteen patients, all of whom had simple exogenous obesity, were tested as to the duration of the ankle jerk. All had normal reflex times, ranging from 0.26 to 0.39 second, with a mean duration of 0.32 second, again not significantly different from the nonobese euthyroid mean of 0.30 second.

Anorexia nervosa. One patient with anorexia nervosa was evaluated with the Achilles tendon reflex test. There had been a weight loss of 50 pounds in the year prior to hospitalization. Hyperthyroidism had been considered strongly as a diagnostic possibility. A reflex duration of 0.30 seconds was recorded. The protein-bound iodine was 6 gamma per 100 ml.

MISCELLANEOUS CONDITIONS. *Uncontrolled tachycardias.* Two patients with auricular fibrillation, poorly controlled with digitalis therapy, were evaluated. One patient, previously referred to, had a reflex duration of 0.20 second and a protein-bound iodine of 15 gamma per 100 ml.

A third patient had a history of one year's duration of multiple paroxysmal supraventricular tachycardias, requiring numerous hospitalizations at which times the patient often presented symptoms of shock. An attempt was made to produce a hypothyroid state by using large doses of methimazole with the hope that this would reduce the frequency of the episodes. In spite of the administration of large doses (90 mg. per day) of the methimazole for two to three months, the Achilles tendon reflex test revealed a time of 0.36 second. A protein-bound iodine, obtained at the time of the test, was 4 gamma per 100 ml. A thiocyanate test was performed because of the unusual resistance the patient showed to the antithyroid therapy.[12] A one-hour uptake of 20 per cent was recorded. One Gm. of potassium thiocyanate was then administered orally. The uptake one hour later was 13 per cent and was 10 per cent at twenty-four hours. The results indicated that the antithyroid drug was not effectively blocking organification as would be expected with the high dose employed and thus explained and confirmed the normal value obtained by the Achilles tendon reflex test.

Neurologic disorders. Two patients with neurologic residua following cerebrovascular accidents, including hyperreflexia of the

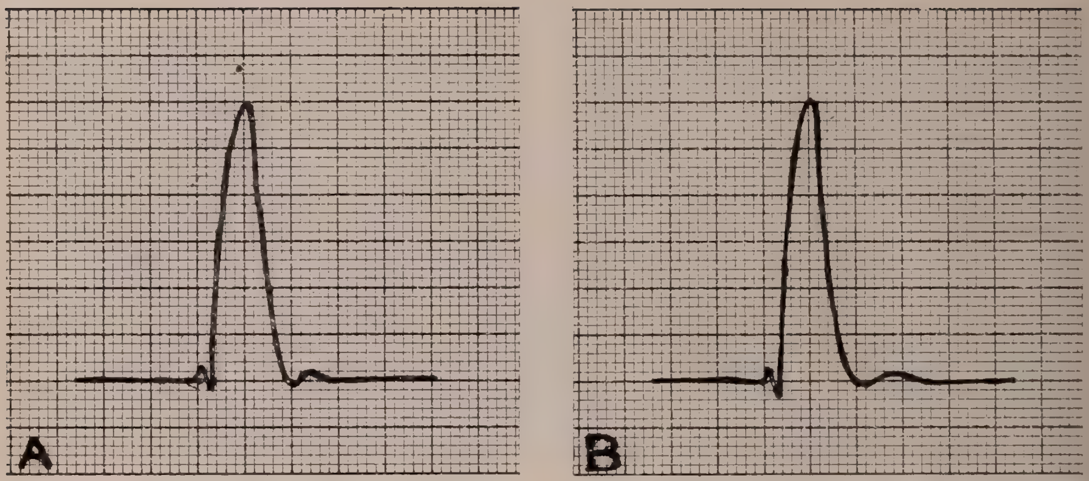

FIGURE 6. Achilles tendon responses of (A) right foot (0.28 second) and (B) left foot (0.28 second) in a euthyroid patient with a herniated nucleus pulposus. Note the differences in the height of the reflex curves, while the duration remains the same.

affected lower extremity, were tested. In each case, the duration of the ankle jerk of the hyperreflexic limb was exactly the same as that of the normal limb, although the contour of the abnormal reflex differed from that of the normal side. The reflex times in both cases were within normal limits, 0.32 and 0.33 second, respectively.

The duration of the Achilles tendon reflex was obtained on a thirty-one-year-old female who was hospitalized because of neurologic findings as a result of a herniated nucleus pulposus. Again, in spite of hyporeflexia of the affected limb, no differences between reflex times on both sides were elicited (0.28 second) (Fig. 6).

One patient with Parkinson's disease was tested and was found to have normal reflex times, with no variation in the reflex duration of either side.

A patient with Huntington's chorea was subjected to the Achilles tendon reflex test, and also proved to have a reflex duration within normal limits (0.32 second).

Finally, a hyperthyroid patient with nonprogressive muscular dystrophy was tested (Fig. 7). The Achilles tendon reflex duration was 0.19 second before therapy and 0.31 second several months after effective antithyroid therapy had been instituted, at which time he appeared clinically euthyroid. Apparently, therefore, as long as the Achilles reflex can be elicited, it seems to be unaffected by local neurologic or vascular disease, and on the basis of this study, it has been shown to be a specific measure of the peripheral activity of thyroid hormone.

Comment

The duration of the Achilles tendon reflex, as measured by the photoelectric cell technic, has proved to be an accurate test of the state of thyroid activity. As previously mentioned, there have been reports dealing with the delayed reflex in hypothyroidism, a fact confirmed in this study. In addition, the Achilles reflex duration has been found to portray accurately thyroid hyperfunction as well, the reflex time being shortened significantly in these cases. Thus, the photoelectric cell technic has markedly increased the diagnostic usefulness of the reflex test through the feature of reproducibility, with only minimal variation on repeated testing, and by virtue of the permanent record that can be obtained for comparison with subsequent records made during a patient's treatment phase.

Once the reliability and validity of this test was established, reflex measurements were obtained in conditions which conceivably could give false positive or false negative diagnostic results such as occur with the determination of the basal metabolic rate. The following conditions were

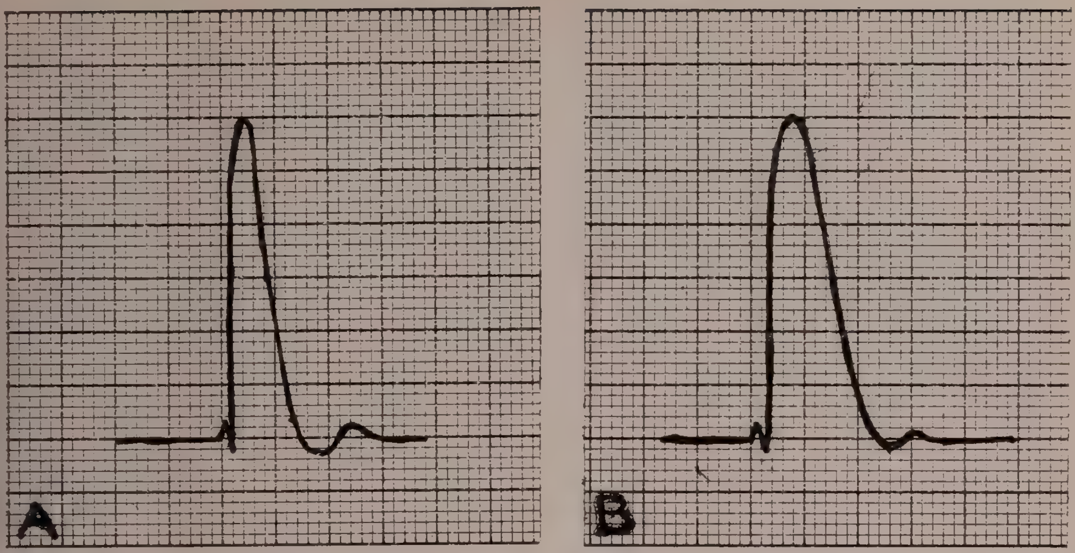

FIGURE 7. (A) Hyperthyroid forty-three-year-old white male with nonprogressive muscular dystrophy. Protein-bound iodine equals 11.6 gamma per 100 ml., serum cholesterol, 145 mg. per 100 ml.; twenty-four-hour I^{131} uptake, 65 per cent; and I^{131} conversion ratio, 85 per cent. Photomotogram equals 0.18 second. (B) Same patient while on therapy with 400 mg. of propylthiouracil daily. Protein-bound iodine equals 4 gamma per 100 ml., and photomotogram, 0.31 second.

found not to interfere with the specificity of the Achilles tendon reflex test as a measure of thyroid function:

Physiologic states. Pregnancy is especially significant since the normal ranges of the other standard tests of thyroid function will be altered in mid and late pregnancy.[7] Most of the reflex durations were obtained in the third trimester.

Obesity may result in an abnormal basal metabolism rate because of the difficulty in obtaining an accurate measure of the body surface area.

Pathologic states. The pathologic states include toxemia, fever, active malignant conditions, agitated states, anorexia nervosa, and neurologic and neuromuscular disorders.

While in every case the reflex time correlated well with the functional state of the thyroid gland as measured by other parameters, there was some overlap. The euthyroid range varied from 0.23 to 0.40 second, whereas the theoretic distribution calculated by 2 standard deviations from the 0.30 second mean was 0.23 to 0.37 second. Three of the 25 hyperthyroid tracings fell within this range, being 0.23, 0.23, and 0.24 second respectively. There is reason to question the 0.24 result, since it was obtained during the first few weeks of the study at a time when the technic of the test had not been standardized.

While the hypothyroid range is presented as 0.41 to 0.64 second, only 2 patients had recordings under 0.46 second (0.41 and 0.44 second). The patient whose reflex time was 0.44 second had already received small doses of L-triiodothyronine. It is reasonable to suspect that the reflex time had been somewhat more prolonged before therapy.

Age, sex, and race had no effect on the reflex duration, the mean time of the youngest and oldest age groups not varying significantly from the mean time of the entire euthyroid group.

The duration of the ankle jerk adjusted toward normal in predictable fashion as corrective therapy was administered to either hyper- or hypothyroid subjects. This change accurately reflected the clinical response of the patient. Even in the case of a hyperthyroid patient with nonprogressive muscular dystrophy, antithyroid therapy resulted in a normal reflex duration.

Finally, it is to be noted that the Achilles reflex test measures but one parameter of thyroid function. No single test is a measure of total thyroid function, and a battery of tests must be obtained to evaluate thyroid status fully. Because of its simplicity, the greatest use of the measurement of reflex duration is suggested as a screening test for thyroid dysfunction and as a means of following patients with thyroid abnormalities on therapy. In the latter instance it offers a much simpler and more accurate technic than the basal metabolic rate, which should now undergo its long overdue demise.

Conclusion

A method of evaluating the functional state of the thyroid gland by measurement of the duration of the ankle jerk has been presented. It has proved to be simple to perform, reliable, valid, and remarkably accurate in the diagnosis of hyper- and hypothyroidism.

Acknowledgment. Thanks are due to the Burdick Company, New York City, for supplying the apparatus necessary for the photomotogram determinations; to Mr. H. Grob for technical assistance; and to I. Musacchio, Ph.D., for help with laboratory determinations. The studies described in this article were supported in part by Grant RG-5162 (C1) from the United States Public Health Service.

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Not true to life

The inference is not justified that our scientifically trained and able doctors are not capable of evaluating critically the publications of new drugs. Doctor friends have told me that the intimate doctor-patient relationship has been damaged by such inferences from Washington and by articles such as the one appearing recently in *Life* which urged patients to press their doctors to prescribe cheaper drugs. Most of you probably saw the *Life* article entitled "A Big Pill to Swallow" but did not see the later advertisement in *Life* or the letters to the editor pointing out numerous errors of fact in the original article, including the fact that the drug on which the article was centered retailed at an average of only 11.3 cents and not 30 cents as *Life* had written.—*Alex Guerry, Jr., President, Brayten Pharmaceutical Company, The Drug Industry—Robbers or Heroes?*

The Direct Current Control System

A Link Between Environment and Organism

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A STUDY WAS UNDERTAKEN *of the problem of the relationship between D.C. (direct current) potentials and regeneration. A complex electrical field was found rather than the expected simple dipole, and its spatial configuration was noted to bear a close relationship to the gross anatomic arrangement of the central nervous system. The D.C. potential gradient was measured on the exposed but otherwise undisturbed main sciatic nerve in the frog. The results were indicative not only of moving charges, but also indicated further that the charge carriers were nonionic and were probably units of the size of electrons. A definite relationship has been established between the time sequence of D.C. changes at the site of a limb amputation and the subsequent healing process. In the human being a similar neural-related pattern was found as in the amphibian. It appeared likely that the organized D.C. activity of the brain was in some way closely related to general behavior, possibly as a controlling mechanism of sorts and that, since the actual D.C. flow of charge carriers was an integral part of the system, then the operating parameters of the system could be influenced by external force fields (magnetic, electrostatic) and by such physical parameters as levels of air ionization.*

FOR MANY YEARS the relationship between D.C. (direct current) electricity and living organisms has been under investigation. Insofar as is known, all forms of life exhibit measurable D.C. potentials on their intact exterior surfaces. Previous studies indicated that these surface potentials were arranged as a simple dipole with cephalocaudal polarity.[1] Studies of these potentials in a variety of animals, including man, indicated some obscure but definite relationship to such factors as embryonic growth,[2] initial responses to injury,[3] healing processes including regeneration,[4] tumor formation,[5] activity of cerebral cortex neurons,[6,7] local[8] and general anesthesia,[9] sleep,[10] hypnosis,[11] schizophrenia,[12] and ovulation.[13] A consideration of these factors reveals that they include the general areas of growth, neural irritability, and cyclic behavior.

The application of direct electrical currents to living organisms, in strengths below the cauterization level, has been reported to produce physiologic effects in the same general areas. Direct current applied fronto-occipitally in human beings is capable of producing sleep and surgical-plane anesthesia depending on the amount of current passed.[14,15] The application of direct current to plants increases the rate of regeneration in an approximate linear fashion with the current density.[16] The complete disappearance of implanted malignant tumors in mice has also been reported following brief daily administrations of direct current for periods of a few weeks.[17] In the central nervous systems of various species the application of small-density direct current has been reported to modulate the spontaneous action potential activity of neurons.[18–20] In all these observations the effect was dependent either on the polarity (positive or negative) of the current or the direction of the imposed D.C. field.

In 1935 Burr,[21] a pioneer in this field of research, postulated that the naturally occurring D.C. potentials had an actual control function and he proposed the electrodynamic theory of life. According to this concept the potentials were quasi electrostatic in nature and were generated by the electrical activity of all of the cells of the organism with no relationship to any discrete internal structures or systems. This concept was at variance with the then-prevailing neurophysiologic concepts of an all-or-none action potential activity of the neuron as the mechanism of communication and control, and accordingly it never received wide support. The intervening years have seen rapid growth in the field of neurophysiology, with a resulting revision of many previously accepted theses and a recognition that many unsolved problems still remained.[22] The interest in D.C. phenomena was sporadic throughout most of this time and was directed primarily toward taxonomic experiments on the results of exposing living organisms to various D.C. densities. Two factors nevertheless remained evident: Living organisms do produce measurable D.C. potentials, and these potentials are to some extent concerned with growth and general behavior.

During the same period these two problems of growth and behavior were subjected to extensive study by the biochemical and neurophysiologic disciplines. Nevertheless, no effective control over growth or behavior has been forthcoming primarily because the basic natural control mechanisms for these parameters of life still remained obscure. However, rapid strides were made in the area of the application of physical sciences to biology. Medical electronics has assumed the stature of an almost independent discipline, biophysics has begun to apply solid state technics and quantum theory to life processes, and control systems analysis has been applied to the study of biologic control systems. These younger disciplines produced new technics, both in instrumentation and analysis, which heretofore had not been applied to the problem of the D.C. potentials in living systems.

Material and method

One of our preliminary studies was directed at the problem of regeneration, with the thought of the possible clinical application in bone-healing processes. The results have far exceeded expectations, and there has emerged a previously unsuspected function of the central nervous system which appears capable of explaining the heterogeneous observations relating direct currents and living organisms.

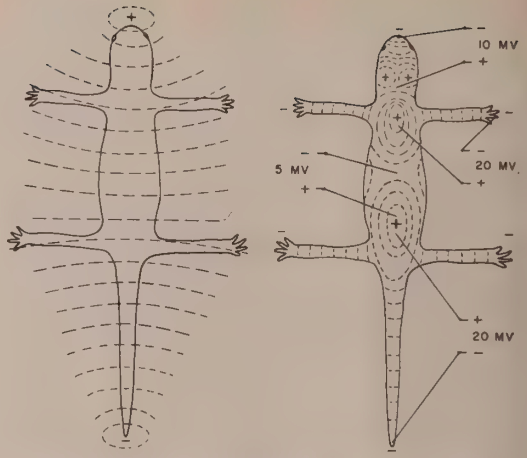

FIGURE 1. D.C. field configuration in amphibian. (Left) Theoretic equipotential lines on basis of dipole field. (Right) Equipotential lines actually found by measurement. Complexities of field, as well as relationship to central nervous system, apparent. Arrows indicate points of standard electrode placement and average values of potentials measured.

Our initial studies were directed toward the precision mapping of the surface D.C. field by determining the lines of equal electrical potential. A complex electrical field was found rather than the expected simple dipole, and its spatial configuration was noted to bear a close relationship to the gross anatomic arrangement of the central nervous system (Fig. 1). Positive areas were located over the cellular aggregates of the neuraxis (cranial, brachial, and lumbar) with increasing negative potentials along the peripheral nerve outflows from each.[23] Analog technics indicated that models of the central nervous system containing D.C. generating sources could produce such a surface field, justifying the hypothesis that the naturally occurring D.C. surface field was generated within and distributed by elements of the central nervous system. This was strengthened by the observations that field potentials on the extremities could be reduced to zero by sectioning the nerve fibers to the extremities and that sectioning the spinal

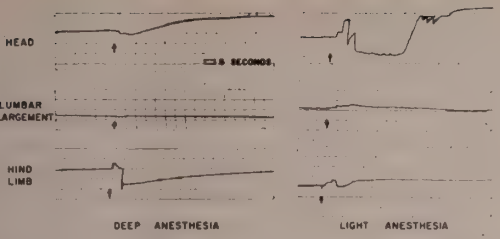

FIGURE 2. Response of D.C. field to hind limb trauma. Fracture of one of long bones in hind limb of a salamander produced at point marked with arrow. Simultaneous recordings made at areas indicated. Upward deflection indicates increasing negativity. Zero offset used to bring recording pens to chart center with amplification used. (Left) Deep anesthesia. Note prompt shift in D.C. potential in injured hind limb, very slight change in lumbar area, and small positive shift in head potential after time lag of two seconds. (Right) Light anesthesia. Head response much greater in magnitude and complexity although lag time remains the same. Head changes definitely not the passive transmission of injury potential but represent active response. (1 millivolt per 2 vertical lines)

cord at the level of the medulla produced severe changes in the field potentials distally, such changes correlating well with the time duration of spinal shock.

In addition, if the D.C. potentials were measured at multiple points on an animal, including the head, a specific series of changes occurred following the application of a traumatic stimulus to the hind limb (Fig. 2). These changes progressed up the neuraxis, reaching the cranial area after a delay of two seconds, and producing an active response. This suggested that the sequence of D.C. field changes had transmitted information regarding trauma. Very specific changes in the field polarity, particularly across the head, were noted with anesthesia. In deep chemical anesthesia, the polarity of the frontal area was found to be positive with respect to the occipital area. Spontaneous slow recovery from anesthesia was associated with a shift through zero to a negative polarity which tended to increase in amplitude until in the normal unanesthetized state the polarity of the frontal area was negative. It is significant that electronarcosis[14,15] is produced by applying a modulated direct current across the head along the fronto-occipital axis with a polarity tending to drive the frontal area positive.

Since the extremities revealed a D.C. potential gradient that was increasingly negative as one proceeded distally, the gradient was measured on the exposed but otherwise undisturbed main sciatic nerve in the frog. This proved also to be negative distally and was fairly linear, being the same along various 1-cm. lengths. Since the potentials measured were direct current in nature and completely unrelated to the action potential activity of the nerves, it appeared that we might well be dealing with an entirely new phenomenon. Standing or electrostatic potentials could not be long maintained in a conducting medium such as a nerve fiber unless they were associated with a continuous flow of electrical charges in some manner analogous to the flow of electricity in a wire connected to a battery. The nerve impulse or action potential does not involve any such activity being basically a traveling wave of membrane depolarization. Present-day theories relate this to a radial movement of ions in and out of the fiber, with no longitudinal transmission of electrical charge. It seemed most probable that we were observing the continuous movement of charges longitudinally in the nerve fiber, and evidence was obtained to substantiate this by utilizing a physical phenomenon, the Hall effect (Fig. 3).

The results obtained were indicative not only of such moving charges, but also indicated further that the charge carriers were nonionic and were probably units of the size of electrons.[24] This would indicate that some phenomenon such as semiconduction- or conduction-band electron transfer was occurring within the nerve fiber. The application of cryogenic technics to exposed nerve fibers provided some confirmatory evidence for this and indicated further that the magnitude of the current flow varied with the state of activity or irritability of the fibers.[25] We had by this time concluded that the surface D.C. potentials are a second-order phenomenon, resulting from the charge transport system associated with the neural tissues. However, charges that move in a D.C. fashion in one direction must ultimately return to their source to complete the circuit.

Our concept of the system at first was that the nerve fibers conducted in one direction, presumably distally, and that the

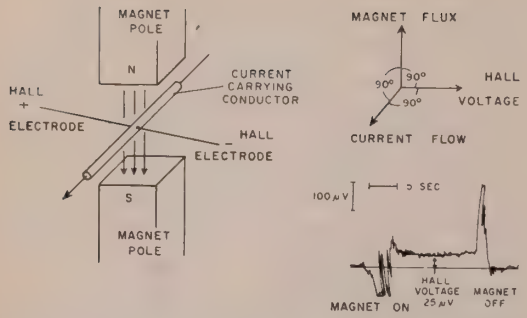

FIGURE 3. The Hall effect. (Left) Schematized basic arrangement necessary for Hall effect experiment. To generate a potential across Hall electrodes, charges must be moving within conductor. (Right) Mutual 90-degree axes necessary illustrated at top. Using nerve outflow in forelimb as analogous to current conductor, Hall effect experiment can be set up. Permanent magnet on movable support furnishes magnetic flux necessary. Representative Hall voltage obtained from one such experiment illustrated at bottom. Steady 25 microvolt change in D.C. voltage obtained during application of magnetic field. Transient wave forms associated with magnet on and magnet off are due to movement of magnet in and out of position. Moving lines of flux generate transient voltages which die out in one or two seconds and contribute nothing to steady Hall voltage.

return path was through the soft tissues or some component thereof. A search for this return path was initially unsuccessful until the routine measurements of the D.C. gradients along the peripheral nerves were extended to the branches of the sciatic nerves. The gradient of the posterior tibial branch was found to be of the same polarity as the main sciatic nerve (negative distally), although considerably higher in magnitude. The gradient along the peroneal branch was then noted to be reversed, that is, positive distally, and lower in magnitude than the posterior tibial branch. The arithmetic sum of the gradients along 1-cm. lengths of the two branches was approximately equal in polarity and magnitude to the D.C. gradient along 1 cm. of the main sciatic. A comparison of the fiber-size spectrum of the two branches revealed that the peroneal branch, which was positive distally, had a preponderance of small myelinated fibers compared with the posterior tibial branch.

Since the smaller fibers are considered to be associated generally with sensory function, a survey of known sensory (dermal) and known motor (muscular) nerves was done. In all cases the sensory nerves had a distal positive gradient, while the motor nerves were distal negative. It is evident that the gradient of a mixed nerve will therefore be the arithmetic sum of the negative and positive gradients of the motor and sensory fibers respectively. Since the normal direction of impulse conduction in a sensory nerve is toward the nerve cell body, the sensory nerve fibers may be viewed as anatomically dendritic in nature. Obviously the motor fibers in a peripheral nerve are anatomically axons. Since all of the sensory nerves (dendrites) were observed to have a D.C. gradient distally positive in polarity and all of the motor nerves (axons) were found to exhibit the opposite polarity, might we be dealing with a D.C. gradient extending longitudinally throughout the entire neural unit: dendrite to cell body to axon? In this regard the previously mentioned works of Gerard and Libet[7,26] are particularly pertinent. They observed such an axodendritic polarization in the cranial neurons of the frog and, most important, related this potential to the activity, as determined by the electroencephalogram, of the same neurons. Goldring and O'Leary[27] have reported that by artificially reversing the potential results in convulsive-type-electroencephalograms while artificially augmenting the potential with the same amount of current, an increase in the voltage of the normal electroencephalogram is produced. In another study, Goldring *et al.*[28] demonstrated the existence of a similar pia ventricular D.C. gradient in human beings and successfully related changes in the neuronal D.C. pattern to changes in the D.C. potentials measured by skin electrodes.

Comment

As a result of all these investigations, we propose that a property common to all neural tissue is an axodendritic electrical polarization (Fig. 4) accompanied by a longitudinal D.C. flow. It is possible to draw a "circuit diagram" for this system as it functions for spinal neurons (Fig. 4B). It is evident that circuit resistance between peripheral terminals (AB) is higher than the resistance be-

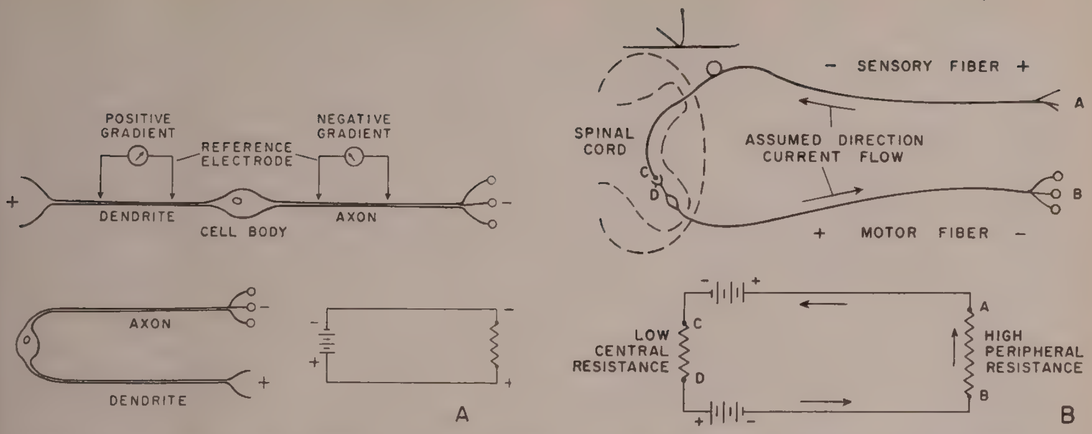

FIGURE 4. (A) Basic axodendritic D.C. polarization of spinal neurons. (Top) Over-all polarization of neuron with illustration of different polarities obtained on dendrite versus axon resulting from position of reference electrode. In studies on peripheral spinal nerves the reference electrode was proximal or nearest to cell body. This is equivalent to reversing voltmeter connections on sensory fibers compared to motor fibers. Therefore, if over-all longitudinal D.C. gradient existed it would be recorded with opposite polarities on each type of fiber. (Lower left) Single neuron bent into loop producing completed circuit. (Lower right) Electronic analog of circuit assuming current source is located solely in cell body. (B) Functioning D.C. circuit composed of two basic neurons. Orientation of each neuron determines its direction of direct current flow. A sensory and motor neuron therefore constitute not only a simple reflex arc but also a complete D.C. circuit. Electrical circuit analog illustrated, again the assumption made that current source is concentrated in cell body. Very narrow gap at central synapse (CD) considered lower in resistance than peripheral path through tissue (AB).

tween central terminals (CD) and that a higher potential therefore will be observed peripherally. The use of such skin-resistance measurements as galvanic skin response as an index of the psychologic state can be interpreted as variations of D.C. flow in such cases. It has been shown that the state of functional activity of cranial neurons, as measured by action potentials, is related directly to the presence of a normal D.C. potential gradient and current flow.[6,7,26] It therefore appears that each neuron is capable of two types of activity: the first being the generation of a D.C. potential accompanied by longitudinal D.C. flow and the second being the generation of rapidly propagating action potentials as disturbances in membrane polarization. The second activity depends on the first being in a normal state. By influencing the rate of message-flow action potentials, the D.C. system qualifies as a data-transmitting control system. In addition it appears to transmit certain types of data such as pain and injury, by variations in its own state: an analog type of data transmission. It also seems to exert controls over certain peripheral as well as central or cranial functions. The reaction times of such an analog system are low but the versatility high; therefore it is thought that possibly this was the original functioning system in the first primitive nerve nets.

It became desirable to evaluate the control functions of this unified D.C. system in regard to the parameters of growth and behavior. Concerning the first, a definite relationship has been established between the time sequence of D.C. changes at the site of a limb amputation and the subsequent type of healing process. Animals demonstrating regenerative abilities followed an entirely different sequence of D.C. changes from that of closely related by nonregenerative forms. Furthermore, the rate of regeneration could be accelerated as well as retarded by artificially implementing or decreasing the magnitude of the measured D.C. field change.[29]

Conclusion

At this time it became technically possible to make long-term D.C. recordings from

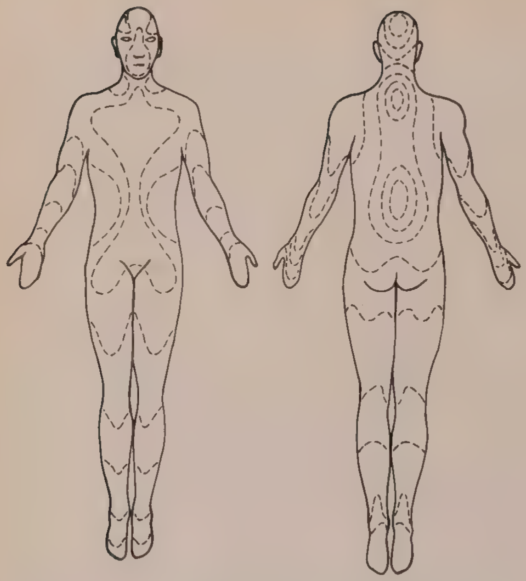

FIGURE 5. Pattern of equipotential D.C. field lines in human being. Similarity in this pattern to that shown by amphibian evident; same relationship to central nervous system.

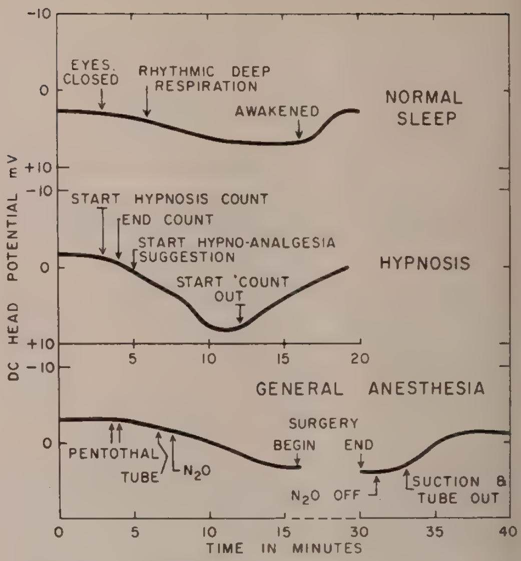

FIGURE 6. Representative changes in transcranial (measured from occiput to frontal region) D.C. potentials of human being during various changes in state of consciousness (sleep, hypnosis, anesthesia). (Top to bottom) All of these associated with shift in positive direction of frontal area.

human beings because of the development of a new type of electrode.[30] Since many papers had dealt with D.C. phenomena in human beings based on the dipole field theory, there appeared little doubt that such D.C. potentials did exist in man. However, because of the generally unsatisfactory nature of the electrodes previously used and the fact that measurements were taken from essentially random points, both the pattern of the field and the significance of the reported changes were in doubt. The first step was to measure the field in the same manner as was done previously with the amphibian. In general the same neural-related pattern was found with differences ascribable to the relative shortening of the spinal cord and the capacitive effects associated with dry skin (Fig. 5).

It was further noted that voltage-regulation curves typical of D.C. sources with internal resistance could be determined along nerve pathways, a fact indicating that the source of the potential could and does supply a current. As with the amphibian, specific changes in the transcortical D.C. potentials were noted with general anesthesia (Fig. 6). It is interesting that the changes noted were of the same polarity as the currents used to produce electronarcosis. In addition, similar polarity shifts were noted in sleep and hypnosis.[31] In all of these states the physiologic level was related to the magnitude of the polarity change. A procaine block of the peripheral nerves produced a drop in the surface potential measured from the brachial area to the palm of the hand (Fig. 7). Two cases with brachial plexus injuries were evaluated. One case with clinical avulsion of the brachial roots demonstrated a zero potential. The other case in which the block was caused by pressure demonstrated complete motor and sensory paralysis immediately postoperatively with zero D.C. gradients. Within forty-eight to seventy-two hours deep pain sensation alone had returned, and this was accompanied by a nearly normal D.C. gradient level. Since deep pain is generally related to C fibers[32] and these C fibers to the phenomenon of "second" or "delayed" pain with a delay time of 0.5 second,[33] the time lag of two seconds noted in the animal's cranial D.C. response to trauma is highly suggestive. A significant relationship was noted between extremity

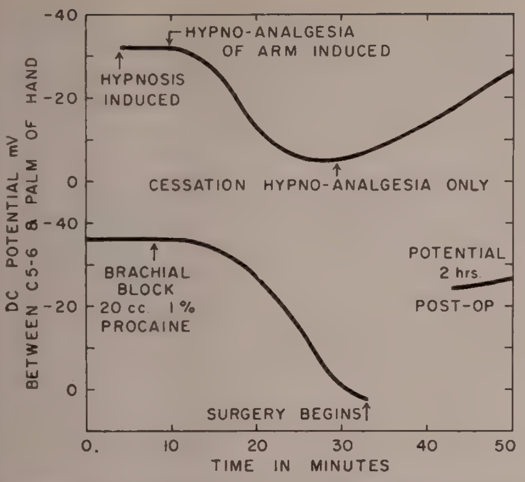

FIGURE 7. Changes in D.C. potential along limb neural gradient (upper arm to palm of hand) associated with chemical nerve block and hypnoanalgesia. In each case local anesthesia associated with drop in normal negative potential.

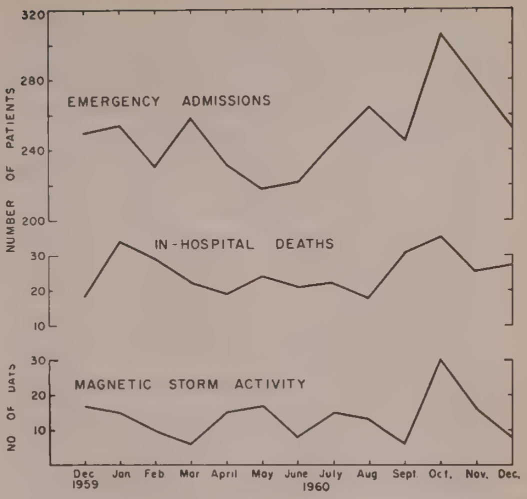

FIGURE 8. Monthly records of numbers of emergency admissions and deaths compared with number of days in which magnetic storms occurred. Magnetic storms global in occurrence and the admission and death rates determined for the Veterans Administration Hospital in Syracuse, New York, only. Rates of hospital admissions and deaths commonly do not follow a real random distribution. Graph indicates there may be relationship between this nonrandom distribution and some geophysical parameter.

D.C. gradients and the production of extremity analgesia by hypnosis. Analgesia in this case was accompanied by a drop in the D.C. potential similar to that noted with a chemical block (Fig. 7). Apparently there is some relationship between cranial areas and the peripheral D.C. gradients which is susceptible to control during the hypnotic state.

Since the cranial D.C. potential appeared to be a particularly important parameter in the state of consciousness or level of irritability in the human being, the possibility that it was the controlling mechanism for biologic cyclic behavior was considered. In a very preliminary study the transcranial D.C. potentials of 2 normal subjects and 2 schizophrenic patients were determined daily for a period of two months. A definite cyclic pattern was evident in all 4 subjects, with a periodicity of approximately twenty-eight days and with all 4 following similar cycles. However, definite differences appeared between the normal and the schizophrenic persons, the significance of which must await further study.

Two considerations of very basic importance were now entertained. First, it appeared quite likely that the organized D.C. activity of the brain was in some way closely related to general behavior, possibly as a controlling mechanism of sorts. Second, since the actual D.C. flow of charge carriers was an integral part of the system, then the operating parameters of the system could be influenced by external force fields (magnetic, electrostatic) and by such physical parameters as levels of air ionization. It is interesting to note in this regard that the suggestion has been made frequently that there is some relationship between psychiatric disturbances and geophysical parameters of the environment. If one compares the incidence of magnetic storms with the incidence of emergency hospital admissions and deaths for a year, some relationship is apparent (Fig. 8).

We have recently reported on a more rigorous statistical evaluation of this possibility.[34] The daily magnetic field intensity measured at Fredricksburg, Virginia, has been correlated with the daily psychiatric admission rate to two Syracuse, New York, hospitals during the past four years. The coefficient of correlation obtained, although low, was highly significant. Because of the crudity of the data used, this result is to be considered as indicating only some possible but promising relationship between psychiatric disturbances and some geophysical parameter, not necessarily a magnetic field. Nevertheless, it is considered highly significant that even with such crude data the result predicted by theoretical analysis was found.

Summary

The D.C. potentials measured on the surface of living organisms appear to be the result of D.C. flow within the central nervous system. This direct current appears to be a phenomenon of nerve fibers in general and is organized into a complex system which is capable of transmitting information and effecting control. Sensory inputs to the system are identified as trauma and external electromagnetic force fields. The system influences and may exert control over growth processes. It determines the basic level of irritability of the neurons themselves and may possibly be related to various aspects of psychologic functioning. This has indicated to us that any comprehensive formulation of psychiatric disorders should take into account these new parameters involving direct current neural mechanisms and their interaction with environmental physical factors.

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Treatment of the Ambulatory Hypertensive Patient*

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IN THE MANAGEMENT *of the ambulatory hypertensive patient, home blood pressure readings generally are not taken, overtreatment is avoided by instructing the patient to reduce his medication immediately if dizziness occurs, and patients usually are not told their exact readings. Drugs which are useful in therapy are the Rauwolfia alkaloids, chlorothiazide derivatives, a combination of the two, chlorothalidone derivative, hydralazine, monamine oxidase inhibitors, peripheral sympathetic blocking agents, and occasionally ganglion-blocking agents. All of these drugs may have side-effects which vary in occurrence and severity. At this time complicated therapy with the more potent drugs seems justified in the male patient with persistently elevated diastolic blood pressure and organ system involvement. However, it is not advised in women in the menopausal-age group or in elderly persons with labile diastolic blood pressures. The end result of treatment, once it is decided on, must be satisfactory blood pressure lowering, and therapy must be titrated until this is achieved.*

FIFTEEN YEARS have elapsed since the introduction of the first orally effective specific antihypertensive medications. Dramatic progress has been made since the days when the lowering of blood pressure was a therapeutic chore and units of the veratrum derivatives had to be measured meticulously in "craw units" to avoid serious side-effects. With the introduction of more effective antihypertensive drugs, adequate treatment of the patient with hypertension should no longer be approached with fear by the practicing physician. The danger of untoward side-effects has been minimized as less toxic preparations have become available so that today the question is not whether or not a patient's blood pressure can be lowered safely, as it usually can, but whether or not the lowering of the blood pressure in a particular patient will actually be beneficial.

Evidence from many centers throughout the world has been accumulated to show that the lowering of blood pressure per se is sufficient treatment to decrease mortality and morbidity in the more serious types of hypertension (Grades III and IV) if medication is administered prior to the onset of severe renal insufficiency.[1-3] The question remains as to whether or not the early treatment of a patient with a labile blood pressure (Grade I) or fixed hypertension with minimal or only moderately severe organ system involvement (Grade II) is either necessary or justified. Recent observations by Smirk[4] suggest that this may be true and that by merely lowering the blood pressure organic changes may be reversed or delayed.

The ambulatory hypertensive patients (Grades I and II) form the largest group of patients seen in practice by the general practitioner. Many of these people are asymptomatic and often lead a benign course for many years. It has been demonstrated, however, that the elevation of blood pressure for any length of time may produce secondary organic changes in the cardiac and renal vascular systems.[5] This has been re-emphasized recently by the results of the Framingham, Massachusetts, study.[6] Morbidity and mortality data in even the "mildest" cases of hypertension also indicate that longevity is decreased.[7]

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* Presented in part at the Course in Cardiology of the Westchester Academy of General Practice, November, 1960.

Although hypertension may be "benign" and many physicians are able to single out cases (especially women) whom they have observed with high blood pressure and no complications for fifteen, twenty, or even twenty-five years, the chances of a normal lifespan in an individual who becomes hypertensive before the age of forty are not good. It is hoped that prolonged treatment of the patient during the early stages of essential or renal hypertension can prevent complications and progression of the disease.

The following data summarize our experience during the past nine years with specific antihypertensive drugs in over 400 ambulatory hypertensive patients and suggest a treatment plan for these individuals.

The treatment of patients with hypertension during its early phases prior to the onset of congestive heart failure, renal failure, or cerebrovascular accidents has been greatly simplified. Hospitalization for long or even short periods of time to achieve blood pressure lowering is no longer necessary. In fact, blood pressure control under hospital conditions often is worthless since drug dosage requirements usually are much less in the hospitalized patient. Therapy is safe and can be tailor-made to the individual in view of the large number of drugs available for use.

Plan of management

All forms of treatable hypertension—namely, coarctation of the aorta, pheochromocytoma, aldosteronism, Cushing's disease, or unilateral renal or unilateral renal vascular disease—must be ruled out before any therapy is undertaken. Often this can be done clinically without recourse to complicated or expensive laboratory procedures. Treatment should be started only after a thorough explanation has been made to the patient of the reason for blood pressure lowering and the type of drugs that are to be used. Above all, optimism should be the keynote of this discussion, since most people are already too blood pressure- or "stroke"-conscious or are frightened at the very mention of the term "high blood pressure." The patient should be informed that treatment is usually effective but is not curative and that once his blood pressure is lowered some medication probably will have to be continued for the rest of his life. It is probably a good idea to mention that some side-effects may occur from drug treatment but that these are not serious and can usually be controlled by alteration of the dosage or changing to another drug. A cooperative patient is most important in any long-term treatment program.

CATEGORIES OF HYPERTENSIVE PATIENTS. The majority of patients with essential hypertension who are seen in a physician's office fall into one of three categories.

The first category includes the young male between the ages of twenty-five and forty, with a diastolic blood pressure between 90 and 110 mm. Hg with or without evidence of early left ventricular hypertrophy with mild or no albuminuria. These patients are usually asymptomatic. The prognosis in the young male with essential hypertension is not a good one if it is considered in the light of "normal" longevity. These patients should be treated despite a lack of symptoms or evidence of marked organ system involvement, and the blood pressure should be lowered to normal levels if possible. Therapy should be selected carefully and pursued until the desired result is obtained. When blood pressure lowering is achieved, as will be outlined, treatment must be continued. We and others have observed several instances of a marked "rebound" of blood pressure to unusually high levels with the onset of congestive heart failure or a cerebrovascular accident following the complete withdrawal of medication in "well-controlled" patients.

In the second category is the menopausal or postmenopausal woman between the ages of forty and fifty-five who has had slightly elevated blood pressure for many years and who is seen with a diastolic blood pressure of between 90 and 110 mm. Hg, occasionally higher. These patients are frequently obese and have many more symptoms than the first group of patients. Headaches, tiredness, dizziness, or gastrointestinal symptoms are mentioned, but very often these are unrelated to the elevated blood pressure. Albuminuria and/or left ventricular hypertrophy are usually not present. In a small number of women with higher diastolic levels cardiac hypertrophy may be noted. The prognosis of this group of individuals, if they are untreated, is considerably better than that of the younger male with an elevation of diastolic blood pressure. Treatment, although indicated, probably should not be pursued as vigorously as with the first group of male patients. If blood pressure can be returned to normal levels without inconvenience, treatment is probably justified, but a drug should be selected that will not make the patient worse. The prognosis without treatment must always be considered against the risk and/or inconvenience of therapy.

The third group consists of patients over the age of fifty-five or sixty who have a significant systolic elevation of the blood pressure with minimal if any diastolic elevation. Treatment here should be aimed at symptomatic relief, if symptoms are present, and lowering of the blood pressure only if the diastolic level is persistently over 100 to 110 mm. Hg. It is in this group of patients that more potent drugs, which produce orthostatic hypotension or a continuing salt diuresis, may produce serious side-effects such as dizziness, fainting, and renal difficulties and in whom the lowering of systolic blood pressure probably will not improve the prognosis. Treatment, if it is decided on, should be pursued with caution, and the least potent drugs should be employed.

Although patients with more advanced hypertensive disease or with complicating renal vascular disease may be seen in the physician's office, the initial management of these patients is often undertaken under controlled conditions in the hospital. Therefore the discussion that follows will not include these groups. The treatment of hypertensive emergencies and accelerated hypertension has been covered elsewhere.[3]

HOME BLOOD PRESSURE READINGS. In the management of the patient with mild to moderately severe hypertensive vascular disease (Grades I and II according to a modification of the Keith, Wagner, and Barker classification), where the less potent drugs are employed, we do not advocate routinely the use of home blood pressure recordings as other groups have urged.[8,9] We have not found it necessary to do so. Since the objective of therapy is to reduce blood pressure to normal or near-normal levels and to prevent wide fluctuations even under stress, the clinic or office readings may often suggest what happens to the patient in a tense business or family situation. It is most unusual in this group of patients to "overshoot" the mark and lower the blood pressure excessively by increasing drug dosages in an attempt to control the "stress" blood pressure readings. In the more severe cases where ganglion blockers or peripheral sympathetic blockers are necessary for treatment, blood pressure readings taken by the physician in his office might suggest that therapy is inadequate and lead to the use of excessive amounts of the more potent drugs. In these instances the argument has been advanced that blood pressure readings taken at home are more useful; these are generally lower, and the adjustment of dosages according to these readings prevents "overtreatment."

OVERTREATMENT. In our experience the danger from overtreating, even when potent agents are used, is eliminated almost completely by advising the patient to reduce his medication automatically if dizziness or faintness is experienced. The taking of blood pressure readings at home makes treatment more complicated, generally focuses the patient's attention on small insignificant pressure changes, and occasionally produces severe psychic reactions if marked variations in the blood pressure readings occur. In an occasional patient with severe disease who is receiving potent drugs and who is not under good control, home recordings for several weeks have helped in the regulation of blood pressure. It must be explained to the patient in these instances that daily and often hourly variations in readings are to be expected.

PATIENT'S KNOWLEDGE OF BLOOD PRESSURE READINGS. Much discussion has occurred with regard to whether or not patients should be told their blood pressure readings. Lay magazines actually instruct their readers that "doctors must tell you your blood pressure." Some patients who know their pressure levels report that they have taken medication in the past and have "responded well" with a fall in blood pressure from 200 to 185 mm. Hg. Others feel disappointed when pressures rise from 165 to 170 mm. Hg from one visit to the next. Because of the average patient's inability to interpret correctly these minor changes in blood pressure and because of the resultant psychic effects of these misinterpretations, we usually do not inform the patient of his or her readings. Rather, he is told: "Your pressure is responding" or "You are doing nicely, but a slight change in medication is necessary for your pressure to be controlled even more adequately." Some patients are given a general idea of the levels of their blood pressure if they travel a great deal where medical care in other areas might become necessary. Hypertensive patients should be encouraged and the disease and its treatment underplayed rather than overemphasized.

The specific antihypertensive drugs that we have found to be most useful are outlined in Table I. Other nonspecific agents such as the barbiturates and the meprobamate derivatives will not be discussed but are certainly useful adjuncts in the treatment of any hypertensive patient. These can be used, as necessary, to supplement the drugs which will be discussed.

TABLE I. Antihypertensive drugs

Drugs	Average Daily Dose (Mg.)*	Mode of Action
Rauwolfia		
Whole root	50 to 100	Central action on sympathetic system; peripheral depletion of catecholamines
Fractions		
Alseroxylon	2	
Reserpine	0.25	
Chlorothiazide and derivatives	1 Gm.	Orally effective diuretics
Hydrochlorothiazide	50 to 100	Probably reduces blood pressure by salt excretion and lowered blood volume; Specific antihypertensive effect?
Benzydroflumethiazide	5 to 10	
Chlorthalidone derivative	100 (three times a week)	
Hydralazine	200 to 250	Probably direct effect on peripheral vessels; blocks some circulating pressor substances
Monamine oxidase inhibitors		
Isocarboxazid	20 to 40	Inhibits breakdown of catecholamines; exact antihypertensive mechanism unknown
Guanethidine sulfate	20 to 200	Peripheral blockade of sympathetic nervous system
Mecamylamine hydrochloride	10 to 50	Ganglion blocker (of both parasympathetic and sympathetic systems)

* Unless otherwise indicated.

Antihypertensive agents

RAUWOLFIA DRUGS. In our experience the Rauwolfia drugs, which have long been used as the initial therapy in most cases, have been disappointing as drugs which are effective by themselves in the treatment of patients with even mild hypertension. Although these agents often produce a bradycardia and a mild sedative action, normotensive blood pressure levels are achieved in only a small number (approximately 20 per cent) of people treated. The Rauwolfia drugs act centrally and probably also play a role in causing a more rapid dissipation of some of the pressor amines such as serotonin and norepinephrine.

The major side-effects of the Rauwolfia drugs include psychic depressions and the possible activation of gastric ulcers. They should probably not be used in depressed individuals or in patients with an ulcer history. Weight gain is also a common side-effect of Rauwolfia administration. In obese individuals who are on a weight-reduction program it is best to avoid the use of these agents, lest a further weight gain produce additional emotional difficulties. If these drugs were potent or lifesaving, one might overlook this latter side-effect, but in view of the mild action and lack of high percentage success of the Rauwolfias, they probably should not be used in obese patients.

The choice of the Rauwolfia preparation to be used is not a critical one. In our experience emotional difficulties have occurred less frequently when the whole root of the drug (Raudixin) has been employed. When they are used in combination with other agents, the Rauwolfia drugs have definitely reduced the amount of the more potent drugs that may be necessary in treatment. These drugs probably still have a place in the routine management of the ambulatory hypertensive patient for the preceding reasons. The dosage is not critical and should be kept at a minimum. In our experience better results are not obtained by doubling or tripling the dosage of the Rauwolfia drugs. The suggested dosage range is noted in Table I.

CHLOROTHIAZIDE DERIVATIVES. The chlorothiazide derivatives probably produce blood pressure lowering by virtue of sodium loss and contraction of blood volume.[10] Some contrary data suggest a "specific" antihypertensive effect,[11] but this has not been confirmed. This group of drugs has proved to be the most effective in the treatment of the patient with mild to moderately severe hypertension without serious renal disease. In those patients with severe renal insufficiency chlorothiazide and its derivatives should be used with great care. In many instances a further reduction of renal flow with increasing azotemia occurs as a result of blood pressure lowering. Renal failure is not, however, an absolute contraindication to the use of diuretic therapy if the blood urea nitrogen is below 70 mg. per 100 ml. and a chlorothiazide drug is deemed necessary to achieve adequate blood pressure lowering. Experience has indicated that in many instances the blood urea nitrogen will rise as blood pressure falls but after a period of from one to three weeks will return to pretreatment levels.

There are few important side-effects from the use of chlorothiazide and similar agents in the ambulatory hypertensive patient. One of the most troublesome is the precipitation of gout. In a large number of patients these drugs produce an elevation of serum uric acid, and in a smaller percentage attacks of gout occur. All patients, especially those in the middle- or older-age groups, should have a uric acid determination done after from four to six weeks of diuretic therapy, especially if any joint symptoms occur. Ideally, blood level determinations should be performed before and at frequent intervals after therapy has begun, but this is usually impractical. If the uric acid level becomes elevated and blood pressure lowering cannot be achieved without these drugs, the concurrent use of probenecid (Benemid), one or two tablets daily, has proved to be a satisfactory method of combating this potentially annoying side-effect.

The lowering of blood potassium by the chlorothiazide derivatives presents the most serious disadvantage to the routine use of these drugs, especially in elderly individuals or in patients with renal impairment. The majority of patients on long-term therapy maintain normal serum potassium levels and do not experience either electrocardiographic or clinical signs of hypokalemia. The possibility exists, however, that serum levels do not reflect actual potassium loss and that chronic depletion, even of a minor degree, may produce long-term organic effects especially on the renal tubules. For this reason, some form of potassium supplements should probably be added to the regimen of the patient who receives continuous chlorothiazide therapy. Skin rashes, purpura, and blood dyscrasias also have occurred in rare instances as a result of the use of these drugs.

The choice of the diuretic to be used is not a critical one. Although on a milligram for milligram basis many newer agents are more potent than the original chlorothiazide preparation (Diuril), the end result of treatment, namely sodium loss and blood pressure lowering, is almost identical with most of the derivatives. Potassium loss may be somewhat less with the benzydroflumethiazide group. Commercially available preparations that contain potassium supplements may offer some advantages over the others, since fewer pills need be taken. For example, Naturetin c K contains 500 mg. of potassium in each tablet. On the usual twice-a-day dosage, 1 Gm. of extra potassium is given. Esidrix-K contains as much as 1 Gm. of potassium in each tablet.

COMBINATION THERAPY. Many Rauwolfia-chlorothiazide derivative-potassium combinations have been made available during the past five years. Although much is to be said against "shot gun" or combination therapy in most diseases, many patients do well on Rauwolfia-diuretic combination therapy. Instead of four to six or even more tablets daily, only two or at most three are needed. This gives the patient a feeling of not being overmedicated or being sick enough to require "lots of drugs." Since the dosage of the Rauwolfia drugs is not critical, an extra tablet to provide more diuresis or one less tablet to provide less diuresis, will often not change the patient's response or increase the side-effects. The availability of different dosage strengths of the Rauwolfia-chlorothiazide derivative combinations gives the physician a wide range of dosages to choose from. The preparation that we have found most satisfactory for routine use has been Rautrax-N (50 mg. Rauwolfia serpentina whole root, 4 mg. benzydroflumethiazide, and 400 mg. potassium chloride, one tablet twice daily). If a combination tablet without additional potassium is desired for a specific reason, Enduronyl (5 mg. Enduron and 0.25 mg. Harmonyl) is a satisfactory preparation.

In many instances the potassium supplements present in the combination tablet may not be enough to provide adequate potassium replacement. The use of orange juice, bananas, paprika, dried apricots, and in some instances supplemental potassium chloride, in the form of the 1-Gm. tablet or liquid potassium triplex, may be indicated. This is especially true in patients with renal disease or in those receiving digitalis.

Utilizing a Rauwolfia and chlorothiazide derivative in combination, normotensive blood pressure levels can be achieved in more than 60 per cent of patients with mild to moderately severe (Grades I and II) essential or renal hypertension.

CHLORTHALIDONE DERIVATIVE. Our experience with a chlorthalidone derivative (Hygroton) is limited, but this drug appears to be a suitable substitute for chlorothiazide if sensitivity or tolerance develops to the latter. Since this drug is longer-acting, it may be given once every other or every third day.

HYDRALAZINE. The use of hydralazine (Apresoline) has been limited during the past five years following reports of the occurrence of a lupus-like or rheumatoid-like syndrome in patients who received large doses of the drug.[12] Our experience with over 250 patients who have received hydralazine during the past eight years has indicated that this syndrome is rare or nonexistent in patients if the dosage range is kept under 300 mg. per day. This symptom complex when it does occur is completely reversible and disappears when medication is stopped. In rare instances symptoms will persist for several months,[13] and the patient will require steroid therapy.

We believe that this drug is useful and should be utilized in the treatment of patients with moderately severe disease if a response to the Rauwolfia-chlorothiazide combination is not forthcoming. The dosage should be increased gradually over a seven- to ten-day period to a maximum of approximately 200 to 250 mg. per day given in four divided doses. The drug should be used with great care in patients with angina or with a previous history of congestive heart failure and/or pulmonary edema because of the increase in cardiac work which may occur as a result of the hydralazine-induced tachycardia. An increase in the heart rate is rarely noted, however, in a patient who has received Rauwolfia drugs first. Combination hydralazine-Rauwolfia and diuretic therapy will result in normal blood pressure levels in over 70 per cent of the patients with moderately severe hypertension.

MONAMINE OXIDASE INHIBITORS. In patients who do not respond to Rauwolfia and/or chlorothiazide or in whom there is a contraindication to the use of one of these drugs, the substitution or addition of a monamine oxidase (MAO) inhibitor such as isocarboxazid (Marplan)* or one of its derivatives often will result in a more satisfactory response.[14] Comparative studies have demonstrated that at present isocarboxazid is the most satisfactory drug of its type for the treatment of hypertension. In the depressed patient or the patient with angina pectoris, psychic stimulation or partial relief of chest pain is frequently seen in addition to blood pressure lowering following the use of this drug. Since orthostatic hypotension frequently results from treatment with an MAO inhibitor, especially when it is combined with diuretic therapy, the patient must be cautioned against standing up suddenly, especially during the first few weeks of treatment. He must be cautioned to reduce drug dosage automatically if dizziness or faintness occurs. In this way serious side-effects will be eliminated. A definite delay in blood pressure response has been noted with isocarboxazid, so that blood pressure lowering should not be expected for approximately seven to ten days. The dosage, therefore, should be kept stable during the first week and should not be increased until after a ten-day period of observation. MAO inhibitors should be used with care in elderly individuals or in patients with a history of cerebrovascular accidents because of the orthostatic effects.

PERIPHERAL SYMPATHETIC BLOCKING AGENTS. In patients with a marked elevation of diastolic blood pressure (in excess of 120 to 130 mm. Hg), the blood pressure occasionally may not be controlled by the use of all of the previously mentioned agents either alone or in combination. In these instances, more potent therapy should be utilized in addition to the other drugs. If a patient is cooperative and intelligent and care is taken to explain drug action and possible side-effects, the use of one of the newer peripheral sympathetic blocking agents such as guanethidine sulfate (Ismelin sulfate) can be undertaken on an outpatient basis. The dosage must be titrated more carefully than with the less potent drugs, and the patient must be examined more frequently. Since orthostatic effects are also noted with guanethidine sulfate, the patient should be cautioned about them. In patients who have not responded to Rauwolfia and chlorothiazide in combination with either an MAO inhibitor or hydralazine, the addition of guanethidine sulfate will lower the blood pressure to normotensive or near normotensive levels in a large percentage of cases. The dosage may be given on a twice-a-day basis or even occasionally once a day because of the long duration of action of the drug. Some blood pressure-lowering effect is usually noted within forty-eight hours after the onset of treatment. The drug is cumulative, and the maximum effect may not be observed for from three to five days. Either 5 or 10 mg. are administered twice daily during the first three to four days, and the dosage is increased gradually after that time until the desired effect is obtained. The average effective dose of guanethidine sulfate has been approximately 30 to 50 mg. per day when it is utilized in combination with other drugs Refractory patients have occasionally required between 200 and 300 mg. daily. The dosage may be reduced slowly after a satisfactory blood pressure lowering has been achieved and maintained for at least a two- to three-month period.

Important reactions to guanethidine sulfate have been limited to postural effects and diarrhea. This latter symptom is often severe but can be controlled by the concurrent use of deodorized tincture of opium or other "constipating" agents.

Excellent blood pressure control also has been obtained with bretylium tosylate (Darenthin), another sympathetic blocking drug, but unfortunately, tolerance develops within a short period of time in most patients who receive this drug.

GANGLION-BLOCKING AGENTS. Although it usually is not necessary to employ ganglion-blocking agents in the treatment of the ambulatory hypertensive patient, especially in view of the excellent results obtained during the past year with the use of guanethidine sulfate, an occasional patient will require the use of a ganglion-blocking agent to obtain a satisfactory result. These individuals have sustained fixed high diastolic blood pressures and definite evidence of multiple organ system involvement. Most often they should be hospitalized. Occasionally, however, with an intelligent patient, treatment is possible on an ambulatory basis.

The ganglion blockers are by far the most potent antihypertensive drugs available. In addition to a sympathetic block, these agents produce a simultaneous blockade of the parasympathetic nervous system with the attendant side-effects such as dryness of the mouth, severe constipation, bladder difficulty, and postural hypotension, occasionally of a severe degree.

Of the many ganglion-blocking agents available, we have found mecamylamine hydrochloride (Inversine hydrochloride) the most effective and easiest agent to employ. This drug is absorbed almost completely from the gastrointestinal tract. In combination with the less potent drugs, the dosage requirement of mecamylamine hydrochloride is usually low enough so that side-effects are minimal. Treatment is begun with 2.5 mg. once daily and gradually increased by increments of 2.5 mg. every three days until the desired blood pressure effect is obtained. It is important to judge the effect by the standing blood pressure since occasionally, if the recumbent pressures are used, the true drug effect is not recognized, and an excessive amount of medication may be given. As soon as a satisfactory blood pressure change toward normotensive levels is noted, a further increase in the dosage should be withheld for a few days to a week and the patient observed before therapy is increased. If patients are instructed regarding the potential side-effects of the ganglion-blocking agents, few serious reactions will occur. They should be cautioned, as with guanethidine sulfate, that if dizziness, weakness, or faintness occurs on standing, the dosage of the drug should be reduced automatically.

Conclusion

It is apparent from the preceding discussion that the effective treatment of the more severe forms of hypertension is often a difficult, expensive, and complicated procedure. However, abundant evidence has been accumulated by many observers which suggests that effective blood pressure lowering will improve the prognosis in these cases. The difficulties in treatment would appear to be justified. It remains to be proved, however, whether or not there is an increase in longevity and decrease in morbidity as a result of the treatment of the ambulatory hypertensive patient with lesser degrees of organ system involvement. It is for this reason that many physicians delay the onset of therapy or are reluctant to use combinations of drugs or to add more potent agents to the basic therapy with the Rauwolfia-chlorothiazide derivatives in the patient with a less severe hypertensive condition even when the blood pressure remains elevated.

Our experience has indicated that in many cases, especially in the male patient with persistently elevated diastolic blood pressure and organ system involvement, effective blood pressure lowering can be obtained only by the use of multiple drugs and often only by the use of the more potent agents. In these individuals for whom the prognosis is relatively poor, the inconvenience of multiple drug therapy would appear to be justified while awaiting the results of longer-term evaluation of a large series of treated cases. However, in women in the menopausal-age group or in elderly persons with labile diastolic blood pressures, complicated therapy would not appear to be justified at this time. If these patients respond to simple treatment, perhaps some benefit will result, but at least no harm will be done. It would appear that a middle-of-the-road approach is the sensible one for the physician to follow at this time, leaving the enthusiastic vigorous treatment to those who are engaged in the long-range evaluation of the problem.

As foolhardy as it may seem to state that all patients achieve a good result and will live longer when their blood pressure is lowered to normal levels, it is equally foolhardy to "treat" a seriously ill hypertensive patient with fixed diastolic pressures only with drugs, such as the Rauwolfia drugs, which have not proved effective in advanced cases. Another example of this is mebutamate (Capla), a centrally acting derivative of meprobamate. Occasionally this drug may lower the blood pressure in an early labile hypertensive patient but certainly should not be expected to be effective in most cases of moderately severe or severe disease.

Often physicians and patients alike believe that "hypertension is being treated" when these relatively ineffective agents are used as the sole treatment in severe cases, and it is only after the occurrence of a cerebral accident or signs of early renal failure that both parties realize that the therapy has been inadequate. The end result of treatment, once it is decided on, must be satisfactory blood pressure lowering, and therapy must be titrated until this is achieved. This is not to say that vascular complications never occur in the vigorously treated hypertensive individual. We have seen episodes of cerebral thrombosis and myocardial infarction occur in patients whom we have considered to be adequately controlled. It is our impression, however, as we have reported previously,[3] that the incidence of these complications is considerably less in patients whose blood pressure has been lowered satisfactorily. Additional proof of this impression is required.

It is the hope that adequate treatment of the patient during the early stages of essential or renal hypertension may prevent or delay the onset of the complications of the disease.

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Mass casualty plan in hospitals

Over five years ago the Joint Commission on Accreditation of Hospitals made the request that in every hospital "there should be a written plan for the care, reception, and evacuation of mass casualties, and that this plan should be coordinated with the inpatient and outpatient services of the hospital. The plan should be rehearsed by key personnel at least twice yearly."

This recommendation was made because it was known that the great majority of hospitals had no coordinated plan for such purposes, and if there was a plan few of the personnel were aware of it. For the most part, hospitals have cooperated, and the Commission has several dozen letters saying, "Thank goodness for this requirement; we were prepared when disaster struck."

This recommendation was originally made to care for local fire, tornado, explosion, poisoning, or transportation accidents. Reports still show, however, that close to 30 per cent of the hospitals surveyed have not carried out our recommendation on this specific item. This should be done immediately.

Now the President of the United States has stressed the need for improving and expediting all facets of Civil Defense. It is essential that every hospital disaster plan be reviewed constantly in the light of developments, local and national. If it is to prove effective, it must be disseminated and known not only to the staff and personnel but to the community, its police, fire, and welfare departments, public utilities, and communications and transportation facilities. In turn it should be an integral part of the State Operational Survival Plan.

Intravenous Abdominal Aortography and Peripheral Arteriography

Diagnostic Value in Arteriosclerotic Abdominal Aortic and Peripheral Vascular Disease*

A MODIFICATION *of the intravenous method of angiocardiography has made possible abdominal aortography and peripheral arteriography by rapid, simultaneous, and bilateral injections of concentrated organic iodides after accurate determination of the circulation time. Over 500 patients have had abdominal aortography and peripheral arteriography with this method. This method is particularly suited for the diagnosis of arteriosclerotic abdominaal ortic and peripheral vascular disease, especially to determine whether or not constructive surgery is indicated and to assess the results of reconstructive vascular surgery, and has advantages over the translumbar method of aortography. It is important to select for intravenous aortography only those patients who are likely to benefit from such studies.*

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In 1959,[1] A MODIFICATION of the Robb-Steinberg intravenous method of angiocardiography, by making rapid, simultaneous, and bilateral injections of concentrated organic iodides after accurate determination of the circulation time, made possible abdominal aortography and peripheral arteriography. Inexpensive needle stopcock units, special 12-gauge syringes, and the use of x-ray equipment which is ordinarily available for gastrointestinal or genitourinary roentgenography make this method of intravenous abdominal aortography and peripheral arteriography readily available for use in the average hospital.

Over 500 patients have had abdominal aortography and peripheral arteriography with the intravenous method which is herein described. In this paper, the essential features of the method and an illustration of its value in the diagnosis of arteriosclerotic abdominal aortic and peripheral vascular disease will be presented.

Method

The intravenous method of abdominal aortography and peripheral arteriography depends on the principles which have been developed for angiocardiography.[1,2] The speed of injection of the contrast medium is essential, and this is accomplished by simultaneously injecting the large veins of both arms. This eliminates the factor of dilution of the contrast material by blood from the opposite innominate vein when only one injection is made and, of course, increases the bolus effect of the contrast material into the circulation. The speed of injection is facilitated also by elevating the arms and having the patient perform respiratory maneuvers.

The time of roentgen exposure of the abdominal aortic or peripheral arteriogram is determined by the preliminary circulation time with sodium dehydrocholate (Decholin Sodium). A standard roentgen technic similar to that of intravenous pyelography, which makes use of the Bucky-Potter grid, is all that is needed for roentgenography of

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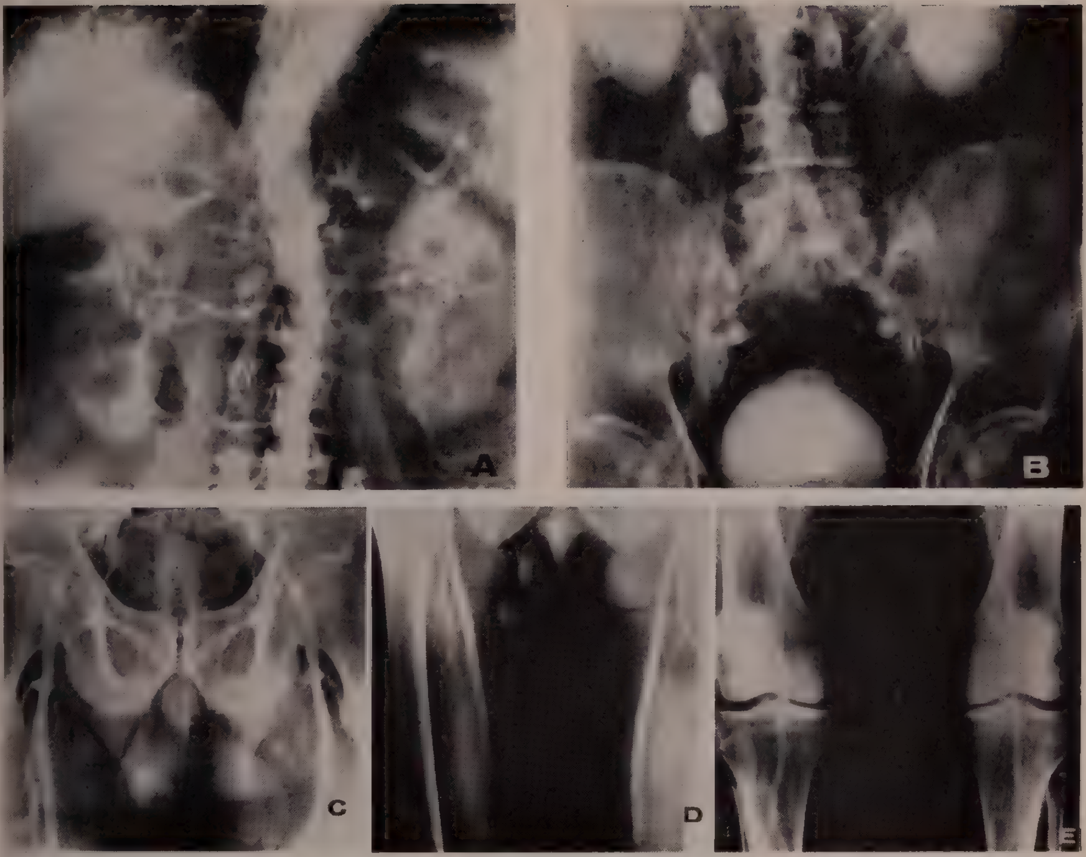

FIGURE 1. Arteriosclerosis and tortuosity of abdominal aortic, aorto-iliac, iliofemoral, and femoral-popliteal arterial systems in sixty-five-year-old man (blood pressure, 136/74). Aorta opacified by bilateral and simultaneous intravenous method of abdominal aortography and peripheral arteriography. Multiple serial exposures utilizing an automatic 12- by 12-inch cassette-shifter permitted study of the abdominal aorta and its branches to the ankle. The body was shifted automatically over the film-changing device during the predetermined circulation time. (A) Abdominal aorta. (B) Bifurcation of abdominal aorta and intact, albeit tortuous, common iliac arteries. (C) Iliofemoral arteries. (D) Sclerotic but intact superficial and deep femoral arteries. (E) Normal femoral-popliteal arterial tree.

the abdominal aorta and its branches. The percutaneous insertion of the Robb-Steinberg 12-gauge needle stopcock unit has been described previously.[3,4] In the absence of a large vein, it may be necessary to perform a cutdown for insertion of the needle. The position of the cannula is then secured by adhesive tape. To make certain that the cannula is properly seated in the vein, an injection of normal physiologic saline to safeguard against extravasation is advisable. The patient is then briefed about the technic of the examination and is instructed about breathing during the examination.

The determination of the preliminary circulation time with the patient supine will serve as a good rehearsal of the patient's participation in the test. Three ml. of a 20 per cent solution of sodium dehydrocholate are mixed with 15 ml. of saline in a 50-ml. syringe and attached to one of the cannulas. Then the arm is elevated, making certain that it is relaxed at the shoulder (this avoids physiologic obstruction of the subclavian vein underneath the first rib). The stopcock is opened, and the patient is instructed to breathe out gently. Then he is asked to breathe in making certain that only a moderate breath is taken, for it is important to avoid the Valsalva maneuver, which tends to delay circulation into the heart. An injection of the sodium dehydrocholate-saline mixture is made simul-

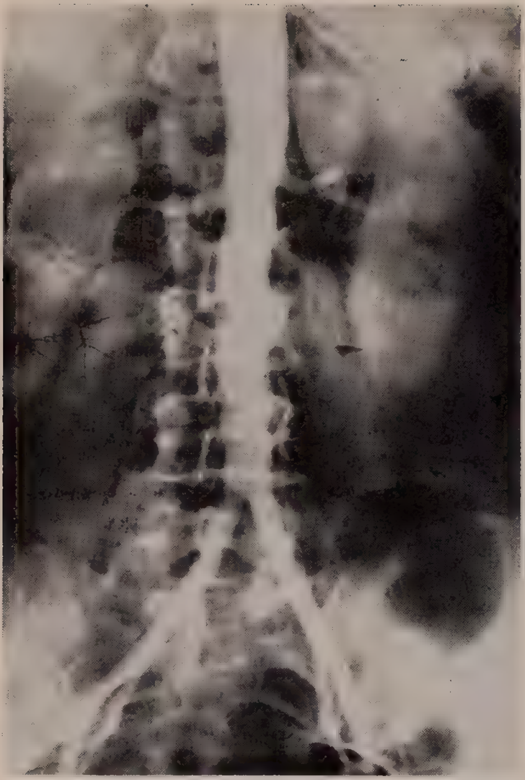

FIGURE 2. Normal intravenous abdominal arteriogram of fifty-three-year-old woman who had an unusually pulsatile aorta that was suspected of being aneurysmal. This film also was made with the automatic multiple-cassette apparatus. Note unusually fine details of the origins of the renal arteries.

taneously with the direction to breathe in. This is also the signal for the technician to start the stop watch. The patient is told to anticipate a bitter taste, and once the injection is completed, he is urged to go through the motion of tasting by smacking the lips, tongue, and mouth. This automatically releases the tendency to perform the Valsalva maneuver. The onset of the bitter taste is recorded by the stop watch. The modified circulation time from arm to tongue is used as a guide for the starting time of the roentgen exposure of the abdominal aorta. If the accuracy of this determination is uncertain, a repeat circulation-time determination is done. The exposure for abdominal aortography is prolonged to two or three seconds and begins one-half second after the circulation time.

The patient is told to anticipate an intense wave of heat soon after the injection of the contrast medium and is assured that it will pass quickly. Then all is ready for aortographic study. The special (12-gauge) Robb-Steinberg syringes are loaded with concentrated organic iodide contrast material, the amount depending on the weight of the patient. A dose of 1 ml. per kilogram of body weight, divided equally for injection into each arm, is advised. Up to 50 ml. in each arm may be necessary for obese patients over 200 pounds. The syringes are attached to the cannulas, the stopcock is opened, and the arms are elevated with a physician standing on a platform on each side of the patient. At the signal, "breathe in," the technician starts the stop watch, and the simultaneous injections are made rapidly and completed in one and one-half to two seconds. Because of viscidity the concentrated contrast agent may be difficult to inject rapidly unless the mixture is warm. The patient is told to breathe naturally. Two or three seconds prior to the selected exposure time, the patient is ordered to stop breathing. A two-second roentgen exposure for abdominal aortography is made while the patient holds his breath. If peripheral arteriography is desired, another exposure of three seconds duration may be made either with a portable roentgen apparatus or with another x-ray tube. The standard grid-cassette technic for lower-extremity roentgenography suffices. If, after inspection, the roentgenogram proves satisfactory, the cannulas may be removed and a tight, temporary bandage applied. There should be no hesitancy in repeating the injection after a short interval, if the patient has tolerated the procedure. Also, if the peripheral circulation at the bifurcation of the iliac arteries is desired, the Bucky grid-cassette may be shifted to include the extremities, and another injection may be made. Pyelography is usually secured five minutes after the completion of the peripheral vascular studies.

Findings

Recently, a motor-driven table which shifts the position of the patient over a 12- by 12-inch, commercially available, auto-

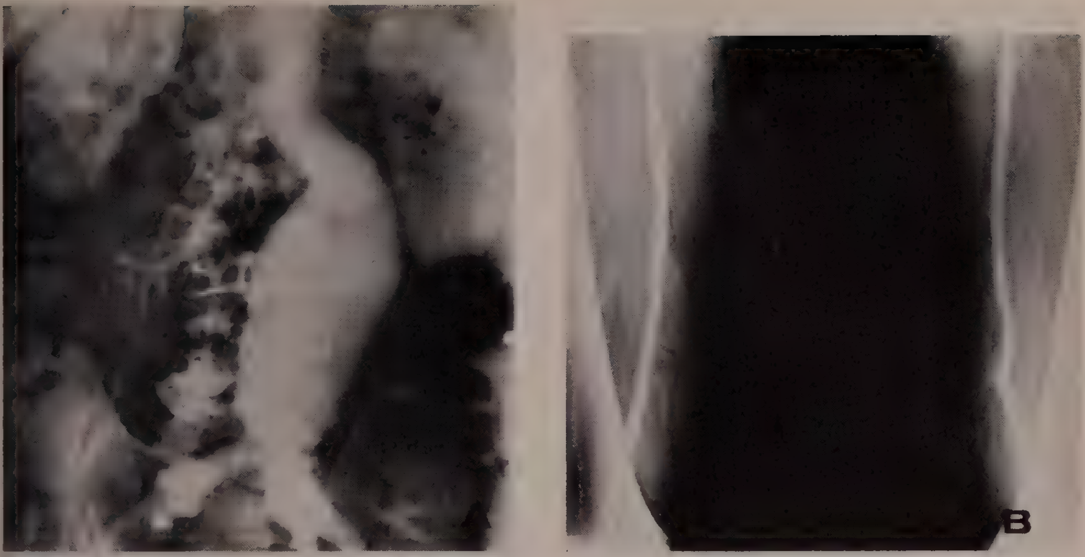

FIGURE 3. Huge arteriosclerotic aneurysm of abdominal aorta successfully resected and replaced by a prosthesis in sixty-four-year-old man. Here also multiple-exposure technics were made. (A) Intravenous abdominal aortogram showing huge aneurysm well below intact renal arteries. (B) Excellent runoff into intact superficial femoral arteries.

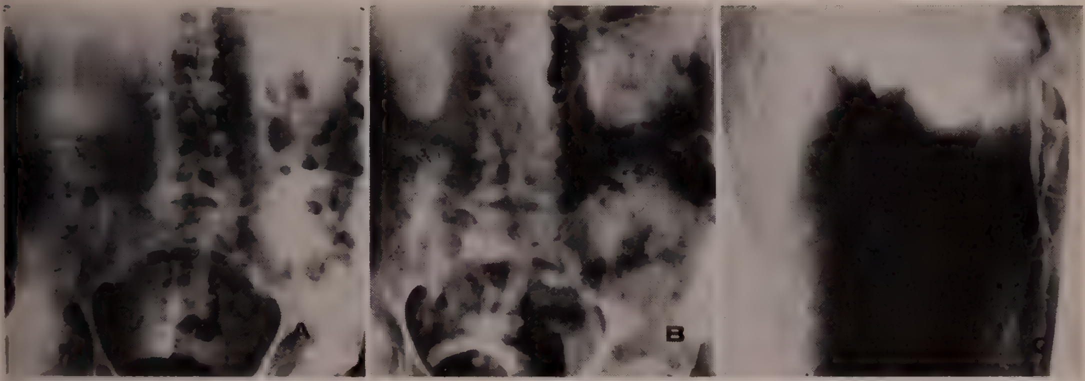

FIGURE 4. Huge sacciform abdomino-iliac arteriosclerotic aneurysm in sixty-two-year-old man with occluded superficial femoral arteries and poor runoff, precluding operation. (A) Control (12- by 12-inch) film showing centrally placed mass extending from second to fifth lumbar vertebrae and lined by calcific walls. (B) Intravenous abdominal aortogram showing origin of aneurysm very close to and probably involving renal arteries. Note huge abdomino-iliac aneurysm lined by thrombus containing calcific outer margins. (C) Poor runoff into legs owing to occlusion of both iliofemoral arteries. Note absence of opacification in calcified right superficial femoral arteries which are in marked contrast to hypertrophied deep femoral arteries. Operation not advised.

matic, serial cassette-changer has been used. This permits a series of exposures beginning at the upper abdomen and ending at the feet (Fig. 1). The method of securing abdominal aortic and peripheral vascular opacification with bilateral simultaneous intravenous injections, however, is unaltered. The shorter exposures which the new apparatus makes possible enhance the visualization of the origins of the renal arteries (Fig. 2). The multiple exposures also make the visualization of the abdominal aorta practically certain with the first injections, especially in the case of abdominal aortic aneurysm wherein blood flow may be unusually slowed (Figs. 3 and 4).

Buckling of the abdominal aorta and common iliac arteries owing to arteriosclerosis

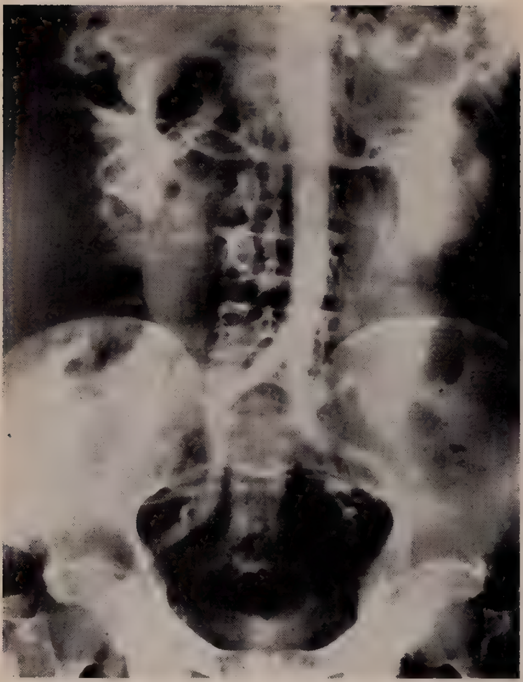

FIGURE 5. Arteriosclerotic tortuous, intravenous abdominal aortogram in sixty-two-year-old man (blood pressure, 140/80). Note tortuous common iliac arteries.

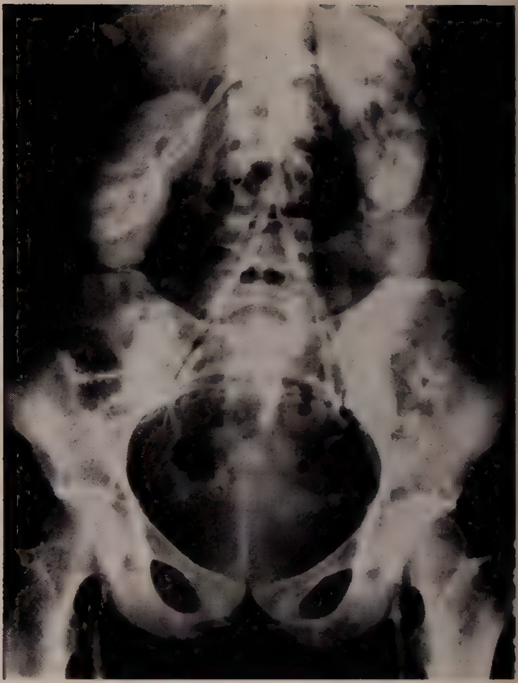

FIGURE 6. Marked arteriosclerotic abdominal aortic endarteritis in forty-three-year-old cigaret-smoking woman (blood pressure, 130/70). Endarterectomy five years earlier was followed by recurrence of severe intermittent claudication. Note marked narrowing of aorta below intact renal arteries and almost complete aortic occlusion at level of the body of the third lumbar vertebra. Below this the aorto-iliac arterial system is markedly hypoplastic. Operation denied patient until she stops smoking.

is demonstrated in Figure 5. The severe arteriosclerotic endarteritis of the abdominal aorta and aortoiliac arterial system (Figs. 6 and 7) in 2 women was striking in that there was marked narrowing and irregularity of the abdominal aorta with hypoplasia of the iliofemoral arterial tree. In 1 patient (Fig. 7) the markedly increased left lower abdominopelvic collateral circulation was owing to partial occlusions of the left common iliac and superficial femoral arteries. Complete thrombotic occlusion of the abdominal aorta below intact renal arteries (the Leriche syndrome) are shown in Figures 8A and 9A. In 1 patient (Fig. 8B) the runoff into intact, although hypoplastic, superficial femoral arteries is strikingly different from that in the other patient whose left common iliac and superficial femoral arteries are partially occluded (Fig. 9B). In another patient who was studied because of a calcific mass adjacent to the left border of the first lumbar vertebra, a poorly filled abdominal aorta was revealed just proximal to the bifurcation of the aorta (Fig. 10A). Aortotomography (Figs. 10B and 10C) demonstrated that the abdominal aorta was intact, but markedly narrowed and with arteriosclerotic plaques along the lower abdominal aortic walls, especially at the bifurcation. The calcified mass, which was seen in the conventional abdominal roentgenogram, was found to be the enlarged and tortuous origin of the inferior mesenteric artery (Fig. 10C). Arteriosclerotic peripheral vascular disease is demonstrated in a patient owing to occlusion of the right superficial femoral artery at the lower third of the right thigh (Fig. 11); in another patient the occlusion was at the left midthigh (Fig. 12).

Comment

Advances in the surgical treatment of atherosclerosis obliterans of the abdominal

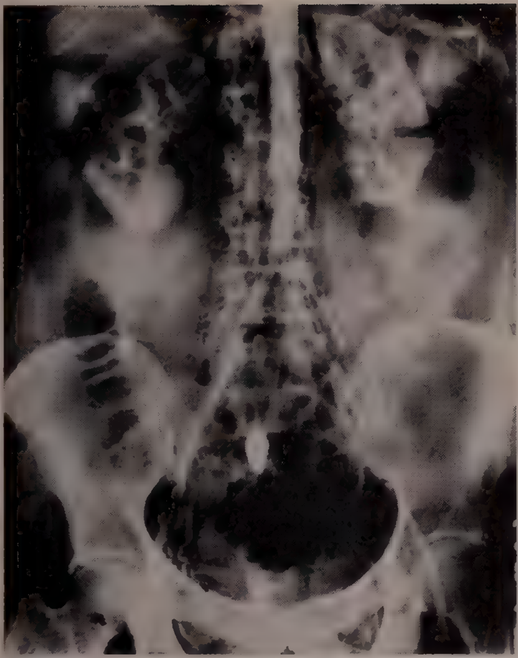

FIGURE 7. Severe arteriosclerotic endarteritic involvement of abdominal aorta and peripheral vascular system in forty-eight-year-old woman. Note diminution in caliber of abdominal aorta at level of the body of the second lumbar vertebra. Left common femoral artery partially occluded from the bifurcation of the aorta to the brim of pelvis. The iliofemoral arteries are hypoplastic. The increased left lower abdominopelvic arterial collaterals are striking. Note iophendylate (Pantopaque) residue in spinal canal owing to myelographic study for suspected spinal disk lesion.

aorta and its major branches, especially the iliac, femoral, and popliteal arteries, has made the diagnosis of disease of these conditions of practical rather than of academic importance. The major sites of obliterative disease occur in the abdominal aorta distal to the renal arteries and in the large arteries leading to and in the lower extremities.[5] The earliest obliterative changes usually occur at or just proximal to the major bifurcation of the arteries. As a result of the gradual and insidious obliteration of the abdominal aorta, which fortunately spares the renal arteries, there is intermittent claudication of the hip, buttock, low back, and calf with easy fatigability.[6-8] With further extension of the process there is involvement of the femoral and popliteal arteries and finally gangrene of the toes.

Palpation of the peripheral pulses, oscillometry, and skin temperature determination are obviously important for the diagnosis of peripheral vascular disease. Indeed, when these simple procedures are performed carefully and thoroughly, a high degree of accuracy in the localization of the occlusive site results. However, it is generally agreed[8,9] that abdominal aortography and peripheral arteriography are essential to determine whether or not constructive surgery is indicated, and of course, to assess the results of reconstructive vascular surgery.[10]

Percutaneous femoral arteriography by simply injecting a dilute organic iodide via an 18-gauge needle inserted into the femoral artery in the groin is usually well tolerated and uncomplicated and results in satisfactory visualization of the ipsilateral lower extremity. This, however, requires a contralateral injection of the opposite femoral artery when both lower extremities need to be compared. These studies, however, do not provide data regarding the condition of the abdominal aorta and iliofemoral tree. Translumbar aortography, therefore, has been widely used.[9-11] In many hands and in thousands of examinations it has been unassociated with untoward reactions. Because of increasing reports of serious complications and death following translumbar aortography,[1,8,11] there has been great reluctance, chiefly because of medicolegal considerations, to use this method. Accordingly, the intravenous method reported previously, although not entirely devoid of fatality,[2] is recommended.

Percutaneous retrograde femoral arteriography as proposed by Seldinger[12] and others[13-16] has come into general use also, especially for renal arteriography. Indeed, it has recently been proposed for aortocerebral angiography.[17] However, it would appear contraindicated in patients with abdominal aortic disease proximal to the femoral arteries. Because of partial arteriosclerotic involvement of the abdominal aorta (Figs. 6 and 7), catheterization of the vessel might cause dislodgment of a thrombus. In the case of total abdominal aortic occlusion owing to arteriosclerosis (Figs. 8A and 9A) and aneurysm (Figs. 3B and 4A), there is the added danger of rupture of

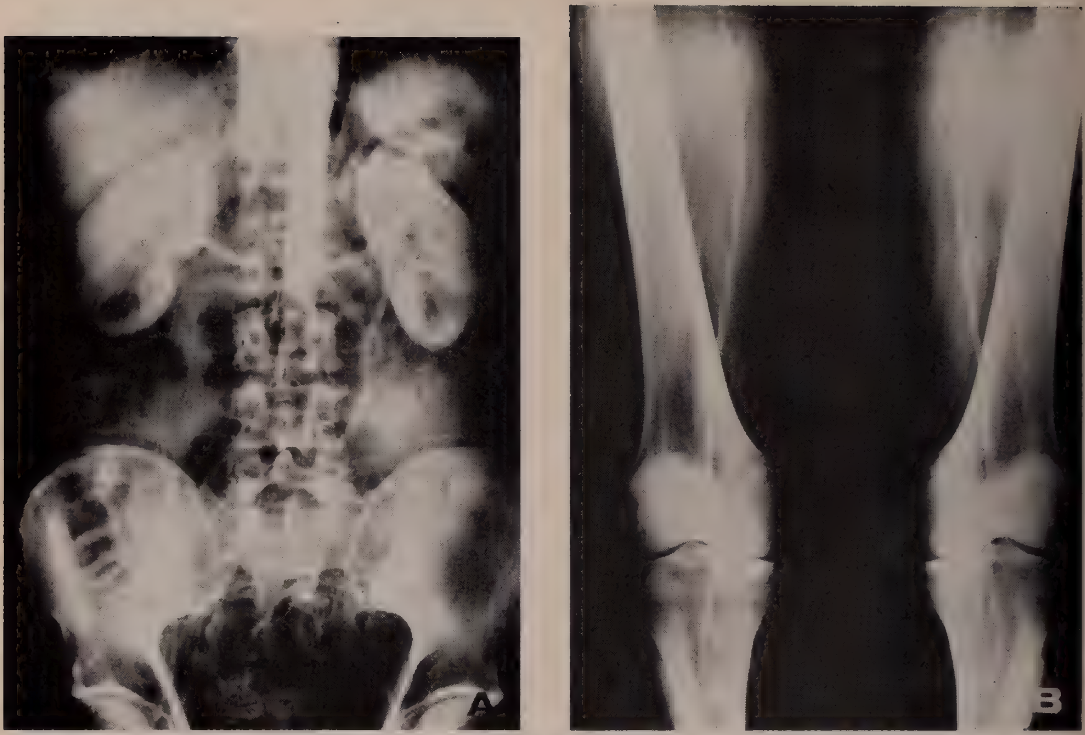

FIGURE 8. Thrombotic occlusion of abdominal aorta (Leriche syndrome) in fifty-three-year-old man successfully treated by endarterectomy, with subsidence of severe disabling hip and leg intermittent claudication. (A) Intravenous abdominal aortogram. Note large left inferior mesenteric artery anastomosing below with hemorrhoidal branches in pelvis. (B) Intact but markedly hypoplastic runoff in legs.

the aorta or aneurysm. Translumbar aortography seems also to be contraindicated in such patients because of the danger of flooding the spinal cord arteries and causing extremity paresis when there is aortic occlusion. In such instances it would appear that intravenous abdominal aortography is the preferable method for aortography.

Arteriosclerosis of the abdominal aorta and its branches is a common disease. The diagnosis of an abdominal aortic aneurysm often depends on the discovery of a pulsatile, expansile mass or on the recognition of calcifications adjacent to the lumbar spine in the conventional abdominal roentgenogram (Fig. 4A).[18] Routine palpation of the abdominal aorta and peripheral vascular system often will be rewarding in the evaluation of hip and leg pains. Indeed, a small percentage of the patients who have been studied with abdominal aortography at this center have had opaque media of a previous myelographic study in the spinal cord. In such instances the low back pain was attributed mistakenly to a spinal disk lesion. Tortuosity of the abdominal aorta and common iliac arteries of varying degree is a common manifestation of arteriosclerosis of the abdominal aorta (Fig. 5). Arteriosclerotic abdominal aortic aneurysm can be of all sizes and shapes (Figs. 3A and 4B). By demonstrating the runoff into the legs, practical and valuable preoperative data can be provided by intravenous arteriography (Figs. 3B, 11, and 12).

Summary

An intravenous method of abdominal aortography and peripheral arteriography, making use of physiologic principles learned during angiocardiography, is particularly suited for the diagnosis of arteriosclerotic abdominal aortic and peripheral vascular disease. Because the apparatus needed for the intravenous injection is inexpensive, regular x-ray equipment ordinarily used for gastrointestinal or genitourinary studies

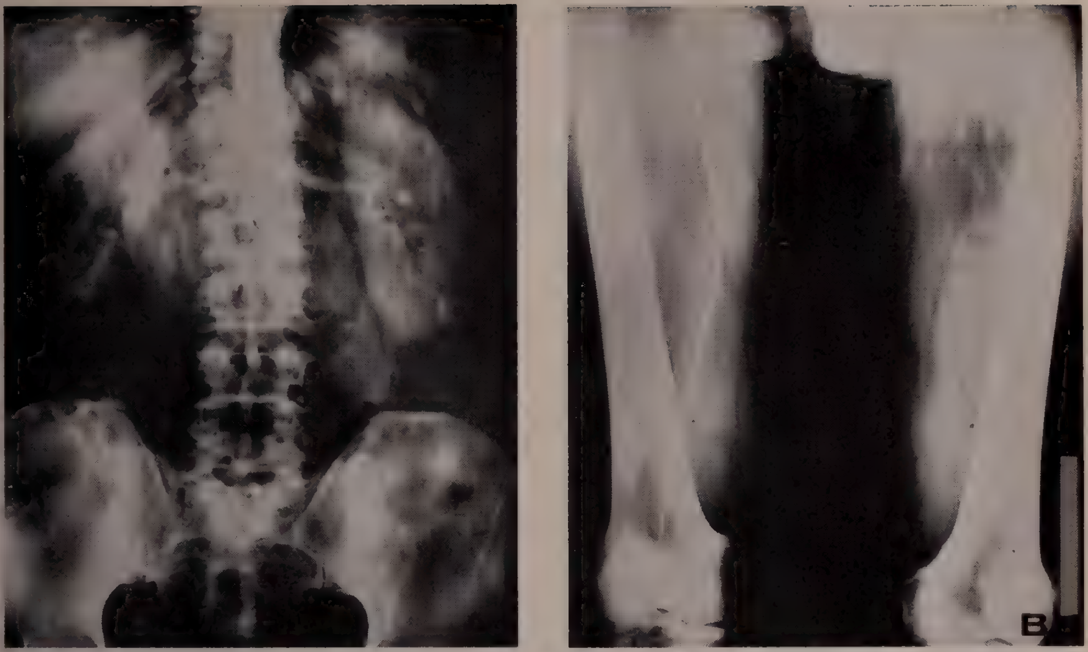

FIGURE 9. Insidious thrombotic occlusion of abdominal aorta in fifty-nine-year-old man. At exploratory operation reconstructive surgery could not be accomplished because of poor runoff into legs. (A) Intravenous abdominal aortogram showing aortic occlusion. Note bilateral markedly enlarged collaterals. (B) Peripheral arteriogram revealing hypoplastic but intact right superficial femoral artery; left superficial femoral artery occluded. Deep femoral branches hypertrophied and markedly tortuous.

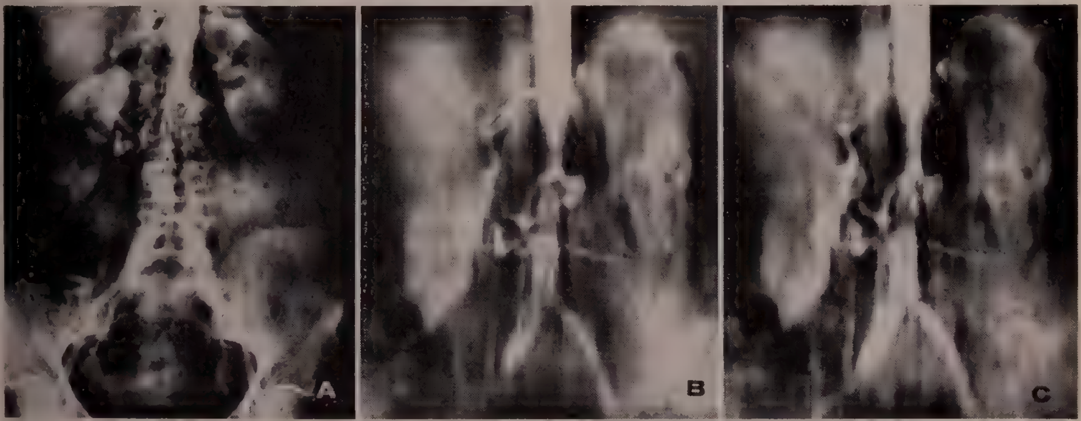

FIGURE 10. Calcified inferior mesenteric artery and severe calcific abdominal aortic arteriosclerosis in fifty-year-old woman. (A) Intravenous abdominal aorta shows poor filling of abdominal aorta below intact renal arteries. Both common iliac arteries, although tortuous and containing multiple calcific plaques, are intact. (B) Aortotomography of opacified aorta at the level of the inferior mesenteric artery. Note enlarged calcified inferior mesenteric artery. (C) Aortotomography at level of the bifurcation of abdominal aorta. Note marked aortic narrowing and irregular contours of aorto-iliac vessels owing to deposits of calcific plaques in walls of arteries.

can be utilized, making the method practical for the small hospital. The intravenous method has, therefore, many obvious advantages over the translumbar method of aortography which has sometimes been associated with serious complications and occasionally death.

The rapid and simultaneous injection of a concentrated organic iodide contrast medium can be made readily by injection into both

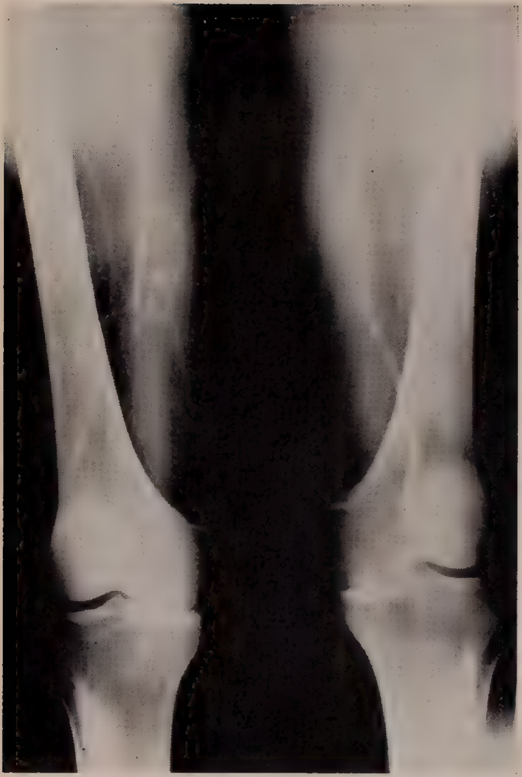

FIGURE 11. Intravenous peripheral arteriography in forty-four-year-old woman showing arteriosclerotic occlusion of right superficial femoral artery inmidthigh region.

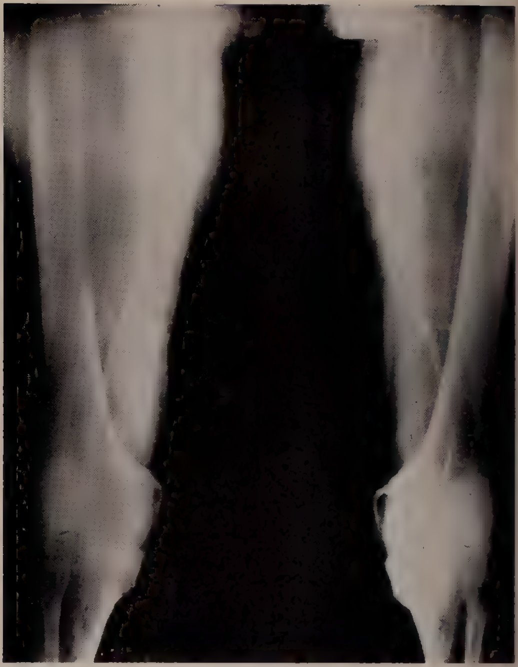

FIGURE 12. Intravenous peripheral arteriography showing arteriosclerotic segmental occlusion in middle of the left thigh in a fifty-five-year-old woman who was successfully treated by venous graft installation.

arms with special syringes attached to Robb-Steinberg cannulas. If dosages of 1 cc. per kilogram of body weight are used, the reaction to the injection of large quantities of the contrast material will be well tolerated. Rarely, and apparently owing to drug sensitivity, death may ensue.

Preliminary testing with the contrast agent cannot designate the patient who will react violently to the intravenous injection. Therefore, it is important to select for angiography only those patients who are likely to benefit from such studies. The arteriosclerotic patient with abdominal aortic endarteritis, aneurysm, or peripheral vascular disease falls into this category. However, because there often is associated cardiovascular, coronary artery, and cerebrovascular arteriosclerotic disease, such patients constitute high-risk cases. Nonetheless, no individual should be denied an examination if there is a prospect of deciding whether or not a patient is operable.

The hazard of intravenous aortography is certainly less than the risk of not treating or incorrectly treating a disease such as an abdominal aortic aneurysm which is prone to rupture. Since abdominal aneurysms are amenable to surgical resection and replacement with a prosthesis, proper diagnosis and evaluation are important for treatment.

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Discussion

STANLEY M. ROGOFF, M.D., *Rochester, New York.* It is a pleasure for me to congratulate Dr. Steinberg for the remarkably simple and useful intravenous approach to arteriography which he and the Minnesota group have developed and popularized in different versions.

As a radiologist speaking to internists, however, perhaps my most valuable contribution can be in the role of the devil's advocate in discussing what has been recognized as a truly significant and stimulating work.

The most pointed question to ask is: To what degree can the intravenous injection really replace direct arterial puncture or arterial catheterization as a method of obtaining satisfactory diagnostic arteriograms of the aorta and of its many significant branches?

There are certain inviolable requirements for producing consistently good arteriograms. A liquid which is opaque to x-rays must be deposited into the high-speed, high-pressure arterial circulation, in such concentration that it will provide an accurate image of the arterial lumen at all critical points.

My bitter experience has been that even when direct arterial puncture or catheterization is employed with efficient mechanical injection aimed precisely at a point of interest, an arteriogram does not always reveal critical detail. There are uncomfortably many reasons: Elevated blood pressure and pulse rate can vitiate arterial contrast; the film can be blurred by the patient's unexpected motion even during exposures as short as 0.1 second; the blood column containing opaque substance may not quite have reached the predicted level at the moment of a single x-ray exposure; or a slight change in the patient's position may be required to bring to light a critical segment of the artery, even though it may be well opacified.

There is a very exciting aspect of Dr. Steinberg's present extension of his classic intravenous angiocardiogram: It is inherently both a safe and simple method. But, lacking any considerable personal experience with it, I would appreciate Dr. Steinberg's comments on whether it is only a gross screening method which can identify relatively gross lesions of the aorta and its major branches. Are there not many surgically significant atherosclerotic lesions of these vessels whose discovery or accurate study still demand direct aimed arteriography, employing arterial punctures and catheters, or mechanical injectors, high-powered x-ray generators, unusual sizes of film, rapid serial film changers—or a combination of these tedious factors? In this category, I believe, are the small atherosclerotic plaques at the orifices of the renal, mesenteric, iliac, carotid, vertebral, and coronary arteries.

My reason for asking such questions is that some of my internist friends are gaining the impression that the intravenous arteriogram has all but replaced the arterial arteriogram. On the other hand, some radiologists and surgeons feel that it is more fairly characterized as a new method which can help to avoid some of the inherent dangers of direct arteriography in selected patients, when such risks are not clinically justifiable.

Use of Whole Blood Transfusions in a General Hospital

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THE USE OF BLOOD has increased steadily over the past few years. It would be difficult to imagine modern medical practice without this wonderful therapeutic tool. Many persons owe their lives to this, and many operations are now possible that would not be possible were it not for the fact that blood is now easily available in large quantities. However, blood is being used in more and more situations and in small quantities. It would be fine if we could use whole blood freely without fear of doing more harm than good. But such is not the case.

It is necessary to re-evaluate the need for transfusions, especially those in which patients receive only 1 pint of blood or less during their hospital stay. Some authors maintain that a 1-pint transfusion should never be given to an adult.[1,2] It is claimed that if a patient needs only 500 to 1,000 cc. of blood, he can get along without it. The reason for the hesitancy in giving blood unless it is absolutely necessary is that transfusions are not without danger. No consistent figures are available on the risk, but the mortality is 1 death in every 1,000 or every 5,000 transfusions. These deaths are due most commonly to hepatitis, overload phenomena or hemolytic reaction. One unit can cause just as severe a reaction as many units.

Because of this concern about the increasing incidence of small transfusions, a survey was made of patients receiving 1- and 2-pint transfusions in a 250-bed division of a general hospital during an eight-month period in 1960. The chart of each patient was reviewed to determine the indication for the transfusion, the results obtained by it, and the reaction to the blood. This study was similar to one made by Morton[3] for a surgical service at another hospital in this same city.

In making the tabulations, bleeding was listed as an indication for transfusion if blood loss of any amount, however small, was mentioned. Any mention of hypotension, falling pulse pressure, elevation of pulse, or comment about shock was listed as "shock." Both pretransfusion and post-transfusion hemoglobin and hematocrit were recorded. The post-transfusion hemoglobin was usually determined the following day. Cases in which no evidence of any of these conditions was present and in which no other reason was given for the transfusion were listed as "no explanation." Babies were excluded from the study, and children were included only if the amount of blood given was less than 4 ml. per pound.

Results

During 1960 932 patients received 2,371 pints of blood. Of these patients, 401 (43 per cent) received only 1 unit of blood during their hospital stay, and 246 (26 per cent) received 2 units of blood (Fig. 1). During the eight-month survey 250 patients in these two groups were studied. The distribution of these patients in respect to their pretransfusion hemoglobin level (Fig. 2) indicates a lack of correlation between small transfusions and the hemoglobin level, although the hemoglobin curve is somewhat lower than normal.

Post-transfusion hemoglobin determinations were done on 75 per cent of the patients. The change in hemoglobin level following the

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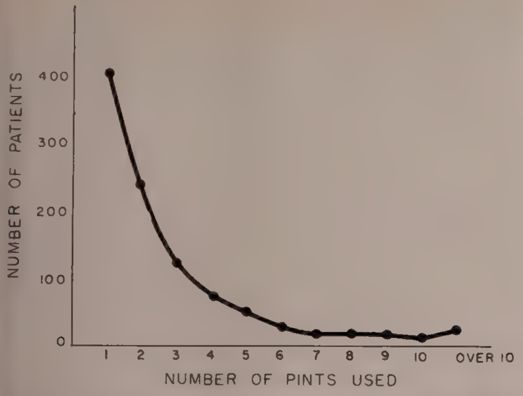

FIGURE 1. Distribution of transfusions (1960); (2,371 pints, 932 patients).

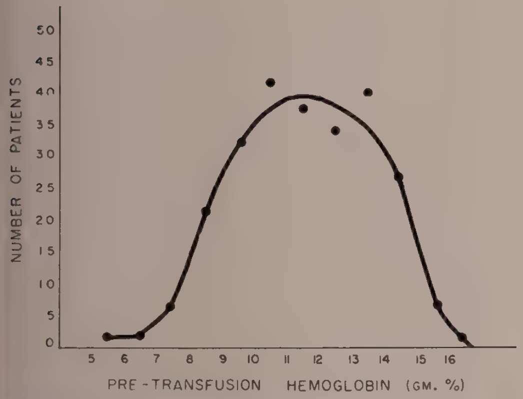

FIGURE 2. Relation to hemoglobin level; 250 patients receiving 1- and 2-pint transfusions.

transfusions (Fig. 3) shows that only those patients with an anemia (hemoglobin below 10 Gm. per 100 ml.) experienced a significant increase in hemoglobin following the transfusions. This was noticed in practically all of the patients, irrespective of bleeding and operation. Considering that 1 pint of blood theoretically produces an increase of 1.5 Gm. per 100 ml. in the hemoglobin level, 14 of the patients with a hemoglobin above 12 Gm. per 100 ml. would have had a drop in the hemoglobin to below 10 Gm. per 100 ml. if they had not received blood. Four of the patients (3 per cent) who were receiving 1 unit of blood and 24 of the patients (30 per cent) who were receiving 2 units of blood would have had a drop in the hemoglobin level to below 7 Gm. per 100 ml. if they had not been transfused. The amount of blood loss was estimated in only 32 of the cases and was less than 700 cc. in all but 6 cases which were between 750 and 1,000 cc.

A SURVEY WAS MADE *of patients receiving 1- and 2-pint transfusions in a 250-bed division of a general hospital during an eight-month period. In this period 932 patients received 2,371 pints of blood; 401 (43 per cent) of these received only 1 unit during their hospital stay, and 246 (26 per cent) received 2 units. Sixty-nine per cent of the patients receiving 1 unit of blood and 58 per cent of those receiving 2 units were given their transfusions in the operating room and the immediate postoperative period. Pyrogenic or allergic reactions with no sequelae occurred after 3 per cent of the transfusions. However, in the past two years 2 serious cases and 1 fatal case of hepatitis have occurred following 1-unit transfusions. Although in retrospect very few of the 1-unit transfusions would have been necessary, at the time there were undoubtedly factors present indicating the need for blood. In about 50 per cent of the cases the 2-pint transfusions were more often of apparent benefit.*

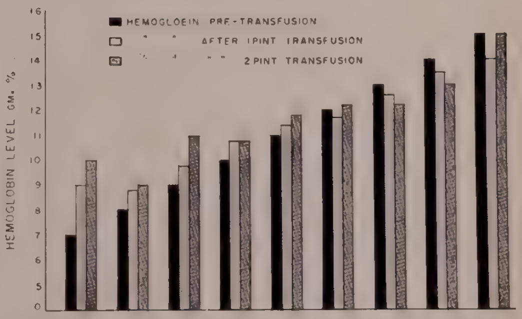

FIGURE 3. Change in hemoglobin level by transfusion (194 patients).

Sixty-nine per cent of the patients who received 1 unit of blood and 58 per cent of the patients who received 2 units of blood were given their transfusions either in the operating room or in the immediate postoperative period (Table I). A lack of explanation for the transfusion was evident in the chart for about half of these patients. Practically all of the patients with high normal hemoglobin levels (above 14 Gm. per 100 ml.) received their blood in the operating room during

TABLE I. Eight-month survey of 250 patients receiving only 1 or 2 pints of blood

Administration of Transfusion	Number of Patients Receiving 1 Pint	Number of Patients Receiving 2 Pints
Given in operating or recovery room	113	44
Bleeding or shock (any evidence, however small)	44	21
No explanation	69	23
Given on floor	53	40
Bleeding	29	30
Anemia	20	9
Shock	3	1
Infection	1	. . .
TOTALS	166	84

TABLE II. Transfusions of 1 and 2 pints given to 35 patients with hemoglobin above 14 Gm. per 100 ml.

Condition	Number of Patients
Gastrectomy	7
Radical mastectomy	5
Thoracotomy	5
Hysterectomy	4
Terminal condition	3
Hip operation	2
Postoperative bleeding	2
Other: (one each: radical neck, skin graft, diaphragmatic hernia, colectomy, nephrectomy, fracture, mitral commissurotomy).	7

major operative procedures (Table II). In 8 of these patients a blood loss estimated to be up to 700 cc. was recorded.

During the period of the survey reactions occurred after 3 per cent of the transfusions and consisted of pyrogenic or allergic reactions with no sequelae apparent. However, in the past two years 2 serious cases and 1 fatal case of hepatitis have occurred following 1-unit transfusions.

The economic aspect of blood transfusions was no small item, although the blood was provided free of charge from voluntary donors by the regional Red Cross Blood Donor Program. The cost of typing and cross-matching the blood and the service charges for the transfusions amounts to about $2,500 a month. This is another example of increasing laboratory costs (Table III).

TABLE III. Amount and cost of blood transfusions (average per month in 1960)

Data	Number	Cost (Dollars)
Admissions (total patients)	1,000	. . .
Patients typed	425	1,500
Pints of blood crossed	650	
Pints of blood used	200	1,000*

* Service charge; blood donated by Regional Red Cross Blood Donor Program.

Comment

The figures obtained in this survey were similar to those obtained in other hospitals. The 43 per cent incidence of single-unit transfusions was comparable with the 36 per cent incidence obtained by Morton[3] in his survey in this same city. As mentioned by him, the retrospective evaluation of blood usage is a matter of opinion, and it is subject to individual variations in interpretation. Using his criteria, Morton discovered that at least 34 per cent and possibly 72 per cent of the single-unit transfusions were unnecessary. While no attempt was made to follow Morton's[3] classification of transfusions as conservative, reasonable, questionable, or unnecessary, a similar conclusion can be reached from the data obtained. Although in retrospect very few 1-pint transfusions would have been necessary, at the time there were undoubtedly factors present indicating the need for blood. For instance, while the loss of 700 cc. of blood is moderate and does not require transfusion, at the time it might not have been known that the bleeding would stop. In about 50 per cent of the cases the 2-pint transfusions were of apparent benefit.

The incidence and results in respect to 1-pint transfusions are in agreement with those reported elsewhere. These data were reviewed ably by Myers[1] who reported similar figures in many hospitals. Not only is the danger of transfusion reaction a constant one to patients, but also it is well to bear in mind the medicolegal import in that "Even if no negligence could be proven in the collection, storage, testing and administration of blood, an action for damages would lie if the plaintiff could prove that the transfusion were not indicated medically."[4]

Summary

Over an eight-month period in a 250-bed division of a general hospital, 250 patients receiving 1- and 2-unit transfusions were reviewed. These patients constitute 70 per cent of the total patients transfused. Of these, 75 per cent were given transfusions either in the operating room or recovery room, in preparation for surgery, or for postoperative hemorrhage. No correlation was found between the number of patients who received small transfusions and the degree of anemia. The transfusions were given to 35 patients with hemoglobin above 14 Gm. per 100 ml. A change in hemoglobin level following transfusion has been tabulated. The similarity of the findings in this survey to those found in other hospitals has been discussed.

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Use of color in hospital decoration

Color should be as carefully prescribed and administered in hospitals as medicine, according to an article by P. H. Knighton in the February 1, 1962, issue of *Hospitals*, Journal of the American Hospital Association. "To both patients and staff, physical surroundings in the hospital present an inescapable 'face' which can either quicken with interest and cheer or remain blank and void of expression." Color should be "purposely prescribed to meet specific needs and be administered with loving care and patient skill by those who are qualified to do so." Each part of the hospital needs special attention. Because invitation and movement are the principal characteristics of entrances and circulation areas, color can be applied boldly, and well-lighted strong colors will help to avoid a tunnel-like appearance. Reception and waiting areas should have an atmosphere of cheer and reassurance, and warm and brilliant, yet not garish, colors should be used. The atmosphere in hospital wards should be one of reassurance, repose, cleanliness, and simple ordered efficiency. This may be fostered by warm and cheerful colors. Since examination and treatment rooms are small and places of concentration, strong color contrasts should be avoided. In surgical suites pale green or pale cream are usually preferred, as pale green obviates the green "after-image" which would appear on white walls after a period of concentration on red wounds. In x-ray rooms bright and attractive colors will help reassure the nervous patients about the complicated and mysterious apparatus.

Management of Osteomyelitis Following Fractures of Extremities

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THE MANAGEMENT of osteomyelitis following a long-bone fracture may be discussed under four general headings: the patient and the extremity; debridement; stabilization of the fracture; and closure of the wound.

Our results and experiences in this problem should be reviewed and compared from time to time in different parts of the country and under different conditions. In this way, we may bring more concerted effort and success in the management of this very serious and disabling complication of an extremity fracture.

It is interesting to look back twenty-five years. In the middle 1930's, all large hospitals had an osteomyelitis ward or service. The majority of the patients on these wards had osteomyelitis due to extremity fractures. The visitor to the hospital had little trouble in locating the osteomyelitis ward, owing to its characteristic and penetrating odor.

Today, we no longer have an osteomyelitis service. Each large hospital, however, can show the visitor its own unfortunate complications, as well as the mistakes of others. The primary reasons for this decrease in the septic complications following fractures of the extremities would seem to be the following:

1. Improvement in the surgery of soft tissues. World War II and the Korean War stimulated the advances in using soft tissues as a definite positive force in wound healing. The invaluable help which the plastic surgeon has given the general surgeon and the orthopedic surgeon accounts for major gains in this field. The close cooperation and teamwork with our plastic surgeon colleagues is one of the advances in the treatment of osteomyelitis following open fractures.
2. Improved technics in the methods of stabilizing the fracture.
3. Improved supportive treatment to the patient. Improved supportive treatment has been accomplished by means of blood replacement and improvement in the patient's general nutritional state.
4. The selective use of antibiotics. Unfortunately there has been at times a tendency to rely on the effectiveness of antibiotics rather than on good surgical technic. There is no question, however, that antibiotics have been a primary factor in localizing and at times eliminating invasive infections of an extremity. It has been a definite help also in combating gas gangrene and tetanus.

The patient and the extremity

The general condition of the patient with a chronic bone infection should be checked carefully. Diabetes should be ruled out. Hypochromic anemia may be a factor in the patient's debility. The nutritional status of the patient needs specific attention as to normal protein and vitamin intake. If the patient is febrile, a blood culture and a urine culture are indicated. Many elective plastic procedures may prove far more successful if the patient's resistance and nutritional state have been improved.

An initial evaluation of the extremity

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* By invitation.

should be made, preferably in cooperation with a plastic surgeon or one well trained in the principles of skin-grafting technics. An over-all plan will give continuity to each phase of wound management. This, in some instances, will account for the success or failure in the management of a chronic bone infection.

Debridement

All infected and devitalized tissue and foreign material of a chronic bone infection should be removed from the wound. This includes the skin edges, muscle and fibrous tissue, and necrosed tendon and bone. Extreme care and attention to detail are required by the surgeon for success in this phase. The "clean-up" process should extend to the depth of the wound and to the extent of infection. The technical steps in accomplishing debridement will depend on the character and extent of the infection.

SMALL DRAINING SINUSES. Small draining sinuses usually indicate a localized process. The exploratory incision should be adequate, however, to reach the origin of the infection. With the complete elimination of necrotic tissues, many wounds at this stage may be closed by a side-to-side suture. If a plate is present on a subcutaneous bone such as the tibia and is not needed to stabilize the fracture, then both the plate and the screws should be removed to allow complete contact of the soft tissues with the bone. A safeguard on initial closure would be the insertion of several small polyethelene tubes for constant drainage, thus eliminating the accumulation of blood or serum.

LARGE OPEN SEPTIC WOUNDS. In the more extensive wounds the problem becomes more complex. As a rule, necrotic bone ends and tendons are exposed in the wound. The soft tissues may be leathery, fibrotic, and inelastic (Fig. 1A).* It is here that the surgeon should seek the help, advice, and cooperation of his plastic surgeon colleague in planning the successive stages of achieving wound closure.

Skin. All necrotic or poorly vascularized skin should be removed by sharp dissection.

IN THE MANAGEMENT *of osteomyelitis following fractures of the extremities, the over-all condition of the patient should be evaluated. All infected and devitalized tissue and foreign material of a chronic bone infection should be removed from the wound. Effective stabilization of the fracture is essential; it may be achieved by plaster cast fixation, cast and transverse wires, compression methods, or intramedullary rod fixation. Closure of the debrided wound may be by direct side-to-side suture, direct sliding or double pedicle graft, rotation or single pedicle graft, or free split-thickness skin graft. Close cooperation with a plastic surgeon is urged throughout management of osteomyelitis.*

Fibrous tissue. Infected and devitalized muscle and fascia should be removed by sharp dissection until pink, retractile tissue is encountered.

Tendons. The exposed necrotic tendon should be inspected carefully. In many instances the tendon, although it may appear to be completely necrotic, may have deep layers which are visible. Therefore, one should be very conservative in the debridement of a tendon. By removing only superficial portions of the tendon in stages, one may save a functional portion of the exposed tendon (Fig. 1B).

Bone. All loose sequestrated bone should be removed from the wound. In those instances where the fracture has healed, the necrotic portion of the cortex of the bone may be removed by a sharp osteotome until viable bleeding bone is encountered. In instances in which there is delayed union or nonunion and the infection involves not only the cortex of the bone, but the medullary cavity as well, the bone ends should be smoothed off by rongeur so that stable end-to-end opposition is obtained. The medullary cavity should then be carefully scraped by curet and all infected tissue removed (Fig. 1B). The surgeon must be prepared to accept some shortening of the extremity. In the tibia, one must remember to do an osteotomy of the fibula to obtain good opposition of the tibial ends.

In infected bone, screws, plates, and bands which have lost their effectiveness as stabiliz-

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* Figures 1 through 6 and 8 through 10 and Table I are reproduced by special permission of the W. B. Saunders Company, Philadelphia, Pennsylvania.[1]

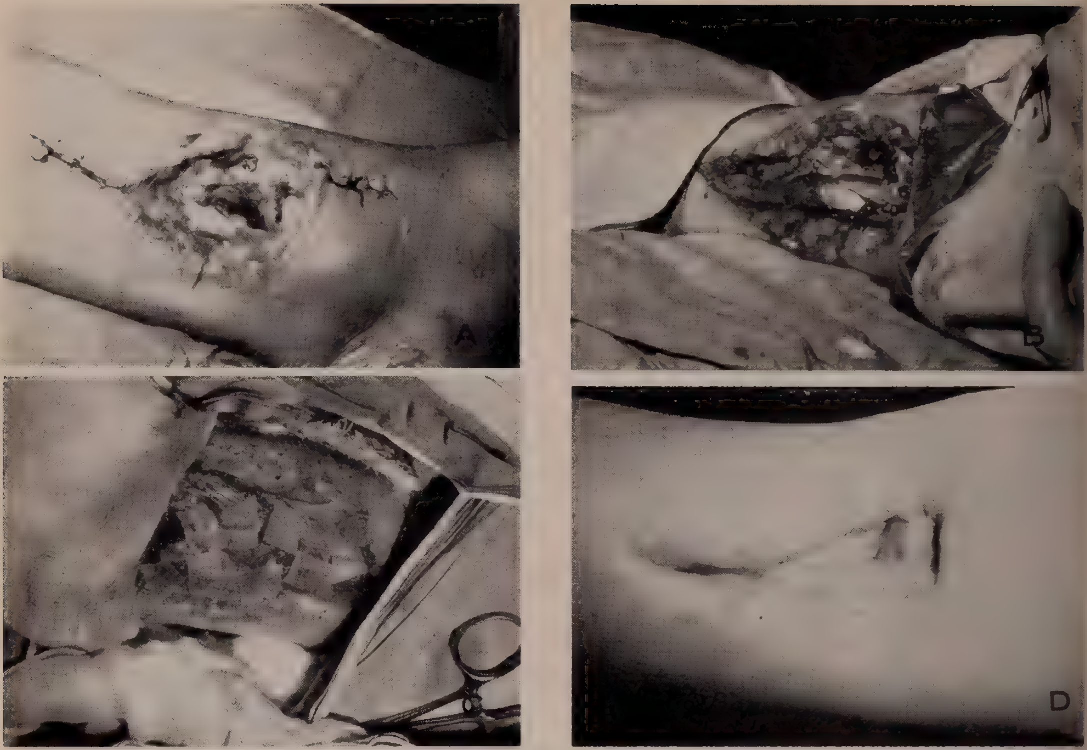

FIGURE 1. (A) Severe septic fracture of lower tibia and fibula in sixty-year-old woman referred to Massachusetts General Hospital in September, 1959. (B) Initial debridement performed September 5 when all devitalized tissue removed from soft tissues, tendons, and bone. Exposed screw removed and saline gauze compress applied and changed daily. (C) Twelve days later split-thickness skin grafts applied to fine granulation covering wound. Four months later wound was completely recovered with no drainage. One year later patient again teaching school and bone union solid. (D) Leg two years after operation. Case illustrates value of complete initial debridement followed by skin grafting.

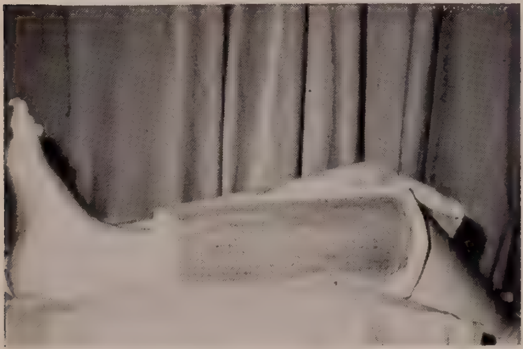

FIGURE 2. Practical way of protecting freshly applied skin grafts—sterile gauze over chicken wire.

ing materials should be removed. Intramedullary rod fixation, on the other hand, may continue to give adequate fixation, even in the presence of infection. If the rod is loose, it can be replaced by a larger rod or a "nesting" of rods. One of the advantages of intramedullary fixation when infection is present is that the soft tissues will have complete and direct contact with the bone.

Stabilization of the fracture

Effective stabilization of the fracture is essential. It is well known that a fracture will heal in the presence of infection if it is stabilized adequately.

Usually, long-bone fractures complicated by osteomyelitis have not healed because of delayed union or definitely established nonunion. Unless the ununited fracture is stabilized securely, subsequent steps in wound closure and soft tissue grafting may not succeed.

PLASTER CAST FIXATION. In some instances the application of a well-molded plaster cast including both of the joints above and below the fractured bones may

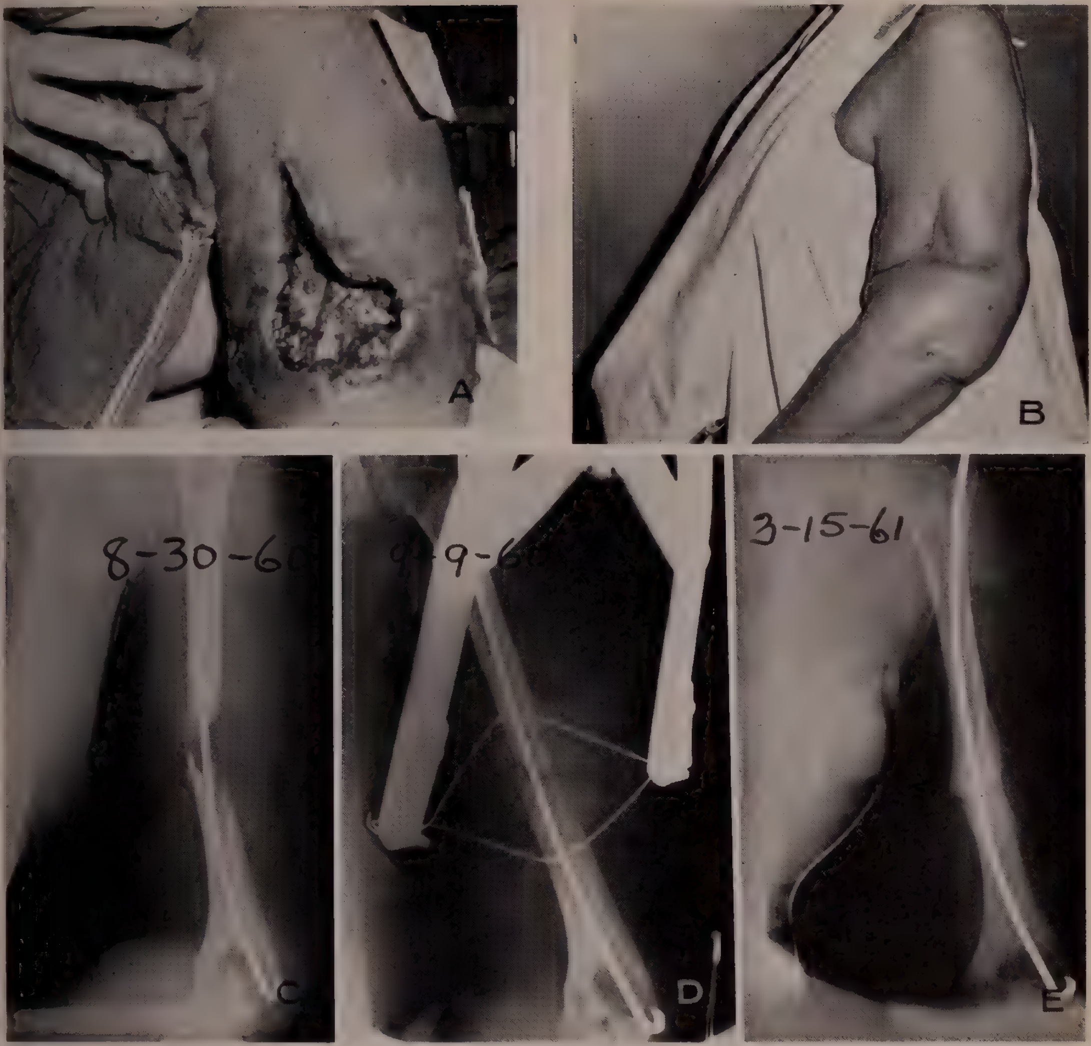

FIGURE 3. Septic nonunion of left humerus in forty-five-year-old woman, April 16, 1960. (A) Large septic draining wound of left arm, April 30, 1960. (B) Appearance of arm one year after injury. (C) Position could not be maintained in repeated shoulder spicas, sling, swathe, and so forth. Rush rod proved ineffective, and wound continued to drain copiously. (D) Greifensteiner method, September 9, 1960: $^3/_{32}$ inch Kirschner wires introduced through humerus above and below fracture site and compression applied. Two weeks after procedure all drainage ceased. (E) Two months later, union of humerus solid, and wires were removed.

afford sufficient support and immobilization. A window may be cut in the cast for the inspection and treatment of the wound. Chicken wire covered with sterile gauze will make a very effective cover protection for the wound (Fig. 2).

Cast and transverse wires. Transverse Kirscher wires or Steinman pins may be inserted through the bone above and below the fracture site. These may be incorporated in a cast, but care should be taken that the fracture is not held apart.

Compression methods. The infected unstable fracture is definitely detrimental to soft tissue healing as well as to bone healing. The striking beneficial effects of stabilizing the septic nonunion are well known. The indolent edema of the extremity is eliminated, circulation is improved, pain is markedly diminished, and the patient finds that he is able to begin active motion of his fingers or toes. Each of these factors has a direct effect on the ability of the soft tissues and the bone to combat infection and initiate

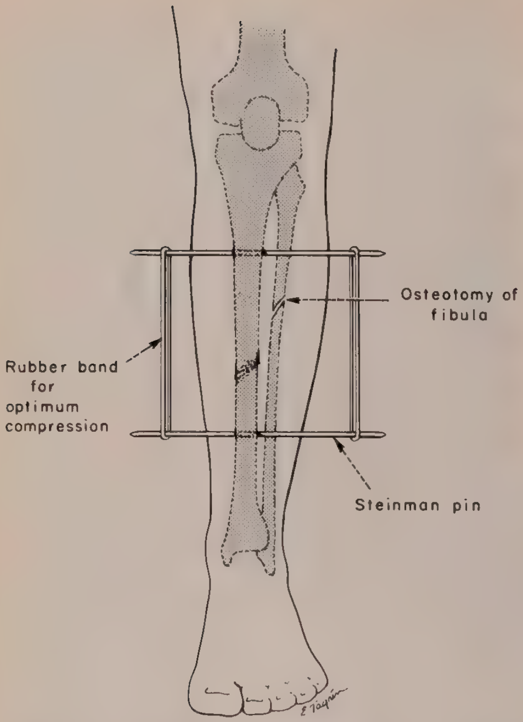

FIGURE 4. King method: compression of bone fragments at fracture site obtained by applying rubber bands around Steinman pins.

repair. The optimum degree of compression should be physiologic, or the amount to give secure stability and bony contact.

Greifensteiner method. Two Kirschner wires ($^3/_{32}$ inch) are introduced through the bone above and below the fracture site and stretched in a stirrup, or spreader, and tightened to bring the fractured fragments into apposition with compression (Fig. 3). This method works best for the humerus. It is not recommended for the forearm fractures.

King method. King[2] has shown the effective use of Steinman pins in which elastic bands are placed around the ends of the pins on both sides to produce compression. He was able to achieve 92 per cent union in 13 infected nonunions. This method works best in the tibia. He had no significant complications (Fig. 4).

Charnley method. The Charnley method[3] of compression can be used also (Fig. 5).

INTRAMEDULLARY FIXATION. Intramedullary rod fixation is being used with increasing frequency today in the treatment of fracture (Fig. 6). In instances when infection complicated the intramedullary pinning and osteomyelitis developed, many of the rods were removed by surgeons in an attempt to eliminate the infection by eliminating the "foreign body." Unfortunately this added to the patient's surgical problems as, in addition to the infection, the patient's extremity was then grossly unstable. Soon it was found that even though infection of the bone occurred, the bone would heal in time if the rod was left in situ (Fig. 6). MacAusland and Eaton[4] have reported the healing time of the fracture and wound in 14 instances of septic intramedullary rod implants (Table I). If the intramedullary rod is loose, it should be replaced by a larger one or a "nesting" of rods. After the fracture has healed, the intramedullary fixation can then be removed and the wound further debrided if necessary.

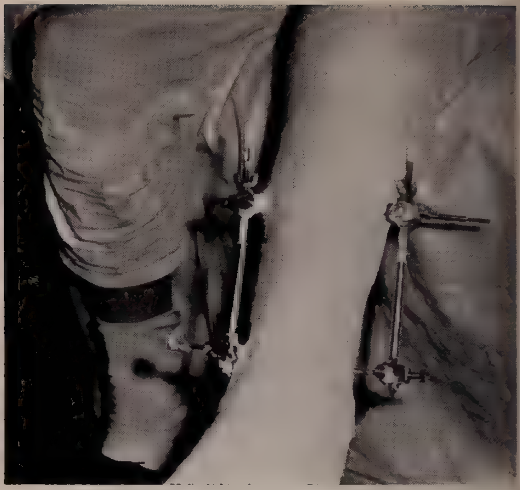

FIGURE 5. Charnley method of applying compression to fracture site, effective when septic nonunion is present.

The formation of a "ring sequestrum" at the fracture site has presented an unusual problem in infected intramedullary rod cases. Should the infected and sequestrated ring be removed early or late? Evidence would favor early removal of the sequestrum.[4]

The intramedullary rod has also been used as a last resort, prior to amputation, in severely infected femoral and tibial shaft infections which have been treated by other

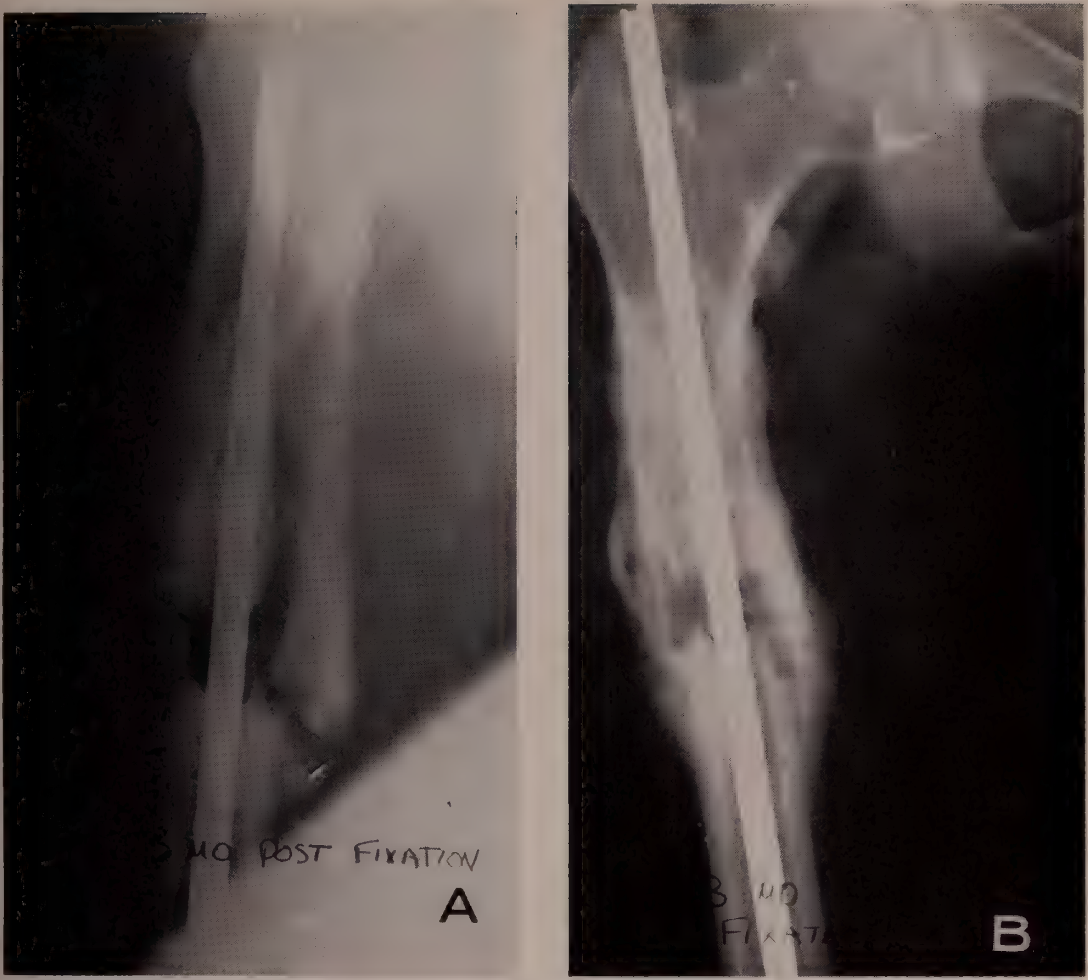

FIGURE 6. (A) Severe sepsis of right femur three months after intramedullary rod fixation in twenty-year-old male. In July, 1955, wound was "pouring" pus. (B) Rod was not removed. Eighteen months later union of femur had occurred, and drainage was reduced to a small sinus. Case illustrated beneficial effect of maintaining stability of fracture in presence of infection.

means. To introduce a rod into the medullary canal of an infected fracture would seem to invite disaster, but experience with a few patients of this character so far has proved otherwise. The author has had experience with 3 severely infected tibial fractures with nonunion, in which an intramedullary rod was introduced as a last resort before amputation. There was no indication of a spread of the infection in any of the 3 fractures. In 2 of these fractures, the leg showed rapid improvement and eventually the fracture and soft tissues healed. In the third fracture, amputation was later performed, chiefly because of extensive soft tissue slough rather than a flare-up or extension of the bone infection. Moe[5] has also pointed out that intramedullary rod fixation of fractures in the presence of bone infection can be performed with very good results.

TABLE I. Experience with 14 septic intramedullary rods

Sepsis	Number of Cases	Fracture United (Months)	Wound Healed (Months)
At fracture site only	9	13	16
Rod tract	5	20	36

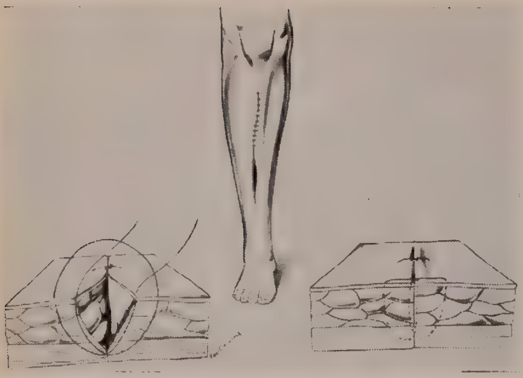

FIGURE 7. Over-and-over suture. Effective closure can be obtained without tension on skin.

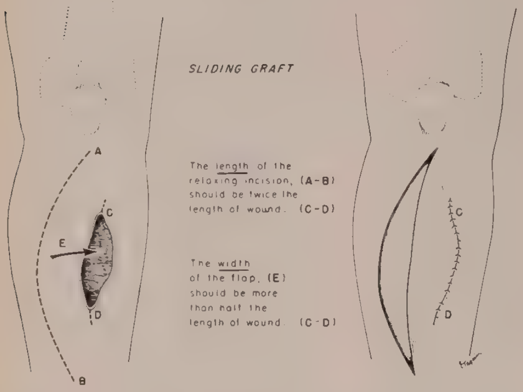
SLIDING GRAFT
A
C
E
D
B
The length of the relaxing incision, (A-B) should be twice the length of wound. (C-D)
The width of the flap, (E) should be more than half the length of wound. (C-D)
C
D

FIGURE 8. Direct sliding or double pedicle graft.

Methods of wound closure

The closure of a debrided wound may be simple or extremely difficult. There are a number of very important considerations such as the size, shape, and location of the wound, and also the condition of the soft tissues of the extremity. In some extremities, the tissues surrounding the wound are soft and elastic; in others the soft tissues may be scarred, fibrotic, and inelastic. Tension on the wound edges should be avoided, regardless of the method elected for closure.

Direct side-to-side suture. If the soft tissues of the extremity are elastic and the size of the wound can be approximated without tension, then direct side-to-side suture will be satisfactory. One should not "force" the wound to close. By extending the length of the incision frequently relaxation may be obtained to afford closure.

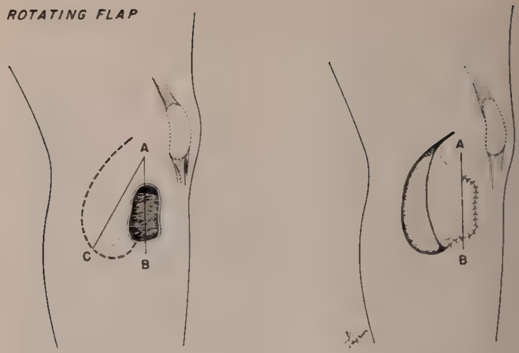

FIGURE 9. Rotation or single pedicle graft.

The type of suture is important. We have found the over-and-over suture very helpful in approximating wound edges and yet avoiding tension (Fig. 7). One or two small polyethylene tubes may be inserted to the depth of the wound for forty-eight hours to remove possible accumulations of serum or blood.

Direct sliding or double pedicle graft. The direct sliding or double pedicle graft (Fig. 8) is particularly applicable to wounds overlying the tibia where the tissues have very little "give." The success of this method will depend on the close observance of specific technical steps. Cannon[6,7] emphasizes two points:

Length. The length of the "relaxing" incision should be twice the length of the primary wound. This would insure adequate blood supply to the flaps. The donor site may be covered by a split-thickness graft.

Width. The width of the intervening flaps should be more than half the length of the wound. This technic, when it is properly performed, has been a safe and very successful method of wound closure.

Rotation or single pedicle graft. The rotation or single pedicle graft (Fig. 9) is particularly applicable around joints such as the hip, knee, and ankle. It can also be used over the tibia, if the defect is not a large one. This method should be thoroughly understood by the surgeon; otherwise he may experience a partial or complete loss of the rotated pedicle.

Free split-thickness skin graft. The free split-thickness skin graft (Fig. 1C and

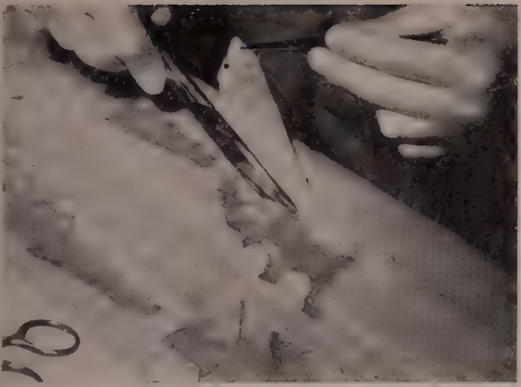

FIGURE 10. Technic of applying skin to sterile petrolatum gauze and cutting grafts to fit surface of wound.

D) is a rapid and very efficacious method of covering large debrided wounds, particularly in long-standing infection or where the soft tissue is not adequate for sliding or rotating. Again, observing specific technical steps is most important in obtaining a successful take of the skin graft.

Following the debridement, the wound should be packed lightly with moist saline gauze and sponges. The dressings should be kept moist and changed daily to fresh ones. We prefer normal saline for tissues although mild antiseptic solutions such as 0.5 per cent Dakin's solution may help to encourage healthy granulations. We agree completely with Cannon[6] that "no topical or parenteral medication has yet replaced faithful mechanical cleansing, careful daily debridement, and frequent changes of dressings." Within six to seven days the wound bed will have become stabilized, the oozing will have diminished, and a fine layer of granulation should cover the wound surface. Fluid accumulations should be reduced to a minimum. Then the surface of the wound is covered with split-thickness skin grafts. Large single sections of skin may be used if the surface of the wound is smooth. As a rule, however, the wound surface may be irregular. We have found that small sections of skin applied carefully with a slight amount of space between the skin islands will allow the exudate of the wound to escape, thus giving a higher percentage of take of the graft. The following technic is suggested: Strips of fresh skin are placed with their external surfaces against sterile petrolatum (Vaseline) gauze. In this way the skin can easily be cut in patterns to desired shapes. The petrolatum on the "top side" of the skin eliminates thickening or hardening of the gauze dressings (Fig. 10). If the wound is fairly dry, a window may be cut over the grafted area and treated with little, if any, gauze dressing (Fig. 2).

Extra sheets of skin may be taken initially, rolled on petrolatum gauze, and preserved at 4 C. in a refrigerator. These can be used on the wound as necessary for a period of approximately five weeks.

Once the wound surface is covered completely, all reparative processes of the soft tissue and bone are stimulated. It is also interesting to note the shrinking effect of the wound cavity once successful coverage is obtained (Fig. 1D). Both the surgeon and the patient may agree that further grafting procedures, which may have been planned, will be unnecessary.

Late plastic procedures can be carried out to fill soft tissue defects using either rope jump grafts for the lower extremity or a direct thoraco-abdominal flap graft for the upper extremity. Bone grafts may be added to aid healing or to strengthen a weak section of the shaft of the bone after the wound surface has been covered successfully.

Summary

The technical steps in the management of osteomyelitis complicating fractures of the extremities are outlined. The success in treatment will depend on the daily, detailed care of the wound and the patient.

With adequate debridement of the wound and stability of the fracture site, the soft tissues can be early approximated, thus functioning as a "positive force" in eliminating the infection.

Teamwork is most important—our plastic surgeon colleagues should be consulted early and often.

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Newborn infants respond to immunization

Proof that babies less than a week old can profit from artificial immunization was reported by John C. Leissring, M.S., John W. Anderson, Ph.D., and David W. Smith, M.D., in the February, 1962, issue of the *American Journal of Diseases of Children.* Antibodies that counteract typhoid fever and tetanus were introduced into the stomachs of 7 babies from twelve hours to five days old. In every baby a rise was found in the number of these antibodies circulating in the blood. This rise indicated that antibodies could be absorbed from the stomach into the blood stream of very young infants, a subject of conflicting reports for the past thirty years. The antibodies were detected by a highly sensitive method of blood analysis, used in this type of study for the first time. The test is believed to detect incompletely formed antibodies in addition to completely formed antibodies. It is possible that even small amounts of antibody given soon after birth could prolong and enhance the immunity passed on to the infant by the mother.

Bendroflumethiazide in Hypertension and Edematous States

Use in Office Practice

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A STUDY OF THE EFFECTIVENESS *in the treatment of hypertension and edema of bendroflumethiazide (Naturetin) in a low-dosage range was undertaken in 38 office patients. The most effective dosage was found to be 5 mg. of bendroflumethiazide with 500 mg. of potassium chloride. All 38 patients responded satisfactorily to treatment. An average fall of 26.8 mm. Hg occurred in the mean blood pressure of the 33 patients with hypertension. Symptoms associated with cardiovascular disease were controlled or lessened in 5 normotensive patients presenting edema and/or pulmonary complaints. Side-effects occurred in 2 patients: mild hypotension in 1 when the drug was given continuously on a once-daily basis, and an exacerbation of gout when the dosage frequency was increased to twice on three times daily. No evidence of tolerance developed even during prolonged therapy. The drug was effective not only in lowering blood pressure and controlling edema, but also in relieving such symptoms as headache, shortness of breath, nocturnal dyspnea, and anginal pain.*

THE USEFULNESS of the benzothiadiazine diuretics in the treatment of hypertension has been appreciated since the first of these agents, chlorothiazide, was first introduced in 1957. As diuretics, these compounds have impressive potency, markedly increasing the urinary volume without producing an unfavorable sodium-potassium excretion ratio.[1] As antihypertensive agents, they are effective in lowering high, but not normal, blood pressure. Moreover, they potentiate the antihypertensive action of a variety of other drugs, including Rauwolfia, Veratrum alkaloids, hydralazine hydrochloride, and guanethidine sulfate, thereby making possible the use of these various agents in considerably reduced dosages.[1]

One of the most recent benzothiadiazine derivatives to command interest is bendroflumethiazide (Naturetin), which is designated chemically as 3-benzyl-3,4-dihydro-6-(trifluoromethyl) - 1,2,4 - benzothiadiazine-7 - sulfonamide - 1,1 - dioxide. This derivative, of low toxicity, is one of the most potent oral diuretics available to date.[1,2] It is gentle in its effect but long-acting, the diuresis often continuing as long as eighteen hours.[3-6] The drug is effective in hypertension for short-term, intermittent, or long-term therapy.[2,3]

Bendroflumethiazide would appear to have particular value in the management of hypertension in patients who are seen in everyday office practice. Besides having a distinctly favorable urinary excretion ratio for sodium and potassium, potassium excretion being increased less than with most of the congeners, bendroflumethiazide increases the excretion of bicarbonate only minimally. Moreover, the excretion of sodium and chloride is so marked that there is no need strictly to limit salt intake by the hypertensive patient.[2] Finally, during the course of therapy, serum electrolytes are not disturbed to a clinically significant degree.[3,7]

Since, for the average patient who is seen in office practice, once-a-day dosage is more convenient than other forms and less likely to result in skipped doses, and because near-maximum sodium excretion occurs at doses of 2.5 mg. of bendroflumethiazide and near-maximum weight losses are seen with doses of 5 mg., it was decided in the present study to try these low doses on a once-a-day

TABLE I. Response of 23 patients with essential hypertension to bendroflumethiazide

			Blood Pressure (Mm. Hg.)				Blood Pressure (Mm. Hg.)		
Case	Sex	Age (Years)	Pre-treatment	Mean	Dosage	Months of Use	Post-treatment	Mean	Difference in Mean*
1	F	. . .	170/100 to 180/100	137	† **	11 8	134/84 to 148/86	113	24
2	F	. . .	206/100	153	. . .	3	144/84 to 148/88	116	37
3	F	. . .	210/96	153	†† *** (1)	9 11	166/82 to 172/90	127	26
4	F	. . .	190/100	145	††	16	156/82 to 168/90	124	21
5	F	. . .	174/92	133	***	1	144/80	112	21
6	F	. . .	204/100	152	***	7	144/80 to 156/90	117	35
7	F	. . .	230/120	175	†	8	144/90 to 180/100	128	47
8	F	. . .	210/110	160	†	17	166/90	128	32
9	F	66	190/102	146	*** (2)	1 1	144/96 to 160/90	122	24
10	F	60	230/136	183	†† ***	3 16	154/100	127	56
11	F	57	178/102	140	†	20	146/78 to 154/82	115	25
12	F	66	194/120	157	†† *** (2)	4 8 6	144/92 to 156/96	122	35
13	M	76	190/100	145	†	14	168/90	129	14
14	F	58	236/128	182	†† *** †††	5 13	164/104	134	48
15	M	71	176/100	138	†	3	144/86 to 156/90	119	19
16	F	71	188/110	149	†† ***	5 8	142/90 to 164/96	123	26
17	F	60	188/104	146	†† ***	4 2	154/96	125	21
18	F	64	164/110	137	**	4	132/82	102	35
19	F	70	184/114	149	† ***	17 3	156/94 to 164/100	128	21
20	F	53	190/120	155	††	(3)	176/108	142	13
21	M	46	176/108	142	†† † *** (2)	1 2 6	132/84	108	34
22	F	70	174/100	137	***	14	138/78 to 148/86	112	25
23	F	53	190/108	149	† **	6 3	156/90 to 166/98	127	22

* Average mean difference: 28.7 mm. Hg.
† Bendroflumethiazide, 2.5 mg. once daily.
** Bendroflumethiazide with potassium, 2.5 mg. once daily.
††Bendroflumethiazide, 5 mg. once daily.
*** Bendroflumethiazide with potassium, 5 mg. once daily.
††† Concomitant therapy with hydrochlorothiazide and reserpine.
(1) Therapy initiated with bendroflumethiazide, 5 mg. twice daily for three days.
(2) Switched to every-other-day schedule.
(3) Patient lost to observation after initial response obtained.

basis for extended periods. Some of the patients in this trial have remained under continuous treatment with bendroflumethiazide for as long as twenty months, with no evidence of undesirable effects or of reduced effectiveness of the medication.

TABLE II. Response to bendroflumethiazide in 10 patients with hypertension associated with cardiovascular disease

			Blood Pressure (Mm. Hg.)				Blood Pressure (Mm. Hg.)		
Case	Sex	Age (Years)	Pre-treatment	Mean	Dosage	Months of Use	Post-treatment	Mean	Difference in Mean*
Hypertensive heart disease									
24	F		186/88	137	† **	1	174/82	128	9
25	F	80	216/106 to 194/96	153	†	20	170/100 to 184/104	139	14
26	F	80	230/110	170	†	15	210/86	148	22
27	M	72	170/90	130	† ††	6 3½	138/84	111	19
28	F	79	204/110	157	†	12	164/96	130	27
29	M	56	230/120	175	†	6	166/98	132	43
Tension headache with chest pain									
30	F	58	144/82	113	†	4	124/80	102	11
Arteriosclerotic heart disease									
31	F	70	190/92	141	***	16	132/74 to 146/86	109	32
Arteriosclerotic and hypertensive heart disease									
32	M	67	184/100	142	†††	6	144/86 to 156/94	120	22
33	M	71	186/104	145	*** †	4 3½	146/90	118	27

* Average mean difference: 22.6 mm. Hg.
† Bendroflumethiazide with potassium, 5 mg. once daily.
** Concomitant therapy with butabarbital sodium and reserpine.
†† Switched to every-other-day schedule.
*** Bendroflumethiazide, 5 mg. once daily.
††† Bendroflumethiazide, 2.5 mg. once daily.

Materials and methods

THE PATIENTS. The present series comprised 38 office patients: 11 men and 27 women. Hypertension was the indication in 33 patients (Tables I and II). Of the remaining 5 patients, 1 had rheumatic heart disease with nocturnal dyspnea, another presented myocardial decompensation with shortness of breath, and 3 had edematous conditions (Table III).

Among those with hypertension, 23 had essential hypertension, 6 had hypertensive heart disease, 2 had arteriosclerosis and hypertensive heart disease, 1 had tension headache, and the remaining patient presented arteriosclerotic heart disease. Four of the 33 hypertensive patients also exhibited varying degrees of edema.

Twenty of the patients had received treatment with digitalis (3), an anticoagulant (1), meralluride (1), and/or benzothiadiazine derivatives other than bendroflumethiazide (18).

THE MEDICATION. Therapy in the present study was initiated with tablets containing 2.5 or 5 mg. of bendroflumethiazide either alone or in combination with 500 mg. of potassium chloride. The usual dosage finally found most desirable was one tablet daily of 5 mg. of bendroflumethiazide with 500 mg. of potassium chloride. At the start of the study no fixed plan was followed in selecting patients to whom the formulations which supplied potassium chloride were given, although these formulations were specified for the 4 patients who were receiving digitalis concurrently because of the increased risk of digitalis intoxications in the presence of a reduced serum potassium.[3] During the course of the study, most patients were switched from bendroflumethiazide alone to the formulations with potassium chloride, when indicated, as shown in the tables.

The duration of therapy was from eighteen to twenty months for 10 of the patients, twelve to eighteen months for 8 patients, six to twelve months for 7 individuals, and from two to six months for 10 subjects. Three patients were treated for less than two months.

TABLE III. Results in 5 patients treated with bendroflumethiazide for conditions other than hypertension

Case	Sex	Age (Years)	Diagnosis	Treatment: Dosage (Mg. per Day)	Treatment: Duration (Months)	Observations
34	M	41	Rheumatic heart disease with nocturnal dyspnea	5	6	Patient remains symptom-free on continued treatment.
35	F	59	Marked ankle edema up to knees (5 to 7 pounds of fluid retained)	5	7	Excellent diuretic effect.
36	M	84	Arteriosclerotic heart disease with auricular fibrillation; ankle edema	2.5	6	Edema controlled with 5 mg. dose daily.
37	M	60	Myocardial decompensation	5	8	Shortness of breath stopped and other symptoms cleared.
38	M	60	Edema of legs with recurrent thrombophlebitis	2.5	19	Good control of edema; able to work regularly without discomfort.

Twenty patients were on various forms of concomitant therapy including digitalis, anticoagulants, sedatives, analgesics, muscle relaxants, appetite suppressants, thyroid preparations, and nitroglycerin. Only 2 of the patients were receiving antihypertensive therapy concomitantly; both of these were receiving reserpine.

Results

All of the 38 patients in this study responded satisfactorily to treatment with bendroflumethiazide. An average fall of 26.8 mm. Hg occurred in the mean blood pressure* of the 33 patients with hypertension. The observations on the 23 patients with essential hypertension are summarized in Table I, and those on the other hypertensive patients are given in Table II. The favorable results noted in the 5 patients treated for conditions other than hypertension are shown in Table III.

Three patients died (Cases 7, 28, and 32), but the death in none was related to the use of bendroflumethiazide. One death resulted from acute myocardial infarction (Case 32), 1 from uremia (Case 7), and 1 from a heart attack while the patient was in a bathtub (Case 28).

Case Reports

CASE 7. A white female, age sixty-five years, was diagnosed as having essential hypertension. The indication for bendroflumethiazide was an incapacitating blood pressure of 230/120 mm. Hg. The patient was a schoolteacher who had had to retire at the age of forty-nine owing to severe headaches and exhaustion from her teaching duties and from commuting on the train. Previous therapy had included an anticoagulant agent, warfarin sodium, for one and one-half years following a stroke.

On bendroflumethiazide, 2.5 mg. once daily, an excellent antihypertensive effect was obtained, and the blood pressure was controlled at 144/90 to 180/100 mg. Hg. She had a sense of well-being on the drug that was stressed on several occasions both by the patient and her husband. However, this patient had renal damage which eventually necessitated the withdrawal of bendroflumethiazide. Death occurred from uremia.

CASE 14. A fifty-eight-year-old Negro female was diagnosed as having essential hypertension. The indication for bendroflumethiazide was a blood pressure of 236/128 mm. Hg. Previous therapy had included rice and low-salt diets for one and one-half years following an attack of cerebral thrombosis that caused slight and transient right-sided paralysis. Concomitant therapy included hydrochlorothiazide with reserpine.

On combination therapy, using bendroflumethiazide, 5 mg. once daily, and bendroflumethiazide with potassium subsequently, 5 mg. once daily, this patient's blood pressure has been controlled at an average level of 164/104 mm. Hg, she is able to work regularly at light cleaning jobs, and she is without symptoms. Since the patient is a widow with a daughter, it has been essential that she work.

CASE 19. A seventy-year-old white female was diagnosed as having essential hypertension, cholecystitis, and typical and recurrent severe head and neck pain. The indication for bendroflumethiazide was a blood pressure of 184/114 mm. Hg. Previous therapy had included chlorothiazide, and the concomitant therapy included sedative and analgesic preparations.

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* Mean blood pressure = one-half the systolic pressure plus the diastolic pressure.

On bendroflumethiazide, 2.5 mg. once daily for seventeen months, followed by bendroflumethiazide with potassium, 5 mg. once daily since then, her blood pressure has been controlled at 156/94 to 164/100 mm. Hg. Recently this patient underwent cholecystectomy and experienced no hypertension problem either during or after surgery.

Case 31. A white female, age seventy years, was diagnosed as having arteriosclerotic heart disease. The indications for bendroflumethiazide were a blood pressure of 190/92 mm. Hg and periodic, severe shortness of breath. Previous therapy had included whole root Rauwolfia serpentina with flumethiazide. There was no concomitant therapy.

Bendroflumethiazide, 5 mg. once daily, produced dramatic results in this patient. Her blood pressure was reduced to a level of 132/74 to 146/86 mm. Hg, and her shortness of breath disappeared. During the sixteen months of bendroflumethiazide therapy this patient was able to carry on her job in a hospital without difficulty, and when her retirement came up recently, she was able to pass the physical examination required for those who want to continue working.

Case 32. The diagnosis for a white male, age sixty-seven years, was arteriosclerotic and hypertensive heart disease with coronary insufficiency and a myocardial infarction two years previously. The indications for bendroflumethiazide were a blood pressure of 184/100 mm. Hg, with symptoms of breathlessness, easy fatigability, edema of the skin, and tension. There had been no previous therapy. The concomitant therapy included an anticoagulant agent, bishydroxycoumarin, and multivitamins.

On bendroflumethiazide, 2.5 mg. once daily, the blood pressure was reduced to an average of 144/86 to 156/94 mm. Hg. This patient experienced a dramatic feeling of well-being when he was started on bendroflumethiazide, and during the six months of therapy there was no edema or dyspnea. Death occurred from acute myocardial infarction.

The following 3 cases are those of nonhypertensive patients and represent the results of bendroflumethiazide therapy in this small group of the series.

Case 34. Rheumatic heart disease with severe damage and continuous fibrillation was the diagnosis for a white male, age forty-one. The indication for bendroflumethiazide was nocturnal dyspnea. His previous therapy had included a digitalis preparation, and this was continued.

On the digitalis therapy plus bendroflumethiazide with potassium, 5 mg. once a day, this patient became symptom-free and was able to return to work. The duration of therapy was six months. The effectiveness of bendroflumethiazide in controlling his nocturnal dyspnea was shown when the patient stopped using bendroflumethiazide for three days and during this period experienced his worst attack of nocturnal dyspnea.

Case 35. A fifty-nine-year-old white female was diagnosed as having edema with retention of an estimated 5 to 7 pounds of fluid in her system. Bendroflumethiazide was indicated for the edema, which was marked from her ankles to her knees. Chlorothiazide and hydrochlorothiazide therapy had been used previously.

When bendroflumethiazide with potassium, 5 mg. once daily, was given, an excellent diuretic effect was obtained. During seven months of bendroflumethiazide therapy, the edema was kept down so well that the patient was able to work as a practical nurse and had no difficulty being on her feet for long intervals.

Case 38. A diagnosis of edema of the legs from recurrent thrombophlebitis was made of a sixty-year-old white male. The indication for bendroflumethiazide was edema and associated leg pains. Previous therapy had included the use of hydrochlorothiazide. There was no concomitant therapy.

Good control of the edema was maintained during six months of therapy with bendroflumethiazide, 2.5 mg. once daily. The patient was able to work regularly and without discomfort. While hydrochlorothiazide had also controlled his severe edema, the patient felt that bendroflumethiazide acted more effectively.

Side-effects

Thirty-six of the 38 patients in this series remained entirely free of untoward effects during the entire period of observation. One of the 2 patients with side-effects (Case 36), edema associated with arteriosclerotic heart disease, experienced faintness on arising and a fall in blood pressure from 130/70 to 110/60 when bendroflumethiazide was given continuously on a daily schedule. The other (Case 37) with myocardial decompensation, experienced a flare-up of previously diagnosed gout when he, on his own responsibility, increased the dosage frequency of bendroflumethiazide from once to twice or three times a day.

No clinical signs of fluid or electrolyte imbalance were seen in any of the patients during the period of study.

Comment

The generally good to excellent results obtained in this series of patients demonstrates the effectiveness of bendroflumethiazide in low daily dosage and demonstrates that such a regimen is appropriate for ambulatory office patients. A single small dose given once daily is worthy of trial in mild to moderate hypertension and in patients requiring continuous therapy for the control of edema. The usual effective dosage was 5 mg. of bendroflumethiazide with 500 mg. of potassium.

It is noteworthy that, among the hypertensive patients, not only were elevated blood pressures lowered and edema controlled or lessened on the low dosages used, but also such symptoms as headache, shortness of breath, nocturnal dyspnea, and anginal pain were relieved. The effectiveness of bendroflumethiazide in relieving these symptoms has been reported previously.[3, 8]

The clinical response in this series to the diuretic action of bendroflumethiazide lends clinical support to the laboratory finding by others that sodium excretion is increased significantly at doses of 2.5 mg.[7] The response to bendroflumethiazide observed in this series also suggests that the restriction of salt intake may not be necessary even on low dosages since salt intake was not limited strictly in the majority of the patients included in the present study.

Summary

Bendroflumethiazide (Naturetin) in dosages of 2.5 mg. or 5 mg. once daily was employed as an antihypertensive and/or as a diuretic in 38 office patients. At the end of this study, potassium was added in all cases. The purpose of the study was to determine the effectiveness of the drug in the low-dosage range. All patients responded favorably, and in the majority of cases the response was remarkably satisfactory. In a few instances, the response could be considered dramatic.

The reduction of the mean blood pressure in the 33 hypertensive subjects averaged 26.8 mm. Hg. Symptoms associated with cardiovascular disease were controlled or lessened in 5 normotensive patients presenting edema and/or pulmonary complaints.

Side-effects occurred in only 2 patients: 1 experienced mild hypotension when the drug was given continuously on a once-daily basis, and the second reported an exacerbation of gout when the dosage frequency was increased to twice or three times daily. No evidence of tolerance to bendroflumethiazide developed even during prolonged therapy.

From the results of this study, bendroflumethiazide appears to be dependably effective in low dosage both as an antihypertensive and as a diuretic agent. In addition, it is invaluable in permitting patients to take salt in moderation while they are under treatment.

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Total Rehabilitation in Home Care Setting

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The Montefiore Hospital Home Care Program was initiated in 1947 with a basic team consisting of a physician, a nurse, and a social worker.[1] Later a physiatrist and a physical therapist were added, and the rehabilitation programs began.[2] In addition, in recent years we have had an industrial homework project, "Jobs for the Homebound,"* which has amplified the range of available occupational and diversional therapies.[3,4] The net effect of all this has been to transform the home from a relatively primitive medical environment into one in which a broad range of medical services and resources can be brought to bear. This build-up in the home medical resources was in no way intended either to compete with or supplant the hospital. However, it did enable us to care for patients in a home setting who would otherwise have remained in the hospital, and it made it possible to bring to these patients the treatment and specialized personnel associated largely with the hospital environment. We have thus been in the fortunate position of being able to evaluate the two different settings from the point of view of the delivery of medical care. With this opportunity we have followed a considerable number of patients back and forth from the hospital to the home and can compare their course and their reactions to treatment in the two environments.[5]

Since we were all hospital-trained and hospital-oriented, there have been many elements of novelty and surprise in the successful care of patients at home. For example, none of us could have anticipated that the home environment for rehabilitation purposes might not only equal the hospital's rehabilitation ward but also that it might, in fact, be superior. Who, indeed, could have predicted that patients apparently incapable of rehabilitation in the hospital would attain major rehabilitation goals in the seemingly less favorable home setting? Nonetheless, such has been the case for some of our patients. It would appear wise to evaluate such results in terms of their applicability to specific patients and to consider whether or not we may have a useful alternative to building more and more institutional facilities.

Advantages of home environment

At first glance the neat, orderly, well-equipped hospital ward seems far more auspicious and far more efficient for its purposes than the somewhat haphazard home environment. Nonetheless, the clutter and the disorder of the home may have its values. We are all familiar with the weak and vertiginous oldster who gets from the bedroom to the kitchen by clutching and leaning onto his tables and chairs. However wavering or uncertain he may seem, he is ambulatory at home. Furthermore, he always has the option of filling any gap in the line of necessary supporting objects with some other article of furniture. In the hospital, on the other hand, we often find the patient safely confined to bed. An organization of brisk, efficient nurses feed him,

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bathe him, and toilet him, all administered in bed. Any locomotor initiative the patient may possess tends to be smothered in this womb-like environment, and before long we find him curled up in a reminiscently fetal position with flexion contractures. To be sure, this might have been avoided if he could have lined up some furniture in the right pattern, but no charge nurse who is oriented for time, place, and person could ever permit this. Inhospital retrogression is familiar to all of us, and we mention it as recorders of events, not as critics. Retrogression does occur often enough to make experienced physicians ambivalent about hospitalizing elderly patients.

The opportunity to hold onto things physically has its equivalent psychologically and symbolically. More than one elderly patient who was able to maintain his orientation at home has collapsed into confusion in the hospital setting. Brief episodes of disorientation at night, with or without the use of sedatives, are followed by longer episodes during the day. Cortical functioning precariously adjusted to the familiar faces and objects of the home may not be transferable into a new environment. We may then witness a transformation of frailty into senility. Such losses of ambulation or onsets of mental decompensation simply mean that the hospital should not be regarded as a universally fit medical environment. The detrimental influences of the hospital environment may have a less notable impact on age groups other than the geriatric, although children are in some ways comparable.

Most patients find hospital routines and hospital noises strange and disquieting. A fair number of them find the hospital environment depressing, and some patients may have an exacerbation of paranoid trends. A considerable group react adversely to the separation from their families and have feelings of isolation which increase as the hospitalization proceeds. They are among the patients who after a time complain of restlessness and require more sedation or become apathetic and show psychomotor retardation. We have been led to conclude that from several points of view the home does have advantages over the hospital, and it is not surprising that some of these advantages may become manifest when one is dealing with the rehabilitation of patients.

On our Home Care Program we have encountered occasional patients who cannot or will not be rehabilitated in a hospital setting but who have fared exceedingly well at home.

Case reports

Case 1. One example of a patient who could not be rehabilitated in a hospital setting was a sixteen-year-old boy with juvenile rheumatoid arthritis. His hips and knees were particularly involved and had kept him virtually bedridden. He spent two continuous years in four major New York hospitals. Major efforts to improve his bedridden status and to make him ambulatory were largely fruitless. At one hospital it was felt that depressive factors might be playing an accessory role, and he was treated on a psychosomatic pavilion for six months. There an intense program of joint effort by rheumatologists and psychiatrists failed to produce significant progress. The patient was finally transferred to Montefiore Hospital where he remained for approximately six months more. At our hospital very earnest efforts to mobilize him were made. He was showered with attention above and beyond the line of duty. Despite all this, the patient continued to complain of severe and almost incapacitating pain on attempted movement, and he remained nonambulatory. At the end of half a year it was a choice of chronic institutionalization or referral to our Home Care Program.

There was a great deal of hesitation over sending this youngster into domiciliary oblivion, and so the Home Care alternative was adopted without any optimistic anticipations. Since the patient was bedridden, elementary nursing procedures had to be taught to his mother. In addition, our physiotherapist and the Home Care nurses became involved actively in the home rehabilitation program. In sharp contrast to two years of the steady course that had been maintained in four hospitals, a gradual but rather striking series of changes occurred over the next few months. Increased exercise tolerance and improved muscle function were followed by increased activities of daily living, and it became apparent that there was an enhanced motivation toward achieving strength and independence. The patient finally became ambulatory on crutches. The patient's education was continued with a teacher for the homebound, entrance examinations were passed successfully, and the young man now attends one of New York City's colleges.

Comment. This early and illuminating experience taught us the following: (1) One cannot necessarily extrapolate from the patient's course in the hospital into the home, and (2) the home may be a more propitious environment for attaining rehabilitation goals.

Orientations, motivations, and goals may be quite different at home. We know, for example, that a patient who has no hesitation in repeatedly calling on the nurse for the bedpan may not want to impose this chore on members of his own household. Instead, he may make strenuous and energetic efforts to get to the bathroom. The rather natural desire at home to get out of bed and into the kitchen for a snack has no exact equivalent in a hospital setting. This boy, visited at home by his teen-age friends, seemed to identify himself with them and their ambulatory status much more affirmatively than he had in the hospital. Undoubtedly, other and more speculative factors of which we are less aware were operative. Such, perhaps, are the somewhat multiple roles ascribed to the mother and father in psychiatric thinking. A parent who wants a son to get up and go to the bathroom may be re-enacting a historic sequence in toilet training that cannot be duplicated in the hospital. Parents constitute a resource freely available within the home, whatever their roles. The use of parental authority is not generally available in the hospital; indeed, the over-anxious parent flitting about the hospital floor is regarded with some negativism as an interference with routine. A variety of experiences have led us to believe that a parental anxiety and concern can be channelled into effective action and support in a Home Care Program.

In this case hospitals had had plenty of opportunities but failed. In other instances, for one or another reason, the patient may not give the hospital the required opportunity.

Case 2. Some two years ago a sixty-year-old orchestra conductor had a disastrous cerebrovascular accident which left him with a complete right hemiplegia and aphasia. It seemed clear that this marked the end of a laudable musical career. He was treated successively in three hospitals including a well-known institute for rehabilitation. In all of them he was strikingly unhappy and depressed, and his hemiplegia and aphasia showed only modest response. He left each institution after a variable period of time, often against medical advice. His capacity to function had shown little improvement when we started him on our Home Care Program several months after his medical catastrophe.

The chief members of the team involved in this patient's case were the physiatrist, the physical therapist, the speech therapist, and the internist, all of whom were sent into his home. Perhaps by good fortune, both the speech therapist and the internist were music lovers with more than an average understanding of all of the difficulties that beset this aphasic exconductor. Goals that seemed almost absurd were set up. The hospital carpenter shop constructed a podium which was brought into the home. It was felt that the podium would have a specifically significant impact on the patient's desire to walk. With a short leg brace on the right lower extremity, practice in mounting the podium was instituted. After several months it was clear that no significantly useful function could be expected from the paralyzed right arm. The patient was persuaded to institute a process of retraining in the art of conducting, using only the left arm. It was found that, fortunately, his musical memory had remained intact. In addition, his previous remarkable capacity for memorizing new scores again became apparent. For some time now he has been conducting concerts both here and abroad, and his performances have been adjudged first rate in every respect.

Comment

Cases such as these 2 are not everyday ones, but they illustrate a valid point. Obviously, if difficult cases can be rehabilitated at home, so can the run-of-the-mill ones. We have, in fact, encountered no difficulty in the routine rehabilitation of scores of patients.[2] Since a patient has to be rehabilitated for functioning in his own environment, it seems both logical and an easing of the transition to continue him on a Home Care Program. When this is done, the patient need not achieve all the desired goals in the hospital. Instead, he is discharged at a time earlier than would otherwise be the case to continue his program in a familiar setting. Even in the absence of a Home Care Program, a failure to follow the rehabilitated patient into his home may be a grievous oversight. We have seen wheelchair patients, who have been trained to toilet themselves, run into an insoluble difficulty on their return home when they are confronted with a too-narrow bathroom door. We have seen arthritic patients retrogress at home in the absence of continued physical therapy. With a paraplegic patient, for example, it seems to us a desirable easing of the family's burden to follow the patient into the home at least for a time.

We have always been of the belief that no one should be sent to the home from the hospital on a Home Care Program without some provision for his spare time at home. All of our patients have, therefore, been given the opportunity of engaging in diversional and work therapy. Such therapy has helped toward specific rehabilitation goals by strengthening muscles and increasing the range of motion. It encourages activity where otherwise passivity and apathy tend to take hold. There have been surprisingly good reactions to arts and crafts such as leather and metal work, weaving, assembling of objects in tiles, and painting on the part of even brain-damaged patients. Of particular interest has been the positive impact of our industrial homework project, "Jobs for the Homebound." This program has enabled patients at home to engage in paid work in the usual manner of a sheltered workshop. Among the types of work performed have been stapling and assembling, the sewing of syringe wrappers and other hospital items, bookbinding, and envelope addressing.

As we have described elsewhere,[3,4] the opportunity to work and make money has many realistic and symbolic values for our chronically ill patients. It has resulted in increased feelings of self-esteem, a more positive attitude toward the procession of the days, and changes toward the normal in the relatedness of the patient to his family. This has been seen even in those patients who have never worked, as with one twenty-three-year-old with muscular dystrophy who earned his first pay on our program and in a sixteen-year-old lad with severe scarring from epidermolysis bullosa[6] who is presently undergoing vocational rehabilitation.

A Home Care Program, like a hospital, can be looked on as an aggregate of facilities and resources, not all of which are necessarily utilized by a specific patient. Obviously, with moribund or senile patients there may be little or no range of services. For various other reasons, including household or other pressures, an otherwise qualified patient may not be responsive to diversional or work therapy. On the other hand, the need may be permanent, as with one of our arthritic patients who continues to receive physical therapy five times a week, year after year. This therapy has been administered by nurses under the supervision of a physical therapist. With the majority of the patients the need is for courses of physical therapy directed toward the achievement of specific goals, after which the therapy is discontinued. The need for diversional or work therapy is generally of indefinite duration.

Results

Keeping in mind that our patients have a variety of chronic illnesses, one can summarize the distribution of the therapeutic programs as follows:

Of 350 patients on the program from 1956 through 1960, 134 received physical therapy. Out of 76 patients with strokes, arthritis, and allied conditions, 64 received physical therapy; in contrast, only 14 of 78 cancer patients and 14 of 83 cardiac patients needed such therapy. Of 133 patients in the group who took part in work and recreational therapy, 123 were deemed not suitable for this and 94 refused the proffered therapy.

It is not difficult to imagine the transformation in an otherwise medically empty home environment as the physiatrist, physical therapist, nurse, internist, occupational therapist, and work therapist come and go. To some extent what results is more than the sum of these parts. From this kind of total care there emerges a reversal of that sense of alienation from normality which impairs the living capacity of many a homebound patient. It must not be supposed, however, that the flow of transactions is purely in one direction or that the benefits are solely those heaped on the patient. Despite the abundance of services, the cost of caring for such a patient at home is far smaller than in the hospital ($5 per day as compared with $30). It is also far more efficient. A patient need not board in the hospital for twenty-three hours out of the day to secure an hour of rehabilitation service. Nor, for that matter, need his care be limited to the time allotted in the Rehabilitation Department. We have found that it is easy enough to teach members of the household to take part in the rehabilitation program. A household member can aid in walking, can stretch out flexion contractures, can apply heat, and so forth, and this can be done repeatedly throughout the day rather than perhaps just once. Parallel bars, walkers, pulleys, wheelchairs, and the like are brought into the home as needed. If, for any reason, rehabilitation at home should falter, the patient can be swiftly returned to the hospital for a brush-up and just as easily returned home again. It seems inescapably logical to us that rehabilitation services should have a home care extension.

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No finer opportunity

Early in the Kefauver hearings, the subcommittee invited testimony from the Arthritis and Rheumatism Foundation. There followed appalling disclosures that some $250 million are spent each year by arthritic patients on useless quack cures . . . . Considering the close attention of the press and public to these proceedings, never had a Congressional inquiry been handed a finer opportunity to launch a public crusade and mobilize national resources to stamp out criminal operatives in the health field. And what happened? Nothing. The investigators were far more interested in getting back to the assault on manufacturers of cortisone and its derivatives which have actually restored millions of cripples and potential cripples to useful, productive life.—*Austin Smith, M.D., President, Pharmaceutical Manufacturers Association, Report to the Nation*

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

A Review of Headache: 1955 to 1961

Part I

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RECENT ADVANCES in the understanding of the mechanism of headache have improved the physician's ability to diagnose and treat headache. It is the purpose of this paper to present a résumé of those articles of outstanding importance on headache during the past six years. Because of the large number of articles published on headache, it was necessary for the authors to be selective in those reviewed.

It is agreed generally that a great majority of the headaches which a physician treats in office practice can be divided into two main categories: muscular contraction headache and vascular headache of the migraine type.

Mechanism

PHYSIOLOGY. The majority of headaches have a strong vascular component. Investigations prior to 1955 demonstrated the vascular changes which occur in the various stages of migraine. There is an initial vasoconstriction of the cranial vessels, and it is associated with the prodromal symptoms. Following vasoconstriction the cranial vessels dilate, and dilatation was associated with the painful phase of the migraine headache. The observation on cranial vessels was conducted with arterial pulse wave recordings; however, in the past five years there has been a shift in emphasis, and experiments have been conducted on the neurochemical aspects of headache.

Earlier work by Ostfeld and Wolff[1] discussed changes in the arteries of the patient associated with headache; however, it was apparent that vascular changes alone could not account for the pain of the vascular headache. A search was made to define a substance or substances which existed in the area of the affected cranial vessels and would have certain physiologic properties to explain the signs and symptoms of the vascular headache. Ostfeld *et al.*[2] and Chapman *et al.*[3,4] have attempted to define the substance which is present at the headache site during or shortly after a migraine attack. In addition to the vasodilatation which occurs during the headache, it is believed, although not proved, that a sterile inflammatory reaction occurs. This sterile inflammatory reaction is produced by the substance in the vicinity of the extracranial arteries. The substance should have properties which would bring about a tissue reaction consisting of increased capillary permeability, lowered pain thresholds, and heightened vulnerability to injury. Such a substance has been identified with various bioassay technics and labeled "neurokinin." Certain properties of the tissue fluid lead to the belief that it is one substance, and a neurokinin-forming enzyme (neurokinase) is present as well. Neurokinin can be distinguished from various known compounds including the potent vasodilator, bradykinin. It is believed to be a polypeptide, but the exact structure is not known. Future work may elaborate the amino acid content of neurokinin.

Ostfeld and Wolff,[5] Ostfeld *et al.*,[6] and Ostfeld, Goodell, and Wolff[7] visualized the bulbar conjunctival vessels during attacks of vascular headache. The conjunctival vessels revealed inconstant vasoconstriction preceding and constant vasodilatation during the headache. Vasoconstriction, with clearing of edema, occurred with the infusion of norepinephrine and simultaneous clearing of the headache. Vasodilator substances permitted fluid to enter the tissue more readily and to act locally, while vasoconstrictor substances constrict the vessels, raise the pain thresholds, and reduce local edema. The observations on the bulbar conjunctival vessels lend further support to the thesis that local vasodilator substances play an important role in vascular headache symptoms. Furthermore, ergotamine tartrate given to subjects with headache reduced the polypeptide content of the tissue fluid as well as cleared the headache. The intradermal injection of neurokinin and neurokinase produced vasodilatation, a lowered pain threshold, and increased capillary permeability. Since these substances are noted in small amounts normally, it may be that with the migraine patient there is an over-reaction of the normal response for dilatation of the cranial arteries, with the characteristic migraine headache. Hansel[8] and Hansel, Hilsinger, and Barrett[9] believe the basic defect lies in the carotid tree, either in the vasa vasorum of the walls of the larger blood vessels or in the arterioles.

Kunkle[10] believes that acetylcholine is responsible for vasodilatation in migraine, and cerebrospinal fluid was bioassayed by means of a clam heart. Positive assay results were found in 5 of 9 migraine subjects. Further study is necessary to implicate acetylcholine as the vasodilating agent. Acetylcholine and histamine are postulated to produce vasodilatation in cluster headaches. The exact mechanism in cluster headaches is speculative, but extracranial vasodilatation probably does occur.[11]

Several studies were conducted with various drugs to elucidate the nature of vascular headaches. Von Reis, Lund, and Sahlgren[12] administered histamine intravenously to patients with recurrent headaches who were headache-free at the time of the study. The temporal arteries were noted to reach their maximal pulsation in twenty to thirty seconds after the injection. The headache began sixty to seventy seconds after the maximum dilatation of the blood vessels. In no instance was headache found during the phase of vasodilatation. From their work it was concluded that the headache develops when the physical changes of vasodilatation are subsiding; the experimentally induced headache may not be analogous to the spontaneously occurring vascular headache. Kimball, Friedman, and Vallejo[13] were unable to induce migraine headaches with serotonin and several other substances; however, they were successful nine out of ten times with 2.5 mg. of intramuscular reserpine. Further studies by Kimball and Friedman[14] with serotonin, acetylcholine, norepinephrine, or histamine were performed on 16 healthy migrainous subjects. None of these substances initiated vascular headaches. Spontaneous headaches could be relieved in three quarters of the patients with adenosine triphosphate, neostigmine, and acetylcholine together. Additional research in neuropharmacology may yield more information about headache mechanisms.

Pichler *et al.*[15] demonstrated that ergotamine tartrate has a prompt and direct peripheral vasoconstrictor action, and there is evidence indicating a lack of central action. Ergotamine tartrate was as effective in sympathectomized as in nonsympathectomized subjects.

A report by Milner[16] comments on the possible relationship between the scotomas of migraine and the spreading depression of Leao observed in rabbits. The neurophysiologic relationship may mean that migraine scotomas are spreading depressions over the cerebral cortex. Additional work along the lines of neurophysiology has not been reported.

The mechanism of the neurologic deficits associated with migraine is not definitely known. Walsh and O'Doherty[17] hypothesized that the ophthalmoplegia associated with migraine is produced by edema of the internal carotid artery in the cavernous sinus, either by direct pressure on the cranial nerves or by compression of the vessels to the nerves. This hypothesis is suggested by the fact that paralysis is of the peripheral type, involvement is of the third, fourth, sixth, and first branch of the fifth cranial nerves, and these nerves run alongside the internal carotid artery in the cavernous sinus. Paralysis typically occurs after many years of simple migraine and hours or days after the headache phase. The onset and subsidence, in addition to the beneficial response to vasoconstrictors, suggest a vascular course for the symptoms and signs.

More recently Verbrugghen[18] and Friedman, Harter, and Merritt[19] suggested that the compression of the third nerve, particularly at the point of its emergence between the posterior cerebral and superior cerebellar arteries, produces the ophthalmoplegia. Friedman, Harter, and Merritt presented carotid angiography in 6 patients who showed no abnormality of the carotid system. In one of their patients vertebral angiography demonstrated segmental narrowing of the basilar artery which may lend support to the suggestion that vascular changes of the basilar system are responsible for the ophthalmoplegia. Rosenbaum[20] uses serial electroencephalograms taken during the course of the disease in hemiplegic migraine to support the notion that cerebral vasoconstriction occurs earlier and that this is followed by focal cerebral edema during vasodilatation. Either phase may have an associated hemiplegic attack because cortical injury may occur during both phases.

Vanderfield,[21] Friedman[22] and Ostfeld and Wolff[23] offer additional reviews of vascular mechanisms of migraine and cluster headaches.

HEREDITY. Many students of migraine believe heredity has an important role in migraine. There have been no statistical studies to establish whether or not such a relationship really exists.

Greppi[24] believes a primary disease disposition is essential for migraine. The primary disease disposition determines the disease but requires the action of factors which can determine or accelerate the development of the tendency to manifest migraine. Greppi believes there are two hereditary constitutional factors—one appears early and the other appears more slowly at a presenile age and is connected with vascular sclerosis.

Blau and Whitty[25] and Rosenbaum[20] emphasize the hereditary tendency in hemiplegic migraine. The family history may be of decisive value, and it is usually of a similar pattern in a family. In this disease there may be an inherited sensitivity in the cortical areas or an undue vascular phenomenon which produces cerebral ischemia and thereby the transient hemiplegia.

WATER, ELECTROLYTE, AND AMINO ACID METABOLISM. Ostfeld and Wolff[26] observed 3 migraine patients, and they revealed that with life-threatening situations there was fluid retention. Relaxation was accompanied by diuresis, and headache occurred at such times. It was felt that overhydration and headache were concomitant but not causally related.

Schottstaedt[27] studied the renal excretion of fluid and electrolytes of headache patients. The alterations in renal excretion correlated with the situation, behavior, and so forth of the subject rather than with the phase of the headache. The alterations in renal excretion were not of etiologic significance in the genesis of vascular headache. The studies on water and electrolyte metabolism were additional confirmations of earlier studies, where it was noted also that changes in body fluid balance were reactions of the body to stressful stimuli.

Preliminary observations by Kimball and Friedman[28] revealed aminoaciduria with particularly noticeable increases in lysine during headaches of the cluster type. The technic of dimensional electrophoresis was employed in identifying the respective amino acids. The search for a defect in amino acid metabolism may be a fruitful approach to cluster headaches as it has been to various other neurologic disorders associated with inborn errors of metabolism.

ENDOCRINOPATHY. Alvarez[29] attempts to explain the basis for the headache periods in migraine patients. Hormonal factors are cited as important since migraine often occurs in girls as they start menstruating or in women during pregnancy. Roberts[30] found that the combined use of sex steroids with other medications offered the best hope of the prevention of migraine. No adequately controlled studies were carried out in an attempt to evaluate hormonal factors in the causation of headache.

Allergy. It is the impression of many clinicians that various allergies are the cause of migraine headaches. Chocolates, nuts, and other foods are cited frequently as the provoking agent for a migraine episode. However, the objective evidence is extremely scant, and the exact relationship of allergy to migraine headaches remains to be defined. Occasionally a patient is seen in whom an allergen is the precipitating agent for a migraine attack. During the past five years there has been little experimental work to confirm any positive relationship. Bickerstaff[31] describes an unusual type of allergen in the case of a forty-year-old woman who contracted a microfilarial infection while in Nigeria. The patient previously had infrequent migraine, but following the parasitic infestation the headaches were very frequent. Besides the headache, swellings over the extremities and a high eosinophil count were present. Treatment for the infection was successful, and the signs and symptoms, as well as the headaches, subsided.

Kaufman[32] analyzed a large group of private medical patients and concluded that food-induced allergies may cause various types of vascular headaches. Furthermore, the headache may be the sole manifestation of the allergy. The elimination of the offending allergen frees the patient of the allergic headaches.

Aird[33] believes that allergy may be one of many stimuli which will cause migraine headaches. Aird cites authenticated cases of migraine secondary to food allergy. Ogden[34] and Carpenter,[35] in examining the histories of migraine patients, are careful to inquire about inhalant allergies as the cause of the headache. Staphylococci and house dust are thought to be frequent inciting agents.

The etiology of cluster headaches is speculative, but Mayer and Kaufmann[36] believe it is a localized anaphylactoid reaction. They have found a high incidence of nasal allergies in their patients with cluster headaches. There is evidence showing that the headaches are a consequence of vasodilatation in the branches of the external carotid artery. The relationship to migraine is controversial. Some authors feel that it is a migraine variant, and others feel that it is a distinct entity.

Muscular. Headaches may be caused by the sustained contraction of the skeletal muscles of the neck or occipital region. Electromyographic observations have demonstrated that procedures which increase action potentials produce pain, and conversely those that diminish the potentials decrease pain. Judovich[37] expressed conflicting opinion; he noted that heightening of the muscle contraction with electrical currents does not increase the headache. However, relief is obtained with vasoconstrictors but is only partially effective for the pain. Judovich believed that the autonomic innervation of the muscles involved was responsible for the headache. It has been suggested that muscle ischemia also may play a role in muscle contraction headaches.

Ostfeld, Reis, and Wolff[38] observed, during anxiety-producing situations, bulbar conjunctival ischemia and arteriolar hypersensitivity to topical levarterenol. During frontal muscle contraction headaches, bulbar conjunctival ischemia occurred. Agents which promote extracranial ischemia intensified muscle contraction headaches, and vasodilator agents alleviated them. There was a parallel between circulatory catecholamine levels and bulbar conjunctival ischemia. From this work, it was inferred that life settings which evoke anxiety and tension produce elevated blood levels of catecholamines and in susceptible individuals may induce muscle contraction headaches and a parallel response with extracranial vasoconstriction.

Dickel *et al.*[39] have been recording neuromuscular tension by electromyography in patients with chronic anxiety and tension states, 500 of whom have had headache as a chief complaint. They have found that the degree of muscle tension and fatigue is related directly to clinical anxiety levels, that localized increases in tension are correlated with the localization of symptoms, and that tension levels can be reduced. The patient attempts to fight off the initial stimulus to contraction and maintains control by willfully increasing the muscle tension. The resulting headache may be compared to the

"Charley horse" of the athlete who tries too hard with his muscles too tight.

More direct studies performed by Onel, Friedman, and Grossman[40] indicate that there is an increased muscle blood flow during muscle contraction headache. Using radioactive Na^{24}, they observed increased muscle flow during muscle contraction headaches; however, the increased blood flow may be relative ischemia during a period of heightened muscle contraction.

Psychologic. The importance of psychologic factors in patients with chronic headache is well documented. The exact mechanism whereby the psyche can produce vascular headaches is conjectural. Kolb[41] has emphasized that frequently the headache is a psychoneurotic expression or the psychophysiologic result of tension or anxiety, and it may be seen in the schizophrenic, manic depressive, and involutional psychotic reactions.

Tissenbaum, Koblentz, and Friedman[42] studied 430 headache patients. Forty-seven per cent were psychogenic, and 33 per cent were post-traumatic. It was emphasized that more patients in the latter group frequently have underlying emotional problems. However, the percentages probably are not representative of the general population, because the patients were studied at a Veterans Administration hospital. Stenback[43] made a study of patients with headaches which were not produced by organic diseases. The author attempted to study the relationship of headache to personality and life stress. Life stress is emphasized in causing headache. Engel[44] presented data on 23 consecutive patients with ulcerative colitis, and they revealed that 20 had suffered from headache. Headaches occurred in 12 patients during remissions. Eight patients with chronic colitis tended to have headaches when diarrhea was less and bleeding was absent. Headaches occurred when the patient felt in control, and this was followed by conscious or unconscious guilt, but the significant object relationship was not jeopardized. Constant bowel bleeding occurred when the patient, to varying degrees, was feeling helpless. Allerton[45] comments that the mechanism in post-traumatic headache usually is psychologic. The history of head trauma is misleading. The author found that these people have a strong pseudomasculine defense or are obsessive, compulsive, personality types. Donahue[46] points to the strong psychologic basis of eyestrain headache. Two thirds of the patients obtained relief by relaxation during reading or working close to an object. In an intensively studied case of a twenty-five-year-old female, 38 attacks of migraine were brought on by situations activating aggressive and hostile conflicts. The recognition of conflict-producing situations at the onset of the migraine attack would cause the headache to subside.

Mullin[47] observed that headaches were a frequent complaint at an isolated Antarctic base. They were blamed in 50 per cent of 37 sick-call entries. Mullin attributes the high incidence to emotional factors, specifically, the need for the careful control of aggression under circumstances of close personal association. Headache was more common in the civilian scientist and officer group than in the enlisted personnel. Garma[48] feels that the scotomas of migraine are related to previous visual psychologic trauma which are repressed. Smith[49] believes that the personality forces which most commonly produce headache are a lack of confidence in one's self, in one's relation to his environment, and an inability to express hostility and resentment. Alvarez[50] noted the temperament of 218 female patients; 95 per cent had a typical, keen, quick, eager mind. They were not definitely less sexual than nonmigrainous females. Blumenthal and Fuchs[51] found psychologic factors paramount in migraine of children, and the headache may be related to their inability to express hostility toward authoritative figures.

Altschule[52] has noted in some instances emotion-evoking situations which include physiologic changes which favor the occurrence of headache. Several different types of mechanisms may be involved. These include vascular changes and excessive muscle contraction which may be part of the reaction to adverse stress. Also, hyperventilation which occurs as part of the reaction to emotional stimuli produces alkalosis, enhancing the perception of pain. The author suggests that the salt and water retention that is present with stress may have a role in headache production, although this may be a parallel, rather than causal, result of stress.

HEADACHE ASSOCIATED WITH INTRACRANIAL DISEASE. There is experimental evidence to show that the headache associated with intracranial tumors is not only a pressure effect. Wolff[53] and Ostfeld[54] point out that traction and displacement of pain-sensitive structures rather than pressure itself is responsible for the headache associated with brain tumors.

Symonds[55] presented 6 cases in which transient severe pain in the head on coughing or straining was the only or outstanding symptom of organic intracranial disease. It was postulated that the increased venous pressure resulting from cough and similar action was capable, in the presence of an already abnormal pressure, of causing headache. There is increased intracranial pressure from venous dilatation at the expense of cerebral capillaries and the expulsion of cerebrospinal fluid. With the cough there may be traction on the vascular and dural structures anchoring the brain to the skull. There also may be injury to intracranial pain-sensitive structures.

Baker and Gottlieb[56] described a case of a simple benign cyst in the choroid plexus of the lateral ventricle which caused intermittent headache and an attack of prolonged unconsciousness. They believed the mechanism of the headache to be a ball valve type of obstruction with an increase in pressure in the lateral temporal horns of the ventricle. The headache was influenced by position changes and cured by the removal of the cyst.

HEADACHES ASSOCIATED WITH ORAL, NASAL, PARANASAL, AND AURAL STRUCTURES. The nasal and paranasal structures are incriminated frequently as the cause of migraine headaches. It is more likely to be the unusual patient who has these structures as the basis of headaches. The studies performed prior to 1955 are the basis of our understanding of the role played by the paranasal structures in headache. McAuliffe, Mueller, and Wolff[57] stated that the mucosa covering the entrance to the paranasal sinuses was found to be the most pain-sensitive of the nasal and paranasal structures. The sinus lining was relatively insensitive. It was emphasized that if headache is not associated with turbinate engorgement and inflammation, it is not the result of disease of the nasal or paranasal structures.

McAuliffe[58] cites experiments performed on the maxillary sinus which demonstrated that increased pressure within the antrum may be associated with pain and headache. Reflex engorgement of the nasal structures was believed to be responsible for the pain produced. Pressure within the sinus is felt as pressure in the side of the face. By cocainization of the turbinate bodies the headache can be made to disappear after the pressure within the sinuses has been increased.

Raymond and Monica[59] and Atterbury and Vazirani[60] report cases of migraine headache relieved by the correction of dental disease; the mechanism by which the headache is brought about is not commented on.

POSTSPINAL PUNCTURE HEADACHE. Bungardner and Burns;[61] Lykins;[62] Wetchler and Brace;[63] Vandan and Dripps;[64] Rosser and Schneider;[65] Alexander, Brown, and Sivak;[66] and Sweeney *et al.*[67] comment on the leakage of cerebrospinal fluid as the mechanism of production of postspinal puncture headache. The current belief is that the leakage of cerebrospinal fluid leads to a fall in the subarachnoid pressure and traction on the pain-sensitive intracranial structures results. Schofield[68] noted that the incidence of headaches fell with advancing age, except for a definite rise in females at the menopause and in patients with acquired syphilis or normal fluids. The data on the duration and time of onset of the headache, on the effects of postural changes, and on visual and auditory phenomena indicate that the postspinal puncture headache syndrome results from decreased cerebrospinal fluid pressure and leakage of cerebrospinal fluid. The manner in which reduction of the pressure may result in headache is believed to be traction on sensitive intracranial structures, but the exact nature and mechanism of these structures has yet to be determined.

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Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
January 5, 1962

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by MARDOQUEO I. SALOMON, M.D.

Fever, Seizures, and Coma

Case history

Salvatore Baldino, M.D.: A forty-two-year-old Negro male was admitted to Knickerbocker Hospital for the first time on July 23, 1961, complaining of headache of one week's duration followed by an episode of unconsciousness. The patient apparently was well until two weeks prior to his admission when he began to complain of malaise and fatigue. During the week prior to admission he felt feverish and lost his appetite. In addition, he developed a persistent, generalized headache. He treated himself with aspirin with little effect. On the morning of admission the patient left the house but returned home about noon stating that he "felt sick." Shortly after this he suddenly became unresponsive and developed shaking movements of his extremities, rolling his eyes and grinding his teeth. In a few minutes he was drowsy but talking and was brought to the emergency room.

The patient suffered from alcoholism and had been drinking heavily for years. There was a questionable past history of tuberculosis. In the past few years he had been hospitalized several times for hepatic cirrhosis and once for pneumonia. On one of these occasions he was told he had diabetes and was given pills to take. He neither followed a diet, checked his urine, nor took his medication regularly. There were no other significant past illnesses, and a system review, according to his wife, was unremarkable.

On physical examination the blood pressure was 140 systolic and 85 diastolic, temperature 102.8 F., pulse 140 per minute and regular, and respirations 24 per minute. The patient appeared well developed but poorly nourished and was acutely ill. He could be aroused but was disoriented and unable to give a history or cooperate. There was no sign of head trauma. The mucous membranes were moist. There was a constant grinding of the teeth but no trismus. The pupils were equal and reacted sluggishly to light. The fundi were normal. His neck was rigid. Respirations were regular, and auscultation of the lungs was unremarkable except for diffuse rhonchi which could be heard generally. The heart sounds were of good quality, and no murmurs or friction rubs were audible. The liver was felt 6 fingerbreadths below the right costal margin. A neurologic examination revealed prominent evidence of meningeal irritation. In addition, there was a left hemiparesis with a coarse tremor of the left upper and lower extremities. The deep tendon reflexes were depressed throughout.

The hemoglobin was 12.5 Gm., and the white blood cell count was 12,000 with 71 per cent polymorphonuclear leukocytes. The urine contained 3 plus albumin and 1 plus sugar with many red cells and 7 white cells per high power field. Skull x-ray films showed normal findings. The spinal fluid was cloudy and contained 1,675 white cells per cu. mm. which were predominantly polymorphonuclear leukocytes. The protein was more than 400 mg. per 100 ml., and sugar was 64 mg. per 100 ml. A gram stain and an acid-fast stain did not reveal bacteria. The fasting blood sugar was 188 mg. per 100 ml. A chest x-ray film revealed a density in the upper field of the right lung with a suggestion of pleural reaction. The findings were consistent with pneumonia or, less likely, tuberculosis. A radiolucency in the upper lobe of the right lung raised the question of a cavity.

On admission, subsequent to the completion of the spinal tap, therapy was instituted with penicillin, sulfadiazine, and chloramphenicol (Chloromycetin) in adequate dosage. Twenty-four hours thereafter, since the spinal fluid culture showed no growth in the light of the clinical picture as then presented, isoniazid and streptomycin were added to the regimen. He continued in a semicomatose condition and had frequent seizures usually beginning on the left side of the body and then becoming generalized. A Babinski sign appeared on the right.

Two days after admission the patient was in a coma; the left-sided findings of tremor and hemiparesis persisted. The temperature was 102 F. Blood and throat cultures were negative. A repeat spinal tap yielded cloudy fluid with a pressure of 220 mm. of water. There were 4,000 cells, predominantly polymorphonuclear leukocytes, with a protein of 166 mg. per 100 ml. and a sugar of 15 mg. per 100 ml. Again no organisms were seen. The white blood count was 9,200, and the sedimentation rate was 104 mm. per hour. The serology gave positive results, and the nonprotein nitrogen was 29 mg. per 100 ml. The urine culture grew out coagulase-negative Staphylococcus aureus on one occasion and Aerobacter aerogenes on another.

The patient's neurologic picture changed very little. On the fourth hospital day chloramphenicol and sulfadiazine were discontinued. At that time the spinal fluid contained 1,000 cells, 48 per cent polymorphonuclear leukocytes and 52 per cent lymphocytes, protein of 140 mg. per 100 ml., and sugar of 30 mg. per 100 ml. By the sixth hospital day the patient had improved and could respond to verbal commands and answer some questions. The left hemiparesis remained, and there were now bilateral Babinski signs. His neck was still stiff.

On the tenth hospital day the patient was alert, obeyed commands, and could identify objects. On the fifteenth hospital day a third lumbar puncture revealed clear fluid with 99 cells, predominantly polymorphonuclear leukocytes, a protein of 109 mg., and sugar of 40 mg. per 100 ml. A chest x-ray film showed considerable clearing of the infiltrate in the upper lobe of the right lung. The temperature was 100 F.

On the seventeenth hospital day the temperature spiked to 104 F. It was felt at first that this was the result of a urinary tract infection since the urine was cloudy and contained many white blood cells. A spinal tap was performed. The patient again became stuporous and developed left-sided convulsive movements. He was started on large doses of antibiotics: penicillin, sulfadiazine, and chloramphenicol. He did not improve and died on the nineteenth hospital day.

Discussion

Mardoqueo I. Salomon, M.D.*: The clinical history of this patient can be outlined in a few sentences. We are dealing with a forty-two-year-old Negro who had a questionable history of tuberculosis in the nonspecified past. During the last few years of his life he developed cirrhosis of the liver, most likely the result of heavy alcoholism and a poor diet. Diabetes mellitus was discovered during this period, but he neglected to control it. Finally, he developed a serious intracranial disease which caused his death in about five weeks. In trying to concatenate these morbid processes into a unity, logical if not nosological, I think a chronologic approach is likely to be helpful, so I shall start with his diabetes mellitus.

There is scarcely any need for me to point out that diabetes mellitus is a disease which starts not at birth but at conception. The blatant expressions of diabetes, such as hyperglycemia and glycosuria, are only two aspects of the malady and not even the most important ones. We now know that many manifestations of the diabetic state, the so-called complications of diabetes, are

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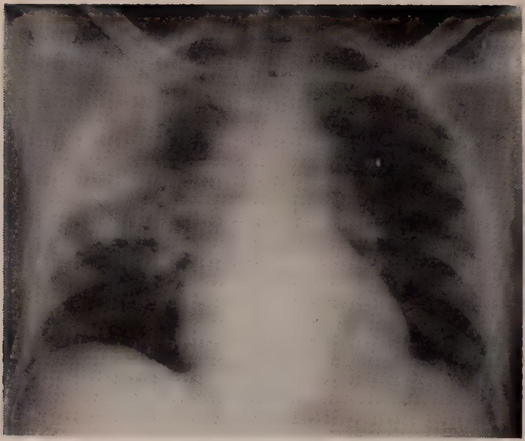

FIGURE 1. Chest roentgenogram on admission showing diffuse infiltration of upper and middle fields of right lung. There is a zone of radiolucency superimposed on the upper portion of the infiltrate.

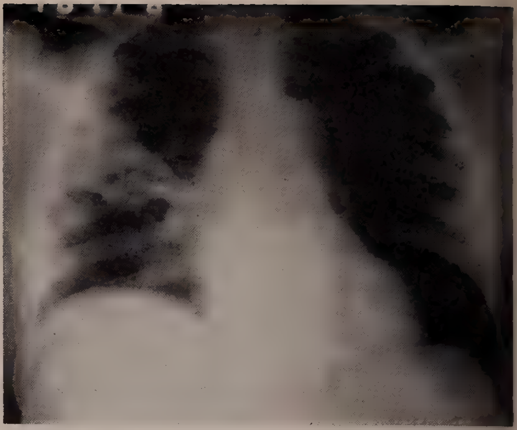

FIGURE 2. Chest roentgenogram two weeks later. A film taken three days previously had shown considerable clearing of the infiltrate, but in this projection the infiltrate is more extensive, somewhat denser, involves both parenchyma and pleura, and contains several small, fairly discrete radiolucent foci.

only the inexorable manifestations that appear irrespective of "good" or "poor" control. Indeed, they may be present before the overt diabetes in the so-called prediabetic stage, or to use a more modern locution, in the stage of diabetes premellitus. I refer to the neuropathy, microangiopathy, nephropathy, and so forth.

The second element in the clinical setting is alcoholism, an acquired habit of our civilization. Both diabetes and alcoholism predispose an individual to tuberculosis, and I am sure that there is no one in this room who has not seen this "complication" in such a clinical setting. There is no need to dwell on hepatic cirrhosis in alcoholic patients. I shall refrain from a circuitous discussion of the relationship of alcoholism to the pathogenesis of cirrhosis. Suffice it to say that alcoholic patients are quite prone to develop it.

At this point we come to the mysterious lung shadow, and I shall ask for a radiologist's opinion.

JOSEPH M. MOYNAHAN, M.D.: The patient was too sick to be brought to the x-ray department, so we are limited to an evaluation of portable films taken with the patient in the supine position. The initial film (Fig. 1) taken shortly after admission shows an area of density in the midfield of the right lung and in the lateral aspect of the upper lobe of the right lung. It appears to be partly parenchymal and partly pleural in nature. A zone of radiolucency is superimposed on the upper portion of the density and raises the question of consolidation with a central cavity. A second chest x-ray film taken two weeks later shows considerable clearing of the infiltrate, but three days later the densities had increased in extent (Fig. 2). Again, there is a suggestion of both parenchymal and pleural involvement in the process. There may be some segmental collapse, and there are several discrete foci of radiolucency. There is no evidence of a hilar mass, but all the films were taken with the patient in the supine position, and the ascending aorta partly obscures the right hilum.

My impression is that the process is pneumonic and that there is an associated pleuritis. There may even be some small abscess cavities, but I do not think the process is likely to be tuberculous, chiefly because of the rapid changes in its roentgenographic appearance. The segmental distribution, pleural reaction, and sharp margins suggest the possibility of an infarct. There is no reason why a large infarct might not develop central areas of necrosis as part of its resolution. However, it would be rather uncommon to see a zone of infarction of this extent involving adjacent areas of both the upper and middle lobes of the right lung.

DR. SALOMON: Well, I see that we are still in the dark as far as the shadows are concerned. We now come to the process that represented the coup de grâce for our patient, namely, the process that caused his malaise and headache, then later the coma, convulsions, and hemiparesis, and finally, most likely, that caused his death.

It is self-evident that the patient had an acute meningitis. The clinical signs and the laboratory study of the spinal fluid admit no alternative. But what kind of meningitis? The constant absence of bacteria, the nugatory effect of intensive antibiotic therapy, and finally the concomitant appearance of left hemiparesis and left Jacksonian epilepsy lead me to believe that this was a sympathetic meningitis, that is, an "aseptic" meningitis provoked by a lesion situated beneath the dura or within the substance of the brain itself.

The Jacksonian fits and the hemiparesis permit some degree of cerebral localization. They suggest a focal lesion in or on the right side of the cerebrum. Admittedly the concept of pyramidal versus extrapyramidal lesions, so emphasized in former years, is no longer tenable since the studies of Power[1] and Travis and Woolsey.[2] Nonetheless, from a practical point of view we may disregard this "re-evaluation of values" and assign the lesion to Brodmann's prerolandic zones 4 and 6. However, whether the lesion is on the surface of those zones or in the subjacent cortex and white matter, or even in the suprajacent subdural space, cannot be determined so easily. The constant grinding of the teeth, a variant of Kojewnikoff's epilepsia partialis continua, would seem to indicate an involvement of the lower prerolandic areas.

Be that as it may, the combination of sympathetic meningitis and a prerolandic lesion do suggest what is commonly termed "a space-occupying lesion." I have never been happy about this unfortunate term, for what lesion could be conceived of as not occupying space?

William B. Ober, M.D.: How about diabetes mellitus as a nonspace-occupying lesion?

Dr. Salomon: I shall leave this heuristic question unanswered to avoid being dragged into problems of epistemology and ontology. Let us consider specific diagnostic possibilities.

The diagnosis of subdural hematoma in a patient with chronic alcoholism cannot be ruled out merely because we have no history of head injury. Such trauma can be overlooked or forgotten easily, especially if the latent period is rather prolonged, as it often is. Papilledema need not be present. Even an ephemeral improvement, as in this particular patient, does not rule out the diagnosis. However, the persistence of polymorphonuclear leukocytes and the low spinal fluid sugar values make me hesitate.

The diagnosis of tuberculoma is difficult to rule out, particularly with the anamnestic shadow of pulmonary tuberculosis. But the pleocytosis is quite high for this diagnosis, a fortiori with such a low sugar. By the same token, lateral sinus thrombosis is a distinct possibility, but I would expect more evidence of ocular signs, either a proptosis or evidence of a lesion damaging the third, fourth, or sixth cranial nerves. In Merwath's syndrome, occlusion of the rolandic veins, the localization of signs and symptoms is compatible; but in this curious entity the foot and the leg are involved first and foremost, which was not the case with our patient.

A solitary brain abscess can develop without an evident primary site of infection, such as a sinusitis or an otitis, congenital heart disease, or perforating skull trauma. Chronic pulmonary suppuration is a fertile ground for a "metastatic" abscess. In patients with brain abscess the pressure of the cerebrospinal fluid is increased, pleocytosis with polymorphonuclear predominance is common, the size of the abscess may lead to nonspecific pressure phenomena, and the location of the abscess may determine the focal signs. A brain abscess can be ushered in by such vague complaints as malaise, fatigue, somnolence, or the like, but the cerebrospinal fluid sugar should not be lowered by an intracerebral abscess. I cannot discard the idea of an abscess, but there are other possibilities to consider.

The protocol contains one rather remarkable set of observations: the relative leukopenia in the presence of fever and an accelerated sedimentation rate. This led me to toy with the possibility of systemic lupus erythematosus. However, even though this protean disease obeys no procrustean rules, I cannot establish such a diagnosis on the strength of the positive data in this case and in the absence of other, more orthodox manifestations. Needless to say, the positive serology findings would come in handy were this a valid line of reasoning.

The relative leukopenia raises the possibility of a fungal infection. Of the number of pathogenic fungi, Nocardia is the most likely because of the involvement of both the central nervous system and the lungs. But no fungi were recovered, and the pulmonary lesions decreased in extent before the patient's death; and so I shall have to discard the idea of a fungus.

Recently, amebiasis has been described as the cause of a somewhat similar clinical picture.[3] For all we know, even the large liver might have been caused by an amebic infection. Nevertheless, the total clinical picture of the case does not fit into the pattern of multiple amebomas.

Almost by exclusion I have to consider an infectious process that would involve the leptomeninges on the convex side of the cerebrum. Specifically, I have lues in mind. Indeed, syphilitic leptomeningitis can cause both the meningeal and the cerebral signs described in this case,[4,5] including in the more fulminating cases the intense polymorphonuclear pleocytosis. Because of its more diffuse character, it could even account for the paradoxical contralateral Babinski sign, even though a slight compression of the pes pedunculi also could cause it. The transient improvement appears to have been quite pronounced; possibly it was the result of penicillin therapy. One might explain the final recrudescence of symptoms to the sudden occlusion of a miopragic cerebral vessel, perhaps under the very impact of a healing process.

MICHAEL S. BRUNO, M.D.: If you are going to make a diagnosis of meningovascular syphilis, how can you account for the low cerebrospinal fluid sugar values?

DR. SALOMON: I have no specific explanation for this. Although spinal fluid sugar is not necessarily reduced in central nervous system lues, I don't think that a low value necessarily excludes the diagnosis.

PERRY BERG, M.D.: The initial spinal fluid sugar value was 64 mg. per 100 ml. which is not necessarily low. However, in a diabetic patient with a blood sugar of 180 mg. this could be low. Was the blood sugar determination done on a specimen drawn at about the same time that the spinal fluid was tapped?

DR. BALDINO: The first spinal tap was done on the evening of admission. The fasting blood sugar was determined on a specimen drawn the following morning.

DR. BERG: Then we cannot be sure of the significance of the first spinal fluid sugar value; bacteria may not have been present in the fluid at that time. Subsequent spinal fluid examinations with the repeatedly low sugar values were done after antibiotics had been administered. It has been observed frequently that bacteria may not grow in media containing antibiotics even in small dilutions, even in the face of a demonstrable infection.

VINCENT VINCI, M.D.: The patient's clinical course suggests to me a fairly well-localized brain abscess, and the sudden development of coma and death would be consistent with the rupture of such an abscess into the subarachnoid space.

DR. SALOMON: This, of course, is a strong possibility, and there is nothing in the protocol to exclude it.

DR. BRUNO: Occasionally negative findings in bacteriologic studies on spinal fluid can be misleading. Not long ago we reported a case of central pontine myelinosis in which the underlying disease was a subdural abscess secondary to acute ethmoid sinusitis.[6] We never were able to get positive spinal fluid cultures in this patient, but at autopsy we did demonstrate streptococci by smear and culture for the abscess. If an intracranial infection is well walled off, bacteria may not be present in the circulating cerebrospinal fluid even with an intense leukocytosis.

LEONARDO DUBINSKY, M.D.: For a known diabetic patient who made no effort to control his carbohydrate metabolism, this patient does not seem to have reacted in the manner one might expect. If he had such a serious bacterial infection of the central nervous system, one would expect hyperglycemia of more than 180 mg., certainly diabetic ketosis, and possibly even diabetic coma. He had none of these

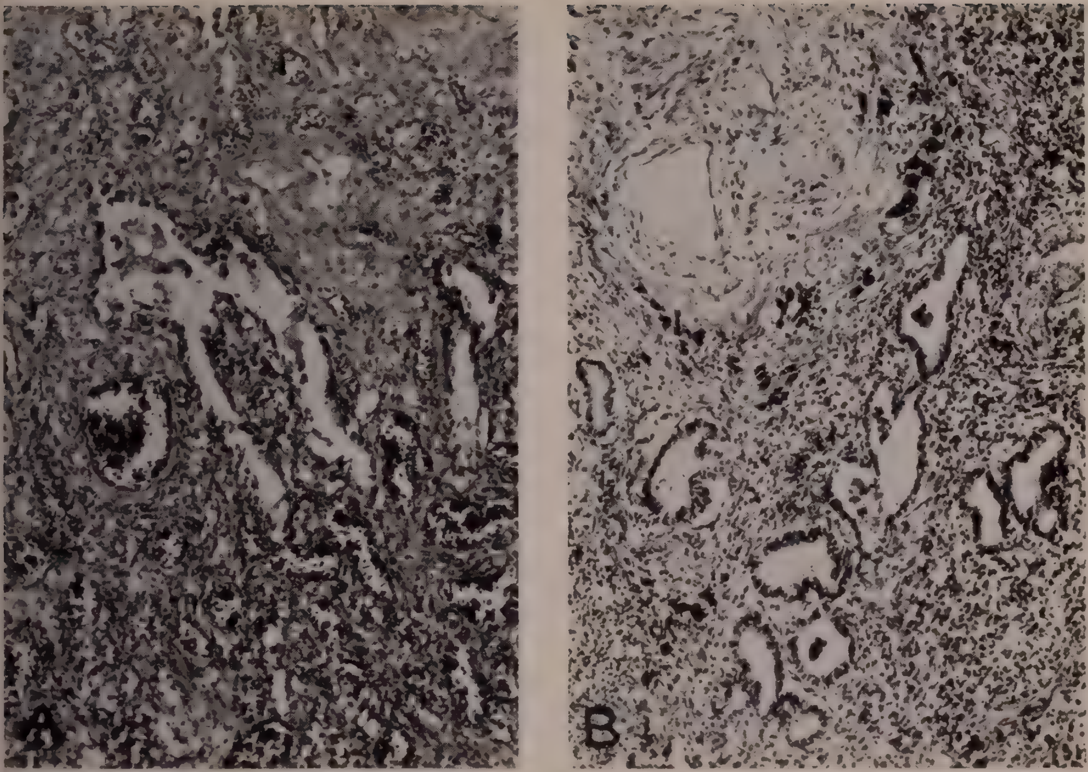

FIGURE 3. (A) Section of upper lobe of right lung showing fibrosis, organization of intra-alveolar exudate, and hyperemia. (B) Area of pulmonary fibrosis and chronic inflammatory exudation showing cuboidal metaplasia of the epithelium of terminal bronchioles or bronchiolar ducts.

phenomena on admission, nor did they develop during his hospital course. The terminal seizures and coma seem to be related definitely to his intracerebral and meningeal disease rather than suggesting diabetic coma.

Dr. Salomon: There are two possible explanations for his failure to behave as one would expect a diabetic patient to. One might conjecture that there was a lessening of the diabetes concomitant with the development of a diabetic nephropathy. There seems to be little clinical or laboratory evidence to support this, but I cannot exclude the possibility. However, a more likely explanation is that his central nervous system infection was not due to one of the usual pathogens, and this is perfectly consistent with my idea that this infection was treponemal.

Jim Harris, M.D.: It was our impression on service that the initial spinal fluid sugar value was low and that the patient probably had a bacterial infection.

David Fine, M.D.: We should remember that low spinal fluid sugar levels are not invariably the result of bacterial infection. One can find low values in carcinoma involving the meninges and in mycotic infections.

Dr. Bruno: Are the cerebrospinal fluid findings consistent with a diagnosis of tuberculous meningitis?

Dr. Fine: They certainly are. Early in the course of tuberculous meningitis the spinal fluid sugar may not be low, or at least not significantly low, and one may see a large number of polymorphonuclear leukocytes. Later in the disease there is a tendency for the sugar levels to fall, and the exudate usually contains a large proportion of lymphocytes.

Clinical diagnoses

1. *Tuberculous meningitis*
2. *Pulmonary tuberculosis*
3. *Portal cirrhosis, liver*

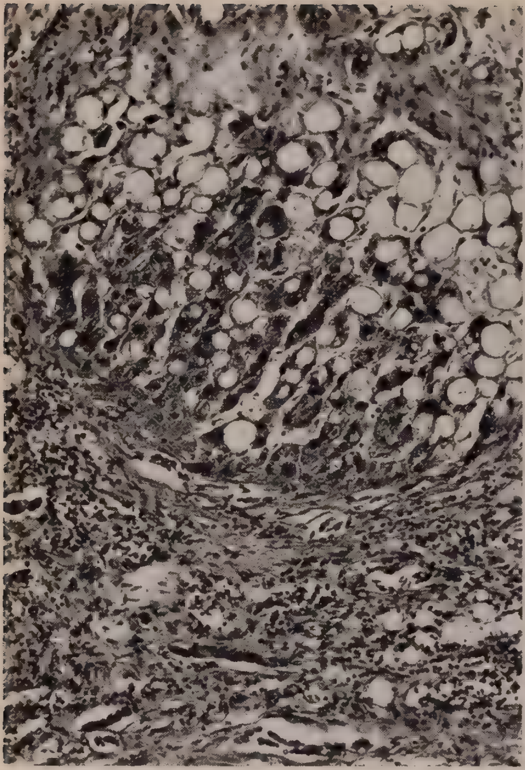

FIGURE 4. Section of liver showing the edge of a regenerating nodule with much fatty metamorphosis. The parenchymatous nodule abuts a zone of fibrosis, lymphocytic infiltration, and bile duct proliferation.

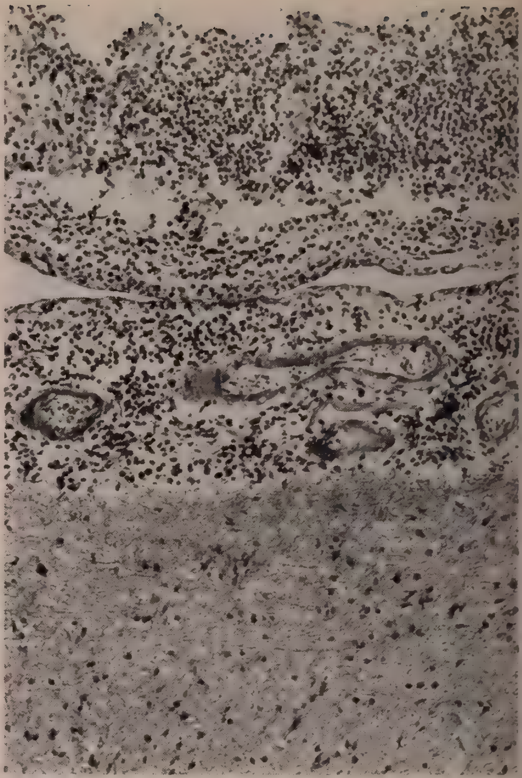

FIGURE 5. The pia-arachnoid is diffusely infiltrated with polymorphonuclear leukocytes, and there is a slight deposition of fibrin.

4. *Diabetes mellitus*

Dr. Salomon's diagnoses

1. *Syphilitic leptomeningitis*
2. *Pulmonary tuberculosis*
3. *Portal cirrhosis, liver*
4. *Diabetes mellitus*

Pathologic report

Dr. Ober: As I stood at the autopsy table, I tried my hand at a bit of clinicopathologic concatenation. The right lung showed a great deal of disease in the upper and middle lobes with much fibrosis and a few small scattered cavities that exuded sticky, purulent material. There was no evidence of caseation. Coupling this with a history of diabetes mellitus and an evident meningitis plus an intracerebral lesion, I had hopes that this might be an example of mucormycosis. However, this guess could not be supported. The pulmonary lesions proved to be those of an organizing, nonspecific pneumonitis, the old-fashioned carnification of the lung. There was evident fibrosis with organization of intra-alveolar exudate (Fig. 3A), and in older areas there was so-called fetalization of alveoli (Fig. 3B). This is not a good term; the spaces lined by cuboidal epithelium probably represent terminal bronchioles or bronchiolar ducts, not alveoli. There was still evident active infection, and the cavities were really small abscesses lined by granulation tissue. There was no real evidence of tuberculosis.

The liver showed a typical nutritional cirrhosis with much fatty metamorphosis (Fig. 4). A histologic documentation for a diagnosis of diabetes mellitus was equivocal.

There was a diffuse meningitis involving the meninges covering the cerebrum and much of the upper part of the spinal cord

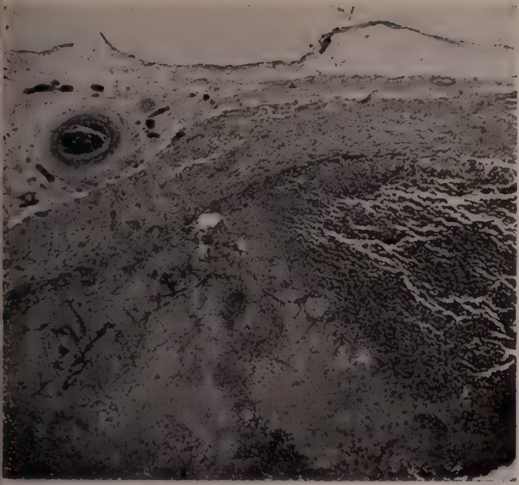

FIGURE 6. Low-power view of the brain abscess in the prerolandic area. Thickened meninges are applied to the surface of a zone of walled-off intracerebral liquefaction necrosis which is almost in contact with the subarachnoid space in this plane of section.

(Fig. 5). In the right prerolandic area, as Dr. Salomon predicted, there was a space-occupying lesion. It proved to be an abscess about 1.8 cm. in diameter (Fig. 6). It was filled with yellowish-green pus, and it involved the cortex and a portion of the underlying white matter. Thickened leptomeninges were adherent to it, and when sectioned, it came within 1 mm. of the subarachnoid space. I have no doubt that the abscess was leaking into the subarachnoid space, that the meningitis was secondary to it, and that there may have been an extensive terminal outpouring of bacteria.

Our postmortem bacteriologic studies were not very helpful. The autopsy was done forty-eight hours after the patient's death, which limits the reliability of the observations. A smear and culture of the pus in the abscess yielded A. aerogenes. It is possible that this patient did have an organizing gram-negative pneumonitis with a metastatic abscess to the brain, and I would commit myself to this diagnosis were it not for the fact that cultures from the upper lobe of the right lung yielded nonhemolytic streptococci. One could, I suppose, explain away the streptococci as indicating secondary, mixed infection of the carnified lung. However, once one begins to explain findings away, it is difficult to know where to draw the line, and one could just as well dismiss the Aerobacter in the brain abscess as a postmortem contaminant which had overgrown the bacteria which were originally there. It is idle to speculate further; all I can really say is that he did have a bacterial abscess in the prefrontal area and that it did leak or rupture into the subarachnoid space.

Dr. Bruno: Most of the physicians who saw this patient felt that this was a tuberculous meningitis. It was not until a final spinal tap was done two days before the patient's death that the clinical diagnosis was changed. We withheld the bacteriologic results of this tap for the sake of the discussion and because they were not reported until after the patient had died. Coagulase-negative staphylococci were grown in quantity from the cerebrospinal fluid on this occasion. There were over 50,000 white blood cells in this specimen, a determination which is strongly suggestive that the abscess leaked.

Dr. Ober: Both A. aerogenes and coagulase-negative Staph. aureus were recovered from the urine during the patient's life, each one on one occasion only. However, there was no evidence of urinary tract infection at autopsy.

Anatomic diagnoses

1. *Brain abscess, right frontal lobe, with diffuse purulent meningitis*
2. *Organizing pneumonitis, right upper and middle lobes*
3. *Portal cirrhosis, liver, nutritional type, with fatty metamorphosis*
4. (*Diabetes mellitus*)

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Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Action of Insulin on Tissues

With Some Remarks on Insulin Antagonism

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ONLY IN A FEW instances of diabetes mellitus can one determine the etiologic factor responsible for the disturbance. Those are the cases associated with hyperfunction of the pituitary (acromegaly), of the adrenal cortex (Cushing's disease), or of the adrenal medulla (pheochromocytoma), or those cases associated with acquired severe pancreatic disease (chronic calculous pancreatitis or carcinoma). The vast majority of diabetic subjects inherit an undefined genetic defect which, operating by an as yet unknown mechanism, leads sooner or later to a disturbance in the hormonal balance, characterized by an absolute or relative lack of insulin. The "mellitus" aspect of diabetes then comes to the fore. It is this aspect, with its well-studied metabolic disturbances, which is amenable to control by insulin or materials evoking insulin secretion. In all humility it must be stated that the important phase of the life of the patient which precedes the onset of hyperglycemia is shrouded in mystery, with some foglights beginning to dispel the shroud slightly. The very serious angiopathy and the crippling neuropathy are indeed cardinal elements of the disease, but their direct relationship to the difficulties in foodstuff metabolism is unclear.

It is evident therefore that inquiry into the nature of the action of insulin and of its antagonists does not promise the answers to many of the problems of diabetes. One may hope, however, in such an inquiry to gain some insight into the "mellitic" phase of the disease and its biochemical peculiarities.[1]

Nature of hormones

Despite the fact the hormones form a most heterogenous group from the vantage point of the chemist (some are proteins, others amino acids, still others steroids), they do constitute a more uniform group from a biologic viewpoint. They are humorally transmitted signal systems.

They serve to integrate organ and cell functions in a manner which appears goal-directed in respect to the organism as a whole, especially in its adaptation to induced changes.

In the test tube, the rates of enzymatic processes depend on concentrations of substrate and catalyst, inorganic ion strengths, pH, substrate removal, and so forth. In the cell, the innumerable chemical reactions are in addition controlled by structural characteristics at the submicroscopic level—the macromolecular complexes, the organelles, and the resulting multitude of surfaces. More and more attention is being paid to these geometric aspects of biologic chemistry despite the difficulties in approach.[2] In a multicellular organism, it would seem likely that it is the role of the hormones (as it is of the peripheral nervous system) to bring about, reversibly, subtle changes in submicroscopic form and thus trigger a change in the functional direction as well as in the rate of a process. This viewpoint is supported in part by the repeated observations that it becomes more and more difficult to elicit a hormonal effect as one proceeds from the whole organism to isolated organs, tissue slices, homogenates, and subcellular preparations. A certain degree of morphologic intactness seems necessary for hormonal (and drug) actions. The gun needs to be at least partially assembled for the demonstration of the action of the trigger.[3,4]

Insulin and enzyme reactions

During the last few years several comprehensive reviews dealing with the mechanism of the action of insulin have been published and the reader is referred to them for detailed references and for a variety of viewpoints.[3-7] Sanger's elucidation of the amino-acid sequence and the structure of the insulin molecule is one of the most brilliant chemical achievements of the recent era. However, thus far the structure of the molecule has remained unrelated to any of its effects, and no notions as to the mode of action can be derived from it. Insulin is a simple protein of unit molecule weight of about 6,000. Since the intravenous injection of 4 micrograms of insulin per kilogram of body weight lowers the blood sugar of a susceptible animal to about 50 per cent from the initial level, it can be calculated that approximately 4,000 molecules are available per cell of assumed average volume of 8,000 cubic microns, or one molecule for every 2 cubic microns. The minimal effective dose of insulin is closer to one fifth of that amount. Thus it is evident that we are dealing with a material of the type associated with active catalysis or the initiation of a chain of reactions.

A concern with the mechanism of action of insulin has long served to bring clinician, biochemist, and physiologist together in an area of common interest and recurring controversy. The existence of the hormone was predicted, and it was named before its isolation; its major biologic properties were outlined before any experience was available with the isolated principle. The sustained interest in this hormone derived from the striking effect of insulin in both clinical and experimental diabetes mellitus and has been paralleled by the repeated biochemical efforts to pinpoint its site of action in the enzymatic scheme of metabolism.[3,8]

Both historically and currently, carbohydrate metabolism occupies the central position in thinking about the action of insulin. A disturbed regulation and utilization of glucose constitutes the hallmark of the metabolic aspect of diabetes, which results from an absolute or relative deficiency in the secretion of insulin. It was soon apparent that the other foodstuffs were not spared in this disturbance and that protein and fat metabolism were, in turn, profoundly influenced by insulin. A variety of physiologic and nutritional schemes were developed to place these disturbances in fat and protein metabolism as secondary consequences of the impaired regulation and utilization of carbohydrate. The remarkable development of enzymology gave considerable meaning and logic to these observations and hypotheses. As enzyme after enzyme was identified and isolated, the stepwise dissimilation and synthesis of carbohydrates, fats, and proteins evolved into the now familiar pathways of intermediary metabolism.

As each new development in this area of biochemistry was fashioned into the expanding schemata of enzymatic steps, certain common points of confluence between carbohydrate, fat, and protein appeared. Based on logic but not evidence, one could point to site after site in the enzyme schemes in which insulin might act to exert its profound and concurrent effects on all the foodstuffs.

The elusive process of attempting to

identify the precise site of the action of insulin paralleled much of the development of our understanding of intermediary metabolism and in no small measure was the concern and work of the same investigators who outlined the enzyme steps.

A series of demonstrations began to appear which invoked enzyme after enzyme as the precise point of action of insulin in intermediary metabolism. None of these proposals, however, met with general acceptance. The failure of adequate experimental repetition, failure to explain the extensive responses to insulin, failure to achieve general demonstration in the many species and tissues which respond to insulin, and, on occasion, failure to achieve consistency between the proposed site of action and the responses in the intact animal all contributed to the ultimate disregard of the various promulgated interactions between specific enzymes and the hormone. A gradual, reluctant, but nevertheless persistent retreat through the enzyme schemes was in evidence, and by about 1945 the initial step in glucose metabolism, its phosphorylation by hexokinase, was generally felt to be the only logical and promising enzyme site for insulin action.[9,10]

Despite the negative results of two or three decades of intensive work along such lines, the general conviction that insulin action would be found in some intimate molecular interaction with a particular enzyme of intermediary metabolism represented the atmosphere of thinking in this area of research. In a sense, hexokinase now represented the last fragment of territory for this approach.

The reports of a direct action of insulin on cell-free hexokinase extracts were greeted enthusiastically for a time. However, in fairly short order, this proposed enzyme-hormone interaction became as untenable as the many previous ones along such lines. Objections were raised on technical and biochemical grounds. Of equal importance were some physiologic inconsistencies. The search for the precise site of the action of insulin had reached a serious impasse. That the hormone was operating to facilitate the entry of glucose into the metabolic pathways at some critical point was clear and obvious.

Sugar transport

The search for the enzyme site of the action of insulin was exhausted at least for the moment, and a new approach to the whole problem was necessary. This new approach, in retrospect, turned out to be a revival and extension of much older speculations.[3] The pendulum swung swiftly to an area of thinking which preceded the all-consuming interest in the biochemical pathways of intermediary metabolism. The structure of the cell, the nature of the packaging of the enzyme equipment into the cellular organelles, and the nature, limitations, and problems raised by the existence of intracellular-extracellular compartments were now considered as possible sites of hormone action. In areas seemingly remote from endocrinology and metabolism, these problems were the central core of investigation. In the biology of microorganisms, in the concern of secretion and absorption, and in the studies of the red cell the movement and transport of materials from the surrounding extracellular fluid to the intracellular compartment have been widely studied and questioned. By contrast, the regulation of metabolism, whether by insulin or by other factors, tacitly assumed free or at least rapid entry and exit of materials from the intracellular site of the enzyme apparatus. The possibility that the confining surface of the cytoplasm, the cell membrane, might constitute a limiting step in the movement of glucose was proposed by the authors' laboratory as a likely site of the action of insulin. This would constitute a step ahead of the known enzymes and hence a step ahead of hexokinase. Insulin would be conceived as regulating the rate of flow of glucose to the enzyme apparatus rather than directly affecting the reaction rates of any critical step of intracellular intermediary metabolism.[3,11-13]

INSULIN AND SUGAR TRANSPORT. Our approach to the problem of sugar transport was to attempt a sharp distinction between the movement of a sugar from one position to another and any subsequent metabolism of that carbohydrate. For glucose, this presented a variety of problems involving either the deduction from the behavior of trace amounts of radioactive glucose or the use of enzyme poisons. Instead, we chose initially to study the behavior of sugars closely related to glucose in structure but for which enzymes are sharply circumscribed. The eviscerated-nephrectomized animal has long been a tool of the metabolic laboratory. Deprived of the liver, intestines, and kidneys, the preparation can survive for many hours or even days with appropriate care. Many areas of function have been studied extensively in this preparation, showing excellent preservation; other functions are acutely lost with extirpation of these viscera. The metabolism of a variety of substances is limited to the liver, intestines, and kidneys. Included among these materials are a variety of sugars. Galactose, the congener of glucose, when injected into the eviscerated-nephrectomized dog is no longer metabolized or excreted. It behaves as an inert material essentially similar to the behavior of urea and creatinine. When a measured amount is introduced intravenously, the blood concentration shows a descending curve for a time until some area of distribution of galactose is reached, and the concentration remains constant. The galactose can now be said to be occupying a space, a volume of water distributed through the body which is available to the sugar. We were able to show that the size of this galactose space was a function of insulin.[3,11] In the absence of added insulin, galactose would occupy about 40 to 45 per cent of the carcass weight. This represented the extracellular fluid space plus the intracellular compartment of certain cells. At any point the addition of insulin resulted in a sharp fall in the blood galactose with the re-establishment of a new equilibrium, representing a distribution space now of 65 to 70 per cent of the carcass weight. Insulin made a space available for the entry of galactose which corresponded to total body water. Having once achieved this widest distribution, additional insulin promoted no further decrease in blood galactose. Carcass analysis revealed that the movement of galactose from the extracellular position to the intracellular compartment previously unavailable without insulin was achieved without any metabolism of the sugar. One could recover the injected material regardless of the area of distribution of galactose or the addition of insulin.

Although this demonstration argued by analogy, it appeared as a most satisfactory scheme for the manner by which insulin regulated the metabolism of glucose. It was proposed that certain cells, presumably those of striated muscle and adipose tissue primarily, were denied free and ready access to the entry of glucose. The intracellular apparatus was capable of very high orders of glucose metabolism with the rate of entry constituting the limiting step. Insulin, in some manner, was conceived as facilitating the movement or transport of the sugar across the cellular surface barrier from its extracellular position to the intracellular compartment. For galactose, in the eviscerated-nephrectomized preparation, this was shown by the manner in which insulin made available a larger space of distribution. Since no further metabolism of galactose was possible, a new equilibrium at a lower concentration in the blood, because of wider distribution, was the end result. For glucose, the greater rate of entry into the cell would result in a greater rate of its metabolism by the intracellular enzymes.

A variety of sugars was tested in this fashion. The sugars employed fell into two categories. Both hexoses and pentoses, which exhibited the same chemical configuration of hydrogens and hydroxyls about carbons 1, 2, and 3 as seen in the glucose molecule, were affected by insulin in promoting their intracellular transport. Those sugars which were modified at these carbon positions were indifferent to the presence or absence of insulin. The insulin-stimulated transport apparatus was pictured as being capable of accepting glucose by virtue of its chemical structure. Coincidentally, sugars of very similar configuration were able to ride the transport system into the interior of the cell and afford the experimental approach described previously.

ACTION OF INSULIN ON TRANSFER OF GLUCOSE. This hypothesis of insulin promoting cellular entry of sugars was examined by a number of workers in various species and isolated tissues.[3-8] Rat, dog, rabbit, cat, and man showed a similar phenomenon. The rat diaphragm, the isolated perfused heart, and the anterior chamber of the eye became tools in the study of the translocation of sugars under the action of insulin. The work of Park *et al.*[14–16] gave particular strength to the glucose transport theory of insulin action by demonstrating directly the phenomenon for glucose in a manner analogous to that seen with the nonutilizable sugars. They argued that the concentration of free glucose inside the cell could be used to distinguish between an action of insulin on permitting glucose entry rather than an action promoting increased enzymatic dissimilation. If insulin promoted an increased entry of glucose then there should be an increase in free intracellular glucose. However, if insulin operated by virtue of directly promoting a greater rate of utilization of glucose by the enzymes, then the free intracellular glucose should diminish and thereby allow further glucose entry as a secondary consequence. Using a number of conditions involving both excess loading with glucose and lowering the temperature of the tissue, these workers were able to show that one of the consequences of exhibition of insulin was a rise in the free intracellular glucose, clearly indicating a primary role of insulin in permitting more glucose to enter the cell. Glucose behaved in a manner quite parallel and analogous to that of galactose. Rapid phosphorylation by hexokinase carried the glucose off into intermediate pathways, maintaining a continuous flow of the sugar into the cell in this fashion. The cell's surface was the limiting step in the metabolism of glucose, and insulin determined the rate of transport of the sugar through the limiting and confining cell membrane.

Turning to the cell membrane in relation to the action of the hormone is at once exciting and highly naïve. The nature and structure of this limiting surface is poorly understood. Much of what is known is deduced from the movement of different materials. Yet such a structure has substance. It can be distorted by a microneedle under a microscope. It can be ruptured and fragmented and it stands between two water compartments of entirely different composition. The evidence which places insulin action at this boundary point is firm and impressive. Going beyond this to propose details as to the nature and structure of the glucose transport system and its relation to insulin is highly conjectural and must be approached cautiously and with considerable reservation.

RELATIONSHIP OF INSULIN TO THE TRANSPORT SYSTEM. Out of the many recent reports of work concerning the relationship of insulin to the transport system has come a variety of findings which do not lend themselves readily to a simple unified picture as initially proposed from the galactose experiments. Many naturally occurring as well as synthetic sugars have been tested in this fashion. The configuration of the sugars acceptable to the insulin-stimulated glucose transport system appears to go beyond the initial findings of the glucose model. Considerable manipulation about carbons 2 and 3 is possible without loss of response to insulin. These variations have been reported in different species and in different isolated tissues.[4–6,8] They may very well reflect the fact that the actual transport apparatus is intrinsically independent of insulin itself. For other cells, there is great species and tissue specificity as to the transport systems for sugars and other substances. The selective entry of materials is a property of organized cells whether of free living microorganisms or of the tissues of multicellular animals. Even closely related species may exhibit different properties of red-cell uptake of sugars. When a systematic comparative study of the chemical configuration requirements of the sugar transport system under discussion is undertaken covering the usual laboratory animals and man and the various tissues employed in research, we may very well have to view insulin as activating the transport system in some fashion, but not determining its precise intrinsic properties. One can view the transport system as a specific property of cell structure, normally held in an inhibited state and activated by the hormone.

Some strength to this view is derived from the work of Randle and Young[5,6] who have shown that anoxia as well as various enzyme poisons, which reduce the oxidative metabolism of the cell, simulate the action of insulin on glucose transport. While there can be many interpretations of these findings, one can propose that part of the normal metabolic function of the cell is to maintain its transport system in a state of inhibition. This would have adaptive meaning since glucose uptake must occur in an orderly, regulated fashion for survival of the organism. A profound and fatal hypoglycemia would be the consequence of rapid glucose uptake in the absence of an increased supply from the gastrointestinal tract or the liver. It may very well be that certain cells such as those of skeletal muscle and adipose tissue are adapted to very high-capacity glucose transport systems for the storage of carbohydrate in the postprandial period. These cells are kept continually in a state of inhibited transport as part of the minute-by-minute maintenance function of their biosynthetic and oxidative activities. At the appropriate times, insulin opposes this inhibition and allows the transport system to operate at higher rates.

Critique of concept

Such a view, which dissociates insulin action from the intrinsic properties of the glucose transport system, might well afford a unified picture to account for the growing evidence that insulin can promote the uptake of amino acids in certain isolated tissues independent of any action on glucose.[17,18] Specific transport systems for the selective uptake of amino acids are very likely, if not essential, to cellular operation. Whether or not such findings of uptake of amino acids by isolated tissues in the absence of glucose will prove to be meaningful in relation to the normal processes of protein metabolism remains to be seen. In any event, these observations do not really threaten this conception of insulin action. It may turn out that insulin opens up an entire area on the mosaic surface of the cell, allowing free access of a number of inhibited transport systems to the materials in the extracellular fluid. The action on glucose would be the most evident and obvious effect. The effects on other constituents may be less apparent but possibly of equal significance.

These three items—the variability in the requirements of chemical configuration, the inhibited rates of glucose uptake with normal oxidative metabolism, and the apparent transport effects of insulin on amino acids—represent but three examples of growing information that derives from examining insulin from the point of view of a membrane regulator. One can certainly anticipate more. Efforts to confine these various phenomena within the structure of a single action of insulin at the cell membrane are hampered by the paucity of detailed information of the nature of this cellular structure. However, this is an area of growing interest and activity. The simple view of the cell membrane as a homogeneous, dialyzing casing for a structureless droplet of cytoplasm has long been challenged. Specific intracellular structures, positioning of enzyme systems, channels, and constant and variable organelles, have already been found in a variety of cells. The association of intracellular enzyme-bearing structures with the membrane itself has been demonstrated in certain instances. The variability in the structure of the confining cell membrane is only one part of the larger and pressing problem of the intimate structure of the cell itself.

Locating insulin action at the surface of the cell will satisfy a large body of experimental data. It will also serve as a most satisfactory explanation for much of what is observed in both the normal regulation of blood sugar and glucose movement as well as the disturbances seen in diabetes mellitus. Nevertheless, it is far from being a complete answer. One can force cellular uptake of glucose by a high concentration of the sugar in the absence of insulin. Indeed one can equate the rate of uptake of insulin-free tissues to that of hyperinsulinized tissues with large amounts of glucose. Some of the metabolic consequences of the glucose which enters the cell, however, are different depending on whether it has achieved entry by high concentration or with the assistance of insulin. The hyperglycemia of the diabetic organism tends to offset the lack of insulin by increasing tissue uptake. But even additional glucose and further hyperglycemia will not correct all the metabolic disturbances which are due to a lack of insulin. Glucose entering cells under the impact of insulin finds a much readier access to glycogen synthesis than to other pathways.[19] Are these simply osmotic consequences of hyperglycemia at the cell's surface, or does the conception of a transport system at a specific site on the cell membrane imply a continuing organization into the depths of the cell channeling the insulin-promoted glucose more effectively into the appropriate enzyme schemes? While the view that insulin acts at the surface of the cell may be correct, the underlying structure of the cell as a whole may convert this action into a more complicated and far-reaching metabolic sequence of events which the entry of glucose by the diffusion effect of concentration can only approximate but not achieve.

Effects of muscular exercise on glucose metabolism

In a somewhat different vein, the glucose transport theory of insulin action reopens the entire question of the effect of muscular work on glucose metabolism. The fact that exercise increases the utilization of glucose in the absence of insulin has been known clinically for a long time. The labile, insulin-sensitive diabetic patient who is controlled with adequate insulin while in bed requires a sharp reduction in insulin once he has returned to full motor activity. This independence of muscular work from insulin in promoting glucose utilization has been carefully studied by Ingle, Nezamis, and Morley[20] and others. The explanation offered originally was simple and adequate. The increased rate of utilization of glucose and conversion to carbon dioxide, water, and contractile energy made room for more glucose and hence, brought it in. Tied to the concept of enzyme steps as a limiting factor this view is consistent. But once having placed the cellular entry of glucose as the limiting factor at rest, it remains so for cells during contraction. This conflict was readily resolved when eviscerated-nephrectomized dogs were subjected to intensive muscular work by electrical stimulation of the hind quarters. Under these circumstances not only was glucose taken up at a higher rate but also nonutilizable sugars of precisely the same chemical configuration as those affected by insulin were afforded intracellular access.[3,12] The authors have shown by cross-transfusion technics that strenuously contracting skeletal muscle releases a humoral material into the blood stream which behaves as does insulin in activating the same sugar transport system across cell surfaces. Not only are the working muscles themselves so affected but also the resting tissues or the tissues of a recipient resting animal in a cross-transfusion experiment experience activation of their sugar transport systems.[21] Apparently a number of humoral materials can act on this specific transport system and allow it to express higher rates of activity. Working muscle regulates its own increased rates of glucose uptake and with more strenuous contraction promotes a generalized increase in sugar uptake by the resting muscles through the release of this as yet unidentified humoral factor.

Insulin and the liver

This finding raises a much wider question To what extent can insulin explain the whole complex of regulation not only of carbohydrate but also of fat and protein; the flux and flow to storage depots, to the liver, to tissues experiencing increased needs? To what extent do changing rates of secretion of insulin and the other relevant hormones completely satisfy the problems of foodstuff regulation in feeding, fasting, and muscular work? Is this example of autoregulation of skeletal muscle an isolated and unique situation? This question is relevant to the matter of insulin effect on the liver. The metabolic behavior of the liver is markedly different in the presence and absence of insulin. The liver of the diabetic organism is busily engaged in gluconeogenesis and ketogenesis. It is relatively or completely insensitive to the effect of food, failing to shut off these activities and to promote lipogenesis, glycogen synthesis, and protein synthesis. Yet, despite these profound shifts in metabolic direction in the absence of insulin, a conclusive demonstration of a direct action of insulin on the liver is lacking or at least very much in question. The response of the liver in the diabetic animal to the administration of insulin is very much delayed, whereas that of skeletal muscle and adipose tissue is almost immediate. The liver shows virtually no restriction to the inflow and outflow of glucose, to its intracellular position both in the presence and absence of insulin. A cellular membrane site of action of insulin in the liver would appear to have little meaning.[22] Are there physiologically meaningful intracellular or cell-free actions of insulin? These have yet to be shown in any consistent fashion. Is the action of insulin on the liver either token in character or absent completely? A direct in vitro action on the liver in a manner comparable to the effects seen after in vivo administration of insulin has not been found. Are the hepatic responses in fact secondary responses to metabolic information sent to it from the peripheral tissues? The manner in which the liver increases glucose output to match the changing needs of the peripheral working muscles is unexplained. The manner in which it shifts to ketogenesis to supply additional caloric needs with progressive fasting is similarly unexplained. Indeed, the whole spectrum of hepatic responses for providing foodstuffs for the periphery in relation to their changing uptakes and in relation to diets and to feeding and fasting are far from adequately understood. It may be that insulin acts exclusively in the periphery and is only one of a number of regulatory devices in the balance between hepatic metabolic activity and the peripheral tissues as storage depots and as utilizers of glucose.

Summary

We can summarize the present status of the subject as follows:

1. In a large number of tissues, comprising the sites of active storage of carbohydrate in the form of glycogen and of fat, insulin acts by opening the "gate" for blood glucose. The enzymatic machinery of intermediary metabolism is activated by the increase in the rate of glucose entry and its consequent phosphorylation.
2. This action leads to increased glycogen storage, lipogenesis, and oxidative breakdown in skeletal muscle, the heart, the connective tissues, and the cells of the adipose tissue.
3. Enhanced carbohydrate metabolism leads to increased esterification of free fatty acids, and therefore fat mobilization is inhibited. Consequently blood fat levels are decreased and the production of ketones is depressed.
4. Protein synthesis from amino acids is favored by increased carbohydrate turnover but may also be influenced directly by insulin via an action of insulin on amino acid incorporation into muscle proteins.[17, 18]
5. Direct effects of insulin on metabolic processes in the liver are more difficult to demonstrate unequivocally. It has been shown recently that in the isolated perfused liver insulin promotes the incorporation of amino acids[23] and inhibits the outflow of potassium.[24] It still is not clear how insulin exerts its effect on liver sugar output and/or glucose uptake.
6. We do not as yet have insight into the actual biochemical mechanism by which insulin and its specific cell receptor jointly produce the primary effect from which all other effects of insulin could be deduced. The site of action for some tissues is located at the cell membrane in close connection with a specific sugar transport system.

Antagonism to insulin

It is quite difficult to provide an adequate definition for insulin antagonism. Operationally this has been measured by the degree of inhibition of the expected lowering of the blood sugar following a particular dose of administered insulin. Such an operational definition is much too broad, since an injection of glucose with the insulin would mask the hormonal effect, and thus glucose could be defined as an insulin antagonist.

Both epinephrine and glucagon exert their major "anti-insulin" effect by just such a mechanism. These hormones lead to rapid liver glycogenolysis and thus "inject" more glucose into the general circulation. In addition, epinephrine limits the rate of glucose phosphorylation, probably by causing an increase in the intracellular content of glucose-6-phosphate. Neither glucagon nor epinephrine inhibit the transmembrane passage of insulin-sensitive sugars.[7]

The glucocorticoids "oppose" insulin action primarily by their stimulatory effect on gluconeogenesis. They do not seem to oppose the rate of transport of glucose into insulin-sensitive tissues.[7]

The pituitary growth hormone may inhibit glucose disposal rates by actions at the level of the fructose phosphate step in glycolysis, but again does not "antagonize" insulin at its effector site.[25]

Under particular conditions the circulating plasma may contain one or more factors, presumably protein in nature, which seem to nullify or depress the expected action of insulin. Of these factors the clearest are the antibodies to exogenous heterospecific insulins. Their mode of action is of course an antigen-antibody combination which competes successfully with the attachment of insulin to its receptor substance.[26,27]

It has been postulated that endogenous insulin may be secreted in a complexed form and that such an insulin-protein complex is inactive. Activation occurs when the compound is disrupted (by a proteolytic enzyme?). While such a system may account for the inhibition of the activity of endogenous insulin, the complexing protein presumably does not oppose the action of exogenously administered insulin.[28]

Resistance to the action of administered insulin has been encountered under a variety of conditions in both animals and man. The antagonists in such instances are found in one or another of the serum protein fractions. Thus in diabetic acidosis one encounters an alpha globulin which may exert its action by hindering the insulin molecule from attachment to its specific cell receptor.[29]

In the rat, the administration of growth hormone leads to the appearance of a B-lipoprotein which in effect opposes insulin action by a mechanism which is not yet clear. Both growth hormone and the glucocorticoids seem necessary to the appearance of this and other protein fractions found in depancreatized cats and dogs.[30,31]

In the mildly obese diabetic patient insulin assay (using the rat diaphragm glucose uptake) shows normal amounts, and insulin added to the plasma of such patients can be recovered. Thus their plasma does not seem to possess an insulin antagonist. However in the uncontrolled severely diabetic individual the basal insulin content is low and added insulin seems to be inactivated. The plasma antagonist in such cases appears to be associated with the albumin fraction of the serum proteins. There is some relation of this plasma component to pituitary activity.[31]

Finally, there are some instances in which extreme insulin resistance exists, but the plasma of such patients contains insulin by assay and may contain it in tremendous amounts after its exogenous administration. Such individuals do not seem to have a circulating antagonist. The resistance (by exclusion) appears to be in the tissues which are normally responsive to the hormone.

Comment

It is evident that this fascinating area of investigation is beset by a myriad of technical and other problems which will take time to resolve. At present we can only state that circulating materials associated with several of the serum proteins may be present which "antagonize" insulin action either by combining with the hormone or by preventing its combination with the effector site. Several of these materials depend for their existence on the activity of pituitary and adrenal hormones. We must curb our speculative enthusiasm concerning the physiologic and/or pathogenetic importance of these "antagonists" in relation to diabetes mellitus until their characterization and possible modes of action become clearer than they are now.

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Number thirty-six in a series of articles on Current Concepts in Diabetes Mellitus

Growth in clinical research

In the past fifteen years there has been a striking growth in clinical research as a two-way bridge between the laboratory and clinical practice. Coupled with this is the achievement of the pharmaceutical industry in the manufacture, quality control, and marketing of new products. In consequence, the lag between scientific discovery and widespread use of new drugs has been shortened.—*Luther Terry, M.D., Surgeon General, U.S. Public Health Service, to 1961 National Health Forum*

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Facial Injury from Anesthesia Mask

THE PROPER STERILIZATION of anesthesia equipment is necessary to prevent cross-infection. Rubber and plastic anesthesia goods will not withstand steam sterilization. Most often rubber goods are washed with or soaked in a germicide between cases. Germicides must be used with great care to avoid face burns.

Case report

A young Negro woman with a diagnosis of sickle cell disease, hemarthrosis, and possible tuberculosis underwent a biopsy of the hip under general anesthesia. A general inhalation agent was administered by face mask for one hour and forty-five minutes. The course of anesthesia and her immediate recovery appeared uneventful.

That evening she complained that her face was more painful than the operative site. Visitors stated that her face appeared to be burned.

No notations were entered on the chart until two and one-half months later. At that time an examination revealed depigmentation on the bridge of the nose, circling the nose, the side of the mouth, and the chin in an oval exactly corresponding to the pressure distribution of an anesthetic face mask. This appeared to be an area of vitiligo or a healed second-degree burn.

Comment

An investigation revealed that the face mask had been soaked for ten minutes in a concentrated solution of a germicide (O-Syl). The manufacturer states that the chemicals in this germicide, which was not used according to his directions, are primarily sensitizers but in high concentrations can be irritating to the skin. The rubber of the face mask will absorb the germicide if the mask is soaked in it. Face mask rubber also contains a substance called Age-Rite Alba, or monobenzoether hydroquinone, which can be leached out of the rubber by the germicide. This substance can produce vitiligo or depigmentation.

Several errors were committed in this case. The face mask was improperly sterilized. The anesthetist failed to elevate the mask from the face at frequent intervals to examine the patient during the conduct of anesthesia. An examination is necessary to detect skin damage which may be caused by irritating chemicals which have been absorbed by the rubber. Rubber goods often are cleaned by inexperienced personnel so that a high index of suspicion is always required.

This girl's face was not examined or

Presented and discussed at a conference held at Bellevue Hospital, New York City, February 5, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

treated by a dermatologist, nor were any notations entered on the chart until legal action had been instituted by the girl's attorney. An ostrich approach to errors in the care of the patient always compounds the harm and the liability.

It is stressed that to disinfect rubber anesthesia equipment, the manufacturer's instructions must be followed strictly to avoid absorption of irritating chemicals, damage to the rubber, and inadequate sterilization.

As an example, the technic of sterilization using the germicide is outlined.

> For anesthesiology rubber tubing and rebreathing bags, flush and rinse with cold water to remove any adhering organic matter. Immerse in 2 per cent germicide solution, allow to act for fifteen minutes . . . but not longer. Drain, immerse in 70 per cent alcohol for one full minute, remove, and wrap in a sterile towel. Allow at least four hours to elapse before using.
>
> Face masks are not to be immersed in the 2 per cent germicide solution; instead, they are wiped with this solution using cotton or a cellulose sponge for this purpose. After wiping with the germicide, wipe with 70 per cent alcohol and allow to dry thoroughly before using.

Other products which may be satisfactory are Betadine and pHisoHex. Ethylene oxide sterilization also may be efficacious.

Number one hundred twenty in a series of Clinical Anesthesia Conferences

Convention paging system

We hope that physicians attending the 156th Annual Convention of the Medical Society of the State of New York will be able to devote all their attention to the interesting program, exciting exhibits, and other features of the meeting. However, if it is necessary, physicians can always be in touch with their offices, their patients, or whoever else may wish to contact them, through the SherPage System. They may be reached by television anywhere at the convention.

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Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
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Year-End Report on Activities of the New York City Poison Control Center

During 1961 the Poison Control Center expanded its services both in magnitude and in scope. Attention was focused this year on professional and lay education, since it is believed that it is the most important weapon in the battle against accidental poisonings. A major emphasis also was placed on the prevention and control of lead poisoning.

A larger number of communities from Upstate New York were served during the year. Over 100 separate communities in Upstate New York and about 50 communities in New Jersey were served on a sustaining basis. Requests for help also were received from Florida, Mississippi, Pennsylvania, Rhode Island, Iowa, Michigan, North Carolina, Virginia, Ohio, Connecticut, Kentucky, Missouri, Massachusetts, Colorado, California, Texas, West Virginia, and the District of Columbia, and Canada, Venezuela, the Dominican Republic, and the West Indies.

Services provided

A marked increase was noted in the number of incidents reported and in the number of requests for help. Requests for help were received on 11,004 incidents as compared with 8,155 in the preceding year. An increase was noted on incidents resulting from medications, household products, rodenticides, insecticides, and those in the miscellaneous category (Table I).

TABLE I. Service statistics

	Number of Incidents	
Toxic Agent	January to October, 1961	January to October, 1960
Internal medications	4,583	3,856
External medications	984	726
Rodenticides	173	119
Insecticides	891	487
Disinfectants	197	147
Detergents	547	291
Lye	138	134
Polishes	141	109
Bleaches	435	339
Solvents	405	316
Cosmetics	759	403
Miscellaneous	2,051	1,228
TOTAL	11,304	8,155

Fatalities

Fewer fatalities were reported during this period as compared with last year (Tables II and III). A reduction was noted in the number of fatalities resulting from barbiturates and from lead poisoning. The marked reduction in fatalities due to lead poisoning is undoubtedly because of the stepped-up efforts of the control program.

TABLE II. Fatalities, January to October, 1961

	Age (Years)							
Toxic Agent	0 to 5	6 to 14	15 to 24	25 to 44	45 to 64	65 and Over	Age Unknown	Total
Barbiturates	...	...	2	3	5	4	1	15
Narcotics	...	...	5	9	1	...	...	15
Sleeping pills	...	...	...	4	4	...	...	8
Lead (confirmed)	6	...	...	...	...	...	...	6
Lead (possible)	1	...	...	...	...	...	...	1
Methyl alcohol	...	...	...	...	3	...	1	4
Cleaning fluid	...	...	...	1	...	...	1	2
Aspirin	1	...	...	...	...	...	...	1
Ammonia	...	...	...	1	...	...	...	1
Talcum powder	1	...	...	...	...	...	...	1
Cheracol	1	...	...	...	...	...	...	1
Podophyllin	...	...	...	...	...	1	...	1
Miltown	...	...	...	...	1	...	...	1
Tranquilizer (unknown)	...	...	...	...	1	...	...	1
Benzol	...	...	1	...	...	...	...	1
J-O Paste	...	...	1	...	...	...	...	1
Sodium fluoride (insecticide)	...	...	1	...	...	...	...	1
Dextro propoxyphene hydrochloride	...	...	...	1	...	...	...	1
Colchicine	1	...	...	...	...	...	...	1
"Ruda" plant (rue?)	...	...	...	...	...	...	1	1
Smoke poisoning	1	...	...	...	...	...	...	1
Plastic bag	...	...	...	...	...	1	...	1
Unknown medication	...	...	8	14	7	4	5	38
TOTALS	12	...	18	33	22	10	9	104

As in the past years, the largest number of fatalities resulted from barbiturates and other sleeping pill medications. In the zero- to five-year age group the number of fatalities was reduced from 22 to 12, and this is chiefly due to the reduction of fatalities caused by lead poisoning.

It may be pointed out that the increased number of requests for help on poisonings does not indicate an increase in the number of poisonings but is due chiefly to the reputation gained by the Poison Control Center as a service agency and to the professional educational program directed at physicians.

Lead poisoning

Lead poisoning also was reported with greater frequency. One hundred fifty-three confirmed cases were reported during the first ten months of 1961 as compared with 123 in the preceding year. In addition, 83 (provisional total) asymptomatic possible lead poisoning cases also were reported during the same period. The increase is believed to be due to an intensification of a case-finding program.

Lay education

Since education is perhaps the most potent single weapon in accidental chemical poisoning prevention, a concerted effort was made during 1961 in this direction in cooperation with the Bureau of Health Education and the Office of Public Relations. All mass communications media were utilized. The radio and television were used extensively and, following each program, thousands of requests for information were received, and literature was disseminated promptly to all who inquired. It also may be said that public health nurses during their home visits, for whatever purpose, carry on a significant health education campaign in looking for hazardous conditions and alerting parents on the indicated corrective measures to be employed.

The Bureau of Health Education developed four very attractive posters on the prevention of accidental poisonings which were distributed to all Department of Health clinics, hospital clinics, and child health stations. Very effective posters also

TABLE III. Fatalities, January to October, 1960

Toxic Agent	Age (Years) 0 to 5	6 to 14	15 to 24	25 to 44	45 to 64	65 and Over	Age Unknown	Total
Barbiturates	...	...	1	6	10	5	3	25
Lead (confirmed)	15	...	...	...	...	...	...	15
Lead (possible)	1	...	...	...	...	...	...	1
Narcotics	...	...	5	8	1	...	1	15
Sleeping pills	...	...	...	3	4	2	...	9
Oil of wintergreen (methyl salicylate)	2	...	...	...	1	...	...	3
Aspirin	2	...	...	...	1	...	...	3
Digitoxin	...	...	...	...	1	1	...	2
Anacin	...	...	...	...	1	...	...	1
Sparine and barbiturate	...	...	...	...	...	1	...	1
Atropine	...	...	...	...	1	...	...	1
Demerol	...	...	...	...	...	1	...	1
Sodium fluoride	...	...	1	...	...	...	...	1
Cyanide	...	...	...	...	1	...	...	1
Lighter fluid	...	...	...	1	...	...	...	1
Furniture polish	1	...	...	...	...	...	...	1
Ammonia	...	...	...	...	...	1	...	1
Drano	1	...	...	...	...	...	...	1
Zonite	...	...	...	1	...	...	...	1
CN disinfectant	...	...	...	...	...	1	...	1
Methyl alcohol	...	...	...	1	...	...	...	1
Quinine and turpentine	...	...	...	1	...	...	...	1
Unknown drugs	...	...	2	15	7	4	1	29
Plastic bag	...	...	...	...	1	...	...	1
TOTALS	22	...	9	36	29	16	5	117

were developed in cooperation with Ross Laboratories, and many thousands of these were distributed to the same facilities and to the maternal and child health staff and all hospital clinics.

Several lay articles on accidental poisonings also were reviewed for *Grolier's Encyclopedia.*

Education of the medical profession

1. As part of a presentation on infant and maternal health for foreign graduate students at the New York Polyclinic Medical School, New York City, the subject of accidental poisoning was discussed in detail.

2. A talk on poisonings was given at the Brooklyn Jewish Hospital before the pediatric and resident staffs.

3. Findings related to poisonings, particularly the human factors involved, were discussed at the workshop of the annual meeting of the Orthopsychiatric Association.

4. The activities of the Poison Control Center also were included as part of an overall seminar on maternal and child health services presented to a group of Long Island University students.

5. A talk on poisonings also was given to students from Hunter College.

6. At the request of the American Academy of General Practice, Queens County Chapter, a discussion on the epidemiology, causation, treatment, and prevention of poisonings was presented at the annual meeting, followed by a lengthy discussion period.

7. A talk on the epidemiology of accidental chemical poisonings was presented to the pediatric and nursing staffs of The Springfield Hospital, Massachusetts, followed in the evening by a formal presentation on accidental chemical poisonings to the staff of The Springfield Hospital and including the pediatricians and general practitioners of Springfield and its environs.

8. At a talk given at Teachers College, Columbia University, New York City, the subject of accidental poisoning also was discussed. The group exhibited considerable interest in the subject and requested health literature which they plan to utilize in their respective localities.

9. A talk on the prevention of poisonings was presented to the pediatric staff of the Booth Memorial Hospital, Flushing. Many physicians from Queens County were present, and considerable audience participation followed.

10. In the course of a presentation on school health services in a workshop at Catholic University, Washington, D.C., the subject of accident prevention was included. Poison control also was discussed as one facet of safety and accident prevention.

11. A talk on the management of poisonings was delivered at the annual meeting of the medical staff of Grasslands Hospital. Considerable interest was elicited followed by a lively discussion.

12. A report on the poison control program was presented at the annual meeting of the New York City and Westchester branches of the American Academy of Pediatrics. The reports were enthusiastically received, and considerable audience participation followed.

13. During October, the Medical Director, as a member of the Accident Prevention Committee of the American Academy of Pediatrics, attended a meeting in Chicago and discussed the activities of the New York City Poison Control Center. At that time he also spoke on this subject at the meeting of the National Association of Poison Control Centers. The possibility of studying fatalities resulting from poisonings in the same manner as perinatal mortality was suggested, and New York City may initiate such a study as a pilot project.

14. A talk on accident prevention and the prevention of accidental poisonings in particular was presented at Coney Island Hospital, Brooklyn. It was heartening to see the interest of all in attendance and the considerable audience participation. Although until now lead poisoning was not reported to any extent from the area which is served by Coney Island Hospital, the physicians showed great interest in the problem, and it was apparent that the diagnosis of lead poisoning in that area is now made with greater frequency.

15. A talk on poisonings was given to the staff of the 635th General Hospital, United States Army Air Force.

16. A talk on poisonings was given before the Subcommittee on Childhood Accidents of the Medical Society of the State of New York.

17. The Medical Director gave a talk to a second-year class at the College of Physicians and Surgeons, Columbia University, New York City, on the epidemiology, causation, and treatment of poisonings.

18. A talk also was given at the postgraduate course of the American College of Chest Physicians on the causation, prevention, and control of accidental poisonings.

19. A presentation on accidental poisonings was given to the physicians to be assigned in the Bureau of Child Health as part of their preservice training course.

20. The Technical Director spoke on the activities of the Poison Control Center at a seminar commemorating the fiftieth anniversary of Fordham University School of Pharmacy.

It is heartening that requests for presentations on accidental poisonings are received with greater frequency than ever before from hospitals, medical schools, and schools of nursing.

Reporting of side-reactions

Working with other agencies, the Center continued to exert vigorous efforts to alert physicians on the importance of reporting side-reactions from drugs or medications used in the treatment of patients. It also requested that physicians report all blood dyscrasias which they may encounter as a result of the use of drugs in their practice. Whenever such reports were received they were forwarded to the Subcommittee on Blood Dyscrasias of the Council on Drugs of the American Medical Association which aims to accumulate sufficient information to determine with certainty whether or not any causal relationship exists between the drug and the reaction obtained.

Publicity

Many talks were given on radio and television on the subject of the prevention of poisonings. Considerable space was devoted to the activities of the New York City Poison Control Center in newspapers, such as the *Daily Mirror*, the *New York Journal*

American, the *New York World Telegram and Sun*, and the *Daily News*, and in magazines, such as the *Pediatric Herald* and the *Medical Tribune*, as well as in the *Journal of the American Medical Association*.

In the special accident prevention issue of the World Health Organization, a page was devoted to the New York City Poison Control Center and included a photograph of the Technical Director and the members of his staff in action.

A representative from the *Pediatric Herald* visited the Center with a view toward obtaining material for publication in a forthcoming issue. The New York *Daily News* also contacted the Center about information on poisonings on the basis of which they published a special feature in the magazine section dealing exclusively with the subject of poison control.

Poison Control Center Technical Advisory Committee

The Poison Control Center Technical Advisory Committee met several times during the year and among the subjects discussed were:

1. A report on the activities of the Poison Control Center for the year 1960 by Harold Jacobziner, M.D.
2. Methyl alcohol poisoning by Jack R. Cooper, M.D., Assistant Professor of Pharmacology, Yale University Medical School.
3. The use of ipecac in the treatment of poisonings by Bernard Davidow, M.D., then Director of Pharmacology, New Drug Institute, New York City.
4. A report on the activities of the Poison Control Center in 1961 and a medical review of poisonings by Dr. Jacobziner.
5. The treatment of radiation overexposure by Roy Albert, M.D., Associate Professor of Industrial Medicine, New York University Medical Center.
6. Toxicologic laboratory service in the Health Department by Dr. Davidow, Chief, Food and Drug Laboratory, City of New York Department of Health.

Other activities

As consultant to the American Medical Association, the Medical Director reviewed many articles on poisoning to determine whether or not they were suitable for publication.

The Medical Director was appointed as a special consultant for the Food and Drug Administration and participated in a special panel of specialists relating to the labeling of hazardous substances. He related the human experience data with turpentine, and as a result of these data it was determined to include turpentine as a hazardous substance.

Case reports

Case 1. A young male Puerto Rican was admitted in a coma to Lincoln Hospital, The Bronx, as a result of a suicide attempt with an unknown roach poison brought from Puerto Rico. The resident physician was advised by us to try to obtain more specific information from the home. Shortly thereafter he called to inquire about a complicated chemical compound which was recognized here as being the formula for parathion, a deadly organic phosphate insecticide.

The routine antidote of atropine was advised in doses which seemed surprisingly large to the resident but which were acceptable in this case. Since the patient had not responded when an inquiry was made a few hours later, the Center recommended that an attempt be made to obtain the new experimental antidote, 2-PAM, developed at Columbia-Presbyterian Medical Center by Edith Nachmansohn, M.D., and Irwin B. Wilson, M.D., and their associates. Dr. Nachmansohn offered to supply the drug and felt that atropine would not be effective in this case and that only 2-PAM might be lifesaving. The drug was administered with dramatic results, and the patient was discharged as recovered on the seventh day following hospitalization.

Case 2. A twenty-three-month-old boy accompanied his father to the cellar and, unobserved, picked up a cup which had been used to measure 100 per cent chlordane, an insecticide, a year before. When the father noticed the child grimacing, he took immediate steps to wash the child's hands and face thoroughly and to induce vomiting. Being a pharmacologist by profession, the father was particularly alert to the toxic possibilities resulting from the ingestion of such a product. The child was normal for several hours but suddenly began to develop tremors and convulsions which are characteristic of chlordane poisoning. He was brought to Jacobi Hospital in The Bronx where he was treated with sedation and was given a thorough neurologic examination. The child was acutely ill for several days and was discharged with residual abnormal electroencephalogram findings. Several days after his discharge, the child was readmitted to the hospital with intestinal symptoms. His progress is being followed.

Case 3. The Poison Control Center has received many calls on the ingestions of deodorant materials by children. Practically all of these have been cases involving the use of paradichlorbenzene, frequently perfumed. A recent call involving a deodorant material by the name of Clear-O-Disc was received. Since information on this product was not in our files, it was thought to be a paradichlorbenzene. A query to the mother, who lived in Stratford, Connecticut, resulted in her sending a small sample to the Poison Control Center where it was identified by odor as consisting of perfumed paraformaldehyde, a poison. This matter has been referred to the Drug Division and the United States Food and Drug Administration for disciplinary action.

Case 4. This one-year-old child was under the supervision of a seventeen-year-old sibling and obtained an aspirin bottle from a low table in the bedroom. The bottle contained an unknown quantity of 5-grain aspirin tablets. The family was entirely unaware of the occurrence, but the child began to vomit, and during the night of the day of the occurrence and the next morning the child was breathing very heavily and was drowsy. An ambulance was called, and the child was taken to a hospital emergency room where his stomach was lavaged, and he was transferred to the Brooklyn Jewish Hospital. On admission to the hospital the patient was dyspneic, hyperneic, and stuporous. The blood salicylate level was 69 mg. per 100 ml., hemoglobin 7.8 Gm. per 100 ml., and the hematocrit 34. In spite of therapy, the child died within one day following admission.

Case 5. A second acute poisoning from parathion occurred locally and was reported to the Poison Control Center. Both of these involved the importation of the product directly from Puerto Rico by newly arrived immigrants. This case was interesting because an unknown woman sold the product to the child's mother as a household insecticide. This was apparently an individual transaction, and the product was not sold through commercial trade channels. The Poison Control Center advised the use of 2-PAM which was successful in the treatment of a previous case of parathion poisoning. It also proved highly successful in this case. An exceedingly large number of requests for reprints are being received for the article on "Parathion Poisoning Successfully Treated with 2-PAM (Pralidoxime Chloride)."*

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* Jacobziner, H., and Raybin, H. W.: Parathion poisoning successfully treated with 2-PAM (pralidoxime chloride), New England J. Med. **265:** 436 (Aug. 31) 1961.

Visitors

The Director of the National Institute of Health from the Netherlands visited the Center with a view toward initiating similar centers in the Netherlands. He requested copies of all forms used and of the plan of operation.

The Director of the National Clearinghouse for Poison Control Centers requested permission to come to New York City and spend some time again observing the activities of our Center. This permission was granted with pleasure.

Articles published

The following articles relating to poison control were also published during this period:

Jacobziner, H., and Raybin, H. W.: Dexedrine, metallic mercury, arsenic, and arnica intoxications, Arch. Pediat. **78:** 19 (Jan.) 1961.

Idem: Proceedings of the New York City Poison Control Advisory Committee meeting, New York State J. Med. **61:** 482 (Feb. 1) 1961.

Idem: Poison control activities in New York City—1960, Arch. Pediat. **78:** 72 (Feb.) 1961.

Idem: Incidents involving detergents, kerosene, and tranquilizers, New York State J. Med. **61:** 944 (Mar. 15) 1961.

Idem: Potassium permanganate poisoning, Arch. Pediat. **78:** 120 (Mar.) 1961.

Idem: Thallium and methapyrilene poisonings, New York State J. Med. **61:** 1345 (Apr. 15) 1961.

Idem: Chloromycetin poisoning, Arch. Pediat. **78:** 159 (Apr.) 1961.

Idem: Cobalt poisoning, *ibid.* **78:** 200 (May) 1961.

Idem: Meprobamate, aspirin, and methyprylon intoxications, New York State J. Med. **61:** 1935 (June 1) 1961.

Idem: The epidemiology of accidental chemical poisonings, Arch. Pediat. **78:** 226 (June) 1961.

Idem: Benztropine methanesulfonate, iron sulfate, and benzocaine intoxication, New York State J. Med. **61:** 2322 (July 1) 1961.

Idem: Plant and insecticide poisonings, *ibid.* **61:** 2463 (July 15) 1961.

Idem: Trioxymethylene (deodorant) poisoning, Arch. Pediat. **78:** 330 (Aug.) 1961.

Idem: Imipramine hydrochloride, trimeprazine, and methapyrilene mixture ingestions, New York State J. Med. **61:** 2811 (Aug. 15) 1961.

Idem: Cobalt and cadmium poisonings, *ibid.* **61:** 3153 (Sept. 15) 1961.

Idem: Turpentine poisoning, Arch. Pediat. **78:** 357 (Sept.) 1961.

Idem: Tetrachloride poisoning, New York State J. Med. **61:** 3506 (Oct. 15) 1961.

Idem: Phosphorus poisoning including two fatal case reports, Arch. Pediat. **78:** 396 (Oct.) 1961.

Reprints of all these articles were distributed to the medical superintendents and poison control officers of New York City hospitals and to many other interested individuals in this country and abroad.

Number eighty-eight in a series of Accidental Chemical Poisonings

Medical Diagnostic Clinics

A series of special articles on rare but important disease entities or medical esoterica

Prepared by the Department of Medicine, St. Vincent's Hospital, New York City

WILLIAM J. GRACE, M.D., Editor
MATTHEW J. FERGUSON, M.D., Associate Editor

A Cardiac Diagnostic

Protocol

A forty-seven-year-old Negro bartender was admitted to the hospital complaining of profound weakness. He had been in apparent good health until eleven months before, when he noted gradually increasing abdominal girth and ankle edema. This was accompanied by a marked loss of physical endurance which had cost him his job four months prior to admission. The patient's medical history was unremarkable except for a "double pneumonia" which had followed a prolonged drinking spree three years earlier. Since that time the patient had abstained from alcohol.

After losing his job, he visited several doctors and hospital outpatient departments. He was told he had cirrhosis and was given various diuretic medications that relieved his ankle edema temporarily. Although he denied exertional dyspnea, orthopnea, and chest pain, he was finally admitted from the hospital emergency room by an intern who thought the patient was in cardiac decompensation.

The physical examination revealed a chronically ill male with a puffy face, lying flat in bed. His temperature was 98.6 F., blood pressure 120/80 mm., pulse 76 per minute, and respirations 14 per minute. The neck veins were visible. The lungs were clear to percussion and auscultation. The heart was not enlarged, and there were no thrills or murmurs. His heart sounds were good, and there was an early protodiastolic third heart sound heard at the apex. The point of maximum impulse was not distinct. Marked abdominal distention with hepatosplenomegaly and shifting dullness were noted. There was 3 plus edema to the midthigh bilaterally.

A laboratory examination revealed borderline liver chemistries with a 1 plus cephalin flocculation and elevated alkaline phosphatase. The chest x-ray film showed clear lungs and a normal-sized heart, with a lack of definition of the cardiophrenic angles. The electrocardiogram showed a tendency toward low voltage, bifid P waves, and inverted T waves. A tuberculin test gave a positive reaction.

COURSE. The absence of diagnostic liver chemistries, abnormal electrocardiographic findings, and the patient's prompt response to a low-sodium diet and diuretics prompted a cardiac investigation. The venous pressure in the antecubital and femoral veins was 300 mm. of water. The circulation time was twenty-six seconds. A paradoxical pulse was not demonstrated. After the patient attained his dry weight, cardiac catheterization was performed. The salient features were as follows: (1) elevated and relatively uniform pressures in the vena cava, right auricle, right ventricle, and pulmonary artery; (2) increased pulmonary capillary pressure; (3) an early diastolic dip and plateau pattern in the right ventricular pressure; and (4) a low resting cardiac output.

The patient underwent cardiac surgery three weeks after his admission.

(Elucidation will be found on page 1257)

Case Report

Rubella Complicated by Arthritis

STANLEY SLATER, M.D.
Brooklyn, New York

THE ONLY COMPLICATION of rubella which usually is considered is the possible effect on a fetus. Despite two recent reports[1,2] of arthritis complicating rubella, this occurrence is apparently not well recognized by many physicians. The purpose of this report is to direct attention again to this complication.

Case report

The patient was a thirty-three-year-old married white female nurse who always had had very slender fingers. Her past history and system review were unremarkable except for two full-term deliveries and one ectopic pregnancy. For about one year prior to her present illness, mild swelling of the fingers had been present on arising in the morning; there had never been any joint pains.

On January 10, 1961, the patient palpated some lymph glands in her neck; this was followed on January 12 by a headache which lasted a few days. A generalized maculopapular rash was first noted on January 13 and had disappeared by January 15. Malaise was present on January 14, but the patient was afebrile throughout the course of the illness. A diagnosis of rubella was made by the attending physician.

On January 15, the proximal interphalangeal joints of the hands were noted by the patient to be swollen and were painful all day, requiring the use of aspirin for relief of the pain. The following day, the wrists and ankles were painful on arising and seemed swollen to the patient. Because of the degree of discomfort, further medical advice was sought.

TABLE I. Results of serology tests

Date	Antistreptolysin O Titer	C-Reactive Protein	Latex Fixation
January 16	1:50	Positive	Negative
February 11	1:50	Negative	Negative

An examination on January 16 revealed the presence of several 1-cm., nontender, anterior and posterior cervical lymph nodes. No splenomegaly was detected. No rash was present, and the remainder of the general examination was unrevealing. An examination of the joints revealed only some early Heberden's nodes with some tightness of the wedding band. There was no tenderness or redness of the joints. The patient was encouraged to continue treatment with salicylates. The pain had disappeared after three days, and when she was seen again on February 11, the patient was symptom-free. It was noted at this time that the wedding band could be moved more freely back and forth over the proximal interphalangeal joint. The patient's daughter had developed rubella on February 2. Table I shows the results of tests performed on the patient's serum by the City of New York Department of Health.

Comment

Johnson and Hall[1] have redirected attention to the presence of transient rheumatic symptoms as a complication of rubella. The patient herein reported fits the clinical features described by them. The symptoms are usually manifested in a young adult, usually of the female sex. The onset of the joint pains and swelling coincide with, or follow shortly, the appearance of the rash and usually last a few days to two weeks.

The ankles, wrists, and hands are the loci usually involved, although Lee *et al.*[2] noted that in their experience the site of predilection in males seemed to be the knee joint. The arthritic complications usually are of short duration and without residua, although some of the patients studied by Lee *et al.* had residual symptoms.

In their 10 cases of rubella with arthritis, Johnson and Hall[1] found positive results of latex-fixation tests in 9 using the euglobulin-inhibition technic. Only 2 of 7 patients with rubella without arthritis showed positive results with this technic. Negative results to a latex-fixation test were obtained when serum alone was used in performing the test, and positive results were obtained in only 2 of the patients with arthritis using euglobulin alone. Lee *et al.*[2] obtained positive results in 4 of 11 patients using the euglobulin-inhibition test and in 1 of 10 patients using F_{11}-coated tanned sheep cells.

Summary

A case of rubella complicated by transient joint symptoms is presented. This combination may be noted more frequently if it is searched for during outbreaks of rubella.

1122 Ocean Avenue, Brooklyn 30

References

1. Johnson, R. E., and Hall, A. P.: Rubella arthritis; report of cases studied by latex tests, New England J. Med. **258:** 743 (Apr. 10) 1958.

2. Lee, P. R., *et al.*: Rubella arthritis. A study of twenty cases, California Med. **93:** 125 (Sept.) 1960.

Pharmaceutical contributions to medicine

Present indications are that in the sixties our growth will be even more fabulous than it was in the fifties and the forties. In that two-decade period more effective new drugs to prevent, diagnose, and treat countless illnesses were discovered than in the entire period of recorded medical history. Eighty per cent of the prescriptions now written could not have been prescribed ten years ago, 1 and $^{1}/_{4}$ million Americans are alive today because of new treatments in the past ten years, and five years have been added to man's lifespan in the last few decades.—*Leonard W. Larson, M.D., President, American Medical Association, to American Association of Medical Assistants*

Medical
Diagnostic
Clinics

ELUCIDATION

Continued from page 1254

Gerke[1] reported that only 36 per cent of 525 autopsy-proved cases of constrictive pericarditis were diagnosed during life. This entity has been a stumbling block and a source of embarrassment to many clinicians despite its remarkably characteristic clinical picture. That it continues to plague us is evidenced by its frequent unsuspected appearance at clinicopathological conferences.

The etiology is varied.[2-4] Tuberculosis is the largest single definite cause. In the majority of cases no specific causative factor can be demonstrated. Pneumococcus, other bacteria, and trauma have been implicated in small numbers of patients.

It is often difficult to determine the onset of this condition unless of course the patient has been diagnosed as having a definite tuberculous pericarditis. A history of acute nonspecific pericarditis is a rarity. Since the constrictive phenomenon must take some time to develop, it follows that the symptoms will be insidious, and hence pinpointing its beginning will be almost impossible. The patient presented here had "double pneumonia" some years before, but it is not certain that this was related. The tuberculin test gave positive results, but this too may be unrelated.

Perhaps the most consistent early symptom of constrictive pericarditis is fatigue. This is due to diminished cardiac output and the inability of the heart to increase this output sufficiently on exertion. Ankle edema and abdominal distention due to hepatomegaly and ascites are typical. Exertional dyspnea and orthopnea are usually absent except late in the course of the disease.

The pertinent physical findings are related to venous hypertension. The neck veins and occasionally facial veins are evident. A paradoxical pulse may be absent in the inactive pericarditis. Wood[5] found it present in only 15 per cent of his cases. In any event, its frequency is overly stressed. The blood pressure and pulse are generally within normal limits. Auricular fibrillation is the most frequently noted arrhythmia (10 to 44 per cent).

Cardiac auscultation is strikingly unremarkable in the uncomplicated case. There are no murmurs. The heart sounds are of good quality. An early protodiastolic third heart sound at the apex is thought to be due to the early limitation of left ventricular filling by the confining pericardial envelope. There is poor definition of the point of maximum impulse. The lungs are clear until late in the disease when pleural effusions may be noted.

Venous pressure is usually between 200 and 400 mm. of water and does not drop significantly after the edema and ascites subside. Hepatojugular reflux can be demonstrated. The circulation time is in the range of twenty to forty seconds. Typically an electrocardiogram shows a tendency toward low voltage, bifid P waves, and inverted T waves. Chest roentgenograms may show normal or enlarged cardiac silhouettes. Pleuropericardial adhesions may cause a lack of definition of the cardiophrenic angles. A quiet heart is observed at fluoroscopy and may be confirmed by kymography. Calcification of the pericardium is noted frequently.

Cardiac catheterization findings reveal a decreased cardiac output which is relatively fixed despite exercise. There is an almost uniform elevation in the vena caval, right atrial, right ventricular end diastolic, pulmonary diastolic, and pulmonary wedge pressures. A characteristic early diastolic dip and plateau pattern is obtained in the right ventricle.

The treatment for constrictive pericarditis is surgical. Brilliant results were obtained in up to 75 per cent of selected patients. The surgical mortality in pericardectomy varies between 10 and 20 per cent.

References

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2. Dalton, J. C., Pearson, R. J., Jr., and White P. D.: Constrictive pericarditis: a review and long-term follow-up of 78 cases, Ann. Int. Med. **45**: 445 (Sept.) 1956.
3. Uglov, F. G.: Diagnosis and surgical treatment of constructive pericarditis, Surgery **47**: 247 (Feb.) 1960.
4. Mortensen, V., and Warburg, E.: Chronic constrictive pericarditis, Acta med. scandinav **131**: 203 (1948).
5. Wood, P.: Chronic constrictive pericarditis, Am. J. Cardiol. **7**: 48 (Jan.) 1961.

MEDICAL SOCIETY
OF THE STATE
OF NEW YORK

Annual Dinner Dance

in honor of

JOHN M. GALBRAITH, M.D.
President

WEDNESDAY
MAY 16, 1962

TERRACE BALLROOM
STATLER HILTON

32nd Street &
Seventh Avenue
New York City

Reception at 7 p.m.

Gourmet Dinner

Music by Ben Cutler

Dress Optional

Subscription $17.50 Per Person

RESERVATION BLANK

make checks payable to:
Medical Society of the State of New York
750 Third Avenue
New York 17, New York

Please send me———tickets for the Annual Dinner Dance on May 16.

Enclosed please find my check for————.

NAME

ADDRESS

Please attach guest list

Reports of Officers

Treasurer

To the House of Delegates, Gentlemen:

As your treasurer reports for 1961, the news is again bad. Figures and statistics can be dull and uninteresting to many of us. This report has, therefore, been divided into two parts. The first will be devoted to a minimum of figures giving highlights of the year while the latter will go into more detail.

The year 1961 ended with a General Fund deficit of $75,598. Our net loss for the year was $54,956. Adding this loss to our deficit at the beginning of 1961—which was $20,642—results in a deficit of $75,598.

If we were to consider our other funds—Investment, Building, Employees Beneficiary, Repair and Replacement—the over-all picture shows a decrease in our net of [$27,423. In other words, we are using the income from our reserve funds to make up losses in the General Fund.

Beginning in September, 1961, we had to borrow cash to provide funds for our general Society operations. The total amount borrowed was exactly a quarter of a million dollars.

As we received dues in 1962, these monies were used to repay our bank loans. When 1962 dues monies are used to pay loans for a prior year, it means that a lesser amount of cash is available for 1962. Depending on how much of our budget is utilized for the first half of 1962, money will again have to be borrowed sometime in August or September. It is to be noted that our 1962 budget forecasts a deficit of almost $139,000.

As to summary details of our financial operations during 1962, Table I is presented herewith. Space does not permit comment on each item, but some highlights are as follows.

Dues. Because of the dues increase of $10.00 which became effective in 1961, dues received amounted to over $833,000.

Journal. Before dues allocation, the JOURNAL resulted in a loss of approximately $124,800. After dues allocation of $125,800, there was a net income of almost $1,000. In Table II, there is presented a schedule of JOURNAL gross income, total expenditures, dues allocated, and final net gain.

Reference to Table II shows that in 1959 gross income was $407,206 with expenditures of $433,940, equalling a net loss before dues allocation of $26,734. In 1960 gross income decreased by $32,254 while expenditures decreased by $23,076. In 1961 gross income decreased again from 1960 by $85,460, while expenditures increased by $3,435. In other words, while gross income was falling rapidly, expenditures were increasing slightly.

The decrease in gross income was the result of causes beyond our control. Similar publications have felt the impact of decreased pharmaceutical advertising. It is fortunate that the JOURNAL is looking forward to a better year in 1962 as regards its gross income. The budget for this department shows an estimated gross income of $316,500 which is equal to an increase of $27,000 over 1961. Expenditures for 1962 are budgeted at $462,198 which is an increase of $47,899.

Administration. In 1956 Administration expense was $134,845. In 1961 it amounted to $270,337—more than doubling during the six-year period. The $270,337 figure increased about 15 per cent over 1960.

The 1962 budgeted expense is $285,955. Included in the figure are:

Salaries	$206,400
Rent	30,000
Electricity	1,500
Telephone and telegraph	4,500
Insurance	3,000
Payroll taxes	6,500
Audit	2,750
Interest on loans	1,300
Tabulating equipment	7,000
	$262,950

There is a total of about $23,000 not detailed above. This latter figure includes postage, stationery and supplies, repairs and service, stenotypist for Council and Trustees meetings, and sundry.

It is to be noted that $7,000 is included for installation of tabulating equipment. It is our belief that once this equipment is installed and operating, the savings in various office operations will be substantial.

Communications. In 1956 the Department of Communications had expenditures of $69,521. This item has increased each year. In 1961 the total was $155,835, equalling an increase of approximately 120 per cent over the six-year period.

Traveling expenses. This includes traveling allowances to Council, Board of Trustees,

TABLE I. Income and Expenditures, 1956 through 1961

	1956	1957	1958	1959	1960	1961
Income						
Members' Dues	$567,476.30	$572,886.30	$574,949.71	$584,644.43	$573,775.00	$833,199.11
JOURNAL (before dues allocation)	*17,965.55**	*12,650.77*	*21,337.48*	*26,734.37*	*35,912.33*	*124,806.95*
Interest	2,645.46	1,627.86	3,337.03	3,460.64	2,603.45	1,829.21
Sundry	...	329.45	32.50	...	...	5,063.31
Transfers to or from other funds	...	...	63,312.53	*53,970.72*	5,629.05	11,743.03
TOTAL INCOME	552,156.21	562,192.84	620,294.29	507,399.98	546,095.17	727,027.71
Expenditures						
Administration	134,845.40	135,965.68	165,804.51	214,926.74	234,958.29	270,337.32
Department of Communications	69,521.64	72,731.42	76,060.05	85,026.72	114,239.92	155,834.73
Legislation Bureau, Albany	26,102.48	29,950.53	31,837.57	28,193.11	24,396.62	15,750.08
Workmen's Compensation Bureau	21,720.68	36,267.97	32,037.42	31,375.26	27,708.51	30,525.30
Bureau of Medical Care Insurance	20,252.03	7,621.43	14,461.59	17,654.02	16,477.52	17,960.04
Scientific Activities	20,890.76	21,704.83	18,454.90	20,172.40	16,101.28	16,501.60
District Branches	3,177.44	3,309.68	3,705.26	4,688.49	4,935.65	3,654.23
Planning Committee for Medical Policies	693.45	420.51	118.92	871.00	1,168.79	631.41
Woman's Auxiliary	6,515.22	9,173.36	8,903.46	5,086.61	7,452.62	8,024.44
Malpractice Insurance and Defense Board	2,439.38	2,154.83	2,081.34	2,149.35	2,320.66	2,287.85
Malpractice Audit	1,250.00	2,000.00	2,000.00	2,067.49	2,000.00	2,000.00
Malpractice Survey	1,250.00	...	...	...	...	...
Counsel—Retainer and Expenses	35,000.00	35,000.00	35,000.00	40,000.00	40,135.00	40,540.00
Traveling Expenses	30,233.17	23,769.28	42,029.80	47,149.82	64,276.68	65,532.46
World Medical Association	...	1,000.00	1,000.00	1,000.00	1,000.00	1,000.00
A.M.A. Conference Room Expense	1,401.30	799.52	2,016.66	4,309.94	10,024.81	8,126.19
Societies for Medical Research	75.00	...	100.00	300.00	...	100.00
Conference of Presidents	75.00	75.00	75.00	75.00	75.00	75.00
Veterans Medical Service Plan	284.51	98.77	2,126.38	*341.78*	184.31	...
Medical Directory	28,103.53	64,674.24	57,334.34	60,204.98	56,866.91	82,130.57
Annual Meeting	5,487.05	12,640.11	19,869.78	25,938 44	23,603.07	36,313.10
Moving Expense and Alterations	732.80	1,840.00	63,312.53	...	...	...
Special Legal Counsel	...	...	...	404.90	...	...
Commission on Medical Services	...	...	...	247.43	550.18	...
Pensions	3,600.00	3,016.20	8,932.40	3,225.82	1,240.30	1,232.40
Empire State Health Council	100.00	...	...	100.00	100.00	100.00
Blood Banks Commission	144.53	231.26	...	...	...	...
A.M.A. Committee on Medical Facilities	...	...	...	277.76	...	...
American Medical Association Convention	...	7,745.95	...	...	...	9,669.30
Blood Banks Association of New York State, Inc.	12,600.00	15,822.86	10,577.14	9,000.00	...	...
Rural Medical Service Committee	850.00	...	19.50	155.51	...	...
Cults, Committee to Combat	2,883.49	1,867.79	598.48	1,944.08	244.90	58.87
Contribution—Refugee Hungarian Physicians	5,000.00	...	...	...	...	...
Contribution—Blood Banks Association of New York State, Inc.	1,400.00	2,400.00	...	...	...	...
Medicare—Tentative Credits to Overhead	*726.20*	726.20	...	...	...	...
Cameron Parish Medical Rehabilitation Fund	...	250.00	...	...	...	...
Management Survey	...	2,721.62	10,784.90	...	...	...
Advisory Committee to Columbia University Study	...	...	210.46	...	...	...

TABLE I. Income and Expenditures, 1956 through 1961 (continued)

Staphylococcal Committee	...	...	771.46	86.79	1,576.05	...
Electrical Survey	...	...	150.00	...	...	...
Membership Drive	...	...	341.61	254.13	...	...
Regional Conference on Resolution 58–49	...	...	...	...	4,643.74	98.88
New York State Council to Improve Health Care of Aged	...	...	...	...	50.00	...
International Congress on Industrial Health	...	...	...	...	3,000.00	...
Special Study, Rural Medical Service Committee and Maternal and Child Welfare Subcommittee	...	...	...	...	1,286.45	...
Forensic Pathology and Medicine Meeting	...	...	...	...	100.00	...
Empire State Medical, Scientific and Educational Foundation, Inc.	...	...	...	...	3,000.00	8,000.00
Relative Values Study for New York State	...	...	...	...	...	112.81
Speakers Seminar	...	...	...	...	...	1,609.38
Federal Legislation Subcommittee	...	...	...	...	...	892.10
Pension Plan Survey	...	...	...	...	...	1,200.00
Personnel Survey	...	...	...	...	...	1,500.00
New York State Association of Professions	...	...	...	...	...	185.50
TOTAL EXPENSE	435,902.66	495,979.04	610,715.46	606,544.01	663,717.26	781,983.56
Net Income	$116,253.55	$ 66,213.80	$ 9,578.83	$ *99,144.03*	$*117,622.09*	$ *54,955.85*

* Italics denote figures in red.

A.M.A. delegates, members of Society committees, the president, the president-elect, the executive vice-president, and others. Almost without exception there are no employes included. In 1956 about $30,200 was spent. In 1961 about $65,500 was spent—more than a 100 per cent increase.

Medical Directory. Because the *Directory* is published every two years, the net expense of each edition is spread over two years. Net costs for each edition beginning with 1957 are:

1957	$ 92,777
1959	117,539
1961	138,502*
1963	170,912 (Budgeted)

Miscellaneous. In October, 1960, the Willers Report was put into effect. This was a study of the job each staff member was doing and its salary value in the New York City area. In implementing the report we increased our salary expense by more than $28,000 annually. None of our executive personnel was included in the study, and therefore no salary increases for this group are included in this figure.

It is to be noted that the Board of Trustees has set up a Building Fund of $500,000 in securities at market value. These securities were transferred from our Investment Fund. Your treasurer heartily agrees with this action. At the present time, we are located in a fairly high rent area. Our rent is now $74,300 per annum. Because of the need for space, it appears we shall have to obtain more space in this area, probably at a cost of $12,000 to $15,000 per annum. Our rent would then approach $90,000. From the financial viewpoint, owning our building would prove to be very practical, particularly if we could obtain property somewhat away from the Grand Central area.

Your treasurer started this report by noting that the news was bad. As this report is being prepared, we know there will be items of expense which have not been budgeted. The following is an estimate of items which will have to be added to our 1962 budget:

Increase in payroll taxes	$ 4,000
Possible increase in postage rates	2,000
Rental of additional space	15,000
Increase in Medicare costs	25,000
	46,000
Present budgeted deficit	139,000
Possible deficit for year	185,000
Accumulated deficits from prior years	75,600
Estimated deficit to December 31, 1962	$260,600

In other words we shall have to find funds

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* This will reduce to the extent that single copies are sold up to the time the next edition is published.

TABLE II. Journal financial status, 1956 through 1961

Year	Gross Income	Expenditures	Net Gain Before Dues Allocation	Dues Allocation	Final Net Gain
1956	319,867	337,832	−17,965	60,610	42,645
1957	364,496	377,147	−12,651	91,635	78,984
1958	377,275	398,613	−21,338	92,062	70,724
1959	407,206	433,940	−26,734	74,568	47,834
1960	374,952	410,864	−35,912	75,532	39,620
1961	289,492	414,299	−124,807	125,800	993

to provide $260,000. There are those who would use our reserves to cover this item. As noted previously, we have already used about $22,000 of reserves in other funds. Reduction of our reserves beyond a certain point will reduce our ability to borrow when cash is needed.

Your treasurer believes that the solution lies in two directions, namely (1) to give thought to increasing dues. If the estimate of $260,600 becomes a fact, we would need a dues increase of approximately $11 per member who pays dues, and (2) to mandate all committees, departments, the Council, and the Board of Trustees to reduce expenditures to a minimum and to live within our income even though some of our services are reduced for a year or two to accomplish this goal. Your treasurer would go so far as to strongly recommend review of the 1962 budget with expense reduction as the aim.

Respectfully submitted,

Maurice J. Dattelbaum, M.D., *Treasurer*

Auditor's Certificate

To the Board of Trustees,
Medical Society of the State of New York:

We have examined the balance sheet of the Medical Society of the State of New York as of December 31, 1961, and the related statement of operating income and expenses and general and other funds for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances.

We did not confirm the unpaid members' dues by correspondence with the members, nor did we confirm the amounts due from the U.S. Government under the "Medicare" program, but with respect to the latter we satisfied ourselves by other auditing procedures.

In our opinion, the accompanying balance sheet and the statement of operating income and expenses and general and other funds present fairly the financial position of the Medical Society of the State of New York as of December 31, 1961, and the results of its operations for the year then ended, in conformity with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

PATTERSON & RIDGWAY
Certified Public Accountants

March 6, 1962

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Statement of Operating Income and Expenses

For the Year Ended December 31, 1961

Operating Income		
Members dues after reserve		$833,199.11
Less: Allocation to JOURNAL circulation income, as authorized by the Board of Trustees		125,800.00
		$707,399.11
Net operating income from JOURNAL		993.05
Interest on savings accounts and treasury bills		1,829.21
Sundries		5,369.31
		$715,590.68
Operating Expenses		
Administrative	$270,337.32	
Department of Communications	155,834.73	
Legislation Bureau, Albany	15,750.08	
Workmen's Compensation Bureau	30,525.30	
Bureau of Medical Care Insurance	17,960.04	
Scientific activities	16,501.60	
Woman's Auxiliary	8,024.44	
District branches	3,654.23	
Planning Committee for Medical Policies	631.41	
Malpractice Insurance and Defense Board	2,287.85	
Malpractice Defense audit	2,000.00	
Legal counsel, retainer and expenses	40,540.00	
Traveling expenses	65,532.46	
American Medical Association expenses	17,795.49	
World Medical Association	1,000.00	
Empire State Medical, Scientific and Educational Foundation	8,000.00	
Pensions	1,232.40	
Sundries	6,734.20	
Medical Directory 1961—portion of loss allocated to current year	81,634.91	
Annual Meeting 1961	36,313.10	
	782,289.56	
Transfer from Repair and Replacement Fund to cover purchases of equipment	11,743.03	
		770,546.53
EXCESS OF EXPENSES OVER INCOME TRANSFERRED TO GENERAL FUND		$ *54,955.85**

* Italics denote figures in red.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Balance Sheet

December 31, 1961

ASSETS

General Fund			
CURRENT ASSETS			
Cash in banks and on hand	$ 85,419.49		
Less: Due American Medical Association	6,535.00		
		$ 78,884.49	
Accounts and notes receivable (after reserves)		35,557.96	
Dues receivable—net, estimated		4,808.00	
Due from other funds, per contra		39,415.25	
Due from U.S. Government "Medicare"		31,832.34	
Inventories		41,852.20	
TOTAL CURRENT ASSETS			$ 232,350.24
PREPAID EXPENSES			
Sundry expenses and deposits			43,126.42
FURNITURE AND FIXTURES			
At nominal value			2.00
ADVANCES (AFTER RESERVE)			
Veterans Medical Service Plan of New York		14,510.53	
Blood Banks Association of New York State		2,500.00	
			17,010.53
Total General Fund			292,489.19
Investment Fund			
Cash in banks		88,324.52	
Investments at cost (market value $677,348.54) (see footnote)		429,929.51	
Accrued interest receivable		2,722.53	
Due from other funds, per contra		15,214.29	
Total Investment Fund			536,190.85
Special Funds Under Control of the Board of Trustees			
BUILDING FUND			
Investments, at cost (market value $501,718.81)	294,025.33		
Accrued interest receivable	1,285.45		
Due from other funds, per contra	3,148.85		
		298,459.63	
EMPLOYEES BENEFICIARY FUND			
Investments, U.S. and other obligations, at cost (market value $67,585.00)	76,727.98		
Accrued interest receivable	573.95		
Due from other funds, per contra	1,730.77		
		79,032.70	
REPAIR AND REPLACEMENT FUND			
Investments, at cost (market value $47,859.63)	49,409.04		
Accrued interest receivable	611.81		
	50,020.85		
Less: Due to other funds	4,543.33		
		45,477.52	
Total Special Funds			422,969.85
Endowment Funds			
Cash in banks		16,021.31	
Less: Due to General Fund, per contra		300.00	
Total Endowment Funds			15,721.31
Pension Fund			
Cash in bank		2,704.21	
Investments, at cost (market value $302,195.37)		284,075.14	
Accrued interest receivable		2,784.45	
Due from General Fund, per contra		3,571.84	
Total Pension Fund			293,135.64
War Memorial Fund			
Cash in bank		6,623.51	
Investments, U.S. Treasury Bonds and Notes (market value $142,050.63)		148,337.52	
Accrued interest receivable		729.60	
		155,690.63	
Less: Due to other funds, per contra		8,073.72	
Total War Memorial Fund			147,616.91
Total Assets			$1,708,123.75

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Balance Sheet

December 31, 1961

LIABILITIES AND FUNDS

General Fund		
CURRENT LIABILITIES		
Notes payable to bank	$250,000.00	
Accounts payable and accruals	45,490.08	
Taxes payable (including withholding)	16,082.26	
Due to other funds, per contra	18,786.13	
TOTAL CURRENT LIABILITIES		$ 330,358.47
DEFERRED CREDITS		
Membership dues 1962	10,000.00	
Annual Meeting 1962	22,823.75	
Sundry	4,904.87	
TOTAL DEFERRED CREDITS		37,728.62
GENERAL FUND		_75,597.90_*
Total General Fund		292,489.19
Investment Fund		
Reserve for depreciation of investments	50,000.00	
Due to other funds, per contra	31,377.82	
Balance	454,813.03	
Total Investment Fund		536,190.85
Special Funds Under Control of the Board of Trustees		
BUILDING FUND	298,459.63	
EMPLOYEES BENEFICIARY FUND	79,032.70	
REPAIR AND REPLACEMENT FUND	45,477.52	
Total Special Funds		422,969.85
Endowment Funds		
Lucien Howe Prize Fund	6,624.89	
Merit H. Cash Prize Fund	2,096.08	
A. Walter Suiter Lectureship Fund	7,000.34	
Total Endowment Funds		15,721.31
Pension Fund		293,135.64
War Memorial Fund		147,616.91
Total Liabilities and Funds		$1,708,123.75

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* Italics denote figures in red.

Note: The Society has a Revolving Fund of $150,000.00 from the U.S. Army ("Medicare" Program), not included in this exhibit. It has claims from physicians, either paid or approved for payment, totaling $224,805.65, that have not yet been reimbursed by the government, and is liable to physicians for claims of $77,090.26. The Society has placed $30,000.00 par value U.S. Treasury Bonds in escrow with a depositary agent of the U.S. Government as a pledge under the "Medicare" contract.

December 31, 1961

Cash in Banks and on Hand

General Fund	$ 85,419.49*
Investment Fund	88,324.52
Pension Fund	2,704.21
Total	176,448.22

* Included $6,535.00 due American Medical Association.

Endowment Funds	
Lucien Howe Prize Fund	6,724.89
Merit H. Cash Prize Fund	2,196.08
A. Walter Suiter Lectureship Fund	7,100.34
Total (Union Dime Savings Bank)	16,021.31
War Memorial Fund	
On deposit	6,623.51

Investments

The investments of the Society are summarized as follows:

	Cost	Market
Investment Fund		
U.S. Treasury Bonds	$ 65,086.22	$ 63,599.38
Industrial and Finance Bonds	47,903.87	49,130.00
Utilities Bonds	113,718.58	113,111.25
Mortgage	542.53	1,251.03
Preferred Stocks	29,501.47	28,570.00
Common Stocks	173,176.84	421,686.88
Total	429,929.51	677,348.54
Building Fund		
U.S. Treasury Bonds	108,124.37	103,972.56
Finance and Utilities Bonds	94,762.64	89,870.00
Common Stocks	91,138.32	307,876.25
Total	294,025.33	501,718.81
Pension Fund		
Utilities Bonds	188,066.27	184,267.00
Bank and Finance Bonds	50,925.00	51,867.50
Common Stocks	45,083.87	66,060.87
Total	284,075.14	302,195.37
Employees Beneficiary Fund		
U.S. Treasury Bonds	31,000.00	27,435.00
Utilities Bonds	35,460.65	31,300.00
Industrial Bonds	10,267.33	8,850.00
Total	76,727.98	67,585.00
Repair and Replacement Fund		
Utilities Bonds	39,567.13	39,318.75
Common Stock	9,841.91	8,540.88
Total	49,409.04	47,859.63
War Memorial Fund		
U.S. Treasury Bonds	$148,337.52	$142,050.63

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Statement of General and Other Funds

For the Year Ended December 31, 1961

	General Fund	Investment Fund	Building Fund	Employees Beneficiary Fund	Repair and Replacement Fund	Pension Fund	War Memorial Fund	Lucien Howe Prize Fund	Merit H. Cash Prize Fund	A. W. Suiter Lectureship Fund
Balance at January 1, 1961.......	*$20,642.05**	$703,354.26	...	$91,971.74	$54,924.67	$273,972.65	$171,104.35	$6,479.32	$2,115.68	$6,841.04
Additions										
Interest on bank balances......	...	2,789.36	...	...	...	...	...	245.57	80.40	259.30
Income from securities.........	...	37,268.56	$2,732.30	2,560.86	2,295.88	10,949.26	5,312.56	...	...	
Profit on sale of securities......	...	9,733.18	...	...	...	...	...	...	...	...
Assessments and contributions received..................	...	...	...	...	...	9,565.97	...	...	...	...
Inter-fund transfer (per contra).	...	...	295,727.33	...	...	...	...	...	...	...
Total Additions.........	...	49,791.10	298,459.63	2,560.86	2,295.88	20,515.23	5,312.56	245.57	80.40	259.30
Deductions										
Custodian and investment service fees................	...	2,605.00	...	...	...	...	...	...	...	...
Prizes.....................	...	...	...	...	...	...	...	100.00	100.00	100.00
Benefits disbursed............	...	...	...	15,499.90	...	1,352.24	28,800.00	...	...	...
Purchases of equipment by General Fund (per contra)...	...	...	...	...	11,743.03†	...	...	...	...	...
Excess of expenses over income.	54,955.85	...	...	...	...	...	...	...	...	...
Inter-fund transfer (per contra)	...	295,727.33	...	...	...	...	...	...	...	...
Total Deductions........	54,955.85	298,332.33	...	15,499.90	11,743.03	1,352.24	28,800.00	100.00	100.00	100.00
Total Increase or (Decrease).....	*54,955.85*	*248,541.23*	298,459.63	*12,939.04*	*9,447.15*	19,162.99	*23,487.44*	145.57	*19.60*	159.30
Balance, December 31, 1961..........	*$75,597.90*	$454,813.03	$298,459.63	$79,032.70	$45,477.52	$293,135.64	$147,616.91	$6,624.89	$2,096.08	$7,000.34

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* Italics denote figures in red.

† Transferred to General Fund. See Statement of Operating Income and Expenses.

Commission on Medical Services—A

Medical Care Insurance

To the House of Delegates, Gentlemen:

The Medical Care Insurance Committee is composed of the following:

Melvin S. Martin, M.D., *Chairman*	Wyoming
Kennedy Creevey, M.D.	Rensselaer
Robert W. Hurd, M.D.	Oneida
Alfred P. Ingegno, M.D.	Kings
C. Otto Lindbeck, M.D.	Chautauqua
Dwight V. Needham, M.D.	Onondaga
Roland E. Stevens, M.D.	Monroe
George P. Farrell, *Adviser*	New York

The committee had one meeting this year, on March 8, 1962, in the offices of the Medical Society in New York City.

At this meeting a letter from the Dental Society of the State of New York referred to us by the Executive Committee was considered. This letter dealt with the relations of the State Dental Society with the various Blue Shield plans of the State. The letter stated the policy of the Dental Society, adopted in December, 1956, which is as follows: "As a matter of general policy, all dental care programs shall be appraised by the Dental Society of the State of New York and not by individuals or branch or district societies." The letter further stated that "A branch society of one of our district (component) societies has entered into and approved a fee schedule for dental care with the administrators of one of the major nonprofit voluntary indemnity group health care programs operating in New York State." After appropriate discussion all members of the committee concurred in the opinion that this is a problem not involving the Medical Society of the State of New York, and that no action was necessary.

A telegram to Henry I. Fineberg, M.D., executive vice-president, Medical Society of the State of New York, from the American Medical Association was referred to our committee by the Executive Committee. It urged support for the A.M.A.-Blue Shield program for medical care for the aged. It was unanimously agreed that the full support of the Society should be given this program.

A resolution from the New York State Chapter of the American Academy of General Practice, urging uniformity of fees for specific procedures, disregarding the specialist or general practitioner situation of the performer of the service, was again considered. The subject of this resolution was considered at length. This resolution had been considered at our last previous meeting, when, because of failing to have a quorum, we expressed no opinion. At the last meeting it was agreed no action on our part was necessary at this time.

It was voted that we give approval for the ensuing year to the following Blue Shield Plans: United Medical Service, Inc., New York City; Western New York Medical Plan, Inc., Buffalo; Genesee Valley Medical Care, Inc., Rochester; Central New York Medical Plan, Inc., Syracuse; Medical and Surgical Care, Inc., Utica; Northeastern New York Medical Service, Inc., Albany; and Chautauqua Region Medical Service, Inc., Jamestown.

Dwight Needham, M.D., introduced a resolution urging the State Society to exert its influence in the coming negotiations for the civil service employes contract concerning diagnostic x-ray coverage. In the present contract, Blue Cross carries the diagnostic x-ray coverage, and it is effective only for in-hospital patients. There are obvious weaknesses in this arrangement. One of these weaknesses is that the patient, for example, a minor accident victim, must pay the cost of the diagnostic x-ray himself. The other weakness is that the patient might insist on being hospitalized in order that the insurance pay the bill for x-rays, thus greatly increasing the cost to Blue Cross out of proportion to the need. This resolution was adopted unanimously.

The committee wishes to express its thanks to the officers of the State Society, to Gerald D. Dorman, M.D., chairman of the Commission on Medical Services, and Henry I. Fineberg, M.D., executive vice-president of the State Medical Society, both of whom attended our meeting, and to Mr. George P. Farrell, director of the Bureau of Medical Care Insurance and adviser to the Medical Care Insurance Committee, who has done so much to assist the committee in its functions.

Respectfully submitted,
MELVIN S. MARTIN, M.D., *Chairman*

Public Medical Care

To the House of Delegates, Gentlemen:

The Public Medical Care Subcommittee is composed of the following:

Marcelle T. Bernard, M.D., *Chairman*	Bronx
Lyman C. Boynton, M.D.	Monroe
Robert J. Collins, M.D.	Onondaga
Karl N. Wechtel, M.D.	Nassau
Earl C. Waterbury, M.D.	Orange
Peter Birkel, M.D., *Adviser*	Albany
Alonzo S. Yerby, M.D., *Adviser*	New York

The subcommittee has held two meetings—January 12, 1962, and March 9, 1962.

MAA Program. The January meeting was devoted to a review of the MAA program in the State as mandated by the Metcalf-McCloskey bill. In advance of the meeting a questionnaire was sent to each county medical society for the following information: Was the program being implemented; were MAA patients and physicians satisfied with its administration; were physicians satisfied with the welfare schedule of allowances paid for medical services to MAA recipients; were the societies in favor of legislation to provide financial assistance to those who qualified under the State bill to purchase voluntary health insurance granting free choice of physician; were county societies in favor of broadening the benefits to include total health care according to the intent of the Kerr-Mills bill?

Forty-one of the 61 county societies responded, representing 94 per cent of the members of the State Society. Thirty-seven indicated the program was being implemented, that MAA recipients objected to being treated as straight welfare patients subject to the same case work investigation and the delay in determining financial responsibility; they would prefer that the program be divorced entirely from welfare.

The reaction of physicians was divided as to the administration of the program by the Welfare Department and the fees paid, and more than a majority were in favor of legislation to provide financial assistance to MAA recipients through the purchase of voluntary health insurance granting free choice of physician; responses were divided as to the broadening of benefits to conform to the intent of the Kerr-Mills bill. Comments from various counties indicated the existence of confusion regarding MAA cases and straight welfare cases.

It was pointed out that the MAA recipient is allowed certain exemptions such as income, cash allowances for certain items, and personal expenses, whereas straight welfare recipients are not allowed these exemptions. An effort is being made by the Department to clarify the differences. Your subcommittee understands that recommendations have been made by the Department to the Legislature for liberalization of the program to include other modalities to conform to the intent of the Kerr-Mills bill.

Dissatisfaction exists among physicians regarding medical care for recipients under the MAA program for two reasons: (1) In most instances MAA recipients are considered as "welfare cases" by local commissioners of welfare and not as medically indigent cases, and (2) the schedule of allowances for MAA cases should be comparable to the "Medicare Program" schedule.

Resolution 61-22. Resolution 61-22, presented by the Medical Society of the County of Ulster, was considered. This related to the prescribing of vitamins for welfare patients according to a recent mandate of the Department of Welfare designating specific illnesses for which vitamins may be prescribed and resolving that the House of Delegates request the State Department to rescind this mandate through its several county departments and to assign control of alleged abuses of welfare regulations to the governing bodies of the county medical societies.

It was pointed out there was no restriction on the prescribing of vitamins for children under age five and no restriction on prescribing therapeutic vitamins for others when medically indicated. The Department does not want to pay for vitamins to be used solely to satisfy the whim of the patient.

Conference with Welfare Department. At the March 9, 1962, meeting, representatives from the Welfare Department presented a comprehensive picture of the workings of the various departments and provided the subcommittee with helpful information for improved liaison. A recommendation was made by Mr. Antonio Sorieri, deputy commissioner, that a member of this subcommittee be appointed as a representative on the Medical Advisory Committee of the Commissioner's group; that many problems of mutual interest to your subcommittee and the Department could be discussed and resolved through this representation. Your subcommittee is in favor of this arrangement.

It was brought to the attention of the subcommittee that consideration was being given to using the facilities of present voluntary nonprofit plans to provide benefits for both welfare and MAA recipients. Premium costs would be paid by the Department.

A suggestion was made by Dr. Birkel that specifically Chapters 505, 540, and 560, of Book 5, were in order for review and revision not only in regard to the regulations but fees as well which were considered to be unrealistic at the present time.

A letter from the Medical Society of the County of Monroe regarding a 1958 resolution whereby fee schedules negotiated between county medical societies and county welfare departments were not required to conform to any fee schedule previously approved by the State Society was presented. It was pointed out that any county society could negotiate with the local commissioner of welfare in the matter of fees but the State reimbursement would be limited to the State schedule in effect, and if the fees locally negotiated were higher than the State schedule the board of supervisors would have to appropriate funds to make up the differential.

Acknowledgments. Your chairman wishes to express her appreciation to the members of her subcommittee for their attendance at meetings, and to Dr. Birkel and Dr. Yerby as advisers.

Respectfully submitted,

MARCELLE BERNARD, M.D., *Chairman*

Convention paging system

We hope that physicians attending the 156th Annual Convention of the Medical Society of the State of New York will be able to devote all their attention to the interesting program, exciting exhibits, and other features of the meeting. However, if it is necessary, physicians can always be in touch with their offices, their patients, or whoever else may wish to contact them through the SherPage System. They may be reached by television anywhere at the convention.

This service is provided through the courtesy of Sherman Laboratories, Detroit, Michigan.

Legislation and Legal Matters

Legislation

To the House of Delegates, Gentlemen:

The Council Committee on Legislation for the year 1961–1962 is composed of the following members:

James M. Blake, M.D., *Chairman*	Schenectady
George J. Lawrence, Jr., M.D., *Vice-Chairman*	Queens
John C. Brady, M.D.	Erie
E. Yale Clarke, M.D.	Warren
E. Craig Coats, M.D.	New York
Walter Einhorn, M.D.	Bronx
Frederic W. Holcomb, M.D.	Ulster
Ralph E. Isabella, M.D.	Schenectady
Henry W. Kaessler, M.D.	Westchester
John A. Kalb, M.D.	Broome
Arthur A. Knapp, M.D.	New York
Charles R. Mathews, M.D.	Monroe
William J. Ryan, M.D.	Onondaga
Herman B. Snow, M.D.	St. Lawrence
Roman R. Violyn, M.D.	Montgomery
Joseph G. Zimring, M.D.	Nassau
Granville W. Larimore, M.D., *Adviser*	Albany

It is with regret that we officially record the death of Aaron Kottler, M.D., a member of the Committee on Legislation. Dr. Kottler was very interested and active in the legislation affairs of the Medical Society and gave freely of his time in this respect.

The Committee on Legislation held its fall meeting in Albany on October 12, 1961, following receipt of the report of the action of the May meeting of the House of Delegates.

The following is a summation of the resolutions submitted to the Committee on Legislation by the House of Delegates and the action which has been taken with reference to these and other resolutions. No report can be given on legislative action on these recommendations inasmuch as this report is being submitted while the Legislature is still in session.

Resolution 61–18 (Onondaga County)—Medical School Scholarships. To provide funds for medical school scholarships annually provided recipients spend a number of years in general practice in a rural community in New York State.

In reviewing this legislation, the Committee on Legislation encountered a number of obstacles that had to be considered, but this legislation was subsequently introduced in the Legislature as follows: Senate Intro. 1015, introduced by Mr. Barrett (Brightwaters), and referred to the Committee on Education; Assembly Intro. 2040, introduced by Mr. Dudo (Lewis County), and referred to the Committee on Ways and Means.

> AN ACT to amend the education law, in relation to authorizing the counties of the state outside the city of New York to award scholarships for professional education in medicine conditioned upon the promise of scholarship holders to practice medicine in such counties for limited periods of time following their licensing as physicians.

Resolution 61–43 (Bronx County)—Tax Deduction for the Cost of Medical Tuition. To permit parents to deduct from their income for tax purposes the cost of tuition for young men and women studying in medical schools.

This was introduced in the Legislature as follows: Senate Intro. 1280, introduced by Mr. Bush (Delancey), and referred to the Committee on Taxation; Assembly Intro. 2570, introduced by Mr. Plumadore (Franklin County), and referred to the Committee on Ways and Means.

> AN ACT to amend the tax law, in relation to deduction of the cost of tuition, textbooks and laboratory fees incurred in connection with attendance at a medical college.

Resolution 61–28 (Albany County)—Medical Practitioners to Organize as an Association for Tax Purposes. To permit medical practitioners to organize as an association for tax purposes.

This was introduced in the Legislature as follows: Senate Intro. 1375, introduced by Mr. Brydges (Wilson); Assembly Intro. 2037, introduced by Mr. Bartlett (Binghamton), and referred to the Committees on Education.

> AN ACT to amend the education law, in relation to authorizing members of any profession to organize an association to engage in the practice of their profession in corporate form, providing for the regulation of such association and of its members and employees, and prescribing their powers and duties.

In addition, there have been subsequent resolutions pertaining to this same subject introduced into the State Legislature.

These resolutions have resulted in a considerable amount of discussion among the professional groups involved. We have been in close association with the New York State Association of the Professions and there is some difference of opinion as to the details concerning this legislation. While this was introduced as a mandated resolution from our House of Delegates, we have suggested to those other interested professional groups that amendments to the resolution, as long as they do not alter the basic concept, are in order. In view of the discussions that have transpired, there is considerable doubt at the present time that this legislation will be passed during this session of the Legislature.

Resolution 61-44 (Queens County)—Legal Responsibility in Performance of Postmortem Cesarean Section. Would permit physicians to use own judgment in cases of advanced pregnancy and where physician has reason to believe that the child is viable in the mother.

The desirability of legislation of this type, as well as other similar legislation affecting autopsy, was thoroughly reviewed by your committee. In the course of discussion it was pointed out that a study is now being made by the State of New York concerning this subject. Therefore, in an attempt to arrive at eventual adequate legislation covering this, it was felt indicated at this time that we advise the study committee of our interest and offer our services. This and a similar resolution also are considered in the recommendation we have previously made by resolution calling for a study of the healing arts. Therefore, it was felt that no specific legislation would be introduced this year, but that we should pursue this subject further unofficially, with the hope that eventually specific corrective legislation could be passed.

Review of the Medical Practice Act (Healing Arts). Based on the recommendation of the reference committee that "it is extremely important that the scope of permissible activity of each paramedical group be accurately defined and enforced..... . At present the limits of therapy permitted to these groups is a matter for interpretation by the Department of Education in an outmoded Medical Practice Act. It is therefore important that this Act be brought up to date."

This resolution, Senate Intro. 10, has been introduced by Mr. Cornell (Scarsdale) into this session of the Legislature. It is doubtful, however, that any specific action will be taken on it. It is encouraging to note that more interest is being expressed relative to this and it is perfectly possible next year that more definitive and stronger action can be sought.

Resolution 61-57 (Queens County)—Only Doctors of Medicine to Practice Psychiatry. To prohibit any person other than a licensed doctor of medicine to treat any human illness or disorder, including mental and emotional disease and personality disorder.

The substitute resolution, which was approved by the reference committee and referred to the Council, was subsequently referred to the Committee on Legislation. The background information pertaining to this problem was accordingly referred to the Governor and the Attorney General.

Property Tax—Medical Societies. This item of legislation was introduced in the Legislature as follows: Senate Intro. 1063, introduced by Mr. Thaler (Forest Hills), and committed to the Committee on Taxation; Assembly Intro. 2183, introduced by Mr. Savarese (Richmond Hill), and referred to the Committee on Taxation.

> AN ACT to amend the real property tax law, in relation to exemption from taxation of real property owned by medical societies.

Exemption from Liability in Emergency Treatment. This legislation was introduced as follows: Senate Intro. 1602, introduced by Mr. Speno (Long Island), and referred to the Committee on Education; Assembly Intro. 2090, introduced by Mr. Bartlett (Warren County), and referred to the Committee on Judiciary.

> AN ACT to amend the education law, in relation to exemption from liability of physicians and surgeons rendering gratuitous emergency treatment.

Medical Assistance to the Aged. Several amendments providing for the extension of services in this area have been introduced in the Legislature. Among them are: (1) To include payments for dental services, eye glasses, physiotherapy, laboratory, and x-ray; (2) allowance retained as a burial reserve; (3) direct grants for clothing and incidental requirements; (4) private duty nursing services; (5) diagnostic screening and preventive services; (6) home health care services; (7) elimination of relative responsibility except for spouse; and (8) establishment of adequate standards as to level, content, and quality of medical services.

The action taken on these and other amendments pertaining to this will be reported in a supplementary report.

The following items of legislation of particular concern to the practice of medicine have been introduced from other sources this year and are being reviewed and followed by your committee and our legislative counsel.

Malpractice. Senate Intro. 1780, introduced by Mr. Hughes (Syracuse), on recommendation of the Laws Revision Commission, and referred to the Committee on Codes; Assembly Intro. 1939, introduced by Mr. Folker (Depew), and referred to the Committee on Codes.

> AN ACT to amend the civil practice act, in relation to time for commencement of action to recover damages for malpractice.

The intent of this legislation is to recover damages for malpractice, whether based on tort, contract, or any other theory. A cause of action for malpractice is deemed to have accrued upon the discovery by the plaintiff or the person under whom he claims of the facts constituting the malpractice, but this provision shall not permit commencement of such an action after six years from the occurrence of the malpractice.

Hypnosis. Senate Intro. 1902, introduced by Mr. Brydges (Wilson), and referred to the Committee on Education; Assembly Intro. 4116, introduced by Mr. Passannante (New York County), and referred to the Committee on Codes.

AN ACT to amend the education law, in relation to restricting the inducing of hypnosis.

The intent of this legislation is to restrict the inducing of hypnosis to physicians, dentists, and certified psychologists; to prohibit exhibitions of hypnosis; and to restrict the teaching of the inducing of hypnosis to educational institutions chartered by the State of New York, all hospitals approved by the State Department of Social Welfare or maintained and operated by any governmental agency or under the jurisdiction of the Department of Hospitals of the City of New York and all courses sponsored by a medical or dental society which is a direct component of a nationally recognized society of the American Medical Association, American Dental Association, or equivalent thereof, or other society or group whose membership is restricted to doctors of medicine, doctors of dentistry, psychologists, psychiatrists, or any one or several of the foregoing.

Phenylketonuria Testing. Assembly Intro. 1032, introduced by Mrs. Lawrence (New York City), and referred to the Committee on Public Health.

AN ACT to amend the public health law, in relation to testing newborn infants for phenylketonuria.

This legislation provides that every newborn infant shall, within two weeks after birth, be subjected to a test for phenylketonuria.

Mental Health Services—Per Capita Aid. Senate Intro. 2312, a Budget Bill, committed to the Committee on Finance.

AN ACT to amend the mental hygiene law, in relation to the per capita limitation on State aid reimbursement for community mental health services.

This legislation would increase the State reimbursement from $1.20 to $1.40 per capita population.

Lien Law. Assembly Intro. 2217, introduced by Mr. Fehrenback (Nassau County), and referred to the Committee on Judiciary.

AN ACT to amend the lien law, in relation to liens of physicians.

Licensure of Clinical Laboratories. Senate Intro. 3212, introduced by Mr. Marchi (Staten Island), and committed to the Committee on Education; and Assembly Intro. 4069, introduced by Mr. Mintz (South Fallsburg), and referred to the Committee on Codes.

AN ACT to amend the education law, in relation to licensing and regulating the practice of bioanalysis.

There have been three different bills introduced into the Legislature calling for the licensing and regulating of the practices of bioanalysts, all of which are essentially and basically the same and would permit the operation of laboratories for medical analysis without medical supervision.

Division of Medical Care (State). Assembly Intro. 208, introduced by Mr. Weiser (New York City), and referred to the Committee on Ways and Means.

AN ACT to amend the executive law, in relation to creating in the executive department a division of medical care, defining its functions, powers and duties, and providing for the appointment and compensation of its officers and employees.

Licensure of X-ray Technicians. Senate Intro. 3093, introduced by Mr. Speno (Long Island), and committed to the Committee on Finance; Assembly Intro. 1588, introduced by Mrs. Lawrence (New York City), and referred to the Committee on Ways and Means.

AN ACT to amend the public health law, in relation to the practice of radiation technology and the creation of a radiation technician advisory board.

Ownership of X-ray Plates. Senate Intro. 1660, introduced by Mr. Bernstein (Bronx), and referred to the Committee on Judiciary; Assembly Intro. 4366, introduced by Mr. Kapelman (Bronx), and referred to the Committee on Judiciary.

AN ACT to amend the personal property law, in relation to the ownership of x-ray plates taken by physicians or hospitals.

This legislation would give title to the patient of any x-ray taken of him and would permit him to demand this as personal property and a physician or hospital would have to surrender the x-ray plate.

AMENDMENTS TO WORKMEN'S COMPENSATION LAW

1. **Selection of Physician.** Senate Intro. 1337, introduced by Mr. Peterson (Odessa), and committed to the Committee on Labor and Industry.

AN ACT to amend the workmen's compensation law, in relation to selection of physician by claimant.

This legislation would permit the patient when medical care is required the right to choose an attending physician from a panel of a reasonable number of competent and qualified physicians to be named by the employer.

2. **Hospital Medical and Surgical Insurance.** Assembly Intro. 2391, introduced by Mr. Arnone (Buffalo), and referred to the Committee on Ways and Means.

An ACT to amend the workmen's compensation law, in relation to required hospital, medical and surgical insurance coverage for covered employees under the disability benefits law, and providing for the establishment and operation of a health insurance unemployment fund to pay premiums for such coverage during periods of unemployment.

3. **Report of Physician.** Senate Intro. 3363, introduced by Mr. Condon (Yonkers), and committed to the Committee on Labor and Industry; Assembly Intro. 4671, introduced by Mr. Dudo (Lewis County), and referred to the Committee on Labor and Industry.

An ACT to amend the workmen's compensation law, in relation to reports of physicians.

This legislation was prepared and introduced at the request of the Bureau of Industrial Health and Workmen's Compensation of the Medical Society of the State of New York and provides that no claim for medical or surgical treatment shall be valid and enforceable, as against such employer or employee, unless within forty-eight hours following the first treatment, or within forty-eight hours after being informed by any of the interested parties that such treatment may come under the provisions of this chapter, the physician giving such treatment furnish a report.

4. **Payment of Bills for Medical Care.** Senate Intro. 3430, introduced by Mr. Condon (Yonkers), and committed to the Committee on Labor and Industry; Assembly Intro. 4670, introduced by Mr. Dudo (Lewis County), and referred to the Committee on Labor and Industry.

AN ACT to amend the workmen's compensation law, in relation to the payment of bills for medical care.

This legislation was prepared by and introduced at the request of the Bureau of Industrial Health and Workmen's Compensation of the Medical Society of the State of New York, and provides unless within thirty days after a bill has been rendered to the employer by the physician or hospital which has treated an injured employe, such employer shall have notified the chairman and such physician or hospital in writing that such employer demands an impartial examination of the fairness of the amount claimed by such physician or hospital for his or its services, the right to such an impartial examination shall be deemed to be waived and the amount claimed by such physician or hospital shall be deemed to be the fair value of the services rendered by him or it and shall be payable within fifteen days thereafter.

Optometric Care. Assembly Intro. 2365, introduced by Mr. Russo (Richmond County), and referred to the Committee on Insurance.

AN ACT to amend the insurance law, in relation to providing medical expense indemnity for optometric care.

This is permissive legislation and would provide medical expense indemnity giving the patient the freedom of choice to select either a physician or optometrist to render such services.

This bill has passed both houses and has been signed by the governor.

Comment. The basic plans of activity of the Committee on Legislation were reviewed by the committee at its fall meeting and a program similar in many respects to that of the previous year was approved. It was the opinion of the committee that we would attempt again this year to keep the various county societies alerted to the legislation activities through the publication of *Capitol News*. Unfortunately, the Department of Communications, whose responsibility this has been in the past to publish and distribute *Capitol News*, was unable to maintain this program with the degree of regularity hoped for this year. Much of the communication to the county societies, therefore, has been through personal contact and personal communication.

The format of meetings with district groups of legislation chairmen and other members of local societies was changed somewhat during this year. In addition to having district meetings with these representatives of the medical profession, we also invited the legislators from the respective areas to these meetings. This led to very thorough and informal discussion of specific items of legislation, as well as medical legislation in general. It seems to be the opinion of the members of the Society participating in this, for the most part at least, that these meetings were more satisfactory and probably should be further encouraged and extended in succeeding years. In addition to this, several of the county societies have sent representative members to the capitol in Albany during the session of the Legislature to visit with their respective legislators. This has proved quite effective and has called to the attention of the legislators that we are, in reality, interested in legislation which affects the medical care of the people of our State.

Although an attempt has been made again this year to encourage members of county societies throughout the State to contact their legislators and to discuss with them the various items of medical legislation, unfortunately too few have done this. While many have worked quite hard in this respect, there are still a large number who have taken no action whatsoever. It seems quite obvious, and often is quoted by the legislators themselves, that if the medical profession is to be effective in regard to medical legislation, it is essential they assume certain responsibilities on a local level, particularly the responsibility for contacting their representatives and discussing matters of importance with them.

The members of your State Legislation Committee and the members of the respective legislation committees of county medical societies can influence to a certain extent legislation affecting medical care. However, the end result in medical legislation—both good and bad—in reality depends on the activities of each individual physician in his day-to-day practice, as well as his willingness to spend at least a little time becoming acquainted with proposed legislation affecting medical practice and discussing such proposals not only with the legislator representing his area but also with his everyday contacts, thus making the opinion of medicine known from a personal and local level.

If we want to have a part in legislation then we must play a part in legislation.

Respectfully submitted,

JAMES M. BLAKE, M.D., *Chairman*

Federal Legislation

Membership of the Federal Legislation Subcommittee is as follows:

George J. Lawrence, Jr., M.D., *Chairman*	Queens
William B. Ayers, M.D.	Nassau
John C. Brady, M.D.	Erie
Harold T. Golden, M.D.	Herkimer
Walter G. Hayward, M.D.	Chautauqua
Solomon Schussheim, M.D.	Kings

The last year has been a most active period for your committee, perhaps the most active since its inception. Detailed reports have been submitted to the Council. The following are the highlights.

Shortly after the House adjourned, a letter was sent to key people, such as presidents, secretaries, and public relations and legislation chairmen, setting forth a program of action stressing contacts with their congressmen to try to obtain their cooperation in opposing H.R. 4222. The *Newsletter* also carried a similar message for all the members of our State Medical Society.

Meetings. A special emergency meeting of all county medical society legislation chairmen was held in Albany on July 12. In spite of the time of the year, when most people were vacationing, there was a very fine turnout. The subcommittee is most grateful for the attendance.

At this meeting your chairman outlined the Federal legislation situation and what he thought future developments would be. He asked for the cooperation of all in doing whatever they could to oppose H.R. 4222, particularly before the House Ways and Means Committee. As a result, when the hearings were held shortly after this meeting, several county medical societies presented statements, and one had a personal representative appear before the committee in Washington.

On July 26, your chairman and Henry I. Fineberg, M.D., executive vice-president, went to Washington and presented the State Medical Society's testimony in opposition to H.R. 4222 to the House Ways and Means Committee. We were given a very cordial reception, particularly by the two New York representatives on the committee, the Hon. Steven B. Derounian and the Hon. Eugene J. Keogh.

Your chairmen and other representatives of our State Society met with Senator George R. Metcalf, Assemblyman Francis P. McCloskey, Raymond W. Houston, State Commissioner of Public Welfare, Alonzo S. Yerby, M.D., executive director of medical care services, New York State Department of Health, and others in regard to the implementation of the Metcalf-McCloskey Law in New York State. As a result of these meetings, we hope that steps will be taken either through proper administration or supplementary legislation to remove the road blocks thus far encountered.

Members of the Woman's Auxiliary, representatives of our Society, including members of the subcommittee and staff, attended the White House Regional Conference held at the Hotel Commodore, New York City, in early fall. The purpose of this conference was to sell the Administration's program for medical care for the aged under Social Security. It was headed by Abraham Ribicoff, Secretary of Health, Education, and Welfare, who bitterly attacked the medical profession. The audience was packed with elderly people who arrived by bus loads or who marched in parade formation to the meeting place. The slanted, unfair method in which this meeting was conducted as a propaganda medium for the Social Security approach stimulated all of us who witnessed the farcical performance to the determination to leave no stone unturned in our fight to defeat H.R. 4222.

Operation Counter-Attack. In November of 1961, "Operation Counter-Attack" was launched. The primary object of this project was to stimulate county medical societies and members to set up small committees of knowledgeable physicians to meet with their congressmen before their return to Washington in January of 1962.

This project called for an intensive five-point program:

(1) Conduct an advertising campaign in local newspapers stating "why" the King-Anderson bill should be defeated.

(2) Contact allied health groups. Purpose: Obtain their support for the preservation of the best medical care by defeating the King-Anderson bill.

(3) Reactivate speakers bureaus. Last year many county medical societies offered the services of their members to organizations, such as Rotary, Kiwanis, PTA, Chamber of Commerce, and the like, to explain medicine's opposition to H.R. 4222. This activity was intensified in 1962.

(4) Write letters to local congressmen and members of the House Ways and Means Committee. Hon. Steven B. Derounian, Republican, Nassau, and Hon. Eugene J. Keogh, Democrat, Kings, are New York's representatives on this key committee.

(5) Enlist the support of the Woman's Auxiliary in all four phases of "Counter-Attack" outlined above.

The first step in "Operation Counter-Attack" was a letter signed by your chairman and sent to all county medical society presidents. Copies were sent to all county legislation chairmen, public relations chairmen, executive secretaries, woman's auxiliary officials, and to members of the Council of our State Medical Society.

In preparation for these meetings, it was suggested that briefing sessions of the doctors involved be held so that they would be armed with facts when they met with their congressmen. Kits were prepared and sent to members of the various committees and executive secretaries. Assistance in conducting these briefing sessions through the personal appearance of Society staff representatives throughout the State and in gathering and forwarding the materials was rendered by the Communications Department. It was necessary to hire outside part-time help to carry out this project.

This was a most ambitious project. As every member of the House knows, it is most difficult to get doctors to go into action on a political subject. Few of us believed that this project could be successful. However, the results were most gratifying.

Actual reports, which can be found in the files of the Communications Department, show that 30 of the 43 congressmen in the State of New York were contacted by local county medical societies. This is something that has never been done before in the history of the State Medical Society. Considering the short period of time the local county societies had to act, and in which your subcommittee had to participate in this project, it was an outstanding achievement. It was brought about by the combined efforts of the local county medical societies with the cooperation of the Council and the Communications Department.

Your chairman would like to point out that a tremendous amount of work was involved in this project. As far as possible there were personal contacts by representatives of the State Society with the local county medical societies. As a result of these personal contacts there were many favorable reports received by State Society headquarters. According to these reports, many of the congressmen who had been on the side of medicine were solidified in their position. On the other hand, there have been many indications that congressmen who had been opposed to medicine's position on the King-Anderson bill were in doubt. In one instance in upstate New York, information provided helped a congressman make up his mind in regard to his position on this bill.

Many other activities were carried on. Copy for articles in county medical society bulletins was prepared and sent to county medical societies throughout the State. Because of the crucial nature of the situation, your subcommittee sent special letters to every member of the Nassau County Medical Society and the Kings County Medical Society urging them to present medicine's views to their representatives on the House Ways and Means Committee. These letters requested that the Nassau County members contact Representative Steven B. Derounian and that the King's County members contact Representative Eugene J. Keogh.

In addition, the January, 1962, issue of the *Newsletter* was dedicated to stimulating activity by every member of the Medical Society of the State of New York in presenting medicine's view in opposition to H.R. 4222.

An example of one of the excellent activities being promoted by local county medical societies is an advertisement which appeared in *Newsday*, a daily publication in the area of Nassau and Suffolk Counties. This advertisement, entitled "Speaking of: Medical Aid to the Aged—Do You Know That—We Already Have Medical Aid to the Aged?," elicited a tremendous response. Your subcommittee recommends that this type of advertisement be sponsored at the local level by every county medical society throughout the State. A copy of the advertisement has been sent to all county medical society executive secretaries.

Although the subcommittee was encouraged by what had been accomplished during 1961, particularly through the cooperation of county medical societies, in the early part of 1962 it became extremely concerned about medicine's failure to present its position to the public. During the last part of 1961, the Administration sent groups of its representatives throughout the country endorsing H.R. 4222. The White House Regional Conference held at the Commodore was one of these meetings. In his State of the Union message, President Kennedy very definitely stated that one of his chief objectives during the 1962 session was the passing of the King-Anderson bill. The President went so far as to hold special breakfast meetings with key people to try to induce them to back his program, including Representative Wilbur D. Mills, chairman, House Ways and Means Committee.

Special Session of House. After a great deal of thoughtful consideration, the subcommittee recommended to the Council that a special session of the House of Delegates be called at the request of the Council to reiterate as of 1962 the Society's opposition to the proposed enactment of the King-Anderson bill, in order to alert the public to the dangers involved and to stimulate the members of our Society into immediate action.

At the January, 1962, session of the Council it was voted that such a session be held. As you know, this special session took place on February 10, 1962, at the Summit Hotel, New York City. Considering the short notice that necessity dictated and the bad weather, the meeting was very well attended. A total of 211 delegates were present. The chairman of the subcommittee wishes, personally and on behalf of his subcommittee, to express deep appreciation to the delegates who sacrificed so much to attend this session.

Four major resolutions of most timely and crucial concern to the people of our State were adopted. Briefly, they (1) rededicated the physician of today to his ideals, recognizing also the obligation to inform public opinion and to express a qualified professional viewpoint where public health legislation is concerned; (2) formed specific proposals to strengthen the Metcalf-McCloskey Act and its State-administered program of medical care to the aged; (3) supported the newly suggested idea of bringing voluntary health insurance plans into the program for the care of the aged; and (4) warned the people and legislators of the dangers inherent in licensing chiropractors.

Washington Visit. On February 27 and 28, and March 1, 1962, the second annual State Medical Society congressional delegation visited Washington. The purpose of this visit was to acquaint our representatives with medicine's views on proposed legislation, particularly the King-Anderson bill, and to build better rapport with them.

The delegation was led by John M. Galbraith, M.D., our president, and Joseph A. Lane, M.D., our president-elect. The remainder of the delegation consisted of the following physicians: Henry I. Fineberg, executive vice-president; William J. Ryan; Bernard J. Pisani; Frederic W. Holcomb, Jr.; Waring Willis; Joseph J. Witt; John C. Brady; Charles R. Matthews; Solomon Schussheim; Leonard J. Heimoff; John H. Powers; William L. Dorr; Ralph S. Emerson; Herbert A. Laughlin; John D. Van Zandt; Michael C. Armao; Vincent J. Tesoriero; and the chairman of your subcommittee. Advisers to the delegation were Jack Pardee, director, and Martin J. Tracey, associate director, Department of Communications.

The following physicians were members of the delegation but were unable to be present because of either inclement weather or illness: William B. Ayers, James M. Blake, William T. Boland, and John D. Naples.

A brief resume of the activities in Washington follows. On the evening of February 27 there was a briefing session at State Medical Society headquarters in the Statler-Hilton by the chairman of your subcommittee and the members of the delegation. On the morning of February 28 there was a breakfast meeting during which the members of the delegation were briefed by members of the Washington staff of the A.M.A.

After the morning briefing session, the delegation was divided into four teams, which were led by Dr. Brady, Dr. Fineberg, Dr. Galbraith, and Dr. Lane. The teams were so set up that each congressman would be visited by a doctor from his local area. These visits continued throughout the morning of February 28. At noon there was a luncheon at the Capitol Hill Club adjacent to the office buildings of the congressmen on the hill.

During the afternoon, the visits to the congressmen were continued, followed by a joint conference with Senators Jacob K. Javits and Kenneth B. Keating in the office of the former. The entire delegation attended this conference. On the evening of February 28, a reception was held for the members of the House and the Senate in the New York Room of the Statler-Hilton. On the morning of March 1, there was a breakfast meeting at which the chairmen of the four teams reported on what had happened during the visits to the congressmen and their reaction to the conference with the two United States senators.

The members of the House will be pleased to learn that one of the most potent weapons that the members of the delegation had was the summary of the actions of the House taken at the special session. This recapitulation, which was presented to the congressmen and the United States senators, made a great impression.

While it is difficult to evaluate what the total effect of the delegation's visit was, certain observations can be made. In the first place, when the delegation appeared in Washington in 1961 they were greeted very amicably and their views were given consideration. During the 1962 visits, the general impression was that more serious consideration was given to the reasons advanced by the various members of the delegation. It was quite evident that one point disturbed many of the congressmen, even those committed to the endorsement of H.R. 4222, that the people were not being told all the facts about the King-Anderson bill.

Thirty-two out of the 43 New York congressmen were contacted. About 20, including our two senators, attended the reception. This is an excellent record.

Special attention is called to the fact that the conference with our two United States senators was most interesting and most encouraging. One year ago, for example, it took a great deal of work on behalf of the staff of our Society to arrange a meeting with the two United States senators. There was some reluctance on the part of the senators to meet with the medical profession. This year, however, there was a different attitude. Both senators were only too happy to meet with our delegation, and gave us considerable time and discussed our problems at great length. Not only were both senators more receptive this year than they were last year, but they also gave definite evidence that they were giving more consideration to our stand in regard to such measures as H.R. 4222.

In summary it can be said that the end result of the two annual trips to Washington by our State Society delegations is that our State Society has gained prestige in the eyes of the members of Congress. There is no doubt that every member of Congress from New York State for or against the position of medicine knows how the State Medical Society stands and respects its views.

Keogh Bill. Action also was taken on another important bill, H.R. 10, the Keogh bill. On receiving notice that public hearings were to be held by the Senate Finance Committee on the proposed law, your chairman sent letters to all county medical societies urging them to express support of the bill to the members of the committee. Your chairman is not happy to report that on August 25 the Senate Finance Committee by a vote of 14 to 3 ordered that a modified version be reported out of committee. This amended bill is a very much watered-down version of the original bill and your chairman questions whether medicine should vigorously support the watered-down version.

For the information of the House, your chairman is taking the liberty of quoting from the legislative round-up of the A.M.A. for September 1, giving a brief idea of what the new proposed law would be:

"As amended by the committee, H.R. 10 would authorize a self-employed individual to contribute 10 per cent of his earned income, or $2,500, whichever is less, toward a retirement plan . . . . A 100 per cent tax deduction would be permitted on the first $1,000 contributed and 50 per cent on the remaining $1,500 . . . . Therefore, the maximum amount deductible for income tax purposes would be $1,750 . . . . A self-employed individual wishing to establish a plan for himself would have to cover all full-time employees with more than three years of service . . . . The benefits for employees would have to be vested in the employee immediately . . . . Benefits would not be payable before age fifty-nine and one-half except in the cast of permanent disability or death . . . . Payment would have to begin at age seventy and one-half . . . . The bill would become effective for taxable years beginning with 1962.

"The House-passed version of H.R. 10 allowed self-employed persons to deduct the full $2,500 . . . . Also, under the House version, only employers who had four or more persons working for them would have to set up a pension program for their employees to take advantage of the plan themselves . . . . The Treasury estimated that the House version would reduce Federal revenues by as much as $358 million a year . . . . As modified by the Senate Finance Committee, the proposal would reduce Federal revenues by about $200 million a year.

"Chances for further action on H.R. 10 this year are slight . . . . The Administration opposes it, and the plan would face a stiff fight on the Senate floor."

At the time this report is being prepared, H.R. 10 has not been voted on by the Senate but can be called up by that body at any moment.

Conclusion. The subcommittee, in conclusion, recommends that the activities of the subcommittee during the past year be continued and intensified, and that appropriate funds be set aside for this purpose. It specifically recommends that the annual visits to Washington be continued.

Your chairman wishes to thank, first of all, the members of his subcommittee and the Council. He also wishes to thank the chairman of the parent committee on legislation, James M. Blake, M.D., and the members of the Washington delegation. He also expresses his appreciation to Henry I. Fineberg, M.D., executive vice-president, for the assistance he has rendered. A vote of thanks also goes to the Society staff members who have assisted him in his efforts, particularly the members of the Department of Communications and especially Mr. Tracey.

We are grateful also to the A.M.A. for the assistance rendered by its field service throughout the year and by its Washington office during our visit to the Capitol.

To Combat Cults

To the House of Delegates, Gentlemen:

The Council Committee to Combat Cults is composed of the following members:

James M. Blake, M.D., *Chairman*	Schenectady
Edward C. Hughes, M.D.	Syracuse
John C. McClintock, M.D.	Albany
John K. Pardee, *Adviser*	New York

An act to amend the education law in relation to the practice of chiropractic, that is, the licensure of this cult, was again introduced this year by Mr. Peterson. Its companion bill was introduced from another source, Mr. Goddard, in the Assembly. In addition to this, a third bill with reference to licensure of chiropractic was introduced by Mr. Mosberg.

The first two items of legislation, those introduced by Mr. Peterson and Mr. Goddard, show considerable change in part over previous years, although basically they are the same bill. Many of the features which we referred to previously have been eliminated in this item of legislation, but it still permits the use of modalities of medical practice and, in reality, does license for the practice of medicine.

This legislation, therefore, has been opposed quite vigorously by your committee. We have again been supported by the State Department of Health, and much of the initiative with reference to opposition to licensure of chiropractic has been taken by Dr. Hilleboe in opposing their use of x-ray.

The activities and pressure with reference to licensure of chiropractic seem to grow more intense each year, and this year it is without question the most intensive campaign for licensure that has been presented for some time.

In view of the misinformation given to the press by Senator Peterson, it was felt desirable that a public hearing be requested. Therefore, the following telegram was sent by your president to Senator Austin Erwin of the Senate Finance Committee and to Assemblyman Fred Preller of the Assembly Ways and Means Committee:

> "In view of inaccurate and misleading information which has been given to the press to the effect that the 'licensure of chiropractic is acceptable to the medical profession,' I, as president of the Medical Society of the State of New York, representing over 25,000 physicians, vehemently refute this statement. The medical profession has and continues to oppose the licensure of chiropractors to practice medicine or to use medical modalities of any type as would be permitted under this proposed legislation.
>
> "Apparently introduction of the Peterson-Goddard chiropractic licensure bills was deliberately delayed until late in the legislative session to prevent a full and complete public discussion. Since the health of the people of the State of New York is seriously involved, we respectfully request a public hearing on these bills to be held by your committee before the committee takes any action."

This subject is still very much alive and whether or not it will be reported from committee for action by the Senate and Assembly is as yet undetermined.

Respectfully submitted,
JAMES M. BLAKE, M.D., *Chairman*

Legal Counsel

To the House of Delegates, Gentlemen:

This is my nineteenth annual report as counsel for the Medical Society of the State of New York. Before being appointed as counsel I was associated with Lloyd Paul Stryker and then with Lorenz J. Brosnan, since graduation from law school in 1928.

Our staff has remained the same as it was last year. Mr. Robert J. Bell, attorney for the Society, and Mr. Harold J. Shapero have continued to prepare and try with great ability a large volume of our litigation. As a matter of fact, I am very proud to say that just as I started to write this report there came in the mail a long opinion in a nonjury case that Mr. Shapero tried and won in Nassau County, and last evening Mr. Bell called me to tell me that after a week-long trial in Queens County, the jury had rendered a unanimous verdict in favor of the defendant. Both of these cases involved a great deal of preliminary work including extensive briefs as well as skillful work in court. Mr. Bell took some time off around Christmas to have surgery performed that he had long postponed, and he came out of it in fine shape. He and I are very grateful for the skillful care that he received and for the many kind letters that members of the medical profession sent to him.

Mr. John J. DeLuca, who has been with us for over twenty years, spends a great part of his time attending examinations before trial and pretrials, which very often set the pattern for the defense of the lawsuit, and also writes briefs and generally assists with the preparation and trial of our cases. Mr. William C. Richardson, who has been with us over twelve years, interviews witnesses, attends examinations before trial and pretrials, and I am pleased to say tried a long difficult Supreme Court case involving multiple defendants and wound up with a defendants' verdict. Mr. J. Richard Burns assists with the trials, manages the office, and is in contact with the offices of the Medical Society taking care of the many matters that constantly arise. He writes a number of opinion letters and has contributed a number of editorials to the NEW YORK STATE JOURNAL OF MEDICINE. Mr. Donald J. Fager has tried cases all over the State of New York and I have received high praise of his work from the judges before whom he appears. Messrs. William C. Ketchum, Jr., Anthony L. Schiavetti, and Andrew A. Goldman are the younger lawyers in the office and all have continued to render excellent service.

There is, in addition to the very large volume of State-wide litigation that requires our attention, an increasing volume of inquiries that must be answered and opinions that must be written in connection with problems of the State Society. It is also necessary that we attend meetings of the Malpractice Insurance and Defense Board, the work of which is quite time consuming, and we assign lawyers to the malpractice committee meetings of the various county societies. Mr. Shapero is assigned to Queens County, Mr. Burns to Westchester County, Mr. DeLuca to Kings County, Mr. Richardson to Bronx and Nassau Counties, and Mr. Fager to New York and Richmond Counties. Mr. Bell, Mr. Fager, and myself attend a number of upstate meetings.

During the last year I talked to the following: the Vermont chapter of the American College of Surgeons at Montpelier, the Tricounty Medical Societies at Utica, a medicolegal conference sponsored by the American Medical Association in New York City, the Erie County Medical Society in Buffalo, a conference on medical-legal problems sponsored by the Defense Research Institute in New York City, a district branch of the New York State Nurses Association, a joint conference of the Cortland County Medical Society and Bar Association, a meeting of the medical staff of the Union Health Center of the International Ladies Garment Workers' Union, the Queens County Catholic Physicians Guild, the Medical Society of the County of Kings, a joint meeting of the Hellenic Medical Association and the Greek-American Lawyers Association in New York City, the medical staff of St. Vincent's Hospital, Bridgeport, Connecticut, and I also taped a panel discussion of medical malpractice on radio station WBAI in New York City. Mr. Bell addressed the Dutchess County Medical Society in Poughkeepsie. Mr. Shapero addressed a joint meeting of the Nassau County Medical Society and Bar Association, the Rockland County Medical Society, students at New York Medical College, and participated in a panel discussion on medical-legal problems sponsored by the Association of the Bar of the City of New York. Mr. Richardson and Mr. Fager continued their series of lectures on medicine and the law to students at New York Medical College.

Malpractice. Every year I have tried to make some comments on the problems involved in malpractice claims and suits. It was John Steinbeck in *East of Eden* who said: "The medical profession is unconsciously irritated by lay knowledge." For a change, I am going to quote from the writings of other lawyers who have much to do with this problem. The Defense Research Institute recently published a monograph on "Medical Malpractice." I wrote one of the articles in which I quoted from "A Professional Liability Primer for Physicians" recently prepared by the Committee on Medical Defense, Massachusetts Medical Society:

> "Throughout the United States and England medical malpractice lawsuits are alarm-

ingly on the increase, and the resultant cost to physicians is skyrocketing. The individual jury awards and out-of-pocket settlements have ranged from nothing to $317,000. In 1959, such costs, including lawyers' fees, court costs, damages, and out-of-court settlements, totaled an estimated $50,000,000. In the same year 6,000 doctors were sued, and it is obvious, therefore, that today's medical school graduate stands a chance of greater than 1 in 8 of being sued, even if he lives in a conservative community. The reasons for the increased incidence of suits are many and varied, but several of these reasons are fairly apparent and concern us seriously.

"Far more than half of all professional liability claims and suits are without the slightest meritorious foundation. This fact may lead the indifferent or uninformed physician to assume that professional liability is not much of a problem, that a great uproar is being made over trifles. But the physician must remember that any patient, including one of his own, when reading of a suit against a physician, may well recall that he himself did not like some particular thing that his physician did to him, that on occasion he was charged too much and then may consider suit as balm for his wounds. He may well say, too: 'Anyway, where there's smoke there's fire!' It is this thought that so well illustrates one very sore facet of the professional liability situation: every physician who is sued is seriously injured by the suit itself. This is true regardless of the justice of the claim. All physicians are in fact injured to some degree by every publicized claim.

"The erroneous opinion exists in many quarters that it is the charlatan, quack, or borderline practitioner who is sued. On the contrary, in some sections of the country, more than half of all the suits have involved practitioners who are above the median of the group in skill, experience, and standing. This may be understandable on the theory that he who has most to lose may be the most readily 'shaken down' to buy his peace."

Attorney Michael R. Gallagher of Cleveland, Ohio, contributed to the monograph excerpts from a radio speech that he had given over a Cleveland station. He speaks of one of the public's current misconceptions as being its

> "failure to comprehend that the practice of medicine is as much an art as it is a science. A decision to operate or not to operate must frequently be made where the various diagnostic aids used are ambiguous or where they point in one direction, while judgment and experience point in another. A doctor should not be placed in the position where honest judgment, conscientiously arrived at, can be the basis for unjustified lawsuits against him."

Another contributor, Edward H. Borgelt of Milwaukee, Wisconsin, stated that:

> "The general situation continues to grow progressively worse and obviously will continue to do so unless something is done in an effort to reverse the trend. Underwriters of this type of insurance are daily becoming more reluctant to cover doctors and there is a report of one doctor, a victim of a verdict in excess of coverage carried, who discontinued the practice of medicine because he did not feel that he could 'afford the jury-imposed premium.'"

I agree with what he calls "Some Factors Which Lead to Medical Malpractice Claims." These are:

> "1. Loose remarks as well as direct criticism, by succeeding physicians.
>
> "2. Notations made on hospital records by interns. (Ill-founded opinions or diagnoses).
>
> "3. Instituting suit for collection of the doctor's bill prior to the expiration of the statutory period within which to bring a medical malpractice suit.
>
> "4. A hostile attitude created by requiring a patient to sit in a waiting room for a long period of time.
>
> "5. Failure to respond 'promptly' to emergency calls.
>
> "6. Information imparted or statements made to the patient by the attending nurse. (*a*) Special precautions are necessary in those cases in which a nurse is included among a patient's relatives.
>
> "7. The giving of privileged information on oral approval. (In some cases, in which the information was not as favorable to the patient as desired, an issue of fact was raised as to whether the doctor had such approval.)
>
> "8. Failure to freely use x-ray for diagnostic and check-up purposes.
>
> "9. Failure to take a complete history which, if taken, would have disclosed reasons why certain procedures should not have been followed.
>
> "10. Disclosure of the fact of malpractice insurance coverage.
>
> "11. In general, the erroneous assumption on the part of the doctor that the old-fashioned relationship between patient and physician still exists.
>
> "12. Failure to obtain written approval to have operation performed by another doctor.
>
> "13. The making of predictions which are too optimistic and which may result in actions for breach of contract.
>
> "14. Failure to confirm instructions in writing when disregarded to the knowledge of the physician; or, in any event, when serious consequences will follow if instructions are not carried out.
>
> "15. Errors in the filling of prescriptions when telephoned to the druggist.
>
> "16. Failure to promptly adequately follow up indications of dissatisfaction with the

physician's services. (Sometimes a frank discussion affords an opportunity to correct mistaken ideas before they grow into actions.)

"17. Failure to arrive at an understanding in advance, particularly when substantial fees are anticipated.

"18. Leaving the city without advance notice to a patient in need of continued care without securing in advance a substitute acceptable to the patient, or in the alternative permitting the patient to select the substitute.

"19. Withholding material facts from a patient who is suffering from a serious ailment. (While there are good reasons why it is done in some cases, the physician does not have the right to withhold such information.)"

Further on Mr. Borgelt comments as follows:

> "The recovery room has proved to be very valuable. Its location, on the same floor, near the operating room, with oxygen tanks and other necessary equipment and trained personnel, provides better care and eliminates some of the dangers and occurrences which have taken place in the past under the old arrangement when a patient was wheeled back to his room directly from the operating table, in a semiconscious condition. However, apparently not all hospitals are equipped with recovery rooms at this time. It is conceivable that since its value has been demonstrated, the failure to provide a recovery room in a given case may be the basis for a claim.
>
> "Surgical sponges are impregnated with radiopaque material and this frequently aids in discovering the cause of postoperative complaints which continue for an excessive period. However, if it is possible to take x-rays before a cavity is closed, would it not be of even more value, and would not this tend to eliminate one of the major sources of medical malpractice claims?
>
> "Would not an insurance company be justified in making the above two procedures —and possibly others—a condition of coverage?
>
> "While it is not a cause—at least directly— for malpractice claims, the failure to keep adequate records often unnecessarily injects issues of fact for a jury. Some ordinary, routine developments are—or may become— important later on. The failure to keep records creates an atmosphere of suspicion, invites contradictory statements from claimants, and tends to add to the problems already presented. In the absence of records, the doctor's word in regard to certain issues is no different or better than the claimant's— in the eyes of a jury. To the extent that the failure to keep adequate records assists in bringing about an adverse result for the doctor, it is a factor in the pressing of subsequent claims, because claimants and their attorneys are encouraged thereby."

There is a very interesting article in the monograph on *res ipsa loquitur* or rule-of-sympathy by R. Crawford Morris of Cleveland, Ohio. It is from an address that he delivered at a medical-legal symposia of the American Medical Association in San Francisco, Louisville, and New York City in the spring of 1961. He quoted the *Saturday Evening Post* has simplified this rule of law to read "someone obviously goofed," and he says "that's not a bad definition but the problem is not quite so simple." As I have told you in my reports before this rule of *res ipsa loquitur*, on translation the thing speaks for itself, has been applied in the State of California with greater frequency than anywhere else. Mr. Morris comments on that situation as follows:

> "Recently there is some indication that the courts, even in California, are beginning to recognize the unfairness to doctors of the rule-of-sympathy perversion of *res ipsa loquitur*.
>
> "The year is 1957, the medical facts are these: Serious impairment of circulation in the legs. Diagnosis by the defendant-doctor orders a translumbar aortogram which is performed at the defendant-hospital by a team of specialists but not by the defendant-doctor. Results of the test reveal aortic block. Next day when patient awakes patient's legs are paralyzed which proves to be permanent. The trial court sent the case to the jury against the defendant-hospital and the defendant-doctor on the theory of *res ipsa loquitur*. The jury returned a verdict against both defendants for $250,000. The Court of Appeals reversed and remanded for new trial for error in the instructions to the jury that *res ipsa loquitur* applied, saying that the trial court should have instructed the jury on *res ipsa loquitur* and let the jury determine whether the facts were such that *res ipsa loquitur* should be applied by the jury. In its opinion the Court of Appeals said:
>
> > 'The application of the doctrine of *res ipsa loquitur* in malpractice cases is a development of comparatively recent years. But gradually the courts awoke to the so-called "conspiracy of silence." This fact, plus the fact that usually the patient is by reason of anesthesia or lack of medical knowledge in no position to know what occurred that resulted in harm to him, forced the courts to attempt to equalize the situation by in some cases placing the burden on the doctor of explaining what occurred in order to overcome an inference of negligence.'
>
> "The great difficulty in the application of the doctrine is to determine where to draw the line. To apply it in all cases where an unexpected result occurs would hamstring the development of medical science. No medical man would dare to use new proce-

dures, especially in surgery, because if injury resulted he would be prima facie guilty of negligence. Thus a great responsibility rests upon the courts—to determine the point at which the doctrine will apply in order to be fair to a patient who has received a result which either common knowledge of laymen or of medical men teaches ordinarily would not occur without negligence, and to be fair to the medical men if there is a result which could occur without negligence and which should not impose upon them the presumption of negligence."

At another part of his talk Mr. Morris says:

"The year is 1960. The jurisdiction is New York. The medical facts are these: Chief complaint—food sticks in the esophagus—chronic; barium x-ray: narrowing of the esophagus. Family doctor refers the patient to the defendant-doctor for esophagoscopy. During the esophagoscopy a rupture occurs at the site of the narrowing in the esophagus. At the trial the plaintiff's proof showed only: (1) the rupture occurred just below the site of the narrowing; (2) defendant-doctor removed the biopsy specimen at the narrowing; (3) defendant knew that scar tissue does not distend as well as healthy tissue; (4) the diameter of the esophagoscope was 12 mm. and the diameter of narrowing was 8 mm.; (5) the rupture occurred when the defendant was applying pressure to pass the esophagoscope past the site of the narrowing. The defendant testified by deposition (1) that he did not discover that the narrowing was scar tissue stricture and not spasm at the time of the esophagoscopy; (2) it didn't look like a scar, it was not white and smooth but thickened; (3) the only way to differentiate the spasm from the scar is by exerting pressure to see if it relaxes; (4) his impression was that it was a spasm; (5) whether spasm or scar stricture, it was necessary to pass the esophagoscope beyond the narrowing to see if there were a cancerous lesion below; (6) he exerted only normal pressure when the rupture occurred; (7) he had done this procedure thousands of times and this sort of rupture does happen occasionally to all doctors; that such ruptures have happened at Mount Sinai Hospital 100 times in the past ten years. Notwithstanding this testimony, the trial court applied *res ipsa loquitur*. Said the New York trial court, in this case:

> 'The facts of the occurrence alone are sufficient to present a prima facie case. The results may be of such a character as to warrant the inference of want of care . . . in the light of the knowledge and experience of the jurors themselves.'

"Just where New York finds jurors who have had experience with esophagoscopies makes one wonder. Says the New York trial court:

> 'Such a duty (to come forward and explain) is now recognized and declared to arise in view of the special relationship such as exists between doctor and patient.'

"But this is not *res ipsa loquitur*, this is a new doctrine, a liability without fault.

"The trial court also held that defendant's explanation, although adequate, was for the jury, saying:

> 'That testimony was sufficient for the jury to consider in exonerating him of the charge of negligence, and in submitting such testimony the defendant met the complaint of the plaintiff in this type of case and situation that the doctor or surgeon should come forward and explain how he discharged his duty to the patient. —So much for the cause of action charging malpractice.'

"Fortunately for the doctor, the jury's verdict was for the defendant. Perhaps these New York jurors really have had experience with esophagoscopies. Who knows?

"But this is not *res ipsa loquitur*. First, this does occasionally happen even where due care is used. Therefore, the occurrence of the rupture is not an inference of negligence. Second, the defendant did explain and this explanation should rebut any *res ipsa loquitur* as a matter of law, and the burden remains on the patient to produce expert witnesses to prove her case.

"Over in New Jersey in 1960 there is a hint of this in a case where judgment was granted to the defendant, on the opening statement alone, which was reversed by the appellate court on the grounds that the plaintiff's proof might show that *res ipsa loquitur* existed, if she proved that the rash on her face, appearing after a general anesthesia during the delivery of a baby, was a 'burn' and not a skin reaction.

"Said the New Jersey appellate court:

> 'We think the present case presents other considerations bespeaking maximum tolerance for the plaintiff's posture—the fact of the patient's unconsciousness when the alleged negligent acts were taking place, and the consequent pooling of the direct evidence of the occurrence in hostile hands, as well as the commonly known difficulty of obtaining expert proofs in support of a malpractice claim.'

"Once again, this is not *res ipsa loquitur* at all, but a rule-of-sympathy for the patient."

He concludes with these words:

"It is easy to accuse; it is difficult to defend. I submit that the safeguard of the law that 'she who affirms must prove' and, in malpractice cases, 'must prove actual negligence by expert testimony,' is sound and should be preserved. And, finally, that we should not travel down the road of liability without fault, certainly not in medical malpractice cases, but should preserve our proven-fault heritage and jury-trial system. To do otherwise is to force the medical profession into the role of insurer, a burden which it cannot and will not bear, with the resultant loss of useful technics and retardation of the progress of medical science. Ultimately, this loss will fall upon the patient himself—who sooner or later may be any one of us."

Attorneys A. Lee Bradford and Paul A. Carlson of Miami, Florida, wrote on "Operating Room Liability" as follows:

> "When a person seeks to hold a doctor liable for the actions of some other person, it should be proved that the person performing the act negligently was under the control and direction of the doctor and following his orders, in contrast to other cases where the doctor has been held liable merely because he is physically present in a room when some person over whom he has no direct control does a negligent act that results in injury to the complaining party."

There has been decided in the last few years a number of cases which are in somewhat oversimplified fashion referred to as the "informed consent cases." Principal among these are *Nathanson v. Kline* (Kansas 1960) 350 Pac. 2nd 1093, which held that a physician violates his duty to his patient and subjects himself to malpractice where no immediate emergency exists if he makes no disclosure of significant facts within his knowledge which are necessary to form the basis of a consent by the patient to the proposed form of treament. This case involved burns consequent upon the administration of cobalt therapy. However, the Court further held that the burden was still on the patient to prove that failure to make reasonable disclosure was a proximate cause of injury.

Another case was *Mitchell v. Robinson* (Mo. 1960) 334 South Western 2nd 11. In this case the Missouri Supreme Court held that the doctors owed the duty to inform a patient who was not in full possession of his faculties of the possible serious hazards of insulin shock therapy.

These cases should not be taken to indicate that a doctor should discuss with a patient every possible consequence of treatment. But where a high incidence of adverse side-effects is a consequence of a particular therapy, such should be mentioned in advance to the patient or a member of his family. The classic statement was made by Judge Cardozo in 1914 when he observed: "Every human being of adult years and sound mind has a right to determine what shall be done with his own body."

You may remember that in one of my past reports I referred to *Ferrara v. Galluchio*, decided by the New York Court of Appeals, which held that a patient might recover against a physician for x-ray burns because she developed "cancer phobia," this despite the fact that she did not have cancer and there was no reasonable expectation that she would develop cancer from her injury. It was based on her statement that a doctor had told her that unless she came in to have her scars looked at every six months she might develop cancer. It was felt that this case was a far extension of the rules applying to mental reaction from injury. Within the year the Court of Appeals set another rather startling precedent in the case of *Battalla v. State of New York*. This case was summarized more recently as follows:

> "The infant plaintiff was placed in a chair lift at the ski center by an employe of the State who failed to secure and properly lock the belt intended to protect the occupant. As a result of this alleged negligent act the infant plaintiff became frightened and hysterical upon the descent, with consequential injuries. The question presented was whether the claim started a cause of action when it alleged that claimant was negligently caused to suffer 'severe emotional, neurological disturbances with residual physical manifestations.' The Court of Claims on a motion to dismiss the complaint held a cause of action was stated. The Appellate Division reversed and dismissed the claim on the authority of the Mitchell case which decided that there could be no recovery for injuries, physical or mental, incurred by fright negligently induced. On an appeal by plaintiff, in a 4-3 decision, the Mitchell case was overrruled and the claim was reinstated. Although noting that the damages or injuries are somewhat speculative and difficult to prove, the majority observed: 'In the difficult cases, we must look to the quality and genuineness of proof, and rely to an extent on the contemporary sophistication of the medical profession and the ability of the court and jury to weed out dishonest claims.'
>
> "Van Voorhis, J., in his dissenting opinion, stated: 'At a time like the present, with constantly enlarging recoveries both in scope and amount in all fields of negligence law, and when an influential portion of the Bar is organized as never before to promote ever-increasing recoveries for the most intangible and elusive injuries, little imagination is required to envision mental illness and psychosomatic medicine as encompassed by the enlargement of the coverage of negligence claims to include this fertile field.' "

There are some recent cases of great interest, particularly to orthopedists, involving suits brought against manufacturing companies for defective prosthetic devices. One case, *Bowles v. Zimmer Manufacturing Company*, an Indiana corporation, decided in the U.S. Court of Appeals, 7th Circuit, May 4, 1960, was brought against the manufacturer of a defective surgical pin used in setting plaintiff's leg fracture in a previous automobile accident for negligence in design and the manufacture of the pin and the breach of warranty in the sale thereof. The plaintiff had recovered a substantial settlement against the motorist who injured him, and a further recovery of $45,000 resulted against the manufacturer. It was held that where a transaction for the sale of the pin originated with the sending of the order by the company in Michigan to the defendant in Indiana which terminated in the insertion of the pin in plaintiff's leg in the hospital, in Michigan the law of Michigan pertaining to implied warranties in the sale applied. It is interesting to read that the pin which bent and then fractured after it had been used to fix a hip was examined by a professor of metallurgy who testified "it was poorly designed, and among the defects referred to was a crack running through the entire length of the pin. Any fluctuation of the leg would cause the crack to widen. This is what happened to the pin in the plaintiff's leg."

In the past I have called attention to the manner in which the Courts are placing particular burdens on the medical profession for untoward consequences of their services. A most recent interesting case was *Kolesar v. United States of America* decided in the U.S. District Court for the Southern District of Florida, Miami Division, August 11, 1961, cited as 198 Fed. Sup. 517. Marrian Kolesar was the dependent wife of a chief petty officer in the U.S. Navy. At the Key West Naval Hospital she had an operation in the nature of exploratory laparotomy scheduled for January 21, 1958. She was thirty-two years of age and considered a good surgical risk. She was prepped and a spinal anesthesia was administered. There is in the decision of the Court a very detailed description of the operation from beginning to end. Following the administration of anesthesia an existing laparotomy scar was excised and it did not bleed. The surgeon immediately announced this fact and asked the anesthesiologist to check the patient. There was reported a blood pressure of 40 over 0 and then 0 and the pulse was unobtainable. Ephedrine was introduced intravenously, and thereafter the anesthesiologist listened to the heart and without comment put the ear plugs in the ears of the surgeon who, after listening, requested a long needle and summoned a general surgeon. One of the doctors who was assisting traumatized the chest, listened for heart sounds, and was then handed a syringe with a long needle containing 2 cc. of ephedrine. After ephedrine was introduced again the heart was listened to and nothing was heard. One of the corpsmen left the operating room and had a chief nurse bring in Levophed. At just about this point a general surgeon appeared on the scene and proceeded to perform an open thoracotomy without the presence of bleeding, and in about 45 seconds from the time he made the incision he had his hand on the patient's heart. After 5 or 10 pumping motions the heart resumed a normal but rapid beat.

As a result of the operation the patient is 100 per cent permanently disabled from brain damage and neurologic deficiency caused by deprivation of oxygen to her brain. She was tube fed for one and a half years following the operation and is incontinent of bowel and bladder. She is not ambulatory but is described as vegetative. Her situation is comparable to that of a paraplegic.

She and her husband were awarded a total of $75,000. The judge found that there was cardiac arrest and circulatory insufficiency at the time of her abdominal incision and she had no obtainable pulse. A period materially in excess of four minutes occurred between the time her incision did not bleed and until effective resuscitative procedures were obtained by manual cardiac massage which restored the flow of blood to the patient's brain. "This constituted a departure from acceptable medical practice. It was generally accepted in the medical profession on January 21, 1958, that a surgeon undertaking surgical procedure should possess, as a part of his qualifications, the ability to perform a thoracotomy and manual cardiac massage. Whatever the semantics of 'arrest,' it cannot be considered accepted medical practice in any community to permit the brain to suffer irreversible damage as a result of an unreasonable lapse of time materially in excess of four minutes."

I have many times called attention to the fact that a physician is not responsible under most circumstances for the breaking of a needle in the course of an injection although a Court may call on him to explain how such an event happened. It is required that to escape liability when part of a needle or a foreign body remains in the patient, the physician fully and fairly inform the plaintiff that such a thing happened. There is some interesting language from a case in the Supreme Court, Nassau County, recently involving a broken needle. Judge Farley after listening to witnesses and reviewing the law applicable to this subject concluded with the following observations:

> "Careful attention was given by this Court to the medical testimony and a great deal of latitude in this regard was permitted to both sides at the trial. The testimony, however, of the doctor* has been of little assistance despite his lengthy recitation of training, degrees, associations, and lecturing. When questioned as to the general practice on the use of a one-inch needle by Long Island dentists, he stated: 'I don't know what they use.' Standards, practices, and skills ordinarily possessed, and employed by a physician, dentist or surgeon, 'in the locality where he practices' (*Pike v. Honsinger*, supra) are important in determining liability in this type of case. He also testified that it would be necessary to penetrate from one to one and one-eighth inches to have effective anesthesia. The fact remains, however, that penetration in this case to the hub of the needle was only about three quarters of an inch and

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* The plaintiff's expert.

the area was effectively anesthetized. Further doubt is cast upon the testimony of this witness, who, when asked how long it would take him to remove the needle from the plaintiff, stated: 'With humility, not more than fifteen minutes.' The hospital records disclose that 'after forty-five minutes of careful attempt it was considered wiser to stop as the patient is over seventy years of age.' The doctor's unequivocal statement that he would recommend further surgery made no impression on this Court. He had never seen the plaintiff and knew nothing of her mental or physical condition although such an inquiry would certainly seem to be a prerequisite to a recommendation of surgical procedure on a seventy-four-year-old woman.

"This Court cannot speculate as to the reason for the needle breaking in the absence of more positive proof than has been presented, nor may it ascribe the break to the technic or methods used by the defendant. There is likewise insufficient evidence to warrant a finding that the defendant acted without reasonable care and diligence in the exercise of his skill or without using his best judgment in applying his knowledge after the discovery of the break. Judgment is accordingly rendered in favor of the defendant and the complaint dismissed."

Comments. I attend, along with my associates, all meetings of the Council, Board of Trustees, and House of Delegates, as well as many committee meetings. I also attend the evening meetings of the Malpractice Insurance and Defense Board. Many matters discussed at these meetings require a great deal of research and deliberation. There is not a day of the week in which we do not receive a number of requests for information from county societies and/or individual members of the Society. We are so aware of the fact that, just as a patient when in trouble is always anxious to get to a doctor, so a doctor when in legal trouble wants to get advice, that we try at all times to have some one available to answer telephone calls. While these calls involve a great variety of matters, I would say that quite typical is the problem of how to come to an understanding with a patient so as to avoid bad feelings and perhaps even litigation. There are many calls by members concerning intramural differences that they are having—one with the other or with the staff of their hospital. One such intramural controversy of recent date occupied several days of the time of State Society officials and your counsel.

From the comments of the many counsel and the opinions in the cases cited above, I have tried to give some impressions of the current malpractice problems facing a physician. Space limitation prevents more of the same.

Since my last report, your counsel has defended a total of 351 new actions brought against members of the Society's Group Plan. These, of course, were in addition to the lawsuits started in previous years and still pending. Claims and events which from past experience will become active lawsuits continued to come to our attention for necessary action in a continuing stream. I also was called on to investigate and defend on the average of three new actions and claims per month against uninsured members of the Society.

I would like to conclude this report with my sincere thanks and appreciation for the assistance so freely given to me by John M. Galbraith, M.D., president; Joseph A. Lane, M.D., president-elect; William L. Wheeler, Jr., M.D., secretary; Maurice J. Dattelbaum, M.D., treasurer; John J. Masterson, M.D., chairman of the Board of Trustees; and Henry I. Fineberg, M.D., executive vice-president; the members of the Malpractice Insurance and Defense Board, and Mr. James M. Arnold, Indemnity Representative of the Society, and his assistant Mr. Frank W. Appleton, having continued their help to me in defending the Society's members.

It was a great tragedy for all of us when we learned of the untimely death of Mr. Dale Snure, executive vice-president of the Employers Mutuals. On several occasions he appeared before the House of Delegates to explain the position of the carrier and the great interest which it took in seeing that the Group Plan worked efficiently. He was a leader in his industry, and a delightful friend of all who knew him.

Respectfully submitted,
William F. Martin, *Legal Counsel*

Medical Communication

Publication

To the House of Delegates, Gentlemen:

The Publication Committee for the year 1961–1962 is composed of the following:

Alfred P. Ingegno, M.D., *Chairman*	Kings
Harold F. Brown, M.D.	Erie
Maurice J. Dattelbaum, M.D.	Kings
Albert H. Douglas, M.D.	Queens
Henry I. Fineberg, M.D.	Queens
William J. Grace, M.D.	New York
William Hammond, M.D.	Westchester
Morris R. Keen, M.D.	Suffolk
Granville W. Larimore, M.D.	Albany
John G. Masterson, M.D.	Kings
Norman S. Moore, M.D.	Tompkins
Reginald R. Steen, M.D.	Nassau
John J. Masterson, M.D., *Adviser*	Kings

The Publication Committee met monthly during the year except in May, July, August, and December.

Because the committee is responsible for the management of the two major Society publications, the NEW YORK STATE JOURNAL OF MEDICINE and the *Medical Directory of New York State*, it was decided to have a stenotypist present to record the verbatim minutes of these meetings.

During 1961 the Publication Committee supervised the completion of two major projects—the publication of the 1961 edition of the *Medical Directory of New York State* and the complete typographic revision of the NEW YORK STATE JOURNAL OF MEDICINE.

New York State Journal of Medicine

As instructed by the House of Delegates, your Publication Committee has devoted its efforts and planning toward carrying out your previous recommendations to improve the content and appearance of the JOURNAL and to increase its readership. This report will detail what has been done toward these goals.

At the March meeting of the Council, a reorganization of the editorial department of the JOURNAL was approved, providing for a part-time editor, an editorial board of six, a group of editorial consultants, and changing the title of executive editor to managing editor. Accordingly, William Hammond, M.D., who had been assistant editor under the late Dr. Redway and acting editor since his death, was appointed editor of the JOURNAL. Further details of the reorganization have not been implemented as yet.

Your chairman and members of the committee believe that the quality of scientific material published in the JOURNAL has improved substantially; the manuscript rejection rate has gone up to approximately 40 per cent; requests for permission to reprint, to quote, to translate, and to use tables and figures have been numerous; the JOURNAL has been cited by many authors; articles have been used as the basis for magazine and newspaper feature stories. We believe that we must reflect in the JOURNAL the high character and quality of medicine practiced in New York State and that the JOURNAL should image the importance of the State Society throughout the profession.

To maintain a continuing program of improvement, the committee, the editor, and the staff have been active in sharing knowledge and exchanging experiences by participation in the work of the American Medical Writers Association, by attending editor conferences, and by appearing as guest speakers for other editor groups. We have also maintained close liaison with the Library of the Medical Society of the County of Kings, the official library for the State Society, and are grateful to Mr. Wesley Draper, librarian, and his staff for their continued cooperation.

Journal Editorial (William Hammond, M.D., Editor; Alvina Rich Lewis, Managing Editor). Starting with the memorial issue on January 1, 1961, honoring our late editor, Laurance D. Redway, M.D., the JOURNAL has appeared twice a month throughout the year with the added Part II of September 1 containing the proceedings of the House of Delegates. The total number of pages in 1961 was 4,486, of which 1,127 were advertising pages (including covers) and 3,433 were text pages; 407 scientific articles were published, representing 905 authors. In addition to general scientific articles, serial material was published as follows: clinicopathologic conferences 22, current concepts in diabetes mellitus 23, rehabilitation conferences 3, accidental chemical poisonings 19, medical care insurance 10, nutrition excerpts 5, maternal welfare 6, recent advances in medicine and surgery 18, diagnostics 8, current anesthesia conferences 12, and history of medicine 5. Regular features are editorials, necrology, medical news, medical meetings, book reviews, letters to the editor, woman's auxiliary news, announcements, filler, and medical school news.

The material published throughout the year has maintained its high standards. The series on diabetes edited by Max Ellenberg, M.D., and Harold Rifkin, M.D., has met with great favor again as it did when we published a similar series several years ago. The papers will be published as a collection in book form by the Blakiston Division, McGraw-Hill. The section on clinicopathologic conferences has been reorganized and Michael Bruno, M.D., and William Ober, M.D., of Knickerbocker Hospital, have been appointed as editors for CPC's for the JOURNAL. They are securing for publication outstanding conferences from many new sources in the State.

In pursuing one of the aims of the JOURNAL, namely, to promote good medical writing, we published an important paper on the subject of conducting and reporting therapeutic trials, by Hart E. Van Riper, M.D., and Donald E. Boyer, Ph.D., a statistician. Reprints of this article are in much demand throughout the country, particularly in medical schools and libraries.

The Associate Editorial Board was of great help as usual in furnishing the Editor with an authoritative critique on all manuscripts relayed to them. The high quality of the papers published attests to the care and discrimination of this board. In place of the annual dinner given to the associate editors a reception was held in honor of John H. Talbott, M.D., editor of the *Journal of the American Medical Association*, at the Saint Moritz Hotel in New York City at the time of the annual meeting of the American Medical Association last June. This was well attended and we entertained many distinguished officers of the American Medical Association as well as editors of other state medical journals throughout the country.

We have also laid the groundwork this year for the annual award of a gold medal and a five hundred dollar cash prize for outstanding medical writing in the JOURNAL, in honor of Dr. Redway. Nominations which may come from the Publication Committee, the Editorial Board, the membership at large, and any subscriber are to be judged during the month of April by the Chairman of the Publication Committee, the Executive Vice-President of the Society, and the Editor. The prize and medal will be awarded at the annual meeting in May.

One of our principal occupations during the latter half of the year was preparing for the changeover in format to begin with Volume 62, issue 1, 1962. This necessitated close and detailed cooperation among the Publication Committee, the JOURNAL staff, the typography consultants, and the printer, Mack Printing Company, Easton, Pennsylvania, to whom we are most grateful for their excellent work and cooperation. Everything went along as planned with the result that the JOURNAL now has a more modern appearance, a format that is more readable, and features which will make the JOURNAL of more lasting use to the reader. Many favorable comments have been received.

Members of the JOURNAL staff take an active part in the American Medical Writers Association and the JOURNAL was privileged to be host to this organization during its annual meeting in New York City, October 5 to 7. The JOURNAL had a booth at this convention and reprints of articles related to medical writing were distributed. The Managing Editor was chairman of the local arrangements committee for the meeting; the Manuscript Editor was cochairman of the program committee, and the Editor was chairman of one of the sessions. In addition, all staff members attended and participated in the convention activities.

On October 29 and 30, the Editor and the Managing Editor attended the biannual meeting of state medical journal editors in Chicago. Practically all facets of medical journal operation were covered at this meeting, by individual speakers and panels. We learned much that can be useful to us in our own operation.

The Editor attended the interim meeting of the American Medical Association in Denver in November. Several of the exhibitors in the scientific exhibits showed interest in publishing their material in the JOURNAL, and some of these are in process at present.

The Managing Editor was guest speaker at a Writers Workshop conducted by the New Jersey Academy of Medicine and has recently been requested to give a series of lectures on medical writing for the New York City Department of Health.

During the year we added to the staff Mrs. Sully Bogardus as research assistant, and she has proved invaluable not only in representing the JOURNAL at local news conferences and meetings but also in working with authors and in preparing the abstracts which are now a regular feature of the JOURNAL.

Much thanks goes to the entire staff so ably supervised by our Managing Editor, Miss Alvina Rich Lewis. These include: Miss Elizabeth C. Smith, manuscript editor; Miss Anne-Marie Fanshaw, Mrs. Joan V. Hughes, and Miss Nele Lape, copy editors; Miss Frances E. Casey, proofreader; Mrs. Sully Bogardus, research assistant, and Mrs. Olga Mielke, editorial secretary.

Journal Business and Advertising (Charles L. Baldwin, Director). During 1961 advertising revenue in the NEW YORK STATE JOURNAL OF MEDICINE decreased from $428,471.95 in 1960 to $325,373.95. This was due to the fact that our largest group of advertisers, the pharmaceutical companies, considerably curtailed their promotional expenditures. They did this down the line, all publications included, because of the pressure of the Kefauver investigation, the F.D.A. regulations on complete disclosure, and the possibility that medical journal advertising might come under the controls of a strict and critical Federal Trade Commission via the Dingell Amendment (H.R. 6471) to the Federal Trade Commission Act.

The latter would make it mandatory for drug product advertising in medical journals to be accompanied by a full disclosure of all the facts on a product, including contraindications which might require two or three extra pages of text per ad. The drug companies claim that if this amendment becomes law they may be forced out of journal advertising, finding it financially impractical to run 2, 3, or 4 pages for each advertisement used.

The NEW YORK STATE JOURNAL OF MEDICINE has had no reserves allocated to it during the past years of high advertising revenues to cushion income crises of this nature. If and when the income picture improves the establishment of such a reserve for future JOURNAL contingencies should be considered. More nonpharmaceutical advertising is being solicited and it is hoped that the future may find electronics and other new fields furnishing advertising material to make up potential further loss of pharmaceutical advertising.

In 1961 we instituted a circulation campaign for readers outside the State, and this at first could only be tested on a trial and error basis. As the year went on, however, we were able to discover through a study of present subscription lists just where our best prospects were to be found. Our results thus far have not been too encouraging, but the duration and degree of effort are not yet sufficient for final judgment. After much discussion, and with Council approval, the Publication Committee plans to continue the campaign for the balance of 1962. Results will then be evaluated to decide whether continued effort is desirable.

We want to thank Miss Camille M. Marra for her fine work as administrative secretary to the Advertising Department during a difficult year. She contributed much in helping to consolidate the reorganized department into a smooth functioning whole. Thanks also go to Mrs. Marcia Werbin who had capably filled Miss Grace West's shoes as advertising production manager. Mrs. Werbin was obliged to resign from our staff for personal reasons in November, 1961, and Mr. Robert W. Miller, formerly filling a similar role on the *Directory*, took over as production manager after having been carefully tutored in all phases of the operation by Mrs. Werbin before she left. Mr. William Wroth, who came to us in January as business supervisor and circulation manager and assistant to the director of business and advertising, resigned in late August to work for his master's degree at the University of Oregon and Mr. Norman Bloomfield was employed to take his place. Mr. Bloomfield's first job was to get a complete breakdown of the JOURNAL paid circulation which is what will assist us henceforward in making the most profitable mailings in our subscription campaign.

In February, 1961, Mrs. Bethany Culhane was employed to keep the books and remit all bills for advertising and subscriptions. At the end of the year the books were in good shape and access to the financial records of the department were readily available. Mr. Joseph Mullaney, mid-West advertising representative for the JOURNAL, did his usual good work in covering that territory and additional territory assigned to him against the odds of a year which saw the previously quoted curtailment of activities by the drug industry.

Late in 1961 after using up an accumulation of old stock we were able to print the JOURNAL on the new 50-pound Energy Coated Book paper which had been approved for use by the Publication Committee earlier in the year. This paper in addition to having far greater opacity than the old type takes print well, and increased reading clarity has added a practical improvement to the better looks of the JOURNAL.

In 1961 the JOURNAL became an official member of the recently organized Association of Medical and Allied Publications, Inc., an organization formed for the purpose of promoting high business standards among publications in the health field and to further the enhancement of printed and bound media as the preferred and superior means of communication of scientific and technical knowledge and to further harmonious relationships between publishers and their advertisers and their advertisers' agencies. Mr. Baldwin was appointed to represent the JOURNAL in this body and was elected secretary of the Association to serve until its next annual meeting in June, 1962.

An attractive new JOURNAL exhibit was shown during the year at the Society's convention in Rochester, at the New York State Health Conference in Rochester, at the American Medical Association meeting in New York City, at the New York Health Exposition, the last two at the Coliseum, and finally at the national convention of the American Medical Writers Association, also in New York City. The exhibit generated much interest wherever it was shown, at the A.M.A. meeting and Health Exposition in particular.

New equipment for the JOURNAL Advertising Department during the year included two electric typewriters and an adding machine. Improved lighting was installed in the department as it was in other areas of the Society's headquarters.

Medical Directory of New York State

The 1961 edition of the *Medical Directory of New York State* was distributed beginning in May of last year, and work was begun immediately on the 1963 edition. The Publication Committee has appointed Dr. Fineberg as a subcommittee to study revisions and improvements for the 1963 *Directory*, and he is now preparing recommendations for our consideration. We plan to streamline the material published.

We are most appreciative of the efficient and careful work of Miss Janet E. Loy, editorial supervisor of the Directory, and her staff.

They are to be complimented for the very low percentage of errors in the 1961 *Directory*.

Directory Editorial (Miss Janet Loy, Supervisor). After completion of the 1961 *Directory*, the *Directory* staff prepared the labels for the delivery of the publication to all members whose dues were paid for the year 1961. A total of 23,440 copies were distributed by December 31, 1961. Of these 19,678 were mailed by the printer or bindery and 3,762 were mailed from the office.

The staff then began to process the mass of mail which had accumulated during the months following the deadline for the 1961 edition. This mail contained changes and additions for the *Directory* cards already in the files, as well as biographical material for physicians who had not previously been listed. Much detail is involved as corrections are made in all necessary files.

Following publication, the cards for physicians who did not send a reply for the current edition were checked with all available sources to secure present addresses and telephone numbers. New information received from inquiries was recorded.

The biographical sections of the 1961 *Directory* were gummed to simplify the pasting of the cards which are sent to each physician requesting data for the 1963 *Directory*. This new procedure seems to be a great improvement and much more satisfactory. The actual cutting and pasting of the individual listings was done outside of the office because the department did not have the time or personnel. Members of the staff marked these cards as to location.

Envelopes were addressed to all physicians, more than 32,000, in the active files. The new pasted *Directory* cards were inserted in the envelopes, after comparing both as to names and addresses, noting changes when necessary, discarding the cards for those who had died or removed from New York State, and inserting unpasted cards for the many physicians whose names were received since the 1961 *Directory*.

There are approximately 175,000 media cards which are used to verify all the necessary qualifications in the individual listings. When each *Directory* is completed, these cards are in order as to hospitals, societies, and so forth. These cards have now been sorted as to location and name of doctor so that they may be brought up to date with the copy cards which will be processed for the 1963 *Directory*.

The number of errors in the 1961 *Directory* which have been brought to our attention has been very small in comparison with the tremendous amount of detail involved. The correct biographical data for these physicians was published in the January 1, 1962, issue of the NEW YORK STATE JOURNAL OF MEDICINE.

Henry I. Fineberg, M.D., chairman of the *Directory* Subcommittee, has given much time and thought to the material published in the *Directory*. At the present time his study has not been completed.

Directory Business and Advertising (Mr. Charles L. Baldwin, Director). The total advertising income from the 1961 edition of the *Directory* was $13,490.49. This was an increase of $4,450.49 over the previous 1959 edition which had an advertising income of $9,040. Most of this increase was due to the sales efforts of Mr. William Wroth who did this in addition to his job with the circulation campaign of the JOURNAL. Mr. Wroth unfortunately left the employ of the Society late in August, 1961.

Sales of individual copies of the *Directory* for 1961 were as follows: the 1959 edition, $452, and the 1961 edition, $32,070, making a total of $32,522. The 1961 edition will, of course, continue to sell through 1962 and into 1963 until the new edition of that year is available.

Mr. Robert W. Miller, who had been in charge of *Directory* advertising production and kept records of sales, and so forth since 1954, was moved up to production manager of the JOURNAL and Mr. Jack O'Brien of the *Directory* staff was promoted to the position vacated by Mr. Miller. We are sure that the same fine handling of the job will continue under Mr. O'Brien as it did during the years of Mr. Miller's stewardship.

Advertising sales for the 1963 edition of the *Directory* will begin early in 1962 and a further increase in volume of advertising sales may be expected. It is also planned to increase the number of copies sold by a strong sales campaign in areas heretofore only skimmed over.

Medical Society Library (Mr. Wesley Draper, Librarian). The Library (functioning through the Library of the Medical Society of the County of Kings) continues to render valuable service to medical research. During the year 5,074 visitors used the Library consulting about 35,000 books in the reading room and withdrawing 10,527 for use outside of the Library. This means that for each day the Library was open there was an average of 20 visitors with 142 books used in the reading room and 42 withdrawn for home use.

The telephone is becoming more valuable to the medical community too busy to call at the Library. Information was supplied for a total of 8,676 such users, an average of about 39 per day. Some of these calls were answered immediately but many required considerable research to find the answers on a wide variety of subjects.

In all bibliographic work errors are almost certain to creep in somewhere. As a contribution toward more accurate bibliographies the Library staff has continued to check for the NEW YORK STATE JOURNAL OF MEDICINE references not found in recent medical indexes. During the year 2,245 references in 205 bibliographies were checked for accuracy and completeness.

As a further contribution to the total medical research program extending far beyond the local area 4,488 volumes were loaned to other libraries and requests for 200 articles comprising 1,342 pages were supplied in photocopy.

In order to function properly it is extremely important to keep the Library up to date with new material as published insofar as possible with limited funds, insufficient staff, and lack of adequate space. During the year, 2,783 volumes were added to the collection bringing the Library's total to approximately 206,000 volumes. These were acquired through gift, exchange, review, and purchase. Approximately three fourths of the amount of money required for the purchase of books, periodical subscriptions, and binding was provided by Library endowments and gifts from individuals, societies, and commercial firms. Most of the individual gifts came through the contribution of $5,500 received from the Medical Library Association of Brooklyn. This is a local "friends of the library" group, organized in 1903 for the specific purpose of securing medical literature for the Library. Practically all the money received has been used exclusively for literature purposes. It has been a very successful venture and many valuable publications are on file which were secured from funds provided by this group. It is now incorporated, with membership open to any who make an annual contribution in the amount of $10 or more.

After much study by a special committee of the Medical Society of the County of Kings and representatives of the State University of New York Downstate Medical Center, recommendations were made to move the Library to the Medical Center and to incorporate it with the library of the Medical Center. Proper provisions were made in the proposed contract with respect to ownership, use, joint management, employment of personnel, storage, and so forth. Specifically, the rights of members of the Medical Society of the State of New York to use of the Library are in no way impaired. The move has been overwhelmingly approved by the membership of the Academy of Medicine of Brooklyn and by all interested parties and is in process of implementation.

Conclusion. Your committee looks forward to continuing improvement in every aspect of the publications it supervises. An ever-widening range of usefulness of the JOURNAL, as mandated by the House of Delegates and the Council, is the goal that governs the functioning of your committee. We believe that since the JOURNAL represents the State Society on library shelves throughout this country and the world, it should continue to have the status not of a mere house organ but of a respected and authorized scientific publication. We also look forward to major improvements in format, content, and usefulness of the *Medical Directory* for 1963. To the extent that these publications do a better and more widely useful job, the problems of adequate advertising income are also helped.

Dr. Hammond, our editor, and Mr. Baldwin, our director of business and advertising, and their respective loyal staffs are to be commended for their efficient and faithful discharge of their responsibilities. Under their guidance we can expect continued progress.

Finally your committee wishes to thank the Council, Trustees, and officers of the Society and this House for their confidence and support. And of course, the executive vice-president, Dr. Fineberg, has been an unfailing bulwark. Your chairman is personally most grateful to the members of the committee. Their interest and devotion make everything possible.

Respectfully submitted,

ALFRED P. INGEGNO, M.D., *Chairman*

Ancillary Groups

Woman's Auxiliary, Advisory to

To the House of Delegates, Gentlemen:

The Advisory Committee to the Woman's Auxiliary consists of the following members:

Norman S. Moore, M.D., *Chairman*	Tompkins
James J. McCartney, M.D.	Nassau
Albert Vander Veer, II, M.D.	Albany

Although formal meetings of the committee were not held during the year, your chairman conferred with the two other members whenever matters were referred to him. Our report will be brief.

Most county medical society auxiliaries have accelerated their legislation programs with special emphasis on implementation of the Kerr-Mills Act and opposition to the King-Anderson bill. For example, the record "Operation Coffee-Cup" was played in local neighborhoods in Schenectady County. The Dutchess County Auxiliary has a special legislation study group. Individual members were reminded many times by the Auxiliary legislation chairman and the president to contact their senators and congressmen.

This year, 201 new Auxiliary members have been added to the rolls throughout the State. The Putnam County Medical Society has approved the organization of an auxiliary. The one in Fulton County has been reactivated.

Several county auxiliaries have cooperated with voluntary health agencies. Many auxiliaries are planning health career days to encourage students to enter the fields of medicine, nursing, and other areas related to the medical profession.

Several revisions of the bylaws are under consideration.

The first State preconvention meeting of the Auxiliary was held in February; plans for the conferences are progressing. Mrs. Harlan English, president of the American Medical Association Auxiliary, will attend the May convention.

A special Auxiliary chairman will work with the Communications Department in the presentation of an exhibit at the State Medical Society meeting in May. This project will be financed by the Auxiliary itself.

The Woman's Auxiliary magazine, *Distaff*, which is published three times yearly, has a new cover and format and the circulation procedure has been completely revised.

During the Fall Conference, held on September 24 to 26, 1961, a successful workshop was conducted for county presidents and presidents-elect. The officers and State chairmen were present.

Twenty counties have made plans to participate in the tenth annual Health Poster Contest in Glens Falls on April 5.

The AAPS Essay Contest (resolution 61–27), endorsed by the Medical Society in May, 1961, has 11 participating counties. However, it has been recommended that this project not be continued next year.

Mrs. Joseph A. Kinnaman, an Auxiliary director from Nassau County, is the new Auxiliary representative to the board of the Physicians' Home. The Auxiliary expects an increase in donations during the coming year.

We would like to thank Mrs. Eugene F. Wolff, president of the Auxiliary, and the officers and members for their cooperation.

Respectfully submitted,
NORMAN S. MOORE, M.D., *Chairman*

Nursing Education

To the House of Delegates, Gentlemen:

The Committee on Nursing Education consists of the following:

Louis M. Rousselot, M.D., *Chairman*	New York
Lester J. Candela, M.D.	Queens
Robert F. McMahon, M.D.	Onondaga
Frank C. Nichols, M.D.	Nassau
Charles M. Smith, M.D.	Seneca

No meetings of the committee have been held during the year 1961–1962 due to the illness of the chairman.

Respectfully submitted,
LOUIS M. ROUSSELOT, M.D., *Chairman*

Prepared by the office of Herman E. Hilleboe, M.D., New York State Commissioner of Health

Laboratories Approved for Diagnostic Procedures in New York State

THE FOLLOWING geographic list, effective November 1, 1961, contains the names of the approved laboratories and their directors. Information regarding the specific procedures for which a laboratory is approved can be obtained from its director.

Albany
- Albany Hospital and Albany Medical College Laboratories—W. A. Thomas, M.D.
- Bender Hygienic Laboratory—J. J. Clemmer, M.D.
- *U.S. Veterans Administration Hospital Laboratory—A. S. Daoud, M.D.

Albion
- Orleans County Laboratories (see Batavia)—J. Tannenberg, M.D.

Amityville
- Brunswick General Hospital Laboratory—L. M. Friedland, M.D.

Amsterdam
- Montgomery County Laboratories, Amsterdam City Hospital, and St. Mary's Hospital—T. S. Velz, M.D.

Auburn
- Cayuga County Laboratory, Auburn Memorial Hospital, and Mercy Hospital—A. E. Harris, M.D.

Ballston Spa
- Saratoga County Laboratories (see Saratoga Springs)—J. Lebowich, M.D.

Batavia
- The Genesee Laboratory—J. Tannenberg, M.D.
- St. Jerome Hospital Laboratory and Genesee Memorial Hospital Laboratory—E. G. Rerrick, M.D.

Bath
- Steuben County Laboratories (see Hornell)—B. J. McClanahan, M.D.
- U.S. Veterans Administration Center Laboratory—W. A. Jarrett, M.D.

Bay Shore
- Southside Hospital Laboratory (see Great Neck)—L. E. Marshall, M.D.

Beacon
- Matteawan State Hospital Laboratory—W. Raab, M.D.
- Highland Hospital Laboratory (see Newburgh)—T. P. B. Payne, M.D.

Binghamton
- Laboratory of the Broome County Blood Center (see Johnson City)—A. A. Kosinski, M.D.
- Kilmer Memorial Laboratory, Binghamton General Hospital—N. Elton, M.D.
- *Our Lady of Lourdes Memorial Hospital Laboratory—W. D. Woods, M.D.

Bronx
- Albert Einstein College of Medicine, Department of Pathlogy—A. A. Angrist, M.D.
- U.S. Veterans Administration Hospital Laboratory—B. S. Gordon, M.D.

Bronxville
- Lawrence Hospital Laboratory—A. A. Eggston, M.D.

Brooklyn
- Brooklyn State Hospital Laboratory—G. Eros, M.D.
- St. Catherine's Hospital Laboratory—M. Wachstein, M.D.

Buffalo
- Buffalo General Hospital Laboratory—E. Witebsky, M.D., K. L. Terplan, M.D.
- Buffalo Regional Blood Center (see Kenmore)—V. Scamurra, M.D.
- Central Cytologic Laboratory—D. N. Shaver, M.D.
- Children's Hospital Laboratory—E. Neter, M.D., K. L. Terplan, M.D.
- Deaconess Hospital Laboratory—B. Fisher, M.D., J. B. Sheffer, M.D.
- E. J. Meyer Memorial Hospital Laboratory—J. M. Benny, M.D., H. Lansky, M.D.
- Emergency Hospital Laboratory—R. T. Quebral, M.D.
- Erie County Laboratory (see Kenmore)—V. Scamurra, M.D.
- Laboratory of the Roswell Park Memorial Institute—E. Neter, M.D., J. W. Pickren, M.D.
- Mercy Hospital Laboratory—A. B. Constantine, M.D.
- Millard Fillmore Hospital Laboratory—A. V. Postoloff, M.D.
- Sisters of Charity Hospital Laboratory—C. F. Becker, M.D.
- U.S. Veterans Administration Hospital Lab-

* Approval pending.

oratory—E. Witebsky, M.D., K. L. Terplan, M.D.

University of Buffalo Virology Laboratory—D. T. Karzon, M.D.

Cambridge

Mary McClellan Hospital Laboratory (see Saratoga Springs)—J. Lebowich, M.D.

Canajoharie

Montgomery County Laboratory (see Amsterdam)—T. S. Velz, M.D.

Canandaigua

F. F. Thompson Memorial Hospital Laboratory—G. Scullard, M.D.

U.S. Veterans Administration Hospital Laboratory—G. Selbach, M.D.

Canastota

Madison County Bacteriological Laboratory (see Oneida)—R. G. Lindauer, M.D.

Canton

St. Lawrence County Laboratories—R. T. Rogers, M.D.

Catskill

Laboratory of the Memorial Hospital of Greene County (see Hudson)—J. Bellamy, M.D.

Central Islip

Central Islip State Hospital Laboratory—F. Weinberg, M.D.

Clifton Springs

Clifton Springs Sanitarium and Clinic Laboratory—G. J. Copeland, M.D.

Cohoes

Cohoes Memorial Hospital Laboratory (see Albany)—J. J. Clemmer, M.D.

Cooperstown

Mary Imogene Bassett Hospital Laboratory and Otsego County Laboratory—C. V. Z. Hawn, M.D.

Corning

Steuben County Laboratories (see Hornell)—B. J. McClanahan, M.D.

Cortland

Cortland Memorial Hospital Laboratory—A. J. Bragoli, M.D.

Dansville

* Livingston County Laboratory—J. S. Grewal, M.D.

Dobbs Ferry

Dobbs Ferry Hospital Laboratory (see North Tarrytown)—J. L. Redmond, M.D.

Dunkirk

Brooks Memorial Hospital Laboratory—V. G. Smith, M.D.

Elmira

Arnot-Ogden Memorial Hospital Laboratory—W. D. Kelly, M.D.

St. Joseph's Hospital Laboratory—J. A. Mitchell, M.D.

Endicott

Endicott-Johnson Medical Department Laboratory and Ideal Hospital Laboratory (see Johnson City)—A. A. Kosinski, M.D.

Farmingdale

Nassau County Tuberculosis Sanatorium Laboratory (see Hempstead)—E. R. Maillard, M.D.

Fulton

Oswego County Division of Laboratories and Research (see Oswego)—E. R. Studenski, M.D.

Geneva

Geneva General Hospital Laboratory—J. W. Walker, M.D.

Glen Cove

Laboratory of the Community Hospital of Glen Cove—T. Robertson, M.D.

Glens Falls

Warren County Bacteriological Laboratory and Foulds Memorial Laboratory—R. H. Stokes, M.D.

Gloversville

Fulton County Laboratory—W. Lanyon, M.D.

Gouverneur

E. J. Noble Hospital Laboratory (see Ogdensburg)—J. F. Majeranowski, M.D.

Gowanda

Cattaraugus County Laboratories (see Olean)—L. D. Moss, M.D.

Great Neck

Laboratories of Dr. Louis E. Marshall—L. E. Marshall, M.D.

Hamilton

Madison County Bacteriological Laboratory (see Oneida)—R. G. Lindauer, M.D.

Helmuth

Gowanda State Hospital Laboratory—W. J. Allexsaht, M.D.

Hempstead

Meadowbrook Hospital Laboratory—V. S. Palladino, M.D.

Nassau County Division of Laboratories and Research—E. R. Maillard, M.D.

Hempstead General Hospital Laboratory—E. J. Felderman, M.D.

Herkimer

Herkimer Memorial Hospital Laboratory (see Utica)—L. G. Thomas, M.D.

Hornell

Steuben County Laboratories in Bethesda Hospital and St. James Mercy Hospital—B. J. McClanahan, M.D.

Hudson

Columbia Memorial Hospital Laboratory—J. Bellamy, M.D.

Huntington

Huntington Hospital Laboratory—C. A. McNicol, M.D.

Islip

South Shore Analytical and Research Laboratory, Inc.—M. L. Rakieten, M.D., F. Weinberg, M.D.

Ithaca

Cornell University Infirmary Laboratory and Tompkins County Laboratory—H. W. Parks, M.D.

Diagnostic Laboratory, New York State Veterinary College—T. F. Benson, D.V.M.

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* Approval pending.

Jamaica
Intercounty Blood Banks Laboratory and the Mary Immaculate Hospital Laboratory—T. J. Hartnett, M.D.

Jamestown
Jamestown Municipal Laboratory—J. W. Mold, M.D.

Johnson City
Charles S. Wilson Memorial Hospital Laboratory—A. A. Kosinski, M.D.

Johnstown
Fulton County Laboratory—W. Lanyon, M.D.

Kenmore
Kenmore Mercy Hospital Laboratory—V. Scamurra, M.D.

Kings Park
Kings Park State Hospital Laboratory—R. M. Cares, M.D.

Kingston
City of Kingston Laboratory, City of Kingston Laboratory in Benedictine Hospital and Kingston Hospital—H. Derman, M.D.

Liberty
Liberty Maimonides Hospital Laboratory—H. Derman, M.D.

Lockport
Lockport Memorial Hospital Laboratory—L. F. Bleyer, M.D.
Mount View Hospital Laboratory—J. F. Mohn, M.D., K. L. Terplan, M.D.

Lowville
Lewis County Laboratory (see Watertown)—F. F. Howatt, M.D.

Manhasset
Manhasset Hospital Laboratory—M. F. Wiener, M.D.
North Shore Hospital Laboratory—S. Gross, M.D.

Massena
St. Lawrence County Laboratories (see Canton)—R. T. Rogers, M.D.

Medina
Orleans County Laboratories (see Batavia)—J. Tannenberg, M.D.

Middletown
Elizabeth A. Horton Memorial Hospital Laboratory and the Middletown State Homeopathic Hospital Laboratory—H. L. Mamelok, M.D.

Mineola
Nassau Hospital Laboratory—L. R. Ferraro, M.D.

Mount Kisco
Northern Westchester Hospital Laboratory—R. A. Fox, M.D.

Mount Vernon
Mount Vernon Hospital Laboratory—J. G. Sharnoff, M.D.

Newark
Newark State School Laboratory—W. J. Welch, M.D.

Newburgh
St. Luke's Hospital Laboratory—T. P. B. Payne, M.D.

New Rochelle
New Rochelle Hospital Laboratory and New Rochelle Professional Building Laboratory—W. C. Schraft, M.D.

New York
Memorial Center for Cancer and Allied Diseases—F. W. Foote, Jr., M.D.
St. Vincent's Hospital Laboratory (see Yonkers)—A. Rottino, M.D.
Trafalgar Hospital Laboratory—J. Gudemann, M.D.

Niagara Falls
Mount St. Mary's Hospital Laboratory—T. T. Bronk, M.D.
Niagara Falls Memorial Hospital Laboratory—F. D. Stone, M.D.
Niagara Falls Public Health Laboratory—I. M. Walker, M.D.

North Tarrytown
Phelps Memorial Hospital Laboratory—J. L. Redmond, M.D.

Norwich
Chenango Memorial Hospital Laboratory—P. T. Cruz, M.D.

Nyack
Nyack Hospital Laboratory—D. E. G. Worcester, M.D.

Ogdensburg
A. Barton Hepburn Hospital Laboratory—J. F. Majeranowski, M.D.
St. Lawrence County Laboratories (see Canton)—R. T. Rogers, M.D.

Olean
Cattaraugus County Laboratories, Olean General Hospital Laboratory, and St. Francis Hospital Laboratory—L. D. Moss, M.D.

Oneida
Madison County Bacteriological Laboratory—R. G. Lindauer, M.D.

Oneonta
Fox Memorial Hospital Laboratory—L. A. Markley, M.D.
Otsego County Laboratory (see Cooperstown)—C. V. Z. Hawn, M.D.

Orangeburg
Rockland State Hospital Laboratory—W. R. Strutton, M.D.

Oswego
Oswego County Division of Laboratories and Research—E. R. Studenski, M.D.

Patchogue
Brookhaven Memorial Hospital Laboratory—W. B. Bissell, M.D.

Penn Yan
Yates County Laboratory (see Canandaigua)—G. Scullard, M.D.

Plattsburgh
Physicians Hospital Laboratory and Champlain Valley Hospital Laboratory—C. W. Petenyi, M.D.

Pomona
Summit Park Sanatorium Laboratory (see Nyack)—D. E. G. Worcester, M.D.

Port Chester
United Hospital Laboratory—T. E. Young, M.D.
Potsdam
St. Lawrence County Laboratories (see Canton)—R. T. Rogers, M.D.
Poughkeepsie
*Hudson River State Hospital Laboratory—J. Morris, M.D.
St. Francis Hospital Laboratory—J. D. Gioia, M.D.
Vassar Brothers Hospital Laboratory—M. L. Dreyfuss, M.D.
Pulaski
Oswego County Laboratory—E. R. Studenski, M.D.
Rochester
Genesee Hospital Laboratory—J. N. Abbott, M.D.
Highland Hospital Laboratory, Dept. of Anatomic Pathology—J. H. Peers, M.D.
Highland Hospital Laboratory, Dept. of Clinical Pathology—J. W. Holler, M.D.
Laboratory of the Rochester Red Cross Regional Blood Bank—W. S. Thomas, M.D.
*Monroe County Health Department Laboratories—R. M. Greendyke, M.D.
*Park Avenue Hospital Laboratory—D. C. Donovan, M.D.
Rochester General Hospital Laboratory—M. G. Bohrod, M.D.
St. Mary's Hospital Laboratory—J. Adler, M.D.
Bacteriological Laboratories of University of Rochester School of Medicine, Strang Memorial and Rochester Municipal Hospitals—H. R. Morgan, M.D., W. B. Hawkins, M.D.
Rome
Rome City Laboratory and Oneida County Hospital Laboratory—D. A. Sunderland, M.D.
Saranac Lake
Laboratory of the General Hospital of Saranac Lake—D. S. Steward, M.D.
Saratoga Springs
Saratoga County Laboratories—J. Lebowich, M.D.
Schenectady
Ellis Hospital Laboratory—G. F. Parkhurst, M.D.
St. Clare's Hospital Laboratory—J. Mauro, M.D.
Star Lake
St. Lawrence County Laboratories (see Canton)—R. T. Rogers, M.D.
Suffern
Good Samaritan Hospital Laboratory—R. T. Bryan, M.D.
Syracuse
American Red Cross Syracuse Regional Blood Center—O. D. Chapman, M.D.
Bureau of Laboratories, Department of Health—R. B. Jamieson, M.D.
Crouse-Irving Hospital Laboratory—J. T. Prior, M.D., R. B. Jamieson, M.D.
Hospital of the Good Shepherd Laboratory, and Syracuse Memorial Hospital Laboratory—J. H. Ferguson, M.D., R. B. Jamieson, M.D.
*St. Joseph's Hospital Laboratory and St. Mary's Hospital Laboratory—C. I. Austin, M.D.
U.S. Veterans Administration Hospital Laboratory—J. A. Schaefer, M.D.
Troy
Cluett Pathological Laboratory, Samaritan Hospital—C. G. Burn, M.D.
Rensselaer County Laboratory—A. W. Wright, M.D.
St. Mary's Hospital Laboratory—J. J. Clemmer, M.D.
Utica
Faxton Hospital Laboratory—L. G. Thomas, M.D.
George Alder Blumer Research Laboratory and Utica City Laboratory—N. M. Levine, M.D.
Laboratory of the Children's Hospital Home of Utica—L. G. Thomas, M.D.
St. Elizabeth Hospital Laboratory—G. C. Walker, M.D.
St. Luke's-Memorial Hospital Center Laboratory—C. E. Davis, M.D.
Valhalla
Westchester County Department of Laboratories and Research—V. A. Bradess, M.D.
Warsaw
Wyoming County Laboratory (see Batavia)—J. Tannenberg, M.D.
Watertown
House of the Good Samaritan Hospital Laboratory—F. F. Howatt, M.D.
Mercy Hospital Laboratory—R. S. Lee, M.D.
West Brentwood
Edgewood Laboratory—A. W. Golfman, M.D.
West Islip
Good Samaritan Hospital Laboratory—A. W. Golfman, M.D.
White Plains
White Plains Hospital Laboratory and White Plains Medical Centre Branch Laboratory—J. Lester, M.D.
Wingdale
Harlem Valley State Hospital Laboratory—L. Loeffler, M.D.
Yonkers
Bureau of Laboratories, Department of Public Health and St. John's Riverside Hospital Laboratory—C. E. DeAngelis, M.D.
St. Joseph's Hospital Laboratory—A. Rottino, M.D.
Yonkers General Hospital Laboratory—M. J. Eisen, M.D.

* Approval pending.

Necrology

Murray Harold Bass, M.D., of New York City, died on March 9 at The Mount Sinai Hospital at the age of seventy-nine. Retired, Dr. Bass graduated in 1907 from Columbia University College of Physicians and Surgeons and interned at The Mount Sinai Hospital. He was a consultant in pediatrics at The Mount Sinai Hospital, where he had formerly been chief of pediatrics, and at St. Joseph's (Far Rockaway), Hackensack, and Barnert Memorial (Paterson, New Jersey), Hospitals. From 1914 to 1919 he was a visiting physician for the Society of the Prevention of Cruelty to Children, for a time was adjunct pediatrician to the Willard Parker Hospital and the Home for Hebrew Infants, and from 1937 to 1942 served as attending pediatrician at the Hospital for Joint Diseases. Dr. Bass was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the American Pediatric Society, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Elfride Evelyn Borg, M.D., of Ridgewood and Huntington, died on October 8, 1961, at her home at the age of sixty-six. Dr. Borg received her medical degree in 1936 from the University of Siena. A former clinical assistant in obstetrics at the Outpatient Department of the Greenpoint Hospital, Dr. Borg was a member of the American Medical Women's Association, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Theodore Boycheff, M.D., of Solvay, died on February 11 at Crouse-Irving Hospital at the age of ninety-two. Dr. Boycheff graduated in 1898 from Syracuse University College of Medicine. Retired in 1954, he had served formerly as health officer for the Town of Geddes and Village of Solvay. Dr. Boycheff was a member of the Onondaga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Warren Britt, M.D., of Tonawanda, died on February 2 at his home at the age of eighty-six. Dr. Britt graduated in 1906 from the University of Buffalo School of Medicine. Retired in 1961, he was a former staff member at Millard Fillmore Hospital and the Edward J. Meyer Memorial Hospital, and an honorary staff member at DeGraff Memorial Hospital. Dr. Britt was a member of the Buffalo Academy of Medicine, the Erie County Medical Society (a past-president), the Medical Society of the State of New York, and the American Medical Association.

Victor Caeti, M.D., of the Bronx, died on October 8, 1961, at the age of sixty-four. Dr. Caeti graduated in 1926 from Eclectic Medical College, Cincinnati. He was a clinical assistant in dermatology and syphilology at Fordham Hospital Outpatient Department.

James Frank Crawford, M.D., of Warsaw, died on October 5, 1961, at the age of seventy-eight. Dr. Crawford graduated in 1911 from the University of Buffalo School of Medicine. He was a member of the Wyoming County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Baptist D'Albora, M.D., of Garden City, died on February 26 at Mercy Hospital, Rockville Centre, at the age of seventy-one. Dr. D'Albora graduated in 1912 from Long Island College Hospital Medical School and interned at St. Mary's Hospital. He was a consultant in gastroenterology at St. Mary's Hospital and past-president of the Alumni Association and the Medical Board and an attending physician at Long Island College Hospital. He was a director of United Medical Service, Inc., and a former member of the New York State Board of Social Welfare. Dr. D'Albora was a Diplomate of the American Board of Internal Medicine (Gastroenterology), a Fellow of the American College of Physicians, and a member of the American Gastro-Enterological Association, the New York Academy of Medicine, the New York Gastroenterological Society, the Brooklyn Society of Internal Medicine, the Morgagni Medical Society of New York, the Kings County Medical Society (a past-president), the Medical Society of the State of New York, and the American Medical Association.

Joseph Samuel Delaney, M.D., of Jackson Heights and New York City, died on November 3, 1961, at the age of forty-eight. Dr. Delaney graduated in 1937 from Queens University Faculty of Medicine, Kingston, Ontario, Canada. He was an attending obstetrician and gynecologist at Misericordia Hospital and assistant attending physician in obstetrics and gynecology at St. Clare's Hospital and City Hospital at Elmhurst. Dr. Delaney was a Fellow of the International College of Surgeons and a member of the New York Celtic Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert E. Graybill, M.D., of Staten Island, died on October 14, 1961, at the age of thirty-four. Dr. Graybill graduated in 1953 from Hahnemann Medical College and Hospital of Philadelphia. He was an assistant attending anesthetist at St. Vincent's Hospital, Staten Island. Dr. Graybill was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Walter W. Hamburger, M.D., of Rochester, died on September 21, 1961, at the age of forty-six. Dr. Hamburger graduated in 1940 from The School of Medicine of the University of Chicago. He was a senior associate in psychiatry at Strong Memorial Hospital. Dr. Hamburger was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Member of the American Pyschiatric Association, and held memberships also in the American Association for Research in Psychosomatic Problems, the American Psychoanalytic Association, the Rochester Academy of Medicine, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Bernard Benjamin Harris, M.D., of Yonkers, died on January 23 at Yonkers Professional Hospital at the age of sixty-one. Dr. Harris graduated in 1924 from Boston University School of Medicine. From 1927 to 1935 he was assistant health officer in the Yonkers Health Department and an attending physician at Leake and Watts Home as well as a former attending physician at the New York Guild for the Jewish Blind. Dr. Harris was a member of the Yonkers Academy of Medicine, the Westchester County Medical Society, and the Medical Society of the State of New York.

John Brennan Horner, M.D., of Albany, died on February 16 at Albany Memorial Hospital at the age of sixty. Dr. Horner graduated in 1926 from the University of Vermont College of Medicine. He was chief of urology at Albany Memorial Hospital and a consultant in urology at Memorial Hospital of Greene County (Catskill). From 1959 to 1960 he was chairman of the executive committee for the Albany Memorial Hospital. Dr. Horner was a Diplomate of the American Board of Urology, a Fellow of the American College of Surgeons, and a member of the American Public Health Association, the American Urological Association, the Northeastern Section of the American Urological Association, the Albany County Medical Society (a past-president), the Medical Society of the State of New York, and the American Medical Association.

Louis E. Klingon, M.D., of Brooklyn, died on August 6, 1961, at the age of seventy-five. Dr. Klingon graduated in 1910 from New York University and Bellevue Hospital Medical School and interned at Bellevue Hospital. He was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Emmet Lucey, M.D., of Staten Island, died on December 1, 1961, at the age of forty-five. Dr. Lucey graduated in 1941 from Columbia University College of Physicians and Surgeons and interned at Bellevue Hospital. He was an associate attending physician in urology at St. Vincent's Hospital, an assistant attending physician in urology at Richmond Memorial Hospital, and an attending physician in urology at Willowbrook State School. Dr. Lucey was a Fellow of the American College of Surgeons and a member of the Richmond County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David J. Maloney, M.D., of Olean, died on February 3 at the Lakeview Hospital (Cleveland, Ohio) at the age of fifty-four. Dr. Maloney graduated in 1936 from Georgetown University School of Medicine. He was an attending physician in anesthesiology at Olean General Hospital. Dr. Maloney was a member of the American Society of Anesthesiologists, Inc., the New York State Society of Anesthesiologists, the Cattaraugus County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ward Beecher Manchester, M.D., of Batavia, retired, died on January 19 at St. Joseph's Hospital, Tampa, Florida, at the age of seventy-nine. Dr. Manchester graduated in 1907 from the University of Buffalo School of Medicine. A past chief of surgical services at the former Batavia Hospital and at St. Jerome Hospital as well as former president of the staffs, he was an honorary surgeon at Genesee Memorial Hospital. One time Genesee County coroner and past-president of the Genesee County Medical Society, Dr. Manchester was loaned to the British government during World War I and served as a captain with a heavy artillery outfit in France.

Harold Leonard Margulies, M.D., of New York City, died on March 11 at his home at the age of fifty. Dr. Margulies received his medical degree from the University of Geneva in 1936. He was a senior clinical assistant attending physician at The Mount Sinai Hospital. Dr. Margulies was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Clay Maxon, M.D., of Chatham, died on February 18 at Albany Medical Center at the age of eighty-four. Dr. Maxon graduated in 1903 from Albany Medical College. Retired, he was a former health officer for Chatham. Dr. Maxon was a member of the Columbia County Medical Society for which he had served as president for two terms, the Medical Society of the State of New York, and the American Medical Association.

John Francis McNeill, M.D., of Beacon, died on March 8 at his home at the age of seventy-three. Dr. McNeill graduated in 1912 from the University of Vermont College of Medicine. He was superintendent of the Matteawan State Hospital for the Criminally Insane. Dr. McNeill was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Life Fellow of the American Psychiatric Association, and a member of the New York Society for Clinical Psychiatry, the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter Ernest Merrick, M.D., of New York City, died on September 12, 1961, at the age of sixty-seven. Dr. Merrick graduated in 1931 from Howard University College of Medicine. He was physiatrist-in-charge at Harlem Hospital and director of physical medicine and rehabilitation at Harlem Hospital Outpatient Department. Dr. Merrick was a member of the Manhattan Central Medical Society.

Greta Prausnitz, M.D., of Flushing, died on October 14, 1961, at the age of fifty-nine. Dr. Prausnitz received her medical degree from the University of Freiburg in 1926. She was an assistant attending physician at Queens Hospital Center and an assistant attending physician in the Cardiac Department at the Queens Hospital Center Outpatient Department. Dr. Prausnitz was a member of the Queens County Medical Society and the Medical Society of the State of New York.

Frank C. Rizzella, M.D., of New York City, died on December 14, 1961, at the age of fifty-three. Dr. Rizzella received his medical degree from the University of Naples in 1935. He was an assistant attending obstetrician and gynecologist at City Hospital at Elmhurst. Dr. Rizzella was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

August H. Stein, M.D., of Oakfield, died on September 6, 1961, at the age of seventy-six. Dr. Stein graduated in 1910 from the University of Buffalo School of Medicine.

Morris Tannenbaum, M.D., of the Bronx, died on July 30, 1961, at the age of fifty-six. Dr. Tannenbaum graduated in 1929 from the University of Maryland School of Medicine and College of Physicians and Surgeons. He was an associate attending physician in chest diseases at Morrisania Hospital and an associate attending physician at the Hospital for Joint Diseases. Dr. Tannenbaum was a Fellow of the American College of Chest Physicians and a member of the the American Academy of Tuberculosis Physicians, the American Trudeau Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas Rankin Thorburn, M.D., of New York City, died on March 8 at Le Roy Hospital at the age of seventy-three. Dr. Thorburn graduated in 1918 from New York Homeopathic Medical College and Flower Hospital. A past-president of the American Osteopathic Society, the Eastern Osteopathic Society, the New York State Osteopathic Society and the Osteopathic Society of the City of New York, Dr. Thorburn was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Brooke Todd, M.D., of Rochester, was killed by an automobile on October 8, 1961, at the age of thirty-seven. Dr. Todd graduated in 1951 from the University of Rochester School of Medicine and Dentistry. He was an assistant attending in obstetrics and gynecology at Strong Memorial and Genesee Memorial Hospitals and chief of obstetrics and gynecology at Park Avenue Hospital.

Gilbert Henry Welch, M.D., of Rochester, died on January 23 at Genesee Memorial Hospital at the age of seventy-four. Dr. Welch graduated in 1910 from the University of Michigan Medical School. He was an associate attending in surgery at Park Avenue Hospital. Dr. Welch was a member of the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Andre Elias Willner, M.D., of New York City and Bayside, died on August 23, 1961, at the age of forty-eight. Dr. Willner graduated in 1943 from the University of California Medical School. He was an assistant attending in surgery at Goldwater Memorial and Lincoln Hospitals and a clinical assistant in surgery at The Mount Sinai Hospital. Dr. Willner was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical Meetings

Joint conference of tuberculosis organizations

The first State-wide meeting to be sponsored by the tuberculosis associations which serve New York State and New York City and by the New York Trudeau Society will be held at the Statler Hilton, Seventh Avenue and 33rd Street, New York City, on Monday, April 16, starting at 9:45 A.M.

Sponsoring organizations for the conference are: Brooklyn Tuberculosis and Health Association, New York State Committee on Tuberculosis and Public Health, New York Trudeau Society, New York Tuberculosis and Health Association, and the Queensboro Tuberculosis and Health Association.

Latin-American Congress of Physical Medicine, Gold Key Award Dinner

The Latin-American Congress of Physical Medicine, The Pan-American Academy of General Practice, and The Spanish-American Society of New York invite all interested persons to attend the Gold Key Award Testimonial Dinner tendered to Charles R. Brooke, M.D., Livingston, New Jersey, and Mario E. Stella, M.D., New York City, on Wednesday, April 25, at the Grand Street Boy's Club, 106 West 55th Street, New York City, from 6:30 to 9:30 P.M.

For information contact: Cassius Lopez deVictoria, M.D., Executive Director, Latin-American Congress of Physical Medicine, 245 East 17th Street, New York 3, New York. Telephone SP 7–2558.

New York Society for Cardiovascular Surgery

The fourteenth annual meeting of the New York Society for Cardiovascular Surgery and the Committee on Cardiovascular Surgery of the New York Heart Association will be held at the New York Academy of Medicine, 2 East 103rd Street, New York City, on Monday, May 7, at 8:30 P.M. in Hosack Hall.

The program will feature a discussion on "Closure of Ventricular Septal Defects—Clinical and Hemodynamic Correlations in 140 Patients Studied Postoperatively by Recatheterization" by C. Walton Lillehei, M.D., Ph.D., professor of surgery, University of Minnesota School of Medicine, Minneapolis, Minnesota. A question period will follow.

For information contact: Lester Blum, M.D., Secretary-Treasurer, New York Society for Cardiovascular Surgery, 101 East 93rd Street, New York 28, New York.

Ira I. Kaplan Lecture

The eleventh annual Ira I. Kaplan Lecture, sponsored by the Radiation Therapy Alumni Association of Bellevue Hospital, will be held on May 10, at 5:00 P.M., in the main auditorium of the New York University School of Medicine. The guest speaker, Oscar V. Batson, M.D., of

Philadelphia, will discuss the relationship of tumor spread to the venous systems.

Symposium on upper and lower extremities amputees

The Mercy Hospital Rehabilitation Center of South Buffalo will sponsor a symposium on upper and lower extremities amputees on May 10, from 9:00 A.M. to 1:00 P.M., in Marion Hall, 360 Choate Avenue, Buffalo 20, New York. Reeve M. Brown, M.D., Buffalo, will be the luncheon speaker.

For information contact: Henry V. Morelewicz, M.D., The Mercy Hospital Rehabilitation Center of South Buffalo, 565 Abbott Road, Buffalo 20, New York.

Heart Association of Greater Miami

The seventh biennial cardiovascular seminar to be sponsored by the Heart Association of Greater Miami will be held May 17 through 19 at the Eden Roc Hotel, Miami Beach, Florida.

The seminar, which will deal primarily with clinical medicine, is directed to internists, cardiologists, and general practitioners.

For information write to: Heart Association of Greater Miami, 253 Southwest 8th Street, Miami 36, Florida.

National Tuberculosis Association

The fifty-eighth annual meeting of the National Tuberculosis Association and the fifty-seventh annual meeting of its medical section, The American Thoracic Society, will be held in Miami Beach, Florida, May 20 through 23. The Deauville and the Carillon will be the headquarter hotels.

For further information write to: National Tuberculosis Association, 1790 Broadway, New York 19, New York.

Memorial Hospital of Long Beach, California

The fourth annual medical staff symposium of the Memorial Hospital of Long Beach, California, will be held at the Hospital, 2801 Atlantic Avenue, Long Beach, California, on Wednesday, May 23. The program will feature papers by staff physicians and by Maxwell Wintrobe, M.D., professor and chairman, Department of Medicine, University of Utah College of Medicine, Salt Lake City, Utah.

For further information write to: George X. Trimble, M.D., Symposium Secretary, Memorial Hospital of Long Beach, Long Beach, California.

American College of Chest Physicians

The following meetings have been scheduled by the American College of Chest Physicians.

Chicago—annual meeting, June 21 through 25, Morrison Hotel; *Los Angeles*—interim session, November 24 and 25, The Ambassador Hotel; and *New Delhi, India*—seventh international congress on diseases of the chest, February 20 through 24, 1963.

For further information concerning these meetings write to: American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

National Conference on Disaster Medical Care

"Community Preparedness for Emergencies" will be the theme of the tenth annual National Conference on Disaster Medical Care to be held in Chicago on June 23, at the Palmer House Hotel. Sponsored by the Council on National Security of the American Medical Association, the one-day meeting immediately precedes the opening of the A.M.A.'s one hundred and eleventh annual meeting.

For further information write to: Department of National Security, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Fifth International Food Congress and Exhibition

More than 120 food companies and related industrial firms will exhibit at the Fifth International Food Congress and Exhibition, September 8 through 16, at the New York Coliseum. Among the exhibits will be a display sponsored by the American Medical Association entitled "Nutrition Nonsense."

Washington State Medical Association

The physicians in the State of Washington have extended an invitation to doctors throughout the country who plan to visit the Seattle World's Fair this September to coincide their trip with the seventy-third annual Washington State Medical Association's meeting in Spokane, September 16 through 19.

For additional information write to: Washington State Medical Association, 1309 Seventh Avenue, Seattle, Washington.

International Society for Rehabilitation of the Disabled

The International Society for Rehabilitation of the Disabled will hold its ninth world congress in Copenhagen, Denmark, June 23 through 29, 1963. The host organization will be The Society and Home for Cripples in Denmark.

For further information write to: International Society for Rehabilitation of the Disabled, 701 First Avenue, New York 17, New York.

Abstracts

Fogel, R. L., Epstein, J. A., Stopak, J. H., and Kupperman, H. S.: Achilles tendon reflex test (photomotogram) as a measure of thyroid function, NEW YORK STATE J. MED. **62:** 1159 (Apr. 15) 1962.

Thyroid function may be evaluated accurately by the use of the Achilles tendon reflex. The duration is measured by a cell attached to a direct-writing electrocardiograph (photomotogram) and is related to the thyroid state of the patient. The principle involved is that the muscle contraction phase of the reflex occurs promptly regardless of the thyroid state of the individual, while relaxation is retarded in hypothyroidism and accelerated in hyperthyroidism. The test requires no special skills. It is not influenced by the emotional status of the patient, nonthyroid metabolic or pulmonary disease, or medication other than thyroid derivatives, nor is it affected by iodine contamination. Pregnancy does not alter the response of the Achilles tendon reflex. There is no discomfort or stress associated with the performance of the technic; hence it is readily accepted by children. The only condition nullifying the value of the test is neuromuscular disease associated with absence of deep tendon reflex. The hyper- and hypothyroid patient's response to therapy may be evaluated by the use of the photomotogram. If the physician is able to use only one test to evaluate thyroid function, the photomotogram would be the one of choice.

Becker, R. O., Bachman, C. H., and Friedman, H.: The direct current control system; a link between environment and organism, NEW YORK STATE J. MED. **62:** 1169 (Apr. 15) 1962.

A study was undertaken of the problem of the relationship between D.C. (direct current) potentials and regeneration. A complex electrical field was found rather than the expected simple dipole, and its spatial configuration was noted to bear a close relationship to the gross anatomic arrangement of the central nervous system. If the D.C. potentials were measured at multiple points on an animal, including the head, a specific series of changes occurred following the application of a traumatic stimulus to the hind limb. Very specific changes in the field polarity, particularly across the head, were noted with anesthesia. The D.C. potential gradient was measured on the exposed but otherwise undisturbed main sciatic nerve in the frog. The results were indicative not only of moving charges, but also indicated further that the charge carriers were nonionic and were probably units of the size of electrons. A definite relationship has been established between the time sequence of D.C. changes at the site of a limb amputation and the subsequent healing process. In the human being the same neural-related pattern was found as in the amphibian with differences ascribable to the relative shortening of the spinal cord and the capacitive effects associated with dry skin. Specific changes in the transcortical D.C. potentials were noted with general anesthesia, sleep, and hypnosis. It appeared likely that the organized D.C. activity of the brain was in some way closely related to general behavior, possibly as a controlling mechanism of sorts and that, since the actual D.C. flow of change of charge carriers was an integral part of the system, then the operating parameters of the system could be influenced by external force fields (magnetic, electrostatic) and by such physical parameters as levels of air ionization. There is some crude evidence of a possible relationship between psychiatric disturbances and geophysical parameters.

Moser, M.: Treatment of the ambulatory hypertensive patient, NEW YORK STATE J. MED. **62:** 1177 (Apr. 15) 1962.

In the management of the ambulatory hypertensive patient, home blood pressure readings generally are not taken, overtreatment is avoided by instructing the patient to reduce his medication immediately if dizziness occurs, and patients usually are not told their exact readings. Drugs which are useful in therapy are the Rauwolfia alkaloids, chlorothiazide derivatives, a combination of the two, chlorothalidone derivative, hydralazine, monamine oxidase inhibitors, peripheral sympathetic blocking agents, and occasionally ganglion-blocking agents. All of these drugs may have side-effects which vary in occurrence and severity. At this time complicated therapy with the more potent drugs seems justified in the male patient with persistently elevated diastolic blood pressure and organ system involvement. However, it is not advised in women in the menopausal-age group or in elderly persons with labile diastolic blood pressures. The end result of treatment, once it is decided on, must be satisfactory blood pressure lowering, and therapy must be titrated until this is achieved.

Steinberg, I.: Intravenous abdominal aortography and peripheral arteriography; diagnostic value in arteriosclerotic abdominal aortic and peripheral vascular disease, NEW YORK STATE J. MED. **62:** 1186 (Apr. 15) 1962.

A modification of the intravenous method of angiocardiography has made possible abdominal aortography and peripheral arteriography by rapid, simultaneous, and bilateral injections of concentrated organic iodides after accurate determination of the circulation time. Inexpensive needles and syringes and the use of x-ray equipment ordinarily available for gastrointestinal or genitourinary roentgenography make this method practical for use in the average hospital. Over 500 patients have had abdominal aortography and peripheral arteriography with this method. This method is particularly suited for the diagnosis of arteriosclerotic abdominal aortic and peripheral vascular disease, especially to determine whether or not constructive surgery is indicated and to assess the results of reconstructive vascular surgery. The intravenous method has advantages over the translumbar method of aortography which had sometimes been associated with serious complications and occasionally death. It is important to select for intravenous aortography only those patients who are likely to benefit from such studies as in rare cases death, apparently caused by drug sensitivity, has occurred.

Bottcher, E. J.: Use of whole blood transfusions in a general hospital, New York State J. Med. **62:** 1196 (Apr. 15) 1962.

A study was made of patients receiving 1- and 2-pint transfusions in a 250-bed division of a general hospital during an eight-month period. In this period 932 patients received 2,371 pints of blood; 401 (43 per cent) of these received only 1 unit during their hospital stay, and 246 (26 per cent) received 2 units. Sixty-nine per cent of the patients receiving 1 unit of blood and 58 per cent of those receiving 2 units were given their transfusions in the operating room and the immediate postoperative period. Pyrogenic or allergic reactions with no sequelae occurred after 3 per cent of the transfusions. However, in the past two years 2 serious cases and 1 fatal case of hepatitis have occurred following 1-unit transfusions. Although in retrospect very few of the 1-unit transfusions would have been necessary, at the time there were undoubtedly factors present indicating the need for blood. In about 50 per cent of the cases the 2-pint transfusions were more often of apparent benefit.

Rowe, C. R.: Management of osteomyelitis following fractures of extremities, New York State J. Med. **62:** 1200 (Apr. 15) 1962.

In the management of osteomyelitis following fractures of the extremities, the over-all condition of the patient should be evaluated. All infected and devitalized tissue and foreign material of a chronic bone infection should be removed from the wound. Effective stabilization of the fracture is essential; it may be achieved by plaster cast fixation, cast and transverse wires, compression methods, or intramedullary rod fixation. Closure of the debrided wound may be by direct side-to-side suture, direct sliding or double pedicle graft, rotation or single pedicle graft, or free split-thickness skin graft. Close cooperation with a plastic surgeon is urged throughout management of osteomyelitis.

Galbraith, J. M.: Bendroflumethiazide in hypertension and edematous states; use in office practice, New York State J. Med. **62:** 1209 (Apr. 15) 1962.

A study of the effectiveness in the treatment of hypertension and edema of bendroflumethiazide (Naturetin) in a low-dosage range was undertaken in 38 office patients. The most effective dosage was found to be 5 mg. of bendroflumethiazide with 500 mg. of potassium chloride. All 38 patients responded satisfactorily to treatment. An average fall of 26.8 mm. Hg occurred in the mean blood pressure of the 33 patients with hypertension. Symptoms associated with cardiovascular disease were controlled or lessened in 5 normotensive patients presenting edema and/or pulmonary complaints. Side-effects occurred in 2 patients: mild hypotension in 1 when the drug was given continuously on a once-daily basis, and an exacerbation of gout when the dosage frequency was increased to twice or three times daily. No evidence of tolerance developed even during prolonged therapy. The drug was effective not only in lowering blood pressure and controlling edema, but also in relieving such symptoms as headache, shortness of breath, nocturnal dyspnea, and anginal pain.

Medical News

Postgraduate pediatric program

Maimonides Hospital of Brooklyn and the State University of New York Downstate Medical Center will present a postgraduate pediatric program May 27 through 29 in the solarium of the Kronish Pavilion at the Hospital, 4802 Tenth Avenue, Brooklyn.

The courses are designed to bring to the pediatrician and the general practitioner advances in theoretical and practical knowledge of the respiratory distress syndrome; bulky stool syndrome; neuromuscular disorders in children; and genetics and chromosomes. The faculty will include speakers from twelve medical centers.

For information write to: Department of Pediatrics, Maimonides Hospital, 4802 Tenth Avenue, Brooklyn 19, New York.

Tightening of regulations for preparations for anemia

The Food and Drug Administration (F.D.A.) proposes to tighten regulation of preparations used to treat pernicious anemia. So-called "intrinsic factor" products would be labeled for sale only on prescription under a proposal published on February 17 in the *Federal Register*.

The statement of policy would also require that any orally-administered drug for the treatment or prevention of pernicious anemia bear a warning stating it is not a reliable substitute for injections of vitamin B_{12} and that periodic examinations and laboratory tests are essential.

Intrinsic factor is an unknown substance prepared from the intestines of food animals which increases vitamin B_{12} absorption in the human stomach. Orally-administered preparations of vitamin B_{12} and intrinsic factor may sometimes mask symptoms and interfere with the diagnosis of pernicious anemia. Intrinsic factor is also regarded as a food additive under the Federal Food, Drug, and Cosmetic Act and cannot be used in foods because there is no covering food additive regulation.

Reprints requested by University of Montreal

The research library of the Institute of Experimental Medicine and Surgery of the University of Montreal has suffered extensive losses due to destruction by fire.

In an attempt to rebuild its library the University has asked the readers of the NEW YORK STATE JOURNAL OF MEDICINE to send them all available reprints of their work, especially those dealing with endocrinology and stress.

The University would also like to point out that its permanent mailing list was destroyed and therefore reprints of its publications will be sent only to those readers who write for them.

Contributions of reprints should be addressed to: Hans Selye, M.D., Professor and Director, Institute of Experimental Medicine and Surgery, University of Montreal, P.O. Box 6128, Montreal 26, Canada.

Course for hospital administrators

The fifth annual Hospital Administrators Development Program sponsored by the Sloan Institute of Hospital Administration under a special grant from the Alfred P. Sloan Foundation will bring together 25 administrators from the United States and abroad for an intensive four-week study of current problems and developments in the field of health administration. The course will begin on June 24 at Cornell University, Ithaca, New York.

Applications for the program will be received from hospital administrators and executives from other health agencies until May 15.

For further information write to: Mr. John Mason Potter, Director, Cornell University News Bureau, 111 Day Hall, Ithaca, New York.

Physician elected officer of military group

Edward A. Barrett, M.D., Mount Kisco, one of the 410 U.S. Army officers selected to attend the associate course of instruction at the Command and General Staff College, Fort Leavenworth, Kansas, has been elected president of the New York Chapter of the Association of Military Surgeons of the United States.

In addition, Dr. Barrett has been appointed to the national executive council of the Association and is chairman of the chapter section.

Membership in the Association of Military Surgeons is open to all who hold or have ever held commissioned rank in the Medical Department of any of the Federal Military Services, the Veterans Administration, or Public Health Service. Membership is also available to those in ancillary medical fields such as nursing, medical service corps, dentistry, medical service specialties, or pharmacy.

For information write to: Lt. Col. Edward A. Barrett, MC, USAR, Headquarters, 912 Surgical Hospital, 2nd Lt. Thomas J. McDonald

U.S. Army Reserve Center, 168–10 Goethals Avenue, Jamaica 32, New York.

Study of air pollution

Herman E. Hilleboe, M.D., State Health Commissioner and chairman of the State Air Pollution Control Board, has announced that a cooperative study of air pollution in Westchester County is being conducted by four local health departments and the State Health Department.

The health departments of Westchester County and the cities of Mount Vernon, New Rochelle, and Yonkers will have an early opportunity to learn what, if any, air pollution problems now exist in their areas. With this knowledge adequate preventive and corrective measures can then be instituted.

Similar studies in Greater Elmira and Erie, Niagara, and Nassau Counties have been completed or are nearing completion. Eventually the whole State will be surveyed as part of the State's air pollution control program.

Fellowships for overseas study

The Association of American Medical Colleges has announced that fellowships to provide a group of young Americans with clinical medical experience in underdeveloped countries have been awarded to 33 junior and senior medical students. The scholarships are made possible by a $60,000 yearly grant from Smith Kline & French Laboratories.

With the current selection, the Association in three years has awarded a total of 92 fellowships for study in 33 countries. This year's students will travel to Thailand, Pakistan, the Philippines, Liberia, India, Tanganyika, Nigeria, Burma, Ethiopia, Peru, Uganda, Borneo, Madagascar, Haiti, Cameroun, Ecuador, Viet Nam, and Southern Rhodesia. They will work in mission hospitals and outpost medical facilities while studying and combating diseases not commonly seen in the United States.

Change in dates for pediatric refresher course

Announcement has been made of a change in dates for the pediatric refresher courses being offered at the University of Buffalo School of Medicine under the sponsorship of the Medical Society of the State of New York and the Bureau of Maternal and Child Health, State of New York Department of Health. The second of the two courses will now be held June 4 through 8 in lieu of June 6 through 10 as previously announced. For full information concerning these courses see Medical News, March 1, page 723.

Personalities

Resigns. Hayden C. Nicholson, M.D., New York City, as executive director of the Hospital Council of Greater New York.

Awarded. Howard A. Rusk, M.D., New York City, a bronze plaque by Cancer Care for his service to the disabled and chronically ill.

Elected. John Mark Hiebert, M.D., Port Washington, as president of the Commerce and Industry Association of New York . . . Leonard J. Raider, M.D., Woodcliff Lake, New Jersey, as president of United Medical Service, Inc . . . . Howard A. Rusk, M.D., New York City, to the board of directors of the Chemical Fund, Inc . . . . John D. Van Zandt, M.D., Tuxedo Park, to the board of directors of United Medical Service, Inc.

Appointed. Arthur Q. Penta, M.D., Schenectady, as president of the section on Oto-Rhino-Laryngology and Broncho-Esophagology of the Pan American Medical Association . . . Calvin W. Tribiano, M.D., Short Hills, New Jersey, as medical director of Walker Laboratories . . . Leo Wollman, M.D., Brooklyn, as a consulting editor to the *Journal of Sex Research.*

Elected. Franz Altmann, M.D., New York City, to the board of directors of the New York League for the Hard of Hearing . . . Leo Wollman, M.D., Brooklyn, to the executive committee of the Society for the Scientific Study of Sex.

Speakers. James A. Brussel, M.D., Assistant Commissioner, State of New York Department of Mental Hygiene, on the topic "Interstate Compact on Mental Health" before the Community Council of Greater New York, on April 10 . . . John M. Galbraith, M.D., president of the Medical Society of the State of New York, on the topic "The Doctor" at a symposium sponsored by the Bronx Chapter of the American College of Surgeons on March 22 . . . Rachmiel Levine, M.D., New York City, the annual Mary Swartz Rose Memorial Lecture, before the Greater New York Dietetic Association on April 9 on the topic "Present Day Concepts of Diabetes from the Genetic and Metabolic Viewpoint" . . . Harvey J. Tompkins, M.D., New York City, on March 12, before the Guild of Catholic Psychiatrists on the subject "Psychiatry and Catholic Education" . . . Frederic Wertham, M.D., New York City, at a meeting of the Association for the Advancement of Psychotherapy on March 23 on the topic "Seduction of the Innocent."

Abstracts in Interlingua

Fogel, R. L., Epstein, J. A., Stopak, J. H., e Kupperman, H. S.: Le photomotogramma del reflexo del tendine de Achilles como test del function thyroidic (*anglese*), New York State J. Med. **62:** 1159 (15 de april) 1962.

Le function del glandula thyroide pote esser evalutate accuratemente a base del reflexo del tendine de Achilles. Le duration del reflexo es mesurate per medio de un cellula que es attachate a un electrocardiographo a registration directe. Isto produce le photomotogramma que pote esser ponite in correlation con le stato thyroidic del patiente. Hic le principio es que le phase del contraction muscular in le reflexo occurre promptemente sin reguardo al stato thyroidic del individuo, durante que le relaxation muscular es relentate in hypothyroidismo e accelerate in hyperthyroidismo. Le test require nulle habilitates special. Illo non es influentiate per le stato emotional del patiente, per le presentia de non-thyroidic morbo metabolic o pulmonar, o per medication altere que derivatos de thyroide. Similemente, illo non es afficite per contamination a iodo. Pregnantia non altera le responsa in le reflexo del tendine de Achilles. Nulle disconforto e nulle stress es associate con le manovra. Ergo illo es prestemente acceptate per juveniles. Le sol condition que pote nullificar le valor del test es morbo neuromuscular associate con absentia de reflexos tendinose profunde. Le responsa del patiente hyperthyroidic e hypothyroidic al therapia pote esser evalutate a base del photomotogramma. Si le medico pote usar non plus que un sol test pro evalutar le function del thyroide, on pote dicer que le photomotogramma debe esser su selection.

Becker, R. O., Bachman, C. H., e Friedman, H.: Le systema regulatori a currente continue; un nexo inter ambiente e organismo (*anglese*), New York State J. Med. **62:** 1169 (15 de april) 1962.

Esseva studiate le problema del relation inter potentiales de currente continue e regeneration. Un complexe campo electric esseva trovate plus tosto que le expectate simple dipolo, e le configuration spatial de ille campo monstrava un intime relation con le disposition anatomic del systema nervose central. Quando le potentiales de currente continue esseva mesurate in varie punctos de un animal, incluse le capite, un serie de specific alterationes occurreva post le application de un stimulo traumatic a un del extremitates posterior. Multo specific alterationes in le polaritate de campo—particularmente a transverso le capite—esseva notate como effecto de anesthesia. Le gradiente del potential de currente continue esseva mesurate in le exponite sed alteremente intacte major nervo sciatic del rana. Le resultatos esseva non solmente indicatori de cargas migrante, illos etiam indicava que le vectores de carga esseva non-ionic e probabilemente unitates del magnitude de electrones. Esseva establite un definite relation inter le chronologia del alterationes de currente continue al sito del amputation de un extremitate e le subsequente processo curatori. In humanos le mesme neuro-relationate configuration esseva trovate como in le amphibio, con differentias ascribibile al relative reduction in le longor del cordon spinal e al effectos capacitatori que es associate con le siccitate del pelle. Alterationes specific esseva notate in le potentiales transcortical de currente continue in association con anesthesia general, somnio, e hypnose. Il pareva probabile que le organisate activitate de currente continue del cerebro esseva intimemente relationate, in un maniera o un altere, con le comportamento general, possibilemente con le function de un mechanismo regulatori. Alora, viste que le fluxo de vectores de carga de currente continue esseva recognoscite como un parte integral del systema, il es justificate supponer que le parametros actuatori del systema pote esser influentiate per externe campos de fortia (de character magnetic o electrostatic) e per parametros physic como per exemplo le ionisation del aere. Il mesmo existe crude indicationes de un possibile relation inter disturbationes psychiatric e parametros geophysic.

Moser, M.: Tractamento del patiente hypertensive ambulatori (*anglese*), New York State J. Med. **62:** 1177 (15 de april) 1962.

In le tractamento de ambulatori patientes hypertensive, lecturas "domiciliari" del tension de sanguine non es usualmente effectuate. Excessos de tractamento es evitate per instruer le patientes de reducer lor medication immediatemente post le occurrentia de vertigine. In general, le patientes non es informate del exacte valor de lor tension. Drogas que es utile in le therapia include alcaloides de rauwolfia, derivatos de chlorothiazido, un combination del duo, derivatos de chlorothalidon, hydralazina, inhibitores de oxydase de monamina, agentes de blocage peripheric e sympathic, e occasionalmente agentes de blocage ganglionic. Omne iste drogas pote haber adverse effectos secundari que varia in occurrentia e in severitate. Al tempore presente, un complexe therapia con le uso del drogas de potentia major pare justificate in le patiente mascule con persistente elevation del tension de sanguine diastolic e affection de systema organic. Tamen, le methodo non es recommendate pro feminas de etate menopausal o pro patientes de etate plus tosto avantiate con labilitate del tension de sanguine diastolic. Le ultime objectivo del tractamento—si un tal es volite—debe esser un satisfacente reduction del tension de sanguine, e le therapia debe esser titrate usque ille objectivo es attingite.

Steinberg, I.: Intravenose aortographia abdominal e arteriographia peripheric; valor diagnostic in arteriosclerotic morbo abdomino-aortic e periphero-vascular (*anglese*), NEW YORK STATE J. MED. **62:** 1186 (15 de april) 1962.

Un modification del intravenose methodo angiocardiographic ha rendite possibile aortographia abdominal e arteriographia peripheric per medio de rapide simultanee injectiones bilateral de concentrate ioduros organic post accurate determinationes del tempore de circulation. Incostose agulias e syringas e le uso del apparatura de radios X que es ordinarimente disponibile pro roentgenographia gastrointestinal e genitourinari rende iste methodo usabile in le hospital median. Plus que 500 patientes ha essite subjicite a aortographia abdominal e arteriographia peripheric secundo iste methodo. Le methodo es particularmente appropriate al uso in le diagnose de arteriosclerotic morbo abdomino-aortic e periphero-vascular, specialmente quando il se tracta de determinar si o non un intervention de chirurgia constructive es indicate e subsequentemente de evalutar le resultatos de reconstructive chirurgia vascular. Le methodo intravenose ha certe avantages in comparation con le methodo translumbar de aortographia, le qual ha occasionalmente essite associate con serie complicationes, mesmo con morte. Es importante seliger pro aortographia intravenose solmente patientes in qui il existe le forte probabilitate que illes va beneficiar ab le resultatos de tal studios, proque in rar casos morte ha occurrite, probabilemente in consequentia de pharmacosensibilitate.

Bottcher, E. J.: Le uso de transfusiones de sanguine total in un hospital general (*anglese*), NEW YORK STATE J. MED. **62:** 1196 (15 de april) 1962.

Esseva effectuate un studio del patientes recipiente transfusiones de 1 e de 2 pintas de sanguine in un division de 250 lectos de un hospital general in le curso de un periodo de octo menses. Durante iste octo menses, 932 patientes recipeva 2.371 pintas de sanguine. De istes, 401 (43 pro cento) recipeva un sol unitate durante lor sojorno al hospital. Duo centos quaranta sex (26 pro cento) recipeva 2 unitates. Sexanta-novem pro cento del recipientes de 1 unitate e 58 pro cento del recipientes de 2 unitates recipeva lor transfusiones in le sala de operationes e durante le periodo immediatemente post-operatori. Reactiones pyrogenic o allergic sin sequellas occurreva post 3 pro cento del transfusiones. Tamen, in le curso del passate duo annos, 2 serie casos e 1 caso mortal de hepatitis ha occurrite post transfusiones de 1 unitate. Ben que il appare in retrospecto que pauchissimes del transfusiones de 1 unitate esseva necessari, al tempore de lor effectuation il habeva sin dubita factores que rendeva evidente que sanguine esseva requirite. In circa 50 pro cento del transfusiones de 2 pintas, le beneficio del manovra esseva plus tosto apparente.

Rowe, C. R.: Tractamento de osteomyelitis post fracturas de extremitate (*anglese*), NEW YORK STATE J. MED. **62:** 1200 (15 de april) 1962.

In le tractamento de osteomyelitis post fracturas de extremitate, le condition general del patiente debe esser evalutate. Omne le inficite e disvitalisate tissu e omne materia estranie de un chronic infection ossee debe esser removite ab le vulnere. Un efficace stabilisation del fractura es essential. Isto pote esser effectuate per fixation sub bandage a gypso, per gypso e transverse filos metallic, per methodos de compression, o per fixation a baculo intramedullari. Post debridement, le vulnere pote esser claudite per sutura directe, per directe graffage a duple pediculo, per graffage de rotation a pediculo simple, o per graffo cutanee libere a spissitate findite. Le plus stricte cooperation con un specialista de chirurgia plastic es urgentemente importante in omne phases del tractamento de osteomyelitis.

Galbraith, J. M.: Bendroflumethiazido in hypertension e statos edematose; uso in le practica del sala de consulta (*anglese*), NEW YORK STATE J. MED. **62:** 1209 (15 de april) 1962.

Esseva interprendite, in 38 patientes de visita al sala de consulta, un studio del efficacia de bendroflumethiazido in basse doses in le tractamento de hypertension e de edema. Esseva trovate que le plus efficace dosage consisteva de 5 mg de bendroflumethiazido con 500 mg de chloruro de kalium. Omne le 38 patientes respondeva satisfacentemente. In le 33 patientes con hypertension, le reduction medie del tension sanguinee medie amontava a 26,8 mm de Hg. In 5 patientes normotensive qui se presentava con edema e/o gravamines pulmonar, le symptomas associate con morbo cardiovascular esseva equilibrate o alleviate. Adverse effectos secundari occurreva in 2 patientes. Leve grados de hypotension occurreva in 1 quando le droga esseva administrate continuemente un vice per die. Exacerbation de gutta occurreva in le altere quando le frequentia del dose esseva augmentate a duo o tres vices per die. Nulle disveloppamento de accostumation esseva apparente in le curso de un prolongate therapia. Le droga esseva efficace non solmente in reducer le tension de sanguine e equilibrar le edema sed etiam in alleviar symptomas como cephalalgia, dyspnea general e nocturne, e dolores anginal.

Books Reviewed

Intra-Abdominal Crises. By Kenneth D. Keele, F.R.C.P., and Norman M. Matheson, F.R.C.S. Octavo of 397 pages, illustrated. Washington, Butterworths, 1961. Cloth, $10.

This meaty book, produced cooperatively by Kenneth D. Keele, a consulting physician of the Ashford Hospital, Middlesex, England, and Norman M. Matheson, a consulting surgeon of the same hospital, has just appeared as a first edition.

One of the main objectives of this book is to resolve the different attitudes of the physician and the surgeon into an urgent "medicosurgical synthesis" when a patient first presents with acute abdominal symptoms.

Of greatest import, of course, is the prompt, correct diagnosis, arrived at by expert history, observation, pertinent laboratory aids, and wise thinking. This is no new subject, but this small book should be of great value for this purpose. It contains concise notes on the most modern diagnostic and treatment technics and would be a handy book to have in the many isolated places to which doctors now go to render aid to the less advanced nations.

The authors believe acute cholecystitis should be allowed to subside before cholecystectomy. The reviewer and many others in this country believe that it is safer to operate as soon as the patient is properly prepared, provided the patient is seen within the first five to seven days. After this period a three-month delay is advisable unless conditions deteriorate, in which case a cholescystostomy might be indicated.

There is a chapter devoted to abdominal crises in the tropics. One part takes up local abdominal disease, and one part covers intra-abdominal crises of general disease. An appendix gives practical notes on some laboratory investigations, including how they are done and what and how they give information. A final index provides quick access to the facts desired in an emergency.

Many interesting problems will be recalled to the minds of the older readers, and probably most will find observations and ideas here that they may wish they had had then.

Besides being compact, useful and interesting, *Intra-Abdominal Crises* by Keele and Matheson is often exciting reading, a not too common finding in medical literature.—William H. Field, M.D.

Symposium: Visual Problems of Color. Two volumes. Octavo, illustrated. New York, Chemical Publishing Company, Inc., 1961. Cloth, $8.50 each.

These two volumes report on the Symposium of the Visual Problems of Color which was held at the National Physical Laboratory, Teddington, England, in September, 1957. Leading biophysicists from eleven countries participated. The majority of the papers are highly technical, but several can be read with interest by the average informed reader.

Perhaps of greatest general interest is the contribution by George Wald, who gave the Selig Hecht Commemorative Lecture. His subject, "Retinal Chemistry and the Physiology of Vision," summarized much of the present knowledge of the chemistry of rhodopsin and of the activity of the cone and rod cells. Two varieties of retinene with different absorption spectra, corresponding to two varieties of vitamin A, are found widely distributed in nature. Opsin, the protein component of visual purple, is species-specific. The photochemical effect appears to be a stereoisomerization from the neo-b (cis) form of retinene to the all-trans form. Regeneration of rhodopsin during dark adaptation requires reconversion to the cis form. It is probable, as Hubbard points out, that the chromophore linkage site on the opsin molecule can be fitted only by the cis form.

Rushton was able to measure the spectral distribution of light reflected from the foveas of normal and deuteranopic subjects. He was able to demonstrate the presence of two photosensitive pigments in normal foveas, but only one in the protanope. Ditchburn reported an interesting experiment in which he was able to eliminate the customary small fixation movements. Under these conditions the hues of perceived colors fade out, as does even light perception. Apparently the on-off effect produced on the individual cone cells by the small fixation movements is a necessary requirement for sustained vision. He could isolate no small retinal areas where any single color receptor predominated. Land's contribution, "Color Vision and the Natural Image," is reprinted from the Proceedings of the National Academy of Sciences. His method of achieving the entire spectral range of colors by projecting two images with white and red light, or a short and a long wave length, is still to be evaluated.

Several papers are devoted to the absorption spectra of rhodopsin found in different species, and there are a few papers on electrophysiology. However the bulk of papers deal with various phases of color matching and the theory of color vision. It is here that any but the advanced student of color vision will bog down in the complex terminology and the intricate geometry of color mixture.—JOSEPH MANDELBAUM, M.D.

Chemicals in Your Food and in Farm Produce: Their Harmful Effects. By Franklin Bicknell, M.D. Duodecimo of 192 pages. New York, Emerson Books Inc., 1961. Cloth, $2.95.

Half-truths are especially dangerous because the other half of the whole is a skillfully hidden lie. The lie may not be an intentional one or a deliberately hidden one at all. But misinformation or uninformed espousal of causes do damage by misinforming the public. The public, for whom incidentally this book is written, is in no position to exercise judgment as to what to accept or to reject. Faddists, antivivisectionists, and health food zealots will refer to this book with delight to shore up their tenuous thinking and to give them "evidence" for what they wish to believe. The reader can infer the nature of the text by the following quotation from it—the context does not matter: "Congenital abnormalities, physical and mental, are mainly caused by the alien substances added to food." This reviewer is very pleased to note that by a return to home-grown or home-prepared foods, inborn errors of metabolism can be wiped out. Similarly innocent statements are also made with respect to the prevention of cancer, cardiovascular disease, and diseases of the nervous system.

The author undoubtedly is not an antivivisectionist nor an antifluoridationist. He states that fluoridation probably is not harmful to the average child or adult but only for the exceptional individual; he mentions the case of a stoker who, drinking 30 pints of water daily, developed "fits," naturally ascribed to fluorine. It is the occasional case—the hearsay, the claptrap of the generalization from a single instance—which is given in support of his views, despite the presence of a respectable bibliography.

Indeed, valid untoward effects from food, as favism, nutmeg poisoning, and so forth, are brought up. But this is overbalanced with such gems as referring to "tinfoil cheese" as "buying food in soft metal containers may not always be wholly desirable, and is certainly in the case of cheese, wantonly costly, compared to buying honest cheese by the pound." The author bemoans food colors and points out the utterly obvious, that dyes in food serve neither a nutritional nor a preservative purpose. But who would buy lard-white margarine even if partially unsaturated? Margarine, bread, and hydrogenated cooking fats (the last with some justice) are called perverted foods.

Note the following in any context: ". . . unconscious realization that flour is now not only a shoddy food but also toxic" can hardly be taken seriously—American nutritionists are accustomed to evaluate consciously.

The author, who emphasizes British problems, presumably feels it important to discuss naturally occurring poisons in food, such as honey poisoning reported by Xenophon in 400 B.C., quail poisoning through birds which have eaten hemlock seeds, hearsay evidence about conditions under which pigeons and rabbits are poisonous, and lettuce poisoning, which we fail to see as being related to his avowed subject, although unrelatedly these are interesting bits of information.

This is one of the better books on which health faddists fluorish. The reason that good space is taken to review this book is to remind physicians that patients are being fed this type of fodder which, worse than uninformative, is misleading in its emphasis as well as in many of its statements, so that physicians may warn patients of the folly of accepting "causes" rather than valid information. In the United States the Food Additives Amendment of the Federal Food, Drug, and Cosmetic Act controls additives to food; the latter is also under the jurisdiction of other parts of the Act. Among valid examples of adequate books, *The Heinz Handbook of Nutrition* (McGraw-Hill, 1960, $5.75) and the 736-page *Food—The Yearbook of Agriculture* (U.S. Department of Agriculture, 1957, $2.25) are suitable for the intelligent layman as well as the professional reader. An excellent nutritional text for the physician is Wohl & Goodhart's *Modern Nutrition in Health & Disease* (Lea & Febiger, 1960, $18.50).—ERWIN DI CYAN, PH.D.

Abdominal Surgery. Edited by Arthur W. Allen, M.D., and David Woolfolk Barrow, M.D. Quarto of 658 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $21.50.

This publication contains contributions from forty-one prominent and carefully selected teachers of surgery. The subjects covered are broad and comprehensive. The printing is clear and easily read. The illustrations are adequate and well done. There is an impressive bibliography and reference list.

The book covers the general principles of the management of the patient in the preoperative period, the operative procedure, and postoperative care. Danger signals are pointed out. The reader is given an understanding of the surgical patient.

The text develops an intelligent approach to surgery of the abdomen. The book goes well beyond the mechanical aspects of surgery and discusses fully the physiologic aspects. It is not an operative manual.—ALAN A. KANE, M.D.

Month in Washington

The American Medical Association said that President Kennedy misstated the real issue when he renewed his request to Congress for legislation that would provide limited health care for the aged under Social Security.

"We believe the American people are entitled to know that the real issue is not medical care versus no medical care for the elderly," Leonard W. Larson, M.D., president of the A.M.A. said.

"The real issue is: Should wage earners and employers be forced to pay a substantial increase in taxes to provide medical care for millions financially able to take care of themselves? No one supporting this proposal has yet presented any evidence that such radical legislation is needed.

"The medical profession is for the Kerr-Mills law to help the aged who need help. We are for voluntary enterprise, including health insurance and prepayment plans for the non-needy aged."

Dr. Larson also disputed other statements on the issue which President Kennedy made in a new health message to Congress. Dr. Larson said that contrary to what Mr. Kennedy said, the Administration's legislation (the King-Anderson bill) could interfere with the patient's freedom of choice of hospital and physician.

It would give the Federal government "such broad power to control the practice of medicine in the nation's hospitals that the Secretary of Health, Education, and Welfare would literally become the czar of American medicine," Dr. Larson said.

Dr. Larson also pointed out that it would not be a health insurance program as President Kennedy said. Instead, it was "political medicine."

"As the Supreme Court of the United States has ruled, Social Security is strictly a tax program with current taxes used principally to provide benefits for those now retired," Dr. Larson said.

President Kennedy's new health message was a summation of various Administration proposals in the field with some additions. It included: Federal aid for construction of medical schools and scholarships for medical students; expanded health research, including a new institute for child health and human development; more funds for the National Institute of Mental Research; Federal loans to help set up group practice clinics; encouragement of states to provide medical services for migrant workers; Federal research and grants to help combat air pollution in cities; a three-year program of Federal assistance to get American children vaccinated against polio, diphtheria, whooping cough, and tetanus. The government would pay the cost of vaccines for all children under five years of age provided state and local communities set up inoculation programs; and establishment of a National Environmental Health Center "to provide a focal point for nationwide activities in the control of air pollution, water pollution, radiation hazards, and occupational hazards."

Prepared by the Washington office of the American Medical Association.

* * *

A broad investigation of cold remedies to determine whether or not their advertising overstates their effectiveness has been started by the Federal Trade Commission.

As a start, the Commission sent questionnaires to 24 major manufacturers of cold remedies. Answers to the questionnaires are mandatory under the Federal Trade Commission Act. When and how many additional manufacturers will receive similar questionnaires has not yet been determined.

The answers to the questionnaires will enable the Commission to make a comprehensive review of problems throughout the entire field and will assist in evaluating scientific evidence claimed for the medicinal preparations.

The survey seeks information on all such preparations offered for the relief or treatment of congestion, irritation, inflammation, infection, allergy, or other conditions involving any part of (1) the head, including the accessory nasal sinuses, (2) the throat, (3) the bronchi, and (4) the chest, or other portions of the respiratory system. The questionnaires also seek information on claims for the relief or treatment of any symptom or manifestation of these ailments.

The Commission's resolution stated that it had reason to believe that certain corporations in offering such products to the public "may have falsely advertised and misrepresented" their efficacy. The resolution added that the public interest required that an investigation be conducted to determine whether or not such advertising was in violation of the Federal Trade Commission Act.

The names of the 24 manufacturers to whom the questionnaires were sent will not be disclosed, an F.T.C. spokesman said.

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956.
2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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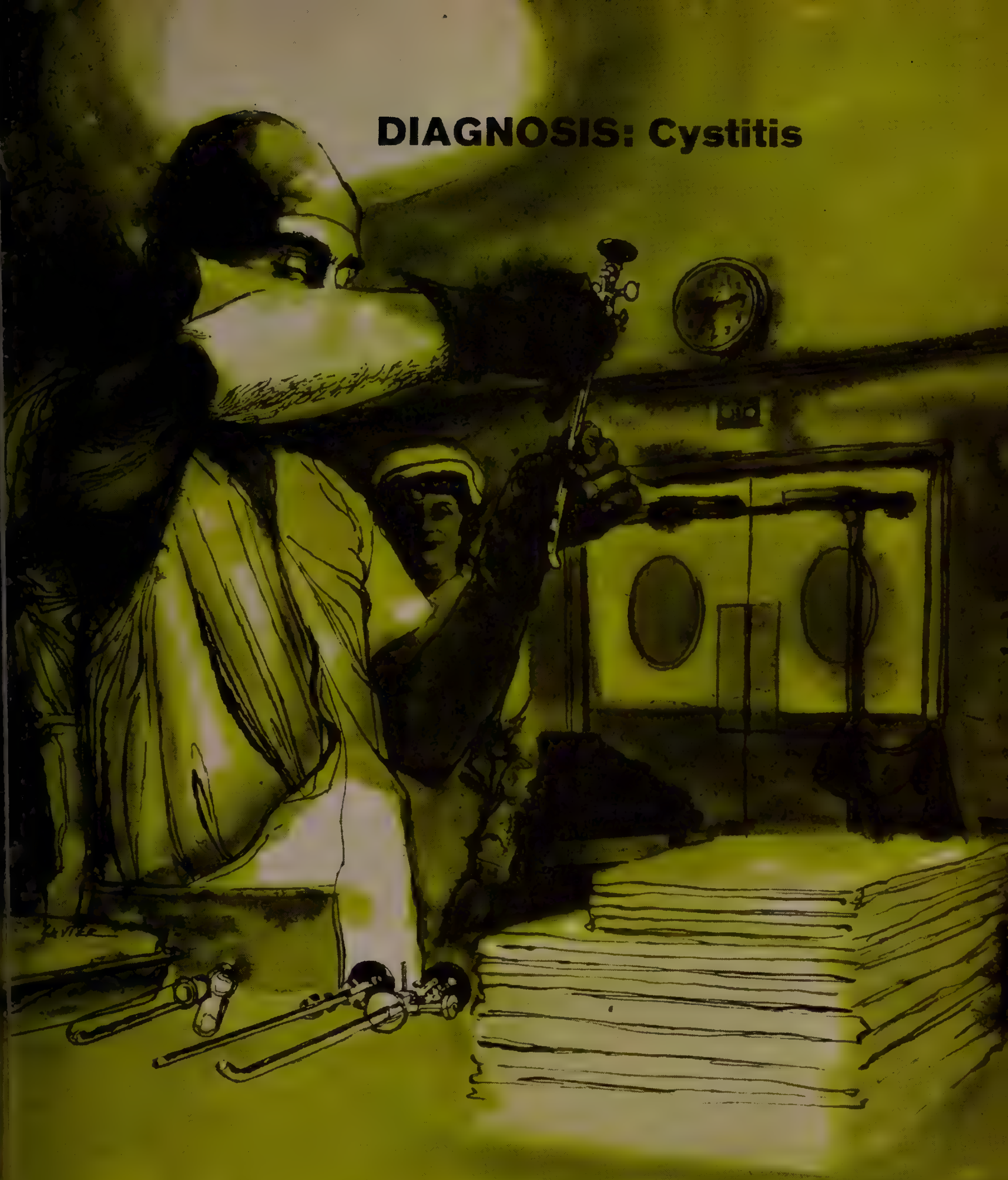

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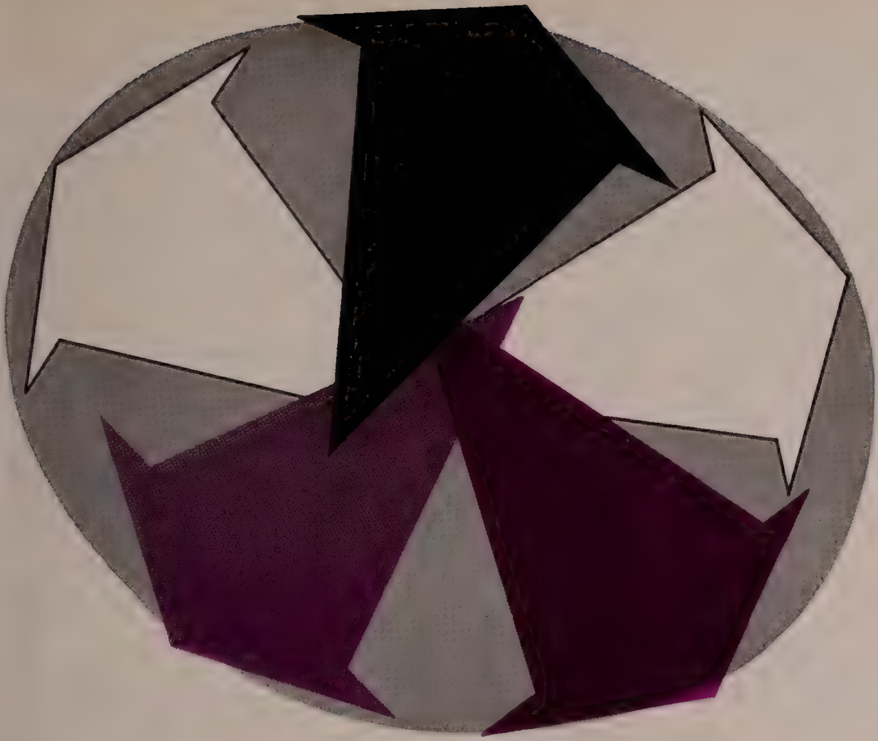

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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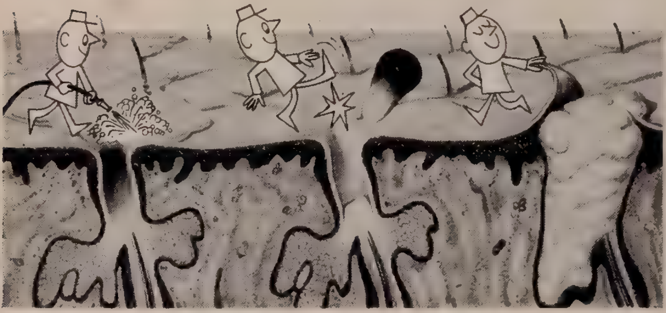

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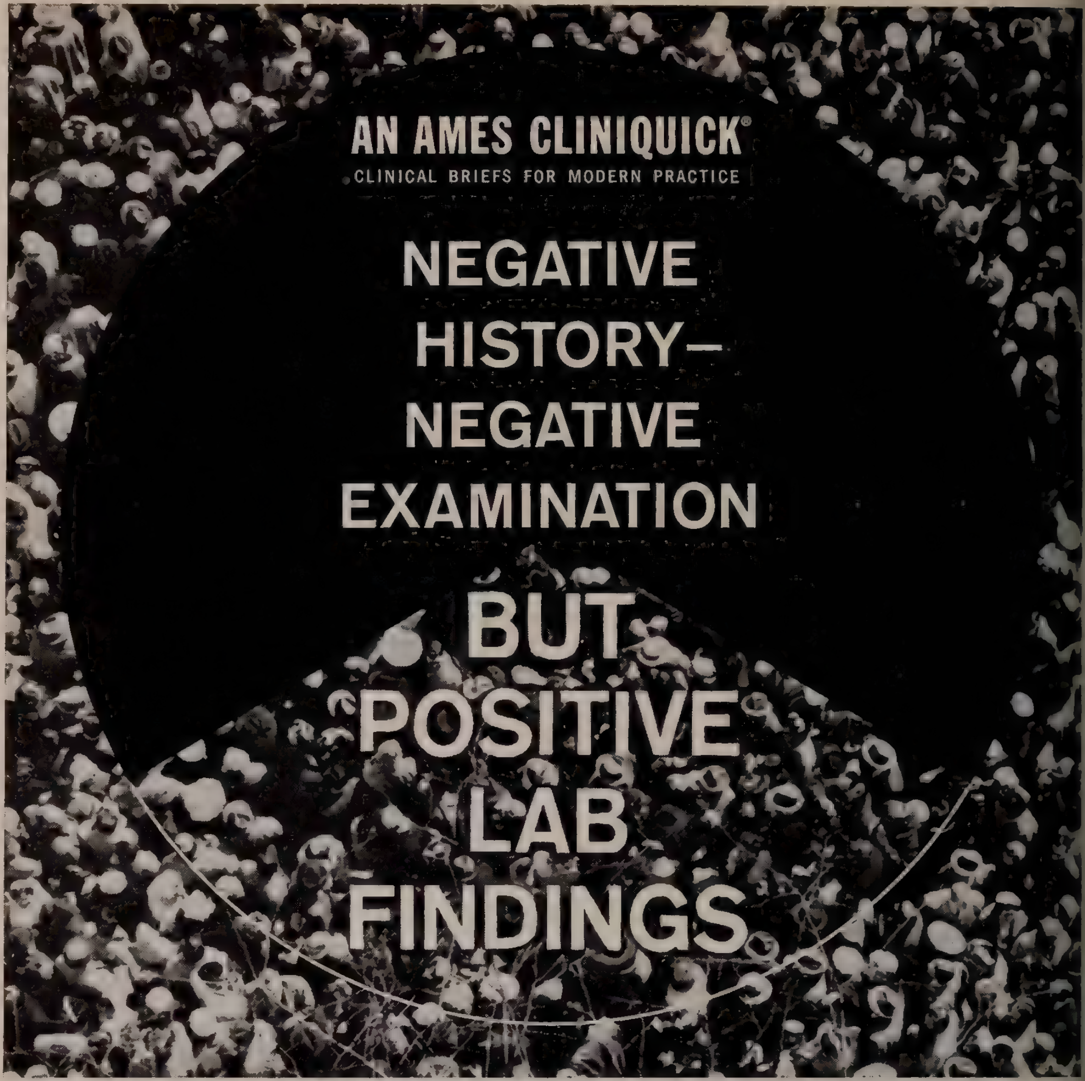
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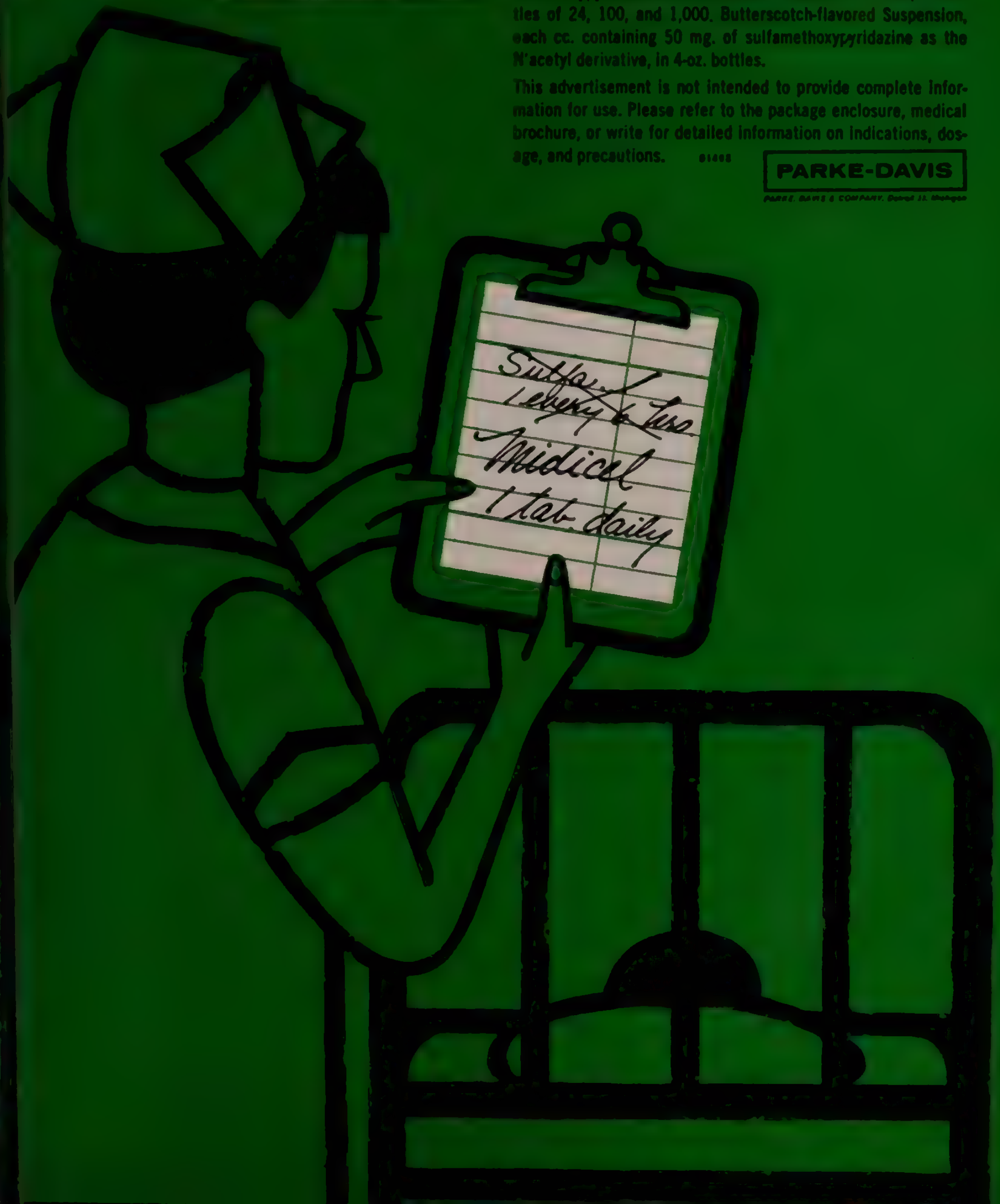
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SECTION ON SPACE MEDICINE at the 1962 Annual Convention, MSSNY

Friday, May 18, 9:00 A.M.
Georgian Room, Statler Hilton, New York City

* * *

SPACE MEDICINE SPECTRA: ANNO V OF SPACE EXPLORATION

1. *Chairman's address:* **The Dynamics of Space Medicine**

   Constantine D. J. Generales, M.D., New York
   Consultant, RCA, David Sarnoff Research Labs and Coordinator of Space Medicine Program, New York Medical College

2. **The United States Government's Role in Current Space Exploration**

   Hon. Victor L. Anfuso, Brooklyn (By invitation)
   House of Representatives, Committee on Science and Astronautics

3. **Unusual Earthly Forms of Life and Extraterrestrial Implications**

   John Pallister, New York (By invitation)
   President Explorers Club; Research Associate, Department of Entomology, American Museum of Natural History

4. **The Significance of the Magnetosphere to Man**

   Alastair G. W. Cameron, Ph.D., New York (By invitation
   Institute for Space Studies, National Aeronautics and Space Administration

5. **Biomedical Engineering as a Physician's Aid**

   Lee B. Lusted, M.D., Rochester
   Associate Professor of Radiology and Biomedical Engineering, The University of Rochester School of Medicine and Dentistry

6. **Life-Like Forms in Carbonaceous Meteorites**

   Bartholomew Nagy, Ph.D., Bronx (By invitation)
   Associate Professor of Chemistry, Fordham University

7. **Electromagnetism and Its Effect on the Organism**

   John H. Heller, Ph.D., Ridgefield, Conn. (By invitation)
   Director, New England Institute of Medical Research

8. **Geomagnetic Environment and its Relationship to Human Biology**

   Robert O. Becker, M.D., Syracuse
   Chief of Orthopedic Section, Veterans Administration Hospital

9. **Selected Topics on Space Medicine in the USSR**

   V. J. Yazdovsky, Moscow, USSR (By invitation)
   Professor, Academy of Sciences of the USSR

10. **The Saturn Program**

    Oswald Lange, Ph.D., Huntsville, Alabama (By invitation)
    Director, Saturn Systems Office, George C. Marshall Space Flight Center

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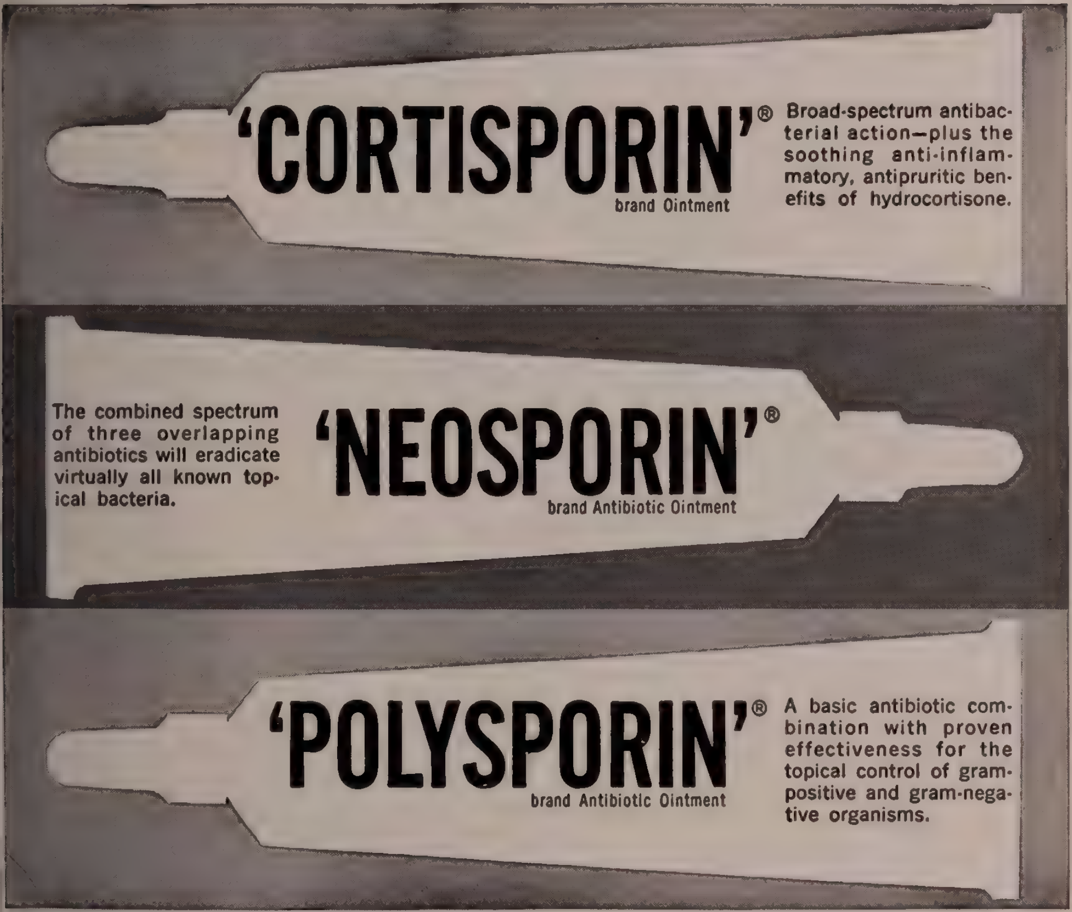

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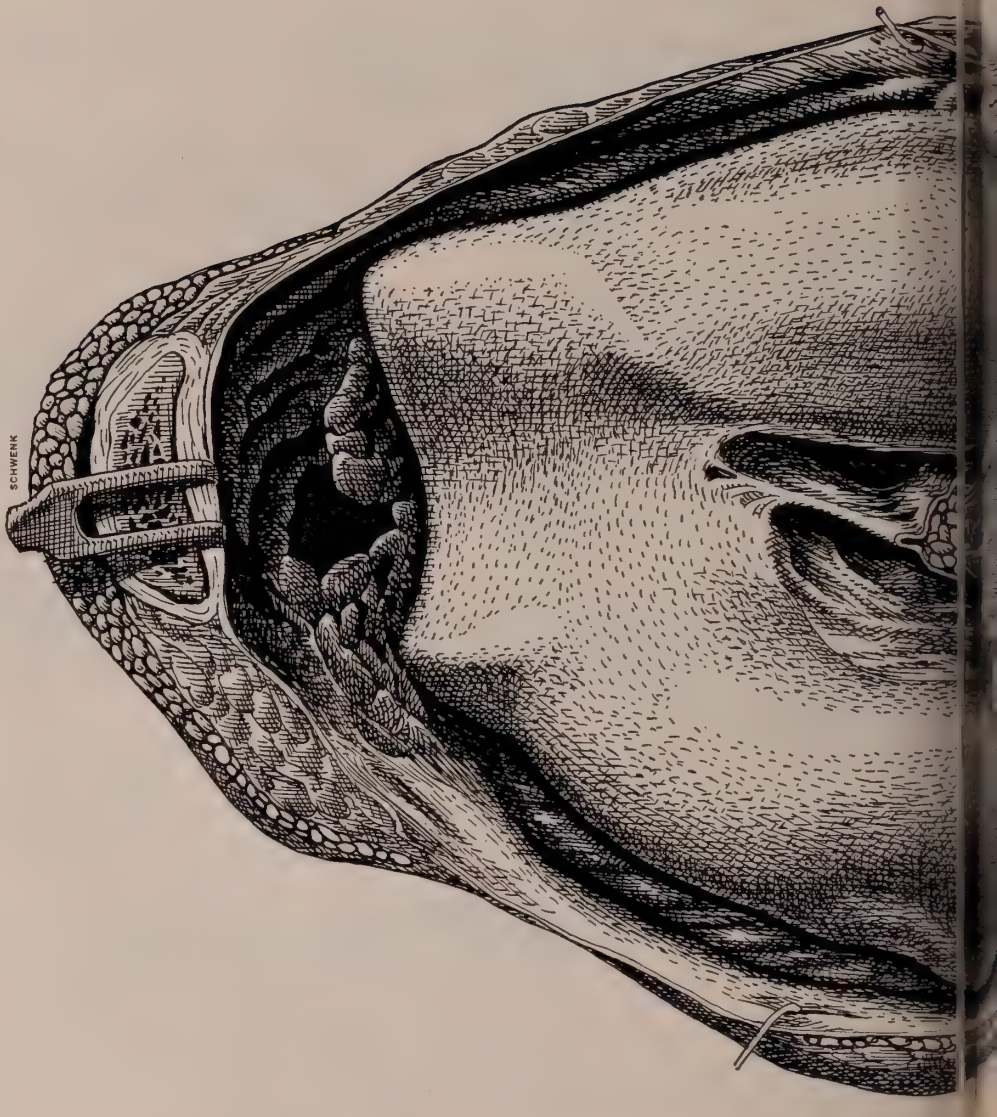

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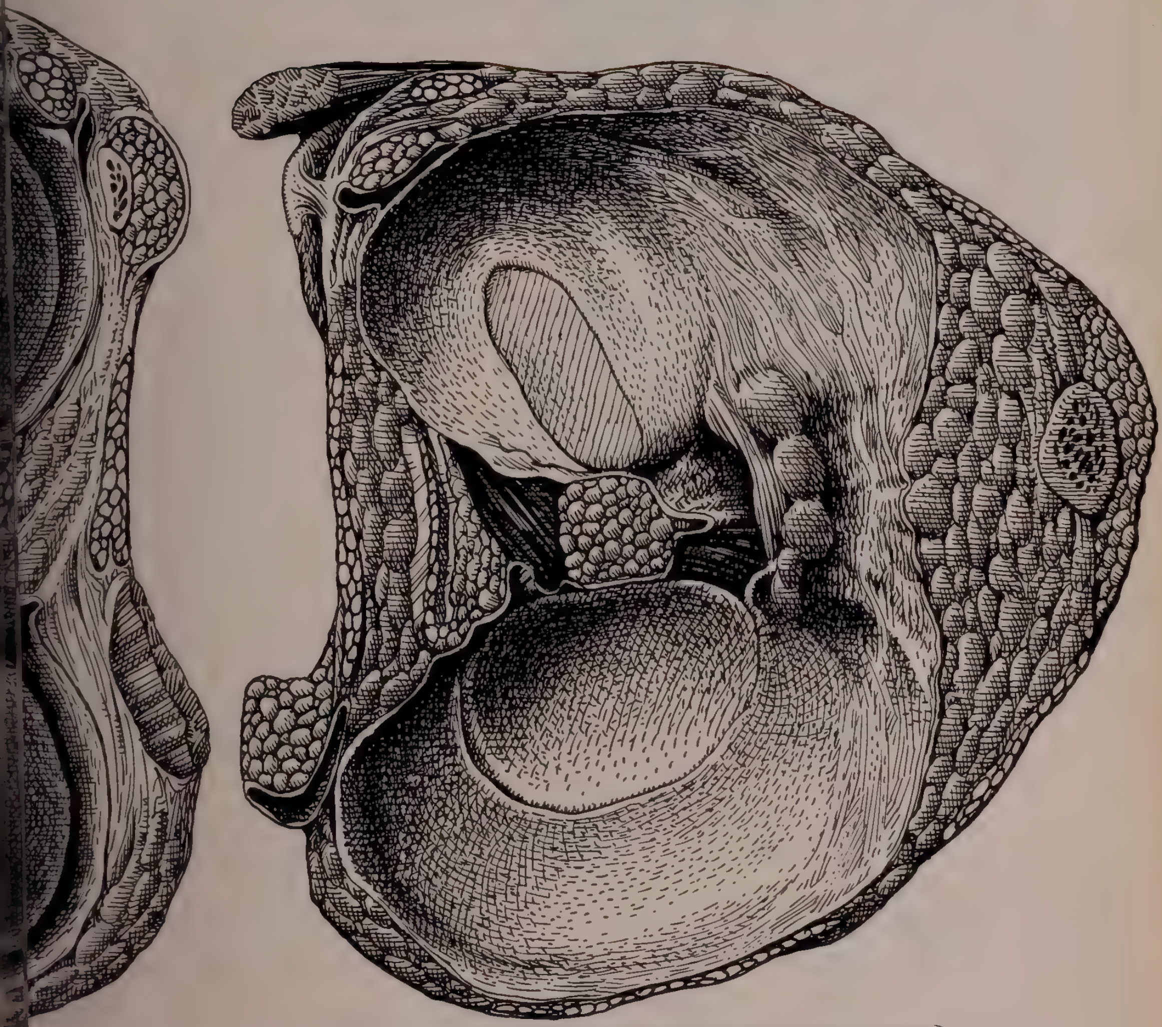

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3:00–5:00	Albert Einstein College of Medicine of Yeshiva University

TUESDAY, MAY 15

1:00–2:30	College of Physicians and Surgeons of Columbia University
2:30–3:30	Public Relations Session
3:30–5:00	University of Buffalo School of Medicine

WEDNESDAY, MAY 16

1:00–2:30	State University of New York, Upstate Medical Center in Syracuse
2:30–3:30	Deans' Panel
3:30–5:00	Cornell University Medical College

THURSDAY, MAY 17

1:00–2:30	State University of New York, Downstate Medical Center
2:30–3:30	Andresen Memorial Lecture
3:30–5:00	New York University School of Medicine

FRIDAY, MAY 18

1:00–2:30	University of Rochester School of Medicine and Dentistry
2:30–3:30	A. Walter Suiter Lecture
3:30–5:00	New York Medical College

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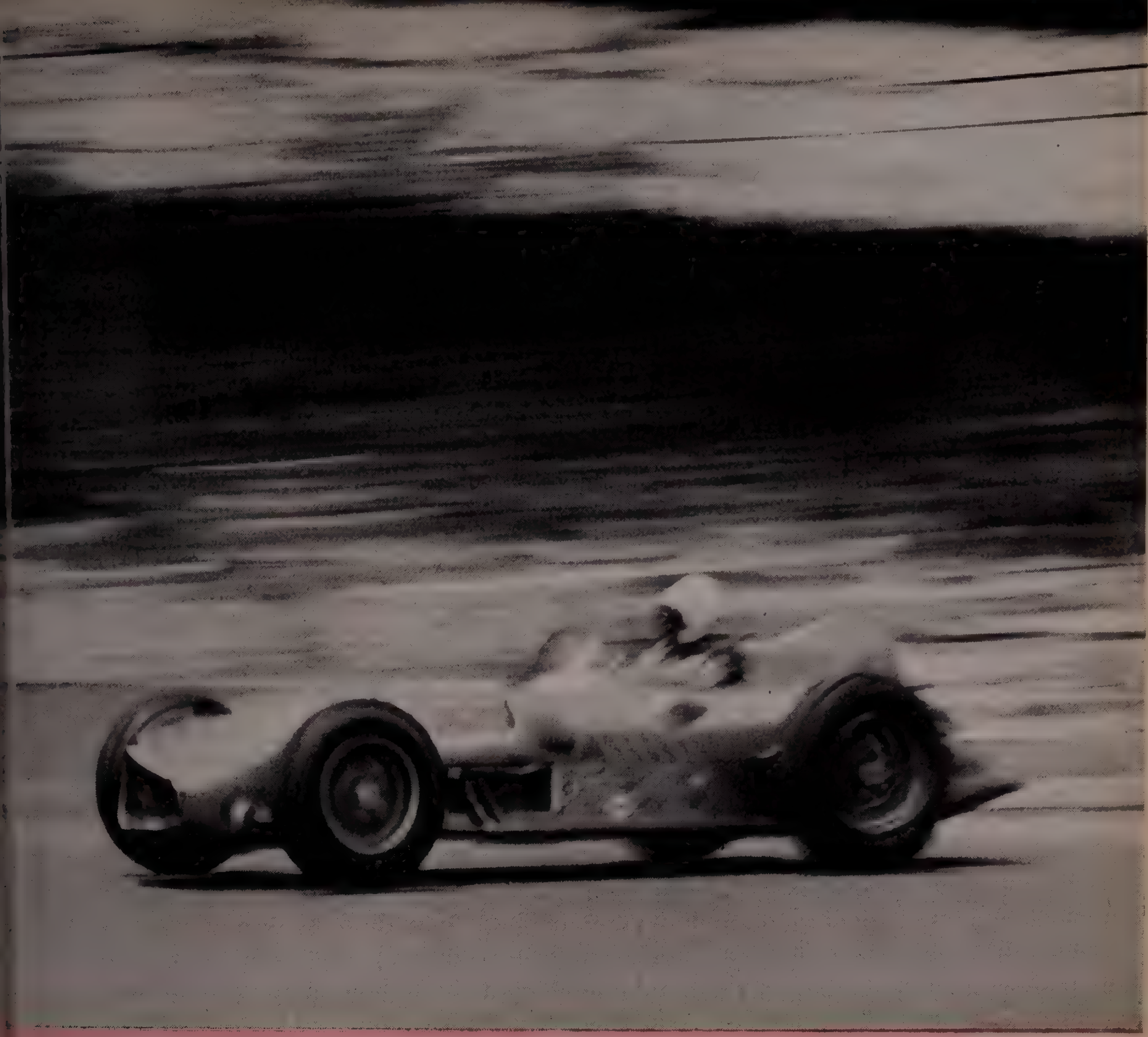

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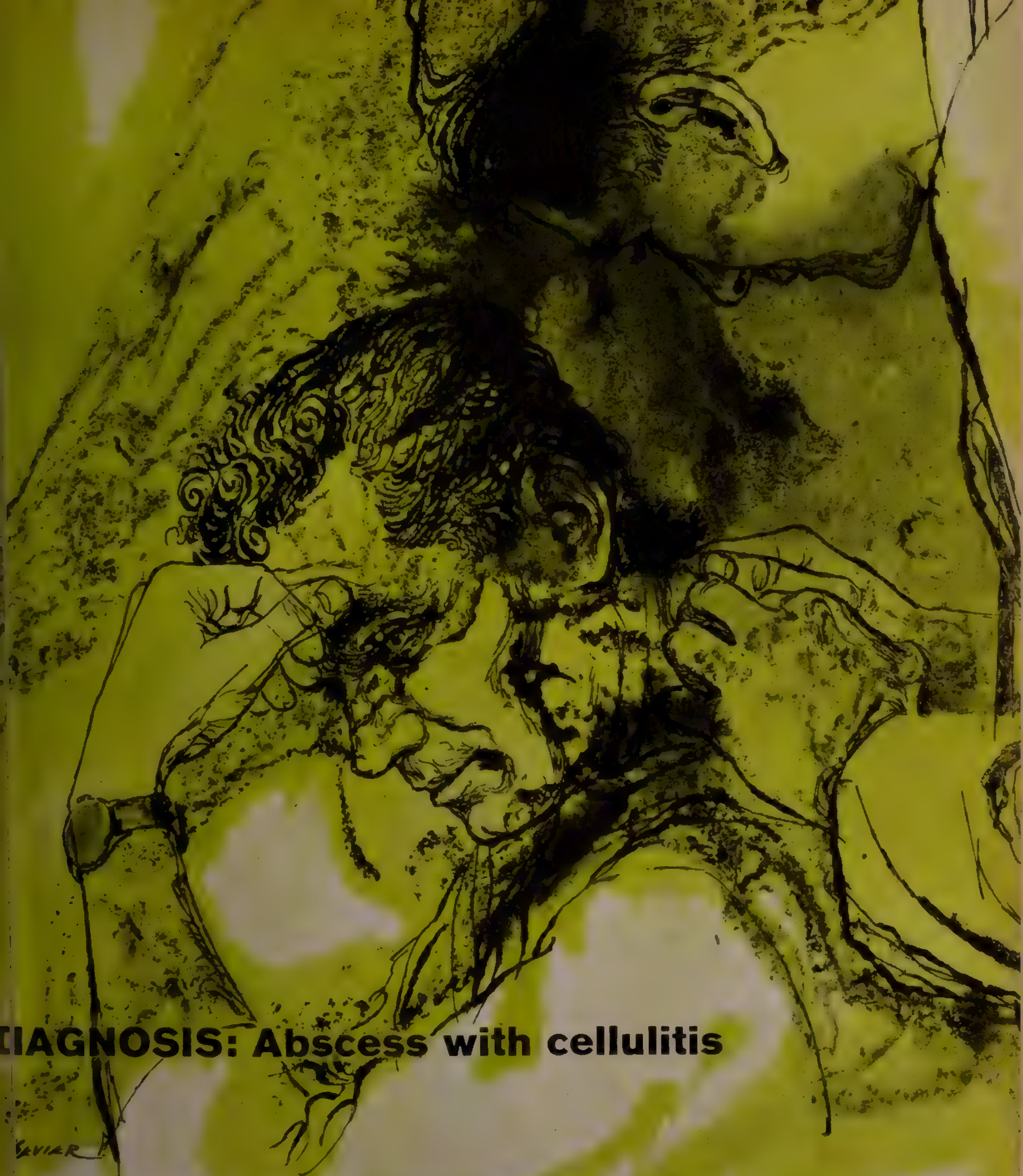

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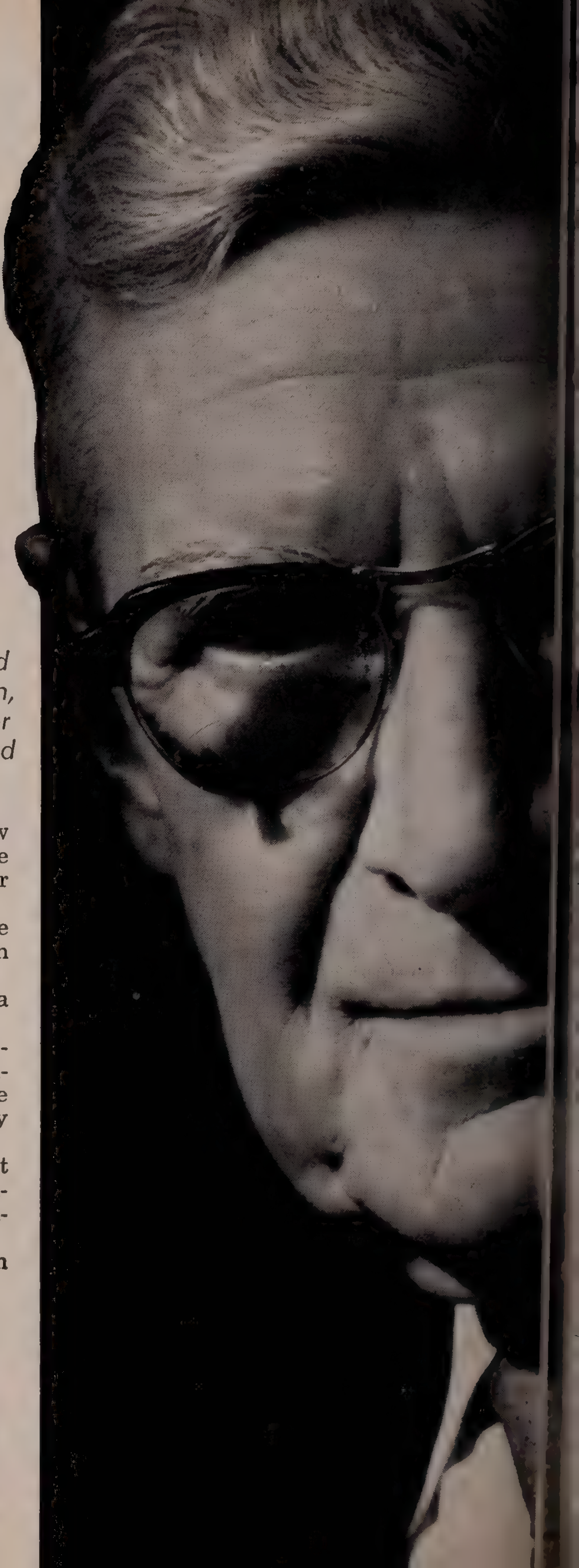

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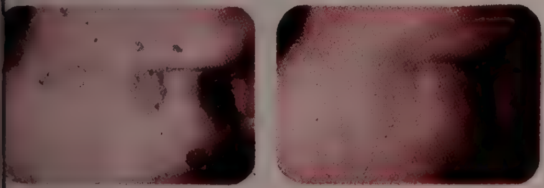

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New York State Journal of Medicine

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Editorials

Wit and wisdom

Humor is a priceless concomitant of wisdom. The truly wise in acquiring their wisdom often acquire also the ability to laugh and to provoke laughter. As we look back on our learning days, the teachers we remember with respect and affection are those who flavored their lectures with humor, whether wry or dry, boisterous or bludgeoning. A famous professor of biochemistry was wont to say, in a fine Scotch burr, toward the end of a long and intricate lecture, when the audience began to show signs of restlessness, "Gentlemen, I have a few more pearls to cast before ye." No one who ever sat at the feet of Andrew MacCallum is likely to forget him.

Such spirits rare in their blooming do appear from time to time. The JOURNAL is fortunate in having enticed into its staff just such a one.

We are pleased to announce that beginning with this issue a monthly column to be known as "Billsbord" will be written for us by William R. Carson, M.D., of Potsdam, New York.

The privilege of knowing Dr. Carson through his column is one our readers will not want to miss. His humor is in the tradition of the late Will Rogers—mischievous and debunking but never needlessly traumatic. Here is medical wit and wisdom, brimful and flowing over, for your enjoyment.

Mental health prospectus

Governor Rockefeller's recommendations to the legislature this year concerning the mental health problems of the people of this State is an orderly, well-reasoned master plan which if implemented should have far-reaching effects.

The over-all objective contemplates intensified application of modern treatment methods in the institutions and in the communities plus expanded and intensified research.

This is to be accomplished by the following means:

1. For mentally ill persons in the State Hospitals.
   (*a*) Intensive retreatment of chronic patients.
   (*b*) Smaller treatment units.
   (*c*) Treatment service designed for special patients.
   (*d*) Improved living conditions.
2. For mentally retarded individuals in the State schools.
   (*a*) Expansion of facilities.
   (*b*) Better care, food, and clothing.
   (*c*) Strengthened central administration direction.
3. For all mentally disabled persons.
   (*a*) Expanded research programs.
   (*b*) Strengthened recruitment and training of personnel.
4. For expanded and coordinated community programs with increased State aid which looks toward the removal of the per capita ceiling.
5. Comprehensive study to modernize admission procedures.

One rewarding facet of these programs is the retreatment of chronic patients.

There are about 30,000 mentally ill patients in the State hospitals who require long-term care and in the past have not responded to treatment.

Many of these patients were admitted prior to the initiation of the dramatic new treatment methods—now provided in all

State hospitals—which have proved so successful on newly admitted patients. Others, while they were exposed on admission to the new treatment methods, did not respond favorably.

Experience at six experimental retreatment units in the State hospitals indicates that with intensive retreatment as many as 10 per cent of these chronic patients can hope to recover and return to their families.

This means new hope for the salvaging of human lives previously considered to be lost. It means also that the State must now set as its goal the intensive retreatment of each chronic patient who has potential for improvement.

As the next major step toward the realization of this goal, the executive budget will provide an increase of over $1 million for seven new special units for the intensive retreatment of chronic patients, thereby more than doubling this aspect of the State's treatment program.

The encouraging results already experienced in this program for chronic patients look forward to the day when these special units will exist in every State hospital, side by side with strengthened and expanded intensive treatment units for the newly admitted and acutely ill patients.

No attack on a problem of such magnitude as mental disorder can advance without research to light the way. From research must come the improved methods of treatment and of prevention of illness and disability.

The State of New York Department of Mental Hygiene recently has made significant contributions along a broad front, ranging from the development and evaluation of psychiatric drug therapy and the establishment of open hospital technics to greater knowledge of the basic chemistry of the nervous system and pioneering work in metabolic disease as a cause of mental retardation.

Still greater efforts are required to realize the potentials for further development, particularly in the areas of mental retardation, child psychiatry, drug addiction, alcoholism, and other conditions.

To meet the needs in research, the State has undertaken a large-scale program for the expansion of its research facilities. This program includes: the Institute for Research in Mental Retardation on Staten Island, the first of its kind in the nation; the Institute for Research in Narcotics Addiction on Ward's Island in New York City; the Institute on Drug Research at Manhattan State Hospital; the expansion for the Research Building at Rockland State Hospital; and the research unit in the new Bronx State Hospital.

Regional mental health boards provide the intimate approach for dealing with mental health needs.

A comprehensive State program for mental health can be effective only if mental health services in the community are strong and are operated in coordination with the services provided by the State.

A mental patient's well-being and his chance for recovery are best served if he can be treated at home while maintaining ties with his family and community. Strong local programs, coordinated with the clinical services of State hospitals, can assure early treatment and, in many cases, recovery before the removal from family and familiar surroundings becomes necessary. In cases requiring hospitalization, such programs can help prevent relapses and maintain patients at home following their release.

The State hospital is no longer a long-term refuge for mentally ill persons from the community, but must be recognized as just one type of facility among a variety of services in the community, designed for all kinds and stages of mental disorders and provided by the State and the localities.

Community clinics and psychiatric units in general hospitals must be extended and enlarged to form a network of accessible facilities serving the community.

Moreover, nursing homes, homes for the aged, and like community facilities, working with community clinics, are more appropriate places of care than the State hospitals for many aged persons with mild mental symptoms. There must be an increase in the use of these facilities, together with increased community psychiatric consultation for this purpose.

This expansion of State-aided community services and their full integration with the State hospital program are of major importance to the future of mental health in New

York.

Important first steps have been taken toward this goal:

In 1960 the legislature raised the per capita ceiling on State reimbursement for community mental health expenditures from $1.00 to $1.20.

In addition, the State has been divided into 10 mental health regions, and regional advisory committees, representing the State institutions and local mental health boards, have undertaken to develop plans for coordinated State-local services.

Much remains to be done. Further legislation is recommended which will raise the per capita ceiling on State reimbursement for community mental health expenditures another 20 cents to $1.40, as a further step in the direction of complete removal of the ceiling, and provide for community mental health boards and directors to participate and cooperate with the State institutions in preadmission screening and posthospital care of mentally disabled persons.

Laws related to the mentally ill need recodifying. Many of the laws relating to admission to mental hospitals are responsive not to today's needs, but to the practices of over a century ago, when the "insane asylum" was used as a fortress for society's protection and not as a hospital for the treatment and rehabilitation of the patient.

Many complex and anachronistic provisions frequently work to the detriment of mentally ill persons who are in need of the modern treatment which mental hospitals now provide.

It has been recognized that the laws relating to admissions are in need of comprehensive revision to reflect the great advances in treatment methods and social attitudes, which have changed the mental hospital from a place of incarceration to a place of hope and cure. At the same time, effective safeguards of due process must be incorporated to protect basic individual rights and liberties.

A comprehensive study of admission procedures under New York State law has been undertaken by a special committee sponsored by the Association of the Bar of the City of New York and Cornell Law School. This special committee has been working closely with the State of New York Department of Mental Hygiene. The committee's report and recommendations are to be published during 1962.

There have been historic breakthroughs during the long transition from the static concept of custodial care for our mentally ill patients to the successful and gratifying treatment concept on which we now base our concern and care.

One great achievement has been that people no longer are afraid to talk about mental illness or to seek care and treatment openly. Mental illness is no longer a silent stigma to be borne in despair without hope; it is a sickness that can be treated effectively.

The advances in treatment of the mentally ill which we can now provide and the intensive research in progress give hope that we may yet attain a major breakthrough comparable in its human significance to that achieved for tuberculosis and infantile paralysis.

Attack on the fourth

Accidents now rank fourth in the United States in causes of death, being exceeded only by heart disease, cancer, and cerebrovascular accident in that order. There has been a remarkable stability in the number of deaths from accidental injury since the late 1930's, but when these are measured against population growth it is evident that the risk of accidental death has actually diminished.

The National Safety Council states that in 1960 accidents caused somewhat over 5 per cent of all deaths in the United States; this represented 9.5 million injuries of which 360,000 resulted in some degree of permanent disability.

Fatal accidents at work have declined from 43 per 100,000 workers in 1937 to 22 per 100,000 workers in 1960—a tribute to safety enforcement by industry.

Deaths from accidents in sports and recreation generally are down—from 21,000 in 1928 to 16,500 in 1960.

Motor vehicle accidental deaths are a vexing problem, 38,200 in 1960, but even here the Safety Council states that, considering the phenomenal increase in mileage traveled, safety in motor vehicle travel has actually increased substantially since early in the century.

Deaths from accidents in the home stand at 30 per cent of all accidental deaths, and almost half of these resulted from falls suffered by persons sixty-five years of age and over.

The greatest opportunity for further progress in reducing accident mortality rests on more public education to prevent accidents in the home. Much is being done in mass education by public health authorities, but this could be further implemented by the practicing physicians who are in and out of people's homes each day. A cautionary word about poor lighting, the ubiquitous scatter rug, or the disorganized medicine cabinet might work wonders. The number of fatal home accidents could be cut appreciably by such a concerted effort to spread the gospel of safety.

Secure sterilization

In view of the prevalence of both virus A and virus B hepatitis, the matter of adequate sterilization of instruments comes to the fore. The known high incidence of infectious hepatitis among drug addicts, whose injection technics are loosely controlled is but one instance.

When one considers that the carrier state in the blood for infectious hepatitis lasts for eight months and for serum hepatitis for five years, the possibility of contamination is relatively high.

The development of disposable materials for office and hospital use over the past several years makes it now possible to have absolute sterilization at reasonable cost.

This cost stands in favorable relation to that of older methods, when depreciation and time cost is figured as the following table* demonstrates:

Approximate cost of disposable and reusable instruments

		Reusable		
Item	Disposable (Cents)	Depreciation (Cents)	Time-Cost† (Minutes) Cents	Total (Cents)
Hypodermic needle	5	..	(2) 8	8
Syringe	10	2	(4) 16	18
Syringe with needle (regular or cartridge type)	12	2	(6) 24	26
Rubber gloves	25	5	(7) 28	33
Lancets	1.5	..	(½) 2	2
Scalpel blades	12	2	(3) 12	14

† Estimated at time-cost of nurse or technician on salary of $2.40 per hour or 4 cents a minute.

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* Medical World News 3: 47 (Jan. 19) 1962.

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	11.00 ☐	12.50 ☐	14.00 ☐	15.50 ☐
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	13.50 ☐	15.00 ☐	16.50 ☐	18.00 ☐
	14.00 ☐	15.50 ☐	17.00 ☐	18.50 ☐
Twin-Bed Room with Bath for two—per day	15.00 ☐	18.00 ☐	20.50 ☐	22.50 ☐
	16.00 ☐	18.50 ☐	21.50 ☐	24.00 ☐
	16.50 ☐	19.50 ☐	22.00 ☐	25.00 ☐
Suite—Living Room, Bed Room and Bath			36.50 ☐	40.00 ☐
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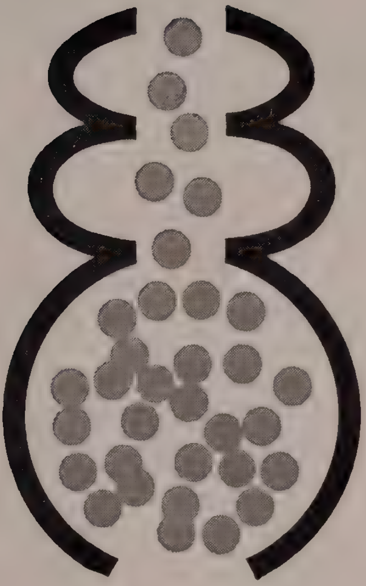

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1. Demeulenaere, L.: Action du R 1132 sur le transit gastrointestinal, Acta Gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.
2. Kasich, A. M.: Treatment of Diarrhea in Irritable Colon, Including Preliminary Observations with a New Antidiarrheal Agent, Diphenoxylate Hydrochloride (Lomotil), Amer. J. Gastroent. 35:46-49 (Jan.) 1961.
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Scientific Articles

An Evaluation of Results of Surgical Correction for Valvular Heart Disease

GEORGE R. HOLSWADE, M.D.
New York City
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New York City

From the Department of Surgery,
The New York Hospital-Cornell Medical Center

GREAT ADVANCES *have been made in the correction of deformities of the heart valves. Both acquired and congenital valvular heart disease have become amenable to surgery with increasing success. The evolution of the surgical treatment for valvular heart disease has progressed through several stages to the present era of partial and complete valve replacement with prosthetic valves. It is too early to evaluate the latter development, and the ultimate composition of the prosthesis has not been determined. The procedure and the results vary with the type of valvular disease. Surgery is particularly successful in congenital valvular stenosis and acquired mitral stenosis. The treatment often is conditioned by widespread involvement of the heart with the presence of other valvular conditions.*

DURING THE PAST thirteen years great advances have been made in the correction of deformities of the heart valves. Both acquired and congenital valvular heart diseases have become amenable to surgery with increasing success. Rheumatic fever has accounted for most acquired deformities of the cardiac valves which have come to surgery, although bacterial endocarditis and trauma have produced defects in heart valves which could be corrected surgically in a few cases. The damage from rheumatic fever has affected the mitral, aortic, and tricuspid valves in that order of frequency, with rare involvement of the pulmonic valve. Congenital valvular heart disease, on the other hand, is seen with greater frequency on the right side of the heart than on the left, and stenosis of the pulmonic valve is one of the more common lesions.

The evolution of the surgical treatment for valvular heart disease has progressed from blind finger fracture and valvulotome cutting and stretching of valves, through direct vision valvuloplasty with the aid of hypothermia and cardiopulmonary bypass, up to the present era of partial and complete valve replacement with prosthetic valves. It is too early at this time to evaluate this latter development properly, and actually one can only speculate now on the future of complete valve replacement. Whether the ultimate form of the device will be anatomically bicuspid or tricuspid or mechanically ball valve is uncertain. Also, the ultimate composition of the prosthesis is undetermined; autografts, homografts, Dacron and Teflon synthetic fabrics, polyurethane, and silicone rubber all have certain drawbacks. Certainly any prosthetic valve will be subjected to tremendous trauma and stress since it will open and close some 37 million times a year.

Acquired tricuspid stenosis

The classic patient with acquired tricuspid stenosis is usually a woman who is considered to have rheumatic mitral stenosis with auricular fibrillation, ascites, and edema. The relative paucity of acute paroxysmal nocturnal dyspnea and the pulmonary

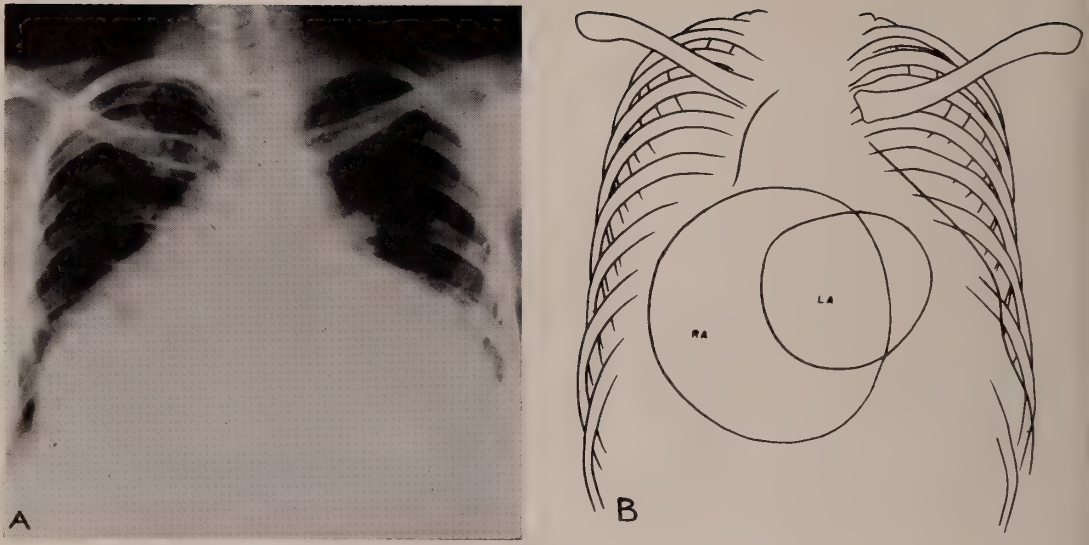

FIGURE 1. Case 1. (A) Roentgenogram of chest showing huge heart with four-chamber enlargement. (B) Line drawing of angiocardiogram showing tremendous right atrium (RA) and large left atrium (LA).[8]

apoplexy type of hemoptysis is important clinically in suggesting the diagnosis of tricuspid stenosis. It is often difficult to distinguish between the murmurs of mitral and tricuspid stenosis, and the final diagnosis usually rests on establishing a transvalvular gradient by cardiac catheterization.

Although acquired tricuspid stenosis is most commonly due to rheumatic fever, it can be caused by systemic lupus erythematosus; carcinoid, endocardial fibroelastosis; and endomyocardial fibrosis. Without damage to the valve leaflets the tricuspid orifice may be obstructed partially by a myxoma arising from the interatrial septum.[1]

Tricuspid stenosis due to rheumatic fever resembles the pathologic changes seen in the mitral valve. The valve leaflets are thickened and scarred. Shortening of the papillary muscles and chordae tendineae produces further distortion of the scarred valve. Fusion of the scarred leaflets occurs at the commissures and in the subvalvular region between the chordae tendineae. Calcifications are encountered much less frequently in the rheumatic tricuspid valve than in the rheumatic mitral valve. An obstruction at the tricuspid valve produces changes in the right atrium with hypertrophy of the wall and chamber enlargement. Isolated tricuspid stenosis is seldom encountered but usually occurs in conjunction with rheumatic involvement of the mitral and aortic valves. Thus it represents, in many cases, only a part of an extensive disease process involving the heart and its valves.

Case 1.[2] A thirty-seven-year-old white woman was admitted to The New York Hospital in March, 1953, in heart failure. There was no history of acute rheumatic fever, but the diagnosis of rheumatic heart disease with mitral stenosis and mitral insufficiency had been made fifteen years previously. For the five years prior to admission she had progression of her cardiac symptoms with marked fluid retention. There were the murmurs of mitral stenosis and insufficiency and tricuspid stenosis and insufficiency. The liver was enlarged, and there was considerable accumulation of fluid in the abdomen and lower extremities.

A roentgenogram of the chest (Fig. 1A) revealed a huge globular heart with four-chamber enlargement but remarkably little pulmonary congestion. An angiocardiogram (Fig. 1B) showed a huge right atrium, 13 by 13 cm. in frontal projection, and a left atrium that was three times the normal size. On cardiac catheterization the mitral valve area was 1.1 sq. cm., the tricuspid valve area was 0.9 sq. cm., and the diastolic gradient over the tricuspid valve was 16 mm. of Hg at rest, increasing to 22 mm. of Hg after exercise. On March 19, 1953, a successful valvulotomy was carried out on a heavily calcified mitral valve, the mitral orifice being increased from less than 1 sq. cm. to between 2 and 3 sq. cm.

At a second operation four weeks later a tricuspid valvulotomy was performed. The surgeon estimated the orifice to be between 0.5 and

1 sq. cm. in an exceedingly thin, flimsy, and already insufficient tricuspid valve. Very slight digital pressure was all that was required to produce a lateral split which increased the orifice to between 3 and 4 sq. cm. and produced further regurgitation. For approximately one year after the operation she was dramatically improved, although the heart remained greatly enlarged, and the murmur of tricuspid insufficiency was more prominent. During the next three years there were repeated episodes of heart failure with increasing fluid retention until she finally died four years after her operation.

Because tricuspid stenosis is associated so frequently with mitral valvular disease which is of greater clinical importance, its correction is usually attempted after the latter has been dealt with. In the case just described this was done in two stages because of the critical condition of the patient, but it may be accomplished at one operation. Bailey and Morse[3] have described a right-sided approach to both valves, and Harken and Black[4] have demonstrated that a finger fracture of both the mitral and the tricuspid valves may be done through the left side of the chest. The patient in the case just presented was improved at first because of the relief of both the mitral and tricuspid stenosis, but the tricuspid insufficiency which was increased at operation undoubtedly was a prominent factor in her eventual downhill course and death. A finger fracture commissurotomy of the tricuspid valve is readily accomplished, but a much lighter touch must be used than on the mitral valve, or serious insufficiency may result.

Congenital anomalies of the tricuspid valve

Congenital tricuspid stenosis or atresia of the tricuspid valve may occur in combination with other cardiac anomalies, the principal ones being atrial septal defect, pulmonary stenosis, and hypoplasia of the right ventricle. Ebstein's anomaly of the tricuspid valve is a rare condition in which the septal and posterior leaflets of the tricuspid valve are attached to the right ventricular wall near its apex. The resultant tricuspid orifice is usually small, and there may be insufficiency. An atrial septal defect nearly always is present in Ebstein's anomaly, and varying degrees of cyanosis are seen.

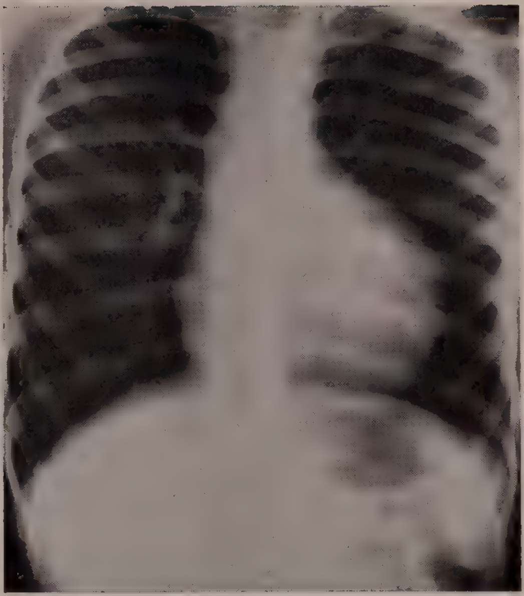

FIGURE 2. Case 2. Roentgenogram of chest showing decreased vascular markings, left ventricular enlargement, and a concavity in the region of the pulmonary artery.

For many years the surgical treatment for tricuspid atresia has been a system artery-pulmonary artery shunt either by a Blalock or Potts procedure. In general, the risk of this operation has been greater in patients with tricuspid stenosis than for patients with tetralogy of Fallot. In a series of 64 patients on whom a Blalock procedure was performed at The New York Hospital-Cornell Medical Center between 1952 and 1958 the operative mortality was 30 per cent for patients with tricuspid atresia and 7 per cent for patients with tetralogy of Fallot. The late results following the shunting procedure have not been too encouraging, with deaths due to heart failure and thrombosis of the shunt and a tendency of the child to outgrow the shunt.

CASE 2. A seven-year-old white boy was admitted to The New York Hospital in 1954 because of increasing cyanosis, dyspnea, and squatting on exertion. There was moderate cyanosis and clubbing of the nails. A soft systolic murmur was heard in the aortic area. An electrocardiogram showed marked left axis deviation. A roentgenogram of the chest (Fig. 2) showed diminished vascular markings, prominence of the left ventricle, and a concavity in the region of the pulmonary artery. Angiocardiograms showed an enlarged right atrium, a rudimentary right ventricle, and no dye passing through the pulmonary artery. The

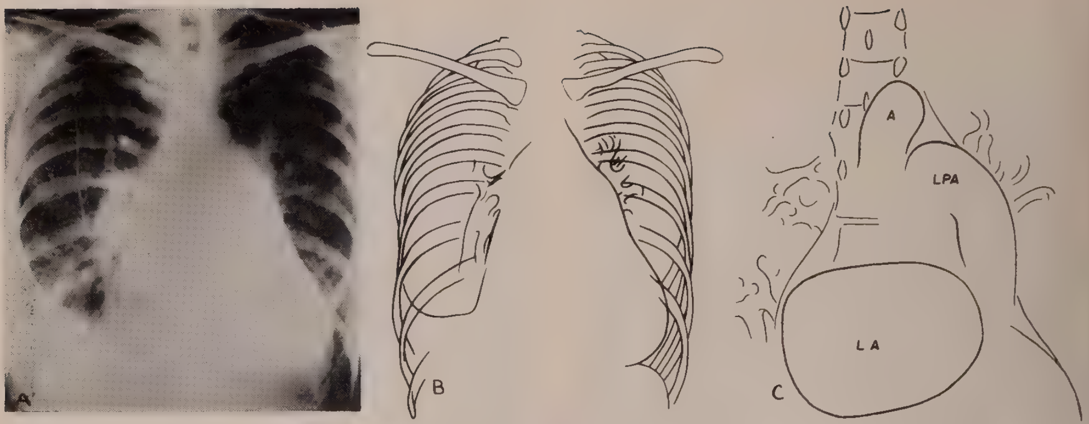

FIGURE 3. Case 3. (A) Roentgenogram of chest. (B) Line drawing showing enlargement of right ventricle and prominent pulmonary artery and branches. (C) Line drawing of angiocardiogram showing greatly dilated left atrium (LA) and pulmonary artery (PA).[8]

hematocrit was 62 and the hemoglobin 20 Gm. per 100 ml. On August 31, 1954, a Blalock procedure was performed. Because of the small size of the pulmonary artery the anastomosis was performed end-to-end between the left subclavian artery and the distal end of the left pulmonary artery. Following the operation the cyanosis was decreased, and his exercise tolerance was increased greatly. When he was last seen four and one-half years after his operation there was minimal cyanosis, and he was able to climb the two flights of stairs in the school he attended. The hemoglobin remained elevated at 18.5 Gm. per 100 ml. A continuous murmur was present.

A more recent procedure for congenital defects of the tricuspid valve has been an anastomosis between the superior vena cava and the distal end of the right pulmonary vein as popularized by Glenn[5] in this country. A similar procedure for patients with decreased pulmonary circulation has been reported from Russia by Bakulev and Kolesnikov.[6] In the Russian version of this operation the anastomosis has been performed end-to-end, necessitating temporary caval occlusion leading to cerebral edema and a high mortality rate of 34 per cent. In this country the performance of an end-to-side anastomosis between the right pulmonary artery and the superior vena cava followed by ligation of the vena cava between the anastomosis and the right atrium has permitted a less hurried anastomosis without the danger inherent in acute temporary obstruction of venous return from the upper portion of the body. This has resulted in a considerably lower mortality rate.

There have been no large series of patients reported who have had superior vena cava to distal right pulmonary artery anastomosis, but the evidence to date indicates that this is a satisfactory procedure. It provides for the direct delivery of venous blood to the lungs, does not increase the work of the left side of the heart, and the work of the right side of the heart is decreased. Edema of the upper extremities has not been a problem. In the small series that has been reported the patients have been improved greatly, and a few patients have been followed for two years.[7] However, the number of patients treated by this procedure is still too small and the follow-up period too short for a complete evaluation.

Acquired tricuspid insufficiency

Acquired tricuspid insufficiency without stenosis is seen most frequently in patients with severe mitral stenosis of long standing. The obstruction at the mitral valve with increased pressure in the pulmonary circulation leads to right ventricular failure and dilatation. As dilatation increases the entire tricuspid ring enlarges. There is no corresponding lengthening of the chordae tendineae, and tricuspid regurgitation occurs in a valve which may not have been primarily affected by rheumatic fever. In our experience 16 per cent of patients coming to mitral valvulotomy have had evidence of significant tricuspid insufficiency, although mitral stenosis has been the predominant lesion.[8]

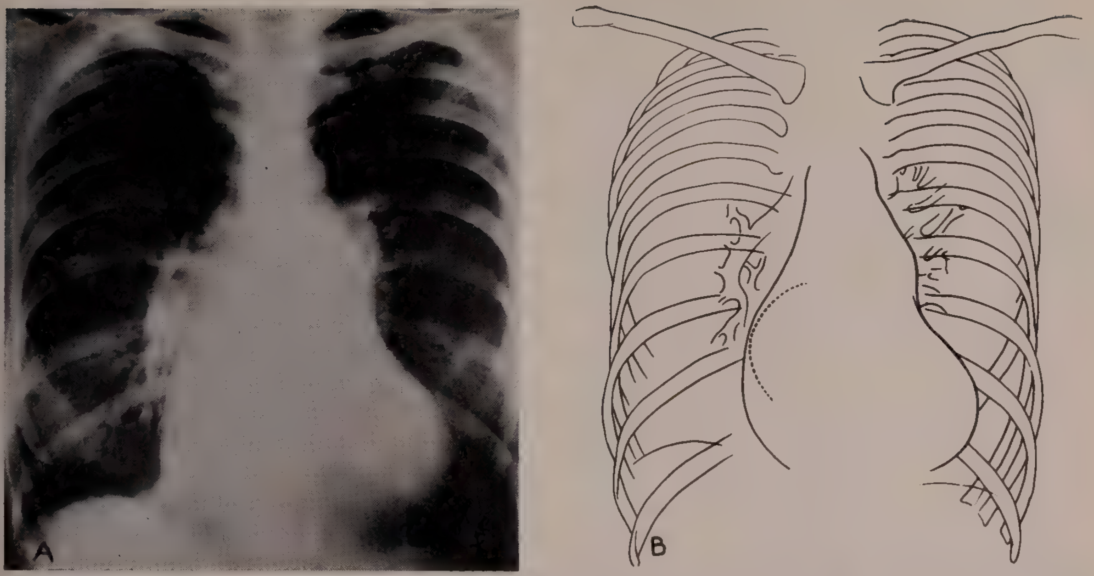

FIGURE 4. Case 3. Two years after operation. (A) Roentgenogram of chest. (B) Line drawing showing considerable decrease in heart size.[8]

The correction of mitral stenosis by finger fracture in such patients has resulted in varying degrees of improvement. The greatest improvement is to be observed among those patients whose rheumatic disease has been of relatively short duration and whose pulmonary vascular bed has not undergone obliterative changes which are irreversible.

Case 3. A forty-seven-year-old woman had rapid progression of exertion dyspnea, orthopnea, and hemoptysis. Auricular fibrillation was present, and there were the murmurs of mitral stenosis and insufficiency and tricuspid insufficiency. The liver was enlarged. The electrocardiogram showed right ventricular hypertrophy. A roentgenogram of the chest (Fig. 3) showed moderate cardiac enlargement with a prominent right ventricular outflow tract, large pulmonary artery, enlarged left atrium, and prominent hila of the lungs. Cardiac catheterization revealed evidence of tricuspid insufficiency along with severe mitral stenosis and greatly increased pulmonary vascular resistance. The cardiac index was well below normal and was further decreased by exercise. After a satisfactory mitral valvulotomy in which the mitral orifice was increased from 0.5 to 3 sq. cm. the patient was greatly improved. A roentgenogram of the chest taken two years after surgery (Fig. 4) showed the cardiac shadow and the pulmonary artery and its branches to be smaller. A cardiac catheterization that was done also two years after the operation showed an increase in the cardiac index which now increased with exercise. Pulmonary vascular resistance, although not normal, was one-third the preoperative figure and increased only slightly with exercise. There was less evidence of tricuspid insufficiency as evidenced by the pressure curve in the right atrium. Five years after the operation she was working full time as a librarian and was able to do all her housework. The murmur of tricuspid insufficiency was still present, but there was no edema and no enlargement of the liver.

Thus the approach to the correction of tricuspid insufficiency in most cases has been an indirect one of relieving the mitral stenosis. The success of this attempt depends on the degree of reversibility of the changes that have resulted primarily from the mitral stenosis.

Some surgeons have advocated a more radical approach to the problem of combined mitral stenosis and tricuspid insufficiency. Julian *et al.*[9] reported a series of 8 patients in whom both valves were approached directly with the aid of cardiopulmonary bypass. His approach was through the right atrium and in turn the atrial septum to do an open commissurotomy on the mitral valve. Then annular plication of the tricuspid valve at two commissures was carried out. The high mortality involved in the open procedure has not led to any extensive application of this technic. Possibly in certain selected cases, now that the technic of extracorporeal circulation has been improved, this procedure can be used more safely.

Acquired pulmonic valvular disease

Acquired stenosis of the pulmonary valve is a rare condition of which rheumatic fever is the most common cause. However, of all the cardiac valves the pulmonic is the valve affected least by the rheumatic process. Autopsy studies on patients who died with rheumatic heart disease have indicated involvement of the pulmonic valve in approximately 5 per cent of the cases. In such cases clinically the pulmonic valve involvement is almost completely overshadowed by disease of the other heart valves. Acquired pulmonic stenosis from causes other than rheumatic fever occurs occasionally and often is associated with systemic diseases, such as malignant carcinoid tumors of the small intestines with metastases, tuberculosis, and diffuse Echinococcus infection. Pulmonic stenosis due to compression of the pulmonary artery by a malignant intrapericardial tumor has been reported.[10]

Pulmonic valvular insufficiency

Insufficiency of the pulmonary valve is an extremely rare form of congenital heart disease. Only a few cases have been reported, and in general it has been regarded as a condition which is well tolerated by the patient and which is compatible with a long life expectancy. However, under certain circumstances pulmonary insufficiency can be the cause of death in infancy.

CASE 4.[11] A two-day-old white male infant was admitted to The New York Hospital on May 1, 1959, in congestive heart failure. The infant was deeply cyanotic with a pulse of 160 per minute and respirations of 90 per minute. There was generalized edema of the face and extremities. A Grade IV rough systolic murmur and a Grade II decrescendo diastolic murmur were heard along the left sternal border from the second to the fourth interspaces. The second heart sound in the pulmonary area was diminished. The liver was enlarged greatly. Chest roentgenograms demonstrated marked right-sided cardiac enlargement. The electrocardiogram showed evidence of right auricular enlargement, incomplete right bundle branch block, and right ventricular hypertrophy. A clinical diagnosis of severe valvular pulmonary stenosis was made. Rapid digitalization and mercurial diuretics resulted in little improvement. An emergency operation was performed under hypothermia for the purpose of opening up what was thought to be a stenosed pulmonic valve. However, when the valve was exposed with inflow occlusion of the vena cava, there was no pulmonary stenosis. Instead there were rudimentary tags of glistening puckered valvular tissue around the dilated annulus resulting in a grossly incompetent pulmonary valve (Fig. 5). Ventricular fibrillation developed, and resuscitative efforts were to no avail. At the postmortem examination the heart weighed twice the normal weight. In addition to the deformity of the pulmonary valve, there was a patent ductus which measured 1 cm. in diameter.

Acquired insufficiency of the pulmonary valve is usually the result of operations performed for pulmonic valvular stenosis. In the early open operations for congenital valvular pulmonic stenosis performed under hypothermia it was a common practice to remove a small portion of the conical tip of the valve. Even in operations performed with extracorporeal circulation where there is plenty of time for a careful examination of the stenosed pulmonic valve and careful plastic procedure on the valve, there are many cases in which an adequate opening of the valve cannot be achieved without producing some pulmonary insufficiency. There is evidence that pulmonary insufficiency produced in this manner is tolerated well unless it is complicated by pulmonary artery hypotension or increased pulmonary blood flow.[12] The degree of valve tissue remaining is also an important factor, as evidenced by Case 4.

Congenital pulmonic valvular stenosis

Stenosis of the pulmonary valve is a fairly common form of congenital heart disease in which the surgical results for the most part have been excellent. It may occur in combination with defects in the ventricular septum, as in tetralogy of Fallot, or it may be associated with defects in the atrial septum. There may be associated patent foramen ovale, but the isolated or pure form is encountered most frequently. This discussion will be concerned with valvular pulmonic stenosis without ventricular septal defects.

In valvular pulmonic stenosis with intact ventricular septum there is little variation

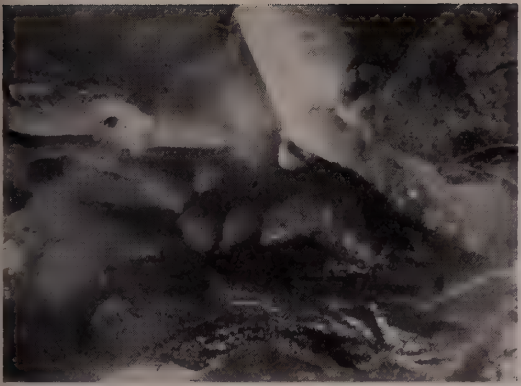

FIGURE 5. Case 4. Autopsy specimen showing rudimentary tags of incompetent pulmonary valve.[11]

in the basic configuration of the valve which consists of a conical-shaped diaphragm with a central opening. The degree of the stenosis varies with the size of the central aperture in the cone. Often the line of diffused commissures may be seen as a radial thickening of the valve on its upper surface. These may be missing centrally, but usually near the annulus of the valve the fused commissures can be identified. Existing independently or in combination with valvular stenosis there may be obstruction in the infundibular portion of the right ventricle. In its simplest form the infundibular obstruction is a mere diaphragm, or infundibular obstruction may be due to localized hypertrophy of cardiac muscle. One of the most interesting forms of infundibular obstruction is that involving the outflow tract to the right ventricle diffusely and resulting from severe valvular obstruction of long standing.

In pulmonic valvular stenosis the pressure in the right ventricle is increased above the normal of 25 mm. Hg. The right ventricular pressure usually exceeds 60 mm. Hg before an operation is warranted. In some cases the right ventricular pressure becomes quite high and may exceed 200 mm. Hg. It has been our policy to determine the pressure gradient over the pulmonic valve preoperatively by cardiac catheterization. A fairly accurate estimate of the right ventricular pressure may be obtained based on the amplitude of the V_1 precordial lead on the electrocardiogram.[13] By selective angiocardiography valuable information may be obtained concerning the anatomy of the valve itself, the pulmonary artery, the outflow tract of the right ventricle, and the degree of the hypertrophy of the right ventricular musculature.

The surgical attempts at correction have followed the patterns accorded other intracardiac lesions. The initial attack was that of Brock[14] of England consisting of a transventricular approach with a valvulotome and a series of dilators. The results following the Brock procedure were unpredictable and far from satisfactory. This indirect approach was followed by the open method first using hypothermia alone and later using extracorporeal circulation. The operation using the artificial heart-lung machine had many advantages over hypothermia alone, the chief of which was the removal of the time restriction for the procedure on the valve. The surgeon was able now not only to correct the valvular deformity more meticulously but to close atrial septal defects, excise obstructing infundibular membranes, and remove hypertrophied muscle from the outflow tract of the right ventricle as indicated. Certainly a more complete operation was possible.

The results following operations for valvular pulmonic stenosis in general have been good. The risk of the operation has been increased considerably in those patients with very high right ventricular pressures and in those patients in whom an immediate drop in right ventricular pressure was not achieved following valvulotomy. In our series of 40 patients operated on by the open technic, 11 operations were performed under hypothermia alone and 29 with the aid of extracorporeal circulation. In this group the age range was from eleven months to fifty-one years. The over-all operative mortality was 10 per cent. However, omitting the patients with preoperative right ventricular pressure in excess of 200 mm. Hg dropped the operative mortality to 6 per cent. The mortality for the group with the high ventricular pressures was 40 per cent.

Three of the four deaths in this series occurred early in the postoperative period in patients in whom a satisfactory reduction in right ventricular pressure had not been achieved despite what appeared to be an adequate pulmonic valvulotomy. In these cases the right ventricular outflow tract remained obstructed because of marked hypertrophy of the right ventricular muscle throughout the outflow tract. In 4 other patients, however, in whom right ventricular pressures remained high immediately after adequate valvulotomy, there was a gradual fall in right ventricular pressure over the course of several months until normal pressures were reached at the time of cardiac catheterization approximately one year following the surgery.[15] Thus it would seem that under these circumstances if the patient can survive the first few days postoperatively, there is an excellent chance that over the course of the next few months the hypertrophied right ventricular muscle will regress, and the right ventricular pressure will fall. Some surgeons have advocated routinely the resection of hypertrophied muscle secondary to valvular obstruction when there is no satisfactory decrease in the gradient over the valve, but this means placing the added burden of a right ventriculotomy on the heart and does not seem justified in all cases. The greatest problem in pulmonic valve surgery today is the selection of cases for the resection of secondarily hypertrophied right ventricular muscle.

In the majority of cases in our series, however, there was a satisfactory fall in the right ventricular pressure after valvulotomy. The average preoperative systolic gradient over the pulmonic valve was 132 mm. Hg. Immediately following the operation the average systolic gradient over the pulmonic valve was 29 mm. Hg. In 2 cases combined infundibular and valvular stenoses were corrected. In 4 cases associated atrial septal defects of the ostium secundum type and in 2 cases patent foramen ovale were closed during the same procedure.

Case 5. A three-year-old white boy had a known heart murmur since birth, but his growth and development had been essentially normal. On physical examination there was a Grade IV harsh systolic murmur loudest in the pulmonic area but heard throughout the precordium. The pulmonic second sound was absent. A roentgenogram of the chest showed dilatation of the pulmonary artery (Fig. 6). An electrocardiogram showed right ventricular hypertrophy. At operation the right ventricular pressure was 175/0, and the pulmonary artery pressure was 20/18 mm. Hg. Six months earlier at cardiac catheterization the right ventricular pressure had been recorded at 110/4 mm. Hg. The patient was placed on the pump-oxygenator, and the pulmonic valve was exposed through the pulmonary artery. The orifice measured 2 mm. in diameter. What was regarded as a satisfactory pulmonary valvulotomy was carried out along the lines of the fused commissures in three directions. There was thickening of the musculature of the right ventricular outflow tract, but there did not appear to be any fixed obstruction. The defect in the pulmonary artery was closed, the patient was taken off extracorporeal circulation, and pressures were measured again and found to be 150/3 mm. Hg in the right ventricle and 20/18 mm. Hg in the pulmonary artery.

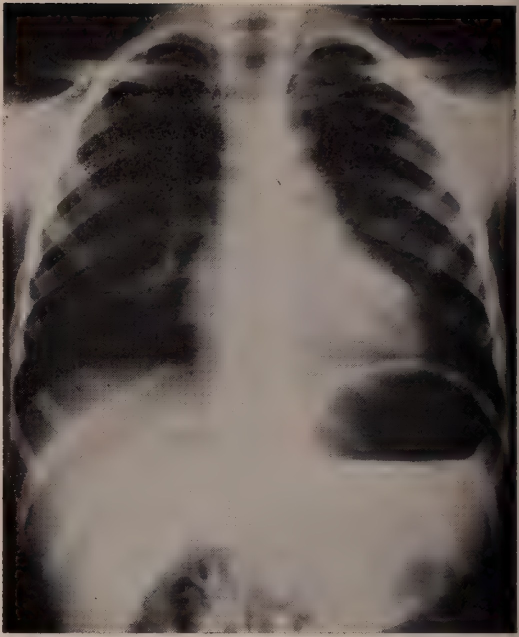

FIGURE 6. Case 5. Preoperative roentgenogram of chest showing a dilated pulmonary artery in a three-year-old child with valvular pulmonic stenosis.

The systolic gradient over the pulmonic valve was now 130 mm. Hg, whereas prior to valvulotomy it had been 155 mm. Hg. This did not seem to us to be a satisfactory reduction in the gradient over the pulmonic valve. Accordingly the patient was placed back on the pump-oxygenator. The pulmonic valve was examined again from above, and the outflow tract of the right ventricle was exposed. The ventricular muscle was greatly thickened, up to 15 mm. in some areas, but there was no definite fixed muscle bar. Sufficient muscle was excised along the outflow tract to permit a channel through the hypertrophied area, and the right ventriculotomy and the defects in the pulmonary artery were closed. After the patient was taken off the extracorporeal circulation the right ventricular pressure was found to be 125/3 mm. Hg and the pulmonary artery pressure 25/23 mm.

Hg. The systolic gradient over the valve was now 100 mm. Hg. We were not satisfied with this gradient but felt that we had done all we were justified in doing. The patient's postoperative course was essentially uncomplicated, and he was discharged ten days following the operation. Serial electrocardiograms have indicated a decrease in the right ventricular pressure. Postoperative cardiac catheterization has not been carried out so far.

There is a need for early operation in pulmonic stenosis with intact ventricular septum. In the case just reported there were no early symptoms. The right ventricular systolic pressure had gone from 110 to 175 mm. Hg in a six-month period. It is likely that with an early operation the greater risk and higher mortality involved with high right ventricular pressures and secondary right ventricular hypertrophy may be avoided.

Congenital deformities of the mitral valve

Congenital anomalies of the mitral valve are exceedingly rare. One rare combination of anomalies combines atresia or stenosis of the mitral and aortic valves with hypoplasia of the left ventricle. Death occurs within the first days or weeks of life, and thus far there has been no successful treatment for this condition. Stenosis of the mitral valve also may be associated with other congenital cardiac defects, such as atrial septal defect (Lutembacher's syndrome), coarctation, and patent ductus arteriosus. Congenital mitral stenosis uncomplicated by other valvular or aortic lesions has been reported, and it too carries a poor prognosis. However, a number of these patients have been subjected to operation.[16] The congenitally stenosed mitral valve differs from the stenosis secondary to rheumatic fever, and to accomplish a satisfactory valvulotomy is considerably more difficult than it is in the rheumatic valve. The usual finding is a conical, thickened diaphragmatic valve with no commissural formation and with short-fused chordae tendineae. However, occasionally a valve may have fused, thin, well-defined commissures that lend themselves readily to finger fracture. Most operations have been performed using a closed technic, but a few have been done open. At The New York Hospital-Cornell Medical Center one has been done by finger fracture and a second has been done employing extracorporeal circulation.

Case 6. An eleven-year-old white girl had gained weight poorly and had had frequent bouts of pneumonia since the age of four months. There was no cyanosis. The blood pressure was 98/72 mm. Hg. Rumbling diastolic and systolic murmurs were present at the apex, and systolic and diastolic murmurs were present in the second left interspace. An electrocardiogram showed right ventricular hypertrophy. A roentgenogram of the chest demonstrated enlargement of the left atrium and pulmonary artery. An angiocardiogram revealed a left-to-right shunt with a markedly enlarged pulmonary artery. Cardiac catheterization revealed the presence of a patent ductus arteriosus with an elevated pulmonary artery pressure of 78/53 mm. Hg and a pulmonary capillary pressure of 21 mm. Hg. At operation a ductus measuring 1.3 cm. in diameter was obliterated, and the mitral valve was examined digitally through the left atrial appendage. It was a funnel-shaped valve with an eccentrically placed orifice measuring 1 sq. cm. By finger fracture a split was obtained along the lines of what normally would have been the fused commissures, and the orifice was enlarged to approximately 2 sq. cm. The diastolic gradient over the mitral valve was 22 mm. Hg before valvulotomy and 10 mm. Hg after valvulotomy. The pulmonary artery pressure fell from 90/60 to 80/52 mm. Hg after mitral commissurotomy, and after permanent obliteration of the patent ductus arteriosus the pulmonary artery pressure fell further to 67/35 mm. Hg. Her early postoperative period was complicated by mild heart failure which responded to digitalis. The diastolic murmur of mitral stenosis was diminished postoperatively. Her general condition improved and appeared to be quite satisfactory. She was lost to follow-up when she left the country three months following her operation.

Congenital mitral insufficiency in most cases is associated with atrial septal defects of the ostium primum variety or atrial-ventricular canal defects. In these a cleft in the middle of the aortic leaflet produces the mitral regurgitation. This is corrected by a few interrupted sutures at the same time the septal defect is repaired. The closure of the cleft in the aortic leaflet alone may not correct the mitral insufficiency completely, since shortened accessory chordae tendineae may prevent the leaflet from functioning competently, and division of these accessory chordae tendineae may be necessary for a good result.[17] Congenital

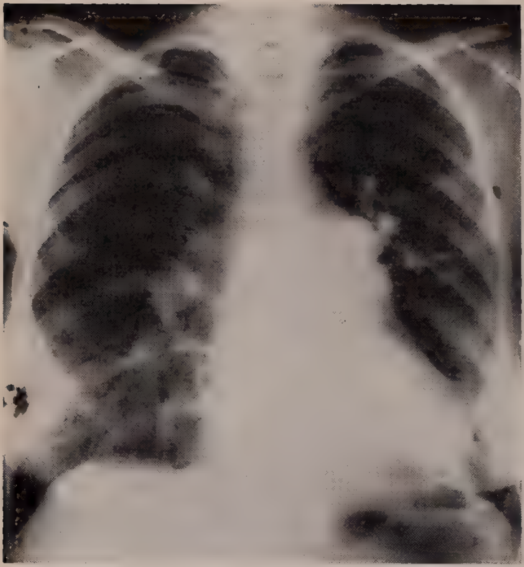

FIGURE 7. Case 7. Roentgenogram of chest in a thirty-four-year-old woman with an ostium primum defect and cleft mitral leaflet showing marked enlargement of the pulmonary artery and some right-sided enlargement.

mitral regurgitation not associated with an ostium primum defect or atrial-ventricular canal defect has been reported, and surgical correction by annular plication using both open and closed methods have been reported in a few isolated cases.[16]

CASE 7. A thirty-four-year-old white woman had known of a heart murmur since the age of two years. She was free of symptoms until the age of thirty-two years when she began to have dyspnea on exertion and increasing easy fatigability. On physical examination the pulmonic second sound was split widely and greater than the aortic second sound. There was a Grade II systolic murmur at the left sternal border in the third and fourth intercostal spaces and a Grade I mid-diastolic murmur at the apex. An electrocardiogram showed incomplete right bundle branch block and left axis deviation. A roentgenogram of the chest revealed an enlarged heart with enlargement of the pulmonary artery segment and enlargement of both the right ventricle and right atrium (Fig. 7).

Cardiac catheterization showed a large left-to-right shunt at the atrial level, and dye studies suggested an ostium primum type of atrial septal defect. At operation when the right atrium was opened using a cardiopulmonary bypass, there was a large atrial septal defect of the ostium primum type with a cleft in the aortic leaflet of the mitral valve. The cleft was repaired using interrupted fine silk sutures, and a patch of compressed Ivalon was used to close the atrial septal defect. A small cleft in the tricuspid valve did not require sutures. Oxygen saturation studies in the operating room demonstrated that the shunt had been obliterated. Postoperatively her course was uncomplicated, and her exercise tolerance has been improved. There is still a faint systolic murmur present to the left of the sternum.

Acquired mitral stenosis

Acquired lesions of the mitral valve are very frequent in our population and are of great clinical importance. Many can be corrected completely by surgery, and many more can be improved. This is particularly true for mitral stenosis, which in this country is due to rheumatic fever with but rare exceptions. The prevalence of mitral stenosis and the great variation in its course has attracted the attention of physicians for a long time. Nonsurgical measures in the treatment of mitral stenosis have consisted largely of the following: (1) limitation of activity to within the cardiac capacity, (2) the judicious use of digitalis, (3) the occasional conversion of auricular fibrillation with quinidine or digitalis, and (4) anticoagulation therapy for emboli. The surgical measures have included: correction of the stenosis, removal of thrombi from the left atrium or its appendage, and the removal of emboli from the arterial tree.

The surgeons have incorporated all the medical adjuncts to support and make their measures more effective. Since Bailey[18] and Harken *et al.*[19] made their early reports in 1948–1949, many surgeons have operated on several thousands of patients for the correction of mitral stenosis or the alleviation of the sequelae and complications that arise from it. In the early beginning of this therapy poor-risk patients were operated on, and there was a period when patients with less than the present accepted indications were operated on because it had been demonstrated that the procedure could be done with little risk if there was little or no advanced disease.

During the first decade the criteria for operation have become well established and so have contraindications. As experience has increased so has the adequacy and thoroughness of mitral commissurotomy with a valve which has not been partially destroyed. Finger fracture or separation of the commissures is more completely done than formerly, and when difficulty is encountered, instruments of a wide range of adaptability may be employed. These instruments range from knives for incision to valvulotomes and dilators which may be inserted through the ventricular wall from below. Stenosed valves that defy correction by the indirect approach are being operated on with open methods in selected cases. Extracorporeal circulation is also the method of choice for patients with large intra-atrial thrombi. The over-all results in patients being subjected to open-heart operation are improving, and they provide a distinct advance for a group of patients who have had a very low salvage incidence previously.

In our experience with over 500 patients operated on for mitral stenosis our results have been similar to others.[20] We have operated on patients who are in Classes 2, 3, and 4 of the New York Heart Association's classification. Our postoperative mortality ranges under 5 per cent. After a decade of experience it is our belief that we can correct mitral stenosis better in those patients in whom it is feasible with less risk than we did five years or more ago. Postoperative complications remain about the same. The postpericardiotomy syndrome consisting of chest pain and temperature elevation continues to occur in about 15 per cent of the patients. An occasional patient, perhaps 3 or 4 each hundred, has been made worse by adding insufficiency so that his disability is increased after the operation. Another small proportion, 4 to 6 per cent, is not improved even though it appears to the surgeon that he has been successful in enlarging the mitral orifice. Some of these patients have had markedly distorted valves with considerable calcification. A lack of mobility of the leaflet at the commissurotomy may contribute to this group of patients that we must consider unimproved but who have not been made worse. Finally we come to consider the patients that we classify as improved. In conjunction with our medical associates this has been estimated at as high as 75 per cent. This, too, is comparable to results reported from other clinics. Because it is not based on objective measurements, it should be regarded as over estimated. There are many factors that contribute to this, not the least of which is the patient-doctor relationship in the treatment of a condition that has been long in the making. Preoperative preparation and postoperative attention probably contribute to the same trend. At the other extreme are those in whom improvement is not only unequivocal but spectacular. Patients who have been bed invalids have been restored to what for them was considered normal activity. They have returned to work and have become self-supporting. Improvement is an elastic term, and we employ it as the ultimate that we may anticipate in the treatment of mitral stenosis due to rheumatic fever. We attack by only freeing the valve that is stenosed by scarring. Whatever else rheumatic fever has done or may do is not likely to be affected by the surgical procedure.

Case 8. A forty-two-year-old white man gave no history of acute rheumatic fever. At the age of twenty he was refused for service in the army because of a heart murmur. For the six years prior to his operation he had increasing difficulty with frequent admissions to the hospital because of congestive heart failure. There was no history of systemic embolization, but he had what was thought to be a pulmonary infarct four months prior to the operation. On admission he was a thin, chronically ill-appearing white male. There was a rough low-pitched diastolic murmur at the apex. An electrocardiogram showed auricular fibrillation and right ventricular hypertrophy. A roentgenogram of the chest showed enlargement of the left atrium and pulmonary artery with increased pulmonary vascular markings (Fig. 8). A finger fracture commissurotomy was planned, but at operation both the left atrial appendage and the left atrium at the base of the appendage were firm and indurated, and to all indications there appeared to be an extensive clot formation within the left atrial appendage and left atrium. Nothing further was done at this time, but two weeks later an open approach using the artificial heart-lung machine was carried out. The left atrium was approached from the right side of the chest through the intra-atrial groove, and an extensive clot formation tightly adherent in the region of the left atrial appendage was found. The mitral valve was heavily calcified, and the opening measured 0.6 sq. cm. The valve was opened to 3 sq. cm., and the calcified leaflets were mobilized as much as possible. Following the operation he was continued on anticoagulants. One year following the operation his exercise tolerance was greatly increased; he is now able to work full time as a bartender, and he feels greatly improved. There have been no systemic emboli.

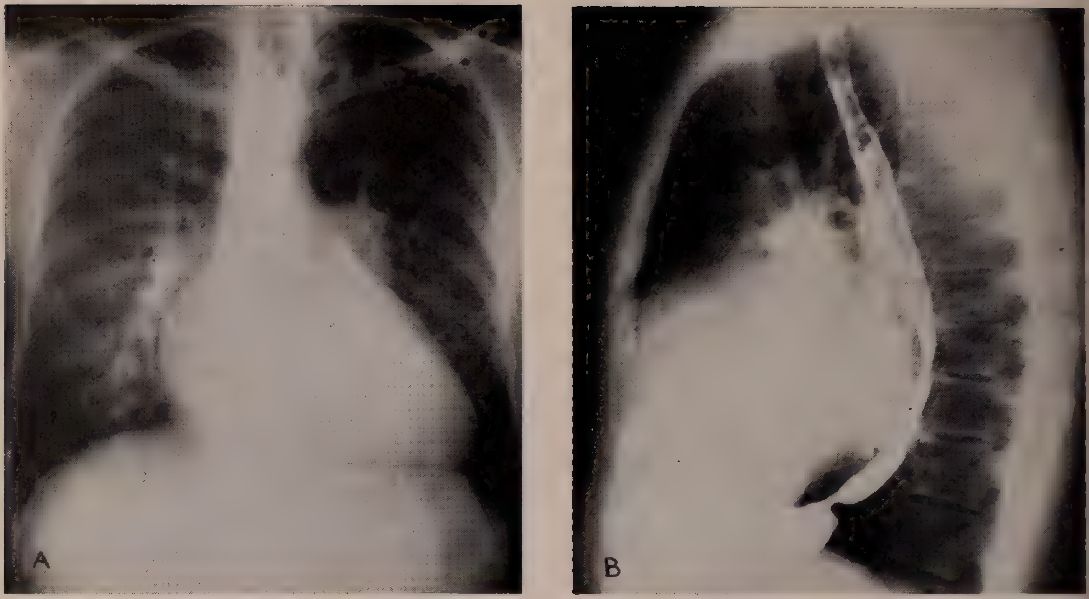

FIGURE 8. Case 8. Preoperative roentgenogram of chest. (A) Posteroanterior view showing increased vascular markings and enlargement of the left atrium and pulmonary artery. (B) Lateral view showing left atrial enlargement.

In our first 400 patients who had a closed-finger fracture mitral valvulotomy 50 per cent of the deaths were associated either directly or indirectly with systemic emboli or thrombi in the left atrium. Had an attempt been made to go ahead with the valvulotomy as a closed procedure at the time of the first operation in Case 8, the result certainly would have been disastrous. It is our policy to perform angiocardiograms on all patients with a history of systemic emboli. When thrombi are demonstrated in the left atrium, an open procedure is done. When the evidence is not quite so clear for thrombi, the pump-oxygenator is kept standing by and is used if necessary. When extensive thrombus formation is encountered unexpectedly, as in the case just described, the open operation is performed two weeks later, and anticoagulants are given during the interval between the operations.

Acquired mitral insufficiency

The loss of valve substance and secondary dilatation of the mitral annulus are the causes of acquired insufficiency of the mitral valve. Rheumatic fever is responsible for the great majority of cases of mitral insufficiency although bacterial endocarditis also can produce it. In some cases of combined mitral stenosis and insufficiency a simple finger fracture of the mitral valve with mobilization of rigid leaflets will result in some improvement in the mitral regurgitation, but these cases are in the minority. In general, the results of surgical procedures for acquired mitral insufficiency have not been outstanding, although small series now are being reported with improved mortality figures and better and longer-lasting results.[21,22]

Early attempts to correct mitral insufficiency were by the closed method and consisted of circumferential suturing of the annulus and external plication of the annulus.[23] When the development of pump-oxygenators permitted an open approach to the valve, internal annular plication became the form of treatment used most frequently.[24] Mattress sutures of heavy silk were placed through the annulus of the valve at the commissure where there was the greatest regurgitation, usually the posterior medial commissure. Often it was necessary to perform a commissurotomy on the fused opposing commissure.[25] The use of heavy suture material buttressed with Ivalon and Teflon have diminished the incidence of these sutures cutting through and tearing out and have improved the long-term results. Various types of plastic procedures have been used to augment a deficient mitral leaflet. The leaflet has been buttressed from beneath with a cigaret of compressed Ivalon.[26] A semiluminar piece of compressed Ivalon has been interposed between the valve leaflet and the annulus.[27] The edge of the leaflet has been extended by sewing on woven Teflon.[28] The mortality figures for the open approach to mitral insufficiency are around 12 to 20 per cent. The majority of patients are said to have been benefited, but long-term follow-ups have not been available.

Case 9. A thirty-two-year-old housewife gave a history of rheumatic fever with St. Vitus dance as a child. A heart murmur was heard at the age of sixteen years, but she had no limitation of activity until four years prior to the operation when she began to have dyspnea on exertion and orthopnea. These symptoms increased progressively. On admission she was a chronically ill-appearing woman with the murmurs of mitral insufficiency and mitral stenosis. The blood pressure was 134/78 mm. Hg, pulse 76, and there was auricular fibrillation. The electrocardiogram showed left ventricular hypertrophy. A roentgenogram of the chest showed generalized enlargement of the heart with enlargement of the left ventricle and left atrium (Fig. 9). The cardiothoracic ratio was 15 to 26. Cardiac catheterization done two years earlier had indicated combined mitral stenosis and insufficiency. It was felt that the predominant lesion was mitral insufficiency, and on April 29, 1958, using the artificial heart-lung machine, the mitral valve was approached by the open technic. The mitral orifice was of the keyhole variety with the area of insufficiency at the anterolateral commissure, the posteromedial commissure being fused. Plication of the annulus at the anterolateral commissure was carried out, and the posteromedial commissure was opened with scissors. The resultant mitral orifice measured approximately 3 sq. cm. It was felt that the insufficiency had been diminished greatly. She was discharged from the hospital twenty-two days after the operation and was greatly improved for a time. Her exercise tolerance increased to the point where she was able to swim under water for short periods, and she did all of her own housework. However, approximately fifteen months following surgery she again developed dyspnea on climbing one flight of stairs, two-pillow orthopnea, and ankle edema. The murmur of mitral stenosis was more marked. Cardiac catheterization revealed evidence of a tight mitral stenosis with greatly elevated pulmonary artery pressure and pulmonary vascular resistance. Eighteen months after the open procedure a closed mitral commissurotomy was performed. The mitral valve orifice was found to measure approximately 1.7 sq. cm., and approximately two thirds of this opening was regurgitation. The sutures at the anterolateral commissure appeared to have held, and the insufficiency was now at the posteromedial commissure. Very little was accomplished at this operation. Although she did recover and seemed temporarily improved, after the second operation her course was progressively downhill, and she expired forty-one months after the first open procedure.

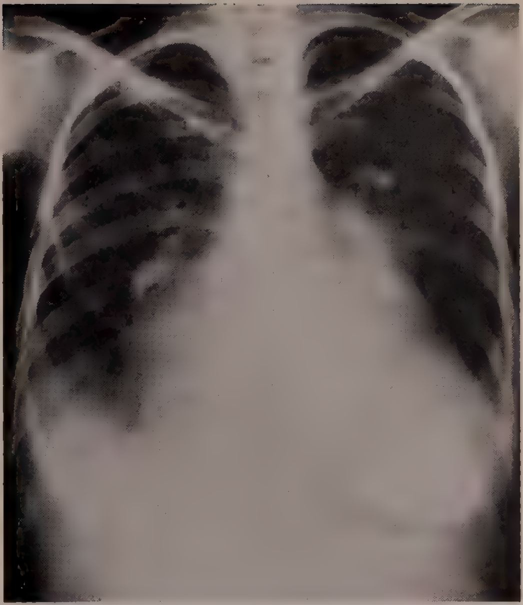

FIGURE 9. Case 9. Anterior roentgenogram of chest in a thirty-two-year-old woman with predominant mitral insufficiency, showing four-chamber enlargement of the heart.

This patient was improved temporarily by annular plication at one commissure, but she subsequently developed combined stenosis and insufficiency at the other commissure one year later. Her condition did not permit a second open procedure. A closed procedure was of no benefit, and she died shortly thereafter.

In patients such as this, total replacement of the mitral valve eventually may become the procedure of choice. At the present time limited numbers of total replacement of the mitral valve with prostheses have been carried out. These prostheses have been in the forms of bicuspid fabric and polyurethane valves corresponding anatomically to the mitral valve,[29] and ball valve prostheses.[30] The numbers of these valves totally replaced so far is small, and the ultimate fate is as yet unknown.

Congenital anomalies of the aortic valve

Aortic regurgitation of a significant degree due to a congenital deformity of the aortic valve probably does exist but is extremely rare, and no surgical treatment for this condition has been carried out thus far. The murmur of aortic insufficiency occasionally may be heard in combination with predominant congenital aortic stenosis, but the systemic signs of aortic regurgitation usually are missing, and the aortic stenosis is the predominant lesion.

Congenital stenosis of the aortic valve, although not one of the more common congenital cardiac anomalies, is being diagnosed more frequently and referred for surgical treatment. The obstruction occurs most commonly at the valvular level in which cases the cusps are thickened, their commissures fused to form a domed-shaped diaphragm with a central opening. Congenital bicuspid valves, while not producing stenosis originally, may in later life be the site of acquired calcific aortic stenosis. In our experience approximately 25 per cent of the adult patients subjected to open correction of acquired aortic stenosis had bicuspid aortic valves.[31] Aortic stenosis may occur at a supravalvular level in a form somewhat similar to that of the classical coarctation of the aorta. The most difficult variety of aortic stenosis to diagnose and treat is the subvalvular form which may be a simple membrane, a ridge of muscle, or a diffused thickening of the musculature of the outflow tract of the left ventricle.

The surgical treatment of congenital aortic stenosis has evolved from the closed transventricular approach through the open approach with hypothermia to the open approach with extracorporeal circulation. Some of the best reported results with a mortality of 8 per cent have been done using deep hypothermia and circulatory arrest.[32] Following an operation the left ventricular pressure may not fall immediately but may continue to diminish for as long as one year after the operation.

Acquired aortic stenosis

Acquired lesions of the aortic valve are second in incidence only to those of the mitral valve. When these are due to rheumatic fever, it is common for the mitral valve to be involved also. It has been estimated that one third of all patients with mitral disease have aortic involvement, and in about one half of the patients with aortic disease the mitral valve is also involved. Rheumatic fever, atherosclerosis, bacterial endocarditis, and syphilis are the generally accepted diseases leading either to stenosis or insufficiency of the aortic valve or to the coexistence of the two.

Aortic stenosis that is severe enough to have produced fainting or attacks of syncope and limitation of activity without cardiac enlargement or evidence of gross coronary artery disease can be corrected by the direct approach using extracorporeal circulation. An aortic valve orifice reduced to a 0.5 sq. cm. area is critical and cannot be tolerated for long. If such a valve is opened to a total valve area even as small as 2 or 3 times the original area without producing significant insufficiency, there may be marked clinical improvement. The most difficult problem is to correct the stenosis without producing or increasing the insufficiency of the valve. Scarring and calcification due to rheumatic fever may have superimposed atherosclerotic changes. The older the pathologic process and the older the patient, the more difficult is the accomplishment of this objective of increasing the orifice and avoiding insufficiency. Coexisting mitral valvular involvement and coronary artery disease tend to reduce the patient's capacity to tolerate the burden of operation. Nevertheless, with the aid of hypothermia and coronary artery perfusion remarkable advancements are being made in the correction of aortic stenosis. The partial and complete replacement of aortic valve leaflets for the treatment of almost completely destroyed valves and valves with marked insufficiency is the next step in the evolution of the surgical treatment of aortic valve disease. At the present time the mortality for this procedure remains fairly high. There are still many technical problems to be solved, and the ideal configuration of the valve and the composition have not been determined.

At open operation using extracorporeal circulation and cardiac arrest by selective hypothermia a great deal can be accomplished by way of removing calcium from leaflets, dividing fused commissures, and in general enlarging the orifice and rendering the leaflets more mobile. In our experience with 33 patients subjected to open operation by this means there were 8 deaths for an over-all mortality of 24 per cent. However, in 11 of these patients there was sufficient mitral stenosis to warrant both aortic and mitral valvulotomies. In these patients with a combined approach there were 4 deaths for an operative mortality of 36 per cent. Twenty-one patients who had an aortic valvulotomy only had a mortality of 20 per cent; if 1 desperately ill patient, whose blood pressure was maintained by norepinephrine and who was operated on as an emergency in the middle of the night, is omitted, there were only 3 deaths in 20 patients, a mortality of 13 per cent. The average gradient across the aortic valve at the time of surgery was 84 mm. Hg, and this gradient was reduced by an average of 60 per cent immediately following the valvulotomy. The clinical course of a number of patients has indicated that there was a further drop in this gradient probably due to a decrease in the degree of muscular hypertrophy in the outflow tract of the left ventricle. Approximately 60 per cent of patients have been improved for periods of a year or more. About 20 per cent have been improved for a shorter time and then have reverted to conditions similar to or worse than their preoperative state. In 1 patient in our series severe aortic insufficiency developed twenty-four hours following the operation, and a second procedure was carried out immediately with the pump-oxygenator to correct the insufficiency.

Case 10. A thirty-seven-year-old white female was said to have a murmur at birth and rheumatic fever at the age of five years. She was free of symptoms until six years before the operation when she developed dyspnea on exertion which increased gradually. Three years prior to the operation she had her first episode of syncope. The blood pressure was 100/70 mm. Hg. There was the systolic thrill and characteristic murmur of aortic stenosis and the murmur of aortic insufficiency. A roentgenogram of the chest showed only a slight enlargement of the heart (Fig. 10). There were calcifications in the region of the aortic valve. The electrocardiogram showed evidence of left ventricular hypertrophy. At cardiac catheterization the pressure in the left ventricle was 227/32 mm. Hg, and the aortic pressure was 104/67 mm. Hg. The aortic valve area was calculated at 0.4 sq. cm. On September 4, 1958, an open aortic valvulotomy was performed using extracorporeal circulation and potassium cardioplegia. A heavily calcified tricuspid valve was enlarged from 0.4 to 2 sq. cm. by dividing the commissures and removing calcium. Ventricular fibrillation developed which required a total of 36 shocks of 350 volts each before the pump-oxygenator could be discontinued. The gradient over the aortic valve had been reduced from 135 to 90 mm. Hg, but the form of the aortic tracings appeared considerably better than that recorded before the valvulotomy. Her postoperative course was complicated by thrombocytopenic purpura, but she responded to treatment, and she was discharged from the hospital five weeks following the operation. She has had remarkable improvement following her operation. There have been no further attacks of syncope, she sleeps with one pillow, does all of her own housework, and can climb four to five flights of stairs. Eighteen months after her operation she underwent a total hysterectomy without difficulty and now, almost three years after her operation, she continues to do extremely well.

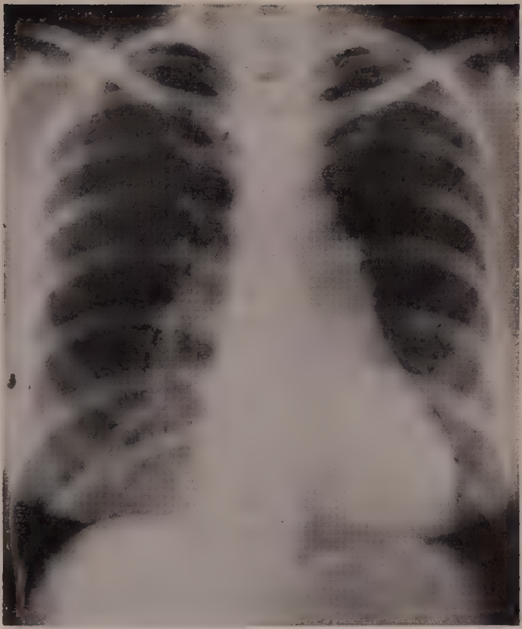

FIGURE 10. Case 10. Preoperative photoroentgenogram of the chest. Despite the small heart size, peak systolic gradient over the aortic valve was 123 mm. Hg in the patient.

Aortic valvular insufficiency

The primary causes of aortic valvular disease have been rheumatic fever and syphilis. Aortic regurgitation also may be produced by acute or subacute bacterial endocarditis through the acute perforation of one cusp or the distortion of one or more cusps during the healing process. Direct or indirect trauma may produce a division or an avulsion of an aortic cusp. The bicuspid congenital valve, such as is frequently associated with coarctation of the aorta, may show some degree of insufficiency and not infrequently is further distorted by endocarditis or rheumatic valvulitis, producing varying degrees of aortic insufficiency and stenosis. In Marfan's syndrome there is an inheritable disorder of connective tissue in which aortic insufficiency results from dilatation of the aortic annulus as aneurysmal dilatation of the ascending aorta develops.

Until the development over seven years ago of the Hufnagel ball valve prosthesis which was inserted into the descending aorta, there was no surgical treatment for aortic insufficiency.[33] Although there have been many objections to the Hufnagel ball valve, including rupture of the suture line, clot formation,[34] hemolysis, and objectionable noise, and it is now considered obsolete in most circles, many patients have received long-lasting benefits from its use.

Case 11. A twenty-one-year-old white male had a known heart murmur since the age of two years. He was small for his age and tired easily, although for the most part he was active throughout his childhood. At thirteen years of age, following cardiac catheterization at another hospital, a diagnosis of ventricular septal defect and pulmonic stenosis was made. At the age of twenty-one, four months prior to the operation, he developed subacute bacterial endocarditis and developed signs and symptoms of acute aortic insufficiency. It was felt that he probably had perforated an aortic cusp. He responded to the usual antibiotic therapy. A roentgenogram of the chest showed four-chamber enlargement of the heart. An electrocardiogram showed right ventricular hypertrophy. His blood pressure was 150/50/0 mm. Hg. There was a typical Corrigan's pulse. There was a diastolic murmur of aortic insufficiency in addition to the systolic murmurs of the ventricular septal defect and pulmonic stenosis. On December 30, 1954, a Hufnagel ball valve prosthesis was inserted into the descending aorta. His immediate postoperative course was uncomplicated. Since his operation he has had a remarkable increase in his exercise tolerance. He has worked full time in an advertising agency, is able to climb stairs, walk indefinitely on the level ground, and sleep with one pillow. Six years after the insertion of the prosthesis he developed auricular fibrillation which was converted with quinidine. Now six-and-one-half years following the operation he continues to do well. The clicking noise of the early type of prosthesis has caused him no concern.

Since the development of the Hufnagel ball valve prosthesis, there have been a number of direct approaches to the problem of aortic valvular insufficiency. The narrowing of the annulus by circumferential suturing and external tucks in the aorta did not meet with much success. Along with the development and improvement in extracorporeal circulation technics have come a variety of open direct approaches to the aortic valve, both for insufficiency and stenosis. Bicuspidization with resection of the noncoronary cusp and sinus has had a limited application with perhaps the best results in Marfan's syndrome.[35] A great variety of plastic procedures have been carried out on the aortic leaflets.[36] These have varied from the simple removal of calcium and mobilization of rigid leaflets to the augmentation and extension of leaflets with prosthetic material and on to partial and total valve replacement.[37,38] The mortality for total valve replacement varies between 14 and 22 per cent with the most experienced surgeons in the country[39] and probably is 50 per cent or more in less experienced hands. The immediate postoperative results in patients with total valve replacement by prosthetic valves are said to be good, yet long-term survival figures are not available. Thus at the present time we appear to be at a period where the Hufnagel ball valve prosthesis is obsolete, yet total valve replacement, and in some cases even partial valve replacement, carries a high mortality and improvement of questionable duration, so that one tends to reserve these for the more severely ill patients.

Summary

The surgical treatments available, the risks of surgery, and the results following surgery have been discussed for congenital and acquired disease of the tricuspid, pulmonary, mitral, and aortic valves. Representative case histories have been presented

to illustrate salient features of surgical treatment for the various valve lesions. Total replacement is the next step forward in the treatment for deformity of the mitral and aortic valves, but at the present time the operative mortality is high and the long term follow-up uncertain.

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Bladder Neck Obstruction as Cause of Fever of Unknown Etiology in Children

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IN FEVER of unknown etiology the urinary tract has always been a place of investigation by physicians in general and pediatricians in particular.[1] The question of what part bladder neck obstruction plays in this important issue becomes more and more significant as the incidence of case finding increases. It is becoming more apparent that obstruction at the bladder neck is the most common cause of urologic difficulties in children. Except for the excision of new growths and plastic procedures on the external genitalia, urology concerns itself almost entirely with the diagnosis and relief of obstruction of the urinary tract.

The importance of bladder neck obstruction in children is becoming very apparent in the increasing number of reports in the literature and is well exemplified in the works of Leadbetter,[2] Marshall, Paguin, and McGovern,[3,4] Stewart,[5,6] Hutch, Bunge, and Flocks,[7] Murphy and Schoenberg,[8] and Hamm and Waterhouse.[9] My study covers a period of some eleven years. In 1956[10] I had the opportunity of presenting our findings and case studies involving 82 patients with various degrees of bladder neck obstruction. Again in 1959[11] I presented a report on 87 patients to the Section on Urology of the Medical Society of the State of New York, and now again I have the pleasure of returning to the Section on Pediatrics with further evaluation and continued study of this difficulty.

There has been extensive work in the field of bladder neck obstruction in relation to the various complications and the etiology of accompanying conditions. Ureteral reflux with bladder neck obstruction presents a much more formidable problem than bladder neck obstruction alone.[12] The various surgical procedures for correction are a separate chapter in pediatric urology.[13] The recognition of these conditions and the methods of diagnosis are most necessary in the evaluation of the problem of bladder neck obstruction.

Material for study

One hundred and twenty-three patients who were admitted to the Northside Division of Rochester General Hospital between 1955 and 1960 were reviewed for evaluation. Fifty-two or 40 per cent were males, and 71 or 60 per cent were females. The ages varied from six months to sixteen years with 87 per cent between two and ten years of age and with a peak incidence at from four to eight years of age (Fig. 1).

Fifty-eight patients or 47 per cent presented symptoms of fever or a significant history of fever. The average duration of symptoms before evaluation was twenty-one months while in the patients with fever it was eighteen months. A re-evaluation of this group, however, revealed that 84 per cent of these had a history of only eleven months. Fever seemed to play a significant part in bringing the patient to the physician for evaluation in about half the time ordinarily seen with other symptoms.

The duration of symptoms before evaluation extended from two weeks to one hundred and eight months. It was apparent that frequency and urgency were long tolerated by the parents, but the occur-

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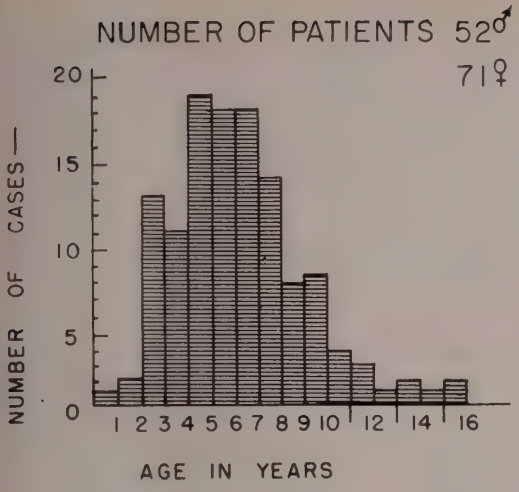

FIGURE 1. Age grouping of 123 children with bladder neck obstruction.

TABLE I. Significant symptoms in 123 patients with bladder neck obstruction

Symptom	Number of Patients	Per Cent of Total
Frequency	79	64.2
Urgency	51	41.5
Abdominal pain	56	45.5
Enuresis		
Day	47	38.2
Night	72	58.5
Straining	21	17.0
No urinary symptoms	21	17.0

A STUDY WAS UNDERTAKEN *of 123 children, of whom 40 per cent were males, and 60 per cent females; 87 per cent were between the ages of two and ten years. Forty-seven per cent presented symptoms of fever or a significant history of fever, which played an important part in bringing the patient to the physician. Frequency, urgency, and abdominal pain are the most common findings in bladder neck obstruction. Nocturnal enuresis occurred in 58 per cent of the patients, day enuresis in 38 per cent. Seventeen per cent were without urinary symptoms. The evaluation of the patients was carried out by urine culture, residual urine determinations, intravenous pyelography, voiding cystogram, and cystoscopy. Types of treatment were: urethral dilatation; cystoscopy and fulguration; transurethral resection; suprapubic resection; and none. Frequently urinary infection has existed longer than indicated in the history; enuresis or the lack of it can be similarly significant. The evaluation of any child with fever of unknown etiology must include a complete urologic study.*

rence of fever, hematuria, and abdominal pain resulted in evaluation at a much earlier moment. Frequency, urgency, and abdominal pain are the most common findings in bladder neck obstruction. Nocturnal enuresis occurred in 58 per cent of the patients while day enuresis, which is more significant, occurred in 38 per cent. Straining to urinate, while a most important point in the history when obtained, could only be elicited on questioning in 17 per cent of the instances. It is most significant that 21 or 17 per cent of the patients who were seen with bladder neck obstruction were without urinary symptoms and were evaluated because of fever, abdominal pain, or general physical debility in the investigation of a child who was doing poorly (Table I).

The evaluation of these patients was carried out by urine culture, residual urine determinations, intravenous pyelography, voiding cystogram, and cystoscopy, with retrograde studies when they were indicated. Most of these patients were studied when they were quiescent between attacks or after they had been given antibiotics or sulfa drugs by their family physicians. In spite of this fact, it is significant that 25 or approximately 20 per cent had positive urine cultures, all but 2 of these showing coliform bacteria.

The evaluation of the intravenous pyelogram was extremely interesting. One hundred and ten of the 123 patients had intravenous pyelography. In only 13 of these instances was it found to be helpful in a diagnosis of bladder neck obstruction. In 26 instances, however, other pathologic conditions involving the upper urinary tract were identified, and in 33 instances retrograde pyelograms were done to confirm or deny the findings on the intravenous pyelograms. It seems apparent, therefore, that the intravenous pyelogram is a necessary part of the evaluation of any patient with symptoms of bladder neck obstruction, not so much to confirm the diagnosis, but to evaluate the status of the upper urinary tract. During part of this study we had attempted to evaluate the bladder by doing a cystogram study using the last films of the intravenous pyelogram when the bladder was filled and attempting voiding cystograms at that time. This has proved to be unreliable as we missed several cases of reflux by this method. If at that time there is still slight retention of dye in either kidney, it is impossible to determine the presence of mild reflux.

Cystographic studies and voiding cystograms were carried out, therefore, on 36 patients, and in 22 of these a definite pathologic condition was demonstrable. In 12 reflux occurred, 5 showing bilateral and 7 unilateral reflux. Trabeculation occurred in 10 as well as in the individuals revealing reflux. At the present time we are evaluating our cystograms, and this will be the subject of a separate report. The cystogram and voiding cystogram are most significant in their contribution and in this study showed definite pathologic conditions in over 60 per cent of the cases examined.

The treatment of these patients is shown in Table II. The total number is greater than the number of patients because some started with urethral dilatations and underwent transurethral resections and finally suprapubic revision of the bladder neck because of their failure to respond to conservative therapy. Cystoscopy was carried out on all patients, and trabeculation was noted in 113. The following cases exemplify some of the various points in the problems of fever and bladder neck obstruction.

TABLE II. Types of treatment in 123 patients with bladder neck obstruction

Treatment	Number of Patients
Urethral dilatation	70
Cystoscopy and fulguration	6
Transurethral resection	27
Suprapubic resection	29
None	3

Case reports

CASE 1. The patient was a two-year-old white female who was referred because of fever and recurrent urinary infection. The child had had recurrent fevers up to 105 F. over a period of eight months. An examination of the urine had revealed an infection which responded to antibiotics but which recurred. She was seen in the office in consultation on January 13, 1959. There was a history of bedwetting which preceded the attacks of urinary infection. She was lethargic with these attacks. There was no wetting in the daytime. Dysuria and frequency appeared with the attacks but not between attacks. Her past history was unremarkable. A catheterized urine revealed: pH, 6; albumin, 0; sugar, 0; and wetdrop examination, negative results. A physical examination revealed a well-developed and well-nourished white child in no acute distress. I thought the right kidney might be palpable and enlarged, but it was nontender. The left could not be felt as such. There was no suprapubic discomfort. Calibration of the urethra revealed it to be somewhat tight to a number 18 French sound. Intravenous pyelography revealed the left side to be entirely within normal limits. On the right side the kidney parenchyma seemed to be a little thinner than normal. The calyces were a little blunter and did not appear as sharp as the left. The bladder density was good, and the contour was normal (Fig. 2A).

The patient was admitted to the Northside Division where cystoscopy and retrograde studies revealed marked contracture of the bladder neck with deep cellule formation. It was decided to give this child a course of urethral dilatations and continuous chemotherapy. She was maintained on a sulfonamide (Lipo Gantrisin), one teaspoonful every day. Urethral dilatations were done over a period of months until the urethra was dilated to a number 24 French sound with ease. She was returned to the office on October 13, 1959, with a history of acute urinary infection. A catheterized urine revealed a moderate amount of pus with clumping. There was a history of some pain on the right side. A voiding cystogram was obtained on October 19, 1959, which revealed reflux into the right kidney and right ureter. There was minimal reflux up the left ureter but none into the kidney (Fig. 2B). She was continued on a course of urethral dilatations and chemotherapy. She was followed periodically until September 20, 1960, at approximately one-month intervals. The urine continued to show negative findings throughout. A check voiding cystogram on September 23, 1960, failed to reveal the presence of any reflux (Fig. 2C). She is not taking any medication. The urethra is not being dilated. She was last seen on January 3, 1961, at which time the urethra accepted a number 24 French sound with ease, and the urine showed negative findings.

CASE 2. The patient was a nine-year-old white girl admitted on October 19, 1958, because of spells of fever, malaise, and urinary infection

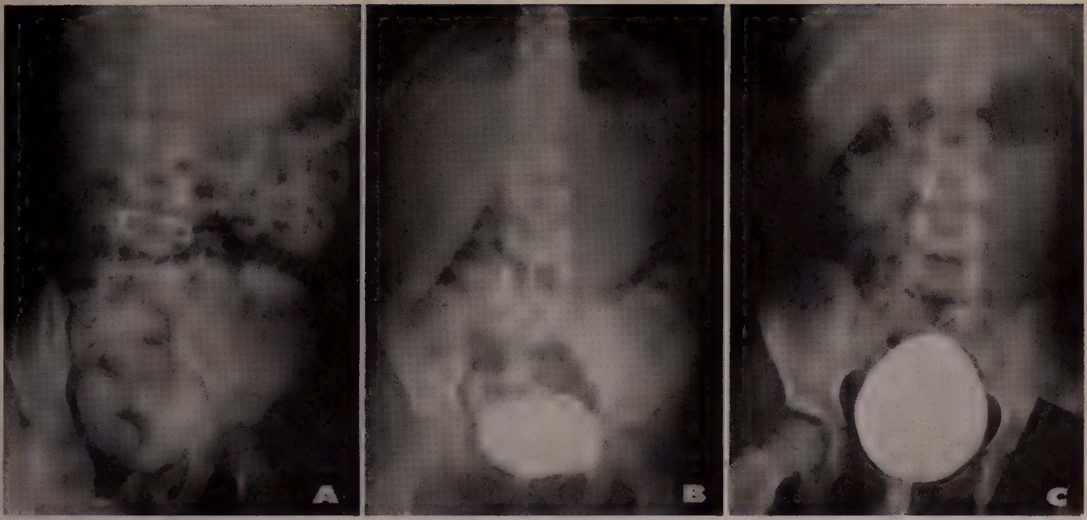

FIGURE 2. Case 1. (A) Intravenous pyelogram on initial work-up. (B) Voiding cystogram showing right ureteral reflux. (C) Voiding cystogram showing absence of ureteral reflux after conservative therapy.

since August, 1958. She had been treated with chemotherapy and antibiotics with improvement and then relapses. She had a sore throat for many days the preceding spring. Repeated urinalyses showed white and red blood cells. A sulfonamide had been given for one week without effect. The mother stated that she recalled numerous episodes of fever, malaise, and vomiting in the past two to three years which had been attributed to tonsillitis, virus, and so forth. The laboratory findings were: hemoglobin, 12.6 Gm., and white blood count, 17,650. The urinalysis showed: pH, 4.5; albumin, trace; sugar, 0; white blood cells, 3 to 9; red blood cells, occasional; blood urea nitrogen, 15 mg. per 100 ml.; urine culture, enterococci; and sedimentation rate, 33 mg. per hour.

The patient responded to chloramphenicol (Chloromycetin). An intravenous pyelogram showed delayed excretion on the left with blunting and distortion of the calyces (Fig. 3A). Cystoscopy and retrograde studies showed only a trace of phenolsulfonphthalein in twenty minutes from the left kidney and 20 per cent from the right. Retrograde pyelograms showed marked distortion of the left kidney with atrophy and evidence of marked chronic pyelonephritis (Fig. 3B). The urethra was very tight. There was marked coarse trabeculation of the bladder with diffuse cystitis cystica. The bladder neck was contracted. A nephrectomy was performed on the left side. The patient tolerated the procedure well. A pathologic examination revealed marked segmental atrophy with chronic pyelonephritis.

The patient was treated in the office with urethral dilatations after the left nephrectomy. On January 7, 1959, she was seen with an apparent flare-up of infection. She did quite well over a period of the next twelve months but showed repeated urinary infection. It was felt that there might be reflux in the ureter on the left side where the kidney had been removed. On May 20, 1959, a voiding cystogram was obtained which revealed a trabeculated bladder with reflux into both ureters, the left ureter being a hydro-ureter (Fig. 3C). She was admitted to the hospital in July, 1959, when the remaining left ureter was resected and a Y-V plasty of the bladder neck was performed. She has been followed in the office from August 4, 1959, and has been maintained on continued medication until the present time. The residual urine varies from 2 to 40 cc. The urine has continued to show negative findings, and she has been afebrile and without urinary infection. A check voiding cystogram obtained on April 3, 1961, still revealed evidence of reflux into the right ureter. An intravenous pyelogram revealed a normally functioning right kidney with some blunting of the calyces and compensatory hypertrophy.

CASE 3. The patient, a six-year-old white female, was first seen in the office on January 14, 1958, in consultation because of recurrent urinary infections and high fever. She had been seen by her pediatrician the first time in August, 1956, because of a high fever. An evaluation at that time had revealed a pyelonephritis. She responded to chemotherapy and antibiotics, but the infections recurred. Pains occurred in both sides and both flanks. There was no frequency in the daytime although she gave a history of wetting the bed about once a week. She had some urgency, and there was dysuria with attacks. A year ago with one attack blood had been noted in the urine. Some vague umbilical pain was present which was relieved by urination although she voided easily. The mother stated that she had been

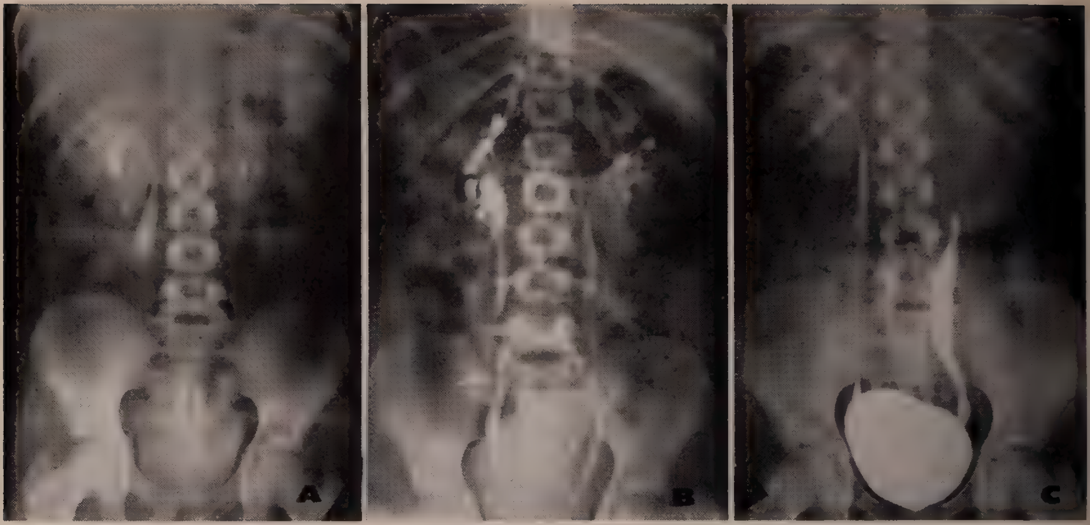

FIGURE 3. Case 2. (A) Intravenous pyelogram on initial work-up showing bilateral changes suggestive of pyelonephritis with marked distortion on left. (B) Retrograde pyelogram confirming findings of intravenous pyelogram. Only a trace of function appeared in twenty minutes from left side—sides reversed. (C) Voiding cystogram showing bilateral ureteral reflux especially up left remaining ureter after nephrectomy.

easy to toilet train. An evaluation of the urine at that time revealed: pH, 6; albumin, 0; sugar, 0; and wetdrop examination, negative results. The patient was a well-developed and well-nourished six-year-old white child in no acute distress. Neither kidney was palpable nor tender. A rectal examination gave negative findings. Calibration of the urethra revealed it to be very tight to a number 18 sound. It was extremely difficult to dilate the urethra. An intravenous pyelogram was essentially within normal limits except for slight trabeculation of the bladder (Fig. 4A). Arrangements were made for dilatations under anesthesia. Dilatation was carried out gradually until a number 24 sound was passed with ease.

She seemed to respond to therapy until July 22, 1958, when she returned with the history of a recent flare-up of acute pyelonephritis. The urine at that time revealed some pus cells. Her difficulties continued with the urine being infected periodically in spite of continued chemotherapy or antibiotics. The patient was admitted to the hospital in January, 1959. The residual varied between 25 and 100 cc. A cystogram revealed bilateral ureteral reflux (Fig. 4B). Transurethral resection of the bladder neck was carried out. She was continued on chemotherapy. The residual urine varied between 5 and 30 cc. She did extremely well maintaining urine with negative findings without urinary symptoms, until June, 1959, at which time the urine showed pus cells with clumps in spite of chemotherapy. She was carried on conservative therapy until October, 1959, at which time she was admitted to the hospital where Y-V plasty of the bladder neck and a Hutch ureteroplasty were carried out on the right side.

Postoperatively the patient has done very well. The urine has shown negative results. On April 16, 1960, a check voiding cystogram revealed no reflux up the right side which was operated on and moderate reflux up the left side (Fig. 4C). The patient since has been followed periodically without urethral dilatation. The residual urine has varied from a few drops to 2 or 3 cc. No medication has been given, and her urine has continued to show negative findings. Her health has been excellent, and there has been no history of urinary infection for over one year and a half. On September 13, 1960, a check intravenous pyelogram revealed the renal architecture to be within normal limits, with excellent concentration bilaterally on the five-minute film (Fig. 4D).

Case 4. The patient is a four-year-old white female child who was seen in the office on October 31, 1956. She had previously been admitted to a hospital because of a high fever of 105 to 106 F. An evaluation had revealed a urinary infection. She had had previous attacks of high fever with vomiting, but no diagnosis had been made of urinary difficulty. She gave a history of wetting the bed at night with occasional wetting in the daytime. Generally the child had not been up to par and would tire easily when at play. Her past history was unremarkable and noncontributory. A urine examination at that time revealed: pH, 5.5; albumin, 0; sugar, 0; and wetdrop examination, 2 to 8 white blood cells with an occasional clump of rodlike bacteria. On physical examination the patient was a thin, somewhat pale female child in no acute dis-

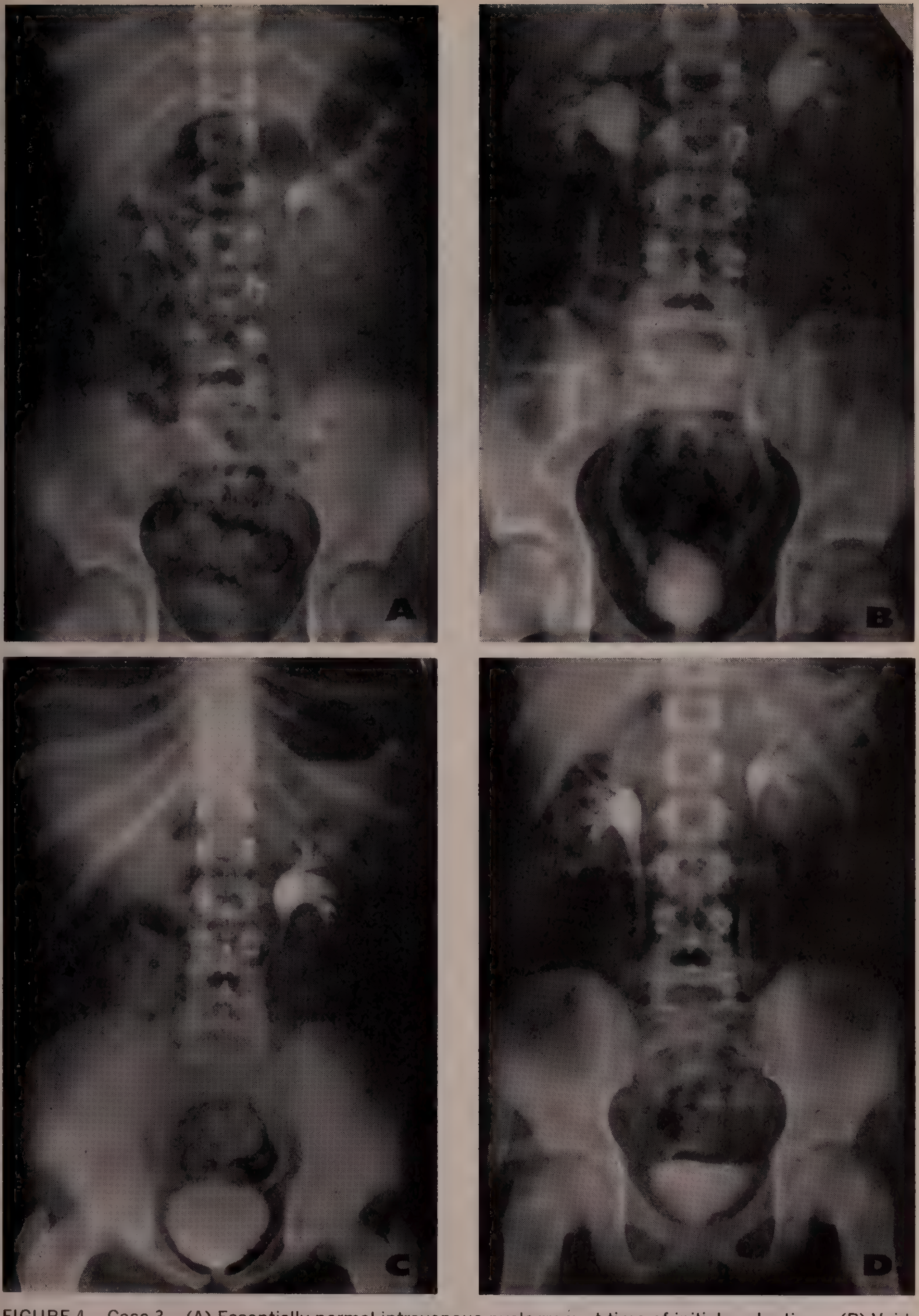

FIGURE 4. Case 3. (A) Essentially normal intravenous pyelogram at time of initial evaluation. (B) Voiding cystogram showing bilateral ureteral reflux. (C) Voiding cystogram after suprapubic Y-V bladder neck reconstruction and ureteroplasty right. Note absence of reflux on right side. (D) Intravenous pyelogram showing excellent function and essentially normal findings one year after surgery.

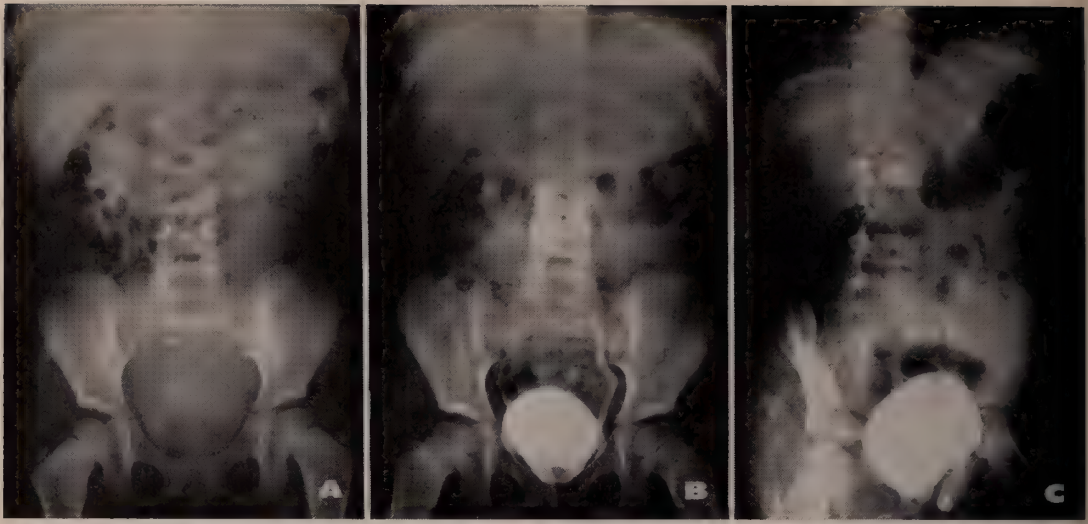

FIGURE 5. Case 4. (A) Intravenous pyelogram at time of initial evaluation. (B) Voiding cystogram showing bilateral ureteral reflux. (C) Voiding cystogram showing absence of ureteral reflux following suprapubic Y-V bladder neck reconstruction and ureteroplasty on left.

tress. Neither kidney was palpable or tender. There was suprapubic discomfort. There was some tenderness along the region of the descending sigmoid colon, but it was filled with feces. A rectal examination confirmed this. Calibration of the urethra revealed it to be somewhat tight to a number 18 French sound. An intravenous pyelogram showed essentially normal findings (Fig. 5A).

The patient was admitted to the hospital for cystoscopy. This revealed a very definite contracture of the bladder neck with coarse trabeculation. The patient was treated with urethral dilatations and continuous chemotherapy. She was seen in the office at one-month intervals until June 16, 1957, at which time she had a flare-up of urinary infection which cleared with chloramphenicol. She continued to have difficulties in spite of continuous chemotherapy and repeated antibiotics until September 27, 1957, when dilatation seemed to be much more effective. The urethra was easily dilated to a number 24 French sound, and she was maintained on one tablet of nitrofurantoin (Furadantin) every other day. She continued to do well until the spring of 1958 when in spite of medication she had recurrence of urinary infections. The residual urine at that time was 25 cc. The patient was admitted to the hospital for re-evaluation. Cystoscopy and fulguration of the bladder neck were carried out. Postoperatively her course was complicated by an infection which responded to chemotherapy. The patient continued to do well for a period of almost one year when she again in August, 1959, had a recurrence of severe urinary infection. This responded to chemotherapy and antibiotics. On October 7, 1959, a voiding cystogram was obtained which revealed trabeculation of the urinary bladder and bilateral ureteral reflux (Fig. 5B). The residual urine at that time was but a few cubic centimeters. The patient continued to do poorly in spite of the fact that the residual urine remained between 2 and 5 cc., and the urine continued to show negative findings. She was admitted to the hospital in December, 1959, at which time a Y-V plasty of the bladder neck and a Hutch ureteroplasty on the left side were carried out. Her postoperative course was entirely benign. She was seen in the office on January 29, 1960, at which time the residual urine was a few drops. The urine showed a few red and white cells. Since that time the child's health has been excellent. There has been no urinary infection. No urethral dilatations have been carried out, and chemotherapy has been discontinued for over a year. On March 3, 1961, a voiding cystogram showed no evidence of reflux on either side (Fig. 5C).

CASE 5. The patient, a five-year-old white male, was admitted to the hospital with convulsions. The mother stated that the child had been well until one day prior to admission when he awoke from his nap and vomited twice. He appeared drowsy and lethargic. He was restless in the night. At 1:15 P.M. the patient had a convulsion. After being seen by his family physician, he was admitted to the hospital. Another convulsion occurred on the way to the hospital, and he was admitted in a comatose state with flaccidity of the right extremities.

The past history was negative and noncontributory. The patient was semicomatose with purposeless motions of the left extremities and flaccidity of the right. A physical examination revealed: blood pressure, 100/40; pulse, 124; and temperature, 103.4 F. The positive phys-

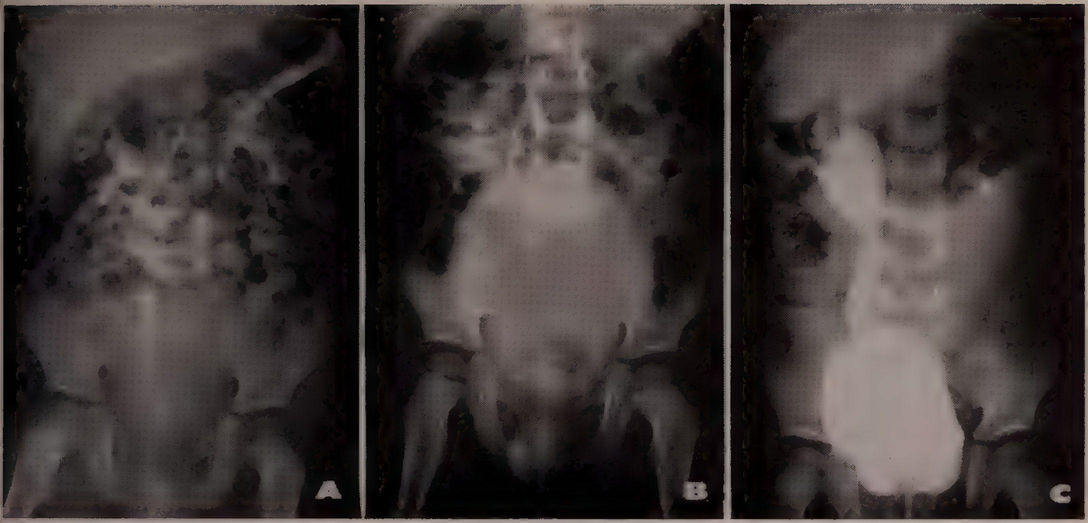

FIGURE 6. Case 5. (A) Intravenous pyelogram at time of initial evaluation. (B) Upright film on intravenous pyelogram revealing markedly dilated bladder. (C) Voiding cystogram showing bilateral ureteral reflux, marked on right.

ical findings were neurologic with absent abdominal and cremasteric reflexes. There was depression of the right reflexes and hyperactivity of the left. The laboratory findings were: white blood count, 37,400, with a shift to the left; hemoglobin, 11.9 Gm.; spinal fluid, 14 cells per cubic centimeter; and Pandy test, negative results. The urinalysis showed: color, amber; albumin, trace; sugar, 0; white blood cells, 6 to 8 per high power field; and red blood cells, 0 to 1 per high power field.

The patient was given penicillin, and the temperature returned to normal within seventy-two hours. Roentgenograms of the chest showed normal findings, and blood cultures showed no growth. His clinical response was good, and all neurologic findings returned to normal. Intravenous pyelography revealed right ureteral dilatation with a ureteral vesical obstruction and a large dilated bladder (Fig. 6A and B). A urologic consultation was requested.

There was no history of urinary difficulty. A physical examination was essentially within normal limits with reference to the genitourinary tract. A voiding cystogram was obtained which revealed an irregular bladder with bilateral ureteral reflux, severe on the right side (Fig. 6C). Cystoscopy showed a markedly trabeculated bladder with contracture of the bladder neck.

The patient was discharged to home on continuous chemotherapy. He was returned to the hospital six weeks later. He had been asymptomatic. A suprapubic Y-V plasty was performed with a wedge resection of the bladder neck. The postoperative course was entirely benign. He was discharged home on the tenth postoperative day. He is being maintained on continuous low-dose chemotherapy and to date is asymptomatic

Comment

It would appear that there is much to be learned from these representative cases. It is apparent from Case 1 that ureteral reflux may disappear with conservative therapy and urethral dilatations. If the bladder neck obstruction is relieved, reflux may disappear.

In Case 2 we can see how in the absence of urinary symptoms repeated fevers were explained away by tonsillitis, sore throats, virus infections, and so forth. This extended over a period of time long enough to allow complete destruction of one kidney. The pathologic condition was extensive and the bladder neck obstruction marked.

Although Case 3 had a few episodes called sore throat and virus before the exact diagnosis was made, no marked renal damage had occurred. Here, however, all forms of conservative therapy were without avail. It was not until surgical correction was carried out that permanent cure was established. This does not mean that conservative therapy is without avail, but it does signify that one must follow these patients and use whatever means are necessary to secure a satisfactory conclusion.

So often when the urethra has been dilated adequately and the residual urine reduced to a few cubic centimeters, the persistence or recurrence of infection has not resulted in further corrective measures. Case 4 exemplifies the need for and the use of bladder neck plastic procedures in these instances. I have 5 female children whose urethras dilated with ease and whose residual urines were insignificant but who had recurrent infections in spite of chemotherapy. All have been cured by suprapubic bladder neck resections.

Urinary infection as a cause of fever of unknown etiology could not be better exemplified than by Case 5. It is most interesting that the intravenous pyelogram suggested a ureterovesical stricture on the right side, but after a more thorough workup the true obstruction was found at the bladder neck.

There have been two areas of thought in pediatric urology which have attracted much of my attention—two areas from which over the past eleven years I have gleaned many cases of bladder neck obstruction. These areas are urinary infection and enuresis.

It has been my impression that frequently urinary infection has existed longer than is indicated in the history. A red throat has explained away many a fever. Since both sore throats and urinary infections respond to the same medication, it may be some time before a urinalysis is performed. With this in mind one must re-examine the rule of thumb which is used by many pediatricians, "I let them have two infections, but after that they are referred for a urologic workup." How sure are you when the first infection occurred?

In the absence of specific urinary symptoms of marked degree, many symptoms are elicited only in retrospect and after detailed questioning. In 21 or 17 per cent of our patients no urinary symptoms were present, and none could be found even on extensive questioning. In this group we find some of the most extreme disease and obstruction.

Enuresis or the lack of it can be similarly significant. Beware of the child who is toilet-trained too early. Bladder neck obstruction can be an aid to early training. The history of early toilet training between one and two years of age plus infrequency of voiding in the daytime is very suggestive of vesical neck obstruction. The bladder capacity should not be great enough to allow such periods of retention. The child at two or three years of age who does not wet at night and who voids only two or three times in the day is usually in for trouble.

The evaluation of any child with fever of unknown etiology must include a urologic study when a definite cause cannot be found. A urinalysis is not sufficient. Urine cultures may reveal an asymptomatic apyuric infection. In chronicity the cellular response may be minimal or absent or intermittent. The use of all the modalities of urologic investigation may be necessary. The pediatrician who is satisfied with an intravenous pyelogram and a urinalysis is going to miss the diagnosis in many of the cases which most need correction.

Summary

In all patients with fever of unknown etiology, urinary infection and, more specifically, bladder neck obstruction, must be suspected as the etiologic factors. Unless a complete urologic evaluation is performed the diagnosis may be missed. Intravenous pyelography and urinalysis by themselves may be insufficient. Bladder neck obstruction with marked involvement of the urinary tract may be present in the absence of urinary symptoms.

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Discussion

William B. Garlick, M.D., *Albany, New York.* I wish to congratulate Dr. Thompson on a very instructive and timely paper. Its great value lies not only in the material presented but more specifically in the very careful follow-up of these patients over a period of years. For only through follow-up can we be sure of our results.

As you all well realize, pediatric urology is a new specialty, and to those of us who are intimately concerned with this, it has been mainly trial and error for we had no one to guide us. The combined experiences of this group are now beginning to pay off in better and correct care of these unfortunate children through proper and early diagnoses.

I think it is safe to say that bladder neck obstruction is rather unique among congenital anomalies in that it often defies detection by ordinary means. Many of these youngsters do not have urinary tract symptoms but rather may have vague gastrointestinal symptoms combined with fever. The urine may or may not have pus, and often it is only in desperation that these youngsters become investigated. Everyone realizes that every youngster cannot be completely worked up every time that fever occurs, but we should all be on the lookout for this common anomaly. I would like to emphasize Dr. Thompson's point that intravenous pyelograms and cultures alone are not enough, for many times these will not be diagnostic; in fact it has been our experience that many times cystoscopy will fail to demonstrate bladder neck obstruction. This may also be true of calibration of the urethra and residual urine. You may wonder, then, how one can find this. We have a set routine on our service for investigating youngsters. We start with cultures and then intravenous pyelography; on the following day, the urethra is calibrated, the residual urine is checked, and a voiding cystogram and a delayed cystogram are done. One must do a voiding cystogram, for many times this is the only way reflux will be demonstrated, thereby making it possible to diagnose the bladder neck obstruction. It is important to do the cystogram at some time other than with the intravenous pyelogram because of confusion with intravenous dye. Cystoscopy and urethroscopy are then carried out and retrograde pyelograms if necessary. The various cystograms are as much a part of our work-up as urine examinations and cultures. In infants and small youngsters who are too young to cooperate, we get a pressure cystogram by passing a Foley catheter, filling the bladder, and then clamping off part of the outlet of the catheter, thereby creating a pinpoint stream and pressure on the bladder. The more the youngster cries, the better. This has been very helpful to us in demonstrating reflux for many times the plain cystogram is not diagnostic.

It is gratifying to see that Dr. Thompson has treated some of these cases conservatively for we believe that there is a place for this type of treatment, as do John K. Lattimer, M.D., and others. However, one must be prepared to do a vesical neck plasty if this does not work within a reasonable length of time.

In one respect, I must disagree with the author. It has been our experience that following vesical neck operations on these youngsters as a rule the reflux will disappear. Therefore, we do not believe in trying to correct reflux by any method until a trial has been given. Many urologists believe that all types of antireflux operations are harmful because of the obstruction created. Be that as it may, it is our belief that in most cases, correction of the bladder neck obstruction alone will cure the patient.

Use of Fe^{59} in Determination of Latent Iron-Binding Capacity

Diagnostic Test in Various Liver Diseases

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THE DIFFICULTY in differentiating clinically the various types of liver disease has produced a multitude of laboratory tests in the attempt to enable more accurate diagnoses. In recent years the serum iron level in various liver diseases has been studied extensively by many investigators[1–7] and appears to have definite value in differential diagnosis. However, since the level of serum iron is controlled in part by the amount of iron-binding protein in the blood,[8] any disease state which produces a change in serum iron levels might be expected to show changes also in the latent and total iron-binding capacity. Therefore the simultaneous determination of serum iron and iron-binding capacity, giving a more complete picture of iron metabolism, might prove more valuable diagnostically than either determination alone. The study presented here was undertaken to test this theory.

SI (serum iron) levels, LIBC (latent iron-binding capacity), and TIBC (total iron-binding capacity), as well as the percentage of saturation of the TIBC, or transferrin, were analyzed in three diseases of the liver: acute hepatitis, Laennec's cirrhosis, and carcinoma. These data were collated as part of an extensive evaluation of various available liver profile tests which is being carried out at the Millard Fillmore Hospital Research Institute on all types of liver disease.

An identical battery of tests was performed on an unselected group of patients who were admitted to the Millard Fillmore Hospital and suspected of having any disease involving the liver. The present study includes only those patients with proved diagnoses of acute hepatitis, Laennec's cirrhosis, and either primary or metastatic carcinoma of the liver, and only the changes observed in the SI, LIBC, and TIBC were considered in these cases. Later the diagnostic importance and interrelationship of these determinations in comparison with others performed in the over-all study will be investigated.

Method

The group studied comprised 41 patients with Laennec's cirrhosis, 19 with acute hepatitis, and 16 with either primary or metastatic carcinoma of the liver, a total of 76 patients. The diagnosis was established either by biopsy or after a review of the attending physician's final diagnosis by three independent observers. In this study hepatitis associated with infectious mononucleosis, serum hepatitis, and infectious (viral) hepatitis were included in the category of acute hepatitis. Cases of leukemia and lymphosarcoma involving the liver were not included in the study.

On each patient the SI was determined by the method of Barkan and Walker.[9] On the same sample of serum the LIBC was determined by a new method developed at this hospital which utilizes Fe^{59}-labeled iron.[10] Briefly, the technic involves the addition of an excess amount of iron labeled with Fe^{59} to serum in vitro and then subject-

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ing this serum to paper electrophoresis. As previously demonstrated by Wallenius,[11] the Fe^{59}-labeled iron will appear in the beta fraction of the electrophoretic strip. When the binding capacity of the beta-1 globulin (transferrin) is exceeded, the remainder of the radioactivity will be found in the gamma globulin zone. The radioactivity present in the beta and gamma globulin zones is equal to the total radioactivity of Fe^{59} added. By counting the proportional amount of radioactivity bound to the beta and gamma fractions, the amount of iron added to the serum that is bound by the beta globulin can be calculated as the LIBC by the following formula:

$$\text{LIBC } (\mu g\%) = \frac{Fe^{59} \text{ in B-globulin} \times Fe^{++}\mu g \text{ added/ml.} \times 100}{Fe^{59} \text{ in B-globulin} + Fe^{59} \text{ in gamma globulin}}$$

Normal values for the LIBC and TIBC by this method are listed in Table I. This procedure, described in detail elsewhere,[10] is carried out easily in the clinical laboratory, and the results are reliable and reproducible. In addition to the SI and LIBC, the TIBC and per cent saturation of the TIBC with iron was calculated for each patient.

A STUDY WAS MADE *of 41 patients with Laennec's cirrhosis, 19 with acute hepatitis, and 16 with either primary or metastatic carcinoma of the liver. The SI (serum iron) and LIBC (latent iron-binding capacity) were determined by electrophoresis using Fe^{59}-labeled iron. The TIBC (total iron-binding capacity) and per cent saturation of the TIBC with iron were calculated also. The significant changes found were: in hepatitis, an increased SI content and TIBC, along with a normal LIBC; in cirrhosis, a normal SI content together with low LIBC and TIBC and a subsequent rise in saturation of the latter; and in carcinoma, a low SI content and a decrease in saturation of the TIBC. The value of the SI determination in differential diagnosis of the liver diseases investigated is increased when it is done in conjunction with determination of the LIBC and calculation of the TIBC and per cent saturation of the TIBC.*

Results

Laennec's cirrhosis. In the group of 41 patients with Laennec's cirrhosis the mean SI level was 117.4 ± 7.5 micrograms per 100 ml. The presence or absence of bleeding or anemia was not considered in the statistical evaluation of these cases.

The LIBC was found to be 199.5 ± 8.1 and the TIBC 316.9 ± 6.1 micrograms per 100 ml. with a saturation of 36.9 ± 0.73 per cent.

Acute hepatitis. In the 19 patients with acute hepatitis the serum iron values ranged from near-normal to highly elevated levels, but none were below normal. This might be accounted for by the fact that the cases were completely unselected as to the activity of the disease at the time of investigation. The mean SI was 164.4 ± 14.5, the LIBC 235.05 ± 18.3 and the TIBC 404.7 ± 20.6 micrograms per 100 ml., with an iron saturation of 40.5 ± 2.5 per cent.

Carcinoma of liver. In the group with carcinoma of the liver also the severity of the disease was not taken into account, nor was the degree of metastatic involvement, bleeding, or the presence of anemia. In these 16 patients the mean was SI 73.9 ± 7.5, the LIBC 202.1 ± 16.3, and the TIBC 276.0 ± 19.4 micrograms per 100 ml. with an iron saturation of 26.9 ± 2.1 per cent (Table I).

The significance of the difference between

TABLE I. Mean values (in micrograms per 100 ml.)* of SI, LIBC, TIBC, and per cent saturation of TIBC observed in the liver diseases studied compared with normal values

Group	Number of Cases	SI	LIBC	TIBC	Saturation (Per Cent)
Normal	21	110.9 ± 6.7	245.5 ± 4.08	355.0 ± 11.3	...
Hepatitis	19	164.4 ± 14.5	235 ± 18.3	404.7 ± 20.6	40.5 ± 2.5
Laennec's cirrhosis	41	117.4 ± 7.5	199.5 ± 8.1	316.9 ± 6.1	36.9 ± 0.73
Carcinoma of liver	16	73.9 ± 7.5	202.1 ± 16.3	276.0 ± 19.4	26.9 ± 2.1

* Mean values and the standard error of the mean are expressed in micrograms per 100 ml. The normal values shown for comparison were obtained on a control group employed in a previous study establishing the validity of the method.

TABLE II. Mean differences in SI, LIBC, and TIBC with t test evaluation of their significance*

Sample Compared	Test	Mean Difference	T Test Values: Found	T Test Values: Required 5 Per Cent Level	T Test Values: Required 1 Per Cent Level	Degrees of Freedom	Remarks
Normal versus hepatitis	SI	43.5	8.5	2.02	2.70	40	No significant difference in LIBC
	LIBC	10.5	1.1				
	TIBC	49.0	5.4				
Normal versus cirrhosis	SI	6.5	2.1	2.0	2.66	60	No significant difference in SI
	LIBC	46.0	11.2				
	TIBC	38.8	12.4				
Normal versus carcinoma of liver	SI	47.0	11.1	2.03	2.73	35	...
	LIBC	43.4	7.8				
	TIBC	79.1	11.2				
Hepatitis versus cirrhosis	SI	47.0	11.4	2.0	2.66	58	...
	LIBC	35.5	6.8				
	TIBC	87.8	18.9				
Hepatitis versus carcinoma of liver	SI	90.5	15.3	2.03	2.75	33	Questionable significance in LIBC
	LIBC	33.9	3.9				
	TIBC	128.7	13.1				
Cirrhosis versus carcinoma of liver	SI	43.5	11.5	2.01	2.68	55	No significance in LIBC
	LIBC	2.6	0.5				
	TIBC	40.9	8.8				

* Statistical evaluation of differences noted between the disease states investigated and between the disease state and the normal as described in the text. The t values found experimentally are compared with the 5 per cent and 1 per cent probability levels. The degrees of freedom are noted for each sample evaluated.

each of these disease categories, as well as between the disease state and the observed normal values of SI, LIBC, and TIBC, was determined by the t test (Table II).

Comment

The rise of the SI to a significant degree above normal levels in acute hepatitis as observed in this study is in agreement with the findings of previous investigators.[1-7] Many of these reports indicate extremely high levels of SI in the range of 300 micrograms per 100 ml. when the determination is made at the time of maximum activity of the disease.

The mechanism of this rise has been a subject of investigation for many years. Reissmann and Dietrich[12] are of the opinion that part of the rise is accounted for by the release of hepatic ferritin when the hepatic cells undergo degeneration. Laudahn[13] also attributes it to the liberation of ferritin due to hypoxia of parenchymal liver cells. The magnitude of the hyperferremia has been reported to follow the extent of liver cell necrosis[14] and can be used to judge the activity of the necrotic phase of acute hepatitis.[15] Thus the elevation of the serum iron level can be a guide to the activity of the disease and can be helpful in prognosis and therapy. Since the SI often follows maximum hyperbilirubinemia, it can also be helpful diagnostically, especially when bilirubin levels are near normal.[16]

The TIBC in acute hepatitis has not been studied as extensively as the SI changes. In the present study the TIBC was definitely elevated above normal values, as was also noted by Lange and Oberhoffer,[1] as well as Mandel.[17]

The rise of the TIBC might be explained by a release of a sequestered phase of transferrin to the circulating phase, as has been postulated to occur in the increase of the TIBC in iron deficiency anemia,[18] due either to cell necrosis or to compensation for the flood of iron into the serum. Laudahn[13] also mentions the release of a beta-globulin complex from the liver during hypoxic states as a possible mechanism of the increased TIBC.

Contrary to the observations in this study, Heidel[5] noted an initial decrease in the TIBC in hepatitis during maximum hyperferremia, followed by a rise toward normal levels.

The cirrhotic patients in this study exhibited relatively normal or slightly above normal SI levels. A few patients had levels significantly higher than normal but not as high as those found in hepatitis. Similar findings have been noted in previous investigations of the SI in Laennec's cirrhosis.[1–7] Levels significantly below normal were rare. The common occurrence of hemolytic anemia with chronic liver disease, which in itself raises SI levels, might account for the SI level remaining normal instead of falling as it does in most other chronic diseases.[19]

In the present study, although the SI remained essentially normal, both the LIBC and TIBC were below the normal range. Similar findings are reported by Heidel[5] who presumes this to be a result of the over-all disturbance of protein metabolism which is characteristic of cirrhosis. Wuhrmann and Jasinski[20] gave the same explanation for this phenomenon.

Rechenberger and Hevelke[21] demonstrated an accelerated removal of intravenous iron in cirrhotic patients, in contrast to its slow removal in hepatitis. Whether or not this is related to the inability of the lowered TIBC to carry iron is an interesting speculation.

As a result of the normal SI levels, together with decreased LIBC and TIBC, the percentage of saturation of the TIBC with iron is increased. The clinical implication of this is readily apparent. Iron which is given to these patients, either orally or parenterally by repeated blood transfusions, could bring about complete transferrin saturation, as in hemochromatosis or hemosiderosis. As previously mentioned there is some evidence of avidity of cirrhotic livers for iron, and this, together with saturation of the transferrin, creates an ideal situation for the production of secondary hemochromatosis.

Goldberg and Smith[22] suggest that an already damaged liver is susceptible to iron overloading and subsequent pigmentary cirrhosis. MacDonald[23] found an increase in iron absorption in experimental animals on a diet which also promotes the development of cirrhotic changes in the liver.

Lowering the serum iron level in various types of malignant disease has been reported previously.[2, 24–26] A decrease of SI in hepatic carcinoma was also noted in this investigation, and, although bleeding was not excluded as a cause, many patients with out anemia or bleeding were found to have low SI levels.

Several explanations for the decreased SI in carcinoma have been offered. Yonehiro *et al.*[27] have demonstrated an increase in the uptake of Fe^{59} by malignant tumors as compared with normal adjacent tissue. Miller and his coworkers,[25] studying anemia and iron metabolism in carcinoma, found that a low SI did not indicate an associated anemia or bleeding, and that normal tissue hemosiderin levels found in liver, spleen, and bone marrow excluded iron deficiency as a cause of the hypoferremia. They further state that the depression of the SI tends to parallel the extent of growth and metastatic spread of the neoplasm.

The finding of a decreased TIBC and LIBC in carcinoma of the liver probably reflects the poor protein metabolism of a damaged liver. The simultaneous finding of a low SI, LIBC, and TIBC corresponds to that seen in infections and inflammatory disease and may have a similar etiologic relationship.

An interesting difference in the behavior of the SI and transferrin levels in cirrhosis and carcinoma is that in carcinoma the per cent saturation was low whereas in cirrhosis it was somewhat elevated. Thus a helpful differentiation between these two diseases, both showing a depression of TIBC levels, may be made by means of these tests.

Conclusion

Applying the t test, the SI levels in the diseases studied all show significant differences.

The increased SI found in acute hepatitis differentiates it from cirrhosis and carcinomas, especially when the TIBC is also elevated. A normal or slightly elevated SI in cirrhosis aids in distinguishing this disease from carcinoma and becomes even more significant when the increase in the per cent saturation of the TIBC is taken into account. In both carcinoma and cirrhosis the TIBC is decreased below normal and considerably lower than that seen in hepatitis.

The latent iron-binding capacity in hepatitis tends to remain normal, whereas in cirrhosis and carcinoma it is significantly decreased. The LIBC and TIBC are both

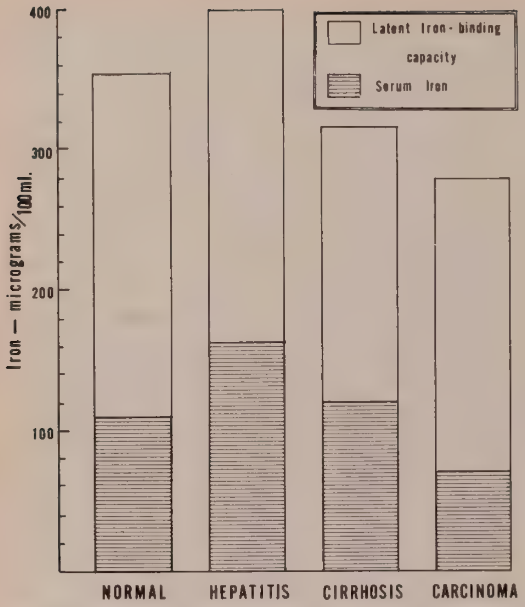

FIGURE 1. Total iron-binding capacity in three liver diseases compared with normal serum values.

lowered in many cases of cirrhosis and carcinoma; indeed no statistically significant difference in these diseases was found in the present study. However, the marked decrease in the per cent saturation of the TIBC in carcinoma as compared with its increase in cirrhosis does provide a diagnostic aid (Fig. 1).

From this study it appears that the value of the serum iron determination in the differential diagnosis of the liver diseases investigated is increased when it is done in conjunction with determination of the LIBC and calculation of the TIBC and per cent saturation of the TIBC.

The significant changes noted in this study are: (1) the rise of SI together with a normal LIBC and obviously increased TIBC in hepatitis; (2) the normal SI with a low LIBC and TIBC and subsequent increase in the per cent saturation of the TIBC in cirrhosis; and (3) the low SI and decreased per cent saturation of the TIBC in carcinoma in contrast to these findings in cirrhosis.

An evaluation of the role played by these tests in differential diagnosis must await the statistical analysis of the results of a large, standardized group of liver profile tests which are currently being studied in this institution in unselected patients with suspected liver disease.

Summary

In the belief that the simultaneous determination of serum iron and iron-binding capacity might prove a more valuable aid in the differential diagnosis of certain liver diseases than either determination alone, this study was undertaken. SI (serum iron) levels, LIBC (latent iron-binding capacity), and TIBC (total iron-binding capacity), as well as the per cent of total saturation of the latter, were determined in 76 patients with hepatitis, cirrhosis, and carcinoma involving the liver.

The LIBC of the serum was determined in vitro by means of a method developed here which utilizes Fe^{59} and paper electrophoresis.

The significant changes found were: in hepatitis, increased SI content and TIBC, along with a normal LIBC; in cirrhosis, a normal SI content together with low LIBC and TIBC and a subsequent rise in saturation of the latter; and in carcinoma, a low SI content and a decrease in saturation of the TIBC.

Likely explanations for these observed changes and their implications in differential diagnosis are discussed.

A proper evaluation of the diagnostic importance of these tests awaits the statistical analysis of a battery of liver profile tests which are being investigated at this institution on a large number of patients who are suspected of having liver disease of various types, of which the present study is a part.

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Convention paging system

We hope that physicians attending the 156th Annual Convention of the Medical Society of the State of New York will be able to devote all their attention to the interesting program, exciting exhibits, and other features of the meeting. However, if it is necessary, physicians can always be in touch with their offices, their patients, or whoever else may wish to contact them, through the SherPage System. They may be reached by television anywhere at the convention.

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Post-Traumatic Aseptic Necrosis of Talus

Preliminary Report

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THE VASCULAR SUPPLY to the talus has been the subject of debate for many years. Sneed in 1925[1] stated that the talus was nourished by numerous small blood vessels and had no main nutrient arteries. He maintained that the small vessels could not be stretched, and therefore avascular necrosis would follow dislocation of the talus. McKeever in 1943[2] postulated that the entire blood supply to the talus was carried in the astragaloscaphoid ligament by branches of the anterior tibial artery, and this view was held widely for many years. Coltart stated in 1952[3] that the talus was supplied by three groups of vessels; if two of the groups were destroyed, necrosis occurred.

Wildenauer in 1950,[4] and more recently Haliburton *et al.*[5] of the Mayo Clinic demonstrated by detailed studies of amputation specimens that the talus was supplied (1) by the three main arteries of the lower leg via a periosteal vascular network which covers all the cartilage-free surfaces, particularly medially, and (2) through two discrete vessels: branches of the posterotibial artery medially and branches of the dorsalis pedis, or lateral malleolar or perforating branch of the peroneal artery, laterally. These two arterial branches, one in the tarsal canal and one in the sinus tarsi, anastomose widely and enter the talus chiefly inferiorly. Thus, although the talus is covered on three fifths of its surface by articular cartilage, it does have a rich blood supply which enters chiefly through the subtalar region. However, injury to the talus may damage this supply sufficiently to produce necrosis.

In a very extensive but short-term study of 228 talus injuries, Coltart[3] found necrosis to be a significant complication in those injuries in which there was a fracture of the talar neck with subluxation or dislocation of the body. He believed necrosis always was evident by eight weeks and that the average time for the regeneration of the body was six months. However, he did not attempt a follow-up study. In fact, the lengthy process of repair and the final effect of treatment on patients who have had aseptic necrosis of a portion of the talus has not been studied adequately.

The preliminary report to be presented here comprises the late results in a series of cases of severe injury to the talus, with particular emphasis on the course of aseptic necrosis.

Materials and methods

The 21 patients in the present study all had significant talus injuries. Minor injuries, such as avulsion flake fractures, were not considered. The study includes many patients of colleagues in Buffalo who were kind enough to allow us to review their case histories and initial roentgenographs and to make follow-up examinations of their patients, including recent, detailed physical and radiographic examinations and comparable studies of the opposite ankle.

The patients studied comprised 12 males

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and 9 females, ranging in age from three to seventy-two years; the average age was thirty-seven years. The mechanism of injury generally was violent; 8 of these patients had fallen from heights varying from 4 to 32 feet. The period of follow-up varied from six months to nine years, the average being five years. The end results were classified as excellent, good, fair, and poor. Occasionally the clinical and radiographic results differed; in this case the two were correlated, and an intermediate result was recorded. Even in the cases with the best results, minimal abnormalities still were present both clinically and radiographically.

Those patients were considered to have excellent results who had few complaints and could indulge in strenuous activities without disability. On examination these patients were found to have less than a 10 per cent loss of subtalar or ankle motion and little if any ankle swelling or calf atrophy. A radiographic examination showed a normal configuration of the talus with little narrowing or sclerosis about the pantalar joints.

Patients were classified as having good results if they had few complaints but did have some pain and limped following strenuous activity. On examination these patients were found to have a 60 per cent or more pantalar motion with only mild ankle swelling or calf atrophy. X-ray changes demonstrated a fairly normal configuration of the talus with mild arthritic changes.

Patients were considered to have fair results if they experienced pain on moderate activity and were found to have from 30 to 60 per cent pantalar motion, moderate ankle swelling, and calf atrophy and if moderate arthritic changes with some loss of normal configuration of the talus were demonstrated roentgenographically.

Those patients were considered to have poor results who had many complaints, much limitation of activity, and a constant limp. These patients had less than 30 per cent of normal ankle and subtalar motion, and radiographs showed severe arthritic changes in the joints about the talus, with deformity of the talus.

TWENTY-ONE PATIENTS *with significant talus injuries were studied; 7 of these developed aseptic necrosis. The early diagnosis of aseptic necrosis was difficult. In later stages evidence of the replacement of the necrotic bone may be seen on the roentgenogram as mottling with irregular zones of decreased density and irregular, thickened trabeculae. In the adult, the articular cartilage overlying the necrotic bone will undergo changes. The treatment of the patients with aseptic necrosis varied. The 3 patients with open injuries were treated with open reductions. In the other 4 patients two fractures simply were immobilized, one was treated first by closed reduction and then open reduction, followed by bone grafting, and the fourth was treated by open reduction. After an average follow-up period of 4.5 years, the end result was excellent in 1 patient, good in 2, fair in 2, and poor in 2. This was far inferior to the over-all late results in the total group of 21 cases.*

The 21 cases studied were divided into three major groups: dislocations, fractures, and fracture-dislocations. Dislocations, in turn, were divided into single, double, or triple, depending on the joints involved. The fracture-dislocations were subdivided into fracture-dislocations of the neck and fracture-dislocations of the body. Five injuries were open. Two of these were dislocations of the talus, while three were fractures of the neck with dislocation of the body.

In 7 of the 21 patients aseptic necrosis occurred. Only this group will be discussed at this time.

The diagnosis of aseptic necrosis in its early stages often was difficult. The body of the talus, if avascular, will not take part in the disuse atrophy occurring in the surrounding bony structures and will appear dense by contrast on the roentgenogram. However, if the extremity has not been protected from weight-bearing, very little disuse atrophy will occur, and an early diagnosis of necrosis may be extremely difficult. In addition, the overlapping malleoli on the lateral roentgenogram often will give the talar body a dense appearance, and therefore comparable studies of the normal ankle are mandatory. Decoulx

TABLE I. Post-traumatic aseptic necrosis of talus in 7 cases

Case	Age (Years)	Sex	Diagnosis	Treatment	Length of Follow-Up (Years)	Late Result
1	37	M	Open complete lateral dislocation	Talus removed completely, washed, and replaced accurately. Non-weight-bearing, 13 months	6	Good
2	37	M	Open fracture neck, with posteromedial dislocation body and fracture medial malleolus	Open reduction with internal fixation medial malleolus. Non-weight-bearing, $1^{1}/_{2}$ years	4	Fair
3	35	F	Fracture neck with dislocation of body	Closed reduction; non-weight-bearing, $8^{1}/_{2}$ months	$1^{1}/_{2}$	Fair
4	41	M	Fracture neck with posteromedial dislocation of body	Closed reduction unsuccessful, then open reduction. Bone grafting for nonunion at 1 year. Weight-bearing before adequate replacement	4	Poor
5	3	F	Fracture neck	Immobilization—few months. Intermittent non-weight-bearing, 3 years	6	Excellent
6	23	M	Open fracture of neck with lateral body dislocation	Open reduction, non-weight-bearing, 3 months	$1^{1}/_{4}$	Good
7	22	M	Markedly comminuted fracture of body	Attempt at open reduction with posterior ankle denervation. Non-weight-bearing, 5 months	9	Poor

and Razemon[6] have suggested tomograms as diagnostic aids.

In later stages evidence of the replacement of the necrotic bone may be seen on the roentgenogram as mottling with irregular zones of decreased density and irregular, thickened trabeculae. In the adult, the articular cartilage overlying the necrotic bone will undergo changes. Narrowing of the articular cartilage spaces after the dead bone has been replaced also is noted. Articular cartilage in the adult presumably depends on synovial fluid and the underlying subchondral bone for nutrition. While the bone is still necrotic, the articular cartilage also is not normal but does maintain its original thickness, apparently existing in a state of "hibernation." When the underlying necrotic bone has been invaded by the advancing vascular fibrous tissue and removed and replaced by new bone, the overlying articular hyaline cartilage is replaced by a thinner, irregular layer of imperfect fibrocartilage. The roentgenogram at this time will demonstrate a narrow joint space, sclerotic changes, and signs of degenerative arthritis. If weight-bearing has not been permitted, the replacement of the necrotic bone will occur so that the architecture of the talar body will remain normal. If, however, there has been weight-bearing before the necrotic bone has been replaced, collapse may occur with fragmentation, spurring, osteocartilaginous loose body formation, and degenerative arthritis.

Aseptic necrosis occurred in 7, or one third, of the total patients. Five of the 7 were males, and 2 were females, ranging in age from three to forty-one years, with an average age of twenty-eight years. In

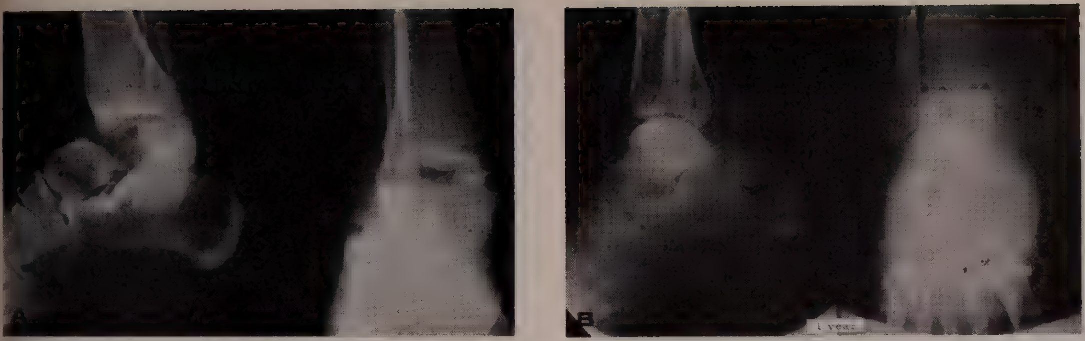

FIGURE 1. Case 1. (A) Closed fracture-dislocation of neck of talus. (B) At one year fracture was ununited and entire body obviously necrotic. Bone-grafting procedure at this time was followed by union of the fracture, and weight-bearing was begun at one year and seven months.

general, their injuries had been violent. Three patients had received open injuries, a higher incidence than in the total group (5 out of 21). The average length of follow-up was 4.5 years. Four of the 7 patients had fractures of the neck of the talus with considerable dislocation of the body, of which two were posteromedial and two lateral. Of the remaining three injuries, one was a fracture of the neck of the talus in a three-year-old child, one was a total dislocation laterally, and one was a severely comminuted fracture of the body of the talus.

Treatment

The treatment of the patients with aseptic necrosis varied. The 3 patients who had open injuries were, of course, treated with open reductions. In the other 4 patients two fractures simply were immobilized, since the position of the fragments was satisfactory. One was treated first by closed reduction and then open reduction, followed by bone grafting. The fourth was treated by open reduction. Of the 7 cases, the end result was excellent in 1 (a young child), good in 2, fair in 2, and poor in 2 (Table I). This was inferior to the over-all late results in the total group of 21 cases.

The following cases are representative of the course of aseptic necrosis following injuries to the talus.

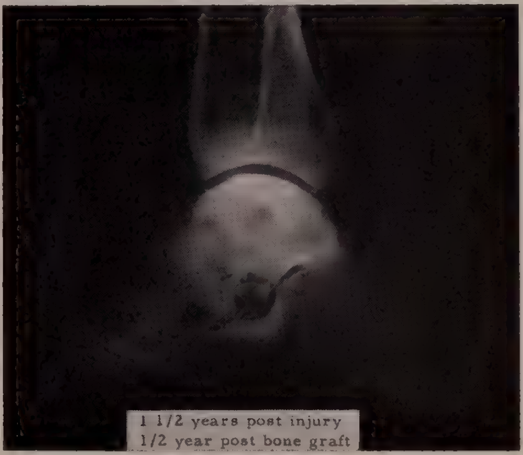

FIGURE 2. Case 1. Fracture healed, and considerable replacement of distal portion of body noted eighteen months after injury.

Case reports

Case 1. This forty-one-year-old construction iron worker fell 15 feet and suffered a closed fracture-dislocation of the neck of the talus with posterior medial dislocation of the body (Fig. 1A). A closed reduction was unsuccessful, and subsequently an open reduction was performed. The patient's ankle was protected from weight-bearing for a full year, after which a roentgenographic examination showed the talar body to be dense and obviously necrotic (Fig. 1B). There was surrounding disuse atrophy, and the fracture line was still visible. Very little replacement of the dead body had occurred. Consequently, autogenous bone grafting across the site of nonunion was performed, utilizing iliac bone. Six months after the bone grafting (eighteen months after the injury) the fracture was healed, and considerable replacement of the distal portion of the body was noted on x-ray examination (Fig. 2). The proximal portion of the body, however, was not yet replaced completely.

Weight-bearing was begun by the patient approximately seven months after the bone-grafting operation. The patient was next seen

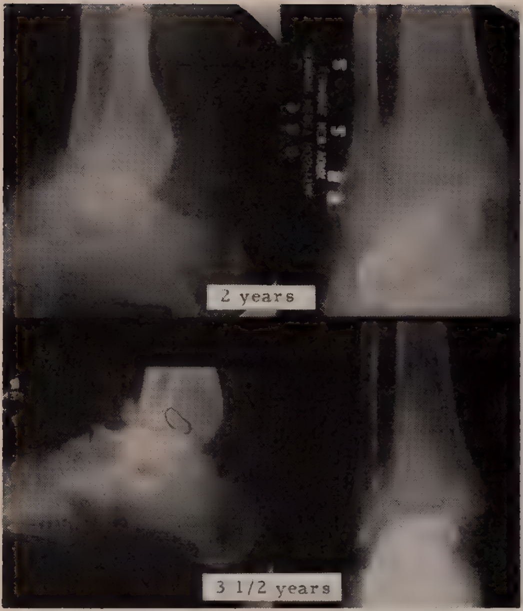

FIGURE 3. Case 1. Two years after injury there were marked collapse and arthritic changes which followed weight-bearing before transformation of the necrotic body was complete. Three and one-half years after injury there was severe degenerative arthritis of the ankle joint, with arthritis in the subtalar and talonavicular joints as well.

about five months later, at which time x-ray films demonstrated a pathologic fracture of the body of the talus with marked collapse of the necrotic bone and irregularity of the upper portion of the body, including spurring and loose body formation (Fig. 3).

Recent x-ray films, made three and one-half years after the original injury, show severe degenerative arthritis of the ankle joint, with arthritis in the subtalar and to some extent the talonavicular joint as well (Fig. 3).

Clinically, however, the patient has surprisingly good function and is classified as having a fair result. He is able to walk a mile or more without pain, although he has some difficulty on uneven ground because of stiffness in his ankle. He has a mild to moderate limp. The ankle joint motion is restricted to 10 degrees with practically no subtalar motion. There is also $4\frac{1}{2}$-cm. ankle swelling and considerable atrophy of the calf and thigh muscles. He is presently doing his regular work as a construction iron worker, but since it is now only four years after his injury, increasing symptoms can be expected.

Comment. One year after the injury there was still no union of the fracture in this case, although union did follow the bone-grafting procedure. The architecture of the talar body was well preserved until weight-bearing was permitted, when collapse of the remaining necrotic portion of the talus occurred, and marked irregularity of the ankle joint and severe degenerative arthritis developed. While this patient has few symptoms at present, the great changes noted on the x-ray and clinical examinations make the prognosis poor.

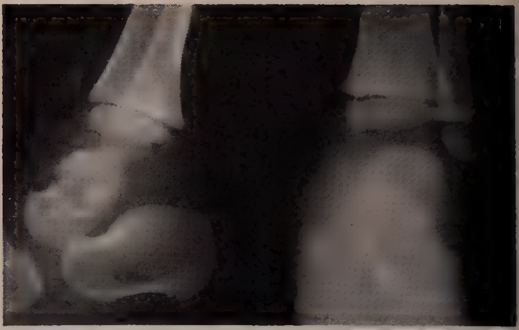

FIGURE 4. Case 2. Closed fracture of neck of talus in three-year-old child.

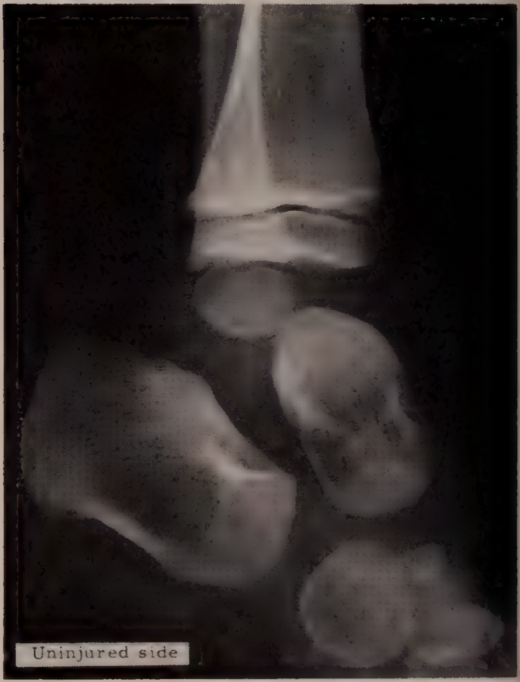

FIGURE 5. Case 2. Denseness of body of uninjured talus illustrates difficulty in diagnosing necrosis.

Case 2. A three-year-old child injured her left ankle in an auto accident and suffered a closed fracture of the neck of the talus, apparently without displacement of the fragments (Fig. 4). A roentgenogram of the uninjured ankle (Fig. 5) showed an apparent increase in density of the body and illustrates the difficulty of making an early diagnosis of necrosis. The treatment consisted of simple immobilization in a plaster dressing.

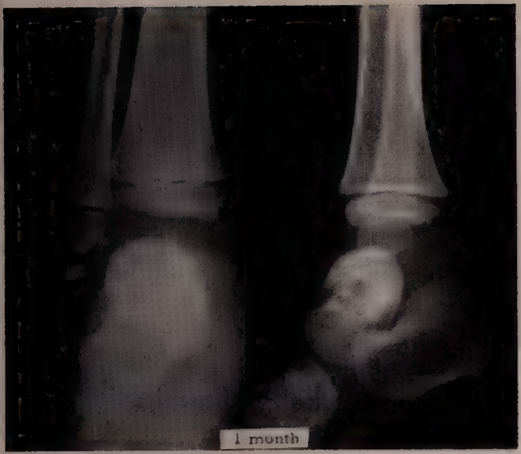

FIGURE 6. Case 2. Necrosis of the body is apparent at one month. Fracture united readily.

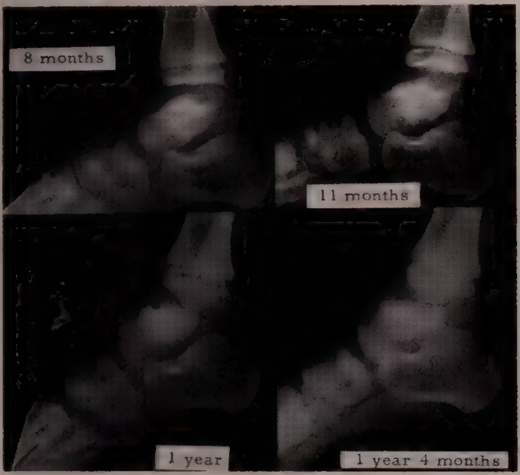

FIGURE 7. Case 2. Subchondral changes of body at ankle joint after eight months. Note course of creeping replacement of the talar body. Central necrosis in body persists after eleven months. Fragmentation of body superiorly present at twelve months. Irregularity and apparent loss of bone substance noted proximally sixteen months later.

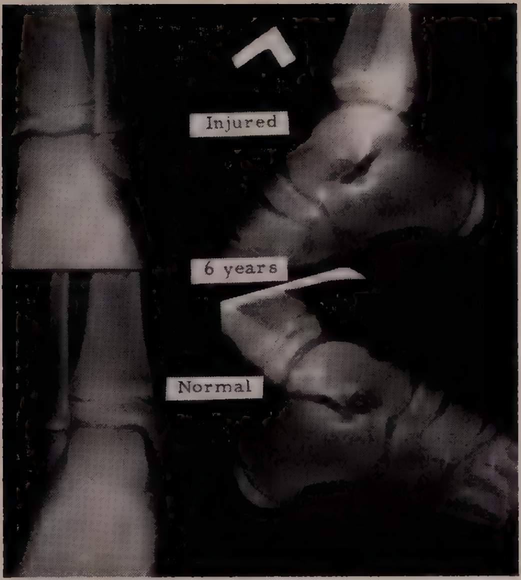

FIGURE 8. Case 2. Six years after injury there was excellent reconstruction of body of talus, width of articular cartilage space at ankle normal, and no evidence of pantalar arthritis.

X-ray films made one month after the injury (Fig. 6) showed that the body of the talus was dense and obviously necrotic and that healing was progressing at the fracture site. Note the lytic area at the fracture site indicating resorption of a portion of the necrotic body. By seven weeks union of the fracture appeared to be quite solid, and further replacement of the necrotic body was occurring. Subsequent x-ray films nine weeks, three and one-half months, and five months later disclosed creeping substitution with subchondral replacement of the necrotic bone. By eight months subchondral changes of the body at the ankle joint were more marked, and at eleven months central necrosis in the body still persisted. At twelve months fragmentation of the body superiorly was present. One year and four months later great irregularity and what appeared to be a loss of bone substance proximally was noted (Fig. 7). At two years and ten months a very irregular pattern of the dome of the body and some density in the midportion were noted.

This child was protected from weight-bearing for about three years, utilizing intermittently walking casts and crutches, with a Perthes' sling. At the end of this time weight-bearing was permitted. When the patient was examined six years after the injury, she had an excellent clinical result. She was asymptomatic and was able to participate in all normal activities. She had a full range of ankle motion, but subtalar motion was mildly restricted. Roentgenograms at that time showed excellent reconstruction of the body of the talus, the width of the articular cartilage space at the ankle was normal, and there was no evidence of pantalar arthritis (Fig. 8).

Comment. This patient received her injury at the age of three years, and as far as could be ascertained, she is the youngest patient with a fracture of the talus reported in the literature. Aseptic necrosis of the body of the talus occurred, although there was no evidence of displacement of the fragments. It is possible, of course, that there was an initial dislocation of the body of the talus which reduced spontaneously before the radiographs were made. It is obvious that the articular cartilage surrounding the body of the talus in this child survived, probably being nourished by synovial fluid. The articular cartilage now is of normal width and has normal function.

Summary

1. Aseptic necrosis of all or a portion of the talus occurred in 7 of 21 patients with severe talar injuries on whom follow-up studies were made to ascertain the late results of such injuries.

2. An early diagnosis of necrosis of a portion of the talus following injury often is difficult and may not be possible for several months. The earliest sign of necrosis is the relative increase in density noted radiographically, which is due to the failure of the necrotic portion to partake in disuse atrophy. Comparable views of the opposite ankle are important to assess the differences in density. Weight-bearing should be avoided until it is certain that the bone is viable.

3. The course of replacement of the necrotic portion of the talus varies with each case.

4. Union of fractures occurred but were sometimes delayed when necrosis was present.

5. When necrosis of the talus occurs in an adult, joint changes can be expected because of the resulting changes in the articular cartilage overlying the necrotic portions of the talus. In the child, however, the articular cartilage may remain normal.

6. It is recommended that if normal architecture of the talus is to be expected, weight-bearing be avoided until significant replacement of necrotic tissue has occurred.

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Increase in pedestrian safety

Life for pedestrians on the streets and roadways of the United States has become safer, according to statisticians of the Metropolitan Life Insurance Company.

The relative frequency of pedestrians killed in motor vehicle mishaps dropped more than 25 per cent between 1949 and 1959—from 5.9 per 100,000 population in 1949 to 4.4 per 100,000 in 1959.

Although male pedestrians recorded the greater improvement in those ten years, their death rate from motor vehicle accidents was nearly three times that among their female counterparts.

The rate among males dropped from 9.0 per 100,000 in 1949 to 6.5 in 1959, somewhat more than one fourth. Among females, the death rate fell from 2.8 to 2.4 per 100,000 or about one seventh.

Autumn and winter months are the most hazardous for pedestrians, in spite of the fact that automobile travel is not at highest level during those periods. The peak periods reflect, in part, the longer hours of dusk and darkness and the consequent decrease in visibility.

Despite the recorded progress, various measures may still be taken to further pedestrian safety. These include the installation of more crosswalks, walk signals, better street lighting, and pedestrian barriers. Also, greater use may be made of adult school-crossing guards and of school safety patrols.

Invasive Carcinoma of the Cervix

Improvement in Therapeutic Results

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THE PRESENT SERIES *is based on a review of 300 cases of invasive carcinoma of the cervix treated from 1940 to 1956. There is a five-year survival of 63 per cent and a ten-year survival of 49.5 per cent in contrast to a 26.2 per cent five-year figure and a 9.6 per cent ten-year result for 328 cases treated from 1926 to 1942. The improvement is reflected in all stages except Stage IV, with the greatest increase in Stage II (66 per cent versus 30 per cent) and Stage III (55 per cent versus 16 per cent). With earlier examinations and improved cytologic technics more cases are discovered in less advanced stages. Radium therapy technics have changed over the years. From 1952 to the present, Fletcher applicators have been in use, and radiocobalt is utilized instead of radium. The number of major complications has decreased as over-all survival figures have improved. The complications were intestinal, urinary tract, and osseous; irradiation accounted for 10 per cent of all the complications, tumor invasion for 11 per cent, and surgical intervention for 3.3 per cent.*

THE TREND in survival in carcinoma of the cervix has improved in each decade in reports from different radiotherapy centers throughout this country and the world. The uniformity of results recorded is rather surprising considering the diversity of patient material and the variety of technics employed. This should not allow, however, for complacency on the part of the therapists and gynecologists involved in the treatment of this disease.

It is essential to evaluate critically the efficacy of any mode of therapy and to consider carefully all the factors that may influence the end results. Not only are five-year survival figures valuable, but longer-term results are vital. Attention to complicating features is important since they add to the morbidity and are not reflected in mortality rates. The periodic re-examination of data is informative in many respects and essential to maintaining a high level of performance. It is in this spirit that the present analysis is offered.

Comparative results of present and previous series

The first analysis of results in the treatment of carcinoma of the cervix by means of irradiation at Strong Memorial and Rochester Municipal Hospitals extended from 1926 to 1942 and included 328 cases.[1] By way of contrast, the present series is based on a review of 300 cases treated from 1940 to 1956 with some overlapping in reporting. The data offered will be presented to allow a comparison with the previous report regarding survival and complications.

In the present review there is a five-year survival of 63 per cent and a ten-year survival of 49.5 per cent in contrast to a 26.2 per cent five-year figure and a 9.6 per cent ten-year result for the first seventeen years at Strong Memorial Hospital (Table I). The improvement in figures is reflected in all

TABLE I. Survival rates in cases of carcinoma of the cervix treated by irradiation at Strong Memorial Hospital

	1940 to 1953			1926 to 1942		
Stage	Total	Number of Survivors	Per Cent	Total	Number of Survivors	Per Cent
Five-year survival						
I	74	61	82.0	58	40	69.0
II	52	34	66.0	83	25	30.0
III	33	18	55.0	107	17	16.0
IV	22	1	4.5	80	4	5.0
Totals	181	114	63.0	328	86	26.2
Ten-year survival						
I	48	29	60.0	58	7	12.0
II	29	15	52.0	83	6	7.0
III	21	10	48.0	107	6	5.0
IV	13	1	7.0	80	1	6.0
Totals	111	55	49.5	328	20	9.6

* There were complications in 22 per cent of the total number of cases from 1940 to 1953 and in 35 per cent from 1926 to 1942.

stages except Stage IV which is to be expected since this stage is incurable for the most part because of the biologic nature of extension and spread. It is gratifying to note that the greatest increase in survival is seen in Stage II (66 per cent versus 30 per cent) and Stage III cases (55 per cent versus 16 per cent). The larger number of Stage II cases renders the results more meaningful than in the Stage III group.

The ten-year survival rates are more striking and indicate that long-term results are improving. Thus the 50 per cent ten-year figure of the present series as compared with approximately 10 per cent for the earlier report is most encouraging. The increased survival applies again to all stages except Stage IV. The fact that longer survivors are free of disease is further evidence of the ability of irradiation to arrest cervical carcinoma in a permanent fashion.

TABLE II. Age distribution of patients with carcinoma of the cervix treated by irradiation at Strong Memorial Hospital

	1927 to 1942		1942 to 1956	
Age (Years)	Number of Patients	Per Cent of Total	Number of Patients	Per Cent of Total
20 to 29	4	4	8	3.3
30 to 39	42	11	46	19.0
40 to 49	103	28	66	27.0
50 to 59	106	29	60	25.0
60 to 69	54	14	36	15.0
70 to 79	17	8	17	7.0
80 to 89	2	2	6	2.5

Reasons for improved results

In the analysis of the preceding figures, many factors must be considered to account for the better results in the recent fifteen-year period. It is most important to define the role of case selection as a factor in the survival percentages. Although changes in technic occur in time, ancillary developments also may have a great impact on results. Before crediting radiotherapeutic developments, an attempt is made to present other facets of the present series that may affect the ultimate outcome.

AGE. The age distribution, one may reason, has shifted toward the earlier years, and perhaps the lack of associated disease contributed to the improved survival figures. This is not borne out in Table II. If the percentages of the total group are tabulated, the similarity of the distribution is striking. The majority of the patients fall between forty and sixty years of age and account for more than half the group. The slight increase in those detected and treated before age forty would hardly weight this present series. No patients under twenty years of age were found.

STAGE OF PRESENTATION. The education of the patient and the physician as to the early signs of a possible malignant condition, such as vaginal bleeding, has led to earlier examinations. When this is added to the success of mass surveys using the Papanicolaou technic, the steady shift of our stages toward Stage I and Stage II becomes understandable. In charting our cases at five-year intervals, this finding is readily observed and appreciated (Fig. 1). The last five-year period (1952 to 1956) has 75 per cent of our cases in the earlier groups as compared with 35 per cent in 1926 to 1932. The value of cytology is without question and has contributed greatly to our better over-all results. The discovery of carcinoma in the less advanced stages lowers the inherent risks of therapeutic procedures and allows for better application of radium with more accuracy in positioning. The control and planning of therapy is therefore more effective and leads to a lowering of complication rates.

It should be emphasized that all staging at Strong Memorial Hospital is done under anesthesia by the gynecologist and a radiotherapist, that every effort is made to follow the rules of the League of Nations, and that all cases are downstaged rather than upstaged. This may in part account for the greater abundance of Stage I and II cases. Thus, if a case is a questionable Stage II or III, the patient is placed in Stage II. In this way our results are made to appear as unfavorable as possible.

The detection of so-called "carcinoma in situ" occurred with sufficient frequency in the past decade that a separate report will deal with this group. These patients were not incorporated in the present series as they were treated surgically rather than by radiation therapy. If these cases were included in our total figures, the over-all results would be better than listed.

HISTOLOGY. The majority of our cases were epidermoid carcinomas and constituted 94.2 per cent of the series. As a rule, the carcinomas were varied in differentiation, but no attempt at grading is offered since it is not routinely done at Strong Memorial Hospital. Adenocarcinoma formed a small percentage as in the previous report, that is, 5.8 per cent, and did not affect the survival figures significantly. Although these latter patients tend to do less well, our figures are too small to justify drawing definite conclusions in regard to the prognosis of histologic types. The histologic distribution is quite similar to the previous series: epidermoid carcinoma, 93 per cent, and adenocarcinoma, 7 per cent. This would not be a factor in explaining the difference in results.

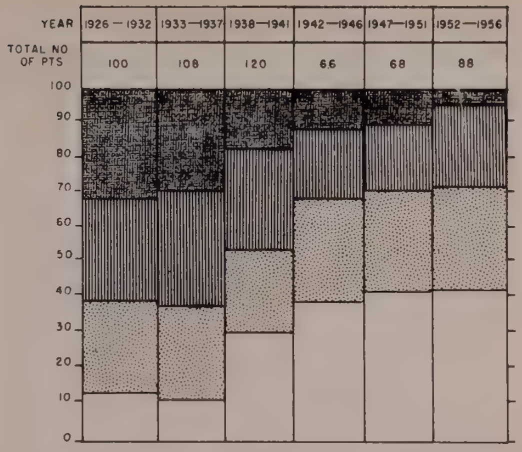

FIGURE 1. Stages of carcinoma of the cervix treated by irradiation at Strong Memorial Hospital, Stage IV indicated by darkest shading.

CHANGING TECHNICS OF RADIATION THERAPY. *Description of technics.* The technics of radiation therapy in carcinoma of the cervix at Strong Memorial Hospital have evolved gradually over the years with the changing of departmental staffs. The treatment plans can be subdivided into five fairly well-defined periods. It is difficult to compare each phase of the treatments employed since records have been kept in varying degrees of detail.

In the first period from 1926 through 1932, the radium applications were short and intense; the dosage was recorded in milligram hours. At least 30 per cent of the cases received 10,000 mg. hours, and 70 per cent received 7,000 mg. hours. External irradiation consisted of massive doses widely separated and at irregular times. No depth-dose calculations are presented. The radiation exposures were measured in milliampere minutes. Nevertheless, the low cure rate and high complication rate suggested that changes in technic were mandatory.

From 1933 through 1937, the radium applications were modified in terms of their intensity. Whereas 70 per cent of the patients received 7,000 mg. hours in the previous group, at least 82 per cent of the cases were below this level. Likewise, the external radiation was given in small total doses, at irregular intervals and widely spaced.

In the third period from 1938 to 1946, more conservative radiation technics were evolved. The T-shaped French cork colpostats were applied in the fornices with 75 mg. distributed equally between the uterine and vaginal parts of the applicator. The dosage employed ranged from 4,500 to 5,000 mg. hours, generally given in a protracted application. External irradiation was delivered to a six-field arrangement employing lateral fields. Daily dose rates of 200 r to two fields were used for a total dose of 1,600 r measured in air to each port. Isodose estimates suggest that adequate doses probably were delivered to pelvic node-bearing areas.

During the years from 1947 to 1951, the fourth period was ushered in with the introduction of the Ernst applicator and Manchester technics. The main advantage of the Ernst applicator was the fixed relationship of vaginal and uterine radium and, hopefully, more uniform pelvic irradiation. The Manchester methods allowed for flexibility when it was indicated. External irradiation was not changed in its factors and generally preceded the use of radium.

From 1952 to the present time, Fletcher applicators have been in use. The separation of vaginal and uterine sources is considered more flexible. Radiocobalt is utilized instead of radium to allow for further control of the dose rate. Two applications are employed with the use of intracavitary sources at the beginning and end of external therapy in earlier cases. Each insertion has been reconstructed three-dimensionally, and doses are calculated from the geometric center of the pelvis to the lateral wall at 1-cm. intervals. All dosages are recorded in rads or roentgens, and isodose plotting of external irradiation allows for the direct determination of depth doses. Generally speaking, point A receives 7,000 to 8,000 r and point B receives 4,000 to 6,000 r depending on the stage of the disease. Oblique ports have been substituted for lateral pelvic fields. Supervoltage irradiation has been followed in advanced cases and when bodily dimensions demanded it. Presently, it is used routinely in all cases.

TABLE III. Improvement in five-year survival rate of patients with carcinoma of the cervix treated by irradiation at Strong Memorial Hospital

All Stages	Total Number of Patients	—Five-Year Survival— Number of Patients	Per Cent
1926 to 1932	100	13	13
1933 to 1937	108	28	26
1938 to 1946	186	89	47
1947 to 1951	68	39	57
1952 to 1956	91	53	58

Survival results according to technics employed. From Table III, one notes that the survival figures have improved as the newer technics have evolved. A more thorough analysis of the data in Table IV does not completely substantiate this observation when it is studied further according to individual stage.

In Stage I, the results from 1933 to the present have been quite good, ranging from a 70 to 80 per cent five-year survival rate. The high figure for the 1933 to 1937 period is a chance occurrence. The 90 per cent figure for 1952 to 1956 is most gratifying, and it should be stressed that it deals with invasive carcinoma only.

In Stage II lesions, a realistic measure of the efficacy of therapy is obtained since the lesion is moderately advanced as well as invasive. The results since 1938 have been surprisingly uniform, despite the evolution of different radium applications. The survival for this stage has remained above the 50 per cent mark, which is above the usual survival figure reported by many major centers. On a year-to-year plotting of figures, the results tend to improve as the familiarity with a technic by staff members increases. It is for this reason that changes in the type of application should be altered only at ten-year intervals and after considerable planning.

The high figure of 50 per cent in Stage III lesions is not significant because the number of cases is limited and the figure higher than expected. Most periods have yielded a 20 per cent survival at five years, and this approximates the average result reported by other groups. In Stage IV the results have been poor and indicate the inadequacy of present technics to cope with this advanced

TABLE IV. Summary of results by stage in carcinoma of the cervix related to technic

Stage	Interval	Incidence: Number of Patients	Incidence: Per Cent	Five-Year Survival: Number of Patients	Five-Year Survival: Per Cent
I	1926 to 1932	12	12.0	3	25.0
	1933 to 1937	11	10.0	11	100.0
	1938 to 1946	60	32.0	47	79.0
	1947 to 1951	29	42.6	21	72.5
	1952 to 1956	38	43.2	34	90.0
II	1926 to 1932	23	23.0	6	26.0
	1933 to 1937	31	28.6	7	22.0
	1938 to 1946	48	26.0	26	54.0
	1947 to 1951	19	28.0	12	63.0
	1952 to 1956	27	29.6	15	56.0
III	1926 to 1932	32	32.0	3	9.4
	1933 to 1937	35	33.0	7	20.0
	1938 to 1946	53	28.5	15	28.0
	1947 to 1951	12	17.7	6	50.0
	1952 to 1956	19	21.6	4	21.0
IV	1926 to 1932	33	33.0	1	3.0
	1933 to 1937	31	28.0	3	9.7
	1938 to 1946	25	30.0	1	0.4
	1947 to 1951	8	11.8	0	0
	1952 to 1956	7	5.7	0	0

TABLE V. Complications in 240 cases of postirradiated carcinoma of the cervix treated at Strong Memorial Hospital from 1940 to 1956

Complication	Total	Radiation: Number of Cases	Radiation: Per Cent	Surgery	Tumor
Intestinal	16	11	4.6	(5)*	5
Urinary	23	8	3.3	3	12
Osseous	15	5	2.1	0	10
TOTALS	54 (22.5 per cent)	24	10.0	8 (3.3 per cent)	27 (11 per cent)

*Contributory role and not counted into total number.

problem. Fortunately fewer cases are encountered in this category. The extensiveness of the disease in this stage results in major complications and distant metastases even if pelvic disease is controlled.

Evaluation of complications. The number of major complications has decreased just as the over-all survival figures have increased, indicating the continued improvement in the evolution of radiation therapy modalities. In the previous report, there were 155 complications in 328 patients (1926 to 1942) for an incidence of 35 per cent as compared with a 22.5 per cent rate in 240 cases (1940 to 1956) in the present survey. As noted, not all of these difficulties can be ascribed to radiotherapy, but the role of tumor invasion and tissue destruction as well as adjuvant surgical therapy must be weighed in each patient. Irradiation per se accounted for 10 per cent of all the complications, tumor invasion for 11 per cent, and surgical intervention for 3.3 per cent. As shown in Table V, the sequelae in postirradiated carcinoma of the cervix are divided into three major areas: intestinal, urinary, and osseous lesions. Multiple organ involvement occurred in 8 cases for an incidence of 3.3 per cent, as there were 45 patients with 54 complications. The majority of cases had only one system affected.

Intestinal complications. Radiation injuries in the small and large intestine were the commonest complication in our series and occurred in 11 patients (4.6 per cent). The bulk of the lesions were in the rectum (8 cases) and were attributed mainly to the radium application. Four fistulas, 2 strictures, and 2 ulcers accounted for all the late rectal sequelae. Regarding the 4 fistulas, 3 patients are alive with their fistula; 2 had diverting colostomies.

Rectal strictures and ulcers occurred only in patients who had severe acute reactions. The onset of symptoms was noted three to six months after the radium application and only occasionally as late as one year. Ulcers respond to conservative measures, such as a low-roughage diet and topical instillations of steroid ointments, whereas the strictures eventually required colostomies.

Small-bowel injuries are always a most serious and life-threatening complication. The patient usually presents symptoms of an acute condition in the abdomen which requires surgical intervention. If bowel complications are not handled carefully, recurrent radiation injuries will develop and require repair laparotomies. One patient died and 1 survived this complication. There were 4 colon complications which were rectocolic fistulas and listed under that category of rectal lesions. Only 1 colonic stricture occurred, and this has been managed conservatively.

Urinary tract. Problems in the urinary tract consisted of ureteral stricture and hydronephrosis (12 patients), fistulas (7 cases), bladder ulcer (2 cases), and severe cystitis (2 cases). The most frequent etiology of ureteral strictures is recurrent carcinoma in the postirradiated patient. Tumor was implicated in 8 instances as compared with 2 occasions for therapeutic maneuvers. One of these latter patients developed her stricture immediately after surgery, and 1 can be attributed to radiotherapy.

Fistulas likewise were commonly due to advanced carcinoma (4 cases) although surgery (2 cases) and irradiation per se (1 case) may be implicated. Only in the latter case did the fistula close spontaneously. Bladder ulcers usually developed six months to one year after the radium application and characteristically were on the posterior wall of the bladder above the trigone. These responded to conservative measures such as irrigations and treatment with Pyridium. Severe cystitis occurred in only 3 patients and was related to secondary infection in 2 patients. These cases recovered following the use of antibiotics.

Osseous lesions. There have been 13 lesions detected to date in the 240 cases under study. Of these, 8 were found to be metastatic in origin, indicating that this finding occurs more frequently than does radionecrosis of bone. Of the 5 cases showing radiation change in bone, there were 3 femoral neck fractures, 1 case having bilateral fractures. Interestingly, there were 2 pubic bone fractures and 3 fractures of the iliac crest. These findings will be described in detail in a separate report.[2] The use of lateral fields was continued through 1951, since femoral neck fractures had been encountered on only 3 occasions in the previous series of 328 cases. Karr[1] felt that 2 of the 3 were due to trauma, leaving only 1 case (0.3 per cent incidence) attributable to irradiation. No femoral neck fractures have occurred since lateral fields were replaced by oblique ports.

Comment

The improvement in results in carcinoma of the cervix at five years and at ten years as compared with an earlier report has been presented. The most important factor influencing the over-all survival figures to date has been the detection of this carcinoma in earlier stages. The shift in staging, due to the Papanicolaou smear test, to a proportionately higher number of carcinoma in situ cases, microinvasive carcinoma, and Stage I lesions is most gratifying. The cure rate for these early cases ranges from 80 to 100 per cent depending on the stage of the lesion. It is predicted that with further long-term reports this cure rate will remain high at ten and fifteen years.

As shown in the analysis of data for our different treatment periods, variations in technic have not altered survival data dramatically in the past three decades. The evolution of technics for the treatment of this disease has been traced and reflects the general evolution of radiation therapy. For the past three decades, the results in all stages except Stage IV have remained uniformly high. Complications due to radiation per se have continued to decrease. Our results compare favorably with those

ABLE VI. Comparative results of five-year survival of patients with carcinoma of the cervix treated by irradiation

	Strong Memorial Hospital (1940 to 1952)		Roswell Park Memorial Institute (1945 to 1952)		Annual Report[3] (To 1948)	
Stage	Number of Cases	Per Cent	Number of Cases	Per Cent	Number of Cases	Per Cent
I	74	82	326	75	4,324	64.9
II	52	66	429	55	6,109	45.9
III	33	55	372	35	3,146	26.0
IV	22	4.5	117	19	178	7.2
TOTALS	181	63.0	1,244	51	13,757	39.8

reported from other institutions (Table VI). The advantages of advances in external irradiation with supervoltage and rotational technics have to be awaited.* Conceivably this may add to survival in more advanced cases since radium therapy is ineffective in delivering the larger doses required to arrest advanced pelvic disease.

The role of surgery in the treatment of carcinoma of the cervix continues to be evaluated in some centers. Although occasional reports show survival figures which approach those achieved with irradiation, they are often attendant on a much higher complication rate. The inability of surgery to yield a high survival in patients with positive nodes has been reported recently by Parsons, Cesare, and Friedell[5] and by Rauscher and Spurny.[6] Evidence for the capacity of radiotherapy to sterilize nodes has been established by the careful work of Rutledge, Tan, and Fletcher.[7] In a series of clinical Stage III patients treated by preoperative irradiation followed by surgery, the incidence of observed positive nodes dropped from an expected value of 65 per cent to 23 per cent. Further support for this thesis is found in Rauscher's series where equal survival results followed the use of postoperative radiotherapy regardless of the use of pelvic lymphadenectomy.

The high complication rate in selected surgical series weighted by Stage I and Stage II cases is the greatest deterrent to the use of surgery. Meigs[8] reported a 24 per cent major complication rate, of which urinary tract fistula predominated. In his appraisal of treatment in carcinoma of the cervix, he stated: "Fistula formation is too frequent, averaging 8.4 to 15 per cent, and pelvic irradiation has but little effect on its frequency." Brunschwig and Frick[9] came to a similar conclusion, reporting a 23.5 per cent incidence of patients with urinary tract fistula alone, exclusive of other complications in a series of 212 cases of exenteration, half of whom remained urologic cripples with nephrostomies, cutaneous ureterostomies, persistent fistulas, or severe incontinence. More recently, Parsons[5] in his series with advances in surgical technic reported a 32 per cent major complication rate plus an 8 per cent mortality rate. Thus one can safely conclude that the 10 per cent complication rate in all systems in our series due to irradiation per se is quite conservative with only 1 urinary tract fistula due to irradiation (0.5 per cent).

A method of screening patients for surgery or radiation therapy would be the best solution for case selection. Work along this line is being pursued actively in many centers. The most widely used tests are the vaginal smears of normal epithelium utilizing Graham's[10] criteria for sensitization response and radiation response before and during irradiation. The approach of Gusberg *et al.*[11] to studying the response of the tumor by deoxyribose nucleic acid (DNA) and ribonucleic acid (RNA) staining technics is another method of finding radioresistant tumors which may be handled more effectively surgically. Other experimental programs are seeking pharmaceuticals that will enhance the responsiveness of tumors to irradiation.[12] Because of the large backlog of detailed data and results, cases of carcinoma of the cervix are a logical group to explore. The use of oxygen, alpha-tocopheral, hormones, and antimetabolites are being employed to this end. The future of radiation therapy in cervical cancer probably will lie in the insight grained in fundamental biologic processes just as in the past the physics of treatment technics was and still is a major contribution.

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* Fletcher, Rutledge, and Chau[4] recently reported a significant improvement in survival in advanced Stage II and Stage III cases with supervoltage technics. In advanced Stage II cases the five-year results improved from 60 to 73 per cent and in Stage III from 37 to 46 per cent.

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Decrease in maternal mortality rate

The mortality of women from conditions associated with pregnancy and childbirth decreased nearly three fifths in the past decade, according to statisticians of the Metropolitan Life Insurance Company.

Provisional figures show there were only 1,360 mothers who died from these causes in the United States during 1960, while births during the same period totaled about 4$^1/_4$ million.

The maternal mortality rate among white women fell from 6.1 per 10,000 live births in 1950 to 2.6 in 1959, a reduction of 57 per cent. The corresponding decrease among nonwhite women was from 22.2 to 10.2 per 10,000 live births, or 54 per cent. Substantial improvement was recorded throughout the childbearing ages.

Each of the major causes of maternal mortality showed a considerable decline in relative frequency during the 1950's. Outstanding progress was made in reducing the death toll from puerperal toxemia and from infections —the mortality rate from the toxemias fell by more than 70 per cent and from puerperal sepsis about two thirds, while that from hemorrhage was reduced by more than half.

Early and continuous prenatal care has contributed greatly to the reduction in maternal mortality. Improvement in obstetric training and practice have also helped. These include advances in the use of anesthesia during delivery, the use of blood transfusions and antibiotics, and better aseptic technics.

Special Problems in Dermatogeriatrics

SKIN DISEASE *in the older patient must be considered by special standards. Dermatogeriatrics is an approach which would correlate the modified responses and special susceptibilities in older persons with patterns of aging. There are four categories of skin diseases which beset senescent patients: obligatory, constitutional, incidental, and inveterate dermatoses. Special problems include nodules of the ears and feet, senile seborrhea, senile tibial erosions, autogenous eczema, seborrheic and senile keratoses, and skin cancer.*

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THE PROBLEM of skin disease in the older patient cannot be considered by ordinary standards. The longer and more complicated history of dermatologic and medical experience, sociologic and psychologic patterns, and economic responsibilities, together with the current medical findings and living conditions, may tend to alter the profile of disease. The frequency and type of disorder, the clinical picture of the presenting dermatitis, its course, and the management and response to treatment may be different in elderly patients.[1-3] Dermatogeriatrics proposes a concept which attempts to balance the cutaneous process with the modified responses and susceptibilities of elderly patients to sharpen diagnosis, reassess treatment, and possibly propose steps for prevention. Dermatogeriatrics may be introduced by suggesting a clinical classification of the skin diseases which beset senescent patients. There are four categories: obligatory, constitutional, incidental, and inveterate dermatoses.

The obligatory diseases occur almost exclusively in elderly patients and, as a rule, are superficial. Nodules of the ears and feet, alopecia and atrophy, senile pruritus, seborrheic and senile keratoses, and epithelioma are examples. In the constitutional group the main process is linked with more profound changes associated with aging. Many of these changes involve the vascular system. Posterioral hypostatic dermatitis, stasis and decubitus ulcers, and tibial erosions are found in this category. Sarcoma and the lymphoblastomas are also included. The incidental group of disorders may occur at any age but present a special problem in elderly patients. Examples of the incidental group are pyroderma, erythema multiforme and drug eruption, neurodermatitis and autoeczema, as well as benign tumors and virus diseases. Last, the inveterate dermatoses are recognized as having an early onset in life but remaining a problem over the years. Psoriasis, discoid lupus erythematosus, tuberculosis, scars and burns, and nevoid conditions fall into this group.

To illustrate some of the special problems in dermatogeriatrics, nodules of the ear and foot, senile seborrhea, senile tibial erosion, autogenous eczema, seborrheic and senile keratoses, and skin cancer were chosen for discussion. These conditions are not necessarily the most common or frequent disorders, but they are intrinsic and, in some instances, represent newer findings in the field.

Nodules of ears and feet[4,5]

Several years ago tender nodules which occur on the anthelix of the ear were recog-

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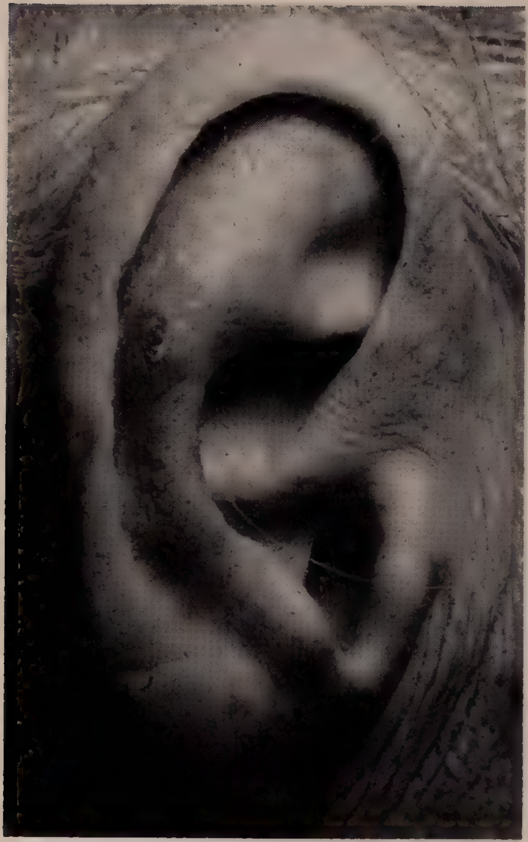

FIGURE 1. Chondrodermatitis anthelicis: single, acute lesion with beginning ulceration (early stage).

nized as a problem in elderly women residing in a hospital-home. About 6 per cent of the patients were affected over a period of eighteen months. The nodules, chondrodermatitis anthelicis, are usually unilateral and initially are crusted or ulcerated, painful, and surrounded by inflammation (Fig. 1). The early lesion measures $^1/_2$ to $1^1/_2$ cc. in diameter. The usual course is from four to six weeks.

Chondrodermatitis anthelicis arises in the patient who is confined to bed for some intercurrent illness and follows trauma on the anthelix from pressure and rubbing on the pillow. Relief may be gained by using a special lamb's skin to cover the pillow and simple antibiotic ointments. The nodules must be differentiated from seborrheic and senile keratoses, epithelioma, epithelial cysts, gouty tophi, and chondrodermatitis nodularis chronica helicis which is clinically similar but which is located on the helix of the ear, mostly in men.

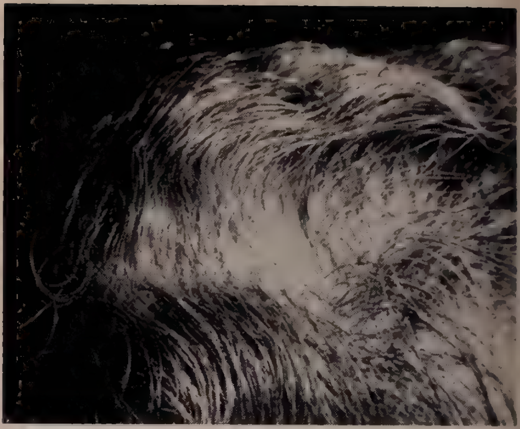

FIGURE 2. Senile seborrhea: diffuse scaling throughout the scalp.

During the study of chondrodermatitis anthelicis a second group of patients was discovered, quite by chance, to have painful nodules located on the bony prominences of the feet and ankles. At times the elbows and lateral surfaces of the knees were involved. These lesions were described as ulcerodermatitis nodularis pedis. The underlying pathologic process was thought to be similar to the anthelix lesions, pressure and rubbing being precipitating factors. Treatment is the same for both conditions.

Senile seborrhea [6]

The scalp of the older patient would not ordinarily be considered a source of trouble. However, many patients who live in institutions or homes have a latent problem. The condition is not inflammatory but appears as a whitish to yellow-brown, odoriferous, adherent scale, diffusely distributed over the scalp and about the hair follicles (Fig. 2). It is sometimes necessary to excoriate the scalp slightly to uncover the amount of involvement. The condition is asymptomatic. However, seborrheic dermatitis may be potentiated and effect the hair margins, face, postauricular areas, chest, and axilla.

An interesting facet of this investigation was turned up when the amount of scale could not be explained entirely on the basis of scalp care. Although a special shampoo was used and proved of value in most cases

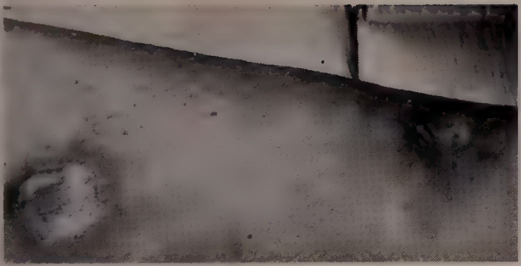

FIGURE 3. Tibial erosion: nummular erosions on the tibia with surrounding inflammation.

in lessening the scale (the frequency of washing remained the same), the severity of the condition was essentially unchanged in some patients. The possibility that senile seborrhea is related to a functional delay in normal exfoliation, a disturbance in keratinization, or to the medical aspects of aging is now being investigated.

Senile tibial erosions

A scratch from a poorly trimmed toenail during sleep, an abrasion from striking one of the many projections on the footrest of a wheel chair, and an excoriation because of pruritus and a dry skin may lead to a superficial tibial erosion (Fig. 3). These lesions appear suddenly, are coin shaped or linear, and are usually multiple. There is a moderate amount of inflammation surrounding the erosion which alternately becomes crusted and exudative. Pain is a problem out of proportion to the size of the lesion, and the course is prolonged, sometimes lasting from twelve to eighteen months.

Senile tibial erosions may reflect mechanisms which underlie the aging process. The lesions are somewhat reminiscent of neurotrophic ulcers seen on the heels of elderly diabetic patients. A study of the neurologic and vascular economy of patients who develop tibial erosions might lead to an insight into some of the pathologic processes of growing old.

Treatment follows general dermatologic principles. Sponging and compressing the lesions remove the crusts, and the application of antibiotic ointments and the use of antibiotics systemically, when indicated, are valuable. An enzymatic type of cream applied on alternate days promotes debridement; however, care must be exercised in the frequency and duration of the application since local irritation is common. Aggressive supportative measures are also necessary.

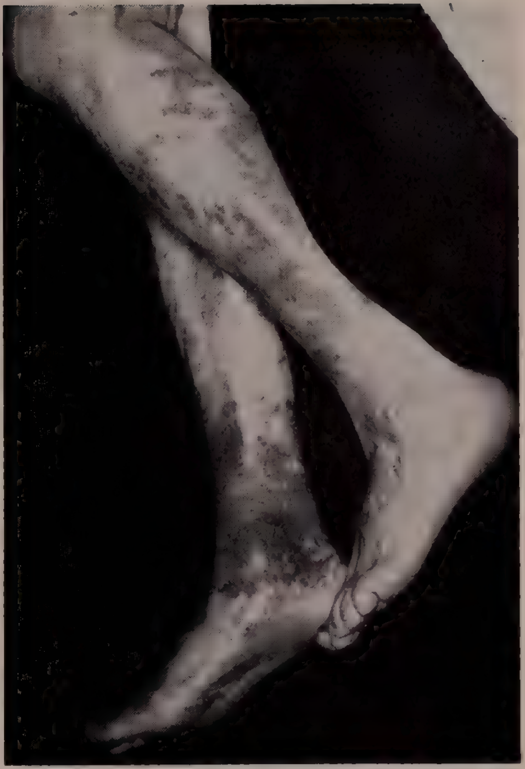

FIGURE 4. Stasis dermatitis and early autoeczema of both legs (organizing stage).

Autogenous eczema[7]

A localized dermatitis such as nummular eczema, stasis dermatitis, seborrheic dermatitis, and tibial erosion may lead to the development of generalized autogenous eczema if treated too aggressively with strong applications, infected, or traumatized. The disorder begins from several days to several weeks after the exacerbation (not always necessary) of the local condition. The early lesion is a vesicle which appears in close proximity to the original dermatitis, then in distant areas. Later the vesicles tend to be grouped, forming orbicular or coin-shaped plaques which, in turn, become confluent, resulting in a generalized dermatitis (Fig. 4).

In the older patient the acute phase of the

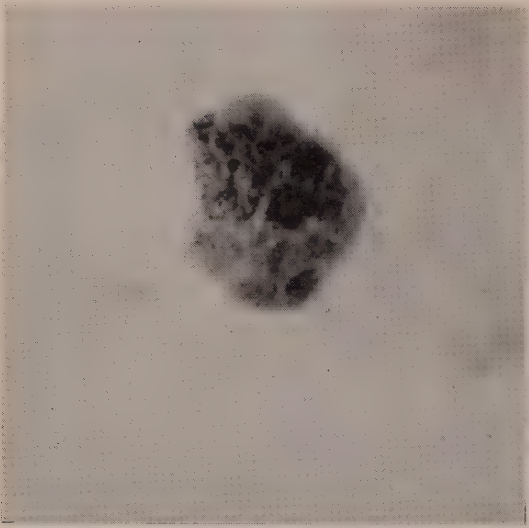

FIGURE 5. Seborrheic verruca: raised, dark, and verrucous lesion on the abdomen.

disorder follows the usual pattern. However, the later stages may be prolonged, lasting months with severe pruritus. The scaling of the resolving dermatitis superimposed on an already dry, senile skin seems to enhance itching. Treatment is difficult because the older skin may not tolerate even the mildest local medication. It is always a temptation to use steroids systemically. However, once begun such a drug must be continued, for relapses are common with decreasing dosage. With the exception of an occasional patient in whom the hazards of treatment have been weighed carefully, conservative treatment is best. Starch or starch and oil baths, antihistamines, steroid ointments, a bland emollient for the resolving dermatitis, and supportative measures constitute well-grounded, if not heroic, therapy. In the long run the course of autogenous eczema may be shorter with conservative management than with systemic steroids.

Seborrheic and senile keratoses[8]

Seborrheic and senile keratoses are common problems in old people. Because senile keratoses are potentially malignant, these lesions must be differentiated and treated individually.

Seborrheic keratoses grow slowly. They measure from $^1/_2$ to 1 cc. in diameter and are sharply circumscribed, round or oval, slightly elevated, and have a rough or moderately verrucous surface. These lesions are covered by a loose, greasy scale and are yellow to deep brown in color. They occur chiefly on the trunk and face. A further stage of the evolution of seborrheic keratoses is the seborrheic verruca. This lesion is darker brown, larger in size, and more verrucous. Neoplastic change is uncommon in the seborrheic type of lesion. If it develops, the locally malignant basal cell epithelioma is the one most likely to occur (Fig. 5).

Senile keratoses are of two types, the raised or papillomatous keratosis and the flat keratosis (Fig. 6). They occur on the areas exposed most frequently to sunlight, namely, the face and dorsa of the hands, the forearms, the ears, and the vermilion border of the lips. The malignant condition which may develop in the senile type of lesion is the prickle or anaplastic cell epithelioma which is most highly malignant.

The raised variety of senile keratosis is well defined, indurated deep gray to black, and covered by a dense and adherent hyperkeratosis. The surface is verrucous and cannot be removed without bleeding. The flat type is smooth, flat, and covered by a dry, fine scale. The margins are irregular and cannot be outlined by palpation. They are gray or sometimes dull red. A history of bleeding from time to time is common.

The treatment of choice for either seborrheic or senile keratosis is electrodesiccation and curettement to complete destruction. The recognition of the senile keratosis warrants removal. There is less urgency in the seborrheic keratosis; however, it may be wise to treat the older, more advanced seborrheic verruca.

Skin cancer[9]

The problem of the diagnosis of skin cancer in elderly patients is essentially that of any age group. Management, however, must take into consideration the additional problems inherent in elderly patients. The treatment of choice is based primarily on an understanding of the process; secondarily, on the size, location, and duration of the lesion; and finally, on the age of the patient.

The dermatologist has a wide choice of

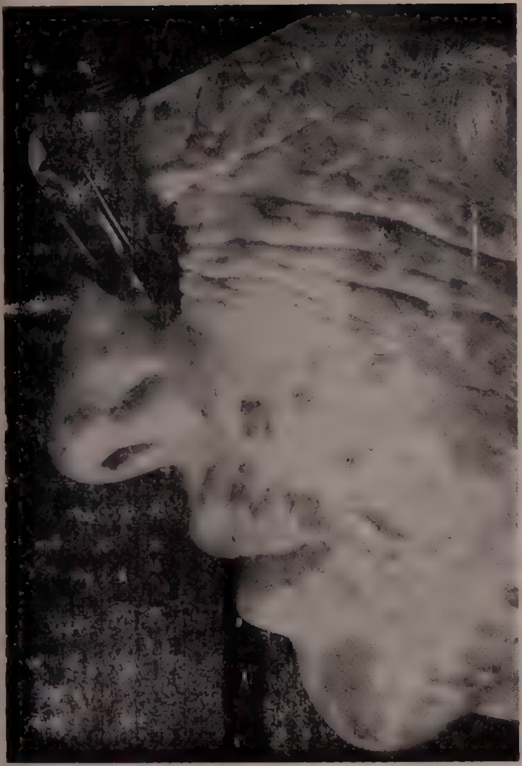

FIGURE 6. Flat and papillomatous senile keratoses (note senile atrophy).

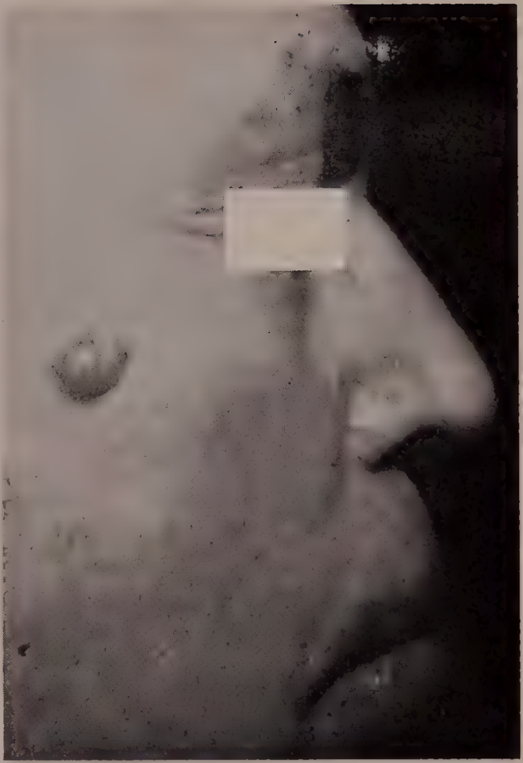

FIGURE 7. Basal cell epithelioma: defined, waxy lesion with telangiectasia.

modalities designed to meet most situations. Electrodesiccation and curettement is especially adapted to older patients (Fig. 7). It is a speedy, simple, and well-controlled method of treatment and is excellent in smaller lesions. Ionizing irradiations or radium may be used for basal cell epithelioma and are particularly well suited for the patient who is physically unable to withstand any surgical procedure. Larger lesions or those in which location is a problem may be treated best with roentgen rays, with the exception of anaplastic epithelioma. In special cases excision may be the treatment of choice. A histologic examination of the edges and undersurface of the specimen will establish the adequacy of the operation. In recurrent lesions and old fibrotic basal cell epithelioma Moh's method of chemotherapy with microscopic control is indicated.[10-12]

Summary

A sound basis for clinical dermatogeriatrics would include a workable definition of the field and a concept which is keyed to the older patient and his problem. In this communication dermatogeriatrics is presented as an approach which would orient the modified responses and special susceptibilities in the older persons to patterns of aging. As an initial step, the dermatoses of elderly patients may be divided into obligatory, constitutional, incidental, and inveterate. Nodules of the ear and foot, senile seborrhea, senile tibial erosion, autogenous eczema, seborrheic and senile keratoses, and skin cancer are discussed as illustrative and special problems in dermatogeriatrics.

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Discussion

JOSEPH J. RUSSO, M.D., *Albany, New York.* I find Dr. Young's classification very useful. It deserves a permanent place in our literature.

Of the many entities that Dr. Young discusses, the eczematous group and pruritus are the ones that present the most trying problems to us in practice. When we are confronted with them, the question of cause, in the first place, and treatment, in the second place, may offer formidable obstacles. These eczematous eruptions are nondescript, small or large, and they arise in almost any area of the body. Are they classified as nummular eczema or contact dermatitis? We call them one or the other, often with tongue in cheek or for want of a better term. New patches appear as the response to treatment is nil or as sensitization and sometimes generalization result. The exact nosology of this large group has always puzzled me. Dr. Young's report describes this group, and the conclusion is drawn that the senile skin has its own peculiar method of responding to external or internal stimuli, conditioned by pathologic-physiologic factors peculiar to the senile skin, a phenomenon as yet not completely understood.

I would like to question Dr. Young on one aspect: How does he manage the elderly patient in his office who presents pruritus alone, from the standpoint of diagnosis and treatment?

Effect of sugars on tooth decay

New evidence has been found of the role played in tooth decay by sugars and carbohydrates in general. This evidence resulted from researches by Dr. Ward Pigman, Dr. James Brasher, and Dr. Theodore Koulourides.

The team of researchers tested the relative ability of various sugars to produce decay in vitro. To do this, they used an experimental apparatus called the "artificial mouth" which reproduces many of the major features of tooth decay and provides an opportunity to study outside the mouth the factors involved in decay.

The "artificial mouth" had been shown previously to produce decay similar to that in the human mouth. It consists of extracted human teeth which are exposed briefly to human saliva. Bacteria in the saliva become attached to the teeth. The teeth are then exposed to drippings of a culture medium suitable for the growth of bacteria. The medium contains nutrients needed for the growth and simulates the saliva which flows over teeth in the human mouth. Bacteria become lodged in the noncleaning areas of the teeth, causing decay in these areas.

The culture medium used in the present study contained various sugars: cane or beet sugar (sucrose), D-glucose (dextrose), milk sugar (lactose), maltose, galactose, mannose, fructose, and soluble starch. The extracted teeth were exposed to the solutions containing these sugars for from eight to twelve hours. The rate of softening was determined by hardness measurements before and after the experiment.

The greatest rate of softening was produced by sucrose, D-glucose, fructose, mannose, lactose, and galactose. No softening was produced in the presence of soluble starch, and maltose showed a markedly slower rate than the other sugars. In the absence of these carbohydrates, no softening of the teeth occurred.

PANEL DISCUSSION

Rehabilitation In New York State

Present Resources and Future Trends

Chairman
WILLIAM H. GEORGI, M.D., Buffalo, New York
Panelists
EUGENE J. TAYLOR, LL.D.,* New York City
Adjunct Associate Professor of Physical Medicine and Rehabilitation, New York University School of Medicine; Vice-Chairman, New York State Governor's Council on Rehabilitation
EDWARD R. SCHLESINGER, M.D., Albany, New York
Assistant Commissioner for Special Health Services, Department of Health, State of New York
ADRIAN LEVY, PH.D.,* Albany, New York
Assistant Commissioner for Vocational Rehabilitation, Department of Education, State of New York

Introduction

William H. Georgi, M.D.: The format of the Section on Physical Medicine has been changed a bit from the past. Usually, we indulge in the clinical and research topics of this section. It is my feeling, however, that in recent years, and more especially in the past year, the welfare and practices of physicians, including specialists in physical medicine and rehabilitation, have been and in the future will be bound up more and more with various organizations on the Federal and state level where rehabilitation is concerned.

It behooves us as physicians to be as intimately aware as possible of the rehabilitation programs at the state level, not only for our information and for the help of our patients, but also so that we may be able to be critical and give helpful suggestions to these areas of service, for the better future benefit of our patients. I have invited a panel of guests, men who are cognizant of many areas of rehabilitation in the State and who have a great deal of information to give us.

I wish to start the panel discussion by asking Mr. Eugene J. Taylor if he would give us a résumé of the report of the Governor's Council on Rehabilitation and perhaps provide us with some aspects of information on this report which do not appear in the written report.

Governor's Council on Rehabilitation

Mr. Eugene J. Taylor: We have had an organization known as the Governor's Council on Rehabilitation here in the State of New York for about two years. When Mr. Rockefeller became Governor, he felt the need for providing some sort of mechanism which could keep him informed and provide him with advice on certain programs that were under way in the State and certain programs that were contemplated.

As your know, we have a number of agencies of the State government that are concerned with the various aspects of rehabilitation: the Department of Health, Department of Welfare, the Department of Mental Hygiene, Department of Education, Workman's Compensation Board, Department of Correction, and a number of other agencies.

There are coordinating mechanisms whereby various branches and agencies of the State government can work together. But when there is a conflict in which the commissioners have differences of opinion, the Governor ends up with conflicting advice.

This Council was designed to weigh the

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* By invitation.

various factors involved and advise the Governor accordingly. The membership of the Council consists of ten people of whom four are physicians, one is a lawyer, and people interested in the various aspects of rehabilitation comprise the rest of the membership.

I think in actuality that although the Governor's Council has not done as much as was contemplated in the area in which it was originally to serve, it has made a rather substantial contribution in other ways. The group meets once each month, with no meetings in July and August, and tries to keep informed on all the activities going on or contemplated within the State: new legislation, new programs, and things of that kind.

I think one of the most helpful devices has been that the Governor's Council has access to the Governor's ear through a direct channel, and from time to time when various commissioners have had programs on which they could not get approval from the director of the budget or some other coordinating branch, the Governor's Council could take the matter under advisement and go directly to the Governor with it. We have had several cases in which rather important things have resulted from this procedure.

We've been making a survey over the last year, a sort of inventory of what some of the needs of the State are and how those needs can be met. The data from that report are now being analyzed and we expect the report will be ready soon.

The few things I want to bring up I hope will not impinge on Dr. Schlesinger and Mr. Levy in their presentations; if I do, they can go ahead and give you more of the details.

Problems in licensing. One thing, for example, which should interest especially the group here, concerns the tremendous shortage of all kinds of rehabilitation personnel in New York State. We've had a particularly difficult problem in physical therapy over the years because of the New York State licensing laws, in which New York State does its own licensing and does not use the standards of the Registry of the American Congress on Physical Medicine and Rehabilitation or of the American Physical Therapy Association or the approval by the Council on Medical Education of the American Medical Association of schools of physical therapy. In other words, every school that wants to be approved by New York State must file a separate set of papers for such approval and must pay the expenses of an officer to come from the State Department of Education to conduct an investigation and visit the school; frankly, people just don't do that.

A boy or girl who graduates from a school outside New York State then must file a paper with the Department of Education and seek special permission to take the licensing examination. That means that a boy or girl who comes to New York from the Midwest at considerable expense to file these papers, does not know, once he arrives and takes a job temporarily, whether or not he'll pass the examination and be permitted to practice here.

A great deal has been achieved in the last few months in developing some uniformity whereby the approval of schools by the Council on Medical Education and Hospitals of the AMA would be acceptable for schools of the State of New York, and also to spell out a little more specifically what the requirements are, for example in basic sciences, for a person to be eligible for licensure in the State. I think once this is done it will be extremely helpful, because we in New York State require far more physical therapists than we produce. We must rely on getting therapists from outside New York State to come into the State if we are going to expand our services here; and to accomplish this will be helpful.

Building policies. Another activity which is illustrative of some of the work of the Governor's Council is an attempt to develop or to get various agencies of the State government to develop policy statements regarding public buildings in New York State. We find that our tax funds are being used, in many instances, to build buildings which are not accessible to people who have severe disabilities, and people in wheel chairs and on crutches cannot get up the steps and use the buildings. We are hopeful that something along this line will be developed, so that a policy statement will be issued that whenever tax funds are involved in public building construction in

New York State a certain minimum code must be followed to make those buildings more accessible.

PROCEDURES. We also have been working with Mr. Levy and with the Governor's Committee on "Employ the Physically Handicapped," the State University of New York, and the State Department of Education, trying to set up procedures whereby physically handicapped students who are applying for admission to colleges in New York State will have a better evaluation or a better chance to be considered and will not be turned down arbitrarily by personnel officers and the university deans and admissions committees who are not familiar with disability and take a rather restricted view of the admission of college students.

The same thing is true of the employment of physically handicapped persons in teaching. Some work is being done along that line which I think will broaden the horizon and opportunities for physically handicapped teachers in the State of New York.

COMMENT. These are examples of some of the things which the Governor's Council does. The Governor's Council is not an operating agency. Its membership serves on a voluntary basis without compensation. It works mostly with the State department agencies concerned with rehabilitation and related services for the handicapped, trying to serve an informational, coordinating, and expediting role. Possibly as we go on into the discussion, I can illustrate some other ways in which the Governor's Council plays a role in New York State.

It's not the purpose of the group to do a once-and-for-all kind of big fact-finding study with recommendations; it's a kind of constant inventory-taking, month in and month out, within the State, trying to seek out some of our weak areas. There are areas which none of us suspect. I'll cite one more example in closing.

In New York State, we have a number of patients, persons with epilepsy, who are committed to State penal institutions. At the State penal institutions we have vocational training programs to try to provide vocational skills for offenders, so that when they are discharged from the penal institutions they will have at least some skills they did not have before through which possibly they can secure employment.

But because of the attitude of those in charge of penal institutions and their lack of knowledge of epilepsy, the epileptic persons who are admitted to our reformatories and penal institutions are not permitted to participate in any of the activity programs because people are afraid they might have a seizure and hurt themselves or someone else. As a result, the man with epilepsy who commits a crime and is sent to a penal institution sits in isolation all the time he is there, not participating in any activity. He is discharged from the penal institution. He has learned no new skill and goes back and commits another crime. This pattern continues.

A pilot project has been started to get a better medical evaluation of these patients from a neurologic standpoint and to get them on a better regimen of drug therapy to control the seizures and give them vocational skills.

We find one branch of our State government, the Governor's Committee on "Employ the Physically Handicapped," preaching that we should employ persons with epilepsy and propagandizing this; and yet we find another branch of the State government denying any opportunity to these people.

DR. GEORGI: Could I ask you one question, Mr. Taylor, while we're on the subject of the Governor's Council? Would you care to spend a few moments in discussing what, if anything, has been done regarding suggestions which might have been made as a result of the questionnaire sent to the 30-odd voluntary agencies by the Governor's Council?

MR. TAYLOR: When those came in, they were analyzed, and then questionnaires were sent out to a number of agencies which were not covered the first time. At the present time, we're completing an analysis of these data and I think it will probably be released in a report next fall.

I do not think we are going to find anything that we did not know already, except some high lights in a few areas of neglected interest.

DR. GEORGI: Thank you, Mr. Taylor. I would like to mention here that I would prefer that we hold off questions until after we have finished the more or less formal part of this discussion, and then I will ask for questions from the floor.

Another aspect in rehabilitation of recent interest is the establishment of primary and secondary rehabilitation centers in the State, and Edward R. Schlesinger, M.D., is in charge of this program and is the authority on it. Dr. Schlesinger will you discuss the present status of this program?

Rehabilitation centers

Edward R. Schlesinger, M.D.: Rehabilitation of the physically handicapped to maximum achievement is a vast problem which will require for attainment the full support of each community and, through the representatives of each community, of the entire State. Citizens' efforts and support must find expression through contributions of time and funds to voluntary agencies and through the support of governmental expenditures for rehabilitation purposes. The ultimate source of both voluntary and governmental efforts is the public. These efforts must not be allowed to diverge as programs develop in the community. On the contrary, the two approaches must continue to develop side by side and even to intermesh in reaching their goal: the rehabilitation of the disabled individual.

I present these somewhat platitudinous remarks at the outset to be sure that my emphasis on new rehabilitation programs within the State government is not misunderstood. These newer developments as well as more traditional activities are designed to supplement and strengthen the efforts of individual citizens, professional groups, and voluntary agencies and facilities and to deepen the bond between individual citizens and practicing physicians.

Rehabilitation services. Many State agencies have been financing or providing rehabilitation services for the physically disabled over a period of years. Mr. Taylor referred to a number of these in his remarks concerning the Governor's Council on Rehabilitation, and there is no need to list them. Some of them are identifiable clearly as rehabilitation, such as the medical rehabilitation program of the Department of Health for the physically disabled under twenty-one years of age and the vocational rehabilitation program of the State Department of Education. These identifiable rehabilitation programs alone came to over $17 million in budgeted Federal, State, and local funds for individual New York State citizens during the 1960–1961 fiscal year alone. In addition to these, there are large sums being spent by agencies whose rehabilitation programs cannot be clearly separated from their total programs. For example, the medical care programs under the State Department of Social Welfare have large rehabilitation components.

The Old Age, Survivor's, and Disability Insurance program under the Department of Social Welfare and the program of the Division of Vocational Rehabilitation similarly have large rehabilitation components. Of course, probably the most rapidly expanding program in the rehabilitation field today is that sponsored by the Workman's Compensation Board. It is clear that the State has a major interest in this field.

Of course, these various programs cannot function in a vacuum. They must call on a host of community resources which are available as conveniently as possible to the disabled person concerned. Furthermore, the services of the various agencies must be related to each other to prevent duplication and avoid any gap between existing services.

Plan for centers. To achieve these goals—the support of rehabilitation centers in strategic locations throughout the State and the promotion of better coordination among the various State agencies in the rehabilitation field—a plan was proposed by the Governor's office late last year. I propose to discuss some aspects of this plan and their implementation to date.

Rehabilitation centers, and particularly the comprehensive rehabilitation centers, are notoriously not self-supporting. Their complex character, involving the team efforts of a group of highly trained, specialized medical and paramedical personnel, makes their costs too great for most disabled persons to meet from their own resources.

Furthermore, voluntary community support for these broad rehabilitation facilities has not been as generous as for some specific disease problems. The resulting financial uncertainty has impeded long-term planning by the existing rehabilitation centers and has discouraged them in many instances in their efforts to broaden and improve their services.

Finally, there are large areas of the State lacking comprehensive rehabilitation centers altogether.

The new plan proposes to provide a financial underpinning to the comprehensive rehabilitation centers in two ways. The first involves the provision of grants to assist the centers in meeting deficits that occur in the establishment, broadening, or improvement of their services.

The second is through payment for individual patient care by the referral and financing of a larger patient load under the various State rehabilitation programs. Since the State services reimburse the rehabilitation centers at least theoretically on a cost base rate for inpatient care, the grants are provided within the maximum set for deficits occurring in the provision of outpatient care.

The provision of these grants on a continuing basis from year to year will encourage long-term planning.

The existing relationships of practicing physicians and the centers will not be disturbed. On the contrary, the new program will help ensure the development of greater resources on which the practicing physician will be able to draw for the benefit of his patients.

Each center is expected to provide comprehensive evaluation. Inpatient and outpatient care must be provided in accordance with the needs of individual patients.

PRIMARY AND SECONDARY CENTERS. Ultimate support is envisioned for a network of about 12 primary and 15 secondary centers, or about one center per 600,000 population.

Both types of centers must be hospital-based, with the primary centers, with one or two exceptions, closely related to the teaching hospitals and medical schools that are located in each of the regions as well as in New York City.

Secondary rehabilitation centers are to be aided in other cities of each region in suitable locations to serve outlying areas most advantageously.

Annual grants not to exceed $50,000 will be provided to each primary center and of not more than $35,000 to each secondary center. The same general range of services is expected to be provided at both primary and secondary centers. However, it is anticipated that the more complex rehabilitation problems will be referred by the secondary center to the primary center. Consultation by personnel in the primary center in the outlying communities will be encouraged.

The New York State Rehabilitation Hospital at West Haverstraw will not be neglected under the new plan. It will continue to serve as a rehabilitation standard-setting and training center and as the center for evaluation and treatment of the most difficult problems, especially those requiring long periods of inpatient care. Through the expansion of its services to include outpatient care, it is planned that the hospital will serve as a primary center for the suburban New York City region.

In addition to the provision of evaluation and treatment services, each center should serve as a focus for the coordination of medical and rehabilitation services within the area.

IMPLEMENTATION. While the State Department of Health has been given immediate responsibility for the implementation of the new State-wide program, it exercises this responsibility under the general advisory review of the Governor's Council on Rehabilitation and with the more detailed advice of the Committee on Rehabilitation of the Interdepartmental Health and Hospital Council. This is a group consisting of the commissioners of the various State agencies that have broad interests in the entire health and hospital field. Its Committee on Rehabilitation consists mainly of those persons in each agency who are actually responsible for the administration of the agency programs. The chairmanship of this group is rotated on an annual basis, and Mr. Adrian Levy is the Chairman this year, and so he may wish to go into this a little further and describe the field research laboratory which I shall only touch on briefly.

The State Department of Health is one of the cooperating agencies in the development of the rehabilitation field laboratory for which special grant funds are now being requested. The field laboratory will be directly under the Interdepartmental Health and Hospital Council.

To quote from the report of the Governor's organization study of State rehabilitation services, "The field laboratory is intended to provide a locus for the study and evaluation of public and voluntary rehabilitation programs and resources and to demonstrate methods by which joint planning and program development can be accomplished. The State-wide plan would help provide basic resources for existing programs. The results of any studies or demonstrations under the field laboratory could be readily applied under the new State-wide plan for rehabilitation centers."

When the State-wide plan was first proposed last October, it was anticipated that not more than two primary centers and one secondary center would be supported on a trial basis for a period of time. However, public and professional reaction to the plan was so favorable that the desirability of stepping up the pace of the program became apparent.

The Rehabilitation Center of the Syracuse University Hospital of the Good Shepherd, a teaching hospital for the Upstate Medical Center, is serving as the pilot primary center under the new program. The center has been broadening its activities into new areas of rehabilitation and has been accepting a steadily increasing number of referrals from State agencies and other sources.

Negotiations are currently under way for the establishment of two secondary centers in the Syracuse area. It seems wise to insist on the development of a primary center in a given region before considering support for secondary centers in that region.

Considerable progress has also been made in the Albany region, in spite of a complicated situation there. The primary center logically belonged to the Albany Hospital because of its teaching affiliations with the Albany Medical College. On the other hand, the Sunnyview Orthopedic and Rehabilitation Center in Schenectady, with its long background in rehabilitation and its particularly highly developed services in certain areas, should certainly not be bypassed, nor could Sunnyview be considered in any sense a secondary center. An arrangement was finally developed under which Sunnyview is to share responsibility in association with the Albany Medical Center Hospital in the provision of services to the Albany region. Close educational ties and consultation services are also being developed between the two institutions.

Elsewhere in the State, preliminary investigations have been made in an effort to implement the program as rapidly as possible.

The new program has served as an impetus to the development of a wide variety of rehabilitation services beyond the immediate relationship of the financial help involved. It is to be hoped that this "seed money" will result in a further flowering of well-conceived rehabilitation services throughout the State.

Dr. Georgi: Thank you, Dr. Schlesinger. I'm now going to ask Mr. Levy if he will discuss some aspects of the current program of the State Division of Vocational Rehabilitation and perhaps go into some of the future plans as related to rehabilitation and our specialty.

Vocational rehabilitation

Mr. Adrian Levy: It really is a privilege for me to be able to talk here at the Society meeting because, strangely enough, I do not think most people realize that the Vocational Rehabilitation program has been in existence for about forty years. We'll finish our fortieth year in July. It has always been amazing to us that while both the medical profession and the general public have a general knowledge that we are in the vocational rehabilitation field, there is really a dearth of knowledge about what the program consists of and its size.

It is rather difficult here, I think, to cover areas which have not already been covered by Mr. Taylor and Dr. Schlesinger, because this is one of the outstanding characteristics of our rehabilitation program in New York State: the fact that we do work together, that we do get involved cooperatively in many of the activities that are being carried on in the rehabilitation field for disabled persons.

However, I will try to give you a picture of our program, what it consists of in general, and something about its size. Let me start with this latter area to give you some idea of what it is.

EXTENT. For the 1960 fiscal year we had on our rolls some 39,000 persons. Generally, we have found, and this was true last year, that we have about 20,000 new referrals during the year. Last year, we rehabilitated into employment 6,300 persons. Now, if you look at the big figures, and then take the 6,300, this does not seem like very much from a percentage viewpoint, and so let us break it down a little bit.

Of our new referrals, we generally find that somewhere around 40 per cent do not get beyond the evaluation stage. The reasons for this are multiple. It may be, and this is quite frequent, that the person does not have an employment handicap. He has a disability, but either it is of a minor nature or he has had sufficient background in training so that he does not need any general counseling or additional service, and a purely placement program is what is required for this person. In these instances, we refer the person to the State Employment Service, to the special placement unit.

There are others who come to us, and a large percentage of those who come to us come on their own or from interested individuals through publicity, not recognizing that we are primarily a vocational rehabilitation agency; and they seek from us care for acute or general medical conditions. We are not a general medical care agency. I shall discuss this a little bit further as I talk about our services. These people are referred to other facilities in the community.

A third group may consist of those who, because of a combination of facts, we feel we are not equipped to help at that appropriate moment. These factors include, obviously, the severity of the disability, the status of the disability and general health, the age factor, and the availability of training and jobs in the community—all types of factors which, when added together and considered in combination, make it appear to us that we are not equipped at the moment to provide for the vocational goals of this person.

However, of those who do get beyond evaluation and do get into the service program as such, we find that 75 per cent, 3 out of 4, do end up rehabilitated into employment. That fourth person generally drops out before the end of the program, or employment, for various reasons, such as: moving out of the State; death during the period as a result of accident or exacerbation of the condition; or, in some instances, the person himself does not feel that he wants to go on and drops out, despite our efforts to motivate him and to work with him toward his goals. We think that 3 out of 4 is a fairly good average, because a couple of years ago I did a survey of some of the other voluntary agencies. This was an unofficial one, done in terms of inquiry of directors of other agencies, and I would guess that this 75 per cent is about 15 to 20 per cent higher than the average in terms of some other agencies.

SOURCES. Now, just a quick picture of the sources of the patients, or clients as we call them, for our program. The largest single source of referral is the health agencies. This includes the medical professions, the clinics, the hospitals, and the special groups or health services, such as the Tuberculosis Association.

Approximately 25 to 28 per cent of our referrals come from these sources. You would be interested in knowing that about 5 per cent of our total referrals come from individual physicians. Approximately 6 to 7 per cent come from what we call our public health agencies and hospitals. This is on both the State and county levels.

A very large percentage of our clients come to us, as I have already said, on the basis of general publicity or word of mouth: about 13 to 15 per cent.

And because we are involved in doing the rehabilitation potential determination for those receiving Old Age and Survivor's Insurance benefits, we find that about 19 per cent of our referrals come from this resource.

The other referrals, of course, come from other agencies, such as from our special arrangements with the Workmen's Compensation Board, where we have counselors assigned to work with the patients and to identify those needing our services; from the school systems, which account for about 8 or 9 per cent of our referrals; and from the State Employment Service, welfare agencies, and, frankly, from every possible resource. We have no limit as to the nature of the referring organizations, whether they be individuals or organizations.

PROGRAM. Now, a little bit about the program. As you know, our program must have employment as its goal for the individual. This is the reason for its being called vocational rehabilitation. And in this program, a determination has to be made as to whether or not the disability constitutes a substantial handicap for employment and whether we can help.

Now, the services provided under this program run the gamut. Certainly one of the most important of the early services is evaluation, and this is comprehensive. We are interested in medical, psychologic, social, educational, and vocational factors. We obtain this information from the available sources in the community and through our own staff, which consists primarily of rehabilitation counselors.

We have been believers for many years in the comprehensive approach to evaluation for the severely disabled. For a long time we have been utilizing those few rehabilitation centers that existed in past years and have been interested in the further development of them.

In our evaluation process, as far as the medical aspects are concerned, we require a general medical report on every patient and the report of a specialist in the area of disability, unless our staff of medical consultants puts in writing that the information contained is sufficient without this specialist report. This information generally concerns something like an old poliomyelitis where there has been no change for years and the patient has received all medical services.

After evaluation, when a person has been accepted in the program, the services which are provided we put under such titles as "physical restoration," "training," and so on. Training can be of two types. It can be vocational training or it can be what we call personal adjustment training, a period during which we try to develop work tolerances and work patterns. Or we—and you might take issue with this, but there's a good reason for it—would consider gait training of a new amputee who has just been fitted with a limb as personal adjustment training, to adjust him to that particular prosthesis.

We do provide maintenance and transportation costs for those undergoing physical restoration or training services where this is necessary and to the extent of the extra cost involved for this particular service. We provide occupational tools and equipment where necessary.

We also are a placement agency. We have a responsibility by law for the placement of the individuals whom we serve because of a written agreement with the State Employment Service. We do joint training with the Employment Service with our staff and their staff and cooperate with them in placement areas.

I have mentioned these services. I should point out to you that there is a needs factor with some of them. The counseling, the guidance, the placement, and the evaluation are provided to all individuals. When the client cannot pay for the physical restoration services, maintenance and transportation, occupational tools, and equipment himself, we participate to the extent that is necessary. We do have a financial needs standard which is liberal.

Since this is a group of physicians, you will be interested to know that we cooperate closely with the State Department of Health in the development and acceptance of standards. We utilize the roster of specialists that the Department of Health requires and sets up as a requirement for our program. We are members of the Hospital Rate Commission, so that we all use the same rates for hospital payments. Our fee schedules for particular services in the medical field are developed jointly with the Department of Health, and we utilize the same maximum fee schedules. For example, we share with the Department of Health an advisory committee in the area of cardiology, the Cardiac Advisory Committee, and we have adopted the standards set forth by the Department of Health.

LIMITS OF SERVICE. I have mentioned physical restoration. I am going to take a couple of more minutes on this because I do want to emphasize that we are not a general medical care agency. This is why we call it physical restoration rather than a medical care service. We provide services which will modify, reduce, or eliminate the handicapping phase of the disability. If this is possible, then we provide this kind of service. However, if the service would be generally beneficial to the individual but would have no effect on the handicapping condition, we do not provide such medical service.

I might mention to you that last year approximately $1 million of our funds were spent on physical restoration services. Within the medical area, about 40 per cent of this was in the diagnostic area. Under our laws, we must utilize other resources. Where resources such as Blue Cross and, for example, the Department of Health's Rehabilitation Bureau are available for persons under twenty-one, these are utilized.

PLACEMENT. Dr. Georgi asked me to speak a little about placement and give a quick picture of it. We have been concerned about this service because obviously we are affected by what happens in the community and in our economic society. We have been putting greater emphasis on this. We have intensified our joint training activities with the employment service. I happen to be chairman of a national group made up of rehabilitation administrators of the State vocational rehabilitation agencies and am Chairman of the Committee on Training. We are sponsoring a national program of intensified placement training for our staffs to assure more active and more effective roles for getting our people into employment.

We have been encouraging the development of a placement program through the facilities that we use, especially in training, to assist in this area. In the area of facilities, obviously, we have been most active with other groups. We coordinate our activities with the Hill-Burton program under John J. Bourke, M.D., and the Department of Health of the State.

We have been active in the program that Dr. Schlesinger just mentioned to you, and as I walked out of my office yesterday evening, I got word that our request for putting a full-time counselor in the first primary center in Syracuse had been approved in the budget. The plan is patterned after our experience in the State Rehabilitation Hospital in West Haverstraw where we have for the past few years assigned a full-time counselor to work with the staff of the hospital, and we intend to do this with each primary center to be sure that we have a comprehensive approach to services to the individual.

I could go on but I do not want to take too much of the initial time. I do want to emphasize again that in all of the rehabilitation activities of the State we have made every effort through the Interdepartmental Health and Hospital Council and with the advice and assistance of the Governor's Council to integrate our approach to services to the disabled. We know we have a long way to go, but we think that we have had a good deal of success in this area.

DR. GEORGI: Thank you, Mr. Levy. As the final part of this formal discussion, I am going to ask Mr. Taylor to discuss something of the study made by New York University of the Workmen's Compensation Board and the Workmen's Compensation Board's problems. Although Mr. Taylor was not a formal member of this committee, he probably knows more about it than anybody else.

Study of Workmen's Compensation Board

MR. TAYLOR: Two years ago New York University undertook a study, at the request of the Workmen's Compensation Board, to see whether or not we could come up with any recommendations on earlier and more effective use of rehabilitation procedures in the treatment of disabled workmen who are beneficiaries of the State of New York Workmen's Compensation Board.

This was done by analyzing a great many data and also by holding a number of hearings throughout the State at which representatives of medicine, labor, business, insurance, public agencies, and interested citizens were invited to participate and express their views.

APPROACH. We took the position that although one cannot really separate medical rehabilitation from vocational rehabilitation, it was essential to do that in this study because the State has a program of vocational rehabilitation that is provided by law, as Mr. Levy has just explained. Also, we recognize that medical rehabilitation is essentially a part of medical care, and this cannot be divorced from medical care.

We took the premise that a great majority of medical rehabilitation procedures can and should be done by the attending physician and in the general hospitals.

But over and above those cases, there are certain types of disabilities which require specialized services and specialized or ancillary personnel such as are usually not available to the average attending physician. It is essential that patients with those disabilities be referred to resources early enough so that complications can be prevented and the person can get the restorative physical medicine rehabilitation services he requires.

FINDINGS. We found that in a great majority of cases under Workmen's Compensation in New York State there is no problem, but there is a small percentage of cases which do constitute problems. Even though the percentage itself is small, the number of persons involved is sufficiently great to warrant that something be done about it.

We find a tremendous difference of opinion among the various groups concerned with Workmen's Compensation and the rehabilitation aspects. Like Mark Twain's classic remark about the weather: Everyone agrees that rehabilitation and mother love are fine ideas, but no one is willing to budge from his position and try to make them more effective.

It is extremely interesting that this report has been attacked rather strongly by different groups: Group A attacks one point saying this is a bad thing; groups B, C, and D say, "No, point 1 is a fine thing but it's point 2 to which we object."

The report itself was based on the premise that the only way to get early referral is through sufficient facilities and the education of all persons concerned to the importance of early referral. We believe, and recommended, that rehabilitation resources which serve disabled workmen should be community resources and should be a part of a battery of general medical rehabilitation services within the community. There was quite universal agreement on that particular point.

We did, however, recognize that, irrespective of what one might think, there is no group in New York State, with one exception, that does not believe pretty much in the free choice of physicians. There is one group of employers who believe that the employers should select the physicians for all types of medical service under Workmen's Compensation.

I think, however, that the great preponderance of opinion in favor of free choice, not only from organized medicine but even stronger from organized labor, means that free choice is the choice in New York State and is going to remain the system which we shall use.

PROBLEMS. One has a problem, however, in trying to find mechanisms whereby one can ensure that this very small percentage of patients are referred early enough to qualified resources for complete evaluation and for comprehensive services. We proposed that this be done by both a quantitative and a qualitative approach, because the Workmen's Compensation Board requires that in certain types of disabilities all cases be reviewed by the Workmen's Compensation Board itself, and that in other cases there should be a time factor.

During the time of the study, the New York Workmen's Compensation Board introduced what they call an "R" form, "R" for rehabilitation, which requires that cases after three months who are still under medical service and receiving compensation benefits be reported with some indication of whether rehabilitation has been considered, whether referral has been made, and so forth. That now has been reduced to two months of cash benefits. If a person is not receiving cash benefits, the report need not be filed.

We had only one piece of legislature in the current session of the Legislature resulting from this New York Workmen's Compensation study, and that was the provision of the penalty of a fine—$25 I think it was—for those agencies who are supposed to file these reports and have not done so. The issue became one on a political basis in which the two political parties voted largely along political lines, and it failed by a very small minority, with organized labor in bitter opposition.

Organized labor is opposed to the current administration of the Workmen's Compensation Board. This creates a very difficult situation in the furtherance of improved services for injured workmen in the State, irrespective of theoretical studies which one produces like the New York Workmen's Compensation study.

COMMENT. I think some good did come out of this study: The very fact that we have had a lot of meetings and a lot of discussions on it and that all of the interested participants have discussed it a great deal has in itself created an educational process that has been rewarding. I think some of the arrangements that have been worked out between the Workmen's Compensation Board and the State Division of Vocational Rehabilitation have shown clearly a great improvement in services for disabled workmen who are eligible for the benefit program described by Mr. Levy.

I think the crux of the matter is the manner of supervision. At the present time, as you know, it's a misdemeanor in New York State for any person to suggest to a compensation patient that he change physicians. If you have a patient under your care and I should say, "How are you getting along?" and he says "Not so hot"; if I say, "Why don't you go and see Dr. X; he's an old friend of mine," I'm subject to a misdemeanor and fine. That is actually the truth.

Now, it does not work out that way, but the very fact that this law does exist makes insurance carriers and certain other groups extremely reticent about making such suggestions.

We did have a pilot unit in New York City that operated for a number of years, in which certain cases were reviewed on paper by physicians and social workers as a unit, and then if it was thought that rehabilitation procedures were indicated which were not being provided at that time, each attending physician was contacted and the suggestion was made that the patient be referred. There was no recommendation as to where the patient should be referred, but only that he be referred for rehabilitation.

When we first started out we found that there was a small percentage of physicians who resisted and resented this, a small percentage of insurance companies, and a small percentage of the patients themselves. But as the program went on over a period of several years the percentages went down constantly. Therefore, I think that we have to develop some sort of a system, which apparently is an educational system, to get all parties to recognize that the best interests of all concerned are heightened by early referral of cases of severe or potentially severe disability to resources that are equipped to handle them.

The report recommended that a pilot unit in the New York district office and similar units be established in all the offices of the Workmen's Compensation Board in the State, recognizing that there were great problems because of a shortage of qualified personnel.

We have obtained no indication that this recommendation is going to be followed or implemented in the very near future, with the exception of the inclusion this year of a very substantial amount within the budget of the Workmen's Compensation Board for rehabilitation, which we assume will be used for this purpose, but this is only an assumption.

Question and answer period

DR. GEORGI: The meeting is now open for questions from the audience. If anybody has anything he'd like to ask any of the participants, I am sure they'd be glad to answer within their abilities.

MR. TAYLOR: I want to make a comment which doesn't refer to New York State, but concerns an item which I think of extreme significance to all of us here and everyone concerned with rehabilitation, which I think has been greatly overlooked.

That is that within the provisions of the Kennedy Administration's plan for medical care for the aged is the provision for physical medicine and rehabilitation services. In other words, most of our Blue Cross and Blue Shield programs, which are on a regional basis as you know, do not include physical medicine and rehabilitation services. But this bill specifically spells out that if a beneficiary of the health insurance elected to go as an outpatient to a physical medicine and rehabilitation service or as an inpatient, that person would be entitled to that care just as though he went for acute medical, surgical, or nursing home care.

I point this out because if this legislation were adopted, it would mean economic barriers for maintenance rehabilitation. The economic barriers to treatment would be removed for about 8 or 9 million people over the age of sixty-five.

Now, under the AMA-backed plan and the legislation which was passed last year, this would be up to the state, the state makes up its own plan with partial Federal financing; this would mean it would be up to the state whether or not it would include these services along with acute medical and surgical services. I think the prospects are that this would be done in practically all states, if not initially at least through amendment as time went on, because if old Mrs. Jones in New Jersey can get this kind of service and her sister-in-law lives in New York and can't, the sister-in-law is going to start demanding it.

I mention this because I don't think the important thing in the context of my comments is whether we have the Kennedy proposal for health care for the aged and Social Security or the AMA plan; the most important thing, in the context of these remarks, is that I think we're going to see prepayment for physical medicine and rehabilitation services for older persons become quite universal within the next year or two. This is a very significant thing as far as practitioners of physical medicine and rehabilitation are concerned and as far as community programs are concerned, because it's going to make a greatly increased demand for services, and more groups that in the past have not had sufficient disability to be supplied those services under public programs or were not eligible for public programs will benefit from such services.

Dr. Georgi: Thank you, Mr. Taylor.

Mr. Levy: I would like to comment on the first part of that. In Michigan, Blue Cross has become interested, and there has been a contract signed between Blue Cross and the Detroit Rehabilitation Institute to cover the services of that institute under the Blue Cross plan. I think this is probably the first break-through. We have other areas where we see interest in this, and I think this is coming even under the Blue Cross Plan, to cover these rehabilitation services.

Mr. Taylor: We are presently negotiating a contract at the Institute of Physical Medicine and Rehabilitation with Blue Cross on an experimental basis, but this will not be open to everyone, but on a limited basis, to get some experience as to what the costs and the actuarial indications would be.

Mr. Levy: May I also comment on Mr. Taylor's remarks about the Workmen's Compensation Board program? I think there are indications, at least to us, that in certain areas they are moving ahead toward the development of medical rehabilitation units.

We started a program a couple of years ago with the Workmen's Compensation Board on a pilot basis in the New York City office, because of the potential number of people that they serve there, in which we actually assigned a staff to the Board to review these cases as they come through. For example, they are reviewed on the "R" form after two months to see whether or not any of these people might benefit from our service. Of course, this is purely voluntary. If we think they will benefit we get in touch with them and offer the services, but we cannot make them take it, obviously.

We have moved this plan up through the State on a gradual basis. At the present time, it's been moved up all the way to the Canadian border along the eastern length of New York. We cover it throughout our White Plains, Poughkeepsie, Albany, and Malone offices. Recently it has moved into the Syracuse region: Syracuse, Binghamton, and Utica. We're now initiating negotiations for starting it in the Long Island area, and then we'll move into Rochester and Buffalo.

One of the things we have found is that people are identifying personnel with the rehabilitation unit—physicians, social workers, and so forth—in the offices around the State with which we will be working, and so this apparently has already started.

Dr. Georgi: I'd like to give Dr. Schlesinger a chance to use the microphone. Dr. Schlesinger, do you have any information to give us regarding the possibility of enlarging the number of types of diseases which the State is planning to offer services for, particularly in the line of State aid? As an example, it is rumored that cystic fibrosis is now going to be included in the group of diseases covered by State aid.

Dr. Schlesinger: The medical rehabilitation program for physically handicapped children has been expanded steadily over the years. As you all know, it started initially as a very limited orthopedic program and now has grown, covering every type of disability for which there is some adequate technic available as far as rehabilitation of the individual is concerned.

Most of these conditions fall into the group of what can be considered definitive problems, that is, conditions for which a single service or a group of services, or at least a single rehabilitation plan which may continue over a period of time, will result in rehabilitation. It has not included conditions for which there was a poor rehabilitation outlook, nor has it included what are essentially long-term medical supervision patients.

With respect to cystic fibrosis, there have been major changes, as far as the condition itself is concerned, from the time when it was almost certainly fatal during the first few years of life. Now that has changed considerably; if the child survives to school age, he has an excellent chance to go through adolescence and early adult life. We don't know how much longer the survival outlook may be because we just haven't been able to follow these persons long enough, so that the question about the outlook for survival is no longer a major factor in this condition.

However, it does pose a different type of approach to the problem from the ones that are currently under the medical rehabilitation program. For this reason, we have not suggested that cystic fibrosis be included automatically within the scope of the program as it has been to a limited extent in a number of New England states. We feel that this problem will require a good deal of study before we arrive at some sound approaches to how it may be met.

The Governor's message included a reference to cystic fibrosis, and that is presumed to be the basis for the rumor. There's no question that it is being given intensive consideration. We hope that if we can get these two demonstrations or surveys off the ground, we'll have the basis for developing a plan. One approach is to obtain as much information as we can on the nature and type of services needed and the cost of the program.

The other is to carry out an intensive survey of a large community in Upstate New York, and Erie County has agreed tentatively to go along with this so that we can get an idea of the size of the problem and relate that to the problem of individual patient care, to get an idea of the ultimate cost of the program.

We are definitely getting into this in one way and another, but it is at the moment on a study basis.

Dr. Georgi: Are there any questions from the audience?

Question: I'd like to ask Mr. Taylor or Mr. Levy whether the Governor's Council on Rehabilitation has done anything about seeing what can be done to facilitate cooperation on the local level between the facilities and services that are already available and the agencies that need these services. This is one of the big problems at the operating level, to get these multiple factors interacting, and I was wondering whether anything had been done or whether there was any prospect of this being done?

Mr. Taylor: When Mr. Rockefeller became Governor, as you know, he brought a number of people into the State government who had reputations for being extremely efficient in management. These people came and presented to the Governor's Council some ideas they had on how the kind of intercooperation within the community which a lot of us feel is essential could be facilitated. They proposed to do this from the top down. Then we did not hear from them for awhile.

When they came back about six months later, they had learned something of the complexities of the rehabilitation problem, and they agreed this could not be done from the top down; it had to be done from the bottom up. Just as one could not sit in Albany and outline a treatment program from a desk for a handicapped child or adult, one cannot sit in Albany or Washington and solve the complexities of intercommunity relationships in Rochester, Buffalo, or Utica.

The result was the program of the development of primary and secondary centers which

Dr. Schlesinger mentioned, believing that only centers could act as focal points in which community rehabilitation planning and cooperation could be developed. I think this is quite true and quite sound, and I think most of the people who are engaged in community planning and social welfare and in medical and hospital care would recognize this, because for one thing they would include on the staff of each of these centers one person whose job would be to be an evaluator, promoter of coordination, information distributor, and so forth. I think this is the only way one can achieve the kind of cooperation that is necessary, and I think this is far more promising than other approaches.

Dr. Schlesinger: There is no question that this is one of the most important aspects of the program. In its absence the whole complicated structure may simply collapse. I think we all know that in some communities there are good rehabilitation centers available which are not being utilized fully for a variety of reasons, not only because financing is scarce but also because there is a lack of awareness of the potentials that are available or the accomplishments that can be achieved through the referral of patients, and there is poor motivation of patients themselves.

In my own discussion I mentioned in passing that on the staff of each of the primary centers there will be a community rehabilitation services coordinator employed under the funds provided through the grant. This is really the only single requirement that we laid down as a uniform thing for all the primary centers. Apart from this one position, it is not necessary to employ any one particular type of person. The centers have to meet generally accepted standards for care which necessitate different types of specialized personnel. We are particularly interested in the person who can serve as a staff person and function on a regional interdepartmental basis with the State agencies. This is only the first step. Without it, we do not see how the thing can function at all.

The State agencies must sit down and work together, as we have succeeded in doing, although it took a lot of doing over a period of several years before we really had them functioning together on the Rehabilitation Committee of the Interdepartmental Council. This has to be carried out within the region and through the region to the various committees, that is, the various communities within the State.

It is not anticipated that these initial coordinating efforts will include the voluntary agencies but that this will be the first step which will then go on, we hope, to the formation of broad coordination within the county, which will include the professional groups and the voluntary agencies.

Mr. Taylor: Paralleling that, of course, will be the large-scale study of the field laboratory in which we hope we can work out some new ways of doing things. At present we have practicing physicians in New York State who conceivably work for six different agencies of the State Government doing general medical examinations, and none of the six forms is the same; if we could get standardization of report forms on such basic things as general physical examinations, I think that would be helpful.

Dr. Georgi: Are there any more questions of the panel?

Dr. Schlesinger: A question concerns the primary center rehabilitation program, particularly the method of financing involved and how the appropriations for this purpose were introduced.

The initial interest, as I indicated, came from the Governor's office itself. As Mr. Taylor mentioned, it stemmed from a desire to develop more effective coordination, the realization that this was already being achieved in large measure on the State level, and that some method had to be worked out to get this into the communities themselves.

As far as the appropriations are concerned, this has posed no great problem because of the tremendous interest of the present administration in the program. When it was started funds were provided through some unexpended funds that were available, and now in the current State budget there is an item of $200,000 which will more than amply carry the program during the current fiscal year at the pace at which it is developing. Ultimately, it is estimated that about half a million dollars or $600,000 will be needed for this purpose each year.

This does not mean that each center is going to get the full $50,000 or $35,000 each year. If so, the amount would probably go up closer to $700,000 or $800,000. But the program is on a deficit financing basis. The centers are reimbursed for deficits incurred in the provision of outpatient services, according to specific positions that are set up in the budget. These are not funds simply to reimburse the centers for current deficits. They are to pay for deficits incurred in expanding services or in improving services and putting on new personnel.

QUESTION: Who introduces such special legislation?

DR. SCHLESINGER: There is no need for specific enabling legislation. The only need is for an item in the executive budget. The Governor's budget includes a line item this year of $200,000 specifically for this purpose. As the needs increase, we hope that amount will be increased proportionately, and ultimately we imagine that it will be in the neighborhood of $500,000 or $600,000. Then the Legislature acts on the budget, and that is all the enabling legislation needed.

The next question, basically is: Has the State Medical Society had an opportunity to review the proposal prior to its introduction? I know that the State Medical Society was kept fully informed of this proposal through its Council Committee on Public Health and Education and through the Council itself, and it was endorsed by the Council; as far as we're concerned, the Medical Society has had a chance to review it. If they felt that there was something controversial in it which required action by the entire Society, I think that they would have referred it through the channels of the House of Delegates.

But, ordinarily, these things are not put before the House of Delegates unless there is something that the Society takes issue with.

This has gotten wide publicity. I'm not sure that the House of Delegates is the proper mechanism for publicizing this. As I say, we discussed the proposal with the proper groups within the Society and we hope that through meetings such as this and through discussions across the State the plan will be given publicity. We have publicized it at every possible opportunity; whenever a new center has received financial support we've attempted to secure broad newspaper publicity through the various channels so as to reach the profession. We hope that this discussion will, through the usual channels, also reach the medical profession.

We're open to any kind of suggestion as to how this can be publicized in the best possible way.

MR. LEVY: Am I correct in assuming that the authority for providing grants to agencies to support and develop facilities and programs is one of long standing, and this is why you don't need enabling legislation here? This is just a matter of utilizing funds for a different type of facility to improve and develop programs? Is this a correct assumption, that this is one of the reasons why the program doesn't have to go in as a separate item of legislation? This is just part of a general program such as is carried out by the Health Department in giving grants.

DR. SCHLESINGER: Would you agree that how the State Society should act is a matter within the State Society itself? We have furnished the information and we are open to discussion of this at length at any time.

MR. TAYLOR: Was it ever suggested by the Council of the State Medical Society that they undertake to notify and inform the members of the county medical societies? This was approved by the State Council and its committee. Did they indicate any willingness to go to the county medical societies and inform them about the development of this program?

MR. LEVY: The question has been asked: Has there been any suggestion in the existing areas where the primary centers are being developed that consideration be given to developing a roster of disabling conditions which might be served and benefited through rehabilitation services?

I do not think we could say a straight "yes" to this in terms of connection with this program; but one of the purposes of the rehabilitation field laboratory is to go into a community to determine, in its broadest sense, what is the best way to organize, integrate; and coordinate the rehabilitation services for disabled people in the community. This is done not only in terms of the medical rehabilitation activities but also as concerns the total adjustment into the community; and this might involve housing conditions, social welfare, employment, and so forth.

Now, there have been, throughout the country, a series of projects in various cities which attempted to meet this problem of identifying the disabled who would benefit from rehabilitation. I think offhand of Knoxville, Tennessee, Kansas City, Missouri, and several others. Thus far our interpretation of this experience is that it has not worked out in each instance as well as we had anticipated: that just getting together to develop such a roster does not indicate that the people are going to get or even require the service. What is necessary is to study the community in depth and study the pattern of organization of services to see whether we can organize a pattern which will provide for continuing attention to the needs of the disabled people, without gaps or duplication.

One last comment before I turn it over: In terms of the development of a roster, I know of no disability group which cannot be benefited in some way by rehabilitation services. I think it's amazing, and certainly it's based on the tremendous advances in medical knowledge and technics, but what is being done for what were considered hopeless conditions just a few years ago is amazing. I do not know of any disability group which has not received services and benefits for at least some of its people through our programs in the State. This is true even in terms of vocational rehabilitation and in terms of multiple sclerosis or muscular dystrophy, disabilities that just eight or nine years ago we would not even accept because we said that they couldn't be rehabilitated vocationally.

QUESTION: Is Division of Vocational Rehabilitation counseling available for all individuals?

MR. LEVY: We've given the idea of providing DVR counseling services much thought, even though they are not in our program. We would love to do this. As a matter of fact, one of the reasons for assigning a counselor to the centers is that the counselor will be available, whether or not we use these services, and can act as part of the center staff.

Certainly we have been interested in this in terms of dealing, for example, with the welfare population. We would even like to get into the retraining problems in terms of automation problems, and so forth.

All I can say to you is that the sizes of the problems in this field are so large in comparison with what we have available in terms of staff and the shortages of personnel that we have not been able to do this. We feel we have to establish priority, and therefore, with the large numbers of disabled persons coming to our doors, we are attempting to serve these people first. In our plan we hope to expand. For example, in the very near future we anticipate putting on an additional 25 counselors. Right now we have a professional staff of over 200 people, and we hope to expand this. I hope that someday we will reach the point where we don't have to think in terms of whether or not a person is eligible for our program, but that if this person can benefit from the kind of counseling services we can provide, he will get them. This is a goal. I'm afraid that I can't say that it can be done right at this moment.

DR. GEORGI: This session is ready to close, and I wish to thank the members of the panel for being our guests today. I am sure we have all learned a great deal about rehabilitation services.

Drug Withdrawal with Promazine Hydrochloride

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FORTY-FIVE PATIENTS *(22 males and 23 females) were treated with promazine hydrochloride (Sparine hydrochloride) for the abstinence syndrome associated with withdrawal of narcotics and barbiturates. In all but 8 cases the addictive drug was stopped abruptly on admission, and full dosage of promazine hydrochloride was started immediately. The daily dose varied from 100 mg. to 1.2 Gm., given intramuscularly in divided doses. Withdrawal was effected easily and without major complications in all cases. All patients seemed relatively comfortable and were accessible to psychotherapy during the withdrawal period. No jaundice or any other significant side-effect developed.*

HABITUATION TO narcotics or the barbiturates is becoming an increasingly important medical and social problem. The treatment of drug addiction and of the associated mental and physical deterioration requires hospitalization. Once withdrawal of the addictive agent has begun, specific symptoms (abstinence syndrome) are soon manifest. The patient suffers cramps, nausea, and severe pain and is insistent in his demands on the hospital staff for relief in the form of additional doses of the drug involved. After the completion of withdrawal the craving usually returns; the high rate of relapse is well known to all physicians. As hospital admissions for the treatment of drug addiction become more numerous, the need increases for a more satisfactory therapeutic regimen than the conventional methods heretofore in use.

In the past insulin coma and subcoma were widely employed. Such measures, it is true, relieve tension and prevent the undesirable effects of withdrawal, but the benefits are associated with many disadvantages. Constant nursing care and supervision are necessary during the first two days of insulin therapy. In addition, this medication cannot be administered indiscriminately to every patient; cardiac disease, diabetes, and age beyond forty-five to fifty years are among the contraindications. Even under optimum conditions there may be danger of cardiac arrest, respiratory distress, or prolonged coma.

In recent years certain of the phenothiazine derivatives have been used with fair results for the treatment of the withdrawal syndrome. However, the clinical response to a number of these compounds is variable. Many patients become extremely drowsy and fatigued; others become confused. Usually there is no acute discomfort as withdrawal continues, but in some cases jaundice may develop during medication with certain of the phenothiazine agents and necessitate the termination of the treatment.

Promazine hydrochloride* appears to combine the more favorable qualities of the various ataractic compounds in the phenothiazine series,[1–5] and contraindications to use of this substance for drug withdrawal are practically nonexistent. Addicts withdrawn with promazine hydrochloride appear less drowsy and fatigued and report greater comfort during the withdrawal regimen than they do under medication with other substances in present use. No jaundice has been reported during treatment of the abstinence syndrome with promazine hydrochloride. The compound is less dangerous than insulin. In addition, withdrawal is completed relatively easily and does not require intensive care nor an excessive

* Promazine hydrochloride is available as Sparine hydrochloride from Wyeth Laboratories, Philadelphia.

expenditure of time on the part of the medical and nursing staff.

Clinical series

Forty-five patients (22 males, ages twenty to seventy-seven years, and 23 females, ages twenty-three to fifty-nine years) were treated for addiction to a variety of drugs, including heroin, morphine, meperidine hydrochloride, and secobarbital and pentobarbital sodium. These patients had been addicted for periods ranging from six months to forty-two years.

On admission all the patients were tense, restless, highly anxious, and frequently depressed. There were many complaints of stomach pains, nausea, and buzzing in the ears. However, most of the patients were cooperative and in several instances actually requested withdrawal. In 37 cases the addictive drug was stopped abruptly on admission and full dosage of promazine hydrochloride was begun immediately. For the other 8 patients withdrawal of the addictive drug was accomplished more slowly. One of these patients was suffering from the complications of diabetes, another had severe hypotension, and a third was in very poor physical condition. Under promazine hydrochloride medication the latter started to eat, and his physical condition began to improve immediately. The addictive drug was withdrawn gradually, accompanied by smaller, slowly increasing doses of promazine hydrochloride. In spite of the smaller doses of promazine hydrochloride administered, withdrawal was completed within one week.

DOSE. Initially, the dose and route of administration were established in pilot studies. The dose was adjusted to the individual needs of the patient and varied from a total of 100 mg. to 1.2 Gm. daily. It was found that the patient responded more satisfactorily when the medication was injected intramuscularly every two or three hours for the first two days and then every three or four hours for three more days. Most patients did well on the following schedule: first and second day, 50 to 100 mg. every two hours, third and fourth days, 50 to 100 mg. every three hours, and on the fifth day, the same dose every four hours. On the sixth day 50 to 100 mg. were injected four times a day. As the patient improved the dose of promazine hydrochloride was gradually reduced until withdrawal was complete; frequently this occurred in five to seven days. On the completion of withdrawal the patient was maintained on promazine hydrochloride in oral doses of 75 to 100 mg. daily for an additional three weeks.

RESULTS. The results supported our original observations[1] and those of others,[2–5] as previously reported. The treatment described produced a state of quiescence and calmness from which the patient could be readily aroused to care for his personal needs or to participate in psychotherapeutic procedures. No patient exhibited signs of tension, restlessness, or craving for the drug to which addiction had been established. All in this series became quiet and tractable, and all adjusted without resistance to hospital routine. Withdrawal was effected easily and without major complications in all cases.

In some barbiturate-addicted patients epileptiform seizures have been reported under prolonged treatment with relatively large doses of certain phenothiazine derivatives.[5] Such seizures occurred in 5 patients in this study who had taken high doses of barbiturate over a long period of time, and 3 of these had hallucinations and extreme confusion. This necessitated a restoration of the barbiturate in doses of 6 to 8 grains (0.4 to 0.5 Gm.) daily. When the dosage of barbiturate was reduced progressively and promazine hydrochloride gradually substituted, confusion cleared, convulsions ceased, and withdrawal was accomplished with no untoward effects. Epileptiform seizures seen in these 5 patients were thought to be related to the abnormal central nervous system stimulation often associated with drug withdrawal. In this study it was found that narcotic addicts seemed to require less care and lower dosage with promazine hydrochloride than did individuals habituated to barbiturates.

No untoward reactions of a clinical nature attributable to promazine hydrochloride developed, except for a few isolated cases of pruritus. No indication of jaundice was observed.

Summary

Promazine hydrochloride was administered to 45 patients for the management of the abstinence syndrome associated with the withdrawal of narcotics and barbiturates. Therapy was instituted immediately on admission, and the addictive drug was withdrawn at once in all but 8 cases. The medication was administered intramuscularly every two to three hours, in divided doses. The total daily dose ranged from 100 mg. to 1.2 Gm. After the initial two-day period, intramuscular injections were continued on a three- to four-hour basis and, after a week, oral medication with promazine hydrochloride was instituted in doses of 75 to 100 mg. daily.

Withdrawal was effected easily and without major complications in all cases. All patients seemed relatively comfortable and were accessible to psychotherapy during the withdrawal period. No jaundice or any other significant side-effect developed.

Promazine hydrochloride provides an effective and relatively safe treatment for the acute symptoms of drug withdrawal.

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Lipids test

A study reported by Stutman *et al.* in the December, 1961, issue of the *American Journal of the Medical Sciences* indicates that the nine-hour postprandial serum optical density is a simple, practical, and efficient tool for screening large populations for abnormalities of lipid metabolism.

The study was conducted in 10 controls (young men) and in 13 young men with coronary heart disease and no prior history of hypertension, diabetes, myxedema, or chronic glomerulonephritis. Preprandial serum lipids were elevated in 12 of these 13 men. In the oral fat loading test, serum fatty acids in the experimental group with coronary heart disease did not return to preprandial levels for at least three hours. While the men were deprived of food over a twenty-four-hour period, serum fatty acids and B-lipoproteins rose in the experimental group at a time that they continued to decrease in the control group. At nine hours, the serum optical density of the experimental group was more than twice the fasting level; this was significantly different from the density of the control group, which had returned to preprandial levels. Total fatty acids and cholesterol were always much higher in the coronary group.

Transmetatarsal Amputation in Arteriosclerotic Diabetic Gangrene

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TRANSMETATARSAL AMPUTATION in the diabetic patient with gangrene has met with moderate success in the hands of various surgeons since McKittrick, McKittrick, and Risley published their report in 1949.[1] The results have varied from 65 per cent healing in Wheelock, McKittrick, and Root's[2] group to 20 per cent in the more severely diseased group reported by Warren *et al.*[3] These cases are not to be confused with the cases of infection or neuropathy without gangrene in diabetic patients, in whom nearly all transmetatarsal amputations are successful.

Since the time spent in the hospital by patients undergoing transmetatarsal amputation is considerable and since the financial burden placed on the patient and his family is no small one, it was decided to determine the fate of all patients who have undergone this operation at The Mount Sinai Hospital since 1955.

Technic of operation

The success of the operation is largely dependent on the maintenance of an adequate blood supply to the long plantar flap. Because the circulation to the plantar aspect of the foot is superior to that on the dorsal, the plantar flap is made long and is brought up and around the transected metatarsals to meet the dorsal skin on the dorsal aspect of the foot (Fig. 1). This technic also places the suture line in a non-weight-bearing area. The utmost care and gentleness should be exercised in fashioning the plantar flap to avoid tissue trauma.

The transection of the metatarsal bones was proximal to their heads at the level of the dorsal skin incision. The approximation of the skin edges was with interrupted sutures of silk or stainless steel wire. If an infection was feared, the flaps were left open and then approximated four to five days later if the wound was clean. The sutures were removed in from fourteen to seventeen days. The wire causes very little reaction in the skin and can easily be left in for that length of time. A posterior plaster splint was used for the protection of the limb, and antibiotics were given to help obviate infections.

Results

During the 1955 to 1960 period 11 transmetatarsal amputations were performed on patients who had diabetes and gangrene. Several different surgeons performed the operations, and therefore, uniform criteria for operation were not used throughout. However, in general, the criteria set forth by Wheelock, McKittrick, and Root[2] were used.

The average hospital stay of the entire group was fifteen and one-half weeks. The patients who healed were in the hospital an average of thirteen weeks, while those who did not heal averaged eighteen weeks. However, it should be noted that 1 patient in the latter group was in the hospital for forty weeks. If this 1 patient is omitted, the average of approximately thirteen weeks holds for both the successful and the unsuccessful cases.

Of the 11 cases, 5 (45 per cent) failed outright and required below-knee amputation. Six cases (55 per cent) healed either primarily or after varying lengths of time subsequent to their discharge from the hospital. Of the 6 cases that healed, 1 patient, a dentist, returned to a gainful occupation. Two of the patients could not be employed because the stump broke down with weight-bearing. One patient did fairly well until he lost his other leg two years after leaving the hospital. He did not work in the interim, however. One patient eventually was able to walk a few steps so that she could feed herself, and 1 patient developed an organic mental syndrome two months after discharge and had to be confined.

Comment

In this series, healing occurred in 55 per cent of the cases, which is not unlike the rate of healing in Wheelock, McKittrick, and Root's[2] series (66 per cent) or in the series of Warren *et al.*[3] (63 per cent). However, only 1 patient in the present series returned to a gainful occupation. Three others can be said to have achieved some limited use from the salvaged leg, although they could not resume an active role in society. In McKittrick's[2] group of 336 patients originally operated on, 218 (57 per cent) were alive and using their limbs at the end of one year, 156 (42 per cent) at the end of three years, and 87 (24 per cent) at the end of five years. In Warren's group of 43 patients, 19 (44 per cent) were living and using their limbs at the time of publication of his paper in 1952.[3] Thus, it would appear that

FROM 1955 TO 1960 *11 transmetatarsal amputations were performed on patients who had diabetes and gangrene. The average hospital stay was fifteen and one-half weeks. Of the 11 cases, 5 (45 per cent) failed outright and required below-knee amputation; 6 cases (55 per cent) healed primarily or after varying lengths of time. Of the 6, 1 returned to a gainful occupation, and 3 achieved some limited use from the salvaged leg. The results are similar to those in other studies. The chance for success and the expense in time and money must be weighed in considering transmetatarsal amputation.*

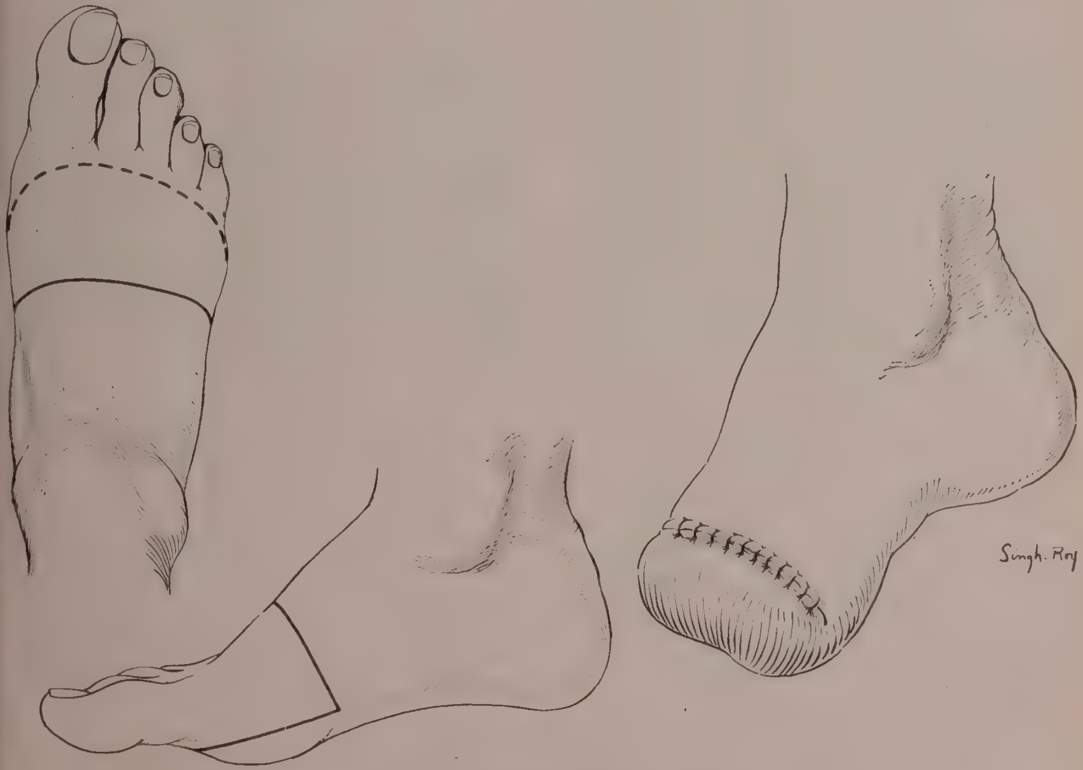

FIGURE 1. Technic of transmetatarsal amputation.

the rate of salvage of a useful limb in the present series is less than that in the two quoted series.

The duration of hospitalization in the present group was similar to that in the quoted series. In view of the salvage rate of useful limbs and in view of the very long hospitalization, it is believed that careful consideration must be given to the great expense that the patient and his family incur in the hope that a comfortable and useful limb will be obtained. Likewise, it must be remembered that many patients become excessively dependent, both physically and mentally, after three to four months in a hospital bed and are unable to assume significant responsibility thereafter. There is no question that a successful result justifies practically any expense. However, because of the expense in time and money and the relatively low salvage rate, the criteria for probable success must be fully understood by the surgeon recommending this operation.

Wheelock, McKittrick, and Root[2] found that approximately 50 per cent of the cases failed if the femoral was the lowermost pulse, 30 per cent failed if the popliteal was the lowermost, and only 25 per cent failed if the dorsalis pedis pulse was the lowermost. They also recommend that the operation not be performed unless rest pain is controlled without narcotics, unless dependent rubor is absent, and unless venous filling in the foot occurs in less than twenty-five seconds. In addition, the plantar skin must be intact, and the dorsal skin must be viable to the metatarsophalangeal joint. Active infection must be under control, and the necrotizing process must be localized by conservative measures. Warren *et al.*[3] call attention to the fact that in their series the patients with no pulses below the femorals, with ischemic rubor, and with rest pain healed in only 2 out of 10 cases.

It is hoped that with the realization of the chance for success and also the realization of the expense involved in attaining that goal, surgeons will employ carefully all of the criteria which have been mentioned previously when transmetatarsal amputation is considered.

Summary

Successful healing of transmetatarsal amputations occurs in approximately 60 per cent of patients with diabetic gangrene. A significantly lower percentage of patients obtain a useful limb for a long period of time.

Attention is drawn to the large expense in time and money involved in the protracted hospitalization, and a plea is made for close adherence to established criteria for operation.

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Nonsurgical Management of Ménière's Disease

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IN MÉNIÈRE'S DISEASE *there is generally a hydrops of the endolymphatic system. Increased pressure within the labyrinth and cochlea produces the characteristic symptoms: vertigo, deafness, and tinnitus. Attacks may last from a few minutes to several days and may recur in weeks or years. The disease may be considered an autonomic dysfunction, possibly caused by a "physical allergy," an all-inclusive term. Endocrine dysfunction and metabolic disturbances have been found in some cases. Other factors to be considered are: overindulgence in alcohol, salt, and certain foods, blocked eustachian tube, upper respiratory or virus infection, and tension and stress. There is no one specific treatment at present. Treatment should include vasodilators, sodium restriction and elimination, anticholinergic drugs, and sedatives.*

THE LITERATURE is replete with theories on the mechanisms involved in producing the symptoms of Ménière's disease. Much experimental work has been done but the conclusions are usually the consequence of deductive reasoning. First of all, there is disagreement as to what should be included under the heading of Ménière's disease. Ordinarily the terms Ménière's disease, Ménière's syndrome, and Ménière's syndrome-complex are applied to that combination of symptoms that includes vertigo, deafness, and tinnitus. Since there may be several combinations of these symptoms, since they vary in form and intensity, and since one symptom may appear without the others, atypical cases (sometimes termed pseudo-Ménière's syndrome) are encountered, and some confusion as to terminology has evolved. In this paper the term Ménière's disease will be used as an all-inclusive one in which the cardinal symptoms appear together or individually.

Symptoms

There is general agreement that in most cases of Ménière's disease there is a hydrops or dropsy of the endolymphatic system. The increased pressure within the labyrinth and within the cochlea produces the symptoms encountered in Ménière's disease, and if this added pressure is great enough or recurs frequently enough, degenerative changes are produced which may be irreversible. The labyrinthine hydrops is considered to have its origin in autonomic dysfunction of the neurovascular system situated in the labyrinth. Arteriospasm and constriction occur, producing labyrinthine ischemia with a secondary effect on the capillaries. This is in the form of injury due either to ischemic effects on the capillary endothelium[1] or to secondary capillary and venule dilatation, causing anoxia and subsequent injury to the endothelium.[2-4] Increased permeability results, and the added amount of endolymph produces the symptoms encountered in Ménière's disease in varying degrees according to the extent of pressure within the labyrinth.

In considering the triad of symptoms that are characteristic of Ménière's disease it must be remembered that these symptoms occur in other disorders, and one should be relatively certain that the vertigo, deafness, and tinnitus are produced by a disease

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within the labyrinth before treatment is instituted. The symptoms may occur simultaneously, but frequently the vertiginous attacks will appear without cochlear symptoms, and the latter sometimes are not accompanied by vertigo. Also, one symptom may appear initially, and it may be hours, days, or months before the others appear. The importance of taking a careful history cannot be overemphasized since much information may be gained by obtaining details of the sensations experienced by the patient.

The victim of Ménière's disease usually complains of a sudden attack of vertigo during the night, perhaps on turning in bed, or on arising in the morning. Sometimes it occurs suddenly during the day and is severe enough for the patient to fall. He may feel that he has lost his sense of balance and will stagger, usually to one side. One must be careful that this attack of so-called vertigo is not a blackout or a fainting spell, for the patient's idea of dizziness varies greatly. Labyrinthine vertigo is quite characteristic; the patient has a sensation of turning in space, or the room seems to revolve around him, and yet there are varying degrees of this dizziness which might be so mild as to include such terms as giddiness, fogginess, unsteadiness, swimming, and so forth. The attacks may last from a few minutes to several hours or days. They are paroxysmal and recur at varying intervals. If the patient is seen at the time of the vertiginous attacks nystagmus is apparent, usually at first to the side of the lesion, later to the opposite side. Nausea and sometimes vomiting occur. Sometimes the individual is confined for weeks, but usually the attack subsides gradually, leaving mild symptoms of unsteadiness which diminish so that the patient is not incapacitated. These remissions may last for several weeks, months, or even years before there is a recurrence.

Caloric tests are sometimes quite normal, but usually we are able to detect that one labyrinth is a little more active than the other, indicating a hypofunction or a hyperfunction of one of them. Unless deafness and tinnitus are taken into account one is sometimes unable to determine by the description of the vertigo, the falling, and the nystagmus which labyrinth is involved, although on caloric testing the hypoactive ear is usually the one that is affected. If one is in doubt as to whether or not the person is describing a true labyrinthine vertigo, the caloric test may be helpful. Frequently this test will produce the same sensations the individual had during the attack.

The patient with Ménière's disease complains of difficulty in hearing. Usually this is unilateral, but attacks of bilateral Ménière's disease are not uncommon. The sensation may be described as a fullness or stuffiness of the ear, or as a "plugged" ear. The cochlear symptoms frequently precede the vertigo, sometimes by several months. The hearing may fluctuate during an attack of Ménière's disease and between the recurrences. This fluctuation, which may occur during any one day or from day to day, is very characteristic of the disease. The hearing defect is perceptive in type and usually involves the low tones, but it may involve the high tones, especially after many recurring episodes. While the hearing defect has a tendency to persist and to increase with repeated attacks, in some patients the hearing improves after the attack and may return to normal. Discrimination for speech is usually reduced much beyond what one would expect from the pure-tone audiogram. Recruitment is always present in the affected ear. Diplacusis and hypersensitivity to loud noises may be experienced and frequently are very annoying to the patient.

The tinnitus also is sometimes very distressing. It is almost always present when the hearing is affected. Although the patient may not be aware of a hearing defect, it can be demonstrated readily by the pure-tone audiogram. The tinnitus is a roaring sound and low pitched but at times may be described as a whistle.

Causes

The partially substantiated theories concerning the mechanisms of endolymphatic hydrops have been mentioned. Apparently in Ménière's disease, there is an autonomic dysfunction which affects the vascular system of the labyrinth. One must look to the causes of this dysfunction to treat Ménière's disease with some semblance of understanding. The effort would be to eliminate the cause, if possible. But experience has shown that this cannot always be done so that frequently it becomes necessary to treat the effect of these unknown causes, that is, the autonomic dysfunction. It is difficult to evaluate truly the efficacy of any treatment because of the well-known fact that Ménière's disease has a tendency toward remissions. It is quite possible that, in many of the mild cases, time alone would have accomplished the same result as certain medications that have been given.

Williams, in his excellent book[2] and in several articles on Ménière's disease,[3,4] has advocated that since autonomic dysfunction apparently produces the vascular changes in the labyrinth one must consider that allergy is the cause of Ménière's disease. He states that autonomic dysfunction and allergy are one and the same, and therefore all cases of labyrinthine hydrops should be treated as an allergy. This does not necessarily mean that they are involved in an antigen-antibody mechanism and can be cured by discovering a food or an inhalant as the cause of the attack. Such is the case in a relatively few sufferers of Ménière's disease. The autonomic dysfunction may be caused by what Williams calls "physical allergy." This is apparently an all-inclusive term.

From a practical standpoint one must consider those factors which may cause this allergy or autonomic dysfunction. Here the history and the general physical examination are most important. A patient may have had asthma, hay fever, urticaria, eczema, histamine headaches, and other allergic manifestations which may give a lead to an antigen-antibody reaction. Sensitivity not only to food, inhalants, or drugs but also to cold, heat, or light may be ascertained. Toxemia or bacterial allergy, probably caused by a focus of infection, may be encountered, and, although this is not a frequent cause of Ménière's disease, an occasional case may be alleviated by the removal of a focus of infection in the teeth.

Endocrine dysfunction and metabolic disturbances have been discovered in some cases. Thyroid deficiency has been known to exist in this disease, and with adequate treatment the symptoms have been relieved. Shambaugh[5] feels that the use of liothyronine (Cytomel) is more efficacious than desiccated thyroid extract. It has been noted that attacks occur in some women at the time of their menses when there is usually fluid retention. With proper treatment these attacks may be avoided. Circulatory disturbances, arteriosclerosis, diabetes, nephritis, hypertension, hypotension, and anemia may be responsible for the symptoms that occur in Ménière's disease.

Occasionally overindulgence in alcohol, tobacco, salt, excessive fluids, and certain foods are factors to be considered. On rare occasions one is surprised by the good effect of inflating a blocked eustachian tube. Very frequently a history is obtained of an upper respiratory infection or a virus infection as the illness that accompanied or just preceded the onset of the symptoms of Ménière's disease. Finally and most important is the consideration of the psychosomatic effect of tension and stress—the effect of emotional upsets and anxiety on the autonomic system, the dysfunction of which produces the local vasospasm that occurs in Ménière's disease.

There are many instances where the actual cause of the attack of Ménière's disease cannot be determined. Also, the acute symptoms are so distressing that they must be alleviated before one can take the time to ferret out the cause of the disturbance. Therefore, in the treatment of Ménière's disease it is best to consider first the management of the acute attack and then outline treatment for the milder disturbances and the long-term care with the hope of preventing recurrences. In addition, it is generally conceded that the sooner treatment is instituted, the more likely are the symptoms to disappear and the hearing to return to normal.

Treatment

Williams[2-4] mentions a plan of action that seems reasonable and merits consideration. Since one is dealing with a vasospasm, vasodilators should be used as a means of restoring the proper balance of fluids in the endolymphatic system. Also, to aid in this imbalance, diet and medications to promote salt elimination are prescribed. And since in dealing with autonomic imbalance there is overactivity of the cholinergic portion of the autonomic nervous system, medication should be given to discourage this hyperactivity. These, then, are the factors to govern the symptomatic treatment of Ménière's disease.

There are many drugs recommended in the treatment of both the acute attack and the milder manifestations of Ménière's disease. There are many methods of utilizing the same drugs. Satisfactory results have been reported by those who seem to be partial to one or more medications. Yet, similar results are recorded by others using different drugs. Some of the methods and medications recommended are mentioned here, and one must outline for himself which course and which drugs he wishes to use.

In the acute attack the patient may be given subcutaneously $^{1}/_{75}$ grain of atropine sulphate to depress the cholinergic action of the autonomic nervous system. Hyoscine has also been used effectively. Ephedrine, 5 to 10 minims given subcutaneously or slowly by intravenous injection, has been used to stimulate the adrenergic autonomic nerves. Dramamine by injection or by suppository has been found helpful in attenuating the acute attack. Phenergan and Benadryl have been used. These probably also act as sedatives. Nicotinic acid is an effective vasodilator, and when it is used in an acute attack in the form of Nicamin by subcutaneous or intravenous injection, it may help to relieve the acute attack. Twenty-five mg. are usually given once or twice a day, and the dose is increased gradually to 100 mg. Histamine is also a vasodilator and is used for its action on the blood vessels and not for purposes of desensitization.

The method of giving histamine advocated by Horton[6] is frequently effective. Histamine phosphate, 2.75 mg., is diluted in 250 cc. of isotonic sodium chloride or glucose solution and is administered by the drip method intravenously at a rate of from 16 to 60 drops a minute according to the tolerance of the patient. If a headache or stomach discomfort occurs the rate must be lowered. The procedure usually takes about an hour and a half. It is given daily until the symptoms subside. Intravenous procaine hydrochloride has also been used with occasional success.[7] A solution of 0.1 per cent in 500 cc. of 5 per cent glucose is given in one dose or divided doses.

When the acute symptoms subside, nicotinic acid, 50 to 100 mg., according to the amount needed to produce a flush, may be given three or four times daily. The patient is more likely to get the flushing if he takes nicotinic acid on an empty stomach. However, some patients cannot tolerate this and must take medication after meals. This drug is continued for an indefinite period of time, but the dosage may be reduced to once a day.

Derlacki[8] obtained good results from the use of histamine in the "optimum dosage technic" of Hansel.[9] He starts with 0.1 cc. histamine diphosphate in a dilution of 1:100,000,000 given subcutaneously. If no reaction is obtained, the following day 0.1 cc. of a 1:10,000,000 dilution is given. The dilution is increased every one to three days until the symptoms are relieved. Then the dosage of this dilution may be increased until the relief of symptoms lasts for from three to seven days. Sublingual histamine is also given.

Not everyone is in agreement concerning the use of the "optimum dosage technic." Walsh[10] advocates giving intradermal tests of the very dilute histamine; the dilution giving the least positive reaction is used subcutaneously, starting with 0.1 cc., and the dosage is increased gradually each three to four days until relief is obtained. This histamine treatment is usually continued for a long period of time in the hope of preventing other attacks.

There are other vasodilators that have been used more or less successfully: Roniacol tartrate, 50 mg., four times a day, and Arlidin, to mention two of them, are given by mouth.

Patients are placed on a salt-free diet as advocated by Furstenberg, Lashmet, and Lathrop,[11] to reduce the sodium content of the body. This encourages the elimination of body fluids, including the fluid of the labyrinth. Ammonium chloride, 15 to 30 mg. three times a day with meals, or potassium chloride is prescribed to eliminate additional fluid and sodium chloride. Acetazolamide (Diamox) has also been used as a diuretic,[12,13] and recently hydrochlorothiazide (HydroDiuril) has been used with success. The salt-free diet should be adhered to as long as possible, and the diuretic medication is gradually reduced as the symptoms subside.

Anticholinergic drugs, such as Banthīne, Pro-Banthīne, Bellergal, and Donnatal, have been given to depress the hyperactive parasympathetic nerve fibers. This supplements the effect of the vasodilators. Some of these contain sedative drugs which are most important in treating not only the anxiety caused by the illness itself but also the stress that may have produced the attack of Ménière's disease to begin with. In any case, a sedative such as phenobarbital or a similar drug should be prescribed. In this connection, everything should be done to relieve the stress or tension that is frequently the cause of the symptoms and that may create recurrences. At times, a personality trait is involved that cannot be easily overcome.

In attempting to prevent subsequent attacks some patients may be carried for a long while on medications such as nicotinic acid and an anticholinergic drug, with the occasional use of ammonium chloride, acetazolamide, or hydrochlorothiazide. If the individuals are tense and anxious they should be kept on a mild sedative. Perhaps a rapid vasodilator, such as nitroglycerin or amyl nitrite, could be carried by the patient and used when he feels the slightest tinnitus, stuffiness of an ear, or dizziness.

Conclusion

The nonsurgical treatment of Ménière's disease is a difficult problem since the causes are not always apparent and the mechanisms involved are only partially substantiated and are somewhat hypothetical. There is no one specific treatment that can be recommended. The treatment should include vasodilators, sodium restriction and elimination, anticholinergic drugs, and sedatives.

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Funerals are expensive

Nobody several years ago survived the series of illnesses that I have had. If someone tells me that the medicines I carry are expensive I must laugh, particularly when I read circulars advertising graves. I would rather pay for a medicine than a grave any day.—*George E. Sokolsky, columnist, King Features Syndicate*

Occult Hypoxemia Complicating Acute and Subacute Intracranial Lesions

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THIS STUDY is concerned with early respiratory insufficiency in acute and subacute intracranial lesions.

A prior knowledge of the association of cerebral and respiratory function is important in understanding their related clinical problems. The influence of respiration on brain function may be demonstrated impressively in the course of intracranial operations, as when carbon dioxide accumulation provokes cerebral edema. In somewhat similar manner, the effect of disordered respiration on brain function is also seen in the variety of pseudotumor cerebri (papilledema secondary to cerebral edema) associated with severe pulmonary insufficiency.[1,2] Conversely, it is well known that brain changes taking place in the course of fulminant intracranial lesions can adversely affect the patient's respiratory exchange.

The existence of a subclinical phase of respiratory insufficiency secondary to central nervous system disorder has been demonstrated by Plum and Wolff[3] in cases of poliomyelitis. Their work suggested that ventilatory failure preceded impaired gas exchange with an apparent sequence of initial hypoventilation, hypoxemia when the vital capacity fell to 1,000–1,200 cc., dyspnea, and cyanosis when the arterial oxygen saturation was 80 per cent or less.

Both cerebral and pulmonary dysfunction may interfere with essential oxygen utilization by the brain. It is known that carbohydrate is the essential foodstuff oxidized by the brain and that the cerebrum is extremely sensitive to oxygen and glucose deprivation.[4,5] Himwich, Bowman, and Fazekas[4] found narrowed cerebral arteriovenous differences in 4 cases of coma which were studied by sampling oxygen levels from femoral artery and internal jugular venous blood.

While such studies suggest that there is a diminished utilization of oxygen by the injured or diseased brain,[4,5] there is also ample evidence of clinical improvement following measures to increase available oxygen.[6-10] This would indicate that the cerebral pathologic process itself may induce respiratory decompensation which significantly decreases available oxygen for the brain's uptake and perpetuates an unfavorable cycle of cerebropulmonary insufficiency.

It has been our impression that cerebropulmonary insufficiency may occur before it is manifested by dyspnea or cyanosis. This phase of intracranial insult may exist without, or prior to, the onset of stupor which for the purpose of this study has been defined arbitrarily as depression of consciousness sufficient to interfere with the ability to take nourishment. The following studies were undertaken to test this hypothesis.

Materials and methods

Ten patients with acute and subacute intracranial disorders (injury, tumor, and cerebral vascular accident) uncomplicated by dyspnea, cyanosis, or other gross evidence of respiratory insufficiency were studied with regard to the oxygen content of their arterial blood (Table I). Other patients with suggestively significant blood-gas findings were not included because of the possible presence of complicating factors such as cardiopulmonary disease or azotemia. The patients studied were characterized by depression of consciousness varying from slight drowsiness, where the ability to take nourishment was not lost, to stupor, where all feeding was artificial.

Although an attempt was made to carry out such studies before definitive therapy such as oxygen administration was started, it was not possible to do this in all instances. Some studies were made without jeopardy to the patient by discontinuing oxygen for about an hour beforehand.

A correlation of arterial oxygen and carbon dioxide studies was carried out in 6 cases (Table II). In 3 cases serial arterial oxygen samplings were taken as the patient emerged from stupor to consciousness. Because of the particular significance of this group, short protocols of their clinical courses are given.

Oxygen and carbon dioxide studies were carried out by the Van Slyke methods. Carbon dioxide determinations were made in each case prior to the determination of oxygen content. Anaerobic conditions were maintained from the drawing of blood to the completion of the analyses to prevent any loss of oxygen or carbon dioxide. Whole blood was studied by collecting the specimen in a heparinized Luer-Lok syringe. A drop or two of mercury was added to facilitate thorough mixing of the specimen. The blood was then transferred directly to a Neill-Van Slyke pipet for carbon dioxide analysis.

Thus, determinations were made of the total carbon dioxide content of whole blood (recorded as volumes per cent) at the actual carbon dioxide tension existing in the arterial circulation. This method reflects more accurately the actual respiratory status of the patient than does the study of carbon dioxide concentration at 40 mm. Hg.

TEN PATIENTS *with acute and subacute intracranial disorders (injury, tumor, and cerebral vascular accident) uncomplicated by dyspnea, cyanosis, or other gross evidence of respiratory insufficiency were studied with regard to the oxygen content of their arterial blood. Anaerobic conditions were maintained throughout. Determinations were made of the carbon dioxide total content of whole blood at the actual carbon dioxide tension existing in the arterial circulation. Patients who, although drowsy, were able to take nourishment had oxygen levels on the borderline of normal or slightly reduced. The remaining patients, too stuporous to take nourishment, showed significant hypoxemia. Oxygen levels rose as the patients regained consciousness. Hypercarbia did not accompany hypoxemia in the cases studied. In such cases early significant hypoxemia may be undetectable by clinical examination alone, since it may not be accompanied by dyspnea, cyanosis, tachycardia, or pulmonary edema.*

TABLE I. Arterial oxygen studies (per cent of saturation) in patient with acute and subacute intracranial disorders not in evident respiratory distress

Patient	Diagnosis	Oxygen	Remarks
1	Ruptured aneurysm	93.0	Drowsy; able to take nourishment at time of study.
2	Thrombotic stroke	95.8	Drowsy; able to take nourishment at time of study.
3	Head injury	92.0	Slightly drowsy two months after injury; able to take nourishment.
4	Brain tumor	91.0	Tube fed four months postoperatively.
5	Thrombotic stroke	91.1	Lethargic; able to take small amount of nourishment; supplemental feeding.
6	Head injury	84.0	Stuporous
7	Brain tumor	86.3	Stuporous
8	Ruptured aneurysm	80.4	Stuporous
9	Head injury	80.4	Stuporous
10	Subarachnoid hemorrhage	87.1	Stuporous

TABLE II. Correlation of arterial oxygen and carbon dioxide levels

Patient	Oxygen Saturation (Per Cent)	Carbon Dioxide (Volumes Per Cent)
2	95.8	41.0
5	91.1	48.3
7	86.3	50.5
8	80.4	42.0
9	80.4	39.4
10	87.1	43.8

It may therefore be expected to give more precise evidence of the presence of acid-base derangements reflecting the ratio of bicarbonate ion to dissolved carbon dioxide.

Results

RELATION OF STATE OF CONSCIOUSNESS TO ARTERIAL OXYGEN CONTENT. Patients who, although drowsy, were able to take nourishment had oxygen levels on the borderline of normal or slightly reduced (Table I). The remaining patients, who were all too stuporous to take nourishment, showed significant hypoxemia. Oxygen levels rose as the patients regained consciousness. This is illustrated in the following 3 cases, 2 of whom received oxygen and 1 of whom did not.

Case 6. A fifty-three-year-old woman sustained an intracranial injury associated with a frontoparietal fracture. Although she remained stuporous and was tube fed for eleven days, oxygen administration was not deemed necessary because of the seeming lack of respiratory distress. Two days after her injury there was persisting stupor, and the oxygen saturation was 84 per cent. Nine days after her injury she was slightly rousable, and her oxygen saturation was 88 per cent. Twenty-six days after the injury the patient was alert, and the oxygen saturation was 99.4 per cent. It is quite apparent that the improvement in consciousness was paralleled by the increased oxygen saturation.

Case 8. A fifty-nine-year-old woman became hemiplegic due to a subarachnoid hemorrhage from a ruptured aneurysm. She was in stupor, and her oxygen saturation was 80.4 per cent. She received intranasal oxygen intermittently during the early phase of her illness. Four days later the patient was alert, and her oxygen saturation was 95.

Case 9. A seventy-eight-year-old man became stuporous as the result of an intracranial injury. The initial arterial study was made two days following the injury when the patient's stupor was observed to deepen. At that time his oxygen saturation was 80.4 per cent. A day later the patient was awake, and the oxygen saturation was 95 per cent.

These studies do not necessarily imply that oxygen administration contributed to the improvement of these patients, as evidenced by the case of patient 6 who did not receive any. It is possible that a lessening of hypoxemia ensued as a result of improvement in the cerebral status alone.

CORRELATION WITH ARTERIAL CARBON DIOXIDE STUDIES. Table II discloses that hypercarbia did not accompany hypoxemia in the group of cases studied, that is, in the nondyspneic range of oxygen unsaturation. This would be in keeping with the clinical observation that some cyanosis can generally be detected when hypercarbia develops.

Comment

Clinically significant hypoxemia, roughly paralleling the impairment of consciousness, was an early accompaniment of the cases of intracranial insult that formed the basis of this study. This occurred without associated clinical evidence of respiratory decompensation, such as dyspnea, cyanosis, or tachycardia.

The anaerobic conditions of whole blood analysis employed in these studies reflect the actual respiratory status of the patient. The absence of hypercarbia, which is a more specific pivotal factor in respiratory acidosis than pH, appears somewhat paradoxical. However, the existence of hypoxemia without hypercarbia under certain conditions, such as disturbance of ventilation-capillary perfusion ratios, suggests areas of further investigation.

The serious import of drowsiness in brain lesions is not only in the damage to centers concerned with consciousness, but also in the associated occult respiratory insufficiency. This associated insufficiency may possibly be one measure of the extent of intracranial insult. The assumption that oxygen lack may exist in such cases of drowsiness despite the absence of overt clinical evidence to suggest it appears justified. At times the existence of hypoxemia has come as a surprise in a patient who appeared, by gross assessment, to be breathing well.

An intracranial insult may still be reversible in the nondyspneic phase of hypoxemia. The presence of obvious respiratory distress indicates that the cerebropulmonary status may have progressed beyond the stage in which corrective measures can be effective. The development of various forms of respiratory obstruction associated with deepening stupor, such as backfalling of the tongue, accumulation of tracheobronchial secretions, and pulmonary edema[11,12] should be regarded as advanced mechanisms in the production of hypoxia,[8,10] signifying possible irreversible brain damage.

The correction of early pulmonary insufficiency in intracranial disorders calls for an assessment of the patient's respiratory status. It would appear, from our studies, that some form of assisted respiration is rational in such cases.

Summary

1. Anaerobic whole blood gas studies of patients suffering from acute and subacute intracranial disorders, characterized by drowsiness or stupor, without associated gross evidence of respiratory insufficiency, disclosed the presence of significant arterial hypoxemia.

2. Hypercarbia did not accompany hypoxemia in the group of cases studied. This seeming paradox and its implications for further study are considered.

3. It appears that early significant hypoxemia in such cases may be undetectable by clinical examination alone, since it may not be accompanied by dyspnea, cyanosis, tachycardia, or pulmonary edema.

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Responsibility of the drug industry

The activities of the universities and their research laboratories and those of the pharmaceutical industry are not competitive but complementary. There is an increasingly broad overlapping of interests. Both do and should have large and effective research programs. It is the prime function of the one to probe and to teach, and it is in our American system the function of the other to do research with the aim of finding and developing new health-giving aids which will come slowly or not at all if we place our dependence on the government, or for that matter on universities, either state or private.—*Lowell T. Coggeshall, M.D., Vice-President, University of Chicago*

A series of review articles
dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

A Review of Headache: 1955 to 1961

Part II

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Diagnosis

About 90 per cent of all headaches encountered in office practice are more or less benign, involving psychophysical factors rather than permanent structural change or serious illness.

For the purposes of this review the headache will be divided into the following diagnostic categories: vascular headache of the migraine type, muscle contraction headache, headache associated with intracranial disorders, headache associated with extracranial disorders, and headache in systemic diseases.

There are a number of general reviews of headache with discussions of frequency for various types of headaches and of the points to be noted in diagnosing the complaint. Reviews have been written by Ouer,[69] Morgan,[70] Graham,[71] Ogden,[72] Friedman,[73] and Nelk.[74] In addition to these, Rooke[75] presents a general review and discusses the differential diagnosis of basilar artery insufficiency and migraine. He stresses that intracranial pathologic conditions must be ruled out in all cases in which the aurae carry over into the headache itself. Blumenthal and Fuchs[76] stress the emotional factors involved in headache, and Friedman[77] points out that glaucoma may manifest itself as eyeball pain with radiation. Keith[78] and Litchfield[79] consider headache in children, and Litchfield notes that headache was an infrequent complaint in a group of 500 pediatric cases. He adds that when headache does occur in children, there is a greater percentage of demonstrable organic pathologic conditions than there is among adults with headache.

Mayer and Kaufmann,[36] and Hilsinger[80] review the various allergic factors in headache patients. Wittich[81] states that with a history of allergy in the family, the incidence of migraine is increased, and reports that eosinophilia occurs during migraine attacks in a higher percentage of patients. Swinney[82] describes 4 patients with headaches which seemed to be the direct result of contact with lanolin.

Vascular headaches of migraine type. There are numerous articles dealing with migraine. In reporting on the incidence of migraine, Magee,[83] in a study carried out at a university clinic, has noted that migraine frequently begins during college years, and feels that this is related to the psychologic stress of college life.

Several authors have advanced specific diagnostic tests for migraine patients. Dalsgaard-Nielsen[84] utilizes pharmacologic tests. Vasodilators, such as nicotinic acid, intravenous vaccine, histamine, or nitroglycerine are employed to induce headache, and the patient compares the induced headache with his usual one. Lund[85] describes specific wave changes in the temporal artery pulsations, which are typical of vascular headaches, and presents a scheme for mathematical analysis of the tracings. Weiglin[86] feels that a comparative determination of the ophthalmic and brachial blood pressures is the only objective method at present for diagnosing vasomotor headaches.

Alvarez,[87] in an article on scotoma in migraine, states that scotoma or a spell of poor vision lasting from twenty to twenty-five minutes is diagnostic of migraine. Lippman[88] reports that he has found three types of dreams in migraine patients and their descendants.

The heading "migraine" includes not only "classical" migraine. It is generally felt that histamine or cluster headache is a variant of migraine.[89,90] Horton[91,92] describes histamine headache as a distinct clinical entity, however, with symptoms differing from those of migraine, trigeminal neuralgia, atypical neuralgia, and other head and face pains. Complete reviews of the subject have been written by Friedman and Mikropoulos,[11] Symonds,[93] and Robinson.[94] The clinical picture appears to be characteristic; males predominate. The onset is usually in the third or fourth decade of life. The duration of a cluster varies but is frequently from several weeks to two months with variable headache-free periods intervening. The headaches always are unilateral, orbital, or frontotemporal in location and occur on the same side with rare prodromata. The predominant associated manifestations are nasal congestion, lacrimation, and ocular injection. The discomfort is severe and is frequently characterized by excruciating, stabbing, or throbbing pains.

To emphasize the protean character of histamine headaches, Quin and Sloan[95] present a case of histamine headache previously diagnosed as trigeminal neuralgia and later as a headache of pheochromocytoma. Unger,[90] apparently disputing the existence of histamine headache, states that he found only three histamine headaches in eighteen years, and the patients had migraine in conjunction with these headaches. He adds that the evidence that histamine causes these headaches is inconclusive.

There has been considerable interest in migraine variants, or equivalents. Blumenthal and Fuchs,[96] and Briggs and Bellomo[97] comment on the manifestations of migraine variants. These may occur as abdominal pain, presenting the symptoms of flatulence, indigestion, biliary disturbance, or even intestinal obstruction, with a history of repeated vague illnesses or family history of headache or biliousness;[96] or the patient may experience precordial pain, palpitations, and tachycardia.[97] Paroxysmal vertigo also may be a migraine equivalent.[97] The symptoms may occur with or without headache. Migraine variants have been reported to be quite common in children.[98–100] Farquhar[101] found that migraine symptoms in children develop chronologically in the order of vomiting, abdominal pain, and finally headache. In older children, all three symptoms are present more commonly. He warns that childhood migraine may present itself as an "acute abdomen." Alvarez[102] feels that migraine is a disease occurring during the third and fourth decades and may recur in middle and late life in very different forms.

Dalsgaard-Nielsen[103] presents a type of headache which he classifies as a group within the interparoxysmal morning headaches. This headache is of a migraine nature but lacks an aura. He calls it hypnocephalaca clinostatica.

In discussing another phase of the migraine complex, Ross[104] distinguishes between major and minor hemiplegic migraine, presenting 6 cases of the latter. In major hemiplegic migraine the aura is more prolonged and persists or increases after the onset of the headache; there is a striking family history of the same type of attacks. In minor hemiplegic migraine the aura sometimes may be followed by ordinary attacks of headache; the family history is not as striking. He concludes that these represent typical migraine attacks with simply an extension of the vasospasm into the rolandic area rather than into the cortex or the retina.

Verbrugghen[18] discusses the differential diagnosis of ophthalmoplegic migraine, nuclear ophthalmoplegia, and pontine tumor, considering particularly aneurysm and myasthenia gravis. The syndrome is described as unilateral headache, often accompanied by nausea and vomiting, with ipsilateral oculomotor palsy and clearly noticeable ptosis following the onset of the headache. The onset of external and internal ophthalmoplegia is rapid, and recovery is slow. The neurologic deficit, however, is not traceable to any lesion. Neurologists used to be extremely skeptical of such a diagnosis, but with the advent of angiography it has become clear that such a condition does indeed exist. According to Horton,[91] however, it is quite rare. He cites the case of an eight-year-old girl. Friedman, Harter, and Merritt[19] present a total of 8 cases out of 5,000 migraine patients with ophthalmoplegia. On a pre-existing headache complex, usually noted before puberty, the patient will develop oculomotor paralysis in conjunction with the headache. The paralysis is most intense as the headache subsides, and it takes days or weeks to subside. The oculomotor nerve, including the pupilloconstrictor fibers, are affected almost invariably. The evidence favors peripheral involvement of the oculomotor nerve as opposed to nuclear brain stem involvement.

Other neurologic signs resulting from migraine have been reported. Robinson[105] cites the case of a thirty-one-and-one-half-year-old man who had mild migraine preceded by mild right homonymous scintillating scotoma. On one occasion he experienced the usual aura, but it persisted with right homonymous hemianopsia with macular sparing. This cleared partially but remained as a dense, right superior quadrant paracentral scotoma, which still lasted after one and one-half years. Wagener[106] suggests that amaurosis fugax—recurrent episodes of usually unilateral blindness terminating as rapidly as they commenced—may be the result of migraine. In 24 out of 138 cases collected from the literature, the diagnosis of migraine was made. Of course, other causes for the blindness should be eliminated before this diagnosis is made.

Ford and Walsh[107] discuss Raeder's syndrome as he has found it in 25 cases. This syndrome consists of an initial unilateral supraorbital headache, followed shortly after onset by ipsilateral ptosis and miosis without loss of sweating on the face (as distinguished from Horner's syndrome). The authors feel that this is merely a series of severe and frequent migraine attacks, with damage done to the oculosympathetic nerve fibers by the repeated dilatation of the internal carotid artery.

The correlation of vascular headaches with abnormal electrical activity in the brain has received a great deal of attention. The studies of Gerson,[108] Selby and Lance,[109] and Camp and Wolff[110] indicate that there is a marked increase in the number of abnormal electroencephalograms in patients with vascular headaches; according to Gerson[108] most authors report from 60 to 75 per cent abnormal tracings in hereditary migraine and from 15 to 25 per cent abnormal tracings in nonhereditary migraine. McCullagh and Ingram[111] believe that in certain instances migraine headaches are related to a family history of cerebral dysrythmia. Camp and Wolff[110] have noticed that in patients with vascular headaches the electroencephalogram abnormalities fall into two broad categories. First there is the nonfocal abnormality of paroxysmal or diffusely occurring 4- to 7-cycles-per-second activity in excessive amounts. In the second category the electroencephalograms show focal abnormalities. The abnormalities are divided into three groups. In one type the electroencephalograms are altered very briefly during the vascular headache with fleeting focal motor or sensory defects. A second group develops abnormalities with the headache of the vascular type and associated with neurologic deficits. The abnormalities subside with the resolution of the clinical signs. The third group have persistent focal defects. They occur most frequently in patients with a neurologic deficit during the vascular headache.

Panzani, Boyer, and Turner[112] state that bilateral synchronous abnormalities are encountered in migrainous subjects but with a marked tendency to unilateral predominance, and Bärtschi-Rochaix[113] reports that the most frequent anomaly in migrainous patients is asymetrical distribution of the amplitude of the alpha wave. Golla and Winter[114] found that the electroencephalogram response curves of 113 headache patients with episodic headaches (whether or not the headache was present) to flickering light of varying frequency differed significantly from the response of a group of 50 controls. The headache patients showed a curve with a constant high response level maintained up to or above twenty flickers per second, while the control group showed a peak response at approximately ten flickers per second, declining rapidly as the stimulus frequency was increased above fourteen flickers per second.

Farquhar,[101] Burke and Peters,[98] Hagbey,[115] Suter *et al.*[99] and Froehlich *et al.*[116] found that there was a strikingly high incidence of abnormal electroencephalograms among children with some form of migraine.

Prichard[117] reported on 19 children with abdominal pain for which no local cause could be found and which was not consistent with the aura of a general seizure. Thirteen of 17 children had normal or only mildly dysrhythmic electroencephalograms; these patients had a family history of migraine. These 17 patients were considered to have abdominal migraine, while the 2 with abnormal electroencephalograms (discharges in the temporal region) and more severe pain did not have a family history of migraine. They were considered to have abdominal epilepsy. The abdominal pain mentioned previously, for example, is generally described as a migraine variant rather than as abdominal epilepsy, partially because of the migranoid character of the syndrome, but partially for euphemistic reasons,[101,115] and yet anticonvulsant drugs were found to be more successful than ergot preparations.[98, 115, 117]

The studies of Snyder,[118] Halpern and Bental,[119] and Karlsson[120] of children, indicate that epilepsy may manifest itself as headache. The headache may or may not resemble migraine. Patients with this syndrome exhibit abnormal electroencephalograms with paroxysmal bursts, often as photic stimulation, and respond well to anticonvulsant medication.[119]

Snyder[118] cites the cases of 2 children with headache and vertigo which were "epileptic equivalents" in whom cerebellar tumors were suspected, but who became completely asymptomatic on anticonvulsants. Ziegler and Torres[121] report the case of a six-and-one-half-year-old boy with left orbital pain occurring on photic stimulation on two occasions (after he watched a movie) and a focal abnormality in the right posterior temporal lateral occipital area. There were no seizures of any type, and it was felt that the severe headaches were focal "epileptic equivalent" phenomena.

A study by Nymgaard,[122] however, failed to reveal any characteristics of epileptic headaches, and he concluded that there is no such entity. Further, Bärtschi-Rochaix[113] concludes that there is no electrobiologic relation between migraine and epilepsy, since in migraine, activation with lights and so forth does not produce an epilepsy pattern on an electroencephalogram tracing, and Alvarez[123,124] states that epilepsy and migraine are the results of separately inherited traits.

Migraine may be of importance in conjunction with other diseases. For example, it is pointed out that migraine may cause a decrease in the gastric emptying time, and Carstairs[125] urges that this fact be taken into account when reviewing radiologic findings and considering gastric surgery. Again, it was found that there was a marked increase in the incidence of toxemia, eclampsia, and convulsions with toxemia in women with migraine. Rotton, Sachtleben, and Friedman[126] further mention that although most migraine patients experienced a remission of symptoms during pregnancy, many of those who did not subsequently became toxemic.

Ask-Upmark[127] points out that migraine is a danger to life by natural as well as by iatrogenic means. An aneurysm may be the cause of migraine, supraventricular tachycardia may be considered an equivalent, and they have possibly fatal consequences. Ergotamine injections have potentially dangerous side-effects, and chronic phenacetin ingestion may result in an interstitial nephritis.

HEADACHE ASSOCIATED WITH INTRACRANIAL DISEASE. Much of the literature deals with intracranial vascular pathology. Chambers[128] presents a review of intracranial aneurysm as the cause of headaches. He emphasizes that the most important factor to note is a change in position, frequency, or character of chronic headache. Cranial nerve signs may be late, and they occur only shortly before rupture. Several case histories of patients with headache arising from intracranial aneurysms are reported.[129–131] Froehlich[129] noted that the headaches were generally migraine-like and appeared abruptly or had changed in some manner from the headaches from which the patient had suffered before. Neurologic signs, particularly ophthalmoplegia, usually were present, but Froehlich reports a case presenting signs of arteriolar spasm in the ophthalmic artery distribution ipsilateral to the pain and papilledema without extraocular palsy.

Smiley[132] cites 2 patients with severe throbbing nuchaloccipital headaches caused by a tortuous basilar artery.

Murphy[133] reports a case of a migrainous patient who suddenly developed headache, loss of vision in the left eye, right hemiplegia, complete amblyopia on the left, and almost global aphasia, apparently as the result of a cerebral infarction after persistent intracranial arteriospasm. Lincoff and Cogan,[134] however, point out that although the syndrome of unilateral frontal headache and oculomotor paralysis is associated most often with intracranial saccular aneurysm, especially when it is of abrupt onset, the syndrome may occur with other types of lesions. He reports 3 such cases as caused by diabetes, 3 by paraclinoid tumor, 1 by leukemia, and 2 by ophthalmoplegic migraine.

In discussing headache caused by intracranial vascular lesions, it is important to note that according to Proudfit,[135] the first clinical sign of thrombosis of the internal carotid artery may be headache. Proudfit has found that of 56 patients with this condition, 28 experienced headache, and headache was the single initial symptom in 11 patients. The head pain almost always was unilateral and always occurred on the side of the arterial involvement. It was not present in the patients who had slowly progressive symptoms but was common in those with episodic symptoms. There was an unexplained association of increased spinal fluid protein with headache.

Headache, of course, also can be the result of a mass lesion. Guest and Jones,[136] however, recommend greater reliance on clinical findings, spinal fluid pressures, and the position of the pineal body shown on skull x-ray films and less use of pneumoencephalography in patients with complaints of headache and/or epilepsy in ruling out mass lesions. In a group of 114 patients with these complaints but with otherwise normal clinical and laboratory findings, only 1 patient was shown to have a mass lesion by pneumoencephalography. But the incidence of brain tumor as shown by pneumoencephalography rose to 26 per cent in patients with abnormal clinical and/or laboratory findings.

HEADACHE ASSOCIATED WITH EXTRACRANIAL DISEASE. There have been numerous contributions about various head and neck structures and their respective headache. Great care must be taken before an oral, posterior neck, or paranasal sinus structure is implicated in headache. Frequently the diagnosis rests on a particular treatment which will give temporary relief, possibly with a placebo effect, and this case is cited as a cure. However, long-term follow-up will reveal a return of the symptoms. Numerous articles appeared which discuss dental and oral causes of headache.[137–141] Bruxism (gnashing, grinding, or clenching of the teeth) is associated with chronic headache. Freese[142] and Monica[143] noted that mandibular muscle spasm may cause pain anywhere in the head or neck and is usually of emotional origin, although organic disease may result in muscle spasm. Trigger areas in muscle and fascia produce a dull aching pain, hyperalgesia, and muscle spasm in the zone of reference. Freese[144] found that ethyl chloride spray to the trigger area may clear up the pain in the zone of reference.

A number of articles have been written on the subject of posterior neck structures as the cause of unilateral or bilateral headaches.[145–150] Travell[151] assigns to the sternomastoid muscle a role in paroxysmal dizziness imbalance, and headache. The diagnosis is established by finding an active trigger mechanism on the sternomastoid muscle on physical examination. The disappearance of the symptom-complex occurs after the trigger area has been blocked.

The ear, nose, and throat structures may result in chronic headache.[152–155] Sellers[153] describes Sluder's headaches. The pain is usually below the hatband line. There may be lacrimation, tightness of the throat, and even dysphagia. There is almost always tenderness at Sluder's point on the mastoid posterior to the external auditory meatus. The diagnosis rests on relief with anesthesia.

The headache which occurs following a whiplash injury to the neck may be caused by concussion; trauma to the second cervical nerve root, spinal accessory nerve, or branches of the occipital or trigeminal nerves; or to a traumatic arteritis.[156]

Vail,[157] in writing about glaucoma headache, states that it must be considered when headache occurs in and around the eyes; it is of sudden onset and is sharp, boring, and prolonged. It must be distinguished from acute iritis, acute conjunctivitis, and histaminic cephalgia.

Friedman, Carton, and Hirano[158] present a discussion of atypical face pain, citing conditions which may be responsible for the pain. They review the data from 294 patients with facial cephalgia and classify them into typical, or primarily neurogenic, neuralgias and atypical, or primarily vascular and psychogenic, neuralgias. Klingman[159] considers a number of etiologies in atypical facial neuralgia, and some are similar to tic douloureux. These include tumor of the fifth nerve, the gasserian ganglion, or tumor in adjacent areas in the middle and posterior fossae, lesions in the cerebellopontile angle, as well as aneurysm of the internal carotid artery or vascular anomaly along the root of the fifth nerve. Intramedullary lesions from the upper cervical cord to the pons may give rise to pain of trigeminal distribution.

Keats[160] described 3 cases of pressure injury to the nerves supplying the scalp with head pain. The injury was caused by a tight face mask harness employed during general anesthesia. It was felt that the greater occipital nerve was damaged by being pressed by the harness against the skull along the posterior occiput.

A very important disease to recognize at the onset is temporal arteritis. Temporal arteritis may cause generalized or localized headaches over the temporal artery. It most frequently occurs after the fifth decade, and the temporal artery may be tender, swollen, and pulseless. Berger and Senders[161] comment on the headaches as severe and throbbing; they are apt to be worse at night and may resist treatment with analgesics. An early diagnosis is important because of the threat of blindness if it is not treated promptly with corticosteroids.[162] It need not be associated with systemic symptoms as reported by Freedland.[163]

MUSCLE CONTRACTION HEADACHES (TENSION HEADACHES). A very common presenting complaint will be ache or sensations of tightness, pressure, or constriction, widely varied in intensity, frequency, and duration, sometimes long-lasting, commonly occipital or suboccipital, and associated with a sustained contraction of skeletal muscles in the absence of permanent structural change. In the past, headaches of this type were referred to as tension headaches; a more recent classification refers to such headaches as muscle contraction headaches.[164] Muscle contraction headaches have been discussed in many reviews of headaches referred to at the beginning of the section on diagnosis.

A careful diagnosis is essential in diagnosing occipital headaches. A recent review by Drake[165] points out that the patient is usually healthy and may also present complaints of nausea, vomiting, dizziness, weakness, irritability, and constipation. Drake also points out that the frequency is variable, and the headache may last for weeks. The muscle contraction headache must be distinguished from conversion headache, migraine, and other vascular headaches. Migraine and muscle contraction headaches were found not to differ in regard to sex, precipitating causes, occurrence, mood change, onset, and termination.

Chambers[166] presents 6 cases which presented symptoms of posterior headaches but were due to serious organic disease. In addition, the presence of less ominous disease should be evaluated before muscle contraction headaches, on a psychic basis, are diagnosed. The muscle contraction headache must be distinguished from migraine and related vascular headaches, conversion reaction, and headaches associated with intracranial lesions, cervical disk disease, cervical osteoarthritis, or spinal-cord tumor.

HEADACHE IN SYSTEMIC DISEASE. Headache may be due to an underlying systemic disease. There have been three reports of headache associated with ocular nerve palsy and other cranial nerve deficits, particularly in diabetic patients.[167–169] In general, a neuritic pathologic condition seems to be the cause of this syndrome more frequently than a vascular pathologic condition in both diabetic and nondiabetic patients. Harris-Jones[168] presents a general discussion of the syndrome, and Waird[169] and Jackson[167] cite case histories. All three have found that recovery occurred independent of treatment.

Atkins[170] suggests that meningitis with Weil's disease may be a cause of migraine.

Walker[171] discusses the relationship between hypertension and migraine. He found the incidence of migraine to be much higher among patients with diastolic blood pressures greater than 100 mm. Hg than it was among those comprising his general case load. Further, the blood pressure was significantly higher in 150 patients than in 150 controls. A correlation between an increased incidence of migraine and an increased blood pressure was present, although not statistically significant, in patients between the ages of forty and fifty and was highly significant in patients over fifty. Walker then considers some of the factors which may be involved in the association of migraine and hypertension; Heathfield[172] suggests that preexisting migraine may be reactivated later in life by hypertension. Walker considers the common occurrence of a family history in both the similarity of personality structures in the two disorders with frequent evidence of suppressed emotional conflicts, and the fact that dilatation and distention of the cranial arteries are involved in producing the headache associated with hypertension and in the migraine headache. However, he mentions that migrainous patients are more likely to have their blood pressures taken than are patients in the general population, and asymptomatic hypertension is likely to be diagnosed in those patients with migraine.

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Clinicopathologic Conference

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Conducted by RULON W. RAWSON, M.D.

Discussed by DONALD B. LOURIA, M.D.

Complications of Chronic Myelogenous Leukemia

Case history

Hugh Sangree, M.D.: A fifty-eight-year-old, single, Greek-born furrier entered the hospital because of fever and epigastric burning of several days duration.

Ten months before he entered the hospital, weight loss without anorexia occurred. He lost 18 pounds and sought medical care when weakness and fatigue led him to stop working. Six months prior to his entry into the hospital his physician found an elevated white blood cell count and hepatosplenomegaly and referred the patient to the Memorial Center Outpatient Clinic.

A review of the past history revealed that gonorrhea at the age of thirty years had been treated with irrigations and that the patient had had a hemorrhoidectomy in 1957 and a tonsillectomy in 1946. For many years he had noted epigastric fullness and discomfort, which appeared after meals, especially with the intake of spicy or fatty foods, and which was partially relieved by bicarbonate of soda. An examination revealed some small, soft, axillary nodes and a palpable liver and spleen which measured, respectively, 5 and 13 cm. below the costal margins. The hemoglobin was 9 Gm. per 100 ml., white blood cell count 360,000, platelets 496,000, and reticulocytes 1.9 per cent. The white blood cell differential contained 3 myeloblasts and many early myeloid forms. A bone marrow aspiration was interpreted as consistent with chronic myelogenous leukemia. The patient was started on chlorambucil, 8 mg. daily. Five months before his entry into the hospital an episode of pain in the left upper quadrant of the abdomen and the left shoulder was accompanied by a friction rub over the spleen. Radiation therapy, 300 r was administered to the splenic area with a gradual diminution of pain. Chlorambucil was discontinued for six weeks while the patient remained asymptomatic with a white blood cell count ranging between 50,000 and 100,000. Three months before his hospital admission he noted weakness and postprandial heartburn. The white blood cell count was 133,000, and chlorambucil was again administered at 14 mg. daily. Two months before his hospital admission a fever of 101 F. with negative pharyngeal and blood cultures responded to tetracycline therapy.

One month before the patient's entry into the hospital a nonproductive cough developed which was unresponsive to sulfonamide therapy. This was associated with anorexia, general weakness, nausea, and burning in the mouth and epigastric area. The platelet count had risen to over 2 million, and the white blood cell count was 62,000. His weight and the hepatosplenomegaly were practically unchanged from the first clinic visit. The dose of chlorambucil was increased to 36 mg. daily. The epigastric distress was partially relieved by antacids. His symptoms persisted along with sore throat, headache, and increasing fever, so that the patient was admitted to the hospital.

A physical examination revealed a well-developed, well-nourished male in no acute distress. The temperature was 104 F., pulse 100, respirations 24, and blood pressure 120/80. The skin was hot and dry. A slight abdominal protuberance, hepatosplenomegaly, and a moderately enlarged prostate were the only abnormalities. The hemoglobin was 10.1 Gm. per 100 ml., white blood cell count 42,000, platelet count 1,082,000, and reticulocytes 1 per cent. The differential count showed 96 adult polymorphonuclear leukocytes, 3 stabs, and 1 lymphocyte. The urine had a specific gravity of 1.010, with 1 plus albumin and no glucose. There were 1 or 2 red blood cells and 2 or 3 white blood cells per high power field. The serum calcium was 8.9 mg. per 100 ml., carbon dioxide 23 mEq., chlorides 102 mEq., potassium 5.4 mEq., and sodium 139 mEq. per liter. The total protein was 5.9 Gm. per 100 ml., with 4.8 Gm. albumin and 1.1 Gm. globulin. The blood sugar was 110 mg. per 100 ml., and creatinine was 2.3 mg. per 100 ml. The prothrombin time was 20 seconds. A chest film and an electrocardiogram were reported as showing normal findings.

On admission blood was taken for culture, and the patient was started on Chloromycetin. A high fever with epigastric and periumbilical pain persisted. On the following day a repeat chest film showed a patchy infiltrate in the mid-field of the right lung. On the third day the blood pressure was noted to be 84/60. An examination revealed diffuse abdominal distention, guarding, direct and rebound tenderness, and active bowel sounds. The hemoglobin was 9.7 Gm. per 100 ml. A gastric aspirate was positive for occult blood, while a stool specimen was negative. The serum amylase was 29 units. Dextran and whole blood were administered, and vasopressors were required to maintain normotensive levels. On the fourth day after admission scattered lung rales were heard, and a chest x-ray film (Fig. 1) showed extensive streaky and patchy infiltrates of a hazy and flocculent nature throughout both lung fields. Penicillin, hydrocortisone, and gamma globulin were added to the regimen.

During the remainder of the course the patient was febrile to a level of 101 or 102 F. despite antipyretics and the addition of novobiocin sodium and polymyxin. The pulse was frequently in the range of 90 to 100 except for one episode of rapid atrial fibrillation. His cough remained minimal and nonproductive. Repeat chest x-ray films (Fig. 2) showed some clearing of infiltrates. However, dyspnea, hyperventilation, marked weakness, and mental confusion were prominent. The results of a lumbar puncture were unremarkable. The blood urea nitrogen gradually rose to 66.5 mg. per 100 ml. despite good urinary output. Ten blood cultures, a throat culture, and febrile agglutinins were negative. A complement

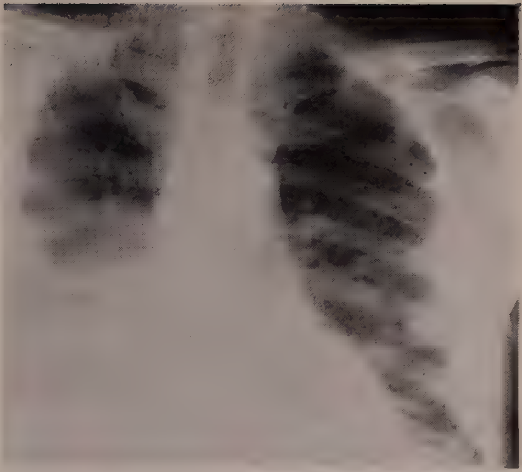

FIGURE 1. Roentgenogram of chest on fourth hospital day shows diffuse infiltration of lower and middle fields of right lung. There is also some haziness in the lower field of the left lung.

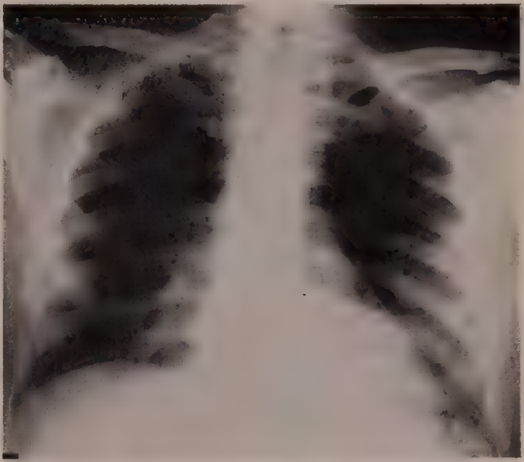

FIGURE 2. Roentgenogram of chest on sixth hospital day shows considerable clearing, although there is persistent infiltration in both hilar areas.

fixation test for herpes simplex showed positive results in a 1:8 dilution on two occasions. Complement fixation tests for Q fever and psittacosis showed negative findings in a 1:4 dilution. Streptococcus MG titers showed negative results in all dilutions.

On the ninth day of hospitalization the patient passed two tarry stools. Shock persisted despite vasopressors and transfusions. Bloody material was noted in the gastric aspirate, the urinary output ceased, and the hemoglobin fell to 8.3 Gm. per 100 ml. The white blood cell count was 60,500, the platelet count 256,000, blood urea nitrogen 95 mg. per 100 ml., and uric acid 13.4 mg. per 100 ml. The patient expired shortly thereafter.

Discussion

Donald B. Louria, M.D.:* Before I begin, there are two items I would like further information about. First, were any lesions of the mouth and skin noted at any time during the last five months?

Dr. Sangree: No oral or cutaneous lesions were seen. About a month or two before his hospital admission when he was given tetracycline, it was thought that he might have a mild pharyngitis.

Dr. Louria: Had he had any animal contacts?

Dr. Sangree: He had been a furrier but had stopped work six months before his admission to the hospital.

Dr. Louria: May we see the x-ray films?

Joseph Fraumeni, M.D.: The chest x-ray film taken on the day of admission showed essentially normal findings. The next film, taken on the third hospital day, shows a definite but hazy infiltrate in the middle and lower lobes of the right lung as well as in the left perihilar area. A film taken the following day shows diffuse infiltration in both lung fields (Fig. 1). The infiltration is not very specific, but it is diffuse and severe. A film taken two days later shows considerable clearing (Fig. 2), although there is persistent infiltration in both hilar areas.

Dr. Louria: We must start out with the assumption that the diagnosis of chronic myelogenous leukemia will stand up. The protocol seems to document it adequately, and I can think of little else that would give the same picture. The question which remains to be solved is what complications arose that produced a rather rapidly fatal illness in a patient who was responding nicely to chemotherapy.

First, I should like to consider what might have been going on in his abdomen to give him epigastric distress progressing to heartburn and finally presenting symptoms of diffuse abdominal pain accompanied by distention and bleeding from the gastrointestinal tract. He might have had an esophagitis with or without a defect at the hiatus, but this would not explain the acute picture seen preterminally. He might have had cholecystitis, but this would not explain the blood in his stomach. Pancreatitis can be associated with gastrointestinal bleeding, often from farther down in the bowel than one might expect. Possibly this is due to the action of proteolytic enzymes being disseminated in the blood stream. However, the normal serum amylase level is somewhat against a diagnosis of pancreatitis. He was a Greek furrier, and the possibility of some form of intra-abdominal echinococcosis must be considered. This has been reported with involvement of the stomach as well as other major viscera. However, there is no real evidence for echinococcal disease, and so I shall discard the possibility.

The most likely cause of his gastrointestinal symptoms is an ulcerative lesion in the stomach or duodenum. Certainly the relief obtained from antacids is consistent with that idea, and the fact that he was on steroid therapy fortifies me in that belief. However, on the evidence at hand I cannot really decide whether such an ulcer was a banal peptic ulcer or the result of a nodular leukemic infiltration of the gastric or duodenal wall. There seems to be little room to doubt that the ulcer was bleeding actively, but it is difficult to decide whether or not it had perforated as well. I suspect it had.

However, in addition to the ulcer which I have placed in his upper gastrointestinal tract, he also had an infectious process, certainly involving the lungs and possibly involving the central nervous system. The cerebrospinal fluid was normal, but this does not completely rule out multiple brain abscesses. About one third of the patients with brain abscesses have normal spinal fluid findings, and the changes in the other two-thirds can be quite variable. However, he had no meningeal signs or real localizing signs of central nervous system disease, and I suspect he did not have bacterial or fungal brain abscesses. I do think that the same infection that might have been in his brain was quite clearly present in his lungs. Looking at the chest x-ray films, I thought transiently of a process characterized by multiple small platelet thrombi or else a diffuse leukemic infiltration of the lungs. However, the rather rapid clearing of the pulmonary infiltrates is inconsistent with such hypotheses, and I must stick to the idea that it is an infectious process.

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Terminal infection is a very common cause of death in patients with leukemia or malignant lymphoma these days, even as it was twenty years ago. However, nowadays we see some of the more uncommon infectious agents; at least we are able to identify them with greater frequency. Whether this is because we can control the more common pathogens or because our microbiology is more sophisticated has been questioned, but I think there is good evidence that the increase in unusual infections is real. Nonetheless, I must consider the more common bacterial pathogens first. Could this patient have had a staphylococcal pneumonia? I doubt it. The classical picture of staphylococcal pneumonia is not present either clinically or radiologically. There is nothing to suggest an abrupt onset of chills and fever, no evidence of lobar consolidation, no x-ray evidence of multiple pulmonary abscesses. Of course, the classical picture need not be present. We are all familiar with the patient whose leukemia is reasonably well controlled but who is admitted with low-grade fever, slight pulmonary infiltration, an unimpressive cough producing little sputum, and in whom we fail to demonstrate anything impressive in his bacterial flora. At postmortem many of these patients show an extensive pneumonic process, more extensive than one might suspect from the chest x-ray films, and staphylococci are found, at times admixed with other pathogens, in the postmortem bacteriologic studies. This patient might very well have had this sort of confluent bronchopneumonia. I cannot exclude it, but there are more attractive possibilities.

Could it be Bacteroides? Again, there is no real evidence. Without peripheral evidence of a bacteroidal infection in his abdomen or a lesion that is likely to seed the blood stream from the urinary tract or the rectum, I think Bacteroides is an unlikely possibility.

Could this be a terminal tuberculous pneumonia? I think it unlikely. There is no evidence for an old, partially arrested focus, and the lesion certainly cleared rapidly on nonantituberculous therapy. Parenthetically, the idea that in diabetic patients tuberculosis is a process of the lower lobe of the lung is a canard. Most of these patients start off with a disease in the upper lobes of the lungs.

Another possibility, a more likely one, is that the etiologic agent is a fungus. If so, there are two possibilities that appeal to me: nocardiosis and disseminated visceral cryptococcosis. I cannot muster enough evidence for cryptococcosis; the fever was too high, the clinical course was very rapid, and the spinal fluid showed negative findings. Nocardiosis is a more likely choice. Studies from this hospital[1] have shown the relatively frequent association of nocardial infection and malignant disease, particularly in patients who have received steroids. On looking over the figures from this institution and adding them to other data in the literature, it becomes evident that about 20 per cent of the nocardiosis reported since 1950 has been in patients receiving adrenal hormones. That is a startlingly high figure when one realizes that the only two mycoses which occur more frequently in steroid-treated patients are candidiasis and aspergillosis. However, it also should be noted that whereas severe moniliasis and aspergillosis have increased markedly in frequency during the antibiotic-steroid era, the over-all number of cases of nocardiosis has not risen strikingly.

What is against the possibility of nocardiosis? Well, the rapid clearing is a little bit against it; the rapid progression is slightly against it; but the fact that he had his terminal infection prior to the administration of adrenal steroids is considerably against it, and I shall have to consider other possibilities.

Let us consider possible rickettsial infections. Could he have Q fever? The chest films are against it. Q fever does not usually produce a disseminated pulmonary infiltrate; it is more usually localized, and 20 to 40 per cent of the cases have no infiltrate at all. However, Q fever can be subacute or even chronic in its course; also, it can mimic other diseases, even lymphoma. Nonetheless, the patient did not really have a good chance of exposure to Q fever, and it is really a very uncommon disease in this part of the country. On that basis alone I would think Q fever unlikely. In addition, I would expect that Q fever would respond to at least one of the antimicrobial drugs that this patient was receiving. I cannot really bring myself to believe that he had Q fever, and certainly there is no evidence for any other of the rickettsial diseases.

This brings me down to the last possibility, probably the most likely one, namely, that he had a virus infection in his lungs. I will eliminate the adenoviruses and the influenza viruses as a group; there are more likely possibilities. I will consider the viruses of primary atypical pneumonia, varicella, herpes, and cytomegalic inclusion disease.

Primary atypical pneumonia when it involves all five lobes is a fearful disease with a mortality that is at least 50 per cent. Against this diagnosis is the x-ray picture. It looks to me as if too much of the infiltrate is interstitial for this to be one of the fatal cases of primary atypical pneumonia. Furthermore, apparently relatively little was found on the physical examination which would be unusual in overwhelming primary atypical pneumonia. The absence of streptococcal MG agglutinins is of no specific help; they are present in 30 to 40 per cent of the cases at most. Also, the extremely rapid downhill course is unusual in primary atypical pneumonia. I should state that the most recent studies suggest that primary atypical pneumonia is not due to a virus but to a pleuropneumonia-like form of a bacterium. One would have expected some response to broad-spectrum antimicrobials.

Could this be an example of varicella pneumonia? The varicella virus produces a diffuse pneumonitis, but the rapid clearing of the chest film is against it. The recovery rate in this pneumonia is in the range of 80 to 90 per cent, or so it seems now that a good many cases have been collected. However, the patients usually have had contact with obvious varicella or herpes zoster and have shown skin lesions preceding the lung involvement by three or four days.

The last possibility which I must eliminate before trying to nail this down as a case of cytomegalic inclusion disease is herpes simplex. The major pieces of evidence in favor of herpes simplex are the two complement fixation tests that showed positive results for the organism at 1:8. It is very hard for me to believe that this was done at the bedside or during the patient's life. I am sure that there must have been some rationale for the investigation of such an unlikely chance. Not being well informed about disseminated herpetic infections, I did a little library work this morning. Apparently there are two types of herpes virus. One is a simian virus which has been associated with encephalitis in patients whose clinical course may start with obscure abdominal pain and who could have viremia. This disease appears only in people who have had contact with monkeys and is primarily the result of monkey bites. I assume that even though this patient was a furrier it is unlikely that he was a monkey furrier; even if he were, he probably would not have been exposed during the last six months. The other form of the virus is the well-known herpes simplex of man. Disseminated herpes simplex occurs mostly in young children and virtually always in association with demonstrable mucocutaneous lesions. Therefore, in this patient it is not likely. However, we have not yet explained the pharyngitis and the burning sensation in his mouth. Is it possible that he had a herpes infection that was either missed or not remarked on? As for the agglutination titers, I am not exactly sure how they can help me. In theory the agglutination titer rises after an infection and then stabilizes, but most adults do not have positive titers. Thus, while a 1:8 titer on two occasions could indicate an active infection, it could equally well represent an infection present for anywhere from two to six months previously with a subsequent maintenance of titer.

I think that cytomegalic inclusion disease fits the known facts more closely. The virus is closely related to the salivary gland virus of rodents. Most commonly, to be sure, it is a disease of infants and children characterized by blood dyscrasias, interstitial pneumonitis, and often accompanied by jaundice and encephalitis. It is rare in the adult, but when it does occur in adults, it is almost invariably a complication of an underlying malignant condition. There are some observers who feel that antimetabolites and steroids increase susceptibility to the disease. In the adult cytomegalic inclusion disease causes a diffuse pneumonitis which may start anywhere in the lungs but which is usually bilateral. The pneumonitis is generally severe, is accompanied by pronounced dyspnea, runs a rapidly progressive course, and death ensues after a very short interval. Evidence of the disease may be present in extrapulmonary sites, notably the liver, spleen, and adrenal glands. I am strongly in favor of the diagnosis of cytomegalic inclusion disease because this patient did have an underlying malignant process and because the disease progressed so rapidly with such paucity of overt symptomatology.

One could argue reasonably that the portal of entry of the cytomegalic virus was the gastrointestinal tract, possibly in an area where a leukemic infiltrate had replaced the normal gastric or duodenal mucosa. If so, the bleeding from the gastrointestinal tract could be ascribed to the interaction of both the underlying malignant condition and the complicating fatal viral infection acting in concert. However, I think it was most probably the pneumonitis that actually proved fatal, and the predominantly interstitial infiltrate which seemed to spread so rapidly from place to place within the lungs, leaving little trace of where it had just been, is rather typical of the pneumonitis of cytomegalic inclusion disease.

I shall make my final clinical diagnosis one of chronic myelogenous leukemia complicated by cytomegalic inclusion disease. I would expect the evidence of viral infection to be very extensive, involving multiple organs. If it isn't cytomegalic inclusion disease, the next best possibility is the herpes virus. I can see no real evidence for bacterial or fungal infection.

BURTON LEE, M.D.: In cytomegalic inclusion disease does the patient have to have had direct contact with rodents?

DR. LOURIA: I don't think so. After all, the disease occurs frequently in newborn infants. In adults it is often associated with a pneumocystis carinii infection, but I don't know what the interrelationship between the two organisms is. I don't know the mode of transmission of cytomegalic inclusion virus.

FRANK L. HORSFALL, JR., M.D.: I don't think anyone knows.

LOTON RASMUSSEN, M.D.: Have you considered the possibility of a poisoning? The principal organs involved seem to be the lungs, liver, and kidneys. There is only one liver function test in the protocol.

DR. LOURIA: I suppose I should have considered an exogenous toxin, possibly an ingested substance, more closely than I did.

DR. LEE: Wouldn't one see the cytomegalic inclusions in the sputum on smear?

DR. LOURIA: One can readily see the inclusion bodies in the sputum of patients with varicella, but I have had no first-hand experience with sputum from patients with cytomegalic inclusion disease.

DR. HORSFALL: You would find cells with intracytoplasmic inclusions in the sputum if there were pulmonary involvement and if you looked for them.

DR. LEE: Do you have to use special methods to demonstrate them?

DR. HORSFALL: No. Any routine stain will show them. The reason they are not seen more often is that we don't think of the virus and don't look. Making smears of sputum has gone out of fashion these days, but one still can make many important diagnoses by this simple method.

HIRSCH KIRSCH, M.D.: Couldn't the abdominal picture be explained on the basis of actinomycosis?

DR. LOURIA: Actinomycosis is the anaerobic relative of Nocardia. Actinomycosis in the lungs rarely produces this sort of disseminated disease. It is a burrowing, undermining type of organism, and I would expect more evidence of consolidation, abscesses, or draining sinuses. Also, I don't know of any evidence that infection with actinomycosis has increased in patients receiving steroids; steroids may provide the setting for infection with Nocardia species, and when severe, a miliary sort of infiltrate may be found. Ergo, if I am wrong about this being a viral infection, nocardiosis is the mycosis that I would consider most seriously.

DR. KIRSCH: It isn't clear to me whether or not you thought he had leukemic infiltrations of the gastrointestinal tract.

DR. LOURIA: I hedged. I think he had an ulcerative process in the gastrointestinal tract that was bleeding and may have perforated. This ulceration may be related to a pre-existing ulcer, it may be the effect of steroids, or it may be leukemic infiltration. I just don't know how to decide that on the evidence at hand.

MAURICE SHILS, M.D.: How often does one see fever and some of this patient's symptoms in patients under prolonged chlorambucil therapy?

RULON W. RAWSON, M.D.: I think it unlikely that chlorambucil would produce this picture. There have been some eczematoid reactions with chlorambucil, and it is conceivable that one could have an allergic reaction, but it isn't likely.

DR. LOURIA: But the mouth burning could be explained by chlorambucil?

DR. RAWSON: Possibly.

JOHN LADUE, M.D.: How do you explain the presence of active bowel sounds with a perforated viscus?

DR. LOURIA: I must concede that the presence of bowel sounds is against the finding of frank perforation of the gastrointestinal tract. However, one does see this phenomenon in patients with ulcerative colitis who undergo perforation; I have heard active bowel sounds in such patients right up to the time of an operation for perforation. I don't know what else could have given this patient an acute condition within the abdomen unless there was some sort of perforation or leakage.

WILLIAM GELLER, M.D.: Could you comment on sporotrichosis?

DR. LOURIA: Sporotrichosis in a visceral form is a really rare disease. There are only a handful of cases in the world literature. It usually develops after exposure to the thorns from rosebushes, and in the few known cases of disseminated sporotrichosis there always has been a local skin lesion, a fairly obvious one, that preceded the dissemination. Perhaps 5, or at most 10, cases of primary pulmonary sporotrichosis have been described, but these have not produced such a fulminant course, and in any case the rarity precludes making that diagnosis without substantial supporting evidence.

Clinical diagnoses

1. *Pneumonitis, type undetermined*
2. *Peptic ulcer, stomach or duodenum, following steroid therapy*
3. *Chronic myelogenous leukemia, in remission following chemotherapy*

Dr. Louria's diagnoses

1. *Cytomegalic inclusion disease, pulmonary and extrapulmonary*
2. *Ulceration of upper gastrointestinal trace, ? leukemic infiltration, ? following steroid therapy*
3. *Chronic myelogenous leukemia, treated*

Pathologic report

H. CLARKE ANDERSON, M.D.: An autopsy disclosed 500 cc. of clear fluid in the abdominal cavity and 1,000 cc. of clear fluid in each pleural cavity. The lungs had a combined weight of 2,500 Gm. with confluent areas of consolidation being grossly apparent. The spleen weighed 900 Gm. and on section showed diffuse pallor and loss of normal follicular markings. There was a great deal of blood in the gastrointestinal tract, mostly as tarry material in the stomach and small bowel. There were no discrete ulcers, but the gastric antrum and duodenum showed numerous small superficial mucosal erosions.

A microscopic examination of the exudate in both lungs showed it to be rather less dense than one would have expected from the gross consolidation and to be chiefly mononuclear in character. Many of the mononuclear cells contained the large, round, basophilic, intranuclear inclusions typical of cytomegalic inclusion disease (Figs. 3 and 4). Similar mononuclear cells with intranuclear inclusions were found in the spleen and adrenal glands in great numbers and also in the thyroid, heart, stomach, duodenum, and pancreas in smaller numbers. Also seen in these sections are smaller, granular, eosinophilic, intracytoplasmic inclusions. As Dr.

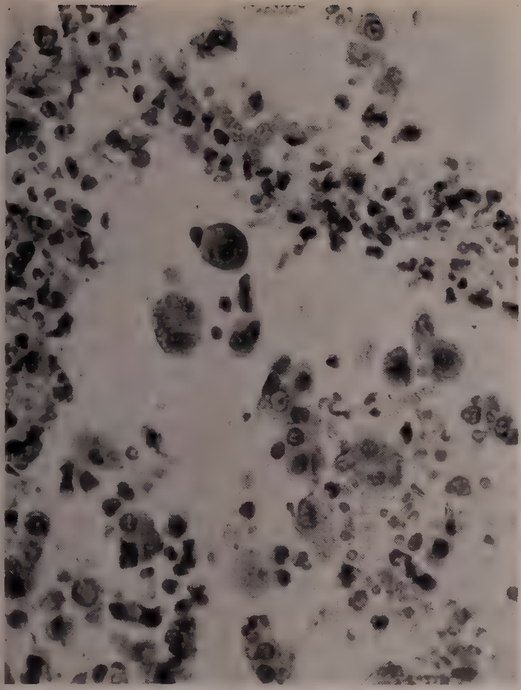

FIGURE 3. Section of lung at autopsy showing an alveolar exudate consisting chiefly of mononuclear cells with a light admixture of other leukocytes. The single, large, dark cell contains an inclusion body.

Louria predicted, the infection was widely disseminated.

I think the massive gastrointestinal hemorrhage was the result of the superficial erosions in the stomach and duodenum (Fig. 5). There was no complete denudation or necrosis, but many of the erosions contained dilated capillaries leading perpendicularly to the surface. There was no perforation of the gastrointestinal tract.

Actually, we could not make a definitive anatomic diagnosis of myelogenous leukemia on the postmortem tissues. The changes in the spleen, bone marrow, and lymph nodes were those characteristic of the disease in remission following effective chemotherapy. The bone marrow was somewhat hypocellular, not an uncommon observation in patients receiving any of a number of antileukemic drugs.

The identification of cytomegalic inclusion disease in tissue depends on how closely one looks for it and on one's awareness of its tinctorial properties. We performed a number of special histopathologic technics in this case, and the results are embodied in Table I.

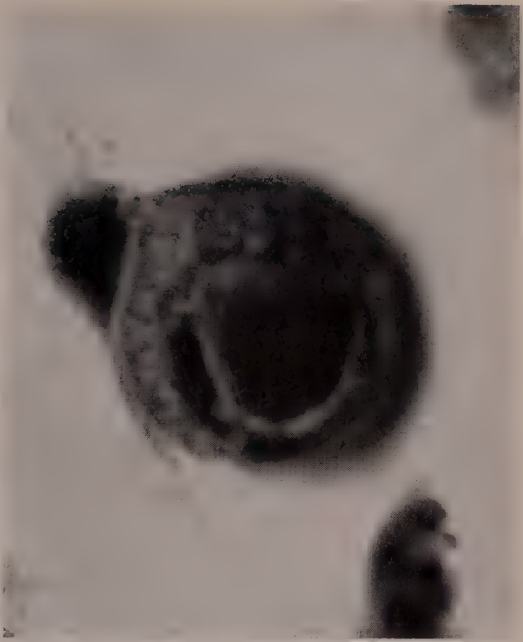

FIGURE 4. Detail of Figure 3 showing the large, round, basophilic, intranuclear inclusion body.

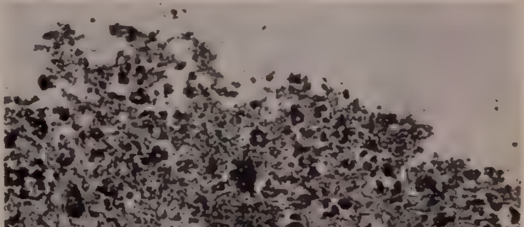

FIGURE 5. Section of gastric mucosa and submucosa at autopsy showing intense vascular engorgement. An extremely dilated blood vessel in the mucosa approaches the surface. Many such vessels were found, and they are interpreted as the source of gastrointestinal bleeding.

TABLE 1. Tinctorial properties of intracytoplasmic and intranuclear inclusion bodies

Stain	Intranuclear Inclusion	Intracytoplasmic Inclusion
Hematoxylin and eosin	Basophilic	Eosinophilic
Feulgen	Positive	Negative
Periodic acid (Schiff)	Negative	Positive
Mallory trichrome	Orange-red	Grey
Methenamine silver	Brown	Unstained
Phosphotungstic acid hematoxylin	Purple	Unstained
Acid-fast (Ziehl-Neelsen)	Negative	Negative

Although absolute proof is lacking that the intranuclear inclusion represents the virus particle itself, the positive Feulgen stain, which indicates a high desoxyribose nucleic acid content, is usually construed as suggestive evidence for this point of view.

Dr. Geller: Were the inclusion bodies seen in the tumor cells themselves?

Dr. Anderson: No, although we couldn't really identify leukemic cells in this treated case.

Dr. Kirsch: What was the nature of the 60,000 white blood cells in the peripheral count at the time of the patient's death?

Dr. Fraumeni: They were mostly adult polymorphonuclear leukocytes.

Anatomic diagnoses

1. Cytomegalic inclusion disease involving lungs, spleen, adrenal glands, thyroid, heart, stomach, duodenum, and pancreas

2. Multiple superficial erosions, stomach and duodenum, with massive gastrointestinal hemorrhage

3. Pleural effusions bilateral, ascites

4. Chronic myelogenous leukemia in remission following chemotherapy

Epicrisis

Dr. Horsfall: Thank you, Dr. Louria, for a most lucid analysis. You have reduced the possibilities to two, herpes simplex vs. cytomegalic inclusion disease, by an exacting process of logic, and you have committed yourself to one of them. Were it not for the two complement fixation tests for herpes, I doubt seriously whether that possibility would even have been entertained.

Dr. Louria: What was the interval between the tests?

Dr. Fraumeni: They were five days apart.

Dr. Horsfall: The serum titers were only 1:8 with herpes simplex virus. If this is, in fact, a reproducible complement fixation result and specific for the virus, it requires some comment, for this is not common, even though it may be found in the serum of a normal person. If the results had been secured by the neutralization test, in contrast to complement fixation, one would expect about 90 per cent of normal persons to show such antibodies. Although an increase in complement fixation titer, if specific, may indicate recent infection, as Dr. Louria pointed out, a constant titer indicates only earlier infection. In this patient we do not know whether the titer was constant or rising.

Reactivation of the herpes virus, since it is carried so commonly, can be anticipated in association with a serious disease process and need not be associated with overt herpetic mucocutaneous lesions. Therefore, the absence of such lesions in this patient does not really rule out herpes simplex.

Can we distinguish between herpes simplex as an explanation for the entire infective process, including the inclusion bodies, and cytomegalic inclusion infection? I think we can, and I will defend this thesis in a moment.

The evidence that this is a case of terminal viral infection rests on two laboratory data, the complement fixation tests which showed positive results for herpes and the morphologic demonstration of the widely distributed intranuclear inclusions. Nuclear inclusions are of considerable interest, but most inclusion bodies are not pathognomonic of a viral infection. The best known inclusion is the Negri body of rabies which, as you know, is cytoplasmic, not intranuclear. There are some eight or nine diseases of man that produce intranuclear inclusions. Briefly, these are: herpes simplex, measles, canine distemper (which may at times infect man), herpes zoster varicellosus, several of the adenoviruses, poliomyelitis, yellow fever, chronic progressive encephalitis of unknown cause, infantile pneumonia (which may be due to an adenovirus), and salivary gland virus, that is, cytomegalic inclusion disease. Only two of this list are pertinent here, herpes simplex and salivary gland virus.

Now, if we may have Dr. Anderson's excellent photograph of the inclusion body again (Fig. 4), we can see that in addition to the large, "owl-eye" intranuclear inclusion which is dense, acidophilic, and surrounded by a translucent halo inside the nuclear membrane, there are a multiplicity of small intracytoplasmic inclusions. These are distributed widely throughout the cell and appear as tiny basophilic dots which on close inspection also are surrounded individually by a clear zone. Similar intracytoplasmic inclusions are present in the other involved viscera. The distinction between herpes and salivary gland virus can be made on this point alone. Herpes simplex produces a type A intranuclear inclusion which does not look like this at all and does not produce intracytoplasmic inclusions. Although it is possible on the basis of laboratory evidence alone, that is, the complement fixation tests, that the patient may have suffered from a recent inapparent herpes simplex infection, his secondary disease, which may indeed have contributed to the fatal outcome, was cytomegalic inclusion disease.

Such a statement is a presumptive diagnosis on morphologic grounds. To pin it down beyond doubt it would be necessary to recover the virus and identify it. This could not be done in this case because the diagnosis was not suspected until the microscopic sections were examined, by which time any attempt at isolation would have failed. So, on these grounds, it is most probable that Dr. Louria's diagnosis of cytomegalic inclusion disease is correct.

I would like to review very briefly what is known of generalized salivary gland virus infection, which is often called cytomegalic inclusion disease. The agent is sometimes called submaxillary gland virus because of its common presence in that organ. The condition may be unfamiliar, for relatively few cases have been described in adults. Only about 35 cases had been reported up to 1960, and these were reviewed by Symmers[2] in a very readable and informative article.

It is important here, as in many viral conditions, to distinguish sharply between infection and disease. We have firm morphologic evidence in this case of infection, but I am less certain that the disease process, as seen during the last two weeks of the patient's life, was attributable to the infectious agent we have identified.

Salivary gland virus infection occurs both in man and in animals and is characterized by the inclusions we have described. They generally are present in several organs, and they are often unassociated with clinical findings. The disease was first described in the 1880's or 1890's and was identified fairly definitely in 1904, although until about 1926 the inclusions were interpreted as being protozoan. The first of the several viruses in the salivary gland group was recovered at the Rockefeller Institute in 1926 by Cole and Kuttner.[3] Later, it was recovered from hamsters, mice, rats, and monkeys, all naturally carrying the agent. It was not until 1956 that the virus was recovered from human beings simultaneously and independently by Smith[4] and by Rowe *et al.*[5] To date, the virus has been obtained many times from adenoid tissue, liver biopsies, and even from urine. All strains, whether rodent, simian, or human, produce the same cytologic changes, the fairly typical intranuclear and intracytoplasmic inclusions. These usually are found in epithelial cells, except in the guinea pig where they are found in mesodermal tissues.

As Dr. Anderson indicated, the basophilic bodies in the nuclei are thought to be largely, if not entirely, desoxyribose nucleic acid associated with protein and may, in fact, represent large clumps of virus particles. The eosinophilic bodies in the cytoplasm are almost certainly not the virus and do not contain desoxyribose nucleic acid. Because of their eosinophilia and other histochemical properties, it is assumed that they are mucopolysaccharide masses that affect biochemical and metabolic functions of the cell. The lesions are most commonly found in the salivary glands, liver bile ducts, renal tubules, and bronchial epithelium. Less frequently, lesions and inclusions are found in the adrenals, as in this case, and in the gastrointestinal epithelium, pancreas, thyroid, and parathyroid. This is quite different from the distribution of herpes simplex which is not distributed in these organs generally and which may affect the central nervous system.

The importance of distinguishing between infection and disease is particularly evident when one considers the data from studies on infants and children. Among 1,700 unselected autopsies in infants, cytomegalic inclusion bodies were found in the salivary glands in from 10 to 15 per cent of the cases.[6] The dissemination of the bodies to other organs is less frequent, probably only in 1 to 2 per cent. In 50 per cent of those individuals in whom it is found as a generalized lesion, usually leading to death, the disease has been associated with so-called pneumocystis carinii pneumonia. The relationship between the two microorganisms is unknown, as Dr. Louria said.

Experimental infection has taught us that there is remarkable specificity for homologous species. This is shown by all of the known types of agents in this group; they will grow only in tissues of the host species that they infect. Human salivary gland virus will grow only in human tissue culture, and until this was attempted in 1956 all efforts to recover the agent had failed.

Both neutralizing and complement-fixing antibodies are present in infected infants and adults. In general, mothers of children who show the disease have antibodies, indicating that they were infected and indeed may have transmitted the agent.

The infection is considerably more widespread than has been appreciated. The frequent recovery of the virus from normal adenoid tissue indicates that it may persist in lymphoid tissue for years. One might speculate that in this patient the infection may date back to infancy and that it was activated by the leukemia and possibly the antileukemic drugs. As Dr. Louria said, some 70 to 80 per cent of the cases in adults have been associated with one or another of the forms of lymphoma or leukemia.

In infants the disease is most often discovered as an entity resembling a blood dyscrasia associated with hepatomegaly and hepatocellular damage. The disease is generally fatal, but the incidental findings in autopsy material show that the infection is by no means rare. In older children the clinical signs vary in terms of the organs involved. Diarrhea, liver damage, renal damage, pneumonia, and cerebral lesions are common. It is frequently superimposed on another debilitating illness, such as pertussis or fibrocystic disease of the pancreas. In adults subclinical infections are probably numerous. How numerous nobody knows. However, no more than 35 cases like this one have been described in adults, and I believe that only in very few instances has the virus actually been recovered and identified. As I have said, in adults it is most commonly associated with a severe underlying disease, and it most commonly manifests itself as a pneumonia. The diagnosis is almost always made on pathologic findings and is rarely suspected on clinical grounds, even though we have seen an instance today in which that was feasible. It is not easy to recover the virus in human cell tissue culture, but it can be done. Complement-fixing antibodies are usually present in individuals who have been heavily infected. Finally, there is no effective treatment yet known, a statement which can be made for all true viral diseases.

DR. ANDERSON: When you said that it was important to distinguish between infection and disease, would you go so far as to imply that the cytomegalic inclusion virus might not have been the immediate cause of death in this patient?

DR. HORSFALL: Precisely. It remains presumptive. The situation is analogous to poliomyelitis, a virus which has infected about 90 per cent of the persons in this latitude over twenty years of age but which has induced recognizable disease in less than 1 per cent of those it infected.

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Current Concepts in Diabetes Mellitus

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Cholelithiasis in the Diabetic Patient

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CURRENT DATA indicate that the surgical management of calculus biliary tract disease in the diabetic patient has a surgical morbidity and mortality only slightly higher than that of the nondiabetic patient.[1-3] The pessimistic attitude toward surgical management that found justification in earlier results is no longer tenable.[4] These more satisfactory surgical results are based on the recognition of distinctive clinical features in symptomatic and asymptomatic diabetic cholelithiasis. This recognition permits an interruption of progressive disease at a time and under such circumstances as permit a total correction of the pathologic situation. Such improvement is a logical sequence of the thirty years of experience with insulin and the eighty years of experience since cholecystectomy was instituted as definitive therapy for calculus cholecystitis.[5] Improved results are to be expected when advantage is taken of the fact that prognostic information can be derived from the clinical course and roentgen findings.

Cholelithiasis is an important and statistically significant public health problem. There is an increasing older population, an increasing diabetic case finding, and with these an increasing finding of patients with cholelithiasis. The incidence of cholelithiasis in routine autopsy material in patients over fifty years of age at Montefiore Hospital is 17 per cent. Various reports from other institutions place it between 10 and 50 per cent, depending on age and sex.[6] All documentation attests to the fact that the incidence of cholelithiasis increases with each decade of life. Furthermore, it is generally conceded that the incidence of calculi in diabetic individuals is somewhat greater than in nondiabetic individuals. The significance of the problem becomes apparent when it is viewed in still another light: Biliary tract disease is the commonest nonmalignant indication for abdominal surgery in the adult.[7]

Etiology

The most logical approach to the problem of cholelithiasis is that of determining the etiology of the stone formation. In spite of the clinical recognition of the relationship to infection (typhoid), endocrine factors (pregnancy and the state of being female), metabolic factors (dietetic and diabetic), and the experimental demonstration that calculus disease is often associated with proximal obstruction, there is as yet no practical method for preventing stone formation. Therefore, the problem of the clinician is to diagnose the entity and to choose the optimum time for therapy in those patients who are most likely to get into difficulty with relatively asymptomatic calculi, and to determine the modality for the management of those with symtomatic disease. It is the duty of the surgeon to perform the operation accurately and completely to correct the disease in the gallbladder as well as in the extrahepatic biliary passages. Both of these desiderata are possible. One is based on an understanding of the pathologic physiology of biliary calculus disease, and the other is predicated on the skilled use of operative methods for securing a complete and totally corrective biliary toilet.[8]

Once calculi have formed, there is no practical external method for influencing the biliary reaction. The pathologic changes in the gallbladder are the sequelae of stones within the lumen of the vesicle as they relate to one another and to the biliary exit at Hartmann's pouch or the cystic duct.[9] The changes in the lumen and the wall are determined by the degree and the duration of the outlet obstruction and probably by the temporal relation existing between the onset of obstruction and the time of emptying of the gallbladder.

A large solitary calculus is usually of the cholesterol type. A stone may reside in an apparently normally-functioning gallbladder, normal in the respect that the patient is asymptomatic and that the oral cholecystogram shows no changes in the gallbladder as reflected by the visualization or the emptying of contrast material. A solitary large calculus can sometimes be identified on the flat roentgen-ray film by a peripheral radiopaque ring shadow. These very large calculi rarely pass into the common duct via the cystic duct. The pathologic sequence initiated by such stones results from the obstruction to the flow of bile. A closed obstructive situation may ensue in which there is no outlet for bile or for the normal mucous membrane secretion derived from the cells in the lining epithelium. Within such a closed system the gradual distention of the organ results in a situation which is analogous to closed-loop intestinal obstruction. Distention of the organ compromises the intramural venous return resulting in edema of the wall. In its more advanced stage, tissue necrosis, secondary infection, and perforation follow. In the early stages of such obstruction the process is purely mechanical and free of a bacterial component. This stage of obstructive cholecystopathy is best characterized as acute obstructive cholecystitis. Such a situation is more likely to be brought about by a large impacted calculus than it is by smaller free-floating stones. These latter, however, may be wedged into the Heisterian valves of the cystic duct and introduce a similar series of events. This grossly distended, tense hemorrhagic gallbladder is histologically characterized by edema and congestion. There is a marked disparity between the observations at surgery and the microscopic examination. This is the early phase of the "acute gallbladder." It is characterized clinically by pain in the upper right quadrant of the abdomen associated with a palpable mass which is the fundus of the obstructed organ and surrounding omentum. Overlying peritoneal signs of tenderness, spasm, and rigidity may obscure the mass as such and indicate only an inflammatory process in the upper right quadrant of the abdomen. Repeatedly it has been observed that there is no reliable correlation between the pathologic state of the obstructed viscus and the intensity of the constitutional response as it is indicated by temperature, pulse rate, or leukocytosis.[10] Secondary infection results in a true empyema of the gallbladder. Suppuration is not encountered as frequently as the general lax use of the term "empyema" would indicate. The disease is usually interrupted earlier or the organ may go on to perforation. Perforations occur either at the fundus, because this is the site of maximum ischemia, or at the site of calculus decubitus ulceration. The perforation is either free or walled off depending on its site and on the rapidity with which the process has developed. At this stage, in the acute episode there is the usual appropriate response as regards the intensity of peritoneal signs and the corroborative laboratory data. In the less usual situation the perforated organ becomes adherent to an adjacent viscus or to the abdominal wall with an ensuing cholecystoenteric, or cholecystocutaneous fistula.

Chronic cholecystitis is the result of repeated insults and results. It results in the progressive thickening and shrinkage of the gallbladder with thickening of its wall, gradual obliteration of the lumen, and progressive loss of demonstrable function. Histologically this is characterized by a mural fibrosis, infiltration of chronic inflammatory cells, and the appearance of Rokitansky-Aschoff sinuses. Acute obstructive cholecystitis is usually engrafted on a chronically diseased gallbladder. Histologically one rarely encounters acute cholecystitis in a gallbladder that has not already been the site of chronic changes. However, the acute episode may be the first symptomatic indication of calculi. There is much evidence to indicate that the early phase of acute obstructive cholecystitis may regress to a chronic inactive stage. This view forms the basis for the nonoperative therapy of the acute episode in the gallbladder.

There has been speculation regarding the role of the choledochus in affections of the gallbladder. Much of this speculation revolves around the question of whether these two systems act sympathetically or independently and on whether or not the choledochus can form calculi independent of the gallbladder. In regard to this latter problem, it has been demonstrated that common duct stones may form although there is a congenital absence of the gallbladder. Histologic studies of the common bile duct in chronic cholecystitis demonstrate, however, that there is no cellular reaction in the duct unless it contains stones. Except for a pericholedochitis the two systems appear to act independently, at least as related to the mural cellular inflammatory response.[11] Common duct stones, in the vast majority of cases, originate in the gallbladder and pass into the common duct via a dilated cystic duct. The histologic inflammatory response observed in common duct biopsies parallels that seen in the similar stage of cholecystitis. The pathologic sequelae are dependent on the relationship of the calculus to the duct size. The common duct is almost always dilated in the presence of gallstones, but the converse is not necessarily true. Choledocholithiasis need not be accompanied by jaundice or hepatic biliary stasis. These complications are a function of the degree of the choledochal obstruction.

The presence of stones in the common duct may be responsible for cholangitis, pancreatitis, and the varying degree of hepatic damage.

Therapy

This brief outline of the salient features in the pathologic physiology of cholelithiasis serves as the basis for therapy. The diabetic response to obstructive and inflammatory disease in the gallbladder generally parallels that seen in other organs. There is a decreased resistance to the inflammatory process so that once the disease and infectious entity has been established it progresses with greater rapidity and with less control than is seen in the normal individual. For example, in acute obstructive cholecystitis of forty-eight hours duration, the gallbladder is found to be in the early gangrenous or preperforative stage more often than in the early phase of edema and congestion. It is noteworthy that this pathologic state often appears in the diabetic patient who has had acute symptoms of less than forty-eight hours duration.

Fifty per cent of the diabetic patients operated on at Montefiore Hospital in the past three years had significant coexistent medical complications in the cardiovascular-renal systems, the lungs, or the body habitus. It is also significant that 20 per cent of the last 50 diabetic patients operated on for biliary tract disease had no prior knowledge of their diabetes; this diagnosis was made on the admission for the biliary symptoms.

Surgical policy

A policy for surgical indications and evaluations has resulted in a 2 per cent mortality in the last 50 diabetic patients who underwent cholecystectomy and choledochotomy or cholecystostomy. However, 50 per cent of this group had significant nonfatal postoperative complications. This policy is predicated on the fact that diabetic individuals tolerate obstructive cholecystopathy poorly and, except if there is a compelling contraindication, early total corrective surgery is indicated. These patients are prepared for surgery by hydration, maximum restoration of hepatic glycogen, and gastric decompression. Liver function tests, an amylase determination, an electrocardiogram, and chest films are part of the routine preoperative evaluation. All cases are managed with the cooperation of an internist. Regular insulin is used regardless of what the prior medication has been.

The surgical procedure aims at a cholecystectomy with evaluation of the common duct by operative cholangiography and choledochoscopy when indicated, so that a total biliary toilet is accomplished.[12,13] This procedure is employed to avoid a surgically uncorrected situation that may later be regarded as a postcholecystectomy syndrome. Pursuant to this policy the only death in the last 50 cases occurred in a seventy-year-old man, admitted three weeks after the onset of symptoms, who had a generalized peritonitis resulting from a free perforation of the gallbladder. Elective surgery in the diabetic patient who is properly prepared, has not, and should not be attended by a greater mortality than in the nondiabetic patient. For the most part poor results have occurred in the acute episodes requiring urgent surgery. Schein, Hurwitt, and Rosenblatt[14] have pointed out that the majority of acute episodes are related to outlet obstruction by large calculi. It is advisable, therefore, to operate electively on all diabetic patients who are found to have large biliary calculi without symptoms, and to operate early or promptly on all symptomatic diabetic patients who have calculi of any size regardless of whether or not the gallbladder functions on cholecystography. A nonvisualized gallbladder with symptoms is likewise an indication for surgery. There is no place in the suitable diabetic patient for "medical management" of symptomatic cholelithiasis, since diet and antibiotics exert no definitive influence on the progress of the pathologic process.

Summary

The pathologic physiology of cholelithiasis and its sequelae is presented.

The diabetic response to acute obstructive cholecystopathy is one of rapid progression to suppuration, localized necrosis, and perforation. Large solitary calculi are a particular menace since they initiate the "acute gallbladder." A policy of early complete biliary toilet for all symptomatic calculi in the diabetic patient and elective cholecystectomy in the presence of large stones has resulted in a 2 per cent mortality in the last 50 such operations on diabetic patients.

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Maternal Welfare

Prepared by the Subcommittee on Maternal and Child Welfare, Committee on Public Health and Education, Medical Society of the State of New York

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Records Unlimited

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PRESUMABLY PHYSICIAN and hospital medical records were used originally to facilitate patient care. Gradually hospital records have been modified to accommodate economic factors such as various types of insurance, medicolegal aspects, medical and nursing undergraduate and postgraduate education, statistical purposes, clinical research, sociologic problems, and other purposes which do not have a direct bearing on the medical care of the patient. Paper work is a factor in the high cost of medical care and, possibly, in some instances it may actually reduce the efficiency of patient care, since it occupies so much of the time of doctors and nurses.

The solution of this problem is receiving much attention at present. Some time ago we surveyed the following maternal death which seems to point up several of the aspects of the problem.

Case report

A thirty-five-year-old multipara had a normal prenatal course. Labor began spontaneously at the thirty-ninth week and was uneventful until shortly before delivery when a terminal abruption of the placenta occurred. A stillborn baby was delivered spontaneously under cyclopropane anesthesia. Approximately one-half hour after delivery the patient developed shock, although there was no evidence of excessive hemorrhage. Appropriate treatment was instituted including whole blood and fibrinogen, since there was evidence of afibrinogenemia. The patient's response was not satisfactory, and several qualified consultants were called. Some active vaginal bleeding occurred, and the uterus was packed. During the first twelve hours the patient received 1,400 cc. of fibrinogen and 4,500 cc. of whole blood. The entire postpartum course was stormy with obstetric, medical, and urologic consultants assisting in the care. An evidence of renal insufficiency developed, with obvious electrolyte imbalance. On the third postpartum day convulsions developed. A lumbar puncture was done on the fourth postpartum day, and the next day it was necessary to do a tracheotomy. Despite the most meticulous diagnostic and treatment management, the patient expired on the sixth postpartum day. An autopsy was performed.

The final diagnosis consisted of the following: intrauterine pregnancy—term-delivered; terminal complete abruptio placenta; afibrinogenemia; complications: bilateral renal necrosis and pituitary necrosis (Sheehan's syndrome); and uterine myometrial infarction.

COMMENT. There is every indication that this patient received adequate prenatal and labor-delivery care. The postpartum attention could well be classified as of an unusually thorough nature; still, modern medicine was unable to save this patient's life. This case summary could be classified as a routine survey of an unfortunate maternal death. The story of how the summary was obtained involves some interesting and pertinent material, in terms of medical records.

The first note of interest involves a matter of vital statistics. The death certificate gave the cause of death as follows: immediate cause—afibrinogenemia due to massive uterine necrosis (?); contributory—Sheehan's syndrome (pituitary necrosis). The certificate was signed by the physician who performed the autopsy.

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* Secretary of the Subcommittee on Maternal and Child Welfare.

This diagnosis might well indicate to an experienced vital statistics expert or a physician that the patient was pregnant, but there is no diagnosis which would indicate a specific relationship with pregnancy to the vital statistic clerk who did not know that afibrinogenemia is usually associated with pregnancy. Actually the patient was a personal friend of an employe in the vital statistic office who was aware of the fact that the patient was pregnant. The staff cross-checked their files and found that the stillbirth certificate, which had been filed several days previously, ascribed the cause of stillbirth to abruptio placenta. Thus the death was coded as a maternal mortality. There is evidence that rather a considerable number of deaths associated with pregnancy are not coded properly because of the manner in which death certificates are filled out.

The summary of the case was made from a photostatic copy of the patient's hospital chart and demonstrates rather dramatically some of the "paper work headaches" facing physicians and hospital personnel. The chart is made up of 107 separate sheets of paper which break down in the following manner:

One admission sheet with final diagnosis and other information.
Four legal requirement sheets, including permit for postmortem examination.
Five sheets pertaining to the stillborn infant.
One sheet designated as anesthetic record for delivery.
One sheet for labor and delivery.
Three consultation sheets.
Eight continuation and progress note sheets with 31 individual notes.
One temperature sheet.
Four blood pressure sheets.
Two special intake and output charts.
One laboratory sheet with 11 hematocrit readings.
Three additional laboratory sheets with general laboratory data.
One sheet with three miscellaneous and five transfusion requests and report sheets attached.
One sheet with forty-nine individual laboratory reports attached, most of which were copied on the laboratory sheets noted previously.
One special laboratory sheet for Wassermann test, blood type, and Rh factor.
One sheet—x-ray request with report.
One sheet—treatment, operative and anesthetic permit for tracheotomy.
One sheet—postoperative sheet pertaining to tracheotomy.
One sheet—anesthesia record for tracheotomy.
One sheet—operative record of tracheotomy.
Five sheets—"Treatment and Doctor's Orders."

The chart actually contained additional sheets, since the "Nurses Note" sheets were not included in the photostatic copy made available to us.

This particular record demonstrated a finding noted repeatedly in the surveying of hospital records of patients with obstetric complications, namely that the summaries in the continuation notes repeat previously recorded data again and again. Details are buried in the progress notes, but they are not recorded in places provided for the specific information in other parts of the chart. It takes hours to analyze such a record for survey purposes. This in itself is relatively unimportant. It is important, however, in terms of the time needed by the attending and consulting physicians in tracking down pertinent information. The tracking down of information is of particular significance if a consultant sees the patient when the attending physician is not present. This example represents a picture of the time expended in tracking down pertinent data, such as laboratory reports and so forth, which at times reaches the point of near frustration.

Comment

The problem of keeping hospital recording within reasonably practical limits will not be easy to solve. It will require the cooperation of many people, including the legal profession, and may well entail either changes in the legislation or the creation of a new legislation.

A few specific points are mentioned which could be constructive. One thing that can be done to improve the efficiency of recording progess notes is to place the "Progress Note" sheet at the front of the chart while the patient is in the hospital.

Consultation sheets. Many hospitals use individual consultation sheets for each consultation. It might be practical to have a single consultation sheet provided, with space for the detailed reason for consultation and the consultant's opinion. The sheet could be devised so that if another consultant was needed, an interval note could be added followed by space for the second consultant's opinion, and so forth.

Laboratory data. It would seem advisable to work out a system of including original laboratory reports in the chart or recording data on specified laboratory sheets, rather than using both methods simultaneously.

Medicolegal permits. It would seem possible to devise a multipurpose permission sheet which could include what might be termed ordinary patient or family permissions such as obstetric and operative procedures, medical and laboratory procedures, releases for clinical research, and others, with a single signature by the patient and/or a responsible member of the family. A space for release against doctor's advice could be provided. The reverse side of the sheet could be used for postmortem examination and postmortem cesarean permissions, to be used at indicated times. This would cut down on individual forms. It is interesting to note in passing that the Law Department of the American Medical Association has prepared forty-seven different types of medicolegal forms covering various commonly and rarely encountered situations.

Much cooperative effort is needed, but uniform forms for history, physical examination, labor and delivery, anesthesia, order and treatment sheets, continuation sheets, and others would prove advantageous to physicians who do obstetrics, hospital personnel involved in the direct and indirect care of the patient, educators, and researchers. A basic principle would involve hospital obstetric records designed primarily for the uncomplicated cases, but with sufficient flexibility to adapt to cases with complications.

Due consideration should be given as to whether or not a single chart will serve the purpose of hospitals with house staffs associated with teaching institutions, hospitals with house staffs of other types, and hospitals without house staffs. It may be impossible to devise a single chart, and three basic charts to accommodate the various categories of obstetric services may be necessary.

Serious consideration should be given to the matter of including all the prenatal data available to the attending physician as part of the patient's hospital record at the time the patient is admitted to the hospital in labor or for prepartum complications.

The discussion of the problems involved in hospital obstetric records has been considered to some degree from their retrospective (research) value. It is more important that the record's value for current patient care be considered. Patient care is accomplished at maximum efficiency when the status of the patient is transmitted by a person-to-person contact, but there are instances, especially in certain types of emergencies, where this method is not practical and the data recorded on the patient's chart must be used.

Summary

There seems to be almost universal agreement among those involved in hospital care of patients that the simplification of records, while maintaining adequate standards of recording necessary data, would be advantageous and economical for the patient. It would allow physicians and others concerned with patient care to devote more time and attention to patient care and expend less time and energy on the paper work involved.

766 Irving Avenue, Syracuse 10

More medical goods and services

People today are using medical goods and services more than they did in years past, partly because they have more education in health matters and partly because higher incomes have raised the standards of what good medical care should be.—*Changing Times, June, 1961*

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
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Car Wax, Imipramine Hydrochloride, and Salicylate Poisoning

The following incidents were reported recently to the New York City Poison Control Center.

Incident 1

Substance Ingested	*Age*	*Sex*
Car Wax	40 years	Male

This incident was reported by a physician from out of town.

About one hour after the patient started waxing his car with wax recommended and sold by the car dealer, he developed severe and diffuse giant urticaria. He had no previous history of hives or allergy. The hives responded at once to adrenalin injection.

An attempt will be made to obtain the exact composition of this product from the manufacturer. We have indicated previously that the concept of "poisoning" reports in the case of drug ingestions also includes side-reactions due to overdosages and untoward reactions. The same interpretation should be extended to reactions resulting from household and other chemical products.

If physicians would report these occurrences routinely to poison control centers, the accumulated resulting information should have beneficial effects. It also may be pointed out that recently the American Academy of Allergy requested its membership to report to their central register all cases of severe allergic reactions resulting from insect bites. Such reactions also should be reported locally to the Poison Control Center.

Incidents 2 and 3

Substance Ingested	*Age*	*Sex*
J-O Roach Paste	6 years	Dog—Male
	Unknown	Dog—Female

The 2 cases cited here were reported to the Poison Control Center by dog owners. One dog was a Dalmatian, and the other was of an unknown variety identified only as "Killer."

The modes of occurrence are as follows:

Dalmation. J-O Paste was put on slices of potatoes to get rid of roaches, and the potatoes were placed where it was thought the children and the dog could not get at them. Evidently the dog reached one from under the tub and ate it. There was about a half-teaspoonful of J-O Paste on a slice of potato. The dog was given salt water and made an unsuccessful attempt to vomit. The next day the dog had diarrhea, but she acted normal and after that was all right.

Killer. There was J-O Paste on a cracker to get rid of roaches. The cracker was on top of the kitchen table close to the wall. The door bell rang, and the dog ran from under the table, hitting one of the table legs and pushing the table from the wall. The cracker fell to the floor, and the dog ate it. That was September 9, 1961. On the same date the dog was given a solution of raw egg and milk. The dog vomited and wouldn't eat. He died some time after 7 A.M. on September 13, 1961, and was found when the owner returned home from work at 6:00 P.M. The American Society for the Prevention of Cruelty of Animals was called.

Our Poison Control Center has cultivated these reports of dog poisonings because of the information elicited from these occurrences. Phosphorus poisonings continue to be a most perplexing problem both in human beings and in animals because of a lack of specific therapeutic measures. The consideration of the curtailment of the use of this product in the home is advisable.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Imipramine Hydrochloride	33 years	Female

This patient took the medication with suicidal intent because her husband had been seeing other women. She took thirty 25-mg. tablets and vomited most of these within two hours following the ingestion. Then she went to a hospital emergency room where her stomach was lavaged with normal saline about three hours following the ingestion.

Since there were no other physical signs or symptoms, after six hours of observation the hospital referred the patient to Bellevue for psychiatric attention.

INCIDENT 5

Substance Ingested	*Age*	*Sex*
Aspirin	3 years	Male

This case was reported by Philip Lustbader, M.D., a pediatrician as well as a supervising physician in the Bureau of Child Health of the Department of Health.

The patient, a three-year-old child, ingested twenty-five 5-grain aspirin tablets while he was presumably under the supervision of his father who was caring for the children while the mother went shopping. The father did not see the patient climb up to the kitchen closet where the aspirin was stored, nor did he see the boy swallow the aspirin. The incident presumably occurred at 10 A.M., but the child was not admitted to the hospital until 5:00 P.M., or seven hours following the ingestion. About a half-hour following the ingestion the patient had several episodes of vomiting. On admission to the hospital the patient had shallow, rapid, irregular respirations, tachycardia, and was semiconscious.

The physical examination on admission revealed a well-developed and well-nourished child, afebrile, and in apparently fair general condition, weighing 28 pounds. The patient did not appear acutely ill. The skin was normal, the lymph nodes were not palpable, an examination of the head produced negative findings, and the lungs were clear. However, there was a tachycardia (200 per minute), and the respirations were shallow, rapid, and irregular (40 per minute).

On admission an emergency carbon dioxide determination showed 28 volumes per cent. Intravenous therapy was started with 8 per cent glucose and water and normal saline. The patient had several episodes of vomiting. He was placed on the critical list the second day after his admission. His temperature rose to 104 F., and his respirations were deep and irregular. He was still tachycardic, and his extremities were cold and clammy. A second carbon dioxide determination was found to be 38 volumes per cent. The patient was placed in an oxygen tent. His blood pressure was 65/20. Intravenous therapy was started with one-sixth molar sodium lactate, 10 cc. per pound of body weight, and was maintained for twenty-four hours. The urine output diminished. Acetone was strongly positive in the urine, and there was a trace of glucose. The albumin was 2 plus.

On the third hospital day the patient was placed on Diamox, 5 mg. per kilogram,

TABLE I. Ingestions reported during a recent weekend

Substance Ingested	Patient	
	Age (Years)	Sex
Ajax cleanser (in eye)	$1^1/_2$	F
Alcohol, rubbing	69	F
Aspirin	$3^1/_2$	F
Aspirin	$2^1/_2$	M
Aspirin	19	M
Aspirin, baby	$2^1/_2$	M
Aspirin, baby	$3^1/_2$	M
Aspirin, baby	$3^1/_2$	F
Aspirin, baby	2	F
Aspirin, baby	5	M
Atropine	3	M
Baby Magic (lotion)	$1^1/_2$	M
Baby Magic (lotion)	1	M
Barbiturates	50	F
Bleach	2	F
Bonadettes (seasickness pills)	2	M
Borax	1	M
Boric acid	82	M
Bromthymol blue	3	M
Carbon dioxide gas	Unknown	M
Cement	9	M
Cement, polystyrene	$1^1/_2$	M
Cement, plastic	2	F
Chloral hydrate	40	F
Clay	$^2/_3$	M
Cleanser	2	F
Clorox	$1^1/_2$	M
Clorox	40	M
Clorox	19	F
Codeine	3	M
Collyrium eye wash	2	M
Colocynth (bitter apple)	27	F
Coricidin (antihistamine)	3	M
DDT	3	M
DDT	5	M
Dehydrating capsule	Unknown	M
Detergent	$1^1/_2$	M
Diaper ointment (perianal)	Unknown	Unknown
Doriden	28	F
Dramamine	2	F
Drano	1	M
Drano	29	F
Dry ice	8	F
Dye (from watch band)	5	M
Equanil	3	M
Floor wax	2	M
Fungicide	63	M
Furniture polish	$1^1/_2$	F
Glue	2	M
Homeopathic teething medication	Unknown	Unknown
Hydrochloric acid and chlorine	52	F
Ink	$3^1/_2$	F
Ink	Unknown	F
Iron salts (from chemistry set)	$6^1/_2$	M
Javelle water	2	M
J-O paste	$3^1/_2$	M
Jumping beans	$1^1/_2$	M
Lead paint	$1^1/_2$	M
Lighter fluid	3	F
Liniment	2	M
Malathion	Unknown	Unknown
Mascara	2	M
Mercury from thermometer	Unknown	M
Mercury from thermometer	1	M
Mosquito killer	2	M
Nail polish remover	$1^1/_2$	M
Nail polish remover	Unknown	Unknown
Nail polish remover	2	M
Naphtha	$^2/_3$	F
Narcotics	24	M
Neo-Synephrine	3	F
Neo-Synephrine	27	M
Oil of citronella	3	F
Oil of citronella	Unknown	Unknown
Oil of wintergreen	2	F
Paint	Unknown	F
Paint remover	23	M
Paradichlorbenzene	2	M
Paste, wallpaper	$^2/_3$	F
Perfume	$1^1/_2$	F
Phenylbutazone	$2^1/_2$	F
Phenylbutazone	$2^1/_2$	M
Potassium permanganate	23	M
Refrigerant	Unknown	F
Refrigerant fumes	Unknown	M
Refrigerant fumes	Unknown	M
Rosex rinse	Unknown	Unknown
Rodenticide	20	F
Rodenticide	$1^1/_2$	F
Sani-Flush	3	M
Serpasil	$3^1/_2$	M
Skotch Ice	Unknown	Unknown
Sleeping pills	22	F
Sleeping pills	33	F
Soap	Unknown	Unknown
Teething lotion	$1^1/_2$	M
Thorazine	2	M
Tintex	2	F
Toilet water	Unknown	Unknown
Triaminicol	23	M
Whiskey	2	M

which was continued for three days. By that time the temperature dropped to 103 F. The urine was still positive for acetone and negative for sugar. The patient also had an episode of hematemesis. From the fourth to seventh hospital days the patient had minimal bloody vomiting. He developed some blue discoloration ecchymosis and swelling associated with blisters over the extremities. The bleeding time was twenty-five minutes and clotting time one hour and thirty minutes. The hemoglobin was 11.5 Gm. per 100 ml., platelets 430,000, and prothrombin time 14 seconds. The patient was started on Vitamin K, 25 mg. a day for three days, and Solu-Cortef, 100 mg., was given intravenously. The child was very lethargic, and the shallow, irregular respirations continued.

On the fifth hospital day the patient developed jaundice (icterus) over the sclerae and skin. The urine output was good, but the urine had a dark amber color. The hemoglobin was 6.5 Gm. per 100 ml. The patient had a tremor over the hands and arms. He was started on 280 cc. of whole blood, the transfusion being given through a cut-down in the left ankle. On the sixth hospital day he also was started on intravenous chloramphenicol (Chloromycetin) 50 mg. per kilogram and penicillin crystallin 1,000,000 units. His temperature still remained high. The patient had a moderately tarry stool (melena) several times a day with about six diaper changes. The hemoglobin again dropped to 6.5 Gm. per 100 ml., and 280 cc. of whole blood was given again. The hand and foot condition became worse with swelling and pain. Fever, tremor, and gangrene in the extremities developed. The gastrointestinal bleeding had stopped by the eighth hospital day.

On the tenth hospital day the hemoglobin dropped to 5 Gm. per 100 ml. A transfusion of 280 cc. of whole blood was given. The patient's condition started to improve, and the intravenous therapy was discontinued.

On the eleventh hospital day he was taking fluids by mouth well but was still running a fever. Because of some gangrenous formation over the right foot, debridement was performed by the surgeon. The patient's temperature still remained elevated, and one hand and one foot were gangrenous. The patient was continued on 150 mg. of chloramphenicol, and procaine penicillin, 600,000 units, was administered every twelve hours. An x-ray film of the chest showed negative findings. An x-ray film of the right foot showed osteomyelitis for which the patient was placed on aqueous penicillin, 3,000,000 units daily.

By March 31, about two and one-half months after admission, the patient's external lesions were completely healed, but both feet were markedly deformed. An x-ray film of both feet showed destructive arthritis and osteomyelitis in the resolving stage. At this time both ankles were fixed in a 90-degree angle by a posterior molded splint. He was moved out of bed and into a wheel chair and exercised his knee joints. The patient was still on antibiotics, but compared with his condition at the time of admission, his general and local conditions were improved markedly.

By the end of April he was standing for progressively longer periods of time. He presented the problem of a shortened heel cord bilaterally. By May 31 the patient was afebrile. He was started on physical therapy three times a week, and it was planned to send him home and have him attend the clinic for further physical therapy.

The patient was discharged on June 1, 1961, with the diagnosis of salicylate poisoning, bronchopneumonia, and osteomyelitis of both the ankles and the hands.

On June 26, he was seen in the Physical Medicine and Rehabilitation clinic at the hospital, where resistance exercises to both hips and both knees were given, in addition to gait training. The patient was continued on this therapy at two subsequent visits. He was seen in the hospital's Traumatic Clinic in August and in September. It was advised that the exercises be continued and that he go swimming and walk in the sand.

While the majority of the aspirin episodes are not associated with severe manifestations or complications, this incident may serve as an additional reminder of the ever-present inherent danger associated with this seemingly "harmless" drug.

Table I lists incidents reported to the New York City Poison Control Center over a recent weekend.

Number eighty-nine in a series on Accidental Chemical Poisonings

Case Report

Atrial Fibrillation with Rapid Ventricular Rate Due to Digitalis

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Lown and Levine in 1954[1] were the first to comment on the emergence of a rapid ventricular rate during atrial fibrillation as a result of digitalization. In 1956 Crouch, Herrmann, and Hejtmancik[2] alluded to the fact that 10 out of 100 cases of digitalis intoxication exhibited atrial fibrillation with a rapid ventricular rate. It was not until 1958, however, that Bacaner[3] reported 3 documented cases of this phenomenon, and recently Friedberg and Donoso[4] have added another case.

The following report describes another instance of atrial fibrillation with a fast ventricular rate due to digitalis administration. The purpose of this report is to emphasize that while atrial fibrillation associated with a rapid ventricular rate commonly indicates the need for digitalization, this entity can also be caused by the administration of digitalis and therefore constitutes an indication for the withdrawal of digitalis.

Case report

A forty-five-year-old Negro male was admitted to Lincoln Hospital with complaints of chest pain, dizzy spells, and palpitations of two days duration.

He had always been in good health and had been able to do hard physical work. He had been symptom-free until May, 1959. At that time he "blacked out" and was admitted to another hospital for a four-week period. A diagnosis of a "supraventricular tachycardia" was made, and, after two unsuccessful attempts to convert the arrhythmia with digitalis, a normal sinus rhythm was established with quinidine. Since then, he has had occasional brief episodes of palpitations and has taken quinidine, 200 mg. twice daily, at these times. In the three months prior to his admission these episodes became more frequent, and he was placed on quinidine, 200 mg. twice daily, throughout this period by his private physician. It has been definitely established that the patient had not received digitalis for the fifteen months prior to admission, that at no time had he received diuretics, steroids, or a low-salt diet, and that there had been no vomiting or diarrhea antedating his hospitalization. Two days prior to admission dizzy spells with palpitations lasting from four to five minutes recurred several times, and on the day prior to admission these symptoms became even more frequent and were associated with mild shortness of breath and precordial aching. In the hour prior to admission, he experienced generalized body weakness, profuse sweating, diffuse precordial pain, and increased dyspnea.

The past history was unremarkable except that a bladder tumor was removed four years previously. There was no history of angina of effort, hypertension, murmurs, rheumatic fever, or the symptoms of hypermetabolism.

A physical examination at the time of admission revealed a well-developed, well-nourished, somewhat apprehensive Negro male. His height was 73 inches, and his weight was 210 pounds. The blood pressure was 130/70, the pulse was 140 and regular, and the respirations were 16 and quiet. The fundi indicated negative findings, and the neck veins were flat. The thyroid was not enlarged or nodular. An examination of the heart disclosed a loud first mitral sound but no murmurs or other abnormalities. The lungs were clear. There was no hepatosplenomegaly, edema, hand tremor, exophthalmos, or lid lag.

A laboratory work-up showed normal findings in the hemoglobin, white blood cell count and differential, fasting blood sugar, blood urea nitrogen, serum electrolytes, serum cholesterol, protein-bound iodide, I^{131} uptake, chest x-ray film, cardiac esophogram, cholecystogram, and upper gastrointestinal tract.

The electrocardiogram at the time of admission showed atrial flutter with a variable but predominantly 2 to 1 auriculoventricular block. The atrial rate was 290 and the ventricular rate was 140 per minute. The P waves were inverted in leads II, III, and aVf.

After the carotid sinus pressure and the sedation failed to alter the arrhythmia, the patient was given digoxin, 1 mg. by mouth, followed by digoxin, 0.5 mg. by mouth, every six hours, for four doses, a total of 3 mg. in the first thirty hours. At the end of this time the electrocardiogram showed atrial fibrillation with a ventricular rate varying between 180 and 240. The QRS complexes were so closely spaced that the absence of P waves could be verified with certainty only during the brief periods of increased atrioventricular block (Fig. 1, lower tracing). On the supposition that the fast ventricular rate and the absence of nausea or vomiting indicated underdigitalization, digoxin, 0.5 mg. by mouth, was administered daily for the next three days. During this time the atrial fibrillation and the fast ventricular rate continued. Despite this persistent cardioacceleration, the patient was virtually asymptomatic, complaining only of mild "fluttering" in his epigastrium, and the gastrointestinal symptoms of digitalis toxicity failed to appear. The digoxin was then stopped, and within forty-eight hours the atrial fibrillation reverted to the pre-existing rhythm. After the lapse of another week, a second course of digitalis was instituted. The patient was given lanatocide C, 0.4 mg. intramuscularly every four hours, for four doses with digoxin, 0.25 mg. by mouth, followed by digoxin, 0.25 mg. by mouth, daily for the following three days. Again atrial fibrillation with a ventricular rate of from 180 to 240 appeared within twenty-four hours after starting digitalis and continued throughout the treatment period. Nausea, vomiting, and circulatory insufficiency failed to appear. On withdrawal of the digitalis, the electrocardiogram again reverted within forty-eight hours to the control record.

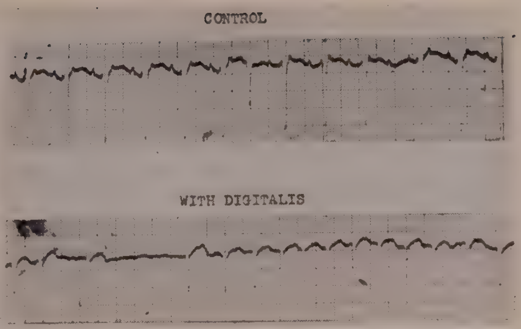

FIGURE 1. Lead V_1 before (upper tracing) and after (lower tracing) digitalization. Control record shows atrial flutter with 2:1 auriculoventricular block, and a ventricular rate of 140 per minute, fusion of an F wave and nodal escape in beat 7, and change from 2:1:3:1 auriculoventricular block between beats 10 and 11. Lower tracing shows atrial fibrillation. F waves are clearly seen during 1.1-second pause between beats 3 and 4. Thereafter, ventricular rate accelerates to 200 per minute, totally obscuring baseline.

After an unsuccessful attempt at conversion with phenylephrine and two unsuccessful trials with quinidine in doses up to 3 Gm. daily, normal sinus rhythm was established and maintained with procaine amide, 250 mg. by mouth, four times daily. A physical examination prior to discharge failed to disclose any murmurs or other cardiac abnormalities, and the heart sounds were now normal. The snapping first mitral sound which was noted during the patient's early hospitalization was attributed to the tachycardia.

During a recent readmission for a recurrence of the arrhythmia, atrial fibrillation with a very rapid ventricular rate again appeared with modest doses of digoxin. This time, however, it was elected to "push" digitalis to the point of gastrointestinal toxicity. This point was reached with 1 mg. of digoxin daily, but even with this dose the rapid ventricular rate failed to slow down.

Comment

The interesting feature of this case is not that atrial fibrillation resulted from digitalization, but rather that the ventricular rate failed to slow down and actually increased to 180 to 240 per minute. The explanation for this phenomenon is difficult to visualize. It is known that digitalis acts on the innervated atrial myocardium to accelerate intra-atrial conduction and to shorten refractoriness.[5] It thus tends to produce atrial fibrillation and to perpetuate and accelerate it, once it has occurred.[4] But digitalis usually slows the ventricular rate in atrial fibrillation by both a vagal effect and by direct action on the auriculoventricular node, and, indeed, atrial fibrillation constitutes one of the prime indications for digitalis.[4,6] Perhaps the experiments of Bordunas *et al.*[7] are germane. They showed that a large dose of digitalis injected directly into the auriculoventricular node may cause a decrease in nodal delay,* and digitalis is known to shorten the refractory period of the ventricular musculature.[8] Perhaps, then, we can tentatively ascribe the production of digitalis-induced atrial fibrillation with a fast ventricular rate to increased impulse formation in the atria, accelerated conduction in the junctional tissue, and hyperreceptivity of the ventricles to these transmitted impulses.

It is of interest that during the periods of atrial fibrillation ventricular rates as high as 240 were recorded without apparent circulatory insufficiency and without the complaint of more than mild epigastric "fluttering." While physiologic experiments have indicated that tachycardia in excess of 180 beats per minute reduces cardiac output progressively, the clinical observation has been made that heart rates over 200 beats per minute are often tolerated for hours or even days without circulatory embarrassment.[9] A case has been recorded of an infant whose ventricular rate was 365.[10]

The close correlation between the development and disappearance of the three bouts of atrial fibrillation with the administration and withdrawal of digitalis leaves no doubt that digitalis was the etiologic factor. That the arrhythmia occurred with what would ordinarily be considered moderate doses of digitalis and that it occurred without gastrointestinal symptoms testifies again to the great individual variations in digitalis sensitivity and to the fact that overdigitalization may produce arrhythmias before gastrointestinal intolerance.[11]

Summary

A case of digitalis-induced atrial fibrillation with a very fast ventricular rate has been described. A review of the literature disclosed only a few previous references to this phenomenon. The point is made that while atrial fibrillation with a rapid ventricular rate usually constitutes an indication for digitalization, this condition can also be induced by digitalis and therefore may be a contraindication to further digitalis therapy.

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* These experiments, however, are open to some criticism. An injection of cocaine and formaldehyde, as well as of acetylstrophanthidin, into the region of the auriculoventricular node of dogs was found to shorten the P-R interval. Moreover, there was no mention of control studies with injection of saline or simply by the insertion of a needle into the region of the auriculoventricular node. The fact that acetylstrophanthidin accelerated auriculoventricular conduction thus may be only a nonspecific effect, in no way related to the pharmacologic properties of the digitalis glycosides. Therefore, the startling proposal that digitalis can quicken atrioventricular conduction must be viewed with some reservations.

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Color test program to be financed by drug industry

A $300,000 two-year public service project to make animal tests on dyes that give drugs their identifying colors was announced today by the prescription drug industry.

Financed by 26 member firms of the Pharmaceutical Manufacturers Association, the program will test seven key colors. Since 1938 the government has certified the safety of every batch of dyes used in food, drugs, and cosmetics, but a 1958 revision of the Federal food and drug laws sets up new and very comprehensive safety tests for color additives. It in effect disqualifies all color additives now in use, in spite of the fact that all of these had been tested for safety during previous years.

The protection of the patient is the primary function of color in drugs. By color-coding their capsules, tablets, and liquids, drug makers help doctors, nurses, and pharmacists ensure that each patient receives the intended medicine in the proper dosage form.

The size and complexity of the program are illustrated by the number of test animals involved—1,460 rats and 180 dogs. Each animal will be subjected to more than 100 times normal human exposure to the test colors. The dogs will become so valuable they are being insured for $20,000 each during the two-year feeding experiment.

Colors that pass all tests will probably be safer than common table salt. When testing is complete, petitions will be filed with the government for certification of the dyes. The animal work for each basic color will cost about $60,000, and the filing fee for each petition is $2,600.

Once the colors are certified, the bulk of the work will have been done as a public service by the drug firms, so that other industries or individuals will be able to file petitions to use these colors in their products without having to repeat the animal safety tests.

Planning for the project began over a year ago when it became apparent that unless the drug makers did the testing, the important color-coding system would be severely hampered.

SYMPOSIUM

The Health Care Issues of the Nineteen Sixties

Chairman
HOWARD R. CRAIG, M.D., New York City

Personal Medicine

T. F. FOX, M.D.
London, England

Editor, **The Lancet**

SOME OF YOU may think of my country as one where the doctor's work has been made official and inhuman. So you may wonder at my coming to plead with you that medicine should be more personal. It's a bad day, you may say, when missions go into reverse, and you have a cannibal preaching in New York. But really the trend toward impersonal medicine is world-wide, and it is due far less to national arrangements than to technologic advances and a technologic attitude of mind. Nowhere are these advances and this attitude more evident than in the United States, and in the depersonalization of medicine, as in so much else, you're probably leading the way.

Even in the most modern clinic, of course, the personal side of practice is not ignored entirely; but it is supposed to matter less and less as science and medical services improve. We have only to look around the world to see that the backward countries, where technology has made least progress, are the ones where most use is still made of personal factors in treating patients. Obviously, the weaker the medical system is, the more personality one needs to put it across. The less the physician's knowledge, the blunter his diagnostic tools, and the feebler his remedies, the more will depend on his inspiring confidence personally.

As we all know, when a practitioner cannot otherwise do anything against disease, his easiest way of inspiring confidence is to claim powers that he does not possess, and it is this element of the bogus in so much personal medicine that has brought it into disrepute in a scientific age. The witch doctor pretends to control good and evil spirits and thereby controls his clients and some of their illnesses. The traditional doctor of China draws on a pharmacopoeia so vast and ancient as to have preternatural authority. Similarly, in older times our own physicians, with their classical learning, their aloofness, and their incredible prescriptions, made themselves appear a mystery. In all countries and all ages, practitioners and healers, orthodox and unorthodox, have supplemented knowledge with a sort of magic. And today we are caught up in a reaction.

Now that we have learned so much and have so many remedies that really work, we thankfully throw away the trappings of the older doctors—the Latin, the pompous manner, the morning coat, and the attention to unimportant details. Good-by, we say, to tricks of conjuring and bedside manners. No longer need the doctor build up his personality. After all, there is nothing subjective about the results of biochemical tests, and the action of a really potent drug is much the same whoever prescribes it. So hurrah for science, objective therapeutics, and open-necked shirts for the physician—once more just an honest man among men!

But if innovators have a fault, it is perhaps a slight tendency to throw every baby out with the bath water. To get rid of the personal magician may be wise but even in a

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technical age, haven't people still a need for personal medical care?

Limitations of technology

It is true that, the more we know, the less we need pretend. And it is true that most people would rather be cured by a competent technician, however impersonal, than killed by their own doctor, however sympathetic. But in thinking that personal medicine has had its day—except perhaps in backward regions—surely we're exaggerating the success to be expected from our technical methods.

And the public is making a similar mistake. In this country, where everyone has the latest information about the mysteries of Mother Nature and of the drug manufacturers, many members of the public are at least as eager as some members of our profession to cut out the "personal nonsense." They still want miracles, of course, but they've transferred their faith from the individual priest of medicine (the practitioner) to the temple of medical science (the hospital), where the wonder-working machines are served by the temple staff. Often, I agree, their faith is justified: Medical science does its best, and sometimes that best is astonishingly good. But if we are to debunk the witch doctor and the general practitioner, we ought also to recognize that the hospital, likewise, does not really practice magic. Although the technical processing of patients has become very complex, the machines and their acolytes cannot always restore health or even life. Despite all our efforts to cure them, people on the whole do not live much longer. In England a man reaching the age of forty may expect to live perhaps two years more than he would have lived a century ago. And in the United States, I rather think, the expectation of life of a man of fifty has actually fallen in one or two recent years.

In brief, the technologic side of medicine is still very far from being so omnipotent and so all-sufficing as to remove all need for the other and older elements in medical care. Hence a good medical organization should still provide personal care by individual doctors, as well as the technical skills of groups of specialists.

Need for individual personal physician

If you ask me what is medically important about this personal care—what is so often missing from medical care as it is practiced nowadays—I would say that what matters most about it is that one doctor accepts continuing responsibility for the patient. He is the patient's own physician, and the patient is his patient.

Even in the days when doctors could seldom do much to alter the course of disease, they were often of immense help to patients and relatives because they so clearly took over the whole management of the case. They may or may not have believed in their remedies, but at any rate they knew, from long experience, that nine times out of ten all that is necessary in an illness is to sustain morale until recovery takes place naturally. The layman usually lacks this reassuring experience which puts the illness into perspective. For my part, I think that people lose a lot if they have no medical practitioner friend whom they can trust and whom they do trust to do his best for them; they lose a lot if, with the help of articles in the magazines, they try to manage their own medical affairs and those of their families. Evidently this is commoner with you than with us, for an English doctor who had started general practice here told me that he had noticed the contrast. In England his patients had treated him as a man they had chosen for his character as well as his knowledge—a man who they believed would regard their problem as his own and personally shoulder their burdens. In a New York suburb, on the other hand, their manner was just what it would be toward an anonymous garage mechanic summoned to deal with a fault in the working of their car. They didn't mind what sort of a man he was. Keeping all responsibility themselves, they wanted only a technician who would explain what had gone wrong and ways in which it might be set right. Which was a pity, because the help people get from a physician depends largely on how they treat him.

For a person to be his own doctor, with a little technical advice now and then, is unwise for another reason. It means that he decides for himself when to see a specialist and which one to see. A very important function of the personal doctor, as I understand it, is to protect his patients from treatment they could do without or would be better without. Modern medicine is very clever; like so many people, I'm personally grateful for having my life saved by it. But it can also be a menace, especially if it is prescribed by someone who doesn't really know the patient and his circumstances. I may be biased, but I trust that any system adopted here will embody one of the good features of our British health service, which is that the patient does not see a specialist unless it is recommended by a general practitioner who has seen him first. This saves time, money, and disappointment. It is better for the patient, for the practitioner, and for the specialist too.

So I believe that the ideal arrangement, in this or any other century, is that everybody should have a doctor who really is his doctor—at any rate so long as they both shall live in the same place, which even here, I am told, is very often for several months at a time. If, in your cities, you eventually decide that medical care shall be given by groups at hospitals instead of by independent practitioners—and I'm inclined to think this a second-best solution—then I think you should still go to great trouble to see that the patient has a sharp and clear personal relationship with one member of the group rather than a hazy relationship with the group as a whole or whoever happens to be on duty. Specialist groups are fine for giving specialist care, but, almost by definition, they are incapable of personal care, which, as I understand it, is the care of a person by a person—by someone who accepts real responsibility for looking after his patient in sickness and in health. The internist member of a group has many technical advantages, but unless he really gets to know his patient and knows his patient's home too, he will still be an imperfect substitute for a family physician.

Hospital care

When the patient reaches a hospital bed, his home physician may no longer have charge of him. In that case, I would say, the hospital ought again to find a substitute. It ought to put the patient under the care of one physician who will be personally responsible for seeing that he gets the greatest possible benefit from his stay, that he gets all the investigation and treatment that he needs, and, still more, that he does not get some investigation which he does not need.

This kind of general protective care is quite different from the occasional visits of the expert on technic who may be going to do the operation or give the final opinion. The person who agrees to be the patient's hospital doctor must try to look at his needs as a whole in proper proportion; he ought to see him at least once a day and keep in touch if need be with his home physician and relatives. For these reasons the personal care of the patient in a hospital often may be undertaken best by relatively junior members of the staff—not by their seniors who are so commonly too busy for such details and are apt to look at patients only through a gastroscope, a cystoscope, or other instruments which give a partial rather than a comprehensive view of the patient's life.

But if I have emphasized the need for patients, in all phases of their illness, to have one doctor of their own and if I have said that one cannot expect the best kind of personal care from a group, this does not mean that the group, in a hospital or anywhere else, should be more impersonal than it can help. Nowadays a great many people in medicine seldom or never speak to patients at all; but, whether they do so often or seldom, anyone trained in or by the profession ought to acquire the professional feeling of personal responsibility toward the patient, as one human being to another, for whatever he does—whether removing the stomach, straightening a pillow, or doing a blood count. Although the hospital is the workshop of specialists, preoccupied with technics, nobody should ever come to think of the patient as a piece of material to be processed; he is a human being—a person, like you or me—not an example of disease. But that needs saying more perhaps in England than in this friendly country, where nobody is just an anonymous type. Even your gangsters, I'm told, put their names on their bullets.

Personal obligation of the physician

And what happens after the patient leaves hospital? Surely there is the same need for the continuous interested care of one person, again the patient's own doctor. Such work, with all it should imply in help to others, can be profoundly satisfying; for although people may have ceased to think of their doctor as a magician, in point of fact he can help them more than ever. The benefits of scientific advance are not confined to institutions, and today there are many kinds of effective treatment that the personal physician can use in his own practice, sparing the patient a visit to the hospital and the hospital a visit from the patient. Finally, when technics fail and the patient has to live with some disability or knows that his life is coming to an end, he wants above all the support of another human being—support which the physician may often give better than anyone else.

In the long run, I believe, the independent personal doctor will not survive at all, unless he concentrates on these things which no hospital can do as well as he can. And I would say that he should give up some of the things any hospital can do better. To survive, he will have to work out a new role based less on the specialist technics he learned in medical school and more on those that are necessary to his particular kind of practice. With a greater interest in preventive medicine, he should become, perhaps, more of a specialist in the art of living.

I am rather certain that, like the people of Athens in Saint Paul's time, we have lately been too much inclined to go out after "some new thing" and have been giving too little thought to the old needs which we aren't really meeting. One reason why so many people go to unqualified healers of one kind or another is that, having tried modern medicine, with its brisk impersonality, its production-line methods, and its rapid turnover, they find they prefer someone who may have odd ideas—a laying on of hands or a laying off of proteins—but who at least listens to all they have to say and seems to give his whole mind to their problem. Explaining why Western medicine doesn't always go down well in the tropics, Dr. Klokke says that Western-trained physicians commonly give an injection so as to close the interview and escape being involved in the patient's troubles. But many patients, East or West, get little help from their doctor unless he does become involved, and, if Western physicians won't do it, these patients would rather go to the witch doctor or the herbalist—in Manhattan as well as in Malaya. Your Dr. Peabody said it all in his famous remark that "the secret of the care of the patient is in caring for the patient."

How can the physician be expected to give this kind of care to anybody who may claim it? Like you or me, surely, he takes a dislike to the man who pushes in the subway or the woman who beats her husband! The answer, of course, is that he is, or should have been, conditioned by his training, with the result that, as soon as he accepts someone as his patient, a quite fresh relationship is established. From the moment the tiresome woman becomes a patient, he is governed by certain inhibitions and certain obligations, as if by a change of mental gear, he ceases to be an ordinary person, with prejudices and easy hostile judgments, and becomes instead her physician, committed to doing his best for her as he sees it. Sometimes this professional relationship is frankly impossible, because one party offends the other too deeply. In which case they must part. Or, all too often, the physician, although he is prepared to take an interest in physical disease, cannot or will not achieve sympathetic understanding and show himself a friend; in which case, although the doctor-patient relationship is correctly preserved, it is too impersonal to be therapeutic. But if the physician is so good a doctor as not to be put off by weakness, folly, grief, sin, or even bad manners, if he places himself at the patient's side, and if he puts the patient's interest before his own, the relationship can be something invaluable. The perfectly perfect physician wouldn't merely like all his patients some of the time or some of his patients all the time; he would like, or at any rate tolerate, all his patients all the time—something even harder to attain than democratic government.

Our medical schools are quite good at giving the future doctor an objective outlook which enables him to keep his head when he is faced with wounds and death, with accident, mania, or disaster. And this is very valuable, indeed essential. But the teachers and the schools will have to decide whether they are content to produce a poker-faced technical expert who will attend to the faulty body as a garage technician attends to a faulty car or whether, even in the modern world, they should still be producing doctors who will feel the same kind of personal obligation toward their patients as was felt by the old physicians. For my own part, I hold that our training lately has been far too much concerned with the body. And in this it is patently old-fashioned. An education which is truly based on science as it has latterly advanced would pay far more attention to the emotions of the patient.

All human relationships demand the repression of some feelings and the cultivation of others, and, as I have said, we are always changing gear as we pass from one relationship to another. To achieve his side of the best kind of doctor-patient relationship, the medical student needs not only a social instinct of toleration and a real desire to help, but also, as I have said already, a fundamental conditioning which takes a very long time. He has to learn to forget himself in the physician, but the physician he becomes must still be a person with a heart as well as a mind, ready to give himself as well as his knowledge.

If this is an ideal to which nobody can attain all the time, it is nevertheless an ideal which has been very powerful in medicine. And it is hardly compatible with the opinion, so often implied, that an essential bond between doctor and patient is a fee for every service rendered. Our medical profession, as W. H. Hamilton told the Committee on Medical Care thirty years ago, has moved "into an epoch in which it has had to make its terms with, to employ pecuniary devices from, and respond to the incentives of, business. . . ." Consequently we may take time to get back to the older tradition in which the service to the patient was always what mattered and the fee, if any, was an honorarium—perhaps only a present to a temple. In the medical profession, as in the lobster, old shells sometimes have to be shed before the new ones grow; maybe the old generation must pass before the new one arises. But meanwhile we needn't pay too much attention to those who say that the instinct to help other people—the wish to apply medical knowledge and skill for their benefit—will wither away unless it is refreshed repeatedly with cash rewards for every task performed. I am all for doctors earning a proper livelihood, but the science and practice of medicine are really much more interesting and attractive, in themselves, than one might suppose from the statements which are made sometimes on behalf of our profession.

Conclusion

Returning to my main theme, I would say this. In planning your development you may be tempted to follow the national genius and put all your money on technology. But, even in these United States, you have a population which is backward in that it consists of human beings with a long racial experience of life in circumstances quite different from those of Lower Manhattan. If people were ever industrial robots, they might need no more than technologic medicine. But actually they are not, and I reckon never will be, and even in the most highly developed parts of the world they still need personal medicine too.

It is because they are aware of this that older people look back wistfully to the horse-and-buggy doctor. I know the horse has died, and the buggy has fallen to bits. But we still have the doctor. And, adapted to modern conditions, he could often, if we wished, be the patient's own doctor—and much the more useful for that.

Some Shifts in Emphasis Between Teaching and Research in Our Medical Schools

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IN A FREE SOCIETY such as ours, the ultimate distribution of manpower is determined by a host of factors, many of which are poorly understood. Presumably the ultimate determinant is the need, or perhaps better, the collective wishes of society. How the latter are translated into actual changes in manpower distribution is understood only partially and is an important research area in sociology.

In the field of medicine and medical science within the past two to three decades, it appears that certain forces have been operating which tend to create some problems for us today. The attractiveness of the whole field of medicine as a career appears to have fallen appreciably as is evidenced by the number of applicants presenting themselves to the nation's medical schools for admission each year. Despite the population increase and the increased enrollment in colleges, the actual number of applicants to medical schools has fallen since the immediate post-World War II period. This has been discussed in other papers and will not be enlarged on here, but the over-all effect is a scarcity of well-qualified applicants to the nation's medical schools at a time when there is general agreement that the total need for physicians and others within the area of health manpower has increased greatly. For this reason, the distribution of effort within the limited group available becomes of increasing interest.

Increase in medical research

Probably the most striking change that has taken place in recent years is the explosive and continuing increase in medical research. This can be measured in many ways: in dollars invested, numbers of people involved, papers published, true advances achieved, and so forth. By any criterion the expansion of effort has been phenomenal. This, I am sure, is a reflection of public interest. The people and the Congress have learned that the fruits of medical research touch on everyone and are central to prosperity and the pursuit of happiness. In fact, it is probable that many people have an exaggerated notion of what can be accomplished by the simple expenditure of additional funds in crash programs. Nevertheless, there has been very great pressure from all sides for increased efforts in the solution of problems related to "the dread diseases." There can be no doubt that the availability of large sums for research has had a powerful influence on the activity of faculties and student bodies in our nation's medical schools.

In former times most medical students who were in financial need took the summer off and worked at odd jobs unrelated to medicine to make ends meet. Now funds are available which allow these students to pursue research projects during their free time and to be paid at least a modest living wage while doing so. The ranks of faculty members in our medical schools have been swelled tremendously during the past two decades, in part through funds available in increased hard core budgets of the schools, but to a much larger extent by monies made available through research grants, research training grants, and the like. The Federal government, because of restrictions in the legislation, has not been allowed to expend monies for straightforward educational purposes, although it must be understood that these faculty members, supported in part or in full by funds earmarked for research, are not expected to devote 100 per cent of their time to that activity. It is clear that teaching and research in most cases go hand in hand. Nevertheless, by law the emphasis must be on research, and the renewal of the grant depends on the satisfactory performance in research.

Another academic fact of life, which is not new, but which has probably been receiving increasing emphasis in recent decades, is that academic promotion is geared more closely to research output than to any other single factor. This is entirely fitting and proper as a general principle, and no one would argue that basic research should not be a prime concern of our universities. At the same time, it cannot be the only concern, with teaching looked on solely as a "load" while research is described as an "opportunity." Both are opportunities, and each in its proper balance is absolutely essential to the ongoing health of our institutions of higher learning.

Career choices are made for a variety of reasons, but there is no doubt that students tend in many instances to emulate their teachers. It is hardly surprising, therefore, that with medical faculties composed predominantly of physicians engaged in academic research and recognized primarily for their accomplishments in investigation, their students should tend to follow in their footsteps when possible. Until recent times a career in academic medicine was reserved for the very small group of dedicated teacher-investigators who sought this life largely because of the intellectual stimulus and usually despite the expectation of very modest financial reward. In fact, until recently, a fairly high proportion of such individuals depended on independent incomes for the maintenance of their families. Although incomes in academic medicine cannot be described as lavish at the present time and, as a matter of fact, further improvement in this situation is needed, nevertheless, it is possible now for young men and women to look forward to a career in medical research even though they have no outside financial support.

Balance of teaching and research

The result has been the gradual trend for more and more people to devote their major time and effort to medical research. The effect in general has been healthy, I believe. Further increases in our research effort are clearly desirable, provided the quality of the research training and the research work can be maintained and so long as the shift of emphasis in a limited pool of medical manpower does not become excessive. As mentioned previously, teaching and research cannot be separated if the health of society is to be maintained. Teachers can rarely be effective for many years if they are removed from the research environment; the field is simply moving too fast. Furthermore, the inquiring mind is an essential prerequisite of a good teacher with the result that the best teachers inevitably desire opportunities to pursue their own research. Hence, one must look on teaching and research not as a dichotomy or as mutually competitive fields, but rather as a composite and inseparable unit.

All that is needed is a balanced recognition, both financially and in academic rewards, for the teaching aspect.

Nursing Care Manpower: How Much and What Kind?

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THE GROWING DILEMMA of health manpower needs is the inevitable result of the rapid population increase with its growing per cent of older people and of the increase in scientific knowledge and the demand of the people for the services required for the application of such knowledge. Highly significant, too, is the fact that patient care is provided by a growing number of types of health personnel and the relationships that have developed among them. Increasing concern for the world's health is a factor in the problem of supplying sufficient manpower to serve needs in this country with a reasonable degree of adequacy.

It is my judgment that the problem of nursing will not be solved by a continuing emphasis on quantity alone. The shortage is a fact. There are aspects to this shortage that relate to quantity, quality, and utilization. These factors go beyond nursing personnel to the usability of allied personnel employed in the institutions offering nursing service. Nursing expands or contracts, especially in hospitals, depending on the availability of others such as dietitians, housekeepers, ward clerks, and messengers. The vanishing of interns in many hospitals is now posing new problems. Who will take up the activities formerly carried by them? What is the potential limit of recruitment into health services and into nursing in particular?

Health manpower problem increasing

The United States Census of 1940 reported just over 1 million persons employed in the

TABLE I. Estimates of professional nurses employed full and part time in the United States, by field of nursing, as of January, 1958 and 1960[1]

Field of Nursing	1958	1960
Hospital and related institutions	291,500	325,000
Private duty	70,000	70,200
Office nurses	37,000	40,000
Public health	28,700	32,400
Occupational health	18,400	18,500
Nursing education	12,400	14,200
Other	2,000	3,700
TOTALS	460,000	504,000

health services industries. Ten years later this figure had increased to 1.6 million, and it appears from the 1960 census that the number has increased to 2.5 million. Among some 18 occupational groups identified by the U.S. Census as engaged in the health services industry, nursing encompasses the single largest group numerically. Within nursing, there are about 500,000 registered nurses. And in the hospitals alone another 470,000 auxiliary workers are employed. If we consider the supply of registered nurses in relation to population, we now have 282 nurses per 100,000. To maintain this ratio as the population increases, it is estimated that 100,000 more registered nurses will be needed by 1970 or a group totaling 605,000. At present more than one fourth of our states have a supply of registered nurses equal to over 300 per 100,000 population, a few have over 400, and still a shortage is claimed. Of the estimated 504,000 currently active nurses, 90,000 are known to be working part time. The actual number may be greater. This nurse force is spread through many types of agencies (Table I).

How nurses are employed

Although hospitals and related institutions still claim the services of more than 60 per cent of the nurses, the trend in percentage distribution of nursing personnel in hospitals is significant (Table II).

TABLE II. Percentage distribution of nursing personnel in hospitals

Personnel	1940	1950	1960
Registered nurses	45	39	30
Practical nurses	8	13	17
Aides	47	48	53

It will be seen that during these twenty years the picture in the nursing management of patient care has changed. The shortage of registered nurses, which became pronounced after World War II, has continued in spite of the fact that larger numbers of students have been and are being recruited for nursing education. During 1960, 49,787 new students were admitted to hospital, college, and junior college schools of nursing, an increase of almost 2,000 over 1959. Admissions to practical nurse schools for the same period showed a slight increase of 200, a total of 23,778.

The introduction of the vast number of auxiliary personnel has introduced a marked change in the responsibility of the nurse. The registered nurse not only must plan for the understanding care of the human needs of patients and the faithful carrying out of the physician's therapeutic orders, her traditional role, but also now imperative is the complex supervisory, teaching, and coordinating functions of creating a team of the several levels now encompassed in nursing personnel, especially in hospitals.

As more nursing in the home is provided, this same team-type of organization for nursing service will extend into the field of public health nursing. Public health nurses, as more independent workers, are better prepared to handle this situation as it increases to meet the continuum of care from hospital to nursing home to natural home. By and large, hospital nurses have not been as well prepared to meet the changes in patient care, to accept the transfer of many complex tasks from doctor to nurse, and to manage without disruption the changing relationships with more articulate and ambulant patients and with the auxiliary personnel who share nursing care. There is a conviction among most thoughtful nurses that the organization of nursing for good quality nursing care must be studied and that more nurses must be prepared to assume the complete range of nursing responsibility. A possible better ratio to aim for of registered nurses to practical nurses and aides might be 50 per cent registered nurses, 30 per cent practical nurses, and 20 per cent aides.

Among the aides should be ward clerks and messengers, to leave the leader nurse, by whatever name she is called, free to assume the responsibilities for direct patient care and for the direction of assisting persons. In the light of the changes in patient care, along with the several groups providing nursing service, where will we find this leader nurse?

Recruitment potential

Over a period of years, professional nursing education has attracted around 3.4 per cent of the seventeen-year-old girls of the country. If by 1970 the aim is to maintain the present ratio of 282 nurses per 100,000 population, the same percentage would need to be attracted each year. Is this enough?

A rather careful estimate of need projected to 1970, based on expected increases in hospital beds, in nursing homes, and the vacancies now in existence, would seem to justify a higher ratio of nurses to population, even to the ratio of 375 per 100,000. Using a midway goal of 310, it would be necessary to recruit 4.5 per cent of the seventeen-year-old girls of the country.

Obviously, the problem revolves around the capacity of the schools and the availability of faculty to serve the students admitted and the possibility of attracting a larger per cent of the young people into nursing education programs. It also revolves around a judgment as to the realistic plan for the education of nurses to assure the quality of patient care which is essential to help each person to maintain health and to recover from illness to the maximum of his potential recovery.

In 1958 the National League for Nursing through an interprofessional committee projected goals for the education of nurses, accepting as the point of departure the existing patterns through which our immediate supply must come. The committee analyzed the situation in terms of the degree of leadership or relative independence inherent in each of these special environments through which nursing reaches the people.

In projecting the type of education deemed to be suitable to prepare nurses, the currently available educational patterns were matched with the responsibility for which nurses need to be prepared (Table III).

TABLE III. Education for responsibility for which nurses need to be prepared[2]

Responsibility	Education
Group I	
Professional nurses who give direct care to patients under supervision	Diploma or associate degree program
Group II	
Professional nursing personnel who hold positions ranging from hospital head nurse and public health staff nurse through service and education administrator	Baccalaureate degree program which lays the foundation for such functions and for graduate study
Group III	
The portion of Group II nurses who become teachers, supervisors, administrators, and consultants	Master's or doctoral degree, study in a functional or clinical area or both

Much experimentation is taking place in curriculum development and improvement of teaching methods. The length of the several education programs is being studied. The needs are about equal across the three groups in Table III, but the crucial need is for faculty and other leaders who are broadly prepared to assume the creative leadership to safeguard today's needs as best as can be and to move us toward the future with wisdom. It must be recognized that a change in practice brings about a change in education in all fields.

Comment

This is a brief discussion of a very complex problem. There is an urgent need for physicians, nurses, hospital administrators, and others dependent on nursing service to assess the situation with objectivity and with some confidence that disruptions need not be the result of reforms. Nurses individually and as a group have deep concern for improving the health care system in an era of costly new technology and mass consuming demand.

I summarize this discussion by giving my firm conviction that nursing service for patients will improve to the extent that fewer layers of personnel are involved in patient care.

I believe there is urgent need for pilot experimental studies, well supported as are some of the studies of the preparation for future physicians. Practical nurses are saying they are not prepared for the tasks they are assigned to perform. Is there need for one-year, two-year, or three-year programs? Could a competent nurse technician be prepared in so many months or so many years of time, eliminating one layer of personnel giving direct patient care? How fast can an adequate proportion be prepared in college programs from which the leadership group will be drawn?

These are some of the issues before us to assure sufficient nurse manpower for the future.

References

1. American Nurses Association: Facts About Nursing, A Statistical Summary 1961 Edition, 1961, p. 8.

2. National League for Nursing: Nurses for a Growing Nation, 1958, p. 23.

Intracardiac illuminator

A new instrument developed by the American Optical Company in conjunction with the Center's Surgical Research Laboratory enables surgeons to seek out and repair heart defects otherwise not visible. The development project was carried out in cooperation with William F. Bernhard, M.D., and Robert E. Gross, M.D., of the Children's Hospital Medical Center in Boston.

Development of the "cold light," called an intracardiac illuminator, was stimulated after the death of a patient who underwent surgery for closure of a ventricular septal defect. During the operation, one hole was seen and repaired in the interventricular septum between the lower chambers of the heart. When the patient was removed from the pump-oxygenator, the heart failed. Later, it was found that three more holes existed in the interventricular septum but had not been seen during surgery. These defects were hidden in the muscular portion of the septum and were not adequately illuminated by the standard operating room lights.

The intracardiac illuminator is composed of a bundle of tiny, hairlike glass fibers in a catheter. The fibers are capable of conducting a beam of light from a distant power source. A pencil-sized probe attached to the flexible light-pipe permits the surgeon to make a detailed inspection of the heart's interior.

Not only does the instrument illuminate the heart chambers and valves, but it also permits transillumination of the muscular and fibrous septum which separates the right and left sides of the heart.

Clinical use of the intracardiac illuminator follows the connection of the patient to the heart-lung machine. With the heart stopped by perfusion of the coronary arteries with cold blood, a small incision is made in the right auricle. The surgeon passes the illuminator probe through the incision into the right ventricle.

After defining the size and shape of the hole in the ventricular septum, the surgeon must determine whether additional defects are present in other areas of the septum. To accomplish this, the illuminator probe is passed beneath the septum to permit transillumination of this structure. Any light which shines through the septal wall immediately indicates the presence of an additional hole needing repair.

Special Article

Writing Style Indicated for Scientific Medical Literature

Some Considerations

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UNDOUBTEDLY, one of the more common complaints with regard to the current scientific literature is that it is "stuffy," unreadable, and, in general, poor competition for the popular reading found in such contemporary magazines as *The Scientific American*, *Fortune*, *Time*, and so on. There are individuals who would make the scientific literature more readable by utilizing lay journalistic technics, applying the "fog" index, or employing such style as that of the *New Yorker* to medical writing.

Other persons cling tenaciously to the precise format of the medical literature of the present and the recent past. And, of course, there are moderates who seek a middle-of-the-road style of writing which might satisfy both extremist camps.

It was the purpose of this survey to consider which of the two styles—the current, detailed, perhaps on occasion dull but obviously disciplined scientific style, or the so-called lay press style—seems to the scientific professions to represent the basic approach from which any consideration of a revision of the literature's style should be undertaken. In other words, which should serve as the base line for revision: the scientific literature as it stands today or a completely modernized stylistic approach? And, further, it was our purpose to consider whether there might, in fact, be a middle-of-the-road approach.

Method

Two expositions of a short scientific experiment which were published as part of an editorial in *Science*** were chosen as the basis for this survey. The two versions of a brief "scientific" investigation, exactly as they appeared in *Science*, appear as Style A and Style B.†† Admittedly, the expositions are caricatures of the literature, but as such they provided a very useful starting point for this survey, notwithstanding and perhaps even because of their exaggerations.

For the purpose of providing a middle-of-the-road version, the information supplied in one or the other of these two versions was reworded into a form (Style C) which reads, we believe, as it might actually appear (again in caricature) in the medical literature, combining therein information from version A which might make the article more readable and interesting with information from version B which would present a more precise

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This report was prepared by the Scientific Manuscripts Committee of the American Association of Dental Editors whose members and others are the authors of this report. This article was prepared for presentation before the annual meeting of the American Association of Dental Editors, October 14, 1961, in Philadelphia, Pennsylvania.

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** Editorial: How to be interesting though factual, Science **126**: 901 (Nov. 1) 1957.

†† Reprinted from *Science* by permission.

scientific exposition of the experimentally obtained data.

A questionnaire dealing with the three versions thus prepared, and included therewith together with the original editorial in *Science*, was addressed to a group of investigators selected at random from among authors of lead articles that had appeared recently in leading medical and dental journals. The sample was taken by searching the current periodical stacks of a major medical library for the authors of lead and second articles appearing in journals other than local bulletins which are published in the United States. Only publications of at least 40 pages in length were searched. Where an address for the author of the lead article was not obtainable readily, this author was passed over in favor of the next. The preparation of the otherwise unselected list was continued until 396 names had been entered.

Each recipient was requested to peruse the three versions of the "manuscript," answer the questionnaire, and return it to us in order that their replies could be tabulated and eventually submitted for publication in a suitable scientific journal.

Examples

STYLE A. Ordinarily, determining whether an egg is cooked or raw, without breaking the shell, poses no special problem. But suppose that several hard-boiled eggs, now cooled, are inadvertently mixed with several raw eggs. How then would you tell them apart? The following method requires no special equipment, only the application of a well-known physical principle. Place each egg on its side and attempt to spin it. If it spins easily, it is cooked; if not, it is raw. Raw eggs do not spin readily because the rotational energy is dissipated in the egg's interior, as dictated by the hydrodynamics of viscous fluids. To confirm the method, break the eggs.

STYLE B. Twelve white eggs were purchased at a supermarket. The eggs were divided into two groups of equal number. The eggs in the first group were boiled seven minutes and allowed to cool; the eggs in the second group were kept as controls. The eggs were mixed. Each egg was placed on its side, and an attempt was made to spin it, after which the egg was broken. It was easy to spin those eggs that subsequently were found to be cooked, but difficult to spin those eggs that proved to be raw.

STYLE C. During the course of experimental studies concerned with the effect of heat on the chicken egg, it was found that occasionally, inadvertently or otherwise, groups of unidentified eggs became mixed. It thus seemed a matter of some importance to determine a reliable test procedure for resorting the experimental material without breaking the shells, which would, of course, destroy the test objects themselves. The spin test was suggested as a sorting technic requiring no special equipment, only the application of a well-known physical principle.

It was the purpose of this study to determine the usefulness of the spin test for ascertaining whether an unbroken egg is cooked or uncooked.

Method. Twelve white, supermarket eggs were divided into two groups of equal number. Six of these were boiled for seven minutes and allowed to cool. Six were kept as untreated controls. The eggs were then mixed "blind."

Each egg was placed on its side and an attempt made to spin it, after which the egg was broken.

Results. Six eggs could be spun readily. All six, when opened, were found to be cooked. The remaining six eggs could not be spun readily; all six of these, when opened, proved to be uncooked.

Discussion. Consideration of the data obtained above suggests that the differentiation between the cooked and uncooked eggs is probably based on the principle of hydrodynamics of viscous fluids which would indicate that a raw egg does not spin readily because its rotational energy is dissipated in its interior.

Summary. A controlled study, undertaken to consider the reliability of a technic for separating cooked and uncooked eggs, revealed that such a differentiation can be made readily by the spin test.

Results

A summary of the information derived from the 115 replies received is presented herewith:*

1. Which of the presentations do you believe to be more appropriate for the presentation of material in the medical literature? A–24, B–16, C–69.
2. Do you object to A? Yes–51, No–55. If so, slightly–21, moderately–18, greatly–12.
   Do you object to B? Yes–81, No–23.

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* A variety of combinations and occasionally inconsistent answers were encountered; for example, not infrequently respondents did not answer all questions, answered more than one portion of a question affirmatively, or replied to one section of a query but not to another.

If so, slightly–18, moderately–31, greatly–31.
Do you object to C? Yes–41, No–48.
If so, slightly–10, moderately–14, greatly–18.

3. If you have indicated that you preferred A, are there ever any situations in which the use of B is indicated in reporting scientific data? Yes–12, No–16; the use of C is indicated in reporting scientific data? Yes–26, No–4.
4. If you have indicated that you preferred B, are there ever any situations in which the use of A is indicated in reporting scientific data? Yes–15, No–4; the use of C is indicated in reporting scientific data? Yes–11, No–7.
5. If you have indicated that you preferred C, are there ever any situations in which the use of A is indicated in reporting scientific data? Yes–47, No–19; the use of B is indicated in reporting scientific data? Yes–33, No–30.
6. Do you believe that there is a middle-of-the-road style of writing between the two extremes (A and B) presented? Yes–88, No–25.
7. If yes, which of the three versions would it be closest to? A–24, B–12, C–42.

Please be sure you have answered the preceding questions before reading the following ones!!

8. Should "lay press" expositions of the contents of an article be confined either to boxes at the beginning of articles, introduction sections, or discussion sections, thus leaving intact the "classical" reporting of the experimental procedures utilized? Yes–73, No–32.
9. Do you feel that the use of the "classical" style for the reporting of a study connotes a disciplined scientific approach whereas a lay press approach might perhaps have disastrous effects if it had been carried over by the investigator to the conduct of the experimental portions of the study? Yes–76, No–22.

Assuming that the same information was available for writing all three versions (A, B, and C), please answer the following questions:

Which version:

10. is the most informative? A–13, B–13, C–89.
11. is the most interesting? A–75, B–11, C–29.
12. is the most readable? A–83, B–16, C–17.
13. would permit the reduplication of the study in your laboratory the most easily? A–4, B–18, C–93.
14. left you the most satisfied? A–26, B–17, C–65.
15. left the least doubt in your mind as to:
    (*a*) the applicability of the test to the problem? A–21, B–17, C–74.
    (*b*) the reliability, usefulness, and precision of the technic? A–9, B–13, C–93.
    (*c*) the reliability of the investigator? A–18, B–15, C–86.
    (*d*) the scientific training and the command of experimental technic of the investigator? A–9, B–14, C–92.
    (*e*) the precision with which the experiment was carried out? A–4, B–13, C–95.
    (*f*) the authenticity of the results? A–7, B–16, C–94.
    (*g*) the appropriateness for the scientific literature? A–12, B–15, C–82.

Now that you have further considered the three versions with additional specific thoughts in mind (questions 8 to 15) and in the light of these answers, may we ask you again to evaluate the three versions as to the following:

1. Which of the three presentations do you believe to be more appropriate for the presentation of material in the medical literature? A–21, B–16, C–78.
2. Do you object to A? Yes–65, No–40. If so, slightly–27, moderately–23, greatly–15.
   Do you object to B? Yes–79, No–25. If so, slightly–14, moderately–28, greatly–33.
   Do you object to C? Yes–34, No–54. If so, slightly–11, moderately–13, greatly–10.
3. If you have indicated that you preferred A, are there ever any situations in which the use of B is indicated in reporting scientific data? Yes–9, No–10; the use of C is indicated in reporting scientific data? Yes–12, No–9.
4. If you have indicated that you preferred B, are there ever any situations in which the use of A is indicated in reporting scientific data? Yes–15, No–4; the use of C is indicated in reporting scientific data? Yes–12, No–5.
5. If you have indicated that you preferred C, are there ever any situations in which the use of A is indicated in reporting scientific data? Yes–50, No–24; the use of B is indicated in reporting scientific data? Yes–33, No–40.
6. Do you believe that there is a middle-of-the-road style of writing between the two extremes (A and B) presented? Yes–79, No–26.
7. If yes, which of the three versions would it be closest to? A–23, B–19, C–38.

Conclusion

We feel that a very substantial majority of respondents were of the opinion that the currently accepted style and format for manuscripts appearing in the scientific literature should remain essentially intact, but that the interest of such articles could and should be augmented by the insertion, in suitable portions of the text, of informative material presented in a more readable manner.

Comment

We apologize to the editors of *Science* for excerpting material "out of context" from their editorial. This editorial was intended primarily to suggest a method for developing a sense of purpose in technical reports. We are anxious to point out that there is no intent to be critical of this need as suggested in the editorial, nor is there any intent to imply by this survey that the editorial was in error in suggesting that the way to get people who begin reading a paper to finish it is to develop such a sense of purpose.

Our studies in this area of investigation are being continued.

Summary

A questionnaire survey was sent to 396 authors of leading articles appearing in the medical and dental literature dealing with their opinions on "Writing Style for the Scientific (Medical and Dental) Literature."

A summary of the information derived from 115 authors who replied suggested that a very substantial majority of respondents were of the opinion that the currently accepted format for manuscripts appearing in the scientific literature should remain essentially intact, but that the interest of such articles could and should be augmented by the insertion, in suitable portions of the text, of informative material presented in a more "readable" manner.

630 West 168th Street, New York 32

Drug costs reduced by competition

Competition explains why antibiotics now cost about one fifth of what they cost a decade ago, on the average. It explains why penicillin prices are now 5 per cent of what they were after World War II. It explains why insulin costs 6 per cent of what it cost thirty years ago; why streptomycin prices dropped 40 per cent in less than a year; and why Salk vaccine prices have been cut in half. Chemotherapy has helped bring good health to 3 million Americans who wouldn't be alive today if prewar rates still applied.—*Edward R. Annis, M.D., in Medical Economics, July 17, 1961*

Industrial Health and Workmen's Compensation

ROBERT KATZ, M.D., Director,
Bureau of Industrial Health and Workmen's Compensation
PETER J. DINATALE, M.D., Chairman,
Council Committee on Industrial Health
CARL F. FREESE, M.D., Chairman,
Council Committee on Workmen's Compensation
Medical Society of the State of New York

Union Health Centers and Their Relationship to Occupational Health Programs

ALTHOUGH THE oldest union health center in the United States dates back to 1913, most health centers were organized during recent years. With the advent of World War II and the widespread adoption of health and welfare programs through collective bargaining, a new stimulus has arisen for the establishment and expansion of union health centers.

This survey attempts to study the services offered by selected union health centers and to correlate them to the objectives and functions of occupational health programs established by management. Special emphasis was placed on such questions as: Does the union health center supplement the occupational health program? Does it interfere with it, duplicate it, or compete with it? The effects on the patients' health and on private and public medical services in the community were considered beyond the scope of the present study.

Function and services of health centers

All the union health centers selected for this study are located in a large metropolitan area and provide nonoccupational medical services to members and/or their dependents. The costs for such services are paid from union welfare funds contributed by management. Each center was visited, and an interview was arranged with the medical director or senior administrative officer. A tour of the center and its facilities was made, and operational data were obtained wherever they were available.

Union health centers were established primarily to offer medical services to union members. However, all but one center in this study extended its services to the spouse and/or other dependents of union members. Nine union health centers were surveyed, serving a total of about 180,000 members and 550,000 dependents (Table I). Membership in union health centers ranged from 2,000 to 50,000. None of the centers rendered care for compensable disorders. Only two centers are utilized for preplacement physical examinations, such services constituting only a small portion of the total services rendered. It may be noteworthy that the centers that did offer such services were directed by physicians trained and experienced in preventive and oc-

TABLE I. Survey study of nine union health centers

Center	Number of Members (Thousands)	Service for—		Services (Per Year)		Utilization (Proportion of Members)	Medical Staff			Remarks
		Spouse	Other Dependents	Diagnostic	Therapeutic		Full Time	Half Time	Part Time	
1	50	X	X	144,000	559,000	1/2	10	7	110	
2	35	. . .	. . .	55,280	22,979	1/3	1	. .	76	Preplacement
3	33	X	. . .	854,901	824,337	1/3	1	. .	70	
4	30	X	. . .	41,632	32,134	1/3	. .	. .	55	
5	10	X	X	5,800	. . .	1/2	. .	. .	6	
6	10	X	X	48,863	28,351	1/2	1	. .	40	
7	8	X	X	5,579	. . .	1/3	1	. .	20	Industrial engineer, preplacement.
8	2	X	X	5,250	5,000	1/2	. .	. .	6	
9	2	X	X	Not available	Not available	1/3	. .	. .	4	

cupational medicine who had medical experience in the industry served by the union membership. The background of the other directors varied from general practice to surgery, orthopedics, internal medicine, and obstetrics and gynecology.

Four of the centers established by unions with a membership of less than 10,000 limited their services to diagnostic procedures only. The remaining five union health centers rendered diagnostic as well as therapeutic care to ambulatory patients. The services of an industrial engineer were available at one center only and were utilized as required to make inspection tours in cooperation with the medical director.

The rate of utilization varied from one half to one third of the eligible members. Only one center offered services during hours which did not interfere with regular working hours. Although few unions had retired members at the inception of their union health center, the number of retired members is increasing steadily, and the number of services rendered to such members is on the rise. With this shift in the character of our population, increasing more rapidly at both ends of the scale, and the prospect of increasing demands on union welfare funds, one might readily surmise that any program of subsistence from any source, voluntary health agencies, or State or Federal government would gain the support of those charged with the administration of union welfare funds.

The physical layout of most of the large centers is quite impressive, and many of them are operated with a fair degree of efficiency. Attempts are noticed to abolish the "clinic atmosphere" and to give the impression of private personal services. Several facilities are equipped with modalities for which there is very little need or use and for which there is a lack of skilled personnel to effect their operation. Thus, the need for a deep roentgen-ray therapy unit in a union health center can be seriously questioned in the face of inadequate facilities for the examination and the reading of routine chest films. Similarly, the presence in one center of two operating rooms equipped for major surgery seems rather extravagant. Although staffing with medical personnel rarely presents a problem, there is at times a shortage of ancillary medical personnel. Combined with underutilization of equipment, this can create an impression of inefficient planning and management. Under these circumstances, the merging of several facilities into one unit may provide a way toward better utilization of personnel and equipment but may lead to insurmountable organizational difficulties.

Comment

Union health centers are the result of the organization of groups of consumers of medical care to arrange for a high quality of comprehensive medical coverage at a reasonable cost without the utilization of previously existing insurance plans (Blue Shield, and others) or facilities (municipal and voluntary hospitals). Thus, a certain number of patients are removed from private and public care institutions and are shifted toward union health centers.

It would be interesting to compare the general health and the improvement of health status of people cared for in the union health center with a similar population group which does not have the benefit of union health care. One could also speculate as to the effects on medical education and research which may or may not benefit from the availability of a fairly homogeneous group of patients of similar socioeconomic background at any one center. The task of evaluation of these aspects of union health center care is a difficult and time-consuming one, and it was not pursued in this study.

The enforced allotment of certain sums of money for health care does not appear to have caused any resentment from the affected people. Since management, which contributes the total cost of union health care, passes this cost on to the consumer, one may question the fairness of the utilization of such funds for the benefit of a select group, the union membership, rather than for the benefit of the entire community of consumers.

Assuming that a large proportion of patients who avail themselves of the service of the union health center would otherwise require the care of "free clinics" at the expense of the public, one may also question the savings in taxpayer contributions which would go toward the maintenance of free municipal clinics which seem to lag behind the increase in the cost of consumer goods attributable to union welfare funds. Admittedly, it is impossible to place an exact value on the good will created by the establishment of union health centers or on the ego satisfaction of the member which may come from attendance at a health center established by his union, compared with the misgivings which he may have in attending a "free clinic" at a municipal hospital outpatients department. Few patients can appreciate the quality of the medical care received or the skill, training, and knowledge of those physicians who minister to them. Although the care received by many participants may not measure up to the expectations, it seems to fill a need of many who, through sheer apathy and ignorance of available community facilities, might go without adequate medical care.

Summary

From the information gathered in this survey, one can conclude that the services offered in most union health centers neither duplicate nor interfere with inplant occupational health programs. The centers could be utilized to supplement such programs, but generally they do not stress the preventive health aspect which is one of the major responsibilities of any good inplant health service.

BILLSBORD

Abandon ye Hippocrates!
  Forget Galen, Hunter, Rush, and Holmes
Lister and Harvey,
  Pasteur, Osler, Pare, Jackson, and Soames
McDougall and Ehrlich,
  Jenner, Bright, Reed, Banting, and Best
Wraiths of the Past!
  Aye, what though we befoul our own nest
A new frontier opens,
  With shining new names and so ye behold
As Messrs. Reuther and Cohen
  Wondrously reveal—as man lives he grows old.

We must admit puzzlement as to the current emphasis on what the consumer wants. This is followed usually by plans for a survey. We have never felt any need for either survey or crystal ball about this matter; for what the consumer wants is Sak's Fifth Avenue service, Macy's inventory, and Sears-Roebuck's prices.

* * *

Couldn't help being intrigued by *Time's* recent subtle pitch for a national health program through the lips of many Englishmen all griping about some facet of their National Health Service but all ending with the declaration they couldn't do without it. This sort of argument could make narcotic addiction acceptable if not advantageous.

* * *

To the physician, old age is an individual accomplishment, to the social planner, it is a group disability.

* * *

We see no significance in the fact that both the surgeon and the burglar use gloves when they work anymore than in the fact there is another profession besides psychiatry that uses a couch to make a living.

* * *

In the unfortunate event that the American people become the victims of some universal health plan under government control, it might well be described by some future historian as follows:

Socialized medicine came to these United States in the middle of the twentieth century:

not as a result of the piteous demands of a large segment of the population left to suffer and die because of lack of funds, until government had no recourse but to establish it;

not because of the brilliant campaign and arguments of its socialistic proponents;

and not due to the demands of a medical profession infested by that strange epidemic of the period characterized by complete absorption in and almost fanatic veneration of security;

but it did come about through this commonplace happenstance: though man as he ages loses his teeth, hair, and at times his memory, he never loses his vote.

* * *

Relative value schedule: (From advertisements in a recent issue of *Hobbies*.)

For Sale—Phi Beta Kappa Key, $12.50.

For Sale—Copper still, not in working condition, as is $18.75.

* * *

We are happy to announce that there will never arise any serious question in this corner about censorship in any of its diverse forms. An agreement has been reached: the Editor allows me to write what I please and I allow him to print what he pleases. Simple but so is,

WRC

Medical Communications Day

SATURDAY
MAY 19, 1962

STATLER HILTON
New York City

sponsored by

NEW YORK STATE JOURNAL OF MEDICINE
Official publication
Medical Society of the State of New York

and

AMERICAN MEDICAL WRITERS ASSOCIATION
Metropolitan New York Chapter

Morning Session

William Hammond, M.D., Scarsdale
Editor, New York State Journal of Medicine, *Presiding*

9:00 A.M. Registration

9:30 A.M. Welcome

Russell L. Cecil, M.D., New York City
President, Metropolitan New York Chapter,
American Medical Writers Association

9:40 A.M. Panel: **New Frontiers in Medical Communication**

Henry I. Fineberg, M.D.
Executive Vice-President and Past-President,
Medical Society of the State of New York, *Chairman*

1. **Communications Systems for Medical Practice**
   Lee B. Lusted, M.D., Rochester, New York
   Professor of Biomedical Engineering and Associate Professor of Radiology
2. **Interchange of Information Through Poison Control Centers in the Nation**
   Henry L. Verhulst, Washington, D. C.
   Director, Poison Control Branch, Division of Accident Prevention, U.S. Public Health Service
3. **Medical Communications: What the Public Really Gets**
   Leona H. Baumgartner, M.D., New York City
   Commissioner of Health, City of New York
4. **Speaking One Language**
   Burgess Gordon, M.D., Chicago, Illinois
   Associate Editor, Journal of the American Medical Association

A question and answer period will follow the four presentations.

12:00 NOON Reception
(*Courtesy Hoffmann-La Roche, Inc., Nutley, New Jersey*)

12:30 P.M. Luncheon

Alfred P. Ingegno, M.D., Brooklyn
Chairman, Publication Committee,
Medical Society of the State of New York, *Presiding*

Address: **Communications and Medical Quackery**

Morris Fishbein, M.D., Chicago, Illinois
Editor, Excerpta Medica,
Past-President, American Medical Writers Association

Afternoon Session

Robert A. Peterman, M.D., Nutley, New Jersey
Hoffmann-La Roche, Inc.; Vice-President, Metropolitan New York Chapter, American Medical Writers Association, *Presiding*

2:30 p.m. Panel: **New Horizons in Medical Communication**

Eric Martin, Ph.D., Fort Lee, New Jersey
Director of Medical Communication, Lederle Laboratories, Pearl River, *Chairman*

1. **The Box and the Button**
   John MacKenzie, New York City
   Executive Secretary, Council on Medical Television
2. **Legal Pitfalls of Medical Communications**
   Andrew J. Graham, Esq., New York City
   Member of firm of Roger, Hoge, and Hills
3. To be announced
4. **The New Horizons**
   Richard H. Orr, M.D., New York City
   Director, Institute for the Advancement of Medical Communications; President, American Medical Writers Association

A question and answer period will follow the four presentations.

5:00 p.m. Reception
(*Courtesy Wallace Laboratories, Cranbury, New Jersey*)

REGISTRATION

Medical Communications Day / Saturday, May 19, 1962

STATLER HILTON, NEW YORK CITY

Sponsored by New York State Journal of Medicine *and* American Medical Writers Association, Metropolitan New York Chapter
Registration Fee: $6.00 for members of the Medical Society of the State of New York or the American Medical Writers Association
$10.00 for nonmembers

Registration fee includes morning and afternoon sessions, luncheon, and receptions.

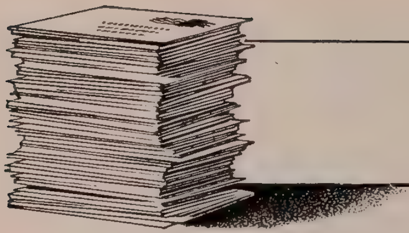
Enclosed is check (or money order) in the amount of .... for ..... reservations for Medical Communications Day on May 19, 1962.

NAME

ADDRESS

AFFILIATION

Please make checks payable to New York State Journal of Medicine; *send to 750 Third Avenue, New York 17, New York.*



Letters to the Editor

AMA membership

To the Editor: It seems to me that in this era of uncertainties the editorial "Shibboleth" is a down-to-earth statement of fact which all the members of our State Society should heed. Our psychiatric group would greatly appreciate your reprinting the editorial by Milton Spiegel, M.D., as an addendum to this letter.

ROBERT J. MEARIN, M.D.

The Mearin Clinic
9 Lafayette Avenue
Brooklyn 17, New York

Shibboleth*

During the first half of the century, revenue from *Journal of the American Medical Association* subscriptions and advertisements sufficed to carry on the herculean tasks of maintaining and raising standards of medical education, hospital internships, and pharmaceuticals and exposing cults, charlatans, and nostrums. Medical licensure, ethics, and economics, which vary from state to state, were left to their respective state medical society. It was not until the mid-1940's, when Federal legislation (Wagner-Murray-Dingell bill) advocating compulsory health insurance was introduced, that the American Medical Association was constrained to leave its ivory towers and enter the political arena. Although it emerged from the fray victorious, its public image had tarnished its shining armor, and its honored escutcheon was bent, bloodied, and besmirched.

Alerted to the threat to free-enterprise private practice, the AMA instituted membership for funds with which to maintain legislative vigilance. Since the threat is nation-wide, it was considered equitable to expect every physician to bear his share. To impose this responsibility, it was resolved to make AMA membership "compulsory." Editorially, in the May, 1960, issue of this *Bulletin*, we decried the use of this word, whose abhorrent connotation alienated many who are outraged by coercion but might have been amenable to an appeal to reason. It was an unfortunate choice that has produced unnecessary repercussions.

Acting as mandated by our membership, our County delegation voted against the proposition, but it passed the House of Delegates by more than the required two-thirds majority. Recently, members of our County Society have been circularized, urging support of a resolution that would absolve them from the necessity of AMA membership. The sparing of any expense is a windfall, and the wish "to get something for nothing" is an understandable human foible. But the impulse to accept, without consideration of consequences, can be foolhardy or disastrous. Troy fell when it succumbed to the old adage "don't look a gift horse in the mouth," despite the exhortations of Laocoon to "beware the Greeks bearing gifts."

There is a modern counterpart of the Trojan horse within the citadel of medicine. The Physicians Forum, which presently urges us to eschew AMA membership because it is "compulsory," has been in the forefront of the fight for compulsory health insurance! Several of its prominent members, distinguished physicians who belong to the AMA, have voiced minority opinion contrary to AMA policy, as is their democratic privilege, testifying and speaking in favor of socialized medicine.

Are we prepared to sell our economic birthright for a mess of pottage? AMA dues cannot be considered excessive for an exalted profession, compared with the cost of craft and industrial union dues, which, as do many national organizations, make membership in the parent organization mandatory. The word "compulsory" is being used as a shibboleth, to divide the forces of medicine into separate camps, creating a diversionary tactic to distract us from the offensive against the ramparts of organized medicine which is soon to be unleashed in Congress. It is a semantic blunder which might well cost us the battle against socialization.

Shall we allow our adversary to sharpen his weapons on the whetstone of semantics? Let us not be too quick to discard majority rule at the bidding of a vociferous minority. Questionable acts by responsible bodies are subject to legal review. If we are to be shackled by the bondage of bureaucracy, let it be by due process of law, not misunderstanding. Let us not be misguided by false prophets and permit a shibboleth to decoy us down the primrose path to socialization.

MILTON B. SPIEGEL, M.D.

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* Reprinted with permission from the January, 1962, issue of the *Bulletin of the Medical Society of the County of Kings and Academy of Medicine of Brooklyn.*

Comment on "Survey of Hysterectomies"

To the Editor: An article with the title of "Survey of Hysterectomies; A Twenty-Four-Year Review" appeared in the December 15, 1961, issue of the NEW YORK STATE JOURNAL OF MEDICINE* which should not be allowed to go unnoticed; in fact it is deserving of wide publicity. A group of surgeons from the Department of Obstetrics and Gynecology of the Beth-El Hospital in Brooklyn report that over a twenty-four-year period (1935 through 1958) they performed 3,548 hysterectomies. That is quite a respectable number for a comparatively young institution of moderate size. But the important part, which is the incentive for this communication, is the fact that hundreds of these hysterectomies were done by the vaginal route. And of still greater significance is the statement that during the year 1958 90 vaginal hysterectomies were done as compared with 207 abdominal hysterectomies. That is a ratio of almost 1 vaginal hysterectomy to 2 abdominal hysterectomies. It is undoubtedly an unprecedented record.

These surgeons deserve great credit for their courage and persistence in performing so large a proportion of vaginal hysterectomies, especially when it is so well known that there is a hostile attitude in certain quarters against the vaginal procedure. And yet the advantages of the vaginal over the abdominal operation, when indicated, can hardly be overestimated. The pain, the abdominal distention, and the nausea and vomiting incident to all the abdominal operations do not occur. There is, of course, no possibility of a postoperative incisional hernia which is not infrequent in the abdominal approach.

It is my firm belief that this marks the beginning of a new era in gynecologic surgery, and it is to be hoped that vaginal hysterectomies will become a more frequent operative procedure in other hospitals than it has been heretofore.

HERMAN SHANN, M.D.

771 East 34th Street
Brooklyn 10, New York

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* Greenberg, M. W., Beilly, J. S., Dissick, J., Tetenbaum, H.: Survey of hysterectomies; a twenty-four-year review, NEW YORK STATE J. MED. **61:** 4163 (Dec. 15) 1961.

Nursing home situation

To the Editor: The series of articles on certain New York City nursing homes, which appeared in the New York *Daily News*, January 10, 11, and 12, 1962, caused much concern among the members of the New York State Nursing Home Association, Inc. Continuing reference to the series of articles by the *Daily News* during recent weeks has increased this concern.

Immediately following the appearance of the articles, our Association sent letters to the editor of the *Daily News* and Miss Kitty Hanson, the author of the articles. Unfortunately at no time has reference been made by the *Daily News* regarding the information and statements which we supplied.

We are aware that the Medical Society of the State of New York has deep interest in adequate health care for aged persons. The Medical Society of the State of New York, as a member of the Joint Council on Health Care for the Aging, works cooperatively with the representatives of the New York State Nursing Home Association, the Hospital Association of New York State, and the Dental Society of the State of New York in helping to develop programs and relationships which will improve this care. With this common interest we thought your readers might be interested in the position of our Association in regard to the *Daily News* articles; therefore, I am enclosing copies of the letters which were sent in connection with these articles, and I am hopeful that you will deem it appropriate to publish our letter to the editor of the *Daily News*.

Letter to the **Daily News**

The series of articles on certain New York City Nursing Homes, which appeared in the New York *Daily News* this week, was a shocking exposé of intolerable conditions which should not be permitted to exist. It is unfortunate that these articles, by direct statement and implication, served to condemn and cast a bad light on all nursing homes in the United States.

As president of the New York State Nursing Home Association, Inc., I wish to call to your attention some pertinent points which are deserving of public attention and which will help the public realize and appreciate that the vast majority of the nursing homes in this State are conducted in an orderly, efficient, and wholesome manner, where the care and comfort of the patient are uppermost in the minds of the administration and staff. These homes are providing a useful, humane, and necessary service for thousands of our aged and infirm people who need care and attention but do not require hospitalization.

Our Association represents approximately 150 nursing homes throughout New York State. We have no members in New York City proper, but we have many members in the suburban counties of New York City.

Our Association, through education and training programs, is constantly seeking to improve and upgrade standards of nursing home care. We are continually working with public agencies, such as the State of New York Department of Social Welfare, State of New York Department of Health, State of New York Department of Mental Hygiene, New York State Office of the Aging, New York State Joint Legislative Committee on Problems of the Aging, and other local health and welfare agencies to carry out this improvement program. In addition, we are constantly working closely with such professional organizations as the Medical Society of the State of New York, the Dental Society of the State of New York, the New York State Hospital Association, various nurses' associations, and other local professional organizations to further improve our standards and acceptance.

In addition, we are cooperating closely with the American Nursing Home Association in the development of an accreditation program which will further enhance the position of nursing homes in health care for aged persons.

Our members attend professional conferences, institutes, workshops, lectures, and many other professional meetings which will improve their abilities to provide better patient care.

We are continually striving to improve our standards and are continually urging public inspection agencies to enforce the regulations to insure a high standard of service in nursing homes.

Just recently Governor Rockefeller proposed the development of a code to upgrade nursing homes and permit them to play a more important role in caring for the aged. In response to this announcement, I dispatched the following telegram to Governor Rockefeller.

> The New York State Nursing Home Association applauds your recommendation for a code to upgrade nursing homes in this State and to increase their importance in the health care for the aged. We wholeheartedly support your proposal and respectfully request an opportunity to have representatives of our Association join with representatives of State agencies and private insurance companies in the development of this code.

I recite all of these details to let you know that there are in New York State many dedicated and competent people running nursing homes, where many patients are receiving high-caliber nursing care by trained medical people. Our efforts with all the public and private agencies can be verified through your own inquiry.

We want the chislers and cheats and incompetents driven out of the nursing home business. We are dedicated people with high standards of service and ethics. We want the public to know that there are many places where the aged can spend comfortable years under expert supervision.

Won't you help us get this message across to your millions of readers?

AUSTIN J. BARRETT, President

New York State Nursing Home Association
685 Linwood Avenue
Buffalo, New York

Infectious hepatitis in heroin addicts

To the Editor: The recent editorial on infectious hepatitis in the NEW YORK STATE JOURNAL OF MEDICINE was of great interest to us.[1] The recurrent outbreaks of hepatitis constitute a major public health problem. However, the endemic form of this disease, particularly among heroin-addicted individuals, has become a serious problem, too. These addicts not only lack a sterile technic in the injections of the drug but also practice unhygienic personal habits which may facilitate the intestinal-oral transmission of the infective agent. Thus it is common to see one addict take a lighted cigaret directly from his lips and give it to a fellow addict who will continue to smoke the same cigaret.

In 1959[2] we surveyed the hospital population of Riverside Hospital, which is devoted to the study and treatment of adolescent drug addicts in New York City, in an attempt to determine the incidence of hepatitis in this group. We elicited a history of icteric hepatitis in 25 per cent and of possible anicteric form in another 6 per cent of the total survey group of 159 patients. We found 5 patients who had clinical evidence of liver disease: 3 were icteric, 4 had hepatomegaly, and 3 had spider angiomas. All had a history of preceding hepatitis. In addition, 48 of the entire group had bilirubinuria.

The problem of hepatitis in pregnant women was discussed by F. J. Schoeneck, M.D.,[3] in the same issue. It is of interest that our survey disclosed that 5 out of the 15 female addicts gave a history of icteric hepatitis; in addition, one had had probable and another one possible anicteric hepatitis. This high incidence raises the possibility that some of the female addicts who become pregnant (and there were 27 such individuals in a three-year period) and who deliver viable infants may be carriers of the hepatitis agents. The recently presented evidence[4] of transplacental transmission of the virus of hepatitis to the newborn infant emphasizes the seriousness of this aspect of the problem of hepatitis among female heroin addicts.

CHARLES R. MESSELOFF, M.D.
RAFAEL R. GAMSO, M.D.

Riverside Hospital
The Bronx, New York

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[1] Editorial: Infectious hepatitis, NEW YORK STATE J. MED. **61**: 4145 (Dec. 15) 1961.

[2] Unpublished data.

[3] Schoeneck, F. J.: Acute viral hepatitis in pregnant women, NEW YORK STATE J. MED. **61**: 4254 (Dec. 15) 1961.

[4] Stokes, J., Jr., *et al.*: The carrier state in viral hepatitis, J.A.M.A. **154**: 1059 (Mar.) 1954.

Necrology

Louis Adler, M.D., of New York City, died on February 14 at the age of seventy. Dr. Adler received his medical degree from the University of Wurzburg in 1922. He was a member of the Rudolf Virchow Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frederick Simon Aron, M.D., of New York City, died on January 21 at the Medical Arts Center Hospital at the age of seventy-three. Dr. Aron received his medical degree from the University of Kiel in 1915. He had practiced in Berlin, Germany, where he was a founder of the German Emigration Office for Physicians and was founder of the American Federation of Jews from Central Europe. Dr. Aron was a member of the Rudolf Virchow Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David Ball, M.D., of New York City, died on December 20, 1961, at the age of sixty-four. Dr. Ball graduated in 1921 from Syracuse University College of Medicine and interned at The Mount Sinai Hospital. He was an associate attending physician at Beth Israel Hospital. Dr. Ball was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harry Elmar Berg, M.D., of Brooklyn, died on March 19 at Coney Island Hospital at the age of fifty-five. Dr. Berg received his medical degree from the University of Basel in 1935 and interned at Israel-Zion Hospital. He was an assistant attending physician at Adelphi Hospital and an assistant attending physician in physical medicine and rehabilitation at the Coney Island Hospital. Dr. Berg was a member of the American Congress of Physical Medicine and Rehabilitation, the New York Academy of Preventive Medicine, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David Brumberg, M.D., of Buffalo, died on February 26 in Miami, Florida, at the age of seventy-eight. Dr. Brumberg graduated in 1908 from the University of Buffalo School of Medicine. He was an honorary physician at the Emergency Hospital of the Diocese of Buffalo and an associate consulting physician at Edward J. Meyer Memorial Hospital. In 1950 he retired as an associate professor of medicine and assistant professor of therapeutics at the University of Buffalo School of Medicine but continued until 1957 at the Lamb Foundation lecturer. Dr. Berg was a Diplomate of the American Board of Internal Medicine and a member of the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Victor Caronna, M.D., of Brooklyn, died on November 2, 1961, at the age of sixty-four. Dr. Caronna received his medical degree from the University of Palermo in 1923. He was a member of the Kings County Medical Society and the Medical Society of the State of New York.

Frances Isham Colonna, M.D., of New York City, died on October 31, 1961, at the age of fifty-nine. Dr. Colonna graduated in 1950 from the State University of New York College of Medicine at New York City. She was an adjunct physician in pediatric psychiatry at the Lenox Hill Hospital and an assistant attending physician in psychiatry at University Hospital. Dr. Colonna was a Member of the American Psychiatric Association and also held memberships in the New York Society for Clinical Psychiatry, the New York City Medical Society on Alcoholism, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Nelson Asahel Craw, M.D., of Fairfield, Connecticut, formerly of the Bronx, died on March 20 in Bridgeport (Connecticut) Hospital at the age of seventy-nine. A charter member of the Bronx County Medical Society, Dr. Craw graduated in 1904 from the Long Island College Hospital School of Medicine. Retired in 1947 Dr. Craw was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Elton Robert Dickson, M.D., of Binghamton, died on December 12, 1961, in Fort Lauderdale, Florida, at the age of sixty-two. Dr. Dickson graduated in 1924 from Albany Medical College. He was deputy city health officer of Binghamton and a senior attending physician at Binghamton General Hospital. Dr. Dickson was a member of the American Academy of General

Practice, the Binghamton Academy of Medicine, the Broome County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Dominick Anthony Di Pasca, M.D., of Levittown, died on January 26 at the age of seventy-six. Dr. Di Pasca graduated in 1907 from the University of Maryland School of Medicine and College of Physicians and Surgeons.

Max Ehrenberg, M.D., of New York City, died on January 31 at the age of sixty-eight. Dr. Ehrenberg graduated in 1920 from New York Homeopathic Medical College and Flower Hospital and interned at Metropolitan Hospital. He was a clinical assistant in dermatology and syphilology at Gouverneur Hospital and Gouverneur Hospital Outpatient Department. Dr. Ehrenberg was a member of the New York County Medical Society and the Medical Society of the State of New York.

Jacob Gillman, M.D., of Jamaica, died on March 20 at Terrace Heights Hospital, Hollis, at the age of fifty. Dr. Gillman graduated from the Royal College of Physicians and Surgeons, Glasgow, Scotland, in 1938. He was a member of the American Academy of General Practice, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Nathaniel Jay Gould, M.D., of the Bronx, died on March 11 at his home at the age of sixty-eight. Dr. Gould graduated in 1913 from the University of Maryland School of Medicine and College of Physicians and Surgeons. He was a consultant in ophthalmology at the Fordham Hospital and at the Bronx Eye and Ear Infirmary. Dr. Gould was a Diplomate of the American Board of Ophthalmology, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the American Geriatrics Society, the Pan American Association of Ophthalmology, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Kristian Gosta Hansson, M.D., of Putney, Vermont, formerly of New York City, died on March 11 at his home at the age of seventy-two. Dr. Hansson graduated in 1923 from Cornell University Medical College. He was director emeritus of physical medicine at the Hospital for Special Surgery, a consulting physician in physical medicine at French Hospital, the New York Infirmary, St. Agnes Hospital (White Plains), and Norwalk (Connecticut) Hospital. Retired in 1956, Dr. Hansson was a Diplomate of the American Board of Physical Medicine and Rehabilitation and a member of the American Congress of Physical Medicine and Rehabilitation, the American Academy of Physical Medicine and Rehabilitation, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Alexander S. Hartstein, M.D., of Syosset, died on December 20, 1961, at the age of sixty-three. Dr. Hartstein graduated in 1921 from New York Homeopathic Medical College and Flower Hospital.

Max Haymann, M.D., of New York City, died on February 17, 1961, at the age of seventy. Dr. Haymann received his medical degree from the University of Erlangen in 1924. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

John Allan Howard, M.D., of Utica, died on February 2 at Utica State Hospital at the age of sixty-three. Dr. Howard graduated in 1926 from Queens University Faculty of Medicine, Ontario, Canada. He was assistant director of Utica State Hospital. Dr. Howard was a member of the Utica Academy of Medicine.

Richard H. M. Joachim, M.D., of Auburn, died on February 28 at the age of sixty-three. Dr. Joachim received his medical degree from the University of Berlin in 1923. He was an attending dermatologist at Auburn Memorial and Mercy Hospitals. Dr. Joachim was a member of the Cayuga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Oscar Kaltner, M.D., of College Point, died on December 11, 1961, at the age of seventy. Dr. Kaltner received his medical degree from the University of Budapest in 1919. He was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Isaac William Karlin, M.D., of Brooklyn, died on January 20 at the Jewish Hospital of Brooklyn at the age of sixty-four. Dr. Karlin graduated in 1924 from the University of Illinois College of Medicine. He was founder and pediatrician-in-charge of the Speech Clinic at the Jewish Hospital, a consultant in speech therapy at the Jewish Chronic Disease Hospital, consulting pediatrician at the National Speech Dispensary, and a former clinical assistant professor of pediatrics at the Yale Graduate School of Medicine. Dr. Karlin was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Edgar Luke, M.D., of Syracuse, died on February 24 at the age of seventy-six. Dr. Luke graduated in 1911 from Syracuse University College of Medicine. He was chief surgeon at People's Hospital, one-time city department of health member, and attending physician at Loretto Rest since its opening. Dr. Luke was a member of the Syracuse Academy of Medicine, the Onondaga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Carter Lee Marshall, M.D., of New York City, died on March 14 at St. Thomas, Virgin Islands, at the age of sixty-three. Dr. Marshall graduated in 1924 from Howard University College of Medicine. He was a former attending physician at Grace-New Haven Community Hospital, assistant dermatologist at Sydenham Hospital, and assistant clinical professor of dermatology at Yale University. Dr. Marshall was a Diplomate of the American Board of Dermatology, Inc., and a member of the American Academy of Dermatology and Syphilology, the North East Dermatology Society, and the Connecticut Medical Society.

Eugene John Miele, M.D., of Freeport, died on February 26 at his home at the age of fifty-six. Dr. Miele received his medical degree from the University of Padova in 1934. He was a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Ida Oshlag, M.D., of New York City, died on February 16 at the age of eighty-seven. Dr. Oshlag graduated in 1908 from the College of Physicians and Surgeons, Boston.

Clarence Ralph Pearson, M.D., of Naples, Florida, formerly of Scottsville, died on December 9, 1961, at the age of sixty-two. Dr. Pearson graduated in 1925 from the University of Vermont College of Medicine. He was an attending physician in general practice at Highland Hospital of Rochester and a consulting physician at St. Mary's Hospital. Dr. Pearson was a member of the American Academy of General Practice, the Rochester Academy of Medicine, the Monroe County Medical Society, and the Medical Society of the State of New York.

Henry F. Quackenbos, M.D., of West Palm Beach, Florida, formerly of Pine Plains and Sharon (Connecticut), died on February 14 at the age of ninety. Dr. Quackenbos graduated in 1893 from Bellevue Hospital Medical College. Retired, he was a Fellow of the American College of Physicians and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Stephen Rath, M.D., of New York City, died on January 10 at the age of fifty-nine. Dr. Rath received his medical degree from the University of Berlin and was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Michael Rosen, M.D., of Brooklyn, died on February 19 at the age of seventy-two. Dr. Rosen graduated in 1914 from Long Island College Hospital Medical School.

Anthony W. Scacciaferro, M.D., of Brooklyn, died on November 22, 1961, at the age of fifty-three. Dr. Scacciaferro graduated in 1932 from Georgetown University School of Medicine. He was an assistant attending pediatrician at St. Vincent's Hospital. Dr. Scacciaferro was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Zelik Sharfin, M.D., of Forest Hills, retired, died on March 20 at Peninsular Hospital at the age of ninety-two. Dr. Sharfin graduated in 1899 from New York University and Bellevue Hospital Medical College. Formerly chief of the pediatric clinic at Beth Israel Hospital, Dr. Sharfin was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Anthony Squillace, M.D., of Brooklyn, died on January 31 at the age of sixty-eight. Dr. Squillace graduated in 1920 from Eclectic Medical College, Cincinnati. He was director of obstetrics and gynecology at Prospect Heights Hospital. Dr. Squillace was a Fellow of the International College of Surgeons and a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George S. Staniland, M.D., of Buffalo, died on February 28 at his home at the age of eighty-five. Dr. Staniland graduated in 1899 from the University of Buffalo School of Medicine. From 1905 to 1925 he was district superintendent of the Metropolitan Life Insurance Company and then a vice-president of the American Kardex Company. During World War I he served as acting city health commissioner and in 1919 was appointed to the board of managers of the City Hospital (now the Edgar J. Meyer Memorial Hospital).

Anne Marie Strauss, M.D., of Kew Gardens, died on January 25 at her home at the age of fifty. Dr. Strauss received her medical degree from the University of Basel in 1936. She was a physician with the Department of Health Tuberculosis Clinic and an assistant attending physician at Queens Hospital Center.

A. Lester Weisberg, M.D., of the Bronx, died on April 23, 1961, at the age of sixty. Dr. Weisberg graduated in 1927 from New York University and Bellevue Hospital Medical College and interned at Morrisania Hospital. He was an associate attending surgeon at Morrisania Hospital. Dr. Weisberg was a member of the American Geriatrics Society, the Bronx Surgical Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frederick Stephen Wetherell, M.D., of Largo, Florida, formerly of Syracuse, died on February 18 at the age of seventy-four. Dr. Wetherell graduated in 1913 from Syracuse University College of Medicine. Retired in 1959, he was a senior gynecologist at St. Joseph's Hospital, a consultant in surgery at St. Lawrence State Hospital, a senior attending surgeon at Syracuse Memorial Hospital, and chief medical officer at the Veterans Administration Regional Office in Syracuse. He helped establish the first cancer clinic in New York City and was a professor emeritus of surgery at the State University of New York College of Medicine. Former president of the Onondaga County Medical Society, Dr. Wetherell was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the American Goiter Association, the American Association of Obstetricians and Gynecologists, the Syracuse Academy of Medicine, the Medical Society of the State of New York, and the American Medical Association.

Lew Winston, M.D., of New York City, died on February 9 at the age of seventy. Dr. Winston received his medical degree from the University of Jurjev in 1916. He was a member of the Russian Medical Society.

Leon R. Wishnow, M.D., of Brooklyn, died on December 11, 1961, at the age of sixty-eight. Dr. Wishnow received his medical degree from the University of Vienna in 1923. He was an assistant attending physician (off service) at Maimonides Hospital. Dr. Wishnow was a member of the Kings County Medical Society and the Medical Society of the State of New York.

Medical Meetings

Symposium on diabetes

The New Jersey State Department of Health in cooperation with The New Jersey Diabetes Association will present its fourth annual spring symposium on diabetes on Wednesday, May 9, from 2:00 to 5:00 P.M., at the Princeton Inn, Princeton, New Jersey. The topic of this year's symposium will be "Employability and Insurability of the Diabetic Patient."

The program is as follows: "Experiences of the American Diabetes Association Committee on Employment," Joseph T. Beardwood, Jr., M.D., Philadelphia; "Rehabilitation and Placement of Diabetics," Abraham H. Kantrow, M.D., New York City; "Diabetes Mellitus in an Employed Population," C. A. D'Alonzo, M.D., Wilmington, Delaware; "Insurability of the Diabetic Patient," A. Henry Clagett, Jr., M.D., Wilmington, Delaware; and "Employment of Diabetics in the Federal Service," Frank McGowan, M.D., New York City.

Symposium on upper and lower extremities amputees

The Mercy Hospital Rehabilitation Center of South Buffalo will sponsor a symposium on upper and lower extremities amputees on May 10, from 9:00 A.M. to 1:00 P.M., in Marion Hall, 360 Choate Avenue, Buffalo 20, New York. Reeve M. Brown, M.D., Buffalo, will be the luncheon speaker.

For information contact: Henry V. Morelewicz, M.D., The Mercy Hospital Rehabilitation Center of South Buffalo, 565 Abbott Road, Buffalo 20, New York.

Student American Medical Association

The annual convention of the Student American Medical Association will be held in Washington, D.C., May 10 through 13, at the Mayflower Hotel.

Fifth annual institute in psychiatry and neurology

"Problems in Aging" will be the topic of the fifth annual institute in psychiatry and neurology at the Veterans Administration Hospital, Coatesville, Pennsylvania, May 16 and 17. The program will consist of panels, lectures, and meetings concerned with the psychiatric, neurologic, and medical aspects of aging. Alvin I. Goldfarb, M.D., New York City, will be among the participants.

For further information write to: Hospital Director, Veterans Administration Hospital, Coatesville, Pennsylvania.

Catholic Hospital Association

The Catholic Hospital Association will hold its annual convention May 21 through 24 at the Kiel Auditorium, St. Louis, Missouri. The theme of the convention is "Our Heritage and Our Future."

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis will present a panel discussion on "Current Psychoanalytic Understandings of Suicide" on May 23 at the New York Academy of Medicine, 103rd Street and Fifth Avenue, New York City.

The panel will consist of: Louis E. DeRosis, M.D., of the Karen Horney School, who will discuss suicide as an intrapsychic phenomenon; Maurice Green, M.D., of the William Alanson White Institute, who will discuss suicide as an interpersonal phenomenon; and Leonard Moss, M.D., of the Columbia School of Psychoanalysis, who will discuss suicide from an adaptational point of view. John Millet, M.D., New York City, will be the moderator.

For information contact: Association for the Advancement of Psychoanalysis, Inc., 329 East 62nd Street, New York 21, New York. Telephone PLaza 2-5267.

Association for Contamination Control

The first annual convention of the American Association for Contamination Control will be held May 28 through 30 at the Jack Tar Hotel, San Francisco, California.

For information contact: Donald M. Petersen, President, Central Vacuum Corporation, 3008 East Olympic Boulevard, Los Angeles 23, California.

Annual Health Conference

The fifty-eighth Annual Health Conference will be held June 11 through 13 in Syracuse. Physicians, nurses, and other public health workers from communities throughout New York State and adjacent states will attend the meeting. The conference serves to provide postgraduate education for professional persons in the health field.

Among the individuals and organizations participating in the function are: the Conference of County, City, and District Health Officers; county and city health department public health nurse administrators; Empire State Health Council; New York State Association of School Physicians; New York State Health Officers Association; New York State Public Health Association; and the New York State School Nurse-Teachers Association.

Association for Physical and Mental Rehabilitation

The sixteenth annual clinical and scientific conference of the Association for Physical and Mental Rehabilitation will be held at the Statler-Hilton Hotel, in Buffalo, July 14 through 20. Problems and accomplishments in the field of rehabilitation will be discussed.

For further information write to: Julian Vogel, Chairman, Public Relations Committee, Association for Physical and Mental Rehabilitation, Inc., 3013 Basque Boulevard, Waco, Texas.

American Society of Cytology

The American Society of Cytology (formerly, the Inter-Society Cytology Council) will hold its tenth annual scientific meeting at the Chase-Park Plaza Hotel, St. Louis, Missouri, November 8 through 10. For further information write to: Paul A. Younge, M.D., Secretary-Treasurer, American Society of Cytology, 1101 Beacon Street, Brookline 46, Massachusetts.

Abstracts

Holswade, G. R., and Glenn, F.: An evaluation of surgical correction for valvular heart disease, New York State J. Med. **62:** 1359 (May 1) 1962.

Great advances have been made in the correction of deformities of the heart valves. Both acquired and congenital valvular heart disease have become amenable to surgery with increasing success. The evolution of the surgical treatment for valvular heart disease has progressed through several stages to the present era of partial and complete valve replacement with prosthetic valves. It is too early to evaluate the latter development, and the ultimate composition of the prosthesis has not been determined. The procedure and the results vary with the type of valvular disease. Surgery is particularly successful in congenital valvular stenosis and acquired mitral stenosis. The treatment often is conditioned by widespread involvement of the heart with the presence of other valvular conditions.

Thompson, H. T.: Bladder neck obstruction as cause of fever of unknown etiology in children, New York State J. Med. **62:** 1376 (May 1) 1962.

A study was undertaken of 123 children, of whom 40 per cent were males, and 60 per cent females; 87 per cent were between the ages of two and ten years. Forty-seven per cent presented symptoms of fever or a significant history of fever, which played an important part in bringing the patient to the physician. Frequency, urgency, and abdominal pain are the most common findings in bladder neck obstruction. Nocturnal enuresis occurred in 58 per cent of the patients, day enuresis in 38 per cent. Seventeen per cent were without urinary symptoms. The evaluation of the patients was carried out by urine culture, residual urine determinations, intravenous pyelography, voiding cystogram, and cystoscopy. Types of treatment were: urethral dilatation; cystoscopy and fulguration; transurethral resection; suprapubic resection; and none. Frequently urinary infection has existed longer than indicated in the history; enuresis or the lack of it can be similarly significant. The evaluation of any child with fever of unknown etiology must include a complete urologic study.

Yeostros, S. J.: Use of Fe^{59} in determination of latent iron-binding capacity; diagnostic test in various liver diseases, New York State J. Med. **62:** 1386 (May 1) 1962.

A study was made of 41 patients with Laennec's cirrhosis, 19 with acute hepatitis, and 16 with either primary or metastatic carcinoma of the liver. The SI (serum iron) and LIBC (latent iron-binding capacity) were determined by electrophoresis using Fe^{59}-labeled iron. The TIBC (total iron-binding capacity) and per cent saturation of the TIBC with iron were calculated also. The significant changes found were: in hepatitis, an increased SI content and TIBC, along with a normal LIBC; in cirrhosis, a normal SI content together with low LIBC and TIBC and a subsequent rise in saturation of the latter; and in carcinoma, a low SI content and a decrease in saturation of the TIBC. The value of the SI determination in differential diagnosis of the liver diseases investigated is increased when it is done in conjunction with determination of the LIBC and calculation of the TIBC and per cent saturation of the TIBC.

Mindell, E. R., Cisek, E. E., and Kartalian, G.: Post-traumatic aseptic necrosis of talus; preliminary report, New York State J. Med. **62:** 1392 (May 1) 1962.

Twenty-one patients with significant talus injuries were studied; 7 of these developed aseptic necrosis. The early diagnosis of aseptic necrosis was difficult. In later stages evidence of the replacement of the necrotic bone may be seen on the roentgenogram as mottling with irregular zones of decreased density and irregular, thickened trabeculae. In the adult, the articular cartilage overlying the necrotic bone will undergo changes. The treatment of the patients with aseptic necrosis varied. The 3 patients with open injuries were treated with open reductions. In the other 4 patients two fractures simply were immobilized, one was treated first by closed reduction and then open reduction, followed by bone grafting, and the fourth was treated by open reduction. After an average follow-up period of 4.5 years, the end result was excellent in 1 patient, good in 2, fair in 2, and poor in 2. This was far inferior to the over-all late results in the total group of 21 cases.

Rubin, P., Lund, C., and Prabasawat, D.: Invasive carcinoma of the cervix; improvement in therapeutic results, New York State J. Med. **62:** 1399 (May 1) 1962.

The present series is based on a review of 300 cases of invasive carcinoma of the cervix treated from 1940 to 1956. There is a five-year survival of 63 per cent and a ten-year survival of 49.5 per cent in contrast to a 26.2 per cent five-year figure and a 9.6 per cent ten-year result for 328 cases treated from 1926 to 1942. The improvement is reflected in all stages except Stage IV, with the greatest increase in Stage II (66 per cent versus 30 per cent) and Stage III (55 per cent versus 16 per cent). With earlier examinations and improved cytologic technics more cases are discovered in less advanced stages. Radium therapy technics have changed over the years. From 1952 to the present, Fletcher applicators have been in use, and radiocobalt is utilized instead of radium. The number of major complications has decreased as over-all survival figures have improved. The complications were intestinal, urinary tract, and osseous; irradiation accounted for 10 per cent of all the complications, tumor invasion for 11 per cent, and surgical intervention for 3.3 per cent.

Young, A. W., Jr.: Special problems in dermatogeriatrics, New York State J. Med. **62:** 1407 (May 1) 1962.

Skin disease in the older patient must be considered by special standards. Dermatogeriatrics is an approach which would correlate the modified responses and special susceptibilities in older persons with patterns of aging. There are four categories of skin diseases which beset senescent patients: obligatory, constitutional, incidental, and inveterate dermatoses. Special problems include nodules of the ears and feet, senile seborrhea, senile tibial erosions, autogenous eczema, seborrheic and senile keratoses, and skin cancer.

Rolo, A.: Drug withdrawal with promazine hydrochloride, New York State J. Med. **62:** 1429 (May 1) 1962.

Forty-five patients (22 males and 23 females) were treated with promazine hydrochloride (Sparine hydrochloride) for the abstinence syndrome associated with withdrawal of narcotics and barbiturates. In all but 8 cases the addictive drug was stopped abruptly on admission, and full dosage of promazine hydrochloride was started immediately. The daily dose varied from 100 mg. to 1.2 Gm., given intramuscularly in divided doses. Withdrawal was effected easily and without major complications in all cases. All patients seemed relatively comfortable and were accessible to psychotherapy during the withdrawal period. No jaundice or any other significant side-effect developed.

Herman, B. E.: Transmetatarsal amputation in arteriosclerotic gangrene, New York State J. Med. **62:** 1432 (May 1) 1962.

From 1955 to 1960 11 transmetatarsal amputations were performed on patients who had diabetes and gangrene. The average hospital stay was fifteen and one-half weeks. Of the 11 cases, 5 (45 per cent) failed outright and required below-knee amputation; 6 cases (55 per cent) healed primarily or after varying lengths of time. Of the 6, 1 returned to a gainful occupation, and 3 achieved some limited use from the salvaged leg. The results are similar to those in other studies. The chance for success and the expense in time and money must be weighed in considering transmetatarsal amputation.

Cracovaner, A. J.: Nonsurgical management of Ménière's disease, New York State J. Med. **62:** 1435 (May 1) 1962.

In Ménière's disease there is generally a hydrops of the endolymphatic system. Increased pressure within the labyrinth and cochlea produces the characteristic symptoms: vertigo, deafness, and tinnitus. Attacks may last from a few minutes to several days and may recur in weeks or years. The disease may be considered an autonomic dysfunction, possibly caused by a "physical allergy," an all-inclusive term. Endocrine dysfunction and metabolic disturbances have been found in some cases. Other factors to be considered are: overindulgence in alcohol, salt, and certain foods, blocked eustachian tube, upper respiratory or virus infection, and tension and stress. There is no one specific treatment at present. Treatment should include vasodilators, sodium restriction and elimination, anticholinergic drugs, and sedatives.

Siris, J. H., Henry, E. I., and Cukier, D. S.: Occult hypoxemia complicating acute and subacute intracranial lesions, New York State J. Med. **62:** 1440 (May 1) 1962.

Ten patients with acute and subacute intracranial disorders (injury, tumor, and cerebral vascular accident) uncomplicated by dyspnea, cyanosis, or other gross evidence of respiratory insufficiency were studied with regard to the oxygen content of their arterial blood. Anaerobic conditions were maintained throughout. Determinations were made of the carbon dioxide total content of whole blood at the actual carbon dioxide tension existing in the arterial circulation. Patients who, although drowsy, were able to take nourishment had oxygen levels on the borderline of normal or slightly reduced. The remaining patients, too stuporous to take nourishment, showed significant hypoxemia. Oxygen levels rose as the patients regained consciousness. Hypercarbia did not accompany hypoxemia in the cases studied. In such cases early significant hypoxemia may be undetectable by clinical examination alone, since it may not be accompanied by dyspnea, cyanosis, tachycardia, or pulmonary edema.

Medical News

Grants offered to residents

The American Geriatrics Society has announced the establishment of three $1,800 grants to encourage resident physicians to devote more time to the study of the medical problems of the aged.

The grants, made possible by Lederle Laboratories, pharmaceuticals division of American Cyanamid Company, will augment salaries paid to residents while they continue their medical education. The individual grants are to be known as the Lederle Residency Supplements and will cover the period July, 1962, to June, 1963.

Application for the grants should be made to: Chairman, Residents and Interns Committee, American Geriatrics Society, 10 Columbus Circle, New York 19, New York. Deadline for applications is May 15.

National survey of prothrombin

The therapeutic benefit from the widespread use of anticoagulant medication makes it imperative that prothrombin measurements be reproducible and that similar levels be used consistently in this country. To stimulate interest in the accuracy and precision of prothrombin measurements, the College of American Pathologists will conduct a national survey.

Those who wish to participate in the prothrombin survey may do so by applying to the Committee for Clinical Pathology Standards of the College of American Pathologists, 2115 Prudential Plaza, Chicago 1, Illinois. In addition to the survey samples, a critique on prothrombin measurements containing suggestions for increasing the reproducibility and accuracy of prothrombin calibrations will be sent to each participant.

Application to participate in the survey should be sent prior to May 1.

Eye teaching day

The Department of Ophthalmology of the Edward J. Meyer Memorial Hospital and the Department of Postgraduate Education of the University of Buffalo School of Medicine will present an eye teaching day on Thursday, May 3, at the Hospital, 462 Grider Street, Buffalo 15, New York.

The program is as follows: Introduction, W. Yerby Jones, M.D., Buffalo; "Survey of Glaucoma in Edward J. Meyer Memorial Hospital Clinic," Robert Griffin, M.D., Buffalo; "Statistics of Case Findings in Glaucoma Detection Clinic," John Armenia, M.D., Buffalo; "Transport Processes in the Lens," Harold Kern, Ph.D., Buffalo; "Problems in Eye Consultation," James McGraw, M.D., Syracuse; "Observation on Vertical Muscles," James Brennan, M.D., Buffalo; "Ophthalmodynamometry," Charles Addington, M.D., Buffalo; and dinner address, Elmer J. Ballintine, M.D., Cleveland, Ohio.

Library appeals for literature

The research library of the Institute of Experimental Medicine and Surgery of the University of Montreal has suffered destruction by fire.

The library represented what is believed to be the largest fully indexed collection of literature on endocrinology and stress in the world (450,000 entries). Started in 1848 at the University of Vienna, the collection was handed down from teacher to pupil for over four generations. As a tool of documentation it was the basis of research planning and the source of literature for all books published by the Institute; in addition, the collection was used extensively by visitors and helped the Institute to answer the innumerable requests for literature received by mail.

Readers who wish to help rebuild the library can do so by contributing new or old reprints, books, or journals dealing with endocrinology, stress, and any other medical subject. Contributions should be addressed to: Institute of Experimental Medicine and Surgery, University of Montreal, P.O. Box 6128, Montreal 26, Canada.

State Sanitary Code amended

The New York State Public Health Council has voted to amend the State Sanitary Code to include precautions relating to materials delivered to and kept in hospital formula rooms. The amendment is effective April 1, 1962. It reads: "Only those materials actually used in the preparation of formulas shall be kept in the formula room. All materials used in the preparation of formulas shall be delivered in the formula room in their original containers."

The amendment was recommended by Herman E. Hilleboe, M.D., State Health Commissioner, following the deaths of 6 infants and the illness of others in the nursery at Binghamton General Hospital. A State Health Department epidemiologic study of these cases indicated that the cause of illness and death was toxemia resulting from high salt intake. The salt was accidentally substituted for sugar in the formula room sugar bin.

New service by hospital

St. Francis Hospital and Sanatorium in Roslyn, Long Island, is initiating a new service for the diagnosis and treatment of patients with thoracic diseases. Consultations are held Wednesdays from 1:30 to 4:00 P.M. Appointments may be made by telephoning Manhasset 7–6200, extension 238.

Symposium on dermatology

New York University Medical Center Post-Graduate Medical School will present a symposium on recent advances in dermatology, May 7 through 9. For further information contact: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that applications for certification in the Board, new and reopened, for the 1963 part 1 examinations are now being accepted. Candidates are urged to make application at the earliest possible date. The deadline for receipt of applications is July 1.

All applicants and candidates for re-examination are required to submit with their application or letter of request a duplicate list of their hospital dismissals for the preceding twelve months made up in accordance with the revised format shown on the last page of the current Bulletin.

Diplomates of the Board are requested to inform the office of the executive secretary of any change in address.

For information write to: Robert L. Faulkner, M.D., Executive Secretary and Treasurer, American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Personalities

New Office. Clyde A. Swift, M.D., for the practice of anesthesiology, in Glens Falls.

Appointed. Clarence Dennis, M.D., Brooklyn, as chairman of a committee on emergency services in Brooklyn . . . Lester J. Evans, M.D., New York City, executive director of the Committee on Medical Education for New York State.

Installed. Edward C. Hughes, M.D., Syracuse, as president of the American College of Obstetricians and Gynecologists . . . Julius Richmond, M.D., Syracuse, as president of the American Psychosomatic Society.

Awarded. Leona Baumgartner, M.D., New York City Commissioner of Health, by the Women's League for Israel, a Four Answers Award in the form of a silver cup for her achievements in public life . . . Henry J. Heimlich, M.D., New Rochelle, the Medaglione di Bronzo Minerva at the fourth international medico-scientific film festival, Turin, Italy, for his motion picture on "Esophageal Replacement with Reversed Gastric Tube."

Elected. George M. Lewis, M.D., New York City, as president and J. Lowry Miller, M.D., New York City, as treasurer of the American Dermatological Association.

Speakers. Morton I. Berson, M.D., New York City, in March before the twelfth annual meeting of the Puerto Rican Chapter of the American College of Surgeons, on the topics "Derma-fat-fascia Grafts for Correcting Bilateral Hemiatrophy of the Face and Building Up the Breasts After Mastectomy" and "Cosmetic Meloplasty—Facelift Operation" . . . James A. Brussel, M.D., Assistant Commissioner, State of New York Department of Mental Hygiene, on the topic "Effectiveness of the Interstate Compact on Mental Health" in Toronto, Canada, on May 6 at the annual conference of the Interstate Mental Health Administrators . . . Stella Chess, M.D., New York City, on March 26 on the subject "Recent Advances in Research in Child Psychiatry" and George Friedman, M.D., New York City, on March 23, on the subject "Legal Aspects of Medical and Nursing Procedures" before the members of the hospital staff of the Veterans Administration Hospital, Northport, Long Island . . . Chas. Murray Gratz, M.D., New York City, in May, in Ciudad de Puebla, Mexico, at the seventh national congress of orthopaedia and traumatology on problems of the pelvis and hip joint . . . John E. Kiley, M.D., Albany, on the use of the artificial kidney in the treatment of kidney diseases at the fifth annual medical teaching day at South Nassau Communities Hospital on April 4 . . . Stanley Lesse, M.D., New York City, on the topic "The Psychological Impact of Advertising on the Individual" at a meeting of the Association for the Advancement of Psychotherapy, on April 23 . . . Leo L. Leveridge, M.D., New York City, on March 15, before the New York Chapter of the Biological Photographic Association on the topics "The Role of the Hospital Photographer in the Production of Professional Medical Motion Pictures" and "Similarities and Differences Between Still Photography and Motion Picture Production" . . . Rachmiel Levine, M.D., New York City, on the treatment of diabetes with oral drugs, and Donald B. Louria, M.D., New York City, on the use of new drugs and antiseptic hospital procedures to help control the spread of bacterial infection in hospitals, at the fifth annual medical teaching day at South Nassau Communities Hospital on April 4 . . . Frederic Wertham, M.D., New York City, at a meeting of the Association for the Advancement of Psychotherapy on April 23.

Abstracts in Interlingua

Holswade, G. R., e Glenn, F.: Un evalutation del correction chirurgic in morbo de valvula cardiac (*anglese*), NEW YORK STATE J. MED. **62:** 1359 (1 de maio) 1962.

Grande progressos ha occurrite in le correction de deformitates del valvulas cardiac. Tanto le acquirite como etiam le congenite formas de morbo del valvulas cardiac es hodie chirurgicamente attaccabile, e le grado de successo progrede. Le evolution del tractamento chirurgic de morbos de valvula cardiac ha passate per plure stadios ante que illo attingeva su stato currente characterisate per le possibilitate de partial e complete reimplaciamentos prosthetic del valvulas natural. Il es non ancora possibile evalutar iste ultime disveloppamento, e le optime composition del prostheses es non ancora fixate. Le technica usate e le resultatos obtenite varia ab un typo de morbo de valvula cardiac al altere. Successos del intervention chirurgic es particularmente notabile in congenite stenosis valvular e in acquirite stenosis mitral. Le forma specific del tractamento es frequentemente conditionate per le presentia de extense affectiones del corde e de altere imperfectiones valvular.

Thompson, H. T.: Obstruction del cervice vesical, como causa de febre de incognite etiologia in juveniles (*anglese*), NEW YORK STATE J. MED. **62:** 1376 (1 de maio) 1962.

Esseva studiate un gruppo de 123 juveniles, 40 pro cento pueros, 60 pro cento pueras, e 87 pro cento de etates de inter duo e dece annos. Quaranta-septe pro cento manifestava symptomas de febre o habeva significative antecedentes de febre. Isto habeva un rolo importante in portar le patiente al attention del medico. Alte frequentia e urgentia del urese e dolores abdominal es le constatationes le plus frequente in casos de obstruction del cervice vesical. Enurese nocturne occurreva in 58 pro cento del patientes, enurese diurne in 38. In 17 pro cento del patientes, nulle symptomas urinari esseva notate. Le evalutation del patientes esseva effectuate per culturation de urina, per determinationes de urina residue, per pyelographia intravenose, per cystogramma in vacuation, e per cystoscopia. Le formas de tractamento esseva: Dilatation urethral, cystoscopia e fulguration, resection transurethral, resection suprapubic, e nihil. In multe casos, infection urinari pare haber essite presente depost plus longe tempores que lo que es indicate per le datos del historia clinic. Enurese e le absentia de illo pote esser similemente significative. Le evalutation de omne caso de un patiente juvenil con febre de incognite etiologia require un complete studio urologic.

Yeostros, S. J.: Le uso de Fe^{59} in le determination del latente capacitate ferro-ligatori; un test de valor diagnostic in varie morbos del hepate (*anglese*), NEW YORK STATE J. MED. **62:** 1386 (1 de maio) 1962.

Esseva facite un studio de 41 patientes con cirrhosis de Laennec, de 19 con hepatitis acute, e de 16 con primari o metastatic carcinoma del hepate. Le ferro del sero (FS) e le latente capacitate ferro-ligatori (LCFL) esseva determinate per electrophorese con le uso de ferro marcate con Fe^{59}. Le total capacitate ferro-ligatori (TCFL) e le procentage de saturation del TCFL con ferro esseva etiam calculate. Esseva trovate le sequente significative alterationes: In hepatitis, augmento de FS e TCFL sed normal LCFL; in cirrhosis, normal FS con basse LCFL e TCFL, sequite de crescente saturation de TCFL; e in carcinoma, basse FS con declino del saturation del TCFL. Le valor del determination de FS pro le diagnose differential del morbos hepatic investigate es augmentate quando illo es executate conjunctemente con le determination del LCFL e le calculation del TCFL e su saturation procentual.

Mindell, E. R., Cisek, E. E., e Kartalian, G.: Necrose aseptic del talus post traumatisation; reporto preliminari (*anglese*), NEW YORK STATE J. MED. **62:** 1392 (1 de maio) 1962.

Esseva studiate 21 patientes con traumatismo significative del talus. Septe de illes disveloppava necrosis aseptic. Le establimento precoce del diagnose de necrose aseptic esseva difficile. In stadios subsequente, reimplaciamento de osso necrotisate pote manifestar se in le roentgenogramma per un apparentia maculate con zonas irregular de reducite densitate e con irregularmente spissificate trabeculas. In adultos, le cartilagine articular que jace supra le osso necrotisate exhibi certe alterationes. Le tractamento usate in iste patientes con necrose aseptic esseva variate. In 3 casos con vulneres aperte, le tractamento consisteva de reduction aperte. Quanto al altere 4 patientes del gruppo de 7, duo fracturas esseva tractate simplemente per immobilisation; in le tertie, reduction claudite esseva usate e, subsequentemente, reduction aperte; le quarte esseva tractate per reduction aperte. Le periodo de controlo post-therapeutic in iste 7 casos esseva 4,5 annos al media. Le resultato final esseva excellente in 1 del casos, bon in 2, satisfacente in 2, e non bon in 2. Le resultato final in le gruppo total de 21 casos esseva marcatemente melior.

Rubin, P., Lund, C., e Prabasawat, D.: Carcinoma invasive del cervice; melioration del resultatos therapeutic (*anglese*), New York State J. Med. **62:** 1399 (1 de maio) 1962.

Le presente studio es un revista de 300 casos de carcinoma invasive del cervice tractate inter 1940 e 1956. Le superviventia quinquenne amonta a 63 pro cento, le superviventia decenne a 49,5 pro cento. Isto contrasta con le superviventia quinquenne de 26,2 pro cento e le superviventia decenne de 9,6 pro cento que esseva obtenite in un gruppo de 328 casos tractate inter 1926 e 1942. Le melioration es reflectite in omne le stadios, excepte stadio IV. Le augmento es le plus marcate in stadio II (66 pro cento in loco de 30 pro cento) e in stadio III (55 pro cento in loco de 16 pro cento). Gratias a plus prompte examines e a plus efficace technicas cytologic, plus numerose casos es discoperite in minus avantiate stadios. Le technica del therapia a radium ha evolvite in le curso del tempore. Depost 1952, applicatores typo Fletcher es in uso, e cobalt radioactive es empleate in loco de radium. Le numero del major complicationes ha declinate in parallela al melioration del cifras de superviventia total. Le complicationes concerneva le intestinos, le vias urinari, e le ossos. Irradiation esseva responsabile pro 10 pro cento de omne le complicationes, invasion tumoric pro 11 pro cento, e intervention chirurgic pro 3,3 pro cento

Young, A. W., Jr.: Problemas special de dermatogeriatrica (*anglese*), New York State J. Med. **62:** 1407 (1 de maio) 1962.

Morbo cutanee in patientes de etate avantiate debe esser considerate a base de standards special. Ab le puncto de vista dermatogeriatric on visa a correlationar le modificate responsas e le susceptibilitates special del subjecto de etate avantiate con le manifestationes del processos invetulatori in general. Es a distinguer quatro categorias de morbo cutanee que affice senescente patientes. Illos es le dermatoses obligatori, constitutional, incidental, e inveterate. Problemas special es nodulos de aure e de pede, seborrhea senil, erosion senil del tibia, eczema autogene, ceratoses seborrheic e senil, e cancere cutanee.

Rolo, A.: Suspension de drogas, effectuate con le uso de hydrochloruro de promazina (*anglese*), New York State J. Med. **62:** 1429 (1 de maio) 1962.

Quaranta-cinque patientes—22 masculos e 23 femininas—esseva tractate con hydrochloruro de promazina (Sparina a hydrochloruro) pro le syndrome de abstinentia associate con le privation de narcoticos e barbituratos. In omne le casos, con 8 exceptiones, le droga potentialmente manicogenic esseva suspendite abruptemente al momento del hospitalisation, e le curso de hydrochloruro de promazina esseva instituite immediatemente in plen doses. Le quantitate diurne variava ab 100 mg ad 1, 2 g, administrate in dividite doses per via intramuscular. Le privation esseva complite facilemente e sin major complicationes in omne le casos. Omne le patientes pareva trovar se relativemente confortabile e esseva accessibile psychotherapeuticamente durante le periodo del disaccostumation. Nulle jalnessa e nulle altere significative effectos adverse secundari esseva notate.

Herman, B. E.: Amputation transmetatarsal in gangrena arteriosclerotic (*anglese*), New York State J. Med. **62:** 1432 (1 de maio) 1962.

Inter 1955 e 1960, 11 amputationes transmetatarsal esseva executate in patientes con diabete e gangrena. Le duration medie del sojorno al hospital esseva dece-cinque septimanas e medie. In 5 del 11 casos (45 pro cento), malsuccesso esseva immediatemente evidente, e amputation infra-geniculari esseva requirite. In le altere 6, coalescimento del vulnere occurreva primarimente o post varie intervallos de tempore. Un del 6 retornava a un occupation remunerative. Tres alteres obteneva un restringite usabilitate del salvate gamba. Le resultatos es simile a illos reportate in altere studios. Le prospecto pro successo e le costos in tempore e moneta debe esser ponderate quando amputation transmetatarsal es sub consideration.

Cracovaner, A. J.: Therapeutica non-chirurgic de morbo de Ménière (*anglese*), New York State J. Med. **62:** 1435 (1 de maio) 1962.

In morbo de Ménière il occurre generalmente hydropisia del systema endolymphatic. Augmento de pression in labyrintho e cochlea produce le characteristic symptomas: Vertigine, surditate, e tinnito. Le attaccos pote durar pauc minutas o plure dies. Illos pote recurrer post septimanas o post annos. Le morbo pote esser considerate como un dysfunction autonome, causate possibilemente per un "allergia physic" (lo que es un termino omni-inclusive). Dysfunction endocrin e disturbationes metabolic ha essite trovate in certe casos. Altere factores que debe esser considerate es excessos in le uso de alcohol, sal, e certe alimentos, blocage del tubo eustachian, infection supero-respiratori o virusal, e tension e stress. Al tempore presente, il non existe un tractamento specific particular. Le tractamento debe includer le uso de vasodilatatores, restriction e elimination de natrium, drogas anticholinergic, e sedativos.

Siris, J. H., Henry, E. I., e Cukier, D. S.: Hypoxemia occulte, como complication de acute e subacute lesiones intracranial (*anglese*), New York State J. Med. **62:** 1440 (1 de maio) 1962.

Dece patientes con acute o subacute disordines intracranial (trauma, tumor, e accidente cerebro-vascular), non complicate per dyspnea, cyanosis, o altere grossier manifestationes de insufficientia respiratori, esseva studiate con respecto al contento de oxygeno in lor sanquine arterial. Conditiones de anaerobia esseva mantenite meticulosemente. Le contento total de bioxydo de carbon in sanguine total esseva determinate sub le conditiones del tension de bioxydo de carbon que de facto existeva in le articulation arterial. Patientes qui, ben que somnolente, esseva capace a ingerer nutrimento habeva nivellos de oxygeno al margine del norma o levemente plus basse. Le remanente patientes, troppo in stupor pro poter alimentar se, monstrava grados significative de hypoxemia. Le nivellos de oxygeno montava in tanto que le patientes reganiava lor conscietate. Hypercapnia non accompaniava hypoxemia in le casos studiate. In tal casos, le prime occurrentia de grados significative de hypoxemia escappa facilemente al detection per examines clinic sol, proque illo pote esser presente non accompaniate de dyspnea, cyanosis, tachycardia, o edema pulmonar.

Announcement

It is called to our attention for the information of our subscribers that the New York City Excise Tax on Gross Receipts imposed pursuant to the General Business and Financial Tax Law is due May 15, 1962. The tax applies to persons conducting any trade, business, profession, vocation, or commercial activity within the City of New York for gain or profit. In general, the tax is based on the gross receipts for the entire calendar year 1961. However, if the taxpayer has reported in a return for a prior period his gross receipts for a portion of such calendar year, the tax is measured by his gross receipts during the balance of the year.

In filing General Business Tax returns on Form B, doctors are required to report thereon as Item 4 the gross receipts (gross fees) from the practice of their profession. Dividends and interest received from investments and profits derived from stock and bond transactions should not be included in the measure of the tax when filing General Business Tax returns if such transactions are occasional transactions of a nature extraneous to the taxpayer's regular activities. In reporting gross receipts, no deduction may be taken for salaries, rent, and other office expenses.

Where a doctor is also a member of a medical group associated with the Health Insurance Plan of Greater New York, the distributive share of the income he receives from the group is not to be included in his gross receipts, since the various medical groups associated with H.I.P. are generally regarded as partnerships and are required to file returns on the basis of their total gross receipts.

In computing gross receipts subject to tax, the taxpayer may take a specific deduction of $10,000.00 from his gross receipts. Tax at the rate of $^{2}/_{5}$ of 1 per cent is to be paid on his gross receipts in excess of $10,000.00. No tax is imposed when the gross receipts do not exceed $10,000.00, and no return need be filed in such case.

The return must be filed on or before May 15, 1962, with the City Collector in the borough in which the taxpayer maintains his office. A remittance for the total amount of tax due, drawn to the order of the City Collector, must accompany the return when filed. Form B for filing this return will be mailed to all taxpayers who have filed returns in prior years. The office of the Comptroller of the City of New York will be pleased to furnish further information or assistance in the preparation of returns.

Woman's Auxiliary

Health Poster Contest

The Tenth Annual State-wide Health Poster Contest, sponsored by the Woman's Auxiliary to the Medical Society of the State of New York, closed on March 30, 1962.

Because of the increase this year in the number of county auxiliaries participating in this worth-while project, it is strongly felt that the aim and purpose of the contest has been recognized as an excellent means of promoting good public relations in the community.

Not only does this contest strive to stimulate health consciousness in our youth, it also encourages the parents of the contestants to realize the importance of guarding their own health as well as that of their families.

From the reports of the county auxiliaries, the contest has been most valuable to the educators of our future citizens, by helping them to execute health programs in their schools. They know that if a student is aware of safeguarding his own health, he develops into a more stable student and one who will achieve success. This year as well as in the past, in spite of other contests running concurrently with the Health Poster Contest, we have had full cooperation from the schools and have been impressed that they realize their responsibility in urging the students on the elementary and high school levels to enter the contest.

The originators of the Health Poster Contest should be congratulated on the annual success that this program has had since its inception. More than 120,000 posters have been submitted over a period of ten years. The county contests have been well executed by the auxiliaries, and many of the judges have been chosen for their expert knowledge of art, along with members of the county medical societies.

Through this contest we feel that we have given to our youth the added dividend of playing an important role in furthering the value of preventive medicine as a prominent asset in every community. The young people are given an insight into the integral part the doctor takes in preserving the lives and health of the citizenry.

Furthermore it is hoped that the continuance of the Health Poster Contest will gain respect, confidence, and esteem for the medical profession.

The State judging will take place in Glens Falls on April 5 in the Schine Queensbury Motor Inn.

The awards will be based on health message, 60 points; originality of design, 25 points; and general appearance, 15 points. A total of $500 in U.S. Savings Bonds has been donated by the Medical Society of the State of New York. Each grade group will receive first and second prizes. Honorable mention certificates will also be awarded. The first prize winner will receive a $125 Savings Bond. (The 1961 winner expressed a desire to continue her education in the field of art.)

The judges scheduled to serve are as follows: Hon. Harry G. Helm, Mayor of the City of Glens Falls; Richard J. Bartlett, State Assemblyman, Warren County; Henry I. Fineberg, M.D., Executive Vice-President, Medical Society of the State of New York; Joseph J. Dodge, Curator, Hyde Collection, Glens Falls; Thomas C. Mahoney, advertising artist, Glens Falls; Dominick A. Zurlo, M.D., President, Warren County Medical Society; E. Y. Clarke, M.D., State Legislation Committee, Warren County Medical Society; Irving R. Juster, M.D., Warren County Medical Society; and John Schuyler, Department of Communications, Medical Society of the State of New York.

MRS. EDWARD P. RYAN, *Chairman*
Health Poster Contest

615 Glen Street
Glens Falls, N. Y.

Medical Schools

Albany Medical College

General research support grant. The National Institutes of Health presented a grant of $126,040 under the new General Research Support Grant program which will enable the College to expand and strengthen its research and many research training programs. Among the new and expanded research activities planned are: development of research programs in the fields of gastroenterology, radiation biology, and medical genetics; enlargement of the Division of Bio-Medical Engineering (the division services, designs and builds much of the medical electronics equipment used at the Center); enlistment of young, promising research personnel; encouragement of basic and applied research projects which do not fit the categories of federal and nonfederal agencies; creation of an office of medical illustration; and provision of more summer research fellowships for medical students and promising high school students.

Symposium. The medical aspects of civil disaster, including the physician's role in the wake of a nuclear attack, was discussed in a special symposium on March 22. James H. Lade, M.D., director of the Bureau of Medical Defense, State Health Department, Lt. General Francis W. Farrell, director, State Civil Defense Commission, and Solomon Garb, M.D., associate professor of pharmacology, University of Missouri School of Medicine, were the speakers. The symposium was arranged by the Medical Education for National Defense Committee (MEND) of the College.

Albert Einstein College of Medicine

New faculty members. Solomon A. Berson, M.D., and Rosalyn Yalow, M.D., have been appointed to the faculty as professor of medicine and radiology and visiting physician at the Bronx Municipal Hospital Center and professor of radiology, respectively. Dr. Berson is currently chief of the Radioisotope Service, the Veterans Administration Hospital, the Bronx, and Dr. Yalow is the assistant chief of the same service. Dr. Yalow also will be assistant director of the Clinical Research Center now being developed at the College and Dr. Berson will direct the isotope activities of the Center.

Faculty appointments, promotions, and fellowships. Department of Anatomy, Anne B. Johnson, M.D., research associate; Department of Medicine, Thomas B. Bradley, Jr., visiting instructor; Department of Pathology; Fernando P. Aleu, M.D., assistant professor, and Nicholas K. Gonates, M.D., instructor (neuropathology); Department of Pediatrics, Bernard Eli Cohen, M.D., visiting associate professor; Department of Surgery, Bernard Herzog, M.D., clinical instructor (dental).

Faculty promotions include Melvin Bronstein, M.D., from clinical instructor to assistant clinical professor in the Department of Ophthalmology; Masamichi Oka, M.D., from visiting instructor to assistant professor in the Department of Pathology; and Chester M. Edelmann, Jr., from instructor to associate in the Department of Pediatrics.

Fellowships have been awarded to Kurt Gerstmann, M.D., and Ivan Herzog, M.D., in the Department of Pathology, and Jack Litwin, M.D., in the Department of Cell Biology.

Research grants. Research grants recently presented to the College from the National Institutes of Health include: National Institute of Neurological Diseases and Blindness to: Saul R. Koreny, M.D., and William T. Norton, M.D., Department of Neurology; Mark Rayport, M.D., Department of Neurological Surgery and Physiology; Dr. Seth K. Sharpless, Department of Pharmacology; Dr. Salome Gluecksohn-Waelsch, Department of Anatomy; Louis Berlin, M.D., Department of Neurology; Dr. Max Hamburgh and Dr. Ernst Scharrer, Department of Anatomy. From the National Institute of Arthritis and Metabolic Diseases: Henry D. Lauson, M.D., and Richard M. Hays, M.D., Department of Medicine. From the National Cancer Institute, Alex B. Novikoff, M.D., and Alfred Angrist, M.D., Department of Pathology. From the National Institute of Allergy and Infectious Diseases, Harry Eagle, M.D., Department of Cell Biology. From the National Heart Institute to: Charles W. Frank, M.D., Department of Medicine.

Columbia University College of Physicians and Surgeons

Rippel foundation. The receipt of a $200,000 grant from the Fannie E. Rippel Foundation for construction of facilities for research in heart disease has been received by the University. The facilities will be housed in the new William Black Medical Research Building at the Columbia-Presbyterian Medical Center. The Rippel Foundation of Newark, New Jersey, is an organization devoted to aiding hospitals and institutions and organizations for the relief and care of aged women, or for treatment of (and research concerning) heart disease or cancer.

Given Foundation Research Fund. A gift of $900,000 has been received by the College from The Irene Heinz Given and John La Porte Given Foundation, Inc., for the establishment of a Given Foundation Research Fund in the Department of Urology. The grant is for the purpose of advancing research and teaching in urology and a portion of the income of this fund will be used to establish a Given Foundation Professorship. Meyer M. Melicow, M.D., has been named the first Given Professor.

Cornell University Medical College

Drive. William A. Barnes, M.D., clinical associate professor of surgery, has been appointed chairman of the medical progress program. David D. Thompson, M.D., associate professor of medicine and associate attending physician at the hospital, has been appointed cochairman.

New York Medical College

Appointed. Warner F. Bowers, M.D., formerly assistant executive director of the International College of Surgeons, joined the full-time faculty on January 1 as professor of clinical surgery.

New York University Medical Center

Appointed. Eugene Moskowitz, M.D., associate clinical professor of physical medicine and rehabilitation, has been appointed consultant to the University of Puerto Rico School of Medicine. Dr. Moskowitz will work with the University's officials in plans for the strengthening and expanding of their teaching, research, and patient-care services in physical medicine and rehabilitation. In connection with his appointment, Dr. Moskowitz spent from March 18 to March 31 at the university.

Visiting professor. Robert L. Bennett, M.D., director, Warm Springs Foundation, was the 1962 Horowitz Visiting Professor of the Department of Physical Medicine and Rehabilitation. The lecture was presented on March 13 and concerned "Orthetics in Physical Medicine." The Horowitz Visiting Professorship was established to honor Louis J. Horowitz, benefactor and one of the original founders of the Institute of Physical Medicine and Rehabilitation.

State University of New York Downstate Medical Center

Lectures. Lucie Jessner, M.D., professor of psychiatry, University of North Carolina, and visiting professor of psychiatry for the month of February at the Center, lectured on "The Development of Identity and Self Awareness in the Child" on February 20.

Guest speaker. Pascal Imperato, fourth-year student, was guest speaker at a meeting of the Center's Parent's Association meeting in March. Mr. Imperato spoke on "Summer Fellowship in Tanganyika." The fellowship was a Smith, Kline and French foreign fellowship awarded last year and Mr. Imperato spent three months working at the Kowak Catholic Hospital.

Symposium. An all-day symposium on "Heart Disease in Infancy" was held at the Center on March 14. Joshua Lynfield, M.D., assistant professor of pediatrics and director of pediatric cardiology, directed the symposium. Speakers were: Abraham M. Rudolph, M.D., associate professor of pediatrics, Albert Einstein College of Medicine; Alexander S. Nadas, M.D., associate clinical professor of pediatrics, Harvard Medical School, and cardiologist, Children's Medical Center, Boston; Sidney Blumenthal, M.D., clinical professor of pediatrics, Columbia-Presbyterian Medical Center; Mary Allen Engle, M.D., associate professor of pediatrics, Cornell University; Eugene F. Doyle, M.D., associate professor of pediatrics, New York University; Dr. Lynfield; and William T. Mustard, M.D., assistant professor of surgery, University of Toronto, and chief, Cardiovascular Surgery, Hospital for Sick Children, Toronto.

State University of New York Upstate Medical Center

Speaker. Dorothy M. Horstmann, M.D., professor of epidemiology and pediatrics, Yale University, spoke on "Notes on a Scientific Mission to the U.S.S.R." in March. The lecture was sponsored by Alpha Epsilon Iota, women's medical sorority. Mrs. Jeanette Schoonmaker, senior medical student and president of the sorority for 1961 to 1962, introduced Dr. Horstmann.

Fellowship. Kenneth Tuerk, junior, has been awarded a Smith, Kline and French Laboratories fellowship which will provide opportunity to travel and study in India during the summer of 1962.

George Birney Broad lecture. Clyde L. Randall, M.D., professor and chairman, Department of Obstetrics and Gynecology, University of Buffalo School of Medicine, delivered the annual George Birney Broad Lecture on March 14. Dr. Randall spoke on "Conservation or Prophylaxis as Regards the Ovary."

University of Rochester School of Medicine and Dentistry

Appointed. John H. Flinn, M.D., director of student health and associate professor of medicine, University of Wisconsin, has been appointed to the newly created post of director of the University's student health program. One of Dr. Flinn's prime responsibilities will be to unify into a single all-University program the health service programs conducted by J. Fletcher McAmmond, M.D., chief medical officer for the River Campus and Eastman School, and Einar Lie, M.D., director of student health at the Medical Center.

Books Received

The following books were received during the month of February, 1962

Atlas of Clinical Endocrinology. By H. Lisser, M.D., and Roberto F. Escamilla, M.D. Second edition. Quarto of 489 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $23.

Textbook of Endocrinology. Edited by Robert H. Williams, M.D. Third edition. Quarto of 1,204 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $21.

Oligophrenia—Mental Deficiency in Children. By M. S. Pevzner. Octavo of 406 pages, illustrated. New York, Consultants Bureau, 1959. Cloth, $15.

General Pathology. Edited by Sir Howard Florey. Third edition. Octavo of 1,104 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $22.

Modern Concepts of Hospital Administration. Edited by Joseph Karlton Owen, Ph.D. Quarto of 823 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $16.

Drugs of Choice 1962–1963. Edited by Walter Modell, M.D. Octavo of 941 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $14.50.

Pharmacology and Therapeutics. By Arthur Grollman, M.D. Fifth edition, revised and enlarged. Octavo of 1,131 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $12.50.

Biological Effects of Freezing and Supercooling. By Audrey U. Smith, M.B. Octavo of 462 pages, illustrated. Baltimore, The Williams & Wilkins Company, 1961. Cloth, $11.

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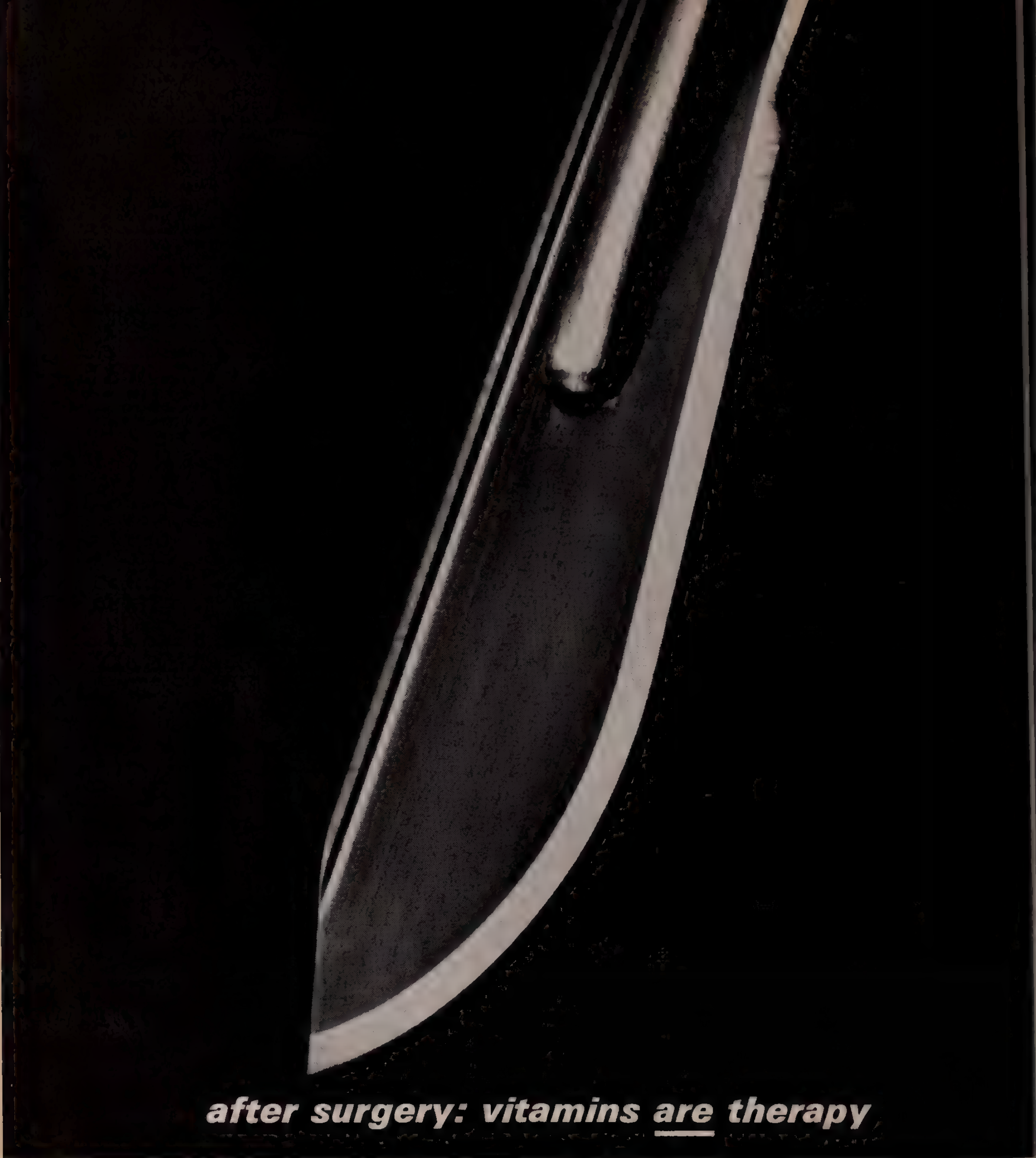

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References: 1. DeNyse, D. L.: M. Times 87:1512 (Nov.) 1959.
2. Gruenberg, F.: Current Therap. Res. 2:1 (Jan.) 1960.

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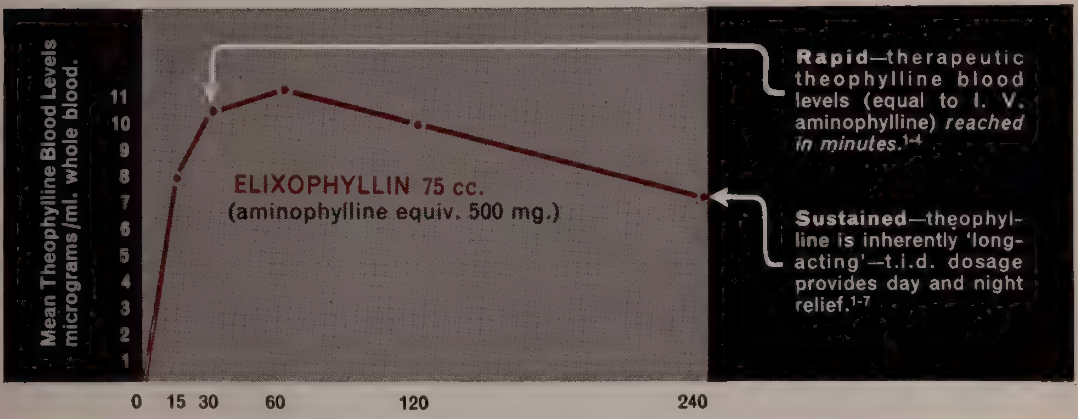

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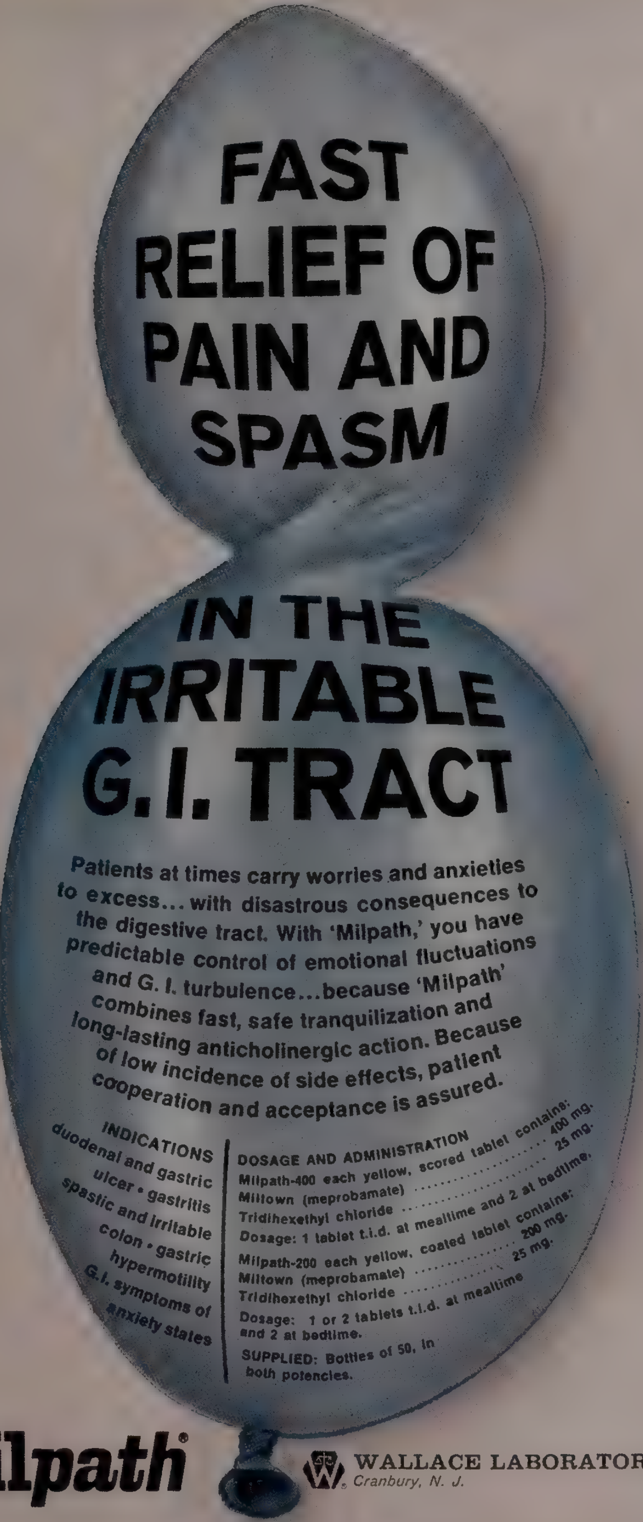

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1. Ford, R. V.: Clin. Res. Notes 2:1 (Dec.) 1959. 2. Ford, R. V.: Cur. Therap. Res. 2:92 (Mar.) 1960. 3. Elliott, J. P., Jr., and Goldman, A. M.: South. M.J. 54:794 (July) 1961.

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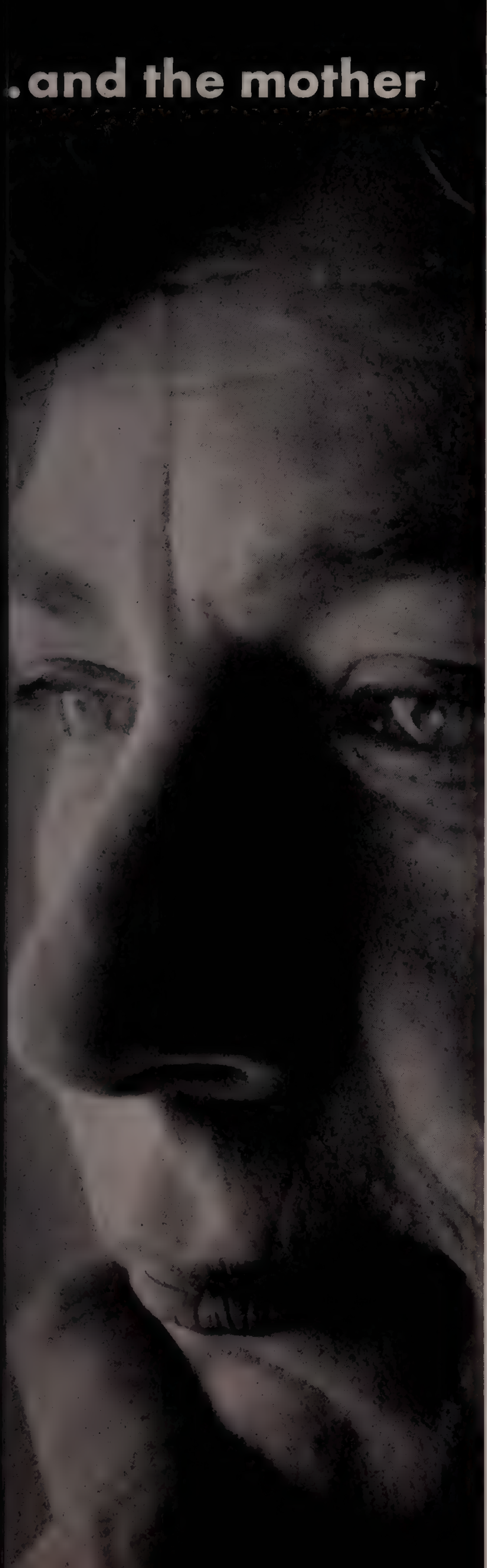

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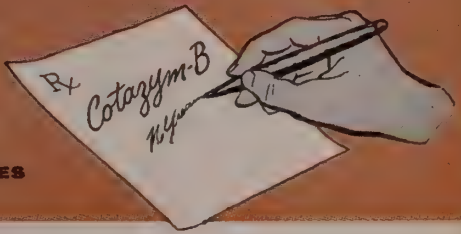

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REFERENCES: 1. Best, E. B., Hightower, N. C., Jr., Williams, B. H., and Carobasi, R. J.: South. M.J. 53:1091, 1960. 2. Analytical Control Laboratories, Organon Inc. 3. Best, E. B., et al.: Symposium at West Orange, N. J., May 11, 1960. 4. Thompson, K. W., and Price, R. T.: Scientific Exhibit Section, A.M.A., Atlantic City, N. J., June 8-12, 1959. 5. Weinstein, J. J.: Discussion in Keifer, E. D., Am. J. Gastro. 35:353, 1961. 6. Ruffin, J. M., McBee, J. W., and Davis, T. D.: Chicago Medicine, Vol. 64, No. 2, June, 1961. 7. Berkowitz, D., and Silk, R.: Scientific Exhibit Section, A.M.A., New York, June 25-30, 1961. 8. Berkowitz, D., and Glassman, S.: N. Y. St. J. Med. 62:58, 1962.

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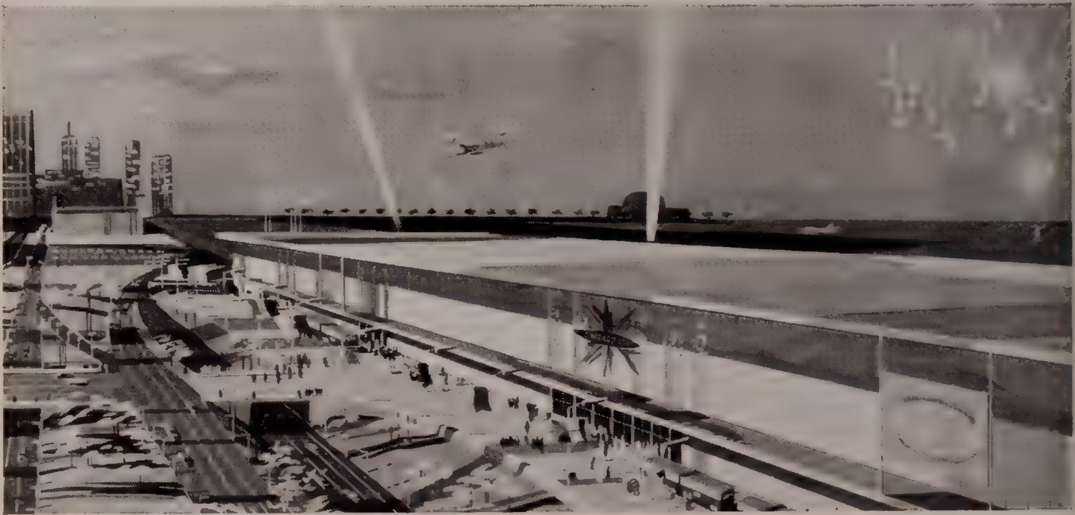

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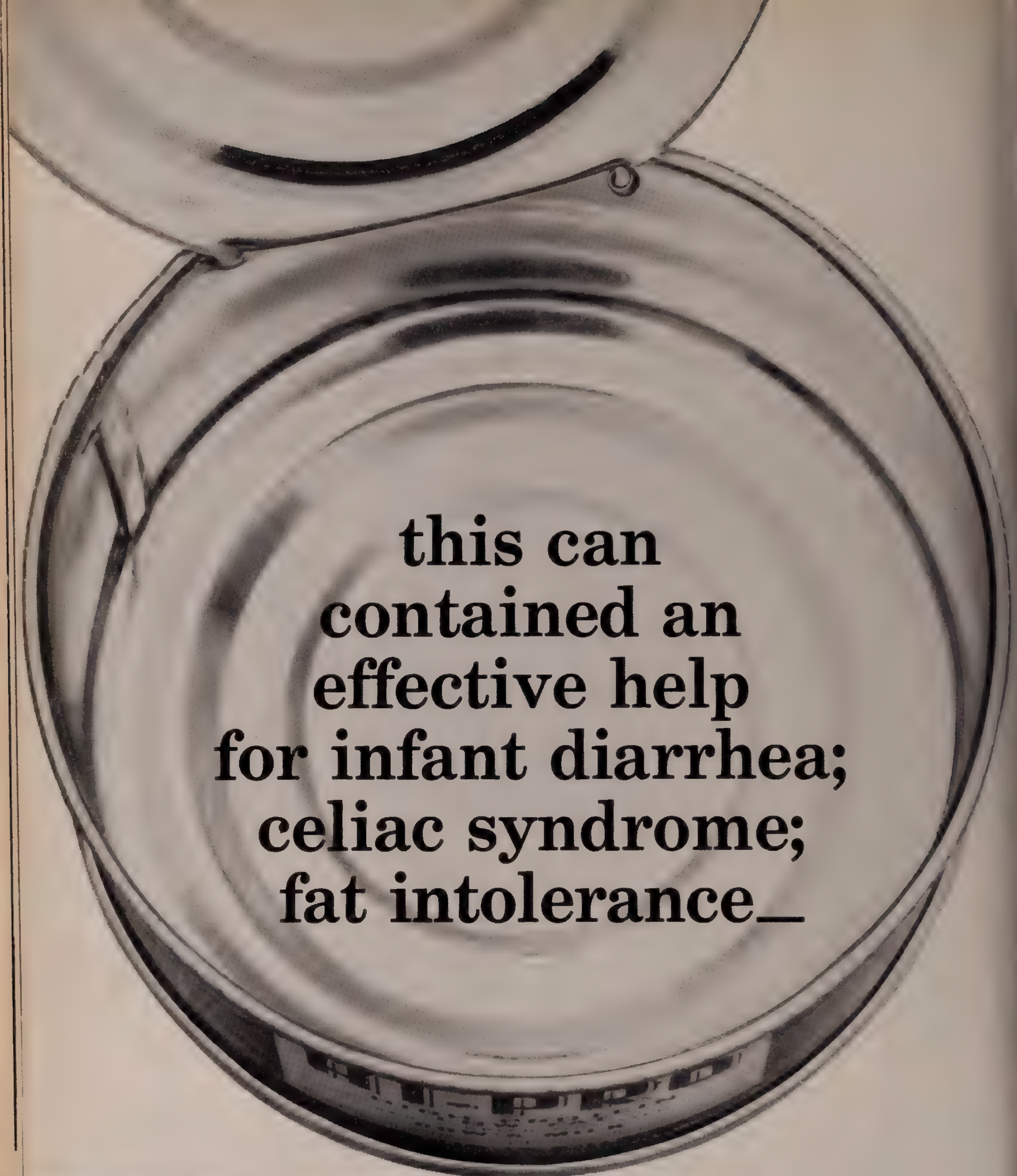
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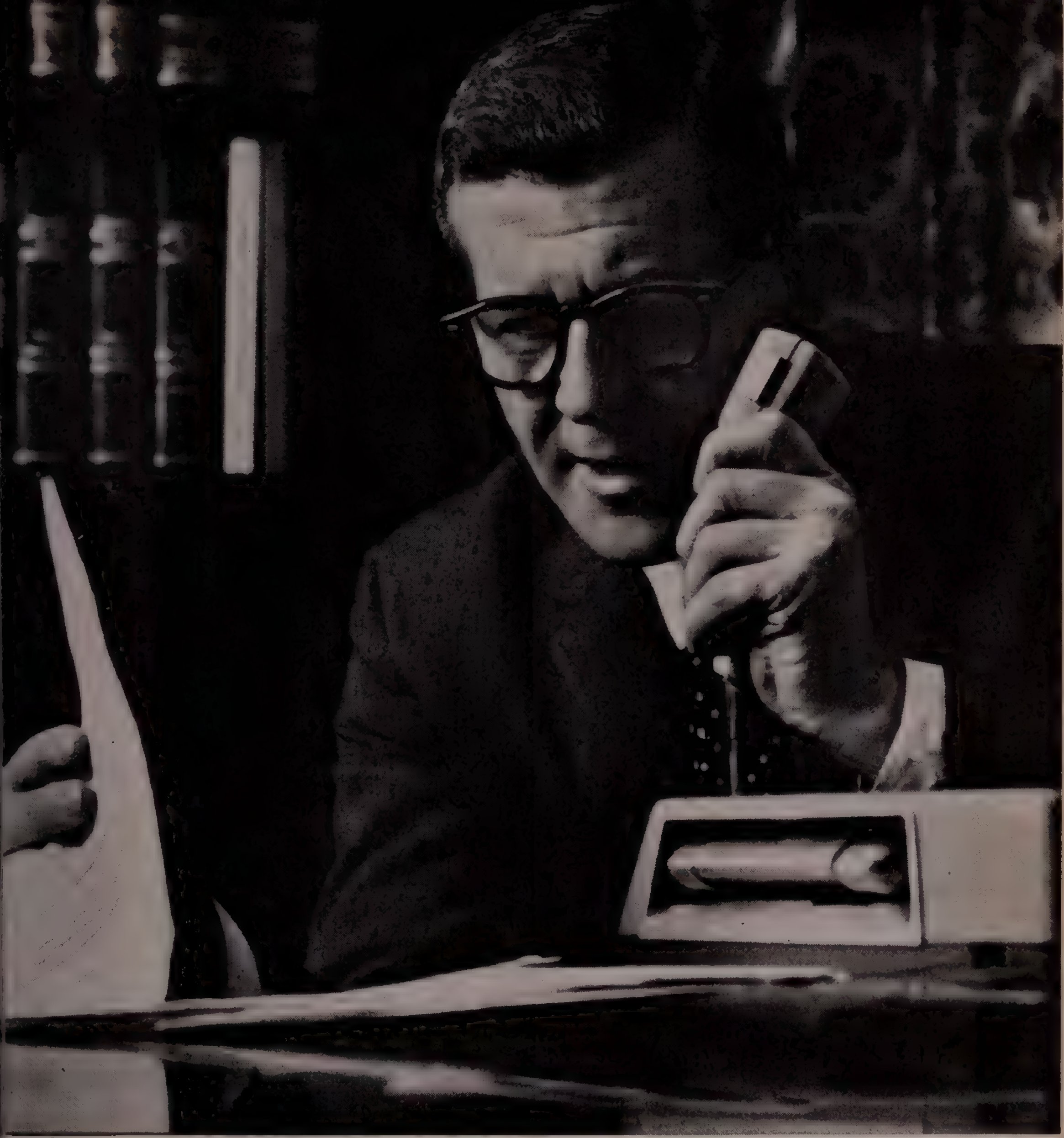

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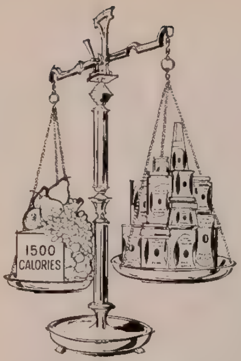

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Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
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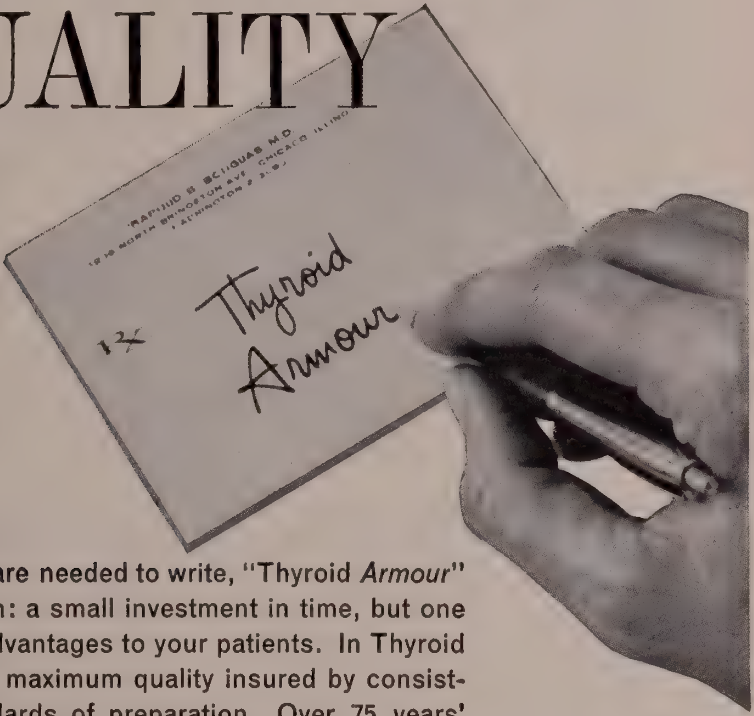

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Technical Exhibits At Medical Meetings

The medical exhibitor, if he expects success, must know his doctors well. Their temperaments cover a spectrum from the archly independent and often innovative individualist to the highly conservative individual. It is up to the exhibitor to understand that different types of physicians "behave" in different ways. Directly to the point: it is basic knowledge for an exhibitor that a physician with a conservative bent is more drawn to medical meetings—both local and out-of-town—than his highly individualistic colleague.

The task of the exhibitor then becomes to tailor his medical meeting presentations to the taste of conservative physicians. Exhibits must offer practical information which doctors can use in daily practice. This does not mean that an exhibitor should engage in a private contest to see how many samples and pieces of literature he can hand out. Such a practice offends good taste and invites legitimate criticism.

A company representative attending a booth at a medical meeting should understand clearly why he is there. His single job is "doctor relations". . . . the cultivation of good will and better understanding for his company. To best achieve this, of course, he should think in terms of supplying doctors with genuinely useful information.

Under these circumstances, what happens to salesmanship? Does salesmanship have a role in a medical exhibition? Of course it does. It is hardly a secret that every company exhibiting at a medical convention would like to see its efforts crowned with increased sales. Yet this does not mean that it is permissible to turn an exhibit into a soapbox for huckstering.

A would-be medical exhibitor can take his cue, however, from the successful salesman. Such a salesman makes it a cardinal rule to do more than describe the merits of the particular product he has to offer; he also works to convince the prospective buyer that he is his ally, genuinely interested in the buyer's well being. This second activity of a good salesman is the main function of a medical exhibit. The job of a medical exhibit is to demonstrate that the company concerned is actually interested in helping the doctor and, indirectly, in helping those persons the doctor serves.

Discussed in such terms, the medical exhibit might, at first, seem a hypocritical and callous device for generating sales. It is not. The successful exhibit must—first and foremost—incorporate a worthwhile message. If it is sincere, if it is honest and if it is interesting, physicians will notice. The benefits to the company from such an exhibit can be very real, even though they are indirect.

Exhibitors planning for a medical convention will do well to keep in mind their role *vis-a-vis* the physician. Whereas company representatives who call on physicians are guests in a doctor's office, the exhibitor is host when the doctor comes to call. It is no courtesy to subject physicians to a repetition of material previously presented by detailmen.

A good exhibit, in the final analysis, is one which helps a physician practice better medicine. One criterion singles out the exhibitor who knows his business; physicians identify his company as one which works conscientiously in their interest.

By D. M. Robertson, Services Manager, Professional Relations, Merck, Sharp and Dohme, Division of Merck & Co., Inc., West Point, Pennsylvania.

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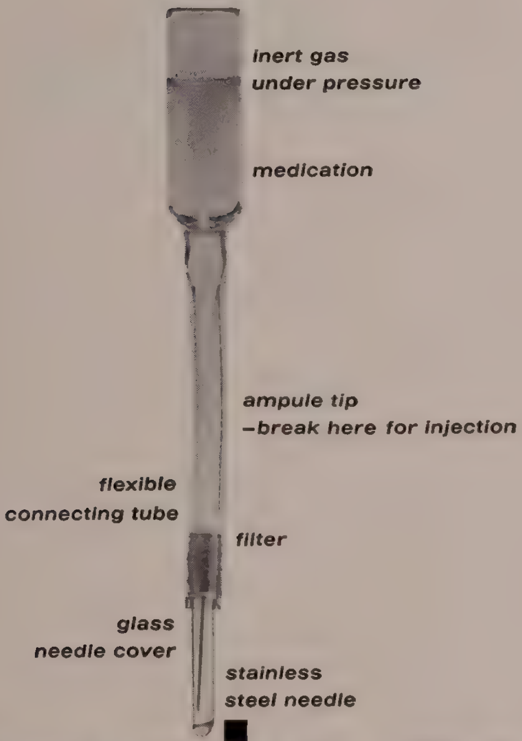

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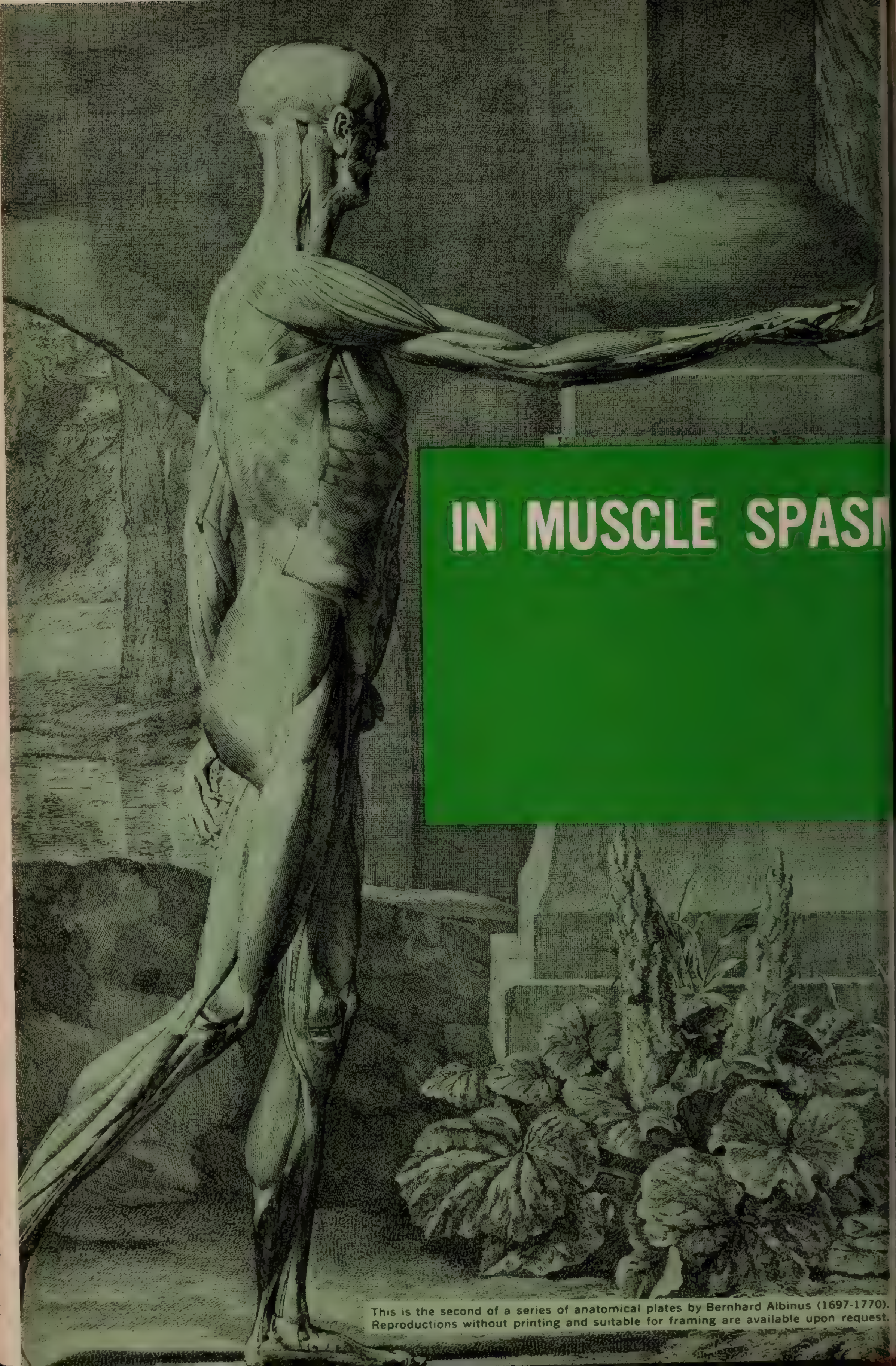
* Feinblatt, T.M., and Ferguson, E.A., Jr., Phenobarbital idosyncrasy, avoidance by use of phenobarbital-niacin, *N. Y. State J. Med.* 62:221-3, Jan. 15, 1962.



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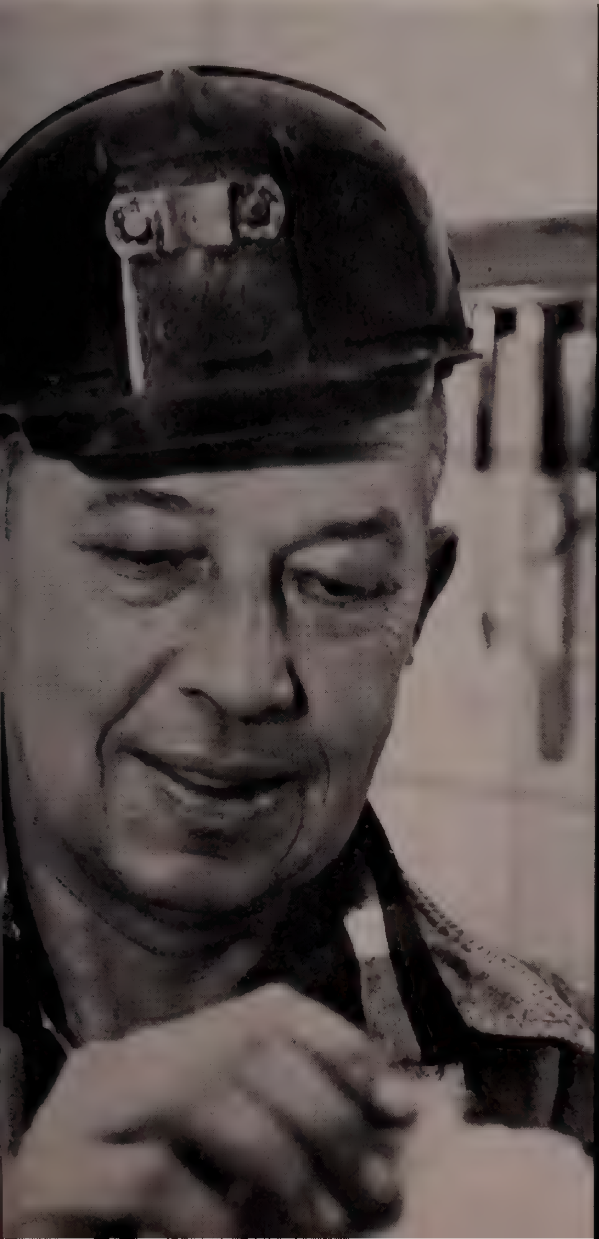

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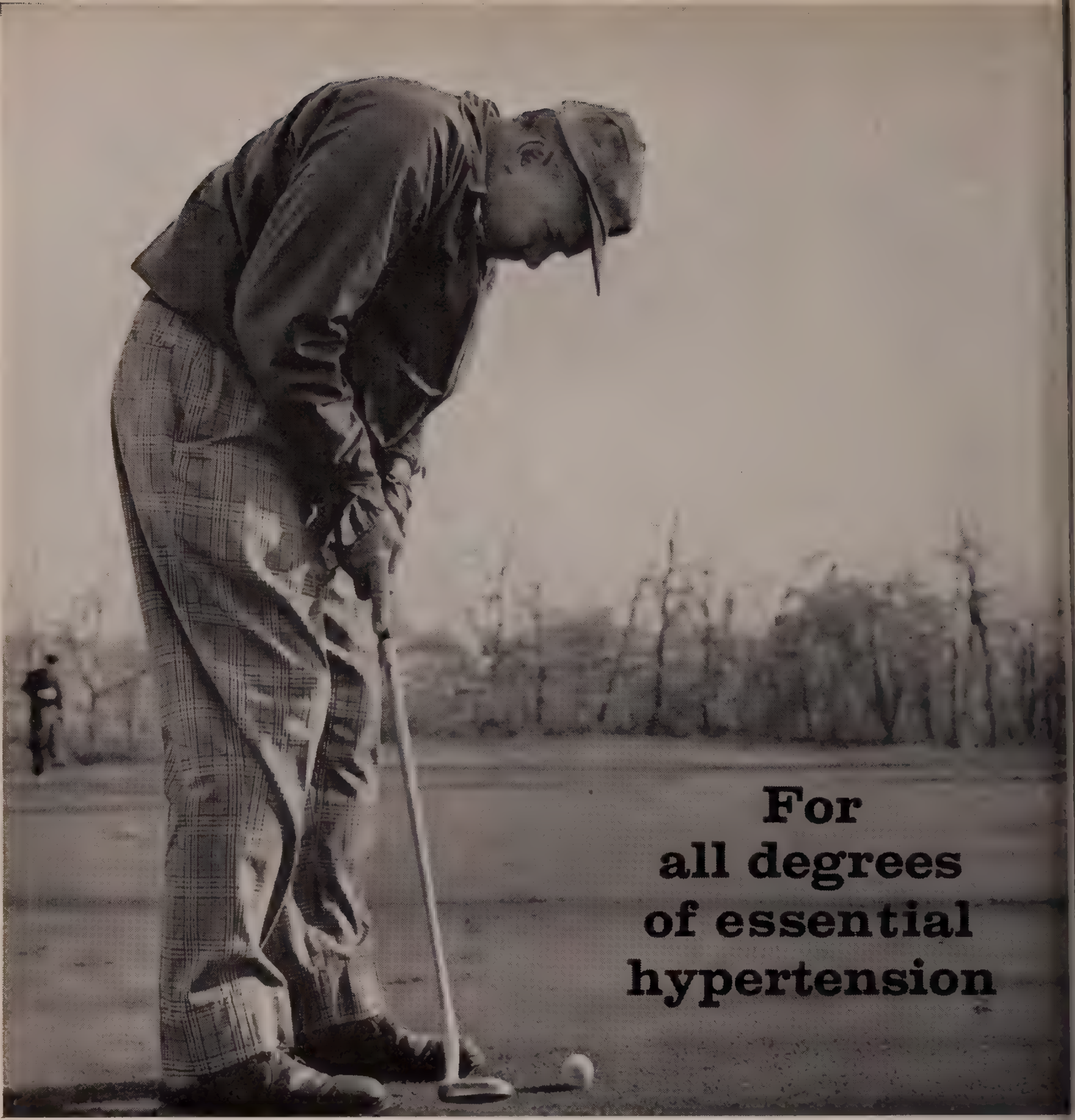

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†Hutchison J. C.: Current Therap. Res. *2*:487 (Oct.) 1960.

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1. Cohen, B. M.: M. Times 88:855 (July) 1960. 2. Cohen, B. M.: Méd. et Hyg. (Genève) #494, p. 210 (Mar. 15) 1961.

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Brightens up the mood, brings down tension

Deprol's balanced action avoids "seesaw" effects of energizers and amphetamines. While energizers and amphetamines may stimulate the patient – *they often aggravate anxiety and tension.*

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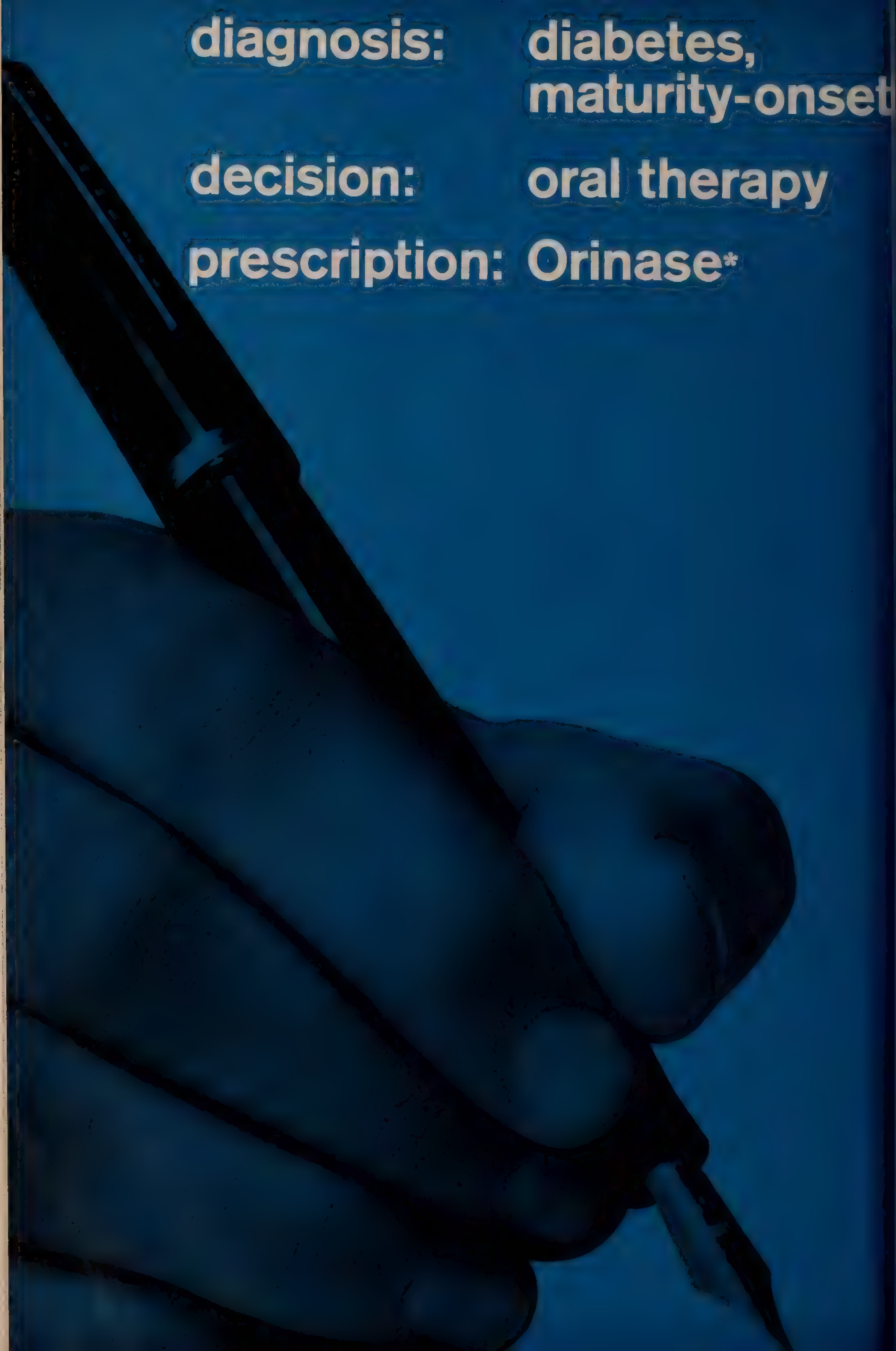
diagnosis: diabetes, maturity-onset
decision: oral therapy
prescription: Orinase*

"It is our practice in those patients in whom oral therapy is indicated to use tolbutamide [Orinase] first."[1]

And when you adopt this approach in newly-discovered, non-ketotic adult diabetics, you provide optimal control in the great majority of instances.

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Indications and effects: The clinical indication for Orinase is stable diabetes mellitus. Its use brings about the lowering of blood sugar; glycosuria diminishes, and such symptoms as pruritus, polyuria, and polyphagia are alleviated.

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Patients receiving insulin (less than 20 units) – discontinue insulin and institute Orinase; (20 to 40 units) – initiate Orinase with a concurrent 30 to 50% reduction in insulin dose with a further careful reduction as response to Orinase is observed; (more than 40 units) – reduce insulin by 20% and initiate Orinase with a further careful reduction in insulin dosage as response to Orinase is observed. In candidates for combined Orinase-insulin therapy, an individualized schedule is usually obtainable during a trial course of two or more weeks.

Contraindications and side effects: Orinase is contraindicated in patients having juvenile or growth-onset, unstable or brittle types of diabetes mellitus; history of diabetic coma, fever, severe trauma or gangrene.

Side effects are mild, transient and limited to approximately 3% of patients. Hypoglycemia and toxic reactions are extremely rare. Hypoglycemia is most likely to occur during the period of transition from insulin to Orinase. Other untoward reactions to Orinase are usually not of a serious nature and consist principally of gastrointestinal disturbances, headache, and variable allergic skin manifestations. The gastrointestinal disturbances (nausea, epigastric fullness, heartburn) and headache appear to be related to the size of the dose, and they frequently disappear when dosage is reduced to maintenance levels or the total daily dose is administered in divided portions after meals. The allergic skin manifestations (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) are transient reactions, which frequently disappear with continued drug administration. However, if the skin reactions persist, Orinase should be discontinued.

Clinical toxicity: Orinase appears to be remarkably free from gross clinical toxicity on the basis of experience accumulated during more than four years of clinical use. Crystalluria or other untoward effects on renal function have not been observed. Long-term studies of hepatic function in humans and experience in over 700,000 diabetics have shown Orinase to be remarkably free of hepatic toxicity. There has been reported only one case of cholestatic jaundice related to Orinase administration, which occurred in a patient with pre-existing liver disease and which rapidly reversed upon discontinuance of the drug.

Each tablet contains:

Tolbutamide .... 0.5 Gm.

Supplied: In bottles of 50 and 200.

Orinase

Upjohn

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January 1962

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[1] Miller, E. D., Jr., and Roller, G. W.: M. Times 89:196 (Feb.) 1961.

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New York State Journal of Medicine

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Editorials

Application of testing data for intelligence

It was not until the very end of the nineteenth century that there was any conception of mental growth or mental measurement. Before that the idea of an orderly sequence of maturation of the intellectual functions had not been considered. Cattell in 1890 was the first to use the term "mental test." Within the next ten years a few attempts were made to develop tests made up of simple motor and perceptual tasks by which the probability of success in school could be predicted. These tests included physical measurements such as height, weight, and lung capacity, tonal memory, speed of simple reactions, estimation of distance, sensitivity to pain, rate of tapping, and so forth. These first tests did not measure intelligence and were not useful in predicting scholastic success, nor did they correlate with the teacher's judgment of the child's ability.

Binet in 1908 conceived the idea of a scale of items which were grouped not only in order of difficulty but also according to the age at which they were usually passed. His approach was different from that of earlier investigators. He attempted to measure more complex performance of the individual and so came closer to measuring intellectual activity. From these tests the child's level of ability could be estimated. Binet testing was rapidly taken up in America.

So many mental tests were devised that Hildreth, in 1945, listed the unbelievable number of 5,294 different tests. This enormous quantity of tests gives evidence of the great interest in America in measuring intellectual capacity.

It is important for physicians to familiarize themselves with the tests found most useful for the children whom they see in their practice. Some knowledge of the reliability and validity of these tests as well as an understanding of what functions they measure is valuable.

The physician cannot rely entirely on his clinical judgment as to whether a child is defective, average, or superior in intelligence. There are simple tests which he can give in his office to assist him in determining this. But beyond this the level of intelligence must usually be ascertained by a well-trained psychologist. The physician needs to understand what the psychologist is telling him in his report. Many of the terms are simple once they are comprehended.

The average intelligence quotient (I.Q.) is 100.

Many tests are scored in mental age (M.A.). The mental age is the score in months or years that a child makes on a test.

The ratio obtained by dividing the mental age in months by the child's chronologic age in months (C.A.) multiplied by 100 is called the I.Q.

$$\text{I.Q.} = \frac{\text{M.A.}}{\text{C.A.}} \times 100$$

If the M.A. and C.A. are the same, the I.Q. is 100.

Certain tests including the Wechsler Intelligence Test Scale for Children (WISC) are arranged so that not only a full score I.Q. is obtained but also a verbal I.Q. and a performance I.Q.

Gesell prefers to use the designation developmental age rather than mental age when younger children are tested on his scale.

The drawing age (D.A.) on the Goodenough Draw-a-Person test correlates closely in normal children with the mental age on the Stanford-Binet test. The drawing age is the score in months that the child obtains when the drawing is scored according to Goodenough.

Educational achievement tests are scored in terms of grade and sometimes age. Reading grade 1.4 means that the child reads at the level of first grade, four months. Reading age 8.2 means he reads at the eight year, two month level, that is, as well as an average child of eight years, two months. These are compared with his school grade placement and his chronologic age at the time of testing.

When children are being tested competitively for admission to special schools or classes the achievement and aptitude test results may be reported in percentiles. This allows comparison with other children so tested. The ninety-eighth percentile means that 2 per cent of the children tested scored better than he did. If he is in the sixty-seventh percentile it means that 33 per cent scored better.

Personality inventory scales and social maturity tests give a measure of the child's social adequacy. This score is usually expressed as social age (S.A.) which is convertible into social quotient (S.Q.) in the same way as the mental age is converted into the I.Q.

Mental tests are technics devised to meet some specific need. Even at best they are still fallible and are dependent not only on the type of test given but also on the training and ability of the one administering the test and the cooperativeness and well-being of the child being tested.

The physician who understands the values and difficulties in mental testing is in a unique position. His rapport with his patient and his wide knowledge of his patient's background allow him to interpret the observations and scores which are presented to him by the psychologist in humane and intelligible terms.

RUTH MORRIS BAKWIN, M.D.

Just like a doctor's prescription

The canons of candor require an analysis of the too often repeated slogan—"just like a doctor's prescription"—which emphasizes compounding. A private survey of retail and hospital pharmacies tells us exactly what a doctor's prescription in 1962 is like. It is not likely to be made up of more than one ingredient. The pharmacies studied were generally agreed that 75 per cent of the prescriptions filled were single directives and only 25 per cent were compounded. One pharmacy estimated as high as 90 per cent were for single items. The trend, of course, has been away from the shotgun to the high-speed rifle. "Just like a doctor's prescription used to be" more nearly expresses the situation. Why should doctors be dragged into the sales pitch anyway?

If it is unethical for a doctor to advertise, is it not just as unethical for doctors to be advertised? Decency finally prevailed when actors dressed in white coats posing as doctors in commercial presentations were removed from the microwaves. Now let us strive to have all mention of doctors removed from this great American folkway.

Every man his own lawyer, billed as "just like a lawyer's brief," makes as much sense.

A new feature

In this issue we inaugurate an expanded "Letters to the Editor" section. This is open to all our readers, and views on any subject pertinent to the practice of medicine are eligible for consideration. We ask only that the views be temperate and constructive.

We ask also that the name and address of the writer be given; however, anonymity by nom de plume or otherwise will be respected if requested.

Here is an opportunity to air that long-incubating idea, ask a question, or offer helpful criticism. "Lay on, Macduff!"

Value of seat belts

It is seldom recognized that approximately 30 per cent of all vehicles manufactured are involved, at one time or another, in injury and fatality-producing accidents. A large number of these accidents occur at speeds of under 40 miles an hour. Physicians probably run more of a risk because of the substantial mileage they drive, often under hazardous conditions.

The importance of using seat belts to minimize the effects of accidents on both short and long trips is well established. The automotive crash injury research at Cornell University and other highly-regarded studies show that many lives can be saved and countless disabling injuries avoided through the use of seat belts in automobiles. Yet many persons, including physicians, have not yet taken advantage of this important safety feature.

When an automobile crashes, the occupants continue to move forward until they hit either the street or some hard portion of the interior. The seat belt serves to "tie" the occupants in the vehicle so that when the vehicle crashes, their deceleration tends to be much less abrupt and consequently severe injury is sustained less often.

Many injuries and deaths result from the driver or a passenger being ejected at the time of impact. Ejection occurs in about 14 per cent of injury-producing accidents. Researchers at Cornell found that ejection multiplies by five times the risk of dangerous or fatal injury. Seat belts keep people from being ejected. Other injuries and deaths result from striking the steering wheel assembly and other surfaces or objects in the car.

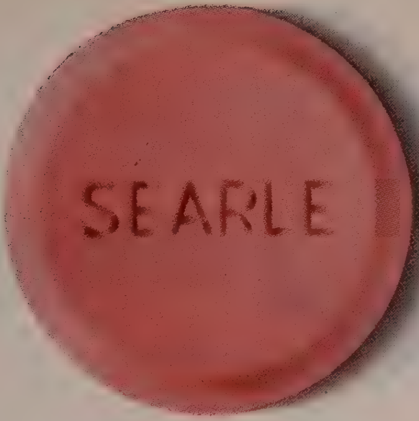
Some of the reasons people give for not using seat belts are that they tend to be uncomfortable, they take too long to put on and take off, and they get dirty if allowed to drag on the floor.

How can these reasons be equated with the benefits?

It is a proved fact that seat belt users have up to 35 per cent less risk of serious injury from these hazards than nonusers. Lap belts, the familiar types of seat belt used in this country, are inexpensive and simple to attach to cars, and if they are worn properly, they are comfortable. In fact, consistent users of seat belts say they are held more firmly in their seat, which adds to the comfort of riding. Passengers in the rear seat who are wearing seat belts also receive excellent protection.

Seat belts are not a panacea for all automobile injuries. But no one can dispute the fact that by using seat belts at all times, the chances of being injured or killed in an automobile accident are greatly diminished. The seat belt will keep the driver behind the wheel in any emergency maneuver, thereby giving him the opportunity he might need to get out of a serious situation. Seat belts also are designed to be opened easily with either hand so the passenger can free himself in seconds.

Common sense dictates that seat belts should be a standard safety feature in all cars and that they should be used. You owe it to yourself, your family, and your patients to save yourself from injury by wearing seat belts. As a physician you have an excellent opportunity to set a good example for others to follow. G. W. L.



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1. Guttmacher, A. F. (Chairman and Moderator): Clinical Experience with and Practical Techniques for the Use of Enovid in Ovulation Control, Transcript of a Closed Circuit Television Symposium, Chicago, G. D. Searle & Co., Jan. 18, 1961, pp. 26-28. 2. For references and review of laboratory and clinical studies, Physicians' Product Brochure No. 67 is available on request.

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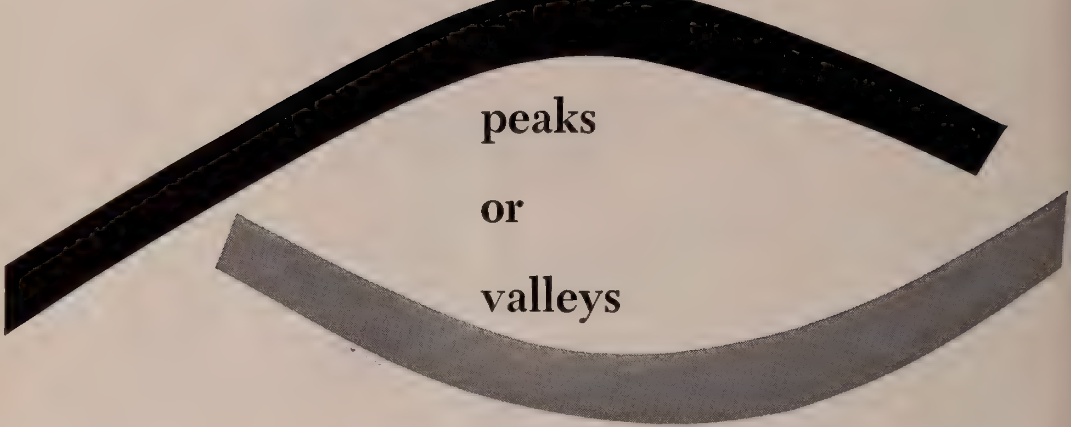

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SYMPOSIUM
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DISCUSSION

Treatment of Hypertension

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Introduction

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RELEVANT TO THE TOPIC of today's program, I believe it is not inappropriate to give a short historical outline of the development of the physical tool which made the study of blood pressure possible, namely that of the sphygmomanometer. The first phase in the development of the measurement of arterial blood pressure began with the direct measurement in animals by

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Stephen Hales in 1733. It was not until 1828, ninety-five years later, that Poiseuille introduced his U-tube form of mercury manometer or hemodynamometer. It was made more sensitive to the small changes in arterial blood pressure by Magendie in 1850 when he interposed a large reservoir partially filled with mercury between both arms of the U tube. Ludwig, in 1847, by adding a float to the long arm of the Poiseuille manometer was able to record arterial blood pressure by kymographic means.

With Herisson in 1834 began the indirect measurement of the blood pressure. By modifying the Poiseuille manometer into his sphygmometer he was the first to be able to demonstrate objectively the force of the arterial pulsations in man. In 1855 Vierordt created the scale-type recording sphygmograph, which by means of balanced weights measured the amount of counterpressure necessary to obliterate the pulsations in the peripheral arteries as an index of blood pressure level. In 1875 to 1876 Marey, a French physiologist, using the Vierordt principle, devised instruments which could compress the blood vessels either of the forearm or of a single finger. The oscillations resulting from the compression were a measure of the arterial blood pressure. Von Basch, a Viennese physician, established the use of indirect blood pressure readings as a practical clinical procedure in man. He is thus recognized as the father of clinical sphygmomanometry. His first instrument was constructed in 1876 and employed a mercury manometer which he replaced with a metal type in 1890. The introduction of the pneumatic cuff by Riva-Rocci in 1896 put clinical sphygmomanometry on its firmest basis. The cuff was 5 cm. wide; it was inflated by a small hand bulb, applied to the upper arm, and connected to either a mercury or anaeroid manometer. The systolic pressure was considered to be the point just before the oscillations disappeared. Von Recklinghausen increased the size of the cuff from 5 cm. to from 12 to 14 cm. for greater accuracy of blood pressure readings. A cuff of this width is still employed today. In 1905 Korotkoff, a Russian physician, first described the auscultatory technic with which we are all familiar and still use today.[1]

New developments

In the present electronic age the development of new instruments for blood pressure recording was inevitable. Indirect, automatic, electronic sphygmomanometers were introduced in July, 1961, in two papers presented at the Fourth International Conference for Medical Electronics.[2,3] One of these machines was conceived and developed by Leslie Edinger, M.D., a general medical practitioner in The Bronx. In these machines the auscultatory method is replaced by the electronic sound or pressure pickup. The pickup device is in the cuff. The cuff is applied to the upper arm and inflated in the usual manner. The registration of the blood pressure is electronic and automatic.

In spite of the medical advances since Hales first measured arterial blood pressure, we still do not know the cause of essential hypertension and the level of normal blood pressure readings. Perhaps some of the speakers on today's program will be able to clarify these points. However, with the introduction of the antihypertensive drugs and oral diuretics, we have advanced considerably in our treatment of hypertension. At the completion of today's program, I am sure that all of us will have advanced our knowledge considerably as far as the physiology, pharmacology, and treatment of this disease are concerned.

The use of the new automatic, electronic sphygmomanometers, especially those which are oriented toward patient use, will help make the treatment of hypertension by the physician more reliable, as the testing of urine at home by the diabetic patient makes the treatment of diabetes more reliable. This type of apparatus also will help to determine the normal base line of blood pressure readings and its fluctuations under various circumstances more accurately and reliably than is possible by our present method.

Newer diagnostic methods such as isotope renograms, angiocardiography, and aortography have enabled us to discover cases of hypertension amenable to surgery. This topic will be discussed further by Dr. De Bakey.

Before this conference proceeds to its working program, in closing I would like to call the attention of this eminent assembly to the following historical facts. It took about one hundred and seventy-five years from the first measurement of arterial blood pressure by Hales in 1733 until an instrument of accuracy was developed so that blood pressure measurements became a routine clinical procedure some fifty-five years ago. It took but a few years recently for its electronic metamorphosis, and I think it will take even less time until it becomes a household article like the thermometer.

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Dilemmas in the Management of Essential Hypertension

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THE DILEMMAS in the management of essential hypertension are encountered in establishing the diagnosis, deciding which patients do and which do not need therapy, selecting appropriate measures for the various phases of the disorder, and altering the therapy in some cases because of complications, the changing needs of the hypertensive patient who is free of detectable complications, and the advisability of sympathectomy in the treatment of the disorder.

Diagnosis

An elevated blood pressure, with no abnormalities found on a routine examination of the urine and in the absence of systemic disorders of which hypertension is a characteristic component, suggests but does not establish the diagnosis of essential hypertension. Indeed, these findings in a patient under forty years of age should be interpreted for what they are: merely indications that parenchymal disease of the kidneys is not at fault and that no systemic disorder which might be the offender has been found. A prompt and favorable response to conservative treatment or a labile response to the amobarbital sodium (Amytal sodium) test in the patient over forty who has a family history of high blood pressure, especially if the patient is a female, strongly suggests a benign essential hypertension. In more severe cases in which there is little or no response to conservative therapy, the failure to identify an etiologic process may be fatal. A functioning pheochromocytoma, although it is rare, may be lethal and yet is curable. It is excluded with reasonable certainty if the cold pressor test reveals a pressor response, the phentolamine (Regitine) and histamine tests show negative results, and there is no undue amount of catecholamines excreted in the urine. A blood pressure reading taken just above the knee which is equal to or higher than that in the brachial artery can be relied on to exclude a coarctation of the aorta.

Hypertension due to unilateral renal disease, be it vascular or infectious, is curable in many instances if the diagnosis is made and acted on early in the hypertensive phase. If the sodium content and volume of urine are approximately the same from each kidney, the rapid and equal excretion of phenolphthalein dye bilaterally suggests that the diagnosis is that of essential hypertension. In the puzzling and severe case the additional information regarding the circulation in the kidneys which can be provided by an aortogram may be valuable, although this study is not without risk and should not be done in patients who are suspected of having a pheochromocytoma. In any event, an aortogram should be reserved for the unsolved case and should then be done only when the risk of doing it is considered to be less than the risk of being deprived of the information it may have to offer.

A negative search for systemic disorders of which hypertension is a characteristic component, notably collagen disease and endocrine disturbance—primarily aldosteronism and Cushing's disease—will favor the diagnosis of essential hypertension.

Selection of patients for treatment

Which patients with essential hypertension should be treated? I may be unorthodox, and certainly there are those who will disagree with me when I make a plea for treatment as soon as the hypertension puts in its appearance. Indeed, when it is practicable, prophylactic treatment, by correction and prevention of overweight and restriction of the salt intake in individuals who give a family history of hypertension, may have much in its favor. To avoid treating patients with intermittent or sustained mild essential hypertension is, I believe, a form of clinical appeasement of undesirable processes. Most, if not all, cases of essential hypertension, as indicated by the studies of Thomas,[1] appear as an intermittent affair and progress, sooner or later, to sustained hypertension.

It is well known and conceded that many cases remain mild and benign, especially in women. Is it not wise to treat these patients? Is it not true that we have no way of predicting which cases, even though free of symptoms, will progress to a fatal ending? One such patient was deprived of treatment for more than ten years because she had no symptoms, even though her blood pressure ranged in the neighborhood of 210 mm. Hg systolic and 110 mm. Hg diastolic. I saw this patient at the age of fifty-three after she had had a hemiplegia. Although renal studies had recently indicated good function, a fatal renal failure complicated the cerebral accident. Was not this a preventable fatality? Let us not forget also that increasing blood pressure is associated with substantial decreases in renal function, as has been reported by Ford.[2] An effective lowering of the blood pressure reverses this unfavorable process, with a significant reduction in the mortality rate.

Selection of appropriate treatment

The basic therapy for all cases of essential hypertension, barring renal failure, will include the correction of overweight. A particularly effective measure in cases of refractory obesity is to subject the patient to a complete fast, allowing only water, weak tea, soft drinks of no caloric value, and vitamins in therapeutic amounts for from ten days to two weeks. The blood pressure decreases, the body weight is reduced by approximately $2^1/_2$ pounds per day, and there is a marked sodium diuresis. I have found this treatment acceptable to the patient, who, almost without exception, is anorexic after the first day.

The need for hypotensive drugs will be minimal if the sodium intake is curtailed sharply: to 2 Gm. in mild cases and to 200 mg. in patients with rather fixed diastolic pressure.

The dosage of hypotensive agents also will depend on the degree of lability of the diastolic pressure. Small doses will suffice if the diastolic pressure decreases below 100 mm. Hg at rest, during an amobarbital sodium test or during conservative therapy. Basic measures as already mentioned, plus combined drug therapy in which the doses are adjusted to achieve the desired effect, will suffice to gain good control in nearly all cases.

General measures

ALTERATION OF THERAPY WITH CHANGING NEEDS. Having achieved reasonably good control of the hypertension, more often than not as the months go by the intensity of the therapy may be lessened without a sacrifice of control. This improvement under medical management from very severe to less severe grades of hypertension is one reason for the virtual disappearance of sympathectomy for patients with essential hypertension. Sympathectomy has a place, however, in the control of severe grades of the disease in the individual who cannot or will not adhere faithfully to the regimen planned for him.

COMPLICATIONS AND THERAPY. The restriction of salt and the use of saluretic agents are contraindicated in cases of severe azotemia (blood urea nitrogen in excess of 80 mg. per 100 ml.). In lesser degrees of azotemia these measures may be tried cautiously, keeping in mind that they precipitate uremia in some cases in which the renal reserve is gone while in others with a modest decrease in the blood pressure the renal function is improved. It is on the chance that the latter experience will be had that these measures are tried in such cases.

The optimal treatment for essential hypertension has not been simplified by the progress which new agents have provided. The opposite is the case. A high degree of individualization is essential, and like the diabetic patients, those with hypertension should be followed closely. This and only this will permit appropriate adjusting of the dosages and changing of the remedies as the need to do so arises.

It is comforting to know that if renal failure is not part of the picture, practically all cases of essential hypertension can be controlled satisfactorily. It is my belief that in mild cases the aim should be to achieve normal blood pressure readings, and in severe cases the achievement of near-normal values will suffice.

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Physiologic Mechanisms in Hypertension*

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SYSTEMIC ARTERIAL blood pressure increases whenever the volume of blood within the systemic arterial tree rises.[1] Since the capacity and the distensibility of the arteries are small, in contrast to the veins, small increments in volume produce large increases in pressure. Changes in the viscosity of the blood appear to be relatively unimportant in the genesis of hypertension, thus leaving two factors: namely, either an increase in cardiac output or a decrease in the caliber of systemic arterioles, either or both of which can increase the arterial blood volume and hence pressure. Increased output distends the arterial tree, and narrow arterioles distend the arteries by obstructing the egress of blood into the capillaries and veins. The flow of blood under these circumstances can become adequate and equal to normal blood flow only by virtue of increased left ventricular work.

Only in acute glomerulonephritis does the hypertension appear to be largely if not entirely attributable to increased cardiac output due to hypervolemia.[2] Although a moderate increase in cardiac output is found in some but not in all early cases of essential hypertension,[3] the most consistent and characteristic feature of this disease is a generalized decrease in the caliber of systemic arterioles, and it is this factor that characterizes most chronic hypertension.

It has long been known that one aspect of this narrowing of the systemic arteriolar bed is structural,[4–6] consisting of intimal proliferation, medial hypertrophy, and, in advanced cases, even fibrinoid necrosis and thrombosis, especially in such regions as the kidney. Whether functional vasoconstriction is increased also or in fact initiates the structural changes has been the subject of controversy for many years.

Vasoconstriction and responsivity

In our laboratory vasoconstriction has been studied in the digit, where flow and pressure could be measured repeatedly during vasodilatation and vasoconstriction and the data converted into an estimate of the work of vasoconstriction. With these methods, resting functional vasoconstriction was found to be increased in essential hypertension.[7] Such an increase could be caused either by increased sympathetic neural firing or by exaggerated responsivity to normal neural discharge or by both factors.

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Since it had been demonstrated that the neurohumor responsible for neurogenic vasoconstriction was NE or norepinephrine, the factor of responsivity was investigated by infusing this substance intravenously and measuring the work of vasoconstriction produced in the digit.[7,8] A two- to tenfold increase in responsivity was found in essential hypertension, suggesting that this factor rather than increased neural discharge was responsible for the increased resting vasoconstriction demonstrated in the disease. Since the effect was brought out after neural blockade by indirect heat and a ganglion-blocking drug, the nervous system seemed exonerated further, and attention was directed toward the function of vascular smooth muscle. It also became clear that in contrast to increased neural firing which could be local, increased responsivity was probably generalized, and this was confirmed when English and Australian workers found similar increases in vascular responsiveness in the forearm skin and muscle of hypertensive subjects.[9,10] The subject, however, had been studied in the digital vessels by direct observation[11] and in the conjunctival vessels by Lee and Holze[12] as well as in the systemic circulation as a whole by Goldenberg *et al.* in 1948,[13] and they too had found an increase in vascular reactivity in hypertension although they did not employ prior neural blockade. Without such a blockade and especially if only pressure is measured,[14–16] the results can be equivocal. In fact in the renal circulation the unblocked vessels of the hypertensive subject seem less responsive than the normal,[15–17] probably because of the factor of autoregulation.[18]

One of the major questions raised by all this work was whether the increased responsivity was merely an artifact found in any type of hypertension, because of the methods used, or whether it was caused by the structural changes in the vessels such as hypertrophy of smooth muscle or arteriolosclerosis. A series of experiments demonstrated that neither of these hypotheses could be sustained. For example, it was demonstrated that the glucocorticosteroids could increase vascular reactivity within a few weeks without producing any increase in blood pressure.[19,20] Also, structural changes similar to those found in essential hypertension are known to occur in Raynaud's disease, and yet the responsivity to NE was normal.[21] What is more, in Raynaud's disease of the vasospastic type, increased vasoconstriction with normal responsivity was found, thus, in contrast to essential hypertension, clearly implicating increased neural firing. Also, in renal hypertension, whether caused by renal artery coarctation, chronic or acute glomerulonephritis, or polycystic kidney, the responsivity to NE was normal, provided mixed cases of renal and essential hypertension were carefully excluded.[22] On the other hand, in essential hypertension even in its earliest phases or in pregnancy with associated toxemia, the responsivity was increased.[23]

The other possibility, namely that increased vascular responsiveness was an intrinsic chemical feature of the vascular smooth muscle of subjects with essential hypertension seemed to be supported by subsequent observations. For example, it was demonstrated that the glucocorticosteroids increased the responsivity more in the hypertensive than in the normotensive person.[20] Aldosterone, on the other hand, increased the responsivity more in the hypertensive than in the normotensive group.[24] Further evidence that sodium was involved in the process could be deduced from experiments which demonstrated that the chlorothiazide group of drugs decreased blood pressure and responsivity in subjects with essential hypertension, but in the normotensive subject, despite salt depletion, these drugs increased the responsivity and failed to alter the blood pressure.[25] That the factor of responsivity is probably what is inherited in the familial transmission of essential hypertension is suggested by Doyle's[26] observation of increased reactivity in the offspring of patients with essential hypertension, prior to any elevation of the blood pressure.

Nature of chemical change

If the chemical nature of this phenomenon seems acceptable, the question is raised as to what the exact chemical change or defect might be. The possibilities again are limited. One may indict the enzymes responsible for the degradation of the vasoactive chemical stimulators or the substances which bind them.[27, 28] On the other hand, the defect may reside in the metabolism of smooth muscle itself.[28] Very little is known about the chemistry of smooth muscle, and the substance responsible for binding NE has not been identified although adenosine triphosphate (ATP) is believed to be involved in this complex.[29] The major enzymes responsible for degrading NE, however, have been identified as catechol-O-methyl transferase and monamine oxidase.[30, 31] Monamine oxidase inhibitors, however they may effect blood pressure, by virtue of their action at the ganglia, do not affect responsivity to NE.[32] The absence of abnormal metabolites of NE in the urine of hypertensive subjects also fails to support the theory that any defect in the metabolism of NE exists in the patient with essential hypertension.[33] It is possible, however, that such a defect might exist in the blood vessel wall and be masked by subsequent metabolism in the liver, nervous system, and other tissue so that the end result represented by urinary metabolites would seem normal. These possibilities must be established or excluded by future investigation.

However, the theory of a specific enzymatic defect must be viewed also in the light of evidence that responsivity in essential hypertension may be demonstrated to be increased not only to NE but also to such a chemically different substance as angiotensin II, an octapeptide.[34] Bumpus, Smeby, and Page[35] have shown, however, that the spatial configuration of this compound is such that its active prostheses may be related to the vasoactive amines. Nevertheless this observation suggests strongly that the defect in hypertension resides either in the binding of vasoactive substances or in the metabolism of smooth muscle, rather than in the absence or modification of a specific degrading enzyme. In this connection it has already been demonstrated that the degradation of angiotensin II labeled with I^{131} is slower in patients with essential hypertension than in normal subjects.[36] This has not as yet been demonstrated for NE.

Precipitating factors

Despite the inherited increased vascular reactivity, hypertension is probably not produced unless there are precipitating factors which bring the tendency into play. Such precipitating factors could be emotional or psychic,[37] ingestion of excessive salt,[38] intercurrent renal disease,[37] and other factors, of which the exact interplay with the vascular system is not clearly understood.

Renal disease is a common complicating feature of essential hypertension and undoubtedly a potentiating factor. The kidneys are particularly vulnerable to ischemic atrophy in hypertension because their local vascular reaction to elevation of the blood pressure is vasoconstriction (autoregulation).[18] Another apparent effect of hypertension on the kidney is to cause it to lose salt on salt loading.[39–41] Whether or not the renal disease also results in excessive secretion of renin and hence resultant angiotensin is not as yet established.[36, 42]

In the later stages of hypertension aldosterone secretion is increased,[43, 44] and all these factors together with arteriolosclerosis and in some cases renal artery stenosis[45, 46] contribute to the final picture of the disease.

Mechanisms of other types of hypertension

The mechanisms of other varieties of hypertension are in some instances more clearly and in others less clearly understood. The hypertension of aortic coarctation is largely mechanical,[47] whereas that of pheochromocytoma is caused by the secretion of norepinephrine and epinephrine by the tumor.[48] The hypertension of Cushing's syndrome may be caused by the effect of the increased glucocorticosteroids secreted on vascular reactivity,[20] whereas aldosterone affects reactivity by virtue of its action on the kidney which results in sodium retention.[24]

Renal hypertension, however, remains the most obscure type physiologically. The retention of salt and water and the secretion of a pressor substance are the two possible mechanisms, either or both of which appear to come into play under certain circumstances. Hypervolemia appears to be largely responsible for the hypertension of acute glomerulonephritis,[2] whereas in chronic nephritis and renovascular hypertension it is possible that angiotensin II is present in excess. The latter is derived from the reaction of renin with hypertensinogen and a converting enzyme and is an octapeptide about 10 times as potent as NE.[49]

It has also been demonstrated in animals that the removal of the kidneys can produce a type of hypertension which is called renoprival[50] and which can be prevented to some extent by the explantation of renal medullary tissue.[51] Whether or not such hypertension exists in man is as yet unclear. It is apparent, however, that the complexity of the mechanisms involved in every patient with hypertension makes the careful study and evaluation of each case mandatory before therapy is initiated.

Summary

Hypertension is produced by an increase in arterial volume caused largely by the narrowing of the systemic arterioles and increased left ventricular force, maintaining a normal cardiac output. The arterioles are more constricted than usual in essential hypertension and also are narrowed structurally. The increased vasoconstriction is caused by increased vascular responsivity to vasoactive substances. This is of chemical origin and is caused either by a defect in degradation or in binding of vasoactive substances or by a defect in the complex responsible for vascular smooth muscle contraction. It is this factor which is inherited in essential hypertension. There are, however, precipitating mechanisms which are variable and poorly understood.

The hypertension of coarctation of the aorta is largely mechanical, whereas steroid hypertension is produced by the effect of those substances on vascular reactivity either directly (glucocorticosteroid) or via sodium retention (aldosterone), whereas in pheochromocytoma the hypertension is produced by increased circulating catecholamines.

The kidneys are unusually vulnerable to hypertension because of local circulatory autoregulation. Tubular function is disturbed also, and it is possible that secondary renal and adrenal (aldosterone) pressor mechanisms are brought into play. Renovascular (Goldblatt) hypertension also may initiate the disease in some cases or complicate other varieties of hypertension. Renal hypertension can be produced by salt and water retention as in acute glomerulonephritis or by the secretion of a pressor substance. The mechanism of renoprival hypertension remains obscure.

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Pharmacology of Antihypertensive Agents

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Before describing the mode and site of action of the various antihypertensive drugs, I would like to summarize briefly what is known about the mechanisms that control the maintenance of arterial blood pressure. Blood pressure varies as the product of cardiac output and peripheral resistance. Peripheral resistance in turn depends on the state of contraction of the arterioles, the elasticity of the arterial walls, the electrolyte distribution in the body, the blood volume, the viscosity of the blood, and unknown factors.

Mechanisms in control of arterial blood pressure

The state of contraction of the arterioles is controlled from the vasomotor center (Fig. 1). This is located in the brain stem in the vicinity of the respiratory center in the floor of the fourth ventricle. The vasomotor center receives messages from the cortex, the carotid sinus and body, and the aortic body. Fibers originating in the vasomotor center pass down the cord in the white matter of the lateral columns to all thoracic and upper second lumbar vertebral segments and form synapses with the connector cells located in the lateral horn of the gray matter. The connector cells give rise to fibers which leave the cord with the anterior roots and pass out to the sympathetic ganglia. The postganglionic excitor fibers commence in the ganglia and go to the vessel wall. Sensory fibers starting in the vessel walls enter the cord through the posterior roots and establish contact with the connector cells, thus completing the reflex arc. These connections are illustrated in Figure 1.

The transmission of impulses in the autonomic nervous system is carried out through neurohormones. Acetylcholine is the mediator released in the sympathetic and parasympathetic ganglia while norepinephrine and epinephrine are released at the effector sites of the sympathetic postganglionic fibers. Many antihypertensive agents reduce the activity of the sympathetic nervous system by interfering with the synthesis of neurohormones, by causing their disappearance from tissues, or by making the tissues less sensitive to their action.

Drugs used in the treatment of hypertension can be divided broadly into two classes: (1) drugs that reduce sympathetic activity and (2) drugs that reduce the sodium content of the body. The cause of essential hypertension, the most common form of hypertensive disease, is unknown, but it appears that it is not caused by an increased activity of the sympathetic system or by an increased salt content of the body. Thus the drugs we have available do not treat the underlying cause of the disease but merely affect a symptom of it.

In this paper I would like to review the site and mode of action of the available remedies and also describe briefly a new agent, mebutamate, that has a different site and mode of action from drugs used up to the present.

Site and mode of action of antihypertensive drugs

There are hundreds of publications describing the pharmacology and mode of action of antihypertensive drugs. Many of them are contradictory. An excellent review has recently been published by Buckley.[1] In the following, I shall classify the agents according to the properties that seem important to me. Figure 2 gives a simple classification of hypotensive agents according to their mode and site of action.

Hydralazine and the nitrites. Drugs that act by direct spasmolytic action on the vessels are hydralazine (Apresoline) and the nitrites. Hydralazine in animals produces a multitude of pharmacologic actions, but it appears to me that its direct effect on vessels may be the most important effect in human beings. Hydralazine can lower the blood

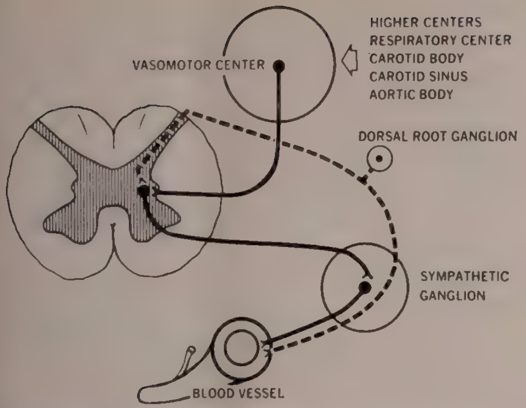

FIGURE 1. Vasomotor center control of contraction of arterioles.

CLASSIFICATION OF HYPOTENSIVE DRUGS ACCORDING TO THEIR MODE AND SITE OF ACTION

1. **Direct action on vessels**
   Hydralazine
   Nitrites
2. **Inhibition of catecholamine synthesis**
   Alpha-methyl-dopa
3. **Depletion of catecholamines**
   Reserpine
   Guanethidine
4. **Insensitivity to catecholamines**
   Phenoxybenzamine
   Ergot
5. **Blockade of ganglia**
   Hexamethonium
   Mecamylamine
   Bretylium
   MAO inhibitors
6. **Reflex vasodilatation**
   Veratrum
   Amidines
7. **Electrolyte control**
   Chlorothiazides
8. **Pressor factor antagonists**
   Antiserotonin · BAS
   Antialdosterone · spironolactone
9. **Vasoconstrictor center**
   Mebutamate
   Barbiturates

FIGURE 2. Classification of antihypertensive agents.

pressure in human beings with high thoracic spinal cord transection and increase blood flow in extremities denervated by sympathectomy.[2] In clinical practice this drug has not found wide application because it is often ineffective and also causes serious side-effects such as orthostatic hypotension, angina, depression, and occasionally a syndrome resembling rheumatoid arthritis and disseminated lupus erythematosus.

The use of nitrites in the treatment of hypertension has been largely abandoned because of their short duration of action and the unpleasant symptoms that they may produce.

ALPHA-METHYL-DOPA. The only available agent that acts by inhibiting the synthesis of catecholamines is alpha-methyl-dopa. This compound inhibits the enzyme decarboxylase so that the precursor of norepinephrine, 3,4-dihydroxyphenylalanine (DOPA) cannot be decarboxylated to dopamine. Alpha-methyl-dopa also inhibits the 5-hydroxytryptamine decarboxylase, thus preventing the synthesis of serotonin from 5-hydroxytryptophan. Clinical results obtained with alpha-methyl-dopa up to the present are said to have been disappointing.

GUANETHIDINE SULFATE. Guanethidine sulfate (Ismelin) reduces blood pressure by producing a depletion of catecholamines from the peripheral nerve endings in blood vessels. This drug, like the recently introduced bretylium tosylate (Darenthin), blocks the effect of sympathetic nerve stimulation without blocking the action of injected norepinephrine. Guanethidine sulfate produces a selective sympathetic inhibition without marked interference with the parasympathetic nervous system. Clinically, the drug has proved to be a reasonably effective antihypertensive agent in the treatment of moderate and severe hypertension. The side-effects produced by guanethidine sulfate are due to the unopposed parasympathetic action and resemble in some respects those observed after the administration of bretylium tosylate and reserpine. The most frequently observed side-effects are nasal stuffiness, diarrhea, inability to ejaculate with retained potency and erections, frequency of micturition, weakness, and depression. Guanethidine sulfate, like many other hypotensive drugs, potentiates certain pressor amines and should not be given to patients who may have received such substances or who are suffering from pheochromocytoma because of the possibility of the occurrence of severe hypertensive reactions.

RAUWOLFIA ALKALOIDS. Reserpine and other Rauwolfia alkaloids produce the depletion of catecholamines and of serotonin from the brain, blood platelets, heart, arterial walls, and elsewhere. It appears that the hypotensive effects of the drug are related to this action.[3] It has been claimed previously that reserpine had a central action which manifested itself by a diminished outflow of sympathetic impulses from the brain. However, this has never been proved. Several investigators have shown that reserpine is completely ineffective in relieving hypertension produced by stimulation of the vasomotor center of the brain.[4–6] These findings speak strongly against a central mode of action of the drug.

The side-effects usually associated with the use of reserpine in hypertensive patients are characteristic of unopposed parasympathetic innervation. If the drug is tolerated, it is of value in the treatment of mild hypertension in tense and anxious patients. It is usually ineffective in more severe cases.

ADRENERGIC BLOCKING AGENTS AND ERGOT. The adrenergic blocking agents and ergot inhibit the effect of catecholamines on blood vessels and thus make them insensitive to the action of neurohormones. These agents act by a receptor site blockade in a way similar to that of atropine, blocking the action of the parasympathetic neurohormone. Of the adrenergic blocking agents, only phenoxybenzamine hydrochloride (Dibenzyline) appears to be of some interest. However, the use of this compound in the treatment of hypertension has been disappointing because of the numerous side-effects observed. These are frequently out of proportion to the benefit derived. The most common side-effects are a feeling of lethargy, dizziness due to reduced cerebral blood flow, and postural hypotension. The results of chronic medication are much less striking than the response to single injections, probably because of the development of compensatory mechanisms.

The use of hydrogenated alkaloids of the ergot group in the treatment of essential hypertension is quite limited. Only modest effects are observed after oral therapy, and tolerance to the hypotensive effects develops rapidly.

GANGLIONIC BLOCKING AGENTS. Ganglionic blocking agents or ganglioplegics were introduced into medicine to produce sympathectomy by chemical means. The first important compound of this kind was hexamethonium chloride which was introduced by Paton and Zaimis in 1948. Many related compounds that are quite similar to it in their actions, such as pentolinium tartrate (Ansolysen), chlorisondamine chloride (Ecolid chloride), and azamethonium (Pendiomide) have since been evaluated. All these agents block nerve impulses in the autonomic ganglia by raising the threshold of the ganglion cells to acetylcholine released at the preganglionic endings. As acetylcholine is the specific neurohormonal transmitter at many different sites, such as the sympathetic ganglia, the parasympathetic end organs, and the myoneural junction, it is quite difficult to produce ganglionic blocking agents that would have specificity or selectivity.

The paralysis of sympathetic ganglia dilates both arteries and veins and abolishes the reflexes which control blood pressure. This gives rise to the most common side-effect—orthostatic (postural) hypotension—which makes the patient faint when he stands up. This is due mainly to the accumulation of the blood in the large dilated veins. The hypotensive action of the ganglioplegics, however, is due only in part to the dilation of the blood vessels. A reduction of the cardiac output plays an important part in the hypotensive action of these agents as it does with certain other antihypertensive drugs.

Serious side-effects of ganglionic blocking agents, other than postural hypotension, are due to symptoms of parasympathetic blockade. The most frequently observed side-effects of this kind are blurred vision, dry mouth, constipation, difficulty in micturition, and impotence. Most of these agents have the additional disadvantage of being poorly absorbed from the gastrointestinal canal and of producing tolerance.

Two recently introduced ganglionic blocking agents, mecamylamine hydrochloride (Inversine) and pempidine tartrate, appear to be more predictable and less erratic in their actions because they are absorbed more completely and with greater regularity. These drugs, however, produce side-effects similar to those produced by the other ganglionic blockers. In addition, severe mental disturbances and tremors following their use have been described.

Recently, a more specific ganglionic blocking agent, bretylium tosylate, has been described which selectively blocks the sympathetic ganglia without affecting transmission in the parasympathetic ganglia. The effects observed with the drug in some respects are similar to those obtained with guanethidine sulfate, but bretylium tosylate has the disadvantage of being absorbed poorly and irregularly. The compound also potentiates the pressor effects of catecholamine and for this reason must not be given to patients suffering from pheochromocytoma. The side-effects of the drug are due to unopposed parasympathetic action and resemble those of guanethidine sulfate and reserpine. In addition, bretylium tosylate also causes parotid pain, and drug tolerance may develop.

Monamine oxidase inhibitors. The monamine oxidase inhibitors act by increasing the concentration of norepinephrine by inhibiting the enzyme that inactivates it. Norepinephrine accumulates in the autonomic ganglia and produces blockage of ganglionic transmission. Because of the toxic effects of these compounds on the liver and the frequent occurrence of a postural-type hypotension, their use as antihypertensive agents has been very limited.

Veratrum alkaloids. The veratrum alkaloids produce an antihypertensive action by a reflex vasodilation which is brought about by stimulation of the sensory nerve endings in the auricles. The cholinergic system is not primarily involved in the vasodilation because the fall in pressure cannot or can only partially be prevented by atropine. Clinically, veratrum therapy by the oral route has proved unsuccessful because of the frequent occurrence of side-effects such as nausea and vomiting.

Certain amidines, such as phenyldiguanidine, also produce a reflex fall of the blood pressure and heart rate by action on the afferent nerve endings of the heart. The clinical effectiveness of these compounds has not been evaluated.

Diuretics. It has been known for some time that diuretics may possess antihypertensive action, but their use in the treatment of hypertension was quite limited until the introduction of the chlorothiazides. These compounds increase the secretion of sodium, potassium, and chloride and produce a reduction in plasma volume. The reduction of plasma volume may be more important than the sodium depletion because the replacement of the plasma deficit with sodium-free dextran abolishes the hypotensive effect on the blood pressure. Clinically, the chlorothiazides are used as a rule in conjunction with other hypotensive drugs. They increase the hypotensive action of antihypertensive drugs and permit their utilization at a lower dosage. The side-effects following chlorothiazide administration are relatively infrequent. The most common are hypokalemia, muscle weakness, and lethargy.

The pressor factors responsible for the maintenance of elevated blood pressure after it once has been established have not been identified with certainty, and antagonists to such factors have not been developed. It is known, however, that aldosterone, which controls the reabsorption of sodium in the renal tubules, may play an important part in the development of hypertension. A specific antagonist to this compound, spironolactone (Aldactone), has been prepared. Spironolactone differs from other diuretics in that it does not affect potassium excretion or even induce the retention of potassium while it increases the excretion of sodium and chloride. Enough experience relating to the value of this drug in the treatment of hypertension is not yet available. A serotonin inhibitor, BAS (1-benzyl-2-methyl-5-methoxy-tryptamine), lowers the blood pressure in experimental animals by competitive inhibition with serotonin. The effects obtained with this compound in human beings do not appear to be impressive.

All the agents discussed up to the present affect blood pressure either by an action on the autonomic nervous system, by changing the electrolyte distribution, or by a direct action on the blood vessel. Mebutamate (Capla, an abbreviation formed from the first letters of "centrally acting pressure-lowering agent") differs from older drugs by producing its hypotensive effect by direct action on the brain stem vasomotor center.

Mebutamate. Mebutamate has no effect on the autonomic nervous system, does not cause ganglionic blockage, and does not modify the circulatory responses to epinephrine, acetylcholine, or serotonin.[7] Cross-circulation experiments confirmed the purely central site of action of mebutamate and showed that the hypotensive effect is produced by a reduction of the vascular peripheral resistance. The cardiac output is not affected.

SIDE-EFFECTS OF SOME USEFUL ANTIHYPERTENSIVE AGENTS

	Postural Hypotension	Parasympathetic Predominance	Parasympathetic Blockade	Sensitivity to catecholamines	Tolerance
Reserpine	−	+	−	+	−
Guanethidine	+	+	−	+	+
Ganglioplegics	+	−	+	+	+
Bretylium	+	+	−	+	+
Adrenolytics	+	−	−	−	+
Chlorothiazides	−	−	−	−	−
Mebutamate	−	−	−	−	−

FIGURE 3. Table showing side-effects of antihypertensive drugs.

The selective action of mebutamate on the vasomotor center of the brain stem is of unusual interest. The electrical stimulation of this area in cats produces a hypertensive response which mebutamate counteracts in a unique fashion. The drug not only elevates the threshold for the pressor response but also limits the rise of blood pressure that could be obtained with supramaximal stimulation. Thus, after mebutamate, even with very intense stimulation, the blood pressure rise remains well below the magnitude of the rise obtained prior to the administration of the drug. No other drug that we have studied had a comparable effect. Reserpine, even in large doses, in confirmation of the findings of others, had no effect on the blood pressure rises elicited by central stimulation, indicating that this drug is devoid of a direct action on the blood pressure-controlling centers. Other drugs commonly used in the treatment of hypertension were also devoid of any effect on the centrally elicited hypertensive responses. The only group of drugs that affected hypertension produced by central stimulation were the barbiturates. These drugs were able to raise the threshold for pressor responses produced by electrical stimulation, but their pressure-lowering action differed from that of mebutamate in being unable to affect or diminish supramaximal blood pressure responses. Thus, after barbiturates, when the intensity of stimulation was increased, blood pressure rises of the same magnitude as prior to the administration of the drug were obtained. By contrast, after mebutamate, a substantial reduction of the magnitude of the response was observed even when stimuli of excessive intensity were used.

There was also another important difference between mebutamate and the barbiturates. The control of the centrally induced hypertension with mebutamate could be obtained in doses that did not affect consciousness and did not anesthetize the animals, while barbiturates produced hypotensive effects only in doses that were hypnotic or anesthetic.

As we do not know the cause of essential hypertension, the object of treatment of this condition has been the lowering of the blood pressure without producing too many unpleasant side-effects. This end is justified because it is known that the mortality of hypertensive patients whose blood pressure has been reduced by drugs is always lower than the mortality of untreated patients. Most drugs available until recently produce too many side-effects to justify their use in the asymptomatic period of the disease. These side-effects are summarized in the table in Figure 3.

Mebutamate does not produce any of the side-effects caused by the older antihypertensive drugs. It does not produce postural hypotension; it does not affect autonomic functions; it does not produce disturbances of the electrolyte balance; and tolerance to its use has not been observed. The only side-effect observed with any frequency is drowsiness, which usually disappears within a few days on continued administration. Mebutamate often makes it possible to lower high blood pressure without unpleasant side-effects, and in this way it may prolong the life of patients in a state that makes it worth living.

There is increasing evidence that the stress and tension of daily living play an important part in the development and progression of essential hypertension. Mebutamate, because of its freedom of side-effects, appears to be an agent ideally suited for the treatment of individuals who react to stresses by an elevation of blood pressure. It will be of interest to see whether or not the administration of mebutamate to such patients will prevent the development of serious hypertensive disease.

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Technic of Drug Evaluation in Hypertension

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THE ANTIHYPERTENSIVE PROPERTIES of mebutamate, as described by Berger and others,[1,2] led to a clinical evaluation of the drug in the treatment of ambulatory hypertensive patients seen in private practice.

Because of the multiplicity of problems which can and do arise in establishing the validity of any antihypertensive agent, rigid criteria were used in conducting the present investigation.

The criteria for drug evaluation are: (1) patient selection and proper diagnosis; (2) controlled study; (3) blood pressure reading and recording; (4) environmental control; (5) patient instruction and control of drug intake; (6) adequate therapeutic and follow-up periods; (7) accurate observation of side-effects; and (8) statistical evaluation.

Selection of patients and proper diagnosis

The first of the criteria includes the selection of patients and proper diagnosis. All patients who could not be depended on to take their medication or to return at specified intervals were excluded from taking part in the study. This included patients who were going on vacation or who were known from past experience to be unreliable. Each patient underwent a thorough physical examination, and the degree of severity of the hypertension in each instance was based on the Smithwick[3] classification.

As a result of this screening procedure, 50 patients ranging in age from thirty-two to seventy-three years, with an average age of fifty-four years, were selected for inclusion in the study. On the basis of the Smithwick classification,[3] 19 patients had Grade I hypertension, 15 had Grade II, 15 had Grade III, and 1 had Grade IV.

Controlled study

The second of the criteria is the establishment of a controlled study. One of the most important factors to be considered is the pretherapy control period. This time period should be of sufficient length to enable all previously prescribed medication and the effects thereof to be eliminated completely so as to avoid any carry-over effect from previous medication or any overlapping effects from previous and present medication. In the present study, the control period for the 50 patients averaged approximately three months and one week. During this period, control pressures were taken and recorded, first with the patient in the supine position and then in the upright position.

Since bias either on the part of the investigator or of the patient must be avoided if an accurate and honest report of the results is to be obtained, a double-blind, crossover procedure should be used. Neither the investigator nor the patient should be cognizant of the composition of the medication being prescribed, and all medications should be identical in appearance and, insofar as is possible, in taste. In the present study, a double-blind crossover procedure was used in which a placebo, mebutamate, mebutamate combined with hydrochlorothiazide, and hydrochlorothiazide alone were compared and evaluated.

The patients were divided into 2 groups of 25 each: The first group of 25 patients, Group A, received the placebo, one tablet, four times daily; mebutamate, one tablet, 300 mg., four times daily; mebutamate, 300 mg. combined with 25 mg. of hydrochlorothiazide, three times daily; and hydrochlorothiazide, 25-mg. tablets, three times daily. For the second group of 25 patients, Group B, the same procedure was used except that mebutamate tablets were given first, followed by the placebo. The first two drugs were given by the double-blind technic, the second two by the single-blind method.

Blood pressure reading and recording

The third criterion involves the proper application of the blood pressure cuff and accurate reading and calibration of the instrument.

The improper application of the blood pressure cuff can cause considerable error in accuracy. A cuff that is too loosely applied will give a much higher blood pressure reading. This is especially true for the obese patient. Also, tissue composition as well as arm circumference can alter blood pressure readings considerably. In the obese patient, for example, there can be a false increase of 20 mm. of mercury or more in systolic pressure in the upper arm as compared with the systolic pressure obtained with the cuff on the forearm. Also, in some obese patients the standard 13-cm. blood pressure cuff cannot be inflated without causing it to bulge, and a larger cuff is indicated to obtain a more accurate determination of the blood pressure.

Little need be said concerning the calibration of the manometer except to state that it should be checked for accuracy before initiating a study.

The importance of the method of determining the systolic and diastolic pressure cannot be overemphasized. Most physicians take the point at which the sounds are first heard as the systolic pressure and the point at which the sound abruptly diminishes as the diastolic pressure. Probably, there would be more accuracy in measuring the blood pressure if the disappearance point were used, as there is approximately a 5- to 10-mm. of mercury difference between the points of diminution and disappearance; however, untrained personnel will have difficulty in determining the point at which the sounds finally disappear.

Also, there is considerable variation in the blood pressure, depending on the time of day and the manner (casual, resting, or basal) in which it is taken. Because of the limitation of time, most practicing physicians take the "casual" blood pressure, that is, one reading with the patient in either the supine or upright position.

In the present study, two "casual" readings were taken at each visit: one with the patient in the supine position and one with the patient in the upright position. In taking the blood pressure, the point at which the sounds were first heard was used as the systolic pressure and the point at which the sound abruptly diminished was used as the diastolic pressure. Whenever possible, the patient was seen at the same time of day at each visit.

Environmental control

The fourth criterion, environmental control and control of the observer-physician, is closely related to criterion three. The patient's environment pertains not only to his physical locale but also to those people with whom he comes in contact.

Since we are treating the patient so that he can continue his normal daily life, he should certainly be seen under circumstances in which he will be living and not under the artificial atmosphere of the hospital or clinic.

In addition to being out of his natural environment, the patient is seen by any number of interns and physicians, not to mention the number of nurses seen in a day. Also, the blood pressure is seldom taken twice by the same intern or nurse. In addition to the fact that the hospitalized patient is apprehensive at best, there is the variability introduced by the difference in the ability of personnel to take accurate blood pressure readings. As mentioned previously, untrained nurses have difficulty in determining the point of final disappearance of Korotkoff sounds and, although the point at which the Korotkoff sounds become muffled may produce more accurate results by the untrained person, it does introduce a variable factor in the results obtained.

In private practice, these problems seldom arise because the physician is well known to the patient, the patient is accustomed to seeing the same physician, and the surroundings are familiar. The fact that the same physician takes and records all blood pressure measurements and uses the same method and procedure each time eliminates most of the variables encountered for hospitalized or clinic patients.

In this study, the patients were seen from two to four times each month, and blood pressure readings were recorded with the patient in the supine and erect positions, each time by the same observer.

Patient instruction and control of drug intake

Two very important points, patient instruction and control of drug intake, which pertain not only to controlled clinical evaluation studies but to general practice as well, comprise the fifth criterion to be considered.

All too frequently, physicians assume that the patient knows how and when to take a prescribed medication, or he will give the patient oral instructions, only to have him forget ten minutes after leaving the office. In the evaluation of any drug, the patient must be impressed with the importance of taking the medication at the prescribed time and in the prescribed amount. If possible, as it was in the present investigation, the necessity of taking the tablets at the prescribed time—one-half hour before meals and at bedtime—was explained to the patient. He was told that the effects of the medication would last for an allotted period of time and that if he failed to take the second dose at the prescribed time he would forfeit most of the improvement gained. It was also emphasized that only the prescribed amount was to be taken, that is, if he did accidentally miss a dose he was not to double up on the next dose.

Only the exact number of tablets to be taken between visits should be given, and the patient should be told to return on a specified date for examination and additional medication. By supplying only the exact number of tablets to be taken within a specified period, the possibility of the patient taking an overdose, accidentally or on purpose, can usually be prevented.

The length of time permitted to elapse between visits also is of importance. This time period should not be too long because a patient who knows he will have to report in one or two weeks will be more conscientious about taking his medication, especially if he knows that the physician is keeping a close check on his progress.

Adequate therapeutic and follow-up periods and observation of side-effects

The next two criteria—adequate therapeutic and follow-up periods, and accurate observation of side-effects—are closely related and will be discussed together.

Some drugs, because of their individual properties, are slow to react in the system, requiring several weeks to produce their full effectiveness; others which act rapidly in the system may produce longer-lasting effects. Because of the wide variability of action among different drugs, adequate time periods should be allotted for each drug being evaluated. During these therapeutic periods, there should be frequent observations of the patient to determine not only the efficacy of the medication and patient response but also any side-effects which may have developed. In the present study each drug was prescribed for a period of one month, and the patients were seen from two to four times each month.

Although there is no difficulty in determining the side-effects which are readily apparent during a follow-up visit, such as the development of a rash, information concerning side-effects which are not readily apparent is difficult to ascertain. Unless the patient provides this information voluntarily, there are only two courses open. The first is to assume that there are no side-effects; the second is to ask the patient

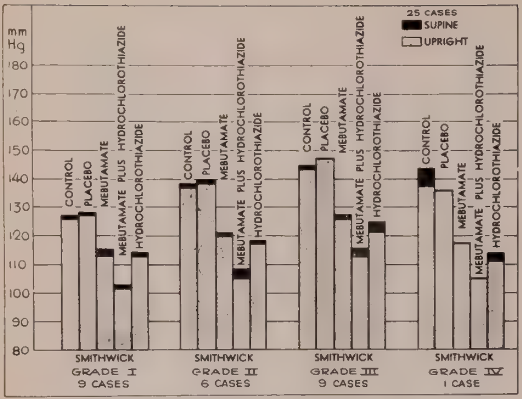

FIGURE 1. Mean arterial pressure in Group A.

if he had any ill effects. The second course is a rather precarious procedure because it involves the power of suggestion. If you suggest or even hint that he might have had a headache or an upset stomach, he will immediately recall having had one. Of course, he may have had an upset stomach or a headache from some totally unrelated cause, but immediately this is associated with the medicine he is taking. Herein lies the difficulty in determining whether or not the side-effect mentioned was directly attributable to the drug. The use of a placebo before or after the drug to be evaluated will frequently confirm or eliminate the drug as the cause of the side-effect; however, side-effects can and do occur with the use of placebo. The consistent reporting of a side-effect by the patient without any suggestion by the physician and the actual observation of a side-effect are the only true criteria for determining those directly attributable to the medication.

Statistical evaluation

The final criterion involves the statistical evaluation of the results. Clinical studies do not always lend themselves to statistical analysis because of the human factors involved. Frequently, the patient will be improved markedly from one standpoint but not improved from another. In relation to blood pressure measurement, however, statistical analysis is certainly applicable in determining whether or not the reductions achieved are significant. In the present study, the reductions obtained were analyzed statistically for each group (A and B) and for each Smithwick classification grade within each group.

Results

The results in Group A may be seen in Figure 1. Reductions obtained on placebo therapy were not statistically significant at the 0.001 level of confidence.

When these patients received mebutamate (second month), based on the control reading, a total reduction of 19 mm. of mercury in systolic pressure and 13 mm. of mercury in diastolic pressure occurred. The reductions obtained on mebutamate were statistically significant at the 0.001 level of confidence.

During the third month when the patients received the combination therapy of mebutamate and hydrochlorothiazide, very marked decreases occurred in both the systolic and diastolic pressures. These reductions were achieved over those already obtained on mebutamate alone. Based on the control reading, this made a total of 39 mm. of mercury decrease in systolic pressure and 21 mm. of mercury decrease in diastolic pressure. Again, the reductions were significant at the 0.001 level of confidence.

During the fourth month on hydrochlorothiazide therapy alone, blood pressure levels approximated those obtained on mebutamate alone. In comparison with control readings, the reductions maintained were significant at the 0.001 level of confidence.

In Group B which received mebutamate as the initial therapy, a reduction in systolic pressure of 21 mm. Hg and in diastolic pressure of 10 mm. Hg (supine) occurred (Fig. 2). In the upright position a reduction of 27 mm. Hg systolic and 11 mm. Hg diastolic were noted. Again, the reductions were significant at the 0.001 confidence level.

On placebo administration during the second month of treatment, blood pressure readings increased in each grade classification in both supine and upright positions. In the supine position the increase was +23/+11 and in the upright position the increase was +28/+11.

The change to the mebutamate-hydrochlorothiazide again caused a marked decrease in both the systolic and diastolic pressures. The average for all the grades was −36/−18 mm. Hg (supine) and −37/−18 mm. Hg (upright).

When hydrochlorothiazide was prescribed alone, again changes from control readings were maintained at levels comparable to mebutamate alone. Reductions were significant at the 0.001 level of confidence.

Side-effects

In Group A during placebo therapy nausea occurred in 3 patients but was transient in 1. During mebutamate therapy, weakness, heartburn, dizziness, or drowsiness occurred in 9 patients but was transient in 3; on hydrochlorothiazide, dyspnea, dizziness, nausea, or orthostatic hypotension occurred in 6 patients but was transient in 5.

In Group B drowsiness and dizziness occurred during mebutamate therapy in 7 patients. Severe dizziness in 1 patient required the discontinuation of the drug. This patient, however, continued with the placebo and sequential therapy until the completion of the study.

In this group the placebo caused drowsiness in 3 patients; combination therapy was accompanied by drowsiness, dizziness, or weakness in 5 patients. On hydrochlorothiazide alone, weakness occurred in 1 patient.

Conclusion

It may be concluded that mebutamate alone, mebutamate combined with hydrochlorothiazide, and hydrochlorothiazide alone are effective in reducing blood pressure at the 0.001 level of confidence. The placebo, given orally, was ineffective in lowering or maintaining reductions in blood pressures. Mebutamate, used alone, and hydrochlorothiazide, used alone, approximated each other in effectiveness in the classification of milder hypertension. Mebutamate seemed slightly more effective in more severe cases. A mebutamate-hydrochlorothiazide combination was much more effective than either drug used alone and was effective in all grades of severity.

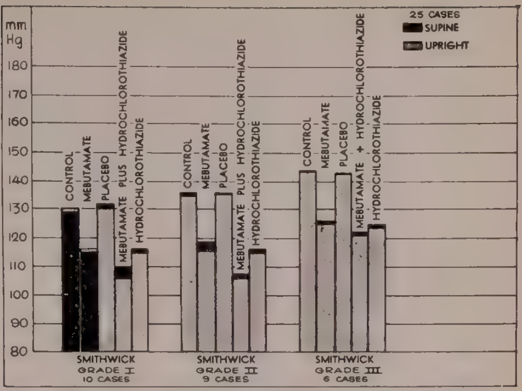

FIGURE 2. Mean arterial pressure in Group B.

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Newer Technics in the Therapy of Renal Hypertension

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RENAL ARTERIAL constriction is an important cause of hypertension. In our experience, approximately 1 in 5 patients with severe hypertension has a renovascular abnormality. Until a decade ago, this condition was treated by nephrectomy; the unsatisfactory results obtained by this method probably are attributable to inadequate knowledge of the disease. The recent availability of renal arteriography and differential renal function studies has resulted in a better understanding of the nature of the disease, and this in turn has led to the correction of the primary cause of the hypertension by the restoration of normal circulation and function of the kidney rather than by removing it. We have treated 115 patients with renovascular hypertension by definitive reconstructive procedures of the renal artery with the restoration of normotensive blood pressure or considerable reduction in blood pressure in a high percentage of cases.

These patients ranged in age from fourteen to seventy-three years, 94 per cent being older than thirty years. There were almost twice as many males (62 per cent) as females (38 per cent).

Types of constriction

Atherosclerosis is the most common cause of renal arterial stenosis. Characteristically, the constriction is localized to the proximal segment of the artery near its orifice or outflow tract from the aorta. After the age of thirty years, this type becomes increasingly prevalent. Thus, 17 per cent of our patients were between the ages of thirty-one and forty years, 25 per cent between the ages of forty-one and fifty years, and 34 per cent between the ages of fifty-one and sixty years. In our experience more than 50 per cent of hypertensive patients older than sixty years have renal arterial stenosis of this type.

Another common atherosclerotic constricting lesion occurs in the accessory renal arteries. This type presents a difficult problem in both diagnosis and treatment. Accessory renal arteries may arise from any segment of the abdominal aorta or iliac arteries. The most common origin is the anterolateral wall of the aorta between the level of the main renal artery and the inferior mesenteric artery. It may be impossible to detect a completely occluded artery. Because of their anterior origin, the aorta may conceal orificial stenosis in anteroposterior arteriograms. These are particularly challenging lesions because they are small and often multiple.

An unusual form of renal arterial stenosis occurring most frequently in relatively young female hypertensive patients is due to intimal and medial fibromuscular proliferation. It appears in the arteriogram as multiple discrete areas of renal arterial narrowing with poststenotic dilation beyond each constricted point. Still another and more unusual type of renal arterial disease causing hypertension is due to an aneurysm of the renal artery.

Complete occlusion of the main renal artery may be readily suspected from excretory pyelograms or radioisotope renograms and confirmed by arteriography. In most cases renal atrophy is so severe that nephrectomy is necessary. If the patency of the primary arterial branches can be maintained by the collateral circulation, it may be possible to conserve the kidney.

Diagnosis

In our experience excretory pyelography has proved of limited diagnostic value. More than 30 per cent of our patients with proved renovascular lesions had no significant pyelographic abnormality. The usual pyelographic evidences of renovascular abnormality in our patients were a delay in the excretion of contrast material and a decrease in the size of one kidney.

A simple diagnostic procedure is radioisotope renography. It indicates the vascular abnormality in a high percentage of cases.

The most accurate indirect diagnostic technic is the split renal function study. This requires the separate collection of urine from each kidney by ureteral catheterization. This shows decreased urine with reduced sodium concentration from kidneys with stenotic renal arteries. The measurement of creatinine, inulin, and para-aminohippurate excretion also may be included in the renal function studies. This procedure has a number of disadvantages and for this reason is employed by us only in patients who present exceptionally difficult diagnostic problems. Not only is it an unpleasant procedure for the patients, but also it is associated with a significant morbidity rate, and its technical performance presents problems.

Renal arteriography is the most reliable method for the definitive diagnosis of renovascular lesions and for planning of the appropriate technic of operation. It can be performed with minimal risk if a few safeguards are observed. These include high insertion of the needle well above the celiac axis, avoidance of a second injection, and limitation of contrast material to less than 30 ml. Translumbar aortic injection of the contrast medium has proved to be the safest and most satisfactory method in our hands. By following these safeguards we have performed more than 2,500 consecutive aortographies with no deaths or other serious complications.

A useful procedure at operation is the determination of simultaneous pulse pressure recordings in the renal artery and aorta. A 5-mm. Hg pressure gradient indicates physiologically significant narrowing in the renal artery.

Technics of renal revascularization

RENAL ARTERY BYPASS. Renal artery bypass is a simple, safe method of revascularization of the kidney in patients with renal arterial stenosis. There are several reasons for this. One is that the segment of the artery that is opened and subsequently sutured is distal to the diseased area, and here the caliber of the artery is usually enlarged by poststenotic dilation. Second, the duration of renal arterial occlusion is minimal. End-to-side anastomosis requires less than ten minutes, which the kidney tolerates well. We usually use an 8-mm. Dacron graft for this purpose, and the proximal end of the bypass is attached to the abdominal aorta. The autogenous saphenous vein is used for the bypass conduit in special cases. In rare suitable anatomic situations the splenic artery can be brought down as a shunt. The bypass principle was used in more than two thirds of our 115 patients.

PATCH-GRAFT ANGIOPLASTY. Patch-graft angioplasty consists of a longitudinal incision in the renal artery across the stenosed area and closure of the defect with an elliptically tailored patch graft. This method was used in 30 per cent of our 115 patients. It may be combined with local endarterectomy.

ASSOCIATED VASCULAR PROCEDURES. As would be expected in a disease caused by atherosclerosis, associated atherosclerotic lesions may occur elsewhere. These are usually occlusive. In addition to the renovascular surgical procedure, 29 per cent of our patients had associated aortoiliac occlusions, which were treated by aortoiliac bypass procedures. The resection of abdominal aortic aneurysms with graft replacement was performed on 6 per cent, and 3 per cent had femoropopliteal bypass operations.

Analysis of results

An analysis of our experience has proved that in properly selected cases the results of correctly performed renal revascularization procedures are most encouraging. Thus, normotensive blood pressure was restored in 80 per cent of our 115 patients, and a striking reduction in blood pressure was achieved in an additional 8 per cent. No improvement occurred in only 6 per cent.

Not only were the immediate results of operation gratifying but also the late results, as indicated by follow-up observations ranging up to four years, have been most satisfactory. Noteworthy has been the improvement in renal function. It is also of particular interest that the revascularized kidney has consistently shown superior function over the other kidney, undoubtedly owing to the severe hypertensive nephrosclerosis in that kidney. In some instances, progressive reduction in blood pressure took place over a period of six months to one year after operation. The total mortality rate including the late deaths was 6 per cent.

Of importance also is the fact that even hypertension of long duration is amenable to surgical correction. Thus, in about one fifth of our patients hypertension has been known to be present for more than seven years, in some longer than eleven years. In most of the cases, however, the hypertension was of short duration—less than three years in about one half of the cases and from three to seven years in about one fourth of the cases.

Summary

The recent availability of renal arteriography and differential renal function studies has led to a better understanding of the nature of renal hypertension due to renal arterial stenosis, so that now it is possible to restore normotensive blood pressure or considerably reduce the blood pressure by properly performed reconstructive surgical procedures on the renal artery in a high percentage of cases.

There are several types of renal arterial constriction. The commonest is due to atherosclerosis. The constriction is typically localized to the proximal segment of the artery near its orifice or outflow tract from the aorta.

Another common atherosclerotic type occurs in the accessory renal arteries. This type presents difficult diagnostic and therapeutic problems but is amenable to surgical treatment. The commonest form of renal arterial stenosis in young hypertensive patients is due to intimal and medial fibromuscular proliferation. Finally, the main renal artery may be completely occluded.

Renal arteriography is the most reliable method for the definitive diagnosis and planning of the appropriate technic of operation. If a few safeguards are observed, the risk of this diagnostic study is negligible.

The most common surgical procedures are renal artery bypass and patch-graft angioplasty. More than two thirds of our 115 patients were treated by the former method and about 30 per cent by the latter. Normotensive blood pressure was restored in 80 per cent of these, and a striking reduction in blood pressure was achieved in an additional 8 per cent. Only 6 per cent obtained no improvement, and 6 per cent eventually died.

Criteria for Use of Antihypertensive Agents

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All areas of clinical medicine have advanced with unprecedented rapidity in recent years. The advances in the field of hypertension have been rapid, catalytic, at times hopeful, and at times frustrating. Reliable data have accumulated to demonstrate that the medical as well as surgical treatment of patients with severe and progressive hypertensive disease may prolong life and that untreated mild and moderate hypertensive disease can shorten life expectancy. No data are available at present to demonstrate that the use of blood pressure-lowering drugs is of value in this latter group. In this somewhat paradoxical situation, we as internists must attempt to decide which patients need vigorous therapy as opposed to those who simply require careful follow-up and reassurance.

The vast majority of patients with hypertensive disease do not seek medical advice because of symptoms relating to hypertension, but rather the detection of blood pressure elevation is an incidental finding in the course of a routine physical examination or an examination for life insurance. Among patients in the lower-income strata and among those who do not consult a physician regularly, symptoms referable to hypertensive disease may often serve as the motivating factor which causes the individual to seek medical advice. In all instances, the approach to the hypertensive patient should be similar. A careful medical history should be elicited with particular reference to the duration of hypertension and/or hypertensive symptoms. Special attention should be given to the evaluation of headaches, episodes of dizziness, occurrences of pain in the renal area, and symptoms referable to early congestive failure. A physical examination should be performed with particular attention to the appearance of the optic fundi, the character of the apical impulse, the heart sounds, and the neurologic examination. The laboratory evaluation should include a complete blood count, serial urinalyses, a determination

TABLE I. Criteria for evaluating the severity of hypertensive disease

Group	Symptoms	Blood Pressure	Retina	Heart	Urine	Renal Function	Central Nervous System
I Mild	None	$\frac{150\text{-}200}{90\text{-}105}$	Normal	Normal	Normal	Normal	Normal
II Moderate	May be none	$\frac{150\text{-}200}{100\text{-}110}$	Grade I and II	Early left ventricular hypertrophy Normal function	Albumin Casts	Slight decrease	Normal
III Severe	Headaches Dizziness Fatigue Early heart failure	Systolic >170 Diastolic >110	Grade II to III	Left ventricular hypertrophy Heart failure	Albumin Casts Red cells	Decreased	Cerebrovascular accident occurs
IV Malignant	Headaches Blurred vision Weakness Weight loss	Systolic >250 Diastolic >140	Grade IV	Left ventricular hypertrophy Heart failure	Albumin Casts Red cells	Markedly decreased	Involvement in many patients

of blood urea nitrogen concentration, an electrocardiogram, a chest roentgenogram, and an intravenous pyelogram. Following this, various other diagnostic tests may be indicated such as quantitative urine cultures, studies for coarctation of the aorta, pharmacologic and chemical tests for pheochromocytoma, evaluation for unilateral renal vascular disease, and evaluation for the possible presence of primary aldosteronism. If all of these data show negative findings, we are probably dealing with a case of essential hypertension, and medical management is indicated.

Numerous methods have been devised for evaluating the severity of hypertensive disease in a given patient. All of these are based on various combinations of clinical and laboratory data. Although some variations are noted, the basic parameters on which the severity of hypertension can be evaluated include the following: (1) lability of blood pressure; (2) levels of diastolic blood pressure; (3) appearance of optic fundi; (4) heart size, determined by x-ray films and/or electrocardiogram; (5) degree of renal functional impairment; (6) cardiac functional status; and (7) central nervous system involvement.

Schemes for quantitating each of these have been devised, and from these figures a numerical index of severity can be determined. Such schemes have merit in that they permit some comparison of different series of hypertensive patients and also permit an evaluation of the effectiveness of a given therapeutic agent. Unfortunately, there has been no uniformity in the schemes presented to date, and as a result, accurate comparisons of groups of hypertensive patients from various clinics cannot be made.

In our clinic, we have not attempted to utilize a numerical index of severity but rather have categorized patients as having mild, moderate, severe, or malignant hypertensive disease. Table I presents the criteria which are utilized in our clinic for evaluating the severity of hypertensive disease and for prescribing initial therapy. It is apparent that there can be considerable overlapping between these categories.

Management of mild, benign hypertensive disease

Patients in the category of mild, benign hypertensive disease have moderate blood pressure elevation which tends to be labile. They are completely asymptomatic and exhibit no evidence of functional or organic deterioration resulting from the hypertensive disease. In this group of patients who can be separated from the normal population only by means of the blood pressure cuff, we select a conservative approach. A suitable diet should be prescribed to correct abnormal body weight; however, severe restrictions of sodium or of other dietary constituents probably is not warranted. The patient's living habits and total life situation should be evaluated, and where practical, appropriate adjustments should be advised. Mild sedatives or tranquilizers in the form of phenobarbital, meprobamate, or similar agents may be of value in that they make the prescribed life restrictions more tolerable. Reassurance should be strong, and periodic follow-up is essential. It is probable that when suitable antihypertensive agents possessing adequate potency and freedom from side-effects are available, patients in this category may also benefit from therapy.

Management of moderate hypertension

Patients who fall into the category of hypertensive disease of moderate severity have a fairly consistent elevation of their blood pressure levels, they usually have no symptoms directly referable to hypertension, and the optic fundi may show changes indicative of Grade I to II hypertensive retinopathy; however, the neurologic examination usually reveals no abnormality. The urine may show minimal albuminuria and occasional casts. The values for renal functional measurements will be moderately decreased. The electrocardiogram usually will demonstrate evidences of early left ventricular hypertrophy; however, as suggested previously, evidences of congestive failure are usually absent. In this group of patients it is generally agreed that specific therapy is indicated.

In our clinic all such patients are treated initially with the thiazides. A wide variety of thiazide derivatives are currently available, and although minor variations have been described in the actions of these agents, there is little difference in clinical response. All of them are potent diuretic agents, all of them are mildly hypotensive, and all tend to produce a moderate degree of hypochloremic alkalosis with mild hypokalemia. Some of the more recently introduced thiazide derivatives which are characterized by prolonged action may have virtue in that they can be administered only once daily or even on alternate days. Until more extensive clinical double-blind and crossover studies have been performed with the various thiazide agents, it is probably advisable for the clinician to select one of the drugs, become acquainted with it, and use it regularly. The thiazide derivatives will produce a moderate but significant reduction in blood pressure in patients in this group.

In some patients it may then be advisable to add Rauwolfia derivatives in small doses. From our own data, we are not convinced that Rauwolfia derivatives add significantly to the welfare of our patients. The hypotensive properties of these agents are minimal, and the side-effects associated with their use may be more serious than the disease for which they are prescribed; as a result we never exceed a daily dose of 0.25 mg. of the alkaloid or 250 mg. of the crude root preparation. If satisfactory control of blood pressure and symptoms cannot be obtained with these agents, then we administer hydralazine, starting with small doses of 10 mg. four times daily and gradually increasing this to a maximum of 400 mg. per day. If a satisfactory control of blood pressure is achieved, the daily ration of hydralazine is then reduced to 100 mg.; however, if blood pressure control is not achieved, then the dose of 400 mg. daily should be maintained only for a brief period of time to avoid the serious complications which may be associated with hydralazine administration. During the past several years, we have been fortunate in that, although we have treated several hundred patients with hydralazine in doses up to 400 mg. daily, we have not observed a single instance of hydralazine disease by administering the drug in this manner.

When they are administered in conjunction with hydralazine, the Rauwolfia derivatives may play an important role in that they serve to modify the tachycardia and palpitations which usually are associated with hydralazine administration.

Various derivatives of veratrum have been utilized in the past for the management of hypertensive disease and continue to be utilized by some groups. Although such agents are of some value in the management of hypertensive crises when they are given intravenously, they are of little therapeutic value for long-term management.

Management of severe hypertension

Patients with severe hypertensive disease usually have persistent blood pressure readings which exceed 170/110, and the optic fundi reveal Grade II to III (Keith-Wagner) changes. Such patients have definite left ventricular hypertrophy on the chest x-ray film and the electrocardiogram and frequently exhibit evidences of congestive failure. A urinalysis reveals albuminuria, casts, and red cells, and the renal function is reduced significantly. This group of patients may have symptoms of hypertensive encephalopathy or may exhibit neurologic deficits resulting from cerebrovascular complications. In this group of patients, the therapeutic agents listed previously should be administered initially in the order described. In addition, complications such as congestive failure and secondary urinary tract infections should be managed with suitable therapeutic agents.

It is in this class of patients that the use of the sympathetic blocking agents should be given a vigorous trial. At present, the agent of choice for this purpose is guanethidine sulfate. The dosage of this drug has to be titrated to the needs of the individual patient, and although it is preferable to do this in the hospital, it may be carried out on an outpatient basis if the patient can be followed carefully at frequent intervals. The incidence of side-effects with this agent has been variable. In the hands of some, the frequency and severity of side-effects have been so overwhelming as to preclude the continued use of this compound in a majority of cases. The major side-effects reported have been profound postural hypotension, fatigue, diarrhea, and loss of ejaculation. Since blood pressure lowering is achieved principally in the upright position and results from a decrease in cardiac output, anginal symptoms and/or congestive failure may develop. Such symptoms together with evidences of nitrogen retention will necessitate a modification in dosage or discontinuance of the drug.

The earlier ganglionic blocking agents such as pentolinium tartrate, mecamylamine hydrochloride, or chlorisondamine chloride may be utilized in this group of patients; however, the side-effects resulting from parasympathetic blockade often tend to limit their usefulness, and in many instances the evidences of parasympathetic blockade may develop before any lowering of blood pressure has been achieved.

Management of malignant hypertension

Malignant hypertensive disease as manifested by rapid progression, severe systemic symptoms, weight loss, and the appearance of papilledema constitutes an indication for the use of any and all of the various hypotensive agents available today. These should be administered sequentially in the manner described previously, except in the presence of acute hypertensive emergencies when the intravenous use of certain other hypotensive agents may be lifesaving. The medical management of malignant hypertension may be likened to walking a tightrope, and the optimum dosage of various hypotensive drugs can result in sustained improvement in the patient's status; suboptimum dosages result in the progression of symptoms while excessive dosages lead to serious side-effects. Fortunately, in those patients who exhibit improvement during therapy, the dosage requirement for hypotensive agents is often reduced with the clinical improvement, and as a result the ratio between the effective dose and the therapeutic dose is significantly increased.

Summary

Great strides have been made in our knowledge of essential hypertension in recent years; however, the fundamental cause remains unknown. Despite this, a number of pharmacologic agents have been developed which possess the capability of lowering blood pressure. When these agents are utilized rationally in patients with severe progressive or malignant hypertensive disease, the mortality and morbidity can be improved significantly. In patients with mild blood pressure elevation who are completely asymptomatic and who exhibit no evidences of organ deterioration resulting from the hypertensive disease, therapy should be conservative at present. Once an agent becomes available which is essentially free of serious side-effects even on long-term administration, then patients in this category should receive therapy also. Patients who fall into the group between these two extremes should be treated with the available hypotensive agents in the hope that blood pressure reduction may serve to avert the ultimate complications which accompany hypertensive disease.

Treatment of Hypertension in Geriatric Practice

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EVEN THOUGH the treatment of hypertension in elderly individuals is generally the same as in younger people, some differences exist. This is especially true with regard to arteriosclerosis which is predominant among elderly individuals. Elderly people are also particularly susceptible to environmental changes and severe psychic stress, which might influence existing hypertension or produce temporary elevation in their blood pressure. This susceptibility reflects the decreased compensatory ability of the elderly body. This decreased compensatory ability of the elderly person's cardiovascular system to cope with the elevated blood pressure is responsible for the development of degenerative cardiovascular disease with or without congestive heart failure which is a common diagnosis in our elderly patients. Various considerations of a general nature are also of special importance in the treatment of elderly hypertensive subjects. A thorough knowledge of the patient is necessary, not only from the point of view of his blood pressure but from every other aspect as well.

First of all, we should lay emphasis on making a definite diagnosis of hypertension before starting any treatment. It is not proper to diagnose hypertensive disease when only the systolic blood pressure is elevated, whereas the diastolic blood pressure is within normal limits; there is no proof at the present time that an elevated systolic blood pressure in elderly persons accompanied by a normal or slightly elevated diastolic blood pressure will cause any degenerative changes in the vessels of the brain and kidneys or other end organs. This elevated systolic blood pressure, caused by increased rigidity of an arteriosclerotic aorta or aortic insufficiency is very common in elderly persons. This simple systolic hypertension must not be treated with antihypertensive drugs. They do not act on the hard pipes of elderly people. These drugs merely act on excessive vasospasm. It is not our aim to lower a 250/90-mm. Hg blood pressure of an arteriosclerotic subject to 150/50 mm. Hg. If the diastolic blood pressure is definitely elevated in repeated readings, we might become concerned that the elderly patient has hypertensive disease. The height of the diastolic blood pressure determines the necessity and the type of treatment.

In our screening procedure we must take into consideration that essential hypertension rarely begins after the individual has passed middle age, but because of the improved medical care more individuals with essential hypertension reach a higher age. We must differentiate the cases of secondary hypertension like the neurologic cases, which are very rare in the older-age group, the cardiovascular diastolic hypertension caused by the coarctation of the aorta, endocrine cases, aldosteronism and pheochromocytoma, and the largest group, the renal cases, especially chronic pyelonephritis, which in elderly subjects is caused by the obstruction of the lower urinary tract.

We believe that individuals with variable degrees of hypertension who have mild occasional symptoms or none at all and few or even no objective findings, but a steady diastolic pressure around 100 mm. Hg or more, accompanied by a systolic pressure of over 150 mm. Hg, should be subjected to more or less vigorous antihypertensive therapy. Especially we want to emphasize that an elderly hypertensive patient who has had a stroke or heart failure needs to be protected as far as possible from the recurrence of such episodes. It is of great importance that not only the elevated blood pressure but also the elderly hypertensive patient with his aging organs should be treated.

Certainly there are many differing opinions concerning hypotensive therapy in elderly patients.

Diet plays a more or less important role in the therapy of hypertension. Master and Lasser[1] contended that lowering the weight to normal in elderly subjects often results in a gratifying decrease of the blood pressure levels. On the other hand, Martin[2] has shown that reduction of obesity is not followed by a significant decrease in the blood pressure, in spite of the fact that an improvement in physical status occurs. Fishberg[3] advocates that a low-sodium diet is a very important antihypertensive measure, but a low-sodium diet has been largely replaced by the thiazide drugs. Low-salt diet has some advantage in the early phase of hypertension, but in the later phase of renal involvement sodium diuresis is a common finding. The success of diet therapy depends on the cooperation of the patient, but generally there is a lack of willingness to cooperate in the elderly individual.

Drug therapy

Sedatives and tranquilizers should be the first choice of therapy in mild hypertension with a diastolic pressure around 100 mm. Hg. Larger doses are needed to help patients over emotionally rough spots, especially elderly subjects with cerebrovascular involvement.

Xanthines are still used occasionally on our elderly patients, but with questionable results.

The pure alkaloid and the crude preparations of Rauwolfia root seem to have the same effect. In one of our earlier studies[4] with reserpine on more than 100 elderly subjects, we noted moderate to severe depression, especially in women after the third month of administration. This depression increased in half the patients during the fifth month of therapy. Two patients had to be placed in the psychiatric ward because of suicidal tendencies.

The thiazide derivatives when used alone are effective in moderately severe hypertension in only half of the patients. Therefore they should be used only in combination with other hypotensive drugs. It is our experience that the long-standing hypertension of elderly patients responds markedly well to combined thiazide therapy. The major complication of thiazide treatment is hypopotassemia. Wilkins[5] recently called attention to digitalis toxicity which may occur on a prolonged digitalis-thiazide regimen. A potassium-rich diet and the intermittent administration of a thiazide seem to be good prophylactic measures. Hyponatremia can be avoided by the allowance of an adequate intake of sodium. After the discontinuance of thiazide administration, the serum potassium level was restored in a short time, whereas the serum sodium remained for a longer time at the lowered level in elderly patients.

Hydralazine might be used occasionally, especially in patients who do not respond adequately to reserpine-chlorothiazide combination therapy. We start with very low initial doses.

Ganglion-blocking agents should be used rarely, if at all, in elderly patients. The undesirable side-effects of the unwanted parasympathetic blockage can create serious problems in the elderly subject. In the elderly male, prostatic hypertrophy is common and may cause urinary obstruction. Mecamylamine hydrochloride is the only ganglion-blocking agent we have used in elderly patients. We experienced some trouble with constipation and severe impaction. Cathartics were given regularly, and this side-effect was adequately eliminated.

Recently we have made clinical studies on a new drug, mebutamate* which acts in a different way from most of the other antihypertensive drugs.

Methods

The subjects studied were selected from the St. Louis Chronic Hospital. All subjects have been inmates for many years. Most of them had been treated before in other institutions for hypertension, and the copies of those records were attached to their present histories. The duration of these known histories of hypertension varied from eleven to thirty-four years. All subjects had for years had periodic laboratory tests including at least a yearly electrocardiogram and x-ray film. The patients were subjected to thorough medical observations by the investigator. Serum sodium, potassium, chloride, and uric acid determinations and a battery of liver tests were also performed during the eight- to ten-week control period. During this period blood pressure readings were taken twice weekly in the morning, between 9:00 and 11:00 A.M. The blood pressures were determined in sitting, standing, and lying positions and, in those 7 subjects who could not stand for various reasons such as leg amputation, arthritis, or hemiplegia, in sitting and supine positions only. The sitting position blood pressure readings were included therefore because most of the subjects spent the greater part of the day seated or rolled slowly around in their wheel chairs. Two readings were made in each position. The pulse rates were taken in the sitting position.

The blood pressures were taken by the investigator and the nurse of the research division. The blood pressure records of the hospital nurses were used for checks but were not included in the reports.

Our original plan called for the discontinuance of all antihypertensive drugs including tranquilizers, especially meprobamates, for at least two weeks, to establish a control level. However, during our preliminary study we found this impractical and even considered it harmful for a number of the patients, especially those who were on a chlorothiazide or hydralazine regimen. Therefore 10 subjects remained on restricted hydrochlorothiazide or reserpine-hydralazine therapy. All the others received placebo tablets irrespective of whether or not they were on antihypertensive drug therapy at the start of the study. Because of this attrition and many others which arise in setting up an experimental study on elderly subjects, our preliminary study required eight weeks. The main purpose of these long pretherapy observations was to eliminate those subjects whose blood pressures showed an excessive variability.

The study was started with 43 patients, but 11 of them were eliminated for various reasons. Two females died of stroke, 6 were discharged to nursing homes, and 3 refused to take tablets after the first signs of oversedation. The end report includes 32 subjects, 24 of them females and 8 males. The ages of these 32 patients ranged from fifty-nine to eighty-six years, with a mean of seventy-one years. Seventeen subjects had electrocardiograms showing left ventricular hypertrophy; 8 subjects had other minor electrocardiographic changes. Eighteen subjects showed an enlargement of the heart on x-ray examination. Three subjects showed old myocardial infarctions. Nine subjects had suffered cerebrovascular accidents with a history of long-standing hypertension.

All patients were started on 300 mg. of mebutamate given three times daily before meals. Seven patients remained on that dose throughout the sixty or more days of therapy. In 5 male subjects it was increased after a few days to 300 mg. given four times daily. Thirteen patients remained for thirty days on 900 mg. and for another thirty days on 1,200 mg. daily. The dosage in 5 patients after thirty to forty-five days of therapy was reduced to 300 mg. in the morning and 150 mg. at noon and in the evening, because of intractable oversedation. In 3 patients 25 mg. of hydrochlorothiazide added after sixty days of mebutamate therapy did not result in signifi-

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* Supplied by Wallace Laboratories, Cranbury, New Jersey.

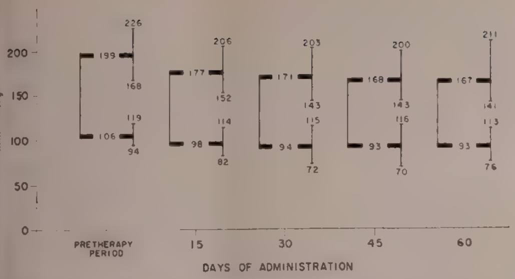

FIGURE 1. Blood pressure changes following daily administration of 900 and 1,200 mg. of mebutamate to 32 elderly subjects. Averages of means of fifteen-day periods.

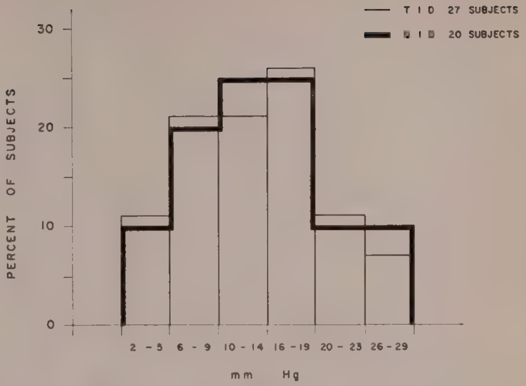

FIGURE 2. Maximum decreases in diastolic blood pressure during sixty days of mebutamate administration.

cant blood pressure reduction. During the mebutamate regimen, 13 to 18 readings were made in each position.

In 20 patients a more intensive study was done. First, to determine the correlation between blood pressures and serum concentrations of mebutamate, blood pressure readings were made at the time of ingestion of 300 mg. of mebutamate, one-half to one hour before and six times hourly thereafter. During this time, blood was drawn for a determination of the concentration of mebutamate in the blood serum at zero, one, two, three, and six hours.* Second, a nine-hour study was established from 7:00 A.M. until 4:00 P.M., to determine the hourly changes in the blood pressure during therapy.

Results

In Figure 1 are given the averages of the mean systolic and mean diastolic blood pressures of 32 elderly subjects during the pretherapy period and the four fifteen-day periods of oral administration of 300 mg. of mebutamate three times and/or four times daily, respectively. The vertical lines show the respective ranges of both systolic and diastolic mean blood pressures. The means are calculated from the readings of all three positions: upright, sitting, and recumbent.

Figure 2 shows the maximal decreases in diastolic blood pressure achieved by the administration of 300 mg. of mebutamate three times and four times daily. These maximum decreases occurred irrespective of the daily dosage in an equal number of the patients during the second, third, and fourth fifteen-day periods of the therapy. On the daily administration of 900 mg. of mebutamate, 3 subjects, and on the 1,200 mg. only 2 subjects, showed no decrease in diastolic pressure. In the 10- to 14- and 16- to 19-mm. Hg drop there were no significant differences between the per cent of patients receiving 900 mg. and those on 1,200 mg. Thirteen of the 27 patients given 900 mg. of mebutamate daily showed a maximum diastolic decrease of from 10 to 19 mm. Hg, as did 11 of 20 subjects receiving 1,200 mg. Three of the 5 subjects whose daily dosage was reduced on account of oversedation to 600 mg. daily, administered in 3 doses, showed a maximum diastolic decrease of 20, 23, and 27 mm. Hg, as compared with a 28, 19, and 23 mm. Hg decrease, respectively, while they were on the 900-mg. dosage.

Figure 3 presents the blood pressure data on an eighty-six-year-old male patient, who has been for years in good physical condition with complaints of slight dizziness, headache, and palpitation. He had known essential hypertension for thirty-four years. There was no evidence of marked cerebrovascular disease. He had left ventricular hypertrophy, traces of albuminuria, 26.1 mg. per 100 ml. blood urea nitrogen, and a satisfactory urinary concentration test for his age. He was treated for many years with xanthines and barbiturates and recently with reserpine and tranquilizers.

Those 3 patients who did not respond to the daily administration of 1,200 mg. of mebutamate produced a 14-, 21-, and 22-mm.

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* The determinations of the serum concentration of mebutamate were done in the Wallace Laboratories.

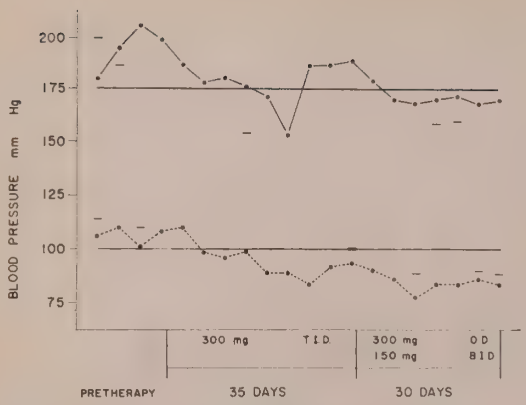

FIGURE 3. Blood pressure changes following mebutamate therapy in an eighty-six-year-old man.

Hg decrease when mebutamate was combined with 75 mg. and 100 mg. of hydrochlorothiazide. Three patients who, prior to the mebutamate therapy, were on reserpine-hydralazine and/or chlorothiazide therapy showed a less than 10-mm. Hg diastolic pressure decrease when they were given mebutamate. Seven of the 11 patients who had been treated successfully with reserpine or a reserpine-chlorothiazide combination prior to this study responded with a 12- to 27-mm. Hg decrease in diastolic pressure to mebutamate administration. A seventy-eight-year-old white woman with arteriosclerotic heart disease and old hemiplegia due to a cerebrovascular accident, who was previously on a digitalis-hydrochlorothiazide regimen, showed a 29-mm. Hg decrease while on digitalis-mebutamate therapy. Her ankle edema increased twice during the mebutamate period; therefore the addition of 25 mg. of hydrochlorothiazide for three days on each occasion was necessary.

The correlation between the diastolic blood pressure changes and the serum concentrations of mebutamate after the administration of 300 mg. of mebutamate was good in 7 cases, fair in another 7 cases, and poor in 6 cases.

Figures 4 and 5 show curves which we consider to denote a good correlation. We must take into consideration that the drug was not the only factor in influencing the blood pressure of the patients; these elderly subjects were also affected by the unusual procedures of hourly blood pressure readings and the 5 blood drawings in the period of six hours.

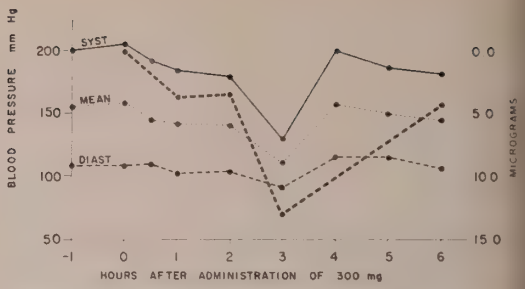

FIGURE 4. Blood pressure changes and serum concentrations of mebutamate in seventy-eight-year-old person following oral administration of 300 mg. of mebutamate, indicated by heavy dotted line.

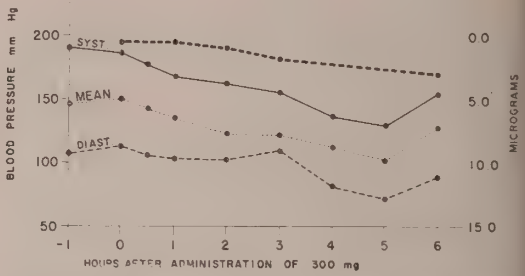

FIGURE 5. Blood pressure changes and serum concentrations of mebutamate in seventy-four-year-old person following oral administration of 300 mg. of mebutamate, indicated by heavy dotted line.

The nine-hour study shows the periodicity of the drug effect. Table I gives the hourly averages and the ranges of blood pressure in the 20 elderly subjects studied. It indicates that the average decrease of the diastolic as well as of the systolic blood pressure was greater after the second dose of 300 mg. of mebutamate than after the first.

Looking at the individual curves, we note that the diastolic blood pressure decrease was greater in 13 out of the 20 subjects after the second daily dose of 300 mg. of mebutamate than after the first daily dose. The peaks of the blood pressure before the second and third daily doses showed a decreasing tendency (Fig. 6). This limited experience on a limited number of elderly subjects suggests some kind of cumulative effect of mebutamate. For technical reasons we could not study the hourly changes after the third and fourth tablets respectively.

TABLE I. Hourly blood pressure changes during oral administration of mebutamate in 300-mg. doses in 20 elderly subjects

Time	Average	Range
7 A.M.	193 105	162-220 80-118
8 A.M.	179 99	158-222 78-128
9 A.M.	170 97	128-210 70-118
10 A.M.	163 95	136-194 62-116
11 A.M.	181 102	140-220 82-128
12 NOON	167 98	148-194 78-118
1 P.M.	158 90	146-186 62-122
2 P.M.	159 92	134-204 88-116
3 P.M.	168 95	142-200 82-114
4 P.M.	175 97	158-200 80-118

There were no significant weight changes during and after therapy.

Clinical symptoms

Among clinical symptoms, the biggest disadvantage associated with mebutamate therapy was oversedation. This annoyed 3 patients so much that they refused to continue therapy after a few days. One female patient was on and off the drug for forty-eight days without getting used to it. Only 2 of the 8 elderly males had trouble with this oversedation, but 13 of the 24 females complained for several days. The omission of several doses of the drug in most cases solved the problem in a few days. In those 5 patients who experienced, in addition to the soporific effect, some drowsiness and dizziness, after thirty to forty-five days of therapy the daily dose of mebutamate was reduced to 600 mg., divided in three doses, for the rest of the study. This reduction in dosage brought about prompt remission of these symptoms, and, as already mentioned, 3 of these 5 subjects showed a continued satisfactory decrease in blood pressure.

Severe constipation occurred in 3 female subjects. This is very close to the rate occurring in our elderly year-long hospital inmates. One of them was previously on mecamylamine hydrochloride therapy.

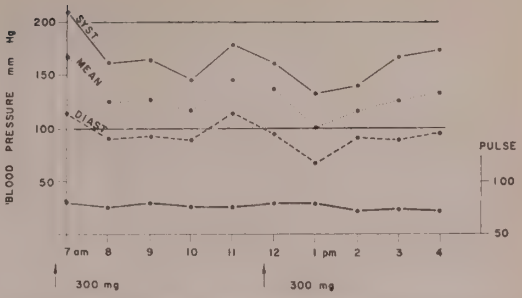

FIGURE 6. Hourly changes in blood pressure during mebutamate administration.

Stomach discomfort and nausea occurred in 5 patients during the second and third weeks of mebutamate regimen, but in all 5 cases this trouble was eliminated when Gelusil was given.

The mean pulse rate during the pretherapy period was 77 per minute with a standard deviation of ±4. In 7 cases there occurred increases in the pulse rate up to 16 per minute when the blood pressure dropped.

A remarkable sense of well-being and marked improvement in mental and physical activity occurred during therapy irrespective of the amount of decrease in blood pressure in most of the elderly patients, even in those who were affected by the soporific side-effect of the drug.

Laboratory data

Table II shows the blood chemical data before and after sixty days of mebutamate therapy. The average of blood urea nitrogen did not change after therapy as compared with pretherapy levels. There were 6 patients with a higher pretherapy level than the accepted normal range, but these higher blood urea nitrogen values are not uncommon in our elderly subjects.

The serum sodium level did not change; the mean level remained the same, 133 mEq. per liter. There were low serum sodium levels in 4 patients, probably on account of the previous thiazide therapy, and 7 patients revealed low serum sodium values for unexplained reasons which did not change significantly during the mebutamate period.

Serum potassium increased slightly in

TABLE II. Average pre- and post-therapy laboratory findings on 32 elderly patients receiving 300 mg. of mebutamate three or four times a day for sixty days

Finding	Pretherapy Average	Pretherapy Range	Post-therapy Average	Post-therapy Range
Cholesterol	258 mg. per 100 ml.	172 to 382	267 mg. per 100 ml.	141 to 408
Blood urea nitrogen	16.3 mg. per 100 ml.	11.6 to 26.1	17.0 mg. per 100 ml.	11.1 to 25.6
Uric acid	4.2 mg. per 100 ml.	2.2 to 5.7	3.9 mg. per 100 ml.	2.8 per 5.1
Sugar	77 mg. per 100 ml.	56 to 110	83 mg. per 100 ml.	62 to 120
Thymol turbidity	3.7 units	1.2 to 11.0	3.4 units	1.1 to 10.6
Cephalin flocculation test	0 to ±1	...	0 to ±1	...
	0 to ±1	...	0 to ±1	...
Alkaline phosphatase	1.9 units	0.1 to 3.7	1.5 units	0.9 to 3.5
Serum sodium	133 mEq. per liter	114 to 142	133 mEq. per liter	116 to 143
Serum potassium	4.0 mEq. per liter	3.4 to 5.0	4.3 mEq. per liter	3.4 to 5.2
Serum chloride	92 mEq. per liter	81 to 97	93 mEq. per liter	86 to 106
Hematocrit	41	32 to 47	41	31 to 47
Hemoglobin	13.8 Gm.	10.5 to 15.8	13.6 Gm.	9.7 to 16.2
White blood count	5,220 cu. mm.	4,130 to 15,000	5,660 cu.mm.	4,150 to 15,700
Polymorph leukocytes	65 per cent	52 to 82	66 per cent	58 to 85
Lymphocytes	27 per cent	13 to 34	28 per cent	18 to 36
Eosinophils	3 per cent	0 to 14	2 per cent	0 to 8

the 4 patients who were, before this study, on a chlorothiazide regimen. On account of the low potassium level in our elderly patients, small amounts of orange juice are offered to them twice daily, especially during the summer months. The serum sodium level did not increase as fast as the potassium. The serum cholesterol levels revealed up-and-down changes in a number of patients, but these changes did not exceed 15 per cent.

Serum copper and serum zinc changes occurred during the study in several patients with a marked increase or decrease, without any correlation with the changes in the blood pressure. Marked increases in serum copper oxidase activity were noted in 50 per cent of the subjects after mebutamate therapy. This increase in oxidase activity was significant at the 0.5 per cent level.

The profiles of urinalysis did not change after therapy.

Summary

Thirty-two elderly patients with a history of long-standing hypertension were studied on a regimen of a new antihypertensive drug, mebutamate. On daily doses of 600, 900, and 1,200 mg. of mebutamate, 19 per cent of the patients responded with a diastolic decrease of 20 to 29 mm. Hg, 49 per cent with a decrease of 11 to 19 mm. Hg, and 32 per cent with a decrease of 2 to 10 mm. Hg.

Fifteen subjects felt a mild to moderate soporific effect, which disappeared within a few days when the doses of mebutamate were reduced.

During mebutamate therapy, all patients expressed a sense of well-being that they had not experienced with any other hypotensive drug.

The hourly blood pressure readings suggest in most of the patients some slight cumulative effect; on the other hand, these hourly observations call for the necessity of sustained-release medication to provide a more even hypotensive effect and blood pressure level during the daytime.

The laboratory data showed no significant changes after therapy in these elderly patients.

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Question and Answer Period

Dr. Duncan: First, I would like Dr. Mendlowitz to give a definition of essential hypertension.

Dr. Mendlowitz: That is a loaded question because nobody knows exactly how to define essential hypertension. I would say that it is a heredity disorder characterized by a progressive elevation in blood pressure beyond what might usually be expected for a particular age, sex, and race in an individual. There are other features of essential hypertension which can be defined more clearly, such as responsivity to various pressor agents, which I spoke about. There are characteristic changes in renal function, which were mentioned also, all of which tend to define and characterize essential hypertension more definitely.

Dr. Duncan: Dr. Mendlowitz, there is a question asking if you would say a few words regarding renoprival hypertension.

Dr. Mendlowitz: That was first described by Grollman and others in Texas when they found that the blood pressure went up in animals whose kidneys were removed. This was a startling observation at the time because until that time it had been assumed by many groups of workers that most hypertension was either produced or certainly influenced by what happened in the kidney. Yet here was blood pressure rising with the kidneys gone. The animals had to be maintained by dialysis in this particular group, and then Muirhead showed that the hypertension could be prevented to some extent by explantation of the medullary substance of the kidney, so that it is a type of hypertension which in some way is caused by the removal of the kidney. Nobody knows exactly what the mechanism of this type of hypertension is, and it is not known whether or not it occurs in human beings.

Dr. Duncan: There is a question addressed to Dr. Berger. Would you please repeat how monamine oxidase inhibitors lower high blood pressure?

Dr. Berger: The monamine oxidase inhibitors act by increasing the concentration of norepinephrine by inhibiting the enzyme that inactivates it. Norepinephrine accumulates in the autonomic ganglia and produces blockage of ganglionic transmission.

Dr. Duncan: Here is another question directed to Dr. Berger. Does mebutamate cause impotence?

Dr. Berger: No, impotence is a symptom of parasympathetic blockage. When the parasympathetic branch of the autonomic system is blocked by a drug, impotence occurs. Mebutamate does not affect the parasympathetic system or for that matter the sympathetic nervous system. For this reason, it does not cause impotence.

Dr. Duncan: This question is directed to me. Do you hospitalize patients on the ten-day no-calorie regimen? Yes, for the first course of the reduction program we do. Our first patient was a physician. He weighed 365 pounds, so it would not be practical to try to reduce his weight to a satisfactory level in one stretch. The initial hospitalization period is rather important, first, to give the patient confidence in the program and, second, to let him realize that, curiously enough, he is not hungry after the first day. It is interesting that this anorexia which develops apparently is related to the appearance of ketones in the plasma. I have had patients after ten days of no calories pleading to be allowed to remain on this program until they had their weight where they wanted it. For the first ten days, for a patient who has a refractory type of obesity, we have them in the hospital. Then subsequent attempts can be made at home, but it is much more satisfactory if it is carried out in the hospital.

Dr. Berger, is mebutamate habit-forming since it is similar to meprobamate?

Dr. Berger: We have no evidence that meprobamate is habit-forming. All the cases of so-called habituation occurred in patients who have been previously addicted to narcotics or habit-forming drugs. I have never heard of a case of habituation in a patient who has not been addicted previously to one of the narcotic drugs. For this reason I believe habituation is not a function of the drug but a function of the personality of the patient.

DR. DUNCAN: Thank you. Dr. Kolodny, a patient is a male, age fifty-five, with varying hypertension of several years standing without symptoms. The right kidney is smaller than the left. Indirect angiography is inconclusive. Would you advise performing a direct femoral aortogram?

DR. KOLODNY: I certainly feel, just glancing at this question and thinking about it casually, that an aortogram would be indicated, but I would certainly want further investigation of that type.

DR. DUNCAN: Dr. Mendlowitz, is the effect of chlorothiazide on decreasing the response of arteriolar musculature to angiotensin due to its diuretic action, indicating sodium, or is it direct, since within five to twenty minutes intravenous infusions do produce decreased responsivity to short-acting sympathomimetics?

DR. MENDLOWITZ: I have a prejudice in that regard. I do not think that there is any definite information. There is some evidence on both sides. Hollander, I think, in Boston, believes that there is a direct action of chlorothiazide on the tissues which can be separated from the sodium-depleting effect. I personally feel that the effect that one observes, with reference to responsivity, is due largely to sodium depletion. I may be wrong about this. I understand that a chlorothiazide derivative has been developed recently which does not eliminate sodium from the kidney but does produce a decrease in blood pressure, and so I think the question cannot be answered, at least not by me. One of the reasons I think that sodium is involved in the process is that aldosterone, which is the other side of the coin, retains sodium and causes an increase in responsivity in hypertensive patients, whereas chlorothiazide produces the opposite effect, in that it decreases sodium. These are all indirect observations.

DR. DUNCAN: This question is directed to me. With the tremendous number of antihypertensive drugs all with different actions and with side-reactions, how can one reasonably expect a general practitioner or even an internist (1) to treat questionable cases and (2) to indicate the cases scientifically and effectively? I think that if one divides the patients with hypertension into certain specified groups either by the Smithwick classification or other methods of grouping, it will give you a plan as to which drugs with different actions will have effect. The second part would be, I think, that one must be familiar with the action of each of these drugs before using them, and, in using them, the additive effect should be looked for. It is true that there is a great number of drugs, and this just points up again the tremendous necessity of individualizing the treatment in these various patients. I do not mean by that that there is just one particular group of drugs that will affect favorably the individual patient because we may have three or four programs that will do the trick, but I would say an adequate evaluation of the degree of severity of the hypertension and a rather thorough knowledge of how each of these drugs acts would be the foundation of treatment.

DR. DUNCAN: Dr. Mendlowitz, how do you explain different readings on both arms when they are taken at the same time and with the patient in the same postion in the absence of mechanical factors, for example, a cervical rib or an aneurysm?

DR. MENDLOWITZ: I do not know whether or not I can explain it. I think that there is a normal difference between the right and the left arm of a few millimeters of mercury—maybe 5 mm. even when readings are taken simultaneously. Of course, one would have to know whether they were taken by the cuff method or by the arterial recordings. There is an error in the cuff method, as you know. Other than that, unless there is a coarctation of the aorta between the innominate artery, on the one hand, and the subclavian on the other, I do not see how you could obtain a very large difference between the two arms.

DR. DUNCAN: This is directed to me in regard to the amobarbital sodium test. How is it carried out? What is the dose and routine administration? The amobarbital sodium test I think has grown in disfavor to a certain extent in the hands of the profession. I think that this is probably because it was misused when surgeons were eager to get hypertensive patients for sympathectomies, and they wanted to get them with the blood pressure as low as possible, with the prospect of better results. They did this test on patients with a very labile type of blood pressure. It showed that it was labile, and sympathectomies were done on many of these patients; postural hypotension resulted, so that the test became somewhat associated with this complication of surgery. If the amobarbital sodium test had been acted on differently and sympathectomy contraindicated in all those patients with labile hypertension, then this difficulty would not have arisen, and I think it would have retained its value.

The actual carrying out of the test can be done the first day the patient comes into the hospital. I would say that it is only when the patient has a severe type of hypertension which we are reasonably sure is not a labile type of hypertension that we would do the amobarbital sodium test. The patient may be admitted at 3:00 P.M. and that evening be given 3 grains of amobarbital sodium after at least four blood pressure readings have been recorded at half-hour intervals. Following one hour, a second dose of 3 grains of amobarbital sodium would be given and an hour later another dose of 3 grains, so that we would have given three doses to the patient, who would be fairly well under the influence of this sedative. If the diastolic pressure does not go down to 100 mm. Hg as a result of this, we consider then that the patient has a rather fixed type of hypertension. It is in those patients that guanethidine sulfate and the ganglion-blocking agents can be given without fear of hypotensive episodes. On the other hand, if it goes below 100 mm. Hg during the course of the test, then we can be on the lookout for hypotensive episodes, so that this is another way we can divide these patients into two groups. If we have fairly good reason to believe or actually know that diastolic pressure goes down to 100 mm. Hg or below after conservative therapy, then we would not do this test. It should only be done when there is no evidence of a lability of the blood pressure. We see no reason for doing this test for patients who are known to have a labile type of diastolic pressure. The route of administration is oral. Dr. Mendlowitz, what levels of blood pressure do you use to separate normotensive from hypertensive patients? What evaluation is placed on the differences in blood pressure readings taken in lying, sitting, and standing positions?

Dr. Mendlowitz: I think I answered this question in part before. That is, it depends on the age and sex of the patient and other factors. For example, if a boy of sixteen has a consistent blood pressure of 140/80, that boy, especially if he has a family history of hypertension, is probably hypertensive. On the other hand, a woman in her seventies, who has a blood pressure of 180/80 or 180/90, may not have essential hypertension at all but may simply have arteriosclerosis with a rather brittle arterial system. I do not think that as a clinician one can make arbitrary designations as to what level of blood pressure a person must have to call something essential hypertension. You cannot do one reading, for example, and say that a patient has essential hypertension. You have to observe the patient and then be convinced in your own mind that the patient has blood pressure levels which are higher than he should have. We have other tests to confirm the diagnosis once essential hypertension is suspected. We do reactivity studies to angiotensin, in which readings are uniformly high, even in patients with earliest hypertension, but these are complicated procedures and are not in wide use.

Dr. Duncan: In regard to the position, would you comment?

Dr. Mendlowitz: I do not think that position has too much to do with it. I know some people have thought that, providing there are no drugs that have been taken, you can differentiate pheochromocytoma from essential hypertension by what the patient does when he stands or lies, in terms of his blood pressure. But I have found that this is so variable that I would not use this as an indication of whether or not the patient had elevated blood pressures caused by an adrenal tumor or some other form of hypertension.

Dr. Duncan: Would you say that episodes of hypertension during emotional disturbances, which are very transient, are due to an increased cardiac output, assuming there is no evidence of hypertensive disease?

Dr. Mendlowitz: I do not know that that has been measured. I think that it is quite well established, as you mentioned in your talk, Dr. Duncan, that people with hypertension do tend to respond to emotional stimuli by elevating their blood pressures more than normal people do. As a matter of fact, this is one of the characteristics of the hypertensive patient. A person who is not a true hypertensive individual, who does not have this underlying trait, may be very disturbed emotionally, and practically nothing or very little will happen. But with a hypertensive person or with one who has the hypertensive characteristic, however you wish to define it, chemically, he will respond to emotion by an exaggerated elevation of his blood pressure. Presumably the blood vessels are hypersensitive, and the stimulus is elaboration of norepinephrine locally via the sympathetic nervous system.

Dr. Duncan: Dr. Kolodny, since we have had saluretic agents, how do you feel about salt? Should we restrict it moderately or severely?

Dr. Kolodny: In my own personal practice I first go by the individual patient. Certain patients will cooperate on a restricted diet of that type for long periods, and others will not. If you have a patient with a relatively severe degree of hypertension on one of the thiazides, certainly salt restriction would be of value if you have to use relatively large doses of the thiazides or a derivative to maintain the antihypertensive effect. In that regard undoubtedly it would be of value to restrict the salt moderately. These old restrictions where they gave 200 to 400 mg. of sodium per day with diets were too difficult for the patient to follow. In my experience, relatively few of them would stay on it for any length of time.

Dr. Duncan: Thank you. We are restricted to one remaining question. I will exercise the prerogative of the moderator to answer this one, seeing that it is directed to me. It comes from a "doubting Thomas," I think. Do you really believe that in essential hypertension the beneficial effects of these patent antihypertensive agents outweigh the side-effects and the symptoms so many patients complain of as a result of taking these drugs? The great advantage of the multitude of drugs is that you can use small doses of several, so that you can get practically no side-effects, or the side-effects are so small that the patients would prefer to have them rather than the symptoms of their hypertension, and you would rather have them too, to reduce the risk to which they are exposed. This question, I would think, comes from someone who suggests that we do not treat hypertensive patients unless they have symptoms.

With my own experience and great interest in hypertension for over thirty-five years, I would say that certainly if patients have a sustained hypertension, modest means should be taken to reduce it. The side-effects will largely be controlled by the physician through the suitable selection of the drugs and the suitable additive effect of several given together, if necessary, or one, if it will do the trick. Most patients who need treatment do better if they are getting two drugs, for instance, chlorothiazide, 250 mg. on alternate days with a quarter grain of phenobarbital, perhaps, twice a day. This may be all they need. They will get no side-effects from that except some increase in urination during the first two days. I feel rather strongly about this because it would look as though there is a suggestion that this disease be allowed to progress to a more dangerous state before we do anything about it. That is what I meant when I said that I considered this a form of "clinical appeasement to pathologic processes" which have a lethal possibility in some cases.

Nutritional and Metabolic Effects of Some Newer Steroids

I. Oxandrolone and Triamcinolone

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A STUDY WAS UNDERTAKEN *of the nutritional and metabolic effects of oxandrolone and triamcinolone. Relative numerical values were determined for the relationship between nitrogen balance and nitrogen intake, designated as the SPAI (steroid protein activity index). Oxandrolone, in doses of 10 to 30 mg. per day for periods of two weeks, exerted high protein anabolic activity in 11 adult males and females recovering from physically disabling episodes. In the same category of patients the administration of 12 to 24 mg. per day of triamcinolone decreased nitrogen retention in 6 out of 8 patients. The reduction in absorbed nitrogen was associated with a statistically significant fall in plasma lysine levels. Neither oxondrolone nor triamcinolone altered appreciably blood levels of sodium, potassium, chlorides, hemoglobin, and hematocrit.*

THE EVER-INCREASING USE of synthetic anabolic and catabolic steroids in a wide range of clinical circumstances has caused concern regarding claims as to the nutritional characteristics of these substances.[1] Assays of steroids for nutritional potency in experimental animals may yield results which are misleading when they are applied to man. Aside from true species differences, the principal source of error seems to arise from the parameters of activity employed. Determinations of the activity of anabolic agents in man are usually based on changes in nitrogen metabolism, while in rats these measurements are frequently based on changes in weight of the levator ani muscle.[2] Values for the catabolic effects of corticosteroids are obtained in terms of weight loss in mice, rats, or dogs, and these findings are seldom applicable to man.[3] These and other uncertainties of interpretation of animal assays make direct determinations of protein activity of steroids in man a prerequisite for their administration.

The consideration of studies employing synthetic or semisynthetic diets[4] or "metabolically stable" subjects[5,6] prompted us to undertake investigations under conditions of measured self-selected food intake with patients who might be expected to require anabolic steroids or corticosteroids. In the course of this work we were able to develop a system for integrating the nitrogen balance data into a scoring index for the metabolic activity of various steroids as part of a long-range structure-activity study. The results of human assays of oxandrolone (17-beta-hydroxy-17-alpha-methyl-2-oxa-5-alpha-androstan-3-one) and triamcinolone (9-alpha-fluoro-16-alpha-hydroxy prednisolone) in terms of the integrated activity index are reported here.

Procedures and methods

The subjects were, for the most part, adult males and females in the recovery phase of episodes resulting in para- or hemiplegia. The age category of the majority of patients was such that a high incidence of hypogonadism could be expected. With few exceptions, the activities of these patients were regulated carefully by a comprehensive program of progressive physical rehabilitation. Subjects were considered for metabolic studies only after they had become well adjusted to their environment and activities, usually within two or three weeks of admis-

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sion to this hospital. The gross nutritional status of all subjects was estimated from tables of the Metropolitan Life Insurance Company.[7] Deviations of the observed weight from desirable weight indicated by these tables are reported as per cent of standard weight (per cent S) in reference to the age-height-weight parameter.

Meals at this institution are prepared to provide an approximate calorie distribution of: protein, 15 per cent; carbohydrate, 50 per cent; and fat, 35 per cent. Tabular measurements of the food intake of patients showed an over-all average daily caloric intake of 2,115, with 75 Gm. of protein. On an average body weight basis, this represents 33 calories and 1.17 Gm. of protein per kilogram of body weight. This range is in good agreement with recommended dietary allowance values.[8] Although the regimen could be expected to provide adequate amounts of critical vitamins and minerals, a vitamin-mineral supplement of recognized potency was given daily on a prophylactic basis.

After the period of adjustment, studies were initiated consisting of successive precontrol and test periods of two weeks duration each. The test substances were given orally in the daily dosage ranges indicated by prior experience. During each week of study, twenty-four-hour urine collections and corresponding diet records were obtained for three or four consecutive days. Fasting blood samples were obtained on the third or fourth day of each week of study. When repeat or multiple studies were done on a patient, the balance periods were separated by a minimum of two weeks.

The daily nitrogen output was determined by the Kjeldahl analysis,[9] and creatinine was determined by the Jaffe reaction.[10] Blood derived from weekly collections was analyzed for hemoglobin,[10] hematocrit,[11] sodium and potassium,[12] chlorides,[13] thymol turbidity,[14] bilirubin,[15] plasma amino nitrogen,[16,17] plasma aminograms,[18,19] and serum glutamic oxalacetic transaminase activity (SGOT).[20]

The average nitrogen balance changes for each period were determined from summations of the daily nitrogen intake, as derived from the tables of Bowes and Church,[21] the total daily urinary nitrogen output determined by Kjeldahl's method, and 10 per cent of the urinary nitrogen as an estimate of fecal nitrogen. Frequent spot checks of the estimated dietary and fecal nitrogen by the Kjeldahl analysis have shown uniform agreement within plus or minus 5 per cent.

Principle of scoring method

An examination of the theory of nitrogen balance as presented by the English investigators, Martin and Robison,[22] and elaborated by Mitchell and Hamilton[23] and Allison[24] disclosed that the effect of steroids and other agents on protein metabolism could be compared more systematically in terms of nitrogen balance to nitrogen intake ratios than in terms of nitrogen output or balance in itself. Further consideration indicated that relative numerical values for this relationship, which we have designated as the SPAI (the steroid protein activity index), is obtained from the equation:

$$\text{SPAI} = \left[\frac{\text{N-bal}_s}{\text{I}} - \frac{\text{N-bal}_c}{\text{I}}\right] \times 100$$

N-bal_s = Average nitrogen balance in grams per day during steroid test periods.

N-bal_c = Average nitrogen balance in grams per day during control periods.

I = Nitrogen intake during steroid and control periods.

The ratios $\frac{\text{N-bal}_s}{\text{I}}$ and $\frac{\text{N-bal}_c}{\text{I}}$ indicate the fraction of dietary protein retained by the body. When the differences of these two ratios are multiplied by 100, the resulting values represent the percentage increase or decrease in nitrogen retention associated with the administration of a test steroid. This treatment of the data has the practical advantage of compensating for changes in the nitrogen intake which may occur in the course of the study. Other things being comparable, the administration of steroids that have anabolic activity should result in a nitrogen balance (N-bal_s) greater than that obtained in the control period (N-bal_c). The SPAI will then have a positive value, and its magnitude will be proportional to the metabolic activity of the test steroid. Conversely, the administration of corticosteroids may result in a nitrogen balance (N-bal_s) less than that obtained in the control period

(N-bal$_c$), and the SPAI will therefore have a proportionately negative value.

Results

The data obtained with oxandrolone in the course of the present investigation are shown in Table I. Since the minimum effective dosage of this steroid had not been definitely established at the outset of the study,[25] initial trials were done with daily dosages of 5 mg. and 10 mg. with patients 2 and 3, respectively. Clearly, the 10-mg. dose was far more effective than the 5-mg. dose. Subsequent assays with doses of 10, 20, and 30 mg. per day disclosed no significant differences in gross nitrogen retention (N-bal$_s$ − N-bal$_c$) and SPAI, so that 10 mg. of oxandrolone could be considered the minimum effective daily dose. It is of interest to note that the metabolic effect of the 20- or 30-mg. dose was not altered by the administration of the steroid in two 10-mg. tablets given at twelve-hour intervals or three 10-mg. tablets given at eight-hour intervals.

The results contained in Table I further indicate that the SPAI is not only a function of the anabolic potency, but also of the dose of the test steroid. Depending on the nutritional state of the patient, underdosage with a highly active anabolic steroid may result in a low or even a negative SPAI which would signify that the prevailing progressive malnutrition of the patient could not be offset by the limited dose of the steroid.

Previously reported results of balance studies with triamcinolone have been rather inconclusive. Hellman *et al.*[26] found little change in nitrogen or potassium balance, but Freyberg, Berntsen, and Hellman,[27] using larger doses of triamcinolone (24 mg. daily or more) with only a moderate protein intake, found that some patients had greater nitrogen loss than during control periods. Curd and Spurr,[25] reporting on 2 patients who received 42 mg. and 82 mg. of triamcinolone per day, respectively, stated that the first patient remained in positive nitrogen balance and the second patient was in negative balance to the extent of 3 Gm. per day. With 2 exceptions, the results of assays with triamcinolone (Table II) indicated that this substance exerts a significant catabolic ef-

TABLE I. Effects of oxandrolone* on the daily nitrogen retention of adults†

Patient	Age (Years)	Sex	Standard Weight (Per Cent)	Diagnosis	Dosage (Mg.)	N-bal$_s$** (Gm.)	I†† (Gm. Nitrogen)	$\frac{\text{N-bal}_s}{\text{I}}$	N-bal$_c$*** (Gm.)	I (Gm. Nitrogen)	$\frac{\text{N-bal}_c}{\text{I}}$	N-bal$_s$-N-bal$_c$ (Gm. Nitrogen)	SPAI
1	60	M	109	Hemiplegia	30	7.2	13.1	0.55	5.1	12.7	0.40	+2.1	+15
1	60	M	109	Hemiplegia	30	8.2	13.6	0.60	5.1	12.7	0.40	+3.1	+20
2	65	M	92	Hemiplegia	5	7.8	14.4	0.54	7.4	14.6	0.51	+0.4	+ 3
3	72	F	98	Hemiplegia	10	4.2	9.1	0.46	1.8	8.6	0.21	+2.4	+25
4	65	M	92	Hemiplegia	20	7.8	12.2	0.64	5.8	11.7	0.50	+2.0	+14
5	63	F	80	Bilateral involvement	30	10.8	15.8	0.68	7.0	15.2	0.49	+3.8	+19
6	70	M	105	Hemiplegia	30	11.5	14.2	0.81	8.9	14.8	0.60	+2.6	+21
7	64	F	. . .	Paraplegia	10	7.4	12.9	0.57	5.0	13.1	0.38	+2.4	+19
8	59	M	114	Multiple sclerosis	20	5.5	12.1	0.45	3.5	11.8	0.30	+2.0	+15
8	59	M	114	Multiple sclerosis	10	8.2	14.6	0.56	6.8	15.5	0.44	+1.4	+12
9	45	M	107	Reaction of hemingeal blastoma	30	10.5	13.6	0.77	9.1	13.6	0.67	+1.4	+10

* Supplied through the courtesy of Thomas Hayes, M.D., of the G. D. Searle Co.
† All results given as average of each study period.
** Average nitrogen balance during steroid test periods.
†† Nitrogen intake during steroid and control periods.
*** Average nitrogen balance during control periods.

TABLE II. Effects of triamcinolone* on the daily nitrogen retention of adults†

Patient	Age (Years)	Sex	Standard Weight (Per Cent)	Diagnosis	Dosage (Mg.)	N-bal$_s$** (Gm.)	I†† (Gm. Nitrogen)	$\frac{\text{N-bal}_s}{\text{I}}$	N-bal$_c$*** (Gm.)	I (Gm. Nitrogen)	$\frac{\text{N-bal}_c}{\text{I}}$	N-bal$_s$-N-bal$_c$ (Gm. Nitrogen)	SPAI
7	64	F	. . .	Paraplegia	12	5.7	13.6	0.42	5.0	13.2	0.38	+0.7	+ 4
8	59	M	114	Multiple sclerosis	12	5.4	16.1	0.34	9.1	16.8	0.54	−3.7	−20
8	59	M	114	Multiple sclerosis	24	6.8	18.0	0.38	9.1	16.8	0.54	−2.3	−16
10	21	M	106	Brain injury (paraparesis)	12	0.8	15.2	0.05	4.6	15.6	0.29	−3.8	−24
10	21	M	106	Brain injury (paraparesis)	24	1.4	15.8	0.09	4.6	15.6	0.29	−3.2	−20
11	80	M	87	Fracture hip (nailed)	12	2.1	15.1	0.14	6.8	14.9	0.46	−4.7	−32
12	65	M	99	Cerebrovascular accident (hemiplegia)	12	4.0	14.3	0.28	8.8	13.7	0.64	−4.8	−36
13	21	M	78	Traumatic quadriplegia	12	1.2	9.8	0.12	0.3	9.5	0.03	+0.09	+ 9

* Kindly supplied to us as Aristocort by Virgil Place, M.D., of the Lederle Laboratories.
† All results given as average of each study period.
**Average nitrogen balance during steroid test periods.
†† Nitrogen intake during steroid and control periods.
*** Average nitrogen balance during control periods.

fect at both the 12 and the 24 mg. per day levels of administration in six of the eight trials. Attention is called to the fact that reduction in nitrogen retention was experienced under conditions of rather high protein intake.

Observations on some clinically important metabolites are recorded in Table III. It would appear from these measurements that the administration of these two steroids for the periods of assay was not associated with significant hematologic or hepatic effects or an appreciable alteration in sodium, potassium, or chloride levels. The serum glutamic oxalacetic transaminase activity was not altered measurably. Changes in the total urinary nitrogen-creatinine ratio followed the expected pattern, namely, a decrease, albeit small, with oxandrolone, and an increase, also small, with triamcinolone. Unfortunately, the magnitude of these changes was too slight to permit an assessment of the metabolic effects of steroids, as proposed by West.[29]

As in our previous experiences with prednisone and prednisolone,[30] chromatographic plasma amino acid analysis disclosed that the decrease in nitrogen retention which occurred with triamcinolone administration was associated with a decrease in the plasma lysine level (Fig. 1). These findings are both well in excess of the 1 per cent level of significance. The small increases in plasma methionine and threonine, although statistically borderline in nature, were similar in magnitude and frequency to those observed in the previous corticosteroid study.

Comment

As mentioned earlier, the principal advantage of the proposed scoring method lies in the fact that the expression of nitrogen balance data in terms of SPAI compensates for the variations in protein intake which may be incurred in the course of the tests. Furthermore, by similar treatment of available data, the relative metabolic activity of other steroids can be ascertained readily. Such a comparison of results reported previously by some of us is shown in Table IV. It will be seen that the relative protein anabolic effects of the newer steroids can be determined easily by assigning a value of

TABLE III. Average effects of steroids on some constituents of the blood and urine

Constituent	Oxandrolone Control (a)	Oxandrolone Test (b)	Oxandrolone (b − a)	Triamcinolone (8*) Control (a)	Triamcinolone (8*) Test (b)	Triamcinolone (8*) (b − a)
Blood						
Hemoglobin (Gm. per 100 ml.)	14.2	14.3	+0.1	12.9	13.8	+0.9
Hematocrit (mm.)	40.1	40.8	+0.7	38.4	41.9	+3.5
Sodium (mEq. per liter)	140.0	139.0	−1.0	146.0	141.0	−5.0
Potassium (mEq. per liter)	4.4	4.4	0	4.7	4.5	−0.2
Chlorides (mEq. per liter)	91.0	91.0	0	91.0	89.0	−2.0
Thymol turbidity (units)	1.9	2.0	+0.1	1.4	1.6	+0.2
Bilirubin (mg. per 100 ml.)	0.5	0.5	0	0.5	0.4	−0.1
Urine						
Total (nitrogen per creatinine)	10.3	8.6	−1.7	10.5	13.3	+2.8

* Indicates number of assays.

unity to the SPAI of testosterone propionate.

As changes from the structure of the naturally occurring steroids become more extensive, there is apparently an increasing disparity between the effects observed in animals and in man.[31] For example, rat assays have shown that the anabolic activity of norethandrolone to testosterone propionate is 1, according to Barnes *et al.*[32] and Saunders and Doggett[33] and 3.5 according to Sala and Baldratti.[34] In our human studies the ratio of 1.4 was found for norethandrolone (Table IV). By means of nitrogen balance experiments, oxandrolone was reported by Saunders and Lennon[25] to have a nitrogen-retaining activity comparable to norethandrolone in castrated rats. On the basis of these animal findings, the suggested dosage for initial clinical trials was 30 mg. per day. The present studies disclose that in man a dose of 10 mg. to 20 mg. per day of oxandrolone gives maximal nitrogen retention. This retention is approximately twice as great as that found for 30 mg. per day of norethandrolone (Table IV).

The present observations in 8 patients suggest that triamcinolone may be less protein catabolic than either prednisone or prednisolone. However, Williams,[38] employing comparable dosages in 3 patients, could find no difference in the protein catabolic effect of triamcinolone or prednisolone. In this connection, attention is called to the fact that the proposed scoring method simplifies the choice and dose of an anabolic steroid which may be considered for the antidoting of the protein catabolic activity of a given corticosteroid. Thus, 10 to 20 mg. per day of oxandrolone (SPAI = +17) could theoretically be expected to offset the catabolic effects of 12 to 24 mg. per day of triamcinolone, SPAI = −17. The data on plasma amino acid levels (Fig. 1) suggest that the protein catabolic effect of triamcinolone may be mitigated also by supplements of lysine.[39] The evaluations of the possible anticatabolic efficacy of these two modalities, when administered singly or in combination with triamcinolone, are in progress.

Summary

Nitrogen balance studies disclosed that the administration of a new synthetic steroid, oxandrolone, at doses of 10 to 30 mg. per day for periods of two weeks, exerted high protein anabolic activity in 11 assays with adult males and females recovering from physically disabling episodes. By the same procedures and in the same category of patients, the administration of 12 to 24 mg. per day of triamcinolone was found to decrease nitrogen retention in six out of eight assays. The observed reduction in absorbed nitrogen was associated with a

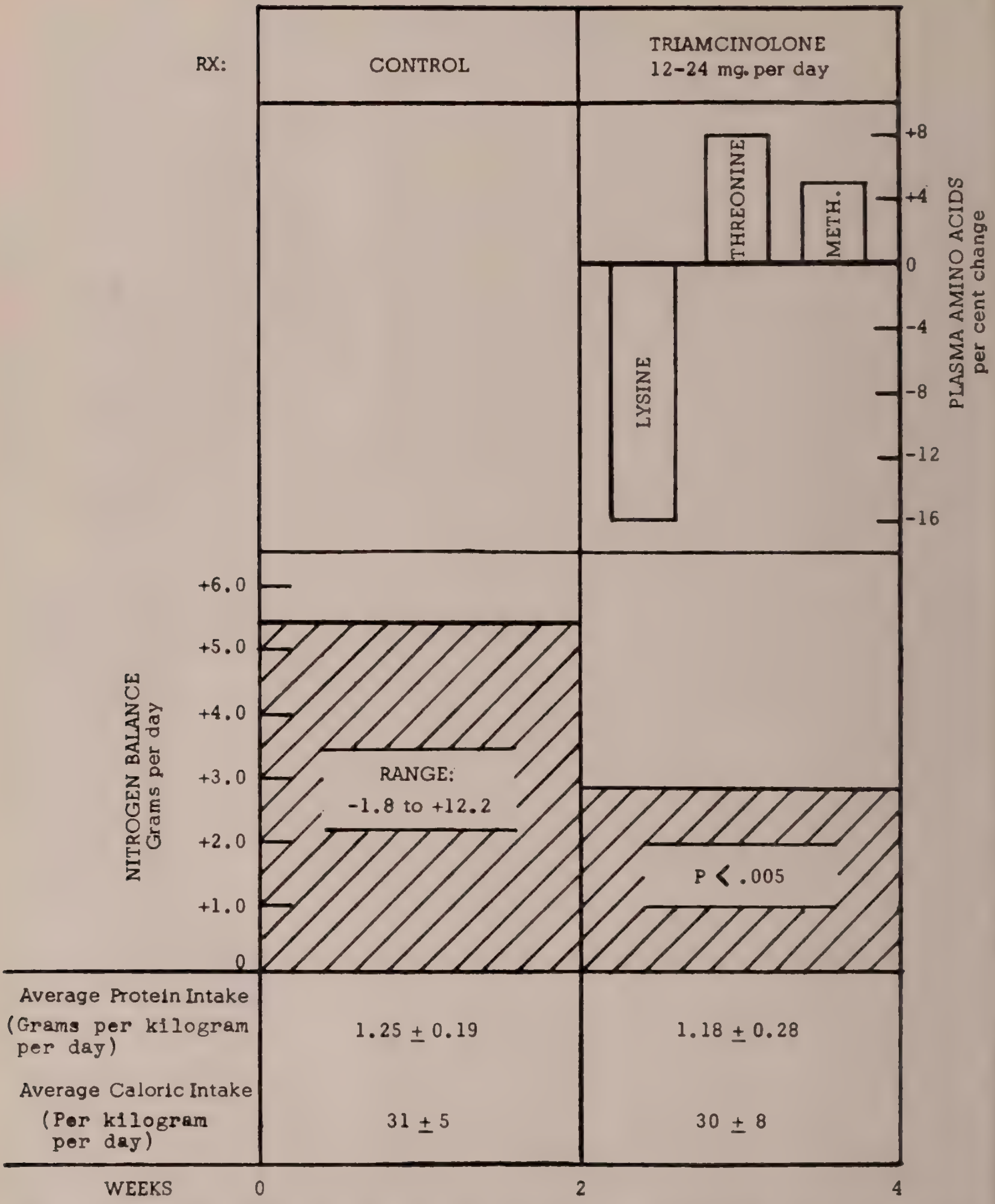

Figure 1. Chart of eight assays with male and female patients, from twenty-one to eighty years of age, recovering from physically disabling episodes. Statistical analyses are given for the effects of triamcinolone on nitrogen-balance and free lysine, threonine, and methionine of plasma.

statistically significant fall in the plasma lysine levels. The administration of both oxandrolone and triamcinolone did not alter appreciably the blood levels of sodium, potassium, chlorides, SGOT, hemoglobin, and hematocrit.

The integration of nitrogen balance data obtained in this and other studies in a scoring method for the protein activity of steroids (SPAI) has been described, and the resulting values have been recorded. It is felt that this expression of the findings per-

TABLE IV. Comparison of protein activity index of some steroids in adults

Steroid	Number of Assays	Dosage Range (Mg. Per Day)	SPAI Range	SPAI Average	SPAI Relative	References
Testosterone propionate	12	10 to 25	0 to +16	+6	1.0	30
19-nortestosterone	14	25 to 75	+4 to +25	+9	1.5	31
Norethandrolone	10	30 to 60	+3 to +28	+8	1.4	32, 33
Oxandrolone	10	10 to 30	+10 to +25	+17	2.8	Present
Prednisone	4	30	−23 to −49	−38	. . .	35, 36
Prednisolone	7	30	−11 to −48	−22	. . .	37, 38
Triamcinolone	8	12 to 24	+4 to −36	−17	. . .	Present

mits a more objective evaluation and comparison of the gross effects of steroids on protein nutrition.

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Alcoholism: Its Cause and Prevention

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SINCE THE PATHOLOGIC consumption of alcoholic beverages is a grave and widespread public health problem, an obligation rests with those concerned with the prevention and treatment of alcoholism to examine the physical and psychologic involvements of the disease. It is important now to emphasize the great need for complete cooperation by the medical profession in the early detection and treatment of alcoholism starting, perhaps, at the "social-drinking" level when this practice among many patients shows the first signs of becoming uncontrolled.

To appreciate how widespread this associated social-medical-psychologic problem has become, we offer these facts and statistics[1,2]:

Of the 70 million drinkers of alcohol in the United States, there are now about 5 million confirmed alcoholic persons—in Massachusetts, approximately 200 thousand. The Federal Bureau of Investigation in its *Uniform Crime Reports* states that drunkenness is the cause of more than 40 per cent of all arrests. In Massachusetts, exclusive of minor traffic violations, more arrests and confinements to jail are made for drunkenness than for all other causes combined.

Studies by Massachusetts tuberculosis sanatoriums and mental hospitals show that the diagnosis of alcoholism, usually in conjunction with other diagnoses, is made in at least 30 per cent of all admissions. The records of chronic disease institutions, public welfare recipients, delinquents and their parents, divorcees, sex offenders, and similar groups disclose higher percentages of alcoholic individuals than should be statistically expected.

American consumers annually spend about 5 per cent of their total budget for alcoholic beverages, an expenditure exceeded only by food, clothing, and housing, and about equal to that for public education.[1] Forty-nine of the 50 states permit the sale and consumption of alcoholic beverages within stated limits. Even the one remaining "dry" state, Mississippi, allows the sale of 3.2 beer and taxes beverages imported into the state.

The vast majority of the 100 million church members in the United States are affiliated with religious organizations which give moral sanction to the moderate use of alcohol.

Why people drink alcohol

Why this great popularity of alcohol? Why do many drink to drunkenness? Worse still, why have 5 million Americans become enslaved to the disease of alcoholism? We visualize alcohol as an instrument used by a number of people with certain types of personalities and in certain social settings for a variety of purposes:

AS A MEDICINE FOR DEPRESSION. Many individuals who suffer a reactive depression or suffer from a depression arising endogenously may partake of alcohol to lift their spirits. For many alcohol is able to wash away momentarily the ugliness evoking depression. The image of the rejected or disappointed individual heading for a bar "to drown his sorrows" is too common to need elaboration. Only one further point is essential, emphasizing that alcohol is a pharmacologic depressant: Some people when they use alcohol as an antidepressant may respond with an intensification of the depression and more serious symptoms

AS A MEANS OF BLURRING PERCEPTUAL INTAKE WHEN THREATENED. The employment of alcohol in perceptual blurring might occur as follows: An individual is aroused homosexually. Since this may be unconsciously desired but consciously tabooed, drinking will permit the flow of soberly repressed instincts. Thereby with drink the individual can engage in forbidden sexual activity and not feel responsible for his actions.

AS AN INSTRUMENT FITTING INTO A SYSTEM OF DEFENSES. Alcohol can be fitted into a system of defenses to make "acting out" possible. With alcohol the latent hostile and aggressive individual may behave this way, being utterly unaware of his reactions under the influence of alcohol. A clinical observation is that persons in this category are incredulous of their contrary behavior with alcohol, whereas the individual whose perception is blurred is aware of his actions but does not blame himself.

AS AN INSTRUMENT TO BREAK DOWN DEFENSES. The person who uses alcohol as an instrument to break down defenses is known to others besides psychiatrists. This is the individual who needs to take drink to perform. In other words, anxiety and tension arousal about writing, speaking before an audience, and so forth is handled by taking a drink before one can perform.

AS AN EMOTIONAL NUTRIENT SOCIALLY. When used in a healthy way, alcohol fulfills an important function in its ceremonial and ritualistic use. When alcohol is so used, as in the preliterate societies and in the Jewish culture, a protection is built up against pathologic usage. However, by using alcohol as an emotional nutrient in an unhealthy way an individual can get care from an otherwise rejecting mate. The mate, when the alcoholic individual is sober, could not and would not tolerate the dependent situation and demands.

AS AN EASE IN SOCIALIZATION. As an ease in socialization alcohol fulfills its greatest role. The cocktail party, that lubricant of social intercourse, would grind to a disastrous halt without alcohol as would the conversation and ease of superficial relationships.

AS A MEANS OF OBTAINING A STATE OF BLISS. People who use alcohol to obtain a state of bliss may seek the hallucinatory effect or oblivion. They use alcohol as they might use morphine. The intensity of the need for oblivion is illustrated by a patient in our experience who, like many an alcoholic individual, was a model husband when sober, but was hostile and abusive when intoxicated. On one occasion, when sober, he showed his wife Skid Row. She was shocked by the drunken derelicts lying in every doorway. He however said to her: "But what's more shocking still is that I envy them their few moments of pleasure." There is nothing that illustrates better the oblivion persons suffering from alcoholism seek endlessly, only to lose it again and again.

AS AN INSTRUMENT FOR ANOTHER'S EMOTIONAL NEEDS. We and others have seen some alcoholic patients whose mates have on the surface argued against their drinking. However, when the husband makes an attempt to halt drinking, the wife's response frequently is in opposition. If sobriety is achieved, the wife becomes more and more disturbed. What in effect has been transpiring is that the husband's drinking, socially unacceptable and overt, was a defense and coverup for the wife's emotional difficulties. If the husband is helped, the problems of the wife are exposed. The drinking of an individual under these circumstances is in part to satisfy the emotional needs of another.

OTHER REASONS. Beyond the reasons and categories noted in the preceding paragraphs, superficial reasons for drinking may be: to keep warm, to cool off, to pep up, to relax, to enjoy the taste, to enjoy the smell, or as a medicinal to fight a cold or increase the appetite. Of course, in some cultures alcohol, especially wine, is used as a liquid in relation to eating.

COMMENT. Based on our clinical observations,[3] our definition of alcoholism is: a chronic behavioral disorder manifested by undue preoccupation with alcohol to the detriment of physical and mental health; a loss of control when drinking has begun, although it may not be carried to the point of intoxication; and a self-destructive attitude in dealing with relationships and life situations. Alcoholism, we believe, is the result of disturbance and deprivation in early infantile experience and the related alterations in basic physiochemical responsiveness; the identification by the alcoholic with significant figures who deal with life problems through the excessive use of alcohol; and a sociocultural milieu which causes ambivalence, conflict, and guilt in the use of alcohol.

It is generally held that alcoholism is primarily a disease of males. We do not agree. The true ratio of males and females suffering from alcoholism is unknown, although the general figure quoted in the medical literature is $5^1/_2$ to 1. Our statistics do not indicate any such vast difference in ratio. Our clinic data show the ratio to be more nearly 4 to 1. As knowledge is disseminated that alcoholism is a disease and therefore is treatable, more and more women are seeking medical assistance. The impression about the number of males versus females suffering from alcoholism may derive from the fact that the male cannot hide his alcoholism as easily as the female. The male's dependence on alcohol resulting in absence from work can be noted quickly. A female, however, in the protected confines of her home can escape social and even intrafamily detection for long periods of time, thereby hiding her disease much longer. Our clinical observation is that the tendency of women to use alcohol more freely than formerly in their social endeavors, coupled with the changing feminine role in society, is resulting in a heightened incidence of alcoholic women.

Many people of both sexes start to drink when they are away from home for protracted periods of time. The college years are a common "trial" period. Although actual figures are unavailable, experience suggests that about 3 to 4 per cent of students who attempt protracted social drinking at college become addicted to alcohol.

A parallel phenomenon exists in our experience, among elderly people. Many individuals will increase their consumption of alcohol following retirement. In time, most revert to their preretirement pattern of controlled drinking. A small percentage, however, become addicted to alcohol at this advanced age.

In our experience, as well as in the experience of others,[4] many alcoholic individuals have a history revealing a significant family figure who depended on alcohol in an uncontrolled manner. Since alcoholism is in part an environmentally, culturally, and emotionally determined condition arising from many complex factors, our experience shows that children of alcoholic parents are in an especially vulnerable position. We have observed a high incidence of alcoholism among children of alcoholic parents. We also have noted that 42 per cent of females and 27 per cent of males suffering from alcoholism had one or more alcoholic parents.

Cultural factors in drinking behavior

Bearing epidemiologic factors in mind, we can gain further understanding of drinking behavior by contrasting preliterate (primitive) practices with contemporary cultural reactions.[5]

The group nature of drinking behavior which is ubiquitous among preliterates seems to be a protecting device, since alcoholism is seldom found among them. The preliterate individual drinks frequently and heavily but seldom uses alcohol as a means of meeting life's problems. Rather he uses it for conviviality and to enhance social relations. Drinking fills a social vacuum. Also, the absence of the Puritan ethic of conscious control of will does not cause ambivalence or conflict with drinking or drunkenness.

Although by our standards the drinking of preliterates may be extreme, possibly pathologic, their drinking is not to the detriment of internal and external needs, and hence, by our definition, they are not alcoholic. The inhabitants of these preliterate societies drink to get drunk. Regardless of the low alcoholic content of most of their beverages, they seek and achieve drunkenness. Our biochemical colleagues would question the possibility of these folk achieving the blood level of 0.15 for drunkenness. A blood level of 0.15 or not, these people get drunk. Here one may differentiate between social-psychologic and pharmacologic-physiologic intoxication. Their intoxication is social-psychologic.

Our look at these primitive people reveals possible suggestions for the socially healthful use of alcohol and points at possible ingredients which produce the alcoholic individual.

In literate contemporary societies, those cultures with a low incidence of alcoholism show drinking attitudes similar to those of preliterate societies, that is, group drinking, no ambivalence, the ritualistic use of alcohol, and the rejection of the use of alcohol to meet life's problems. On the other hand, cultures with a high incidence of alcoholism have drinking practices in opposition to the healthy attitudes of the preliterates, that is, guilt and ambivalence, solitary drinking, no ritualistic involvement with alcohol, and the accepted use of alcohol to meet life's problems.

The comparison of preliterate peoples with American suburbanites is interesting and revealing but suggests that caution must be exercised in extrapolating practices from one group to another. The suburbanite's protection is less well structured and less intense than that of the preliterate individual. Also, the social controls and pressure brought upon the deviant American suburbanite are different from those brought upon the deviant preliterate individual. Last, the definitions, sets, controls, and so forth, established by preliterate societies are more easily learned and managed than those of the modern American whose social values derive from amorphous and at times distant influences. In their resulting indistinction, the American's social values are more conducive to anxiety than to a sense of security.

The host: man

Clearly the combination of the agent (alcohol) and the host (man) does not necessarily lead to alcoholism. But some men and women, many in certain groups, do become addicted to alcohol.

What about the host, man?

One can make a generalization about man as a machine: It applies to men physiologically, biochemically, socially, and, we believe, psychically. The generalization is this: Man strives toward a state of equilibrium. Bernard[4] recognized this striving in his studies of the vasomotor system, but it was Cannon[5] who evolved the concept of homeostatic mechanisms, whereby the physiologic mechanism strives to correct imbalance by appropriate safety measures and recreates the level of equilibrium it formerly enjoyed. Biochemical malfunction has multiple systems which are corrective in the direction of equilibrium, and certainly psychologic concepts of mental mechanisms, including Freud's formulation of id, ego, and superego, are seen as maintaining the psychic base line of the individual. Psychiatric symptoms are generally viewed as restitutive phenomena; the symptoms are an attempt to achieve equilibrium. These phenomena apply also to man as a social being.

All of man's internal and external activity from conception to death is to maintain effectively environments within his base line of equilibrium or organization. Situations or emotions which result in inexplicable and frightening sensations threaten the tendency toward the desired equilibrium. Hence, just as physiologic and biochemical alarm and corrective systems operate, so does the psyche attempt to warn and alleviate. Mass communication and the destruction of protective natural barriers have unleashed a flood of new anxieties and tensions on the world of today. Cultural boundaries which were safe and directive no longer exist. The individual caught between two cultures cannot stay there. He must either withdraw into himself or join the greater culture around him. The action of withdrawing or the action of joining can be visualized as a striving toward equilibrium.

As life becomes more complex and more troubled, as new sources of anxiety are introduced before old sources are eliminated, the individual in most cultures of today must seek for newer and additional methods to maintain equilibrium. This attempt at maintaining cultural and psychologic equilibrium has been alluded to as "coping with life."

What are some of the newer and additional means of coping with psychologic disequilibrium? There is psychologic treatment: psychoanalysis or psychotherapy. By these technics an individual attempts to learn and correct behavioral abnormalities which have prevented his managing the new influx of stress and strain. He seeks through therapy a new formula of adaptive behavior for the present and uncertain future. Others use tranquilizers and drugs. Many others become involved in organizational activity or create a background of distraction through radio or television to prevent more threatening stimuli from coming into awareness. Some are freed from stress by the onset of physical illness, while others develop neurotic symptoms or psychotic mechanisms. Some coping mechanisms are subtle; some are obvious; some completely take over the individual and become a way of life. One such response is alcoholism. The alcoholic individual in trying to maintain his state of equilibrium becomes disastrously involved in his semisuicidal attachment to his coping method, alcoholism. This results in gradual and eventual complete rejection and social ostracism.

Etiology

We reject single causal explanations of alcoholism. Instead we consider the etiology of alcoholism from a dynamic, interrelated perspective. This includes the consideration of prenatal influences, personality development, and cultural influences as they are reflected in the individual's personality and attitude toward alcohol.

PRENATAL AND BIRTH FACTORS. Montagu[6] states that the "constitution is the sum total of the structural, functional, and psychological characters of the organism." The genetic potentialities as in later development are influenced by internal and external factors of environment. Therefore, we consider consitution as a dynamic process rather than a fixed entity. Although the genetic potentialities may be limited, the environmental influence will act on them in varying ways. Genes therefore may be influenced to develop differently their potentialities with different end results as a consequence of the environmental influence in which they operate. Just as the infant, the child, and the adult can be affected by environmental factors to go in certain directions within limits, so can the developing fetus be environmentally affected. Therefore, a disturbed prenatal period, (be it physical, chemical, or emotional), can provide the personality bedrock on which the psychosocial symptom of alcoholism develops.

At birth the newborn infant is faced with a new set of stimuli. These stimuli, involving internal and external needs of uncountable number, will have an effect on personality development. Not only are internal and external stimuli being received that will affect the personality and emotions of the newborn child, but also a social change takes place. Guarded by the bastion of uterine tissue, the fetus does not come into direct contact with another being. At birth, with the dilation of the cervix, social interaction with other people begins. Direct contact with all sorts of people and their social expectations becomes manifest.

Based on our clinical observations, we draw two major developmental strands together. On the psychologic side it is this: that there is a prenatal bedrock of personality influences which serves as the foundation on which an infinitesimal number of stimuli are brought to bear. Also, that with birth, the human being for the first time becomes directly affected by social and cultural influences.

PSYCHOLOGIC FACTORS. Now let us focus and elaborate on the psychologic "strand" of the future alcoholic individual. As we have suggested previously, the personality problems we will describe for the alcoholic subject are not exclusive to alcoholism. Lying in his crib, even to the expert observer, the infant later to become addicted to alcohol will look no different from other infants. If his prenatal period has been a "difficult" one (physically, emotionally, or both), he may be an irritable, tense, difficult baby. He will not be any different, however, from other infants who may become future psychiatric patients in any category, nor any different from reasonably, stable, functioning adults. We reject the concept that alcoholic individuals are born, not made.

One facet of the psychologic strand is that it is inseparable from the physiologic and biochemical strands. It is intertwined intimately with physiologic and biochemical responses, which are as much an individual reaction as emotional. For example, one of our patients had anxiety about not being fed, although he had ample money and food, because as a child his family was impoverished and he frequently went without meals. Just as he possesses psychologic patterns of response to this early anxiety, his physiologic and biochemical responses are directed toward the early patterns of not being fed. They are tied together as a Gordian knot, and no legal or surgical separation is possible. Emotional life cannot be separated from the physical, just as physical responses cannot be divorced from the emotional.

Physiologic factors. A second factor to take into account is that patterns of emotional and physiologic response become fixed, and this fixation varies from individual to individual. Various levels of patterning of response will be established at different periods in development. If we view the newborn infant as relatively free of patterns of response and literally a wide-open receptacle for direction, it is natural to see that input will have the greatest significance at the earliest stages of development. When patterns have begun to evolve, the potentiality for input significance is diminished.

A third observation is that patterns of response follow "the path of least resistance." When confronting a choice between the familiar and the less familiar pathway, most will choose the familiar. It is safe and less threatening. Consequently, once a developing human being has chosen a pathway a number of times, it has become familiar; the tendency to follow it in the future is enhanced.

When we move from psychologic development in general to look specifically at the development of the alcoholic individual, we see that certain common psychologic generalities occur, although specific events will vary with the individual. What are these generalities and what do they mean to the alcoholic person?

On the basis of long-term observation of alcoholic subjects in psychotherapy, we have classified the psychologic strand of the alcoholic individual as a perversion of oral behavior.[7] By this we mean that during the course of psychosexual development, the alcoholic individual was emotionally traumatized during the earliest stage—the oral. As a consequence of this trauma, fixation occurred when the individual's means of achieving security and release of tension was by means of stimulation of the oral cavity. This orality may have been heightened further by prenatal or constitutional factors. Because in alcoholism instinctual oral wishes are gratified directly and without anxiety, we recognize this pattern of gratification as a perversion rather than a neurotic mechanism, which is a disguised, anxiety-ridden converse of a perversion.

During the oral stage of development, the infant is seemingly omnipotent. Whatever he wants, whenever he desires, fulfillment must occur. Through his mouth he derives sustenance, expresses destructiveness and love, and exerts his power. Giving figures (mothers, mother surrogates) are not perceived as separate and having separate needs of their own. Rather, all people are perceived as existing only to serve.

An alcoholic individual is not too different. Relations do not evolve which are derived from mutual respect—give and take and recognition of the individuality of the other. The attitude of the alcoholic person is that of infantile demand. The orality component of alcoholism manifests itself in every relation. Not only must alcohol be consumed and consumed but also all people with whom he has relations must be symbolically devoured by the alcoholic individual. Regardless of how much one attempts to satiate the needs of an oral personality, there is bound to be failure. For satiation of the omnipotent, all-consuming, devouring oral need is impossible. Hence the alcoholic individual fails, and those attempting to "feed" him fail. For example, the wife who has tried to do everything to please her husband and has been unsuccessful decides to let him have his alcohol. She even goes out and buys it for him, thinking that this may improve their relations. He responds by making new demands which assure failure of this relationship.

Can we then indict an alcoholic personality? Immediately the answer is no. Although there are many common personality traits, there is no single personality configuration common to all pathologic drinkers. We believe any personality type may use alcohol pathologically to alleviate anxiety, to make instinctual impulses acceptable, to strengthen defense measures, and to provide narcosis against painful reality. We believe the level of psychosexual development achieved prior to the onset of pathologic behavior will determine the severity of the alcoholism and the severity of the regression. In other words, the patient who has been healthy for much of his life and has formerly achieved positive goals will be easier to treat than the patient who has been emotionally disturbed most of his life and who has many life failures in his history.

Alcoholic individuals, while perhaps suffering variable personality and highly individualized conflicts, have common threads of difficulty. The pre-alcoholic subject has been rendered vulnerable to alcohol by security-threatening experiences of emotional deprivation. As we use the word deprivation, it means an absence of a stable emotional relationship with a mother figure. This deprivation may manifest itself in many ways, such as an overtly rejecting mother, a withdrawn mother, a dead mother, a frequently intoxicated mother, an absent mother, an overprotective mother, and so forth. Although we are cautious about extrapolating from animal behavior to human reaction we nevertheless are impressed with the work of Seitz[8] who reported that kittens suffering early deprivation of their mothers showed low tolerance to frustration, rage, emotional lability, poor adaption to stress situations, and diminished learning capacity. These responses are not too unlike the reactions of alcoholic individuals as we have seen them.

How does alcohol fill the needs of the alcoholic subject? Alcohol for the alcoholic individual is a substance dispelling tension and depression. It alleviates a sense of aloneness; it gives readily available, instantaneous pleasure; it permits mastery and simultaneous expression of hostile feelings; it provides a built-in guarantee of suffering, punishment and alleviation of guilt, and feeds back sufficient stress for continued drinking. The role fulfilled by alcohol in the personality of the alcohol addict goes beyond just tension release. Alcohol permits the alcoholic individual to deny his underlying depression. This depression resulting from deprivation of an emotional and physical relationship early in life is most severe. This severity results because the cause of depression occurs at the very foundation of personality development and colors forever further emotional influence. The fact that alcohol has a special role and fulfills a special need for the alcoholic individual we believe precludes the possibility that all individuals can become alcoholic.

Social factors. It is not merely the beverage itself but, as noted earlier, the constellation of attitudes surrounding it that are important. Playing an important role in the etiology of alcoholism is the element of ambivalence. Ambivalence may be defined as contrary or opposite feelings toward a subject existing concurrently. Underlying drinking attitudes in our culture is that of the Puritan ethic which condemned as evil all things bringing pleasure to the senses. The Puritan belief held that drinking led to sexual misbehavior. The essence of the ascetic Puritan pattern is hostility toward the spontaneous, impulsive enjoyment of life and what it has to offer. Although there has been a decline of religious ardor affiliated with Puritanism, the personality type based on these values has become an American ideal—an end in itself. Thus, the ideal Puritanic personality, basing his inhibition on distrust of impulse and deliberately controlling all emotional life, finds all use of alcohol, even moderate, as potentially antithetic to Puritan values.

In the present cultural climate of America, where diverse cultural groups are being rapidly assimilated and acculturated, the Puritan ethic, by remaining the ego ideal, brings into conflict the acquired ideal with the values of the previous culture. Hence, this rise in conflict and ambivalence with a greater potential for predisposing attitudes may lead to the pathologic use of alcohol. Of course, with destruction of natural barriers and the ease of communication of ideas and attitudes, ambivalent attitudes spring forth in many societies besides our own.

An additional factor in modern American drinking practices which encourages the pathologic use of alcohol is first of all the attempt to "tightrope" drink, that is, to drink to reach a delicate point midway between sobriety and drunkenness. This attempt is often doomed to failure because the multiple factors determining an individual's response to alcohol vary. Thus, dissatisfaction and partial failure is common in American drinking. Another factor is that the group protection of preliterate societies is lacking in the American small, mobile family nucleus. The development and emphasis on utilitarian drinking (drinking for purposes of social medication) is yet another unwholesome contemporary attitude.

Other sociocultural attitudes and practices contributory to alcoholism are clandestine drinking and disapproved drinking. For example, by focusing negatively on alcohol and by developing extreme negative role models, young Mormon people, when rebelling, are likely to use alcohol in an uncontrolled manner.

Therefore, we feel, as does Snyder,[9] that "... the problem of alcohol ... cannot be understood apart from a consideration of the broader sociocultural matrix in which drinking occurs." Drinking itself cannot be the exclusive cause of alcoholism, as demonstrated by the orthodox Jews and the Italians. Virtually every member of these groups drinks with negligible alcoholism.

Alcohol must be available. Associated with the physical availability of alcohol as a beverage, the pharmacologic effects of alcohol are important. As a pharmacologic agent, alcohol is useful as a central nervous system depressant. Tension, fear, anxiety, and conflict can be alleviated temporarily by the consumption of alcohol.

In summary, to cause alcoholism—and perhaps any disease or condition—there must exist multifaceted sociocultural phenomena operating significantly in conjunction with psychophysical processes. Therefore, what we propose is an etiologic framework not especially weighted toward any discipline.

We view alcoholism as the final trunk line evolving out of many feeder lines of influence.

Primary prevention

How does one prevent alcoholism? The traditional view in a public health perusal of prevention involves the agent-host-environment continuum. Although the host and environmental factors appear completely interwoven in the etiology of alcoholism, the agent, alcohol, stands out clearly.

Can we, therefore, manipulate the supply and availability of the agent in a way that will prevent alcoholism from occurring? There are some possible procedures: (1) Forbid the sale and/or use of alcohol by legal or social measures; (2) legally limit the sale and/or use to certain people at certain times and in certain places; and (3) alter the chemical composition of alcohol so that so-called "habit-forming properties" or toxic properties are removed or reduced.

FORBIDDING SALE. Forbidding the sale of alcohol is a well-known technic familiar to most adult observers in the United States, since the Prohibition Amendment (Eighteenth) to the United States Constitution is still recent history. The theory of prohibition sounds reasonable. Only the reality of manufacture and distribution dooms it to failure. Alcohol, in one form or another, can easily be produced by any farmer, by any high school chemistry student, or by any informed citizen. It is unrealistic to consider that by legislative fiat (the magic wand supposedly removing all problems) alcohol can be removed from use by society.

Most men (and increasingly women) have been and are alcohol users, and there is no valid reason to expect that this situation will change. No invention which meets social needs and which is a part of man's culture will be discarded unless more meaningful and clearly superior alternatives are offered.

LEGAL LIMITATIONS. Does the failure of prohibition then preclude legal measures? The answer is no. There are some legal measures which might exercise some control on drinking and subsequently affect drinking attitudes and practices. They include, among other suggestions, very high taxes on all alcoholic beverages.

The major question is whether or not governmental action affects the amount consumed by alcoholic individuals or social drinkers. Since many natural social experiments have remained largely removed from scientific inquiry, we have no definite answer. We are of the impression that such manipulation is of doubtful value in reducing alcoholism rates. Legal controls are more likely to affect the social drinker than the person addicted to alcohol. We feel, however, that measures such as the tax measure suggested previously are more subtle and less challenging to drinkers, both social and pathologic, than measures for prohibition. Hence, opportunities for developing unhealthy attitudes are reduced. Certainly indirect legal controls will not do the harm of outright prohibition and very likely could help to deter some of the nonalcoholic excesses occasionally associated even with social drinking.

CHEMICAL ALTERATION. Another possible method of manipulating the agent, alcohol, would be an attempt to alter the chemical composition so that the so-called "habit-forming" properties are removed. These habit-forming properties are substances acting as depressants on the central nervous system. Such depressants reduce inhibitions, and the entire release pattern follows. The response of inhibitory release, to varying degrees, is the goal of both social and pathologic drinkers. Although conceivably the removal of tension-reducing properties could be accomplished, we are certain this maneuver would be doomed to failure. Man would surely return again to the manufacturing of his own supply of the real beverage. It is this very depressant quality which accounts for the endless popularity of alcohol.

Although we may consider impractical the removal of alcohol's potential for tension release, it is practical, however, to manipulate chemically the other components of beverage alcohol. These components, called congeners, are those ingredients, other than ethyl alcohol and water, in beverage alcohol. We do not suggest that such chemical manipulation will reduce the rate of alcoholism or prevent alcoholism. Rather, we feel, that there exist positive gains to such manipulation which may alter the features of our drinking behavior.

Congeners are made up of volatile and nonvolatile components. The volatile part derives primarily from the grain and secondarily from the fermentation and aging process. The nonvolatile fraction consists of many materials, notably tannins which are drawn from the wood during the process of aging. Essentially the longer a whiskey is barreled, the higher will be its percentage of congeners. Further the blended whiskeys contain significantly fewer total congeners by weight than straight or bonded whiskeys or cognac. Therefore, cognac, bonded liquor, and aged whiskey—the more costly and more sought-after beverages—are higher in congener content than the cheaper, younger, blended whiskeys.

The total number of congeners is estimated[10] to be in the several hundreds. Snell[11] isolated seven major congeners for analysis: fusel oil, total acids (as acetic acid), esters (as ethyl acetate), aldehydes (as acetaldehyde), furfural, tannins, and total solids. Other observers[12] have found that vodka contains only one-tenth the amount of congeners found in whiskey.

What do the congeners do? We do not have all the answers relating to congener effect, but we know that color, flavor, and bouquet of whiskey are all influenced by the congeners. What other effects do congeners have? In a general way, and there are exceptions, a high incidence of congeners gives alcohol a high toxicity level, as many of the congeners are highly poisonous substances (fusel oil, furfural, tannins, and so forth). The toxic effects of congeners in whiskey are exerted by the slowing down of the rate of metabolism of alcohol, thereby enhancing undesirable side-effects. Although Haggard, Greenberg, and Cohen[12] have suggested that there may exist some yet unidentified congeners which affect liver function in a physiologically desirable way, most contemporary investigators agree that beverages with high congener content, when contrasted with those of low content, affect adversely the rate of alcohol's disappearance from the body. This results in a slower rate of recovery from intoxication, more severe hangover effects, diminished motor response, poorer judgment, and a decrease of learned skills.

We assume that most people drink alcoholic beverages for the narcotizing effects. Since we feel that people will not give up the social mechanism of drinking, it would appear advantageous that they at least recover their equilibrium and skills as quickly as possible after drinking. Congeners act against this desirable goal. As McKennis and Hagg[10] stated: "The physiologic studies already cited demonstrate that control of congeners, as achieved through manufacturing and blending techniques which regulate their type and quantity, can lead to either an increase or decrease in toxic effects. For the consumer, the latter is certainly more desirable." Since congener content can be influenced materially by altering the distillation and aging process (as has been done with vodka-type whiskey by a filtering process over heavy charcoal), we feel that every effort should be expanded for their removal.

Modern research has yet to improve the method of activated charcoal for filtering purposes. This process was developed in 1811 by the Russian chemist Smirnoff. Even today, in the United States all vodka is not subjected to this process, although the most commonly available vodka is exclusively filtered by activated charcoal. This process, when used as a subsequent process to modern day distillations, apparently results in a spirit containing less harmful congeneric substances than any other distilled alcoholic product manufactured to date.

What about congener influence on alcoholic individuals? The only suggestion of variation in the rate of individuals addicted to alcohol comes from Damrau and Liddy[13] who suggest that ". . . vodka (a low congener beverage) does not appeal to alcoholics and does not provide the complete psychological satisfaction which they demand." Our own experience does not support this contention. Our patients do not sip or flavor their drinks; they drink for the effect. Although whiskey may be the preferred beverage (as it is for 80 per cent of American drinkers, social and immoderate),[14] alcoholic individuals will not refuse alternate beverages if whiskey is unavailable. Further, alcoholic subjects in their attempts to control their drinking frequently switch brands and types of beverage.

From the point of view of primary prevention of alcoholism, we believe that the alcohol beverage industry has an obligation to its consumers and to the medical profession who must treat the problem of alcoholism, to "clean up" their beverages. We believe that as a public health measure the alcohol beverage industry must reduce—and reduce drastically—the toxic congeners now present in most forms of distilled spirits. Major scientific evidence indicates that most congeners have a toxic effect and that there are less toxic effects from beverages with a lower congener content. The liquor industry could utilize the same filtration method they already employ for the reduction of congeners in vodka. To maintain the smell, taste, and appearance of the different types of beverages, nontoxic flavoring, coloring, and aromatic substances could be substituted.

MODEL FOR DRINKING BEHAVIOR. Another apparent deterrant to alcoholism is the creation of a role model of ritualistic drinking. The legitimizing of alcohol or its use with meals, as the Italians have done, appears to be preventive. The development of a clear, unequivocal model for drinking behavior is important. Experiencing alcohol in a low content alcohol beverage at a young age in a socially acceptable situation can only help foster guiltless drinking attitudes.

It is important that alcohol never be defined as a magic substance able to meet all needs. If this image does not develop, alcohol is less likely to be fitted into an emotional system as a defense or symptom mechanism.

Drinking to drunkenness, if it occurs, should be in a "safe" setting, that is, an occasion at which the use of alcohol is sanctioned. Certainly, the group drinking behavior of preliterate cultures seems to be a protective device even when drinking to drunkenness results. The use of alcohol by preliterate societies (prior to contamination by Western civilization) for conviviality and to enhance social relations rather than as a means of meeting life's problems results in little ambivalence or guilt regarding alcohol and hence almost no alcoholism.

EDUCATION IN USE OF ALCOHOL. If we are to learn from the experience of others, we must see that the teaching of alcohol use be presented in a manner to promote less potentially socially destructive methods of dealing with the beverage. We also must keep in mind Bales'[15] suggestion that cultures must provide mechanisms to meet inner tensions. If not alcohol, something else will be necessary. As we consider the development of healthy and preventive cultural attitudes, we must guard against the dangers of arbitrary total prohibition, for the admonition never to drink, particularly in the complex society of today, frequently brings about the opposite result.

Another broad category of primary prevention leads us to consider the question of alcohol education through the public school system.

Is there a rationale for alcohol education? Demone[2] in a presentation to a group of teachers stated:

> I would like to suggest that you are also in an appropriate position to bring about more objective attitudes toward alcohol. If we can agree that people have attitudes which we can identify and manipulate, it is reasonable to suppose that anyone with an extended and intimate relationship with young people can help them. This means that a chance for people to talk, look, and think about alcohol in a healthy and rational way can be of assistance to them. They should be allowed to look at alcohol, at the reasons people drink and do not drink, because eventually they are going to have to make their own decisions. You can assist them to make sensible decisions, as you do in other health and social problem areas.

In a similar conference, Pasciutti[16] emphasized that the curiosity of children regarding alcohol manifests itself early and in many ways. They ask many questions pertaining to why people drink, why people stagger, and why some people act strangely after drinking. According to Pasciutti, "The question of alcoholism looms large in their minds." If Pasciutti's emphasis is correct, then one simple function of alcohol education is information. Children deserve and should receive unvarnished facts and objective answers.

A typical statement of objectives in alcohol education appears in the manual on alcohol education for teachers of New Hampshire.[17] The stated objectives are simple and straightforward:

> (1) The presentation without bias of scientific information concerning the nature, use, and effect of alcohol on the individual and society; (2) to develop sound attitudes toward alcohol problems which will result in effective patterns of behavior in society; (3) to develop an understanding that alcoholism is an illness which is a public health problem susceptible to prevention and treatment; (4) to develop a sense of responsibility for one's own welfare and that of others regarding the use of alcohol through knowledge of the types of controls which have been used in relation to the production, distribution, and use of alcohol.

Perhaps the most significant accomplishment of these stated objectives is that they have been accepted by New Hampshire's Temperance League ("drys") and by representatives of the Licensed Beverage Industry ("wets") emphasizing a rare union.

The pitfall that should be avoided is that of expecting too much of school education programs. Although these programs can help, home, church, and group influences ultimately will be more important. School programs cannot alter a poor or inadequate socialization process. They might, however, counteract some of its influence. Certainly students will bring to the classroom a series of different attitudes toward alcohol and therefore create a better understanding of the problem.

Mental hygiene

For preventive mental health measures to be effective we need some means of developing healthy emotional relationships early in life and throughout life. This would result in flexible adaptable personalities having a greater capacity to withstand emotional and physical trauma.

If alcoholism is the result of disturbed emotional, physiochemical, and sociocultural factors, one cannot just take away the alcohol and provide no restituting substitute. Alcoholics Anonymous has recognized this. Let us hope that supposedly more sophisticated professional groups will experience similar insight.

Treatment

Actually to cure an alcoholic individual, means to restore him by treatment to a state where his drinking could fall within the norms of social imbibing. This is, at present, impossible. Regardless of the mode and success of treatment, the true alcoholic individual does not and cannot drink socially. If the intertwined psychologic, physiologic, and social factors we described are causative, then cure is unlikely. Treatment for cure's sake would need technics for altering all genetic, psychologic, and physiologic systems as well as the social attitudes relating to the etiology of alcoholism. These technics would have to operate at the level of earliest influence. Hence, psychologic treatment can touch only portions of personality aberrations. In the same way, physiologic treatments affect only part of the disturbed response patterns, and social attitudes can be altered only in part. When the recovered alcoholic person drinks, the effectiveness of recently learned emotional and behavioral responses diminishes, bringing to the surface infantile, primitive conflicts. In time the recovered alcoholic individual responds to alcohol with a reawakening and strengthening of his deprived feelings. With this comes a pathophysiologic response to alcohol resulting in regression to the previous, alcoholism state.

Realistic alternatives to producing perfect beings or complete cures include: earlier case finding, crisis intervention, and strengthening of caretaking community programs. Child guidance programs to aid children with evidence of inadequate coping mechanisms are very important. Then by individual or group treatment of parents and child we can attempt to develop a more flexible and adequate personality structure.

Another alternative is to reduce somehow the stress of life and the increased unpredictability of events. Here, too, as with mental health, the necessary omnipotence is unavailable. Furthermore, we ought not to make life—in our enthusiasm for health measures—so healthy and problem-free that it is just not worth living, even if we possessed the necessary knowledge and skills to do so.

The possible genetic factors effecting the development of alcoholism may eventually be handled through new technics to affect the fetus in utero or by means of natural selection.

For the present, however, the interrelationship of precipitating and contributory factors of alcoholism suggests that the best approach is by simultaneously working on all frontiers: research, treatment, and prevention. A spirit of scientific inquiry is the necessary ingredient for success. In contrast with poliomyelitis, for example, a magic vaccine probably will never be found for this complicated social-behavioral health problem. Progress at best will be slow and steady. Our initial goal is merely to reduce the rate at which alcoholism is occurring.

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Use of CCC in Treatment of Alcoholic Patients at Meadowbrook Hospital

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THE MAGNITUDE of the alcoholic problem in Nassau County may be estimated from the fact that from 30 to 40 per cent of all the patients admitted to the psychiatric observation ward of Meadowbrook Hospital, the county general hospital, are alcoholic, either acutely intoxicated or with an alcoholic psychosis. The need to do something about the problem in a preventive and therapeutic way has been recognized for some time by the hospital authorities. Consequently, six years ago the Special Treatment Clinic was organized. This was a clinic for the psychotherapeutic treatment of chronic alcoholic patients which functioned until the winter of 1959. It was finally closed because only 5 per cent of the alcoholic patients referred to it on discharge from the psychiatric ward ever followed through with an application at the clinic. Of the group which did report, only a few ever became sober or stayed in treatment. It finally became evident that the experiment was too costly to continue and the clinic was abandoned. The function was taken over by the Mental Hygiene Clinic which previously had not accepted alcoholic patients.

Methods and Materials

Experimental work with CCC or citrated calcium carbimide (Temposil) was begun in the Mental Hygiene Clinic in June, 1959, and has continued until the present. CCC was selected over disulfiram (Antabuse), since CCC has been demonstrated to be much safer for indiscriminate use in the type of alcoholic patients who are found on the psychiatric ward because of its lack of hypotensive effects.[1,2] This lack of hypotensive effects obviated the need for keeping the patient under observation while he was tested with alcohol to demonstrate its effect in the presence of CCC.

The census of the alcoholic ward is always so great that a rapid turnover is essential to prevent serious overcrowding. For the first six months each alcoholic patient who was ready for discharge was asked if he wished to take CCC and return to the clinic for a follow-up examination. In cases in which the problem was serious and the patient was reluctant, the patient's family was consulted as to their desire to supervise the taking of the CCC tablets by the patient on a daily or twice-daily basis. If either the patient or his family agreed, the patient was given a month's supply of CCC, and an appointment to return to the Mental Hygiene Clinic was made. Twenty per cent of the patients have returned for treatment in the Mental Hygiene Clinic; only 5 per cent had returned to the Special Treatment Clinic. A disappointingly small number of patients kept their return appointment, but enough information was obtained from readmissions on the ward to show that many of them had taken the CCC tablets until they were used up but had not bothered to return for more tablets. However, other patients had discarded the medication as soon as they left the hospital. The policy was changed in January, 1960, so that only a week's supply of CCC was given on discharge, and the patient was asked to return before the week was over for a new supply and a new appointment. This served to put the initiative on the

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TABLE I. Duration of sobriety in months

Duration (Months)	Number of Patients in Mental Hygiene Clinic*	Number of Patients in Special Treatment Clinic†
0	7	7
$^{1}/_{4}$	1	1
$^{1}/_{2}$	1	2
1	20	2
2	10	. .
3	4	. .
4	2	1
5	9	. .
6 and over	3	1
TOTALS	57	14

* Range (in months)—0 to 11; median—1.
† Range (in months)—0 to 6; median—$^{1}/_{8}$.

EXPERIMENTAL WORK *with CCC or citrated calcium carbimide (Temposil) was begun in 1959 at the Mental Hygiene Clinic. Twenty per cent of the patients discharged on CCC have returned to the clinic for treatment in comparison with only 5 per cent who returned to the previous Special Treatment Clinic without treatment with CCC. CCC is a valuable adjunct in attaining sobriety. It has no side-effects when not mixed with alcohol; it fortifies the patient's will at its weakest point and is a proper symbol of the patient's willingness to try to abstain from drinking; it may be given without the patient's knowledge at the discretion of the physician and the patient's family; and it provides a clear-cut index of the patient's sobriety.*

patient or his family, minimized the previous waste of tablets, and effectively separated "the sheep from the goats."

Working with alcoholic patients who are staying sober and "getting back on their feet" is a rewarding experience while the sobriety lasts. Their decadent appearance disappears, their health improves, they are full of good intentions, they and their families are happy, and everything appears hopeful. Then suddenly they miss an appointment, do not respond to a follow-up letter, and can safely be assumed to have relapsed. Soon they reappear on the ward with another bout of delirium tremens. In all fairness, however, it is shown on the follow-up examination that some of them have maintained their sobriety and have dropped out simply because they could not take time off from work to return to the clinic or because they "wanted to do it alone."

It is extremely difficult to evaluate a treatment for alcoholism because of the uncertain nature of the alcoholic patient. To get an index of the effectiveness of CCC in the Mental Hygiene Clinic, the records of the Clinic were tabulated on the basis of duration of abstinence, number of interviews, and number of relapses. As a comparison, all of the alcoholic patients admitted to the Special Treatment Clinic were sampled randomly, and 50 cases were selected. From these 50 cases only 14 were found in which comparable data could be obtained because the Special Treatment Clinic put no stress on sobriety in itself and frequently did not mention whether a patient was drinking or not. The distributions are given in Tables I and II. As discouraging as the figures are for the CCC group, they can be seen to be superior to the psychotherapeutic group in duration of sobriety.

TABLE II. Number of interviews and relapse rate

Status Per Patient	Mental Hygiene Clinic	Special Treatment Clinic
Number of interviews		
Range	0 to 17	0 to 23
Median	1	1
Number of relapses		
Range	0 to 2	0 to 2
Median	1	1

One difficulty in the evaluation of progress in CCC treatment in this hospital clinic is the inherent bias in the selection of cases. The majority of patients have been selected from those patients hospitalized on the ward, and these patients in themselves are a highly select group. A goodly proportion are patients who have had one or more attacks of delirium tremens. Such patients are notoriously prone to "give up drinking" after such an attack since it is invariably a shocking experience. Therefore, it is questionable if such patients have "reformed" owing to the CCC medication or simply because of the fear of a repetition of the delirium tremens which they have experienced. However, we have a number of patients who have begun drinking immediately on discharge from the hospital, and on subsequent admissions we have been able to prevent this by discharging them with CCC in their systems, much to their families' gratification.

Contrary to expectations, the addition of alcoholic patients to the rolls of the Mental Hygiene Clinic has added little extra burden. They are handled mostly by one person, me. I see them briefly on a once-a-month basis and have attempted only to reassure them, reinforce their good intentions, and renew their medication. Occasionally a patient had neurotic symptoms, depression, or behavior problems for which more intensive therapy was necessary. These patients, in addition to their CCC appointments, were given more intensive therapy by a clinic psychiatrist or a social worker. The actual number of these patients was very small and represented less than 4 per cent of the total. I was struck by the "normality" of the majority of the alcoholic patients, once they had been sober for a month or two. Even depressions which had been present on discharge from the hospital lifted, psychopathic behavior disappeared, and anxiety became nonexistent. Therefore, it is wise to wait for a period of time after sobriety has been achieved before diagnosing underlying psychopathology, since it may indeed be reactive to the alcoholism itself, rather than the other way around, as is usually assumed.

Several types of interference to CCC therapy were encountered. The commonest type was the tendency to rationalize not taking the drug with the statement that the patients were told in Alcoholics Anonymous that drugs are a crutch and that the problem must be fought out alone by will power, Alcoholics Anonymous, and religion. However, Alcoholics Anonymous authorities have assured me that this does not represent an official position of the organization. I attempt to counter this rationalization with the advice that as long as a crutch is needed, there is no shame in using one. I point out that having CCC in the system may reinforce the will power at the point that it is most sorely tempted and thus prevent taking the one drink that may lead to a return to alcoholism.

A happy by-product of CCC therapy was the discovery that in some patients there results a loss of the desire to drink. I am told repeatedly of such patients who act as bartenders at private parties and who are able to drink soda instead of alcohol. Whether or not this is truly a physiologic effect of the drug is moot, but I see no harm in suggesting this possibility to patients to reinforce their determination to stay on the medication.

A few patients have attempted to drink while taking CCC. At least 1 patient that I know of had been able to do this by titrating the beer she drinks against the physiologic effects of the CCC and has managed to have a bottle of beer or two daily under these circumstances. However, her ability to "control" her drinking in this manner did not last long, and she began to cheat on the CCC and shortly relapsed into complete alcoholism. Other patients have cheated by secreting the tablets in the cheek and later spitting them out, and 1 patient would swallow the drug and then, after his wife had left for work, would vomit it up.

In a few cases, where the situation seemed desperate enough, I have given a supply to the spouse to be given surreptitiously to the patient. This technic has been used effectively in Canada.[3] By experience, it was found that CCC crushed into a powder mixes well enough with cooked cereal, spaghetti, mashed potatoes, creamed vegetables, and similar foods. It is insoluble in fluids. Not one of these experiments was completely successful, but in several instances wives were able to bring about a reduction in the amount of alcohol ingested by their husbands.

One case is interesting in that the patient, who was incorrigibly alcoholic and who had undergone a portacaval shunt for cirrhosis, was given 100 mg. of CCC daily in his food by his wife and mother, and at no time did he have a reaction. Later, on his next admission for delirium tremens, he was given 100 mg. of CCC and challenged with intravenous alcohol, with no reaction.

Undesirable side-effects from CCC were relatively rare and usually mild. Only 1 patient had a readmission for a CCC-alcohol reaction and this required no treatment. Patients ordinarily went to bed and fell asleep. The symptoms noted most frequently from the CCC-alcohol combination were: lobster-red flush of face, dyspnea, cough, palpitation, anxiety, general malaise and inability to continue drinking at the time, headache, and, in 1 case stupor. One patient, who had made three serious suicide attempts while drinking, remained sober for five months while on CCC medication, but after this he relapsed and finally succeeded in killing himself with carbon monoxide from his car exhaust.

Unlike disulfiram, at no time in this series were any side-effects noted that could be attributed to CCC alone. In the clinic it was observed repeatedly that patients usually kept their appointments only when they were taking CCC regularly and staying sober. Once they relapsed into drinking, they usually dropped from sight completely, although they might appear again at a later date.

Their cases are usually closed with the comment, borrowed from another conflict: "missing and presumed lost."

Summary

In conclusion, it may be stated that although CCC (Temposil) is not a treatment for alcoholism, sobriety is, and CCC is a valuable adjunct in this treatment. CCC has the following advantages:

It appears entirely harmless.

It has no side-effects when not mixed with alcohol.

It fortifies the patient's will at its weakest point.

It is a proper symbol of the patient's willingness to try to abstain from drinking.

It may, if necessary, be given without the patient's knowledge, at the discretion of the physician and the patient's family.

It provides a clear-cut behavioral index of the patient's sobriety.

Keeping the alcoholic patient sober increases his chances of seeking follow-up treatment and has improved the rate of return to sobriety from 5 to 20 per cent. The only serious shortcoming of CCC is the brevity of its action.

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Report on special margarines

The difference between special diet margarines and regular margarines is not very great from the standpoint of average consumption of the individual, according to the Council on Foods and Nutrition of the American Medical Association.

Special margarines differ from regular margarines in having a higher polyunsaturated fatty acid content. The nutritional significance of the increased amount of polyunsaturates in special margarines has not been documented. On the basis of the average per capita consumption of margarine, the extra amount of polyunsaturates made available by the use of special margarine is not very great.

A comparison of six special margarines with regular margarines showed that the polyunsaturated fatty acid content of the special products was considerably greater, in most instances more than double that of the conventional products. However, there was little difference in the saturated fatty acid content between the two types of margarines.

There is no scientific evidence that the source of the polyunsaturates used in margarines has any therapeutic significance. Cottonseed, corn, soya bean, or safflower oil can serve as the source.

Transventricular Mitral Commissurotomy

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ALTHOUGH COMMISSUROTOMY commonly relieves symptoms of mitral stenosis, when patients are followed over a long period of time, the rate of recurrence is increased progressively. In Bailey, Zimmerman, and Likoff's[1] original series of patients followed over one year, for example, only 55 per cent of them have maintained their improvement. Already 12 per cent of those patients operated on before 1952 have been reoperated on for recurrent stenosis.

Recurrent stenosis usually follows an initially inadequate procedure. An early relief of symptoms, then, is inevitably followed by a progressive deterioration. Less often, a refusion of the leaflets may occur because of an incomplete mobilization and recurrent episodes of rheumatic infection. In our own experience with more than 200 patients, restenosis occurred in only 1 instance following an apparently adequate commissurotomy. This case was that of a fifteen-year-old girl in whom digital commissurotomy resulted in a wide separation of the leaflets and an excellent early result. Recurrent episodes of rheumatic fever supervened, however, and four years later the patient expired. An autopsy revealed a restenosis of the leaflets which could not now be separated even with maximal digital pressure.

When the mitral orifice is enlarged to at least 2 fingerbreadths and a reasonably normal degree of leaflet mobility is achieved, one may anticipate an excellent result, with a sustained relief of symptoms. In almost half of our patients at the present time we find it necessary to use a valvulotome to obtain this kind of result. Optimally, the instrument should be one which can be introduced safely alongside the finger. The surgeon should be able to engage it accurately in the commissures, with little likelihood of producing a major degree of incompetence with the incision. Because occasionally we have produced a major grade of insufficiency following instrumentation, our search for a more effective technic has continued.

In Great Britain, Logan and Turner,[2] in France, Dubost,[3] and in the United States, Gerbode[4] and Cooley and Stoneburner[5] have employed a two-bladed dilator to separate the leaflets along the line of commissural fusion. Dubost proposed that the dilator be introduced blindly through the left auricular appendage and opened after it had been felt to traverse the mitral orifice. The others have recommended transventricular insertion of the dilator. In either event, when the dilator is engaged accurately and the blades are opened, an anatomically precise disruption of the commissures is usually accomplished. Gerbode[4] states that serious incompetence has not occurred in any of his patients so treated.

We have adopted transventricular dilatation in instances where an adequate commissurotomy requires instrumentation. We believe that if this technic is employed properly, one may achieve a mitral orifice of maximal diameter. We believe further that one must be prepared to accept the possibility of a serious grade of insufficiency, should the separation of the commissures be inaccurate in this admittedly uncontrolled technic. In contradistinction to what one finds in reviewing other results, this has occurred twice in our small series of patients.

MITRAL COMMISSUROTOMY, *performed with a transventricular dilator, is another technic for instrumental correction of mitral stenosis. The technic is particularly useful in instances of obliteration or attenuation of the auricular appendage, or in secondary commissurotomies. Much emphasis is placed on the surgeon's guiding the dilator through the mitral orifice into the left atrial cavity. Significant insufficiency, a major complication in all types of instrumental commissurotomy, occurred twice in this series of 14 patients.*

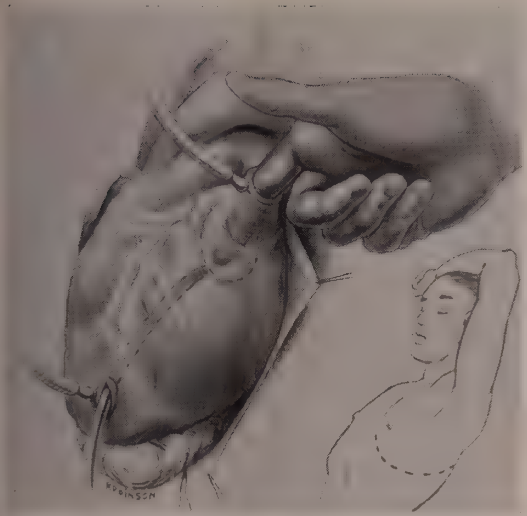

FIGURE 1. Right index finger, inserted through left auricular appendage, traverses stenotic valve and engages dilator within left ventricular cavity. Inset: Incision is curvilinear one through fifth left interspace. Preferentially, this is posterolateral incision.

Technic

In most instances the patient is operated on in the right lateral recumbent position. Alternatively, he may be placed in an exaggerated anterolateral position, with the left side elevated by a sandbag. In either event, the incision is through the left fifth interspace (Fig. 1). The lung is retracted backward and down, and the pericardium is opened behind the phrenic nerve. Above, the pericardial incision extends over the pulmonary artery, and below, curving backward, it extends about 3 cm. below the atrioventricular sulcus, exposing the left atrium and its auricular appendage.

A number 2 silk purse-string suture is placed around the left auricular appendage and is incorporated in a Rumel tourniquet. When the nature of the condition has been identified and it is apparent that instrumentation is required, the finger is withdrawn and a Satinsky clamp is applied around the base of the appendage. The pericardial incision is extended downward and posteriorly, exposing the apex of the heart. A tagged sponge is packed into the pericardial space behind the cardiac apex, displacing it forward into the operative field.

A number 2 silk purse-string suture is placed around an avascular portion of the apex, taking three bites over an area which is approximately 2.5 cm. in diameter. A bridge of tissue of approximately 2 ml. is left between each stitch. This suture is then also incorporated into a Rumel tourniquet. The surgeon again introduces his right index finger into the left auricular appendage, while the first assistant, standing opposite him, concentrates on guiding the instrument through the mitral valve. Using a bistoury knife and being careful to avoid cutting the purse-string suture, the assistant makes a 4-mm. stab wound into the left ventricle within the center of the purse-string suture.

A two-bladed dilator (Glover aortic dilator) is now introduced through this incision, while the second assistant gently tightens the purse-string suture to control blood loss which is rarely significant (Fig. 1). As the dilator is pushed into the left ventricular chamber, the surgeon pushes his right index finger through the mitral valve orifice, feels the tip of the dilator and, retracting his finger, guides it back into the left atrium (Figs. 2 and 3). The dilator is now positioned so that its blades lie accurately within the mitral orifice, and the instrument is rotated 45 degrees to the patient's left so that, when the blades open, they will do so in the line of the commissures (Fig. 3). It is of the utmost importance that the surgeon confirm the fact that the dilator is free of entanglement with the chordae tendineae

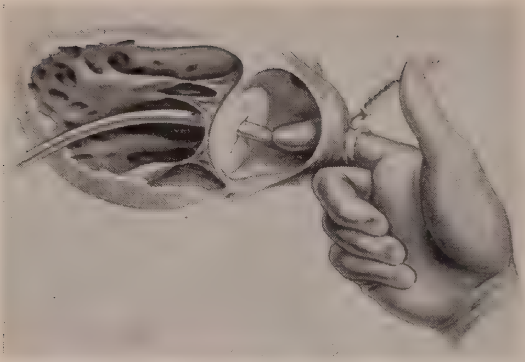

FIGURE 2. Cutaway illustration of index finger engaging dilator within cavity of left ventricle.

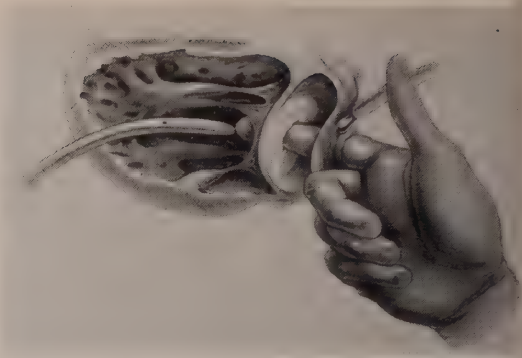

FIGURE 3. Index finger has guided dilator through stenotic valve.

cordis or valve tissues when it is opened. It may therefore be necessary to introduce and withdraw the instrument several times before the surgeon has determined, by palpation, that it is accurately engaged. As the assistant slowly opens the dilator, one can feel the leaflets being separated forcibly (Fig. 4). On completion of the commissurotomy, the instrument is withdrawn from the heart, and the incision in the left ventricular myocardium is closed with several interrupted 00 silk sutures on an atraumatic needle. The purse-string suture is removed, if possible. If not, the ends are tied together loosely, and the excess is removed. The intra-auricular finger reexamines the valve. Usually both commissures, and always the posterior one, will be found to be widely opened. If the anterior commissure is not opened, it may be necessary to incise it with a valvulotome.

Comment

Mitral commissurotomy, performed with a transventricular dilator, is another technic for instrumental correction of mitral stenosis. The surgeon need not accept an inadequate commissurotomy because of anatomic difficulties. The densely fibrosed and fused commissures that do not fracture with careful but vigorous finger manipulation, yield readily to the pressure exerted simultaneously to both commissures by the expanding two-bladed dilator. We must, however, be prepared to accept, as a potential complication of this as well as other instrumental technics, the risk of a serious grade of insufficiency.

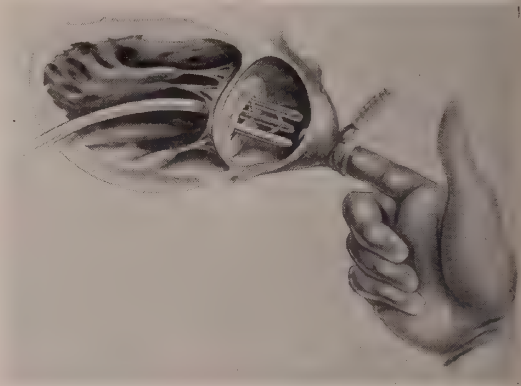

FIGURE 4. Finger has been retracted further, and dilator is opened to its fullest extent (3.9 cm.).

Not infrequently, the left auricular appendage is short and friable, and vigorous finger manipulation may then be dangerous because of the possibility of a tear extending into the left atrium. In these instances it is much safer to use the dilator and to limit finger manipulation to guiding the instrument into place. In our small group of patients there have been 5 instances where the neck of the appendage has been so narrow that it prevented entry of the index finger. This anatomic difficulty is readily circumvented by employing transventricular dilatation, with the fifth finger acting as a guide for an accurate placement of the instrument.

Transventricular dilatation should prove to be a valuable adjunctive approach to

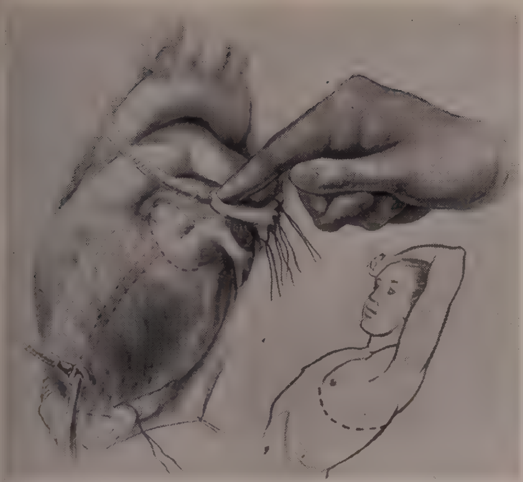

FIGURE 5. In secondary mitral commissurotomy, index finger has been introduced into left atrium by way of superior pulmonary vein. Dilator has been guided through stenotic valve into cavity of left atrium. Inset: Incision is through left fifth interspace. Preferentially, this is by way of posterolateral approach.

secondary operations on the mitral valve (Fig. 5). These operations are always more difficult than the primary operation because the auricular appendage has been removed, and the left atrium must be entered through its wall or through one of the pulmonary veins. In addition, the valve is usually resistant to finger fracture and requires manipulation with a valvulotome. Under such circumstances we have employed transventricular dilatation under the guidance of a finger inserted through the superior pulmonary vein.

Much emphasis is placed on the surgeon's guiding the dilator through the mitral orifice into the left atrial cavity. This avoids inadvertent entanglement with the chordae tendineae cordis or valve tissue and laceration of the leaflet, or uncontrolled separation of the commissures with massive regurgitation.

Summary

1. We have presented our technic of transventricular dilatation of the mitral valve.
2. This technic is especially useful in instances of obliteration or attenuation of the auricular appendage, or in secondary commissurotomies.
3. Significant insufficiency, which occurred twice in this series of 14 patients, is a major complication, as it is in all types of instrumental commissurotomy.*

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* Since this report was submitted, we have successfully utilized this technic in another 12 patients.

Mast Cells and Thrombosis

A Correlative Study

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IT IS WELL KNOWN that a hemorrhagic tendency is part of the clinical pattern of human "mastocytosis" (urticaria pigmentosa and/or mast-cell leukemia). These hemorrhagic proclivities have been attributed to the increased production and release of heparin resulting from the increased numbers of mast cells. In the literature no mention is made of the possible results or effects of a decrease in the number of mast cells in the human body. Such a decrease may result in intravascular thrombosis, just the opposite effect from that noted in an increase in these cells. This report concerns the preliminary findings of a study of autopsy material correlating the number of mast cells in the skin with the presence or absence of intravascular thrombosis.

Materials and methods

Skin samples were taken from the epigastrium of cadavers in 100 consecutive autopsies. The tissue was fixed in 12 per cent formalin and processed for embedding in paraffin. Sections, 7 microns in thickness, were stained with Bismarck brown which is an excellent stain for the granules in the cytoplasm of mast cells. Counts were made to determine the number of mast cells occurring in a field obtained with 10 × ocular and 43 × objective. Since mast cells are more numerous in the upper part of the dermis, to have an average count for the entire skin, the counts were started in the subepithelial zone proceeding downward toward the lowest part of the dermis and then proceeding upward, counting in this way 20 fields. The counts of each field were added, and the total was divided by 20. The result of this division was considered the average count for that particular sample of skin.

Two points should be emphasized: (1) The autopsies were performed in the routine way with no special effort placed on a search for intravascular thrombosis; and (2) the skin counts were performed without the author's knowledge as to whether or not thrombosis was found by the prosector. In fact, the correlations of this study were done only at the end of the count of all the skin samples. The thromboses considered here refer only to those found in large vessels, particularly pulmonary arteries, coronary vessels, and iliac veins. Microscopic thrombosis or infarctions were not included.

Results

The results of the present study are shown in Table I. It shows that the average counts ranged from 1 to 14 mast cells, and it can be seen that cases with counts of 6 or less have a high percentage of thrombosis (38 per cent) whereas cases with an average count of above 6 show a sharp decline in thrombotic phenomena (6 per cent).

The number of cases falling into each individual group is small. Therefore, one cannot determine the statistical significance of individual groups, and for that reason they were not shown in the table.

Comment

Mast cells are apparently connective tissue cells. They are found in the stroma

TABLE I. Mast cells in epigastrium of cadavers in 100 consecutive autopsies

Average Number of Mast Cells	Total Number of Cases	—Thrombosis— Number of Cases	Per Cent
1 to 6	70	27	38
7 to 14	30	2	6

SKIN SAMPLES *were taken from the epigastrium of cadavers in 100 consecutive autopsies. The average counts of mast cells ranged from 1 to 14; cases with counts of 6 or less had a high percentage of thrombosis (38 per cent) whereas cases with an average count of above 6 showed a sharp decline in thrombotic phenomena (6 per cent). This finding might indicate that low counts of mast cells in the skin are associated with low levels of blood heparin.*

of healthy and sick tissues[1,2] in amounts which have never been determined accurately. They are absent from certain tissues such as those of the central nervous system, adrenal glands, and anterior lobe of the pituitary. They have been found in the bone marrow only in occasional instances, particularly in cases in which there was some degree of marrow depression.[3]

Cells with the morphology of tissue mast cells have been seen in the blood in some instances of the so-called mast-cell leukemia.[4,5]

Their relative absence from the bone marrow precludes a common origin with the blood cells, particularly the blood basophils with which they were linked in the old literature. However, the possibility of a relationship between both types of cells has been raised in recent years.[6,7]

The morphology of mast cells in tissue culture has been studied by Paff, Bloom, and Reilly.[8] The function of these cells in human beings is not clearly understood, although considerable evidence has been accumulated to indicate that they produce and probably release histamine, heparin, and hyaluronic acid.[7,9]

The presence of heparin in these cells may be related to heparin activity in the blood stream. Clinical observations of patients with urticaria pigmentosa, now recognized as a systemic disorder[10,11] characterized by increased numbers of mast cells in the tissues, show that a hemorrhagic tendency is frequently observed. This hemorrhagic tendency may be spontaneous[11,12] or may be produced by minor injuries of the skin.[13] Urbach, Bell, and Jacobson[14] were able to demonstrate increased heparin activity of the serum in patients with urticaria pigmentosa after rubbing the skin with a towel. Oliver, Bloom, and Mangieri[15] found 50 times more heparin in mast-cell tumor of dogs than in normal dog liver. Similar findings had been reported in human beings.[4] Köksal[16] extracted from mouse mast cells a substance capable of inhibiting the coagulation of fresh mouse blood.

It is of interest that the survivors from the explosion of the atomic bomb in Hiroshima and Nagasaki developed a hemorrhagic state characterized not only by thrombocytopenia but also by increased amounts of mast cells in the tissue.[17,18] This may be related to the finding of Allen and Jacobson[19] who, after the irradiation of dogs, found thrombocytopenia and hyperheparinemia with disturbances in blood coagulation. The bleeding tendencies of these animals were controlled by injecting into them toluidine blue in spite of the fact that thrombocytopenia, if present, was not improved.

The results of the present study suggest a direct relationship between a decrease in the number of mast cells in the skin and the presence of vascular thrombosis. This finding might indicate that low counts of mast cells in the skin are associated with low levels of blood heparin. However, no measurement of the level of heparin in the blood was determined in this study. Further correlative studies are necessary to clarify the issue.

Summary

Mast cells were counted in samples of skin taken from the abdomen in autopsy cases, and a range of 1 to 14 was found. These counts were correlated with the presence or absence of intravascular throm-

bosis in large vessels. The percentage of thrombosis was considerably higher in cases with 6 or less mast cells, whereas a sharp decline in thrombotic phenomena was apparent in cases with counts of above 6.

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Use of dimenhydrinate in labor

According to an article by Scott *et al.* in the January 1, 1962, issue of the *American Journal of Obstetrics and Gynecology*, the administration of dimenhydrinate (Dramamine) to patients in labor had useful effects attributable to its antihistamine component, diphenhydramine. Antihistamines appear to have a definite place in the management of labor.

All of the 322 patients included in this study were (1) selected by the criteria of vertex presentation, intact membranes, and vaginal delivery and (2) premedicated with meperidine, scopolamine, and secobarbital. About half of them were given an intravenous injection of 100 mg. of dimenhydrinate over a two-minute period when the patient was entering the active phase of the first stage of labor. Analgesic and sedative drugs were given whenever needed by the patient. Comparisons of dimenhydrinate-treated and control groups showed that this drug had the following effects: It shortened the first stage of labor by 25 per cent in primigravidas and by 15 per cent in multigravidas and did not prolong the second or third stage; it tranquilized the patients almost immediately, usually for the duration of labor; it potentiated analgesia and enhanced the ability to tolerate pain; and it did not increase the number or type of complications—all infants had good color and spontaneous respirations and cry. The shortening of labor might have been due to general relaxation together with a reduction of cervical spasm due to histamine release.

Management of Osteoarthritic Knee

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THE OSTEOARTHRITIC KNEE *is affected by a slow degenerative wear and tear phenomenon which may start in the second or third decade of life, although most patients do not present symptoms until the fourth or fifth decade. Edema and hypervascularity of the synovia are among the first pathologic findings, along with changes in the cartilage. In most cases rest of the affected joint, generally with a Jordan splint, affords prompt relief. Operative management is reserved for patients who have not responded to conservative therapy and who have persistent pain. The operative procedure depends on the case. Postoperatively a massive compression bandage is applied, quadriceps pinching exercises are begun within twenty-four hours, and the patient is allowed to walk within a week, with emphasis on obtaining complete extension of the knee joint for proper stability.*

WHILE BY definition arthritis implies an inflammation of a joint, strictly speaking there is no active inflammation in the degenerating osteoarthritic joints which are the subject of this report. This condition may be referred to more properly as arthrosis, but that term has never acquired widespread acceptance.

We shall limit our discussion to knees affected by a slow degenerative wear and tear phenomenon, and we shall refer to this condition as osteoarthritis. Excluded from this report are cases having infectious, rheumatoid, rheumatic, or other causes.

The degenerative process may start quite early, in the second or third decade of life, although most patients do not become symptomatic until the fourth or fifth decade. Women are affected more frequently than men. Usually patients exhibit slowly increasing symptomatology which can be initiated by minor trauma or anatomic structural variations of the bones comprising the knee joint. Bowing of the legs, knock knees, or deformities in a contiguous hip or ankle joint may increase stress and may be responsible for knee joint degeneration. Wear and tear on the joint may also be increased by obesity and by sudden movements that produce stress and strain on the ligaments of the knee joint. Pain is often localized on the inner side of the joint, is usually insidious at onset, and may be initiated or aggravated by a minor traumatic episode. Once present, pain may be aggravated by prolonged standing, walking, and especially by arising from the sitting position.

Pathology

Among the first pathologic findings of osteoarthritis are edema and hypervascularity of the synovia. The articular cartilage is discolored and shows evidence of degeneration. Fibrillation of the cartilage is seen. There is a loss of elasticity with a gradual thinning of the cartilage, resulting in a narrowing of the joint space. Eventually the underlying bone becomes sclerotic, eburnated, and exposed. Mild pannus formation is sometimes seen, and eventually there are extensive productive changes at the articular margins with hypertrophy of

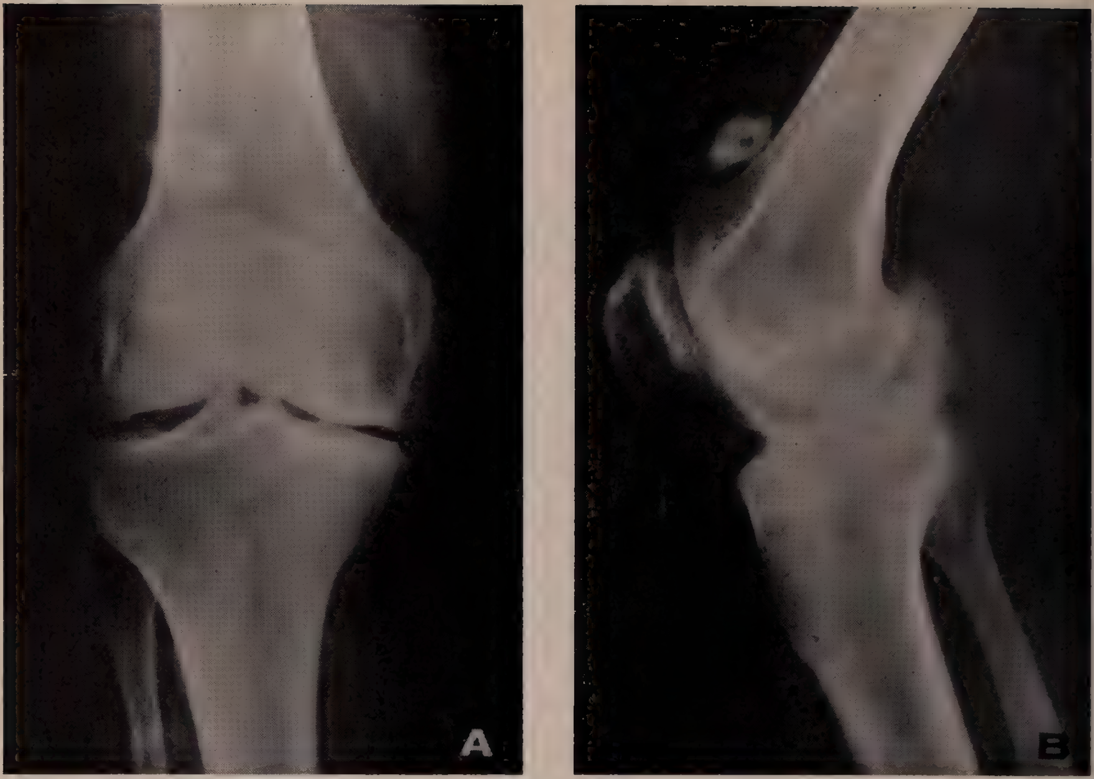

FIGURE 1. (A and B) Preoperative anteroposterior and lateral views showing free joint body in quadriceps pouch, extensive arthritic lipping of articular surface of patella, narrowing and irregularity of medial joint space, with extensive lipping of medial joint surfaces.

bone at the margins of the articular cartilage. X-ray films of the knee reflect the destructive cartilaginous changes by visualizing a narrowing of the joint space, particularly on the medial side. Also noted in x-ray films are local sclerosis and proliferative changes at the joint margins and, at times, free joint bodies.

Orthopedic management

Every attempt should be made to correct static deformities that may be apparent. For example, genu varum deformities, with secondary pronation of the feet, can be compensated for by wearing an orthopedic oxford with inner heel wedges and scaphoid pads to remove some of the strain from the tibial collateral ligaments. In most cases rest of the affected joint affords prompt relief. For the past twenty years we have been using a Jordon splint which is essentially a piano felt pad $^3/_8$ inch in thickness, 15 inches in length, and 5 inches in width, reinforced with three or four stainless steel struts. It is fastened behind the knee with an elastoplast bandage and reinforced with adhesive strapping. Thus considerable support is obtained with a trace of mobility in the knee. It has the advantage of affording sufficient immobilization without producing secondary stiffness which one sees so often after immobilization in plaster. We have, at times, used intra-articular Hydrocortone in conjunction with the immobilization, but we have not noted any appreciable difference in our results and have therefore discontinued its use. At the end of three weeks the splint is removed and reapplied with an ace bandage, to be worn for a period of two weeks during the waking hours. The splint is then discarded, and the ace bandage is worn alone for an additional two weeks. By this time the great majority

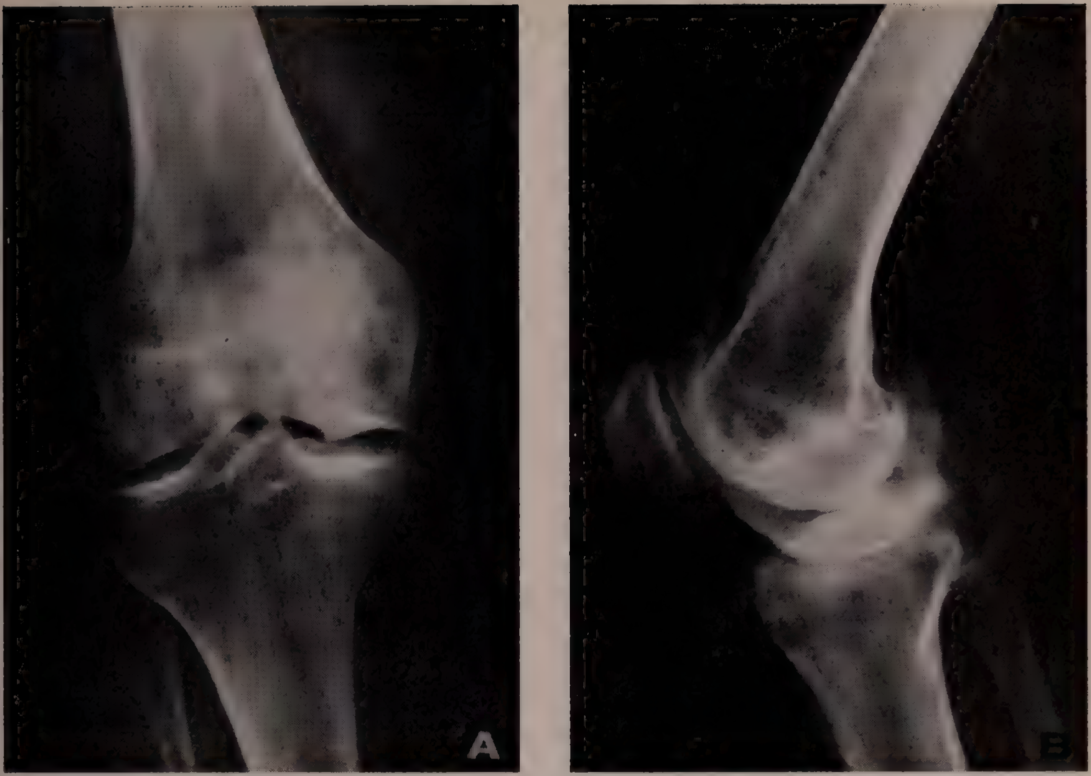

FIGURE 2. (A and B) Postoperative views of same patient showing removal of joint body and osteophytes about medial joint line and patella.

of patients are completely relieved of their pain and are indeed very grateful.

Operative treatment

Operative intervention is reserved for those patients who have not responded to an adequate course of nonoperative or conservative therapy and have persistent pain and swelling, usually on the medial side of the joint. The joint itself, as judged by x-ray film, should not show too much disruption, and it is desirable to have at least some cartilaginous covering over the articular surfaces of the femur and tibia. Prior to operation our patients are forewarned that the postoperative period may be rather trying.

We do not have a "standard" operation for the arthritic knee. We avoid indiscriminate surgery on these patients, but we do perform adequate surgery to relieve the symptomatology. Many times an internal menisectomy for the removal of a degenerated, fibrillated, and fragmented meniscus is all that is necessary. On the other hand, if the menisci appear healthy, they are left in situ while other areas of involvement are corrected. While synovectomy ordinarily is not indicated in osteoarthritis, we have done complete or partial synovectomies when the necessity arose. We have seen patients in whom one side of the synovial membrane, usually the medial half, has been thickened, granular, and edematous as a result of the chronic irritative process, secondary to joint degeneration. These patients have done very well with partial synovectomy. Synovectomy is carried medially and laterally to the cartilage line, and osteophytes are removed not only from the margins of the articular cartilage, but also at the joint line (Figs. 1 to 4). It is not uncommon to find a small osteophyte imbedded loosely between

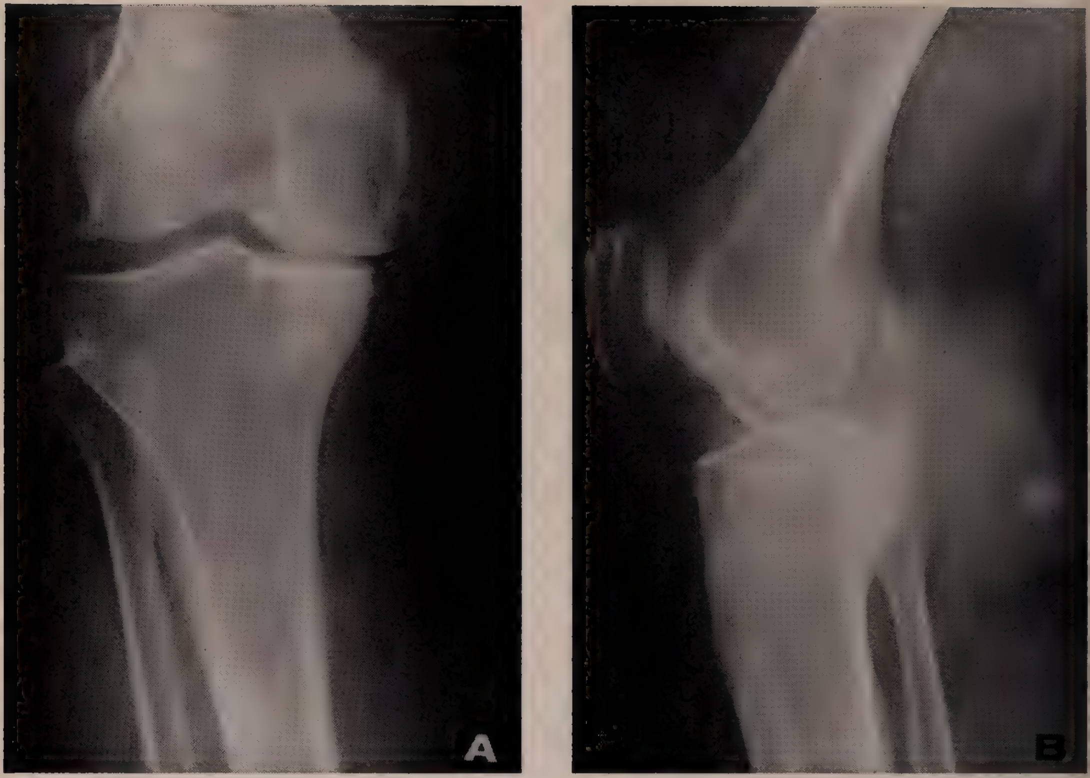

FIGURE 3. (A and B) Preoperative and lateral views. Note free joint body in outer compartment of knee and large osteophyte formation over medial femoral condyle.

the articular margin and the tibial collateral ligament. The authors employ a median or lateral parapatellar incision but do not hesitate to augment it with a second capsular incision in back of the tibial or fibular collateral ligament for adequate exposure of the posterior compartment of the knee joint. We have not resorted to patellectomy except on rare occasions. However, we have often thinned out the patella and reflected synovial membrane from the articular side of the quadriceps tendon over the denuded and thinned-out and smoothed patella.

Postoperatively, a massive compression bandage is applied using laparotomy pads and a plentiful supply of Webril over which an ace bandage running from the toes to the groin is applied. Quadriceps setting exercises are begun within twenty-four hours, and we allow the patient to walk, usually within a week, emphasizing at all times the necessity for obtaining complete extension of the knee joint for proper stability.

We have used leg traction postoperatively, but we see no advantage over a firm, massive compression dressing. Our goal is to obtain a knee that can be extended fully and can flex to 80 or 90 degrees. If at the end of six weeks the patient cannot flex the knee to 90 degrees, especially if there is a cessation of progressive improvement in flexion, the knee is manipulated under anesthesia. It is flexed gently to 70 or 80 degrees without using undue force, and a compression bandage is applied for two or three days. Active physiotherapy with resistive exercises is reinstituted.

Summary

We wish to emphasize that under the described form of management osteoarthritis of the knee is not a hopeless condition. In the great majority of cases conservative treatment is sufficient, but for those few

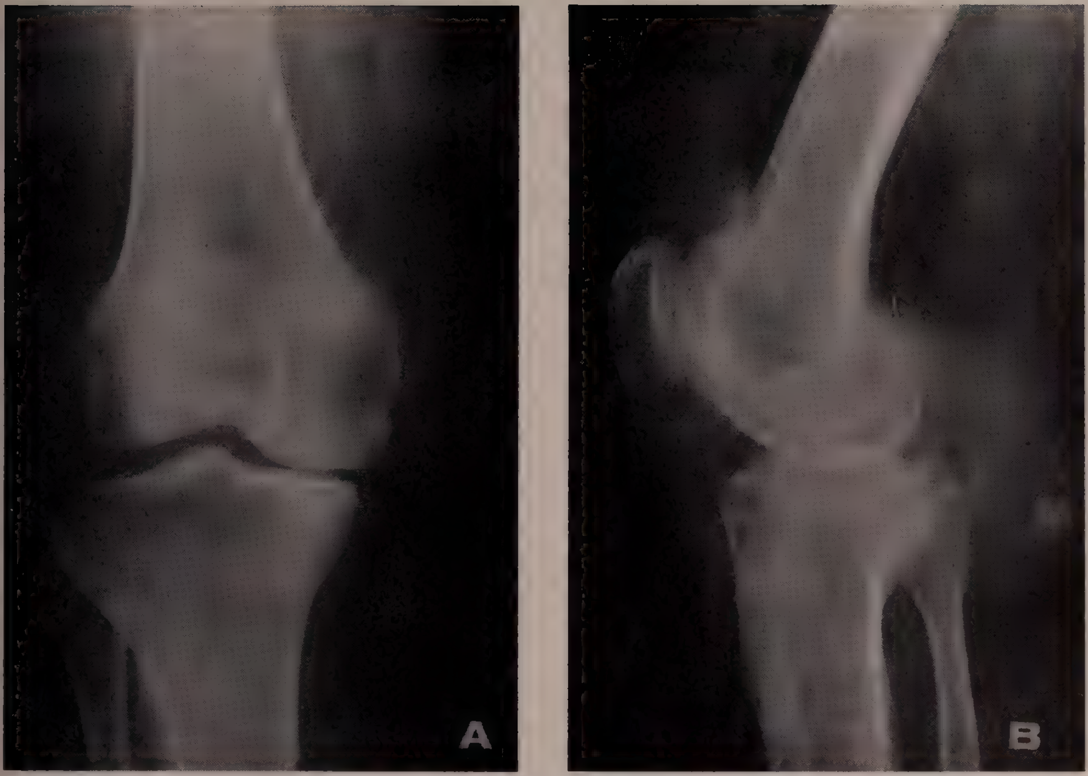

FIGURE 4. (A and B) Postoperative views; joint body has been removed, and osteophytes have been excised.

patients who are not helped by conservative treatment surgery can be a valuable therapeutic adjunct. The patient can be helped materially if the proper therapeutic regimen, as outlined in this report, is adapted to his needs.

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Scientific session held at the
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PROCEEDINGS

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MURRAY DWORETZKY, M.D., AND SHEPPARD SIEGAL, M.D.
Editors

Immune Globulins

Structural and Functional Studies*

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ANTIBODIES IN MAN and in most species of animals studied so far are associated with a group of structurally and functionally closely related proteins collectively referred to as the "immune globulins" or "the group of gamma globulins."[1] These proteins include a major component which makes up more than 90 per cent of the total, known as the 7S gamma globulin fraction and two minor fractions, known as the 19S gamma globulin (beta-2M globulin) and the beta-2A globulin. Because of their common antibody function, it has recently been suggested that these two minor components, which in normal serum make up less than 10 per cent of the immune globulins, be called gamma-1A and gamma-1M globulins.[2] This would be better than the older, somewhat confusing terminology, since it is based on functional, as well as structural, properties of these proteins.

Properties

Table I summarizes some of the physicochemical and biologic properties of these three major types of antibody-containing proteins. All of them migrate with the gamma or slow beta globulins on electrophoresis, depending on the medium employed. Both 7S gamma globulin and gamma-1A globulin have sedimentation coefficients of approximately 7S (Svedberg

TABLE I. Physicochemical and biological properties of immune globulins

Properties	7S γ Globulin	19S γ (γ_1M; β_2M) Globulin	β_2A (γ_1A) Globulin
Physicochemical			
S rate	7S	19S	7S
Molecular weight	160,000	±1,000,000	?
Electrophoretic mobility	γ globulin	Fast γ globulin	Fast γ—β globulin
Carbohydrate (per cent)	2.5	10.0	10.7
Antigenic specificity	+	++	+
Biological			
Placental transfer	Yes	No	No
React with rheumatoid factor	Yes	No	No
Fix to skin (PCA)	Yes	No	No

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* Supported by the Arthritis and Rheumatism Foundation and the United States Public Health Service, Grants A-2954 and A-1431 (C2).

units), while the gamma-1M globulin has a sedimentation rate of 19S. Gamma-1M globulin has a molecular weight of about a million, while that of 7S gamma globulin is approximately 165,000. The molecular weight of the gamma-1A globulin is not known but probably approximates that of 7S gamma globulin. Each of these proteins contains carbohydrate: 7S gamma globulin about 2.5 per cent, and the gamma-1A and gamma-1M globulins approximately 10 per cent carbohydrate. Of particular value in studying these proteins are their antigenic properties which further confirm their close structural relationships. Immunologic studies have shown that while each of these proteins possesses certain unique antigenic determinant groups which distinguishes it from each of the other immune globulins, they also contain certain common antigenic groups which cause them to cross-react when examined with antisera to these proteins.

In certain proliferative disorders of the plasmocytic or lymphocytic cell series there are produced structurally closely related paraproteins which are, however, generally devoid of antibody activity. These are the myeloma proteins corresponding to the 7S gamma or gamma-1A globulins and the macroglobulins related to the gamma-1M globulin. Since these proteins are present in these abnormal sera in large amounts and can be isolated more readily in a state of purity than their normal counterparts, they are frequently employed to study the properties of these proteins, and many of the results reported in the literature have been obtained with such preparations.

While each of the immune globulins has as its major biologic function the capacity to combine with and to neutralize specific antigens which may be injurious to the host. the 7S gamma globulins possess a number of other interesting biologic properties which distinguish them from the other two members of the immune globulins. First as shown in Table I, only 7S gamma globulin can cross the placenta to appear in the blood of the newborn infant. Neither the gamma-1A nor the larger gamma-1M globulin can traverse the placenta, and they are, therefore, virtually completely absent from cord blood. This property is of particular practical importance since in cases of A, B, O group or Rh factor incompatibility in the newborn infant, only maternal antibodies associated with the 7S gamma globulin fraction can cross the placenta and cause tissue damage in the offspring, while antibodies in the maternal circulation associated with the other two proteins do not reach the offspring and are, therefore, not injurious to the newborn infant. A similar situation appears to exist in the case of white blood cell and platelet incompatibilities. Second, only 7S gamma globulin can fix to the skin as measured by passive cutaneous anaphylaxis (PCA), while neither gamma-1A nor gamma-1M globulins can do so. The importance of this property in causing tissue damage is poorly understood. Third, only 7S gamma globulin can react with rheumatoid factor, while the other proteins in this group lack the determinant groups against which rheumatoid factor is directed. The possible reasons for these properties of 7S gamma globulin are currently under study and will be discussed subsequently.

Association of antibodies with gamma globulin fractions

Most antibodies in man and in all other species are associated with the 7S gamma globulin fraction. However, a few antibodies are frequently associated with the gamma-1M globulin fraction. Some of these are listed in Table II and have been summarized recently by Kunkel.[3] It appears likely that others classically associated with the 7S gamma globulin fraction may belong to the gamma-1M globulin at some stages during the immune response. Because of difficulties in isolating the gamma-1A globulin in a pure state, this fraction has been less well studied. However, it too appears to contain a number of antibodies.[1] Little is known of the factors that determine the type of antibody produced to a given antigenic stimulus. It would appear that the stage of immunization, the nature of the antigen, the route of administration, and possibly certain genetically determined factors may play a role. For example, when rabbits are immunized with sheep cells, their initial antibody response is primarily a 19S gamma globulin, whereas at a later

TABLE II. High molecular weight antibodies and substances in man

Antibodies
Rh saline agglutinins
Isoagglutinins*
Cold agglutinins
Heterophil antibodies
Streptococcal M.G. antibodies*
Wassermann antibodies*
Typhoid O agglutinins*
Paratyphoid agglutinins*
Penicillin antibodies†
Leukagglutinins*
Antinuclear antibodies†
Thyroid antibodies†
Other substances
Properdin
Rheumatoid factors
Macroglobulins

* Frequently.
† Rarely.

stage of immunization 7S gamma globulins are produced in large amounts.[4] Similarly, in man it appears that the initial response of the newborn infant, as well as the adult subject, immunized with a mixture of typhoid-paratyphoid vaccines as well as with certain other antigens, is an antibody associated with the gamma-1M fraction, while after a more prolonged immunization and during the secondary response 7S gamma globulin antibodies are produced.[5] While the nature of the antigen and the route of administration probably also have an effect on the type of antibody produced, their exact role has not been as well defined and appears quite complex, since the same antigen may result in the production of both types of antibody in the same subject over prolonged periods of time. This is particularly true of blood group substances and the complex, poorly defined agents responsible for the production of Wassermann antibodies in syphilis, each of which frequently induces the prolonged formation of antibodies associated with both the 7S gamma globulins and gamma-1M globulins in the same subject. Finally, the nature of the antibody may be determined in part by as yet poorly defined characteristics of the host. Thus, subjects belonging to blood group O produce isoagglutinins associated primarily with the 7S gamma globulins, while isoagglutinins in persons with blood groups A or B more often belong to the gamma-1M globulin fraction.[6] Recent studies also suggest that this may be modified by the presence of the rheumatoid factor, since subjects belonging to blood group O who possess the rheumatoid factor may produce 7S gamma globulin isoagglutinins less readily than normal group O subjects.[7]

Structure and function

Because of their large size and complex structure, the immune globulins have not lent themselves readily to precise structural analyses such as those which have recently succeeded in elucidating the exact amino acid sequence of smaller proteins, such as insulin and ribonuclease. However, by applying a number of physicochemical and immunologic technics to the study of these proteins and some of the smaller units derived from them, it has been possible to gain a better understanding of their structure and to correlate some of their structural and functional properties. As a result of such studies, it is becoming increasingly apparent that although each of the immune globulins possesses certain unique properties which allow it to be distinguished from the other members of the group, the antibody function common to all of them reflects certain basic similarities in their structure. Such studies have been most successfully performed with 7S gamma globulins but are also in progress with the gamma-1M and gamma-1A globulins.

In 1958 Porter[8] succeeded in breaking down 7S rabbit gamma globulin with papain and cysteine to fragments with sedimentation coefficients of 3.5S and in separating these fragments by chromatography on diethylaminoethyl cellulose. Two of the fragments so obtained (fragments I and II) had molecular weights of approximately 50,000. Each of these fragments contained a single antibody-combining site and therefore behaved like a univalent antibody, while fragment III, which had a molecular weight of about 80,000, failed to combine with antigen. Subsequent studies have shown that it too retained a biologic significance, since it contained the site necessary for fixing to the skin,[9] for combining with rheumatoid factor,[10,11] and since it alone can cross the placenta readily while fragments I and II fail to do so.[12] When human 7S gamma globulin is similarly treated, it too yields 3.5S units which can be separated by somewhat different chromatographic technics into a component (B) with a fast electrophoretic mobility, which is rich in hexoses but devoid of antibody-combining activity, and two fragments (A and C) of slower electrophoretic mobility which retain the ability to combine with antigen.[13] When each of these fragments is tested with an antiserum to 7S gamma globulin, fragments A and C give a reaction of identity, although differing in electrophoretic mobility, while fragment B is antigenically unique. In the case of human gamma globulin, papain digestion results in the destruction of the site necessary for skin fixation[14]; however, fragment B retains the ability to combine with rheumatoid factor to give a soluble complex composed of one molecule of rheumatoid factor and five or six molecules of the fragment.[15] While this technic of degrading 7S gamma globulin has yielded a great deal of information on the structure of gamma globulin and has permitted the isolation of several biologically active fragments from a number of different antibodies, it now appears that more precise chemical technics, especially those that selectively break disulfide bonds,[16] may yield even more definitive information of the precise structure of the immune globulins.

In the case of the gamma-1M globulin, an important finding which opens new pathways to the study of the proteins was the observation in 1957 by Deutsch and Morton[17] that these proteins are composed of 7S units which are held together by disulfide bonds that are readily broken by treatment with sulfydryl reagents. In all instances this dissociation is accompanied by a loss of antibody activity but appears to be reversible when the sulfydryl reagent is removed, if pure proteins are used.

A study of the units produced from the gamma-1M globulin in this fashion has demonstrated that the units differ from native 7S gamma globulin in a number of ways, and that the 19S gamma globulin cannot be simply a polymer of 7S gamma globulin.[18] Thus, when accurate sedimentation studies are performed, these fragments obtained from the gamma-1M globulin have an s rate of 7.5 to 8S compared with 6.5S for native 7S gamma globulin. In addition, they differ from 7S gamma globulin in their chromatographic behavior on diethylaminoethyl cellulose in being richer in hexose and in resembling native gamma-1M globulin rather than 7S gamma globulin in their antigenic properties. The ease of dissociation of these proteins, which is accompanied by a complete loss of antibody activity in all instances studied to date, serves as an excellent presumptive test for gamma-1M antibodies. This inactivation, together with the lack of placental passage, serves as an excellent screening technic for 19S gamma globulin antibodies. Because of this ready inactivation, sulfydryl reagents, especially penicillamine, have been used with some success in the treatment of certain patients with symptoms secondary to cold agglutinins, macroglobulins, and cryoglobulins of the gamma-1M type, and it seems possible that such measures may be useful in other disease states resulting from the presence of high molecular weight antibodies.

While detailed studies of the structure of gamma-1M and gamma-1A globulins have not yet progressed to the stage achieved for 7S gamma globulin, it has been possible to obtain a better definition of their relationships by comparing these proteins with the 3.5S units of 7S gamma globulin. Such studies have demonstrated conclusively that the gamma-1M, gamma-1A, and the closely related Bence Jones proteins cross-react with 7S gamma globulin by virtue of antigenic determinant groups associated with those fragments of 7S gamma globulin which have the antibody-combining site, while the antigenic specificity of the 7S gamma globulin molecule resides in fragment B which is devoid of antibody-combining sites.[19] A similar cross reaction has also been demonstrated between gamma-1M rabbit globulin and fragments I and II derived from 7S rabbit gamma globulin.[20] Here too the antigenic specificity of the 7S gamma globulin resides in fragment III. It would thus appear possible that some of the biologic functions unique for 7S gamma globulin may be associated with this fragment of the molecule which also has some structural specificity.

Thus, the application to immunology of some of the newer methods of protein chemistry has yielded a great deal of information relating the structure of these molecules to some of their functions. However, a great deal remains to be learned, not only about the ultrastructure of the immune globulins, but also about such basic questions as the nature of the immune response, the type of cell involved in the production of different immune globulins, the factors that determine the type of antibody produced, and the basic mechanisms of the production and release of antibodies by these cells. These problems are under study in many laboratories and the answers may soon be forthcoming.

Question and answer period

JOSEPH FRIES, M.D.: Thank you, Dr. Franklin. The measure of the success of a scientific presentation is the number of questions which it stimulates, and I am sure you have many. May I exercise a President's prerogative of asking the first question?

There are at least two reports that I know of in which anaphylactic reactions resulted from the injection of gamma globulin. These reports have been variously reported in the literature. No comment is made on the likely antigenic component within the gamma globulin—I am not talking about additives of contaminants. Would the speaker care to discuss the possibilities?

DR. FRANKLIN: This is the type of question that deserves a long answer, and it is really open to a number of different interpretations and touches on many of the fundamental questions in immunology at the present time.

There are a number of possibilities which immediately come to mind. First of all, when you prepare gamma globulin, as is done commercially by the Cohn procedure, there results a certain amount of aggregation of the molecules. Larger molecules and polymers are formed, and at least in experimental animals, when these are injected intravenously, they can cause anaphylaxis and when injected into the skin, they can elicit an immediate or delayed inflammatory reaction. This type of reaction is unlikely in these subjects, however, since we have been fairly sure that the injections were not intravenous.

Another possibility is that the subject may have had certain allergies to start with, and the gamma globulin that he received may have been contaminated with some of the corresponding allergens derived from the donor population. For instance, somebody who is sensitive to some kind of food may have gotten gamma globulin from a pool that contained some of the foodstuffs to which he is allergic. Again, this does not seem too likely because this would be a much more frequent occurrence when one considers the large amounts of gamma globulin now given to allergic patients.

I think that by far the most provocative and most interesting approach to this problem comes out of some very recent work which has shown, or at least given suggestions, that gamma globulins in different human beings and in different species of animals show certain individual variations from one subject to another. A number of workers have now been able to produce antibodies to gamma globulin in experimental animals by the injection of homologous gamma globulin. Thus, by immunizing a guinea pig with guinea pig gamma globulin or a rabbit with rabbit gamma globulin, it is possible to induce the formation of antibodies which react with a wide variety of gamma globulins from many species.

In the case of human gamma globulin, this problem does not lend itself quite as readily to an experimental approach. However, on the basis of the gram grouping, the human population has been divided into different gamma globulin types which have been recognized as an outgrowth of the work on rheumatoid factors. It now appears that the human population can be divided into at least seven major gamma globulin groups. Although the differences among them appear to be subtle and at present detectable only by complex technics employing selected sera from patients with rheumatoid arthritis, it is quite conceivable that sooner or later some subjects may develop antibodies to injected gamma globulins of a different type and develop symptoms similar to those described in these patients.

Recently we worked with a five-year-old boy who was falsely diagnosed as being agammaglobulinemic. He had significant levels of gamma globulin, but they were lower than normal. This child had received injections of gamma globulin for many years, and when we first saw him, we did the usual rheumatoid factor tests because of the frequent association of rheumatoid arthritis with agammaglobulinemia. To our amazement, with rabbit gamma globulin this boy reacted very strongly in the sensitized sheep cell agglutination reaction, so that it looked, at least from the preliminary studies, as if he might indeed have developed antibodies to gamma globulin which he had received. Unfortunately two subsequent studies, as well as latex fixation tests, indicated negative results even after stimulation with gamma globulin, so that we have no explanation for our initial finding. We expect to follow this boy further and to challenge him again with gamma globulin.

QUESTION: Is there any difference in the quantity, as well as the quality, of the gamma globulin in the allergic patient, as compared with the nonallergic patient?

DR. FRANKLIN: To the best of my knowledge there are no striking differences between these two groups. I think the methods we have available at the present time are so crude that we are just not in a position to measure any minute differences in the qualitative as well as the quantitative properties of these proteins if such should exist. I think it is quite conceivable that aside from specific antibodies such as reagins or blocking antibodies, there may be other differences of which we are not aware at this time.

QUESTION: Many of our allergic children are highly susceptible to infections of all sorts. Most of them have normal gamma globulin. Do you postulate this is a qualitative difference in gamma globulin, or do you think it has nothing at all to do with the gamma globulin?

DR. FRANKLIN: I think that this question really gets into the whole problem of host defense mechanisms, and in concentrating on gamma globulin, I may have unintentionally given the false impression that this is the sole mechanism involved. There are many different substances and different mechanisms, cellular as well as humoral, and we have just dissected out one little fragment of this complex group. I think that we cannot really attribute all of the defects in defense mechanisms to this particular sphere of interest. The leukocytes and the reticuloendothelial system all play a very important role, as do a number of more or less well characterized humoral factors, such as properdin and others.

ELY PERLMAN, M.D.: With the fluorescent technic, are you able to show any difference between the site of production of 19S as compared with the site of production of 7S gamma globulin?

DR. FRANKLIN: In my opinion, and I feel it quite strongly, on the basis of some of our own work as well as on the basis of what we see in the bone marrows and lymph nodes of subjects with macroglobulinemia, the 19S gamma globulins are produced, at least in part, by some cells which are closely related structurally to the lymphocyte, whereas the 7S gamma globulin, and this is generally accepted, is produced by a plasma cell. However, things may not be quite so simple since there is some work in the literature which seems to indicate that both types of gamma globulin are produced by plasma cells. I do not know of any work that shows that a single plasma cell can produce two different types of gamma globulin, and such an occurrence seems a bit unlikely. As a result of these discrepancies, the site of 19S gamma globulin production remains a little in doubt. It may be a plasma cell, and it may be a lymphocyte-like cell.

DR. FRIES: May I express the thanks of the New York Allergy Society to Dr. Franklin for giving us all a stimulating and informative evening.

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USAN, term to designate generic drug names

USAN (United States Adopted Names) will be the new term applied to nonproprietary names of drugs by the recently formed Drug Nomenclature Committee of the American Medical Association and the United States Pharmacopeia. The primary objective of the new committee is to find a single, suitable, nonproprietary name for each drug in general use. The term "USAN" does not mean that the names are adopted by or have scientific sanction from the Federal government.

The term, U.S. Adopted Names, applies only to those names chosen by the AMA-USP Nomenclature Committee since its establishment in June, 1961. While, in general, the committee is concerned with USAN for new drugs, it has acted on some generic names that were in use prior to June of last year.

To date, the committee, with increasing cooperation from individual pharmaceutical firms, has assigned U.S. Adopted Names to more than 100 new compounds of therapeutic interest. Lists of USAN are now being made available for publication.

Because proposals for USAN may originate wherever pharmaceutical research is in progress, they may differ considerably in both derivation and length. Through an Advisory Panel on Pharmaceutical Nomenclature, the committee is studying the general principles for coining nonproprietary names. These principles will be circulated widely among all who have occasion to propose names, in order that the future names for drugs may be less subject to criticism on the grounds of being too long, unwieldy, and hard to pronounce.

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

A Review of Headache: 1955 to 1961

Part III

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Treatment

Obtaining objectivity creates a problem in evaluating drugs for the treatment of headache. Thus it is especially important that double-blind technics, with placebos and standards of comparison be utilized.[173] It is equally important to remember that the success of a drug depends on the personalities of both the doctor and the patient.[174] Recent articles by Ogden,[175] Blumenthal and Fuchs,[176] Friedman and Merritt,[177] and Rushton[178] have discussed the general treatment of headache.

Migraine. The principal advances over the past five years in the symptomatic treatment of migraine have been in the development and use of new ergot derivatives, combinations of ergot and other medications, and new routes of administration. An encouraging breakthrough in the prophylaxis of migraine may have occurred with the introduction of 1-methyl-D-lysergic acid butanolamide (UML-491).

Ergotamine tartrate remains as the drug of choice in the symptomatic treatment of migraine. In a series of 2,500 migraine patients at the Montefiore Hospital Headache Unit, ergotamine tartrate, alone or in combination, by all routes of administration gave good relief in 50 per cent.[179] Eighty-three per cent obtained symptomatic relief with ergotamine and caffeine. Combinations of these two ingredients with pentobarbital sodium and Bellafoline (Cafergot P-B) are particularly effective in the anxious patient.[179–181] Others have found that chlorpromazine adds to the effectiveness of ergotamine.[180,182] Dihydroergotamine (D.H.E. 45) requires larger doses but is useful in patients who react poorly to ergotamine and is less likely to produce gastrointestinal symptoms and vascular side-effects.[182,183] In a limited study a tablet containing ergotamine tartrate, caffeine, belladonna alkaloids, and acetophenetidin (Wigraine) was found to be very effective in the symptomatic treatment of migraine.[184] A rectal suppository, containing ergotamine tartrate, caffeine, scopolamine aminoxide, and chloral hydrate has been recommended.[185] Blumenthal and Fuchs[186] have reported good results in headache patients with severe nausea and vomiting with a tablet containing ergotamine tartrate, caffeine, and cyclizine, an antiemetic.

Oral administration is the most practical route in patients without nausea and vomiting and in whom there is a definite prodromal period during which medication can be taken. Rectal suppositories, especially ergotamine tartrate with caffeine alkaloid (Cafergot) and those two ingredients with Bellafoline and pentobarbital sodium, have been very effective in those patients who cannot retain their oral medication.[178] Intravenous ergotamine tartrate (Gynergen) or dihydroergotamine is indicated when the headache reaches a maximal intensity in a short time, and 80 to 85 per cent success has been reported by this route.[176,179] Recently, Graham, Malvea, and Graham,[187] Speed,[188] and others,[185,189] have reported excellent results with orally inhaled ergotamine (Medihaler). This offers both rapid action and convenience but does give a slight increase in the incidence of side-reactions. Sublingual ergotamine tartrate also has been recommended.[190]

In a series of 1,200 patients given ergotamine tartrate and caffeine alkaloid orally or rectally, side-reactions occurred in 10 per cent.[179] The incidence rose to 16 per cent in 108 patients who were given ergotamine parenterally. However, 62 per cent of these reactions were nausea and vomiting; other reported reactions have included abdominal pain, leg cramps, vertigo, diarrhea, and thrombophlebitis.[191] Lippman[192] and others[182,193] have stressed that prolonged or overfrequent use of ergotamine actually may increase the frequency of attacks, either by tolerance or a rebound phenomenon. An editorial in the *British Medical Journal* advises that ergotamine compounds be used only for the severe migraine syndrome, and then as rarely as possible and in the smallest effective dosage.[194] On the other hand, Blumenthal and Fuchs[195] feel that many patients can tolerate higher doses of ergot derivatives than physicians normally are willing to give, and they illustrate their point with 4 patients who had been taking massive doses of ergotamine over a period of years without toxicity. Friedman, Von Storch, and Araki[179] have concluded, on the basis of their own cases and a review of the literature, that when well-known contraindications are observed, the problem of serious complications to ergotamine therapy becomes negligible.

The effectiveness of ergotamine in migraine apparently is related to the vasoconstriction which it produces in the extra- and intracranial branches of the external carotid artery. Pichler *et al.*[196] have shown that the action of the drug is on a peripheral site.

There are several alternatives for the patient in whom ergotamine gives no response or is contraindicated (pregnancy, coronary heart disease, peripheral vascular disease, impaired hepatic or renal function, thyrotoxicosis, and others). Results comparable to those obtained with ergot preparations have been reported with methylisooctenylamine (Octin) given orally or subcutaneously.[197] This drug does not produce gangrene and does not stimulate the myocardium but has caused transient hypertension. A multitude of other drugs have been recommended for the treatment of migraine, and although some may have been effective in an individual case, most have been shown over the years to be not useful. The use of some, such as nicotinic acid[198] and vitamins,[199,200] is inconsistent with our understanding of the mechanism of migraine; others, such as deanol,[201] dimenhydrinate (Dramamine),[202] urea,[203] and steroids,[193,204] offer little hope for the migraine patient. Hunter and Ross[205] and Vincent[206] have been able to reduce both headaches and drug intake by means of psychotherapy. Analgesics may be useful if cranial muscle spasm accompanies the attack.

In children with migraine, Burke and Peters[98] have found acetylsalicylic acid to be the drug of choice. Ergotamine is useful but less effective in children.

The symptomatic treatment of cluster headaches is made even more difficult by two factors. First, the early intensity and brief duration of the headache demand a drug with rapid action, and second, the frequency of the headaches during the bouts predisposes the patient to ergot toxicity when such drugs are used. Robinson,[94] in a thorough review of the subject, recommended treatment with vasoconstrictors, preferably ergotamine tartrate subcutaneously, before the headache has started. Graham, Malvea, and Graham[187] were able to relieve 36 per cent of the headaches in fifteen minutes and 71 per cent within forty-five minutes, by using aerosol ergotamine tartrate. An initial trial with antihistaminics[176] or with the inhalation of 100 per cent oxygen has been suggested. These failing, parenteral ergotamine tartrate, dihydroergotamine, or adrenalin may be required. Prolonged headaches are amenable to oral or rectal ergotamine tartrate and caffeine alkaloid.

It is the problem of preventing both migraine and cluster headaches which has received the greatest attention from investigators over the past five years. The major advance has been the introduction of 1-methyl-D-lysergic acid butanolamide (UML-491). Sicuteri,[207] Friedman,[208] Graham,[209] and Friedman and Losin[210] report a good response in 65 to 85 per cent of their migraine and cluster patients on prophylactic UML-491. The drug is administered orally in an average dose of 6 mg. per day. Side-reactions have occurred in about 12 per cent and consist primarily of giddiness, difficulty in concentration, nausea, and epigastric pain. Peripheral vascular insufficiency has been reported as a complication of UML therapy, but it has responded to the discontinuation of the medicine. UML has no direct effect on the peripheral circulation in animals,[208] but Dalessio *et al.*,[211] working in Wolff's laboratories, have shown that it may act by increasing sensitivity to endogenous and exogenous constrictor agents. Using UML in their experimental model employing the bulbar conjunctival vessels, they found that alone it did not produce any vascular changes but that it did increase the sensitivity of these vessels to local norepinephrine. Wolff's group also has shown that UML will markedly diminish sterile inflammatory reactions, although it has no effect on plasma or urine steroid levels. UML is a potent blocker of serotonin-produced edema, and Friedman and Losin[210] have suggested a local site of action, with the prevention of edema formation and/or the breakdown of polypeptide substances. Sicuteri[207] has reported success in the symptomatic treatment of migraine and cluster headaches with UML, but Graham[209] and Friedman[208] have not been able to reproduce these results.

Several other measures have been recommended for the prophylaxis of migraine. Ergotamine itself is too toxic for prolonged use, but success has been reported with a sublingual vasorelaxant (Hydergine) and oral drops of dihydroergotamine.[212–214] According to Greene,[215] urea is the drug of choice, and he also reports success with carbachol. A decrease in the frequency and severity of migraine also has been obtained with prochlorperazine (Compazine),[216,217] but in a double-blind study on 28 children with migraine, daily prochlorperazine produced no improvement.[218] Leyton[219] recommends a treatment program including chorionic gonadotropin injections, neostigmine (Prostigmin) desensitization, carbachol, and Bellergal, but the studies lack controls, and the results remain to be duplicated.

The effectiveness of histamine desensitization[176,178] for the prevention of cluster headache has been questioned by several authors.[94,100] Sicuteri *et al.*[220] have suggested a program of protected desensitization in which the headache is treated with 48-80, a histamine liberator, under the protection of a synthetic antihistaminic. Ergotamine tartrate is useful for prophylaxis in cluster headache, and Symonds[93] has described a program of self-administered intramuscular injections, 0.5 mg. three times a day for five days of each week.[221] Other routes advised include rectal suppositories at bedtime[222] and subcutaneous injections.[223]

MUSCLE CONTRACTION HEADACHE (TENSION). The symptomatic treatment of tension headaches with a sedative or analgesic alone will give only 50 to 60 per cent improvement[173] as compared to 40 to 45 per cent improvement with placebos. There is no significant difference in the results with a variety of analgesics, for example, A.S.A., A.P.C., Darvon, or codeine.[224,225] Good results can be raised to 71 per cent by using combinations of analgesics and sedatives or analgesics and tranquilizers.[173,226]

Tunis[202] found dimenhydrinate or triethanolamine to be successful in 80 per cent of 130 patients with vasculographic evidence of temporal artery constriction. Preliminary results with carisoprodol (Soma), a muscle relaxant with analgesic properties, have shown significant rates of improvement.[173]

The introduction of the tranquilizers has provided a means to reduce the patient's reaction to adverse stress, thus diminishing the frequency of such headaches. Chemically, these drugs can be classified into the following groups: phenothiazines, Rauwolfia derivatives, diphenylmethanes, substituted propanediols, and methaminodiazepoxide. Success, varying from 50 to 72 per cent improvement, has been reported with the tranquilizers.[227–229] Best results have been reported with methaminodiazepoxide (Librium) and with meprobamate (Miltown, Equanil). The side-effects of the tranquilizers have consisted of nausea, fatigue, and dizziness, and can be counteracted with amphetamine or by taking the tranquilizers at mealtime.

A group of drugs, commonly referred to as antidepressants or mood-elevators, has been found to be useful in many patients with tension headaches. Most of these are monoamine oxidase inhibitors and hydrazine analogues of iproniazid.[230,231] Examples, in order of decreasing activity, include isocarboxazide (Marplan), phenelzine (Nardil), and nialamide (Niamid). Their effect is usually to stimulate psychomotor activity, although in some patients they produce sedation or a relaxing effect.

Psychotherapy should be considered in the chronic forms of tension headache.[232] The therapy need not be formal; the practitioner is well suited to offer supportive psychotherapy, and the results may be gratifying. The available means of treatment can be offered in combination or singly depending on the particular requirements of the patient.

HYPERTENSIVE HEADACHES. Reserpine appears to be the drug of choice for hypertensive headaches, producing relief in 77 per cent of those with elevated blood pressure, but only in 49 per cent of the tension group and 45 per cent of the migraine group.[233] The drug caused an identical blood pressure drop in those who were not relieved of headache. Barrett and Hansell,[234] however, have found reserpine to be effective in all vascular headaches. Potassium thiocyanate also has been recommended.[176] Ellis[235] feels that sympathectomy will relieve headache in the majority of cases of essential hypertension.

POSTSPINAL-PUNCTURE HEADACHE. Considerable attention has been devoted over the past five years to the problem of postlumbar puncture headache, and many suggestions have been offered. The average incidence of headaches in 20 to 30 per cent of the patients undergoing spinal tap has been reduced to 5 per cent or less by eighteen hours of bed rest,[236] lying in the prone position for three hours,[237] hydration with 1,000 cc. of Ringer's lactate with 5 per cent glucose and intravenous vitamins,[238] intramuscular Pitressin,[239] A.S.A. and ergotamine tartrate with caffeine alkaloid,[240] 50 to 100 mg. of 1 per cent procaine intravenously,[241] and by the injection of 10 to 120 cc. of saline into the caudal canal.[242] Dihydroergocristine or the vasorelaxant mentioned have been found to be useful in both spinal headache and postconcussion headache.[243] Fly *et al.*[244] have found that the volume of gas introduced in pneumoencephalography affects the duration of headache but not its severity. Cortisone, 50 mg. every six hours orally, to a total of 400 mg., will relieve those postpneumoencephalogram headaches which have an organic basis.

ATYPICAL FACIAL NEURALGIA. The injection of trigger points with 2 per cent procaine has been recommended by Reichert[245] for the treatment of atypical facial neuralgia. Ray,[246] in a review of numerous neurosurgical procedures, has concluded that the results of surgical treatment of atypical facial neuralgias are discouraging.

TEMPORAL ARTERITIS. Treatment has consisted of biopsy of the temporal artery and relief of the head pain frequently follows such a procedure. A local injection with procaine also has produced relief of the head pain.[247] Birkhead, Wagener, and Shick[162] reported on 55 patients with temporal arteritis: 21 patients had pain in the head when treatment was started. The headache of 18 patients was ameliorated within the first forty-eight hours of treatment. Corticosteroids were used in the 55 patients: 52 patients received cortisone, and 3 patients received prednisone. The authors concluded that corticosteroids are indicated in all patients with temporal arteritis. Treatment should begin at the time the diagnosis is made and should be continued until the symptoms of the disease have subsided and the erythrocyte sedimentation rate returns to normal. The drug should be discontinued gradually and the patient observed for relapse. The main object of corticosteroid administration is to prevent progression of ocular lesions; if untreated, the patient may progress to bilateral blindness.

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Unexplained infant deaths involve several factors

Although the problem of sudden and unexpected death in infancy remains unsolved, a postmortem study of 29 infants and a review of the literature by J. D. Collins and P. G. Piper in the October, 1961, issue of the *Wisconsin Medical Journal* suggest that the mechanism of death in these patients depends on a number of factors, rather than a single cause.

Complete autopsies, including examination of the central nervous system, were performed. Cultures for bacteria in blood, lungs, spleen, and meninges were taken routinely. In some cases, viral studies were made on tissue and body fluid samples; serum protein electrophoretic studies were made in 3 cases. Routine hematoxylin and eosin stains were done, along with special stains when indicated.

The authors found in their own series, and in those of most other investigators, a histologic complex consisting of emphysema, pulmonary congestion and edema, interalveolar thickening with an increased mononuclear infiltration, hyperplasia of the bone marrow, and reactive hyperplasia of the lymphoid system.

Although the histologic picture suggests infection, the authors feel that the small number of viral agents isolated as well as lack of positive bacterial cultures do not support this view. A selective factor based on the maturity of the child, rather than a single agent, may be the etiologic factor.

Since the majority of children do not die from suffocation, physicians are urged to refrain from attributing an unexplained death to accidental suffocation. Such a diagnosis is unfair to the parents and may cause guilt feelings. They urge that autopsy include examination of all viscera and the central nervous system, thorough bacterial and viral cultures, and serum protein electrophoretic studies. It is suggested that all circumstances prior to death be investigated by the police, social worker, and family physician.—*Pediatric Currents, Ross Laboratories*

Clinicopathologic Conference

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Conducted by JOHN W. PICKREN, M.D.
Discussed by ROBERT TARAIL, M.D.

Medical and Surgical Complications of Diabetes Mellitus

Case history

At the age of forty-five years the patient developed irregular vaginal bleeding associated with clots. On physical examination the only abnormal findings were a scar of the cervix and small leiomyomas of the uterine fundus. Biopsies were taken and were reported as hyperplastic endometrium and chronic cervicitis. A urinalysis showed a trace of reducing substance and no albumin. Two tubes tandem of 50 mg. of radium were inserted into the uterus, and she received 1,600 mg. hours of irradiation. At the age of fifty years she was noted to have diabetes, and over the ensuing fourteen years she required globin insulin of up to 35 to 40 units daily.

At the age of sixty-four years she developed a productive cough, epigastric pain, and vomiting. A chest roentgenogram showed several round infiltrations in both lung fields; the largest was about 3 cm. in diameter. The diaphragmatic leaflets were clear and regular. The heart was not enlarged, but there was some rounding of the left ventricle. The aorta was slightly tortuous. She was afebrile. Her blood pressure was normal on most occasions except for hypertensive readings on two occasions, the highest value being 205/100.

A funduscopic examination showed an exudate on the right and arteriosclerotic vessels bilaterally. Her heart and lungs were normal on physical examination. An examination of the abdomen revealed a large, ill-defined, cystic mass in the right upper quadrant. A sigmoidoscopic examination was unrevealing for a distance of 17 cm. The hemoglobin was 9.1 Gm. per 100 ml., and the leukocyte count was 8,500 per cubic centimeter with a differential of 4 stab forms, 51 segmented neutrophils, and 45 lymphocytes. Several urinalyses revealed a 4 plus albumin and a 3 to 4 plus reducing substance. Acetone was noted on one occasion. A serologic test for syphilis produced negative results. The fasting blood sugar ranged from 242 to 498 mg. per 100 ml. The blood nonprotein nitrogen ranged from 37 to 51 mg. per 100 ml. The serum electrolytes and plasma proteins were normal. Her serum carbon dioxide content was 23 millimols per liter. A flat x-ray film of the abdomen showed that both kidneys were well outlined and normal in size, shape, and position. Intravenous and retrograde pyelograms, a cholecystogram, a barium enema, and an upper gastrointestinal x-ray study disclosed no abnormalities. An electrocardiogram showed flat or slightly inverted T waves in all limb leads and in V_5 and V_6. The QRS waves were of high voltage in the chest leads. These changes were interpreted as consistent with left ventricular hypertrophy.

Increasing vomiting and abdominal distention appeared, and crystalline insulin was substituted for globin insulin in preparation for a diagnostic laparotomy. She was given digitalis. Chlorpromazine hydrochloride was administered without relief of the emesis. An abdominal exploration was carried out. A greatly enlarged liver was seen, and a biopsy showed normal hepatic architecture. The enlarged liver seemed to depress the right kidney, tilting its lower pole forward. The only other abnormal findings were small nodules on the uterus which were biopsied; they proved to be small leiomyomas.

The blood pressure fell and remained in the range of 90/50 for several hours. On the first postoperative day she was given 2 L. of 5 per cent dextrose in water. Twenty-five units of crystalline insulin were added to each bottle of infusion. During this day she complained of dizziness and lethargy. On the second postoperative day the patient continued to vomit and complained of feeling giddy as though she were going into insulin shock. Her respirations were deep but regular, her face was flushed, and she was very restless. The carbon dioxide was 8 millimols per liter; serum chloride 73 mEq., serum sodium 118 mEq., and serum potassium 6.5 mEq. per liter; nonprotein nitrogen 121 mg. per 100 ml.; and blood sugar 1,400 mg. per 100 ml. Her urine contained 4 plus sugar and acetone. Treatment for diabetic acidosis was initiated. She was oliguric for twelve hours. In a period of twenty-four hours a total of 5.3 L. of fluid, 133 mEq. of sodium bicarbonate, 335 mEq. of sodium chloride, and 500 units of crystalline insulin were given to her. Seven hours after initiation of these therapeutic measures her blood sugar had dropped to 500 mg. per 100 ml. After twenty-four hours the blood sugar was 130 mg. per 100 ml., and the nonprotein nitrogen had fallen to 92 mg. per 100 ml. The serum chloride rose to 90 mEq. and the serum sodium to 128 mEq. per liter, and the carbon dioxide to 23.2 millimols per liter. The serum potassium fell to 3.5 mEq. per liter. There was no significant glycosuria. Another electrocardiogram was performed, and it showed several changes from the previous tracing with a depression of the S-T segment in leads I and aVl, an elevation of the S-T segment in leads III and aVf, and a slight inversion of the T waves in leads II, III, and V_6. These were interpreted as showing myocardial anoxia and digitalis effect. She developed numbness in the right leg, and rales were heard at the bases of both lungs. The left dorsalis pedis pulse was not palpable, but the left leg appeared normal in all other respects. On the fifth postoperative day there was an episode of flushing, sweating, and weakness during a glucose infusion. These symptoms were relieved by the intravenous administration of 20 ml. of 50 per cent dextrose. On this day the nonprotein nitrogen was 53 mg. per 100 ml., and the blood sugar was 336 mg. per 100 ml. During the sixth postoperative day the patient appeared alert and in no distress. While sitting in her bed, she suddenly fell back, became cyanotic, and her pupils dilated rapidly. Resuscitation procedures failed, and the patient was pronounced dead.

Discussion

Robert Tarail, M.D.: Before proceeding, may I see the x-ray films?

I. Jakimow, M.D.: A roentgenographic examination of the chest on admission showed nodular densities in both lung fields (Fig. 1). The largest was located in the lower lobe of the left lung. A small nodular density near the upper aspect of the left hilum can be localized from the lateral projection in the upper lobe of the left lung. A third nodular density was present in the middle lobe of the right lung close to the hilum and close to the minor fissure. The films do not reveal pleural reaction or a pathologic condition of the bone. The heart and mediastinum were within normal limits.

Radiologically, these findings may be the result of many things, such as transient eosinophilic infiltration, Wegner's granulomatosis, infarction, gumma, or abscess. All of these diseases probably can be ruled out by the clinical and laboratory findings in this case.

There are two other more likely possibilities: First, it may represent multiple granulomas. The absence of calcification is a point against this diagnosis. Second, it may represent multiple pulmonary metastases. Statistically one should consider pulmonary

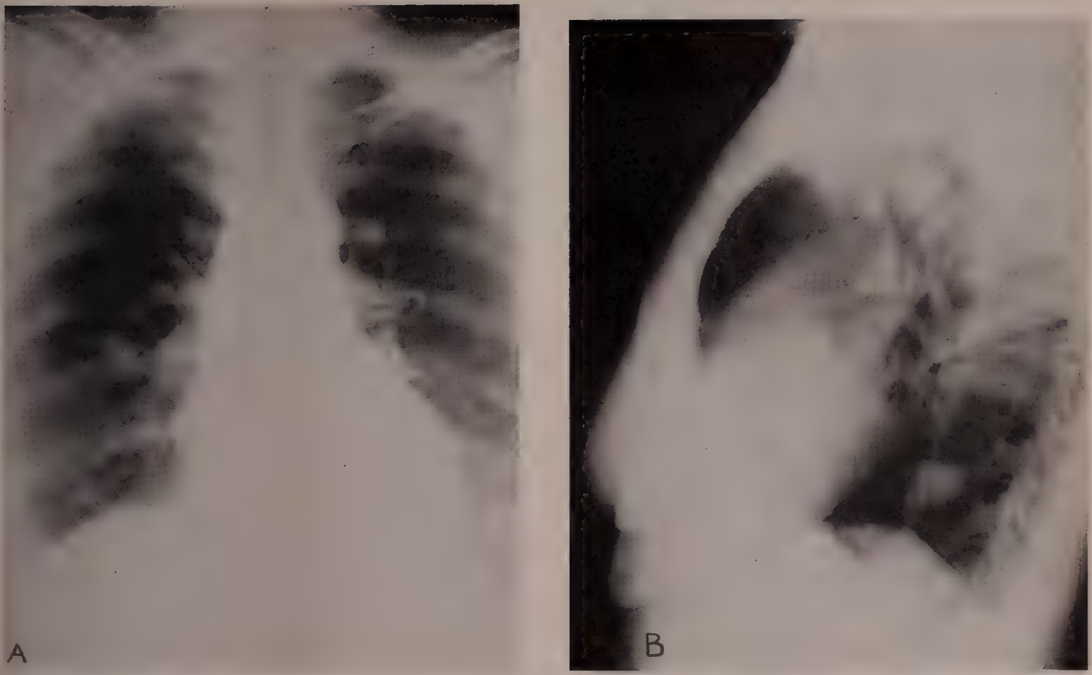

FIGURE 1. (A) Posteroanterior view of chest shows nodular formations in the left lower lobe, left upper lobe, and right middle lobe of the lungs. (B) Lateral view of chest shows same findings. These pictures are consistent with the findings in patients with multiple lung metastases.

metastases from an inapparent primary site as the most probable disease that would cast shadows of this type.

The patient also had other radiologic studies. Examinations of the colon, gallbladder, urinary tract, and upper gastrointestinal tract revealed essentially normal findings.

Dr. Tarail: I hope you agree with me, Dr. Jakimow, when I say that the absence of cardiac enlargement as reported in the protocol does not exclude cardiac hypertrophy at autopsy. In a patient who died recently we felt that there was impressive clinical evidence of coronary atherosclerosis and hypertensive heart disease. X-ray films of the heart and fluoroscopy did not disclose enlargement. At autopsy the heart weighed 600 Gm., and the patient weighed only about 40 Kg. In regard to the round shadows in the lung fields seen on x-ray examination, I am unable to propose a definite diagnosis. I appear to have good company, since Dr. Jakimow exercised similar reserve. I would contend that the infiltrations do not bear much relationship to the important clinical aspects of this case.

Prior to Dr. Jakimow's description of the roentgen findings, I had surmised from the protocol that the pulmonary lesions were most consistent with a granuloma, such as inactive tuberculosis. But after having heard Dr. Jakimow's differential diagnosis, and having seen the films, I am inclined to agree with his preference for metastatic cancer. Intelligent speculation concerning the nature of a possible primary tumor is made difficult by the absence of anything in the protocol to suggest a primary site.

Now for some of the cardinal problems. In the first place I think it is quite clear that our patient had diabetes mellitus. At the end of the first paragraph of the protocol we learn that "At the age of fifty years she was noted to have diabetes, and over the ensuing fourteen years she required globin insulin of up to 35 to 40 units daily." The protocol documents the presence of persistent hyperglycemic glycosuria, thereby fulfilling a salient prerequisite for the diagnosis of diabetes mellitus.

Also portrayed in the protocol are several of the tricky diagnostic dilemmas posed by the diabetic patient. For the moment we shall single out the mass in the liver which evidently perplexed the patient's physicians. The gamut of diagnostic studies culminated in a laparotomy. An enlarged liver was found.

Why do patients with diabetes develop hepatomegaly? For decades now, an evanescent, recurring enlargement of the liver of the "now you see it, now you don't" variety has been found during the course of diabetic acidosis and coma. This is obviously an unsuitable explanation in the present case. The greatly enlarged liver is described in the protocol as having a normal architecture histologically. Such livers have been observed in patients with well-controlled diabetes with normal conventional tests of hepatic function. The nature of this hepatomegaly is poorly understood. Fatty metamorphosis has been described on occasion. In other instances glycogen deposition may account for the phenomenon.

Next, we must consider what kind of kidney disease this patient had. First, I believe the hypertension was of renal origin. Second, the intense proteinuria is consistent with a nephrotic syndrome. The latter, as you recall, is defined as having the following components: proteinuria, hypoproteinemia because of a lowered serum albumin, edema, and elevation of serum cholesterol. Our patient had proteinuria, but edema and hypercholesteremia are not mentioned. The serum proteins are described as normal. This may have been but one measurement, and perhaps the total protein concentration was in fact normal at that time because of dehydration.

Concentrations of blood nonprotein nitrogen as high as 121 mg. per 100 ml. point to advanced renal failure. Superimposed dehydration and diabetic acidosis probably contributed to the elevations of nonprotein nitrogen. Various x-ray studies of the kidneys disclosed no abnormalities, consistent with the varieties of renal disease which our patient probably had.

The renal findings fit the diagnosis of capillary glomerulosclerosis (Kimmelstiel-Wilson syndrome) unequivocally. As you recall, this disorder is comprised, at the clinical level, of diabetes associated with proteinuria, a lowering of plasma albumin, edema, arterial hypertension, and, frequently, abnormally high alpha-2 globulin. Usually there is associated diabetic retinopathy and neuropathy. Statistically, the chances that our patient had diabetic capillary glomerulosclerosis are overwhelmingly high. For the sake of completeness we may list other, very unlikely, causes of nephrotic syndrome: chronic glomerulonephritis; collagen disease, especially disseminated lupus; amyloidosis; secondary syphilis; allergic reactions to drugs (especially those used in treating epilepsy), to weeds, and to bee stings; renel vein thrombosis; constrictive pericarditis; and the "pure lipoid nephrosis" of childhood.

Although no x-ray evidence of urinary tract obstruction was found, the patient was oliguric for twelve hours. When authentic oliguria supervenes during the course of diabetes, it is well to consider the possibility of pyelonephritis so severe as to produce necrosis of renal papillae (necrotizing papillitis). I will exclude this diagnosis because of the brevity of the oliguria and other features of the subsequent course. However, I do believe on statistical grounds that our patient did have chronic and/or acute pyelonephritis despite the fact that pertinent data are not cited in the protocol.

Now for a little vignette. At necropsy, the kidneys may have shown "glycogen nephrosis." Although this occurs in less than 10 per cent of diabetic patients, it is perhaps more common in, and reflects, excessive hyperglycemia and intense glycosuria. If the kidneys were stained for glycogen, I would expect Dr. Pickren to find infiltration of renal tubular epithelial cells with this substance. Interestingly enough, there is no known functional correlate of this histologic finding.

My final venture into the thorny path of renal diagnosis predicts the presence of benign nephrosclerosis.

Was there diabetic retinopathy? The protocol states: "A funduscopic examination showed an exudate in the right eye and bilateral arteriosclerotic vessels." If our assumption of diabetic glomerulosclerosis is correct, it is very likely that diabetic retinopathy was present. Moreover, a histologic examination of the retina would likely confirm this hypothesis. The high points of this vascular disorder include: (1)

The characteristic, early aneurysmal dilation of finer retinal vessels, particularly in the perimacular area. A careful ophthalmoscopic examination at this stage shows only clusters of tiny red spots which simulate punctate hemorrhages. (2) Later, frank hemorrhages, waxy, and cotton-wool exudates develop. Visual impairment tends to wax and wane with spontaneous increase and remission of these lesions. Therefore, at this stage it is "convenient" to study the effects of widely divergent therapeutic regimens, for if this is done without suitable controls, an improvement of vision is almost inevitable using any program which permits the patient to survive long enough. (3) Proliferating retinopathy coupled with advanced atherosclerotic changes may be regarded as the final, irretrievable stage.

Data concerning diabetic neuropathy are conspicuous in the protocol by their absence. Nevertheless, I contend that neuropathy was present. This is based on an almost invariable association of the Kimmelstiel-Wilson syndrome, diabetic retinopathy, and neuropathy. This triad has been epitomized by the term "diabetic triopathy," since the three phenomena may be considered as manifestations of the common denominator of vascular disease in diabetic patients.

The currently insoluble problems of diabetic vascular disease usher in our discussion of this patient's heart ailment. I feel quite confident that a heavy heart was found at autopsy for reasons already considered earlier. I believe that the two major causes of heart disease were arterial hypertension and atherosclerosis of the coronary vessels. It must be rare, indeed, for a sixty-four-year-old who had diabetes for at least fourteen years to escape significant coronary atherosclerosis.

The description of the first electrocardiogram does, indeed, support the interpretation of "myocardial disease and possibly left ventricular hypertrophy." The nasty episode of hypotension following the abdominal exploration and liver biopsy probably represented hemorrhagic and/or traumatic shock rather than myocardial infarction or a sudden decrease of coronary blood flow as primary events.

A summary of differences in the second electrocardiogram when contrasted with the first suggests: T_1 is no longer inverted or flat, and there is no T inversion in V_5; S-T segments have become depressed in leads I and aVl and elevated in leads III and aVf. These findings are not those of potassium deficiency, and I agree with the interpretations in the protocol, namely, myocardial anoxia and digitalis effect. Moreover, it is well to recall at this point that digitalis is extremely versatile, on occasion, in producing all manner of electrocardiographic changes even in the absence of expected ST-T depressions.

To continue in a vascular vein: "She developed numbness in the right leg, and rales were heard at the bases of both lungs. The left dorsalis pedis pulse was not palpable." The failure to feel this pulsation has little meaning unless we know whether or not it was palpable earlier in the game. Bilateral basal rales raise the question of a failing left portion of the heart. Finally, numbness of the right leg may suggest phlebothrombosis or neuropathy.

Following the laparotomy the patient developed a constellation of metabolic and electrolytic disturbances which are both unusual and puzzling. On the first postoperative day the carbohydrate intake was only 100 Gm. which is really insufficient. To meet metabolic requirements an intake of 200 to 300 Gm. of glucose with appropriate crystalline insulin dosage is usually necessary. I do think that the short supply of glucose explains the postoperative hypoglycemia.

However, by the second postoperative day the blood sugar had risen to 1,400 mg. per 100 ml., an extraordinary value, and the patient was in diabetic acidosis. I am not sure when the blood specimen was drawn in relation to the time of a glucose infusion. It is wholly likely that the value is artifactitiously high because the specimen was taken while an infusion was running in. Nonetheless, the chemical evidence of major derangements of electrolyte metabolism and acidosis is striking. The elevated nonprotein nitrogen level is primafacie evidence of acute renal failure coupled with dehydration. The striking depression of serum bicarbonate reflects the combined effects of diabetic acidosis and renal failure.

The tremendous reduction of serum

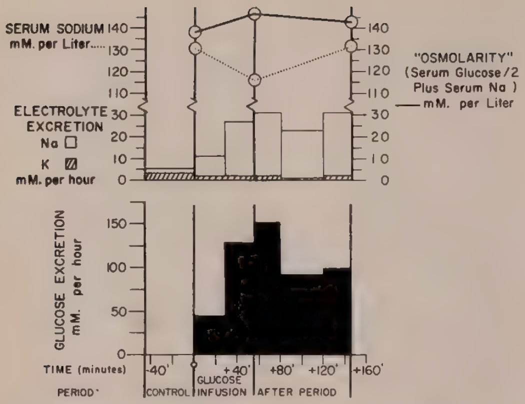

FIGURE 2. Effects of massive injection of glucose on serum sodium and osmolality.

sodium and chloride deserves further comment at least because of its rarity in diabetic acidosis. Following are the mechanisms of hyponatremia in diabetic acidosis which may be involved in this situation.

1. Extrarenal loss of sodium
2. Renal losses
    - Glycosuria, ketonuria
    - Salt wastage
    - Diuretics
3. Hyperglycemia
4. Hyperlipemia, lactescence
5. Adrenocortical failure
6. Dysfunction of cellular membranes
7. Dilution

Of these factors, only the first three merit serious consideration in our patient. Thus, she had the characteristic gastrointestinal loss of sodium and chloride by vomiting, probably coupled with limited or absent intake of these ions. Salt loss via the urine probably proceeded rapidly because of intense glycosuria and ketonuria, but I strongly doubt that salt wastage accompanying renal failure played a role, nor did the use of diuretics.

So far we have failed to account for the hyponatremia. Although vomiting coupled with intense glycosuria and ketonuria are regular concomitants of diabetic acidosis, they simply do not lead per se to hyponatremia of more than a slight degree because of correlative changes in the water metabolism. The outlandish hyperglycemia (1,400 mg. per 100 ml.), on the other hand, is almost certainly the primary mechanism. Why do I say this?

The role of elevation of plasma glucose in generating reduced concentrations of sodium and chloride was investigated some years ago by Seldin and myself[1,2] in normal subjects and in patients with diabetic acidosis. Figure 2 exemplifies our findings. Serum sodium during water diuresis immediately prior to the intravenous infusion of glucose in a normal subject was 131 millimols per liter. Our index of plasma osmolality came to 138 millimols per liter. Hypertonic glucose was then injected rapidly and produced a precipitous fall of sodium to 116 millimols per liter. This was associated with rapid elevations of plasma sugar and osmolality. After the recovery period the plasma glucose fell, there was a slight fall in our crude index of osmolality, and sodium rose to its control concentration.

We have inferred from such observations that the cataclysmic drop in concentrations of plasma sodium and chloride are related significantly to an increase in the osmolality of extracellular fluid induced by the load of glucose. This increased osmolality caused by glucose results in the withdrawal of water from intracellular fluids, dilution of extracellular fluid, and lowers plasma sodium and chloride.

An important lesson in regard to treatment is implicit in these observations and in our studies of this phenomenon in diabetic acidosis.[2] Under the latter circumstance, we have shown that plasma osmolality and effective osmotic pressure is increased, despite marked hyponatremia, because of the large increment of glucose in the plasma. Therefore, vigorous therapy with sodium salts, such as occurred in the present case, must be deferred until insulin has produced a major reduction in the blood sugar. Otherwise, a large sodium load during massive hyperglycemia may serve only either to perpetuate or to increase intracellular dehydration.

Now for the terminal episode—sudden death on the sixth postoperative day. Hamman[3] aptly defined sudden death as "death coming quickly and unexpectedly." It "need not be instantaneous nor can it be long delayed." It "comes reasonably quickly under circumstances when its immediate arrival is unexpected." The death of our patient fulfills these criteria all too well.

TABLE I. Leading causes of death in diabetes mellitus

Causes	Period of Time: Naunyn-Allen Era 1898 to 1922 (Per Cent)	Banting Era 1922 to 1950 (Per Cent)	1950 to 1957 (Per Cent)
Acidotic coma	47.7	4.5	1.2
Cardiorenovascular (atherosclerotic)	21.1	62.8	75.9
Infections	11.2	10.0	5.2
Cancer	3.2	9.2	10.4
Tuberculosis	4.9	2.7	0.7
Other*	11.9	10.8	6.6
Total patients	1,162	11,877	5,016

* Includes insulin reactions, other circulatory and rheumatic heart disease, accidents, inanition, suicide, and unknown.

Table I[4] provides an interesting historical perspective of the causes of death in patients with diabetes over the past fifty years. Before the achievements of Banting and Best, which culminated in insulin treatment, death from uncontrolled diabetes predominated. Cardiorenovascular deaths were comparatively infrequent, although prominent. But in clear contrast, complications attributable directly to the immediate consequences of uncontrolled diabetes (acidosis, infection, and tuberculosis) accounted for 64 per cent of the deaths. Before insulin became available the diagnosis of diabetes in children particularly and of severe diabetes in adults had disastrous implications for the patient and his family tantamount to those of certain forms of cancer today.

The life-saving gift of insulin during the Banting era (Table I) curtailed the latter complications dramatically to 17 per cent at the expense of the equally dramatic upswing of vascular deaths to 63 per cent. Finally, we wrestle currently with the fact that death in diabetes, as probably exemplified by our patient, may be ascribed in three fourths of the cases to cardiorenovascular phenomena. For the most part these are atherosclerotic in their genesis. Thus, advances in the chemotherapy of infections and in the management of the disturbed carbohydrate metabolism presumably have relegated deaths from acidosis, "nonspecific" infection, and tuberculosis to the low figure of 7 per cent.

Returning to the terminal event in our patient, the recollection of electrocardiographic evidence suggestive of myocardial anoxia stands out. My opinion that sudden death resulted from myocardial infarction and coronary thrombosis is based on this antemortem evidence of myocardial anoxia coupled with the common knowledge of the high incidence of coronary atherosclerosis in elderly diabetic patients. Massive pulmonary embolism is a second, less likely, possibility.

In his classic paper Hamman[3] points out that if violence, trauma, and poisoning are excluded, about 9 out of 10 cases of sudden death are of cardiovascular origin, such as heart failure, hemorrhage, arterial embolism, and arterial thrombosis. Further, he says that 65 per cent of all sudden deaths are of cardiac origin, and 65 per cent of these are due to disease of the coronary arteries.

Clinical diagnoses

1. *Diabetes mellitus*
2. *Metastases to lungs*
3. *Myocardial infarction or pulmonary embolus*

Dr. Tarail's diagnoses

1. *Diabetes mellitus*
2. *Hepatomegaly of diabetes mellitus*
3. *Diabetic with capillary glomerulosclerosis*
4. *Diabetic retinopathy*
5. *Diabetic neuropathy*
6. *Diabetic "triopathy"*
7. *Pyelonephritis*
8. *Benign nephrosclerosis*
9. *Glycogen nephrosis*
10. *Pulmonary infiltrations, ? metastases, ? granuloma*
11. *Leiomyomas of uterus*

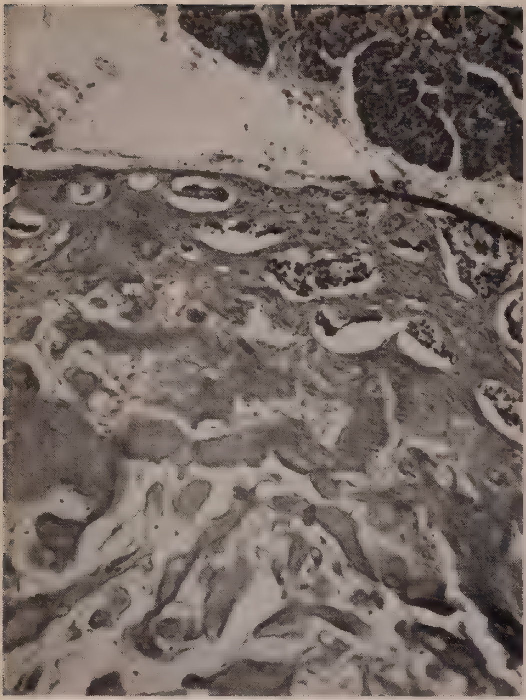

FIGURE 3. Photomicrograph of pancreas shows a partially hyalinized, enlarged islet of Langerhans. Note proliferation of cells on periphery of the mass and central fibrosis (hematoxylin and eosin stain).

12. Hypertensive coronary atherosclerotic heart disease

13. Sudden death on the basis of either myocardial infarction or massive pulmonary embolism

Pathologic report

John W. Pickren, M.D.: I must compliment Dr. Tarail on his astuteness and prescience. He has "stolen the thunder" from the pathologist by predicting most of the abnormal anatomic findings. These abnormalities are those frequently found in association with the physiologic defect of diabetes. Diabetes is a strange disease in that one generally assumes that in a malady of apparent hormone dysfunction an anatomic abnormality should be recognizable in the organ of secretion. But in diabetes this is not always true. It is apparent that the diabetic state may result from an imbalance in the normal interaction of the islet pancreatic cells, anterior pituitary, and adrenals. Experimentally, severe and fatal diabetes can be produced by destroying the beta islet cells either by extirpating the pancreas as performed by von Mering and Minkowski in 1889[5] or by the administration of alloxan which selectively kills beta islet cells. However, autopsy studies on diabetic cadavers have shown that more often than not the islets are apparently normal. Hyalinization, necrosis, and fibrosis of the islets may be seen.

In this patient the only islet cell deviation from normal was the presence of one large islet representing either an adenoma or hyperplasia. The central portion was partially fibrosed and calcified (Fig. 3). Warren[6] states that islets do not submit tamely to hyalinization since the growth of islet cells occurs during the hyalinization process. This enlarged islet may represent such a phenomenon. The acinar tissue of the pancreas was the site of considerable change. Acute and chronic fat necrosis was present. Such involvement may have been the cause of the epigastric pain and emesis perceived by the patient, but it is in no way related to her diabetes.

In this patient's kidneys either nodular or diffuse glomerulosclerosis involved practically every glomerulus. Intercapillary glomerulosclerosis was first described by Kimmelstiel and Wilson in 1936.[7] Since that time it has been learned that the lesion is almost pathognomonic of diabetes of long duration (ten years). It rarely occurs in patients without diabetes.[8] There is a definite male preponderance. In the nodular form microscopic accumulations of acellular material are deposited as spheroid masses between the glomerular capillaries. In the diffuse form similar material is deposited evenly between the glomerular capillaries.[9] Both types of deposition were present in this patient (Fig. 4). Glycogen nephrosis was not present. A sufficient interval had elapsed between the episode of hyperglycemia and death for any increased deposition of glycogen into the epithelial cells of the convoluted tubules and Henle's loop to revert to normal.

This patient's heart weighed 450 Gm., a definite enlargement. Both the left and right ventricles were thickened, the left to 1.8 cm. and the right to 0.5 cm. In association with the enlargement of the heart, the walls of arteries throughout the body, but

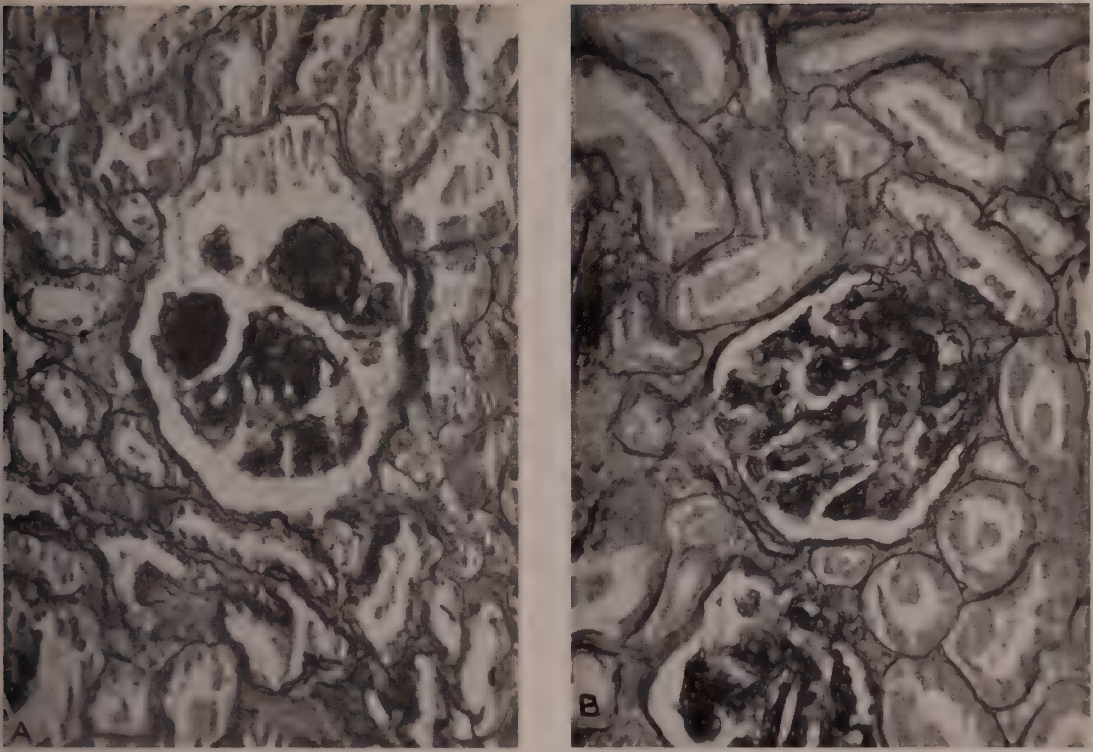

FIGURE 4. (A) Photomicrograph of kidney discloses nodular spheroid masses of acellular material deposited between the glomerular capillaries. (B) Deposition of similar amorphous material but in a diffuse pattern between the glomerular capillaries. (Periodic Acid-Schiff).

more pronounced in the kidneys (nephrosclerosis), were thickened from a deposition of fibrinoid material beneath the intima. These changes are in agreement with the two hypertensive blood pressure readings given in the protocol. Hypertension is seen in over 50 per cent of patients with diabetes. In addition to the hypertension, this patient also suffered from myocardial infarction. On the posterior aspect of the left ventricle the epicardium showed a 5 by 7 cm. area of congestion and fine fibrinous exudate. The infarction lay deep to this area and involved the posterior myocardium and the interventricular septum. The central portion of the infarcted tissue was pale yellowish-grey, and the margins were hemorrhagic. I would estimate that the infarct was of four to ten days duration. The posterior descending branch of the right coronary artery was occluded completely by a recent thrombus. The other coronary vessels showed only minimal sclerotic changes.

In addition to the infarctions of the heart, others were found. In the rectosigmoid, approximately 19 cm. from the anus, gross congestion and microscopic epithelial necrosis were associated with thrombotic occlusion of the veins. A small infarct occurred in the anterior lobe of the pituitary gland. These infarctions were similar in duration to the one in the heart.

Now, what were the lesions in the lungs that brought the patient to the hospital? They were epithelioid granulomas; the largest measured 5 cm. in maximum diameter. Stains and study for acid-fast bacilli and fungi did not disclose the offending agent. However, it is known that tuberculosis occurs two to three times as frequently in diabetic patients as in individuals without diabetes.

The liver was normal in size. Its earlier enlargement was apparently of the evanescent type about which Dr. Tarail spoke. The leiomyomas of the uterus were insignificant.

In summary, this patient had clinical and anatomic changes suggestive of diabetes. Most of her other difficulties may be related to this disorder. Her terminal episode was the result of coronary occlusion with cardiac infarction.

Anatomic diagnoses

1. *Diabetes mellitus, clinical*
2. *Capillary glomerulosclerosis (nodular and diffuse)*
3. *Benign nephrosclerosis*
4. *Hypertensive cardiovascular disease*
5. *Coronary occlusion with myocardial infarction*
6. *Infarctions of rectosigmoid and pituitary*
7. *Acute and chronic pancreatitis*
8. *Granulomas of lung*
9. *Leiomyomas of uterus*
10. *? Hyperplasia or ? adenoma of islet of pancreas*

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Meckel's diverticulum in infants and children

According to a report by Wellington Hung, M.D., in the November, 1961, issue of *Clinical Proceedings of the Children's Hospital of the District of Columbia,* 22 children with Meckel's diverticulum seen over a period of seven and one-half years were analyzed for age, sex, symptoms, histology, and other relevant data. In 3 of these patients, the diverticulum was an incidental finding during surgery undertaken for other indications (1 herniorrhaphy and 2 appendectomies); in the other 19 diverticulectomy was the primary intent of the procedure, based on characteristic symptoms. The complications which may occur in Meckel's diverticulum to produce the symptoms include infection, peptic ulceration, hemorrhage, perforation, intestinal obstruction, volvulus, intussusception, and neoplasm. Meckel's diverticulum is a potential source of danger in the abdomen, whereas removal of an uncomplicated diverticulum is simple and safe. The condition should be looked for when at operation the clinical findings that led to the procedure cannot be otherwise explained. If found in the course of an operation, it should be removed if there are not contraindications to additional surgery. In this series there were no deaths, and there have not been any readmissions for recurring symptoms.

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Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

Urogenital Complications in Diabetes

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COMPLICATIONS involving the genitourinary tract are frequent in patients with diabetes and represent an important aspect of their long-term care. The urologic entities described herein are not restricted to diabetes. However, they occur more often in the diabetic patient, are more serious, present altered clinical manifestations, and unfavorably influence the diabetic status itself. Effective treatment must be etiologically oriented, prompt, vigorous, and often of prolonged duration.

For purposes of classification, one can divide urogenital complications into those primarily the result of infection and those related to the obstructive effects of diabetic neuropathy on the urinary passages. Clinically, these mechanisms are usually combined in varying degrees, one leading to and reinforcing the other.

The specific Kimmelstiel-Wilson nephropathy is the subject of a prior article in this series and will not be included in this discussion.[1]

Acute pyelonephritis

Acute pyelonephritis is a common and serious complication of diabetes. Significant acute renal infection has been found in approximately 20 per cent of postmortem examinations of diabetic patients as compared with only 4 per cent of a comparable group of nondiabetic patients.[2–6] Because of the paucity of urinary complaints and physical findings, the pyelonephritis was often clinically unsuspected in the diabetic patients, although it was a principal cause of death.

Acute renal infection is more prevalent in the older-age group, with women predominating. The onset is usually sudden with systemic manifestations such as chills, vomiting, drowsiness, and prostration. Sepsis may be confirmed by the finding of a gram-negative bacteremia. Although the patient is seriously ill, urinary symptoms such as loin pain, costovertebral angle tenderness, and dysuria are not necessarily striking. The blood urea nitrogen and white blood cell count are elevated. Pyuria is variable and often disproportionately minor. Usually gram-negative pathogens are found in the urine, but enterococci and Staphylococcus aureus are also causative agents.

Unless adequately treated, the disease process may progress relentlessly. Phlebitis of the renal veins and perinephric extension can occur. Renal function is regularly impaired. Insulin requirements increase rapidly, and diabetic control becomes difficult to maintain. The combination of drowsiness, vomiting, and renal failure may mimic the picture of diabetic coma and draw attention from the underlying urinary infection. The common complaint of anterior abdominal pain and vomiting, possibly the result of perinephric involvement, may lead to the erroneous diagnosis of acute cholecystitis, peritonitis, or acute intestinal obstruction.

The treatment of acute urinary tract infections depends on the identity of the offending organisms. One of the broad spectrum drugs is used in high dosage until sensitivity studies indicate the antimicrobial agent of choice. Therapy must be prompt, vigorous, and sustained until all signs and symptoms have disappeared and until the urine cultures have remained sterile for a period of at least two or three weeks. The need for even longer-term use of antibiotics in these patients has not yet been clearly defined.

Why pyelonephritis is more likely to occur in patients with diabetes is not known with certainty. That such patients are generally more susceptible to infections such as carbuncles and tuberculosis is well known; a similar susceptibility to renal infections is possible. An immunologic defect has been postulated but not established.

Some investigators have found asymptomatic bacilluria to be more common among diabetic individuals than in the general population.[7] Other observers have failed to confirm this higher incidence, but even in their studies it has been evident that the diabetic patient usually has a bacterial count of millions of colonies per milliliter as compared with the nondiabetic patient whose asymptomatic bacteriuria rarely rises above 100,000 per milliliter.[8] This higher level of bacteriuria, coupled with the ever-present possibility of residual urine caused by neuropathic obstructive changes in the bladder and ureters and the excellent culture medium offered by the sugar-laden urine, can readily account for the predisposition of the diabetic patient to more frequent and more serious urinary tract infections.

Renal papillary necrosis

Renal papillary necrosis or necrotizing papillitis was first described pathologically by Friedreich in 1877.[9] Its association with diabetes was emphasized fifty years later by Gunther[10] and is now well accepted. It does occur in the nondiabetic patient, especially in the presence of lower urinary tract obstruction. Robbins and Angrist[11] estimate the incidence of renal papillary necrosis to be 3.2 to 5 per cent in diabetic patients coming to necropsy. Of the 226 postmortem examinations done at the Joslin Clinic between 1950 and 1955, 11 cases or 4.1 per cent were found, females predominating in the ratio of 9:2. There were 8 unilateral and 3 bilateral cases.[12]

Two clinical pictures are associated with renal papillary necrosis: (1) acute fulminating, with signs of overwhelming sepsis and little reference to the urinary tract except for rapidly progressing renal failure; (2) subacute or smoldering renal infection present for a long time, with acute exacerbations of fever, chills, flank pain, and occasionally hematuria. There may be typical renal colic with the passage of sequestered renal papillae.[13]

The condition may be reasonably suspected in diabetic patients with severe urinary tract infection showing a sudden increase in symptoms and signs of infection, disproportionate acidosis, rapidly rising blood urea nitrogen, and/or oliguria, anuria, or bacteremia.

The characteristic pathologic lesions closely resemble infarcts and are localized to the medulla. Many authors have stressed the vulnerability of the papillary blood supply which consists of small, thin-walled vessels that carry the arterial blood along the papilla and pass directly into veins by U-shaped loops. Compression of these vessels by interstitial edema, inflammatory exudate, and an elevated intrapelvic pressure could readily lead to ischemia and papillary infarction. A comparable pathologic picture has been produced in rats by occluding the venous drainage of the kidney. Venous obstruction represented by venous and capillary thrombi very likely also plays a part in the pathogenesis of this condition in human beings.[14,15]

Laboratory findings include pyuria, leukocytosis, an elevated sedimentation rate, and an increasing azotemia. The urine culture is variable, commonly yielding Escherichia coli, Proteus vulgaris, or Aerobacter aerogenes. A gram-negative bacteremia is not infrequent.

The roentgenographic features in this entity are the result of destruction of the papillae and the associated inflammatory changes. Accordingly, they vary with the stage of the disease at which the examination is made. The earliest evidence on intravenous pyelography is a delay in, or complete failure of visualization of the involved kidney. Mild to moderate dilatation of the collecting system may be seen. Later, as a result of necrosis and sloughing of the renal papillae, a mottled moth-eaten appearance of the fornix appears, simulating that seen in tuberculosis. Retrograde pyelography may visualize the halos or "ring shadows" that represent the subsequent defect.[16]

Necrotizing papillary necrosis is likely to occur in a kidney previously damaged by a combination of vascular and inflammatory insults. Patients in whom such episodes have been known to occur, particularly the elderly female or the male with prostatic obstruction, should not be subjected to catheterization or instrumentation, except for stringent indication.

In the acute phase of this disorder, vigorous treatment is necessary using the antibiotic of choice, preferably either by intravenous or by intramuscular route in massive dose. Even potentially nephrotoxic agents such as neomycin, kanamycin, and so forth should be employed if sensitivity studies of the organisms cultured from the urine or blood indicate their marked superiority to other antimicrobials. It is imperative that the blood pressure be maintained, thus providing good renal perfusion. Vasopressors such as Aramine or Levophed bitartrate are used when required. Blood transfusions and oxygen therapy may also be of help. A nephrectomy in carefully selected cases of demonstrated unilateral disease may be lifesaving. Despite energetic treatment, the case fatality rate remains very high.

An additional comment may be made here on gram-negative bacteremia which is of frequent occurrence in diabetic subjects. Of a total of 454 cases of gram-negative bacteremia collected from the literature, 12 per cent were in diabetic patients, and in the vast majority of them an acute urinary tract infection was present.[17,18] Catheterization or needless instrumental manipulation of infected urinary tracts accounted for a large number of these cases.

The association of fever and shock in a diabetic patient should lead one to suspect the presence of an underlying urinary tract infection even when the usual urinary symptoms are lacking. This is a most serious complication and must be treated immediately and energetically.

Neurogenic vesical dysfunction

Neurogenic vesical dysfunction is an important manifestation of diabetic neuropathy and occurs frequently in patients with diabetes of long duration. Occasionally, in the presence of other neurologic findings, it is difficult to make the clinical differentiation from true tabes dorsalis of syphilitic origin. Because of the similarity of the two conditions, one may speak of diabetic pseudotabes.

Diabetic neuropathy results in diminished bladder sensation, thus leading to urinary retention and to an atonic distended bladder. The onset is insidious with gradually increasing intervals between voidings until the bladder reaches quite large volumes. The stream is weak and the patient usually must strain to urinate. Often overflow incontinence develops. In the older male diabetic patient there is generally an additional prostatic factor. In such situations the usual picture is that of prostatic obstruction, that is, urinary frequency, nocturia, and a growing residual urine. Cystoscopic examination in the uncomplicated neurogenic type reveals only a large, atonic bladder with fine trabeculation. In the prostatic type, typical deep trabeculation and cellule formation are evident. The urine commonly is infected.[19]

The voided urine sugar determination is an unreliable guide to insulin therapy when there is significant residual urine. One may find the patient in hypoglycemic shock at the very time the urine sugar is 4 plus. This paradox finds ready explanation in the fact that the voided specimen is a sample of urine which has accumulated over several hours and therefore does not truly reflect the current blood-sugar level.

The treatment of chronic vesical dysfunction consists in relieving the bladder retention and in eliminating any concomitant urinary infection. In mild cases, and when no prostatic obstruction is present, relief can often be obtained by the use of parasympatheticomimetic drugs, such as Urecholine chloride given in sufficiently large doses. When medical treatment alone is unsatisfactory, transurethral electroresection of the bladder outlet has been employed in both sexes and yields good results.[20,21]

If, in addition to the neural factor, there is considerable prostatic enlargement, open surgery is indicated, employing the type of prostatectomy best suited to the particular case in question. Hypotensive episodes must be guarded against during the surgical and postoperative period, and urethral catheter drainage should be terminated as soon as possible. It is important to maintain the patient under appropriate antibiotic cover.

Neurogenic ureterectasis

The ureter not uncommonly participates in the neuropathic process in cases of long-standing vesical dysfunction. Ureterectasis of variable degree eventuates, the dilatation at times attaining the dimensions of the small bowel. Residual urine accumulating in such ureters readily becomes infected and leads to recurrent bouts of pyelonephritis. Detritus and inflammatory products often become the nidus for stone formation which provides an additional factor to perpetuate and intensify the infection. The vicious cycle of residual ureteral urine, infection, and stone formation may end with disastrous consequences to the involved kidney.

If a stone is present, it must be removed surgically, or cystoscopically if that method is feasible. The treatment of the infection is the same as that described for vesical dysfunction.

Primary diabetic pneumaturia

The passage of gas in the urine in the absence of a fistulous connection with the bowel, and without antecedent instrumentation, is rare. It does occur in the diabetic patient where a gas-producing infection develops in one who carries a large residual urine. The most common organisms capable of such marked gas production are E. coli, A. aerogenes, and yeasts. Analyses of the gas present in several cases have shown varying concentrations of carbon dioxide, hydrogen, nitrogen, and methane. The gases are insoluble in the urine and are odorless. The urine is usually alkaline in reaction, and the sugar concentration is low because of the bacterial fermentation.[22]

A roentgenographic examination may offer the first clue to the presence of an accumulation of gas in the urinary bladder. A rounded or pyriform gas shadow in the suprapubic region is noted. Excretory cystography shows the opaque contrast medium capped by a large amount of gas within the distended bladder. A fluid level can be demonstrated with the patient in an upright position.[23]

There is an explosive passage of gas after the bladder is emptied of urine when either a catheter or an instrument is passed. Evidences of a cystitis and of obstruction can be observed cystoscopically.

The treatment is that of the underlying infection and obstruction as already described under neurogenic vesical dysfunction. Strict diabetic control is desirable to reduce the glycosuria.

Cystitis emphysematosa

Cystitis emphysematosa is a more serious condition in which gas production is not only present in the bladder but also in vesicles within the bladder wall and in the surrounding tissue planes. Cystitis emphysematosa has been associated with diabetes in approximately 50 per cent of all reported cases. It is most likely to occur when vesical trauma and generalized debility are superimposed on a gas-producing urinary tract infection in a person with hyperglycemia. The pathologic findings consist of a gray, edematous thickened bladder wall with numerous small (1 to 5 mm.) vesicles covering the mucosal surface and protruding into the lumen. Usually the vesicles are lined by splintered fibers representing the compressed tissue planes produced by gaseous distention. Hemorrhage around the vesicles is invariable.[24]

An x-ray examination demonstrates a radiolucent ring about the bladder. Cystoscopically, one sees a striking silvery sheen reflected from the vesicles which are rupturing and sending bubbles of gas toward the dome of the bladder.

An active systemic and antibiotic treatment, as outlined previously is required in these usually debilitated patients.

Fertility

Sperm counts and ejaculatory volumes of diabetic males are reasonably normal; sperm motility is somewhat diminished. There is a slightly higher incidence of abortion reported among the nondiabetic wives of diabetic men than among those in a control group. No significant differences have been observed in the incidence of premature births, stillborn infants, malformations, or in the birth weights and sex ratio of offspring.[25,26]

Impotence

Impotence, either erectile, ejaculative, or both, is a common complaint of male diabetic patients. Its incidence is from two to five times higher at all ages than in the nondiabetic population. The disturbance usually begins as a difficulty in maintaining normal erection and may progress to total impotence. Libido usually persists. In those who do become impotent, 60 per cent give evidence of their affliction within five years of the onset of diabetes.[27] A neuropathy involving the lumbar and/or sacral cord or the sympathetic and parasympathetic innervation of the erectile mechanism may underlie this sexual dysfunction.

There is no satisfactory treatment at this time for the neurogenic component, although vitamin B preparations and parasympatheticomimetic drugs have been advocated. Effective therapy includes a sympathetic understanding by the physician and a highly particularized approach to each patient.[28] Improvement in the general health of the patient, reassurance, and suggestive therapy may occasionally yield good results.

Calcification of the vasa deferentia

Calcification of the vasa deferentia, while not specific, is a frequent occurrence in diabetes.[29] In an unselected group of 100 male diabetic patients, it was demonstrated radiographically in 11. It is essentially asymptomatic and was detected when roentgenograms of the pelvis were taken for other reasons. The calcified structures are seen as roughly symmetrical tubular shadows approximately the caliber of medium-sized arteries low in the midpelvis.

The pathogenesis is unknown. It is not the result of intraluminal vasal infection, but it is probably degenerative in nature. There is no correlation between the severity of the diabetes and the presence of calcification of the vasa.[30]

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Number thirty-eight in a series of articles on Current Concepts in Diabetes Mellitus

Announcement

It is called to our attention for the information of our subscribers that the New York City Excise Tax on Gross Receipts imposed pursuant to the General Business and Financial Tax Law is due May 15, 1962. The tax applies to persons conducting any trade, business, profession, vocation, or commercial activity within the City of New York for gain or profit. In general, the tax is based on the gross receipts for the entire calendar year 1961. However, if the taxpayer has reported in a return for a prior period his gross receipts for a portion of such calendar year, the tax is measured by his gross receipts during the balance of the year.

In filing General Business Tax returns on Form B, doctors are required to report thereon as Item 4 the gross receipts (gross fees) from the practice of their profession. Dividends and interest received from investments and profits derived from stock and bond transactions should not be included in the measure of the tax when filing General Business Tax returns if such transactions are occasional transactions of a nature extraneous to the taxpayer's regular activities. In reporting gross receipts, no deduction may be taken for salaries, rent, and other office expenses.

Where a doctor is also a member of a medical group associated with the Health Insurance Plan of Greater New York, the distributive share of the income he receives from the group is not to be included in his gross receipts, since the various medical groups associated with H.I.P. are generally regarded as partnerships and are required to file returns on the basis of their total gross receipts.

In computing gross receipts subject to tax, the taxpayer may take a specific deduction of $10,000.00 from his gross receipts. Tax at the rate of $^2/_5$ of 1 per cent is to be paid on his gross receipts in excess of $10,000.00. No tax is imposed when the gross receipts do not exceed $10,000.00, and no return need be filed in such case.

The return must be filed on or before May 15, 1962, with the City Collector in the borough in which the taxpayer maintains his office. A remittance for the total amount of tax due, drawn to the order of the City Collector, must accompany the return when filed. Form B for filing this return will be mailed to all taxpayers who have filed returns in prior years. The office of the Comptroller of the City of New York will be pleased to furnish further information or assistance in the preparation of returns.

Nutrition Excerpts

Prepared with the cooperation of the faculty of the Graduate School of Nutrition, Cornell University, Ithaca, New York

R. A. NELSON, M.D., Editor

Predicting Body Fatness of Young Women on the Basis of Skinfolds

CHARLOTTE M. YOUNG, PH.D.
Ithaca, New York

In an earlier Nutrition Excerpt[1] we presented data on the body fatness of normal young women as determined by the densitometric technic. The young women were found to average 28.69 ± 4.856 per cent of their body weight as fat, a figure over two and one-half times as high as that for young men of comparable age and status. At that time it was pointed out that, in the absence of facilities to make density measurements, the very simple technic of skinfold thicknesses measured with a calibrated caliper in well-chosen spots would seem to give a better indication of relative fatness than the other more elaborate chemical procedures used. Obviously if the determination of body fatness is to be applicable to the work of the clinician, a method must be found that is reasonably accurate and efficient yet relatively inexpensive in terms of time and cost.[2]

Study objectives

The question arose: Could specific gravity (easily converted to body fatness) be predicted on the basis of some simpler measurement such as skinfold thickness? For young and for middle-aged men, based on density and skinfold measurements Brožek and Keys[3] presented such equations. Pascale *et al.*[4] also gave an equation for young men. As recently as 1960 Chinn and Allen[5] presented an equation for estimating body fat in men based on the measurement of two skinfolds, weight, height, and age. However, no satisfactory equation has been proposed for young women, probably because of the lack of fundamental data for a sufficient number of women on which it could be based. With the publication of our report[6] such data were available, and the task of formulating a prediction equation for specific gravity based on skinfold measurements was undertaken.[2] (Specific gravity may be converted easily to percentage body weight as fat by the Rathbun-Pace formula.[7])

Methods and materials

The basic data used in the formulation consisted of measurements of density, skinfold thicknesses at 12 sites, and "standard weight" of 94 young women of normal weight, ages seventeen to thirty years. The process used in arriving at the choice and number of skinfolds to be used in the final equations has been reported in detail elsewhere.[2] Essentially it consists of determining the intercorrelations between skinfolds and density and on the basis of these eventually formulating linear regression equations. Obviously, from the standpoint of convenience, one would wish to use an equation which involved as few measurements as possible and yet did not give significantly different predictions statistically from those resulting from a more elaborate set of measurements.

In formulating a predictive equation for middle-aged men, Brožek and Keys[3] found that adding relative weight as a variable enhanced the effectiveness of predicting specific gravity from skinfolds. Since young women are more comparable to middle-aged men than to young men with regard to body fatness,[1] in the selection of equations it seemed wise to see how the inclusion of percentage standard weight as a variable, in addition to various combinations of skinfolds, would affect the prediction.

The 12 skinfold sites for which thickness measurements were available included: the chin, under the mandible; below the tip of the scapula; the chest, midaxillary border of the pectoralis major and at the xyphoid level on the midaxillary line; the lateral aspect of the thorax over the lower rib midway between the axilla and the iliac crest; the waist, on the midaxillary line, halfway between the lower rib and the iliac crest; the abdomen, just to the right of the umbilicus and also halfway between the umbilicus and the pubis on the midline (referred to subsequently as the "pubis"); the supra-ilium on the midaxillary line; the upper arm, over the triceps midway between the tip of the acromial process of the scapulas and the tip of the elbow; the thigh, halfway down over the rectus femoris muscle; and the knee, over the patella.

From the various prediction equations derived it was apparent that if skinfold thicknesses alone were to be used to predict specific gravity in young women an equation involving six sites seemed to be the one of choice:

$$\text{Predicted specific gravity} = 1.0647 - 0.0003444X_1 - 0.0001557X_2 - 0.0002803X_4 - 0.0006181X_5 + 0.0005768X_8 - 0.0004001X_{12}$$

Where X_1 = pubis-abdomen, halfway between the umbilicus and pubis on the midline; X_2 = lower rib; X_4 = supra-ilium; X_5 = chin; X_8 = chest (pectoralis major); and X_{12} = knee.

The multiple correlation coefficient of the specific gravities predicted using such an equation and those determined was 0.7218 with a standard deviation of differences of 0.0066 units of specific gravity. Since a change of 0.001 unit of specific gravity is roughly equivalent to a 0.5 per cent change in body weight as fat, for two thirds of the individuals for whom such a prediction equation might be used the predicted per cent body weight as fat would be within 3.3 per cent of the densitometrically determined body weight as fat.

TABLE I. Conversion of values for specific gravity of man to fat content on basis of equation: per cent fat = 100 (5.548/specific gravity −5.004)*

Body Specific Gravity	Per Cent Fat of Body Weight	Body Specific Gravity	Per Cent Fat of Body Weight
1.002	49.3	1.052	23.0
1.004	48.2	1.054	22.0
1.006	47.1	1.056	21.0
1.008	46.0	1.058	20.0
1.010	44.9	1.060	19.0
1.012	43.8	1.062	18.0
1.014	42.7	1.064	17.0
1.016	41.7	1.066	16.1
1.018	40.6	1.068	15.1
1.020	39.5	1.070	14.1
1.022	38.5	1.072	13.1
1.024	37.4	1.074	12.2
1.026	36.3	1.076	11.2
1.028	35.3	1.078	10.3
1.030	34.2	1.080	9.3
1.032	33.2	1.082	8.4
1.034	32.2	1.084	7.4
1.036	31.1	1.086	6.5
1.038	30.1	1.088	5.5
1.040	29.1	1.090	4.6
1.042	28.0	1.092	3.7
1.044	27.0	1.094	2.7
1.046	26.0	1.096	1.8
1.048	25.0	1.098	0.9
1.050	24.0	1.100	0.0

* Reproduced from Rathbun and Pace.[7]

However, in almost all cases the inclusion of the percentage of standard weight as a variable in prediction equations using various numbers of skinfolds increased the accuracy of the prediction of specific gravity at a statistically significant level. Perhaps, then, if percentage standard weight were used in the prediction equation a lesser number of skinfolds might need to be measured. Such proved to be the case. For young women, when standard weight was included as a variable, there was no significant advantage in predicting specific gravity by using twelve, six, or two skinfolds over using one. The skinfold of choice appeared to be the one referred to previously as pubis, located at a point halfway between the umbilicus and the pubis on the midabdominal line. Percentage standard weight is based on average weight per sex, age, and height in the *Build and Blood Pressure Study, 1959*[8] taken as 100.

For young women, then, the practical equation of choice for predicting specific gravity proved to be:

$$\text{Specific gravity} = 1.0884 - 0.0004231X_1 - 0.0003401X_{13}$$

When X_1 = skinfold on midabdominal line halfway between the umbilicus and pubis (expressed in millimeters); and X_{13} = percentage standard weight (average weight per height, age, and sex.)[8]

The predicted specific gravity may be converted easily to per cent fat of body weight by use of the Rathbun-Pace equation.[7]

$$\text{Per cent fat} = 100\left(\frac{5.548}{\text{specific gravity}} - 5.044\right)$$

Table I may be used to convert values for body specific gravity to fat content.

Using the preceding equation to derive specific gravity, there was a correlation of 0.699 and a standard deviation of differences of ±0.0068 between derived and densitometrically determined values for the 94 normal-weight young women studied. These figures compare with values of 0.743 and ±0.0086 which Brožek and Keys found for middle-aged men.

Summary

For young women, the specific gravity (and hence body fatness) may be predicted on the basis of a single skinfold (midabdominal line halfway between the umbilicus and pubis) and percentage of standard weight. An equation for the prediction is presented. Similar equations previously have been available for young and middle-aged men.

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Number twenty-eight in a new series of Nutrition Excerpts

Correction

The reader's attention is called to the following author's correction in the Nutrition Excerpt series: Maynard, L. A.: Trace elements, New York State J. Med. **26:** 544 (Feb. 15) 1962, page 544, second column, line 31, delete the words "in normal pregnancy."

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

VALENTINO D. B. MAZZIA, M.D., Chairman
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Radial Nerve Palsy From Intramuscular Injection

Anesthetists frequently prescribe and occasionally administer various medications intramuscularly. A site often utilized for the injection is the deltoid region. If the intramuscular injection is not placed carefully, radial nerve injury may result.

Case report

A forty-seven-year-old male was admitted to the emergency room with compound fractures of both legs incurred in an automobile accident. The history and physical examinations otherwise were noncontributory. His admission blood pressure was 120/60 mm. Hg, pulse 104 per minute, and respirations 22 per minute. The admission hematocrit was 39, and no pathologic findings were noted in the urinalysis.

Because the patient was complaining of severe pain, 100 mg. of meperidine were administered intramuscularly in the left arm while he was in the emergency room.

In the operating room forty-five minutes later he was found to be apprehensive and in acute distress. An additional 50 mg. of meperidine hydrochloride and 0.4 mg. of atropine sulfate were administered intravenously. The anesthetic induction and maintenance for the open reduction and fixation of both legs was cyclopropane-oxygen in a closed-circle absorption system. One thousand cc. of whole blood were administered intravenously in the left arm to replace the 800 cc. of blood estimated to have been lost during surgery.

The patient awoke from the anesthetic promptly and immediately began to complain of weakness in the left hand.

A neurologic consultant examined the patient on the following day when wrist drop on the left was noted. The muscle strength was strong in the shoulder group, biceps, triceps, thenar group, and flexor carpi ulnaris. The muscle strength was weak or absent in the brachioradialis, extensor carpi radialis, supinator muscle, extensor digitorum communis, and extensor carpi ulnaris. There was no sensory loss, and the skin was noted to be sweating normally.

The impression was that he had a left radial nerve palsy above the innervation of the brachioradialis muscle.

The patient's hand was placed in a splint, and physiotherapy was begun promptly. Healing of the fractures and recovery of the nerve progressed satisfactorily, and the patient was discharged as recovered at the end of eight weeks.

Comment

The clinical picture of radial nerve palsy varies in accordance with the site of the

Presented and discussed at a conference held at Bellevue Hospital, New York City, February 5, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

injury. An injury to the nerve in the forearm results in a partial wrist drop. Damage to the nerve above the elbow causes an inability to dorsiflex the hand at the wrist or the fingers at the metacarpophalangeal joint. A lesion proximal to the midhumerus causes a loss of power in the brachioradialis. Because the radial nerve carries few sensory fibers and its fields of innervation are shared by other nerves, the sensory deficit in radial nerve palsy is usually minimal.

An examination of this patient revealed that the site of the injury must have been near the lateral intermuscular septum just above the innervation of the brachioradialis muscle. This site is distal to the recommended site for intramuscular injection in the deltoid muscle. This injury probably was caused by the meperidine injection in the emergency room.

The upper part of the deltoid covers the prominence of the shoulder and its joint and is not recommended as an injection site because of the nonyielding tendons and septa. The lower part of the deltoid has similar septa which ascend from the tendon into the muscle substance close to the axillary nerve.

Only the very small area between the upper and lower portions of the deltoid should be used as injection sites. This small area begins about 2 fingerbreadths below the acromion. Injections should not be made into the lower or middle third of the arm. Only a very limited quantity of fluid can be injected into the deltoid.

It should be noted that usually radial nerve palsy subsequent to anesthesia and surgery is due to pressure on the posterior cord of the brachial plexus caused by hyperextension of the upper part of the arm. Occasionally, pressure on the nerve in the forearm against the edge of the operating table or by an arm board also may produce an injury.

The anesthetist and the surgeon must protect the patient vigilantly from these nerve injuries.

Number one hundred twenty-one in a series of Clinical Anesthesia Conferences

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The job of drug research

We need to improve and extend research in every area and at every level. In particular we need a strong and productive pharmaceutical industry capable of producing and refining drugs that are far better than we have today. We need to extend and strengthen government regulation of the industry to the end that the public be more fully protected against dangerous or counterfeit drugs or those that are made by a fly-by-night organization in unsanitary conditions. . . . We also need to support strongly those industrial organizations which take pride in their regulations, which order their relations with the profession on a high plane, and which do the main heavy job of translating scientific knowledge into sound and useful drugs.—*Dr. Vannevar Bush to Association of Military Surgeons*

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
HAROLD JACOBZINER, M.D., Assistant Commissioner,
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Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Rhubarb Poisoning

THIS ARTICLE is an outgrowth of the following correspondence from Pauline G. Stitt, M.D., Chief, Home Medical Service, and Associate Professor of Preventive Medicine and Pediatrics at Massachusetts Memorial Hospital in Boston.

> In my favorite part of my favorite paper, Lewis Nichols' page, "In and Out of Books," *New York Times* Book Review, on Sunday, December 17, 1961, I ran across an item that I think should come to your attention because of your well-known vigilance regarding poisoning in childhood.
>
> The item was called "Postscript," and it said that the new *Larousse Gastronomique* states that rhubarb leaves can be "eaten like spinach." J. B. Priestley warned the British publisher that such leaves are dangerous. Over here Crown used an erratum note and queried the University of Rochester and the New York health authorities regarding evidence of their being poisonous and was told there was "no evidence."
>
> I read that with alarm, for rhubarb leaves have a long history of extreme toxicity. This first came to my attention in the late 1930's or early 1940's because of a catastrophe in Alabama. When I heard about it, I did some reading and found several well-supported incidents in the literature. (The cases usually were fatal and usually involved children.)
>
> At that time I was practicing in Upstate New York where rhubarb is a favorite garden product, so I paid heed to the literature. Once alerted, I never forgot, and in the intervening years have noticed with interest how case reports continue to occur. I have no references at hand but think the Index Medicus will disclose several that I seem to recall having seen within the last five years.

In our reply to Dr. Stitt we agreed about the toxicity of rhubarb, and stated that information citing "no evidence" of rhubarb leaf poisoning did not come from the Poison Control Center.

Rhubarb, or Rheum rhaponticum, is a coarse, perennial herb of the buckwheat family. It has large leaves and small clusters of flowers on a tall, fleshy stalk. The leaf stalks generally are used in cooking. The dried roots also are used for medicinal purposes, that is, as cathartics and tonics. Rhubarb is grown all over the United States, and the leaf blade contains the toxic part, oxalic acid, and other oxalates. It is said to contain about 1 per cent or less of the toxic material. The leaf stalk, which is generally used for cooking and baking, is not toxic. It is used for preparing sauces and appetizing pies.

However, poisoning can and does occur from eating large amounts of raw or cooked leaves or blades of rhubarb which contain the toxin, oxalic acid, and oxalates.

Signs and symptoms

The symptoms are essentially the same as those which one encounters in oxalic acid poisoning, since this is the etiologic agent which causes the poisoning.

Oxalic acid and the oxalates have a corrosive and irritant action on the gastrointestinal mucosa. Therefore, the early symptoms of rhubarb poisoning are burning in the mouth, throat, and esophagus; thirst; nausea; dysphagia; recurrent vomiting; epigastric and abdominal pains; and diarrhea. Because of the corrosive action on the gastrointestinal mucosa, the vomitus is often bloody. The stools also may be bloody. Epistaxis is also encountered frequently. The pulse becomes weak, slow, and irregular, and there is a distinct drop in the blood pressure. The heart may show evidence of dilatation, the respiratory rate is lowered, and the respirations are weak. Kidney damage is always present and is manifested by the symptoms of oliguria, albuminuria, oxaluria, hematuria, anuria, and uremia in severe cases. Headaches, muscular cramps, trismus, and twitchings of the facial muscles are common. Paresthesias and exaggerated reflexes also may be present. The pupils are dilated and sluggish in reaction. Amaurosis also may occur. In severe cases there may be convulsions, stupor, and coma, and death will ensue rapidly from circulatory collapse.

The symptoms usually appear soon after ingestion, and even death may occur rapidly within several hours following the onset. At times, however, the symptoms may be delayed. In some cases the gastrointestinal symptoms may be absent entirely, and the presenting manifestations may be those related entirely to the central nervous system.

The lethal dose of oxalate for adults is said to be in the neighborhood of 20 Gm., and the lethal dose for children is much lower, perhaps between 5 and 10 Gm. However, a fatality has been reported following the ingestion of 5 Gm. The symptoms in that case were a very weak pulse and a very rapid collapse following convulsions.

Absorption and pathogenesis

Oxalates are absorbed readily from the intestines. Following absorption the oxalates combine with the blood calcium to form calcium oxalate which is excreted by the kidney. This reduces the level of ionized calcium in the body fluids. The resultant hypocalcemia produces an hyperirritability of the central nervous system which at times causes tetany and twitchings of the skeletal muscles. It also causes a disturbance of the heart. The kidney damage is caused both by the obstruction of the renal tubules by the crystals of calcium oxalate and by the chemical action of the oxalate ion. The oxalate crystals in the ureter, kidney, and bladder also cause pain, oxaluria, oliguria, and hematuria.

Diagnosis

A poisoning may be suspected whenever a history of rhubarb leaves ingestion is obtained. The diagnosis may be confirmed by laboratory findings, such as the presence of an oxaluria and a hypocalcemia. The presenting symptoms of a hypocalcemia and those due to the corrosive action of oxalic acid also may prove helpful.

Treatment

The treatment of rhubarb poisoning is essentially the same as that for oxalic acid poisoning. As a first aid measure milk, cheese, milk of magnesia, lime water, chalk, or any dilute solution of a calcium salt may be given. Magnesium sulfate also may be given as a cathartic. A gastric lavage with lime water or other calcium salt is beneficial. This should not be done, however, if corrosion of the mucosa of the mouth or esophagus is already present. The vomiting may be helped by the administration of demulcents. A 5 per cent solution of calcium chloride or large amounts of milk may be given to delay the absorption caused by the formation of insoluble calcium oxalate. Hypocalcemia should be treated by the parenteral administration of calcium gluconate or some other calcium salt. The intravenous use of calcium chloride or calcium gluconate, however, has been questioned recently. If shock is present, it should be vigorously treated. The treatment in the main is supportive and symptomatic.

One of the reasons why more cases of rhubarb poisoning do not occur is that the leaves which contain the toxic product generally are not eaten, and second, the oxalic acid contained in the rhubarb leaf blade is said to be less than 1 per cent.

The New York City Poison Control Center has not received any reports as yet of rhubarb poisoning. A visiting physician from Finland, however, informed us of a fatal case of rhubarb poisoning. It occurred in a two-year-old orphan child who was in an orphanage and who was fed rhubarb leaves from the orphanage garden by an older child.

Another fatality from rhubarb also was reported by Tallqvist and Vaananen.* A five-year-old girl was admitted to the hospital in a semistupor. The early symptoms were nausea and lethargy. On the following morning the child's condition became worse. She vomited four times, and the vomitus appeared dark in color. As per instructions, the child was given a sedative and was brought to the hospital twenty-four hours following the onset of her symptoms. Oxalic acid poisoning was suspected because of the typical presenting symptoms. The diagnosis was confirmed by a urinalysis which revealed oxaluria. On further detailed questioning it was revealed that the child was playing in the garden picking rhubarb leaves and tasting some of them. She showed a great liking for the taste of rhubarb, whereupon her playmates fed her a considerable amount of the raw rhubarb leaves. In spite of heroic therapy with calcium gluconate and stimulants, the patient expired within two days of the occurrence.

It is possible that the frequency of rhubarb poisoning is higher in rural areas than in metropolitan centers.

Many fatalities from rhubarb poisoning occur in grazing sheep and cattle which ingest large portions of rhubarb leaves while in pastures where rhubarb is grown.

Physicians should be mindful of the possibility of rhubarb poisoning and should alert parents on the potential existing hazards, particularly if children are permitted to play in gardens or other areas where rhubarb is grown and where the possibility of ingesting rhubarb leaves exists.

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* Tallqvist, H., and Vaananen, I.: Death of a child from oxalic acid poisoning due to eating rhubarb leaves, Ann. Paediat. Fenn. **6**: 144 (1960).

Number ninety in a series of Accidental Chemical Poisonings

A fortune is spent, but nobody is richer

The medically needy are today a minority amid a majority of sufficiency and affluence. Accordingly, they can be identified and helped on the local level with success and thoroughness never before possible. Nevertheless, our apostles of affluence propose coast-to-coast spending schemes that offer too little to those who need it and a dividend to those who don't. This is very much like the legend of the eccentric who leaves a million dollars to be distributed in $1 bills to one million people. A fortune is spent, but nobody is richer. When the fortune spent is public money, everybody is that much poorer.—*Austin Smith, M.D., to Pharmaceutical Manufacturers Association*

Case Reports

Hypogammaglobulinemia, Arthritis, Sprue, and Megaloblastic Anemia

IRA GREEN, M.D.
Bronx, New York
ROBERT J. SPERBER, M.D.
Bronx, New York

From the Department of Hematology, Laboratory Division, Montefiore Hospital

THE CAUSE AND NATURE of hypogammaglobulinemia are poorly understood. The fact that a variety of other illnesses is commonly associated with both congenital and acquired hypogammaglobulinemia adds further interest to this disease complex.

An analysis of cases of hypogammaglobulinemia may lead to a better understanding of their causes and may also show more clearly the normal mechanisms of antibody production. The pathogeneses of the diseases which are frequently associated with hypogammaglobulinemia may also be clarified.

Case report

A twenty-seven-year-old white male surveyor's helper had four admissions to the Bronx Veterans Administration Hospital. He was first discovered to have hypogammaglobulinemia at the Walter Reed Army Hospital in 1953.

The patient's mother related his early history as follows:

He had been delivered after a full-term pregnancy in June, 1933. This had been the third normal pregnancy for the mother who was thirty-two years old at the time. The mother's health was good except for a history of pulmonary tuberculosis in early childhood. Both older brothers, as well as a younger sister had no history suggestive of hypogammaglobulinemia or connective tissue disorders. The father died at the age of fifty-eight years of Bright's disease and heart disease of an unknown type. The patient was a normal baby and was breast-fed until the age of six months. He was then given powdered milk supplements. The diet contained no added vitamins. The patient's general course is outlined in Figure 1. At seven months he had a left mastoid infection which required surgical intervention. Scarlet fever and mumps occurred at the age of three years, and varicella occurred at the age of four years. Between illnesses he was well. He had his first episode of lobar pneumonia when he was eleven years old. He was treated successfully with penicillin in the hospital. Shortly after this a second mastoid infection occurred. Between the ages of eleven and nineteen years he had five episodes of bronchopneumonia which required hospitalization. These infections responded to penicillin therapy.

In May, 1953, the patient entered the United States Army. Within a week, he was hospitalized with pneumonia of the lower lobe of the left lung. Because he responded poorly to conventional therapy at the base hospital, he was transferred to the Walter Reed Army Hospital. Here the diagnosis of hypogammaglobulinemia was established shortly after admission. The physical findings showed evidence of pneumonia of the lower lobe of the left lung. There were small nontender anterior cervical, supraclavicular, and axillary nodes. A low globulin was noted on an ordinary albumin-globulin ratio. A scanning of the electrophoretic pattern showed the gamma globulin to be 110 mg. per 100 ml. No

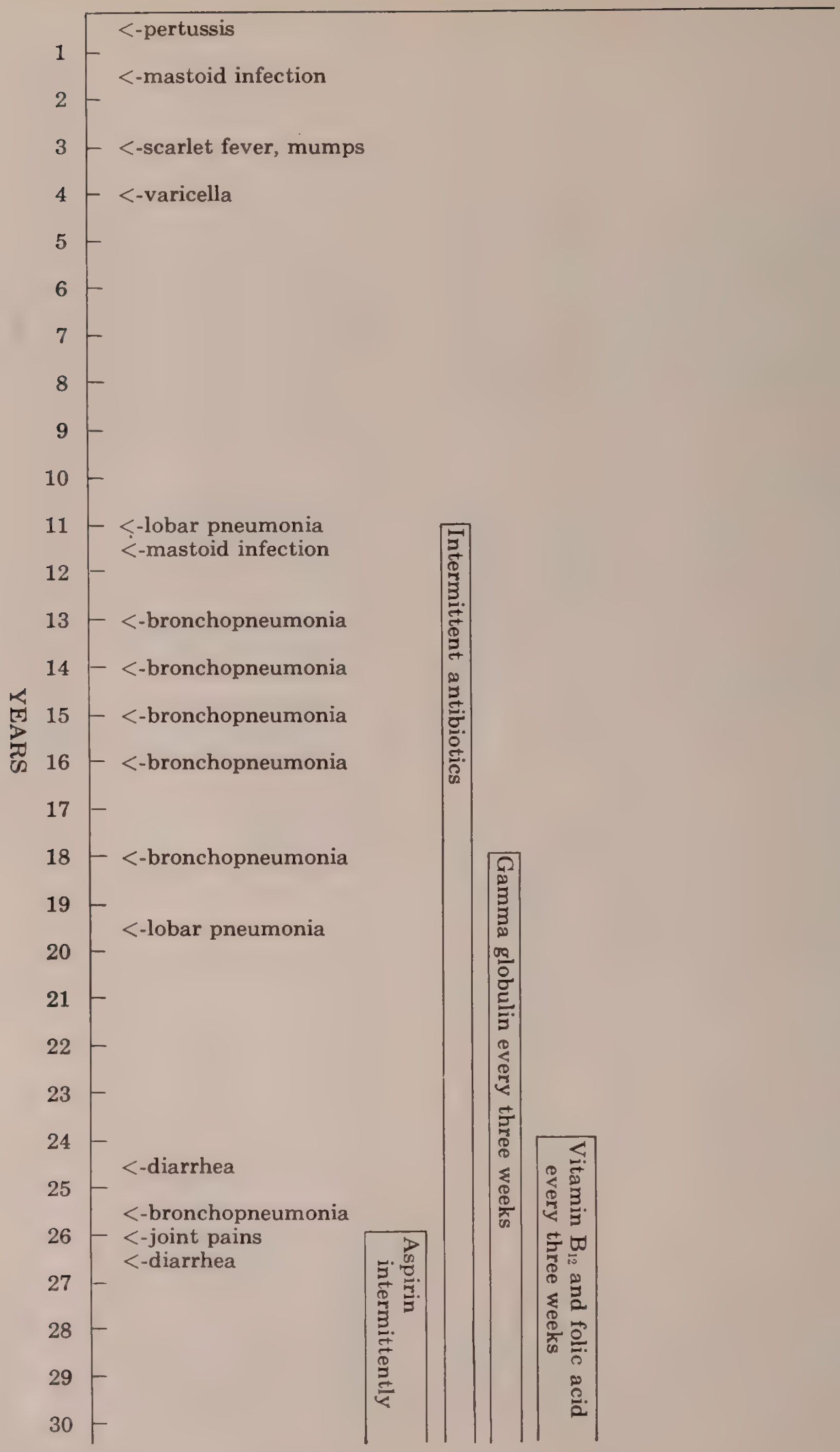

FIGURE 1. Medical history of patient and corresponding treatment.

spleen was felt. The laboratory findings are summarized in Table I. Additional special studies at this time (1953) were: skin tests for tuberculosis, coccidioidomycosis, and blastomycosis and a serologic test for syphilis, all of which indicated negative findings. The cephalin flocculation test showed negative results, the thymol turbidity was 4, and the bilirubin was 0.6 mg. The radioactive iodine uptake was 13 per cent in twenty-four hours. The 17-ketosteroid excretion was 30 mg. per twenty-four hours. Bronchograms showed minimal bronchiectasis bilaterally. The results of a barium enema were normal.

The patient's pneumonia responded gradually to antibiotic therapy and parenteral gamma globulin. His mother, sister, two brothers, and two cousins were examined in 1953 and were found to have normal serum patterns by electrophoretic analysis. No studies for the rheumatoid factor were done at this time.

In January, 1955, the patient was admitted to the Bronx Veterans Hospital for further investigation. At this time the spleen was easily felt 3 cm. below the left costal margin. The laboratory work is shown in Table I. I^{131}-tagged gamma globulin had a half life of twenty-one days after injection into the patient. While in the hospital, the patient had an episode of bronchitis with temperature elevation. This was treated with tetracycline. The patient was seen as an outpatient, and he continued to receive gamma globulin 20 cc. intramuscularly every three to four weeks. Intermittent episodes of bronchitis were treated with tetracycline.

On March 5, 1958, the patient returned to the Bronx Veterans Administration Hospital with gastrointestinal symptoms. He complained of diarrhea, gaseousness, insomnia, and weakness. He was given kaopectate and an antispasmodic drug without benefit. The physical examination was essentially unchanged. The hemoglobin was 12.2 Gm. per 100 ml. Previously, his hemoglobin had been 16 Gm. per 100 ml. The white blood count ranged from 4,000 to 7,000 per cubic millimeter, with normal differentials. There were from 168,000 to 240,000 platelets per cubic millimeter. A urinalysis was normal. The results of the

TABLE 1. Results of laboratory studies of vitamin B_{12} absorption before and after treatment with antibiotics

Physical Data	Dates May, 1953	November, 1953	March, 1955	March, 1958	May, 1959	January 9, 1961	January 30, 1961
Hemoglobin (Gm. per 100 ml.)	10 to 11	15	14.8	13	15	. . .	. . .
White blood count per cubic millimeter	6,200	12,000	7,850	5,000	7,400	. . .	. . .
Gamma globulin (mg. per 100 ml.)	110*	. . .	. . .	40†	. . .	. . .	. . .
Bone marrow	Myeloid hyperplasia, no plasma cells.	. . .	Dilute marrow, no plasma cells.	Megaloblastoid to normoblastic marrow	. . .	. . .	. . .
Typhoid immunization	Negative result after stimulation	. . .	. . .	Negative result after stimulation	. . .	. . .	. . .
Schilling test**	. . .	. . .	. . .	Without intrinsic factor 0.1 per cent; with intrinsic factor, 2.7 per cent.	. . .	Without intrinsic factor, 0.4 per cent; with intrinsic factor, 2.6 per cent.	After antibiotic therapy, 0.9 per cent without intrinsic factor.

* Scanning electrophoretic pattern.
† Gel-diffusion technic.
** Twenty-four hour urinary excretion, Co^{60} (radioactive cobalt), vitamin B_{12}.

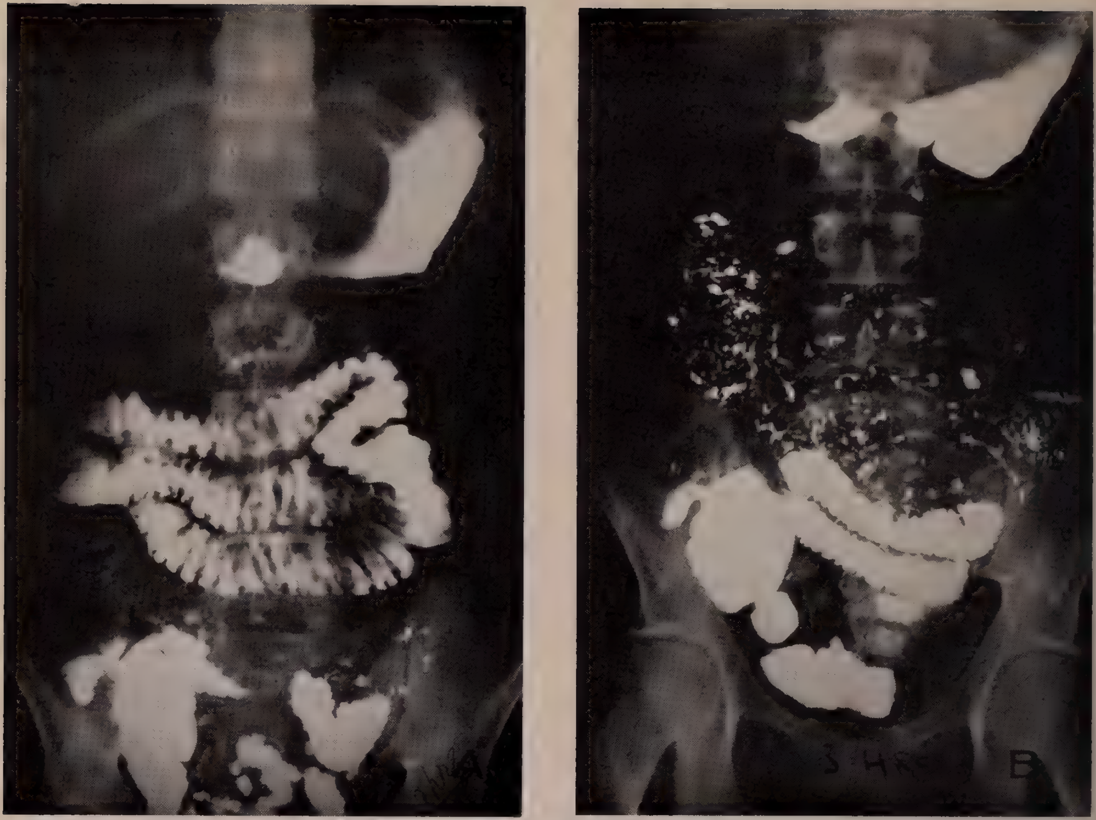

FIGURE 2. (A) Small-bowel series after two hours, with gastric retention still present. Jejunal loops show thickening of valvulas conniventes, with segmentation of barium column and slight flocculation of barium. (B) Small-bowel series after three hours, with gastric retention still present and flocculation of barium in jejunal loops.

Coombs test were negative. The serum sodium, potassium, carbon, carbon dioxide, calcium, phosphorus, bilirubin, and the prothrombin time were all normal. The total protein was 4.9 Gm. per 100 ml., the albumin was 4 Gm. per 100 ml., and the globulin was 0.9 Gm. per 100 ml. Using an agar-diffusion technic, the patient was found to have a 40 mg. per 100 ml. globulin.* There were no red blood count isoantibodies demonstrable at this time. Typhoid and paratyphoid agglutinins again indicated negative findings. Stools for culture, ova, and parasites did not show any pathogenic bacteria. No hydrochloric acid was found on gastric aspiration after adequate histamine stimulation and by the Diagnex test. The serum carotene was 94 gammas per 100 ml., and the oral glucose tolerance curve was flat. After three days on a 100-Gm. fat diet, the twenty-four-hour stool collection weighed 411 Gm. and contained 27.8 Gm. of total fat and 23.1 of fatty acids (normal is 5 Gm. of total fat). A bone-marrow aspiration showed erythroid hyperplasia with megaloblastoid changes in the erythroid series.

A proctoscopy and a barium enema were normal. A gastrointestinal series showed moderate gastric retention and thickening, and hypertrophy of the jejunal loops was noted. In addition, irregular clumping of barium in the small intestine was present (Fig. 2). A Schilling test done without the intrinsic factor showed a twenty-four-hour urinary excretion of 0.1 per cent. After the intrinsic factor, the excretion of vitamin B_{12} was 2.7 per cent. The patient noted a feeling of well-being and a return of his appetite within twenty-four-hours after the adminis-

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* Done by L. Korngold, M.D., Sloan-Kettering Institute, New York City.

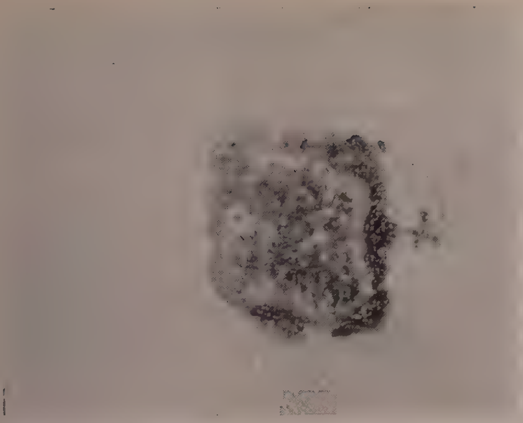

FIGURE 3. Disintegrated homograft, raw graft bed, partially covered by exudate, after twenty-two days.

tration of vitamin B_{12}. His hemoglobin rose from 12.2 to 14.6 Gm. per 100 ml. There was a reversion to normoblastic proliferation in the bone marrow. Vitamin B_{12} (100 micrograms) and folic acid (15 mg.), intramuscularly every three weeks, were added to his regimen.

During this admission, the patient was given a homograft with a split-thickness skin graft (0.0012).[1] This graft was rejected normally in fourteen days (Fig. 3). In June, 1958, the patient was hospitalized for another episode of bronchopneumonia. In November, 1958, the patient developed bilateral pains and stiffness in his fingers, wrists, elbows, and knees. There was no directly antecedent infection or sore throat. The proximal interphalangeal joints showed swelling bilaterally. X-ray films of the joints showed no bony changes. The symptoms responded to 4 Gm. aspirin per day. After two weeks the dosage was tapered. The patient continued to have intermittent arthralgia and he takes aspirin when necessary.

While the patient was having joint symptoms, his serum was studied for macroglobins and the rheumatoid factor.* Neither was found. In December, 1958, the patient had an exacerbation of diarrhea. There was poor response to antispasmodics, sedation, kaopectate, and later Sulfasuxidine. The patient was given a gluten-free diet for one month. His symptoms started to improve almost simultaneously with the start of the diet. However, the symptoms did not recur after the cessation of the diet.

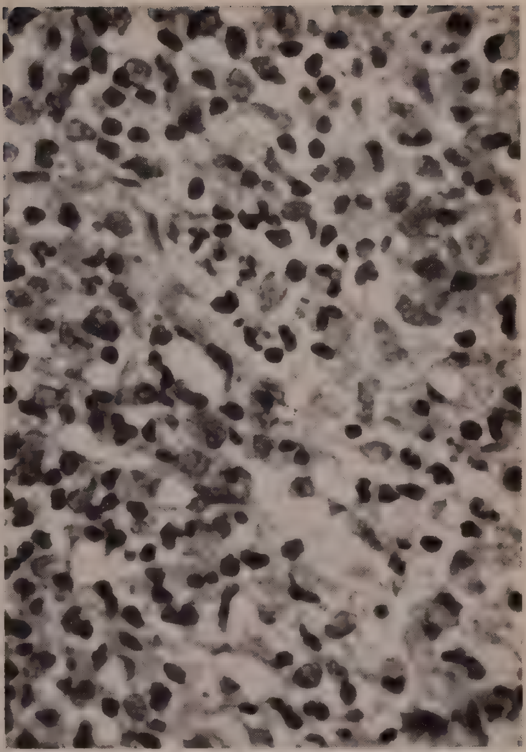

FIGURE 4. Infiltrate in submucosa consisting of round cells and polymorphonuclear leukocytes (hematoxylin and eosin stain X 560).

On February 2, 1959, a peroral Shiner tube biopsy of the distal duodenum was performed. Because of tangential section, the height of the villi could not be evaluated. However, there was an increased number of lymphocytes and especially polymorphonuclear leukocytes in the lamina propria and submucosa. No plasma cells were seen (Fig. 4). In January, 1961, the patient had further studies of vitamin B_{12} absorption before and after antibiotics. The results are seen in Table I.

At present (March, 1961) the patient is working full-time. He has intermittent joint pain and diarrhea. In spite of an enlarged spleen, there is no hematologic evidence of hypersplenism. He is subject to frequent mild upper-respiratory illnesses which are easily controlled with tetracycline.

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Comment

The patient's hypogammaglobulinemia is probably of the early acquired type. The rather high level of gamma globulin, the absence of family history, the benign course during the first ten years of life, and the normal homograft rejection are in favor of the acquired type of hypogammaglobulinemia.

The fact that connective-tissue disease[2,3] and sprue-like syndromes[4–6] are associated with hypogammaglobulinemia may have several possible causes. First, each one may be the consequence of some basic defect which determines both the inability to produce antibodies and also produces the secondary manifestations. Second, the associated illnesses may be simply due to the absence of gamma globulin and circulating antibodies. One consequence of absent antibodies is the decreased ability to handle exogenous pathogens. The arthritic and gastrointestinal complications may each belong to the same or separate divisions of the two broad categories mentioned previously.

The association of rheumatoid arthritis with hypogammaglobulinemia is of interest, since it was thought at one time that the rheumatoid factor might be related directly to the pathogenesis of rheumatoid arthritis. The high incidence of an illness identical pathologically to rheumatoid arthritis in patients with hypogammaglobulinemia has been one of the main arguments against the pathogenetic role of rheumatoid factor. Since patients with both congenital and acquired hypogammaglobulinemia get arthritis and since the underlying defect in these illnesses is probably different, a common "defect in mesenchyme," as postulated by Good and Rotstein,[3] which determines hypogammaglobulinemia and arthritis is unlikely.

There is another and quite paradoxical mechanism of the high frequency of arthritis in patients with hypogammaglobulinemia. Because of the cellular infiltration of lymphocytes and plasma cells into the synovium and because of the resemblance of these lesions to immunologically produced lesions of experimental arthritis in animals, it has been thought that rheumatoid arthritis may represent some type of auto-immune disease.[7] The presence of the cellular infiltrate suggests that if immune processes are operating, they are probably of the delayed variety. There is highly suggestive evidence that the presence of circulating antibodies may actually inhibit or prevent sensitivity of the delayed type. The most definite evidence comes from the work of Snell and Kaliss[8,9] which is concerned with the interference of the homograft rejection phenomenon (a type of delayed sensitivity) by circulating antibodies. This phenomena has been called "enhancement." The mechanism for this unexpected finding is now thought to be based on the "walling off" of the antigenic material coming from the graft by the circulating antibodies. Chase[10] also mentions that the production of delayed sensitivity in guinea pigs by organic compounds is greatly interfered with by the presence of circulating antibodies directed against the antigen used to produce the delayed sensitivity. Finally, there is the well-known clinical observation that there is an inverse relationship between the development of delayed-type skin allergy and circulating antibodies in patients with deep mycoses.[11]

We are therefore suggesting that it is not the presence but the absence of circulating globulin which may set the stage for immune reactions of the delayed type. The absence of "inhibitory globulin" factors in patients with rheumatoid arthritis and hypogammaglobulinemia is highly suggestive in this regard.[12,13] The high incidence of rheumatoid arthritis in patients with both congenital and acquired hypogammaglobulinemia suggests that "enhancement" by gamma globulin may be a normal mechanism in healthy people for preventing auto-immune aggression of the delayed type.

The high frequency of sprue-like syndromes in patients with hypogammaglobulinemia has been noted previously. The exact reason for malabsorption in these cases is not known. Again, either the intestinal lesion and hypogammaglobulinemia arise from a common defect or the malabsorption arises secondarily as a result of low levels of gamma globulin. The recent embryologic observations that lymphocytes arise in part from endoderm, as does the intestinal epithelium, give some weight to the first possibility.[14]

An absence of circulating antibodies could predispose to growth of bacteria in the small intestine. These bacteria could damage the intestinal mucosa structurally or could compete with the intestinal mucosa for nutrients. Very good evidence of the latter mechanism is present in patients and rats with "blind loop" anemias.[15] Here, vitamin-B_{12} malabsorption can be corrected by eliminating the bacteria by antibiotics.[16]

In our patient the biopsy showed increased numbers of polymorphonuclear neutrophil leukocytes. These cells according to one reviewer[17] of the histologic section are distinctly unusual in ordinary nontropical sprue in which lymphocytes and plasma cells predominate.[18,19] Since antibiotics failed to correct vitamin B_{12} malabsorption in this patient (Table I), his condition does not seem to be due to a "blind loop" mechanism. Auto-immune phenomena have been demonstrated in patients with colitis.[20] A mechanism similar to that outlined for the pathogenesis of the arthritis seen in patients with hypogammaglobulinemia may also be operating to cause the intestinal defects. The data in this patient are not sufficient in helping to choose among the several mechanisms mentioned for the frequency of intestinal malabsorption seen in patients with hypogammaglobulinemia. Low gamma globulin due to the failure of gamma globulin production is not seen in nontropical sprue.

Frequently these patients are treated with antibiotics for prophylactic reasons and also for definite episodes of infection. "Broad spectrum" antibiotics can cause diarrhea, but a malabsorption syndrome is seen only after treatment with neomycin.[21] Our patient was not treated with this drug.

The alleged ability of patients with congenital hypogammaglobulinemia permanently to accept skin homografts is not at present consistent with the fact that these patients can develop and transmit delayed sensitivity.[22] In view of the many technical difficulties involved in evaluating skin-homograft survival, further skin homografting should be performed in patients with both congenital and acquired hypogammaglobulinemia.

The fact that our patient had a perfectly normal homograft rejection phenomenon in spite of a globulin level of 40 mg. per 100 ml. strengthens the impression gained from animal experimentation that circulating antibodies have very little to do with the rejection of solid-tissue homografts.

Summary

A case report of early acquired hypogammaglobulinemia has been presented to show the course and complicating illnesses of hypogammaglobulinemia. Certain data and speculations as to the relationship between hypogammaglobulinemia and the frequently associated illnesses were offered.

Addendum*

Because of the recently reported high incidence of rheumatoid factor in relatives of patients with hypogammaglobulinemia, this patient's mother, sister, and brother were studied for the presence of rheumatoid factor and antinuclear globulin. These factors were absent. The gamma globulin levels of these relatives were again found to be normal.

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Calming the irritable infant with a simple tonal device

According to an article by Jay R. Olsen, M.D., and Edward N. Nelson, M.D., in the December, 1961, issue of *Minnesota Medicine*, it has often been observed that babies, irritable and sleepless although dry and well, are often lulled to sleep by certain sounds: the hum and vibration of a moving automobile or the sound of some sort of noise-making device nearby. These observations prompted experiments with a small transistorized device designed to emit a constant tone (Slumber Tone). This paper is a preliminary report on twelve weeks of experience with the device in the hospital nursery and in the home.

The device produced the desired results in 90 per cent of the infants exposed to tone. The effect could be repeated consistently in the same infant provided he was not ill, wet, or hungry. If any of these conditions prevailed, the device would not work. Also, it was not always successful on first exposure if environmental conditions were not favorable, such as a noisy examining room; once at home, however, many of these fussy infants rapidly became calm and fell asleep on exposure to the tone. Once the infant passes the age of seven months, the device has little calming effect. The immediate response is one of calming, resembling that which occurs when the child is picked up and held. Calming is usually instantaneous, and the child goes to sleep in thirty seconds to five minutes. Usually the baby will remain asleep if the tone is then stopped.

Remarkable Activity of an Elderly Man with Coronary Heart Disease

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THAT REGULAR physical activity appears to exert a protective action against coronary heart disease and sudden death in that condition has been observed by several authors.

Morris and his coworkers[1–3] reported that men in physically active jobs have less frequent, less severe, and later coronary heart disease in middle age than sedentary workers and that the incidence of sudden death in coronary heart disease was much greater among less active persons.

Kraus,[4] who ascribes to inactivity an important role in the production of disease, considers also coronary heart disease to be a "hypokinetic disease." The role played by a lack of exercise in the production of disease and the role of exercise in the prevention of heart disease and in cardiac rehabilitation has been extensively discussed and stressed by Kraus and Raab.[5]

Spain and Bradess,[6] analyzing a population group for the factors thought to be involved in the development of coronary atherosclerosis, found that the men who had engaged in sedentary occupations tended to die from coronary occlusion at a younger age than those whose occupation involved considerable physical activity. Strenuous activity was associated only infrequently with the episode of acute coronary occlusion that preceded death.

Wolffe[7] found evidence of atherosclerosis in a surprisingly high percentage of 300 top executives with curtailed physical activities but found little evidence of atherosclerosis in 300 athletes actively engaged in vigorous physical activities. Marathon runners in the fifth and sixth decade showed no evidence of atherosclerosis in the vessels of the lower extremities, and good circulatory efficiency was demonstrated.

Also Walker[8] mentions that most evidence indicates that physical activity protects against rather than promotes atherosclerosis. He points out that physically active workers with coronary artery disease have a lower early mortality rate and a longer survival from the onset of their disease than sedentary workers.

Luongo[9] points to the "evidence that sedentary living and poor health habits are the real culprits in coronary disease and not hard work, overexercise or occupational stress." May[10] also has stated that sedentary living conditions predispose people to coronary heart disease.

An explanation for the damaging effect of inactivity on cardiovascular function and structure has been given by Raab and his coworkers.[11–14] Raab states: "The underlying mechanism seems to consist in a deterioration of cholinergic vagal counterregulatory effectiveness against the injurious influence of uninhibited sympathetic-adrenergic activity upon myocardial oxygen economy and myocardial mechanical efficiency."[11]

Regarding the possibility of resuming work after coronary thrombosis, several authors have stated that the outlook for return to work for patients with coronary heart disease is generally favorable.

Williams *et al.*[15] report in a questionnaire survey of general practitioners that, among the answers to the question of experience in rehabilitation of patients with coronary artery disease, "experience was cited to show that most of these patients were able to return not only to work but to their previous occupation without a great deal of restriction."

Price[16] points to the accumulated evidence that a large number of garment workers have a form of benign coronary thrombosis with myocardial infarction which evidently occurs mostly in older-age groups and carries with it a not unfavorable outlook for continued employment.

Crain and Missal[17] found further confirmation that the outlook for return to work is more favorable than is generally thought for industrial employes who have suffered a myocardial infarction.

The experiences of the Work Classification Unit of the Los Angeles County Heart Association[18] "confirm the impression that many patients with cardiovascular disease who could work are not allowed to work or are kept below safe capacity."

The following case is presented as a contribution to the observations about the work of old people with coronary heart disease and about the protective action of work in that connection.

Case report

A seventy-one-year-old white male patient was admitted to the New York State Veterans' Camp on September 11, 1953. There was no history of heart disease, chest pain, or dyspnea. The patient reported that as a young man he practiced many sports such as rowing, skating, baseball, and hockey playing; he was in the Navy for ten years. Later he was a businessman. He did physical work in his free time and walked a lot as a pastime. The patient stated that he worked physically "because he wanted to keep his health in shape." The physical examination revealed the presence of a varicose ulcer at the left ankle, blood pressure of 170/90, weight of 196 pounds, and height of 5 feet $8^1/_2$ inches. After healing of the varicose ulcer, the patient started to do general outdoor labor in the camp, for example, lawn and hedge work, also work in the forest such as cutting trees, digging holes for pipes, and shoveling snow. He performed this kind of work for about three and one-half years; during all that time he made no complaints whatsoever indicating the presence of a coronary artery disease.

In June, 1957, he left the camp and worked outside as a caretaker. At that time he did very hard work such as lumber work, sawing wood, tearing down a barn, and building a bridge. And with that unusually heavy work he did not care for sufficient rest. He reported later: "I put too much on me." On August 8, 1957, about one and one-half months after starting the unusually heavy work, he felt during work a severe epigastric and substernal pain, radiating to the jaws, also pain in both arms, and he broke out in profuse cold sweat. The next day he experienced a similar attack. On that day he was brought to the Veterans' Camp and admitted to the infirmary.

On examination his pulse rate was 40 per minute, regular, his blood pressure 110/80, and his temperature 98.4 F.; the heart sounds were clear, the lungs were clear to percussion and auscultation, there was no engorgement of the neck veins, and no edema was present. The abdomen was soft, with no tenderness or resistance, and no masses were palpable. Electrocardiograms taken on August 10 and 20 and September 10, 1957, revealed the following findings: Q_2 and Q_3, aVf, and V_6 were present with inversion of T_2 and T_3, aVf, and V_6. These findings were constant in all the three dates mentioned; they revealed the presence of a ventricular myocardial disease with old posterior wall infarction (Fig. 1). Consequently the conclusion was: The patient, unknown to him, had previously suffered a posterior wall infarction. The attacks on August 8 and 9, 1957, were caused by episodes of coronary insufficiency. An x-ray film of the chest for heart size taken on September 16, 1957, showed the heart to be within normal limits with a left ventricular preponderance. There was a suggestion of an atheromatous plaque within the knob of the aorta and widening of the aortic shadow. Blunting of the left costophrenic angle was present. During his stay in the infirmary the patient suffered intermittently from anginal syndrome which gradually subsided. He was treated with nitroglycerin sublingually and meperidine hydrochloride (Demerol) subcutaneously. His pulse rate gradually increased to 55 and 60 beats per minute and his blood pressure to 130/80. On September 16, 1957, he was discharged from the infirmary.

One month after his discharge he started to do the same work as he performed before the cardiac episode against the warning of

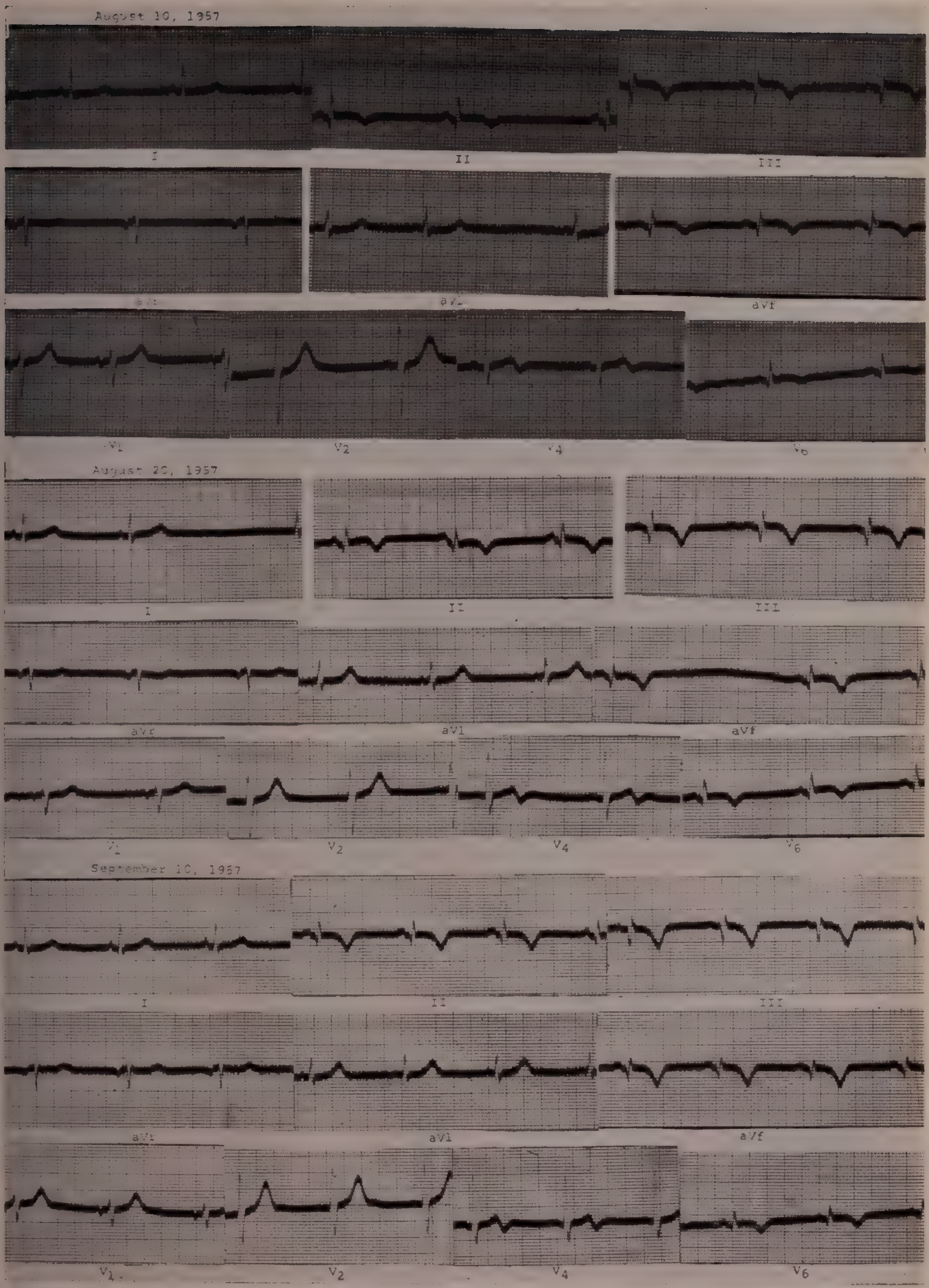
August 10, 1957
I
II
III
aVr
aVl
aVf
V1
V2
V4
V6
August 20, 1957
I
II
III
aVr
aVl
aVf
V1
V2
V4
V6
September 10, 1957
I
II
III
aVr
aVl
aVf
V1
V2
V4
V6

FIGURE 1. Electrocardiograms taken on August 10 and 20 and September 10, 1957. Note persistence of following findings on all three dates: Q_2 and Q_3, aVf, and V_6, inversion of T_2 and T_3, aVf, and V_6. Conclusion: old posterior wall infarction.

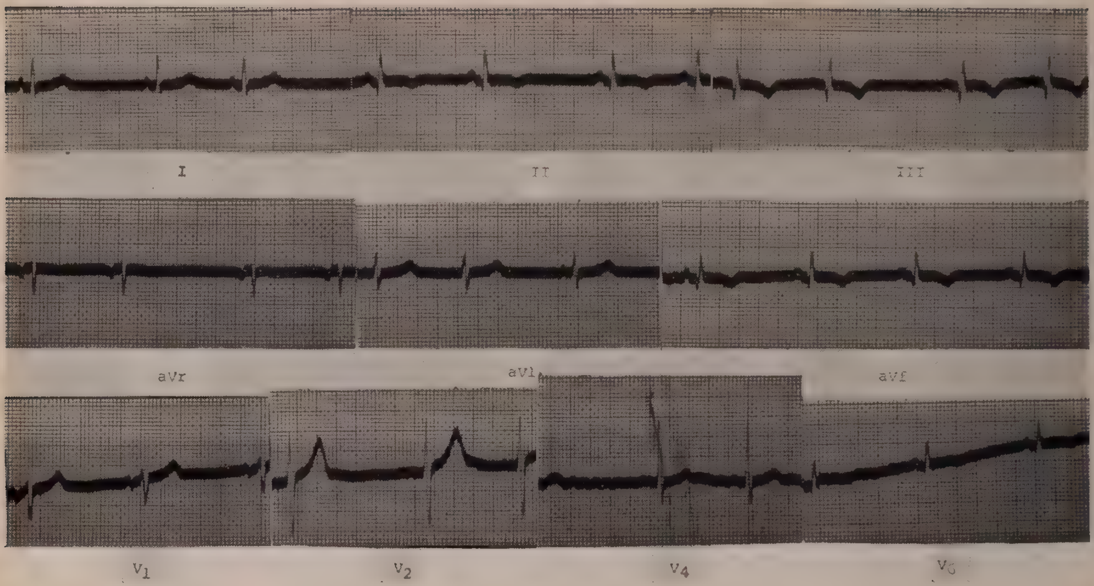

FIGURE 2. December 6, 1957: no significant changes from earlier tracings.

the medical department. An electrocardiogram taken on December 6, 1957, revealed no significant changes from the previous tracings (Fig. 2). The patient worked without any complaints until October 2, 1958, when he fractured his right lateral malleolus during work. The fracture healed perfectly, and he resumed his work on January 14, 1959. The interpretation of an electrocardiogram taken on January 8, 1959, was: As compared with the tracing of December 6, 1957, T_2 and T_3, aVf, and V_6 were less deeply inverted, and the posterior wall infarction was old (Fig. 3).

On January 25, 1959, the patient cleaned a ramp about three blocks long and 20 feet wide from snow 2 inches deep within about five and one-half hours; it was the fourth time he had done such work since January 15, 1959. A clinical examination which was made on January 29, 1959, revealed an excellent general appearance. The patient had no complaints whatsoever; no clinical pathologic condition was found. The blood pressure was 150/85 and the pulse rate 72 per minute with a regular rhythm.

The patient continued to work in the same way as before. In October, 1959, he reported that he felt excellent and was still doing outdoor labor at the age of seventy-seven. In February, 1960, he was admitted to the infirmary for a respiratory infection which lasted for sixteen days. In March, 1960, that is, more than two and one-half years after the described cardiac episode, he again removed snow after each of several snowstorms. In June, 1961, he still was doing outdoor work at the age of seventy-eight.

Comment

Some of the effects of training leading to a greater work capacity manifest themselves in a longer duration of effort before exhaustion, ability to attain a greater minute volume of ventilation and a greater oxygen consumption during exhausting work, greater mechanical efficiency as indicated by a lower oxygen consumption for a given amount of work, lower resting heart rate, smaller increase of heart rate during moderate work, larger stroke volume, and more rapid return of heart rate and blood pressure to normal following activity.[19] By a planned program of exercise the work capacity of the heart can be improved.[20]

In contrast, inactivity appears to be an important contributing pathogenetic factor in myocardial degeneration and cardiovascular disease. In this connection, Raab[11–14] has stressed the role of the neurohormones in cardiovascular pathogenesis. "A constant adrenergic preponderance, as it prevails in the untrained heart, creates an

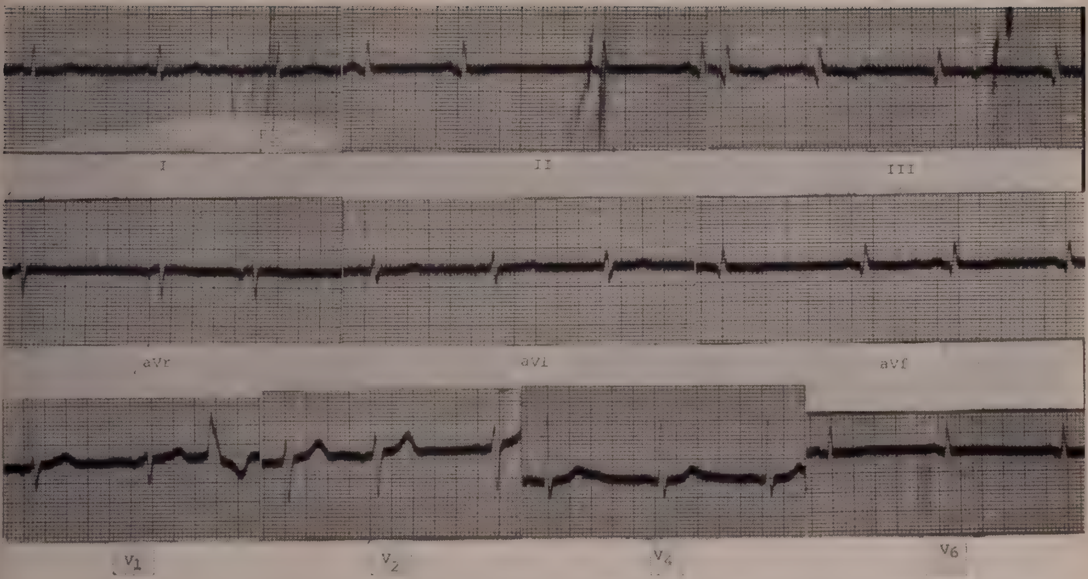

FIGURE 3. January 8, 1959: T_2 and T_3, aVf, and V_6 less deeply inverted than on previous tracings.

initially latent unfavorable metabolic situation. Adreno-sympathetic overactivity is apt to bring on catastrophe when additional catecholamine-'toxifying' circumstances, which increase the metabolic vulnerability of the myocardium, coincide with it. Such circumstances are: coronary sclerosis, arterial hypertension, cardiac hypertrophy, overactivity of the thyroid hormone and of adrenal mineralocorticoids."[5] Selye[21] points to the probability that the cardiotoxic effect of epinephrine depends on a "conditioning" for the effects of other potentially pathogenic stimuli, for example, cardiac stimulants or bacterial or viral infections.

We have, furthermore, to consider the influence of the mental attitude of the working person on work efficiency. The experiments of Stevenson, Duncan, and Wolff[22] have revealed that the work efficiency of healthy persons as well as cardiac patients was decreased in a mental state of anxiety but increased in a balanced state of mind.

Raab[11] has pointed to the detrimental effects of the cortical and hypothalamic mechanisms of anxieties on the neurovegetative biochemical equilibrium in the cardiovascular system. Emotional stresses seem to exert a damaging influence on the heart through sympathetic stimulation of the heart muscles and by promoting atherogenesis through elevations of the serum cholesterol level.[5]

The observation that work which is done cheerfully and within certain limits often appears to have a beneficial effect on coronary heart disease is supported by experiences that return to work was enhanced in patients with coronary heart disease who liked that kind of work, whereas rehabilitation appeared to be difficult in those cardiac patients who disliked their work.[23]

The cheerful mental attitude in which our patient performed his work was of paramount importance. Very probably the same kind and amount of work done with dislike or resentment would have exerted a detrimental effect on the patient's heart.

In this patient, who liked to do physical work all his life, a certain amount of work appeared to have a definitely beneficial effect. The kind of work performed by him would have to be considered as too strenuous for an untrained man of his age. However, for him it could be classified as only moderately strenuous and adequate.

This work enjoyed by the patient appeared to have also a protective action. Because even when this patient, who, unknown to him, previously had a myocardial infarction, did at a time very heavy work exceeding the work capacity of his heart, he did not again suffer a myocardial infarction but only temporary attacks of coronary insufficiency. Also the fact that he recovered so completely that at the age of seventy-five he was able to resume his previous work points to the protective effects of his training which include the acquired ability of improving the coronary blood flow during work and the development of a beneficially high vagal tone which prevents adrenergic preponderance, improves oxygen economy of the heart muscle, and increases efficiency.[5,11]

Furthermore, we have to assume that this protective influence is also based on the acquisition of the faculty to develop an appropriate collateral circulation in the coronary vessels compensating for the loss of circulation caused by narrowing or obstruction of a coronary artery. That assumption is supported by reports of an unusually rich development of the capillary network of athletes' hearts[24] and by the observation that the total coronary bed in exercised animals is augmented.[25] The importance of building up a collateral circulation in the coronary vessels in anticipation of eventual coronary occlusions or excess demands on the myocardium has been stressed by Green and Borousch.[26]

Physical work can be considered to be a form of "alarming stimulus" placing the body in a state of general stress.[27,28] We know from the work of Selye that, on one hand, "complete absence of stress is incompatible with life"[29] and that, on the other hand, there are "transitional steps between physiologic adaptive processes to stress and strain of everyday life and severe alarm reactions which cause death during the shock phase."[30]

These observations are in accordance with the law of Arndt-Schulz[31]: "Weak stimuli excite physiologic activity, moderately strong ones favor it, strong ones retard it, and very strong ones arrest it."

The conclusion appears to be justified that an insufficient amount of physical activity—which is a form of an alarming stimulus—is a conditioning factor[28] promoting the breakdown of the heart in form of myocardial infarction.

In contrast to that effect of insufficient exercise, the appropriate amount of physical work appears to be just the opposite of a conditioning factor in the production of coronary heart disease. Consequently the appropriate amount of exercise deserves in that connection the name of a "counterconditioning factor."

An excessive amount of physical activity, as demonstrated by the aforementioned case, is a specific damaging agent. Its damaging effect apparently was diminished in that patient by the counterconditioning effect of previous training.

This case also proves that coronary heart disease does not exclude the possibility of physical work even at an advanced age.

The determination of the optimal prophylactic and therapeutic activity dose which includes the most appropriate quality and quantity of individually adapted exercise with all its ramifications opens a wide field of research. It is a part of the search for the "optimal preventive and therapeutic alarming stimuli."[32]

Summary

The case of a seventy-five-year-old, physically trained man with an old posterior wall infarction who performed comparatively strenuous work is presented because it shows the protective action of training and of work cheerfully performed even at an advanced age.

Especially interesting is the fact that even after a bout of excessive work this patient suffered only temporary attacks of coronary insufficiency, a few months after which he resumed his previous regular physical work which he continued to do for years without any untoward effect.

Acknowledgment. The author wishes to thank Irving R. Juster, M.D., and George E. Hubbard, former Superintendent of the New York State Veterans' Camp, for their help in preparing this report and Curtis P. Bight, M.D., for his constructive criticism.

70-B Glasco Turnpike

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Regional enteritis in children

According to an article by Wilton H. Bunch, M.D., Arthur I. Kugel, M.D., and Jacob Janzen, M.D., in second quarter, 1961, issue of *Medical Arts and Sciences*, both acute and chronic regional enteritis occur in children, although either form is rare. A study of 12 cases collected from four hospitals supports the consensus that the peak incidence of the acute form occurs at about five years of age; the chronic type occurs with increasing frequency after ten years and is rarely found under that age. The peak incidence of the chronic form occurs at about age twenty-seven. Except for the higher incidence of the acute form in early childhood, the course of the disease is similar in all age groups. Surgery is not indicated in acute regional enteritis in childhood. Since the appendix is rarely involved, its removal is comparatively safe.

Angiocardiography in a Community Hospital

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Robb and Steinberg in 1938[1] announced a practical method for the visualization of the cardiac chambers and the great vessels in the living patient. In the ensuing years refinements in technics and equipment have made angiocardiography a commonplace procedure in all modern medical centers.

In many community hospitals, however, there has been some reluctance to expand the available diagnostic facilities to include angiocardiography. Modern sophisticated angiocardiographic equipment is beyond the financial resources of many smaller hospitals, and when one considers the ready access to extensively equipped medical centers throughout the country, it would be unreasonably wasteful for all of the medical institutions to obtain such elaborate equipment for occasional use.

About one year ago an unexpected modest donation was given to us, earmarked for the purchase of needed equipment by one of our neurosurgeons. A comparatively inexpensive rapid film changer for cerebral angiography was obtained. Using this unit for angiocardiography, we have solved some interesting problems which we believe to be of more than casual interest, particularly to those in circumstances similar to ours.

Technic

All patients were fasted for six hours. Suitable barbiturate sedation to alleviate apprehension was given to all patients one hour before the procedure. After antiseptic skin preparation, a number 13 needle was inserted into a suitable vein in the right forearm through a weal of 1 per cent procaine hydrochloride. After threading the needle well into the vein, it was attached to a Robb syringe containing 50 cc. of 90 per cent Hypaque, warmed to decrease its viscosity. With the patient's arm elevated and with the patient holding his breath, the injection was made as rapidly as possible by hand. The seriograph was set to take two films each second, a total of 12 films in all. If we were interested primarily in the pulmonary circulation, exposures were begun the instant the injection was begun. When the aorta or one of its branches was of prime concern, the sequence was started as soon as the injection was completed. There have been no reactions. We have not found it necessary to repeat the injection except in a few instances. A total of 1 cc. per kilogram of body weight may be given safely for one study, and by simultaneous injection of half the total dose in each arm to the average-sized adult patient opacification of the abdominal aorta may be obtained by the intravenous method. A cutdown may be necessary if the obtainable veins are not of sufficient caliber for easy percutaneous puncture.

Case reports

Case 1. A fifty-seven-year-old white female was admitted on January 29, 1959, with the diagnosis of mediastinal tumor. For several weeks prior to entry she had been awakened from sleep with difficulty in breathing and a feeling of tightness in the chest, associated with weakness. Aside from a cholecystectomy performed three years previously, she had enjoyed apparent good health. Six years ago, she was informed that her chest x-ray film was abnormal; however, she chose to ignore that report. A physical examination presented a well-nourished, well-developed woman, appearing perfectly well. The blood pressure

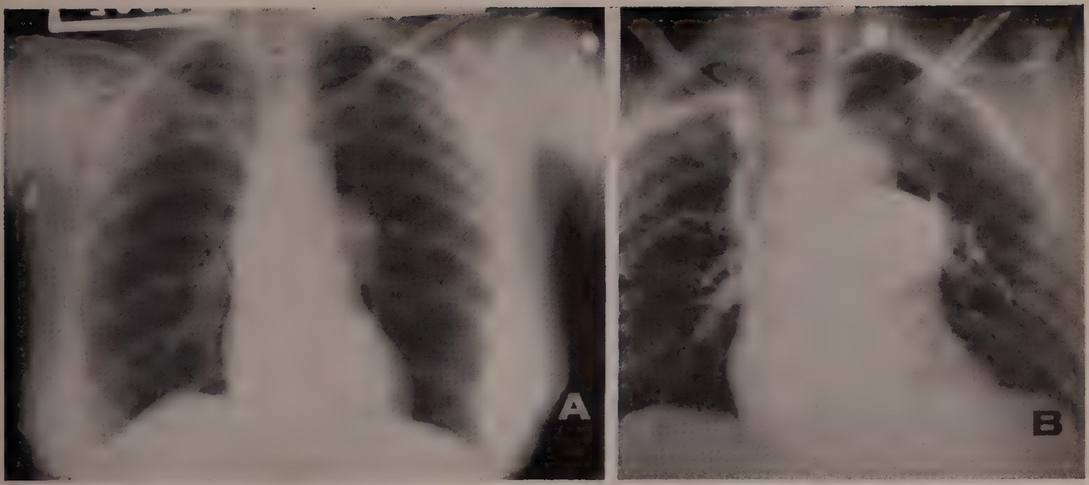

FIGURE 1. Case 1. (A) Angiocardiogram showing rounded shadow in left hilum. (B) Angiocardiogram demonstrating aneurysmal dilatation of left pulmonary artery.

was 160 systolic and 105 mm. Hg diastolic. The only positive finding was a systolic murmur in the second left intercostal space, with a normal pulmonic second sound. A chest film showed a smooth rounded mass in the left hilum which was pulsatile on fluoroscopy. The electrocardiogram was normal. Angiocardiography revealed that this mass was an aneurysmal left pulmonary artery (Fig. 1). Cardiac catheterization, performed elsewhere to rule out possible causes for this finding, was essentially normal. There was a 10 mm. of mercury gradient between the right ventricle and the pulmonary artery, which we did not consider of such significance as to warrant the conclusive diagnosis of pulmonary stenosis. The right ventricular pressure was 34.5/5.5, while the pulmonary pressure was 24.4/11.1. The systemic and pulmonary flows were equal. There was no evidence of intra- or extracardiac shunt. We were unable to demonstrate conclusively any of the known causes of pulmonary artery dilatation.

Comment. There are many causes of pulmonary artery dilatation without true aneurysm formation. Broadly speaking, congenital lesions of the heart, such as pulmonary valvular stenosis, and defects characterized by left to right shunts and consequently high flow through this circuit result many times in an enlargement of the main artery and its branches. Diseases of the lungs and their vascular beds which result in pulmonary hypertension are associated frequently with an enlargement of the pulmonary artery. Since we were unable to demonstrate conclusively any known cause in our case, we classify it as one of idiopathic pulmonary artery dilatation.

A true aneurysm of the pulmonary artery is a very rare lesion, compared with aneurysm of the aorta. Groedel[2] reports the pulmonary lesion as occurring once to every 250 aortic aneurysms. Deterling and Clagett[3] reviewed the literature and were able to collect 36 autopsy-proved cases of pulmonary artery aneurysm. They considered only autopsy-proved cases in their analysis. This was an incidence of 1 in 17,000 autopsies. The cases which they analyzed all had pathologic evidence of vessel wall destruction. Slightly more than 30 per cent of these cases had proved syphilis. The other associated conditions were patent ductus arteriosus in 20 per cent and interventricular septal defect in 9 per cent. Four of the deaths were due to rupture of the aneurysm—2 to bursting into the pericardium, the other 2 to perforating the bronchus—while heart failure was the most common cause of death in the other patients. The age distribution in this group is also of interest as is the sex of the involved patients. There were approximately an equal number of men and women, whereas in aortic aneurysm men were by far in the majority, the ratio being about 6 to 1. Thirty per cent of the patients were less than thirty years of age. In more than half of the 36 cases reviewed there was a harsh systolic murmur heard in the pulmonic area, while a palpable thrill was present in 8 patients. The associated symptoms in Deterling and Clagett's[3] reviewed cases, in the order of frequency of occurrence, were dyspnea, cyanosis, edema, cough, hemoptysis, and chest pain. The radiographic finding was generally that of a discrete rounded shadow at the hilum. There was pulsation on fluoroscopy with associated transmitted pulsation in the smaller vessels of the lungs, giving rise to Pezzi's sign or the "hilar dance." There were some cases, however, in which no pulsation was seen, so that the absence of this sign does not rule out the diagnosis. These authors also reported a case in which the diagnosis of aneurysm was made in a thirty-seven-year-old individual, and surgical treatment was attempted. Because of the extent of the lesion, the procedure was abandoned, and the patient expired three days later. The postmortem examination confirmed the diagnosis and demonstrated a patent ductus of 1-cm. diameter, marked arteriosclerosis, and associated diffuse thrombosis and hyalinization of the small pulmonary vessels.

Israels[4] has reported an autopsy-proved case of an aneurysm involving both the right and left pulmonary arteries. Sections showed arteriosclerosis of the pulmonary vessels, with thrombosis of the smaller radicles. This patient also has demonstrated a harsh murmur in the second and third left intercostal space.

Dotter and Steinberg[5] have reported 2 instances of aneurysmal dilatation of the left pulmonary artery demonstrated by angiocardiography. They termed this condition "congenital pulmonary artery aneurysm," and described it as an organic dilatation which cannot be accounted for by any known cause of pulmonary artery dilatation. "Idiopathic dilatation of the pulmonary artery" is another term applied to the dilation of the vessel without demonstrable cause. Van Buchem *et al.*[6] have presented 5 cases proved by angiocardiography in which cardiac catheterization showed no hemodynamic abnormalities.

The fate of the involved vessels in pulmonary artery dilation of unknown cause offers interesting speculation. It is said repeatedly that this is a benign condition, yet an analysis of the fluid mechanics involved in dilated elastic conduits would indicate otherwise. Once dilatation has occurred from whatever cause, it would seem that the Bernoulli principle would apply.[7] This law states that a widened lumen slows the stream of fluid. Slowing of the stream then increases the lateral pressure in the elastic conduit, causing further dilatation. Thus a cycle is developed, limited only by the rigidity of the vessel wall and the surrounding structures. If structural fatigue occurs with vessel wall damage, a true aneurysm results. Because of the low pressure in the pulmonary circuit, this would not occur as often as in the systemic circuit. Theoretically, however, if a patient with idiopathic dilatation of the pulmonary artery lives long enough, a true aneursym should develop eventually. Moreover, should 1 of these patients with idiopathic dilatation develop pulmonary hypertension from whatever cause, the process would be hastened.

It is only by following these patients to autopsy that the true course and prognosis of this condition will be known. Certainly a rapid enlargement of a previously dilated pulmonary artery in the idiopathic group should be viewed with considerable suspicion, and surgical treatment should be considered.

Case 2. A forty-year-old white female was admitted on May 15, 1959, with a two-day history of hemoptysis. Her past history revealed a similar episode at the age of seventeen years. She also stated that she had had many bouts of bronchitis in the past. A hysterectomy for fibromyomata had been performed in 1945. Except for decreased breath sounds on the left side, there were no significant findings. An x-ray examination of the chest revealed an increased volume of the right lung, with a shift of the mediastinum to the left side. A bronchoscopy was normal. Bronchial washings were reported as showing some suspicious cells, possibly malignant. The patient was discharged, only to be read-

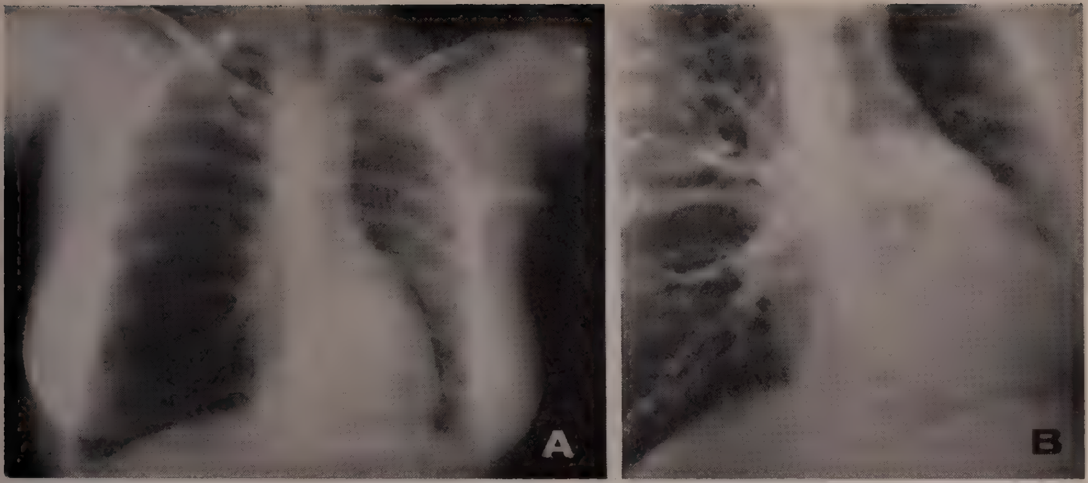

FIGURE 2. Case 2. (A) Angiocardiogram showing posteroanterior view of chest. Right lung is overinflated and mediastinum is displaced to left. Left lung is hypoplastic and occupies smaller volume than normal. (B) Angiocardiogram showing absence of pulmonary artery going to left lung.

mitted five weeks later for a rebronchoscopy. The findings at this time were those of chronic bronchitis in the left lower lobe bronchus which were verified by a biopsy. It was also noted that the left bronchial tree was smaller in caliber than the right side. A bronchogram revealed no anomalies. Because these findings were compatible with those found in the congenital absence of the pulmonary artery to the left lung, an angiocardiogram was performed. This study showed a complete absence of the main branch of the pulmonary artery to the left lung (Fig. 2). There was no other cardiovascular anomaly demonstrated.

Comment. The congenital absence of a main branch of the pulmonary artery was once thought to be extremely rare. In 1952 Madoff, Gaensler, and Streider[8] reported a case diagnosed by angiocardiography, in which they were able to demonstrate a systemic vessel from the aortic arch to the lung. In 1953 Steinberg, Dotter, and Lukas[9] reported 2 cases demonstrated by that technic. In 1 patient the left side was involved and in the other the right side. Cardiac catheterization was performed in 1 patient, at which time it was found that the resting pulmonary artery pressure was normal despite the fact that there was twice the normal blood flow through the uninvolved lung. Mild pulmonary hypertension did develop with exercise, however, and during this time the cardiac output doubled. These findings were felt to be similar to those of a patient with a surgical pneumonectomy.

The normal pulmonary vascular bed is large enough to allow a threefold increase in flow without an increase in pressure. With greater flow the pressure begins to rise, assuming, of course, that there is no pulmonary vascular disease, such as is known to develop in patients with prolonged large left-to-right shunts.

In 1954 Flynn, Siebens, and Williams[10] presented 1 instance of the anomaly. Their patient presented symptoms of hemoptysis. This case was also proved by angiocardiography, although the radiologic signs were classical. A bronchospirometry revealed that the oxygen uptake on the affected side was only 4 per cent, although it accounted for 43 per cent of the total ventilation. The arterial blood was fully saturated, while cardiac catheterization showed minimally elevated pulmonary artery pressure. The cause of the hemoptysis was felt to be an enlargement of the bronchial circulation. An increase in the bronchial circulation has been shown to occur in dogs after a ligation of the main branch artery to a given side. That increased bronchial circulation in man also occurs is demonstrable in patients with congenital heart disease in whom there is a small amount of pulmonary flow due to outflow tract obstruction. In open correction of the tetralogy of Fallot the bronchial collateral flow may present a formidable problem in perfusion.

Maier[11] analyzed 3 cases of proved absence of the right pulmonary artery. One of his patients was operated on because of repeated pulmonary infections, hemoptysis, and a productive cough. A pneumonectomy was done on the affected side. The diagnosis of an absent pulmonary artery had been established preoperatively by angiocardiography. There was no pulmonary artery to the resected lung, although there was a systemic vessel arising high in the chest and entering the upper portion of the lung. Maier's second case was diagnosed by an angiocardiogram, and here dilated bronchial vessels on the plain film of the chest gave the appearance of an inflammatory infiltrate. The third case concerned an infant who died of pneumonia and demonstrated at autopsy the anomaly of absent right pulmonary artery. Here again a systemic artery was found, this one arising from the ascending aorta and supplying the right lung. The vessel was 2.7 cm. in diameter.

Maier[11] also presented 3 cases of hypoplastic lung. In this anomaly the roentgenographic picture may be similar to that of a congenital absence of a pulmonary artery, although the bronchogram will usually differentiate the two conditions. Those lungs also had a systemic blood supply coming through the diaphragm, although there was a small pulmonary artery in 2 instances. In the severe hypoplastic lung bronchial anomalies with congenital bronchial cyst formation and bronchiectasis constitute most of the maldeveloped lung. The lung may consist of only one lobe, with a bronchial tree which does not correspond to any single normal lobe. The 3 cases analyzed all involved the right side. The radiologic picture was one of marked displacement of the heart into the right chest, giving the picture of dextrocardia.

Madoff, in his discussion of this report by Maier,[11] reported on the bronchospirometric findings in a case he studied with absent right pulmonary artery. With the patient breathing room air, the affected side took up no oxygen; while breathing 100 per cent oxygen, however, the affected side took up 7 per cent oxygen. The normal left lung took up 93 per cent oxygen. Then, supplying pure oxygen to the right or affected side and room air to the left or good side, there was an uptake of 18 per cent oxygen on the right side and 83 per cent oxygen on the left side. He was able to calculate the bronchial circulation to the affected side as 7 per cent of the left ventricular output, compared with 1 per cent, which is the normal systemic blood flow to that lung.

Schneiderman[12] reported an autopsy-proved case of an absent right pulmonary artery in which a systemic artery from the ascending aorta to the lung was present. He reviewed the published autopsy and the surgically proved cases and found that all of them had a systemic artery from the aorta or one of its branches to the affected lung. His search also revealed that in the absence of the left pulmonary artery associated cardiovascular anomalies, such as the tetrology of Fallot, were frequent, whereas when the right side was so affected, it was an isolated defect, except in rare instances. That this condition is being more readily recognized was demonstrated by Fisher and Van Epps[13] who collected and analyzed 7 cases, 6 of which involved the right side. In most of their cases there was a murmur heard in the pulmonic area, ascribed to the increased flow through the single main artery present.

The radiologic findings in this anomaly are readily recognizable. They consist of an overdeveloped lung, with a shift of the mediastinum to the opposite side and an absence of the main pulmonary artery shadow on the affected side. Pulmonary vascularity is absent on the involved side, and the bronchogram is normal, as opposed to the entity of congenital hypoplastic lung where anomalies of the bronchial tree are usually present. It may also be possible to demonstrate a systemic blood supply to the affected side by angiocardiography, in addition to the demonstration of an absent pulmonary artery, as Madoff, Gaensler, and Streider[8] and Maier[11] were able to do in their cases.

The prognosis in this anomaly without associated intracardiac defects is good. One reported case was fifty-six years old. A major affliction in the normal lung, however,

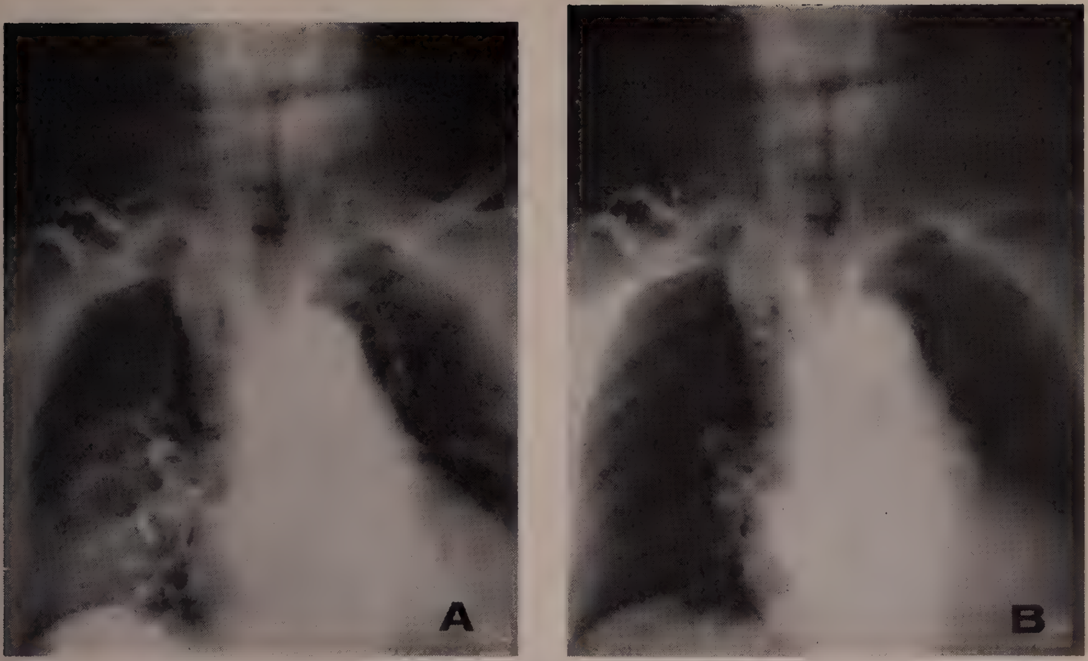

FIGURE 3. Case 3. (A) Angiocardiogram demonstrating buckling of innominate artery. (B) Angiocardiogram showing borders of innominate artery marked for diagrammatic purposes.

would be of more serious import than in the normal individual, and the patient ought to be made aware of this fact. For this reason, the diagnosis should be made conclusively by angiocardiography when the radiologic signs are suggestive.

CASE 3. A seventy-four-year-old white female was admitted on February 24, 1959, complaining of a swelling of the right side of her face which was present on arising in the morning. The admitting physician had felt a strong pulsation in the right supraclavicular area which he felt might be an aneurysm of the innominate artery. The patient had been known to have had ankle edema in the past. A physical examination revealed a well-developed, well-nourished white female in apparent good health. Her blood pressure was 190/90. There was a prominent pulsation in the right supraclavicular area on the right side. No definite mass was felt. There was no bruit heard over this area. Aside from minimal ankle edema, the remainder of the examination was normal. A chest x-ray film revealed a slight prominence of the right superior mediastinal shadow. Angiocardiography demonstrated very clearly a tortuous innominate artery (Fig. 3).

Comment. Although an aneurysm of the innominate artery is a rather uncommon lesion, a buckling of the innominate artery occurs rather frequently. That the two conditions can occur together is shown by the case reported by Kirby and Johnson[14] in which an aneurysm of the innominate artery associated with tortuosity in a hypertensive patient was treated by resection and end-to-end anastomosis.

Parkinson, Bedford, and Almond[15] studied this entity and came to the conclusion that a tortuous innominate or common carotid artery is a more common cause of pulsatile swelling in the neck than an aneurysm of these vessels and found that most of the patients with a tortuous innominate or common carotid artery were hypertensive.

Hsu and Kistin,[16] in an extensive review of a buckled innominate artery, presented 16 cases which they had collected in a two-year period. Nine of their cases were hypertensive. Two of them had a widened superior mediastinal shadow demonstrated by x-ray film. One patient was thirty-

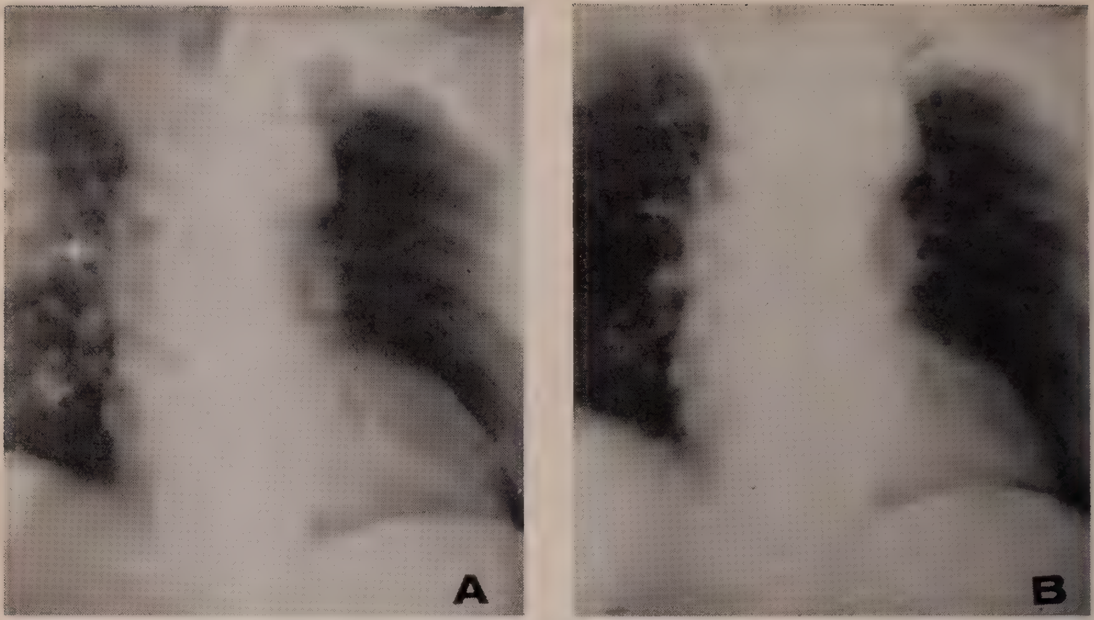

FIGURE 4. Case 4. (A) Control film taken prior to injection of contrast media. (B) Contrast media in aorta during angiocardiography. Thickened wall of aorta is clearly visible in descending aorta above cardiac shadow.

four years of age and had coarctation of the aorta. The other 15 patients were between fifty-one and eighty-three years of age. Thirteen out of 16 of the patients were women, and most of them were obese. These authors also noted that buckling of the common carotid may cause bulging of the pharyngeal wall and may be mistaken for an abcess. Indeed, they referred to a case in the literature where drainage was done, in such an instance, with the predictable result. One of their patients was explored for an aneurysm and died following surgery.

Honig, Dubilier, and Steinberg[17] report a series of 12 cases proved by angiocardiography. In a series of 104 angiocardiograms done in hypertensive patients they found 12 instances of a tortuous innominate artery. Eight of their patients were women, and 8 of the total were hypertensive. A bruit was heard over palpable pulsations at the base of the neck in 3 out of 4 patients. One of their cases had a thoracotomy for mediastinal tumor, and none was found. A postoperative angiocardiogram showed a tortuous innominate artery. Benzier, Katz, and Pitman[18] collected 12 cases of this entity during a mass survey for chest disease. Three cases were subsequently proved by angiocardiography. The incidence in patients over fifty years of age was 4.9 per cent.

The right border of the superior mediastinal shadow on x-ray film is formed by the superior vena cava and the right innominate vein. As a result of the degenerative changes due to hypertension and arteriosclerosis, the aorta elongates and becomes tortuous. As this occurs, the arch becomes somewhat elevated, causing the innominate artery to buckle. This event causes a prominence in the right border of the superior mediastinum which may be confused with a mediastinal tumor or a lesion of the lung, a substernal thyroid, or an aneurysm of the innominate or common carotid artery. This lesion, although perfectly benign and requiring no treatment, should be considered in the differential diagnosis of all pulsating masses in the supraclavicular area, the suprasternal area, and masses presenting in the right superior mediastinal area.

CASE 4. A fifty-two-year old white male was admitted to the hospital on October 10, 1959, with a one-hour history of a severe tearing pain in the left upper chest, associated with profuse sweating and weakness. The pain radiated down the chest and through to the back. The patient was a known hypertensive of two years duration, and for one week prior to admission he had been having mild intermittent chest pain.

A physical examination revealed an acutely ill patient complaining at the time of chest and upper abdominal pain and requiring morphine for relief. The blood pressure was 200/120, the pulse was 120, and the temperature was 100 F. Fundi showed marked thinning of the arterioles. The chest was clear and the heart sounds were normal. The abdomen at examination was completely normal. All peripheral pulses were present. An electrocardiogram was within normal limits except for nonspecific T-wave changes. Because of the upper abdominal pain, a serum amylase was done and found to be in the normal range. An x-ray film of the chest was suggestive of a widened aortic shadow. During the next twelve hours the pain remained severe and moved into the upper abdomen. Eighteen hours after admission an angiocardiogram was performed to confirm the suspected diagnosis of dissecting aneurysm of the aorta. The thickened aortic wall, typical of this disease, was clearly demonstrated (Fig. 4). During an intravenous pyelography, a nonfunctioning left kidney gave further evidence of the extent of dissection, and it was felt that surgery was urgent.

Twenty hours after admission, anesthesia was induced, and hypothermia was begun. A left thoracotomy was carried out when the patient's temperature had reached 93 F. On entry into the left pleural space through the bed of the resected fifth rib, a small amount of serosanguineous fluid was encountered. The ecchymotic aorta could be seen through the overlying pleura. On incising the pleura, the aorta was found to be irregularly thickened from the level of the subclavian artery to the diaphragm. The aorta was mobilized, and several intercostal arteries were ligated. With the temperature at 90 F., a pair of coarctation clamps were applied, 4 to 5 inches below the origin of the subclavian artery, and the aorta was completely transected. A window of the intima from the proximal aorta was excised to allow for the re-entry of the stream into the main channel below. The intima was sutured to the adventitia in the distal segment, thereby obliterating the false lumen in the lower segment. The aorta was then reanastomosed. The duration of cross-clamping was twenty-five minutes. Prior to occlusion, Arfonad was given to reduce the blood pressure to 120 systolic. After slowly removing the clamps, the blood pressure fell to 100 systolic. Aramine was started intravenously, and the pressure was maintained at 160/80. This medication was required for about eight hours. Its discontinuance prior to this was associated with falls in blood pressure to below 100. A tracheotomy was done eight hours after surgery because of difficulty with secretions. There was no evidence of cord or brain damage as a result of the aortic occlusion, and the patient moved all his extremities without difficulty. The urine output during the first twenty-four hours postoperatively was 470 cc.

Thirty-six hours postoperatively the patient experienced a generalized convulsive seizure from which he recovered spontaneously. Several hours later a similar episode occurred. At this time the heart sounds became inaudible. The chest was rapidly opened, and the heart was seen to be in ventricular fibrillation. Successful defibrillation was carried out, and normal rhythm was maintained for thirty minutes, when fibrillation recurred. Further efforts at resuscitation were to no avail.

An autopsy showed aortic dissection beginning at the origin of the subclavian artery and extending down to the external iliac arteries. The suture line in the thoracic aorta was satisfactory. The left kidney showed hemorrhagic infarction, with dissection of the renal artery on that side. There was a point of narrowing in the vessel, distal to the limit of the dissection. The other kidney was normal. The aorta was the site of extensive atherosclerosis.

Comment. Although isolated cases of surgical intervention for dissecting an aneurysm are reported dating back to 1935, it remained for DeBakey, Cooley, and Creech[19] to make a concentrated attack on this problem and to demonstrate that surgical treatment was feasible. Their approach to the problem via the thoracic aorta was based on the pathologic findings of Shennan[20] and of Gore and Seiwert[21] who noted that in the acute cases that came to autopsy the process had involved the thoracic aorta in between 95 and 98 per cent. The abdominal aorta was involved by an extension from the thoracic aorta in between 35 and 55 per cent. Gore and Seiwert also observed that, whereas between 85 to 95 per cent of the acute cases died of hemorrhage from rupture of the outer wall of the aorta, rupture occurred in the abdominal aorta in only 2 per cent of the cases. The surgical principle applied by DeBakey, Cooley, and Creech[19] was the deliberate creation of what may occur spontaneously in the healed case, namely, a point of re-entry into the main channel. This procedure allows the more peripheral circulation to be through the normal channel and removes the great tension on the outer wall of the more proximal vessel which, if unrelieved, leads so often to its rupture.

Although the diagnosis of a dissecting aneurysm is frequently made with considerable accuracy on clinical and ordinary radiologic study alone, it may at other times present great difficulty, particularly in the acute case. Prior to the establishment of a sound operative procedure for this condition, it was of academic interest, but of little practical importance if the differentiation from acute myocardial infarction was not always made. Once surgery is contemplated, however, a correct diagnosis becomes imperative. Warren, Beckwith, and Muller[22] report 1 case out of a series of 5 surgically treated dissecting aneurysms where this error was made. That particular patient had a normal electrocardiogram and signs of pericardial tamponade. He had collapsed with transient paraplegia. At operation a large hemopericardium was found, but there was no evidence of an aortic rupture. The patient expired and at autopsy was found to have a large myocardial infarct.

The radiologic aspect of a dissecting aneurysm was reviewed extensively by Lodwick.[23] He correlated the x-ray film findings with the autopsy findings and was able to point up certain diagnostic features. A widening of the supracardiac shadow was found in most cases. Some of the patients showed a widening of the aortic knob, while a thickening of the aortic wall was occasionally demonstrated, even without the use of contrast media. Also noted frequently was the obliteration of the notch below the aortic knob. In view of the fascinating work of Ponsetti and Baird,[24] who were able to produce aortic dissection and kyphosis in growing rate by feeding them a diet of seeds of sweet peas, Lodwick[23] looked for spinal abnormalities in his cases. He was able to demonstrate mild dorsal scoliosis in 2 out of 3 patients who died of a dissecting aneurysm. These patients had medial necrosis of the aorta, the dissection having begun in the ascending aorta.

The angiocardiographic findings in aortic dissection were first reported by Golden and Weens.[25] The diagnostic features in this study consist of a thickened aortic wall appearing as a double shadow of varying thickness, caused by the abnormal channel contrasted to the opacified main channel. Angiocardiography offers a method which is accurate, although probably not infallible in the acute stage.

The patient with a rupture of the aorta into the pleural space or abdominal cavity of course is not such a great dilemma to the surgeon, since hemorrhage in itself is an indication for surgery. In such a situation opacification of the pleural space or mediastinum by blood would make the demonstration of the thickened wall of the aorta almost impossible by angiocardiography.

Comment

It has not been our purpose to discuss the applications, indications, or contraindications of angiocardiography. Many learned reports have been written on angiocardiography in the past twenty-two years, since its first clinical application, and indeed it would be pretentious on our part to discuss it. It does occur to us, however, that too little emphasis has been placed on this technic as a tool which can be, and should be, available in the smaller community hospitals where a significant percentage of the thoracic surgery in this country is now done. This field of surgery is certainly no longer restricted to the teaching centers, and many a surgeon will, on occasion, find himself face to face at operation with a lesion with which he would have been able to deal successfully, had an accurate preoperative diagnosis allowed for proper preparation as to equipment and surgical assistance.

Although in our case the outcome of a dissecting aneurysm of the aorta was unsuccessful, the indications for surgery were clearly defined and the diagnosis was assured. This particular patient was in no condition to be moved and certainly, from all available autopsy data concerned with this disease, very few of the acute cases will ever be in a condition to be transferred safely to medical centers. With the present diffusion of capable surgeons throughout the country, the early definitive diagnosis of this affliction by angiocardiography should make possible some significant salvage among these patients, wherever they may be.

A final consideration relative to angiocardiography, but certainly not a small one, is the pure joy that comes from being able to settle a diagnostic problem which was formerly out of reach on one's home ground. The thrill of making a correct diagnosis is after all one of the great satisfactions of medicine, but it is not necessary that these findings come only at the time of autopsy.

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The Physician's Responsibilities Under the Second Injury Law

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THE PURPOSE of this report is to help clarify the role of the physician, his responsibilities and his privileges, in the successful administration of the Second Injury Law. The basic objectives of this law, as part of the Workmen's Compensation Law, are as follows:

1. An injured employe should be compensated for all the disability which he suffers as a result of an industrial injury.
2. Employers should be encouraged to employ the physically handicapped. Furthermore, if a person so employed should suffer a subsequent industrial injury, his employer should not be penalized by the imposition of greater liability than would be the case if the employe did not have a pre-existing physical impairment. The employer should be entitled to limited liability.[1]

To make this law applicable to any individual case, the employer must comply with five specific provisions of the Second Injury Law.

Provisions of the Second Injury Law

PROVISION 1. The previous handicap must be a permanent physical condition serious enough to be or likely to be a limiting handicap to employment. It may be a previous workmen's compensation injury but not necessarily. It may be a disablement as a result of accident and disease or a congenital condition. For example:

CASE 1. A paraplegic person, whose paraplegia was the result of a noncompensable injury, sustained an injury to his right wrist. It resulted in a 60 per cent loss of use of the right hand. This second injury interfered with the use of crutches. An award for permanent total disability was affirmed. *Conway* v. *Aluminum & Brass Company*, 279 App. Div. 82; 304 N.Y. Rep. 571.

PROVISION 2. The employer must have knowledge of the previous permanent physical handicap of the employe. This knowledge is basic to the employment decision. For example:

CASE 2. An employe consulted his doctor and learned that he had heart disease. In talking with his employer about his poor health he was advised to "take it easy." The employer had not been told about the heart trouble. The case was disallowed in respect to the Second Injury Law and it was held that the employer did not have knowledge of prior permanent physical impairment. *Caggiano* v. *Cella*, 281 App. Div. 1050.

CASE 3. A claimant was suffering from a previous permanent physical impairment. The condition was obvious to anyone who saw the claimant and was likely to influence adversely any employer in hiring him. The employer believed the condition to be permanent. The decision was made in favor of the employer, and reimbursement from the Special Fund was ordered.

PROVISION 3. The second injury must be caused by an accident that arises out of and in the course of employment or by an occupational disease causing disability or death for which the employer is required to

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provide benefits under compensation law. For example:

Case 4. A claimant who has a permanent partial disability sustains an injury away from work which is not covered by compensation. Such a case does not come under the Second Injury Law.

Provision 4. The second injury must result in a permanent disability, caused by both conditions, that is materially and substantially greater because of the previous handicap than that which would have resulted from the second injury alone. In both cases, it must be established that either the injury or the death would not have occurred except for the presence of such preexisting permanent physical impairment. For example:

Case 5. A factory worker, who limped since childhood owing to shortening of the right leg, strained his back in the course of lifting a box of supplies. This case was disallowed for reimbursement under the Second Injury Law because the combined disability of the first and second injuries was not materially and substantially greater than the second accident would have caused alone.

Case 6. A workman had previously lost 45 per cent use of his right hand in an employment accident. He then suffered a second injury that caused the loss of use of 85 per cent of his opposite left arm. The decision was made that the employer was entitled to reimbursement from the Special Fund for all compensation payable in excess of one hundred four weeks, since permanent disability after both injuries was greater than would have resulted from the subsequent injury alone: *Wason* v. *Mover & Pratt, Inc.*

Provision 5. Claims for reimbursement from the Special Fund must be filed with the Board in writing by the employer or by his carrier, in his behalf, prior to the final determination that the resulting disability is permanent, but in no case more than one hundred four weeks after the date of disability or death.

Under the Second Injury Law the employer of a permanently partially disabled worker has only a limited direct financial responsibility if the handicapped worker should be injured further or disabled. At most the employer or his insurance carrier is liable for compensation benefits and medical care for only one hundred four weeks. It is significant that the Law specifies permanent disabilities without reference to any specific diagnosis.[2] The records reveal that many employes come to work with known permanent disabilities (cardiac or other) and then sustain a covered accident, resulting in an additional degree of permanent disability (cardiac or other).[3] Under these circumstances the employer's payments are limited to one hundred four weeks, although the claimant may thereafter continue to receive payments through the Special Disability Fund for extended periods or for life.

A useful Second Injury Law may thus stimulate the hiring of the cardiac or other disabled person, spread the cost of future injuries, and relieve the burden from a particular employer.

Medical testimony

The medical testimony necessary and sufficient to establish the validity of a case is undoubtedly the most important single item in the correlation of all evidence before a case can be disposed of. From 65 to 80 per cent of all litigation in our courts requires some type of medical report or testimony, and 7 out of 10 personal injury cases are decided on medical rather than legal consideration. It is obvious from these figures that the medical profession has an increasingly important part in the administration of justice.[4]

The difference between law and medicine is the method of approach insofar as the discovery of truth is concerned. The lawyer attempts to maintain his position by argument and contention with the opposing counsel. His professional life is one of advocacy of a cause. His object is to magnify his own arguments and to belittle those of his opponent.

The physician, on the other hand, does not live by contention. His training is in the free and open atmosphere of the laboratory, hospital, sick room, or private office. He demands full and frank discussion and disclosure of all phases of a case. All factors pertaining to the case are brought to light and evaluated. When all the pertinent data are collected, he correlates them and forms a judgment with reference to the illness. By training and practice therefore the whole tempo and attitude of the day-to-day experience of the physician and of the lawyer are totally different.

It may be noted that the law and the courts demand to know the results of disability evaluation in more or less inflexible absolute terms. From the medical examiner's point of view, the factors involved in the evaluation of medical impairment are endowed with large margins of unavoidable variables and error. To satisfy the letter of the law, the physician is confronted by the enigma of trying to convert medical variables to legal quasi judicial constants. Since we are dealing basically with human elements throughout, the problems become difficult to evaluate at best.[5]

Expert testimony

In the presentation of cases before the courts expert testimony is often brought in. A model Expert Testimony Act was approved in New York State in 1937 and 1943. The reason for this act was summed up in a prefatory note which said:

> Parties constantly employ experts upon the strength of their bias which may range from professional prejudice to naked perjury. There can be no doubt of the need of expert testimony. The problem is how to eliminate the evils of bias and partisanship which shape it.[6]

What is expected of the examining physician with regard to the Second Injury Law is valid evidence of the claimant's functional capacity or the extent of his incapacity. Physicians are trained to think in terms of diagnosis and treatment. It is not enough to diagnose the case in point. It is even more important to evaluate the severity of the malady and come to a conclusion as to its permanency. The examining physician, in this respect, becomes the diagnostician and prognostician.

In addition, the physician is expected to arrive at a conclusion with reasonable medical certainty in respect to evaluating the combined severity of two separate injuries.

The physician may establish a case by merely quoting from his records that the claimant had a previous injury which resulted in a permanent disability. This portion of the testimony involves the subject of "knowledge."

There are these three important facts that the physician can and must establish for clarification of the case: (1) knowledge, (2) permanency of medical impairment, and (3), the most important, a medical opinion about the magnitude of the impairment of the two superimposed injuries as compared with the possible results of each injury sustained separately.

Disability evaluation

The evaluation of permanent disabilities in the Workmen's Compensation Board in the State of New York may be divided into four groups.

The first involves schedulable injuries of the extremities. There are definite values established by law assigned to the loss or loss of use of an extremity, for example an arm which is assigned three hundred twelve weeks of total disability at $55 per week, effective July 1, 1962. The lower extremity is assigned two hundred eighty-eight weeks of total disability at $55 per week. There are commensurate values for portions of an extremity.

The second group comprises injuries to the body or vital organs or systems resulting in permanent disabilities but disposed of eventually by a "lump sum, nonschedule adjustment." The lump sum is arrived at by an agreement which is reached by mutual consent of the claimant or his attorney and the carrier or his representative.

The evaluation of disability resulting from systemic injuries is a very complex subject. Two of the main reasons are (1) systemic injuries do not lend themselves easily to a percentage loss-of-use evaluation as is the case when evaluating injuries of the extremities; and (2) the medical and legal criteria used are at variance. For convenience, disabilities in this category have been classified as mild, moderate, or marked partial disability, temporary or permanent; total disability; or no disability.

The third group is one in which the right of compensation has been established and compensation has been paid for not less than three months, in which the continuance of disability and future earning capacity cannot be ascertained with reasonable certainty. In such cases the Workmen's Compensation Board may, in the interest of justice, approve a nonschedule lump sum adjustment agreed to between the claimant and the employer or his insurance carrier.

The fourth group involves cases in which the evaluation of permanent total disability is made. In such cases the employe is paid $66^2/_3$ per cent of his average weekly wages during the continuance of such disability, determined on the basis of his average weekly wages for the year prior to his accident. The maximum weekly benefit rate of $55 is applicable in accidents or disablement which occur after July 1, 1962.

Legally, there may be three different concepts of permanent disability: (1) inability to earn full wages, (2) total disability to perform any other work, and (3) actual incapacity to perform the work in the occupation in which the claimant was engaged at the time of the accident. The disability in such instances is based on the significance of medical impairment as it relates to the customary work or to any other job opening that the employer is able to provide.

The term permanent impairment should be used to designate a purely medical condition. It refers to any anatomic or functional abnormality or loss after maximum medical treatment and when the condition has reached a permanent state.

The term permanent disability should be used to denote the legal disposition of a case and involves the inclusion of other than medical factors concerned in the case. In other words, a claimant, when his injury has reached a permanent state and there is permanent medical impairment from which there results a change in his ability to perform his so-called "customary work," may be classified as having a permanent disability.

It is most important for the examining physician to become aware of his proper place in the evaluation of disability. The final rating when a compensation case is disposed of is a quasi judicial action, that is, a legal, not medical, responsibility. Nonmedical factors which go into this determination, such as industrial disability, age, sex, and social condition, have proved extremely difficult to measure. For this reason, permanent impairment which is determined by the physician is in fact the sole or real criterion when determining a disability far more often than is readily acknowledged. The numerous problems confronting the examining physician thus assume the greatest importance for the equitable disposition of a case.

The evaluation of permanent impairment from systemic injuries involves a knowledge of anatomy, physiology, general pathology, and pathogenesis, and their objective correlation. Each of the factors mentioned carries with it a large margin of unavoidable error which is compounded when an attempt is made to add the factors up and convert them to a single finding.

As of 1959 fewer than one third of the nation's workmen's compensation laws have "subsequent injury funds" that cover radiation injuries. Whether or not the later disability due to exposure to radiation is a proper charge of the Second Injury Fund is a moot question. There is in New York State a "Slow Starting Occupational Disease Law" which imposes liability on the employer, or if insured his carrier, for delayed disability due to radiation, provided notice of the disability is given to the employer within ninety days after the disablement and after knowledge that the disease is or was due to the nature of the employment.

The intent of the Workmen's Compensation Law is

> That every person in this State who works for a living is entitled to maintain his independence and self-support even after he has been physically handicapped by injury or disease.
>
> That any plan which will reasonably, equitably, and practically operate to break down hindrances and remove obstacles to the employment of partially disabled persons is of vital importance to the State and its people.

Summary

The physician's role in helping to solve the problems related to the Second Injury Law is the most important part of the case record.

It involves consideration of the first injury, its severity and prognosis, and the potential

physical capacity for employment.

His knowledge must be broad rather than specialized, and he must be aware of sociopsychologic interests and motivations.

When a second injury is superimposed, the many problems already encountered become intensified and more complex.

At this point, the physician deals with the law, industry, labor, insurance, social workers, education centers, lawyers, and a mass of clerical work.

A correlation of all factors now brings the doctor to the point of determining, to the best of his ability, the claimant's remaining functional capacity to satisfy the legal procedure.

From these medical deliberations and findings the Workmen's Compensation Board will be able to determine whether or not the Second Injury Law is applicable.

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Influence of Sodium in the Potable Waters on the Low-Sodium Diet in Cardiovascular Therapy

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THE USE OF the low-sodium diet in the treatment of essential hypertension and congestive heart failure makes it important for physicians to consider the possible influence of the sodium content of the drinking water on the total daily sodium intake.

In an article in the May 7, 1949, issue of the *Journal of the American Medical Association*, Cole* made the observation that the sodium content of the water becomes important when it reaches 10 mg. per 100 ml. (100 parts per million of sodium ion).

Fortunately, most of the natural waters in New York State do not contain appreciable concentrations of sodium. Tests have revealed that the drinking waters of Albany and Syracuse have a sodium content of 0.2 mg. per 100 ml., that of New York City and Rochester 0.3 mg., and that of Buffalo 0.7 mg. These amounts are subject to seasonal fluctuations, but there is little likelihood of the concentrations ever reaching sufficient magnitude to have significant influence on dietary therapy.

Exceptions may occur in some communities in the central part of the State where the drinking water is obtained from wells near salt deposits or shale formation where sodium carbonate might be present. Even in these instances, the concentration of sodium ion is usually less than 10 mg. per 100 ml.

* Cole, S. L.: Tap water sodium in the low salt diet, J.A.M.A. **140:** 19 (May 7) 1949.

TABLE I. Communities utilizing zeolite softening plants

Place	County	Hardness of Raw Water (Parts per Million)*
Belfast	Allegany	250
Bethlehem	Albany	180
Bolivar	Allegany	170
Canastota	Madison	350
Cazenovia	Madison	310
Chittenango	Madison	440
Clyde	Wayne	740
Dexter	Jefferson	290
East Aurora	Erie	340
East Rochester	Monroe	280
Elba	Genesee	1,000
Fillmore	Allegany	140
Fultonville	Montgomery	350
Greenville	Greene	200
Houghton	Allegany	140
Ilion	Herkimer	360
Latham	Albany	150
Manchester	Ontario	300
Munnsville	Madison	800
New Windsor	Orange	144
Oakfield	Genesee	330
Palatine Bridge	Montgomery	350
Riverview Village	Dutchess	350
Rose, N. Rose	Wayne	230
Sauquoit	Oneida	290
Scottsville	Monroe	900
Sharon Springs	Schoharie (auxiliary well)	820
Solvay	Onondaga	740
Stockport	Columbia	172
Thornwood	Westchester	200
Union Springs	Cayuga	410
Wappingers Falls	Dutchess	180
Yorktown	Westchester	190

* Prior to softening.

Effects of zeolite process

Hard waters softened by the zeolite process, however, contain a concentration of sodium equivalent to the calcium and magnesium removed by the softening process. If water with the hardness of 300 parts per million were softened to the usual standard of 80 parts per million hardness, the process would result in the presence of 100 parts per million of sodium ion in the treated water. The treatment of water with lesser degrees of initial hardness would not result in clinically significant amounts of sodium ion, provided the softening process was not carried below 80 parts per million hardness.

Zeolite softening plants are utilized in the treatment of public water supplies in the communities listed in Table I. In addition, zeolite softening plants are being used extensively in private dwellings, particularly in hard-water areas of the State.

Advice for physicians and health officers

Physicians utilizing the low-sodium diet for patients residing in areas where the sodium ion of the drinking water might be in excess of 10 mg. per 100 ml. (100 parts per million) would do well to confer with the local health officer for further information regarding this item. The State of New York Department of Health, through its Division of Environmental Health Services, will be glad to assist local health departments in conducting studies on the local water supply regarding sodium content, if the indications arise.

Should the local water supply have a significantly high concentration of sodium ion, it will be necessary for the patient to purchase special drinking water. Obviously, all purchased water should likewise be checked for sodium content.

SATURDAY
MAY 19, 1962

STATLER HILTON
New York City

Medical Communications Day

sponsored by

NEW YORK STATE JOURNAL OF MEDICINE
Official publication
Medical Society of the State of New York

and

AMERICAN MEDICAL WRITERS ASSOCIATION
Metropolitan New York Chapter

Morning Session

William Hammond, M.D., Scarsdale
Editor, New York State Journal of Medicine, *Presiding*

9:00 A.M. Registration

9:30 A.M. Welcome

Russell L. Cecil, M.D., New York City
President, Metropolitan New York Chapter,
American Medical Writers Association

9:40 A.M. Panel: **New Frontiers in Medical Communication**

Henry I. Fineberg, M.D.
Executive Vice-President and Past-President,
Medical Society of the State of New York, *Chairman*

1. **Communications Systems for Medical Practice**

Lee B. Lusted, M.D., Rochester, New York
Professor of Biomedical Engineering and Associate Professor of Radiology

2. **Interchange of Information Through Poison Control Centers in the Nation**

Henry L. Verhulst, Washington, D. C.
Director, Poison Control Branch, Division of Accident Prevention, U.S. Public Health Service

3. **Medical Communications: What the Public Really Gets**

Leona H. Baumgartner, M.D., New York City
Commissioner of Health, City of New York

4. **Speaking One Language**

Burgess Gordon, M.D., Chicago, Illinois
Associate Editor, Journal of the American Medical Association

A question and answer period will follow the four presentations.

12:00 NOON Reception
(*Courtesy Hoffmann-La Roche, Inc., Nutley, New Jersey*)

12:30 P.M. Luncheon

Alfred P. Ingegno, M.D., Brooklyn
Chairman, Publication Committee,
Medical Society of the State of New York, *Presiding*

ADDRESS: **Communications and Medical Quackery**
MORRIS FISHBEIN, M.D., Chicago, Illinois
Editor, Excerpta Medica,
Past-President, American Medical Writers Association

Afternoon Session

ROBERT A. PETERMAN, M.D., Nutley, New Jersey
Hoffmann-La Roche, Inc.; Vice-President, Metropolitan New York Chapter, American Medical Writers Association, *Presiding*

2:30 P.M. PANEL: **New Horizons in Medical Communication**
ERIC MARTIN, Ph.D., Fort Lee, New Jersey
Director of Medical Communication, Lederle Laboratories, Pearl River, *Chairman*

1. **The Box and the Button**
   JOHN MACKENZIE, New York City
   Executive Secretary, Council on Medical Television
2. **Legal Pitfalls of Medical Communications**
   ANDREW J. GRAHAM, Esq., New York City
   Member of firm of Roger, Hoge, and Hills
3. To be announced
4. **The New Horizons**
   RICHARD H. ORR, M.D., New York City
   Director, Institute for the Advancement of Medical Communications; President, American Medical Writers Association

A question and answer period will follow the four presentations.

5:00 P.M. Reception
(*Courtesy Wallace Laboratories, Cranbury, New Jersey*)

REGISTRATION

Medical Communications Day / Saturday, May 19, 1962

STATLER HILTON, NEW YORK CITY

Sponsored by New York State Journal of Medicine *and* American Medical Writers Association, Metropolitan New York Chapter
Registration Fee: $6.00 for members of the Medical Society of the State of New York or the American Medical Writers Association
$10.00 for nonmembers

Registration fee includes morning and afternoon sessions, luncheon, and receptions.

Enclosed is check (or money order) in the amount of .... *for* ..... *reservations for Medical Communications Day on May 19, 1962.*

NAME

ADDRESS

AFFILIATION

Please make checks payable to NEW YORK STATE JOURNAL OF MEDICINE; *send to 750 Third Avenue, New York 17, New York.*

Necrology

Charles H. Alessi, M.D., of Rome, died on March 20 at Rome Hospital at the age of sixty-two. Dr. Alessi graduated in 1927 from the University of Buffalo School of Medicine. He was an attending surgeon at Rome and Murphy Memorial Hospitals. Dr. Alessi was a member of the American Academy of General Practice, the Oneida County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Miller Allerton, M.D., of Port Crane, died on March 9 at his home at the age of eighty. Dr. Allerton graduated in 1906 from the University of Maryland School of Medicine and College of Physicians and Surgeons. Retired in 1945, he had been former chief of the medical staff at Binghamton City Hospital (now General Hospital) and at his death was a senior attending physician there. Dr. Allerton was a member and past-president of the Binghamton Academy of Medicine and the Broome County Medical Society, and a member of the Medical Society of the State of New York, and the American Medical Association.

Hyman Belsky, M.D., of Mount Vernon, died on March 31 at Mount Vernon Hospital at the age of fifty-nine. Dr. Belsky graduated in 1927 from the University of Maryland School of Medicine and College of Physicians and Surgeons. He was chief of medicine and chairman of the medical board of Mount Vernon Hospital and an associate attending physician at the Bronx Municipal Hospital Center. Dr. Belsky was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the New York Academy of Medicine, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Archie Leigh Dean, M.D., of New York City and Pleasantville, drowned while swimming in the Gulf of Mexico on March 28 at the age of seventy. Dr. Dean graduated in 1917 from Cornell University Medical College. A former professor of urology at Cornell Medical College, he was a consulting urologist at Vassar Brothers Hospital, Poughkeepsie, and an emeritus genitourinary surgeon at Memorial Hospital for Cancer and Allied Diseases. Dr. Dean was a Diplomate of the American Board of Urology and a member of the American Association of Genito-Urinary Surgeons, the American Urological Association, the New York Academy of Medicine, the Clinical Society of Genito-Urinary Surgeons, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Perry Bartlette Hough, M.D., of New Rochelle, died on April 7 at his home at the age of eighty-eight. Dr. Hough graduated in 1899 from New York University and Bellevue Hospital Medical School and interned at City Hospital and New York Eye and Ear Infirmary. He was a consultant ophthalmologist at City Hospital at Elmhurst, and at Knickerbocker and Sea View Hospitals. Dr. Hough was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Kirk, Jr., M.D., of Troy, died on March 18 at the Sharpe Homestead at the age of eighty-nine. Dr. Kirk graduated in 1899 from Albany Medical College. He was an attending neurologist at Leonard Hospital and an examining neuropsychiatrist at the Albany Veterans Administration.

Macy Levi Lerner, M.D., of Rochester, died on March 7 at his office at the age of seventy-two. Dr. Lerner graduated in 1914 from Jefferson Medical College of Philadelphia. He was an associate attending ophthalmologic surgeon at Strong Memorial Hospital and a consulting ophthalmologist at Genesee Memorial and Rochester General Hospitals. Dr. Lerner was a Diplomate of the American Board of Ophthalmology (one of the first certified), a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the Rochester Academy of Medicine (honorary life member), the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James Hoyt Lewis, M.D., of Buffalo, died on March 11 at his home at the age of eighty-five. Dr. Lewis graduated in 1901 from Columbia University College of Physicians and Surgeons and interned at New York Hospital. He was a consulting surgeon at Buffalo General Hospital, a consulting surgeon at the Bethlehem Steel Company clinic, former chief surgeon at the old

Moses Taylor Hospital in Lackawanna, and for many years a professor of anatomy at the University of Buffalo School of Medicine. Dr. Lewis was a Fellow of the American College of Surgeons and a member of the Buffalo Academy of Medicine, the Buffalo Surgical Society, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Herman Mendlowitz, M.D., of Brookyln, retired, died on April 1 at Maimonides Hospital of Brooklyn at the age of seventy-nine. Dr. Mendlowitz graduated in 1903 from New York University and Bellevue Hospital Medical School.

Max Pomerance, M.D., of Brooklyn, died on March 27 at Beth-El Hospital at the age of sixty-one. Dr. Pomerance graduated in 1928 from Long Island College Hospital Medical School and interned at Beth-El Hospital. He was attending cardiologist at Beth-El Hospital and Beth-El Hospital Outpatient Department, assistant attending cardiologist at Polyclinic Hospital, and an associate attending cardiologist at Polyclinic Hospital Outpatient Department. Dr. Pomerance was a Diplomate of the American Board of Internal Medicine (Cardiovascular Diseases), a Fellow of the American College of Physicians, a Fellow of the American College of Cardiology, and a member of the East New York Medical Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Bruno O. Charles Pribram, M.D., of New York City, died on March 13 at the age of seventy-three in Bavaria, Germany. Dr. Pribram received his medical degree from the University of Vienna in 1913. He was a Fellow of the American College of Surgeons and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Schleifstein, M.D., of Albany, died on March 9 at the age of sixty-one. Dr. Schleifstein graduated in 1924 from McGill University Faculty of Medicine. Retired in February, 1962, as chief pathologist of the New York State Health Department's division of laboratories and research, for the last ten years he was chairman of the postgraduate training committee of the State Association of Public Health Laboratories and had been a former chairman of the Section on Pathology and Clinical Pathology of the Medical Society of the State of New York. Dr. Schleifstein was a Diplomate of the American Board of Pathology (Clinical Pathology and Pathologic Anatomy), a Fellow of the American College of Pathologists, and a member of the Society of American Bacteriologists, the American Association of Pathologists and Bacteriologists, the American Public Health Association, the American Society of Clinical Pathologists, the American Society of Tropical Medicine and Hygiene, the New York State Society of Pathologists, the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Charles Schmidt, M.D., of Brooklyn, died on April 7 while visiting in Oswegatchie at the age of sixty-one. Dr. Schmidt graduated in 1930 from Georgetown University School of Medicine. He was deputy medical superintendent of Kings County Hospital.

Edmund Bernard Sullivan, M.D., of Mount Vernon, died on April 3 at his home at the age of seventy-three. Dr. Sullivan graduated in 1914 from Fordham University School of Medicine and interned at Manhattan Eye, Ear and Throat and Bellevue Hospitals. He was a consulting otolaryngologist at Mount Vernon Hospital. Dr. Sullivan was a Diplomate of the American Board of Otolaryngology and a member of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Francis W. White, M.D., of New York City, died on March 29 at Midtown Hospital at the age of eighty-five. Dr. White graduated in 1903 from Jefferson Medical College of Philadelphia. He was a consulting otolaryngologist at Manhattan Eye, Ear and Throat and North Hudson Hospitals (Weehawken, New Jersey), and an honorary member of the medical staff of Grasslands Hospital (Valhalla). Dr. White was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Laryngological, Rhinological and Otological Society, the New York Academy of Medicine, the New York Otological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Abstracts

Albanese, A. A., Lorenze, E. J., and Orto, L. A.: Nutritional and metabolic effects of some newer steroids. I. Oxandrolone and triamcinolone, New York State J. Med. **62:** 1607 (May 15) 1962.

A study was undertaken of the nutritional and metabolic effects of oxandrolone and triamcinolone. Relative numerical values were determined for the relationship between nitrogen balance and nitrogen intake, designated as the SPAI (steroid protein activity index). Oxandrolone, in doses of 10 to 30 mg. per day for periods of two weeks, exerted high protein anabolic activity in 11 adult males and females recovering from physically disabling episodes. In the same category of patients the administration of 12 to 24 mg. per day of triamcinolone decreased nitrogen retention in 6 out of 8 patients. The reduction in absorbed nitrogen was associated with a statistically significant fall in plasma lysine levels. Neither oxandrolone nor triamcinolone altered appreciably blood levels of sodium, potassium, chlorides, hemoglobin, and hematocrit.

Peck, R. E.: Use of CCC in treatment of alcoholic patients at Meadowbrook Hospital, New York State J. Med. **62:** 1626 (May 15) 1962.

Experimental work with CCC or citrated calcium carbimide (Temposil) was begun in 1959 at the Mental Hygiene Clinic. Twenty per cent of the patients discharged on CCC have returned to the clinic for treatment in comparison with only 5 per cent who returned to the previous Special Treatment Clinic without treatment with CCC. CCC is a valuable adjunct in attaining sobriety. It has no side-effects when not mixed with alcohol; it fortifies the patient's will at its weakest point and is a proper symbol of the patient's willingness to try to abstain from drinking; it may be given without the patient's knowledge at the discretion of the physician and the patient's family; and it provides a clear-cut index of the patient's sobriety.

Crastnopol, P., Seidenberg, B., and Braunstein, E. A.: Transventricular mitral commissurotomy, New York State J. Med. **62:** 1630 (May 15) 1962.

Mitral commissurotomy, performed with a transventricular dilator, is another technic for instrumental correction of mitral stenosis. The technic is particularly useful in instances of obliteration or attenuation of the auricular appendage, or in secondary commissurotomies. Much emphasis is placed on the surgeon's guiding the dilator through the mitral orifice into the left atrial cavity. Significant insufficiency, a major complication in all types of instrumental commissurotomy, occurred twice in this series of 14 patients.

De La Pava, S., and Pickren, J. W.: Mast cells and thrombosis; a correlative study, New York State J. Med. **62:** 1634 (May 15) 1962.

Skin samples were taken from the epigastrium of cadavers in 100 consecutive autopsies. The average counts of mast cells ranged from 1 to 14; cases with counts of 6 or less had a high percentage of thrombosis (38 per cent) whereas cases with an average count of above 6 showed a sharp decline in thrombotic phenomena (6 per cent). This finding might indicate that low counts of mast cells in the skin are associated with low levels of blood heparin.

Kenin, A., Levine, J., and Spinner, M.: Management of osteoarthritic knee, New York State J. Med. **62:** 1637 (May 15) 1962.

The osteoarthritic knee is affected by a slow degenerative wear and tear phenomenon which may start in the second or third decade of life, although most patients do not present symptoms until the fourth or fifth decade. Edema and hypervascularity of the synovia are among the first pathologic findings, along with changes in the cartilage. In most cases rest of the affected joint, generally with a Jordan splint, affords prompt relief. Operative management is reserved for patients who have not responded to conservative therapy and who have persistent pain. The operative procedure depends on the case. Postoperatively a massive compression bandage is applied, quadriceps pinching exercises are begun within twenty-four hours, and the patient is allowed to walk within a week, with emphasis on obtaining complete extension of the knee joint for proper stability.

Abstracts in Interlingua

Albanese, A. A., Lorenze, E. J., e Orto, L. A.: Effectos nutritional e metabolic de certe nove steroides. I. Oxandrolona e triamcinolona (*anglese*), NEW YORK STATE J. MED. **62:** 1607 (15 de maio) 1962.

Esseva interprendite un studio del effectos nutritional e metabolic de oxandrolona e triamcinolona. Relative valores numeric esseva determinate pro le relation inter le balancia de nitrogeno e le ingestion de nitrogeno. Pro isto le termino "indice del activitate proteinic de steroide" esseva introducite. (Abbreviation anglese: SPAI.) Oxandrolona—in doses de 10 a 30 mg per die durante periodos de duo septimanas—manifestava un alte activitate de anabolismo proteinic in 11 adultos mascule e feminin in stadio de recuperation ab physicamente invalidante episodios. In 6 ex 8 patientes del mesme categoria, 12 a 24 mg de triamcinolona per die reduceva le retention de nitrogeno. Le reduction in absorbite nitrogeno esseva associate con un statisticamente significative declino del nivellos plasmatic de lysina. Ni oxandrolona ni triamcinolona alterava appreciabilemente le nivellos sanguinee de natrium, kalium, chloruro, e hemoglobina o le valor del hematocrite.

Peck, R. E.: Le uso de therapia a CCC in le tractamento de patientes de alcoholismo al Hospital Meadowbrook (*anglese*), NEW YORK STATE J. MED. **62:** 1626 (15 de maio) 1962.

Travalio experimental con citrate carbimido de calcium (CCC; Temposil) esseva comenciate al Clinica pro Hygiene Mental in 1959. Vinti pro cento del patientes dimittite con prescriptiones de CCC ha retornate al clinica pro tractamento additional, a comparar con solmente 5 pro cento de retornatos post previe programmas de Tractamento Special in que CCC non esseva usate. CCC es un utile adjuncto al interprisa de establir sobrietate. Illo ha nulle adverse effectos secundari si illo non es miscite con alcohol. Illo reinfortia le determination del patiente in le area le plus debile e representa un appropriate symbolo pro le prestessa del patiente de effortiar se a abandonar le biber. Illo pote esser administrate sin informar le patiente, i.e. al discretion del medico e del familia del patiente. E illo provide un nette indice del sobrietate del patiente.

Crastnopol, P., Seidenberg, B., e Braunstein, E. A.: Commisurotomia mitral transventricular (*anglese*), NEW YORK STATE J. MED. **62:** 1630 (15 de maio) 1962.

Commissurotomia mitral effectuate con un dilatator transventricular es un technica additional pro le correction instrumental de stenosis mitral. Le technica es particularmente utile in casos de oblitteration o de attenuation del appendices auricular o in commissurotomias secundari. Es sublineate multo emphaticamente le importantia de que le chirurgo guida correctemente le dilatator via le orificio mitral ad in le cavitate sinistro-atrial. Un grado significative de insufficientia, lo que es un major complication in omne generes de commissurotomia instrumental, occurreva duo vices in le hic-reportate serie de 14 patientes.

De La Pava, S., e Pickren, J. W.: Mastocytos e thrombose; un studio correlative (*anglese*), NEW YORK STATE J. MED. **62:** 1634 (15 de maio) 1962.

Specimens de pelle esseva obtenite ab le epigastrion de cadaveres in 100 necropsias consecutive. Le numeration medie del mastocytos variava inter 1 e 14. Casos con numerationes de 6 o minus habeva un alte procentage de thromboses (38 pro cento), durante que casos con un numeration medie de plus que 6 monstrava un forte declino de phenomenos thrombotic (6 pro cento). Iste constatation significa possibilemente que basse numerationes de mastocytos in le pelle es associate con basse nivellos de heparina in le sanguine.

Kenin, A., Levine, J., e Spinner, M.: Tractamento del genu osteoarthritic (*anglese*), NEW YORK STATE J. MED. **62:** 1637 (15 de maio) 1962.

Le genu osteoarthritic es afficite de un lente phenomeno de detrition que pote initiar se durante le secunde o tertie decennio del vita, ben que in le majoritate del casos le patiente presenta symptomas solmente in le quarte o quinte. Edema e hypervascularitate del synovios es inter le prime constatationes pathologic. Iste disveloppamento occurre in concomitantia con alterationes del cartilagine. In le majoritate del casos, reposo del afficite articulation, generalmente con un ferula de Jordan, resulta in prompte alleviation. Intervention chirurgic es reservate al casos in que le patiente non responde al therapia conservatori e suffre persistente dolores. Le typo de operation depende del caso individual. Post le operation un massive bandage de compression es applicate. Exercitios a pinceage del quadricipe es comenciate intra vinti-quatro horas. Ambulation es permissible intra un septimana. Attention debe esser prestate al obtention de un extension complete del articulation genicular con le objectivo de restaurar le correcte stabilitate.

Month in Washington

Supporters of the King-Anderson bill stepped up their campaign as the House Ways and Means Committee neared a showdown vote on the legislation which would provide limited health care for the aged under Social Security.

The Kennedy Administration took over the leadership in the drive with the President accepting an invitation to address a rally in Madison Square Garden, New York City, on May 20 sponsored by the National Council of Senior Citizens for Health Care Through Social Security.

The Administration also was organizing citizens' committees in individual states to whip up grass roots pressure for the bill. The President was asking prominent persons, such as former Democratic governor and U.S. senator Edwin C. Johnson in Colorado, to head such committees.

After personally pledging their support to the legislation in a White House call on the President, 27 physicians formed The Physicians Committee for Health Care for the Aged Through Social Security headed by Caldwell B. Esselstyn, M.D., of New York City, president of the Group Health Association of America. Most of the 27 are educators, hospital administrators, or are in other administrative posts. A majority are members of the A.M.A.

Pointing out that the White House was able to muster only an insignificant number of doctors for the King-Anderson bill, an A.M.A. spokesman said at least 90 per cent of the nation's 261,000 physicians are opposed to the legislation.

The intensified Administration drive made it imperative that physicians and other opponents of the Social Security approach go all-out at this time in their efforts against the King-Anderson bill.

A vote was expected in the Ways and Means Committee in May or June at the latest.

Sen. Robert S. Kerr (D., Okla.), reaffirmed his opposition to the King-Anderson bill but said he expected it would come up on the Senate floor for a vote. He said he and Rep. Wilbur D. Mills (D., Ark.), chairman of the Ways and Means Committee, were conferring on legislation that would expand the Kerr-Mills program, which has the wholehearted support of the A.M.A., to cover more aged persons.

Under the leadership of Rep. William E. Miller (R., N.Y.), who is also chairman of the Republican National Committee, some Republican Congressmen got behind the so-called Bow bill which would permit aged persons to reduce their Federal income taxes by up to $125 a year to cover health insurance premiums. The government also would issue to persons sixty-five years old and older who pay no income taxes, or who pay less than $125, a certificate with which to purchase health insurance.

* * *

The Public Health Service licensed Type III oral poliomyelitis vaccine but left the decision to local health officials and physicians as to whether the oral or the Salk vaccine, or both, would be used this year.

Types I and II oral polio vaccine had been licensed last year, and Type III was the last of the series needed for protection against all three types of polio. Production and availability of the oral vaccine will be a major factor in the extent of its use this year.

The P.H.S. conclusion on local immunization programs was recommended by a special advisory committee to the Surgeon General and was in line with a policy adopted by the A.M.A. House of Delegates at Denver last November.

The P.H.S. gave five guidelines for the local programs:

1. Organizers of community drives must be assured that adequate supplies are available before such programs are undertaken.
2. All persons in those groups selected by the community should receive vaccine regardless of past polio immunization history.
3. In general, vaccination programs using either vaccine must have careful planning and achieve a maximum of support from official and voluntary health and medical groups.
4. The plans should assure the ready availability of the vaccine in all areas of the community and for all persons within the selected target groups. Special emphasis must be directed to those areas and population groups having the lowest levels of immunization. Community-wide programs should achieve the immunization of the maximum number of persons but no less than 80 per cent of the preschool children in all socioeconomic groups.
5. A continuing program of immunization of infants should be incorporated as an essential feature of all organized community-wide programs.

The P.H.S. also recommended that the three types of oral vaccines be administered sequentially, each in monovalent form at intervals of about six weeks.

"Optimally," the P.H.S. said, "large scale immunization campaigns with oral poliovirus vaccines should be conducted during the winter or spring months."

Prepared by the Washington office of the American Medical Association, Washington, D.C.

Luther L. Terry, M.D., Surgeon General of the P.H.S., termed the licensing of the Type III oral vaccine as "another major step toward the final conquest of paralytic poliomyelitis."

"Now, two effective weapons, the formaldehyde-inactivated vaccine and the oral vaccine, are available for general use," Dr. Terry said. "Their proper application should accelerate the decline in poliomyelitis and could lead to the early elimination of the disease."

The P.H.S. called for emphasis this year on vaccination of the unimmunized and inadequately protected with one or the other of "these effective vaccines (or a combination so long as there is at least a complete series of either) and also to the initiation of as many well-organized community-wide programs as the supply of vaccines will permit."

The P.H.S. set four priorities in use of the polio vaccines: (1) Vaccination programs in areas threatened with epidemics. The P.H.S. Communicable Disease Center at Atlanta, Georgia, will keep on hand supplies of oral vaccine to meet this need; (2) routine immunization of infants, starting when six weeks old and completed in twelve months; (3) immunization of preschool children; (4) immunization of young adults and parents of young children.

Medical Meetings

New York State Society of Industrial Medicine and the Clinical Society of the New York Diabetes Association

There will be a joint meeting of the New York State Society of Industrial Medicine and the Clinical Society of the New York Diabetes Association on Thursday, May 24, at the New York Academy of Medicine, 2 East 103rd Street, New York City, at 5:00 P.M. The meeting will consist of a symposium on "Employability of the Diabetic."

Speakers will include the following: Leonid S. Snegireff, M.D., D.P.H., associate professor of chronic disease control, Harvard School of Public Health, Massachusetts; Borris A. Kornblith, M.D., Workmen's Compensation Board, State of New York; B. B. Loomis, employe and public relations manager, Humble Oil and Refining Company; Gerald Friedman, M.D., president, New York State Society of Industrial Medicine, and chairman, Clinical Society of the New York Diabetes Association; Harold Brandaleone, M.D., associate clinical professor of medicine, New York University College of Medicine; and Abraham Kantrow, M.D., chairman, Vocational and Counselling Service, New York Diabetes Association, New York City.

For information contact: New York State Society of Industrial Medicine, 30 Rockefeller Plaza, New York 20, New York.

Section on Ophthalmology, Nassau Academy of Medicine

The Section on Ophthalmology, Nassau Academy of Medicine, will hold a meeting at the Academy on May 28. Gilbert Baum, M.D., Port Chester, will be the guest speaker.

For information contact: Arthur E. Merz, M.D., F.A.C.S., Secretary-Treasurer, Section on Ophthalmology, Nassau Academy of Medicine, 520 Franklin Avenue, Garden City, New York.

Pharmaceutical Society of the State of New York

The eighty-fourth annual convention of the Pharmaceutical Society of the State of New York will be held at the Lido Hotel, Lido Beach, Long Island, June 8 through 13.

Thirteenth international ornithologic congress

More than 600 leading scientific ornithologists from throughout the world will gather at Cornell University June 17 through 24 for the thirteenth international ornithologic congress. A special symposium on the role of birds as factors in the spreading of virus diseases has been arranged in cooperation with the U.S. Public Health Service.

The American Neurological Association

The eighty-seventh annual meeting of The American Neurological Association will be held at the Claridge Hotel, Atlantic City, New Jersey, June 18 through 20. For information write to: Melvin D. Yahr, M.D., Secretary, Neurological Institute, 710 West 168th Street, New York 32, New York.

American Nuclear Society

The annual meeting of the American Nuclear Society will be held in Boston, June 18 through 21, at the Statler Hilton Hotel. One of the special features of the meeting will be a review of biologic and medical aspects of radiation led by Shields Warren, M.D., scientific director, New England Deaconess Hospital.

For further information contact: Mr. Ted Eaton, Arthur D. Little, Inc., 25 Acorn Park, Cambridge 40, Massachusetts.

American College of Chest Physicians

The American College of Chest Physicians will hold a five-day meeting at the Morrison Hotel, Chicago, June 21 through 25. The meeting will include postgraduate seminars, open forums, a cine symposium, round-table luncheon sessions, and motion pictures.

For information write to: Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Society for Surgery of the Alimentary Tract

The Society for Surgery of the Alimentary Tract will meet in Chicago at the Sheraton Hotel on Sunday, June 24. Don W. Fawcett, M.D., professor and chairman, Department of Anatomy, Harvard Medical School, Boston, will present a special address entitled "Electron Microscopy Studies of the Pancreas as Related to Function."

For further information concerning the meeting contact: Robert Turell, M.D., 25 East 83rd Street, New York 28, New York.

Saranac symposium on tuberculosis

The eleventh annual symposium for general practitioners on tuberculosis and other pulmonary diseases will be held in Saranac Lake, July 9 through 13. Sessions will be held at the Hotel Saranac and at various sanatoria and laboratories in the area.

The symposium is acceptable for twenty-seven hours of category 1 credit by the American Academy of General Practice.

For information write to: Registrar, Symposium for General Practitioners on Tuberculosis and Other Pulmonary Diseases, P.O. Box 627, Saranac Lake, New York.

American Public Health Association

The American Public Health Association's ninetieth annual meeting, the first in the South in twenty-five years, is scheduled for Miami Beach, Florida, October 15 through 19. The Fontainebleau Hotel will serve as headquarters for the meeting.

For further information contact: Mr. George Schless, Schless and Company, 59 East 54th Street, New York 22, New York.

Northeastern proctologic conference cruise

The New England Proctologic Society, the New Jersey Proctologic Society, the New York Society of Colon and Rectal Surgeons, and the Pennsylvania Proctologic Society will hold a conference cruise November 7 through 16. The ports-of-call of the nine-day cruise are San Juan, Puerto Rico, and St. Croix and St. Thomas, Virgin Islands.

For information contact: Sydney D. Weston, M.D., 1 Hanson Place, Brooklyn, New York.

Medical News

Women physicians invited to brunch

The American Medical Women's Association extends an invitation to all women physicians attending the A.M.A. annual meeting in Chicago to be their guests at a brunch on Sunday, June 24, at 11: 00 A.M., at the Essex Inn.

Those wishing to attend should write to: American Medical Women's Association, 1790 Broadway, New York 19, New York.

Drug reaffirmed as nonaddicting

The Bureau of Narcotics has published in the *Federal Register* of March 24, 1962, a ruling that reaffirms the status of dextro propoxyphene (Darvon) as a nonaddicting drug.

Introduced by Eli Lilly and Company in 1957, dextro propoxyphene came into wide use as a nonaddicting oral analgesic. Following a hearing on the drug's status as a nonnarcotic, the Bureau made a ruling which assures that it will continue to be available on a regular prescription.

Award offered to oral surgeons

The American Society of Oral Surgeons has announced the opening of a competition for a cash award to be presented at the forty-fourth annual meeting of the society in New Orleans, October 24 through 27. The award will be for superior original manuscripts concerning any phase of research related to oral surgery during the current year.

For further information write to: American Society of Oral Surgeons, 840 North Lake Shore Drive, Chicago 11, Illinois.

Bronx hospitals to merge

A merger of The Bronx Hospital and The Lebanon Hospital was approved on April 10 by the boards of trustees of both voluntary, nonprofit institutions. The two general hospitals will be combined into a new 600-bed complex to be called The Bronx-Lebanon Hospital Center. The combined institutions will serve the south, central, and west areas of the Bronx.

Medical self-help training program

The State Health Department has distributed approximately 600 medical self-help training program kits to local civil defense jurisdictions in New York State, according to a report issued by Herman E. Hilleboe, M.D., Commissioner, State of New York Department of Health.

The program is part of a nationwide mass educational effort sponsored by the American Medical Association and the United States Public Health Service. Plans to implement the program in New York State were developed recently at a meeting of General F. W. Farrell, director, New York State Civil Defense Commission; James H. Lade, M.D., director, Bureau of Medical Defense, State of New York Department of Health; and Edward A. Burkhardt, M.D., chairman, Committee on Disaster Medical Care, Medical Society of the State of New York.

"The objective of this program is to teach American families how to survive in a national disaster—to meet their health needs when the services of physicians are not available," Dr. Hilleboe said.

Air pollution rules in effect

Rules to prevent air pollution from new sources, recently adopted by the Air Pollution Control Board, are now in force, Herman E. Hilleboe, M.D., Commissioner, State of New York Department of Health, and chairman of the Air Pollution Control Board, has announced.

The new rules were effective April 1. They require the review and approval of plans for construction or modification of dumps of all kinds, office building and apartment house incinerators and heating plants, stone crushing operations, manufacturing processes, power plants, and other sources of air contamination.

Copies of the rules and guides for designers of air pollution control systems are available on request from: State Air Pollution Control Board, 84 Holland Avenue, Albany 8, New York.

Incidence of hepatitis increases

The number of cases of viral hepatitis in New York City reported so far this year is about half the number reported in the same period last year, Leona Baumgartner, M.D., Commissioner, the City of New York Department of Health, has reported. Yet the number of cases this year is more than twice the average number for the same period in each of the ten years 1951 through 1960. There have been 357 cases of hepatitis reported as of April 16, against 708 for the same period last year. The average number for the corresponding period each year during the ten-year period was 149.

Physician to write history

George Rosen, M.D., New York City, professor of Public Health Education at the Columbia University School of Public Health and Administrative Medicine, has been invited by the National Institutes of Health to develop a plan for a history of the Institutes.

The U.S. Public Health Service, of which the National Institutes of Health is the research arm, has awarded Columbia a planning grant of $37,081 for this study.

Eastman Kodak receives health achievement award

Eastman Kodak Company, Rochester, has received the 1962 Health Achievement in Industry Award of the Industrial Medical Association for "excellence in the field of occupational health."

Refresher courses in basic sciences

Refresher courses in anatomy and histology, biochemistry, and physiology will be offered by the basic science departments at the School of Dentistry of Fairleigh Dickinson University, Teaneck, New Jersey, during June and July. The courses are designed to assist in preparing residents and interns for state and national board examinations and foreign students in preparing for the foreign students examination. Practicing physicians and dentists wishing to keep abreast with recent advances and nomenclature are also invited to attend.

For further information write to: Mrs. Claire Parker, Dental Research Building, Fairleigh Dickinson University, Teaneck, New Jersey.

Blood bank standards revised

The basic document for voluntary accreditation of blood banks has been revised and is available for distribution, the Joint Blood Council has announced. *Standards for a Blood Transfusion Service*, third edition, 1962, provides improved guidelines for evaluating and conducting an acceptable blood transfusion service in hospitals and community blood banks.

Copies may be obtained for $1.00 from: Joint Blood Council, 1500 Massachusetts Avenue, N.W., Washington 5, D.C.

Course in occupational medicine

"Occupational Medicine," a full-time course for physicians, will be given for eight weeks from September 17 through November 9, by the New York University Post-Graduate Medical School.

The course content covers preventive medicine, including epidemiology and biostatistics, administrative medicine, occupational diseases, and industrial hygiene.

For further information write to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

Leaflet detailing work clothing safety

A leaflet issued jointly by the National Safety Council and the Institute of Industrial Launderers is being offered without cost to interested persons. It describes the "seven deadly sins" of garment safety which make defective and unsafe work garments one of the most common causes of lost-time accidents in American business and industry.

The leaflet is available from the Institute of Industrial Launderers, 1833 Jefferson Place, N.W., Washington, D.C.

Personalities

Elected. Henriette R. Klein, M.D., New York City, as president of the New York Society for Clinical Psychiatry . . . John M. Walker, M.D., Greenwich, Connecticut, as chairman of the executive committee and chief executive officer of Memorial Hospital for Cancer and Allied Diseases, New York City.

Appointed. Lawrence W. Friedmann, M.D., Jackson Heights, as associate medical director of the Institute for the Crippled and Disabled, New York City . . . John Roderick Heller, M.D., New York City, as a member of the City of New York Board of Health . . . George A. Jervis, M.D., Thiells, as research director of the Joseph P. Kennedy, Jr. Foundation . . .W. Cecil Johnston, M.D., Dannemora, as director of Matteawan State Hospital for the criminally insane . . . . Arthur W. Wright, M.D., Albany, to the New York State Board of Regents.

Awarded. Leona Baumgartner, M.D., New York City, Commissioner, the City of New York Department of Health, the annual Samuel J. Crumbine Award of the Kansas State Public Health Association, in recognition of her meritorious service in public health . . . Herman E. Hilleboe, M.D., Albany, Commissioner, State of New York Department of Health, the annual medallion award of the Foundation for Research of the New York Academy of Osteopathy in recognition of his contributions in the fields of public health, health research, and health education . . . Paul Reznikoff, M.D., New York City, the annual award of distinction of the Cornell University Medical College Alumni Association for his outstanding contributions to medicine.

Speakers. Edward Bien, M.D., Bethpage, on April 5, at a public forum on arthritis at the Nassau Academy of Medicine . . . James A. Brussel, M.D., New York City, Assistant Commissioner, State of New York Department of

Mental Hygiene, on the topic "Mental Health, New York State," before the Josephine Karet League, New Rochelle, on May 22 . . . Arthur J. Cracovaner, M.D., New York City, on the "Management of Carcinoma of the Larynx" at the two hundred twenty-eighth meeting of the Eastern New York Eye, Ear, Nose and Throat Association on March 1 . . . Andrew C. Fleck, Jr., M.D., Albany, on April 17 at a meeting of the New York State Commission on Tuberculosis and Public Health, Inc . . . . Nicolai Gioscia, M.D., Mineola, on April 12, before the staff of the Veterans Administration Hospital, Northport, Long Island, on the topic "The Mental Health Board in Operation" . . . Morris Herman, M.D., New York City, on the topic "The Psychiatrist and the Court" at a meeting of the Society of Medical Jurisprudence, April 9 . . . Max N. Howard, M.D., New York City, on April 11 at a panel discussion in Chicago on the topic "Planning for Natural and Industrial Disasters" . . . R. Townley Paton, M.D., New York City, on the topic "Indications and Contraindications of Keratoplasty" on April 23 . . . James H. Sterner, M.D., Rochester, in Chicago on April 10, on the subject of industrial health . . . Alexandra Symonds, M.D., Brooklyn, on "Special Problems in the Treatment of Adolescents" at a meeting of the Association for the Advancement of Psychotherapy on April 27 . . . William N. Young, M.D., Halesite, on April 11 at a panel discussion in Chicago on the topic "Planning for Natural and Industrial Disasters."

Rising incidence of chronic respiratory disease

Increasing concern is being shown by medical and health authorities because of the rising incidence of chronic respiratory disease. Evidence of this is found in the upward trend of the death rates from those conditions. The recorded death rates from chronic respiratory diseases have shown a sizable increase in the past decade, according to statisticians of the Metropolitan Life Insurance Company.

The combined mortality from these diseases—namely, chronic bronchitis, the chronic pneumonias, bronchiectasis, and emphysema—rose fairly steadily from about 5 per 100,000 population in 1949 to 10 per 100,000 in 1959.

The rise in mortality was particularly rapid among males. The rate more than doubled among both white and nonwhite males during the decade, while among females the increase amounted to approximately 50 per cent.

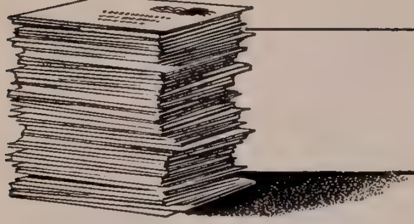
Emphysema alone accounted for slightly more than half of the total increase in mortality. The recorded death rate from this disease in 1958 to 1959 was no less than 6 times that in 1949 to 1950. Chronic pneumonia was the only other disease in which a relatively large increase in mortality was recorded.

For chronic bronchitis, the death rate among white males at ages forty-five and over rose by 11 per cent between 1949 to 1950 and 1956 to 1957, reflecting chiefly the marked increases at ages fifty-five to seventy-four. Among white females, however, this rate dropped about one third at ages forty-five and above.

During the same period, the death rate from asthma fell in each age group among both males and females.

The over-all increase in mortality attributed to the chronic respiratory diseases represents in part the growing proportion of people at the older ages. The rise is also a consequence of the increasing number of people with persisting lung changes due to previous acute respiratory infections.

Years ago, many of these people would have succumbed to such infections; now they survive but with residual respiratory impairment. Air pollution, too, has probably contributed to the increase in respiratory irritants.



Letters to the Editor

Cancer in situ of uterine cervix

To the Editor: Dissatisfaction with the results of the treatment of invasive carcinoma of the cervix uteri has stimulated a widespread, aggressive campaign of cervical Papanicolaou testing. Wishful thinking has led the research gynecologist to believe that finding of "cancer in situ" (intra-epithelial carcinoma) will annihilate any vestige of invasive cancer of the cervix. Controlled research efforts are to be encouraged, but in the human being mistakes may be forgiven only on a limited scale. The question is now raised: What will be the price of the present vigorous effort in the war against this scourge of humanity?

Ferguson,[1] writing in a journal for practitioners, would inject the physician into the private sex life of every female teen-ager who can have a vaginal examination. He would perform frequent cervical smears. In an early report on precocious adolescents with a predilection for infection of the cervix, he has found 66 patients with Class III Papanicolaou smears and 10 cases of cancer in situ. Another patient, a prostitute and heroin addict, had a hysterectomy and one ovary removed for a tubo-ovarian abscess. Prostitutes and heroin addicts have been cured and tubo-ovarian abscesses healed; invalids of this type have turned into useful, healthy individuals rearing fine families.

Most gynecologists are willing to wait until women with cancer in situ have children before they employ heroic measures; but the handwriting on the wall points to hysterectomy in many, even before they have progeny. Beecham[2] with 139 cases of cancer in situ and 2 operative deaths, with an average patient age of thirty-six years, is not satisfied with his results from partial hysterectomy because 5 other patients in this series have already developed invasive cancer of the cervix.

Tumor boards are advising practicing gynecologists to hunt down cancer in situ aggressively and treat it actively. Those gynecologists who readily remove the wombs of fertile women do not need much encouragement to remove the wombs of the adolescent.

However, carcinoma in situ is still a field beclouded with ambiguity. Serious differences of opinion regarding the etiology, diagnosis, and prognosis of this condition exist. Diverse criteria of recognition and form of therapy exist, even in the highest ranks of gynecology. Terms such as reserve cell hyperplasia, dysplasia, and squamous metaplasia add to the confusion. In many cases, histologic evidence of an in situ lesion vanishes, never to reappear. Ferguson's indication of "cancer" smears—Class III Papanicolaou smears of cervicitis—disappear when the cervicitis is healed. One may suggest a similar consideration for the disappearance of cancer in situ. The womb with cancer in situ (if a carcinogenic irritation persists?) develops invasive cancer more readily. Other methods of cure rather than the extirpation of the uterus must be considered seriously and conscientiously. The removal of the uterus usually means the removal of the ovaries with resultant surgical menopause, osteoporosis, and premature coronary heart disease. Moreover, the loss of an endocrine target organ has been known to lead to cancer of the stimulating endocrine organ. Besides, prophylactic surgery does not sound practical in an age when we see multiple cancers in five different organs.

Controlled experiments are needed and should be welcomed.

Almost one half of the girls in Ferguson's series refused to submit to therapy. Presumably the skilled investigator acquainted them with the research problem involved, as well as the possible dire consequences of their refusal. Their wishes should be respected. Until more is known of any advantage of the suggested remedial measures they will serve as the controls that all research needs. Vigorous attention to prophylactic hygienic measures and treatment of infections should precede prophylactic hysterectomy. The fertility or expectations of our future mothers should not be sacrificed on the altars of research. We must prevent rapa expectare de utero immaturo.

BERNARD SELIGMAN, M.D.

163 Ocean Avenue
Brooklyn 25, New York

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[1] Ferguson, J. H.: Positive cancer smears in teenage girls, J.A.M.A. **178**: 365 (Oct. 28) 1961.

[2] Beecham, C. T., and Carlin, E. S.: The management of cancer in situ, New York Academy of Sciences, New York City, December 9, 1961.

Mental ability of premature children

To the Editor: Apparently there is some evidence that premature children have an increased chance of less-than-average mental ability.

Would you comment as to the validity of these studies and whether or not this topic should be discussed with the parents.

G. Eugene McCrae, M.D.

Reply

An infant is classified as premature when the birth weight is 2,500 Gm. (5 pounds, 8 ounces) or less. This definition is generally recognized as unsatisfactory inasmuch as a 5¹/₂-pound baby may be full term, or it may be an immature fetus that would have developed greatly if it had carried to forty weeks. Hence, the first requirement in any follow-up study of premature infants is exact information about the cases reported, with suitable control groups.

In 1953,[1] Alm studied 999 premature babies and 1,002 controls. The author concluded that among the surviving premature children, there was a greater incidence of paralysis, epilepsy, and mental deficiency than among the controls.

Drillien[2] of Edinburgh studied the mental development of 595 children and determined that the developmental quotient fell steadily with decreasing birth weight at all ages, with repeated testing from six months to two years.

Knobloch and a group of workers at Johns Hopkins in Baltimore reported in 1956[3] on the results of testing 500 premature children and 492 full-term controls at approximately forty weeks of age. In the total premature group, approximately 75 per cent were normal, while 88 per cent of the controls were normal. In the smallest infants, weighing 1,500 Gm. or less at birth, only 50.9 per cent were normal.

In New York City in 1958,[4] Dann *et al.* at Cornell studied 73 cases of premature children with a birth weight of 1,000 Gm. (2 pounds, 4 ounces) or less, who were followed for from three to four years. The results showed a wide range of I.Q. (59 to 142) with an average of 94. This was significantly below the 107 found in 34 full-term siblings.

The evidence is piling up, and the more precise the conditions of the data collection are, the poorer the showing of the light-weight premature children in brain function is.

Discussing this with parents is another problem. The parents of premature children tend to be overprotective and through their own anxieties lay the groundwork for behavior disturbances in these children. It would seem better to stress that the majority of premature children "catch up" by their second birthday, or even before. To add the fear of retardation to the burden of prematurity is not justified from the statistical studies at hand. However, these figures can help to explain "why"—if and when retardation does become evident.

Gertrude M. Hyde, M.D.

County Office Building
White Plains, New York

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[1] Alm, I.: The long-term prognosis for prematurely born children; a follow-up study of 999 premature boys born in wedlock and of 1002 controls, Acta pædiat. (supp.) **42:** 1 (May) 1953.

[2] Drillien, C. M.: A longitudinal study of the growth and development of prematurely and maturely born children. III. Mental development, Arch. Dis. Childhood **34:** 37 (Feb.) 1959.

[3] Knobloch, H., Rider, R., Harper, P., and Pasamanick, B.: Neuropsychiatric sequelae of prematurity; a longitudinal study, J.A.M.A. **161:** 581 (June 16) 1956.

[4] Dann, M., Levine, S. Z., and New, E. V.: The development of prematurely born children with birth weights or minimal postnatal weights of 1,000 grams or less, Pediatrics **22:** 1037 (Dec.) 1958.

Continuing education for physicians

To the Editor: The recent reports on the congressional investigation of the drug industry have pointed up one glaring defect in the present practice of medicine. The apparent necessity for the drug firms to spend large sums of money in educating the doctors in the use of their products indicates that they have filled a vacuum which the doctors themselves may have created. Why have we not educated ourselves? Many do take advantage of the excellent programs provided by the various societies and groups—that of the Academy of General Practice is an excellent example.

This zeal is not universal, but it could be made so in the following way. At the time for renewal of the license to practice medicine the licensee shall present to the education department a certificate of attendance at an accepted refresher course given during the previous licensing period.

These courses need be no longer nor shorter than two weeks. They should be arranged by medical societies and medical schools, and they should cover the pharmacology of important new drugs and the usefulness of important new laboratory tests, new diagnostic methods, and improvements in therapy.

In this way everyone would at least be exposed to the word, not just the perceptive few, and the doctors would be back in the business of their own education.

Humphrey Magruder, M.D.

Exiled Cuban physicians

To the Editor: During recent months many Cuban physicians have escaped to the United States. The greatest concentration of Cuban physicians in exile is in Florida with many of them in the Miami area. Because of the many Cuban medical exiles in this country and because most of them left Cuba with few or no financial assets, their economic situation is perilous.

The Cuban physician escapees have formed the Cuban Medical Association in Exile. Enrique Huertas, M.D., serves as president of the association which is located at 213 Aragon Avenue, Coral Gables, Florida, P.O. Box 1016. The telephone number is HI 6-9902.

Dr. Huertas has made a request for any assistance or cooperation which the American Hospital Association may provide in the placement of Cuban physicians in hospitals. The American Medical Association is contributing $1,000 per month for six months to underwrite expenses for the office of the Cuban Medical Association in Exile.

Recognizing the plight of these exiles, we encourage the employment of these Cuban physicians wherever it is legitimately possible and practical. However, hospitals cannot afford to jeopardize their standards of medical and patient care by the employment of unqualified Cuban physicians in exile in positions where direct patient care responsibility must be exercised. The standards and requirements of the Educational Council for Foreign Medical Graduates, listing by the American Hospital Association, accreditation by the Joint Commission on Accreditation of Hospitals, and approval for internships and residencies by the American Medical Association should not and have not been waived for these exiles. The hospitals of the United States must continue to guard assiduously the standards of care provided to the patients they serve. To lower them could result in loss of various approvals and could create unfortunate medicolegal problems for hospitals in which unqualified physicians are giving patient care.

How then may hospitals assist in helping to meet the economic and professional needs and desires of these physicians? If the Cuban physician has been qualified under ECFMG or has a valid license to practice from one of the states, he can be given patient care responsibilities. Those Cuban physicians who do not qualify for patient care may be employed in several ways, that is, in technical positions in laboratories, x-ray procedures, pharmacy, medical records, and so forth. It is also possible for them to serve as interpreters, providing their command of English permits accurate communication with members of the medical staff and nursing and other hospital personnel.

The Cuban physicians in exile deserve every assistance which can properly be offered them, and the American Hospital Association hopes that the hospitals of this country will extend such assistance in every way practical and possible.

EDWIN L. CROSBY, M.D.

American Hospital Association
840 North Lake Shore Drive
Chicago 11, Illinois

Need for more adequate first-aid kits

To the Editor: Many patients request information about first-aid supplies for trips, camping, and the like. In my opinion, most if not all commercially available first-aid kits are grossly inadequate. For example most still contain crude scissors which don't cut, reels of one-half inch gauze, and good, old inadequate antiseptic. I would recommend that a subcommittee of the Medical Society of the State of New York be charged with the responsibility of formulating practical and effective groups of supplies for the home, pleasure trips, camping, and perhaps national emergencies.

GEORGE E. MOORE, M.D.

Roswell Park Memorial Institute
Buffalo 3, New York

Books Received

The following books were received during the month of March, 1962

An Atlas of Head and Neck Surgery. By John M. Loré, Jr., M.D. Quarto of 490 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $25.

A Textbook of Obstetrics. By Duncan E. Reid, M.D. Quarto of 1,087 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $18.50.

Current Therapy—1962. Edited by Howard F. Conn, M.D. Quarto of 790 pages. Philadelphia, W. B. Saunders Company, 1962. Cloth, $12.50.

The Medical Clinics of North America. Veterans Administration Hospitals Number. March, 1962. The Management of Medical Emergencies. Benjamin B. Wells, M.D., Marc J. Musser, M.D., and Robert J. McClaughry, M.D., guest editors. Octavo. Philadephia, W. B. Saunders Company, 1962. Published bi-monthy (six numbers a year). Cloth, $18 net; Paper, $15 net.

Henry Ford Hospital International Symposium on Otosclerosis. Edited by Harold F. Schuknecht, M.D. Octavo of 660 pages, illustrated. Boston, Little, Brown and Company, 1962. Cloth, $18.50.

Clinical Radiology of the Oesophagus. By Marcel Brombart. Translated by Sheila Kenny, M.D. Octavo of 383 pages, illustrated. Bristol, John Wright & Sons LTD, (Baltimore, The Williams & Wilkins Company), 1961. Cloth, $15.

Higher Cerebral Functions and their Clinical Disorders. By Benno Schlesinger, M.D. Quarto of 560 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $14.75.

Clinical Immunology and Allergy. By Leo H. Criep, M.D. Quarto of 582 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $18.75.

Hallucinations. Edited by Louis Jolyon West, M.D. Octavo of 295 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $9.75.

Management of Emotional Disorders. By A. H. Chapman, M.D. Octavo of 259 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1962. Cloth, $8.50.

First International Conference on Congenital Malformations, London, England, July 18–22, 1960. Compiled and edited for the International Medical Congress, LTD. Quarto of 314 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $7.50.

A Textbook of Comparative Endocrinology. By Aubrey Gorbman, Ph.D., and Howard A. Bern, Ph.D. Octavo of 468 pages, illustrated. New York, John Wiley & Sons, Inc., 1962. Cloth, $12.50.

Dissemination of Cancer; Prevention and Therapy. By Warren H. Cole, M.D., Gerald O. McDonald, M.D., Stuart S. Roberts, M.D., and Harry W. Southwick, M.D. Octavo of 462 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $12.75.

Surgery of the Ambulatory Child. By S. Frank Redo, M.D. Octavo of 340 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $8.50.

Drug Therapy. By Frank C. Ferguson, Jr., M.D. Duodecimo of 411 pages. Philadelphia, Lea & Febiger, 1962. Cloth, $7.50.

Practical Management of the Obese Patient. By Frank L. Bigsby, M.D., and Caeytano Muniz, M.D. Octavo of 151 pages. New York, Intercontinental Medical Book Corporation, 1962. Cloth, $4.00.

Modern Concepts of Psychoanalysis. Edited by Leon Salzman, M.D., and Jules H. Masserman, M.D. Octavo of 210 pages. New York, Philosophical Library, 1962. Cloth, $4.75.

Basic Anxiety; A New Psychobiological Concept. By Walter J. Garre, M.D. Octavo of 123 pages. New York, Philosophical Library, 1962. Cloth, $5.00.

The Doctors' Dilemmas. By Louis Lasagna, M.D. Octavo of 306 pages. New York, Harper & Brothers, 1962. Cloth, $4.95.

Symposium on Angiotensin. Edited by J. Edwin Wood, M.D., and Raymond P. Ahlquist, Ph.D. Quarto. New York, The American Heart Association, Inc., 1962. Paper, $2.50. (American Heart Association Monograph Number Three)

Books Reviewed

The Medical Clinics of North America. Nationwide Number. March, 1961. Hypertension and Its Treatment. Irvine H. Page, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bimonthly (six numbers a year). Cloth, $18 net; Paper, $15 net.

Irvine H. Page, M.D., is the guest editor and gives the foreword. The book is divided into two parts concerning pathogenesis and treatment.

The authors are all well-known authorities on the subject of hypertension and come from various places. The effects of vascular disease are discussed at length, as are renal disease, aldosteronism, and arterial hypertension. The principles of treatment with special precautions and detailed drug therapy are presented, including hydralazine, guanethidine, and Darenthin, with many tables to help in bringing out specific points. Surgical treatment of hypertension and toxemia of pregnancy and its treatment are discussed also.—VINCENT ANNUNZIATA, M.D.

Recent Advances in Human Genetics. Edited by L. S. Penrose, M.D. Octavo of 194 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $8.00.

In this small book, a distinguished group of British and American scientists present in a series of eight essays a number of topics of timely interest to students of human heredity. L. S. Penrose, editor of the volume, has prepared the first chapter on mutation, while D. G. Harden has prepared an excellent review of the recent work on human chromosomes in a well-illustrated and interestingly written second chapter. Of the remainder of the book, the most noteworthy chapter is that of Sarah B. Holt, who has succeeded in crystallizing several instructive and useful facts regarding the inheritance of fingerprint patterns, while other chapters deal with sex abnormalities, abnormal hemoglobins, gene order, and statistical methods.

The book suffers from its narrowness of scope and the omission of several important aspects of modern human genetics. For example, there is no chapter on the heredity of the blood groups, especially, the Rh-Hr types, or erythroblastosis. The chief mention of the blood groups are the citations on pages 121 and 148 of the claimed associations between A-B-O groups and disease, as if they were established facts, whereas these reports have actually been shown to be fallacious. The chapter on statistical methods by C. A. B. Smith, one of the world's foremost biometricians, whose book *Biomathematics* is an excellent standard text on the subject, is too sketchy to be of much help to beginners and too superficial to be of much interest to those acquainted with the subject. This work, like many other recent books, suffers from its overemphasis of biomathematical methods and calculations, with resulting misapplication, and appears to overlook the fact that mathematics is no substitute for common sense and accurate laboratory work. For example, the chapter by Renwick on gene order cites certain reports with spurious statistical evidence of linkage as proof of the demonstration of linkage in man.

Despite its faults, this book should be included in the library of all students of human heredity. However, at eight dollars, this small volume is overpriced.—A. S. WIENER, M.D.

Henry Ford Hospital International Symposium: Blood Platelets. Edited by Shirley A. Johnson, Ph.D., Raymond W. Monto, M.D., John W. Rebuck, M.D., and Robert C. Horn, Jr., M.D. Octavo of 732 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $18.50.

This is a comprehensive presentation of the morphology, physiology, biochemistry, and pathology of blood platelets which is the result of an international symposium which took place at the Henry Ford Hospital, Detroit, Michigan.

The list of editors, participants, and discussants is an index of the quality of the material presented. There is an introduction which is followed by discussions on the historical facets of the subject.

Then follows a consideration of platelets in blood vessel integrity, platelet clumping, physiology, and pathology of hemostasis; their relation to bleeding time and mechanism in blood coagulation; platelet fractions; and metabolism and clot retraction of platelets.

After a banquet speech one has enough strength to pursue a discussion of altered platelet function; hematopoietic aspects and physical properties of platelets; labeling, life span, and preservation of platelets; and last, immunologic aspects of platelets.

For one interested in this fertile field of thrombocytology, this work is more than adequate.—MAURICE MORRISON, M.D.

The Cardiac Arrhythmias. By Brendan Phibbs, M.D. Octavo of 128 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $7.50.

This short book by Brendan Phibbs of the Casper Clinic is well written and well illustrated. Basic physiology is covered adequately, and there are informative schematic drawings. The more complex arrhythmias are not discussed. This is no great gap since the volume is intended for general practitioners, for whom it will be a useful introduction to the field.—MILTON PLOTZ, M.D.

Advances in Blood Grouping. By Alexander S. Wiener, M.D. Quarto of 549 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $11.

This book represents a collection of the author's multiple contributions to the field of immunohematology since 1953. Fifty-eight papers are presented as one text with a subject and author index. The reader, who is able, is taken through the major and minor problems relating to all known blood groups. The material covered lacks easy readability but is a superb compendium written in the author's own style and terminology; it includes a discussion of recent blood group advances and a review of previous ones.

This book is ideally suited as a reference source wherein specific information may be found. It is unlikely that the average physician or student would find this compilation a source of easily digestible information. This book belongs in every hospital library.—ALAN N. MORRISON, M.D.

The Question of Fertility. By Georges Valensin, M.D. Octavo of 296 pages. Garden City, N. Y., Doubleday & Company, Inc., 1960. Cloth, $4.50.

This extremely interesting book translated from the French covers all phases of the subject. The style is delightful, sometimes almost breezy. Often the writer goes deep into the history of fertility or the lack of it in the "birds and the bees" as well as in the two- and four-footed animals. He alludes briefly to the technics of artificial insemination in all forms of life; he touches on parthenogensis and philosophizes on the advantages and disadvantages of a race of amazons, should predetermination of sex become a possibility.

The religious and moral attitudes toward artificial insemination using a donor, as it applies in various cultures, makes up an important part of the book. Also mentioned are the legal implications.

In all, this volume is a worth-while addition to the library. Any adverse criticism would have to be limited to a tendency to make a point based on too few cases.—SANFORD KAMINESTER, M.D.

General Anaesthesia. Volume 1: Basic Principles. Volume II: Techniques, Special Fields and Hazards. Edited by Frankis T. Evans, M.B., and Cecil Gray, M.D. Octavo. Two volumes, illustrated. London, Butterworth & Co. (Publishers) Ltd., 1959. Cloth, $29.50 per set.

These two volumes consist of monographs on the physiologic basis of general anesthesia. The work is a collaborative text written by more than 40 of England's best physiologists, scientists, and anesthetists.

In the first volume, the best chapters are on the physiology of the nervous system and on muscle relaxants. It is indicative of English practice that local and regional technics are omitted even where they would be indicated, as in obstetrics, and that so much space is devoted to muscle relaxants.

The second volume does not match the high standard of factual background and physiologic substrate of the first. The outstanding chapter is Dr. Mushin's on the physiology of the endocrine system with relation to anesthesia. The chapter on obstetric analgesia must have been written for midwives. The chapter on special technics includes such anachronisms as asphyxial methods with nitrous oxide and primary and secondary saturation.

Perhaps because the text is a collaborative venture, the critical approach to problems in anesthesia is missing. It is recommended as a general reference text for one's library.—SAMUEL BERKOWITZ, M.D.

Atlas of Surgical Operations. By Robert M. Zollinger, M.D., and Elliott C. Cutler, M.D. Third edition. Folio of 236 pages, illustrated. New York, The Macmillan Company, 1961. Cloth, $18.

Dr. Zollinger, in his busy day, has found time to produce a new edition of this well-known atlas. There is no doubt that well-documented visual aids like these are necessary for good teaching. The preface indicates that a second volume will appear soon with many of the newer surgical procedures that have been developed since this book first went to press. This will be a welcome addition to the field of visual aids in surgery. The volume has its greatest usefulness for residents in training. A different color of paper and good black and white drawings would be preferable.—PHILIP E. LEAR, M.D.

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References: 1. DeNyse, D. L.: M. Times 87:1512 (Nov.) 1959.
2. Gruenberg, F.: Current Therap. Res. 2:1 (Jan.) 1960.

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SYMPOSIA . . .

SURGICAL TREATMENT OF ACQUIRED CARDIOV CULAR DISEASE—Dr. Master, Moderator, following his add on FADS AND PUBLIC OPINION IN HEART DISEA McCormick Place, Room D, 9 a.m.

SPECIAL PROBLEMS—EMPHYSEMA, BIOPSY FOR S COIDOSIS, TOBACCO SMOKE, AND CARDIAC RESUS TATION. McCormick Place, Room D, 10:55 a.m.

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SYMPOSIUM . . .

INHALATION THERAPY—PHYSIOLOGICAL PRINCIPL METHODOLOGIES, AND CLINICAL APPLICATIONS (sented in cooperation with AMA Section on Anesthesiology Pathology and Physiology)—Dr. Robert D. Dripps, Universit Pennsylvania Hospital, Philadelphia, Moderator. McCormick Pl Room D, 1:30 p.m.

FIRESIDE CONFERENCES . . .

30 tables, each with a moderator and panel of experts discussing m aspects of cardiopulmonary diseases. Morrison Hotel, 8:15 p.r

See Convention Number, J.A.M.A., May 19, for complete scientific program, advance registration, hotel accommodations, and luncheon reservation forms.

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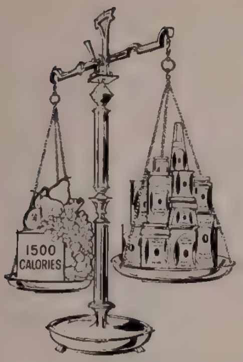

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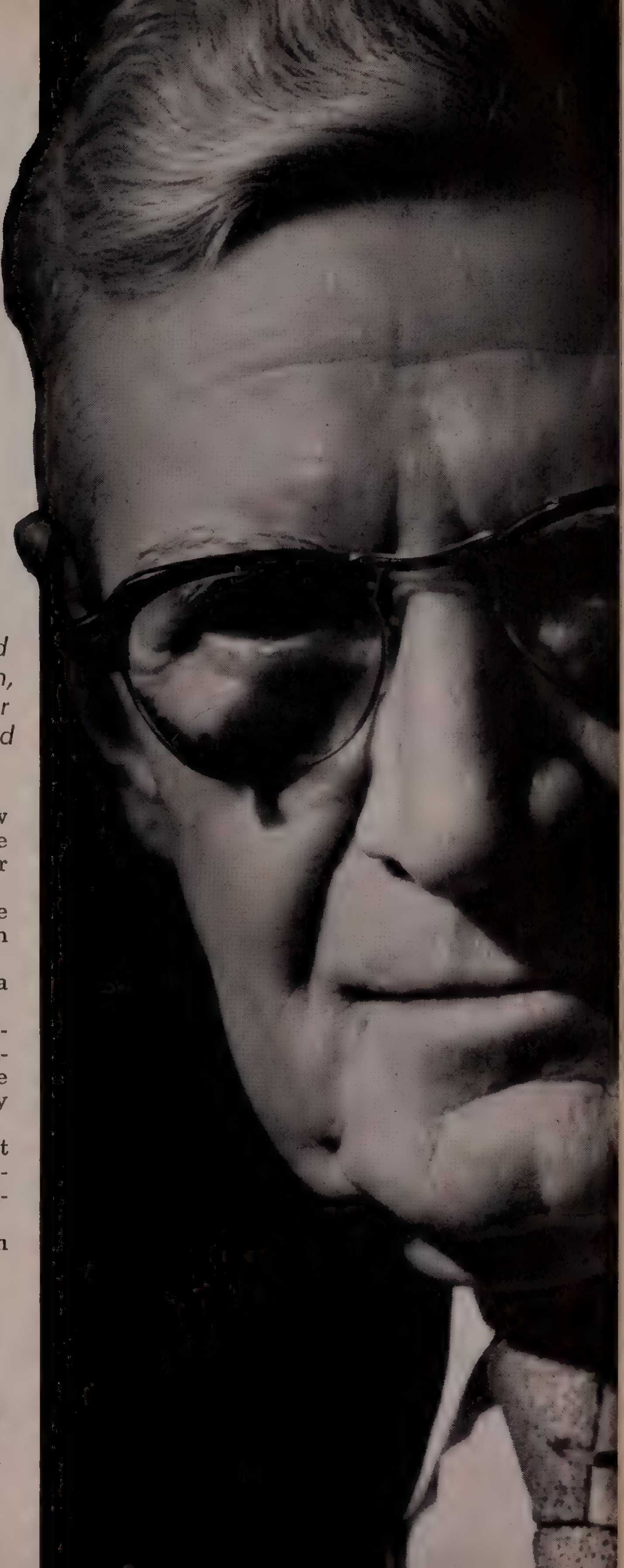

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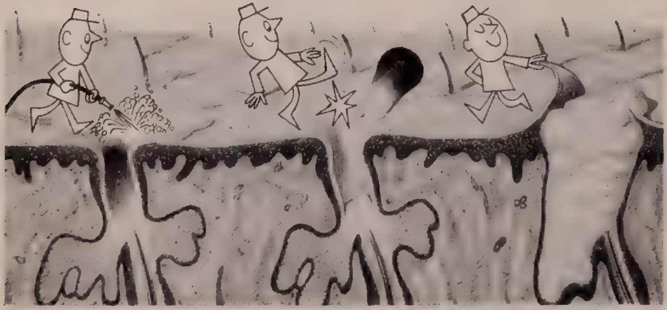

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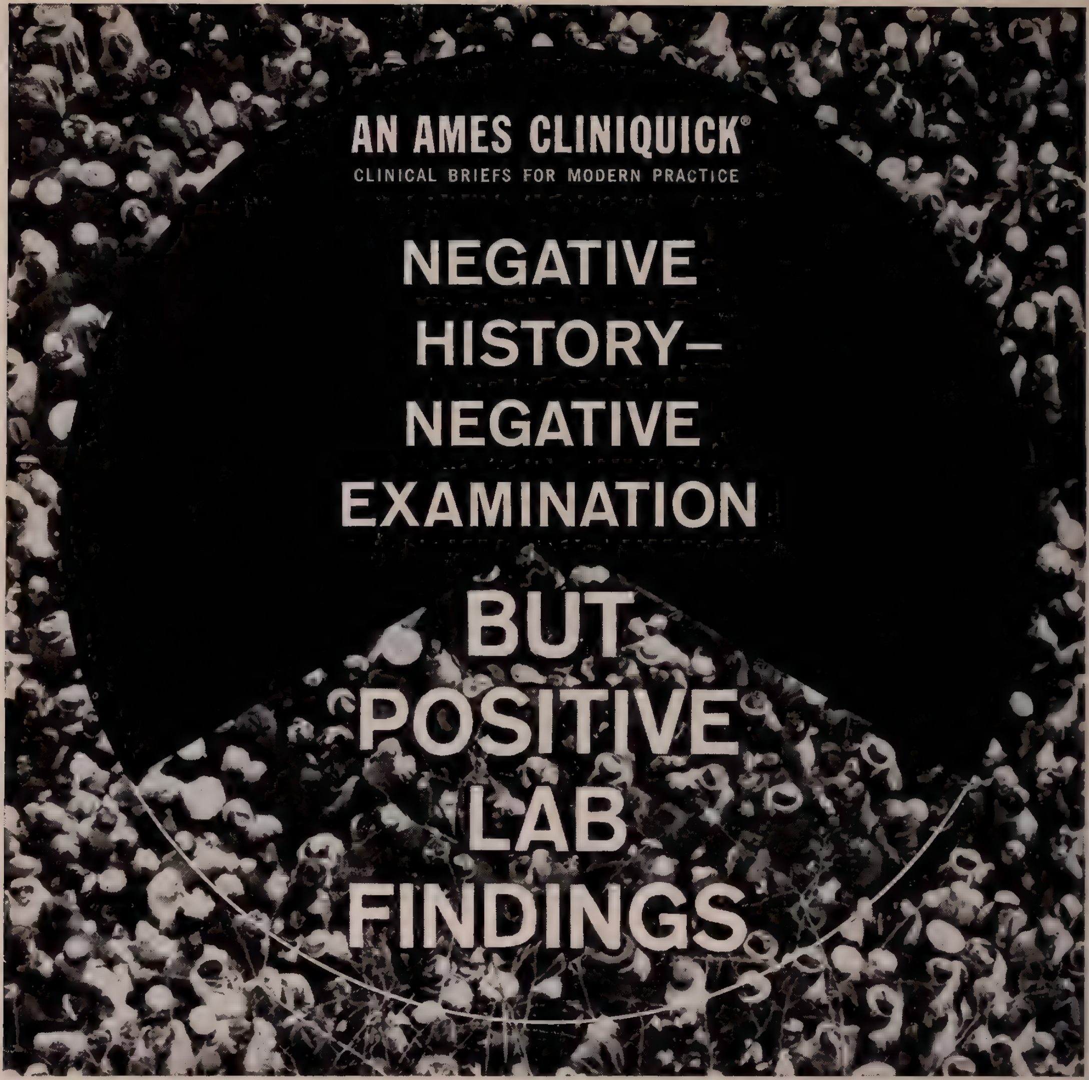
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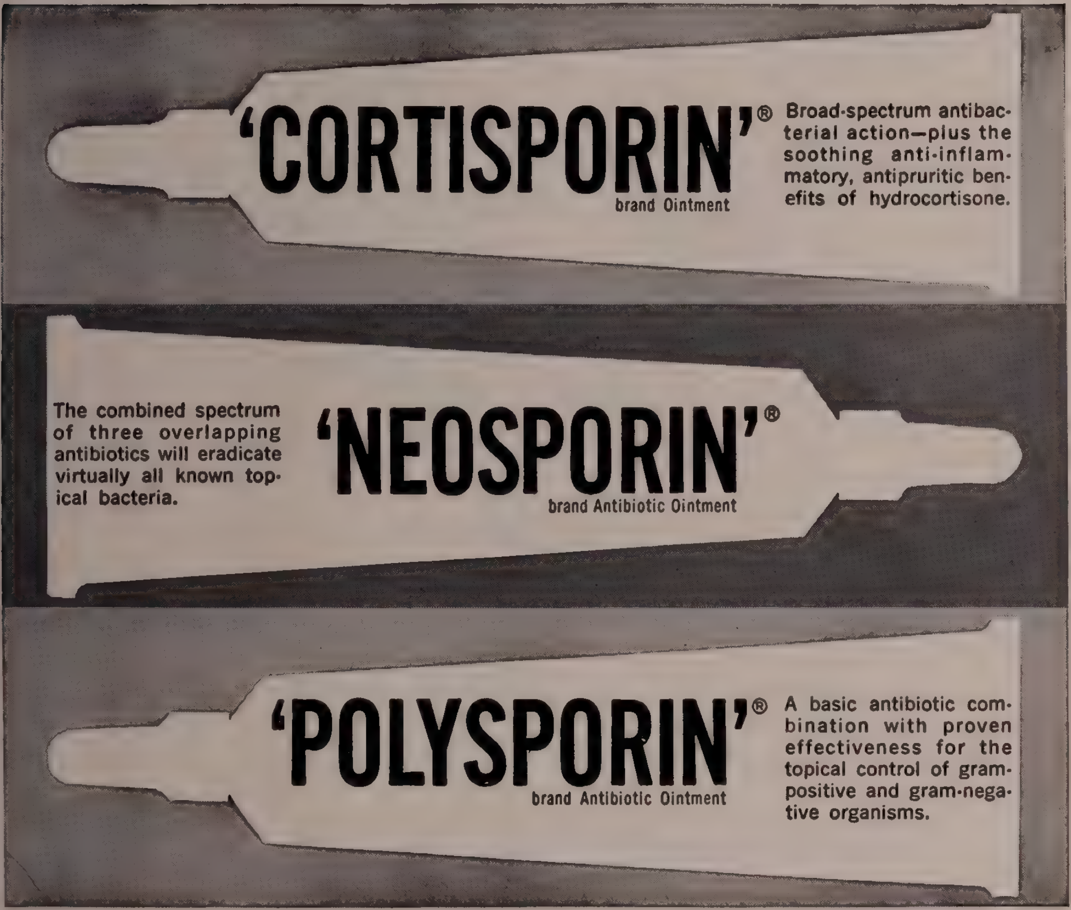
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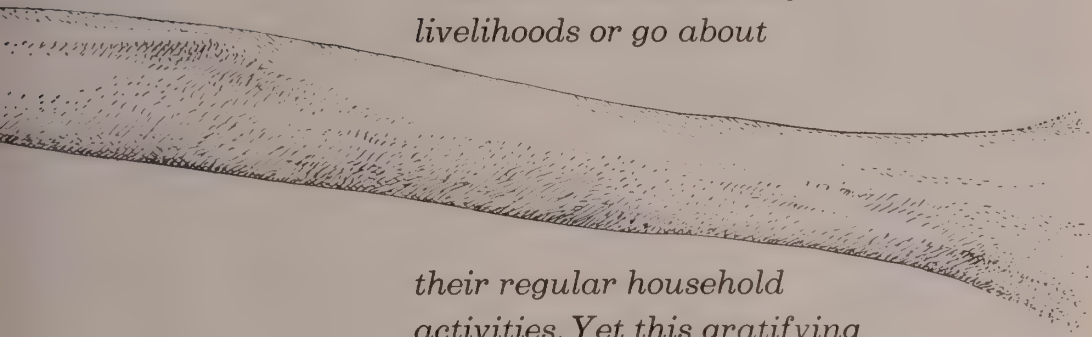

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To halt the increase in venereal disease

There is no doubt that in recent years there has been a real increase in infectious venereal disease in the United States, particularly among teen-agers. As reflected in reported cases of primary and secondary syphilis, venereal disease was on the increase until 1947, declined substantially from 1948 through 1953, and then leveled off. Since 1957 it has been rising sharply. In 1961 several hundred more cases of primary and secondary syphilis were reported than in 1951, a decade before, and over 6,000 more than in 1960. There is every indication that there will be a further sharp increase in venereal disease in 1962.

The number of infectious syphilis cases in the fifteen- to nineteen-year age group increased by 59 per cent between 1959 and 1960 and is still rising steeply.

Since 1950, per capita expenditures for venereal disease control have decreased from 20 cents to 12 cents in 1961. This includes sums spent by state, local, and Federal governments. It is inescapable that the drive against venereal disease during World War II achieved results and that its effect was apparent during the eight years after the war. Since then the record has been growing.

Meeting the problem of syphilis and gonorrhea obviously need not await further laboratory discoveries. We have the armamentarium to cure these ailments. The drugs we have are effective, and they are administered easily and quickly. We have what was only dreamed of twenty-five years ago. The problem lies not in the tools we have, but in our neglect, and this is shameful.

The Federal government intends to launch a new drive against venereal disease. Some of the money will be spent for especially trained health department representatives who will visit private physicians to enlist their cooperation and offer diagnostic and epidemiologic services. Why is this to be done? Because evidence indicates that in 50 per cent of all cases of syphilis physicians do not report as they are required to. In other words, for every 2 cases of syphilis, the physician breaks the law once. More important is the fact that the practicing physician can seldom take the time to trace all contacts.

It should not be necessary to mention in this JOURNAL that to control venereal disease the persons who are spreading these diseases must be found and treated. This is not being done as it can and must be done. Thousands of cases each year are not reported, and therefore the patients are not interviewed to seek other sources of infection.

There are obvious reasons why physicians do not report cases of venereal disease. These reasons are not adequate. Venereal disease is a chain reaction. A single source of infection can lead to scores of victims, and each of these can repeat the process. Adequate reporting now can eliminate the need for even greater inconvenience and embarrassment later, for if the chain of infection is not broken at every opportunity now, much sterner measures may be needed to deal with the vast increase in cases that is certain to result.

In venereal disease the physician has a responsibility not only to his own patient, but also to others who may be infected from the same source. The individual physician must help as a partner in his community in meeting this problem. If he will do his part, the present shocking rise in venereal disease can be stopped and reversed.

Counterclockwise drugs

Men learn or understand best by comparison or by analogy. The new can be best encompassed by viewing it in the framework of the familiar, the old, which endows many emotionally charged issues with perspective and proportion. Perhaps in that sense we may view dispassionately the questions of new drugs and drug patents, which have become an emotionally charged orgy. If we turn the clock back twenty-five years, it will allow us a view not embellished with the trivia, the peripheral barnacles, the self-aggrandizement, and the destructiveness with which the question of drug patents is viewed.

When we turn the clock twenty-five years back, to 1937, we will be in a period where the present therapeutic era had just opened. We were then smugly ensconced for sulfanilamide and sulfapyridine had been introduced just about then. Antibiotics—even penicillin—the antihistamines, or cortisone, which subsequently led to the various adrenal corticosteroids, were unknown.

But for patients who were seen within the last month or any recent month, 100 per cent of physicians responsive to advances in therapeutics prescribed, in preponderant proportion, drugs which did not exist twenty-five years ago. The existence and use of these newer drugs are directly due to our patent structure.

Most of the newer drugs are covered by patents. Pharmaceutical manufacturers remain in business because the profit from their operations enables them to exist and to sponsor research leading to new drugs; these new drugs advance therapeutics. One must not overlook too that the profit from a successful drug also enables a manufacturer to maintain on the market an unprofitable drug merely because a small number of physicians demand it.

One of the practices in the industry which is the target of attack is profit; another is the patent structure. And legislation is proposed to limit drug patents severely.

Apparently no one has called the attention of the legislators to the fact that another type of patent structure, namely the copyright laws, thrives justifiably. The plain fact is that the business of publishers also runs on profit. Few if any publishers would take the risks of publishing a new book unless they were assured of a monopoly for a reasonable period of time. In their case, a reasonable time is two periods of twenty-eight years each which are allotted them to profit through such valid, legal monopoly.

In this light it is inconsistent to look on drug patents as if they were public enemies to be harassed or legislated out of existence. In this context it is incongruous to have compulsory licensing of copyrights and as illogical to have compulsory licensing of drug patents, or any patents.

The pressure on the part of this Administration to limit exclusive use of drug patents to three years will undoubtedly result in a contraction of research efforts. Surely if the motivation is reduced the incentive will be much decreased. Under those circumstances we may look forward to the low degree of invention and discovery that is found in countries with a low level of incentive. Their contribution to therapeutic advances is the piracy of patents from enterprising countries.

In this instance we can profit from Bismarck's dictum which applies here: "Fools learn from experience—wise men from the experience of others."

Should restriction of drug patents become a reality, the rate of appearance of new drugs will be severely slowed down; the profit motive and hence the incentive will have shrunk. Then the choice of drugs and literature will be much smaller, and United States drug development will have regressed to the low rate of inventiveness of certain foreign countries. That would hardly be progress. No one contends that all new drugs—or even the majority of them—are fundamental advances. Some are mediocre; others are downright poor. Many of the latter are not marketed; but even in those which are marketed there is a natural process of selection through which drugs die.

But there is no restriction on what drug to choose. The greater the number of drugs the larger the choice. The competent physician will choose the drug he prescribes on the basis of his knowledge and particularly on the basis of his thoughtful evaluation of the data which manufacturers distribute in behalf of the drug.

A related complaint has to do with advertising material. It is chic to complain about the quantity of the advertising brochures disseminated by manufacturers in behalf of their drugs. It has become a status symbol of the sage to voice such complaint. But quantity as such is no cause for complaint; nothing stops a physician-recipient from exercising discrimination and thoughtful selection. Analogous European literature, on the other hand, is of considerably lower caliber, and selection and discrimination are certainly more difficult when the choice is smaller.

The advances of drug therapy in the United States are thus tied directly to the integrity of our patent system. Reducing the exclusive use of one's own patents unquestionably will inhibit markedly advances of drug therapy in the United States.

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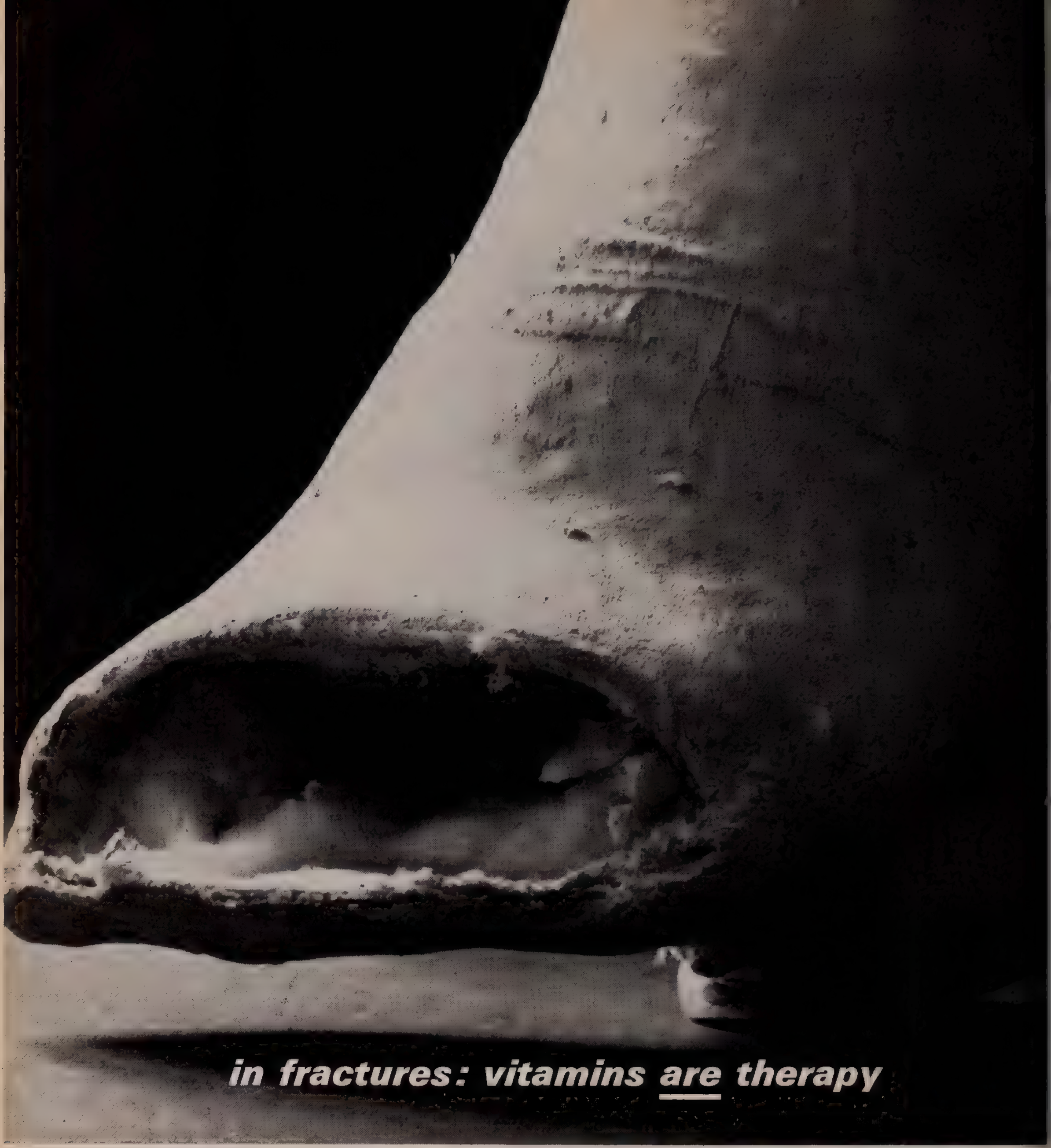

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Mass Immunization with Sabin and Cox Oral Poliomyelitis Vaccines

Experience in Monroe and Tompkins Counties, New York, 1960

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IN 1960 A MASS POLIOMYELITIS *immunization program was conducted in Monroe County, using Sabin oral monovalent vaccine administered in three doses to preschool and school age groups, and in Tompkins County, using Cox oral trivalent vaccine administered in a single dose to all age groups. Both vaccines are easily administered, tasteless, and acceptable to all age groups. There were 6 cases of cutaneous allergic manifestations, possibly owing to penicillin sensitivity, following feeding of the Sabin vaccine; many minor suspected reactions were reported after the first dose of Sabin vaccine but fewer after the second and third doses; also minor gastrointestinal complaints were prevalent after administration of the Cox vaccine. The 1960 poliomyelitis season in Monroe County was similar to that of recent years; none of the 7 cases of paralytic disease had been given Sabin vaccine. No poliomyelitis occurred in Tompkins County in 1960. In comparing the oral vaccines according to per cent of fourfold or greater rises in antibody titers, Type I Sabin and Type III Cox were excellent as original and booster antigens. Type III Sabin and Type II Cox were much less effective. Because of the comparatively poor showing of Type III Sabin vaccine and the increasing importance of Type III as a cause of paralytic poliomyelitis, an immunization schedule of at least two doses of Salk vaccine followed by boosters of Sabin vaccine is recommended.*

IN THE SPRING of 1960 it appeared likely that one or more varieties of living attenuated poliomyelitis immunizing agents would be favorably considered for licensure by the United States Public Health Service. Herman E. Hilleboe, M.D., State Health Commissioner, suggested that several areas in New York should undertake programs with the agents then under consideration to gain experience in their use. Monroe County was offered the opportunity to use the Sabin type vaccine in the preschool- and school-age groups. Tompkins County was offered the use of the Cox type vaccine for all age groups.

Community background

Monroe County, New York, is an Upstate New York community which includes the third largest city in the State, Rochester, an extensive suburban area and a peripheral rural area. The population of Monroe County, according to the 1960 preliminary census figures, is 586,387. Of this number 318,611 are in the City of Rochester and, of course, there is a concentration in the first and second ring townships. There were approximately 25,000 nonwhite people enumerated in the 1960 census, the vast majority in the City of Rochester.

The area has a stable economy, by most standards would be considered generally prosperous, has a high level of interest in medical matters on the part of its population, is the location of a well-known medical school and medical center, and has other attributes which can be expected to contribute to a cooperative attitude toward reasonably well-established health programs. A county health department was established in 1958. It serves the schools in the City of Rochester, but not in the rest of the County.

Tompkins County with Ithaca, its only city, the county seat, is situated in the south central part of New York State in the Finger Lakes Region. In 1960 its population totaled about 66,000 of which approximately 13,000 were students at Cornell University and Ithaca College; the remainder was about equally divided between greater Ithaca and the rural and village populations. The Tompkins County Health Department, established in 1947, provides general health services throughout the county, not including, however, health services in the schools which are the responsibility of the six individual school systems.

Objectives

The objectives of this program were simple. We wished to gain general experience in the handling and administration of the different oral vaccines. We wished to determine the ease and speed with which the material could be administered and to experiment to a certain extent with methods of administration. We wished to sense the degree of public acceptance of such material, to determine through short-term surveillance whether or not there were reactions associated with the administration of the vaccine, to determine through intermediate-term surveillance whether or not neuroparalytic accidents might occur, and through long-term surveillance whether or not there would be any measurable effect on the incidence of poliomyelitis during the poliomyelitis season that would follow. We also wished to estimate roughly the distribution and character of enteric cytopathogenic agents in the community before and after feeding, in case any interfering agents were prevalent.

It is emphasized that no attempt was made to conduct a controlled type of study such as the 1954 poliomyelitis vaccination field trials in which both counties participated.[1] At the time of the study Tompkins County was just completing a county-wide program for the administration of the third dose of Salk vaccine. In Monroe County substantially satisfactory immunization levels with Salk vaccine have been achieved since 1954. The poliomyelitis immunization status of several segments of the population in Rochester was estimated in 1959 and again in 1960 using the quota sampling technic developed by Serfling, Cornell, and Sherman[2] of the Communicable Disease Center, United States Public Health Service. The 1960 sample showed an extremely favorable immunization status. From 82 to 100 per cent of the persons sampled in the age group five through nineteen years gave a history of having had three or more injections of conventional vaccine. Under these circumstances it was considered unlikely that any differential attack rates could be detected by doing a controlled study in either county.

Procedure

There was little time for slow and meticulous organization. The definitive request to conduct the program was received May 3.

In each county the approval of the Board of Health, the Medical Society, and the different school systems was rapidly obtained.

Because the decision to undertake these programs was made so late in the school year, only two types of the Sabin vaccine were to be fed (Types I and III) at that time. Type II was scheduled for the fall of the year. Both counties relied on mass media such as the press, radio, and television

TABLE I. Persons fed living Sabin poliomyelitis vaccine by age group and type fed, with available populations and percentages fed, Monroe County, 1960

		Poliomyelitis Vaccine					
		Type I		Type III		Type II	
Age Group (Years)	1960 Population*	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)
0 to 1	13,076	837	6.4	775	5.9	566	4.3
1 to 5†	58,061	13,011	22.4	13,477	23.2	8,414	14.5
5 to 18†	134,111	95,913	71.5	92,675	69.1	89,867	67.0
18 plus	...	4,122	...	4,044	...	3,377	...
TOTALS	...	113,883	...	110,971	...	102,224	...
TOTALS EXCLUDING 18 PLUS	205,248	109,761	53.5	106,927	52.1	98,847	48.2

* Preliminary figures.

† Half of population aged five allocated to each category.

for the distribution of information to the public. There was excellent cooperation from these groups. Letters to parents were distributed through the school systems. It was decided to exclude Cornell University students because they were already in the midst of final examinations.

To estimate the character and prevalence of the intestinal viral flora, approximately 100 rectal swabs were obtained from children attending clinics in the central part of Rochester immediately before the feeding was to start. This area was chosen because it was thought that the highest frequency of enterovirus infection would be detected there. The examinations were performed by Paul Fiset, M.D., in the virus laboratory at the University of Rochester's School of Medicine and Dentistry. This laboratory is supported by a contract with the Monroe County Health Department. No cytopathogenic agents were detected in the specimens collected. In the period from January 1960 to April 1960, however, 5 isolations of Type I poliomyelitis virus were made on routine examination of stool specimens at this laboratory. None of these patients had clinical poliomyelitis. Samples were obtained also from individuals in Tompkins County. These were examined by the State of New York Department of Health laboratory and found to be negative.

The Sabin vaccine was diluted so that there were approximately 2×10^5 PFU (plaque forming units) of virus present in 0.1 ml. of suspension for Type I; 3×10^5 PFU for Type II; and 1×10^5 PFU for Type III. This suspension was dispensed in approximately 45 ml. quantities in dropper bottles. The droppers were calibrated to deliver roughly 0.1 ml. for each two drops. The original plan was to prepare a simple syrup in plastic squeeze bottles similar to ketchup dispensers, to dispense this simple syrup in plastic teaspoons, to place two drops of vaccine in the syrup, and then to feed the syrup and vaccine mixture to the children by the spoons. This plan was generally followed. It was soon discovered, however, that the vaccine had no unpleasant taste and the two drops could easily be placed on the tongues of cooperative children directly from the dropper. However, this was found to be inadvisable with the very young children who frequently attempted to lick the dropper and thus possibly contaminated the whole bottle of vaccine.

Supplies of Sabin vaccine were offered to private practitioners who felt that they would have substantial numbers of children to immunize in their own offices. Few physicians responded to this offer. Thus, the burden of the program fell almost entirely on the Monroe County Health Department. Table I shows the numbers of persons fed the indicated types of vaccine at the specified ages.

The Cox vaccine was trivalent in form, the concentration of virus in the vaccine dose was 5×10^5 TCD_{50} (50 per cent tissue culture infective doses) of Type II. It was supplied directly from the Lederle Laboratories to the Tompkins County Health Department in cherry-flavored liquid form in 50-dose bottles with measuring dose pipettes. The vaccine was measured into

TABLE II. Acceptance of Sabin vaccine immunization by socioeconomic area, elementary schools, Rochester, New York

Socioeconomic Area	Number of Schools	Range of Acceptance (Per Cent)	Median of Acceptance (Per Cent)
Upper	24	71.0 to 100	84.3
Middle	29	66.7 to 96.6	78.0
Low	19	58.3 to 93.9	73.9

TABLE III. Individuals fed living Cox poliomyelitis virus vaccine by age group with available populations and per cent fed

Age Group (Years)	1960 Population	Fed (Number)	Fed (Per Cent)
0 to 1	1,455	480	33.0
1 to 4	5,365	2,963	55.2
5 to 19	18,065	13,200	73.0
20 to 49	18,467	13,269	71.8
Totals	43,352	29,912	69.0

paper cups by means of a Cornwall Luer-Lok syringe with continuous pipette outfit. To this was added about 1/2 ounce of nonchlorinated water from large carboys with positive-pressure mechanism through plastic tubing. Some children were fed directly with medicine droppers. Thirty thousand persons were fed the Cox vaccine in schools, industries, businesses, and public clinics. Seventy-eight per cent of those enrolled, 13,200 school children, received the vaccine.

The Cox vaccine was also offered to the private physician for the immunization of his patients. As with Monroe County, comparatively few physicians took advantage of this offer.

The Sabin vaccine is apparently quite stable. The Type I vaccine which had been diluted but then refrozen when a substantial amount was not used, was furnished to John Paul, M.D., and his associates for the Middletown, Connecticut, project. We are informed that this particular material still had an adequate titer of virus after it had been thawed.[3]

Acceptance

As Table I indicates, the participation of the preschool-age group in the Sabin program was poor compared with the school-age group. Several factors accounted for this. There was heavy rain for the first three days of the week during which Type I was fed to the preschool children. Very few of the practicing physicians undertook to feed the vaccine, and the parent had to take the preschool child to a specified clinic. It was much simpler merely to sign the permission slip for the school-age child.

Some observations were made on the frequency of acceptance of the oral vaccine according to socioeconomic grouping.[4,5] It is now well known[6] that the lower socioeconomic part of the population in certain cities has been in difficulty with poliomyelitis in recent years, and the evidence points to low immunization rates as a responsible factor. In this program, vaccine was freely available without cost to the recipient, the school children were all given the same opportunity to participate, and yet in Rochester the elementary schools showed differences when classified according to the socioeconomic area served, as is illustrated in Table II. Schools in the county outside of Rochester are not classifiable in this manner, nor are the secondary schools.

Acceptance of the Cox vaccine varied from a low of 65 per cent of the pupils in a rural grade school to almost 100 per cent in a rural central school. Economic or educational status of the parents had little effect. Interestingly, in those over twenty years of age, 30 per cent had not received the Salk immunizations. Many of these adults stated they feared the parenteral immunizations. In addition, acceptance was influenced by the need for only one clinic visit instead of the three required by Salk vaccine. These figures are shown in Table III. Excluding college students, approximately two thirds of the population under fifty years of age participated.

Blood specimens

To estimate antibody response it was decided to obtain approximately one blood specimen from every 200 persons receiving the Sabin vaccine, preferably from persons who had received little or no formalin-inactivated vaccine. About 300 paired specimens were secured. The second specimen to complete the paired serologic specimens was not collected until one month after feeding Type II in November. These results will be discussed later in this paper.

In Tompkins County 235 paired blood specimens were collected from the school-age group and 265 from volunteers in the special mass clinics. No attempt was made to choose those individuals with no history of Salk immunization. These bloods were collected prior to and one month after feeding.

Surveillance

At the time this program was started it was difficult to secure information on reactions that could be attributed to the material. The general statement that there were "no reactions" was hard to believe. We were aware, through personal communications, that urticaria had been observed following feeding of the Cox vaccine in Dade County, Florida.[7] Shortly after the beginning of the second day of feeding of the Sabin vaccine a sixteen-year-old girl with a history of severe penicillin sensitivity developed generalized and moderately severe urticaria within minutes of receiving the vaccine. She was admitted temporarily to a nearby hospital emergency department but was promptly relieved of her symptoms by appropriate treatment. This was the first of approximately 6 instances of cutaneous allergic manifestations which developed anywhere between minutes to forty-eight hours after the Sabin vaccine had been fed. Four of these 6 persons had clear histories of previous manifestations of penicillin sensitivity. The other 2 individuals were not known to be sensitive to penicillin.

There were many telephone calls regarding suspected reactions. The majority of these were concerned with reports of headache, stiff neck, backache, and similar symptoms occurring anywhere between one to six hours after the vaccine had been fed. In these instances a simple reassurance was sufficient to allay parental anxiety. More serious symptoms or signs were followed up by one of four Monroe County Health Department physicians. In the course of visiting this latter category of cases, measles, dermatitis venenata, acute glomerulonephritis, acute gastroenteritis, and respiratory infections were found. Only one instance of aseptic meningitis came to the attention of the Monroe County Health Department subsequent to the initial feedings of the material and within a reasonable period of time. This girl had not been fed vaccine although 75 per cent of her classmates in school had received it. No agent was isolated from stool specimens, and paired blood specimens failed to show a rise in antibody titer against any of the types of poliomyelitis virus. The etiology of this illness, therefore, remains undetermined.

Very little was reported in the way of reactions following the second and third doses of Sabin vaccine. Possibly the parents of the participants had lost their anxiety to a certain degree by this time; possibly there was a self-elimination of those who had minor problems when Type I was fed. Only 1 additional case of urticaria was reported following the administration of Type II.

Although wild enteric viruses were not isolated from fecal specimens in Tompkins County, prior to and during the month of feeding of the Cox vaccine, there was prevalent in the community an illness of from twenty-four to seventy-two hours duration consisting of a rather severe headache for twenty-four hours followed by a gastrointestinal upset in some and in others a pharyngitis. A surveillance checksheet was sent to every physician in Tompkins County with a request to report any symptoms which might be associated with the vaccine. Schools were asked to report any suspicious illness. When the second blood specimen was taken from the adults, each was asked about any symptoms.

Some individuals, predominately adults, reported the onset of the syndrome mentioned previously within twelve to seventy-two hours after taking the vaccine. Three allergic reactions, 2 of circumoral edema, and 1 of hives in a highly sensitive child were seen, despite the fact that there was no penicillin in the vaccine. Two persons had arthralgias, which were believed to be coincidental. No person is known to have had any signs of meningeal irritation or central nervous system involvement. We were fortunate that the vaccine was not administered during our poliomyelitis season.

TABLE IV. Reported cases of poliomyelitis and aseptic meningitis in Monroe County, 1960

Age (Years)	Sex	Onset	Clinical Diagnosis	Immunizations Salk	Immunizations Sabin	Virology Stool	Virology Cerebrospinal Fluid
37	M	May 14	Polio encephalitis	0	0	No satisfactory specimens	. . .
16	F	June 22	Aseptic meningitis	3	0	Negative	. . .
31	F	August 10	Aseptic meningitis	0	0	Negative	. . .
27	F*	August 18	Paralytic polio	0	0	Negative	. . .
3	F	September 4	Paralytic polio	3	0	. . .	. . .
9	F	September 8	Paralytic polio	0	0	Type I	. . .
$1^1/_2$	M	September 14	Paralytic polio	0	0	. . .	Type I
$3^1/_2$	F	October 14	Paralytic polio	0	0	Negative	. . .
20	F	November 5	Paralytic polio	0	0	Type I	. . .

* Pregnant.

Poliomyelitis during 1960

Monroe County's experience with poliomyelitis during the so-called poliomyelitis season of 1960 did not differ from recent years. During 1960 there were 7 cases of paralytic disease. One in a thirty-seven-year-old man was fatal. The diagnosis was made on the basis of histopathologic findings, and no satisfactory specimens were available for virus studies. The onset of poliomyelitis in this fatal case was two days before his children were fed Type I virus. The 6 other paralytic cases were twenty-seven, twenty, nine, three, three and a half, and one and a half years of age. One case was in a pregnant woman. In 2 instances Type I poliomyelitis virus was isolated from stool specimens. The same virus was isolated from the cerebrospinal fluid of a third case. None had been fed Sabin vaccine nor had any family members received the vaccine. The three-year-old child had received three doses of Salk vaccine (Table IV).

There was only 1 additional case of aseptic meningitis reported in August of 1960. Virus isolation was not successful in this case.

No poliomyelitis occurred in Tompkins County in 1960. Late in the fall one boy developed a nonparalytic disease which proved to be of ECHO virus etiology.

Serologic findings

It is difficult to compare the serologic findings from the two areas. There were 272 blood samples from individuals under twenty in Monroe County and only 141 from the same age group in Tompkins County. In addition, in Tompkins County, no attempt was made to draw bloods from those with little or no Salk immunization history.

Of the 307 paired bloods examined from Monroe County, 90 had received no Salk vaccine, and 217 had received one or more doses. There were 27 triple-negative reactions among these 307 before Sabin vaccine feeding. Fifteen of these had received no Salk immunization; 12 had received one or more Salk vaccine injections. Of these 12, 3 had received one, 8 had received two, and 1 had received four Salk immunizations. Since every child did not receive all three types of vaccine, conversion rates are based on the numbers actually fed. Of the 27 triple-negative reactions as a whole, 26 out of 27 (96.3 per cent) fed Type I converted from a titer of less than 4 to 4 or more; 17 out of the 22 fed Type II (77.3 per cent) converted; 20 out of 25 fed Type III (80 per cent) converted (Table V).

In the Sabin vaccine group as a whole, without regard to previous Salk immunization, 98 or 31.1 per cent had an antibody

TABLE V. Triple negative conversions without regard to Salk immunization history Sabin Vaccine Program, Monroe County

Poliomyelitis Virus Vaccine	Number Fed	Converted to Antibody Titers of 4 or More (Number)	(Per Cent)
Type I	27	26	96.3
Type II	22	17	77.3
Type III	25	20	80.0

titer of less than 4 to Type I, 56 or 18.2 per cent a titer of less than 4 to Type II, and 115 or 37.4 per cent had a titer of less than 4 to Type III. If conversion rates are calculated on the basis of those actually fed the individual types (Table VI) we find that 93.7 per cent converted to an antibody titer of 4 or more for those fed Type I, 83.3 per cent for those fed Type II, and 70.6 per cent for those fed Type III. Again the conversion rates would appear to be better for Type I than for Type II or Type III. What proportion of these conversions may be due to cross immunity or natural infections is difficult to say. Interestingly enough, there were 5 individuals who converted although they were not fed homotypic vaccine. Three converted from a titer of less than 4 to 4 or more for Type II and two converted from a titer of less than 4 to 4 or more for Type III. It was not determined whether or not siblings of these converters had been fed virus. If conversion rates for the Sabin vaccine are examined according to the number of Salk immunizations, Type III conversions would appear to be somewhat influenced by two or more Salk vaccine immunizations (Table VI). When no Salk vaccine had been given, the conversion rate was 61.4 per cent for Type III. With one dose of Salk material the conversion rate was 61.0 per cent, but with two previous doses the conversion rate jumped to 79 per cent. These numbers are small.

There was no difference in conversion rates when they were calculated in relation to the length of time since the last Salk injection. The time interval used was two years.

In Tompkins County there were only 6 triple-negative reactions, none of which converted to triple positive. There was little

TABLE VI. Percentage of conversions from under four to four or more antibody titers by number of previous Salk immunizations

Salk Immunizations (Number)	Sabin Vaccine						Cox Vaccine					
	Type I		Type II		Type III		Type I		Type II		Type III	
	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)
0	41/46	89.1	29/35	80	27/44	61.4	20/23	87	14/26	53.8	31/37	83.8
1	20/20	100	5/6	83	9/15	60	5/6	83.3	...	...	7/9	77.7
2	18/19	94.7	10/11	90.9	23/29	79	1/2	50	1/2	50	5/6	83.3
3 or more	11/11	100	1/2	50	18/21	85.9	19/20	95	1/1	100	37/38	97.4
TOTALS	90/96	93.7	45/54	83.3	77/109	70.6	45/51	88.2	16/29	55.1	80/90	88.8

chance for natural infection affecting Tompkins County results as all bloods were drawn within a month of the feeding.

In both areas prefeeding antibody titers for those who had received Salk vaccine were the best for Type II and the poorest for Type III. In comparing the oral vaccines according to per cent of fourfold or greater rises, Type I Sabin and Type III Cox were excellent as original and booster antigens. Type III Sabin and Type II Cox were much less effective.

Summary

The poliomyelitis experience of both communities following the administration of the vaccines has been good, but not strikingly better than before oral feedings. There were no known neuroparalytic incidents either during or following the initial administrations. During 1960, none of the poliomyelitis cases reported, nor any member of their families, had received the vaccines.

Both monovalent and trivalent vaccines are easily administered, tasteless, and acceptable to all age groups. However, for continuing use by either the Health Department or the private physician, the administration of a trivalent vaccine would be more practicable. Because we know that individuals have little regard for maintaining their own immunization records and that many move from area to area and from physician to physician, we would prefer to use a trivalent material, three times if necessary, rather than monovalent.

Much has been said regarding the greater acceptability of oral versus parenteral immunization. Experience with the Sabin vaccine would seem to indicate relatively little difference. Acceptance seems to be related to socioeconomic status. The oral vaccine has the distinct advantage of being easier to give in a door-to-door campaign, however, and is apparently more acceptable to adults as was seen in Tompkins County.

Although we cannot show that the urticarias noted with the Sabin vaccine were due to penicillin, we feel it would be a distinct advantage to have a penicillin-free vaccine. The amount of penicillin in this vaccine per dose was 7 units. Of those with the most immediate and severe reactions, several had a history of a severe penicillin reaction in the past. On the other hand, we know that many youngsters supposedly sensitive to penicillin were fed this vaccine without reaction. The fact that there were fewer calls regarding supposed reactions following the feeding of Type III and Type II may have been due to a lessening of anxiety on the part of the parents or may have been due to a self-screening of those who blamed reactions on the first administration.

Since the Cox vaccine has not been approved for public distribution a discussion of its use seems out of place. In view of the comparatively poor showing of Type III Sabin vaccine it might be wise to consider an immunization schedule of at least two doses of Salk vaccine, followed by boosters of Sabin vaccine at appropriate intervals, particularly in view of the increasing importance of Type III as a cause of paralytic poliomyelitis.

It has been postulated that the use of the Sabin vaccine eliminates wild poliomyelitis virus from the community. This was not the experience in Monroe County. Poliomyelitis virus Type I was isolated from 4 of the 7 cases in 1960. Perhaps the failure to eliminate wild poliomyelitis virus was due to the small percentage of preschool children who received the vaccine.

It has also been postulated that the oral vaccine would be ideal for mass administration on an emergency basis when an epidemic of known type has arisen. This hypothesis is under test as of this writing in Onondaga, Madison, and Oneida Counties in New York State. Admittedly the administration of the vaccine is easily and rapidly done. We would question whether or not in the event of an epidemic the determination of poliomyelitis virus type and the mass feeding of type-specific vaccine can be carried out with speed sufficient to influence the course of such an epidemic.

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Car "cowcatcher" might end some pedestrian injuries

A "cowcatcher" design was recommended for automobiles as a way to reduce pedestrian injuries. The recommendation was based on a study of 200 persons who were struck and killed by cars in Manhattan during an eighteen-month period; the study was conducted by Cornell University Medical College, the New York City Police Department, and the Office of the Chief Medical Examiner of New York, and reported in the April 14, 1962, issue of the *Journal of the American Medical Association.*

Considerable progress also has been made in identifying and modifying specific features of the interior automobile design which frequently cause injury. Some progress also has been made in eliminating some external projections and modifying sharp angles and curves. However, further study of the possibility of creating external automobile designs with greater energy-absorbing potential is needed. It is possible that a "cowcatcher" design, which will cradle the pedestrian more effectively, may eliminate some of the injuries now associated with secondary impact against the pavement.

It has been estimated that 4 per cent of all automobiles manufactured will at some time strike and injure a pedestrian. About 300,000 pedestrians each year sustain varying degrees of injury when struck by motor vehicles, and in urban areas they account for the great majority of all injuries related to motor vehicles.

Although the study was concerned primarily with injuries sustained by the victims, the findings also indicated that in more than three fourths of the accidents in which responsibility could be reasonably ascribed, that is, 147 of 191 accidents, the pedestrian had directly initiated the chain of events involving himself in the accident by violating some pedestrian safety regulation. Further evidence of the responsibility of the pedestrian on many occasions was the presence of alcohol in the blood or brain tissue. This was found to be a factor in 75 per cent of the fatal pedestrian accidents in New York City.

Antibody Response to Two Different Live Poliomyelitis Virus Vaccines

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During 1960 a public health exercise in the large-scale oral administration of two different live poliomyelitis virus vaccines (Sabin and Cox) was carried out in two cities of New York State (Rochester and Ithaca).[1] A unique opportunity was thus presented to study two "rival" vaccines under conditions where the immunizing characteristics, as measured by antibody titers, could be compared. The comparison consisted of systematic double-blind, controlled titrations in each of two laboratories, one* of which has been the source of a great many of the published serum titers in the past.[2,3] Pre- and postvaccine blood specimens were collected from groups of volunteers in each city. This report presents the results of neutralizing antibody studies on these blood specimens.

The Sabin vaccine,[4]† in monovalent form, was administered orally in Rochester (Monroe County) during 1960 according to the following schedule: Type I in May; Type III in June; and Type II in November. Postvaccine blood specimens were collected between December 13, 1960, and February 26, 1961. The concentration of virus in each dose of vaccine was as follows: poliomyelitis virus I, 2 × 10^5 PFU (plaque forming units); poliomyelitis virus II, 3 × 10^5 PFU; and poliomyelitis virus III, 1 × 10^5 PFU.[5]

The Cox vaccine,[6]** in trivalent form, was administered orally as a single dose in

TABLE I. Relationship between prevaccine titers and the percentage of fourfold or greater antibody rises* to poliomyelitis virus Types I, II, and III, following vaccination with Sabin vaccine and with Cox vaccine

		Poliomyelitis Virus								
		Type I			Type II			Type III		
		Sera	Rises		Sera	Rises		Sera	Rises	
Vaccine	Prevaccine Titer	(Number)	(Number)	(Per Cent)	(Number)	(Number)	(Per Cent)	(Number)	(Number)	(Per Cent)
Sabin	<4	85	79	92.9	49	42	85.7	104	72	69.2
	4	22	19	86.3	20	17	85.0	29	23	79.3
	16	48	40	83.3	54	48	88.8	40	24	60.0
	64	67	34	50.7	47	34	72.3	48	21	43.7
	256	41	16	39.0	67	31	46.2	44	11	25.0
	1,024	22	...	...	48	...	...	20	...	...
TOTALS		285	188	71.4	285	172	72.5	285	151	56.9
Cox	<4	34	31	91.1	18	7	38.8	64	56	87.5
	4	31	25	80.6	16	9	56.2	33	30	90.9
	16	41	30	73.1	43	26	60.4	52	43	82.7
	64	70	36	51.4	78	40	51.2	51	38	74.5
	256	71	23	32.4	82	30	36.5	50	17	34.0
	1,024	69	...	...	79	...	...	66	...	...
TOTALS		316	145	58.7	316	112	47.2	316	184	73.6

* Where percentage of sera showing fourfold antibody rise has been calulcated, sera having titers of 1,024 in the prevaccine serum have been omitted from consideration; a rise in titer from a base line of 1,024 was impossible to demonstrate under the conditions of the test.

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* Microbiological Associates, Inc., Bethesda, Maryland.

† Supplied by courtesy of Albert B. Sabin, M.D., The Children's Hospital Research Foundation, Cincinnati, Ohio.

** Supplied by courtesy of Dr. Herald Cox, Lederle Laboratories, Pearl River, New York.

Ithaca (Tompkins County) during May and June, 1960. Postvaccine blood specimens were collected approximately one month after vaccine feeding. The concentration of virus in the vaccine dose was as follows: 5×10^5 TCD_{50} (50 per cent tissue culture infective doses) of Types I and III, and 6×10^5 TCD_{50} of Type II.

Tests in tissue culture of 100 prevaccine fecal specimens from volunteers in Rochester* failed to indicate that any enteric viruses were active at the start of the study; 67 similar fecal specimens from Ithaca tested in our laboratory in tissue culture and in infant mice yielded only one isolate of Coxsackie A16 virus. The two experimental groups of sera were kept the same size, although there was some difference in age distribution between the two groups; the results are based on tests on a total of 601 serum pairs of which 285 received Sabin vaccine and 316 received Cox vaccine. The difference in group size is a consequence of some of the original Sabin vaccinees dropping out of the test before receiving all three of their vaccine feedings.

A COMPARISON, *consisting of systematic double-blind, controlled titrations of pre- and postvaccine blood specimens from volunteers, was made between Sabin poliomyelitis vaccine in monovalent form, administered orally in three doses in Rochester (Monroe County) and Cox vaccine in trivalent form, administered orally as a single dose in Ithaca (Tompkins County). A neutralization test in primary cynomolgus monkey kidney tissue using a CPE (cytopathic effect) end point and a metabolic inhibition neutralization test in monkey kidney cells were performed. Types I and II Sabin vaccine were of approximately equal antigenicity while Type III produced somewhat less antibody response, whether the population was classified according to age or according to Salk vaccination status. In general the booster effect decreased with all three types as the amount of prevaccination antibody increased. Cox Type III vaccine was a better antigen than Types I and II. Both vaccines performed especially well in the elimination of antibody gaps when the vaccinee had received previous Salk immunization.*

Methods

Serum was withdrawn aseptically from each blood specimen and immediately frozen and stored at −20 C. until tested. Before testing, the sera were coded by replacing the laboratory identification numbers with random numbers.[7] Sera were arranged in groups so that the two sera of each pair were always tested simultaneously, but the laboratory doing the testing did not know the key to the random numbers, and therefore,

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* Tested by Dr. Paul Fiset, University of Rochester, School of Medicine and Dentistry, Rochester, New York.

TABLE II. Relationship between prevaccine titer and percentage of fourfold or greater antibody rises* to poliomyelitis virus Types I, II, and III following vaccination with Sabin vaccine, shown according to age groups

		Poliomyelitis Virus								
		Type I			Type II			Type III		
			Rises			Rises			Rises	
Age Group (Years)	Pre-vaccine Titer	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)
0 to 10	<4	27	27	100.0	14	12	85.7	32	24	75.0
	4	1	1	100.0	7	7	100.0	2	1	50.0
	16	7	5	71.4	8	7	87.5	9	6	66.6
	64	7	4	57.1	7	6	85.7	3	1	33.3
	256	4	3	75.0	10	6	60.0	1	0	0.0
	1,024	4	...	...	4	...	...	3	...	...
TOTALS		50	40	86.9	50	38	82.6	50	32	68.0
11 to 20	<4	53	50	94.3	32	28	87.5	68	46	67.6
	4	20	17	85.0	12	9	75.0	26	21	80.7
	16	39	33	84.6	45	41	91.1	31	18	58.0
	64	57	27	47.3	37	25	67.5	39	18	46.1
	256	35	13	37.1	53	23	43.3	41	11	26.8
	1,024	18	...	...	43	...	...	17	...	...
TOTALS		222	140	68.6	222	126	70.3	222	114	55.6

* Where percentage of sera showing fourfold antibody rise has been calculated, sera having titers of 1,024 in the prevaccine serum have been omitted from consideration; a rise in titer from a base line of 1,024 was impossible to demonstrate under the conditions of the test.

TABLE III. Relationship between prevaccine titer and percentage of fourfold or greater antibody rises* to the three types of poliomyelitis virus following vaccination with Cox vaccine, shown according to age groups

Age Group (Years)	Pre-vaccine Titer	Poliomyelitis Virus Type I Sera (Number)	Type I Rises (Number)	Type I Rises (Per Cent)	Type II Sera (Number)	Type II Rises (Number)	Type II Rises (Per Cent)	Type III Sera (Number)	Type III Rises (Number)	Type III Rises (Per Cent)
0 to 10	<4	5	5	100.0	1	0	0.0	15	15	100.0
	4	5	3	60.0	1	1	100.0	5	5	100.0
	16	2	1	50.0	4	3	75.0	7	6	85.7
	64	14	8	57.1	11	4	36.3	5	4	80.0
	256	6	0	0.0	6	3	50.0	1	0	0.0
	1,024	2	...	...	11	...	...	1	...	...
Totals		34	17	53.1	34	11	47.8	34	30	90.9
11 to 20	<4	9	9	100.0	1	0	0.0	16	15	93.7
	4	10	10	100.0	5	3	60.0	10	10	100.0
	16	16	15	93.7	17	10	58.8	14	14	100.0
	64	25	13	52.0	28	13	46.4	24	21	87.5
	256	22	10	45.4	28	11	39.2	19	12	63.1
	1,024	25	...	...	28	...	...	24	...	...
Totals		107	57	69.5	107	37	46.8	107	72	86.7
21 to 30	<4	8	6	75.0	5	2	40.0	9	7	77.7
	4	4	3	75.0	0	0	...	2	2	100.0
	16	3	2	66.6	5	2	40.0	9	8	88.8
	64	5	3	60.0	11	7	63.6	4	2	50.0
	256	11	5	45.4	10	3	30.0	8	0	0.0
	1,024	10	...	...	10	...	...	9	...	...
Totals		41	19	61.2	41	14	45.1	41	19	59.3
31 to 40	<4	4	3	75.0	3	1	33.3	11	9	81.8
	4	5	4	80.0	2	1	50.0	5	3	60.0
	16	10	7	70.0	9	4	44.4	10	7	70.0
	64	13	4	30.7	11	6	54.5	5	0	0.0
	256	11	3	27.2	17	5	29.4	8	3	37.5
	1,024	16	...	...	17	...	...	20	...	...
Totals		59	21	48.8	59	17	40.4	59	22	56.4
41 plus	<4	8	8	100.0	8	4	50.0	13	10	76.9
	4	7	5	71.4	7	4	57.1	11	10	90.9
	16	9	4	44.4	8	7	87.5	11	8	72.7
	64	13	8	61.5	16	9	56.2	12	10	83.3
	256	20	5	25.0	21	8	38.0	14	2	14.2
	1,024	16	...	...	13	...	...	12	...	...
Totals		73	30	52.6	73	32	53.3	73	40	65.5

* Where percentage of sera showing fourfold antibody rise has been calculated, sera having titers of 1,024 in the prevaccine serum have been omitted from consideration; a rise in titer from a base line of 1,024 was impossible to demonstrate under the conditions of the test.

did not know from which city the sera originated or which sera constituted a pair. Each group of sera included one positive and one negative control, which were coded in the same way as the test sera.

Two laboratories participated in the serologic testing: the Division of Laboratories and Research, State of New York Department of Health, Albany, and a commercial laboratory, Microbiological Associates, Inc., Bethesda, Maryland. The New York State laboratory performed a neutralization test in primary cynomolgus monkey kidney tissue using a CPE (cytopathic effect) end point. Microbiological Associates performed a metabolic inhibition neutralization test in monkey kidney cells. Both laboratories used a test dose of virus of approximately 100 TCD_{50}. Both laboratories tested the sera in dilutions of 1:4, 1:16, 1:64, 1:256, and 1:1,024, and in all cases titer is defined as the highest initial dilution of serum giving complete neutralization of the test dose of virus. In the calculation of fourfold or greater antibody rises, a change of titer from less than 4 to 4, was counted as a positive antibody rise. Duplicate tests by both laboratories on identical sera show a high degree of correlation between these two methods.

CPE NEUTRALIZATION TEST AS PERFORMED BY THE NEW YORK STATE LABORA-

TABLE IV. Influence of prior Salk immunization on the relationship between prevaccine titer and percentage of fourfold or greater antibody rises* to the three types of poliomyelitis virus following vaccination with Sabin vaccine

		Poliomyelitis Virus								
		Type I			Type II			Type III		
			Rises			Rises			Rises	
Number of Salk Immunizations	Prevaccine Titer	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)
0	<4	36	31	86.1	31	27	87.0	39	22	56.4
	4	5	3	60.0	2	2	100.0	9	5	55.5
	16	12	10	83.3	10	9	90.0	6	4	66.6
	64	14	10	71.4	13	10	76.9	13	6	46.1
	256	8	4	50.0	15	7	46.6	6	2	33.3
	1,024	1	...	...	5	...	...	3	...	...
TOTALS		76	58	77.3	76	55	77.4	76	39	53.4
1	<4	15	15	100.0	4	3	75.0	12	7	58.3
	4	2	2	100.0	6	5	83.3	1	1	100.0
	16	4	2	50.0	4	4	100.0	7	3	42.8
	64	6	5	83.3	7	5	71.4	7	4	57.1
	256	7	2	28.5	9	5	55.5	7	2	28.5
	1,024	2	...	...	6	...	...	2	...	...
TOTALS		36	26	76.4	36	22	73.3	36	17	50.0
2	<4	19	18	94.7	9	8	88.8	29	22	75.8
	4	11	10	90.9	6	4	66.6	7	6	85.7
	16	13	11	84.6	22	19	86.3	11	8	72.7
	64	17	7	41.1	9	7	77.7	17	5	29.4
	256	14	6	42.8	22	9	40.9	17	5	29.4
	1,024	12	...	...	18	...	...	5	...	...
TOTALS		86	52	70.2	86	47	69.1	86	46	56.7
3 or more	<4	14	14	100.0	5	4	80.0	24	21	87.5
	4	4	4	100.0	5	5	100.0	12	11	91.6
	16	19	17	89.4	18	16	88.8	16	9	56.2
	64	30	12	40.0	18	12	66.6	10	5	50.0
	256	12	4	33.3	21	10	47.6	14	2	14.2
	1,024	7	...	...	19	...	...	10	...	...
TOTALS		86	51	64.5	86	47	70.1	86	48	63.1

* Where percentage of sera showing fourfold antibody rise has been calculated, sera having titers of 1,024 in the prevaccine serum have been omitted from consideration; a rise in titer from a base line of 1,024 was impossible to demonstrate under the conditions of the test.

TORY. For the CPE neutralization test the sera were inactivated at 56 C. for thirty minutes. Each serum dilution was mixed with an equal volume of virus previously titrated to contain approximately 100 TCD_{50}, and the mixture was allowed to remain at room temperature for three hours. One-tenth ml. of each mixture was inoculated into each of two monkey kidney tubes, and all tubes were examined daily thereafter for cytopathic effect. The end point of the test was the day the virus titration confirmed the presence of 100 TCD_{50} of virus in the test dose and was usually five to seven days after inoculation.

METABOLIC INHIBITION TEST AS PERFORMED BY MICROBIOLOGICAL ASSOCIATES.[8] For the metabolic inhibition test the sera were inactivated at 56 C. for thirty minutes. Each serum dilution was mixed with 100 TCD_{50} of virus, and the mixture was allowed to remain at room temperature for one to two hours. Each mixture was inoculated into one tube containing a suspension of monkey kidney cells. The test was read at the time when the control test dose of virus (100 TCD_{50}) showed its color change.

Results

The results are based on tests performed on 601 pairs of sera 316 of which came from volunteers receiving the Cox vaccine and 285 from volunteers receiving the Sabin vaccine. The data from these tests were decoded and entered on multisort cards by punching holes according to a previously determined code; the cards were then sorted to extract the following information:

1. The percentage of fourfold or greater antibody rises according to virus type, antibody type, and prevaccine titer (Table I).

TABLE V. Influence of prior Salk immunization on the relationship between prevaccine titer and percentage of fourfold or greater antibody rises* to the three types of poliomyelitis virus following vaccination with Cox vaccine

		Poliomyelitis Virus								
		Type I			Type II			Type III		
			Rises			Rises			Rises	
Number of Salk Immunizations	Prevaccine Titer	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)	Sera (Number)	(Number)	(Per Cent)
0	<4	13	12	92.3	15	5	33.3	21	17	80.9
	4	8	6	75.0	5	4	80.0	9	8	88.8
	16	7	4	57.1	10	7	70.0	10	7	70.0
	64	7	2	28.5	9	6	66.6	9	5	55.5
	256	13	3	23.0	8	4	50.0	1	0	0.0
	1,024	2	...	...	3	...	...	0	...	...
TOTALS		50	27	56.2	50	26	55.3	50	37	74.0
1	<4	3	2	66.6	0	0	...	7	5	71.4
	4	4	3	75.0	0	0	...	4	2	50.0
	16	5	3	60.0	3	2	66.6	6	4	66.6
	64	5	3	60.0	6	2	33.3	9	7	77.7
	256	10	3	30.0	14	6	42.8	3	2	66.6
	1,024	9	...	...	13	...	...	7	...	...
TOTALS		36	14	51.8	36	10	43.4	36	20	68.9
2	<4	2	1	50.0	2	1	50.0	4	3	75.0
	4	2	2	100.0	4	1	25.0	2	2	100.0
	16	5	4	80.0	2	2	100.0	4	3	75.0
	64	4	3	75.0	6	3	50.0	4	3	75.0
	256	7	2	28.5	7	4	57.1	5	2	40.0
	1,024	6	...	...	5	...	...	7	...	...
TOTALS		26	12	60.0	26	11	52.3	26	13	68.4
3 or more	<4	15	15	100.0	1	1	100.0	32	31	96.8
	4	17	14	82.3	7	4	57.1	17	17	100.0
	16	23	18	78.2	28	15	53.5	31	29	93.5
	64	54	28	51.8	57	29	50.8	27	21	77.7
	256	40	15	37.5	51	16	31.3	41	13	31.7
	1,024	51	...	...	56	...	...	52	...	...
TOTALS		200	90	60.4	200	65	45.1	200	111	75.0

* Where percentage of sera showing fourfold antibody rise has been calculated, sera having titers of 1,024 in the prevaccine serum have been omitted from consideration; a rise in titer from a base line of 1,024 was impossible to demonstrate under the conditions of the test. In 4 persons the Salk status was unknown.

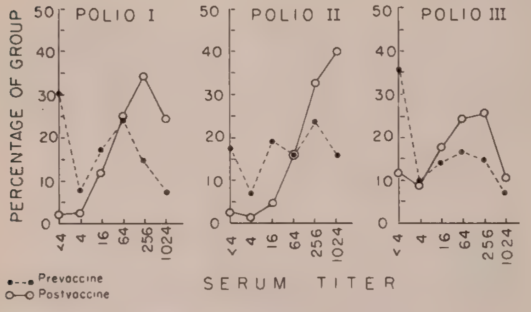

FIGURE 1. Antibody profiles of the data shown in Table VII. Sabin vaccine, pre- and postvaccine titers.

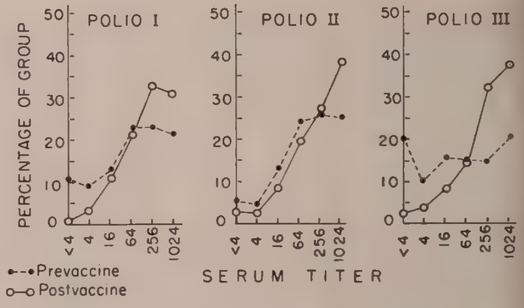

FIGURE 2. Antibody profiles of the data shown in Table VII. Cox vaccine, pre- and postvaccine titers.

2. The percentage of fourfold antibody rises according to age group, vaccine type, antibody type, and prevaccine titer (Tables II and III). An analysis of the results in terms of age has only been carried up to age twenty for the Sabin vaccinees (Rochester) since 95 per cent were below age twenty.

3. The percentage of fourfold antibody rises according to Salk vaccination status, vaccine and antibody type, and prevaccine titer (Tables IV and V).

4. Conversions of triple negatives (Table VI).

5. Distribution of pre- and postvaccine

TABLE VI. Postvaccine antibody titer of triple negative sera following administration of Sabin vaccine and Cox vaccine, shown according to age and number of Salk vaccinations previously received

Vaccine	Vacinee's Age (Years)	Salk Vaccinations (Number)	Postvaccine Titer Poliomyelitis Virus		
			Type I	Type II	Type III
Sabin	15	4	64	4	64
	9	2	256	1,024	<4
	12	2	256	1,024	16
	3	4	16	<4	64
	12	2	64	64	16
	10	2	256	64	<4
	4	0	16	<4	16
	7	2	256	64	16
	13	0	256	64	16
	14	2	16	<4	16
	11	3	256	64	4
	14	0	1,024	64	64
	2	0	1,024	64	256
	13	0	1,024	1,024	1,024
	28	0	<4	<4	<4
	10	2	16	16	16
	16	1	1,024	1,024	64
	9	0	256	64	<4
	10	0	1,024	64	64
	4	1	1,024	1,024	<4
	13	0	256	64	16
Cox	24	2	<4	16	<4
	22	0	16	<4	4
	26	0	16	<4	<4
	27	0	<4	<4	16
	5	0	64	<4	64
	36	0	256	<4	<4

Sabin vaccine: 21 triple negatives; 13 conversions to triple positive, 61.9 per cent.
Cox vaccine: 6 triple negatives; 0 conversions to triple positive.

titers and antibody profiles based on the previously mentioned figures (Table VII and Figs. 1 and 2).

A general summary of the results of this study is presented in Table VIII.

Comments

In comparing over-all percentage rises, it is necessary to bear in mind that the age distribution of the study population affects these results, and that this distribution was not identical in the two populations studied (see Tables II and III); therefore, for accurate comparisons, figures from the same age groups should be used.

Another unavoidable difference between the two groups occurred in the time intervals between the first and second bleedings. In the case of the Cox vaccine the interval was only one month, whereas the interval for the Sabin group was almost six months, owing to the spacing of feedings with the three types. This longer interval allowed time for changes in antibody level, particularly in the case of the first feedings with Types I and III, and for exposure to wild poliomyelitis virus. In point of fact, there were 5 clear-cut cases of paralytic poliomyelitis in the area (Rochester) of the Sabin group, 3 of which were identified as Type I. To cover the possibility that antibody rises of less than 4 to 4 were not true fourfold rises, a count was made of the number of rises in this category; the total was 34 such rises in the Sabin vaccine and 12 in the Cox group, of which 24 occurred with Type III antibody. These numbers were not large enough to affect the over-all results significantly, but if they are deducted from the totals shown, their distribution is such that the conclusions stated are emphasized rather than diminished.

Table I indicates that Types I and II

TABLE VII. Distribution of pre- and postvaccine antibody titers* according to vaccine type

		Poliomyelitis Virus											
		Type I				Type II				Type III			
		Prevaccine Titer		Postvaccine Titer		Prevaccine Titer		Postvaccine Titer		Prevaccine Titer		Postvaccine Titer	
		Persons				Persons				Persons			
Vaccine	Titer	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)	(Number)	(Per Cent)
Sabin	<4	85	29.8	6	2.1	49	17.2	7	2.4	104	36.5	34	11.9
	4	22	7.7	8	2.8	20	7.0	5	1.8	29	10.2	27	9.5
	16	48	16.9	34	11.9	54	19.0	15	5.3	40	14.0	49	17.2
	64	67	23.5	70	24.6	47	16.5	47	16.5	48	16.9	70	24.6
	256	41	14.4	99	34.7	67	23.5	95	33.3	44	15.4	73	25.6
	1,024	22	7.7	68	23.9	48	16.8	116	40.7	20	7.0	32	11.2
TOTALS		285	100.0	285	100.0	285	100.0	285	100.0	285	100.0	285	100.0
Cox	<4	34	10.8	4	1.2	18	5.7	12	3.8	64	20.3	8	2.5
	4	31	9.8	10	3.2	16	5.1	9	2.9	33	10.4	12	3.8
	16	41	13.0	35	11.1	43	13.6	27	8.5	52	16.5	27	8.5
	64	70	22.1	67	21.2	78	24.7	62	19.6	51	16.1	49	15.5
	256	71	22.5	102	32.3	82	25.9	85	26.9	50	15.8	101	32.0
	1,024	69	21.8	98	31.0	79	25.0	121	38.3	66	20.9	119	37.7
TOTALS		316	100.0	316	100.0	316	100.0	316	100.0	316	100.0	316	100.0

* Results are also expressed as antibody profiles in Figures 1 and 2.

TABLE VIII. Summarized results of vaccine study in terms of analysis of antibody levels for the two types of vaccine used

		Percentage of		Overall Percentage of Fourfold Rises by								
				Age Group (Years)					Salk Vaccinations (Number)			
Poliomyelitis Virus Type	Vaccine Type	Fourfold Rises	Fourfold Rises (Single Negatives)	0 to 10	11 to 20	21 to 30	31 to 40	41 plus	0	1	2	3 or more
I	Sabin	71.4	92.9	86.9	68.6	...	...	...	77.3	76.4	70.2	64.5
	Cox	58.7	91.1	53.1	69.5	61.2	48.8	52.6	56.2	51.8	60.0	60.4
II	Sabin	72.5	85.7	82.6	70.3	...	...	...	77.4	73.3	69.1	70.1
	Cox	47.2	38.8	47.8	46.8	45.1	40.4	53.3	55.3	43.4	52.3	45.1
III	Sabin	56.9	69.2	68.0	55.6	...	...	...	53.4	50.0	56.7	63.1
	Cox	73.6	87.5	90.9	86.7	59.3	56.4	65.5	74.0	68.9	68.4	75.0

Sabin vaccine were of approximately equal antigenicity while Type III produced somewhat less antibody response. This finding held true when the population was classified according to age (Table II) or according to Salk vaccination status (Table IV). In general the booster effect decreased with all three types as the amount of prevaccination antibody increased. In those volunteers who had no prevaccination antibody for one of the three types, there still remained a certain number who had no antibody after vaccination (Table I). This is true for poliomyelitis virus Type III more than for the other two types. An interesting finding in the cases of poliomyelitis virus Types I and III was that individuals who had no prevaccination antibody responded better to the Sabin vaccine when they had Salk immunization than when they did not, even though the Salk immunization gave them no detectable antibody (Table IV).

Table I also shows that Cox Type III vaccine was a better antigen than Types I and II. The response of volunteers in the age group zero to ten years to Type III Cox vaccine was especially good (Table III). As is the case with the Sabin vaccine, in general the booster effect of Cox vaccine decreases with all three types as the amount of prevaccination antibody increases. With all three types there were some individuals who had no antibody after receiving the vaccine. Individuals who had no prevaccination antibody responded better to the Cox vaccine when they had Salk immunization than when they did not, even though the Salk immunization alone gave them no detectable antibody (Table V).

With reference to Table VII relating the distribution of antibody titers to the type of vaccine given, it is necessary to point out that in the Sabin (Rochester) group an effort was made by the personnel selecting the volunteers to accept individuals who had received no previous Salk immunizations. This gives a slight bias to this group toward triple negative status (Table VI) and, presumably, in view of the findings of Table V, also toward a somewhat lower final antibody titer.

It will be apparent to the discerning reader that in addition to those discussed here, many other factors bear upon the final evaluation of these results. However, the aim of this paper is to present the results of the study, rather than to review them in terms of the many publications and opinions concerning this frequently controversial topic. It is to be hoped that all the published data may be correlated before long in a general review of the field of live poliomyelitis virus vaccination.

In general it can be said that Type III Sabin vaccine was somewhat poorer antigenically than Types I and II; Types I and II Cox vaccine also seemed to be of low potency, but a good response followed the use of this Type III vaccine. Both vaccines performed especially well in the elimination of antibody gaps when the vaccinee had received previous Salk immunization.

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Mental Health: Current Problems in Developing Effective Community Programs

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ONE CANNOT consider "current problems" without some reference to recent history, nor can one do so without reference to the immediate future. Perhaps saying this is no more than to utter a truism. Nevertheless, in my opinion, whatever focus we obtain will be gained as a result of our efforts at using the two dimensions in time in the form of brackets around the present.

We aren't always adept at this process, of course. A recent example of this inability to assess and predict appeared in the newspapers some time ago.[1] According to the story, in 1830 bankers in Shawneetown, Illinois, were asked for a $3,000 loan by the founding fathers of a remote village. The request was rejected on the grounds that the village was "too far from Shawneetown to ever amount to anything." Shawneetown today is described as a quiet little town on the banks of the Ohio. Its mayor and most influential banker recently decided it was time to journey to the remote place and present, in person, a proclamation to Mayor Richard J. Daley admitting that Shawneetown had erred about the future of Chicago one hundred thirty years ago. This surely underscores the uncertainty of appraisals even when the best efforts are engaged in the process.

Charcot, the great French neurologist of the last century, is quoted as observing that "disease is from old and nothing about it changes. It is we who change as we learn to recognize what was formerly imperceptible."[2] A difficult task is the seeing of an old problem in a new and advantageous light. We are being encouraged increasingly to hope that an old problem, that of mental illness, at this period in time is being seen in a new light. There is evidence that the care of the mentally ill is being altered according to new vision. This means that new problems may emerge or take on a new urgency now and in the decade ahead.

One of the hopeful signs of the newer approach to mental illness and emotional disturbance emerged within the past few years here in New York. Without the slightest exaggeration it may be said that in 1954 the New York State Legislature opened a new era in the history of the care of the mentally ill of this nation. By enacting the Community Mental Health Services Act,[3] which had as its high purpose "the development of preventive, rehabilitative and treatment services through new community mental health programs and the improvement and expansion of existing community services," New York State established a course which since has been followed in a number of other progressive states. To a considerable extent, the original purposes have been achieved within the confines of the law in New York State. Now, for further advances to be made, the law must be modified to permit them.

In the enactment of the precedent-making new law, the legislature included certain limitations on the extent to which the State government would participate financially in sharing with local government the cost of community programs. Over the past six years of experience under the Act very little concern has developed with respect to the fifty-fifty rate of sharing between the State and local governments. On the matter of per capita limitation, however, a strong con-

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sensus for change has evolved. Increasingly, authorities have come to view any per capita limitation as now obsolete (whether at the original limit of one dollar; or, at one dollar and twenty cents, as enacted in the last legislature; or, at any other future-assigned amount). This is not to say that the original measure should not have included a per capita limitation; authorities who then supported the first legislation now recommend abandonment of the per capita formulation in erecting the ceiling on reimbursement.

One of the significant accomplishments under the Act has been the achievement of recognition by local governments that responsibility for mental health services may be centrally placed. As used in the Act, "community mental health" is indeed a unifying concept useful for purposes of increasing the effectiveness of government action in a difficult field. The term actually embraces a great many, different disabling conditions, which fact increases the complexities of planning and purveying services. In itself, this great range of disorders speaks eloquently for the removal of the per capita restriction on developments in the field. This must be regarded as the primary desideratum for further advances to be made in mental health.

Problem complexity

Even if "mental illness" were a single disorder caused by a single agent of disease producing a uniform picture from the clinical point of view, the requirements of the act for four categories of service (inpatient, outpatient, rehabilitation, and educational) would present a complex group of responsibilities on state and local governments. In fact, these responsibilities are more complicated because mental illness does not conform to so simple a group of characteristics. Mental disorders are numerous; they are varied in type; they occur at different ages; and, as they occur, they are handled in a wide range of situations. Measures of prevention, early diagnosis, treatment, and rehabilitation for one type of disorder do not necessarily apply to another. The need is thus generated for a richly diversified program of services in any community of much size and complexity.

Services are demanded and supplied under community programs which emphasize the need of one particular group or another: by age group (for example, the aged, children); by diagnostic group (for example, narcotic addicts, retardates); by social system of involvement (for example, school children, prisoners, ex-mental patients); and by region (residents of a given area). No matter which group is selected, an excellent case can be made for increased services. The fact seems to be irrefutable: We are nowhere near the saturation of any community with needed services. As a result of this scarcity of required services and as a consequence of the limitation on available funds, persons interested in special groups are thrown into competition for the modest amounts appropriated. Such rivalry actually may interfere with the optimum advancement of a community mental health program. In the determined effort to win support for a particular group, boards and legislators are requested to seek legislation to exempt services of a certain type from accountability under the Act. Thus, the per capita restriction forces program judgments to be considered in the legislature rather than at the local level where the responsibility for planning must rest.

Obviously, community approaches to so complex a group of problems and disorders must be numerous in type as well as frequency. Of necessity, too, many different kinds of workers will be engaged in the several components of a mental health program; further, many different agencies will be called on to bear some part of the responsibility for action. In this vast staging of concern there are many roles to be played, and many new parts are now being written. The "master script" is far from a completed document.

We aim toward the objectives of mental health by means of imperfect instruments at best. In many ways we are confronted with the same problems in planning which faced public health advocates a century ago. Without knowing the exact cause of the contagious and infectious diseases, campaigns were waged on a generalized principle that filth was associated with disease. History records that advances were made when cleanliness was substituted for dirty conditions, although advances became much more rapid with the specific discovery of an agent of a disease. We know that many chronic and degenerative diseases did not yield either to the antifilth campaigns or to the scientific advances of bacteriology. Mental illness is one great residual group of this type, which for the most part still must be addressed in nonspecific terms.

The newer mental hospital

One factor of which many are convinced, as we look ahead into the 1960's, is that we have an outmoded system of care for the mentally ill patient. Early last year, a 12-man group of experts recommended the eventual elimination of large custodial mental hospitals.[4] Small regional, community facilities are foreseen as the type to be developed in the replacement of the old system. In these, patients would be allowed more freedom. Programs would include occupational and recreational therapy, educational planning, group therapy, and activities that mesh with the general life of the communities in which these smaller hospitals would be located. This concept of care gains ever more support. As it does, the weight of responsibility appears increasingly certain to undergo a further shift toward local government.

What are some of the indices that give hope and cause concern for the planning of community programs? We have just experienced the fifth consecutive year in which the number of resident patients in the mental hospitals of the State of New York has declined.[5] Thus, a local trend continues which in 1956 was established as a national phenomenon. The annual increase in resident patients for fifty-three years (from 1902 to 1955) had shown a definite rise from year to year. Nationally, this number had become a greater than four-fold increase over the resident patients enumerated in mental hospitals in 1902.[6]

That the upward trend was probably in part related to an ever-increasing population must be acknowledged. However, the rate of hospitalization for each 100,000 of the civilian population clearly demonstrates that the increases in mental hospital residents were not caused simply by the numerical expansion of persons within our boundaries. Concurrently with the reduction in numbers of resident patients in New York City, there is an increase in admissions to mental hospitals. Although first admissions continue to constitute the larger proportion of all admissions in the national setting, the size of the proportion has decreased. Between the years 1922 and 1959, there is a four-fold rise in the rates for readmissions over the nation as a whole.[6] This may be viewed in at least two ways. It may be considered a manifestation of insufficient rehabilitative care in the community or it may be considered evidence of an improvement in the utilization of short-term hospitalization for mental illness. More likely it is a product of both in combination with other factors.

We also see clearly an increase in the number of patients on convalescent care in the community. In New York City, for example, the census of patients on after-care has increased 30 per cent or more since these clinics were established in 1954.[7] Furthermore, the number of direct discharges to the community, without a period of convalescent care, has increased as has the number of voluntary admissions to mental hospitals.[5]

All of these trends may be viewed as part of the changing character of mental patient care. A serious question to be asked is whether or not any segment, government, profession, or community is prepared so that full advantage may be taken of the changes which we are now able to glimpse.

At the time of its enactment into law, the Act could hardly have incorporated features allowing for the impact on communities of trends which were developed to revolutionize the care of the mentally ill. After all, the Act scarcely foreshadowed two emerging developments in the field of psychiatric care: (1) the improved methods of handling patients in the mental hospital (including increased use of voluntary admissions and open hospitals), and (2) the successful application of the new pharmaceuticals.

The Community Mental Health Services Act, however, provides local government with a most timely opportunity to participate in a coordination of efforts which are aimed toward improved systems of care. Even more significantly, the opportunity has been afforded local government to observe the effect on it and its citizens of the newer psychiatric practices. The view is a sobering one in the implications for expanding community responsibilities.

Psychiatric rehabilitation services

The rehabilitation issue for state and local governments is underscored by these trends. Satisfaction cannot be taken in the declining numbers of resident patients in mental hospitals even though this represents a gain to the community of improved and recovering patients. We realize that at the same time, heavy responsibility inevitably falls on the local community to insure long-term recoveries and preclude relapses. The provision of aftercare and rehabilitation becomes increasingly important to forestall the unnecessary readmission of patients to state hospitals.

The mental hospital of today is not only different from that of two decades ago, it is changed from that of only ten years ago. A new appreciation of the treatment potential of the patient has led to a welcome reduction in the use of restraintive technics. The introduction of the tranquilizing drugs has pushed reformation in the same direction.

The implications of the newer developments really transcend the hospital walls. More than ever, the hospital is enabled to (and indeed must) come to terms with community supports in the aftercare process. The need for advances to be made in extramural programs for the recovering mentally ill patient commands renewed attention. This evolution, if not revolution, which is being witnessed in the mental hospitals will not be confined within the walls of an institution or within the organization of a department. The effects will be perceived in many related areas of public concern.

There is active interest among the concerned leadership of the community in enterprises for the rehabilitation of the mentally ill. A spectrum of services is visualized in which such program modifications may be found as night hospital, day hospital, sheltered workshop, half-way house, family care, expatient club, and aftercare clinics.[8] A bridge between the hospital and the community is envisioned, built according to the individual needs of the patient. This is the great challenge with which the community is now faced — a result of the revolution in care which has commenced in the mental hospital. The challenge will not be met without additional funds.

Because of the division of responsibility for different aspects of care for the mentally ill between the state and local governments, precautionary steps must be taken to assure that the development of needed rehabilitation services takes place. Among the four categories specified in the original legislation, "psychiatric rehabilitation services for persons suffering from psychiatric disorders" would appear to be one offering the greatest undeveloped potential for community programs. This is, in part, because of the relative state of underdevelopment in the field of rehabilitation and mental health. The continuation of a fixed ceiling, under which the sharing of costs for rehabilitation must be crowded, will allow for no substantial new achievement in what promises to be one of the most demanding areas in the decade ahead.

Inpatient psychiatric services in general hospitals

During the past few years within the psychiatric profession the concept of continuity of care has gained wider acceptance as a basic operational assumption. Briefly stated this view holds that the patient ideally should be given definitive treatment as soon as possible, as near to home as possible, with as few changes as possible in treatment personnel, and with a properly graduated return to home and community. Our present system of hospitals was built in an era which was not characterized by the same expectancy of hope for the patient as now obtains. Therefore, today's patient in yesterday's system may find it difficult to obtain treatment promptly, may need to be cared for at a considerable distance from home, and may suffer a complete change in treatment personnel when returned to the community on aftercare status.

The distance between the local community and the state institution led, until the enactment of the Community Mental Health Services Act, to a precise division in the cost of caring for the mentally ill. The local facilities provided only temporary care until the patient could be received at the state hospital. Thereafter, the responsibility was agreed to be that of the state. Fortunately for patient care, this cleavage is no longer so clear.

The treatment programs in general hospitals have been promoted under the Community Mental Health Services Act so that increasing numbers of patients may not need to be sent on to remote mental hospitals to receive early effective treatment. The old attitudes and policies are undergoing slow but definite change in response to the newer advances in psychiatry.

The advances include recent undertakings of modest proportions in terms of dollars, but of rich promise in terms of improved patient care. Included here, too, are such innovations as day hospital care, night hospital care, and community center care. The concept of less than twenty-four hour hospital care in the general hospital psychiatric service is gaining wide acceptance. A flexible method, it enables the patient to receive the amount and kind of treatment needed without total separation from his family and his work.[9] There are obvious economic advantages to the patient, his family, the community, and the government.

We are confident that we are about to see hospitalization for mental illness in a new perspective in the decade before us. We are now encouraged to say that the system of care may be altered so that every effort may be made to prevent unnecessary hospitalization. Through the new methods we now may prevent that noneffectiveness which resulted from the old system of remote hospitalization. To be able to provide, as near to home as possible, the kind of services which will prevent unnecessary state hospitalization, unnecessary commitment, and unnecessarily long periods of care in institutions, new programs and new patterns of care are needed. The establishment and development of these new beneficial programs ought not to be impeded by a lack of available funds.

Outpatient psychiatric clinics

An arresting development is clearly discernible in the growth pattern of outpatient and community clinics in the city. Very recently the one hundredth psychiatric clinic license was granted by the State Department of Mental Hygiene. Some of the licensed clinics have branches in different locations from the parent and these, when added to the licensed number, make 122 reporting units.[10] The utilization of community clinics is reflected not alone in growth in numbers of reporting units, but also by the increased services rendered as well as an increasing demand for services.

Of the licensed group, 16 are municipal clinics, 46 clinics have a contractual relationship with the Community Mental Health Board, and 38 clinics are without such a connection. Fifty-two of the clinics are for all age groups, 22 are for children, 9 are for adults only, and 17 are in various special categories of service.

The clinics not in contract with this Board must be considered as an undeveloped potential in this important area of service. Furthermore, many clinics already engaged in service under an arrangement with the Board are ready to expand but for additional funds needed. Both groups of clinics represent a prospective increase in services which might develop up to twice the amount of service currently being so received.

How important an increase in services of this type is to the welfare of children may be expressed in one important way: only 9 of the licensed clinics are for adults alone. Children and their parents stand to gain to a very substantial degree if services in community and outpatient clinics are expanded. There is much work to be done, and the opportunities may be seized only if sufficient funds are made available for new and expanded outpatient psychiatric services.

The need of children and their parents for a mental health resource has been accepted since shortly after the turn of the century. My own respect and admiration for the work of child guidance clinics is perhaps conditioned by having been a part of such a unit in the District of Columbia. Personally, I feel that some of the contemporary criticism of the child guidance clinics is from a very narrow view of over-all mental health needs. I would like to quote a thirty-five-year-old statement of Adolf Meyer[11] on this point:

> We are at times made to believe that all our mental hygiene work and effort aims largely at the prevention of insanity and crime, just as the early advocates of psychopathic hospitals made it look as if, through the creation of a psychopathic hospital in each state, the existing state hospital care would then be made less expensive, and perhaps in part unnecessary. To be sure, early work means a heading off of some of the disastrous depths of aberration and deviation, and much unnecessary blundering. But the chief goal is much more direct. It offers prompter and more and more enlightened help both to the patient and family and to the community in respect to really new problems largely left to themselves before; it is a direct service to the positive needs and opportunities of the community in behalf of what I reemphasize as health, happiness, efficiency, and social adaptation.

For my part, I do not believe that the child guidance clinic can be cast aside because it has not prevented juvenile delinquency or insanity.

The trends outlined mean to me that a wide range of services, of which the child guidance clinic is but one, must be contemplated to confront the multiple faces of mental illness. To me, also, it becomes increasingly clear that effective liaison between mental health agencies of varying types is prerequisite to better service.

Consultation and educational services

We have scarcely begun to implement our consultation and educational services, which are envisioned as a potentially great resource in the preventive field of endeavor. These, too, must be developed if we are to be better equipped throughout our helping services to deal early and effectively with adjustment problems.

Mental health consultation as an operational activity is still in infancy. It would appear, however, that work along these lines could be of immense value. Recent work done in Massachusetts demonstrates the value of this service and offers constructive suggestions to others interested.[12,13] Mental health consultation is distinguished from clinical consultation in that it does not mean the mental examination of a patient by mental health personnel; rather, it is mental health personnel working with the staffs of various agencies in an effort to help cope more adequately with evidences of disturbed mental health as these evidences are encountered.

The great promise of this approach is in the early point of the attack before problems are so entrenched as to require highly specialized methods for solution. The added value of the approach is in the improved performance of society's "gatekeepers" of mental health — teachers, nurses, judges, probation officers, and a vast group of other helping specialists.

The aging population

There are other trends which may have important effects on the mental health program plans of the future. We can scarcely hazard guesses about certain of them, so indistinct do they emerge, not so much as to fact as to effect. The aging population is one such well-defined, well-established trend. Expressed in one way, now at age sixty-five one may expect to live fourteen years longer, according to the average life expectancy.[14] However, it is expressed, life expectancy has been increased, and an ever-larger proportion of the aged in the population is to be expected. This confronts us with the need to provide adequate mental health services to a group which has had little such attention before. Evidence is accumulating that substantial numbers of mildly to moderately disturbed elderly patients are being cared for in homes for the aged and in nursing homes. The provision of services suitable to this portion of the population may require a considerable reorientation of community clinic programs.

Consultation services suitable to the the caretakers of the elderly infirm may call for an especially interested staff based in community-oriented facilities. Probably most mental health centers would have to augment their staffs and widen their programs to provide such services.

Prepayment for psychiatric care

We do not yet know how to plan for the impact of increased interest in providing prepaid care for psychiatric conditions. This coverage, which has been approached by insurance experts with some trepidation, now appears to be viewed in a more favorable light. How the policy holder will make use of his inpatient care provision, when this becomes possible, will be the object of study on many counts. This field of prepaid medical care is one in which mental health is a certain participant, although the extent of future involvement of mental health personnel is by no means clear.

Future issues in development

If one reviews the pattern of development in public health, and if one reviews the historical bases of mental hygiene, a number of historic guidelines become evident. These guidelines have had application in the development of medical care services and ought to be considered as indicative of important problem areas in planning for new approaches in mental illness.[15]

First, for an increasingly important share of the work, local government organizations must be anticipated to accept responsibility. Other auspices may be expected to be engaged for certain parts of the work, of course, but the greatest portion of responsibility will be within the hands of local governments as it is with respect to other health areas. If, indeed, this is the pattern for the future, it will present a problem area which will not be traversed easily. This has to do with the matter of financing during the difficult period of transition. At the present time, the state has almost complete responsibility for care. There have been some encroachments on this from the Federal government through the programs of care in the Veterans Administration and the U.S. Public Health Service. With the passage in this State of the Community Mental Health Services Act of 1954, the dividing line of fiscal responsibility became blurred between State and local governments. That this cleavage is no longer clear may be fortunate in planning patient care, although difficulties may be foreseen as new programs are proposed. Time-honored policies affecting the division of responsibility between governments do not yield easily to the forces for change.

Second, to effect a systematic reduction in health problems, an adequate organization with appropriate operations is needed. Not infrequently, an adequate organization depends on the availability of sufficient numbers of trained personnel. However, the emphasis here is not only on the manpower problem, although this is expected to complicate plans and operations during the next decade. On the contrary, the problem to which I refer is the one of arranging transorganizational approaches and interagency efforts. In the complexities of providing for community mental health services, not only are government lines to be crossed but so are department lines within governments, agency lines within communities, and disciplinary lines within agencies. This will provide the second great area for problem solving. Here I refer to the problems relating to the specialist heritage in the fields of medicine and public health. There will be many opportunities for professional workers of one discipline to resist advances undertaken by another discipline. However, with so much work remaining to be done, the resolution of agency and organizational rivalries and professional jealousies must be patiently and doggedly identified and resolved.[16]

The importance of the scientific basis for advances requires little more emphasis in our time than events of the day have given it. Paradoxically, the importance of scientific advance may act to present the third area of difficulty in the times ahead. Clearly, the effort at obtaining increasingly improved data concerning mental illness and health must be strengthened. All of this needs almost not to be said. But we must be reminded that more progress likely will be based on empiric observation in this field before precise scientific data are at hand. This should be recognized without detracting from the field. In our day of rapid technologic advances, it is sometimes difficult to justify programs which cannot be supported scientifically. We are obliged to move forward with whatever we have learned, and we cannot be deterred by those who would scoff because of the inexact nature of our predictions.

Summary

In summarizing my views, I submit that the opportunities which are ahead in developing community programs may be seized in accordance with our abilities:

1. To continue the advances being made in the mental hospitals, overcoming the isolation of the mental hospital and of the patient from the community;
2. To develop and elaborate new extramural programs for the rehabilitative phase of medical care;
3. To develop and expand preventive services which obviate unnecessary hospitalization or commitment;
4. To facilitate a greater sharing between all levels of government, local, state, and Federal, in the provision of psychiatric care in keeping with the newer knowledge available;
5. To perfect adequate organizations and systems aimed at the reduction of the problem which may involve many agencies and professions; and,
6. To utilize information available in this complex and important field as a basis for innovation and new departures.

If the community is prepared to accept the humanitarian responsibilities of mental health, it then may be prepared to answer affirmatively the question whether or not inevitably increasing cost for care of the psychiatric patient will be assumed. An attractive consideration is the possibility that community mental health measures will result in a diminution of the amount of money which is necessary to be spent for the maintenance of vast outmoded hospitals for the chronic care of the mentally ill. Certainly intriguing is the thought that at worst what may happen will be simply the transfer of monies expended in the chronic care system to a local system of community mental health services, with no increased cost to the taxpayers. To me it would seem that more likely at the outset will be increases in expenditures during the period of transition and evolution in the care of the mentally ill. For us to begin to come to grips with this on the local scene, the State government will have to participate as a full partner in the development of such services. This cannot now be accomplished in New York State under the limitations imposed on the community mental health services program. Therefore, we must look toward the complete removal of the ceiling on mental health expenditure sharing between State and local governments.

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Indications for Artificial Dialysis

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From ancient to recent times physicians have sought artificial means to rid the body of accumulated metabolites and toxins in the presence of failure or inadequacy of the normal excretory organs. Purging, phlebotomizing, and induced diaphoresis are examples of efforts in the past. Abel, Rowntree, and Turner[1] gave birth to the modern era in 1912 when they first demonstrated vividiffusion or hemodialysis publicly. Their early artificial kidney, consisting of collodion membranes and leech anticoagulant, is now well known. The development of the technics of dialysis which are presently used required an increased understanding of fluid and electrolyte balance, the development of the newer anticoagulants, and the introduction of cellophane semipermeable membranes. With the exception of the resin exchange-type artificial kidney, modern artificial kidneys utilize a cellophane membrane and heparin as an anticoagulant.

The cellophane membrane has a pore radius similar to the human glomerular capillary. This means that the various blood constituents of molecular size below that of serum albumin will pass through the membrane if there is a gradient across it. The direction of exchange is of course dependent on this gradient, and it permits diffusion to the blood of substances as well as their removal. The artificial kidneys as presently constructed have no counterpart to the renal tubules and therefore none of the homeostatic functions of the human kidney tubules.

Artificial dialysis is used in the treatment of a diverse group of diseases that may be divided into four major categories. These are: (1) acute renal insufficiency; (2) intoxication with dialyzable non-nephrotoxic agents; (3) selective forms of chronic renal disease; and (4) intractable uremia, overhydration, or metabolic coma in patients with either surgically or medically reversible disease. We shall illustrate each category and discuss the indications for dialysis in individual cases.

The indications for dialysis in a specific case cannot be listed succinctly because dialysis is but one of the modalities of therapy employed in each case. The medical measures to regulate acid-base and fluid balance, to supply calories, and to sustain the cardiovascular and respiratory function are paramount and complement each other. Not all patients with the diseases listed previously require dialysis, just as not all peptic ulcers require surgery. Perhaps at first glance a better understanding of medical management might seem to lessen the need for dialysis. Closer supervision of medical needs can save the lives of those with milder forms of disease, but in prolonging the lives of those with severe disease the aid of dialysis will be required more often, as indicated by Merrill,[2] and should permit a decreasing mortality.

The Fourth Division, Urologic Service, at Bellevue Hospital acquired its first artificial kidney in 1951. Between 1951 and 1958 over 100 dialyses were performed. The original apparatus was a Kolff rotating drum-type dialyzer, considerably more cumbersome than the Kolff[3] disposable twin coil unit now in use. Interestingly, during the earlier period peritoneal dialysis was performed frequently, but since the acquisition of the twin coil disposable unit, peritoneal dialysis has been used infrequently. In 1959 we acquired two disposable twin coil units. One is used at Bellevue Hospital and the other at University Hospital. In the period from January, 1959, to December, 1960, 26 patients have been dialyzed and form the basis of this report. Table I shows the distribution of cases and survivals of this group.

Acute renal insufficiency

Acute renal and presumably reversible insufficiency is the now classic condition which benefited by artificial dialysis. Included in this category is renal insufficiency following transfusion incompatibilities, severe trauma, extensive burns, heavy metal intoxication, obstetric catastrophes, and other causes of renal ischemia and tubular necrosis. The primary therapy, no matter what the etiology, remains medical, as described previously. Although we have no absolute criteria or easily applicable formulas to determine the need for dialysis, we have learned to use the available clinical and laboratory guides. The clinical parameters are related primarily to changes in the nervous system and manifest themselves as increasing irritability and progressive clouding of the sensorium. The laboratory or biochemical indicators are useful collectively rather than individually. A rising serum potassium level of above 6.5 to 7.0 mEq. per liter despite adequate exchange resin therapy, a rapidly rising blood urea nitrogen usually greater than 200 mg. per 100 ml., and increasing acidosis despite bicarbonate replacement with the carbon dioxide combining power below 15 mEq. per liter have been the most useful indicators. The biochemical and clinical changes are concurrent in most cases and occur in cases requiring dialysis despite attempts to correct and compensate for the changes in the physiology during renal insufficiency. Other clinical and laboratory changes associated with acute renal insufficiency include a bleeding diathesis; nausea; occasional ileus; diarrhea; retention of creatinine, uric acid, and phosphates; and depression of serum calcium, but these have been less useful indicators of the need for dialysis.

ARTIFICIAL DIALYSIS *is used in the treatment of acute renal insufficiency, intoxication with dialyzable non-nephrotoxic agents, selective forms of chronic renal disease, and intractable uremia, overhydration, or metabolic coma in patients with either surgically or medically reversible disease. From January, 1959, to December, 1960, 26 patients have been dialyzed, using a disposable twin coil unit. The indications for dialysis must be determined in conjunction with medical measures to regulate acid-base and fluid balance, to supply calories, and to sustain the cardiovascular and respiratory function.*

TABLE I. Patients dialyzed between January, 1959, and December, 1960, by the Fourth Division, Urologic Service, New York University Medical Center

Category	Description of Cases	Number Dialyzed	Number of Survivals
I	Acute tubular insufficiency	10	4
	Renal cortical necrosis	3	0
	Ethylene glycol intoxication	1	0
	Acute glomerulonephritis with anuria in adults	3	0
II	Barbiturate intoxication	2	2
	Sedative intoxication	1	1
	Salicylate intoxication	1	1
III	Chronic renal disease	3	1
IV	Obstructive uropathy preparatory for surgery	1	1
	Metabolic coma (hepatic insufficiency)	1	0
TOTALS		26	10

Included under the category of acute renal insufficiency in our series are 3 cases of confluent renal cortical necrosis proved at autopsy, 1 case of probable ethylene glycol intoxication, and 1 patient with acute renal insufficiency following a septic abortion who expired from gram-negative septicemia during the diuretic phase. The survival of such cases at present is still exceptional despite dialysis. A separate category of acute renal insufficiency is the adult with acute or subacute glomerulonephritis with anuria. Unlike the child with this disease, recovery is unusual in the adult. Our experience has been limited to 3 cases each of whom eventually succumbed without evidence of entering a diuretic phase.

Intoxication with non-nephrotoxic dialyzable substances

Intoxication with non-nephrotoxic dialyzable substances includes accidental and intentional ingestion of substances such as barbiturates, other soporifics, salicylates, bromides, potassium thiocyanate, and ammonia compounds. At an institution such as Bellevue Hospital an average of over 100 cases of attempted chemically induced poisonings are seen annually. From our own figures few of these require dialysis as the survival rate with supportive measures is excellent in the usual case. However, the need for dialysis increases with an increased dosage of intoxicant, and even before the blood level can be determined clinically we have been guided by the patient's ability or inability to maintain respiratory and cardiovascular function and the clinical changes manifested over a period of time. Prior to dialysis gastric lavage, analeptics, vasopressors, respirators, endotracheal tubes, and tracheostomy have been utilized as indicated. Those occasional patients who are unable to maintain their vital functions despite supportive measures have been benefited by dialysis. The preceding remarks apply particularly to barbiturates and other soporifics which, despite the route of excretion, are all dialyzable. Salicylates, and more particularly methylsalicylate, require dialysis because of their toxicity in relatively small doses. According to Goodman and Gilman[4] as little as 4 ml. of methylsalicylate may be fatal in children. Despite the severity of intoxication, the survival rates are good. Each of our 4 cases survived.

Chronic renal disease

The role of dialysis in chronic renal insufficiency is limited at present. The 3 patients with chronic renal disease who underwent dialysis in our series include 1 with an acute history in whom the possibility of reversibility could not be ruled out, a patient with lupus nephritis, and 1 patient with polycystic disease. This last patient is a forty-eight-year-old male with intractable uremia who was comatose despite essentially balanced serum electrolytes. The daily urinary output exceeded 1,500 ml. and increased in the presence of increased fluid intake. Hemodialysis resulted in the patient regaining consciousness within two hours, and the patient, although azotemic, remained oriented and fully conscious for six months before requiring a second dialysis. He continues to require careful regulation of his fluid and electrolyte intake. It is difficult to draw conclusions on the basis of 3 cases, but we emphasize the urinary output in this last case. The urinary volume may be the significant factor in determining the value of dialysis at present for chronic renal disease, as has been commented on by Keleman and Kolff.[5] They state: "A volume of 1500 ml/24 must be reached in order to sustain any improvement brought about by dialysis." The role of dialysis in chronic renal diseases will increase after the development of either external or internal dialysis units or chambers that allow for daily, inexpensive, outpatient therapy.

Intractable uremia, overhydration, or metabolic coma

Two of our recent cases illustrate the fourth of the categories of diseases benefited by dialysis. One was a patient, age thirty-two, with a solitary giant hydronephrotic kidney; he was uremic, comatose, and edematous when first seen. A nephrostomy was indicated but considered of greater risk than dialysis. Twenty-four hours after a six-hour hemodialysis, a nephrostomy was performed. The patient survived for eighteen months, part of which time he was gainfully employed. His death was the result of renal insufficiency. Terminally the urinary output had decreased below 400 ml. per twenty-four hours. The second patient illustrates a metabolic derangement benefited by hemodialysis. The patient was comatose as a result of hepatic insufficiency secondary to Laennec's cirrhosis of the liver. Following dialysis he regained consciousness, but no significant hepatic regeneration occurred, and the patient lapsed back into coma and expired within one month of dialysis.

Summary

The indications for artificial dialysis in a series of 26 cases treated during a two-year period have been reviewed.

Although it is not absolute, sufficient experience has been gained in the management of such cases to enable reasonable certainty of the indications for dialysis in the individual case. Not included in the clinical material have been the cases referred to us for dialysis for whom other forms of therapy were indicated or those so terminal that they expired shortly after their arrival at the hospital. Included in this material are cases of unrecognized obstructive uropathy, problems of severe electrolyte and water imbalance which were managed medically, and patients who expired less than two hours after their transfer to our hospital. These cases are cited to dramatize the need for the proper diagnosis of the cause of anuria and uremia when they are present, for the proper medical management of such cases, and for the avoidance of fatal delays in recognizing the need for dialysis when it is indicated.

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Good nursery schools offer advantages

A nursery school operated professionally and competently has strong advantages for most children at the age of three or four, according to an article by Dr. Willard Abraham in the April, 1962, issue of *Today's Health*. However, nursery schools are not the answer for all childhood problems of insecurity, speech, and slow maturing. They will not compensate for the rejection a child may feel when a new baby enters the home scene, and they cannot make up for a broken home, parents who never wanted him in the first place, or a mother who puts her pleasures or luxuries ahead of him. They can be of only limited help in these situations.

Nursery schools represent "a wedge toward the bigger world which the child can enter gradually." They also offer "an open door to the beginning of science, numbers, music, and art, to concepts of time and space—and another link in the reading process."

Most children can profit from this expanded experience, but only if the child is ready to be away from home part of the day, the school supplements, rather than duplicates the home, and the staff, equipment, and physical setting are appropriate to the child's needs.

Serial Serum Enzymes in Infectious Mononucleosis*

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AN ATTEMPT WAS MADE *to correlate serial serum enzymes with the clinical course of infectious mononucleosis. The SGO-T (serum glutamic oxalacetic transaminase) level was elevated in 31 of 36 patients (86 per cent) with infectious mononucleosis. The SGP-T (serum glutamic pyruvic transaminase) level was elevated in 21 cases (66 per cent), normal in 10, and not obtained in 5. LDH (lactic dehydrogenase) activity was increased in all of the 7 patients studied; in 2 cases it was elevated when the SGO-T and SGP-T levels were within normal limits. In 80 per cent of the cases the highest transaminase levels were recorded during the first two weeks following the onset of symptoms, indicating that hepatic alterations occur early in the course of infectious mononucleosis, but they returned to normal in all of the patients, during the third to fifth week of illness in two thirds of the patients. Serum transaminase levels were normal in 18 cases of rubella, which may mimic infectious mononucleosis.*

HEPATIC INVOLVEMENT in infectious mononucleosis has been well documented by clinical, laboratory, and biopsy data.[1–7] Numerous reports have likewise indicated the value of serum enzymes, particularly SGO-T (serum glutamic oxalacetic transaminase) and SGP-T (serum glutamic pyruvic transaminase) as an index of liver cell injury.[8–11]

Rennie and Wróblewski[12] have recorded the value of serum transaminase in infectious mononucleosis, which the authors felt reflected closely the nonicteric as well as the icteric hepatitis seen in their cases.

Material and methods

An attempt was made to correlate serial serum enzymes with the clinical course of infectious mononucleosis. Weekly SGO-T and SGP-T levels were obtained in 36 hospitalized cases of infectious mononucleosis admitted to the United States Naval Hospital, Bethesda, Maryland. Serial serum LDH (lactic dehydrogenase) activity was evaluated in the last 7 cases. All of the patients had a positive absorbed heterophil antibody titer and were followed with weekly heterophil titer tests, liver function studies, complete blood counts, and electrocardiograms.

Results

The SGO-T level was elevated in 31 of 36 patients (86 per cent) with infectious mononucleosis. It was consistently higher than the SGP-T level (Table I). The values ranged from 47 to 716 units (normal 5 to 40 units). The SGP-T was elevated in 21 cases (66 per cent), normal in 10, and not obtained in 5. Serum values varied from 44 to 402 units (normal 5 to 35 units).

The SGO-T and SGP-T levels were noted to be normal during the prodromal phase of infectious mononucleosis in 2 patients who developed their illness while they were on the medical service for

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* The opinions or assertions contained herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

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TABLE I. Comparison of serum enzymes as indexes of infectious mononucleosis in 36 patients

Patient Number	Highest SGO-T	Highest SGP-T	Days from Onset of Illness to Highest Transaminase	Absorbed Heterophil Antibody Titer
1	74	18	7	1:896
2	98	33	7	1:896
3	113	44	14	1:448
4	49	14	1	1:3,584
5	48	12	26	1:28
6	325	Not done	10	1:1,792
7	62	Not done	5	1:896
8	91	46	12	1:448
9	110	132	14	1:112
10	131	107	16	1:3,584
11	31	20	3	1:7,168
12	114	86	22	1:448
13	116	108	11	1:448
14	88	48	21	1:448
15	75	91	9	1:224
16	80	54	8	1:448
17	53	61	17	1:448
18	328	221	10	1:448
19	188	140	5	1:3,584
20	176	140	10	1:1,792
21	55	30	14	1:448
22	48	33	3	1:14
23	450	220	17	1:448
24	23	17	7	1:112
25	176	188	3	1:1,792
26	169	79	13	1:448
27	162	75	10	1:448
28	406	402	18	1:224
29	60	Not done	7	1:1,792
30	716	Not done	7	1:448
31	14	13	..	1:28
32	19	17	..	1:448
33	30	9	..	1:896
34	47	44	11	1:112
35	68	63	9	1:224
36	109	94	14	1:896

nonrelated problems. The serum transaminase level and heterophil antibody titer both rose to significant levels after one week and only at the time of the acute phase of infectious mononucleosis.

LDH activity was increased in all of the 7 patients studied. In 2 cases LDH activity was elevated when the SGO-T and SGP-T levels were within normal limits.

Comment

In 80 per cent of the cases the highest transaminase levels were recorded during the first two weeks following the onset of symptoms (Table I). This would imply that hepatic alterations occur early in the course of infectious mononucleosis. Serum lactic dehydrogenase activity and serum transaminase levels returned to normal in all of the patients who were followed in this survey, and in two thirds of the patients this was achieved during the third to fifth week of illness. With the aid of serial liver biopsies Nelson and Darragh[7] concluded that the usual course of hepatitis in infectious mononucleosis is from two to four weeks. Serial serum transaminase, therefore, would tend to support their data.

An abnormal thymol turbidity or cephalin flocculation was noted in 25 of 29 patients. Frequently the evidence of compromised liver function persisted for several weeks after the serum transaminase returned to normal. The Bromsulphalein test performed on admission gave normal results in 9 of 11 cases of nonicteric hepatitis, indicating its questionable diagnostic value in infectious mononucleosis.

The electrocardiograms were within normal limits in 24 of 26 cases in which they were obtained. In one case it was compatible with pericarditis, and a second patient's electrocardiogram revealed nonspecific T-wave changes. The SGO-T is usually normal in pericarditis, although an occasional elevation has been recorded.[13]

In the course of this study we encountered a mild epidemic of rubella. Four cases with rash, fever, pharyngitis, diffuse adenopathy, and splenomegaly mimicked infectious mononucleosis. The SGO-T and SGP-T levels were normal in 18 cases of rubella, and the normal transaminase lent added support to the normal heterophil titers.

Summary

1. Serum SGO-T (glutamic oxalacetic transaminase) and SGP-T (serum glutamic pyruvic transaminase) levels are commonly elevated in infectious mononucleosis and often aid in establishing a working diagnosis.

2. Elevated transaminase values most probably reflect hepatic involvement, although pericardial disease must be excluded by serial electrocardiograms.

3. The early prognostic value of serum transaminase in infectious mononucleosis is open to question since it gave negative reactions in the prodromal phase of 2 cases.

4. Serum transaminase determinations have been consistently normal in rubella and may be used as an added laboratory test in the differentiation from infectious mononucleosis.

5. Since increased activity was obtained in 7 consecutive cases, lactic dehydrogenase activity may be a more sensitive indicator of liver or cardiac involvement in infectious mononucleosis.

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Gamma Globulin in the Prevention of Upper Respiratory Infections in Children

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A DOUBLE-BLIND STUDY *was performed on 143 children from one to nine years of age with histories of frequent upper respiratory infection to evaluate the prophylactic value of gamma globulin. Half of the children received 0.2 cc. of gamma globulin per pound of body weight at monthly intervals for five months. The alternate patients received equal amounts of saline. The results were identical for the two groups as a whole. However, of 16 asthmatic children in the study, the asthmatic patients on gamma globulin had about one-half as many upper respiratory infections as the asthmatic patients on placebo, and they had fewer asthma attacks. Two thirds of the parents, irrespective of the agent given, thought the children had improved. No members of the gamma globulin group had measles. Chickenpox and mumps occurred in both groups. It is possible that asthmatic and maybe all allergic children have a specific deficiency of their gamma globulin which prevents an adequate antibody formation and causes the allergic response to upper respiratory infections.*

THE EFFICACY of gamma globulin in the treatment of infectious asthma has been reported by Friedlaender, Friedlaender, and Weiner[1] and Brown and Botstein.[2] It was the impression of Brown and Botstein that the beneficial effect of gamma globulin in decreasing the number of asthma attacks was due to the decrease in the number of upper respiratory infections suffered by those patients. The following study was undertaken to determine whether or not gamma globulin is an effective agent in the prevention of upper respiratory infections not only in the asthmatic child but also in an average pediatric population.

Material and method

In November, 1959, all members of the Montefiore Hospital Medical Group who had children between the ages of one and nine years were invited to participate in the study. Each child participating was to receive either gamma globulin or saline during the winter months of 1959 to 1960. Parents of 143 children volunteered for the study and signed a pledge to follow the program through to its completion. As expected, most of the children had histories of frequent upper respiratory infections in previous years. They were still an average group however, without clinical histories of hypogammaglobulinemia. The gamma globulin levels were not determined. The majority of the patients came from families with several children. Ninety-seven participants had siblings in the study. Only the nurse knew and kept the record of the patients who received gamma globulin or saline throughout the study. This fact was not disclosed either to the investigators or to the parents of the participants until the statistical evaluation of the results was completed. The gamma globulin, contributed for the study by the American Red Cross, was a 16 per cent solution of the globulin fraction of pooled normal human plasma (1 cc. contained 165 mg. ± 15 mg. of pure gamma globulin). Every month, the

TABLE I. Months of observation of 143 children by type of agent*

Months of Observation	Gamma Globulin	Saline	Total
1	6	6	12
2	2	3	5
3	7	8	15
4	49	44	93
5	8	10	18
Total children	72	71	143
Total months of observation	267	262	529
Average months per child	3.71	3.69	3.70

* Each child was given one injection of gamma globulin or saline placebo at beginning of each month of observation.

TABLE II. Average number of upper respiratory infections per child per month by type of agent

Considerations	Gamma Globulin	Saline	Total
Number of children	72	71	143
Number of months observed	267	262	529
Number of upper respiratory infections	130	127	257
Average number upper respiratory infections per child per month	0.487	0.485	0.486

TABLE III. Average number of upper respiratory infections per child per month by type of agent and age of child

Age of Child (Years)	Gamma Globulin	Saline	Total
1 to 2.9	0.62	0.59	0.60
3 to 4.9	0.41	0.44	0.42
5 to 6.9	0.49	0.44	0.47
7 to 8.9	0.32	0.38	0.34
All children	0.487	0.485	0.486

even-numbered patients received 0.2 cc. of gamma globulin solution per pound of body weight (0.075 Gm. per kilogram) and the odd-numbered patients the same amount of normal saline. The dose was usually divided into two portions and injected intramuscularly deep into both buttocks. Not all patients received five injections since some patients joined the study after November, 1959, and some did not report for their last injections. Table I shows that the majority received four injections and few had less than two injections. There was no significant difference in the number of injections received by the gamma globulin and the control groups. Since not all the patients were treated and observed for five months, the results were evaluated in terms of person-months of observation. An observation month starts with the date of the patient's injection and ends one month later.

Results

No adverse reactions were observed in either group. In the following evaluation, the effect of the agent is expressed in the number of upper respiratory infections per patient per observation month. At each monthly visit the participants were examined by the pediatrician. Every upper respiratory infection, whether seen by the pediatrician or only reported by the parent, was recorded in the patient's chart. In addition, the charts contained records of all office visits and house calls during the interval. (In Montefiore Medical Group every house visit is made part of the chart.) Included in the census was each "cold" (with or without fever), sore throat, otitis, tonsillitis, bronchitis, pneumonia, and laryngitis. Not included were the so-called "intestinal virus" infections, with vomiting and diarrhea but without evidence of upper respiratory involvement. The infectious childhood diseases (mumps, chickenpox, and measles) were considered separately. An attempt was made to differentiate between mild and severe infections, using as a guide whether or not an antibiotic was given. This classification had to be dropped since indications for treatment were dependent more on the personal judgment of the pediatrician (six pediatricians in the Montefiore Medical Group were attending our study children) than on the severity of the infection.

As shown in Table II, the results are identical for the two groups as a whole. There is also no evidence that gamma globulin has a cumulative effect since there is no decrease in the number of infections per month throughout the duration of the study.

Our previous experience with asthmatic children[2] suggested that gamma globulin might be more effective in preventing up-

TABLE IV. Average number of upper respiratory infections per child per month by type of agent and sibship of child

Sibship of Child	Gamma Globulin	Saline	Total
Single	0.42	0.47	0.45
Sibling	0.50	0.49	0.50
All children	0.487	0.485	0.486

per respiratory infections in preschool-age children than in the older-age group. Table III shows that the number of upper respiratory infections decreased similarly in the gamma globulin and control groups with the increasing age of the children.

There is also no significant difference in the frequency of upper respiratory infections in the 46 single children as compared with the 97 sibling children of our series. In both the gamma globulin and the saline group the participants with siblings were not significantly different from single children (Table IV).

The possibility that gamma globulin might be more effective in the asthmatic child than in the nonasthmatic patient was also investigated. In both groups there were 16 children who had had at least one asthmatic attack, of whom only 2 were severely asthmatic (one in each group). None of these children had received gamma globulin prior to this investigation and were not included in our previous report.[2]

The response of all children on gamma globulin or placebo was the same (0.487 vs. 0.485). However, asthmatic children responded quite differently from nonasthmatic children, and this difference was also true between asthmatic children on gamma globulin or on placebo. Table V indicates that asthmatic patients on gamma globulin had about one-half as many upper respiratory infections as asthmatic patients on placebo. The response of all nonasthmatic children was alike, whether on gamma globulin or on placebo. In addition, for all those on placebo, asthmatic patients did more poorly than did nonasthmatic children.

When one considers the asthmatic children only, the results are similar. Table VI compares those asthmatic patients who had asthma attacks with those not having such attacks. Here, whether the patient with asthma on gamma globulin had asthma attacks or not, he had about half as many upper respiratory infections as the asthmatic patient on placebo. Also the asthmatic child on gamma globulin with attacks had fewer upper respiratory infections than those without attacks and on gamma globulin.

Table VII is based on numbers too small for significance. But indications here accord with previous data. Fewer of the asthmatic patients on gamma globulin had asthma attacks than did those on placebo and also had fewer such attacks and upper respiratory infections.

One of the interesting features of any double-blind study is the comparison of the objective with the subjective evaluations of the agent and the placebo. Accordingly, the parents of the participants of this study were polled to see whether or not they thought the injections had improved the health of their child during this winter as compared with previous winters.

The questionnaire was answered by the parents of 106 out of the 143 participants. Two thirds of the parents, irrespective of the agent given, thought the children had improved (Table VIII).

Infectious childhood diseases

As expected, no members of the gamma globulin group had measles. Chickenpox

TABLE V. Average number of upper respiratory infections per child per month by type of agent and asthmatic status*

Status	Number of Children	Gamma Globulin	Number of Children	Saline	Total
Asthmatic	7	0.32	9	0.65	0.50
Nonasthmatic	65	0.51	62	0.46	0.48
All children	72	0.487	71	0.485	0.486

Chi-square less than 0.05.
* Asthmatic child, one with history of asthma.

TABLE VI. Average number of upper respiratory infections per child per month by type of agent and attack status,* asthmatic only†

Status	Gamma Globulin	Saline	Total
Attacked	0.22	0.62	0.50
Not attacked	0.36	0.69	0.50
All asthmatic children	0.32	0.65	0.50

Chi-square less than 0.05.

* Attacked = asthmatic child having one or more asthma attack. Asthma attack also counted as upper respiratory infection.

† Asthmatic child, one with history of asthma.

and mumps occurred in both groups. Three patients in the gamma globulin group had chickenpox during the fourth week after their last injection. Mumps also occurred in 1 of 3 intimately exposed children in spite of gamma globulin. In the saline group there was 1 instance of measles, 3 of chickenpox, and 2 of mumps, while 1 child with known exposure within his family escaped mumps.

Comment

Jackson, Dowling, and Anderson[3] observed that pooled gamma globulin neutralized certain viruses in vitro, causing a reduction of upper respiratory infections. This double-blind study showed no evidence that gamma globulin given intramuscularly reduced the number of upper respiratory infections in children. Even in large doses there appears to be no valid rationale for the use of gamma globulin as a prophylactic for frequent upper respiratory infections in a nonasthmatic child.

Two thirds of the parents of the participants in our study felt that their children had improved, even on monthly saline injections. The "improvement" during this winter as compared with the previous winter may be due to the psychologic value of periodic visits to the pediatrician or to treatment with injections. Another factor is the expected reduction in the rate of upper respiratory infection with the progressing age of the patient.

TABLE VII. Number and per cent of asthma attacks by type of agent, asthmatic only

Number of Asthma Attacks Per Child	Gamma Globulin	Saline	Total
0	5	4	9
1	2	3	5
2	...	1	1
3	...	...	...
4	...	1	1
All asthmatic children	7	9	16
Per cent had attack	28.6	55.6	43.8
Number of attacks, total	2	9	11
Average number attacks per child	0.29	1	0.69
Total months observed	31	37	68
Average number attacks per child per month	0.06	0.24	0.16

TABLE VIII. Evaluation by 106 parents of children's responses to agents

Evaluation	Gamma Globulin (49) (Per Cent)	Saline (57) (Per Cent)	Total (106) (Per Cent)
Excellent	24.5	28.1	26.4
Improved	42.9	36.8	39.6
No help	32.6	35.1	34.0

However, the prophylactic use of gamma globulin in the allergic child seems to be of value. In our present series only the few participants with histories of asthma seemed to benefit from gamma globulin. Although 16 children constitute a very small series, the results confirm our previous experience. In a recent report by Gordon and Spencer,[4] 15 out of 17 patients with borderline or moderate hypogammaglobulinemia had a personal or family history of severe allergy and showed dramatic reduction in the rate and severity of upper respiratory infections after monthly injections of even small doses of gamma globulin. In our previous investigation of asthmatic children[2] there were no cases of hypogammaglobulinemia, and yet gamma globulin was effective clinically. Gordon and Spencer suspect that the core of the problem is not so much the quantity as the quality of the gamma globulin given. The ability to produce antibodies is not related to the ability to maintain a normal level of gamma globulin.[5] Barandun, Huser, and Hassig[6] confirmed the fact that patients with normal gamma globulin levels can be deficient in antibody formation. Their patients presented the full clinical picture of the agammaglobulinemia syndrome, failed to produce antibodies after immunization with diphtheria and typhoid, and one of them took a homologous skin graft. These authors also mention the frequency of an allergic "tendency" among their patients.

It is possible that asthmatic or maybe all allergic children have a specific deficiency of their gamma globulin which prevents an adequate antibody formation and causes the allergic response to upper respiratory infections. While we do not advocate the use of gamma globulin routinely for every child and even for a vaguely "allergic" child, we feel it should be given a trial in all children whose asthma is secondary to upper respiratory infections.

Summary

1. One hundred forty-three children from one to nine years of age, with histories of frequent upper respiratory infection, were submitted to a double-blind study to evaluate the prophylactic value of gamma globulin. The gamma globulin levels were not determined.

2. From November, 1959, through late March, 1960, 72 patients received 0.2 cc. of gamma globulin solution per pound body weight (0.075 Gm. per kilogram) at monthly intervals, while 71 alternate patients received equal amounts of saline.

3. At the conclusion of five months the number of upper respiratory infections per month was practically identical in both groups.

4. Sixteen of the 143 patients had a history of asthma. The 7 in the gamma globulin group suffered 0.32 upper respiratory infections per month as compared with 0.487 infections per month of the whole gamma globulin group. There were only 2 attacks of asthma in the 7 patients (2 patients, each suffered one attack). The 9 asthmatic children in the saline group had a total of 0.65 upper respiratory infections per month, as compared with 0.485 per month of the whole saline group. Five of the 9 patients suffered a total of 9 asthma attacks.

5. Two thirds of the parents of the participants in both groups reported improvement in their children as compared with the previous winter, and one-third found the injections ineffective.

6. Gamma globulin was not effective in the prevention of chickenpox and mumps.

7. We do not recommend gamma globulin for the prevention of upper respiratory infections in the average child but only in the child who suffers from asthma secondary to upper respiratory infections.

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Detection of Bladder Distention by Suprapubic Percussion

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Bladder distention may escape detection on physical examination if its telltale signs are not sought by the examiner. These signs are suprapubic distention, dullness, or a mass in the suprapubic region.

Some of the data from a study on the topographic anatomy of the bladder are reported here because we have been unable to find statements in standard textbooks of urology or physical diagnosis relative to the amount of urine which is necessary to distend a bladder enough to cause the presence of suprapubic dullness or a mass.

Whenever practical, indirect methods to discover the presence of residual urine in the bladder are preferable to the direct method of urethral catheterization. This is a basic principle among urologists. The information reported here will be useful in this regard.

Materials and methods

The subjects for this study were adult patients from the urologic, surgical, gynecologic, medical, or rehabilitation-medical services of the Bronx Municipal Hospital Center, who had indwelling catheters. Their bladders were instilled aseptically with measured increments of 50 cc. of sterile saline or of 5 per cent sodium iodide solution to which 0.5 Gm. of neomycin per liter were added. The filling was carried to the point of maximum tolerance only. The lower portion of each patient's abdomen was percussed after each increment of filling, and the findings were noted on a life-size chart in centimeters. Simultaneous cystograms were performed on some of the patients. The entire procedure was repeated as the bladder was emptied of its contents by increments.

Data complete enough for our purpose were gathered from 29 adult patients, 24 males and 5 females. The results are consistent enough to be significant. Data were discarded when the patients were too weak to continue the test; if they voided around the catheter, vitiating the accuracy of our measurements; and from 1 patient whose bladder was surgically suspended against the abdominal wall. The results are summarized in Table I.

Results

The consistency of the results justifies the following generalizations:

1. In only one instance was suprapubic dullness encountered when less than 100 cc. of fluid were present in the bladder.
2. The average filling of the bladder which permitted the detection of an unmistakable 1 cm. or 1 fingerbreadth of dullness above the symphysis was 134 cc., in 29 observations.
3. Deviations from the average could be explained by obesity, gaseous distention, or elevation of the bladder by suspension from a previous suprapubic scar.

These findings are interpreted to mean that when otherwise unexplained suprapubic dullness is found, the bladder probably contains more than 100 cc. of urine. If this is found immediately after the patient voids, it represents pathologically increased residual urine. Since such an amount represents a clinically significant residual urine, the finding of a distended bladder should

TABLE I. Degree of bladder filling at which suprapubic dullness was first detected (dullness 1 cm. above symphysis)

	Number of Patients	Bladder Filling (Cc. to Nearest 12.5 Cc.
	2	200
	3	175
	7	150
	9	125
	7	100
	1	75
TOTAL	29	

TWENTY-NINE ADULT PATIENTS *with indwelling catheters were studied by percussion for bladder distention. In only one instance was suprapubic dullness encountered when less than 100 cc. of fluid were present in the bladder. The average filling of the bladder which permitted the detection of 1 cm. or 1 fingerbreadth of dullness above the symphysis was 134 cc. If the results of abdominal percussion, intravenous urogram, and phenolsulfonphthalein tests are inconclusive, or if the patient's condition demands more immediate action, as in the case of fever and pain, then diagnostic catheterization is indicated.*

direct the management to urologic principles of study and therapy.

Comment

A distinction must be made between catheterization for diagnosis and catheterization for therapy. In patients with urinary retention therapeutic catheterization is indicated without hesitation whatever the diagnosis. The present discussion is confined to the problem of catheterization for diagnosis where there is no such clear-cut therapeutic indication. The decision to catheterize then depends on the possible sequelae of discomfort, infection, slight hematuria, or acute urinary retention, as weighed against the sequelae of undetected and untreated residual urine in the bladder.

Pathologic physiology of residual urine

Briefly, the common consequences of undrained residual urine can be:

1. Calculus formation
2. Acute urinary retention
3. Hydronephrosis, bilateral or unilateral
4. Renal failure and uremia
5. Cystitis
6. Pyelonephritis
7. Septicemia
8. Death.

Most of the foregoing do not develop acutely. Indeed, they may sometimes be clinically silent. Urinary retention need not develop acutely, but may be chronic. Urinary retention must be considered in the differential diagnosis of these conditions when they are present without other explanation.

Causes for residual urine may be:

1. Benign prostatic hypertrophy
2. Vesical neck contracture
3. Urethral stricture
4. Carcinoma of the prostate
5. Bladder calculus
6. Neurogenic bladder
7. Urethral meatal stenosis
8. Urethral tumor or calculus
9. Foreign body
10. Severe phimosis
11. Urethral valve
12. Debility
13. Retention secondary to psychologic causes
14. Retention secondary to drugs, such as Banthīne and morphine
15. Acute postoperative or postanesthetic retention
16. Reflex retention (painful hemorrhoids).

Diagnostic approach to detection of bladder distention

In the diagnostic study to explain bladder distention or residual urine, a search should be made for a history of previous episodes of retention, impairment in the size and force of the urinary stream, frequency, nocturia, a history suggestive of instrumental or gonorrheal stricture of the urethra, or a decrease in urinary output. Following this, the physical examination should seek evidence of a distended bladder, enlarged prostate, or a palpable urethral lesion.

In this context, let us re-examine the use of the urethral catheter in the light of the demonstration that persistent suprapubic dullness or a mass, otherwise unexplained, denotes at least 100 and usually 150 cc. of bladder content.

With the persistence of the suprapubic dullness or mass after voiding, one can separate patients with an obvious residual urine from those who, despite the absence of physical signs, may or may not have a significant bladder residual. Patients in the first group do not need diagnostic catheterization. Confirmation that this dullness or mass indeed represents a distended bladder may be obtained radiographically by intravenous urography with a postvoiding film provided that renal function is adequate.[1]

With the newer agents, excretion is successful even in the presence of mild renal failure, such as when the blood urea nitrogen is 40 mg. per 100 ml.

In the second group, with the occult or absent residual urine, where the patient has no demonstrable bladder dullness or mass, further indirect tests may succeed in ruling out the presence of residual urine. Such tests are the postvoiding film of the intravenous urogram and the various fractional phenolsulfonphthalein tests.[2,3]

If residual urine is present in the absence of physical findings, it probably represents less than 150 cc. or even less than 100 cc. It is just in this range that the postvoiding cystogram is most accurate as a semiquantitative estimate of residual urine.[2] Also, the residual urine can be calculated from a fractional phenolsulfonphthalein test according to the method of Cotran and Kass.[4]

If the residual urine is over 60 cc., and often if it is over 30 cc., the failure of the bladder to empty nevertheless may be implicated as a cause of the urinary infection, renal failure, or other condition being studied. No rules can be established relating the clinical significance of a residual urine to its volume. This is a matter for clinical judgment in each individual case.

Role of catheterization

If the results of abdominal percussion, the intravenous urogram, and the phenolsulfonphthalein tests are inconclusive, or if the patient's condition demands more immediate action, as in the case of fever, pain, and so forth, then catheterization is indicated.

The safe approach to the use of the catheter must be made along classic urologic lines, such as the exclusion of all patients in whom catheterization can be avoided, the knowledge of contraindications and complications, and the use of the proper technic.

Catheterization must be recognized as a minor surgical procedure to be performed by properly trained technicians or professional personnel with proper equipment and preparation. It should not be done without assistance, draping, or sterile technic.[5]

Rigorous precautions can reduce secondary infections after diagnostic catheterization to the vanishing point in the normal bladder. Recent confirmation of this classic urologic observation has come from Braude.[6]

Hesitation or procrastination in performing indicated catheterization will allow progression of the disease, if it is caused by bladder malfunction. Even though uremia may lessen with hydration, or the fever of an infection may subside with antibiotic therapy, the disease process is merely masked and not removed.

The present revulsion against the abuse of the catheter must not be allowed to swing so far that the profession ignores the valid indications for its diagnostic use.

Summary

1. A distended bladder often can be detected on physical examination by percussion, palpation, or inspection, if this possibility is borne in mind by the examiner. The average contents of a bladder first detectable by percussion in 29 adult patients was 134 cc. and in only one instance was it under 100 cc. (1 cm. suprapubic dullness).

2. On the other hand, the inability to percuss or palpate a bladder may not rule out the presence of significant residual urine. By using one of several indirect tests of bladder emptying, patients with

normal excretion of phenolsulfonphthalein or adequate excretion of hypaque may be spared diagnostic catheterization to demonstrate the absence of residual urine.

3. These findings can be helpful in detecting the patient with occult urinary retention and may spare some patients diagnostic catheterization until a more propitious time. They may help other patients by hastening relief from uremia or severe urinary infection by pointing out the need for catheterization.

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Reduction in mortality rate from appendicitis

Marked progress has been made in the control of deaths from appendicitis in the last two decades, according to a Metropolitan Life Insurance Company report.

In 1959 the death rate from appendicitis in the United States was only 1.0 per 100,000 population—a 60 per cent decrease from the rate a decade ago and a 90 per cent drop from 1939.

This improvement extended over all age groups, but it was especially notable in the age range of from one to thirty-four years, where the mortality rate fell 96 per cent in two decades. Currently, the rate does not exceed 0.6 per 100,000 at any age group under forty-five and is only 2.0 per 100,000 at ages fifty-five to sixty four.

A major factor in these gains has been the control of peritonitis and other infections through the use of antibiotics. Diagnostic procedures also have improved, along with advances in surgical technics and preoperative and postoperative treatment of patients.

Despite the remarkable gains achieved, appendicitis continues to be an important medical problem because of its relative frequency. Based on the current National Health Survey, there were about 417,000 persons in this country hospitalized for appendicitis in the year from July, 1957, to June, 1958. Of this number, nearly 90 per cent were treated surgically.

Altogether, appendicitis patients spent a total of 2,709,000 days in short-stay hospitals during that year.

Comparison of Hexylcaine and Tetracaine as Topical Anesthetics in Gastroenterologic Procedures

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THE USE OF hexylcaine hydrochloride (Cyclaine hydrochloride) as a topical anesthetic in 500 gastroenterologic procedures was compared with tetracaine hydrochloride (Pontocaine hydrochloride), used in 100 cases. Tetracaine hydrochloride was administered always with a certain amount of uneasiness because of the possibility of a severe or fatal reaction, as has been reported.[1] Clinical studies and investigations with hexylcaine hydrochloride have shown good results with low toxicity, and there have been no reported fatalities.[2–6] This encouraged me to use hexylcaine hydrochloride routinely and also in procedures in which anesthesia was not used formerly, as in esophageal bougienage and even in intubation for simple gastric analysis.

TABLE I. Type of procedures performed

Procedure	Cases Treated With Hexylcaine Hydrochloride	Cases Treated With Tetracaine Hydrochloride
Gastroscopy	210	67
Gastroscopy with gastric-brush biopsy	35	21
Esophagogastroscopy	50	5
Esophagoscopy	53	5
Esophagoscopy with punch biopsies	34	2
Gastric-brush biopsy alone	18	...
Esophageal dilatation, bougienage, and intubations	100	...
TOTALS	500	100

Method and dosage

Five hundred patients received topical anesthesia with hexylcaine hydrochloride, and 100 patients received topical anesthesia with tetracaine hydrochloride for a variety of gastroenterologic procedures (Table I). Preanesthetic medication was used for major cases, such as gastroscopy, esophagoscopy, pneumatic dilatation of the terminal esophagus in achalasia, and esophageal tamponade. Preanesthetic medication was not used for minor procedures, such as gastric-brush biopsies* without gastroscopy, esophageal bougienage, dilatation with mercury-filled dilators, and intubation for gastric analysis.

The preanesthetic medication was approximately standard for all cases and consisted of 1 to 2 grains of Luminal sodium, 20 to 40 mg. of Benadryl hydrochloride, $^1/_{150}$ to $^1/_{75}$ grains of atropine, and 50 to 75 mg. of Demerol hydrochloride by injection forty-five minutes prior to the procedure. The tetracaine hydrochloride was prepared by diluting 5 cc. of 2 per cent tetracaine hydrochloride with 15 cc. of water, making a total of 20 cc. of $^1/_2$ per cent tetracaine hydrochloride. This solution was divided into three portions of about 7 cc. each for gargling. The patient, in a sitting position, was instructed to take and hold a portion of the solution in his mouth and gargle four times (that is, four prolonged exhalations with the head hyperextended), lowering his head between gargles to breathe. Five and ten minutes later he would repeat the procedure with the second and third 7-cc. portions of the diluted tetracaine hydrochloride.

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* This refers to the use of the rotating brush method, as used in the Papanicolaou cytologic procedure. Two devices were used, namely, the Ayre rotating brush and the Nieburgs' rotating brush. The brush in the Ayre device consists of retractable soft bristles, whereas the Nieburgs' brush device consists of retractable nylon fibers. Otherwise, they are much the same, both permitting extrusion, rotation, and retraction of the brushes.

Hexylcaine hydrochloride was used undiluted as a 5 per cent solution. Five cc. of the solution were given as one gargle to the patient who held it in his mouth and gargled three times with it, as described previously.

On rare occasions a throat spray was used on those patients who were unable to gargle. To avoid accidental swallowing of the anesthetic, each person was instructed carefully, and he had to demonstrate his ability to carry out the gargling procedure first with water without choking, coughing, or swallowing the liquid. Following this, he was given the anesthetic gargle. Hyaluronidase or epinephrine mixed in the solution, the swabbing of the hypopharynx with the anesthetic, and the installation of anesthetic through a hypopharyngeal tube were not used for reasons which are discussed later in this report.

A COMPARISON WAS MADE *between hexylcaine hydrochloride (Cyclaine hydrochloride) used as a topical anesthetic in 500 cases and tetracaine hydrochloride (Pontocaine hydrochloride) in 100 cases. Preanesthetic medication was given only for major procedures. With tetracaine 5 out of 100 patients had unsatisfactory anesthesia, resulting in unsuccessful or incomplete procedures. There were no failures with hexylcaine. The time consumed in administering the anesthetic was from ten to twenty minutes for tetracaine and from two to three minutes for hexylcaine. There were no adverse reactions to either anesthetic. The relative safety of hexylcaine and the simplicity of its administration permit its use in minor procedures as well as in major ones.*

Results

With the use of tetracaine hydrochloride 5 out of 100 patients (5 per cent) had unsatisfactory anesthesia, resulting in unsuccessful or incomplete procedures (Table II). The application of additional anesthetic usually was of no benefit because the patient had become excited or frightened by then, making further instrumentation impossible. With hexylcaine hydrochloride there were no failures.

The time consumed in administering the anesthetic, using as an end point the loss of the pharyngeal gag reflexes, was from ten to twenty minutes for tetracaine hydrochloride and from two to three minutes for hexylcaine hydrochloride. There were no adverse reactions to either of the anesthetics during this study.

Comment

Hexylcaine hydrochloride was found more satisfactory in clinical use than tetracaine hydrochloride. Of striking advantage was

TABLE II. Comparison of hexylcaine hydrochloride and tetracaine hydrochloride

Type of Anesthetic	Number of Cases	Dose	Time Consumed in Anesthesia	Number with Poor Anesthesia	Percentage with Poor Anesthesia	Reactions
Hexylcaine hydrochloride	500	One 5-cc. portion, gargled three times	Three to four minutes	0	0	0
Tetracaine hydrochloride	100	Three 7-cc. portions, each gargled three times*	Ten to twenty minutes	5	5	0

* See "Method and Dosage" section for details of technic.

the brief time consumed in administering the anesthetic which shortened each procedure considerably, curtailing the operating room time, as well as the time spent by the doctors, nurses, and personnel. Immediately after the hexylcaine hydrochloride gargle, the patient was positioned, the instruments were lubricated, and the instrumentation was begun.

The small amount of time necessary to achieve anesthesia with hexylcaine hydrochloride, the simplicity of its administration, and its relative safety permitted its use for minor procedures which had been done previously without anesthesia. The application of hexylcaine hydrochloride in office procedures has been found very practical.

In administering topical anesthesia careful attention must be given to keeping the level of absorbed blood to a minimum. The danger of systemic reaction is in proportion to the concentration reached by the drug in the blood, and the most important protection is to limit each dose given.[7] The absorption from mucous membranes is considerable, and experimentally this absorption gives blood levels comparable to equal doses injected intravenously.[7] The maximal topical dose of hexylcaine hydrochloride is calculated to be about 7 cc.[7] Since excellent results can be achieved with a 5-cc. dose in gastroenterologic procedures, it is risky to use a greater quantity. It also appears unnecessary to have patients gargle more than the three breaths, as described previously. Having patients gargle 10 cc. of the solution for a duration of five minutes, as described in a recent article,[8] seems to be an unnecessarily large dose.

The use of throat sprays leads to overdosage and should be avoided when possible. The injection, through a hypopharyngeal tube, of an extra few cubic centimeters of anesthetic, none of which is recovered, also leads to overdosage; besides, it causes coughing and gagging and converts a relaxed, cooperative patient into an anxious and difficult one. The use of 5 per cent hexylcaine hydrochloride jelly on the endoscopic instrument should also be avoided, since once enough anesthesia is obtained for introduction of the instrument, there is no need for more. The anesthesia lasts at least twice as long as it takes to do an endoscopic procedure, obviating the need for a prolongation of the anesthesia by the use of jellies. Training the patient, by having him gargle first with water, has been found very valuable in preventing aspiration (with rapid absorption of the drug) and accidental swallowing. About 1 out of 30 patient swallowed the entire mouthful of water at the first trial. If the patient swallows the anesthetic gargle by error, it is not felt that another dose should be given. A case has been reported of a severe, but not fatal, reaction which occurred when a second 10 cc. of hexylcaine hydrochloride were given after the first 10 cc. were accidently swallowed.[8] Epinephrine is not used with the hexylcaine hydrochloride because it does not retard the absorption of the topically applied anesthetic, as it does when used by infiltration.[7]

Premedication is of considerable importance. The barbiturate and the antihistamine, besides sedating the patient, serve to prevent reactions. Besides decreasing the amount of interfering secretions, atropine retards absorption.[7] Premedication was not used in the minor cases because in these cases the patient was given only one gargle of about ten seconds duration. This has been found to be sufficient for these purposes.

Summary

1. The results of the use of hexylcaine hydrochloride (Cyclaine hydrochloride) as a topical anesthetic in 500 gastroenterologic procedures were compared with those of tetracaine hydrochloride (Pontocaine hydrochloride), used in 100 cases.

2. Hexylcaine hydrochloride was found to give superior results in the dosages used, and a striking advantage was found in the rapidity of its action and in the brief time consumed in inducing topical anesthesia.

3. It is felt that the relative safety of hexylcaine hydrochloride and the simplicity of its administration permits its use in minor procedures such as gastric analysis, as well as in major ones.

4. The technic of obtaining topical anesthesia has been described, and the factors promoting safety from systemic reactions have been discussed.

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Sedentary habits cause backache

Exercise is the answer to backache caused by sedentary habits, according to an article by Hans Kraus, M.D., and Sonya Weber, D.Sc., in the April, 1962, issue of *Archives of Environmental Health.* Their conclusion was based on a study of 52 psychoanalysts, a highly sedentary group, and on earlier research by Dr. Kraus.

Each analyst was tested to determine his muscle deficiencies, and exercises were specifically prescribed to overcome these weaknesses. The exercises started with gentle movements and were increased gradually as strength and flexibility improved. After the exercises were learned, the analysts were told to perform them at home at least once a day for from five to twenty minutes.

The researchers were able to follow the progress of 26 of the 52 analysts for from two to ten years. Of the 26, who originally complained of low back pain along with pain in the upper back, neck, shoulder area, and legs, 8 had no pain at all, and 18 had definite relief from pain at their final examination. All showed considerable improvement in muscle strength and flexibility. In some cases pain recurred when exercises were suspended.

Lack of exercise may operate in different ways to produce painful muscular conditions. "It may cause weakness and stiffness in muscles, since—as is generally known—a muscle only maintains the efficiency at which it is ordinarily used. On the other hand, inability to respond to stimuli and the need to assume identical posture for long periods of time may store tension in certain muscle groups and manifest itself in considerable pain. This category is usually referred to as 'tension syndrome' and includes many cases of stiff neck, painful shoulder, painful upper and lower back, and painful leg and arm muscles."

To gain an impression of the magnitude of complaints among analysts possibly due to underexercise and unreleased tension, the researchers also sent a questionnaire to the 750 members of the American Psychoanalytical Association. A total of 489 questionnaires were returned. Of these, 144 analysts exercised and had no pain; 107 did not exercise at all and had pain; 47 had pain which was relieved by exercise; 52 had pain despite physical activity; 29 did not exercise at all and had no pain; 44 reported an organic disease involving the lower back; and the remaining 66 could not be evaluated.

If the unevaluated group and those with organic disease are disregarded, it can be inferred that the remaining 379 analysts would not have had pain if they had performed sufficient and appropriate exercises.

The chances of preventing back pain in persons in such a sedentary occupation as that of a psychoanalyst can be improved by such simple measures as changing chairs frequently when working; taking five-minute breaks for mild exercise such as walking up and down; incorporating ten to thirty minutes of exercises into the daily routine; developing walking habits, including stairs, and engaging in some such activity as walking, swimming, tennis, or gardening on weekends and on one weekday.

Congenital Dysplasia of the Hip

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HASS[1] ADOPTS THE VIEW, in a recent publication, that every newborn infant should have a roentgenologic examination of the hips as part of a routine check-up. He feels that congenital dysplasia of the hips can be identified radiologically in the first months of life, long before physical signs of dysplasia become evident. An acetabular angle of 30 degrees or more denotes the presence of a predislocation of the hip. Treatment during this period offers effective prophylaxis.

Caffey and his coworkers,[2] however, reporting on 627 newborn infants, found no support for a congenital dysplasia-predislocation hypothesis of congenital dislocation of the hip. They seriously doubted that predislocation of the hip in early infancy actually existed as a recognizable entity. Asymmetry of skin folds, extra skin folds, and limitation of abduction of the flexed thigh were present in more than one half of the infants who were later shown to be normal by repeated radiologic and clinical examination. Their work indicated further that an acetabular angle of 30 degrees did not separate normal from abnormal angles. These observers found that the incidence of angles larger than 29 degrees in white female infants was 44 per cent in the right hip and 54 per cent in the left hip. If 30 degrees had been adopted as a criterion for the diagnosis of dysplasia of the hip, one-half the newborn white females would have been subjected to prophylactic treatment. In regard to acetabular angles, Coleman[3] felt that the position of the beak of the femoral neck in relation to Perkins' line reflected more accurately the basic defect in congenital dysplasia of the hip. This is a line dropped perpendicularly from the most lateral point of ossification of the acetabular roof. The point corresponds to the anterior-inferior iliac spine. He found that in 25 of 43 hips, the beak of the femoral neck was unequivocally lateral to this line.

The purpose of this paper is to explore the usefulness of present-day clinical and radiologic signs of congenital dysplasia of the hip.

Patient material and observations

The 386 newborn infants included in this study were examined twice in the first week of life for clinical signs of dysplasia of the hip. The group consisted of 199 boys and 187 girls. The physical signs sought were limitation of abduction of the flexed thigh, Ortolani's jerk of entry and exit, and a jerk of exit. In the presence of these findings a roentgenogram of the hips was taken. In the first week of life this occurred in only Case 1 (Fig. 1). In this patient, both Ortolani's jerk of entry and exit and a limitation of abduction of the flexed thigh were elicited.

As the 366 normal infants in this study were followed through their first year of life, it became readily apparent that asymmetry of skin folds, extra skin folds, partially concealed labium majus on one side, and differences in the length of the extremities were not indicative of underlying dysplasia of the hip. Skin folds were asymmetric in 27.5 per cent, extra skin folds were present in 9.1 per cent, one leg appeared to be shorter in 0.4 per cent, and the labium majus was partially concealed on one side in 4 per cent. Roughly 2 out of 5 patients showed at least one of these signs at one month of age. However, it should be noted that practically all infants with congenital dysplasia of the hip had one or more of these frequently meaningless signs (Table I). These signs should alert one to the possibility of dysplasia of the hip. Tests for abduction at one month of age showed bilateral 80- to 90-degree abduction in 87 per cent, 70- to 79-degree bilateral abduction in 12 per cent, and 60- to 69-degree bilateral ab-

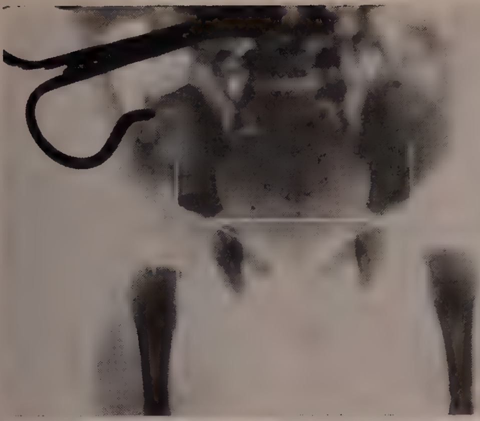

FIGURE 1. Roentgenogram of Case 1 with jerk of entry and exit of left hip on physical examination. Acetabular indexes below average. Lateral disposition of left femoral neck apparent.

IN 386 NEWBORN INFANTS *examined twice in the first week of life, 20 cases of dysplasia of the hip were found, an incidence of 5.1 per cent. Of the 366 normal infants, followed through their first years of life, asymmetry of skin folds, extra skin folds, partially concealed labium majus on one side, and differences in the length of the extremities were misleading and not indicative of underlying dysplasia of the hip. The following clinical and roentgenologic data are indicative of congenital dysplasia of the hip: limitation of abduction of the flexed thigh, jerk of entry and exit, and jerk of exit. Roentgenograms which are taken of infants who are suspected of having a dysplastic hip will support the diagnosis in 50 per cent of cases. No warning clinical signs of congenital dysplasia of the hip were found at birth in 19 infants who were later shown to have abnormal hips.*

duction in 0.9 per cent. Abduction was unequal on the two sides in 3.7 per cent. After the second month abduction is in the range of 70 to 80 degrees. Abduction limited to 60 degrees or less should warrant roentgenographic examination.

On examination of the hips, if an infant had a jerk of entry and exit or a jerk of exit he was considered to have congenital dysplasia. These important clinical signs were demonstrated in 5 infants. An x-ray examination of infants with these findings was corroborative except in one instance (Tables I and II). Unilateral limitation of abduction of the flexed thigh was found in 31 cases. In 14 of these, the roentgenograms also suggested dysplasia of the hip (Tables I and II). Bilateral limitation of abduction was found in 3 infants. In 1 of these, the roentgenogram supported a diagnosis of dysplastic hip disease. In the 19 infants with normal findings on x-ray films, the limitation of abduction failed to persist for more than two months.

Comment

The 20 infants shown in Table I represent the number of congenital dysplasias of the hip found in a group of 386. These infants have been examined at regular intervals to the present date. The incidence of dysplasia in this small series is high, 5.1 per cent. Coleman[3] reported an incidence of 1 in every 110. Harris'[4] incidence was 0.10 per cent at birth. These figures lead one to believe that congenital dysplasia of the hip in the United States is not as uncommon as is generally believed.

Since some continue to use the measure of the acetabular angle as a basis for or against the diagnosis of congenital dysplasia of the hip, an understanding of just what it represents would seem important. It is an indication of the state of ossification of the caudal edge of the ossification center of the ilium. The tilt of this ilial ossification center may not correspond with the tilt of the real, invisible cartilaginous roof. A recognition of the limited value of the acetabular angle as a diagnostic criterion for dysplasia of the hip is obvious. Harris[5] suggests that acetabular measurements in the later months of infancy be used in the same way as height-weight tables are used. Thus, an acetabular angle of 31 degrees in an infant of four months or older would fall beyond two standard deviations. This finding in conjunction with clinical observations could substantiate a diagnosis of dysplasia of the hip. Since a difference of 5 degrees between the two acetabular angles falls beyond two standard deviations, this measurement would also be of value in diagnosing unilateral dysplasia of the hip.[5]

TABLE I. Summary of findings in individual cases

Case Sex Delivery	Congenital Dysplasia Diagnosis Age	Clinical Signs	Roentgenologic Findings	Treatment Duration	Results
1 M Breech	Left hip with subluxation 1 day	Jerk of entry and exit; limitation of abduction of left hip; asymmetric folds	RAA* 28 LAA †30 Lateral disposition of beak of left femoral neck in relation to Perkins' line	Plaster cast and FPS** 6 months	$3\frac{1}{2}$-year follow-up Normal hips
2 F Cephalic (Fig. 2)	Bilateral of hips with subluxation 1 month	Jerk of entry and exit, right hip; limitation of abduction, left hip; asymmetrical folds; shortening of left labium majus	RAA 42 LAA 52 Bilateral lateral disposition of femoral neck in relation to Perkins' line	Plaster cast and FPS 6 months	$2\frac{1}{2}$-year follow-up Normal hips
3 F Cesarean section in breech position	Left hip with subluxation 2 months	Jerk of entry and exit, left hip; limitation of abduction, left hip; asymmetric folds; shortening of left labium majus	RAA 31 LAA 48 Lateral disposition of beak of left femoral neck in relation to Perkins' line	Plaster cast and FPS 8 months	$2\frac{1}{2}$-year follow-up Normal hips
4 F Cephalic	Left hip with subluxation 5 weeks	Jerk of entry and exit; limitation of abduction, left hip; shortening of left labium majus	RAA 25 LAA 45 Lateral disposition of beak of left femoral neck in relation to Perkins' line	Plaster cast and FPS 8 months	$2\frac{1}{2}$-year follow-up Normal hips
5 F Cephalic	Left hip with subluxation 1 month	Limitation of abduction, left hip; extra fold on right thigh; shortening of left labium majus	RAA 28 LAA 33 Lateral disposition of beak of left femoral neck in relation to Perkins' line	Lost to follow-up	
6 F Cephalic	Right hip with subluxation 4 months	Limitation of abduction of right hip; asymmetric folds	RAA 39 LAA 30 Lateral disposition of beak of right femoral neck in relation to Perkins' line	Plaster cast	Under treatment
7 F Cephalic	Left hip with subluxation $2\frac{1}{2}$ months	Limitation of abduction, left hip; asymmetric folds	RAA 27 LAA 32 Left femur displaced cephalad and laterad	FPS 4 months	16-month follow-up Normal hips
8 F Cephalic	Left hip with subluxation 3 months	Limitation of abduction, left hip; asymmetric folds	RAA 29 LAA 37 Left femur displaced laterad	FPS 5 months	1-year follow-up Normal hips
9 M Cephalic	Left hip with subluxation 3 months	Limitation of abduction, left hip; asymmetric folds	RAA 30 LAA 39 Left femur displaced laterad	FPS 4 months	2-year follow-up Normal hips
10 F Breech	Bilateral with subluxation of left hip 3 months	Bilateral limitation of abduction of hips	RAA 35 LAA 35 Left femur displaced laterad	FPS 5 months	$1\frac{1}{2}$-year follow-up Normal hips
11 F Cephalic	Left hip 4 months	Limitation of abduction, left hip; asymmetric folds; shortening of left labium majus	RAA 22 LAA 29 Shallow left acetabular fossa	FPS 4 months	$3\frac{1}{2}$-year follow-up Normal hips
12 F Cephalic	Left hip 4 months	Limitation of abduction, left hip; asymmetric folds	RAA 24 LAA 32 Shallow left acetabular fossa	FPS 7 months	$1\frac{1}{2}$-year follow-up Normal hips
13 F Cephalic	Left hip 2 months	Limitation of abduction, left hip; asymmetric fold; shortening of left labium majus	RAA 29 LAA 35 Shallow left acetabular fossa	FPS 4 months	2-year follow-up Normal hips
14 F Cephalic	Left hip 4 months	Limitation of abduction, left hip; asymmetric folds; shortening of left labium majus	RAA 25 LAA 32 Shallow left acetabular fossa	FPS 4 months	$2\frac{1}{2}$-year follow-up Normal hips
15 F Breech	Left hip 2 months	Limitation of abduction, left hip; asymmetric folds; shortening of left labium majus	RAA 29 LAA 35 Shallow left acetabular fossa	FPS 5 months	$1\frac{1}{2}$-year follow-up Normal hips
16 F Cephalic	Left hip 2 months	Limitation of abduction, left hip; jerk of exit; asymmetric folds	RAA 27 LAA 31 Shallow left acetabular fossa	FPS 4 months	$1\frac{1}{2}$-year follow-up Normal hips
17 M Cephalic	Left hip 7 months	Limitation of abduction, left hip; asymmetric folds	RAA 24 LAA 29 Poorly developed left femoral capital epiphysis	FPS 4 months	14-month follow-up Normal hips

Table I (continued)

Case Sex Delivery	Congenital Dysplasia Diagnosis Age	Clinical Signs	Roentgenologic Findings	Treatment Duration	Results
18 F Cephalic	Left hip $4\frac{1}{2}$ months	Limitation of abduction, left hip; asymmetric folds	RAA 25 LAA 30 Shallow left acetabular fossa	FPS 4 months	1-year follow-up Normal hips
19 F Cephalic	Left hip 3 months	Limitation of abduction, left hip; asymmetric folds	RAA 22 LAA 27 Poorly developed left femoral capital epiphysis	FPS 5 months	11-month follow-up Normal hips
20 F Cephalic	Left hip 4 months	Limitation of abduction, left hip; asymmetric folds	RAA 28 LAA 32 Shallow left acetabular fossa; asymmetry in Shenton's line	FPS 3 months	8-month follow-up Normal hips

* RAA = right acetabular angle.
† LAA = left acetabular angle.
** FPS = Freijka pillow splint.

Coleman[3] feels that more attention should be paid to the position of the beak of the femoral neck in relation to Perkins' line. He reported the position of the beak to be lateral to the line in 58.1 per cent of abnormal hips. In this study, in 7 of 22 abnormal hips, the beak of the femoral neck fell lateral to Perkins' line.

According to our observations, a limitation of abduction of the flexed thigh, a jerk of entry and exit, and a jerk of exit are the only reliable clinical signs of hip dysplasia. Infants with a jerk of entry and exit had x-ray films of the hip which supported a diagnosis of dysplasia in every instance. A jerk of exit was demonstrated in 1 infant. The x-ray appearance of this infant's pelvis was equivocal. However, it was felt that clinical displaceability of the femoral head established a diagnosis of dysplasia despite the roentgenographic findings.[3] A palpable jerk of entry is elicited by abducting the flexed thigh and levering the femoral head into the acetabulum. Following this maneuver, if the thigh is adducted, the head will slip over the posterior acetabular rim, producing the jerk of exit. A palpable jerk of exit may be elicited by flexing and slightly abducting the hips. While the pelvis is fixed on one side by vertical pressure on the thigh, an attempt is made to displace the opposite hip laterally or posteriorly. Infants with unilateral limitation of abduction of the flexed thigh had x-ray films which supported the diagnosis of dysplasia in 45 per cent of cases.

Conclusion

It is clear that criteria for the diagnosis of congenital dysplasia of the hip is in a state of flux. What is dysplasia to some may not be according to others. The possibility, therefore, that some of these abnormalities may pass undiagnosed in the early months is a real one. It seems reasonable that the diagnosis and treatment of congenital dysplasia of the

TABLE II. Correlation of x-ray findings with clinical signs

Clinical Signs of Congenital Dysplasia of Hip	Number of Cases X-Rayed	X-Ray Findings			Diagnosis	
		Abnormal	Equivocal	Normal	Simple Dysplasia	Subluxation
Unilateral limitation of abduction	31	14	0	17	9	5
Bilateral limitation of abduction	3	1	0	2	0	1
Jerk of entry and exit	4	4	0	0	0	4
Jerk of exit	1	0	1	0	1	0
TOTALS	39	19	1	19	10	10

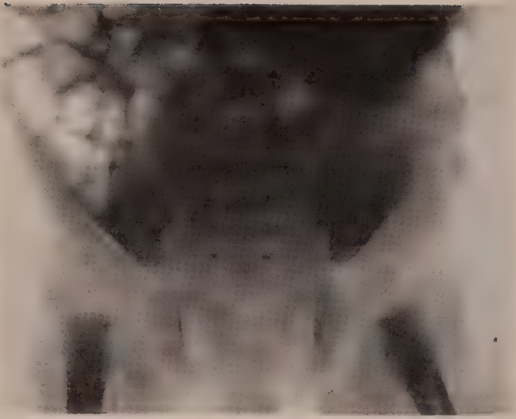

FIGURE 2. Roentgenogram of Case 2 with jerk of entry and exit of right hip and normal left hip on physical examination. Acetabular indexes above average. Bilateral lateral disposition of femoral neck in relation to Perkins' line apparent.

hip can be based on the following clinical and roentgenologic criteria: (1) displaceability of the femoral neck or jerk of exit; (2) a jerk of entry and exit; and (3) unequivocal limitation of abduction of the flexed thigh combined with (*a*) an acetabular angle of 40 degrees or more in the first three months of life and 31 degrees afterwards (two standard deviations from the mean), (*b*) lateral disposition of the beak of the femoral neck in relation to Perkins' line, or (*c*) a difference of 5 degrees in the acetabular angle of the sides (two standard deviations from the mean).[5]

Summary

From a group of 386 infants, 20 with congenital dysplasia of the hip are presented. This is a surprisingly high incidence, yet no new or unknown criteria were utilized. Repeated careful evaluation of the hips in each infant should result in a clinical diagnosis in the first four months of life. Roentgenograms that are taken of infants who are suspected of having a dysplastic hip will support the diagnosis in 50 per cent of cases.

No warning clinical signs of congenital dysplasia of the hip were found at birth in 19 infants who were later shown to have abnormal hips. This supports the view of Caffey *et al.*[2] that predislocation of the hip does not exist as a recognizable clinical entity in the newborn infant.

Since routine x-ray films of the pelvis were not done at birth, we cannot comment from facts on the usefulness of such a procedure. However, interpretation of roentgenograms of the hip in the newborn period is extremely difficult. We urge, therefore, that x-ray films be done in this period only if a jerk of entry and exit is obtained or if clinical displaceability of the hip is present. Infants with limitation of abduction of the flexed thigh may be followed to at least four months of age. Roentgenograms obtained at this time will permit a more accurate evaluation.

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Control of Swelling in Sports Injuries

A Key to Prompt and Complete Recovery

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A STUDY WAS UNDERTAKEN *to determine adequate treatment of post-traumatic swelling in sports injuries. A preliminary series of 40 professional boxers who had absorbed varying degrees of facial damage were examined periodically after their bouts; none received antiswelling treatment. The examination two to three hours after the bout provided a more accurate estimate of damage than the immediate examination. Another series of 163 professional boxers were treated with buccal amylase (Buclamase). The observable damage was the same at the immediate and two- to three-hour examination. The rates of recovery were markedly superior to the preliminary series. In the buccal amylase series the results were excellent or good in 88 per cent of the cases, while only 25 per cent of the results in the preliminary series were excellent or good. Buccal amylase was most effective when started immediately after injury.*

SPORTS INJURIES run the gamut from simple contusions and strains to dislocations, multiple fractures, and ruptures; but a complication common to almost all these injuries is post-traumatic swelling. To a generally significant degree, the manner in which the initial swelling is controlled will influence the rate and quality of healing. All physicians, and trainers and coaches too, are presumed to be familiar with this maxim. Yet our experience in the examination and treatment of thousands of athletes, mostly professional boxers, has revealed that much post-traumatic swelling either goes untreated or is treated inadequately, to the detriment of the boy's sports career. The scar tissue on the boxer's face as a result of poor healing is a target for reinjury in subsequent bouts. The excessive fibrosis from a muscle contusion ("charleyhorse") or ligament tear when edema or hematoma slows healing may produce a handicapped, injury-prone athlete. These residual effects of injury can be minimized by adequate control of the swelling, and the athlete can be returned to full activity at an earlier date as well.

As a part of its medical program for the protection of professional boxers, the State of New York Division of State Athletic Commission has studied the problem of post-traumatic swelling and has sought practical means to improve the boxer's recovery from the contusions and lacerations which are an inevitable part of his trade. Two major considerations influenced our approach to this subject: first, the observation that the standard antiswelling procedures were often inadequate or impractical, and second, the suspicion that many cases which could have been aided materially by antiswelling measures went untreated because the symptoms were not evident at the time of the first examination.

It has long been standard practice to apply ice packs immediately after bouts to facial injuries of professional boxers. The benefits of ice are fully appreciated by

TABLE I. Facial damage, untreated, in 40 boxers

Classification of Damage	Number of Cases	Progress of Repair: Excellent	Good	Fair	Poor
Immediate					
Minor	14	2	3	9	. .
Moderate	21	2	3	10	6
Severe	5	. .	. .	3	2
After two hours					
Minor	6	2	3	1	. .
Moderate	26	2	3	18	3
Severe	8	. .	. .	3	5

trainers and boxers, who in fact employ it between the rounds of a bout. Therefore, if the boxer returns to the dressing room with obvious swelling over the cheekbones or brows, it is almost certain that ice packs will be applied for twenty or thirty minutes. There is no doubt that initial swelling is reduced by the vasconstrictor action of ice packs when they are thus applied promptly after trauma, and yet this is only a temporary measure which may be followed by a reactionary vasodilation as the body attempts to counteract the reduced skin temperature. Repeated applications of ice at intervals over the next day or two are necessary since the inflammatory reaction to trauma continues for up to forty-eight hours. Compliance with this regimen is difficult to obtain, and at best the results are not ideal.

Perhaps a more serious deficiency in the usual handling of swelling from sports injuries results from a failure to recognize that reactionary edema may follow several hours after trauma. Hemorrhaging from damaged blood vessels produces rapid early swelling, but reactionary edema may take several hours to develop. Frequently a boxer will receive numerous heavy blows about the head and show no marked signs of damage. He is unconcerned about what he cannot see or feel, and he is anxious to get in the shower and relax, so that he does not welcome treatment. The examining physician may anticipate later inflammation and swelling, but it is unlikely that he will have either the conviction or the authority to enforce inconvenient treatment in a situation which seems equivocal and of minor significance. Treatment may be sought later when severe swelling is present, but the eradication of established swelling is a far more difficult proposition than controlling it before it gets started.

Methods and materials

With these considerations in mind, clinical studies were initiated in the fall of 1959. The subjects were professional boxers who appeared in bouts in New York City during the 1959 to 1960 boxing season and part of the 1960 to 1961 season. Initially, a series of 40 boxers who had absorbed varying degrees of facial damage in bouts was studied to determine the relationship of immediate swelling and swelling which developed several hours later to the subsequent repair of contusions and lacerations. None of these 40 boxers received antiswelling treatment after their bouts or during the course of subsequent observation. Panel physicians of the Commission examined the boxers immediately after their bouts and recorded their estimate of the degree of damage sustained by each boxer as minor, moderate, or severe. This estimate did not relate to the amount of punishment the boxer had absorbed in his bout but rather to the physical signs of damage observable. The same physician re-examined the boxer two to three hours after the bout and again recorded his estimate of damage. Examinations on subsequent days provided data for an evaluation of the rate of recovery in terms of excellent, good, fair, or poor.

Table I summarizes the findings of this preliminary study. The significant point apparent from these statistics is that the immediate examination is not a reliable indicator of the extent of inflammation and swelling which ultimately may develop as a result of trauma. It will be noted that there was a marked shift in the estimates of damage toward the severe category at the later examinations. And the pattern for the rate of recovery coincided much more closely with the damage estimated at the two- to three-hour examination than with the immediate estimates. From these findings we conclude that the physician who examines an athlete soon after injury should assume that consequential swelling may develop, even though it is not then apparent, and should take

TABLE II. Facial damage, treated by buccal amylase, in 163 boxers

Classification	Damage		Progress of Repair			
	Immediate	After Two Hours	Excellent	Good	Fair	Poor
Minor	57	52	28	26	3	. .
Moderate	90	95	33	47	8	2
Severe	16	16	2	7	4	3

immediate steps to control it. The advantages of starting antiswelling treatment early are considerable, so it is unwise and impractical to withhold treatment until it is established that inflammation is consequential.

The second and major objective of our program was to find an improved method of controlling post-traumatic swelling, one which would provide practical as well as effective therapy. It was logical to consider the use of an anti-inflammatory drug, and the preparation which we selected for trial was buccal amylase.* This product came to our attention as a result of its successful use in a large series of orthopedic cases by Thompson, Glick, and Silverstein.[1] It suited our needs better than other enzyme preparations in several ways. First, it is reported to be completely free of local irritating effects or other side-effects. The mode of action of this drug, to the extent that it is known, is also intriguing. Animal tests indicate that buccal amylase inhibits the abnormal capillary permeability which follows trauma or irritation. Thus, the effect should be somewhat analogous to that of ice packs in that the initial effusion of fluids into the damaged tissues would be inhibited, that is, swelling could be checked before it became established. However, since this is not a vasoconstrictor action, as in the case of cold therapy, the "rebound" or vasodilating reaction would be avoided, and the continued administration of buccal amylase might be expected to control the swelling until the inflammatory process had subsided. The buccal form of this enzyme was considered advantageous, as opposed to an enteric-coated oral form, since the rapidity of action was important for our purposes.

A series of 163 well-documented cases in which judgments as to the results of anti-inflammatory therapy were justified were eventually accumulated. Medication was provided to many other boxers who could not be included in the statistics because of their failure to appear for later examinations, usually because they were out-of-town boxers who returned home. The examination procedure was the same as in the preliminary series of untreated boxers. Panel physicians examined each injured boxer immediately after his bout and estimated the extent of observable damage. The same physician examined the boxer two to three hours later and again recorded his estimate of damage apparent at that time. The examinations on subsequent days were, in the case of all 163 boxers in the series, made by one member of the panel (Dr. Campbell). Buccal amylase was administered at the time of the first examination after the bout, 2 tablets placed between the upper lip and gum and allowed to dissolve slowly. Subsequent dosage was 2 tablets four times a day for four days, or until all signs of inflammation disappeared.

Results

The results of the buccal amylase series are summarized in Table II. They reveal two striking differences from the experience with the untreated boxers recorded in Table I. The estimates of observable damage at the two- to three-hour examination coincided closely with those recorded immediately after the bout; that is, there was virtually no increase in the swelling during this interval, whereas in the untreated boxers increased swelling was noted in a high percentage of cases. Additionally, the rates of recovery were markedly superior to the preliminary series. In the buccal amylase series, the healing results were classified as excellent or good in 88 per cent of the cases, while of the results in the untreated series only 25 per cent were classified as excellent or good. There was no evidence of deleterious effects from the early anti-inflammatory therapy in any case in this series.

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* The alpha amylase used in this study was supplied as Buclamase tablets by Rystan Company, Mount Vernon, New York.

Another noteworthy point became clear in the course of this series: the importance of starting buccal amylase therapy soon after injury. There were a number of boxers who initially declined to use the buccal amylase tablets, primarily because they felt their injuries were not sufficiently severe to require any treatment. Some of these men returned later for treatment when inflammation had developed, and they were given supplies of the enzyme tablets. Case records were incomplete in most of these cases, but in those which could be followed up it appeared that the treatment was definitely helpful. Yet there was a strong impression among the examining physicians that the results were not comparable with those obtained when treatment was started soon after injury. This observation coincides with the report of Thompson, Glick, and Silverstein[1] who noted a difference between the "dramatic" results obtained when ankle sprains were treated early and the somewhat slower recovery when treatment with buccal amylase was delayed. It is also pertinent that particularly outstanding results were reported by Monica[2] in a dental trial on post-extraction cases where the clinician was able to initiate buccal amylase treatment immediately after the extractions.

Comment

We conclude from the data developed in these trials that anti-inflammatory therapy should be initiated routinely immediately following bouts for boxers who have sustained any degree of facial damage. It is apparent that the absence of marked swelling at this time is no justification for omitting such treatment. Such an omission may result in the later development of an inflammation which goes untreated; and even when a subsequent examination results in the initiation of treatment at that time, the effectiveness of anti-inflammatory therapy will be diminished by the delay.

The buccal amylase preparation used in these trials proved to be highly effective and practical for our purposes. We cannot say whether this is the best available modality for an inflammation following trauma, for the trials compared its use with untreated cases and not with other forms of anti-inflammatory therapy. Yet it is clear that buccal amylase provides a means of controlling swelling that is uniquely suited to the treatment of sports injuries such as the facial contusions and lacerations which were the subject of these clinical trials. Its action is rapid, it appears to be without side-effects, and the dosage form is convenient. These attributes make buccal amylase a desirable vehicle for implementing the routine, early anti-inflammatory therapy which we recommend.

While these trials were concerned with injuries peculiar to boxing, the findings are pertinent to other sports injuries. The poor healing of a facial contusion, where organization of the underlying tissues produces scar tissue highly susceptible to reinjury, is comparable to the ankle or knee injury in which slow repair results in inflexible tissues and restricted motion. The control of swelling is by no means the only type of prompt treatment that is essential for sports injuries, but it is one requirement in almost any such injury if optimal healing is to be obtained. Facilities for initiating effective antiswelling treatment immediately after injury would seem to be as important in football, basketball, skiing, and other injury-producing sports as in boxing.

Summary

It is generally recognized that the degree to which swelling is controlled in sports injuries influences significantly the rate and quality of healing. Yet much post-traumatic swelling goes untreated or is treated inadequately. Clinical studies were conducted by the New York State Athletic Commission to develop a consistent, effective policy for postbout treatment of professional boxers.

A series of 40 untreated boxers with varying degrees of facial damage were studied to determine the relationship of immediate

swelling, and swelling which developed later, to the rate of recovery. There was a marked increase in the extent of swelling noted in examinations two to three hours after bouts in comparison with examinations immediately after bouts. A definite correlation was revealed between the rate of recovery and the extent of swelling at the two- to three-hour examinations in these untreated cases. On the other hand, the extent of swelling noted immediately after bouts did not prove to be a reliable indicator of how much swelling would develop later or of the relative rate of recovery that might be expected.

A second series of 163 boxers in which buccal amylase was employed as an anti-inflammatory agent was studied. Treatment was initiated immediately after bouts and continued for four days, or as needed. Among these treated boxers there was virtually no increase in swelling during the interval between the immediate examination and the two- to three-hour examination. In 88 per cent of the cases the rates of recovery were classified as excellent or good as opposed to 25 per cent similarly classified in the series of untreated boxers. In an additional group of boxers where buccal amylase therapy was started later when severe swelling was established, the results were considered good but inferior to those obtained with immediate treatment.

Routine anti-inflammatory therapy for boxers, even when tissue damage appears minor, seems justified, and treatment should be initiated as early as possible. Buccal amylase provides an effective and practical vehicle for implementing this recommended policy.

The pertinence of these findings to other types of sports injuries is discussed.

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Hydroxyzine in treatment of rheumatic chorea in children

A comparative study of the effects of hydroxyzine (Atarax) and phenobarbitone in 22 children with rheumatic (Sydenham's) chorea, reported by A. El-Ghomi, M.D., and Y. W. Aboul-Dahab, M.R.C.P., in the December, 1961, issue of *Archives of Pediatrics*, indicates that hydroxyzine is the superior tranquilizer for this purpose and perhaps the most effective drug available for the treatment of the condition. In 3 of the 12 patients who were given the hydroxyzine a trial of reserpine followed. Hydroxyzine proved better than phenobarbitone in controlling the abnormal movements and in the immediate cure of the disease. All the 12 treated cases benefited from hydroxyzine, with definite improvement evident in 7 of them after a week or less and after two weeks in 11. Of 9 cases treated with hydroxyzine alone for at least three weeks, 6 recovered completely or almost so within three weeks. Among the controls (the 10 patients on phenobarbitone) no patient definitely improved within one week, and only a single case did so within two weeks. Of 9 cases followed up, there were no recoveries in less than three weeks, and 2 cases suffered side-effects consisting of drowsiness and ataxy. In 1 of them the dosage had to be decreased. One of the patients on hydroxyzine experienced mild drowsiness which disappeared without reducing the dose. There were no changes in pulse, blood pressure, or blood picture.

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Hazards of Abdominal Paracentesis in the Cirrhotic Patient

Part I

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IT IS GENERALLY appreciated that patients with parenchymal disease of the liver tolerate stress poorly. Varix hemorrhage, surgical operation, varied infections, and paracentesis are not infrequently responsible for initiating hepatic failure and coma. Abdominal paracentesis, although a comparatively minor procedure, may be followed by disturbances in electrolyte and water balance, metabolic changes, hemodynamic derangements, peritonitis, traumatic hemorrhage, and other complications. Such clinical sequelae can be very puzzling and deceptive. Their full appreciation and careful interpretation are indispensable for prophylactic purposes and also for judicious corrective treatment. This paper documents these varied complications encountered in the course of a study of a large series of patients with cirrhosis of the liver on the wards of Bellevue Hospital and may be classified as follows:

1. Precipitation of varix rupture
2. Suppuration: abdominal wall abscess, peritonitis
3. Hemorrhage within abdominal wall, peritoneal cavity
4. Low-salt syndrome
5. Liver failure
6. Kidney failure
7. Ammonia encephalopathy
8. Hypokalemia
9. Hemodynamic alterations
10. Protein depletion
11. Colon bacillus bacteremia
12. Perforation peptic ulcer.

Precipitation of varix rupture

The rupture of an esophageal varicosity precipitated by paracentesis was observed in 6 cirrhotic patients. A hemorrhage transpired within nine hours after the tap in 4 patients, after twenty-four hours in 1, and three days thereafter in another. Three patients died, and in these perforated varicose veins were verified at autopsy.

This sequence of events is explicable by an analysis of the alterations in respiratory dynamics before and after paracentesis. The passage of blood from the abdomen to the chest is achieved by the force of the heart beat transmitted to the veins through the capillaries and facilitated by movements of the thoracic cage, a downward thrust of the diaphragm, and variations in intra-abdominal pressure. The distention of the abdomen by massive ascites results in ventilatory insufficiency characterized by a reduction in the total lung capacity and its subdivisions and a decrease in maximum breathing capacity and breathing reserve.[1] Moreover, ascites is accompanied by the elevation and immobilization of the diaphragm and stiffening of the abdominal wall, which produce platelike atelectases in the basal lung fields, promote a shallow type of respiration, and render the thoracic cage-abdominal wall breathing unit comparatively rigid.

Pulmonary ventilation in its various phases improves when the ascitic fluid is drained: the respiratory excursions increase in amplitude and breathing becomes deeper. However, maximum improvement may be delayed for several days after paracentesis as the painful puncture wound heals, the abdominal wall regains its tone, and the patient regains his strength.

The consequent greater and improved respiratory excursions enhance the venous return heartward. In addition, a large volume of blood, which has been sequestered in the splanchnic area because of a slow circulatory velocity on the basis of portal bed block, is suddenly mobilized and circulated through the esophagogastric pathways, jeopardizing the integrity of the varicosities.[2] Evidence has been documented that a precipitous upheaval in circulatory dynamics within the splanchnic and portal venous systems appears to be a necessary prerequisite for initiating varix rupture and for the profuse bleeding that usually characterizes this pathologic entity.[3] As indicated, over-all pulmonary ventilation may not improve maximally until several days after the abdominal puncture and thus may explain the time lag between the drainage procedure and the onset of vein rupture. Furthermore, voluntary coughing to rid the bronchial tree of accumulated secretions can accentuate the altered dynamics brought about by the elimination of the peritoneal fluid and thus enhance the possibility of varix rupture.[2] There is a suggestive parallelism between the altered pressure gradients within the intestinal lumen and the vascular dynamics that follow paracentesis, which respectively are etiologic in the perforation of a peptic ulcer, as will be seen, or in the rupture of an esophageal varix. Rupture from a mesenteric and a retroperitoneal varix, both with fatal hemoperitoneum following paracentesis, has been recorded.[4,5] Other instances of varix rupture which are precipitated by trocar drainage of ascitic fluid are cited in the literature.[2,6]

Abdominal wall and peritoneal suppuration

This complication occurred in 7 patients.

CASE REPORTS. *Case 1.* Four paracenteses were performed over a period of seven weeks in this seventy-year-old male cirrhotic patient. All the paracenteses yielded clear, yellow fluid. Ten days after the last tap the patient complained of griping abdominal pain, nausea, and distention. The temperature rose to 102 F. and the white blood cell count to 21,750. A diagnostic abdominal puncture recovered turbid peritoneal fluid that was loaded with segmental polymorphonuclear leukocytes and grew out pneumococcus type 6 in pure culture. Antibiotics were administered, but unfortunately the clinical course was complicated by fatal bleeding from esophageal varices that was precipitated by an indwelling Miller-Abbott tube, utilized to control intestinal ileus. A necropsy disclosed the presence of an acute fibrinopurulent peritonitis in addition to portal cirrhosis, splenomegaly, and ruptured esophageal varicosities.

Case 2. This patient's ascitic abdomen was tapped three times over a span of two and one-half months, finally yielding a turbid yellow fluid containing 22,000 leukocytes per cubic millimeter that lay in a fine fibrin mesh. Transitory neuropsychiatric signs and symptoms developed. Ascites soon reaccumulated and was associated with marked edema of the abdominal wall. The clinical course deteriorated gradually with the development of jaundice, stupor, and finally a deep coma.

A necropsy showed that several old paracentetic scars were present in the right lower quadrant of the abdomen. The right rectus muscle was necrotic and fragmented by a dissecting abscess that extended through the rectus sheath posteriorly around to the lumbodorsal fascia on the right side and also into the space of Retzius. Small pockets of pus also were present around the prostate gland and the rectum. About 2 L. of turbid yellow ascitic fluid were present. Figure 1 illustrates the abscess in the anterior abdominal wall. Additional and very interesting findings included syphilitic hepar lobatum of the liver with gumma formation, thrombosis of the portal vein, and esophageal varices.

Case 3. This seventy-three-year-old cirrhotic patient was subjected to eight intercurrent paracenteses because of refractory ascites over a period of two and one-half years. A fever up to 101 F. not infrequently followed the tap which on some occasions leaked peritoneal fluid for from one to several days. The seventh and eighth drainage procedures took place three weeks apart. Within twenty-four hours after the eighth drainage, which evacuated 6,700 cc. of turbid brownish fluid, the patient lapsed into a stupor and soon thereafter expired in a deep coma.

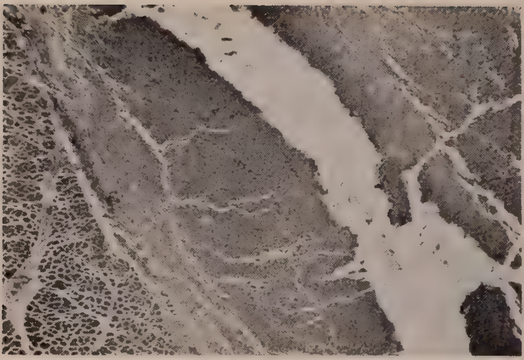

FIGURE 1. Case 2. Postparacentetic abscess in anterior abdominal wall. Purulent exudate fills the rectus sheath and transversalis fascia. The inflammatory process also extended through the fascia to peritoneum that was covered by fibrinous exudate (hematoxylin and eosin stain).

The necropsy findings showed numerous abscesses deep in the abdominal wall, directly adjacent to the abdominal paracentetic scars. Some were filled with brownish, others with green-yellow pus. Figure 2 represents a microscopic section of the involved abdominal wall. About 3,000 cc. of turbid, dark-brown fluid filled the peritoneal cavity that showed signs of an acute generalized peritonitis. Besides an advanced cirrhosis, esophageal varices and a portal vein thrombosis also were present.

Case 4. This fifty-four-year-old female with a long-standing history of alcoholism had experienced one episode of hematemesis but was subject to intractable ascites. A splenorenal shunt was performed in June, 1950. The ascites subsided for a period of one year but again recurred. She had continued to drink heavily. Repeated paracenteses again were undertaken, the final one on March 3, 1953. When the bandage dressing and sutures were removed from the most recent puncture wound, the latter appeared to be infected. Simultaneously, the patient complained of diffuse abdominal pain and tenderness. She deteriorated clinically, neuropsychiatric signs and symptoms supervened, and she expired on March 31, 1953.

At necropsy the left rectus muscle was necrotic and was the seat of an abscess. Overlying the abscess were four healed paracentetic scars. The abscess extended widely through the abdominal tunics from the midline to the left lower ribs above and the left anterior superior iliac spine below. The peritoneal surfaces and abdominal viscera were covered with a thick fibrinopurulent exudate. A postmortem culture of the ascitic fluid, abdominal wall abscess, and peritoneal pus isolated Bacillus coli, clostridia, and enterococci.

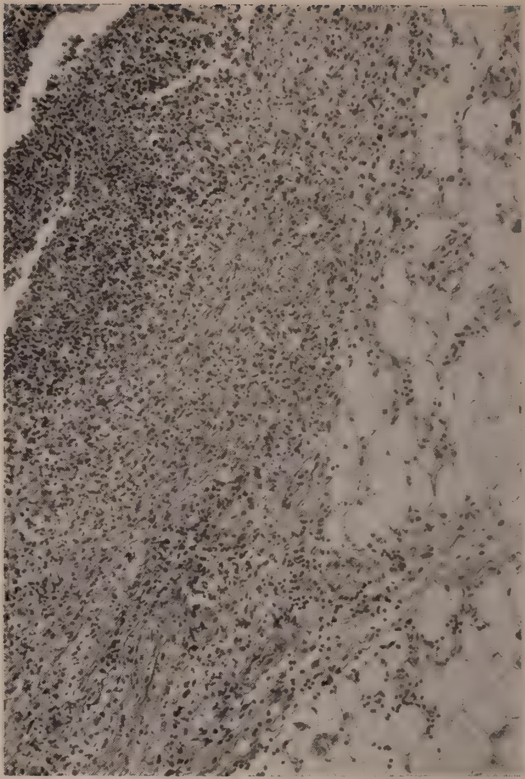

FIGURE 2. Case 3. Acute inflammatory reaction with abscess formation in subcutaneous tissues postparacentesis (hematoxylin and eosin stain).

Case 5. Five paracenteses were performed in this forty-nine-year-old cirrhotic patient over a period of one month. A fever ranging up to 103 F. was noted after the second and the last drainage procedures. Following the last procedure the patient complained of vague, diffuse, abdominal pain. Apathy, stupor, jaundice, and finally a deep coma supervened from which the patient expired.

At autopsy two black, necrotic-edged puncture wounds of the skin were noted below the umbilicus, each measuring 1 cm. in diameter. The margins of one were still approximated by suture material. Dissection revealed that these wounds extended through the abdominal walls and peritoneum. Signs of a widespread peritonitis were apparent in addition to portal cirrhosis, congestive splenomegaly, and esophageal varicosities. Hemolytic streptococci were cultured from the peritoneal exudate.

Case 6. Hepatic decompensation, manifested principally by jaundice and ascites, characterized the clinical course of this fifty-year-old alcoholic patient. Forty-eight hours after an apparently uneventful paracentesis midway between the umbilicus and the pubis, the patient lapsed into a stupor and finally into a deep coma from which he failed to recover.

A necropsy disclosed a small puncture wound in the peritoneum at the paracentetic site which was only partially healed. The visceral peritoneum was injected along a loop of small bowel. There was no evidence of frank perforation, but a microscopic study revealed the submucosal layers to be edematous and to contain many polymorphonuclear leukocytes, lymphocytes, and precipitated protein. This reaction extended to the subserosal fat.

The pathologic diagnosis was phlegmon of the small intestine.

Case 7. This forty-six-year-old male had "never been sick in his life" until two months prior to his entry into Bellevue Hospital after he developed ascites. Ten abdominal paracenteses had been performed by his private physician, the most recent having taken place the day before his hospital admission. He appeared both acutely and chronically ill. Multiple subumbilical paracentetic scars were evident, and ascitic fluid leaked actively from a fresh drainage wound. Icterus appeared, the temperature and white blood count rose, and he ultimately expired in a coma.

At necropsy the peritoneal cavity contained about 4,000 cc. of cloudy, brown fluid with stringy flakes of puslike exudate. A fibrinous exudate coated the entire peritoneal cavity and also the intestinal serosa. The diagnosis was acute generalized peritonitis, portal cirrhosis, congestive splenomegaly, and cardioesophageal varices.

Thus, among the foregoing 7 cases, there were 3 instances of abdominal wall suppuration additionally associated with peritonitis, 3 cases of solitary peritonitis, and 1 case of phlegmon of the intestine. Certain features bear emphasis. The paracentetic wounds can heal and become well scarred notwithstanding the presence of an underlying or adjacent abdominal wall abscess. Furthermore, there may be no regional subjective symptoms or objective physical changes that would betray the presence of such a localized suppurative process which, however, may be obscured by edema or brawny induration of the abdominal parietes. The abscess may dissect throughout the layers of the abdominal wall and extend widely to the rib margins above, the anterior superior iliac spine below, and even posteriorly to the lumbodorsal area, and of course, it may serve as a nidus of infection of the peritoneal cavity.

Among the factors that predispose toward wound infection and the development of purulent collections in the abdominal wall are: (1) lack of asepsis; (2) unnecessary, long, preliminary skin incisions; (3) unduly patulous paracentetic wounds; (4) persistent and chronic leakage of ascitic fluid that infiltrates the regional tissues, affording a good soil for bacterial contamination; (5) edema of the abdominal wall; and (6) poor healing of tissues in the nutritionally deficient cirrhotic patient whose liver additionally is less proficient in synthesizing or elaborating the protein complexes that are necessary for antibacterial defense mechanisms.

Peritonitis complicating paracentesis is due to bacterial soiling implanted directly by the penetrating trocar or represents the extension of an infection from an incipient abdominal wall abscess. Rarely will the trocar perforate a loop of bowel, which generally slips away from the point of the instrument unless it is adherent to the peritoneum at the puncture site. This accident occurred in 1 patient, since fecal material was noted on the withdrawn trocar, and laparotomy was undertaken promptly with a preoperative diagnosis of a perforated bowel. On exposure, numerous loops of intestine were noted to be attached to the anterior abdominal wall. The ascitic fluid, however, appeared entirely clear and later was shown to be culturally negative. No obvious bowel perforation could be discerned. Apparently, the edges of the perforation were sealed over promptly without peritoneal contamination. Madden,[7] on the other hand, cites a case wherein "transgression of the lumen occurred with a complicating peritonitis which was the immediate cause of death." MacDonald and Mallory[8] document 3 cirrhotic patients with peritonitis that followed repeated paracenteses. It should be emphasized that the peritoneal infection may be low-grade, insidious in onset, and not clinically apparent for several days to two weeks after its inception. It may be entirely unsuspected in the obtunded cirrhotic patient and may be the surreptitious cause for the clinical deterioration of the patient, which is erroneously believed to be due to progressive liver failure rather than an underlying iatrogenic peritonitis.

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Number one hundred twelve in a series of Recent Advances in Medicine and Surgery. Parts II and III will appear in the June 15 and July 1, 1962, issues of the JOURNAL.

Fatigue common symptom of depression

The single most common symptom of depression is fatigue, according to an article by John D. Stoeckle, M.D., and Gerald E. Davidson, M.D., in the April 14, 1962, issue of the *Journal of the American Medical Association.* A large number of persons seek medical aid for bodily complaints, often severe, which may or may not be related to a disease, and many of these persons with so-called functional disease are suffering symptoms of depression.

From patients seen at the Medical Clinic of the Massachusetts General Hospital over a four-year period, this depressive reaction was found to follow a wide variety of events which came as a psychic shock to the patient and produced a feeling of personal loss. The three main types of shock which precipitated the depression among the group observed were bodily injury, loss of a sense of security, and separation from a loved person.

"The single most common symptom of disturbance in bodily feelings was a loss of the feeling of well-being. The patient complained of fatigue, tiredness, or 'heavy' feelings. The fatigue was often overwhelming and made daily activity very difficult. The usual obligations to oneself and to family, friends, or job could not be fulfilled. The spectrum of this depressive fatigue varied from a general feeling of being 'tired all the time' to inability to work or get out of bed in the morning."

Disturbances in sleep patterns and eating habits as well as a feeling of helplessness, hopelessness, irritability, and resentment were other common symptoms. Generally, the patients felt a distressing loss of self-esteem and withdrew their interest in people, objects, and activities.

Such cases can be treated. "In the mourning process, time is needed to allow for the acceptance of the loss and for redirection of goals and object relations." Through the technics of psychotherapy the physician can remove the patient's grieving, helplessness, hopelessness, and sometimes anger, somethings by letting him talk it out, and the patient also can be helped to adapt to his loss.

"It is often difficult to realize that many losses are irrevocable and that illness will continue until the patient is able to accept these facts. The course of depression may be chronic, like that of many other medical diseases and its modification likewise difficult. However, many reactions to acute losses are self-limited and, if not, can often be alleviated."

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Kings County Hospital Medical Center
Brooklyn, New York
April 20, 1961

Conducted by S. M. ARONSON, M.D.

Discussed by HANS OPPENHEIMER, M.D.

Disorientation, Focal Neurologic Signs, and Death in Ten Days

Case history

A forty-year-old Negro male was brought to the emergency room of a neighboring hospital by the police on August 16, 1960, because of disorientation and confused behavior. There was no indication of any recent trauma. Because of his disturbed state the patient was transferred immediately to Kings County Hospital Medical Center. No further history could be obtained at this time.

The initial examination in the psychiatric admitting room of Kings County Hospital noted that the patient was found disoriented and confused. He had a right homonymous hemianopsia and a positive Romberg sign. On this basis the patient was referred to neurosurgery.

A physical examination on his admission to the neurosurgical service showed the patient to be strikingly confused, disoriented, and belligerent. In response to questions regarding his immediate complaint, the patient described occasional difficulties in walking. The patient was well developed and nourished and showed no evidence of recent trauma, despite a careful examination. However, a few old scars on the right side of the forehead were noted. The pupils were equal and reactive to light. The neck was supple. No abnormalities of the chest or abdomen were seen. The extremities exhibited no deformities or impairment of movement, although one observer noted a hypotonia of both legs. Sensation was intact throughout. Some difficulties in the performance of finger-to-nose testing were noted. The patient showed an ataxia in attempting to walk. The reflexes were depressed mildly throughout, but were present generally.

Shortly after his admission the patient exhibited severe restlessness and agitation. He became violent to a degree which required physical restraint. A further examination at this time disclosed no papilledema. The pupils were equal and reactive to light. A mild right facial paresis was seen. No gross deficit of motor function was evident otherwise. His coordination was grossly intact. There was no apparent loss of any of the sensory capacities. In the succeeding two days the state of agitation was unchanged. He used foul language constantly and repeatedly talked of killing himself. No further change in his neurologic status was evident in his first few days of hospitalization. His temperature rose on the third day to 101 F.

The severe agitation persisted despite constant sedation, and psychiatric re-evaluation was requested. On the second hospital day the consultant noted that the patient reacted in a very confused and threatening manner. His speech was rambling, incoherent, and irrelevant. His mood was agitated, disturbed, and threatening. His affect was intensely constricted at times and definitely inappropriate. The patient seemed to be preoccupied with death and stated that he was going to die. He described auditory hallucinations in which he heard God speaking to him. The sensorium was definitely clouded. His memory was impaired. Insight and judgment were completely lacking. Because of the difficulty in managing the patient on an open ward, he was transferred to a closed psychiatric ward on the seventh hospital day.

An examination on the eighth hospital day on the psychiatric service disclosed that the patient complained of generalized pains. The pupils were dilated and reacted sluggishly to light. The neck was supple. Crackling rales were heard over the base of the right lung. The limbs showed a definite but mild flaccid paresis. The patient seemed to be unable to move the right arm. The reflexes were uniformly diminished throughout. The knee jerks were absent. No pathologic reflexes were found. His temperature continued to be elevated, occasionally as high as 102 F. The pulse was 130 per minute, respirations 24 per minute, and blood pressure 90/70 mm. Hg.

Later that same day the patient became lethargic. A repeat examination at this time showed a right hemiparesis. No pathologic reflexes were elicited. The knee jerks were absent bilaterally. No change was noted in the optic fundi. During the evening the patient vomited approximately 300 cc. of coffee-ground material. Because of the apparent progression of the neurologic deficit the patient was re-examined by the neurosurgical service. The consultant confirmed the lethargy and the right hemiparesis. No papilledema was evident. The temperature was 101.4 F. A lumbar puncture was performed, and clear fluid was obtained under normal pressure. A Pandy test was 3 plus. Four white blood cells were seen on microscopic examination. Smears for bacteria, including acid-fast organisms, were reported as negative. Cultures were negative.

The next day the patient was retransferred to neurosurgery. On the cessation of sedation the patient became somewhat more alert and was capable of brief and elementary conversation. Percutaneous carotid arteriography was attempted but was unsuccessful.

The patient's lethargy deepened despite an avoidance of any further sedation. The fever continued without appreciable fluctuation at a level of 101 to 102 F. The hypotensive state of 90/70 mm. Hg also persisted. The patient mumbled incoherently but was not as violent as had been noted previously. The patient was found dead in bed at 1:45 A.M. ten days after his admission.

Further laboratory data included a blood urea nitrogen of 15 mg. per 100 ml., fasting blood sugar of 81 mg. per 100 ml., and chest and skull x-ray films which were reported as showing negative findings. The hemoglobin was 15.5 Gm. per 100 ml., and the white blood cell count was 16,400 cubic millimeters (84 per cent polymorphonuclear neutrophil leukocytes and 16 per cent lymphoctyes). The urinalysis produced no important findings.

Discussion

HANS OPPENHEIMER, M.D.: The cases which the psychiatrist is called on to discuss at clinicopathologic conferences invariably are patients with fatal brain lesions which produce, while the patient is alive, so-called psychiatric signs, in addition to other manifestations. Broadly speaking, the organic psychiatric syndromes, apart from focal pictures, such as frontal or temporal lobe syndromes or certain forms of epilepsy, are either dementias or deliria, the former more chronic and insidious, the latter more acute and dramatic. Each in a way has its own characteristic symptomatology. The present case is no exception. But before going into the clinical discussion of the history and findings I will, with your permission, make some comments on what one may call the meaning or the neurodynamic interpretation of psychiatric organicity. I hope that this theoretic discussion will contribute toward a better understanding of the clinical manifestations in the present case.

About eighty years ago Jackson set forth his ideas about the evolution and dissolution of the nervous system in his classical Croonian Lectures, and in more modern times Goldstein* added his terminology and insight toward a more holistic conception of brain damage. Jackson, like Freud, combined in his work a broad intuitive insight with sober, painstaking, detailed observations of clinical data. Neither alone would do; both together make for genius. As you know, Jackson conceived of the nervous system as an entity functionally consisting of lowest, middle, and highest levels. This stratification, while very broadly anatomic, was in essence physiologically conceived. Both phylogeny and ontogeny reveal this evolution from the lowest to the highest levels. Brain damage reverses this process and direction; the organic or neurologic, and indeed the neuropsychiatric symptom, is an expression of a reversal of the process of evolution, a dissolution. Goldstein uses the term dedifferentiation.

To understand the Jacksonian concept let us first recall his ideas concerning the essential features of the various levels. The lowest levels, for example, the spinal cord reflex, are most organized (fixed), least complex, most automatic, phylogenetically the oldest, and least vulnerable. By contrast the highest levels, for example, the prefrontal association areas, are least organized and therefore capable of choice or alternative function of a more fluent, flexible adaptation and are perhaps still capable of evolution; most complex (of higher functional capability); least automatic, which is another way of saying most voluntary; phylogenetically most recent; and unfortunately, if I may be subjective, most vulnerable to damage. The latter fact, which is known also as Jackson's law, can be demonstrated easily in daily clinical experience. In ordinary hemiplegia for instance, the arm is more paralyzed than the leg, the hand more than the arm, and the fingers more than the hand. In dementia the abstract functions suffer first and the concrete performances either not at all or later. In aphasia propositional speech is lost before either automatic or emotional speech is impaired.

Jackson has further taught us that in case of either general or focal brain lesions or, as he called it, uniform or local dissolution, the resulting symptom does not reflect merely a defect resulting from the dissolution of the highest level, but at the same time activity of the next lower level, the then highest level of evolution remaining. This latter activity is not only present, but, in accordance with Anstie's principle, it is exaggerated. Each symptom thus shows a combination of negative features (dissolution suffered) and positive features (evolution remaining). If dissolution were complete, with no positive symptom remaining, death would ensue. It is easy to illustrate this Jacksonian law with well-known clinical examples, including some of our patient's own symptoms. A patient with beginning dementia is unable to name objects; he cannot apply the noun which categorizes the object. It is a feature of Goldstein's amnestic aphasia. Instead, he usually describes or demonstrates the use of the object. The latter, a concrete way of dealing with an object, is a positive symptom; the inability to name it, an abstract way of dealing with it, is a negative symptom. A patient with verbal paraphasia substitutes a wrong word, which may be in the cluster of associated concepts, thus "doing the best he can," a positive symptom. His failure to use the right word constitutes the negative symptom aspect of verbal paraphasia. With some risk of oversimplification one may call any form of psychologic regression, either perceptual, verbal, or ideational, a positive symptom or an inferior form of adaptation.

I should like to look at two outstanding symptoms that our patient had in the light of some of Jackson's theories. Clinically, the patient's over-all mental state may be called a delirium with focal neurologic signs. There is disorientation, which is a perceptual catastrophe, and excessive agitation over a prolonged period, which is a severe motor dissolution of a uniform type. The disorientation in organicity is characterized by the patient believing himself to be in familiar surroundings, animate, inanimate, temporal, and situational. Semantically, "dysorientation" would be more accurate. The patients have an orientation but not the right one. The former is the positive, the latter the negative aspect of the symptom of disorientation. The mistaking of the unfamiliar for the familiar indicates the relative stability of lower levels of orientation which by habit, frequent experience, and (in Goldstein's terms) concreteness due to familiarity are more fixed or organized and less vulnerable to the process of dissolution.

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* Goldstein, K.: Frontal lobotomy and impairment of abstract attitude, J. Nerv. & Ment. Dis. 110: 93 (1949).

I shall now review the clinical aspects of the case as presented in the abstract. A forty-year-old man was brought to the hospital in a state of disorientation and confusion. There was no further history as to trauma, intoxication, duration, or development of the presenting symptomatology. It was noted that he had a right homonymous hemianopsia. With due respect to the examiner I would, in view of the mental state of the patient, not base a definite localization of a lesion on this finding. A positive Romberg sign also was described. Later, on the neurosurgical service, he was found to have ataxia and some difficulty performing the finger-to-nose test. There was some history of difficulty in walking. Neither cerebellar disease nor tabes would produce the mental picture of severe dementia, but ataxia may accompany frontal lobe lesions, and we will keep this in mind. Soon after his admission to the neurosurgical service to which he was transferred because of a suggestion of a focal brain lesion accompanying the dementia, he became belligerent and severely agitated and remained so for most of the ten days of his remaining life. I consider the agitation an indication of a profound, uniform dissolution. Neither during this examination nor at any subsequent examination was there any evidence of increased intracranial pressure. It is most unusual, to say the least, to have a space-occupying intracranial lesion big enough to cause a delirium-like clinical picture without a substantial increase in intracranial pressure. Furthermore, lethargy, not agitation, is a feature of intracranial hypertension.

We notice that the pupils were equal and reacted to light; this is surely of no help in making a diagnosis. I now invite your attention to the development of a progressive right hemiparesis, first in the form of a right central facial paralysis. One may well ask whether or not we are not dealing after all with a unilateral lesion. The use of foul language, while possibly indicative of emotional incontinence of the organic variety, is of no help toward a diagnosis in a disoriented and agitated patient. Auditory hallucinations are rather uncommon in organicity; visual hallucinations are the rule. Our patient heard the voice of God talking to him. Since there is no doubt about organicity in this case, we must recall that a small percentage of patients with organic cerebral disease, for example, 5 per cent of paretic patients, may present schizophreniform pictures. Toward the end the patient became lethargic, and the pupils were dilated and reacted sluggishly to light. The spinal fluid examination showed a 3 plus Pandy reaction and 4 cells. No serologic findings were available.

We have here a clinical picture which, despite some confusing elements and the absence of an adequate history, permits us to draw conclusions as to the most likely diagnosis. The patient had a severe dementia with almost delirium-like agitation and severe impairment of consciousness without signs of increased intracranial pressure. Therefore, the mental picture cannot be due to a space-occupying lesion, despite the presence of progressive neurologic signs. Subdural hematoma in its early stages need not be accompanied by intracranial hypertension, but if it is fatal, it is so because of intolerable brain pressure. It is mainly on this basis that I would rule out this lesion.

The x-ray films of the skull and the chest, as demonstrated by William Gannon, M.D., show normal findings.

Therefore, I visualize a rapidly progressive cortical destruction with both uniform (delirium) and local (hemiparesis) dissolution. The choice lies between degenerative and inflammatory lesions.

Alzheimer's disease is not as rapidly fatal and invariably is accompanied by asymbolia, which our patient did not have; nor is there an increase in the protein content of the spinal fluid in presenile dementia. As to a diffuse inflammatory condition, we can rule out meningitis because of the spinal fluid findings and tuberculous meningitis because of the absence of basal signs (cranial nerve palsies). Considering the mental picture, the rapidly progressive paralysis, the spinal fluid protein, the age of the patient, the severe agitation, and perhaps even the described ataxia and ultimate pupillary paralysis, I would consider it most likely that the patient died of a fulminating, so-called galloping type of general paresis.

Clinical diagnoses

1. *Acute psychosis*
2. *? Schizophrenia*
3. *? Toxic delirium*

Dr. Oppenheimer's diagnosis

General paresis

Pathologic report

S. M. Aronson, M.D.: A complete autopsy was performed ten hours after death. The body configuration and state of nutrition were normal. No cutaneous abnormalities were recorded. The heart weighed 290 Gm. and displayed a minimal left ventricular preponderance. Some pulmonic edema and terminal aspiration of gastric contents also were demonstrated. Otherwise, the thoracic and abdominal viscera were unremarkable.

The brain weighed 1,280 Gm. The intracranial dura and associated venous sinuses were normal on gross examination. The cerebral hemispheres were approximately symmetric and of normal external shape. No areas of malacia, exudate, or hemorrhage were seen externally. No ventral herniations were apparent. The arteries at the base of the brain were distributed normally, were of average caliber, and showed no mural abnormalities. The brain stem and cerebellum were normal externally.

Cross sections of the cerebral hemispheres disclosed no gross changes of the cortex, subjacent white matter, or basal ganglia. The ventricular system was of a normal cross-sectional area. No neoplasms, areas of necrosis, malacia, or other gross changes were seen. Similarly, the brain stem, cerebellum, and spinal cord showed grossly unremarkable findings.

Histologic preparations, however, showed extensive neurocellular and reactive alterations, particularly in sections of the frontal, parietal, and temporal lobes. The cellularity of the leptomeninges, supratentorially, was increased mildly. The cellular infiltrate of the subarachnoid space was pleomorphic with modest numbers of plasma cells, lymphocytes, and mononuclear cells. Within the underlying cortex there was a total disruption of the normal, orderly, cortical architecture. Neurons were destroyed haphazardly in association with an irregularly severe, spongy, rarefaction of the tissues. A diffuse glial response also was evident. An extensive protoplasmic astrocytosis was noted throughout, more marked in the middle cortical lamina. Many of the nerve cells which managed to survive showed varying stages of distortion, basophilia, and sclerosis. An abortive microgliosis, fairly characteristic for this disease, was seen readily in the areas of cortical involvement. The reacting microglial cells were increased appreciably in number but did not venture beyond an intermediate stage of responsiveness, rarely achieving the phagocytic form. Instead, they appeared as mildly hypertrophic, elongated cells with but a modicum of visible cytoplasm. These are, of course, the classical rod cells (Fig. 1).

Many of the perivascular spaces surrounding the draining veins within the cortex were filled with collections of lymphocytes, macrophages, and plasma cells (perivascular cuffing). With appropriate staining reactions, namely, Prussian blue procedure, iron granules could be demonstrated in the perivascular phagocytes. The subcortical white matter showed a minimal loss of myelin and a mild reactive gliosis. Attempts were made to demonstrate histologically the existence of bacterial or spirochetal organisms in the parenchyma. These attempts were uniformly unsuccessful.

The qualitative changes described were noted in all supratentorial cortical areas, although they were more severe in the frontal and parietal lobes. The basal ganglia and hypothalamic nuclei demonstrated comparable changes but of far less magnitude. Within the midbrain, pons, medulla, cerebellum, and spinal cord, occasional blood vessels were surrounded by increased numbers of lymphocytes, but no parenchymatous neuronal degeneration or

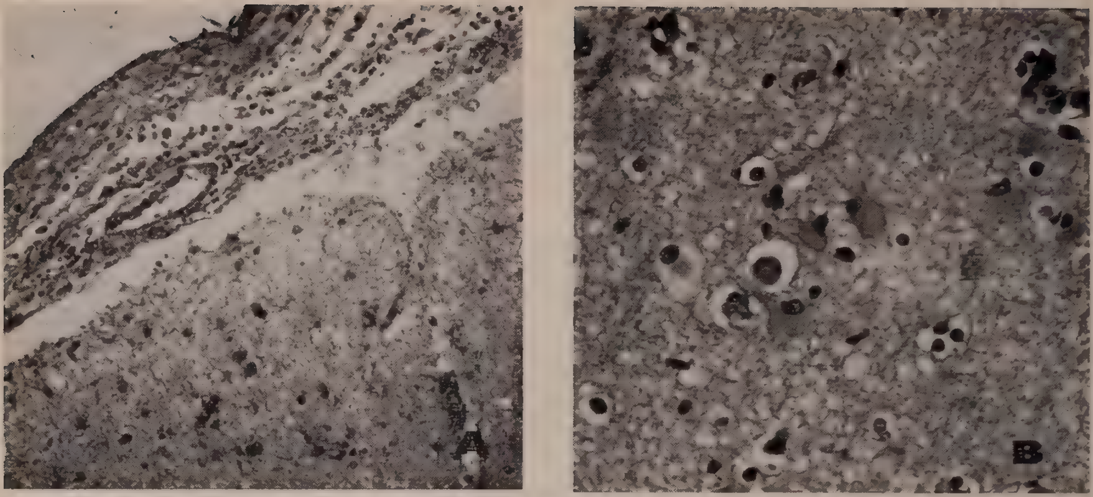

FIGURE 1. (A) Frontal lobe leptomeninges showing mild inflammatory cell infiltration. The superficial cortex is rarefied and gliotic (hematoxylin and eosin stain). (B) Frontal cortex showing loss of neurons, numerous protoplasmic astrocytes, and a few rod cells.

other neuroglial response was evident. The very mild subacute leptomeningitis described previously also was seen in the infratentorial and spinal sections.

The collective pathologic complex, that is, diffuse cerebral cortical involvement to the relative exclusion of the infratentorial gray matter, cortical spongy degeneration, disruption of neurocellular architecture, diffuse astrocytosis, the peculiar form of microgliosis (rod-cell formation), mild interstitial and leptomeningeal inflammation with numerous plasma cells and iron granules in perivascular and subarachnoid phagocytes are consistent with the diagnosis of acute luetic encephalitis (general paresis).

We have one further fragment of laboratory evidence to substantiate this impression. A specimen of cerebrospinal fluid was examined and was found to produce a strongly positive reaction for syphilis (Kolmer test). This information became available only after the patient died. In addition, a diligent search of this patient's previous hospital encounters finally disclosed records indicating a positive serum reaction as well. Neither of these two laboratory observations was included in the clinical protocol made available to Dr. Oppenheimer because it was felt that this information was not available to the members of the clinical services during the patient's last hospitalization.

TABLE I. Incidence of nervous system infection in autopsy population at Institute of Pathology, Kings County Hospital Medical Center, 1954 to 1960

Infection	Number of Cases
Leptomeningitis	
Pneumococcus	41
Meningococcus	16
Hemophilus influenzae	4
Miscellaneous suppurative	53
Tuberculosis	29
Fungus	6
Lues	2
Total	151
Abscess	
Macroscopic, suppurative	22
Microscopic, suppurative, diffuse	40
Tuberculosis	3
Fungus	1
Total	66
Encephalomyelitis	
Poliomyelitis	14
Miscellaneous viral agents	5
Lues (tabes dorsalis)	2
Lues (general paresis)	1
Total	22

A few further observations might be pertinent regarding this case. First, no evidence was found in any of the viscera to suggest the possibility of further luetic involvement. Second, there were no mesencephalic or spinal lesions to indicate the coexistence of any tabetic components. No endarteritis obliterans was observed in the intracranial tissues.

The gross nervous system changes ascribed classically to dementia paralytica were not seen in this case. The diffusely thickened and fibrotic leptomeninges tightly adherent to shrunken and separated cerebral gyri, the narrowed cerebral cortices, the increased consistency of the cortical and subcortical tissues, the secondarily dilated ventricles with a granular ependymitis, and the normal infratentorial tissues are the changes to be seen in an individual who shows tangible clinical evidence of neurosyphilis for a few years. A minority of patients with paresis display an unremitting delirium at the onset of the cerebral phase of syphilis and often die within weeks (galloping neurosyphilis). The case under discussion is in this category.

This is the first case of general paresis coming to autopsy at this hospital in the last decade. The autopsy protocols for the years 1921 and 1922 (Kings County Hospital) were reviewed. Luetic infection, both of the nervous and cardiovascular system, was a relatively common observation.

For comparative purposes a review also was made of autopsy data at Kings County Hospital (1954–1960) concerning nervous system infection encountered at autopsy. It will be noted that the treponema accounts for less than 2 per cent of all such cases in this enlightened age (Table I).

Anatomic diagnosis

Acute luetic meningo-encephalitis.

New non-narcotic antitussive agent

In a series of 49 adult patients suffering from cough associated with respiratory conditions, all but 6 enjoyed good to excellent relief from a new non-narcotic antitussive agent, pipazethate (Theratuss), according to an article by William I. Gefter, M.D., in the September, 1961, issue of the *Pennsylvania Medical Journal*. This agent has emerged from the quest for antitussive agents which would replace the narcotic component in cough mixtures. While opiates, particularly morphine and codeine, are effective, they carry the hazard of habituation. Also, codeine in high dosage tends to dry the mucous membranes and to stimulate the cerebral centers.

Unlike codeine, pipazethate appears to remain effective and usually nontoxic at high dosage levels. Adverse side-effects occurred in 4 cases, but in 1 of these the side-effect (a dry choking sensation in the throat when the tablet was taken) was offset by relief of the cough. The side-effects were sufficiently severe to warrant discontinuance of medication in only 2 patients. One patient who did not respond to other drugs received no benefit from this drug either.

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Current Concepts in Diabetes Mellitus

MAX ELLENBERG, M.D., and HAROLD RIFKIN, M.D., Editors

The Future in the Field of Diabetes

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MANY STUDENTS of diabetes have stressed the fact that our knowledge of this subject is extremely rudimentary. Surveys of the incidence of the disorder have, of course, been made in some parts of the world, but the number is not great and the complete knowledge which we desire is not available in any country. In most countries no studies in this field have been made. I have been in many parts of the world where practically nothing is known about the dietary habits of diabetic individuals, where a study of the inheritance of the disorder has not even been contemplated, and where few, if any, reliable autopsy records have been secured. I wonder which will be the first country to make a comprehensive survey of the incidence of diabetes.

The statisticians would have to tell us what must be done to provide a reasonable idea of the country-wide incidence. Great authorities have exhorted the doctors to examine the urine of more patients, secure the results of analyses of the blood, and to concentrate on the known relatives of diabetic patients and on all individuals who are overweight. Certainly all medical societies and hospitals and all doctors should be urged to continue the work and to provide larger masses of relevant data.

It is difficult to find statements suggesting that the public health service of a country should be stimulated and encouraged to help in making a comprehensive survey of diabetes. We all appreciate that the public health services of many countries including our own have made many outstanding advances which only an organization of this type could contribute. There is surely no insuperable obstacle to a combined effort by the medical profession and the public health service to determine the true incidence of diabetes. There would be many more new cases brought to the attention of the practicing physician, and he would be able to apply modern knowledge to their early treatment. A large number of patients would be greatly benefited. Some day all well-developed countries will know the incidence of diabetes in their populations and will be able to trace readily the hereditary influence. The only acceptable goal is complete knowledge of the situation. Detection drives are very productive and eminently worth while, but a comprehensive survey with provision for following all borderline cases for prolonged periods is needed.

The tests for the detection of diabetes are being further improved, and even more conclusive evidence will be obtained, so that most of the individuals, and only those, who would later develop frank diabetes will be selected. The pioneer scientists who have been responsible for detection of what we call the "prediabetic state" must train their successors, and facilities must be provided so that there is a continuous flow, for the foreseeable future, of this type of information. The findings obviously should be applied on a large scale to the detection of very early diabetes. We must do this when the pilot studies have established the most satisfactory procedures.

Role of genetic lesions

There is more and more evidence that diabetes is hereditary. I have discussed elsewhere[1] a simple classification of the possible genetic lesions which could lead to the diabetic state. These include all the factors which might cause failure in the formation or the liberation of insulin. There might be failure of the supply of the essential building stones, failure in one or more of the enzymes that are responsible for the synthesis of insulin, or failure in the mechanisms which regulate the rate of synthesis and liberation. A genetic lesion might affect any one of the various membranes through which insulin has to pass before reaching the nearest capillary. There might be excessive binding or destruction of insulin or a failure in the mechanism which normally liberates insulin from its bound form. This area of investigation is one of the many active foci in the insulin field, and the rapid advances will certainly make radical changes in our views. The exact nature of the binding of insulin is being attacked vigorously by Antoniades, Renold, Steinke, and their colleagues. Work on insulin degradation, pioneered by Mirsky, is progressing, and Williams and his group and Stetten are investigating another fascinating insulin-inactivating mechanism which the latter termed the "insulin transhydrogenase system."

Role of beta-cell lesions

Many of us have discussed the present information regarding lesions of the beta cells in the diabetic state. Experts can detect histologic lesions in these cells in essentially every case of diabetes, but in approximately half of them the changes are slight. We all know that the lesions in the beta cells are advanced and that the capacity to make insulin is seriously impaired in growth-onset diabetes. Comprehensive studies of electron microscopic changes in the beta cells in diabetic individuals are being made, and a great deal of work in this area is essential.

My colleagues and others have shown that in maturity-onset diabetes some 40 per cent of the normal insulin content remains in the beta cells. We must remember, however, that most of these patients were treated carefully with insulin. How much insulin would these pancreata have contained, or how much would have been present in the blood, if these patients had died without receiving any insulin? What would have been the picture of the beta cells? The pancreatic lesions that we see in spite of insulin treatment are, in more than 90 per cent of instances, the only endocrine abnormality detectable morphologically in all types of human diabetes. Some investigators recently have reported an increased level of insulin-like activity in the blood in untreated juvenile diabetic subjects, and this has been interpreted as evidence for an extrapancreatic lesion. While this interpretation may prove to be correct, it is entirely possible that a primary beta-cell lesion might make these cells abnormally susceptible to normal stimuli and thus be responsible for the raised level of blood insulin.

But we all accept the fact that in many human diabetic patients there are ample stores of insulin in the pancreas, and the insulin-like activity of the blood may be high. As yet we have insufficient data on the effect of a standard dose of dextrose on the level of blood insulin. There have been several reports[2] indicating that response of blood insulin to dextrose is delayed in diabetic individuals who have apparently normal fasting blood levels of insulin. The rate of the disappearance of a test dose of labeled insulin will have to be determined routinely. In the future the response of different tissues will have to be estimated. How does adipose tissue respond? What about muscle? Is the liver reacting normally to a physiologic amount of insulin? When we were ignorant of the true complexity of the situation, diabetes appeared to be a rather simple and straightforward disease!

The average daily dose of insulin for all diabetic individuals is probably about 40 units; only a very small proportion of diabetic patients—less then 1 per cent—are resistant, and in our intensive search for all the possible causes of human diabetes we must not neglect the obvious, that is, that most of the many millions of patients respond well to about the same amount of insulin that is secreted daily by the normal pancreas. This does not mean that the primary seat of the disorder is in the beta cells, but it does mean that these cells are failing to respond to whatever situation exists by providing what, in most cases, appears to be a very moderate amount of additional insulin in a normal physiologic form. There should be emphasis, therefore, on diabetes as a disorder of compensation. We will have to explain the puzzling fact that there is so little evidence of an increased demand for insulin in human or canine spontaneous diabetes. Why do we not see the hyperplasia of beta cells in human diabetes which can be produced under similar conditions in the rat?

Role of the glands

The various steps which I have followed in discussing the beta cells and their secretion, insulin, apply also to the glands that may produce diabetogenic substances. For example, the production of somatotropin might be increased by an abnormally great activity of the acidophilic cells of the anterior pituitary or by an overproduction of the building stones from which the hormone is constructed. It is possible, although I suppose not very likely, that a genetic lesion could result in the excessive activity of some enzyme which plays a part in the production of somatotropin. There might be a failure in a normal mechanism which keeps the rate of formation of somatotropin under homeostatic control. Some of the membranes through which somatotropin has to pass might become, through genetic abnormalities, more permeable than they are under physiologic conditions. Somatotropin may exist in the bound as well as in the free form, and a decreased binding could conceivably cause an excess of activity. There might be a failure in the mechanisms which normally destroy somatotropin. There might be lesions in the tissues on which somatotropin normally acts, and an increased susceptibility to this hormone is a possibility.

My friend and one-time colleague Young[3] has recently reviewed the findings, many of which were obtained in his own laboratory, supporting the view that an abnormally high level of serum-growth hormone may be an important factor in some cases of diabetes. The following points from his paper may be emphasized here: Randle has found that in certain untreated and treated diabetic patients abnormally high levels of serum-growth hormone are observed. The findings in animals suggest that a transient rise in serum-growth hormone, without the production of any signs of acromegaly, might result in permanent pancreatic diabetes in human patients. The persistence of an increased level of anterior pituitary activity manifested by a hypersomatotropinemia may play a role in the production of the complications of diabetes. We know that insulin counteracts many of the pathologic effects of an excess of somatotropin, and I may state my conviction again here that thus far we have not learned how to compensate completely for the loss of the physiologic liberation of insulin by periodic injections of it.

Similar considerations could be applied to the other glands which may produce diabetogenic substances. It is unnecessary to trace these for the thyroid, adrenal cortex, the adrenal medulla, or alpha cells of the pancreas.

Other factors

In the future we will be able to separate and assay accurately all of the factors that interfere with the action of insulin or which produce an excess activity of the diabetogenic factors.

In addition to the great variety of factors which may affect the amount of active insulin or the amount of active somatotropin, which we may use as the prototype of the diabetogenic agents, there is a vast area comprised of the cells and metabolic processes on which these hormones act, where departure from the normal could produce diabetes. There might be one or more abnormalities in the transport system for glucose across the cellular membrane of muscle or adipose tissue. These abnormalities might be in areas on which insulin or somatotropin act or in processes vital to the normal metabolism on which these hormones have no effect. In other words, one or more of the lesions in certain diabetic individuals could conceivably be in a metabolic process which is independent of the endocrine system. There is, as yet, no conclusive evidence that such a diabetes-producing lesion occurs, and an attempt to discuss the possibilities in detail would take me beyond my depth in intermediate metabolism.

When there is a normal amount of any physiologic factor which acts as one of the balancing mechanisms to insulin, that is, to preserve homeostasis, I feel that the best term to describe this substance is "physiologic opponent." Certain factors which may at times be physiologic opponents may on other occasions, and perhaps usually, function synergistically with insulin—for example, somatotropin. An excess of a physiologic opponent may be termed an "antagonist," which is a slightly stronger word in my vocabulary than "opponent." An inhibitor has been defined as a substance which, in the absence of added insulin, decreases the process which insulin accelerates, for example, glucose uptake by skeletal muscle. This is a useful, but rather subtle distinction, since the inhibitor that works in the absence of added insulin may be antagonizing traces of insulin which remain in normal or diabetic tissues.

As you no doubt know, a binding substance may be present as a physiologic entity in pancreas and blood, as the observations of Lindner and of Antoniades, Beigelman, and Renold suggest, or the binding substance might be created by the method of preparation of insulin, or conceivably even produced as a result of some metabolic abnormality.

The results of electrophoretic studies suggest that, in addition to the anti-insulin factors, the chemistry of which is more or less known, that is, the other hormones, at least four types of anti-insulin factors may be recognized, associated with gamma globulins, beta globulins, alpha globulins, or albumen. Some of these may prove to be abnormal products of the endocrine glands. As I have stated previously, antibodies are of great practical importance in the treatment of diabetes and in the assay of insulin in the blood. There is no evidence that they play a role in the etiology of diabetes, that is, a case of diabetes due to an autoimmune reaction has not been established.

Knowledge through study and testing

How can we proceed to determine which of the many genetic abnormalities operate in the production of diabetes? All direct and indirect approaches must be used. The current literature abounds in significant papers on this subject. It is obvious that one particular avenue of approach must be used to the fullest extent that is clinically permissible. This is the comprehensive study of the most sensitive and reliable technics of all the systems I have mentioned in experimental animals and even more extensively in human individuals who are most likely to become diabetic. Where will the first abnormality be detected? Will the site vary from case to case? Will, for example, a detectable decrease in insulin liberation or a measurable increase in some pituitary factor be the first abnormality recognized? Claims for each of these already have been made. Will the fascinating new knowledge of the biochemistry of genetics enable the physicians of tomorrow to neutralize or counteract the effects of the abnormal gene or genes? That would bring us close to our ultimate goal, the prevention of diabetes.

Since I have been thinking about insulin for over forty years, I find it easier to let my imagination run with this hormone rather than with the others which are also significant in relation to diabetes. The fine work of Sanger on the structure of insulin is, of course, a great landmark, but there is still much more to be done before the orientation of all the links in the chain is perfectly understood. I listened recently to a fascinating review by Dr. Barbara Low of the new knowledge gained by x-radiography of crystals of insulin. Further understanding of the chemistry of insulin may help to make available even more satisfactory slow-acting preparations. Eventually insulin will, of course, be made synthetically, but there is apparently a great deal more to be learned before this can be accomplished. Dixon and Wilson, working in the University of Toronto, have separated the two chains of insulin, both of which are inactive, and have been able to reunite them with a recovery of a definite amount, albeit small, of physiologic activity. This is not what we mean when we speak of the synthesis of insulin, but it is a great advance.

I have discussed many times, the possibility that insulin will eventually be given by mouth, and I am still persuaded that this is by no means an impossibility.

We need to know a great deal more about the factors which are responsible for the liberation of insulin, and we must keep in mind the possibility that some physiologic substance or mixture of substances will be found which acts as a much more potent stimulant of insulin liberation than do any of the oral hypoglycemic agents. It will be unfortunate if the physiologic stimulant of insulin liberation turns out to be ineffective when it is administered by mouth!

There has been a wealth of literature on the action of these oral agents and it is now well established that their main action is to liberate insulin. They appear to inhibit the new production of sugar in the liver more than insulin does. In some apparently uncomplicated cases of mild diabetes the response to a test dose of tolbutamide has been found to be subnormal. There are obviously many possibilities which might explain this finding. I will not discuss in detail the most recent knowledge of the actions of the various oral hypoglycemic agents and will refrain even from mentioning those which are not associated with the liberation of the antidiabetic hormone! I do realize, however, that the elucidation of the mechanism of action of these latter substances could make an important contribution to our knowledge of the etiology of diabetes.

Role of testing apparatus

The invention and development of new apparatus—automation if you wish—is affecting all aspects of medical research and treatment. A brief description of the contrast between a laboratory in which I worked in 1921 and one which I am now equipping and in which I would like to work for the next twenty years, might be interesting. The problems of the two periods are rather similar. I wish to follow blood sugars, liver fat, and glycogen, certain aspects of protein metabolism, to analyze expired air, to look at histologic preparations of the islands of Langerhans, to assay the insulin in the pancreas and other tissues—in short to advance knowledge of the physiologic significance of insulin.

In 1921 we had the first model of the Duboscq-Leitz colorimeter. This was our most expensive apparatus, costing approximately $250. The microscope cost $100. The standard glassware and reagents, the metabolism cages, the syringes, sterilizers, and so forth may have pushed the total to nearly $1,000. We had no technical assistance and for the first several months received no stipends. Later we were given $60 a month. This was perfectly normal for the times. The same pattern would have been followed in most other countries. (It was not normal nor did it prove possible to continue these arrangements in the Department of Physiology after we had established the effects of insulin on depancreatized dogs. Banting and I were given appointments in other University departments soon after we presented our first paper on November 14, 1921, but this is another story.)

In 1961, in large part through the generosity of The Wellcome Trust, several new research laboratories have been constructed in The Banting and Best Department of Medical Research. In the one which is for my own use I hope to have available the following standard equipment: an autoanalyzer for the continuous recording of blood sugar ($5,000); an amino acid analyzer ($15,000); gas chromotography apparatus for fatty acids ($4,500); recording apparatus for oxygen and carbon dioxide in expired air ($2,500); automatic scintillation counter ($10,000); a recording spectrophotometer ($10,000); an electron microscope ($36,000); centrifuges for the preparation of cell fractions ($7,500); and standard apparatus for paper chromatography ($1,000). All of these are or will be available but admittedly are not and will not all be concentrated in my personal laboratory, The total cost with the usual accessories will be about $95,000. This is not an extravagant plan. Laboratories devoted to other types of research would require much more expensive apparatus. The contrast with 1921, however, needs no emphasis.

In addition to the equipment listed one will also need a research associate and a part-time secretary. At least three highly skilled technicians will be required. Happily salaries have also increased.

Goals for the future

While savoring the memory of the "good old days" of research in diabetes, I am not reacting against the present situation. I think that it is wonderful and full of immense promise.

We must have a great deal more clerical and mechanical help in scanning, selecting, summarizing, and cataloguing the huge volume of relevant scientific literature which confronts us. We must be able to formulate our problems clearly and to plan the attack on them with first-rate scientific strategy. Then mechanical devices, kept in perfect order, can be the tireless servants of the investigator who must not inundate his mind with more data than it can evaluate and utilize. In the future the mechanical aids to research will be more complicated, more efficient, more expensive, and more productive. It is our duty to attract, select, and train investigators who can use these devices intelligently and to the full and who will always place the real advance of knowledge above a demonstration of the amazing capacity of new apparatus to perform wonders. The advance in knowledge of diabetes must continue to throw a bright light on the whole field of medicine.

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Number thirty-nine and last in a series of articles on Current Concepts in Diabetes Mellitus

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Monobenzone not safe for bleaching skin

Monobenzone, a color-inhibiting chemical compound, cannot be used safely or reliably to bleach extensive skin areas, according to an editorial in the April 28, 1962, issue of the *Journal of the American Medical Association.* There is a high incidence of irritation and allergic reaction encountered with the use of this compound. An even greater problem is the lack of predictability of its effect on skin color. While many persons fail to respond to monobenzone, others develop unsightly and sometimes apparently permanent white spots which may extend beyond the area to which the agent is applied, and in still others increased pigmentation occurs.

Cardiovascular Spotlight

Prepared by the Subcommittee on Heart Disease, Council Committee on Public Health and Education, Medical Society of the State of New York

J. G. FRED HISS, M.D., Editor

Clinical Role of Angiocardiography*

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ANGIOCARDIOGRAPHY TODAY differs from angiocardiography of a decade ago in almost all but the name. Formerly, a rather poorly tolerated contrast fluid was injected by hand through a cannula tied into an arm vein of a patient, and a few x-ray films were exposed in one plane in the hope of getting a picture of diagnostic value. There was considerable discomfort for the patient, and the radiation hazard to the physician or technician was significant. Today's procedure is smoother, safer, and more informative because of several technical developments. This procedure is now usually combined with cardiac catheterization and associated studies of circulatory pressures, flows, dye-dilution curves, and other measurements. The contrast is therefore injected directly into a specific chamber, either by direct puncture or by right or left heart catheterization, using a side-hole catheter to prevent recoil. Other improvements are due to the work of the chemist and engineer. The modern contrast materials are much better tolerated by the patient than previous compounds and can be injected in 100-ml. amounts or more.[1] Automatic syringes for the rapid injection of large amounts of contrast at body temperature are now available. X-ray films can be taken more rapidly and easily, and simultaneous films in two planes are possible at frequencies up to 12 films per second or x-ray movies at 60 frames per second. The image amplifier permits fluoroscopy with much lower roentgen-ray exposure for the patient and the operator.

In this report we will not discuss the technic of making these observations, the precautions to be observed, or the signs of any specific cardiovascular lesions. Rather, we will outline briefly the type of information which contrast radiography of the cardiovascular system can provide and we will suggest some of the conditions in which it is indicated.

Seriogram and cinefluorogram technics

Two technics are currently popular for studying the cardiovascular system radiologically with contrast. One technic involves making a series of roentgen-ray exposures directly on film of various sizes up to 12 by 12 inches or larger. The film, either in rolls or in cut form, is changed rapidly as direct exposures are made, preferably simultaneously in two planes. These seriograms may be taken as rapidly as 12 per second, but each one is viewed separately and compared with earlier and subsequent films. With good apparatus and good

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* Material for this report was taken from work supported by the John A. Hartford Foundation and Dent Family Foundation.

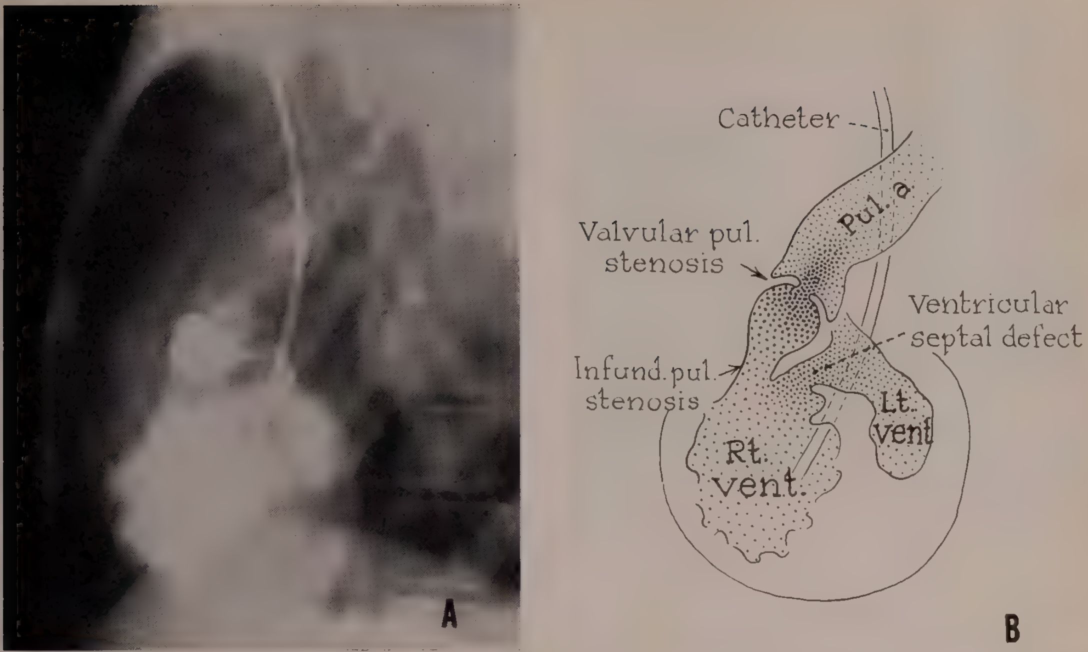

FIGURE 1. (A) Tetralogy of Fallot, lateral projection. Contrast injected into right ventricle demonstrates high ventricular septal defect, infundibular stenosis, and valvular pulmonic stenosis. (B) Diagram clarifying (A).

technic the resolution and detail are as good as standard roentgenography.

The other technic, cinefluorography, consists of photographing the amplified image of a fluoroscopic screen with either a 16- or 35-mm. movie camera, with up to 60 exposures per second. The resultant movie film can be viewed at slower speeds to give a slow-motion effect or frame by frame. The quality of motion given by this technic portrays the action of the heart vividly and makes the time dimension particularly comprehensible. The individual frames generally lack the definition which the larger seriograms provide.

The complementary advantages of the two technics are well illustrated in the study of abnormal shunts in congenital heart disease. Cinefluorography has proved effective in demonstrating either an atrial or ventricular septal defect. Usually, the left anterior oblique projection is used to view the septum on end. If the abnormal shunt is small, the angiogram may catch a mere puff of contrast, visible on cine only by nature of the motion. Seriograms provide a static representation of these events and therefore show a small shunt less well. However, they often give better anatomic detail when they do show a shunt,[2] permitting more accurate estimations of size and location of the abnormal opening with relation to other structures and giving valuable information useful in planning the surgical approach[3] (Figs. 1 and 2).

Similar complementary advantages pertain to the two technics in the study of valvular regurgitation. If contrast is injected into the left ventricle, small degrees of regurgitation may appear in the cineradiogram as puffs of contrast into the left atrium which might be missed on the seriograms. The degree of mitral regurgitation may be estimated in a rough way by the size and density of the regurgitant stream. The degree of error in such observations has not at present been defined clearly. In such a case seriograms provide information of a different nature. Under favorable circumstances, the volumes of the left atrium and left ventricle can be estimated from a series of paired pictures during several cardiac cycles as the bolus of contrast passes through the heart. A discrepancy in the

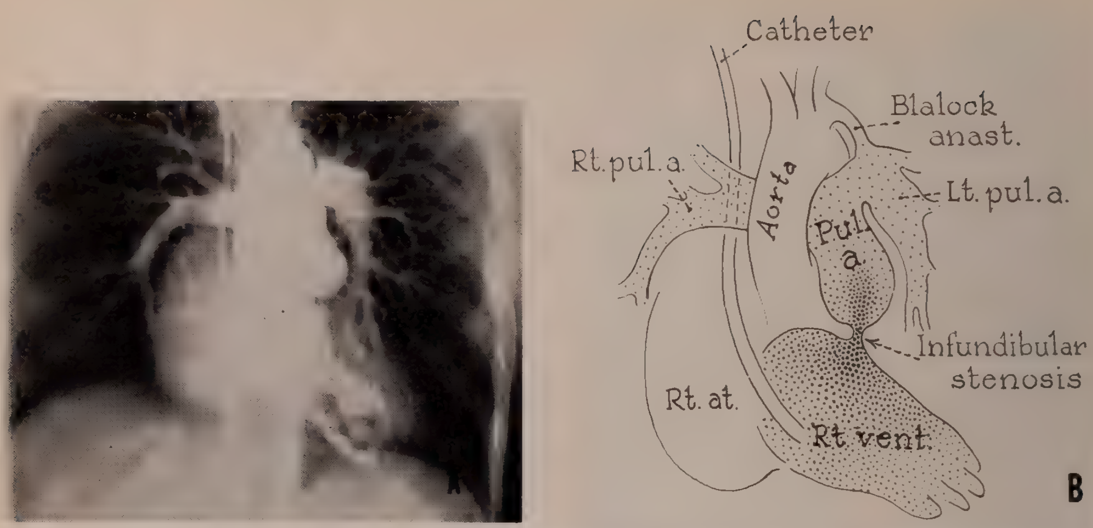

FIGURE 2. (A) Tetralogy of Fallot, anteroposterior projection, right ventricular injection. Contrast deposited in right ventricle has now opacified both pulmonary artery and aorta. Infundibular stenosis and results of previous Blalock operation (left subclavian to pulmonary artery anastomosis) are well visualized. (B) Diagram clarifying (A).

normal volume relationships between the left atrium and the ventricle can then be used to estimate the degree of regurgitation.[4,5]

Additional technics. Valvular stenosis is often demonstrable by contrast technics because the valve cusps can be seen to be restricted in their movement. A thickening and calcification of a valve may also be evident. Mitral stenosis often results in the stagnation of blood and therefore an indirect indication of mitral stenosis can be inferred from the abnormal persistence of contrast in the left atrium. Where pressure and flow measurements give inconclusive information about pulmonary stenosis (small pressure gradient in the presence of a high flow), contrast studies can be relied on to demonstrate the immobility of the fused valve cusps and their failure to open (Fig. 1). Large films in particular can differentiate infundibular from valvular stenosis, a distinction with important practical consequences as far as surgical relief is concerned. Pericardial effusion and tumors of the heart are other conditions in which radiographic visualization may be useful.

When the root of the aorta is opacified by a bolus of contrast, the two coronary arteries are usually outlined with either seriograms or cinefluorograms.[6,7] Irregularities of the lumen or localized obstructions can be visualized. A more precise technic which yields a better view of the coronary circulation is that of Sones[8] which involves catheterizing the ostium of either coronary artery with a special catheter. A small amount of contrast is injected directly into the mouth of one coronary artery during cinefluorography. The observation may be repeated several times in each vessel, if necessary. The demonstration of good coronary artery circulation in a normal person with anginal symptoms may be as important as the localization of coronary artery obstruction.

For the study of the functional integrity of other vascular structures, especially arteries, the seriograms are generally more useful than cinefluorograms. The aorta or its branches can be well visualized by contrast material which may be injected directly by retrograde arterial catheterization. Such study is indicated in all post-traumatic aneurysms, some degenerative aneurysms, and some cerebral vascular insufficiencies. Another approach to visualizing the aorta involves injection into the pulmonary artery, with exposures delayed until the contrast has perfused the lungs and returned to the left side of the heart. The renal vessels may be studied in a similar manner[9] (Fig.

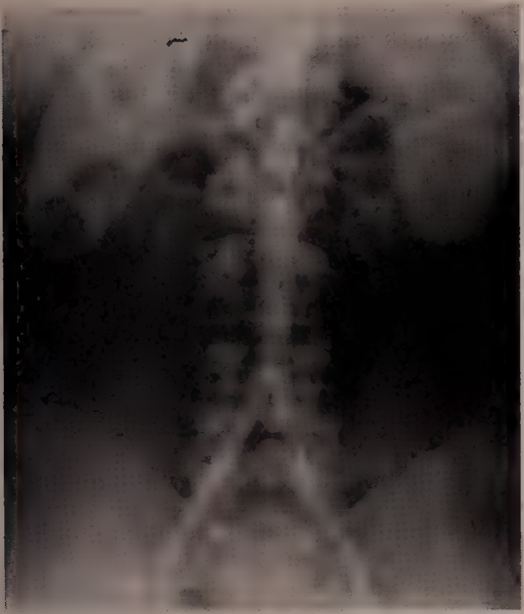

FIGURE 3. Normal aortogram obtained after pulmonary artery injection of contrast demonstrates quality of film obtained by this technic. Renal arteries, aorta, and common iliacs appear free of disease.

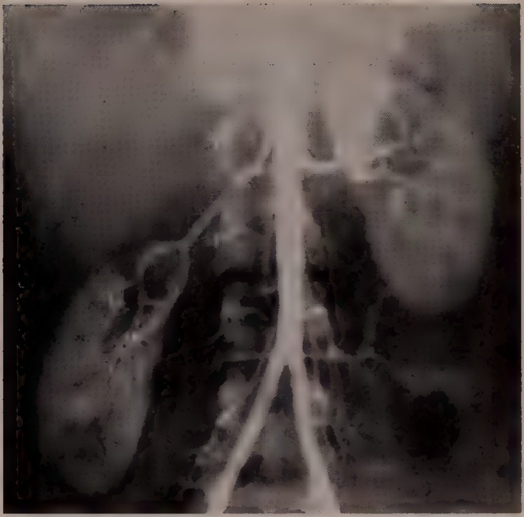

FIGURE 4. Normal aortogram obtained after aortic injection of contrast demonstrates greater clarity of film obtained by this technic. Right kidney is low.

3). A more direct approach to the renal arteries involves the Seldinger technic which consists of successive percutaneous insertions in a femoral artery of a large bore needle, a special catheter guide, and a plastic catheter. The catheter tip can then be inserted selectively in either renal artery and contrast injected directly,[10] or a bolus of contrast may be injected near the site of origin of the renal arteries for bilateral visualization. Films obtained after aortic injection (Fig. 4) are so superior to those following pulmonary artery injection that, with rare exceptions, we now utilize only the direct approach.

The pulmonary vasculature is altered in many types of heart disease, particularly those associated with pulmonary hypertension.[11,12] The caliber and number of branches of the pulmonary arteries can be studied systematically with contrast injections. Contrast injected through an end-hole catheter wedged in a radicle of the pulmonary artery gives a detailed picture of the vascular structures in that one lobule.[13]

The portal venous system can be outlined by the injection of contrast into the splenic pulp through a needle inserted percutaneously into the spleen. Such pictures may demonstrate esophageal varices and may have negative value in ruling out esophageal varices in patients with gastrointestinal bleeding of unknown origin.[14]

Comment

We need to be reminded of the relatively large number of adult patients who suffer from congenital cardiovascular lesions. Among our adult patients, over the past year's experience, we have demonstrated the detailed anatomy in cases of congenital aortic stenosis, pulmonic stenosis, ventricular septal defect, atrial septal defect, patent ductus arteriosus, coarctation of the aorta, tetralogy of Fallot, and corrected transposition of the great vessels.

As experience with angiocardiography grows, its contributions and limitations will be further defined. The relative merits of seriograms and cinefluorograms will become more obvious. For the present it is important to remember both technics and consider their use in all diagnostic problems with vascular implications. A complete study replaces speculation with precise diagnosis, a requisite in the preoperative evaluation of any patient.

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Improved biopsy can detect precancerous lung

Precancerous lung conditions can now be detected by an improved type of biopsy, according to an article by John J. Nolan, M.D., and William F. Enos, M.D., in the April 21, 1962, issue of the *Journal of the American Medical Association*. The sponge biopsy technic can detect in living persons the premalignant and malignant changes in lung tissue related to cigaret smoking and lung cancer previously discovered in a study of autopsy material from 400 men who died of lung cancer and other causes.

On the basis of this finding it is recommended that the habitual cigaret smoker who shows a change in cough habit, even with a chest roentgenogram which shows negative findings, undergo a lung examination including a sponge biopsy. If atypical changes in the lung tissue are found, the smoker should be warned of the increased risk of developing invasive lung cancer if he persists in his addiction.

Cancer of the lung now causes more deaths than any other form of cancer in men, and its incidence is increasing in men and women. As it is not likely that cigaret smoking will disappear from the American scene, early diagnosis offers the only logical solution to this increasing problem.

Sponge biopsy has been used in the past to diagnose cancer of the skin, mouth, cervix, and stomach. In the respiratory tract the suspicious area is rubbed vigorously with a cellulose sponge. Tissue particles are trapped by the sponge, removed, and examined microscopically. The diagostic results are as accurate as those derived from punch biopsies. This method can eliminate the necessity of a punch biopsy and the risks associated with the use of a sharp punch instrument. In addition the sponge is inserted by means of a flexible carrier and can reach areas which the inflexible punch instrument cannot.

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Amniotic Fluid Embolism and Anesthesia

THE CORRECT DIAGNOSIS of the etiologic factors of acute cardiovascular collapse associated with anesthesia is of the utmost importance. Empiric treatment or therapy directed by an incorrect presumptive diagnosis may aggravate rather than alleviate the condition.

Case report

A forty-year-old multipara was admitted at term following a third episode of painless vaginal bleeding. She had hemorrhaged profusely in the third and seventh months of gestation and had required a vaginal pack to control the earlier episodes. During the remainder of her pregnancy the patient had spotted intermittently. On the basis of the painless bleeding and an anterior floating vertex, placenta previa was suspected. On appropriate examination with a provision for performing an immediate cesarean section this diagnosis was not confirmed, nor was a low-lying placenta observed. Hence, the patient was returned to the ward to await spontaneous labor.

One week after admission the patient developed irregular abdominal pain, and dark red blood was passed per the vagina. The uterus was soft. Irregular contractions were noted, but the uterus relaxed well between contractions. The fetal heart rate was 144 per minute.

At this time the membranes were ruptured artificially. Clear amniotic fluid was observed. One-half hour later the patient complained of severe abdominal pain over the uterus and had generalized abdominal rigidity. The fetal heart rate was 200 per minute. The maternal blood pressure was 90/40 mm. Hg, and the pulse rate was 140 per minute. The presumptive diagnosis was that of abruptio placentae with fetal distress for which an immediate cesarean section was scheduled.

The preanesthetic medication was atropine sulfate 0.4 mg. intramuscularly. In the operating room the blood pressure was observed to fall from 145/85 to 105/80 mm. Hg. The pulse rate was 90 per minute, and the respiratory rate was 40 per minute. Oxygen by mask was administered while the patient was being prepared and draped. Anesthesia was induced with cyclopropane and oxygen, and orotracheal intubation was performed readily with a number 8 Portex tube following 40 mg. of succinylcholine intravenously.

On incision the blood was noted to be dark. The blood pressure was not auscultable at this time, nor was a radial pulse palpable. However, the apical heart rate was heard at 140 per minute. Cyclopropane was discontinued, and oxygen was administered for the remainder of the operation. Surgery was continued while 500 ml. of blood were administered under pressure followed by 800 ml. of 5 per cent dextrose in water. Systolic beats then were heard at 60

Presented and discussed at a conference held at Bellevue Hospital, New York City, February 5, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

mm. Hg, and the apical pulse rate varied between 140 and 160 per minute. A second unit of blood was transfused. Mephentermine sulfate, 5 mg., was given intravenously, and methylprednisolone, 80 mg., was infused, but without any improvement in the patient's condition.

When the abdomen was entered, approximately 200 ml. of straw-colored fluid was noted. The uterus was dusky and edematous. A subserosal hematoma was discovered over the right anterior surface of the uterus. The uterus and membranes were incised. The amniotic fluid was grossly bloody and heavily loaded with meconium. Approximately 300 ml. of blood and blood clots were present in the uterine cavity. The neonate was delivered in poor condition and never respired spontaneously. The placenta was attached to the anterior fundic wall of the uterus and was partially separated. A large hematoma of the right broad ligament was noted with evidence of subperitoneal bleeding over the right lower portion of the uterus. Both ovaries were normal.

In view of the large hematoma, a subtotal hysterectomy was begun. At this point, one-half hour after the induction of anesthesia, neither the blood pressure nor the apical pulse could be obtained. Closed-chest cardiac massage was instituted, and in approximately thirty seconds a beat was auscultated at the apex. No blood pressure or palpable peripheral pulse was discerned. A supracervical hysterectomy was completed rapidly. Following this, the right broad ligament was opened, and approximately 700 ml. of clotted blood were evacuated. At this point, approximately two hours after the start of anesthesia, an auscultable pressure at 110/70 mm. Hg was noted at the radial artery. The pulse rate was 140 per minute. The abdomen was closed rapidly, and the operation was terminated two hours and fifteen minutes after the start of anesthesia. The estimated operative blood loss was about 800 ml.

The patient was detained in the operating suite for approximately two hours because of the inability to auscult a blood pressure or palpate a radial pulse consistently. She seemed to have air hunger and received oxygen by mask. However, the patient was conscious, alert, communicated with the operator, asked questions regarding the infant, and so forth. During this period she received 200 mg. of hydrocortisone intravenously and intramuscularly. Mephentermine sulfate, 4 mg., was given intravenously, followed shortly by 5 mg. of phenylephrine hydrochloride in 500 ml. of 5 per cent dextrose in water. None of these measures had any significant effect.

After two hours the patient was transferred to the recovery suite. At this time her clotting time was three minutes, and the fibrinogen level was 174 mg. per 100 ml. Nasal oxygen therapy was instituted. The patient's condition continued to deteriorate. The pulse rate was 160 per minute. Three additional blood transfusions were given, raising the total blood administered to 2,500 ml. during the operative and postoperative period but without producing an auscultable blood pressure. Levarterenol, 4 micrograms per liter, was substituted for the phenylephrine hydrochloride, and this concentration was increased gradually to 16 micrograms per liter, but without response. The pulse rate remained at approximately 140 per minute. Lanatoside C, 0.8 mg., was given intravenously without effectively changing the patient's status. When the ventilation became ineffective, the patient's trachea was reintubated and connected to a ventilator. Approximately four hours after the end of the operation the patient had a grand mal seizure which was believed to be secondary to cerebral anoxia.

Forty-five minutes later spontaneous respirations were absent, and the patient expired five hours after the end of the operation. The blood group and type were rechecked and were found to be compatible. No signs antemortem of intra-abdominal bleeding were evidenced.

At necropsy the significant findings were 800 ml. of clotted blood at the right broad ligament and significant amniotic fluid emboli within the pulmonary artery branches and arterioles.

Comment

This case report illustrates an extremely skillfully managed general anesthetic. The cessation of cardiac function was managed properly. Unfortunately, the patient's disease precluded survival by the conventional modalities of therapy.

Amniotic fluid embolism has been reviewed intensively by Schnider and Moya.* Usually it occurs in a multiparous female with a normal prenatal course. The most characteristic feature is excessively strong, vigorous contractions, which are sufficient either to tear the myometrium or to rupture the fetal membranes at the uteroplacental site. In either case, the uterine diastasis permits the entrance of amniotic fluid into the systemic circulation. The amniotic fluid detritus embolizes to the pulmonary vessels, where a mechanical blockage and probably a generalized reflex or "anaphylactoid" pulmonary vasoconstriction are caused. Clinically, this is evidenced by hyperpnea, tachypnea, and dyspnea. Failure on the right side of the heart tends to occur, and pulmonary edema is common. Shock and anoxemia develop rapidly. Convulsions are not unusual, and coagulation defects are common late findings. This syndrome does not respond well to therapy, and death usually supervenes within two or three hours.

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* Schnider, S. M., and Moya, F. M.: Amniotic fluid embolism, Anesthesiology **22**: 108 (Jan.-Feb.) 1961.

In this patient the diagnosis was obscured by the previous history of bleeding, by the very evident abruptio placentae, by the relatively severe blood loss preceding and incident to the cesarean section, and by the large hematoma at the broad ligament. In addition, the uterine contractions were not severe, and insufficient thought was given to the possibility that the area of the abruption might serve as a portal of entry if the membranes were ruptured. Furthermore, the clinical course seemed to be more protracted than was consistent with the syndrome; nor did pulmonary edema or a coagulation defect occur.

However, several findings were accorded insufficient attention. First, the shock was inconsistent with the past and present blood loss and did not respond sufficiently to apparently adequate whole blood replacement and vasopressor therapy. Second, air hunger was a significantly prominent feature. Third, convulsions are not the usual consequence of hemorrhagic shock. These inconsistencies should have prompted an earlier reconsideration of the original diagnosis.

How might an earlier diagnosis have altered the treatment? Positive pressure ventilation with a high oxygen environment might have been instituted earlier to combat anoxemia and pulmonary congestion. Blood replacement would not have been carried out so energetically. Vasopressors, such as mephentermine sulfate, which has cardiac inotropic activity and may not increase pulmonary vasoconstriction, might be better advised than the known pulmonary vasoconstrictors, phenylephrine hydrochloride and levarterenol.

These measures, together with the judicious use of pulmonary vasodilators, such as aminophylline, might serve to lessen the spasm, thus decreasing the outflow resistance of the right side of the heart and increasing its contractility.

It is conceded that the prognosis of amniotic fluid embolism is poor and that none of these measures might have altered this patient's clinical course. However, the therapy which was instituted, while excellent in many details, was not entirely to her advantage.

Should the diagnosis of amniotic fluid embolism be entertained seriously, and the usual supportive measures outlined here prove inadequate, perhaps a cardiopulmonary bypass with thoracotomy and aspiration of the emboli should be considered.

Number one hundred twenty-two in a series of Clinical Anesthesia Conferences

Sports accidents

Accidents sustained in sports and recreation account for about 5,000 fatalities a year in the United States and for a much greater number of serious injuries, it is estimated by statisticians of Metropolitan Life Insurance Company.

Approximately 2,500 of these deaths result from accidents among persons swimming or playing in the water, while an additional 1,000 are due to boating mishaps. The remainder of the death toll from sports and recreation is attributable mainly to the use of airplanes for pleasure flying, hunting, and participation in various other popular sports.

"Sports and recreation are responsible for only a relatively small portion of the total accident mortality. Nevertheless, the need for accident prevention in this area is underscored by the fact that several million Americans participate in competitive sports, such as baseball, football, and boxing, and a far greater number engage in swimming, boating, skiing, fishing, hunting, and other recreational activities."

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Zinc Chloride Poisoning (Solder)

THE FOLLOWING INCIDENT was reported recently to the New York City Poison Control Center.

Substance Ingested	*Age*	*Sex*
Soldering Paste	$6^1/_2$ years	Male

Approximately twenty hours after the patient's ingestion of zinc chloride, the Poison Control Center was consulted about the therapeutic measures to be employed. The advice given was to use symptomatic and supportive therapy. The Public Health nurse who visited the home to obtain more precise information about the mode of occurrence related as follows:

Around 8:30 A.M. on December 25, 1961, Patient 1, six and one-half years old, drank a small amount of Yager Soldering Salts that his father had in a soft-drink bottle on the kitchen floor. He used it in repairing radios and had obtained it from a friend who owned a garment plant and used it to repair or oil sewing machines. The parents were sleeping at the time since they had been at the hospital most of the previous night with a diabetic sibling (Patient 2), five and one-half years old, who was critically ill. The child's older brother, eight years old, was up and around the apartment. He wakened his father at once and told him that Patient 1 had drunk the solder solution. The father immediately gave the child large amounts of milk with warm water to drink, causing repeated vomiting. The child showed no symptoms but was unable to retain ginger ale or any liquids later on in the day.

Circumstances required the parents to leave the two children with the father's mother and aunt. The children remained at their grandmother's home overnight. The victim was unable to retain anything and complained of pains in his abdomen. His parents picked him up at 10 A.M. on December 26, 1961, and took him to the emergency ward at the local hospital. The father obtained the original container of Yager Soldering Salts which he gave to a physician at the emergency ward. He was told it was not harmful and that the child probably would have a "sick stomach." The father claimed that the physician called the City of New York Department of Health Poison Control Center and read the label to the person who answered the telephone. The child was admitted to the hospital because he complained of abdominal pain and because his brother (Patient 2) had died of a hypoglycemia.

Apparently Patient 1 complained of more severe pain that afternoon. After surgical consultation an operation was decided on for possible intestinal block or appendicitis. The child's condition improved after the operation.

However, the telephone operator at the hospital phoned the father at home on January 3, 1962, seven days following the operation, and told him the child was dead.

According to the Public Health nurse the diabetic sibling (Patient 2), the brother of the victim, five and one-half years of age, fell at home on December 16, 1961, knocking out two front teeth and cutting his gums. Two sutures were taken in the emergency room at the local hospital immediately after the accident. He was kept home from school the following week. The sutures were removed on December 22, 1961, and the child appeared well. The mother took the child shopping with her on December 23, 1961, and he complained of not feeling well that afternoon. A doctor was called who made a diagnosis of pneumonia and called an ambulance which took the child to the hospital. A chest x-ray film and routine urinalysis were done while the child was at the emergency ward. The patient was admitted to the hospital for an immediate work-up in the inpatient service because the urine was positive for sugar.

The hospital physician telephoned the family at 10 P.M. on December 24, 1961, because the child's condition was poor. The mother and father went to the hospital. The child died at 3:20 A.M., December 25, 1961.

The epidemiologist's report on the diabetic patient stated that the child, a known diabetic patient, was admitted to the hospital on December 23, 1961, with a diagnosis of an acute respiratory infection and diabetic ketosis. A urinalysis showed a 4 plus reaction, and the blood sugar was 232 mg. per 100 ml.

He was given 40 units of regular insulin intramuscularly and other symptomatic therapy. Soon after the insulin injection he became pallid and had repeated convulsive seizures. An emergency blood sugar showed 43 mg. per 100 ml., and the carbon dioxide-combining power was 53 volumes per cent.

Respiratory difficulty was noted, and an emergency tracheotomy was done. A nose and throat culture on December 24, 1961, showed Escherichia coli and Streptococcus mitis organisms.

His condition deteriorated, and he expired on December 25, 1961. An autopsy was performed on the same day, and the findings included edema of the viscera, post-tracheotomy with mediastinal emphysema, gastroenteritis with 500 cc. of brownish fluid in the peritoneal cavity, edema of the brain, and hypoglycemic shock. There was no indication that the patient had consumed any solder paste, as had his brother.

A report from the hospital superintendent in reply to an inquiry from the Poison Control Center on the 2 fatalities follows:

> Patient 2 was admitted to the hospital on December 23, 1961. The autopsy did not reveal any findings due to the ingestion of poisoning.
>
> His brother (Patient 1) was admitted on December 25, 1961, with the diagnosis of gastroenteritis. The father stated that the boy had ingested some "paint," which included zinc chloride, twenty-four hours prior to admission.
>
> The boy complained of generalized abdominal pain, mostly in the right lower quadrant, on palpation. Intravenous feeding was started. He was seen by the attending surgeon who reported that the child had some tenderness and intermittent rigidity which seemed to be on a voluntary basis. The x-ray films showed abdominal distention, especially of the large bowel.
>
> On December 27, 1961, a total gastrectomy was done under general anesthesia. The findings were necrosis of the entire stomach from the esophagus to the pylorus. The colon was moderately distended, and the appendix appeared to be normal. There were 1,500 cc. of brownish fluid in the peritoneal cavity, and there were numerous nodes in the mesentery of the small intestine. He left the operating room in fair condition.
>
> After the operation the patient still complained of pain in the abdominal area. He vomited yellowish, thick liquid. On January 3, 1962, he was exceedingly restless, became very pale and cyanotic after vomiting, and lapsed into a comatose state. He was pronounced dead at 4:35 A.M.
>
> The case was referred to the office of the Medical Examiner. The cause of death was corrosive gastritis, for which an operation was performed, and hepatic necrosis due to the ingestion of soldering salts, for which a chemical examination is pending.

This solder preparation was reported as

containing approximately 96 per cent zinc chloride and a small amount of ammonium chloride. Zinc chloride is used by itself or in a combination as a soldering flux in soldering operations. Cases of zinc chloride poisoning usually occur from ingestion. However, one massive outbreak has been reported due to zinc chloride fumes. When ingested, zinc chloride has a marked corrosive action on the gastrointestinal tract. It produces a whitish membrane with large exfoliations, producing many reddish, denuded areas. Perforation of the stomach and ulcerations also may occur.

The symptoms include pain in the mouth, throat, and epigastrium; salivation; edema; massive swelling of the lips; and not infrequently, edema of the glottis. There is also excessive salivation, difficulty in swallowing, and recurrent bouts of violent vomiting. Usually there is severe abdominal pain followed by bloody diarrhea. There is a rapid but weak pulse, a drop in the blood pressure, stertorous respirations, and the skin becomes cold and clammy.

When death occurs, it is generally due to circulatory collapse and shock from peritonitis resulting from the perforation of the gastrointestinal tract. When death does not occur within several hours, damage to the kidney also will occur and will be accompanied by albuminuria, hemoglobinuria, and an oliguria.

In some cases muscular weakness, muscular spasms, aphonia, and sensory disturbances occur. It also has been reported that zinc appears to be toxic to the hemopoietic system, since in some cases zinc will cause a microcytic hypochromic anemia. Similar to potassium permanganate, zinc chloride also has been used as an abortifacient causing corrosion of the vagina and uterus and death from collapse.

Von Oettingen* cites a case where the accidental rectal administration of a 50 per cent aqueous solution of zinc chloride, although immediately removed by lavage, resulted in pallor, severe tenesmus, extensive ulceration of the rectal mucosa with extensive hemorrhages, and later complete stenosis of the rectum above the anus.

Lethal dose

The lethal dose shows considerable variations. A fatality was reported in a person following the ingestion of $3^1/_2$ Gm. On the other hand, recoveries have been reported after the ingestion of 90 Gm.

Zinc is a bluish white metal, widely used in industry in galvanizing, coating of iron utensils, soldering, printing, wood preserving, fireproofing, and dyeing. Formerly, zinc stearate also was used extensively in dusting powders, causing many fatalities from such use in infants. The cause of such fatalities was perhaps caused by a mechanical action of the powder which was inhaled by the child and which caused a bronchopneumonia.

Zinc compounds also have been used therapeutically with questionable value as astringents, deodorants, abortifacients, antiseptics, and for local applications.

A diet deficient in zinc will result in poor growth and the loss of hair in animals because of faulty enzymatic activity. Metallic zinc is said to be inert, but some of its salts, such as the sulfate and chloride, are toxic. Poisonings have been reported from the inhalation and ingestion of zinc compounds.

It has not been proved definitely that acid foods stored in zinc-galvanized containers will dissolve a sufficient amount of the metal to cause harmful effects, apart from emesis. However, the use of such vessels for the storage of acid foods is not advocated.

Zinc chloride (butter of zinc) is a soluble salt and is used in soldering preparations, in preserving fluids for dead bodies, as a preservative of railway ties, as a cauterizing agent, and as an escharotic, astringent, and disinfectant. When it comes in contact with the skin, it may cause an inflammation, burn, and a dermatitis.

The inhalation of zinc chloride fumes may cause respiratory tract irritation, a tracheitis, bronchitis, aphonia, and other respiratory difficulties.

Most of the severe poisonings, however, result from the accidental or intentional (suicidal) ingestion of the product. Zinc is excreted through the large bowel and the kidneys.

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* Von Oettingen, W. F.: Poisoning; A Guide to Clinical Diagnosis and Treatment, 2nd ed., Philadelphia, W. B. Saunders Co., 1958, p. 597.

Chronic zinc poisoning

"Metal fume fever" is an industrial disease caused by chronic zinc poisoning. It is also known as "brass-founders ague," "spelter shakes," or "zinc chills." It is due to the inhalation of fine particles in fumes of the metallic oxide of metals, such as zinc, copper, lead, mercury, and cadmium.

The symptoms of such chronic poisoning are not unlike those of influenza, such as generalized aches and pains, vomiting, nausea, weakness, pains in the extremities, chills, rapid pulse, hyperpyrexia, cough, diarrhea, and a metallic taste in the mouth. Exhaustion to the point of prostration is not uncommon. The disease is self-limiting, lasting from several days to two weeks and leaving no permanent injury.

Treatment

No specific antidote is available for zinc poisoning, although dimercaprol has been suggested. The treatment is entirely supportive and symptomatic including gastric lavage and the use of demulcents.

One must be very cautious, however, in passing the gastric tube, not to injure the inflamed mucosa. Water and milk are fluids to be used in the gastric lavage. It is important that the patient be observed carefully during convalescence for complications, such as strictures, anemia, and so forth.

In addition to the use of zinc chloride as a soldering agent, solutions of acids, especially hydrochloride, are used frequently. Zinc chloride made into a paste with petrolatum, as well as rosin, constitute other agents in common use.

Several days following the zinc chloride fatality a fatality in a seventy-two-year-old male resulting from the ingestion of a soldering hydrochloride preparation was reported to the Poison Control Center.

Although it was reported as an accidental occurrence, it may have been of suicidal intent. The patient was admitted to a hospital emergency room where he expired shortly thereafter.

Soldering preparations have been in wide use for many years, and it is very fortunate that although the case fatality rate is high, the number of incidents have been low. Regrettably, this low incidence cannot be ascribed to any intelligent warnings on the part of the manufacturers. In the first fatality there were no warnings of any kind on the label. As a matter of fact, the container stresses "no fumes, no acids, and no corrosives" in large letters with no warnings as to the possible physiologic injuries and with no regard to care and storage.

It is to be noted that the labels on large-sized industrial containers of both zinc chloride, granular and fused, and zinc chloride 50 per cent solution, warn against severe skin irritations and contact with the eyes. The mention of the hazard of ingestion is notable by its absence. The failure of chemical manufacturers to discuss the hazards of ingestion on the labels of bulk containers is a general one. It is believed that this absence may act as a trap to the packager of small-sized containers, since he undoubtedly uses the wholesale-size labels on the materials which he received as a guide to the retail label.

It is to be noted that the new Federal Hazardous Labeling Act does not control the labeling of industrial-size containers. The New York City and State laws, however, do not make any distinction between household and industrial-sized containers. It is regrettable that Congress did not give the U.S. Food and Drug Administration the requested jurisdiction over the labeling of large-sized containers. The Administration, as well as the A.M.A., favored the legislation of both household and industrial packings.

While most soldering agents contain a corrosive agent, there is a varying degree of corrosiveness, and not all contain zinc. Because of the amount of home radio construction and home repairs in general, soldering preparations are distributed widely and represent an area where new-found caution is to be employed. On the other hand, numerous ingestions reported to this Center of pharmaceutical preparations containing zinc oxide and calamine have been notably unimportant in their sequelae. This should be especially comforting to pediatricians who so frequently are confronted with the ingestions of ointments used in infant care.

The use of zinc sulfate as an emetic fortunately has never been noted in reports to this Center.

This Center receives numerous calls about children who have licked the "white liquid" on dry cell batteries. This substance is a mixture of ammonium chloride and zinc chloride. We have been recommending milk of magnesia (for neutralization) and milk in these cases. There has been only local oral irritation reported. The amounts of zinc chloride formed by the chemical reaction with the zinc battery casing apparently is too small to cause major damage. Finally, the use of zinc chloride powder in toy chemistry kits warrants a second thought.

Number ninety-one in a series of Accidental Chemical Poisonings

Hospital planning in England

During the next ten years England will do away with her large mental institutions, moving their patients into general hospitals, according to an article by Dr. Brian Abel-Smith in the May 1, 1962, issue of *Hospitals*.

The change is part of a new long-range program of hospital planning and construction under which Britain will spend 500 million pounds (slightly more than 1.4 billion dollars) in the next ten years.

Moving the mental patients has two objectives: to teach the public to regard mental illness in the same way in which they regard any other illness, and to bring the standards of provision for mental patients up to those for other patients. Extensive home-care programs, outpatient facilities, and day-hospital facilities are also being planned for the care of mentally ill patients.

The over-all hospital planning is veering toward the all-purpose comprehensive general hospital and away from the specialty hospital, based on the principle that no medical specialty can flourish if it is cut off from the mainstream of medicine. Hospitals of between 300 and 800 beds in size are being planned, since they are probably most efficient and economical.

The most critical problem is that of providing for chronically sick persons. Experience has shown that the problems of proper medical and nursing care for the chronically ill cannot be overcome without bringing them under the same medical and nursing control as that of the acute hospital. The plans call for abolishing what is called the nursing home in the United States.

Another problem of long-term planning is determining the bed need. During World War II, England hospital experts estimated the bed need at 5 per 1,000 population, but extensive studies since the war have shown the need at little more than 3 acute beds. It has also been found that the need varies between different areas of the country and can vary rapidly over time as medical technics and medical fashions change.

A study showed that "areas which already had fewer beds seemed to need fewer beds, while those having more beds needed all the beds they had. Despite all the talk about haphazard hospital development, it appeared that supply was nearly equal to demand," Dr. Abel-Smith said, continuing:

"What we had discovered was Say's law. Within limits, supply creates its own demand. When general practitioners know that hospital beds are short, they don't hospitalize patients who are not desperately in need. . . . When hospital doctors know that beds are short, they reduce the length of stay. When they know they are plentiful, they increase the length of stay."

Statistical studies provide useful yardsticks in planning, but they must be used with common sense. A compromise must be worked out between the demand for beds as calculated by statistics and the demand expressed by physicians and citizens of the region. Hospital planning must also be done within the framework of all medical and social services.

Case Reports

Rupture of the Spleen in Infectious Mononucleosis

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Rupture of the spleen is a catastrophic complication that may occur in the course of an otherwise uneventful case of infectious mononucleosis. It is important for the attending physician to be aware that this untoward event may occur spontaneously or following an inconsequential and easily forgotten trauma, and to be prepared to make a rapid diagnosis and follow through with appropriate therapy.

Case report

A sixteen-year-old white youth was admitted to the hospital on August 9, 1959, complaining of pain in the left upper part of the abdomen radiating to the left shoulder and associated with weakness and dizziness. Six hours prior to his admission he had been playing with his younger brother and had received a very light blow to the upper portion of the abdomen. Following this minor episode he was well for two hours before discomfort in the upper part of the abdomen set in.

The patient related that he had been under a physician's care for the previous three weeks because of weakness, sore throat, enlarged lymph glands, and fever. Penicillin had been prescribed, but he had been discharged from treatment shortly before the present illness.

On admission the patient was pale, restless, and perspired freely. His temperature was 99.8 F., the pulse 128, and the blood pressure 120/60. The tonsils were enlarged, but the pharynx was not inflamed. Enlarged nontender cervical, axillary, and inguinal lymph nodes were noted. The abdomen was distended slightly. There was marked tenderness throughout the epigastrium and the left upper quadrant of the abdomen, with associated muscle spasm. The liver and spleen could not be palpated.

Laboratory tests on admission revealed a hemoglobin of 10.2 Gm. per 100 ml. The white blood cell count was 5,800 with 49 per cent neutrophils, 1 per cent monocytes, and 50 per cent lymphocytes. The latter were considered atypical.

Free blood was demonstrated in the peritoneal cavity by a needle puncture and aspiration. This fact, combined with the history of a sore throat and the presence of enlarged lymph nodes, led to a diagnosis of splenic rupture following minor trauma in a patient with infectious mononucleosis.

At an abdominal exploration performed shortly following the patient's admission there were found 2 L. of free blood in the peritoneal cavity. The spleen was four times its normal size and presented a large, deep laceration on its external surface. An uneventful splenectomy was performed, at which time two enlarged hilar lymph nodes also were removed.

The postoperative course was benign, and the patient was discharged from the hospital on the thirteenth postoperative day. A heterophil antibody test performed on the first postoperative day yielded a titer of 1:896.

Pathologic report

Gross examination. The first specimen on gross examination was a spleen 17 by 14

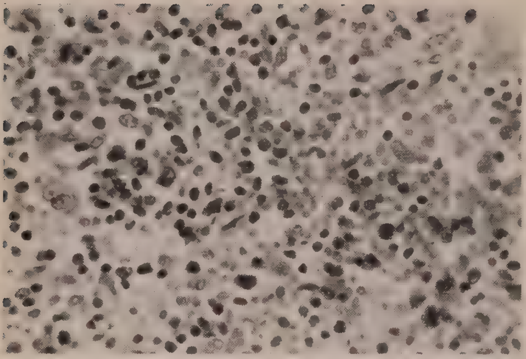

FIGURE 1. Section of spleen showing several large atypical lymphocytes characteristic of infectious mononucleosis.

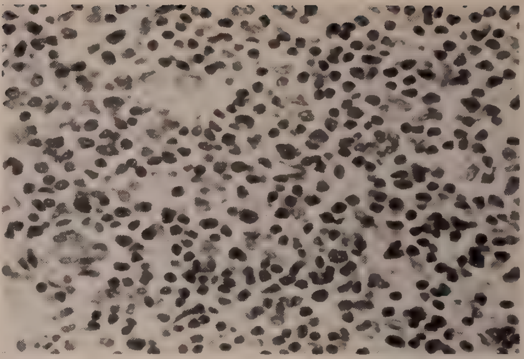

FIGURE 2. Section of lymph node from hilum of spleen demonstrating the atypical lymphocytes of infectious mononucleosis.

by 7 cm. The outer surface was grey-blue. In the notch and extending out onto the lateral external surface were several irregular deep lacerations. On section, the pulp was soft. The cut surface revealed milium-like grey nodules in large numbers. The second specimen consisted of two adjoining lymph nodes, the larger of which was 2.5 cm. long. The outer surface was greyish-tan. The cut surface was grey-red.

Microscopic examination. Sections of the spleen on microscopic examination showed a moderately well-preserved architecture. The lymph follicles were reduced slightly in size and number. The pulp, on the other hand, was markedly congested, and the sinusoids were distended with red blood cells. The pulp was crowded with polymorphonuclear leukocytes, plasma cells, and eosinophils. In addition, there were in the sinusoids many large, atypical lymphocytes compatible with the diagnosis of infectious mononucleosis (Fig. 1).

Sections of the lymph nodes showed moderately well-preserved cytoarchitecture. The lymph follicles were intact. The sinusoids were distended with blood, and the lymph spaces were crowded with polymorphonuclear leukocytes and the atypical lymphocytes of infectious mononucleosis (Fig. 2).

Comment

Spontaneous rupture of the spleen in infectious mononucleosis was first described by King in 1941.[1] Subsequent reports of similar cases without precipitating trauma have appeared with moderate frequency in the literature.[2-13] Several other authors have reported splenic rupture in infectious mononucleosis and on close questioning of the patients have been able to assign blame to relatively trivial events, such as the act of defecation,[4,14] catharsis,[4] the act of climbing into bed,[4] and abdominal examination.[4,15] In the present authors' case a light blow on the abdomen during a mock boxing match between brothers resulted in rupture of the spleen.

The important points to be made are that the benign course of a case of infectious mononucleosis can be marred suddenly by rupture of the spleen either spontaneously or following minor trauma, and an examination of the abdomen of a patient suspected of having infectious mononucleosis must be performed with utmost gentleness.

Summary

Another case of rupture of the spleen in infectious mononucleosis is presented. Sudden shock without apparent cause in patients with this disease should draw attention to the spleen so that appropriate therapy can be administered without delay.

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Live poliomyelitis vaccine schedule for infants

Two schedules for immunizing infants with oral live poliomyelitis virus vaccine were reported generally satisfactory by Randolph Batson, M.D., Amos Christie, M.D., and William J. Chestham, M.D., in the April 21, 1962, issue of the *Journal of the American Medical Association*. Considering the desirability of immunizing infants against poliomyelitis at the same time that other immunization procedures are performed, it is advised that vaccine against Types I, III, and II be given singly in that order at six weeks, twelve weeks, and eighteen weeks of age or that vaccine combining all three types of poliomyelitis virus be given at six, twelve, and eighteen weeks.

Infants immunized on these two schedules developed the highest level of protection in a study in which 90 infants were fed Sabin vaccine on five different schedules.

Infants immunized on the first schedule did not respond to Type II vaccine as well as had been expected. This may have been due to interference from other intestinal viruses which are prevalent during the summer and autumn when the poliomyelitis vaccine was administered.

In view of such possible failures, an additional dose combining all three types of poliomyelitis virus should be considered at a later date.

The study also indicated that even a high level of immunity transmitted by the mother to the infant did not block the immunizing effect of the vaccine.

No adverse reactions were associated with the vaccine, and no difficulties were encountered in administering it.

Bacterial Endocarditis Complicating Ventriculoatrial Shunt

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In the surgical treatment of infantile hydrocephalus, interest has been revived in those procedures which are designed to divert cerebrospinal fluid into the circulatory system.[1,2] Although ventriculoatrial shunt presently seems preferable, there are many factors limiting its effectiveness.[2-4] One sequel incident to the presence of the tube in the right atrium is the production of a fatal bacterial endocarditis. The clinicopathologic features of this complication are illustrated by the sequence of events recorded in the present report.

Case report

A Negro boy, age five months, was admitted to a hospital for progressive enlargement of the head. Hydrocephalus was reported to have been present at birth, and after the first month of life a ventriculoperitoneal shunt was performed. At the time of transfer to Kings County Hospital four months later, it was apparent that the shunt was ineffectual.

A physical examination disclosed an infant manifesting the obvious characteristics of hydrocephalus. The occipitobregmatic circumference was 57 cm. The anterior fontanel was enlarged and bulged to a mild degree. Craniofacial disproportion was marked, and the scalp veins were exceptionally prominent. The pupils reacted normally to light stimulation, extraocular muscle movements were appropriate, and a funduscopic examination did not reveal any abnormality. All muscle reflexes and movements of the limbs were normal. The previously installed tube for the ventriculoperitoneal shunt was palpable and in the proper position. Escape of cerebrospinal fluid into the subcutaneous tissues along the course of the tube was not evident. A roentgenographic examination of the skull demonstrated the craniofacial characteristic of hydrocephalus. The white blood cell count was 12,000 per cubic millimeter. The hemoglobin content was 11 Gm. per 100 ml. A urinalysis gave normal results.

An intermittent fever without an apparent cause was noted shortly after admission to the hospital. Intramuscular aqueous penicillin, 600,000 units, was administered daily for fourteen days. During this period decubitus ulcers appeared over the scalp from which Staphylococcus aureus, coagulase positive, was obtained by culture. Organisms could not be cultured from the peripheral venous blood. Partial healing took place in the ulcers after local antibiotic therapy and change in points of pressure. The head continued to enlarge, however, necessitating the performance of a ventriculoatrial shunt with a Pudenz-Heyer tube. Immediately after surgery and for the subsequent six weeks the circumference of the head decreased. The anterior fontanel remained depressed, and the general clinical state of the child improved. However, at the end of this period and again without an apparent cause, fever reappeared and was associated with bulging of the anterior fontanel. Thereafter, progressive weight loss ensued, associated with apathy and loss of appetite. The head continued to enlarge. Fever persisted until death occurred eleven weeks after operation.

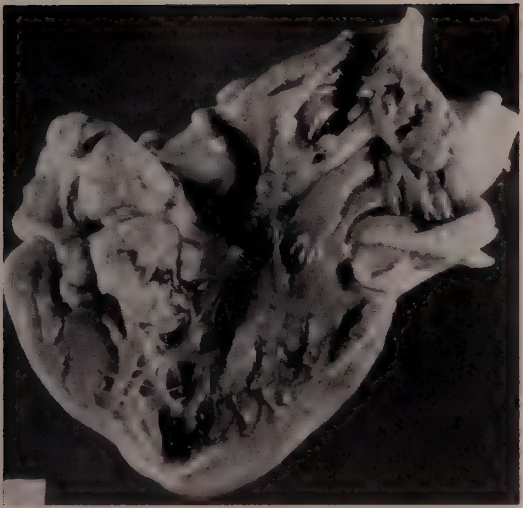

FIGURE 1. Vegetative bacterial endocarditis of the tricuspid valve with friable masses and extension of vegetations to adjacent endocardium.

Necropsy findings

The body was that of a poorly developed child. The cranial vault was approximately twice the usual size. A 2-cm. skin ulcer was present over each temporal region. The sagittal suture was open, and the anterior fontanel was greatly enlarged.

The heart weighed 27.5 Gm. The foramen ovale was minimally patent. Most of the atrial surfaces of the posterior and medial tricuspid leaflets were covered with a friable, granular, yellow substance averaging 1 cm. in thickness. This material also covered the adjacent portions of the chordae tendineae and the ventricular and atrial endocardium from which it projected into the entrance of the superior vena cava (Fig. 1). The superior surface of the anterior leaflet was covered with similar vegetations. A microscopic examination showed the vegetations to be composed of fibrin and colonies of gram-positive cocci (Fig. 2). The subjacent atrial wall and tricuspid valve showed necrosis with fibrin replacement, gram-positive cocci, and infiltration by neutrophils. The myocardium in proximity to the vegetations was diffusely infiltrated with lymphocytes and macrophages. There were several small abscesses in the myocardium.

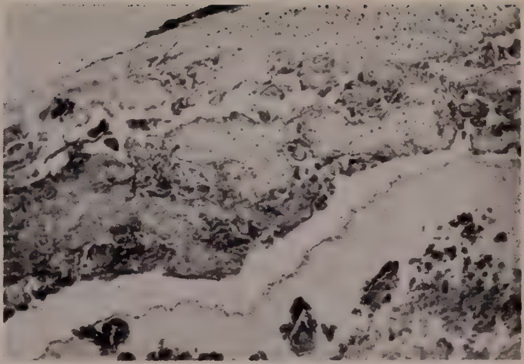

FIGURE 2. Detail of bacterial vegetation showing inflammatory infiltration. The black masses represent bacterial colonies (hematoxylin and eosin stain).

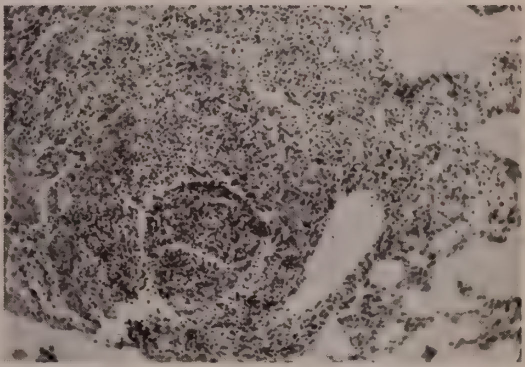

FIGURE 3. Lung parenchyma containing acute inflammatory infiltrate and small abscess (hematoxylin and eosin stain).

The lungs contained diffuse hemorrhagic foci with acute inflammatory infiltrations and small scattered abscesses (Fig. 3). Emboli of fibrin and gram-positive cocci were seen in the smaller arteries.

The kidneys showed a horseshoe configuration (Fig. 4). Areas of interstitial hemorrhage were scattered throughout. All glomeruli observed contained hyaline thrombi, and many contained clusters of gram-positive cocci. Scattered interstitial microabscesses were present containing clumps of cocci and fibrin.

Staph. aureus, coagulase positive, was obtained in pure culture from the vegetations of the tricuspid valve and heart blood. In the kidney and bronchi there was an admixture of gram-negative enteric bacilli. A mixed growth of staphylococcus and pneumococcus was obtained from the cerebrospinal fluid.

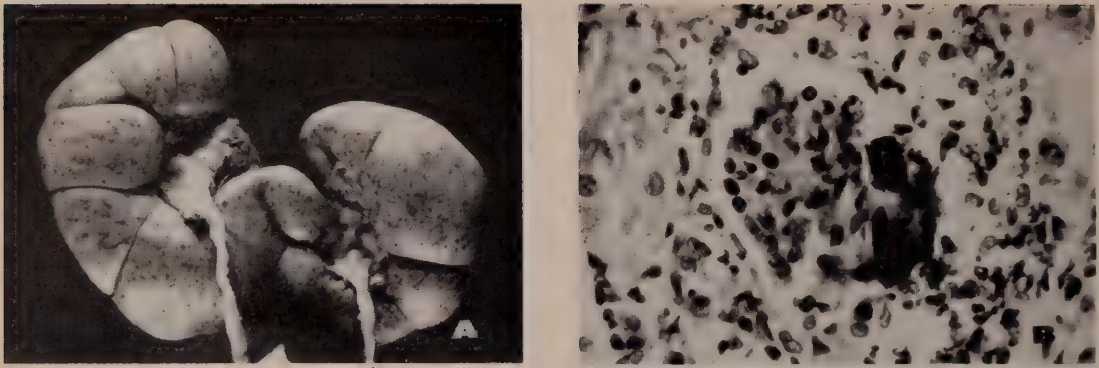

FIGURE 4. (A) Petechiae on cortex of kidney giving "fleabitten" appearance. (B) Focal glomerulonephritis with acute necrosis and bacterial growth in glomerular tuft (hematoxylin and eosin stain).

The cerebral hemispheres were enlarged and fluctuant. The gyri were flattened. Areas of atrophic cortex were seen over the occipital and temporal lobes. A portion of ventriculoatrial shunt tubing was found emerging from the ventricular system through the cortex. Serial sections showed the ventricles to be massively dilated. The cortex and subjacent white matter were greatly attenuated. The ependymal lining was thickened and granular. The aqueduct of Sylvius was atretic at the level of the intercollicular sulcus. The fourth ventricle was grossly dilated. The leptomeninges in all microscopic sections were infiltrated with a mixed exudate of lymphocytes and polymorphonuclear leukocytes. The gray matter showed a diffuse decrease in ganglion cells with intense gliosis. Scanty amounts of exudate were scattered over the lining of the ventricular system. The cerebellum showed moderate atrophy. There was atresia of the calamus scriptorius.

Comment

Isolated tricuspid bacterial endocarditis is a rarely encountered pathologic entity, particularly in the absence of a pre-existing congenital, rheumatic, luetic, or arteriosclerotic valvular defect. Reactions to foreign bodies within the heart cavities, such as thrombi within the lumen and mural thrombi with subsequent pulmonary embolization, have been observed by others.[3,5] The application of metal clips to the heart valves in laboratory animals with superimposed bacteremia has resulted in bacterial endocarditis,[6] but the clinical production of this pathologic state has not been recorded in man. In the present instance, a foreign body in the right side of the heart and the coexisting bacteremia apparently were the determining factors in the establishment of such a lesion. Of significance is the fact that the presence of an endocardial infection was not considered during the patient's life. It is possible that other children have succumbed to a similar but unrecognized complication of the ventriculoatrial shunt. The recognition of the syndrome should prompt a transfer of the shunt to another suitable area and the administration of appropriate antibiotic therapy.

Summary

An instance of fatal bacterial endocarditis following a ventriculoatrial shunt for hydrocephalus is described. The importance of its recognition is mentioned.

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An Unusual Form of Cutaneous Sarcoidosis

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In 1869 Jonathan Hutchinson[1] recorded what was probably the first description of a case of cutaneous sarcoidosis. Since then there have been numerous contributions by Besnier, Boeck, Schaumann,[2] and many others which have extended widely our knowledge of the clinical forms that sarcoidosis can assume. By now it is apparent that the cutaneous and systemic manifestations of sarcoidosis may present such a variety of symptoms that this condition may be listed among the "great imitators" along with syphilis, tuberculosis, leprosy, the deep mycoses, and drug eruptions.

We herewith report a case of sarcoidosis in universal distribution on the skin, as part of a systematized process of sarcoidosis, that took the form of perifollicular pustules and papules. In a review of the English literature of the past ten years, we have been unable to find a case that was precisely like ours.

Case report

A thirty-five year-old, obese Negro man fell acutely ill about one year ago and was admitted to a hospital with fever, headache, dizziness, weakness, joint pain, and an extensive eruption. Laboratory studies at that time revealed 2 plus albuminuria and total serum proteins of 8.4 Gm. per 100 ml. with an albumin to globulin ratio of about 1. A biopsy of the skin showed as granulomatous tissue. No definite diagnosis was made at that time. The patient improved after adrenocorticosteroid therapy and was discharged. About five months later, he grew worse and was admitted to Bellevue Hospital for dermatologic and general medical investigation. The symptoms were the same. The past personal history was not remarkable. He was born in Mississippi and lived there until the age of twenty when he moved to New York City. His occupation is that of a cook. There is no past history of active tuberculosis.

A general physical examination revealed the following abnormal findings: The temperature was 102.2 F., and the pulse was 118. Nontender lymphadenopathy involving the cervical, axillary, and inguinal nodes was present. A systolic murmur was heard at the cardiac apex. Hepatosplenomegaly was noted. The large joints of all the extremities were swollen, warm, and tender. A neurologic examination revealed a slight gross tremor at rest and weakness of all the extremities, more marked in the upper than in the lower. The left eye is missing, having been enucleated after an injury long ago. There had been a 120-pound loss in weight (from 360 to 240) in nine months.

An examination of the skin showed an extensive eruption that consisted of perifollicular pustules and papules scattered over the face, trunk, and extremities (Fig. 1). The individual lesions measured from 1 to 3 mm. in diameter. On the face, the papules were smooth of surface, flattened, and round or oval. On the rest of the body, the surface of each papule was hyperkeratotic and pierced by a short, thick hair. Furthermore, there were areas of scaling on the trunk and extremities. The scales were thin, dry, and attached somewhat loosely to the underlying papules.

Numerous laboratory tests were performed with the following important results: The peripheral blood showed 10.5 Gm. per 100 ml. of hemoglobin with hypochromic erythrocytes. The erythrocyte sedimentation rate (Westergren) was 38 to 42 mm. per

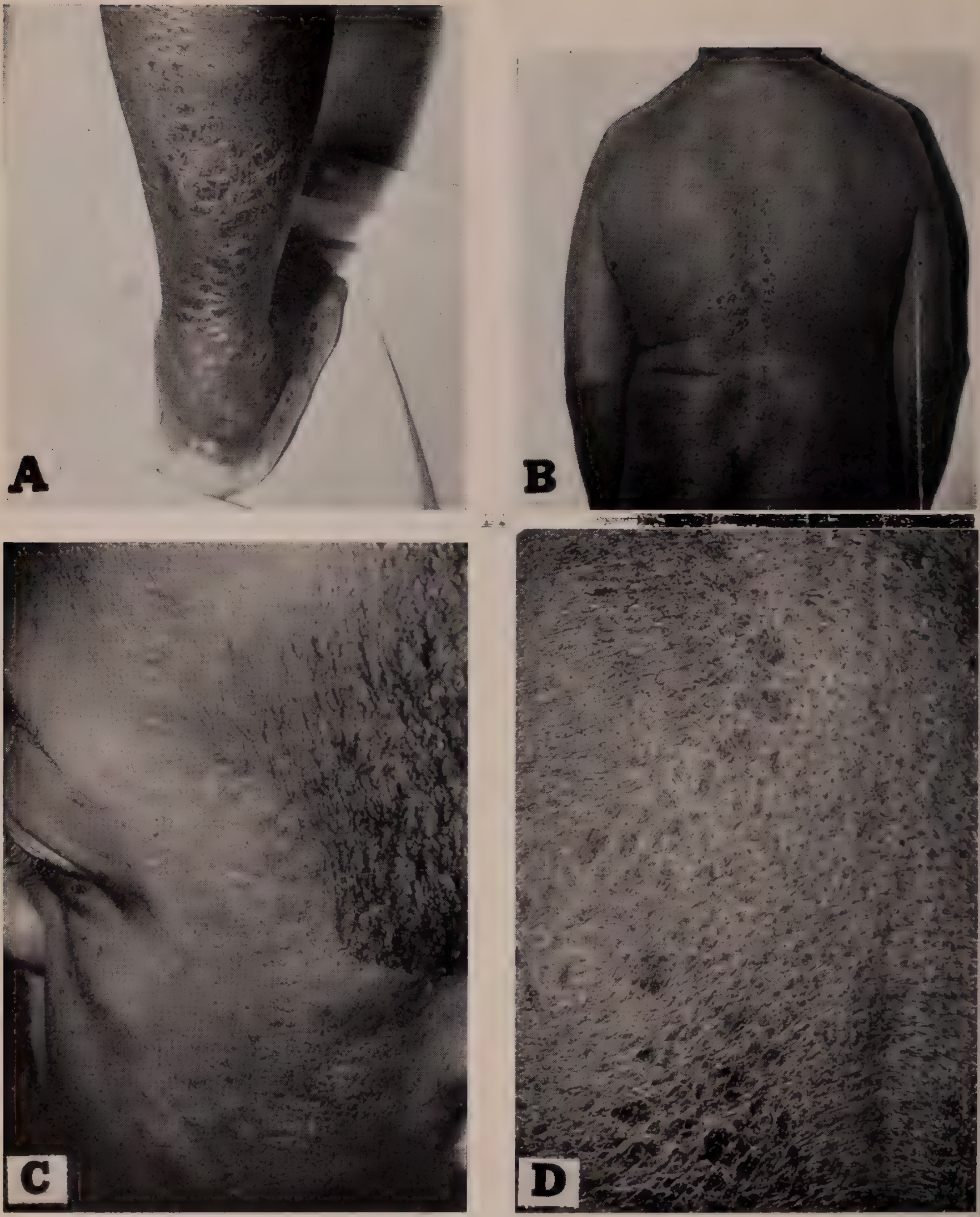

FIGURE 1. Clinical aspects of cutaneous sarcoidosis with lesions in perifollicular position. (A) Process on a leg; (B) on the back; (C) on the face; and (D) on the back in enlarged detail.

hour (normal 0 to 9). The urinalysis showed 2 plus albuminuria. The blood urea nitrogen was 16 to 23 mg. per 100 ml. (normal 10 to 20), and the uric acid was 6.3 to 8 mg. per 100 ml. (normal 2 to 4). The Bromsulphalein clearance showed 17 per cent retention after forty-five minutes (normal 0 to 5 per cent); cephalin flocculation showed 2 plus (normal 0 to 1); and thymol turbidity showed 23.5 units

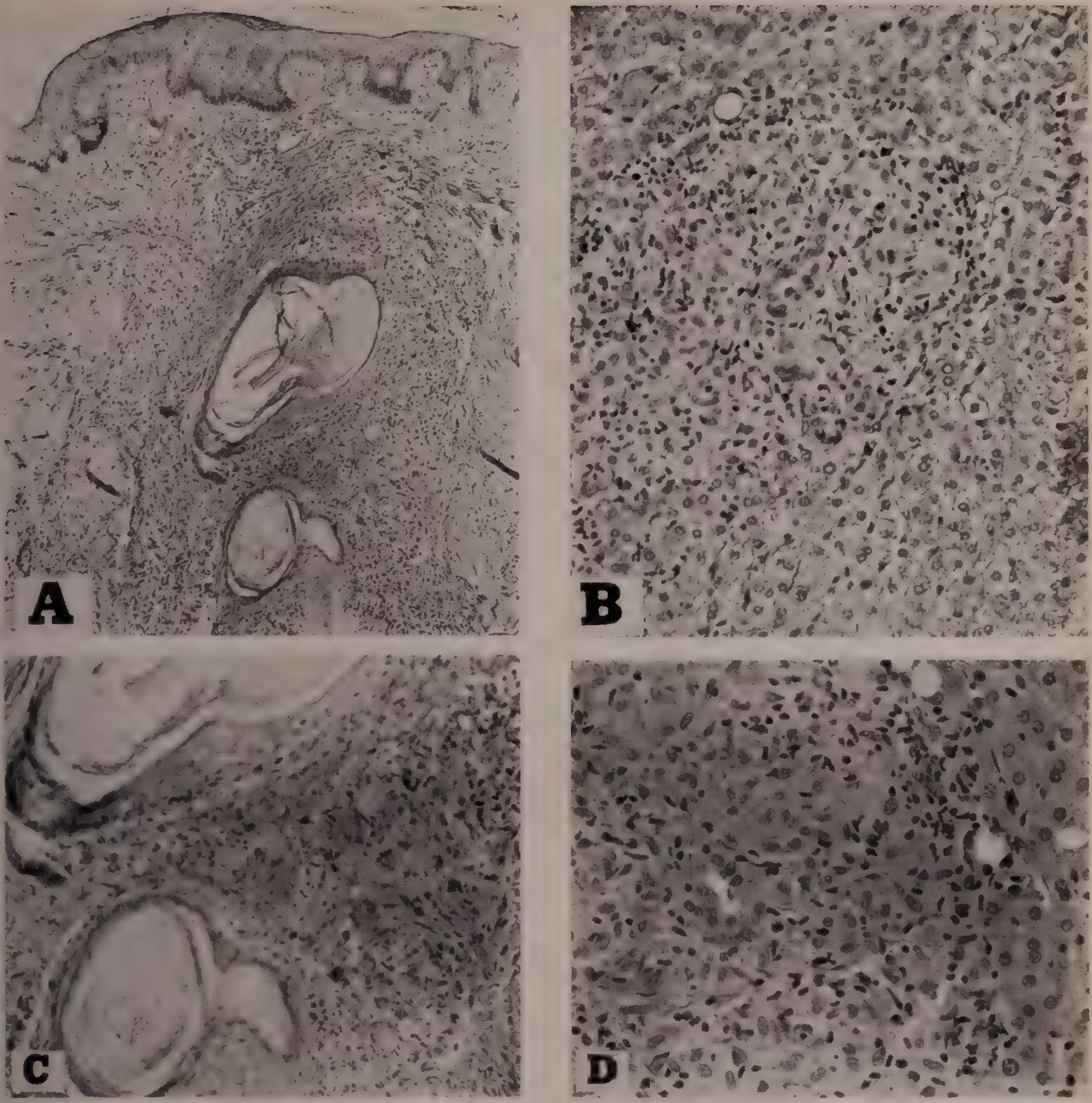

FIGURE 2. Histologic aspects of sarcoidosis. (A and C) Process around a follicle in low and high power magnification. (B and D) Process in the liver in low and high power magnification.

(normal 0 to 5). The total serum proteins were 7.6 Gm. per 100 ml.; the albumin-globulin partition was 3 and 4.6 Gm. respectively, and the albumin-globulin ratio was 0.65 (normal 1.8). Cultures of pustules yielded Staphylococcus aureus, coagulase-positive.

The following pertinent tests gave negative or normal results: alkaline phosphatase, serum calcium, smears for the lupus erythematosus cell, latex agglutination, C-reactive protein, electrophoretic pattern of serum protein, and serologic tests for syphilis.

Still more laboratory investigations of interest were as follows: A tuberculin test with second-strength protein purified derivative (equivalent to 1:100 of old tuberculin) gave negative results. The electrocardiogram showed normal findings. Radiography of the chest and long bones failed to show any pathologic condition. Electroencephalography revealed a diffuse abnormality.

Two skin biopsies were performed. One biopsy was of a follicular hyperkeratotic papule on the chest (Fig. 2A and C); the other was of one of the scaly areas overlying the papules on the back of the trunk. In both sections, sarcoidal infiltrate was seen, and the histologic reading of one of the representative sections, as interpreted by Arthur Hyman, M.D., was as follows:

> The epidermis shows a considerable deposit of pigment in the basal zone and is thinned in one area. The uppermost cutis under this thinned epidermis shows an ill-defined aggregate of epithelioid cells with a streak of lymphocytic types beneath it. Toward the middle of the sections, the cutis, except for its uppermost part, is occupied by a well-defined almost encapsulated collection of epithelioid cells with a few Langhans' giant cells and a slight admixture of lymphocytes. This infiltrate surrounds the cross sections of a hair follicle and is directly related to it. The diagnosis is sarcoidal reaction.

Acid-fast stains of tissue sections did not reveal any tubercle or lepra bacilli. An examination under the polarizing microscope showed no doubly refractile bodies.

Two Kveim tests were done seriatim. A biopsy of the first one which was performed after four weeks showed a granulomatous infiltrate which was insufficient for diagnosis. The second biopsy was performed after six weeks and was interpreted by Dr. Hyman as follows:

> The epidermis is not remarkable. The cutis to its depth shows well-defined masses, sheets, and round groups of edematous epithelioid cells with considerable scattered small round cell infiltrate. In the upper parts, there are a number of Langhans' giant cells. The diagnosis is a positive reaction to the Kveim test.

A scalene lymph node biopsy showed nests of epithelioid cells consistent with the diagnosis of sarcoidosis.

A liver biopsy was reported as granulomatous lesion of undetermined etiology (Fig. 2B and D); Boeck's sarcoid was considered a good possibility, but a definite diagnosis could not be made. A kidney biopsy showed a normal kidney.

The course of the patient in the hospital was as follows: On admission, he was given acetylsalicylic acid (10 grains every four hours) for pain, and novobiocin (1.5 Gm. per day) for the pustular element of the eruption. Topically he received potassium permanganate baths and an emulsion containing 3 per cent iodochlorhydroxyquin (Vioform). Within a few weeks, the pustular element of the eruption cleared. Antibiotics were discontinued, and topical medication was reduced to a simple petrolatum emollient.

Several weeks later, the patient developed more frequent episodes of joint pains although the swelling and tenderness of the joints had by now subsided. These pains were no longer controlled by acetylsalicylic acid. Therefore methylprednisolone was administered (24 mg. per day in divided doses). An improvement in the fever, arthralgia, and generalized weakness ensued. The lymphadenopathy became less marked especially in the cervical region. However, the headaches, dizziness, and skin eruption appeared to be unaffected by the steroid therapy. A recent tapering-off of the methylprednisolone to 16 mg. per day has resulted in exacerbation of those symptoms which it appeared to control at the higher level.

Comment

A process in the skin is frequently the first and sometimes the only detectable sign of sarcoidosis. Since the involvement of other organs may be concurrent or sooner or later may become concurrent, it is necessary to be familiar with the clinical varieties of cutaneous sarcoidosis to investigate for the possibility and probability of other organ involvement.

In parts of the world where sarcoidosis is common or where it has been investigated intensively (for example, in Scandinavia), elaborate morphologic classifications of cutaneous sarcoidosis have been evolved.[3] We may adapt these classifications to our part of the world as follows:

COMMON FORMS OF CUTANEOUS SARCOIDOSIS. Papular, nodular, and plaque forms are solid elevations on the skin that may be of near skin color or somewhat reddish and of no consistent patterned distribution, although they are found most frequently on the cheeks, the nose, and the lateral sides of the arms.

UNCOMMON FORMS OF CUTANEOUS SARCOIDOSIS. Lupoid types are tumefactions that are dusky red or purple (lupus pernio) when they are located on the chilblain areas (fingers and toes) or red and telangiectatic when they are located on the nose or around the eyes (angiolupoid).

Lupus vulgaris-like forms may conceivably be nothing more than true lupus vulgaris that has gone on to sarcoidal transition.

Annular formation may result from central healing of nodular lesions and sometimes shows atrophy at the center.

Psoriasiform appearances may supervene when sarcoid lesions are scaly and happen to localize on the sites of predilection of psoriasis or occur in patients with a tendency to psoriasis.

Lupus erythematosus-like pictures may be simulated when a sarcoidal process is located on the face, especially the "butterfly area." The pernio and angiolupoid forms may come to this at times.

Erythema nodosum-like lesions may occur and be clinically indistinguishable from the more banal appearances of erythema nodosum.

This list of the morphologic possibilities of cutaneous sarcoidosis probably can be lengthened considerably. For example, old scars have been found to develop sarcoid papules.[3] Papulo- and noduloulcerative forms that resemble papulonecrotic tuberculid[4] and erythema induratum[5] have been recorded. Sarcoidosis has been symptomatic of erythroderma and what appeared to be urticaria.[2] Eruptions as vague as the polymorphous light eruptions and occurring in the light-exposed areas have been resolved to be sarcoidosis.[6] Finally, sarcoidosis has been found to affect the mucous membranes rarely.[7] The nasal mucosa is most susceptible to such involvement. Ulceration is common in such sites, and stenosis may be a consequence of scar-healing.

Schaumann,[2] however, stated that pustules are never seen in Boeck's sarcoid. Our case presented pustules in addition to papules in perifollicular location. In fact, the general differential diagnosis of the superficial pyodermas was our first avenue of investigation. The question now is whether the pustulation in our case was an inherent part of the process or an incidental matter. We think it was inherent and consequent on the location of the sarcoid process around the follicular apparatus. In this site and so close to externality, we imagine the sarcoid infiltrates ulcerated as they sometimes do in less superficial positions. The finding of staphylococci in such pustules is not surprising since contamination with the ubiquitous staphylococcus can be expected on any break in cutaneous integrity, especially in perifollicular areas. In any event, the pustulation misled us for a while before we discovered the true nature of the process.

Summary

A case of systemic sarcoidosis is reported in which cutaneous involvement took the form of pustules and papules around hair follicles. Morphologic varieties of cutaneous sarcoidosis are reviewed briefly.

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Medical Care Insurance

A series of articles on health insurance prepared by the Associated Blue Shield Plans of New York State

LEONARD J. RAIDER, M.D., Editor

Voluntary Health Care Programs Today

An Appraisal of Accomplishments and Opportunities for Growth*

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AN ESTIMATED 132 million persons, or well over 70 per cent of those who are eligible for enrollment, have some form of voluntary health insurance—an accomplishment of great national importance and one which needs to be emphasized continually. The rate of enrollment has decreased of necessity, but total enrollment continues to grow, and there is room for further growth. Estimates indicate, for example, that 90 per cent of the approximately 17 million people living in New York State have some coverage.

But almost more remarkable than enrollment has been the growth in the extent of health insurance benefits. In spite of continual inflation in various components of medical care such as hospitalization, benefits to insured persons are growing rapidly as measured in constant dollars paid by health insurance agencies. This is logical since basic policies for medical and hospital care are being improved and extended, and medical expenses, such as those for hom and office physician visits and drugs, ar being covered by Blue Shield, Blue Cross and insurance companies. Probably a many as 40 million people now have suc extended coverage aimed at high costs.

This is impressive progress, yet the question remains of whether or not we ar approaching health insurance goals in term of what the American public wants. Blu Shield officers are inevitably concerne with such vital factors as fee schedules service benefits, physician acceptance, an the solvency of the prepayment organizations. Often these concerns are misinterpreted with the public not fully understanding administrative requirements an the need for voluntary support. However Blue Shield is voluntary health insurance participation is voluntary, and success i dependent on understanding and acceptanc by both subscribers and physicians. Blu Shield must be concerned with practica and consequential administrative and relationship problems, but equally important it must bring leadership to the professio in understanding how the success of th operation will be judged by the public. It is within this equation between publi and professional acceptance that I wish t comment on several important aspect related to Blue Shield.

Incidentally, this interplay is vastly different in our voluntary setting from wha it is under a compulsory governmenta program. But the place of government i health insurance is not resolved and neve will be as long as government insurance i an untried alternative. It will be used continually as a base for criticism of voluntary methods. Whether or not we have a breakthrough as is currently embodied in the King-Anderson Bill depends on the public's judgment concerning the success of voluntary effort in meeting public needs.

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* Adapted from a speech given at the Annual Program Conference, National Association of Blue Shield Plans, Chicago, Illinois, October 23 and 24, 1961.

It is wise to remember that there has been little expansion of government in the health field in recent years. Of total expenditures for personal medical care of $10,807,100,000 from 1949 to 1950, about 21.8 per cent came through government financing. By 1959 to 1960, a decade later, total expenditures had increased to $23,665,200,000, but the proportion financed by government is not greater but is slightly less, at 20.6 per cent. In spite of some increase in government programs such as Medicare and care for veterans and Indians, then, there has been no major change in the portion of personal medical care expenditures financed by government in the past ten years, and the major portion of government expenditures for personal health services continues to be for the care of mentally ill persons and those with tuberculosis and other long-term chronic illnesses.

Crucial issues

It seems to me that Blue Shield is concerned with several crucial issues that must be well understood and controlled to the general satisfaction of the public if voluntary health insurance is to continue as the primary financing mechanism for medical care. These issues are as follows:

PRICE. In the face of increased expenditures for medical care, the question that is continually raised is whether or not the increases in units of service—visits to the physician, admissions to hospitals, and use of prescription drugs—are necessary, and whether or not the price of a unit of service is justified. I believe that there is evidence with which to defend the present use of medical services and prevailing prices, although I will not try to describe such evidence here. But I do wish to point out that for physicians the focus is on fee schedules, the effect that insurance has on these schedules, and the total payment by the population for increased benefits. To what extent the conviction is well founded I do not know, but the public feels to a distressing degree that insurance inflates professional fees. There are ways to meet this criticism, but they require great effort by the profession.

USE. The use of services, particularly hospital care, is another serious problem. And the use of surgical services is being questioned also. I was astounded when a sample of physicians in an Eastern state stated on interview that in their opinion there is needless use of hospitals not only by their associates, but also by themselves individually. I know that the public demands more hospital care, not only when life is at stake, but also often when the hospital means greater comfort, reassurance, and convenience. To me these reasons seem defensible, but if they do not seem so to the profession or do not justify increased use, then they certainly will not be acceptable to the insured population, particularly as premiums rise. Any excessive or unnecessary incidence of surgery is wholly beyond understanding, and there needs to be assurance that such is not the case.

QUALITY. A third, if overlapping, area of vulnerability is the quality of medical care. The public is becoming more sophisticated in its demand for medical care and its judgment of results. This foreshadows even more criticism of the quality of medical care as related to the qualifications of physicians performing various services, their interrelationships for consultation, and the effectiveness of the efforts they make toward acquiring the most up-to-date knowledge with which to treat patients. The more complex issues involved in these criticisms have been of concern to the profession for years. The increased sophistication of a public with higher educational levels and larger incomes is reflected directly in increased demand. And higher demand is stimulated by the great amount of public information on health matters in the press and through every medium of communication. This all adds up to greater pressure on the profession to intensify their efforts at upgrading the quality of care and to insure that the public understands professional concern for such upgrading.

Many aspects of medical prepayment could be discussed. Among other matters is the need for enrolling more people and for the retailoring of some benefits so that a large segment of the public may have greater protection when illness necessitates higher expenditures for many or all types of medical care: physicians' services, hospitalization, drugs, and sometimes nursing home care. We can demonstrate that consequential progress is being made along these lines, but efforts must remain steady and persistent.

The three issues mentioned—use, price, and quality of medical care—call for the attention of everyone concerned with the success of voluntary health insurance and with maintaining public acceptance of such insurance as the primary way people pay for medical care. Further, it needs to be remembered and emphasized that there is little indication that these three issues would be resolved or better handled under a government system. In fact, I believe that the contrary might be true. Nonetheless, these are important issues for the average man who, in living longer, can well expect to impose many demands for medical care during his lifetime.

Major opportunities

These are crucial times, too, for Blue Shield. The three major criticisms mentioned present the greatest challenge to Blue Shield as they do to all voluntary health insurance, but they also present major opportunities, if I measure the situation correctly.

Sponsored by the medical profession, Blue Shield has been criticized for professional control and urged to include more lay representation on its governing boards. This may well be a wise course to follow, but I think the primary strength of Blue Shield is its physician support and the opportunity it provides the profession to come to grips with the serious criticism confronting them related to the use, price and quality of medical care. In my opinio Blue Shield provides a potentially excellen program with which the profession can aver criticism, maintaining control where it i necessary and giving reassurance to th public.

There is a simplicity in indemnity payments, and, in fact, some Blue Shield plan have not moved from that simple relationship of fiscal intermediary between subscriber and physician. The service benefit with all the administrative problems i imposes—the necessity for fee schedules and, more importantly, physician acceptance of such schedules—also provides th mechanism for public reassurance concerning the validity of pricing of physicians services. With or without the servic benefit, Blue Shield could operate withou concern for the validity of use or for th quality of care for which payment is made But it has so much to offer a beleaguere profession when it feels the need for joint approach to these problems that cannot but believe that its role will continually receive more recognition. Organization and administration are resisted b the profession as unwelcome but inevitabl components of medical care in these times yet professional success for the physician i dependent on his learning how to us organizations such as Blue Shield.

Success is partly a matter of more effective organization. It is also a matter c informing the public of what has bee accomplished, and certainly there is muc to report. It is a truism that in the lon run the public and their representative in government make the decision as t whether or not the voluntary system wit all of its accomplishments and opportunitie is to continue as the method of choice.

Number seventeen in a series of special articles on Medical Care Insurance

Medical History of Genesee County

Early Settlement to War of 1812

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THE CAMPAIGN OF General John Sullivan against the Iroquois Indians in 1778 revealed to many of his troops the beauty and fertility of Western New York. After the peace treaty was signed in 1783, a few hardy pioneers such as Charles Wilbur and Capt. John Ganson moved into the area which is now Genesee County. However, it was not until Joseph Ellicott made the survey of the Holland Purchase in 1798 and established the Land Office in 1801 that settlement began on any scale. The population of Batavia was 40 in 1801 and increased tenfold by 1805.

Illnesses of frontier life

Although the country was beautiful and fertile, it was not a healthy region, as attested by Ellicott himself and by other travelers. The chief disease was known as "fever and ague." This was undoubtedly malaria, as the terrain was very marshy and mosquitoes were plentiful. Ellicott remarks in his *Journal* for June, 1801, "The mosquitoes probably never were more plentiful. During the expedition (to Buffalo Creek) I calculate that I have lost by them at least four ounces of blood." On August 25, 1801, he states in a letter, "I am sorry to inform you that many of the settlers are grievously afflicted with ague and fevers; and one worthy industrious man has fallen a victim. He has left a wife and three children to lament his loss." The sickness apparently continued throughout the entire summer and fall, for Ellicott wrote again on November 7, 1801:

> This season has been extremely unfavorable for business in this part of the country, as well on account of the continual rains as that of almost the whole of the people in the infant settlement having been afflicted with the Bilious and other fevers, which circumstance has greatly retarded all our operations as well as the settlement and add to the catalogue of our misfortunes.

Another account of the diseases of the region with some views on their possible etiology is given by Timothy Dwight, an early visitor to Western New York, in his book, *Travels in New England and New York,* published in London in 1823. He states:

> The diseases which principally prevail here (New England and New York) are the "fever and ague," intermittents without ague and bilious remittents. "Fever and ague" may be considered as nearly universal; almost all the inhabitants being sooner or later seized with it within a few years of their immigration. This disease from the violence of its affections, and long continuance, its return at the same season for several successive years, and the lasting impression which it often leaves on the constitution is regarded by the people of New England with a kind of horror. The other two diseases, though common to most parts of the country, are yet much more predominate in particular places. Along the Genesee they all abound. They are frequent also, as I was informed, on the southern shores of Lake Ontario, and in spots around the outlets of most of the smaller lakes and in various others. A tract around the Onondaga salt springs is still more sickly and fatal.
>
> To the evils mentioned above I ought to add the exposure of the recent settlers to walking and working a great part of their time in moist ground; the badness of their houses; the poorness of their fare; together

> with the difficulty of obtaining proper medicines, good nurses and skillful physicians. Nor ought it to be forgotten, that the streams are frequently choked, rendered sluggish, and raised in many places above their usual height by the timber which is cut down, or which, being girdled is suffered to fall into their channels. In this manner they affect the atmosphere in as noxious a manner as mill ponds and other artificial accumulations of water.

Obviously, the early settlements in Western New York were extremely unhealthy habitations. There was at this period no exact knowledge of the causation of these fevers and no specific or very effective treatment. One of the wives of the earliest settlers of Le Roy tells of the Indians helping her treat her family, sick with a prevailing influenza, by means of the Indian sweat. The procedure was to dig holes in the ground and put in hot stones, over which hot water was poured. The patients were then placed in the steam and covered with blankets until they were well "sweated." A cure was often effected by this means. Another regime for the "fever and ague" is given in a letter from Robert Morris to Charles Williamson, the land agent, in the summer of 1794. His advice was as follows:

> I have received in due course your several letters of the 2nd and 22nd of June and of the 1st of August and sorry I am to perceive by the last that you had then the ague and fever. I fear you do not take good care of yourself. You should avoid the morning and the evening dews and sleep warm, live well and drink good Madeira wine. Surely if these things are properly attended to, the ague will abandon you and I hope to hear soon that it is gone.

Other perils of frontier life

Frontier life presented other perils in addition to illness. Accidents were frequent, and wild animals and snakes were also troublesome. Bears were common, wolves were plentiful, and rattlesnakes were frequent invaders of the settlers' cabins. John Maud, an English traveler, gives this account in his memoirs of a rattlesnake bite and its treatment in the year 1800:

> On Flint Creek, between Naples and Geneva, Mr. Armstrong gave me a large rattle of 10 joints, lately taken from a rattlesnake which had bit his brother. On receiving the bite the youth tied a string very tight around his leg, a little above the wound; for this purpose a withe of the bark of white ash is the best as it infalliably prevents the poison from ascending beyond it. He then went home and cut off a piece of flesh from his leg where the fangs had entered, squeezed out the blood, and put salt and indigo into the wound, over which he held a piece of the flesh of the rattlesnake; when this grew putrid, which it did in a few minutes, he applied a fresh piece till he had used up all the snake. For a few hours his leg continued swelled, and much yellow matter oozed from the wound; he was, however, enabled to go to his work the second day. I was shown the best antidote for the bite of a rattlesnake; these antidotes are numerous. The plant I was now presented with I do not recall having before seen. It was Solomon's Seal.

This prompt and vigorous treatment was apparently most successful.

It must be remembered that during this period, roughly from 1800 to 1812, Genesee County was definitely a frontier or backwoods region. For example, the population of New York City was estimated at 182,247 in 1774. There was a vast difference between medical practice in a city of that size and a frontier territory. The pioneer physicians had many hardships to face. They had to ride on horseback along the trails and through the woods with their own drugs from herbs and barks, and few of their patients were able to pay them much of anything for their services.

Fee schedules

Some idea of the types of medical practice at the beginning of the nineteenth century can be obtained from a fee schedule published by the New York City physicians about 1800. Among other items, we find the following types of medications: powders, pills, boluses, electuaries, mixtures, decoctions, tinctures, infusions, lotions, cerates, and blister plasters. The prices were from $0.12 a dose for most of them up to $2 for a large blister plaster. Fees for various services were as follows:

Medical Service	Dollars
Dressing wounds	1 to 2
Applying cupping glasses	4
Bleeding in arm	1
Bleeding in foot	2
Attending in smallpox	5 to 10

Puncture in oedematous swellings	2
Inserting spue	2
Inserting seton	5
Introducing catheter first time	5
Reducing simple fracture	10 to 20
Reducing compound fracture	30
Setting dislocations	5 to 20
Reducing hernia	25
Amputating breast	50
Amputating arm or leg	50
Operation for aneurysm	100
Operation for hernia	125
Operation of lithotomy	125
Operation of trepanning	100
Under midwifery we find the following charges:	
For a common case	15 to 25
For tedious or difficult case	25 to 50

Frontier physicians

In spite of the difficulties of practice, between 15 and 20 physicians ventured into Genesee County between 1800 and 1812. The first was David McCracken, M.D., who came there in 1801. His name is listed in an association of Western New York physicians in that very year. In January, 1802, he bought lot 8, section 10 of the survey, a tract of 152 acres for $418. We know little more about him, except that he moved to Rochester in 1818.

Joseph Alvord, M.D., came to Batavia in 1802 and was slain in the attack of Lewiston in 1813. A David Fairchild, M.D., was reported as living in Le Roy in 1802, but he did not remain there. Reuben Town, M.D., who practiced irregularly, was mentioned as living in Batavia in 1803. In the same year Le Roy gained its first settled practitioner, William Coe, M.D., who also devoted his evenings to teaching. In the year 1805 Ella Smith, M.D., came to Le Roy, and in 1806 or 1807 Levi Ward, M.D., came to Bergen from Connecticut. It is said that Dr. Ward came to the new country to find a home for himself and his family rather than to practice his profession. He was one of the most active of the early settlers. He built the first frame house in the Bergen area, the first marriage was held in his house, he opened the first store in Bergen in 1808, and he was the first supervisor. In 1817 he moved to Rochester where he lived to the age of ninety years. He was a delegate from the Genesee County Medical Society to the New York State Medical Society meeting in Albany in 1810.

In 1808 Benjamin Hill, M.D., came to Le Roy. He bought 448 acres of land and departed, but returned some years later to settle there. The same year a more permanent resident came to the community, Fred Fitch, M.D. He is described as a skillful physician of good standing. He is also described as eccentric, stirring, enterprising, and fond of military display. He is said to have raised a company of artillery of which he became captain. While attending a "general training" exercise with his company at Stafford, he stabbed himself in the leg while demonstrating his prowess at sword play. As a result, his leg was amputated. He eventually moved from this region to Ypsilanti, Michigan, where he died.

In 1810 Charles Chaffee, M.D., came to Alexander, Elijah Stoddard, M.D., came to Pembroke, and William Sheldon, M.D., came to Le Roy. Dr. Sheldon became an important and valued citizen of the community of Le Roy. He came to Le Roy on horseback from Bennington, Vermont. His saddle bags contained medicines, a lancet, and a turnkey for pulling teeth. He was penniless when he arrived at Ganson's Tavern to rest for the night. The innkeeper's wife became ill during the night, and Dr. Sheldon was called to attend her. Later he was prevailed on to settle there and take up practice. During the War of 1812 he was made captain of a volunteer militia company and an aide-de-camp to Gen. Daniel Davis. He was acting in this capacity at the Battle of Fort Erie and was near the General when the latter sustained his fatal wound. Dr. Sheldon went through seven skirmishes unharmed, but was captured at Black Rock and was imprisoned for six months at Montreal. He served several terms as supervisor and as sheriff and died in June, 1874.

The records show John Z. Ross, M.D., as living in Batavia in 1811, the death of John Hall, M.D., in Alexander in 1812, and also, in 1812, the presence of Silas Taylor, M.D., in Byron and Abel Tennent, M.D., and Daniel White, M.D., in Pavilion. The following account is quoted in full from an old *Gazeteer:*

> Dr. Daniel White, the first practitioner in

what was Covington was a surgeon in the War of 1812. He was very skillful, had a large practice over what is now Pavilion, gave calomel and whiskey freely as the practice was, and was more companionable than constant as his wife believed. He was a leading member and champion of the Masonic order. While leading a grand Masonic procession on "St. John's day," at Pavilion, arrayed in royal robes, his wife, who had more temper than self respect, and who frequently gave her husband the benefit of it, brought up the rear, dressed in the most slatternly garments imaginable. Their daughter Volina was the first child born in the town.

The population of Batavia in 1812 was about 1,500, and the entire county was showing a steady and rapid growth. This was interrupted by the War of 1812. The settlements were not involved in the skirmishes, but the sound of the cannons from the battles of the Niagara frontier were heard frequently. The Genesee County settlements became a haven for refugees from the frontier villages, a rallying point for troops, and a site for the care of wounded soldiers. Gen. Winfield Scott, who was wounded at Lundy's Lane, was taken by litter to the Ganson Tavern in Le Roy where his wounds were cared for.

There were apparently four of these early physicians involved in the War of 1812: Dr. Fitch who raised and trained a company of militia, Dr. White of Pavilion, Dr. Sheldon, aide-de-camp to General Davis and later a prisoner of war, and Dr. Alvord, killed in the raid of Lewiston.

As would be expected, the war caused a serious disruption of the affairs of the settlement, and it was not until about 1818 that things began to return to normal in Genesee County. From this point on, growth was steady and rapid, so that by 1830 the population of Batavia was estimated at about 4,264 and that of Genesee County was thought to be 26,008.

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Fingerprints clue to mental illness

Patients suffering schizophrenia were found to have a high incidence of unusual fingerprints in a study reported by Theophile Raphael, M.D., and Louise G. Raphael in the April 21, 1962, issue of the *Journal of the American Medical Association*. These findings support the theory that a genetic deficiency results in a vulnerability to a variety of disorders and abnormalities. Fingerprints develop during the third and fourth months of pregnancy, and abnormal prints have been linked to such congenital conditions as epilepsy and mongolism.

The fingerprints of 100 male patients aged twelve to sixty-seven in a mental hospital were compared with Scotland Yard fingerprints, the largest, most complete and reliable series for the general population.

The comparison revealed that among patients there was an increased incidence of whorls and arches. The patients had fewer ulnar loops than the normal population group. A striking difference was the high incidence of short, broken lines in the center of whorls among the patients as contrasted with the orderly concentric circles among the normal population. This "ridge dissociation" found frequently among the patients is rare in the general population.

These findings raise the possibility of detecting vulnerability to various abnormalities and disorders and warrant more intensive investigation.

BILLSBORD

Random Remnant from the Department of Trivia

Lo! how aspirin and Anacin and, yea, the wrestler's mat
Have lost their TV glamour and "the twist" is now old hat!
Now a new vexatious problem bugs every square and every cat
Is it saturates or unsaturates that make a head grow fat?

Ole Doc

"Times sure change," muttered ole Doc on his recent morning visit; "bout the only place you can see a truss these days is in the surgeons' dressing room."

* * *

"Means Test," ole Doc snorted, "one hears so much about the degradation of charity, the humiliation of others knowing a person needs help, and the consequent affront to the dignity of an individual, it gets harder and harder to remember that we once were taught that charity was a virtue and pride akin to sin."

* * *

One needed no calendar or sentimental ballad to realize that spring had arrived on schedule and with all banners flying. The sun was warm enough to cause shedding of overcoat with all the alacrity which in the days of the dear departed institution of burlesque one associated with the opening bars of "A Pretty Girl is Like a Melody." If you hadn't seen your first robin one of the group crowding the office had. The maples were tapped reported the G.P., and the general conversation was not concerned with either virus, stock market, or problems both personal and professional but instead was of summer camps, boats, or golf. The only extraneous note was the attitude of ole Doc; not exactly dejected but sort of grumpy and subdued. His mood was soon noted and the pack seized their rare and unexpected opportunity to turn on him, mocking his lack of vitality and accusing him of endocrine atrophy, jealousy of their youth, and preoccupation with the past. For the first time they sensed the great advantage that always tips the scales on the side of youth—that if you can't out-experience, out-smart, or out-think them you can always out-wait them.

The old man took it and after their departure drawled in a quizzical manner, "You know they're right. When one senses the lack of inner response to such a spring day, he can't help regret the past. If a man is lucky there are only two annual events he has to fear when he is old, the annual college reunion and spring—for these are stark, even brutally realistic mirrors to record the fact that, regardless of illusion, one not only grows old but also does not escape the toll such a process exacts. I don't dislike spring. I don't want winter to go on and on. It's just that it no longer gives me that inner kick, that inner reaction my mother thought she could control with sulphur and molasses but which I know can never be controlled until it is destroyed by age. Once spring meant marbles, then baseball, then women, and now—income tax! I honestly don't think I want to be young again. In fact I am sure I don't. I couldn't stand the dreary prospect of a future made up of Kennedy after Kennedy and their respective Jacks and Jills. No, I don't want to be young again; I just wish I wasn't so damn old!"

* * *

"Marriage," pontificated ole Doc, "sometimes explodes and disintegrates at the first period of stress; sort of dies by crisis at about the time she begins to think of it in terms of a ring around the bathtub instead of around a finger. And then again it just sort of peters out by lysis but you know it is dead when he buys his own can opener and she orders a second morning newspaper."

* * *

The daily bull session was almost over before ole Doc came in obviously ruffled and sputtering about the parking situation. One could sense he was brimming over with more than his usual quota of discontent at the world of today, and all it took was a casual question to get him started.

"The trite phrase 'the customer is always right' used to be very popular but as is true of most generalizations it was not always valid. However, it did create a philosophy of service and a code of behavior that brought satisfaction to the customer and profits to the merchant. The premise of today could be expressed as a question: Has the customer any rights? Companies build modern establishments; they hire trained personnel men and psychologists to study human reactions. But are they used for the comfort or service of the customer? No! they are all busy in employer-employe relationships. They build parking places or pressure the community to install parking meters. For customers? Well that is what they say, but most of them are appropriated and used by the employes. I am not antiemploye. I want them to have everything the traffic allows, but it is about time someone realized that stores were not built to make jobs or provide economic stability but to serve the public; that railroads and busses were not established to provide economic security and opportunity to some depressed area but to serve a public need for transportation facilities; and that hospitals were built to care for patients and not for the care and feeding of employes nor as a means to enhance the prestige or satiate the ambition of any one of us."

* * *

When the daily bull session seems sterile and desultory it usually can be enlivened by teasing ole Doc about one or the other of his two pet peeves—the Yankees or golf. Today he was the unwilling recipient of many apparently well-intentioned suggestions as to the adaptability of golf for a man his age, accompanied by generous offers of free instruction. As expected this precipitated violent reaction, even more vehement than usual. "Let me tell you this," he scolded as he wagged his finger under my nose. "If I need to walk for exercise I can walk without having eighteen silly flags to show me the way, and if I need a cane I'll buy a stick and not have some defenseless youngster toting my luggage, and if I want to pay someone to cut grass it will be on my own lawn! The only difference between golf and begging on the street is that in golf it's the blind man that is trying to put something in a cup."

WRC

Chronic drug therapy and anesthesia

The administration of certain drugs now in common use prior to surgery may influence profoundly the reaction of the patient to anesthesia and surgical stress, according to an article by C. R. Stephen, M.D., in the September, 1961, issue of the *Journal of the Tennessee State Medical Association*. Phenothiazine compounds and certain antihypertensive drugs, especially the Rauwolfia derivatives, may, in combination with the anesthetic, induce severe hypotension.

If corticosteroids have been given, the possibility of adrenocortical suppression must be considered, with consequent reduced ability of the patients to withstand surgical stress. In such cases, supplementary cortisone should be given in appropriate amounts preoperatively.

Some antibiotics also have a curarizing effect, and the anesthesiologist should know if such drugs have been given. There are also certain hazards associated with rapid digitalization twenty-four to forty-eight hours before the operation. A careful history of drug administration should be elicited from all surgical candidates so that proper steps can be taken to avoid complications from this source during and after the operation.

Necrology

Julius B. Bailin, M.D., of the Bronx, died on April 12 at Hunts Point Hospital at the age of sixty-seven. Dr. Bailin graduated in 1923 from Columbia University College of Physicians and Surgeons and interned at Lincoln Hospital. He was director of the Talbot Center for Treatment of Alcoholism and a member of the board of managers of the Bronx Union YMCA. Dr. Bailin was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Martin Barad, M.D., of New York City, died on April 25 at The Mount Sinai Hospital at the age of thirty-five. Dr. Barad graduated in 1953 from the State University of New York at Syracuse College of Medicine and interned at The Mount Sinai and Bronx Veterans Administration Hospitals. He was an assistant attending psychiatrist at Vanderbilt Clinic, an attending psychiatrist at the Hospital and Home for Aged and Infirm Hebrews, and an instructor at the Psychoanalytic Clinic of Columbia University. Dr. Barad was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), an Associate of the American Psychiatric Association, and a member of the Association for Research in Nervous & Mental Disease, the New York Society for Clinical Psychiatry, the New York County Medical Society, and the Medical Society of the State of New York.

Clarence Walter Barth, M.D., retired, of Schaghticoke, died on March 28 at his home at the age of sixty-seven. Dr. Barth graduated in 1918 from Albany Medical College and was a Life Fellow of the American Psychiatric Association.

Harold R. Brown, M.D., of New York City, died on April 4 at the Brooklyn Veterans Administration Hospital at the age of sixty-eight. Dr. Brown graduated in 1917 from Fordham University School of Medicine. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Eugene Calvelli, M.D., of Port Washington, died on April 23 at his home at the age of eighty-two. Dr. Calvelli graduated in 1916 from New York University and Bellevue Hospital Medical School. He was a consulting cardiologist at Nassau Hospital, St. Joseph's (Far Rockaway) Hospital, Mercy Hospital (Rockville Centre), Nassau County Tuberculosis Hospital, and Community Hospital at Glen Cove, a consulting physician at Meadowbrook Hospital, and a senior attending physician at St. Francis Hospital (Roslyn). Believed to have been the first cardiologist to practice in Nassau County, he had formerly taught at the New York University College of Medicine, retiring as assistant clinical professor of medicine. A past-president of the Nassau County Medical Society, Dr. Calvelli was a Fellow of the American College of Cardiology, a Fellow of the American College of Physicians, and a member of the New York Academy of Medicine, the Medical Society of the State of New York, and the American Medical Association.

Newton David Chapman, M.D., of Port Richmond, died on April 23 at his home at the age of ninety-four. Dr. Chapman graduated in 1892 from New York University College of Medicine. Retired, he was a member of the Richmond County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry David Diamond, M.D., of New York City, died on April 8 at Memorial Hospital at the age of forty-four. Dr. Diamond graduated in 1944 from the University of Louisville School of Medicine. He was an attending physician and chief of the Lymphoma Service at Memorial Hospital for Cancer and Allied Diseases and the James Ewing Hospital, an attending physician at New York Hospital Outpatient Department, and a consulting physician in neoplastic disease at the New York Infirmary. Since 1946 he had served on the faculty of Cornell University Medical College as clinical associate professor of medicine. Dr. Diamond was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the American Association for Cancer Research, the American Federation for Clinical Research, the American Radium Society, the American Society of Hematology, the James Ewing Society, the International Society of Hematology, the Society for the Study of Blood, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Julius Dobkin, M.D., of the Bronx, died on April 18 at Lebanon Hospital at the age of fifty-four. Dr. Dobkin graduated in 1936 from New York Medical College and interned at Metropolitan Hospital. He was a clinical assistant attending pediatrician at Lebanon Hospital. Dr. Dobkin was a member of the American Academy of General Practice, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Heyward Harris, M.D., of New Rochelle, retired, died on April 26 at his home at the age of sixty-one. Dr. Harris graduated in 1927 from New York Homeopathic Medical College and Flower Hospital. He was a Member of the American Psychiatric Association.

Bernard Kantrowitz, M.D., retired, of New York City, died on April 17 at Montefiore Hospital at the age of seventy-eight. Dr. Kantrowitz graduated in 1907 from Long Island College Hospital Medical School.

Robert Lenz, M.D., of New York City, died on April 11 at the Bergen Pines County Hospital at the age of seventy. Dr. Lenz received his medical degree from the University of Vienna in 1911. He was a member of the American Trudeau Society, the New York County Medical Society, and the Medical Society of the State of New York.

Kenneth Duncan Nichol, M.D., of Brooklyn, died on February 11 at his home in Monroe at the age of fifty-nine. Dr. Nichol graduated in 1923 from the University of Toronto Faculty of Medicine. He was an attending pediatrician at Methodist Hospital of Brooklyn. Dr. Nichol was a Diplomate of the American Board of Pediatrics and a member of the Brooklyn Academy of Pediatrics, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Russell Lowell Putnam, M.D., of New York City, retired, died on April 19 at New York Hospital at the age of ninety-two. Dr. Putnam graduated in 1895 from Harvard Medical School. He was a consulting surgeon at Lincoln Hospital. Dr. Putnam was a Fellow of the American College of Surgeons and a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Miron Tabor, M.D., of Woodside, died on February 18 at the age of seventy. Dr. Tabor received his medical degree from the University of Prague in 1920. He was a member of the Queens County Medical Society and the Medical Society of the State of New York.

John McNamara Vetter, M.D., of New York City, died on April 17 at St. Barnabas Hospital for the Chronically Ill at the age of thirty. Dr. Vetter graduated in 1957 from New York Medical College. He was a resident surgeon of the Second Surgical Cornell Division, Bellevue Hospital.

Live birth survival rate

Almost 98 per cent of the babies born alive in the United States survive, according to an article in the May, 1962, issue of *Today's Health*. The downward trend in infant mortality dipped to 26 per 1,000 births in 1956, an all-time low for any year up to that time. In 1957 and 1958, a slight increase in infant deaths under one year of age was reported. But the rate dropped again in 1959 and in 1960. In 1960, 5,000 more babies were saved than in 1958, and the rate per 1,000 live births hit an all-time low of 25.7. The record is especially impressive, considering the greatly increased number of births annually over the past eight years. Since 1954 at least 4.2 million live births have been recorded annually: 8 each minute, 480 each hour, and 11,520 each day of every year.

Medical Meetings

Eye Residents Association of The New York Hospital-Cornell University Medical College

The third annual meeting of the Eye Residents Association of The New York Hospital-Cornell University Medical College was held on April 16 and 17 at The New York Hospital.

Symposium on oral disease

A joint medical and dental symposium on oral disease will be held on Friday, June 1, in the Empire Room of the Waldorf-Astoria Hotel, New York City. Leonard W. Larson, M.D., president of the American Medical Association, will be the principal speaker at the meeting which is sponsored by the American Geriatrics Society. All interested physicians and dentists are invited to attend.

Metropolitan Chapter, Professional Group on Bio-Medical Electronics

The Metropolitan Chapter of the Professional Group on Bio-Medical Electronics will hold a meeting on June 5 at 8:00 P.M. in Welch Hall at the Rockefeller Institute, 67th Street and York Avenue, New York City. G. Peter Halberg, M.D., director, Electroretinography Service, New York Medical College, will speak on the subject "Organization of an Electroretinography (ERG) Service." A premeeting dinner will be held at the Sutton Restaurant, 1063 First Avenue, New York City.

A.M.A. and the American College of Chest Physicians

The American Medical Association and the American College of Chest Physicians will hold a combined scientific session at McCormick Place, Chicago's new convention center, on Monday, June 25. This will be the closing day of the five-day meeting of the chest physicians and the opening day of the American Medical Association's annual meeting. Arthur M. Master, M.D., New York City, will deliver the opening address at the joint meeting. His topic will be "Fads and Public Opinion in Heart Disease."

Rocky Mountain cancer conference

The sixteenth annual Rocky Mountain cancer conference, cosponsored by the Colorado Division of the American Cancer Society and the Colorado Medical Society, will be held in Denver, Colorado, in the Brown Palace West Hotel, July 13 and 14.

A feature of the meeting will be panel discussions on "Neoplasms Complicating Pregnancy" and "Carcinoma of the Colon." Among the guest speakers will be George E. Moore, M.D., of Buffalo.

For further information write to: Rocky Mountain Cancer Conference, 1809 East 18th Avenue, Denver 18, Colorado.

Congress on occupational health

The twenty-second congress on occupational health will be held in Boston on October 2 and 3. The two-day meeting at the Somerset Hotel is sponsored by the American Medical Association's Council on Occupational Health.

Subjects to be discussed at the congress include: history and problems of occupational health in New England, small plant occupational health programs, confidentiality of occupational health records, human factors in accidents, mental and emotional problems in the worker, and occupational health and workmen's compensation problems posed by handicapped workers.

For information write to: Council on Occupational Health, American Medical Association, 535 North Dearborn, Chicago 10, Illinois.

American Society of Cytology

The American Society of Cytology (formerly the Inter-Society Cytology Council) will hold its tenth annual scientific meeting at the Chase-Park Plaza Hotel, St. Louis, Missouri, November 8 through 10. For further information write to: Paul A. Younge, M.D., Secretary-Treasurer, American Society of Cytology, 1101 Beacon Street, Brookline 46, Massachusetts.

University of Texas M. D. Anderson Hospital and Tumor Institute

A clinical conference on "Tumors of the Skin" will be held at The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas, November 9 and 10. The etiology, epidemiology, diagnosis, and treatment of skin tumors will be discussed in lectures and panel discussions. Among the invited guest speakers is Herbert Traenkle, M.D., Roswell Park Memorial Institute, Buffalo.

For further information contact: J. Leslie Smith, Jr., M.D., Department of Pathology, The University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston 25, Texas.

Abstracts

Rathbun, M. L., Broad, R. H., Font, W., Milham, S., and Ames, W. R.: Mass immunization with Sabin and Cox oral poliomyelitis vaccines; experience in Monroe and Tompkins Counties, New York, 1960, New York State J. Med. **62:** 1767 (June 1) 1962.

In 1960 a mass poliomyelitis immunization program was conducted in Monroe County, using Sabin oral monovalent vaccine administered in three doses to preschool and school age groups, and in Tompkins County, using Cox oral trivalent vaccine administered in a single dose to all age groups. Both vaccines are easily administered, tasteless, and acceptable to all age groups. There were 6 cases of cutaneous allergic manifestations, possibly owing to penicillin sensitivity, following feeding of the Sabin vaccine; many minor suspected reactions were reported after the first dose of Sabin vaccine but fewer after the second and third doses; also minor gastrointestinal complaints were prevalent after administration of the Cox vaccine. The 1960 poliomyelitis season in Monroe County was similar to that of recent years; none of the 7 cases of paralytic disease had been given Sabin vaccine. No poliomyelitis occurred in Tompkins County in 1960. In comparing the oral vaccines according to per cent of fourfold or greater rises in antibody titers, Type I Sabin and Type III Cox were excellent as original and booster antigens. Type III Sabin and Type II Cox were much less effective. Because of the comparatively poor showing of Type III Sabin vaccine and the increasing importance of Type III as a cause of paralytic poliomyelitis, an immunization schedule of at least two doses of Salk vaccine, followed by boosters of Sabin vaccine is recommended.

Hotchin, J., Plager, H., Decher, W., and Jacobs, J.: Antibody response to two different live poliomyelitis virus vaccines, New York State J. Med. **62:** 1776 (June 1) 1962.

A comparison, consisting of systematic double-blind, controlled titrations of pre- and postvaccine blood specimens from volunteers, was made between Sabin poliomyelitis vaccine in monovalent form, administered orally in three doses in Rochester (Monroe County) and Cox vaccine in trivalent form, administered orally as a single dose in Ithaca (Tompkins County). A neutralization test in primary cynomolgus monkey kidney tissue using a CPE (cytopathic effect) end point and a metabolic inhibition neutralization test in monkey kidney cells were performed. Types I and II Sabin vaccine were of approximately equal antigenicity while Type III produced somewhat less antibody response, whether the population was classified according to age or according to Salk vaccination status. In general the booster effect decreased with all three types as the amount of prevaccination antibody increased. Cox Type III vaccine was a better antigen than Types I and II. Both vaccines performed especially well in the elimination of antibody gaps when the vaccinee had received previous Salk immunization.

Tessler, A. N., Morales, P. A., and Hotchkiss, R. S.: Indications for artificial dialysis, New York State J. Med. **62:** 1792 (June 1) 1962.

Artificial dialysis is used in the treatment of acute renal insufficiency, intoxication with dialyzable non-nephrotoxic agents, selective forms of chronic renal disease, and intractable uremia, overhydration, or metabolic coma in patients with either surgically or medically reversible disease. From January, 1959, to December, 1960, 26 patients have been dialyzed, using a disposable twin coil unit. The indications for dialysis must be determined in conjunction with medical measures to regulate acid-base and fluid balance, to supply calories, and to sustain the cardiovascular and respiratory function.

Gold, J. A., O'Connell, F., and Caldwell, F.: Serial serum enzymes in infectious mononucleosis, New York State J. Med. **62:** 1796 (June 1) 1962.

An attempt was made to correlate serial serum enzymes with the clinical course of infectious mononucleosis. The SGO-T (serum glutamic oxalacetic transaminase) level was elevated in 31 of 36 patients (86 per cent) with infectious mononucleosis. The SGP-T (serum glutamic pyruvic transaminase) level was elevated in 21 cases (66 per cent), normal in 10, and not obtained in 5. LDH (lactic dehydrogenase) activity was increased in all of the 7 patients studied; in 2 cases it was elevated when the SGO-T and SGP-T levels were within normal limits. In 80 per cent of the cases the highest transaminase levels were recorded during the first two weeks following the onset of symptoms, indicating that hepatic alterations occur early in the course of infectious mononucleosis, but they returned to normal in all of the patients, during the third to fifth week of illness in two thirds of the patients. Serum transaminase levels were normal in 18 cases of rubella, which may mimic infectious mononucleosis.

Botstein, A., and Brown, E. B.: Gamma globulin in the prevention of upper respiratory infections in children, NEW YORK STATE J. MED. **62:** 1799 (June 1) 1962.

A double-blind study was performed on 143 children from one to nine years of age with histories of frequent upper respiratory infection to evaluate the prophylactic value of gamma globulin. Half of the children received 0.2 cc. of gamma globulin per pound of body weight at monthly intervals for five months. The alternate patients received equal amounts of saline. The results were identical for the two groups as a whole. However, of 16 asthmatic children in the study, the asthmatic patients on gamma globulin had about one-half as many upper respiratory infections as the asthmatic patients on placebo, and fewer asthma attacks. Two thirds of the parents, irrespective of the agent given, thought the children had improved. No members of the gamma globulin groups had measles. Chickenpox and mumps occurred in both groups. It is possible that asthmatic and maybe all allergic children have a specific deficiency of their gamma globulin which prevents an adequate antibody formation and causes the allergic response to upper respiratory infections.

Boyarsky, S., and Goldenberg, J.: Detection of bladder distention by suprapubic percussion, NEW YORK STATE J. MED. **62:** 1804 (June 1) 1962.

Twenty-nine adult patients with indwelling catheters were studied by percussion for bladder distention. In only one instance was suprapubic dullness encountered when less than 100 cc. of fluid were present in the bladder. The average filling of the bladder which permitted the detection of 1 cm. or 1 fingerbreadth of dullness above the symphysis was 134 cc. If the results of abdominal percussion, intravenous urogram, and phenolsulfonphthalein tests are inconclusive, or if the patient's condition demands more immediate action, as in the case of fever and pain, then diagnostic catheterization is indicated.

Sasson, L.: Comparison of hexylcaine and tetracaine as topical anesthetics in gastroenterologic procedures, NEW YORK STATE J. MED. **62:** 1808 (June 1) 1962.

A comparison was made between hexylcaine hydrochloride (Cyclaine hydrochloride) used as a topical anesthetic in 500 cases and tetracaine hydrochloride (Pontocaine hydrochloride) in 100 cases. Preanesthetic medication was given only for major procedures. With tetracaine 5 out of 100 patients had unsatisfactory anesthesia, resulting in unsuccessful or incomplete procedures. There were no failures with hexylcaine. The time consumed in administering the anesthetic was from ten to twenty minutes for tetracaine and from two to three minutes for hexylcaine. There were no adverse reactions to either anesthetic. The relative safety of hexylcaine and the simplicity of its administration permit its use in minor procedures as well as in major ones.

Giannattasio, R. C.: Congenital dysplasia of the hip, NEW YORK STATE J. MED. **62:** 1812 (June 1) 1962.

In 386 newborn infants examined twice in the first week of life, 20 cases of dysplasia of the hip were found, an incidence of 5.1 per cent. Of the 366 normal infants, followed through their first years of life, asymmetry of skin folds, extra skin folds, partially concealed labium majus on one side, and differences in the length of the extremities were misleading and not indicative of underlying dysplasia of the hip. The following clinical and roentgenologic data are indicative of congenital dysplasia of the hip: limitation of abduction of the flexed thigh, jerk of entry and exit, and jerk of exit. Roentgenograms which are taken of infants who are suspected of having a dysplastic hip will support the diagnosis in 50 per cent of cases. No warning clinical signs of congenital dysplasia of the hip were found at birth in 19 infants who were later shown to have abnormal hips.

Stevens, M. A., McCown, I. A., and Campbell, E. A.: Control of swelling in sports injuries; a key to prompt and complete recovery, NEW YORK STATE J. MED. **62:** 1817 (June 1) 1962

A study was undertaken to determine adequate treatment of post-traumatic swelling in sports injuries. A preliminary series of 40 professional boxers who had absorbed varying degrees of facial damage were examined periodically after their bouts; none received antiswelling treatment. The examination two to three hours after the bout provided a more accurate estimate of damage than the immediate examination. Another series of 163 professional boxers were treated with buccal amylase (Buclamase). The observable damage was the same at the immediate and two- to three-hour examination. The rates of recovery were markedly superior to the preliminary series. In the buccal amylase series the results were excellent or good in 88 per cent of the cases, while only 25 per cent of the results in the preliminary series were excellent or good. Buccal amylase was most effective when started immediately after injury.

Abstracts in Interlingua

Rathbun, M. L., Broad, R. H., Font, W., Milham, S., e Ames, W. R.: Immunisation in massa con oral vaccinos contra poliomyelitis de Sabin e Cox; experientias in 1960 in le contatos Monroe e Tompkins de New York (*anglese*), NEW YORK STATE J. MED. **62:** 1767 (1 de junio) 1962.

In 1960 un programma de immunisation in massa contra poliomyelitis esseva executate in le contato Monroe, con le uso de monovalente vaccino oral de Sabin administrate in tres doses a juveniles de gruppos de etate prescholari e scholari, e in le contato Tompkins, con le uso de trivalente vaccino oral de Cox administrate in un sol dose a subjectos de omne gruppos de etate. Ambe le vaccinos esseva facile a administrar; ambes esseva sin sapor e acceptabile a omne gruppos de etate. Sex casos de manifestationes de allergia cutanee occurreva post le ingestion del vaccino de Sabin, possibilemente in consequentia de sensibilitate a penicillina. Multe suspecte reactiones minor esseva reportate post le prime dose de vaccino de Sabin. Tal reportos esseva minus numerose post le secunde e le tertie dose. Minor gravamines gastrointestinal esseva frequente post le administration del vaccino de Cox. Le saison de poliomyelitis in 1960 in le contato Monroe esseva simile a illos de altere annos in le recente passato. Nulle del 7 casos de poliomyelitis paralytic occurreva in un subjecto tractate con le vaccino de Sabin. In le contato Tompkins, nulle poliomyelitis occurreva in le anno 1960. Un comparation del procentages de casos con augmentos quadruplice o plus in le titros de anticorpore demonstra que Typo I de Sabin e Typo III de Cox esseva excellente como antigeno original e como antigeno de stimulo additional. Typo III de Sabin e Typo II de Cox esseva multo minus efficace. Viste le comparativemente debile performance de vaccino Typo III de Sabin e le crescente importantia de Typo III como causa de poliomyelitis paralytic, un programma de immunisation es recommendate in que al minus duo doses de vaccino de Salk es sequite de stimulation additional per vaccino de Sabin.

Hotchin, J., Plager, H., Decher, W., e Jacobs, J.: Responsa anticorporee a duo differente vaccinos de vive virus de poliomyelitis (*anglese*), NEW YORK STATE J. MED. **62:** 1776 (1 de junio) 1962.

Esseva effectuate un comparation inter le vaccino de poliomyelitis Sabin in forma monovalente, administrate per via oral in tres doses in Rochester (contato Monroe, New York), e le vaccino de poliomyelitis Cox in forma trivalente, administrate per via oral in doses unic in Ithaca (contato Tompkins, New York), per medio de systematic essayages controlate a duple anonymato titrante specimens de sanguine pre- e postvaccinal ab gruppos de voluntarios in le citates mentionate. Esseva effectuate tests de neutralisation in primari tissu renal de simias cynomolgos (con le uso de un puncto terminal del effecto cytopathic) e tests de neutralisation del inhibition metabolic in cellulas de ren simian. Typos I e II del vaccino Sabin esseva de approximativemente le mesme antigenicitate. Typo III produceva un responsa anticorporee alique minus pronunciate, sin reguardo a si le population esseva classate secunde le etate o secundo le stato con respecto al vaccination Salk. A generalmente parlar, le effecto de stimulo additional declinava in omne le tres typos in tanto que le nivello del anticorpore prevaccinal montava. Vaccino de Typo III de Cox esseva un melior antigeno que Typos I e II. Ambe vaccinos se provava particularmente efficace in le elimination de lacunas de anticorpore quando le vaccinato habeva recipite un previe immunisation Salk.

Tessler, A. N., Morales, P. A., e Hotchkiss, R. S.: Indicationes pro le dialyse (*anglese*), NEW YORK STATE J. MED. **62:** 1792 (1 de junio) 1962.

Dialyse artificial es usate in le tractamento de acute insufficientia renal, intoxication con dialysabile agentes non-nephrotoxic, formas seligite de chronic morbo renal, e intractabile uremia, hyperhydratation, o coma metabolic in patientes con morbo de reversibilitate chirurgic o medical. Inter januario 1959 e decembre 1960, un total de 26 patientes esseva dialysate con le uso de un instrumento a serpentinos gemine non-reusabile. Le indicationes pro un dialyse debe esser determinate in conjunction con mesuras medical pro regular le balancias acido-base e de liquido, pro provider calorias, e pro sustener le function cardiovascular e respiratori.

Gold, J. A., O'Connell, F., e Caldwell, F.: Determinationes serial del enzymas del sero in mononucleosis infectiose (*anglese*), NEW YORK STATE J. MED. **62:** 1796 (1 de junio) 1962.

Esseva interprendite le essayo de correlationar le valores de determinationes serial de enzymas del sero con le curso de mononucleosis infectiose. Le nivello de transaminase glutamic-oxaloacetic del sero (T-GOS) esseva elevate in 31 de 36 patientes con mononucleosis infectiose (86 pro cento). Le nivello de transaminase glutamicpyruvic del sero (T-GPS) esseva elevate in 21 del 36 (66 pro cento), normal in 10, e non determinate in 5. Le activitate de dishydrogenase lactic (DHL) esseva elevate in omne le 7 patientes assi studiate. In 2, illo esseva elevate quando le nivellos de T-GOS e T-GPS esseva intra le limites del norma. In 80 pro cento del casos le plus alte nivellos de transaminase esseva registrate durante le prime duo septimanas post le declaration del symptomas, lo que indica que alterationes hepatic occurre precocemente in le curso de mononucleosis infectiose. Tamen, in omne le patientes ille nivellos retornava a valores normal, in duo tertios del patientes durante le intervallo ab le tertie al quinte septimana del maladia. Le nivellos seral de transaminase esseva normal in 18 casos de rubella que es un condition que alteremente pote mimar mononucleosis infectiose.

Botstein, A., e Brown, E. B.: Globulina gamma in le prevention de infectiones superorespiratori in juveniles (*anglese*), New York State J. Med. **62:** 1799 (1 de junio) 1962.

Esseva effectuate un studio a duple anonymato in 143 juveniles de etates de inter un e novem annos con antecedentes de frequente infectiones supero-respiratori, con le objectivo de determinar le valor prophylactic de globulina gamma. Un medietate del juveniles recipeva 0,2 ml de globulina gamma per libra de peso corporee a intervallos de un mense durante un periodo de cinque menses. In le remanente membros del gruppo, correspondente quantitates de solution salin esseva administrate. Le resultatos esseva identic pro le duo subgruppos como totales. Tamen, inter le 16 asthmaticos includite in le studio, le recipientes de globulina gamma habeva circa un medietate del numero de infectiones supero-respiratori occurrente in le recipientes del placebo, e le numero de lor attaccos asthmatic esseva etiam plus basse. Duo tertios del parentes, sin reguardo a qual agente habeva essite usate, pensava que lor filios se trovava melio. Nulle membro del gruppo recipiente globulina gamma habeva rubeola. Varicella e parotiditis occurreva in ambe subgruppos. Il es possibile que juveniles con asthma e possibilemente juveniles con allergias in general ha un specific deficientia de globulina gamma, lo que preveni le formation adequate de anticorpore e causa le responsa allergic a infectiones supero-respiratori.

Boyarsky, S., e Goldenberg, J.: Detection de distension del vesica per medio de percussion suprapubic (*anglese*), New York State J. Med. **62:** 1804 (1 de junio) 1962.

Vinti-novem adulte patientes con catheteres n sito esseva studiate per percussion pro distension del vesica. Un surde sono suprapubic in le presentia de minus que 100 ml de liquido in le vesica esseva constatate in solmente un occasion. Le replenation medie del vesica que permitteva le detection de 1 cm de surditate supra le symphyse esseva 134 ml. Si le resultatos de percussion abdominal, de urographia intravenose, e del test a phenolsulfonphthaleina remane ambigue o si le patiente se trova in un condition que require un action plus immediate (como per exemplo in le presentia de febre o de dolor), catheterismo diagnostic es indicate.

Sasson, L.: Comparation de hexylcaina con tetracaina como anestheticos topic in manovras gastroenterologic (*anglese*), New York State J. Med. **62:** 1808 (1 de junio) 1962.

Esseva comparate hydrochloruro de hexylcaina (hydrochloruro de Cyclaina) e hydrochloruro de tetracaina (hydrochloruro de Pontocaina) usate com anesthetico topic in 500 e 100 casos respectivemente. Medication preanesthetic esseva usate solmente in major interventiones. Con tetracaina, 5 del 100 patientes obteneva non-satisfacente grados de anesthesia, con le resultato de insuccessose o incomplete operationes. Con hexylcaina nulle malsuccesso esseva incontrate. Le tempore requirite pro le administration del anesthetico esseva inter dece e vinti minutas in le caso de tetracaina e inter duo e tres minutas in le caso de hexylcaina. Nulle adverse reactiones esseva constatate post le un o le altere agente. Le relative innocentia, de hexylcaina e le simplicitate de su administration permitte su uso in minor operationes e etiam in majores.

Giannattasio, R. C.: Dysplasia congenite del coxa (*anglese*), New York State J. Med. **62:** 1812 (1 de junio) 1962.

In un serie de 386 neonatos, examinate duo vices in le curso del prima septimana de lor vita, 20 casos de dysplasia del coxa esseva trovate. Isto representa un incidentia de 5, 1 pro cento. In le 366 normales, tenite sub observation durante le prime annos de lor vita, le occurrentia de asymmetria de plicas cutanee, le presentia de plicas cutanee extranumerari, un partialmente celate labio major a un latere, e differentias in le longor del extremitates non esseva valide como signos de un subjacente dysplasia del coxa. Del altere latere, constatationes clinic e roentgenologic que es valide como indicationes de congenite dysplasia del coxa es: limitation del abduction del flectite femore, abruptessa de entrata e de exito, e abruptessa de exito. Roentgenographias de infantes suspicite de haber dysplasia del coxa supporta le diagnose in 50 pro cento del casos. Nulle premonitori signo clinic de congenite dysplasia del coxa esseva trovate al tempore del nascentia in 19 infantes in qui anormalitate del coxa esseva constatate subsequentemente.

Stevens, M. A., McCown, I. A., e Campbell, E. A.: Tractamento de tumescentias in vulneres de sport; un factor cardinal in le complete e prompte restablimento (*anglese*), NEW YORK STATE J. MED. **62:** 1817 (1 de junio) 1962.

Esseva interprendite un studio pro determinar lo que representa un adequate tractamento de tumescentia post-traumatic in vulnerationes de sportistas. Un serie preliminari de 40 boxatores professional (qui habeva suffrite varie grados de traumatismo facial) esseva examinate periodicamente post lor matches. Nulle del homines in iste gruppo recipeva un tractamento anti tumescentia. Le examine duo a tres horas post le match provideva un melior mesura del damnification que le examine immediate. U serie subsequente de 163 boxatores profes sional esseva tractate con amylase bucc (Buclamase). Le observabile grados de damnif cation esseva le mesmes in le examines im mediate e post duo o tres horas como in le seri preliminari. Sed le progresso del restabliment esseva marcatemente plus favorabile. In l serie tractate con amylase buccal, le resultat esseva excellente o bon in 88 pro cento del caso durante que in le serie preliminari excellent o bon resultatos amontava a solmente 25 pr cento. Amylase buccal esseva le plus efficac quando su uso esseva initiate immediatement post le injuria.

Medical Schools

Albany Medical College

Commencement speaker. Willard C. Rappleye, M.D., former dean of the faculty of medicine at Columbia University College of Physicians and Surgeons and now president of the Josiah Macy, Jr. Foundation, will deliver the principal address at the 133rd commencement exercises on June 3.

Assistant dean. Dr. Eugene H. Horn, associate professor, Department of Anatomy, has been appointed an assistant dean of the College. Dr. Horn will serve as coordinator of research and training grant programs, assist in the preparation of grant applications, counsel faculty with regard to appropriate sources for research and training funds, and determine the readiness of applications for submission to granting agencies. Dr. Horn will also represent the College in the planning, development, and method of operation of a proposed dormitory for medical students and students of the Albany Law School. Other responsibilities will include supervision of procurement of classroom equipment and audiovisual aids, as well as planning the operation and development of the College's expanding animal research facilities.

Workshop. A workshop sponsored by th Association of Rehabilitation Facilities Upstate New York was held in April at th Albany Center Hospital. Topics presente were: "Public Assistance—Its Nature an Scope," "Problems of Rehabilitation of Socia Welfare Recipients," and "Research Project– Disabled Parents of Dependent Children."

Albert Einstein College of Medicine

Colloquium. "Viruses and Cancer" was th subject of a colloquium held in connection wit the fourth annual commencement on May 25 Participants were: Dr. Peyton Rous, Rockefeller Institute, who discussed "The Effect of th Tumor Viruses on Scientific Thought"; Ludwi Gross, M.D., chief, Cancer Research Unit Veterans Administration Hospital, the Bronx spoke on "Isolation and Serial Cell—Fre Passage in Mice and Rats of the Mouse Leukemia Virus"; Dr. Charlotte Friend, Sloan Kettering Institute, presented "Virus-Induce Leukemia of Mice"; Dr. Sarah Stewart, National Institutes of Health, discussed "The Vira Transformation of Cells"; Dr. Aaron Bendich

Sloan-Kettering Institute, "Infectious Nucleic Acids and Cancer"; Dr. W. Ray Bryan, National Institutes of Health, was a discussant. Other speakers and their topics were: Dr. Salvatore Luria, professor of biology, Massachusetts Institute of Technology, "Viral Control of Enzyme Production"; Dr. Harry Rubin, professor of virology, University of California, "Cell Alteration and Host Response Following Infection with RNA-Containing Tumor Viruses"; Dr. Renato Dulbecco, professor of biology, California Institute of Technology, "The Neoplastic Transformation of Tissue Culture Cells by Polyoma Virus"; and Frank L. Horsfall, Jr., M.D., president and director, Sloan-Kettering Institute for Cancer Research, gave the summary.

Irving London, M.D., professor and chairman, Department of Medicine, served as moderator of the Colloquium.

Columbia University College of Physicians and Surgeons

Grant. The Rockefeller Foundation presented a $400,000 grant toward the construction of the new William Black Medical Research Building. The building, for which ground was broken recently, will be one of the largest devoted to medical research in the United States.

Appointed. John V. Taggart, M.D., professor of medicine, has been appointed professor of physiology and chairman, Department of Physiology, to be effective July 1. Dr. Taggert first joined the College in 1946 as an instructor in medicine and was appointed full professor of medicine in 1958. Dr. Taggart will continue as professor of medicine.

Cornell University Medical College

Research career awards. Edwin D. Kilbourne, M.D., professor of public health and director, Division of Virus Research, and Ralph E. Peterson, M.D., associate professor of medcine and director, Subdepartment of Endocrinology, have been granted awards by the National Institutes of Health which will permit hem to devote most of their time and effort to esearch and to the teaching of research. The rants cover an initial five-year period and rovide salary, anticipated periodic increases, nd fringe benefits. Each award is granted ith the intention of continuing Federal support or the full career of the individual.

rofessor and chairman. William F. Scherer, M.D., has been named professor and chairman, epartment of Microbiology and Immunology, nd will succeed Dr. James M. Neill who will tire after thirty-one years of service. Dr. cherer is presently professor of microbiology at e University of Minnesota Medical School d will assume his new post July 1.

New York University Medical Center

Institute of Industrial Medicine. The Institute of Industrial Medicine has begun an expanded research program in Sterling Forest under the directorship of Norton Nelson, M.D., director of the Institute and professor of industrial medicine. The expanded research program will include studies of lung cancer, air-borne diseases, radiation hazards, and other environmental and occupational diseases. A graduate teaching program will be instituted in which graduate students will conduct research and attend classes.

State University of New York Downstate Medical Center

Research grants. During the first three months of 1962 43 research grants totaling $808,764 have been received by the Center. In addition, a grant of $72,690 was received from the National Institutes of Health for graduate training in clinical ophthalmology. All but three of the awards were to support specific projects, 22 for renewals of work already in progress, and 18 for new research. The largest grant of $201,399 was made under the new General Research Support Grant Program of the National Institutes of Health to provide general support for research and research training projects. Another grant of $5,000 from Warner Lambert Company is to support general surgical research and the third grant of $4,590 from the National Fund for Medical Education is to be used for noncategorical basic research. Twenty-three of the 40 grants for specific projects came from the National Institutes of Health; three from the Health Research Council of the City of New York; five from the Upjohn Company; two each from the American Cancer Society and the Life Insurance Medical Research Fund; and one each from United Cerebral Palsy, Charles Pfizer, White Laboratories, Inc., the James Picker Foundation, and the Roswell Park Division of Health Research, Inc.

New faculty members. Four new faculty members have been appointed clinical assistant professors. Appointed in the Department of Medicine have been Ernest Lehman, M.D., Norman Shaftel, M.D., and Stanley Stark, M.D. The fourth appointment, in the Division of Orthopedics of the Department of Surgery, was Henry D. Isenberg, Ph.D.

Visiting professor. Franz Leuthardt, professor and chairman, Department of Biochemistry, University of Zurich, Switerland, was visiting professor of biochemistry for the month of April. On April 9 Professor Leuthardt delivered a major lecture on "Some Problems of Fructose Metabolism."

Special lectures. Alexander G. Bearn, M.D., Rockefeller Institute, delivered the Annual Murray B. Gordon Memorial Lecture on April 23. Dr. Bearn's subject was "Genetic Heterogeneity Among the Serum Proteins." On April 26, Henry L. Bockus, M.D., professor of medicine emeritus, University of Pennsylvania Graduate School of Medicine, delivered the Albert F. R. Andresen Memorial Lecture on "The Mechanism of Abdominal Pain."

State University of New York Upstate Medical Center

Otolaryngology postgraduate teaching day. The twelfth annual postgraduate teaching day in otolaryngology was held in March. Alfred Doust, M.D., professor and chairman, Department of Otolaryngology, was in charge of the program. Out-of-town speakers were: Dr. Rex Bunker, Santurce, Puerto Rico, "Problem Foreign Body Cases," and Dr. Assad S. Khoury, Washington, D.C., "Juvenile Laryngeal Papilloma." Dr. Lawrence R. Boies, professor, Department of Otolaryngology, University of Minnesota Medical School, addressed the evening session which was a combined meeting with the Central New York Eye, Ear, Nose and Throat Society.

Medical Center faculty participating and topics were: "Progress Report on Laryngeal Investigations," Sidney T. Dana, M.D., "Changing Trends in Middle Ear Grafting," Siroos Amiri, M.D., "The Artificial Nose," Lee R. Stoner, M.D., "Monaural vs. Binaural Hearing," Herbert N. Wright, M.D., "Diagnostic Otologic Problems," Gordon D. Hoople, M.D., "Problem of the Caudal End of the Septum," Norman E. Johnson, M.D., and "Rehabilitating the Head and Neck Cancer Patient," George A. Sisson, M.D.

Other Syracuse doctors assisting in the program were Wesley H. Bradley, M.D., and Dav L. Poushter, M.D.

University of Rochester School of Medicine and Dentistry

Dedication ceremonies. The new Rehabi tation and Diagnostic Center was dedicated April 13 with a tour of the new facility and public symposium. Participating in the sy posium were: John E. Fogarty, U.S. congres man from Rhode Island who spoke on "Heal Facilities—Key to a Better Life," Herman Hilleboe, M.D., New York State Commission of Health, "Rehabilitation is a Communi Affair," David Frost M.D., assistant direct for health and medical activities, Office Vocational Rehabilitation, Department Health, Education, and Welfare, "Rehabilit tion and Comprehensive Patient Care," ar Robert L. Berg, M.D., Albert D. Kais Professor of Preventive Medicine and Cor munity Health and director of the new cente "Teaching a Long-Range View in Patient Care

Five-year grant. The National Institutes Health has awarded a five-year grant of $289,5 for training radiotherapists to meet the prese and future needs for cancer therapy in th country. Under the direction of Philip Rubi M.D., chief of the Division of Radiati Therapy and Isotopes, and Louis H. Hempe mann, Jr., M.D., chairman of the Departme of Radiology, the program began June The program in radiobiology is aimed at t post-doctoral level and fellowships for th program will be offered to men who have M.D D.D.S., or C.V.M. degrees.

Appointed. Frank W. McKee, M.D., wh graduated from the University in 1943 has bee appointed associate dean of the Medical Scho and professor of pathology to be effective July

Medical News

Course in gastroenterology

The annual course in postgraduate gastroenterology of the American College of Gastroenterology will be given at the Morrison Hotel in Chicago, November 1 through 3. The moderators will be Owen H. Wangensteen, M.D., chairman and head of the Department of Surgery of the University of Minnesota School of Medicine, and I. Snapper, M.D., director of medical education, Beth-El Hospital, Brooklyn.

From the medical as well as the surgical viewpoint the subject matter will consist of the diagnosis and treatment of gastrointestinal diseases and comprehensive discussions of diseases of the mouth, esophagus, stomach, pancreas, spleen, liver and gallbladder, and colon and rectum.

For further information write to: American College of Gastroenterology, 33 West 60th Street, New York 23, New York.

North Shore Hospital opens new eye clinic

North Shore Hospital, Manhasset, Long Island, has announced the opening of a new Eye Clinic and Comprehensive Eye Service.

Operating under the Hospital's Division of Surgery, the Eye Clinic will provide outpatient care to the medically indigent. The service is designed to take care of inhospital patients and provide consultation to other services. Ira Kaufman, M.D., Great Neck, will direct the new service.

Prospective clinic patients may call Manhasset 7–5000 to arrange for an appointment with the Registrar of the Outpatient Department. Appointments can also be made on referral from a private physician, social agency, the Department of Health, the Department of Welfare, or other similar agencies.

Postgraduate courses for eye specialists

The Institute of Ophthalmology of the Americas of The New York Eye and Ear Infirmary, New York City, has announced that the fifth series of postgraduate courses for specialists in ophthalmology will be given from September 6 through November 1.

The courses include the following: Advances in Ocular Prostheses; Anomalies of Extraocular Muscles, including Ptosis; Application and Use of the Indirect Ophthalmoscope; Biomicroscopy; Biomicroscopy, Using Near Ultraviolet, Cobalt Blue, Polarized, and Infrared Light; Clinical Bacteriology; Clinical Problems of Tear Formation; Complications of Ophthalmologic Surgery; Contact Lenses, Electrophysiology and Applied Physiology of the Eye; Enucleation and Evisceration; Glaucoma; Gonioscopy; Keratectomies and Keratoplasties; Lacrimal Sac Surgery; Light Coagulation (Meyer-Schwickerat Apparatus); and Low-Vision Aids.

Also: Medical Mathematics; Ocular Biochemistry; Ocular Geriatrics; Ocular Neuro-Ophthalmology; Ocular Photography; Ocular Radiology; Ocular Therapeutics; Ophthalmoscopy; Orthoptics; Pathology; Pediatric Ophthalmology; Perimetry; Physiological Optics; Plastic Eye Surgery; Pleoptics and Macular Function Testing; Psychosomatic Factors in Ophthalmology; Radioisotopes in Ophthalmology; Recent Advances in Cataract Surgery; Refraction; Retinal Detachment; Surgery of the Orbit; Tonography; and Uveitis.

For additional information write to: Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3, New York.

Women physicians invited to brunch

The American Medical Women's Association extends an invitation to all women physicians attending the A.M.A. annual meeting in Chicago to be their guests at a brunch on Sunday, June 24, at 11:00 A.M., at the Essex Inn.

Those wishing to attend should write to: American Medical Women's Association, 1790 Broadway, New York 19, New York.

Treatment for teen-age drug addicts

A new center for the treatment of teen-age narcotics addicts will be opened in July or August at Sea View Hospital on Staten Island. Alexander W. Kruger, M.D., Brooklyn, will be in charge of the new facility which is expected to have a capacity of about 60 patients. All patients will come to the hospital on a voluntary basis.

Smith Kline & French Foundation grants

More than 300 agencies throughout the nation received grants totaling $631,675 from the Smith Kline & French Foundation during

1961, the trustees have announced. Last year's grants raised the amount distributed by the Foundation since its establishment in 1952 to $4,657,898.

Essay competition for medical students

Junior and senior students of all medical schools in this country have been invited to submit entries to "The Annual Walter Reed Memorial Essay Competition of The Brooklyn Hospital." Three cash prizes will be offered: $1,000, $750, and $500.

The closing date for this year's competition is March 1, 1963. Essays should be from 5,000 to 10,000 words in length and submitted in triplicate. The prize-winning essays will be the property of The Brooklyn Hospital for suitable publication.

Essays should be sent to: Abraham G. White, M.D., Director of Medical Education, The Brooklyn Hospital, 121 Dekalb Avenue, Brooklyn 1, New York.

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology has announced that applications for certification in the American Board of Obstetrics and Gynecology, new and reopened, part 1, and requests for re-examination in part 2 are now being accepted. All applications and requests for re-examination are to be received in the office of the executive secretary and treasurer on or before July 1. No applications will be accepted after that date.

After July 1, 1962, the Board will require a minimum of three years of approved progressive residency training for admission to the examinations. After that date, training by preceptorship will not be acceptable.

In order to be well informed of the present requirements for membership candidates are urged to review the current Bulletin of the Board, a copy of which may be had by writing to: American Board of Obstetrics and Gynecology, Office of the Executive Secretary and Treasurer, Robert L. Faulkner, M.D., 2105 Adelbert Road, Cleveland 6, Ohio.

Louis H. Bauer receives award

The Aerospace Medical Association paid a special tribute to its founder and first president Louis H. Bauer, M.D., of Rockville Centre, on April 11 during the Association's thirty-third annual meeting in Atlantic City.

Dr. Bauer, a pioneer in aerospace medicine, was presented with a bronze plaque for his "... leadership in founding the Aerospace Medical Association and its journal and in recognition of his outstanding contributions to the development and progress of civil and military aviation medicine." (See Figure 1.)

FIGURE 1. Rear Admiral J. L. Holland, USN, MC, (right) commanding officer of the U. S. Navy Aviation Medical Center, Pensacola, Florida, presents Louis H. Bauer, M.D., with a bronze plaque from the Aerospace Medical Association.

Personalities

Elected. Martin Cherkasky, M.D., Bronx, as vice-president of the Greater New York Hospital Association.

Awarded. Rieva Rosh, M.D., New York City, the Humanitarian Award of the Greater New York and New Jersey Council of Auxiliaries of the American Medical Center at Denver for her contributions in the field of radiology . . . Otis B. Schreuder, M.D., Jamaica, the Howard K. Edwards Award of the Aerospace Medical Association in recognition of his achievement in the practice of clinical aerospace medicine . . . George H. Whipple, M.D., Rochester, the Jessie Stevenson Kovalenko Medal by the National Academy of Sciences for his contributions to medical science.

Appointed. Ira Kaufman, M.D., Great Neck, as attending-in-charge of the newly-created Department of Ophthalmology at North Shore Hospital, Manhasset . . . Michael J. Lepore, M.D., New York City, as director of the newly-established Upjohn Gastrointestinal Service at Roosevelt Hospital . . . James M. Murphy, M.D., Willard, as assistant commissioner in charge of the Division of Special Services of the Department of Mental Hygiene of the State of New York . . . Anthony N. Mustille, M.D., Helmuth, as director of Willard State Hospital in Seneca County . . . Arthur Zitrin, M.D., New York City, as director of psychiatry for the City of New York Department of Hospitals.

Speakers. Evan Calkins, M.D., Buffalo, on the subject "Parameters of Rheumatoid Disease Research" on May 23 at a symposium on rheumatoid arthritis sponsored by the Academy of Medicine of New Jersey and The National Foundation in conjunction with the Department of Health of the State of New Jersey . . . Marvin Block, M.D., Buffalo, on April 25 at a symposium sponsored by *The Reader's Digest* on the problem of alcoholism in women . . . Saul Farber, M.D., Brooklyn, on May 7 at a symposium on renal metabolism sponsored by the Downstate Medical Center of the State University of New York . . . Ruth Fox, M.D., New York City, on April 25 at a symposium sponsored by *The Reader's Digest* on the subject of alcoholism in women . . . Alfred Freedman, M.D., New York City, on April 23 at a meeting of the New York County Medical Society on the subject of narcotics addiction . . . Constantine Generales, M.D., New York City, on April 12 before the Pi Lambda Theta Women's Honor Society at Teachers College, Columbia University, on the subject "Space Progress and Ethics" . . . Gerhard Giebish, M.D., New York City, on May 7 at a symposium on renal metabolism sponsored by the Downstate Medical Center of the State University of New York . . . Paul H. Hoch, M.D., Commissioner, State of New York Department of Mental Hygiene, at a meeting of the New York State Association of Community Mental Health Boards on April 30 in New York City . . . Currier McEwen, M.D., Charles Ragan, Jr., M.D., and Paul Weiss, M.D., New York City, on the subject "Clinical Aspects of Rheumatoid Arthritis" on May 23 at a symposium on rheumatoid arthritis sponsored by the Academy of Medicine of New Jersey and The National Foundation in conjunction with the Department of Health of the State of New Jersey . . . Lewis Thomas, M.D., and Arthur Zitrin, M.D., New York City, at a meeting of the New York County Medical Society on April 23 on the subject of narcotics addiction.

Antiradiation drug developments

The development of antiradiation drugs has progressed to a point where they do not kill dogs but not to a point where they are without risk for people, according to an article by David Jacobus, M.D., and Major Michael P. Dacquisto in the September, 1961, issue of *Military Medicine*. The first drugs tested killed about 10 per cent of the animals without any exposure to radiation. On the more recent mixtures, no dog has died, but they suffer obvious side-reactions, the most common being emesis, hyperactivity, methemoglobinemia, and some hypotension.

In the limited numbers of dogs used, it appears that the mixture chiefly used provided at least 50 per cent reduction in the amount of injury over that sustained by the control dogs. For example, 95 dogs given a radiation dose of 775 r had a mean survival time of 10.9 days, whereas 23 dogs chemically pretreated survived more than sixty days and were still alive twenty-seven months later. On a dose of 1,500 r, 39 control animals had a mean survival time of 4.2 days, while 28 pretreated animals had a mean survival time of 12.6 days on the same radiation dosage.

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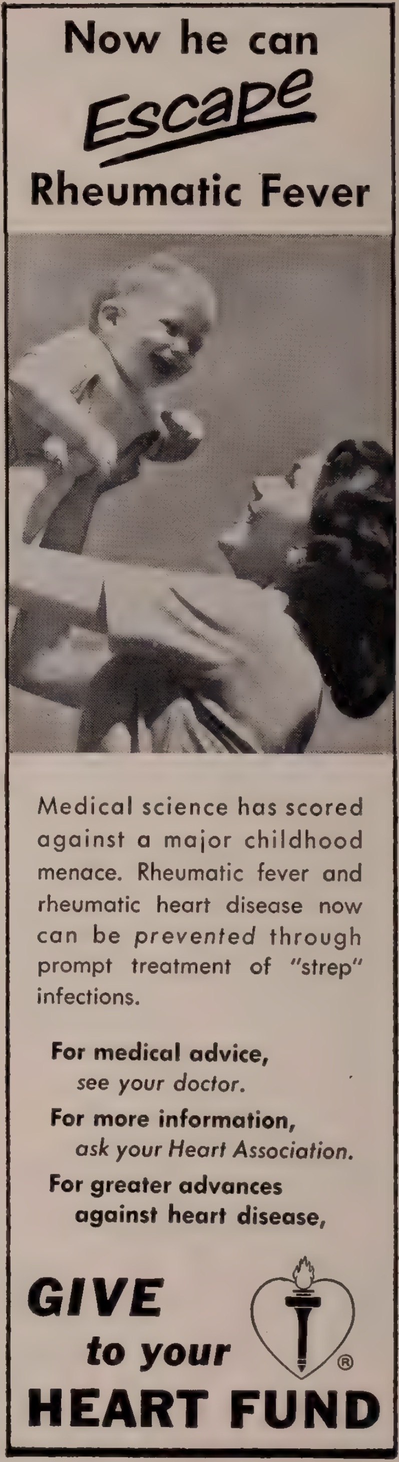

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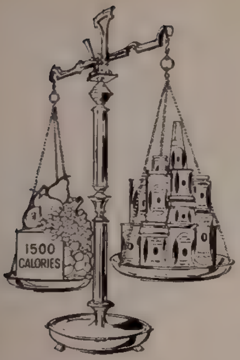

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Brown Gravy	1 tbsp.	7	21

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The Editors of the JOURNAL *assume no responsibility for opinions and claims expressed in the articles contributed by individual authors. Contributions accepted for original publication only.*

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1946 Infection and Chronic Lymphocytic Leukemia, A Review of 61 Cases
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1953 The Misdiagnosis of Glaucoma
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1962 Turner's Syndrome, Review of Literature and Report of Case in Newborn Infant
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1977 Hospital Management of Adolescent Patients
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1990 Effect of Isocarboxazid on Relief of Anginal Pain
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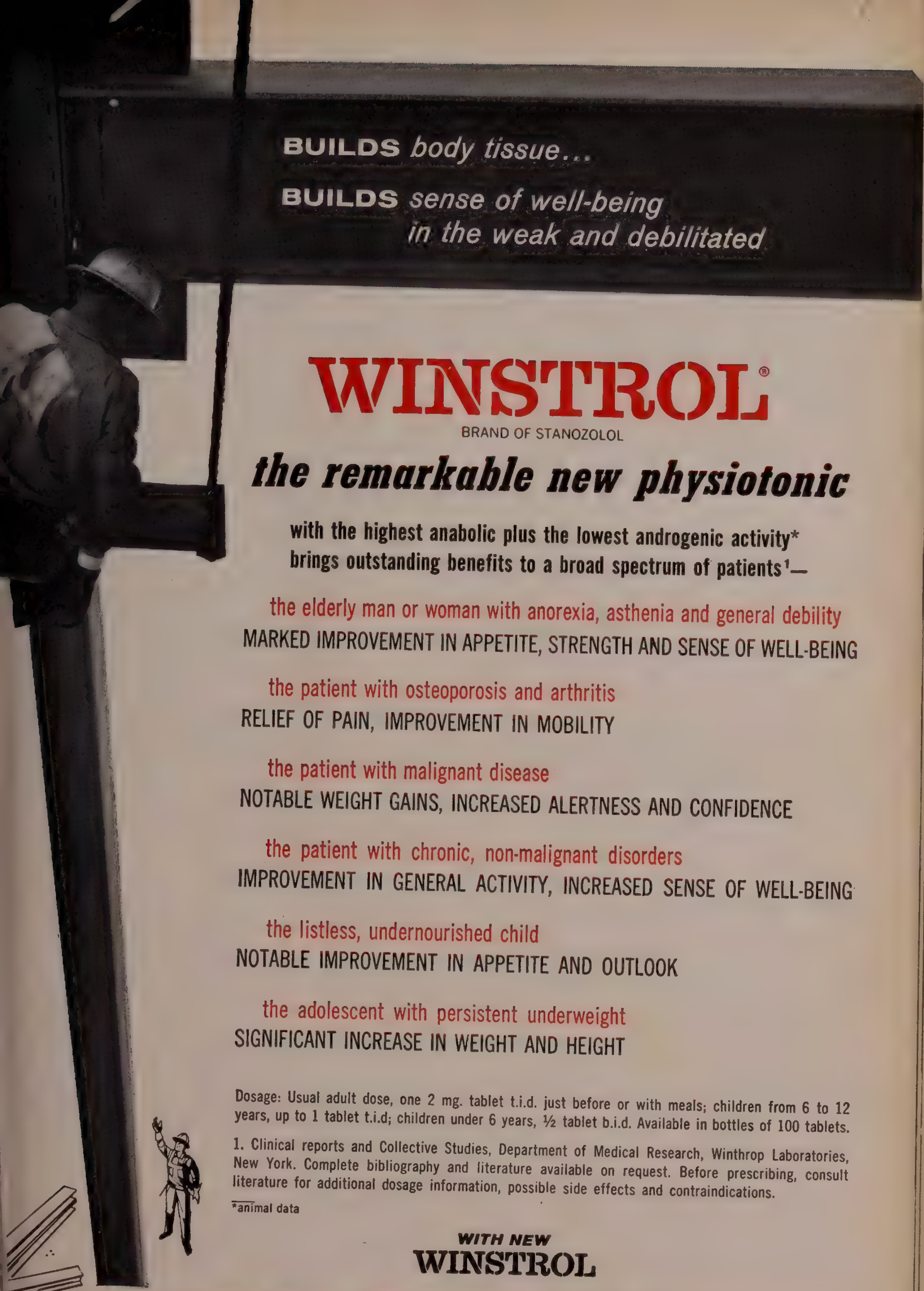
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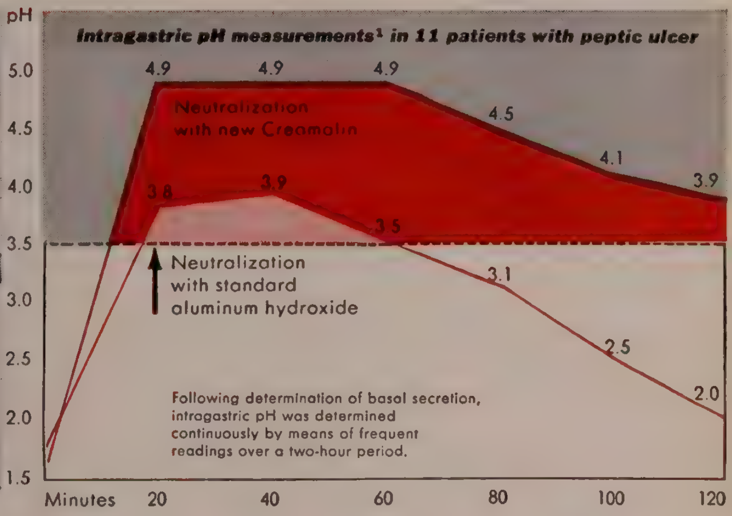
Intragastric pH measurements[1] in 11 patients with peptic ulcer
pH
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Minutes
20
40
60
80
100
120
4.9
4.9
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3.9
3.5
3.1
2.5
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References: **1.** Schwartz, I. R.: *Current Therap. Res.* 3:29, Feb., 1961. **2.** Beekman, S. M.: *J. Am. Pharm. A.* (Scient. Ed.) 49:191, April, 1960. **3.** Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A.* (Scient. Ed.) 48:381, July, 1959. **4.** Data in the files of the Department of Medical Research, Winthrop Laboratories. **5.** Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: *J. Am. Pharm. A.* (Scient. Ed.) 48:384, July, 1959.

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Morning stiffness may be reduced or even eliminated as a result of therapy with the only steroid in long-acting form. And the slow, steady release of steroid makes it possible in some cases to reduce the frequency of administration and/or the total daily steroid dosage.

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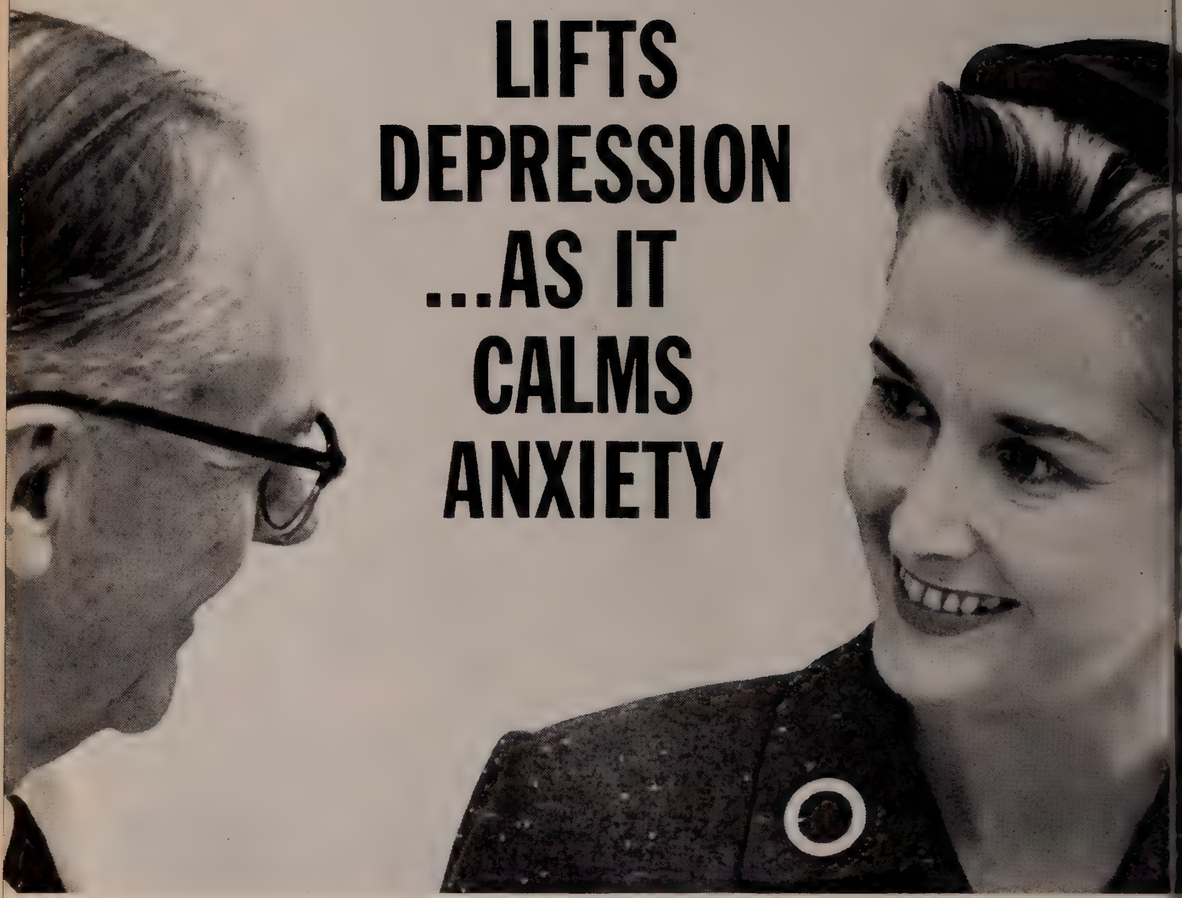
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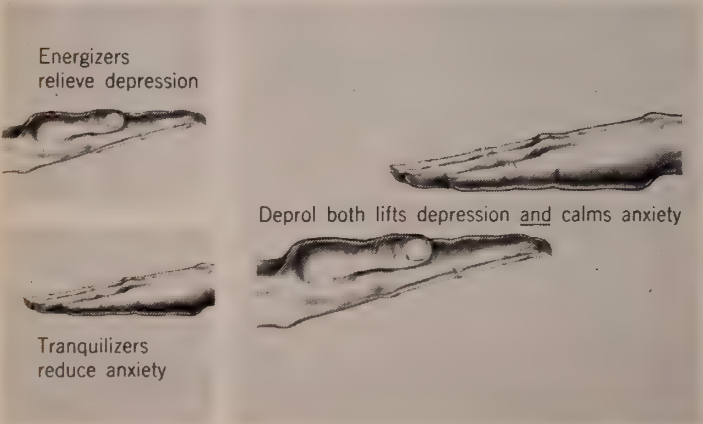
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relieve depression
Deprol both lifts depression and calms anxiety
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reduce anxiety

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be increased gradually up to 3 tablets q.i.d. With establishment of relief, the dose may be reduced gradually to maintenance levels.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets.

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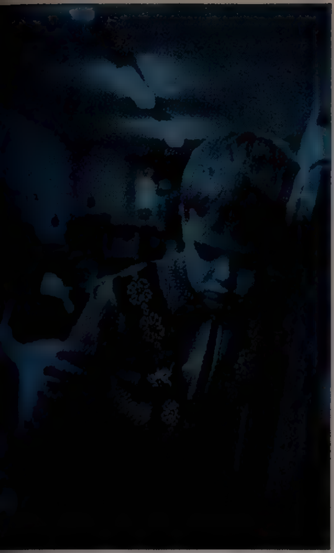

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This advertisement is not intended to provide complete information for use. Please refer to the package enclosure, medical brochure, or write for detailed information on indications, dosage, and precautions.

*Roseman, E.: Neurology 11:912, 1961.

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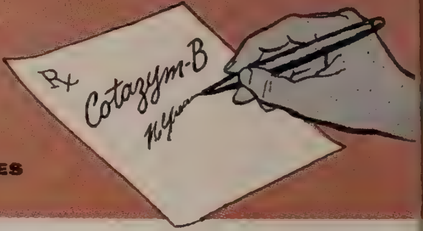

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Dosage: 1 or 2 tablets with water just before each meal.

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REFERENCES: 1. Best, E. B., Hightower, N. C., Jr., Williams, B. H., and Carobasi, R. J.: South. M.J. 53:1091, 1960. 2. Analytical Control Laboratories, Organon Inc. 3. Best, E. B., et al.: Symposium at West Orange, N. J., May 11, 1960. 4. Thompson, K. W., and Price, R. T.: Scientific Exhibit Section, A.M.A., Atlantic City, N. J., June 8-12, 1959. 5. Weinstein, J. J.: Discussion in Keifer, E. D., Am. J. Gastro. 35:353, 1961. 6. Ruffin, J. M., McBee, J. W., and Davis, T. D.: Chicago Medicine, Vol. 64, No. 2, June, 1961. 7. Berkowitz, D., and Silk, R.: Scientific Exhibit Section, A.M.A., New York, June 25-30, 1961. 8. Berkowitz, D., and Glassman, S.: N. Y. St. J. Med. 62:58, 1962.

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The patient looks better, feels more confident as **COSMEDICAKE** helps improve her appearance while the skin lesions heal.

*__COSMEDICAKE__ contains colloidal sulfur, benzalkonium chloride, salicylic acid and hexachlorophene in a smooth, greaseless base. Supplied in four skin-matching colors.

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1. Berger, R.A., Clinical Medicine, Sept. 1961.

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* Feinblatt, T.M., and Ferguson, E.A., Jr., Phenobarbital idosyncrasy, avoidance by use of phenobarbital-niacin, *N. Y. State J. Med.* 62:221-3, Jan. 15, 1962.

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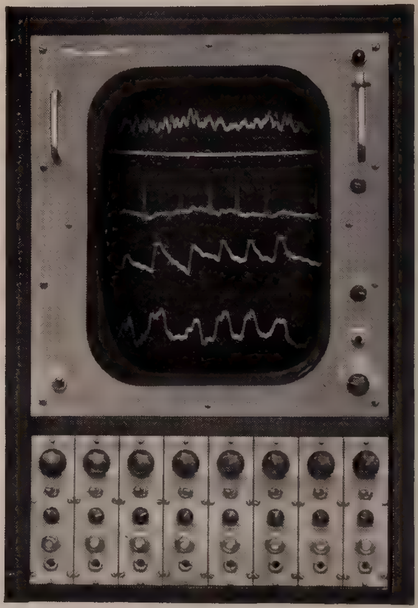

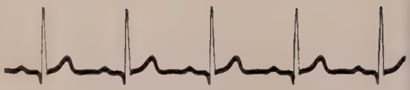

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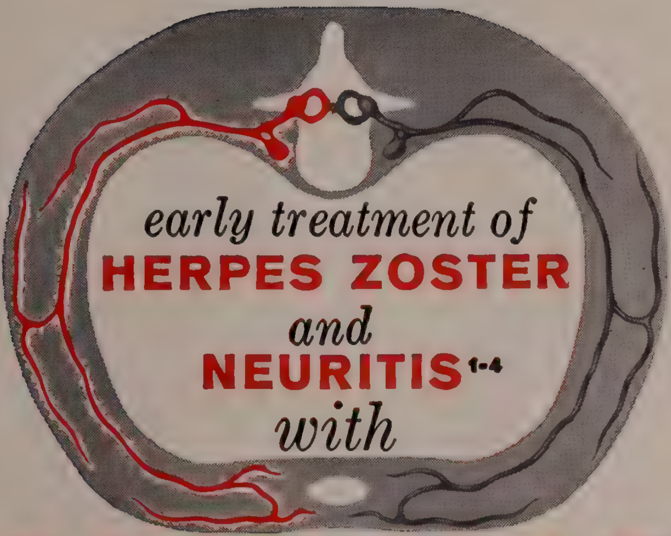

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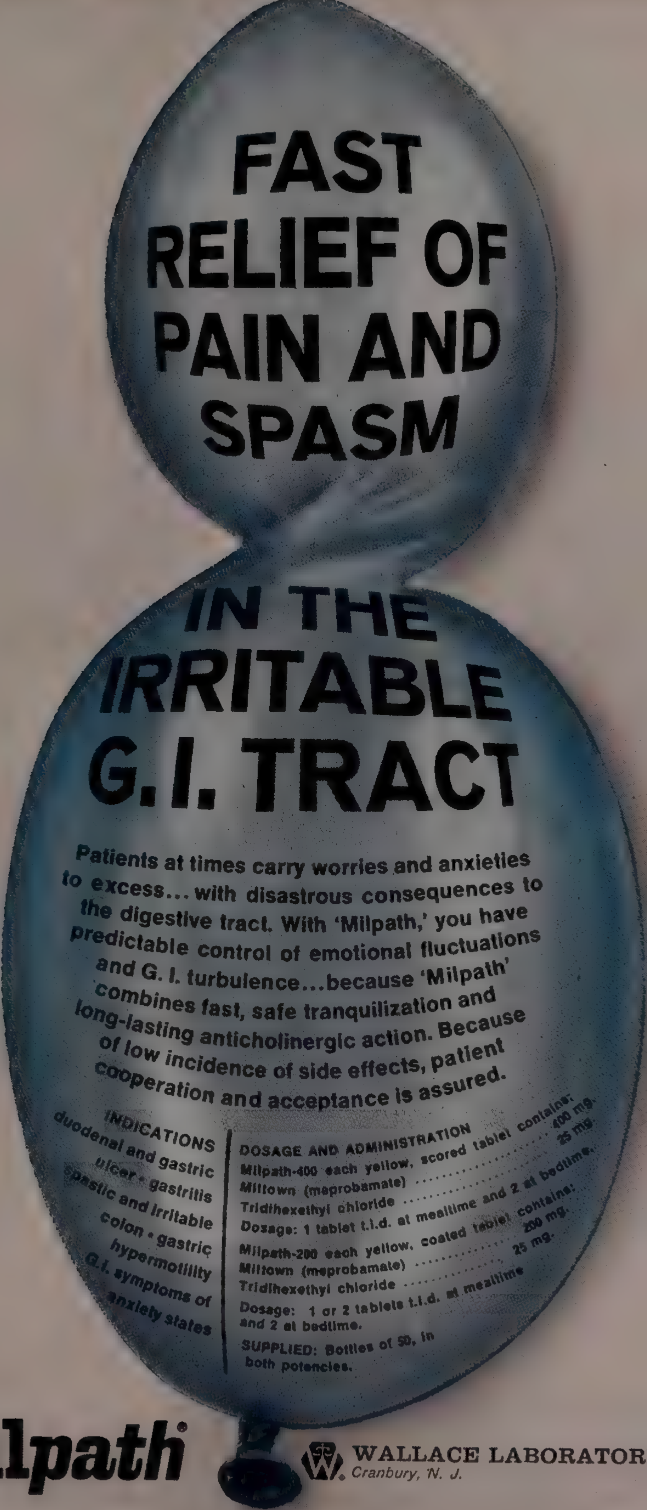
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1. Ford, R. V.: Clin. Res. Notes 2:1 (Dec.) 1959. 2. Ford, R. V.: Cur. Therap. Res. 2:92 (Mar.) 1960. 3. Elliott, J. P., Jr., and Goldman, A. M.: South. M.J. 54:794 (July) 1961.

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Council on Drugs: J.A.M.A. *176*:594 (May 20) 1961.

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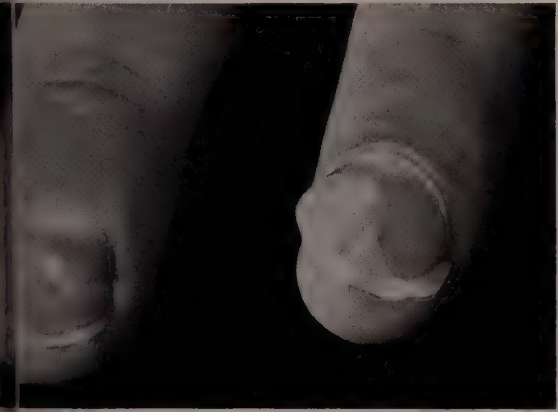
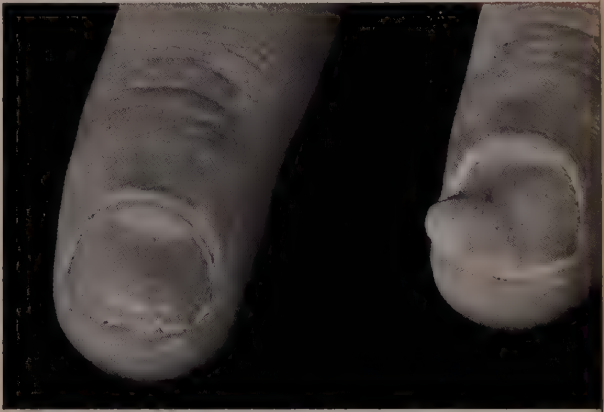


2 April 19, 1961.



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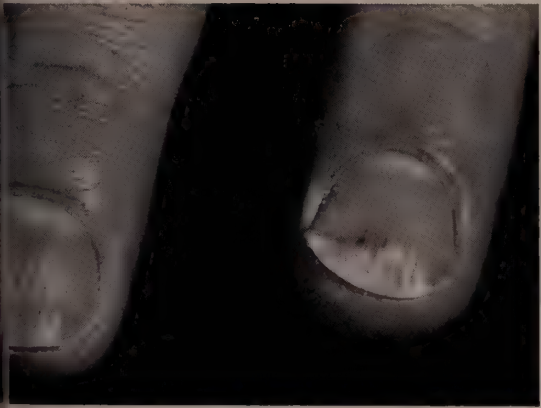

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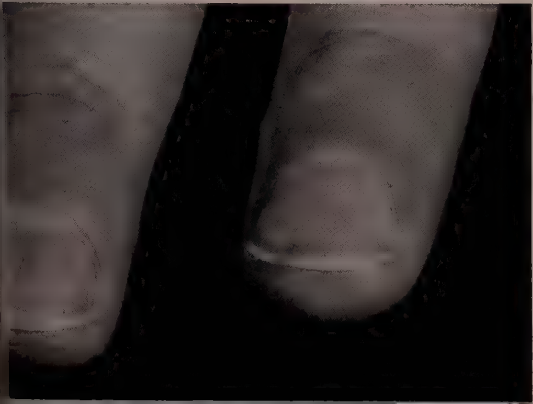
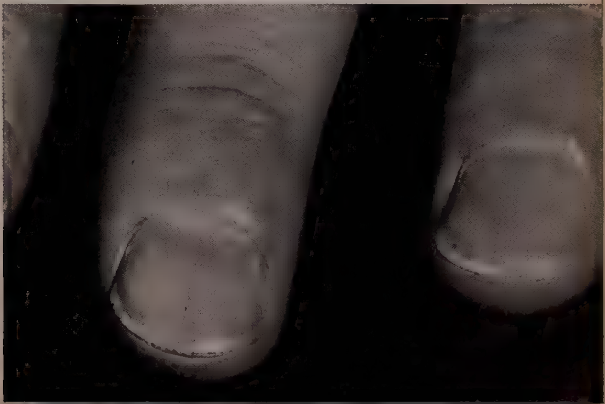
June 19, 1961 — therapy with FULVICIN stopped.



5 July 19, 1961 — four-week follow-up.



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1. Cohen, B. M.: M. Times 88:855 (July) 1960. 2. Cohen, B. M.: Méd. et Hyg. (Genève) #494, p. 210 (Mar. 15) 1961.

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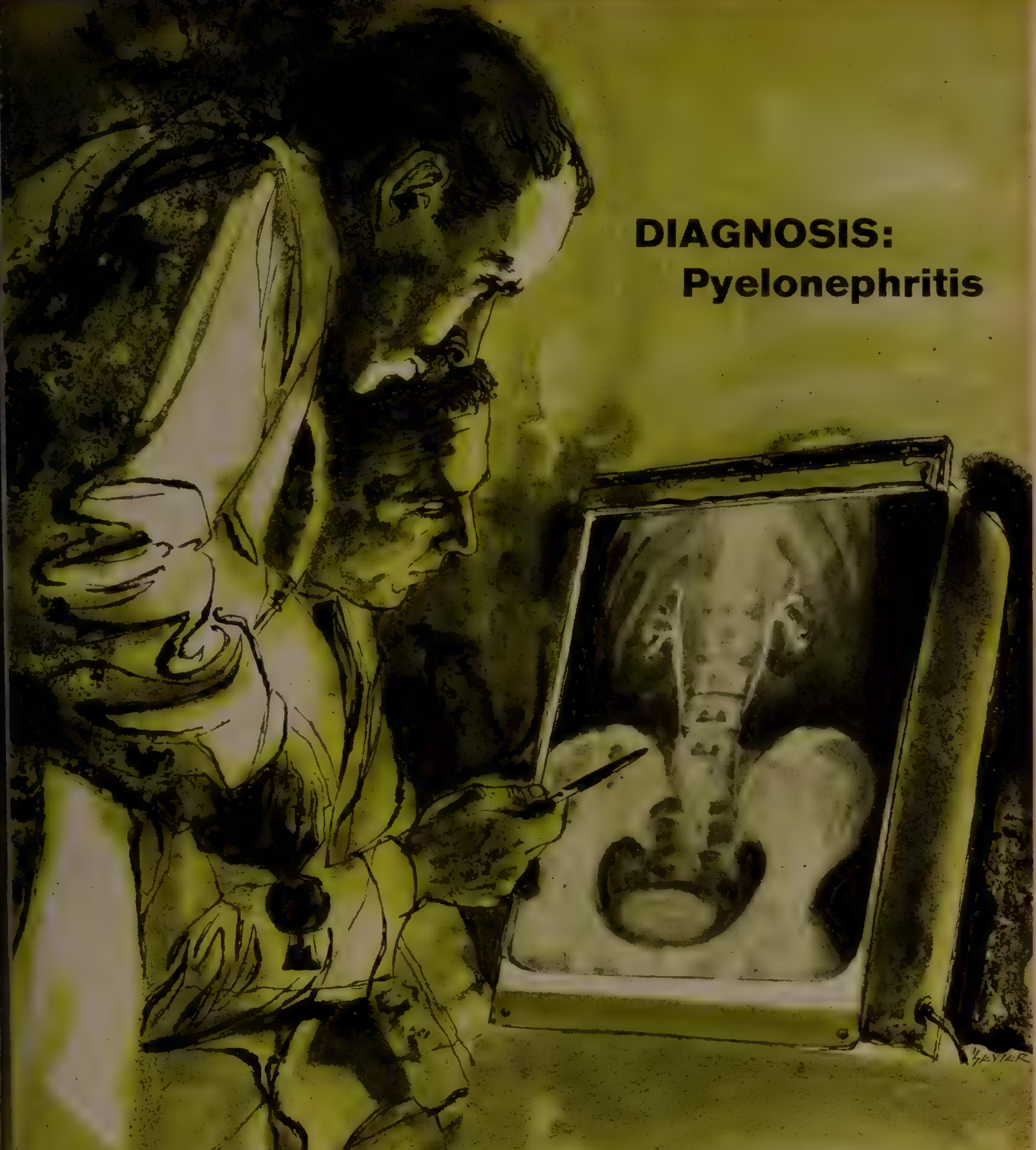

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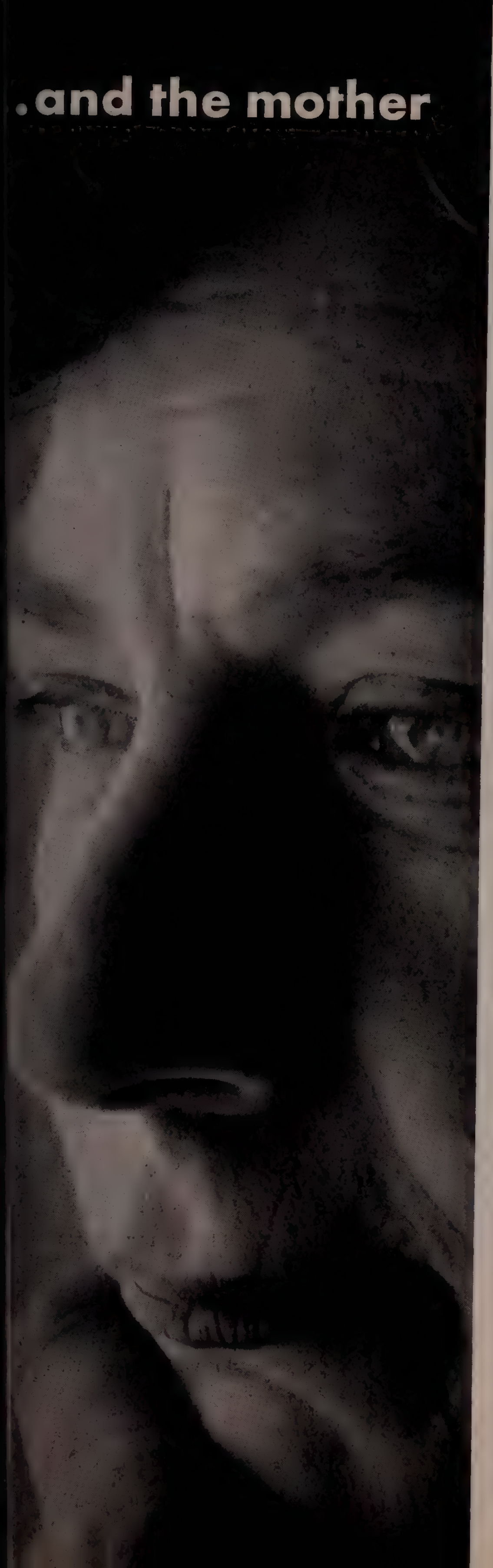

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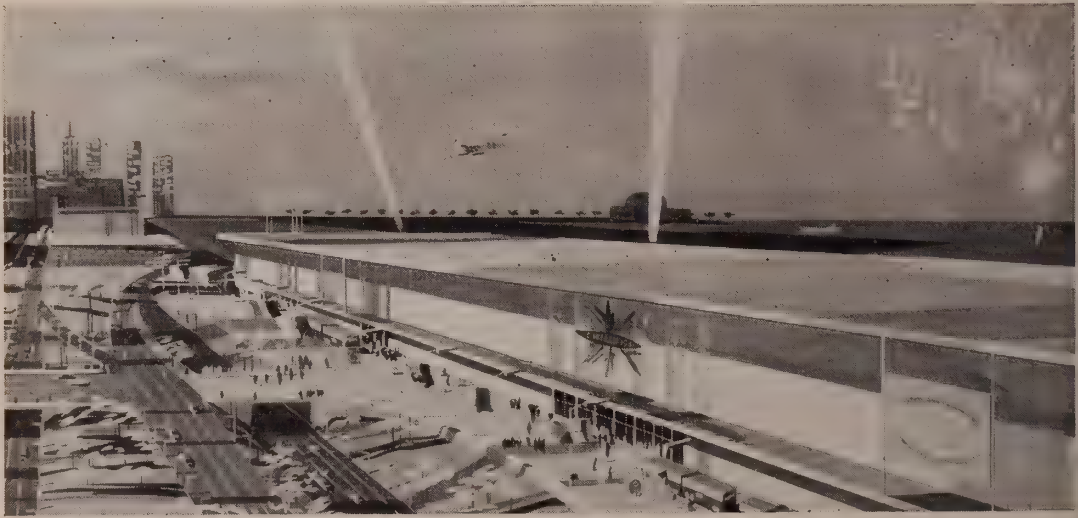

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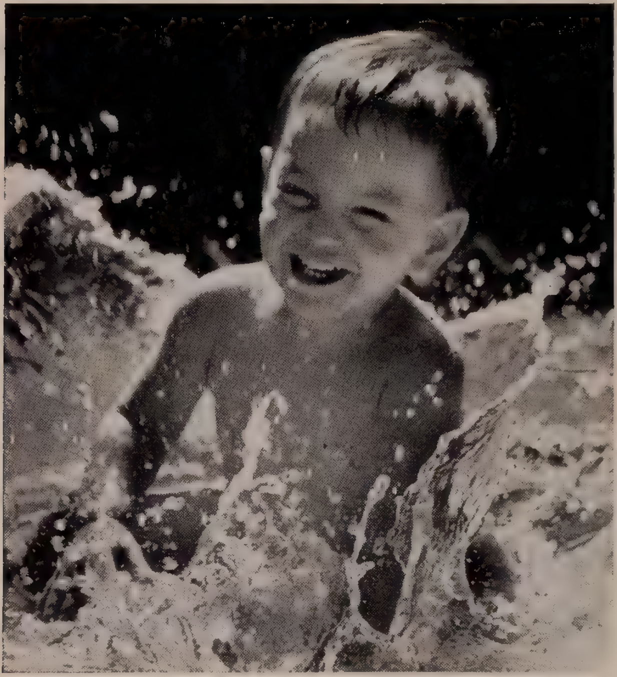

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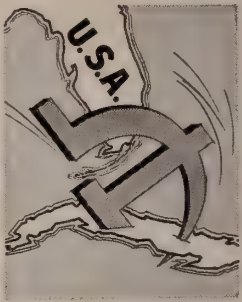

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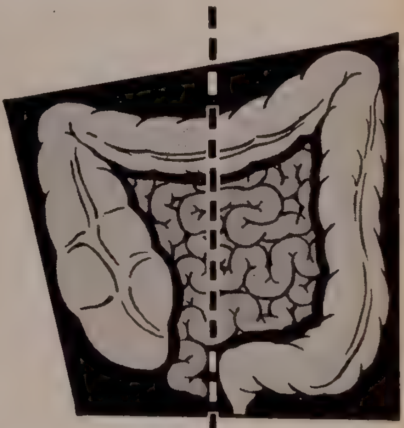

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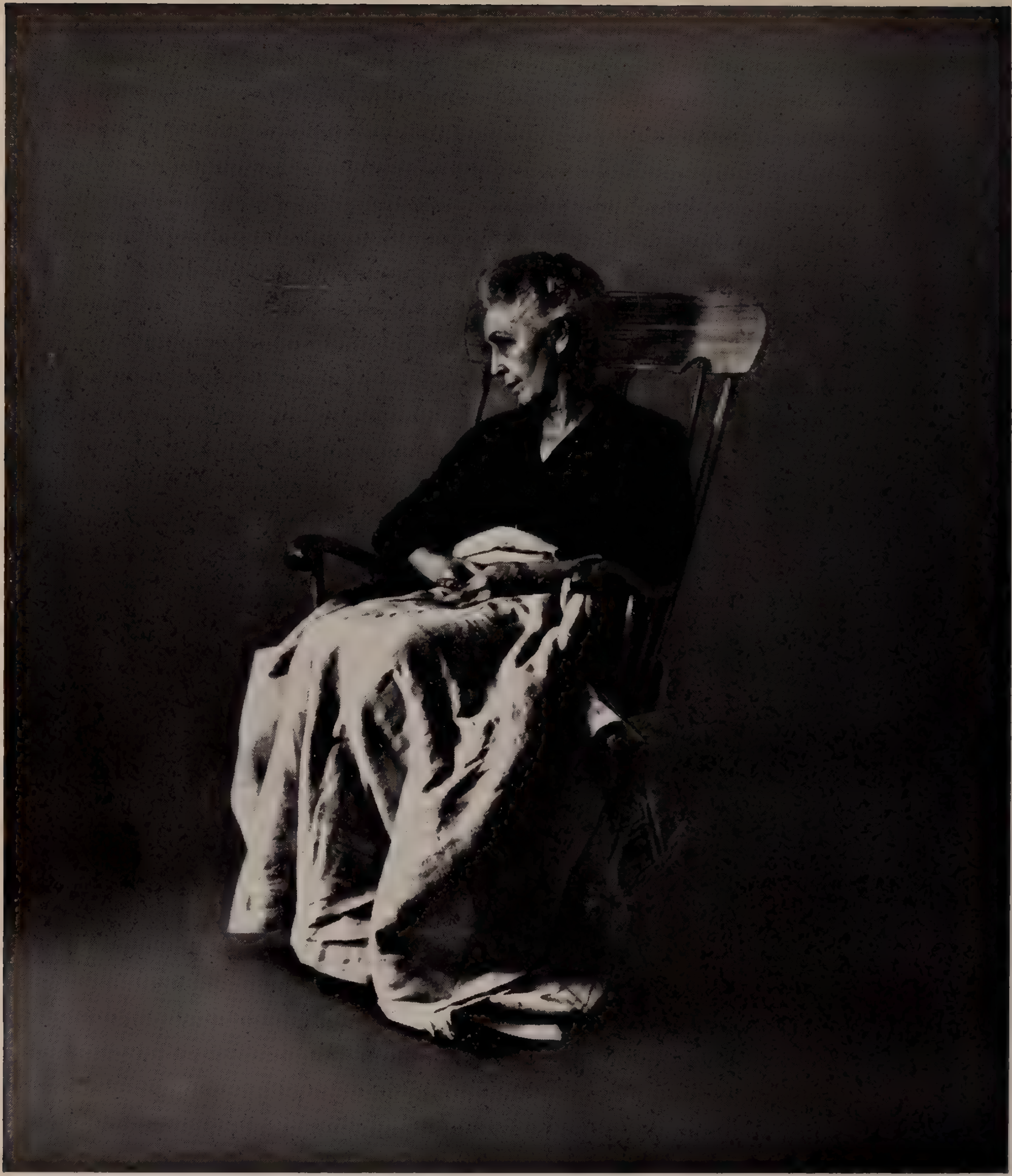

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Editorials

Trends in graduate education

A recently published survey of the 1961 graduates of Columbia College discloses that the proportion of those going on to higher study over those terminating at college level is 8.5 to 1.

The professional schools attracted the greater number distributed through medicine, law, engineering, business, theology, dentistry, architecture, journalism, and education.

Out of a class of 360, medical study led the list with 94 students enrolled in medical schools throughout the country. Law was close behind with 89, and engineering was third with 33.

Whereas 45 per cent of the class was engaged in the aforementioned professional studies, only 20 per cent were enrolled in graduate schools in the arts and sciences. The most popular studies here were, in order, English 18, history 13, and physics 13.

It would seem that, for the majority, undergraduate experience is the beginning and not the end of higher education. It is encouraging to note that medical study leads all others and that while we have been led to believe that pure science, particularly physics, was making inroads on student attention, this study at least does not show it.

However, the implications are plain for all parents—prepare for a greater educational budget and hope for progeny smart enough to obtain scholarships.

The need for public health nurses

Everyone is aware of the shortage of nurses generally, but the lack is particularly pressing in the public health field. At a time when services to the increasing school population, the increasing aged population, and the increasing number of chronic disease patients are expanding, the number of career public health nurses, the key persons in delivering public health services, is shrinking.

A recent report from the Commissioner of the New York City Department of Health discloses that, during the ten-year period from 1950 to 1960, each year the Department ended with fewer public health nurses than when the year began. In 1950 there were 850 public health nurses on the staff; at the end of 1959 there were 577.

This slow and steady attrition was met in several ways—first by relieving the available public health nurses from clerical and other duties not requiring skill. The position of public health assistant was created to function at this level and 431 of them are assisting in this way. Registered nurses without public health training were employed, but the number of these available has declined. The use of married nurses who could devote part-time and at the same time carry on their home and family duties was of considerable help. At the present time, 113 part-time nurses are on the staff furnishing the equivalent of 49 full-time nurses. The services of the visiting nurse associations have been used on a contract basis. These services amount to the equivalent of 25 full-time nurses. A salary increase has also been instituted. However, at the end of 1960 there was an increase of only three public health nurses over the number on the staff at the end of 1959. The Commissioner states, "While the numerical increase, three, is insignificant the fact that a ten-year trend has been halted, if not reversed, does give at least a glimmer of hope."

Some idea of the magnitude of the public health nursing service provided in the city of New York may be gained by the following list of their activities:

Eighty child health stations where approximately 200,000 infants and preschool children made 955,662 visits;

Twenty-five tuberculosis clinics where about 80,000 patients and contacts made 524,065 visits;

Thirteen social hygiene clinics where approximately 45,000 patients and contacts made 239,218 visits;

Three cancer clinics where about 5,000 persons made 21,864 visits;

An adult diagnostic center where about 3,000 patients made 5,467 visits;

Seven working paper clinics where 218,777 medical examinations were given to adolescents seeking permission to go to work;

Five clinics where antirabic, typhoid-preventive, and other shots were given to more than 50,000 persons;

Six cardiac clinics where 7,448 children with possible heart conditions made 8,259 visits;

One orthopedic clinic where 721 children with orthopedic handicaps were examined and consultation services given;

Seven nutrition clinics where more than 10,000 persons made more than 70,000 visits for treatment and consultation;

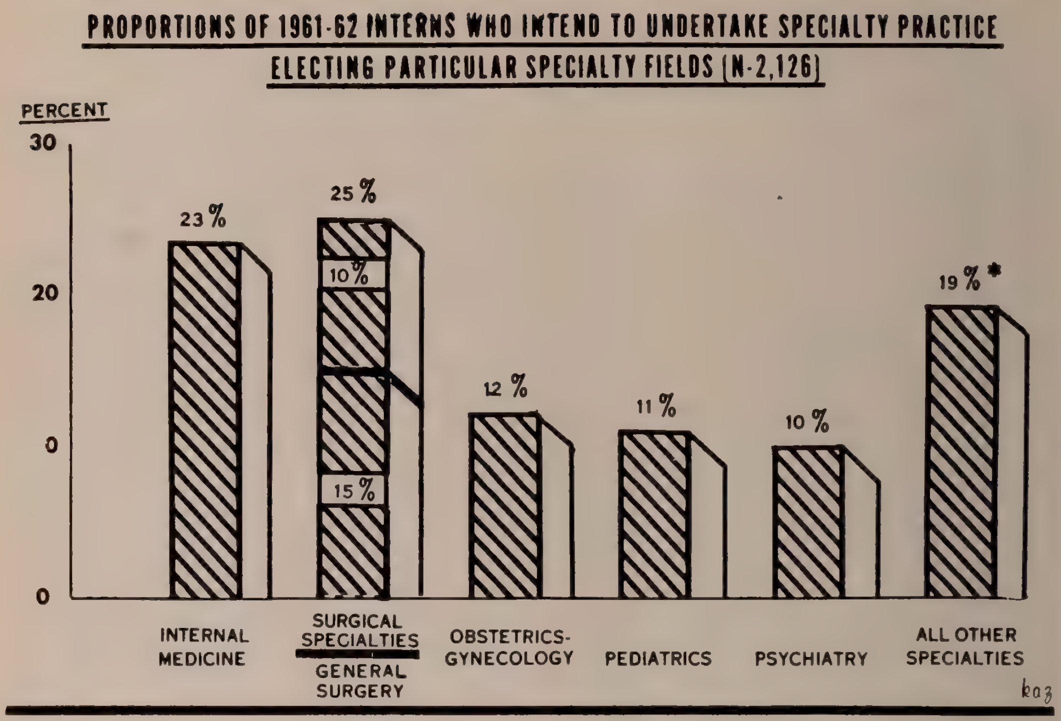
Two diabetes centers and three temporary special diabetes clinics where 36,554 visits were made;

Nurses also served in the school health services of the Department—in 1,151 public and parochial elementary schools with 83,600 pupils and 20 day care centers attended by approximately 100,000 children under six;

Nurses made 433,091 home visits to mothers and infants, to preschool children, to school children with physical defects or other problems, to children and adults with acute communicable diseases, to diabetes and tuberculosis patients, to venereal disease patients, and as part of the hospital home care program and rehabilitation project.

As the number of nurses graduated each year increases, a rise which statistics are beginning to indicate, we trust that the Public Health Service will obtain its just share to carry on this important work.

"Will you tell the doctor to take me off his rounds today? I'm too sick to see him."



*Includes: Radiology, 4%; Ophthalmology and Otolaryngology, 4%; Pathology, 3%; Anesthesiology, 2%; Dermatology, Physical Medicine, Public Health, Preventive Medicine and Rehabilitation, 6%.

FIGURE 1. Fields of specialization chosen by 1961 medical school graduates.

Trends in medical careers

The Association of American Medical Colleges in a recent report tells what young doctors choose to do today as compared with their choices ten years ago.

The data from graduates of medical schools of the class of 1950 were collected in 1959 after they had been in practice. The data on the classes of 1961 were obtained two months after graduation, during internship.

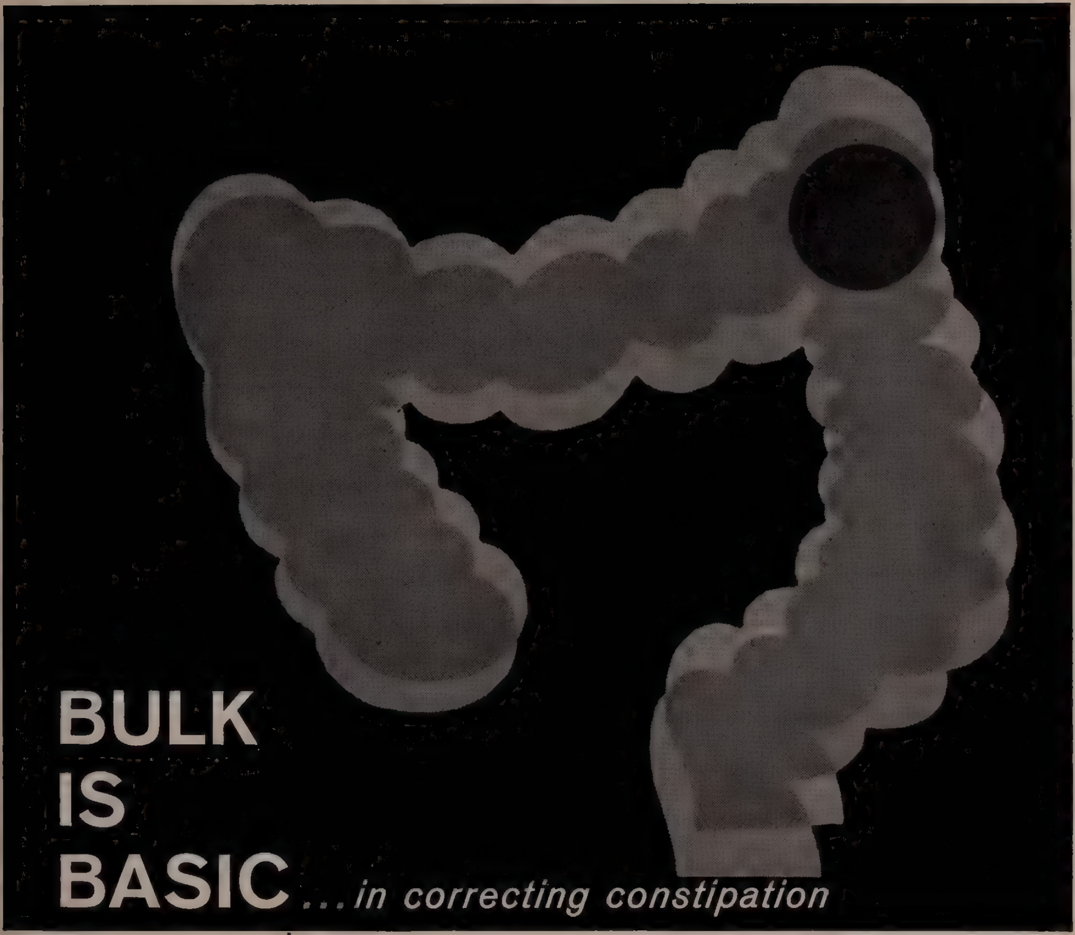
In 1950 63 per cent chose specialty practice, 33 per cent chose general or family practice, and 4 per cent chose research and teaching.

In 1961 78 per cent chose specialty practice, 18 per cent chose general or family practice, and 4 per cent chose research and teaching.

Thus from 1950 to 1961 there has been a net increase of 15 per cent of graduates desiring to enter specialty practice and a corresponding 15 per cent decrease in those choosing general or family practice. The proportions opting for research and teaching has remained unchanged throughout this period.

A further breakdown of the 78 per cent of the 1961 class who expect to enter specialization shows in the accompanying figure what proportions elect particular fields.

How will this trend affect the health care coverage of an expanding population? Among the specialists one group is suited to provide a general type of medical care within the framework of its specialty—internal medicine. Much will be expected of this group in applying their special skills broadly. We see this gradually evolving. Provided interest in and of the patient is maintained, the evolution of medical practice should hold no fears for anyone.



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1. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 6, Baltimore, The Williams & Wilkins Company, 1955, p. 578.

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Scientific Articles

Evaluation of Routine Postoperative Electrocardiography

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ROUTINE POSTOPERATIVE *electrocardiograms were taken on 782 patients, of whom 321 (41 per cent) had normal recordings. The electrocardiograms of the remaining 461 patients revealed either abnormalities of rate, rhythm, or conduction or myocardial changes suggestive of disease. Of these, 56 would have been detected by applying criteria representing the major cardiovascular problems encountered in the recovery room, 48 were detected by a preoperative electrocardiogram, and 167 were not detected prior to operation. However, in all but 2 of the latter the abnormalities of the electrocardiogram resulted from chronic heart disease. It appears that changes that occur as the result of operative and postoperative medical and physiologic phenomena can be detected by recording a postoperative electrocardiogram on patients showing marked bradycardia or arrhythmia, sudden unexplained tachycardia, hypoxia, or hypotension not amenable to the restoration of circulating fluid volume. However, a routine preoperative electrocardiogram is indicated for every patient scheduled for operation.*

A COMPREHENSIVE REVIEW of the complications encountered in the recovery room during the course of several years revealed a sufficient number of cardiovascular difficulties to warrant further investigation. To facilitate the diagnosis of these complications, a study of the electrocardiogram in the immediate postoperative period was conducted from October, 1958, to July, 1960. Since the services of a full-time technician were not available at this time, the study was confined to four categories which represented the major portion of the cardiovascular problems encountered in the recovery room. These categories were: (1) arrhythmia, (2) bradycardia (pulse under 60 beats per minute), (3) tachycardia (pulse over 120 beats per minute), and (4) "evaluation," a general term including patients with known preexisting severe chronic cardiac disease, hypotension, respiratory difficulties, massive blood replacement, and those patients anesthetized by the technic of induced hypotension. During the period of the study a total of 1,000 patients or 1 out of every 10 patients admitted to the recovery room fulfilled the qualifications necessary for inclusion in the series.

A complete review of the study and its findings has been reported by Schweizer and Howland.[1] The most significant factor was the discovery of 11 cases of myocardial infarction. Since the signs and symptoms were atypical in every case, the recovery room electrocardiogram was the essential element in the detection and early institution of therapy in these patients. The study also revealed that myocardial disease was present in a large percentage of patients who developed an arrhythmia or a pulse rate below 60 per minute in the postoperative period. Benign tachycardia in the first twenty-four hours after surgery proved to be a relatively rare occurrence. In the majority of patients serious medical or physiologic disturbances were responsible for the appearance of a pulse rate higher than 120 per minute.

Since this first series revealed the importance of the postoperative electrocardiogram in the detection and differential diagnosis of cardiovascular problems, a second series utilizing every patient in the recovery room was instituted to determine whether or not routine postoperative electrocardiography would add further information to that obtained by limiting the procedure to specified categories. The results obtained in the second series are discussed in the present report.

Source of material

The 782 patients comprising the second study included every patient admitted to the recovery room of Memorial Hospital between the hours of 9:00 A.M. and 5:00 P.M. for a period of three months. Whenever possible, a 12-lead electrocardiogram was recorded by a nurse technician on the patient's admission to the recovery room and repeated just prior to discharge for return to the wards. Follow-up electrocardiograms were taken on the floors on all patients with abnormal tracings. The electrocardiograms were interpreted either by us or by a resident in cardiology. A consultation with an attending cardiologist was obtained on all cases presenting problems in differential diagnosis.

Results

In the group of 782 patients, 321, or 41 per cent, had completely normal postoperative electrocardiograms. The recordings of the remaining 461 patients revealed either abnormalities of rate, rhythm, or conduction, or showed changes suggestive of myocardial disease.

The types of arrhythmias and disorders of conduction (Table I) were similar to those in the first series. An increase in the number of cases of first-degree heart block, bundle branch block, and delayed intraventricular conduction is understandable, since these conduction defects would not have been detected by the criteria of the first study unless they had been associated with a palpable arrhythmia. The incidence of myocardial disease in the group was 60 per cent of the total, exactly the same as in the first series.

TABLE I. Arrhythmias and disorders of conduction

Type of Arrhythmia or Conduction Disorder	Number of Cases
Auricular premature contractions	7
Nodal and supraventricular premature contractions	4
Ventricular premature contractions	30
Ectopic pacemaker	2
Preexcitation (Wolff-Parkinson-White) syndrome	1
Nodal rhythm	1
First-degree heart block	12
Bundle branch block	23
Complete auriculoventricular dissociation	1
Delayed intraventricular conduction	13
Auricular fibrillation	5
TOTAL	99

Further similarities between the two series were discovered in the case of the bradycardias and tachycardias. In both studies it was observed that patients subjected to operation in the regions of the breast and perineum were more prone to develop bradycardia than those patients with operative sites elsewhere in the body. Sixty-three per cent of the group of patients with postoperative bradycardia in series 2 had pathologic conditions located in the breast or perineum in comparison with 62 per cent in the first series. The incidence of myocardial disease among the bradycardias was slightly less in the second series, 20 per cent in contrast to 40 per cent in series 1.

All the cases of tachycardia that developed in the immediate postoperative period in both series 1 and series 2 were sinus in origin and averaged in rate from 120 to 140 beats per minute. Table II indicates that the majority of cases of marked tachycardia represented a serious physiologic or medical disturbance which required prompt therapeutic measures. In both studies respiratory complications and hypovolemia due either to a decrease in total blood volume or a plasma deficiency alone were the major causes of a rapid pulse rate in the twenty-four-hour period after operation. Only 34 of 151 patients presented no obvious reason

TABLE II. Etiology of tachycardia in series 1 and series 2

Indications	Number of Patients Series 1	Number of Patients Series 2
Respiratory complications	14	6
Hypovolemia		
Total blood volume	16	13
Plasma deficiency	10	6
Severe preoperative myocardial disease	15	0
Miscellaneous	6	6
Preoperative tachycardia with adequate medical reason	25	0
No obvious cause	34	0
TOTALS	120	31

for the tachycardia.

The most interesting results in series 2 were found in an analysis of the total incidence of myocardial disease (Table III). In the entire group of 782 patients, 271, or 35 per cent, showed electrocardiographic evidence of cardiac pathologic conditions including flattening or inversion of the T wave; depression of the S-T segment; delayed intraventricular conduction; bundle branch block; nodal rhythm; auriculoventricular dissociation; auricular fibrillation; and changes indicative of old myocardial infarction, cor pulmonale, or left ventricular hypertrophy. Of these 271 patients, 56 would have been detected by applying the criteria of the first study, and another 48 were picked up by a preoperative electrocardiogram. The remaining 167 patients (61 per cent of the total) were not discovered prior to operation. Only 2 of these 167 patients showed electrocardiographic changes indicative of myocardial damage attributable directly to untoward incidents of the operative and postoperative period. In all the other cases the abnormalities of the electrocardiogram resulted from chronic heart disease, including 30 instances of old myocardial infarction. An example of an old anterior myocardial infarction which was missed by the failure to take a preoperative electrocardiogram is shown in Figure 1A.

Although no case of myocardial infarction was found in the group of patients on whom electrocardiograms were obtained during the course of the three-month period of study of series 2, 1 patient developed a coronary occlusion within a few hours after leaving the recovery room. No electrocardiogram was obtained on this patient, since he was admitted to the recovery room after 5:00 P.M. and displayed no clinical evidence of cardiovascular difficulty. There were, however, 3 cases of severe myocardial ischemia which were differentiated from subendocardial infarction solely by transaminase determinations and serial electrocardiograms. The electrocardiograms of 1 of these patients is shown in Figure 1B.

TABLE III. Types of myocardial disease

Indications	Number of Cases
Old infarction	38
Cor pulmonale	5
Severe myocardial ischemia	3
Myocardial damage	135
Bradycardia with myocardial disease	30
Arrhythmia or conduction defect with myocardial disease	60
TOTAL	271

Comment

To justify the recording of an electrocardiogram on every postoperative patient, it is necessary to determine how much, if any, additional information was obtained from the routine electrocardiograms of series 2 in comparison with the selected cases of series 1.

One of the most important aspects of the first study was the detection of 11 myocardial infarctions. In each case the symptoms and signs were so atypical that the diagnosis would have been delayed or missed entirely in the absence of postoperative electrocardiography.

Since a limited study produced such valuable information, it was anticipated that routine postoperative electrocardiography would result in an even better detection of the "silent coronary." On the contrary, study number 2 failed to reveal a single case of myocardial infarction during the hours in which electrocardiograms were recorded. Since the 1 patient who developed a myocardial infarction several hours subsequent to discharge from the recovery room was admitted after 5:00 P.M. and showed no clinical signs of cardiovascular abnormality

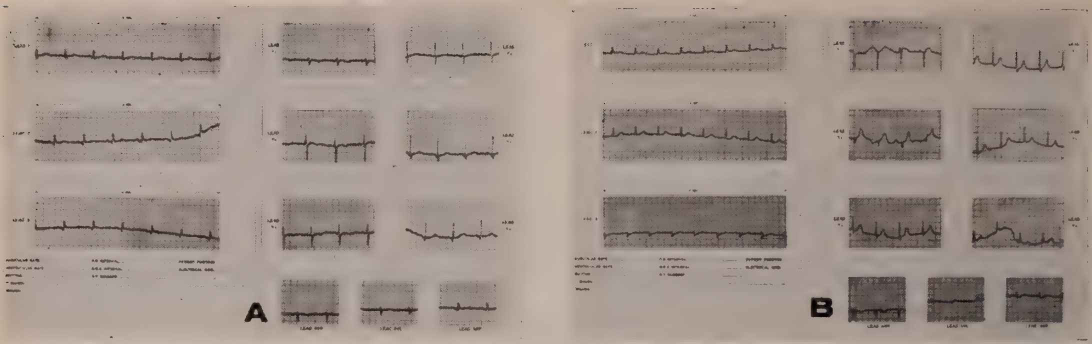

FIGURE 1. (A) Old posterior myocardial infarction, diagnosed for first time by electrocardiogram, in recovery room. (B) Interpretation by cardiologist: slight elevation of S-T segment 1, slight depression of S-T segments 2, 3, and V_3 to V_6. Abnormal tracing suggestive of acute injury pattern to lateral wall.

necessitating an electrocardiogram during the night, it is impossible to determine whether or not early electrocardiographic changes were present during the period of his stay in the recovery room. One case in 782 in series 2 bears out the ratio of approximately 1 out of 1,000 cases (11 in 10,000 in series 1) of myocardial infarction occurring in the first twenty-four hours after operation.

Confirmatory evidence for the relatively large number of cases of myocardial infarction reported in the two series of our study and for the absence of typical signs and symptoms is supplied by the investigations of Wroblewski and La Due,[2] Mendelsohn and Monheit,[3] and Driscoll *et al.*[4] Wroblewski and La Due[2] reported the incidence of myocardial infarction in the period after operation as 0.8 per cent (15 infarctions in approximately 20,000 operations). In this group 60 per cent of the patients developed evidence of infarction within three days after surgery with 4 cases occurring either on the operative or the first postoperative day. Only 4 of the 15 patients had typical symptoms of precordial pain. Driscoll *et al.*[4] detected 12 acute myocardial infarctions in 496 patients studied by electrocardiogram during the course of the first twenty-four hours after operation. Of these 12 cases, 6 would have been missed by reliance on clinical signs alone. In a series of 50 patients studied by Mendelsohn and Monheit[3] after biliary tract surgery, there were 4 cases of myocardial infarction and 5 patients with electrocardiographic changes suggestive of ischemia. All 4 cases of infarction were of the "silent variety." In addition to these investigations, recent series reported by Lindberg *et al.*[5] and Stokes and Dawber[6] suggest that myocardial infarction can occur with minimal or no symptoms or signs of cardiovascular difficulty.

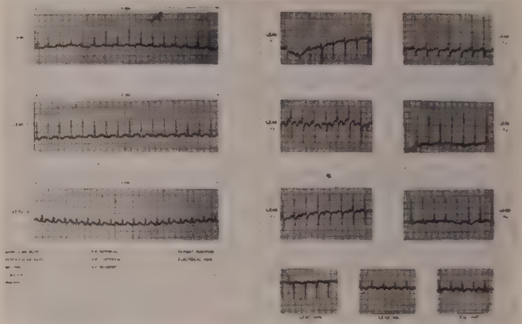

FIGURE 2. Myocardial ischemia following massive blood loss.

The number of cases and types of abnormality in the group of bradycardias, tachycardias, and arrhythmias were strikingly similar in the two series. Routine electrocardiography added very little to the information obtained by limiting the study to the categories established for the first series.

The most interesting results were obtained in the group of 271 patients with electrocardiograms indicating the presence of myocardial disease. By applying the criteria of the first study, 30 of these patients belonged in the category of bradycardias, 24 in the arrhythmias, and 2 in "evaluation." Another 48 cases were detected by a preoperative electrocardiogram, leaving 167 cases (61 per cent of the total) which were discovered for the first time by a routine postoperative electrocardiogram. On the surface this constitutes an excellent argument

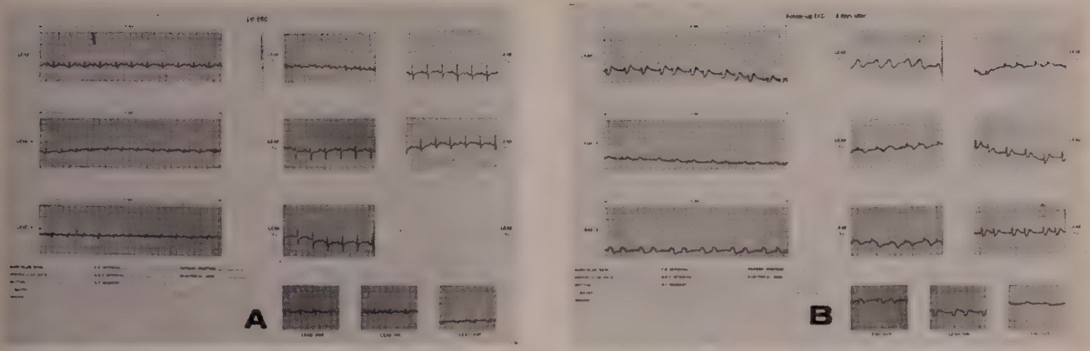

FIGURE 3. (A) Abnormal tracing suggestive of acute cor pulmonale, probably due to pulmonary embolism. (B) Follow-up tracing, six days post-operatively: tracing indicative of further acute right ventricular ischemia secondary to acute pulmonary infarction.

for recording an electrocardiogram on every postoperative patient. Further analysis reveals, however, that only 2 of the 167 cases represented recent myocardial damage which was directly dependent on events of the operative and postoperative period. One of these 2 was a case of a severe myocardial ischemia (Fig. 2) following massive blood loss in the operating room, and the other of a cor pulmonale (Fig. 3) in a patient who had been subjected to a laparothoracotomy for gastric cancer. In the remaining 165 cases the cardiac changes recorded on the electrocardiogram were chronic in nature and were present prior to operation. Included in this group were 30 old myocardial infarctions. All of these cases could have been detected to greater advantage by a preoperative electrocardiogram.

As a result of these two studies, we have reached the conclusion that routine postoperative electrocardiography is not justified, since the information revealed by this means adds very little to that obtained by limiting the technic to the criteria employed in the first study. Changes that occur as the result of operative and postoperative medical and physiologic phenomena can be detected by recording a postoperative electrocardiogram on patients showing marked bradycardia or arrhythmia, sudden unexplained tachycardia, hypoxia, or hypotension not amenable to the restoration of circulating fluid volume. Since many of the cases of myocardial disease detected by the postoperative electrocardiogram represented the chronic cardiac pathologic conditions which existed prior to surgery, we feel that a routine preoperative electrocardiogram is indicated in every patient scheduled for general or spinal anesthesia or major surgery.

Summary

1. Postoperative electrocardiography is not indicated for every patient admitted to the recovery room.

2. Cardiovascular abnormalities resulting from events of the operative and immediate postoperative period can be detected by limiting the recovery room electrocardiogram to patients with (1) sudden unexplained tachycardia, (2) hypotension unresponsive to fluid replacement, (3) marked bradycardia or arrhythmia, and (4) lack of oxygenation due to any cause.

3. A routine preoperative electrocardiogram is indicated for every patient scheduled for operation.

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Infection and Chronic Lymphocytic Leukemia

A Review of 61 Cases

THE HOSPITAL RECORDS *of 61 patients with chronic lymphocytic leukemia, or CLL, were studied. Infection and anemia were the principal causes of hospital admissions. Thirty-seven patients (61 per cent) had a total of 84 clinically evident infections: 33 episodes of pneumonia, 18 skin infections, 10 genitourinary infections, 8 bacteremia infections, and 26 other infections. There appeared to be no correlation between use of adrenal corticosteroids, radiation, or cytotoxic agents and the occurrence of infections. The frequency of infection and the incidence of acquired hemolytic anemia suggest that the immune response is distorted and inadequate in chronic lymphocytic leukemia, but the exact cause has not been determined.*

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THE CLINICAL ENTITY which is included in the term chronic lymphocytic leukemia, or CLL, presents itself in different ways to the patient and the physician. It is a disorder which is relatively easy to describe, but the breadth of the definition can be varied. It would appear that the most simple description is that CLL is a progressive and irreversible disorder of lymphocytic tissue which is characterized by increased numbers of mature-appearing lymphocytes in the peripheral blood and tissue; frequent enlargement of the lymph nodes, spleen, and liver; and which has a duration usually measured in years. One of the areas of discussion relating to this disease concerns how frequently CLL causes symptoms. To minimize the malignant aspects of chronic lymphocytic leukemia, some would substitute the term "chronic lymphocytosis," indicating that this is a relatively benign disorder in most patients and causes few symptoms.[1] Such a viewpoint can be supported by the clinician's attitude toward the disease or by studies which show that the disease exists in substantial numbers of people who have no symptoms attributable to CLL. Since CLL is commonly a disease of the later years of life when symptoms due to aging become more frequent, it is, at times, difficult to separate symptoms into different etiologic classifications.

As the disease is most frequently encountered, patients have symptoms that can be related directly or indirectly to the leukemic process. In some patients these symptoms are relatively minor and interfere little with their normal life. With progression the disease can produce manifestations that require hospital care, and in some instances the disease is related causally to a patient's death.

It is the purpose of this study to present information concerning the symptomatic illnesses associated with chronic lymphocytic leukemia when such illness was severe enough to admit the patient to a clinic or a hospital. This study does not describe the entire gamut of symptomatic illness in CLL, but only that portion which appears most important to the patient and his physician.

This study is based on a review of the records of 61 patients with chronic lymphocytic leukemia from five major hospitals in one community and from a tumor clinic. It is realized that the cause of hospital admission is the result of an interplay of many factors, not all of which are strictly within the area of clinical medicine. In a retrospective study such as this, it is impossible to equate the relative importance of each factor at the particular time the patient entered the hospital or clinic. Certainly the manifestations of disease, the patient's and physician's sensitivity to symptoms, the socioeconomic setting of the patient, and the judgment and experience of the admitting physician are some of the factors which play a role in the decision concerning hospital or clinic admission.

Materials and methods

The patient records of five Syracuse, New York, hospitals and an outpatient tumor clinic were reviewed for over as long a time as adequate records were available. The periods varied from four to twelve years prior to June, 1959. No cases were included in the series in which there was reasonable doubt concerning the diagnosis of chronic lymphocytic leukemia. All the patients included in this series had a high white blood cell count with a persistent absolute lymphocytosis of predominantly mature lymphocytes. In the majority of patients there also was an enlargement of the liver, spleen, and/or lymph nodes. Patients with obvious blastic leukemia, even if the cell type appeared to be lymphocytic, were not included. Because of the retrospective nature of this study, the observations on some patients were limited.

Results

The records of 61 patients were examined and included in this study. The sex and age distributions of these patients are indicated on Table I.

TABLE I. Age at the time of diagnosis of chronic lymphocytic leukemia

Sex	Number of Patients	Mean Age (Years)	Median Age (Years)
Male	39	64.5	65
Female	22	68.5	69
TOTAL	61	65.9	66

Of the total group of 61 patients, 13 are still alive, 13 were lost to follow-up, and 3 had their disease discovered a few days before their deaths. The remaining 32 cases were followed from the time of diagnosis to death. The mean duration of the disease (diagnosis to death) was 2.5 years with a range of from two weeks to nine years. Two years after the diagnoses were made 47 per cent of the group of 32 patients with a complete follow-up were living. Four years after the diagnoses 19 per cent were living, and six years after the diagnoses 9 per cent were living. There was no correlation found between the duration of the disease and the patient's age at the onset of the disease.

In reviewing the records it became obvious that infection was a frequent event in the patients studied. Thirty-seven patients (61 per cent) of the entire group of 61 patients had a total of 84 clinically evident infections. Although the infections were symptomatic in each case, objective evidence was required for their inclusion in the study as infections. The objective evidence included visible abscesses; an infiltration of the lung which was demonstrated by an x-ray examination and which disappeared with anti-infective therapy; and a febrile episode with positive blood, urine, or sputum cultures which, when treated as an infection, resulted in lysis of the fever and negative cultures. Infections of the respiratory tract, including bronchitis with cough and fever, were not listed as infections unless positive bacterial cultures were obtained. Twenty-two of the patients with infection and 10 patients who had no evident infection were followed from the time of diagnosis to the time of death. There was no significant difference between these two groups in the duration of the disease.

The primary cause for hospital admission was determined after a review of the chart correlating the patient's complaint with the objective clinical findings. The entire group of 61 patients had 193 hospital admissions. Forty-one of these admissions were primarily for infection, 14 primarily for bleeding, and 38 primarily for anemia without obvious bleeding. There also were 46 admissions for other causes related to chronic lymphocytic leukemia, for example, weakness, fever, lymphadenopathy, and so forth, and 54 admissions for reasons not directly related

TABLE II. Etiology of infections isolated

Etiology	Number of Infection Episodes
Coliform	11
Diplococcus pneumoniae	10
Micrococcus pyogenes (Staphylococcus)	5
Streptococci	5
Herpes simplex (clinical diagnosis)	4
Hemophilus influenza	3
Pseudomonas aeruginosa	2
Herpes zoster (clinical diagnosis)	2
Proteus vulgaris	1

to the patient's leukemia, for example, appendicitis, herniorrhaphy, and so forth. Twenty-six of the 32 cases that were followed from the time of diagnosis until the time of death had hospital admissions connected with their chronic lymphocytic leukemia. Sixty-three per cent of the hospital admissions that were primarily for infection occurred in the last year of the patients' lives. Over 90 per cent of the hospital admissions which were primarily for bleeding and anemia and 45 per cent of the admissions for other causes related to CLL occurred during the year preceding death.

The most common infection encountered among the entire group of 61 patients was pneumonia. There were 33 episodes of pneumonia, 6 of which were terminal. In 5 of the 6 terminal pneumonia cases an absolute neutropenia (less than 2,700 neutrophils per cubic millimeter) were found at the onset of the infection. There were 18 skin infections, 10 genitourinary infections, 8 bacteremia infections, and 26 other infections. All of the bacteremia infections were symptomatic and were without an obvious source for the introduction of the bacteria. The infecting organisms in the 8 bacteremia infections were 2 Pseudomonas aeruginosa (both terminal), 5 coliform organisms (2 terminal cases, 3 recovered), and 1 streptococcus (terminal).

In considering the etiology of the entire group of infections, positive cultures were included only if they were accompanied by a symptomatic infection. The most commonly isolated organisms were coliform bacilli, which were cultured during 11 episodes of infection, and Diplococcus pneumoniae, which was obtained in 10 instances. Staphylococci and streptococci were each isolated 5 times. Two cases of herpes zoster also were diagnosed clinically. The various organisms isolated from the entire group of 61 patients during evident episodes of infection are shown in Table II.

When available, the white blood cell count and the differential count taken at the onset of the infection were analyzed primarily for infection for each of the hospital admissions. This represented the initial diagnostic laboratory examination of the patient, and in most instances it was done before any type of therapy was instituted. The normal total leukocyte count is arbitrarily defined at from 5,000 to 10,000 white blood cells per cubic millimeter and the normal absolute neutrophil count at from 2,700 to 6,200 per cubic millimeter. It was found that 75 per cent of the patients had a leukocytosis, and 56 per cent of the patients had a neutropenia at the onset of their infection (Table III).

In this review, patients receiving adrenal corticosteroids at any time during the course of their illness had no greater incidence of infection than those patients who did not receive this therapy. In 50 per cent of the episodes of infection the patient had received either antileukemic chemotherapy or x-irradiation in the three-month period preceding the infection. There appeared to be

TABLE III. Total leukocyte and neutrophil count during infection

	White Blood Cells		Neutrophils	
Findings	Number of Infections	Total (Cubic Millimeters)	Number of Infections	Count Per Cubic Millimeter
Less than normal	5	<5,500	35	<2,700
Normal	11	5,000 to 10,000	15	2,700 to 6,200
Greater than normal	49	>10,000	13	>6,200
No information	30	...	32	...

TABLE IV. Age distribution of patients with infection and chronic lymphocytic leukemia

Age at Diagnosis (Years)	Number of Patients	Number of Patients with Infection	Number of Episodes of Infection
21 to 30	1	1	4
31 to 40	1	1	2
41 to 50	5	4	6
51 to 60	9	4	10
61 to 70	22	14	33
71 to 80	19	10	26
81 to 90	3	2	2
91 to 100	1	1	1
TOTALS	61	37	84

no provable correlation between the judicious use of radiation or cytotoxic agents and the occurrence of infections. Older patients with CLL showed no greater tendency to acquire infections than did younger CLL patients. The number of patients in the younger-age groups are small, however (Table IV).

In the group of 37 patients with a history of infection, 11 had hilar node enlargement noted on chest x-ray films. Seven patients with hilar node enlargement had episodes of pneumonia. Twenty-two had no hilar nodes, and 4 had questionable hilar nodes noted on chest x-ray films. Thirteen of this group of 26 patients had episodes of pneumonia.

Comment

This study was undertaken to determine why patients with chronic lymphocytic leukemia enter the hospital. Emphasis was placed on infectious disease for two reasons: (1) infections are a major cause of morbidity in CLL, and (2) the corroborative laboratory data were more complete for infections than for other complications, such as anemia and bleeding.

The occurrence of infections in patients with chronic lymphocytic leukemia has been noted for many years. As early as 1902 and 1903 there were reports of pneumonia complicating CLL.[2,3] Wintrobe and Hasenbush[4] noted that 38 per cent of the patients with CLL had infections, whereas 28 per cent of the patients with chronic myelocytic leukemia, or CML, developed infections. In his study there were 10 episodes of pneumonia among the 47 patients with CLL and none among the 39 cases with CML. Pisciotta and Hirschboeck[5] reviewed the causes of death of 54 patients with CLL and found that 4 died of pneumonia. Kirshbaum and Preuss[6] studied over 14,000 necropsies at the Cook County Hospital and found 23 cases of CLL, 14 of whom died of pneumonia and 8 of whom showed massive gross bleeding. The occurrence of infections with gram-negative organisms has long been a problem in the care of patients with leukemia. Silver *et al.*[7] found Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa to be the most frequently encountered organisms in a group of patients with acute leukemia. Forkner *et al.*[8] studied 23 patients with Pseudomonas septicemia and found that 13 of these patients had leukemia, and 2 of these had the chronic lymphocytic type. A recent report emphasized the high incidence of infection, including pneumonia, in CLL, and describes some aspects of the disturbed immune response in this disease.[9] It appears that there is a defect in the immune response in some patients with chronic lymphocytic leukemia which causes an increased susceptibility to bacterial infection.

One consideration would be whether or not the defect is the result of decreased phagocytic activity. The quantitation of total phagocytic activity in the body is difficult, if not impossible. Not all infective agents are ingested actively by phagocytic cells, but many bacteria are. Not all bacteria are destroyed even if they enter a cell. The phagocytic mechanism includes those cells, such as the neutrophil, monocyte, and histiocyte, which are distributed to local sites of infection, as well as the phagocytic cells fixed within the vascular system that screen particulate material from the circulation. Clinically one measures only a fraction of this phagocytic function when the neutrophils are enumerated in the peripheral blood. It is by inference that we assume that an appropriate neutrophil response to local infection occurs when the peripheral count increases, since the phagocytic activity at the site of infection is the more important aspect in the control of infection by this means. In this study the neutrophil response, as measured in the peripheral blood at the onset of infection, appeared to be less than that which is normally seen with bacterial infection or was absent altogether. Obviously this is explicable in a number of ways. The patients studied are in the older-age group, and the neutrophil response to infection in the aged may be diminished. Early in infection at any age the absolute number of neutrophils in the blood may not be increased. It is appealing to relate the lack of neutrophil response in these patients directly to their lymphocytic leukemia. Although information on this specific point in this study is not available, one could suppose that so much infiltration of the marrow cavity by lymphocytes had occurred that it impaired effective and rapid myelopoiesis. It is also possible that the extra medullary leukocyte pool, which is presumably the most readily available source of neutrophils, is diminished in these patients or that the stimulus for the redistribution of these cells to the infective site is lacking.[10] Whatever the explanation, the neutrophil response to infection in some patients with CLL is less than expected and may play a role in increased susceptibility to infection.

The role of the lymphocyte and lymphocytic tissue in the control of infective agents certainly is not understood completely. The classic barrier theory proposed by Virchow[11] that the lymph vessels channel particulate material, such as bacteria, to regional nodes where phagocytosis by fixed macrophage occurs appears to be a part of the immune response. However, as Yoffey[12] suggests, this system not only may have a limited capacity but actually can facilitate the distribution of infection. The latter certainly could be true if the normal structure of the lymph node was distorted and/or if the phagocytes present in the node were diminished or inhibited. Normal lymph node architecture is frequently altered in CLL.[13] The distortion of the nodal architecture suggests that organisms which obtain access to afferent lymph vessels could pass more readily into the large lymph channels and eventually into the blood stream. The incidence of bacteremia in this study may indicate that this occurs and that it occurs more frequently in terminal disease when there is quantitatively more lymphatic tissue involved.

The cytologic source of soluble antibody has been a subject for continuing examination and discussion. Harris and Harris[14] have reviewed this subject and presented evidence which supports both the plasma cell and the lymphocyte as a source of antibody globulin. Since their review, other studies[15,16] have appeared which continue to support one or another view of the principal cell type involved in the production of antibodies. The lymphocyte and plasma cells not only are frequently closely associated physically, but also probably are related genetically either through common derivation or interconversion. Schultz[15] suggests in his review that following the initial exposure to an antigen there is a proliferation of plasma cells with a simultaneous appearance of antibody protein.

Whichever primary cell type is responsible for the production of most of the soluble circulating antibody, physically and genetically it appears to be related in part to lymphocytic tissue. With this assumption it is not difficult to suppose that the antibody portion of the immune response would be quantitatively and qualitatively disturbed in a disease which affects the growth pattern and metabolism of lymphocytic tissue. Many investigators have noted abnormalities in serum gamma globulin levels in patients with CLL. Hypogammaglobulinemia has been reported in from 10 to 50 per cent of patients with CLL.[17-22] The depression in gamma globulin levels generally occurred late in the disease and was not found by all investigators to be accompanied by an increased incidence of infections.[18,19] Hypergammaglobulinemia also has been reported in CLL patients.[17,22] In spite of the varying gamma globulin levels reported in CLL, almost all the patients with this disease have little or no antibody response to certain injected antigens.[23-26] Properdin levels have been reported as normal[27] and decreased.[28] Complement has been shown to be present in a normal amount in CLL.[28]

More speculation is possible if we include the observations of Nossal and Lederberg[29] concerning the production of antibodies by single cells. These studies appear to indicate that the single lymphocyte has the capacity to produce only one or at most two specific types of antibodies. Coons, Leduc, and Connolly's[30] observation of the distribution of antibodies in lymphocytic tissue also indicates that not all cells produce all antibodies and that clones of similar cells are stimulated to replicate and to produce antibodies to a specific response.

One hypothesis that might be drawn from such studies is that there is considerable heterogeneity, in a genetic sense, in lymphocytic tissue; that there are numerous cell lines, morphologically similar but genetically different. This could be supported by Burnet's[31] hypothesis of clonal selection in immunity. This genetic difference expresses itself in the individual cell's ability to respond to a specific antigen. If this be the case, then it is also possible that in chronic lymphocytic leukemia there have been developed specific clones of cells which have a limited ability to produce large varieties of antibodies because they are genetically rather homogeneous.

It is possible to include in the hypothesis of homogeneity of cell population in CLL some of the other immune phenomena seen with CLL. The most obvious of these is acquired hemolytic anemia. Acquired hemolytic anemia is observed with some frequency in CLL.[32] Although the mechanism of this disorder is not understood in detail, it may involve both soluble agents, such as plasma proteins which could influence red cell surface or metabolism, and aberrant tissue and cell mechanisms which decrease the survival of erythrocytes. If there was functional hypertrophy of certain cell lines which produce particular proteins that adversely affect erythrocytes, it would not be surprising that some patients would develop hemolytic anemia in association with CLL on this basis.

Summary

The hospital records of 61 patients with chronic lymphocytic leukemia were reviewed. The principal causes of hospital admissions were found to be infection and anemia. Pneumonia was the most commonly occurring infection in this study. There were eight bacteremia infections, seven of which were caused by gram-negative organisms. Over 90 per cent of the serious anemia and bleeding episodes occurred in the last year of life, whereas only 63 per cent of the infections occurred in the last year of life.

The administration of corticosteroids or alkylating agents did not appear to increase the occurrence of infections among the patients studied in this series. The frequency of infection and the incidence of acquired hemolytic anemia suggest that the immune response is distorted and inadequate in chronic lymphocytic leukemia. The possible causes of the disturbed immunity are discussed.

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Closed-chest massage in stillborn infant

Closed-chest heart massage has been used successfully to resuscitate a stillborn infant, according to an article by Sylvan N. Surks, M.D., and William Ladner, M.D., in the April 28, 1962, issue of the *Journal of the American Medical Association*. Less than one minute after the baby was delivered artificial respiration and closed-chest heart massage were begun. An anesthesiologist performed the heart massage, using two fingers to apply intermittent pressure to the infant's breastbone overlying the heart.

Resuscitation continued approximately seven minutes before the baby began breathing spontaneously. About two minutes later the respirations became regular. The baby was discharged from the hospital in good condition five days later, and at three months of age showed no damage to the brain or nervous system.

From this case and similar reports, it appears that newborn infants can withstand the moderate chest compression necessary to activate the heart. This type of massage should be the preferred method of resuscitation in stillborn infants when resuscitation is deemed feasible. Since closed-chest heart massage can be started immediately, this technic should be expected to reduce the incidence of neurologic damage in resuscitated stillborn infants.

The Misdiagnosis of Glaucoma

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FALSE DIAGNOSIS of glaucoma may be made in patients in whom the disease does not exist and the patient subjected erroneously to medical or surgical therapy. Correct diagnosis with the use of a Schiotz tonometer depends on reliability of the instrument, use of a correct calibration scale, and recognition of the error of reproducibility of tonometer readings. Misdiagnosis may be made on the basis of misinterpretation of the following: high normative ocular tensions, high ocular rigidity, changes of the disk and visual fields caused by other conditions, and visual fields with normal disks.

AT PRESENT both the ophthalmologist and his medical colleagues are being urged to practice routine tonometry so that early cases of glaucoma may be detected. Simultaneously there has been a concentrated effort to develop diagnostic procedures such as tonography which will be of aid in determining early cases of glaucoma. Errors can be made with our present diagnostic technics for glaucoma so that the diagnosis of glaucoma may be made in patients in whom the disease does not exist. When a patient has been thus misdiagnosed, he may be subjected erroneously to either medical or surgical therapy. Wrong diagnoses will lead also to a false concept of glaucoma in regard to the course, prognosis, and adequate therapy.

There are various types of misdiagnosis of glaucoma. The most important and common of these is the misdiagnosis of chronic open-angle glaucoma from the normal, and this paper will concern itself primarily with this type. To establish if the misdiagnosis has been made, it is exceedingly important that the criteria for the diagnosis of chronic open-angle glaucoma are clear. In this author's opinion, until further knowledge is obtained concerning the relation between ocular tension and field loss, any combination of two of the following factors will be considered adequate for the diagnosis of chronic open-angle glaucoma and therefore adequate for therapy to avoid field loss: persistent elevated ocular tension; difference between the two eyes greater than 4 mm. Hg; low coefficient of outflow by tonography or high P o/c by water-provocative tonography; and field and/or disk change. The author is well aware that patients may carry elevated ocular tensions for a considerable period of time and even have abnormal tonographic values without showing field changes.

TABLE I. Survey of adequacy of Schiotz tonometers from July 1, 1959, to June 30, 1960[1]

Make	Total Serviced	Rejected for Discard (Per Cent)	Corrected (Per Cent)	Meeting Standards (Per Cent)
American	484	2.9	37.6	59.5
Foreign	178	27.5	31.5	41.0
TOTALS	662	9.5	36.0	54.5

Since tonometry, either impression or applanation, tonography, and field and disk changes are used for the diagnosis of chronic open-angle glaucoma, a knowledge of the errors which can arise using these technics are needed to avoid a misdiagnosis. The purpose of this paper is to point out how these errors are made and can be avoided.

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TABLE II. Calibration scale for Schiotz tonometers (millimeters of mercury) with 5.5-Gm. and 7.5-Gm. weights

Scale Reading	1948		1954		1955	
	5.5	7.5	5.5	7.5	5.5	7.5
3.5	25.4	37.2	22.2	34.2	22.4	33.0
4	23.4	34.7	20.4	31.8	20.6	30.4
6	16.9	26.5	14.6	23.5	14.6	21.9
7	14.2	23.0	12.4	20.2	12.2	18.5

Tonometry

Since the Schiotz tonometer is the main instrument used in routine tonometry, the following discussion is based on this instrument.

THE INSTRUMENT. The Schiotz tonometer is a delicate mechanical instrument which is subject to wear and tear and requires a periodic evaluation of its satisfactory working order. As with any other instrument, it is the responsibility of the user to make sure that the instrument is adequate and gives reliable measurements. Table I has been taken from the report of the Committee on Standardization of Tonometers of the American Academy of Ophthalmology and Otolaryngology by the R. O. Gulden Schiotz Tonometer Service of Philadelphia covering the year July 1, 1959, to June 30, 1960.[1] It indicates that even 2.9 per cent of American-made tonometers had to be rejected or discarded as being entirely inadequate for repair, and almost a little over a third had to be corrected. Therefore, in the hands of their owners these tonometers probably were estimating ocular tension inaccurately. If the instrument registered on the high side of normal, the ophthalmologist using this instrument may have been making the diagnosis of glaucoma on the basis of elevated tension when actually the instrument was at fault. Every ophthalmologist should have at least two Schiotz tonometers so that one can be sent in and checked regularly.

CALIBRATION SCALE. Not only is it important to have an adequate tonometer, but it is also important to use the correct calibration scale. The limits of what is considered to be the normal ocular tension are based on the surveys of large populations in terms of both scale reading and millimeters of mercury using the 1955 calibration scale. The errors involved in using scales older than that of 1955 are shown in Table II. If the ophthalmologist is using scale readings only, then very little confusion will result with changes in the calibration scale. However, if he is using millimeters of mercury, then, as shown in Table II, for the same scale reading the 1955 scale has lower values in millimeters of mercury. Therefore what will be considered abnormal tensions on the 1948 scale will be borderline or normal on the 1955 scale.

REPRODUCIBILITY OR ERROR OF SCHIOTZ TONOMETER READING. One must always remember that the Schiotz tonometer, like any other instrument, has a certain error associated with it, that is, if the same individual took repeated measurements on a model eye in which the pressure was held stationary, then there would be a certain range of values. For the Schiotz tonometer this spread of values for any particular reading is about ±0.5 scale readings.[2,3] Table III illustrates this point using the 4-scale reading for the 5.5-Gm. weight and the 6-scale reading for the 7.5-Gm. weight which represent almost the upper limits of normality for ocular tension. A 4-scale reading actually could be 3.5 to 4.5, and a 6-reading could be 5.5 to 6.5. Therefore the spread of ocular tensions are 3.5 mm. Hg with the 5.5-Gm. weight and 3.7 mm. Hg for the 7.5-Gm. weight. This error represents ideal conditions and is probably larger in everyday practice with such effects as lid squeezing, movement of the eyes, and position of the tonometer. The error of a Schiotz reading is also increased when one patient

TABLE III. Error of a Schiotz tonometer reading—±0.5 scale readings

Tonometer Scale Reading	Weight (Gm.)	Mm. Hg (1955)	Error	
			Scale Reading	Mm. Hg (1955)
4	5.5	20.6	3.5 to 4.5	22.4 to 18.9
6	7.5	21.9	5.5 to 6.5	23.8 to 20.1

TABLE IV. Error of one tonometer reading based on glaucoma surveys

Year	Place	Number of Patients Screened	Referred for Further Glaucoma Tests (Per Cent)	Glaucoma* (Per Cent)	False Positive (Per Cent)
1944	Philadelphia, Pennsylvania	10,000	12.3	1.5	11.8
1953	Cleveland, Ohio	12,825	12.8	2.3	10.5
1955	Kings Park, New York	6,373	6.7	2.4	4.3
1956 to 1957	Southern California	3,958	10.8	2.5	8.3
1958	Pittsburgh, Pennsylvania	20,994	5.7	1.8	3.9
Average			9.7	2.1	7.8

* Calculated percentage includes estimated percentage of glaucoma patients of those not followed up, assuming percentage of glaucoma patients similiar to that of patients followed up.

sees different ophthalmologists who may have standardized tonometers but who show variations between each other in reading the same ocular tension. Unless one recognizes the error of the tonometer then one or two readings which happen to be on the high side of the error range, that is 3.5 with the 5.5- or 5.5 with the 7.5-Gm. weight may indicate that the patient has glaucoma while actually the patient's tensions may be entirely normal.

The error of single tonometer readings can again be pointed out vividly by analyzing the data from glaucoma surveys which have been carried out using one tonometer reading on large numbers of patients.[3,4] Table IV shows such an analysis of surveys in which an average of 9.7 per cent of the patients were referred for further glaucoma tests based on one tonometric examination, and only 2.1 per cent were actually found to have the disease. Therefore for approximately every 1 patient with glaucoma who was detected, 4 patients were referred. Of course a great deal of the high percentage of false positive findings is undoubtedly due to patients having tensions taken for the first time, but some of it is probably due to variation or errors in tonometric examination.

Misinterpretation of high normative ocular tensions

Beside the preceding factors of instrument errors, calibrations errors, and the error of the reproducibility of measurement, an unawareness that the distribution of ocular tensions in a normal population appears to be that of a normal distribution curve may also lead to misdiagnosis. There are then a number of individuals at the extreme ends of the curve who will show very high or low tensions. When these individuals are examined and followed carefully, they are found to be normal and do not exhibit any other indication of glaucoma aside from a high ocular tension. Figure 1A, taken from Leydhecker,[5] indicates his data on a survey of ocular tensions of 10,000 persons. This curve, as Leydhecker points out, is the result of two curves or two distribution patterns, one being the normal distribution pattern for the population and the other containing the abnormal ocular tensions of the glaucomatous patients. Figure 1B, also taken from Leydhecker,[5] shows the normal distribution curve which has been extrapolated from Figure 1A. There are a number of individuals who have tensions over 20 mm. Hg, and in fact Figure 2 indicates how many individuals have elevated tensions.[5] Almost 0.5 per cent of the total population had tensions greater than 25 mm. Hg. Therefore when measuring ocular tensions, one must expect to find individuals who will have so-called high normative ocular tension. When these patients are examined carefully with other diagnostic means such as visual fields and water-provocative tonography, no indication of any abnormality is found. These patients could be easily and readily labeled as glaucoma. The following is a case report of a patient who falls into this group of normative high ocular tensions and who received medication for a period of eleven years until the correct diagnosis was made.

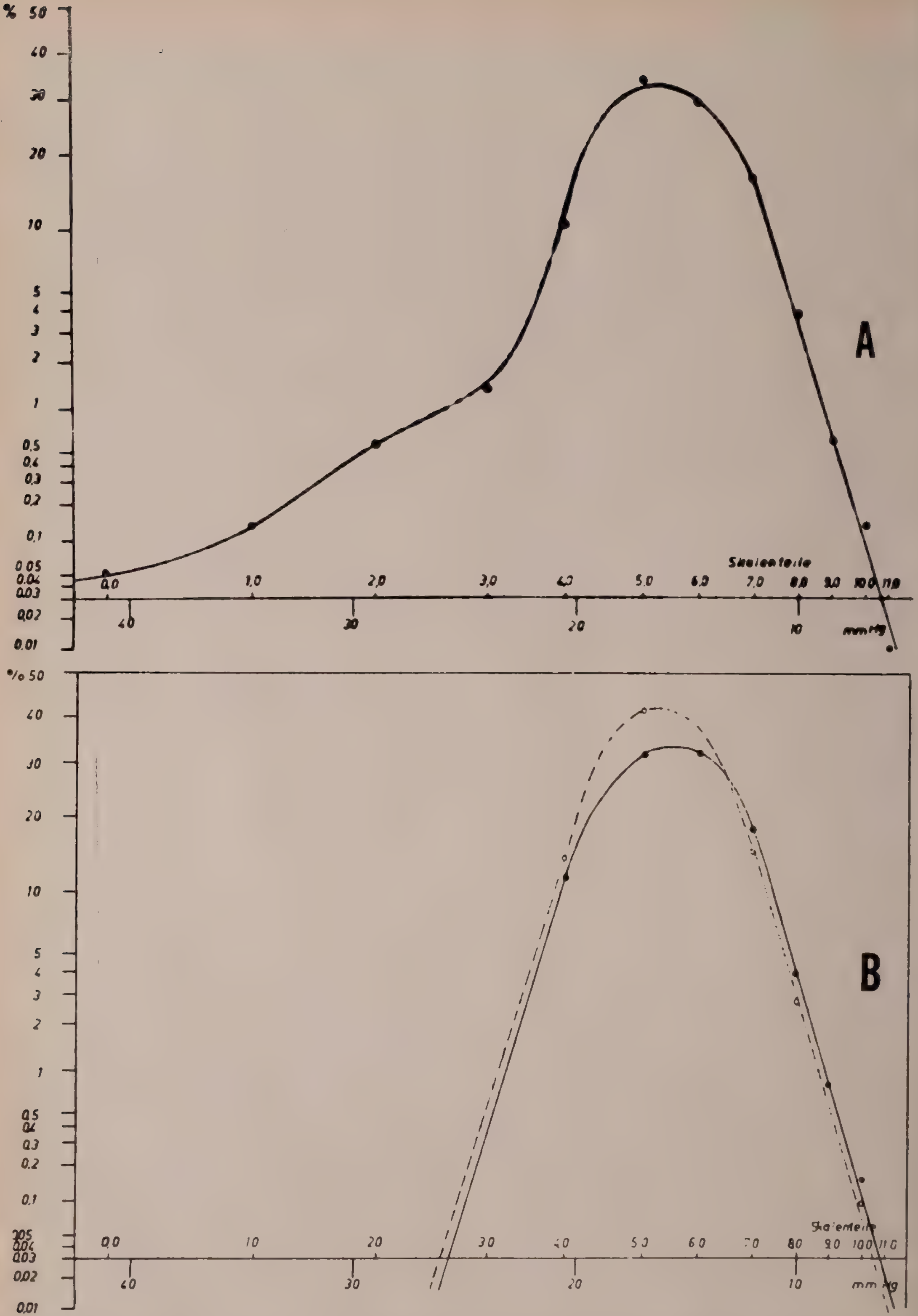

FIGURE 1. (A) Logarithmic frequency distribution curve of ocular tensions (Schiotz) of 19,880 eyes in 10,000 patients without symptoms. (B) Extrapolated logarithmic frequency distribution taken from (A) after exclusion of glaucomatous eyes. (Reproduced with permission of authors and publishers, Ferdinand Enker Verlag, Stuttgart.[6])

CASE 1. A white female first saw her ophthalmologist at the age of forty with intermittent sharp pains in both eyes accompanied by headaches. Her ocular tensions averaged 29 mm. Hg in the right eye and 27 in the left eye. The visual acuity was 20/20 in both eyes, the disks were normal, and the central fields were slightly constricted to 20 to 25 degrees. The ocular tension diurnal variation was less than 3 mm. Hg in both eyes. The angles were open. The patient was placed on 2 per cent pilocarpine which reduced her tensions to 21 mm. Hg in both eyes. Over the next ten years the patient was seen at regular intervals, and her ocular pain was diagnosed as tension headaches. When she was seen eleven years after the initial diagnosis and her medication discontinued, her tensions averaged 26 mm. Hg in the right eye and 25 mm. Hg in the left eye. The visual acuities were 20/20 in both eyes. The disk was normal and the central fields full and normal. Her tonographic values showed a normal outflow, and the patient had a normal ocular rigidity.

Misinterpretation of high ocular rigidity

When performing Schiotz tonometry, besides measuring ocular tension one is determining ocular rigidity, that is, the indentation that the plunger makes in the eye depends not only on the pressure but also on the elasticity or rigidity of the ocular coats. In patients who have highly rigid or unelastic walls, the plunger will sink in very small distances compared with those who have normal elasticity, and therefore the scale reading will be low and the tension registered as high. The danger is therefore that individuals who may have normal ocular tensions but increased ocular rigidities will be labeled as having glaucoma and will be treated as such. Table V illustrates this point in a qualitative manner as to how one can determine whether or not a patient has elevated ocular rigidities by using Friedenwald's[2] method of several independent determinations using two weights. If the pressure reading in millimeters of mercury with the 10-Gm. weight is consistently greater than the reading with the 5.5-Gm. weight, then the patient has increased ocular rigidity. The error range of these tonometric readings is indicated also in the last column of Table V.

The factor of ocular rigidity can be eliminated almost entirely by using the Goldmann applanation tonometer. The importance of ocular rigidity in determining the ocular tension is shown by Figure 3 taken from Goldmann and Schmidt[6] which shows the variation of scale reading for the 7.5-Gm. weight for one tension of 24 mm. Hg with changes of ocular rigidity. Slight increases in ocular rigidity will give large decreases in scale readings, indicating highly elevated ocular tensions. Since 19 per cent of routine office patients have ocular rigidities above 0.0250, according to Drance,[7] one may expect to encounter patients with misdiagnosed glaucoma who have increased ocular rigidities. An example of this problem is given in Table VI which shows what happens when one has increased ocular rigidity with a borderline ocular tension by Schiotz tonometry. In this case the patient's ocular rigidity or K value was 0.053 which was chosen for this example because it was highly elevated. However, the tension readings for the 5.5- and 10-Gm. weight were respectively 22.4, which is certainly a borderline reading, and 27.2 which is certainly elevated. One would think that on the basis of these tensions this patient would be regarded as highly suspicious of having glaucoma especially on the basis of the 10-Gm. weight reading. However, the patient's true tension was only 12 mm. Hg. Thus the misdiagnosis of glaucoma can be made easily by ignoring the factor of ocular rigidity. An actual case representing such an instance is shown in the following:

CASE 2. A white female first saw her ophthalmologist at the age of thirty-four. At this time the diagnosis of glaucoma was made based on ocular tensions ranging from 22 to 29 mm. Hg in the right eye and 23 to 29 mm. Hg in the left eye. The visual acuity in both eyes was 20/20. The optic disks showed questionable early cupping. The central fields were full and normal. The patient had a narrow angle and a negative reaction to a mydriatic test. A basal iridectomy was done on the left eye, and the postoperative tension ranged from 22 to 31 mm. Hg in the right eye and from 23 to 29 mm. Hg in the left eye. Three years later because the tension in the left eye was 32 mm. Hg, a cyclodialysis was done. After eleven years the visual acuity in both eyes was 20/20; the optic disks were normal, the central fields were full and normal, and the tensions without medication ranged as before surgery. The tensions in both eyes measured with Schiotz tonometers of two weights were as follows: 17.3 mm. Hg with a 5.5-Gm. weight and 23 mm. Hg with a 10-Gm.

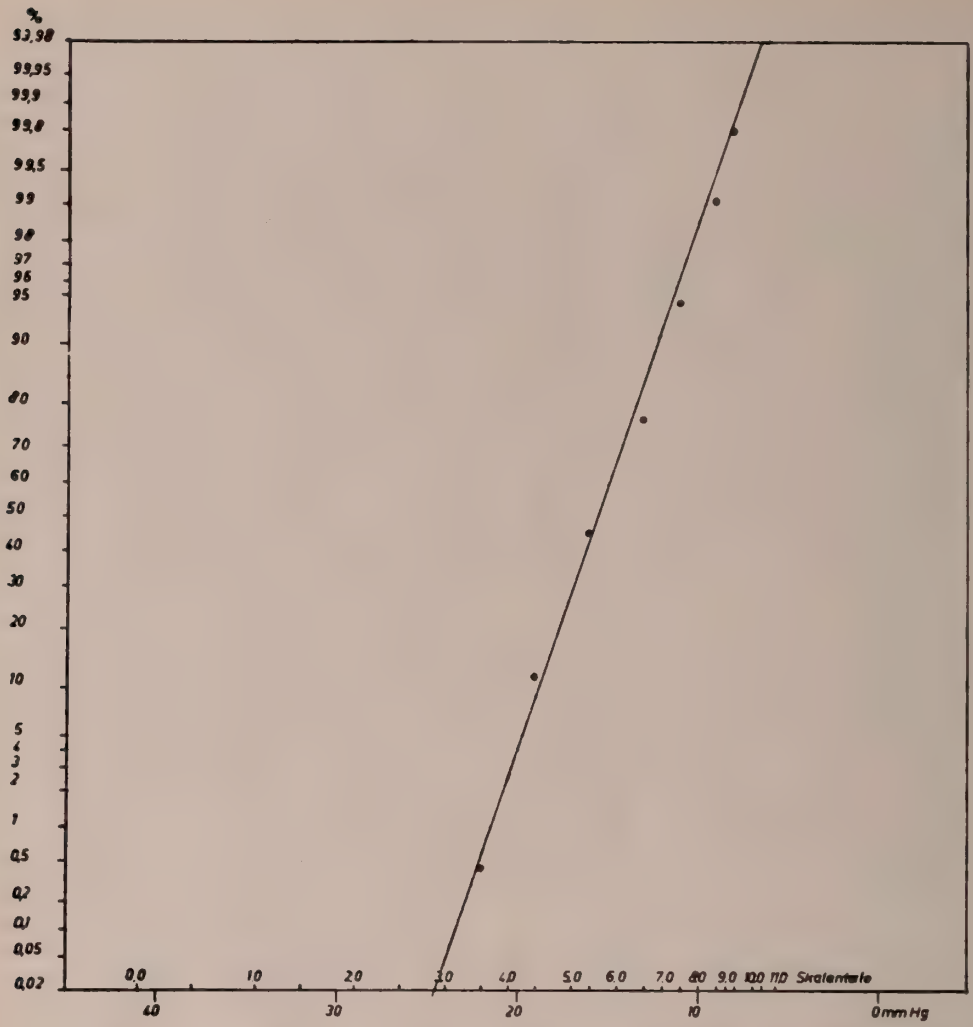

FIGURE 2. Probability distribution curve of data in Figure 1B. (Reproduced with permission of authors and publishers, Ferdinand Enker Verlag, Stuttgart.[5])

TABLE V. Qualitative determination of ocular rigidity with Schiotz tonometry using two weights

Tonometer Scale Reading	Weight (Gm.)	Mm. Hg (1955)	Error Range (Mm. Hg, 1955)
4.0	5.5	20.6	18.9 to 22.4
8.5	10.0	21.3	19.5 to 23.1

If the 10-Gm. weight reading is greater than 22.4 mm. Hg, the ocular rigidity is increased; if the 10-Gm. weight reading is less than 18.9 mm. Hg, the ocular rigidity is decreased.

weight. The ocular rigidity (K) was calculated to be 0.051, and the true ocular tension was 9 mm. Hg (1955 scale).

The importance of ocular rigidity also is a factor in estimating tonographic values since the standard tonographic tables assume normal ocular rigidity. At present the value of routine ocular rigidity determinations in tonography is not firmly established. However, deviations from normal ocular rigidity can cause large variations in the outflow value.

Misinterpretation of changes of the disk and visual fields

The entity of pseudoglaucoma has been well enumerated by Blazar and Scheie.[8] In

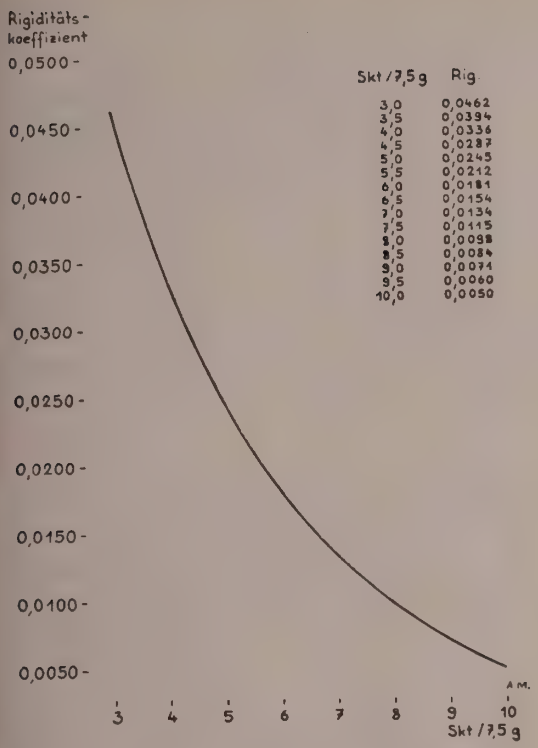

FIGURE 3. Effect of ocular rigidity on Schiotz tonometer scale reading (7.5-Gm. weight) with an ocular tension of 24 mm. Hg. (Reproduced with permission of authors and publishers, S. Karger Verlag, Bern.[6])

TABLE VI. Increased ocular rigidity with Schiotz tonometry with borderline ocular tension

	—Weight (Gm.)—	
Finding	5.5	10.0
Tonometer scale reading	3.5	7.0
Tension (mm. Hg, 1955)	22.4	27.2
Ocular rigidity (K)	0.053	
True tension (mm. Hg, 1955)	12	

these cases the disk and field changes appear similar to those which are seen in glaucoma, but no pressure or outflow abnormalities are found, and a definite etiologic factor can be implicated. The possible causes are: tumors arising near the optic chiasm; congenital anomalies, including oblique insertion of the optic nerve, branching of the vessels behind the lamina cribosa so that branches appear at the disk margin, coloboma of the optic disk, and colobomas within the optic nerve sheath; syphilitic optic nerve atrophy; optic neuritis (retrobulbar neuritis); and sclerosis of the internal carotid arteries. In all of these conditions since typical glaucomatous disk and field changes occur, one can easily see that, if on these individuals errors are made on tonometry or the patients' tensions and tonographic values are borderline, they can be misdiagnosed as glaucomatous. Figure 4, taken from Blazar and Scheie,[8] indicates 3 such cases of pituitary tumor, syphilitic optic atrophy, and calcification of the internal carotids. Similarly Chamlin[9] has documented cases of optic neuritis with paracentral nerve fiber bundle defects sparing fixation. Another example where the misdiagnosis of glaucoma can be made has been shown by Goldmann[10] (Fig. 5), where medial ectasia of the fundus exists, that is, one area of the disk or one part of the globe is depressed more posteriorly in one meridian than another. Here again an arcuate scotoma may be detected extending from the blind spot to the nasal field and may be confused with a true baring of the blind spot. Adding the appropriate correcting lens will eliminate the scotoma.

Misinterpretation of visual fields with normal disks

A number of other clinical entities can show identical field changes to those in glaucoma and yet have normal disks. Again if the tensions are borderline and some of the other studies are suspicious, one can easily misdiagnose as having early glaucoma these individuals who have shown little or no disk changes. An excellent example of such a condition is retrobulbar neuritis.[9] Figure 6 is taken from Traquair[11] illustrating a field change easily imitating glaucoma. Traquair[12] also illustrates a choroiditis juxtapapillaris which again can give a typical glaucomatous field defect. This of course would be recognized by a careful fundus examination. Figure 7 shows that a glaucomatous field defect can be obtained easily from a patient in whose eye the illumination is decreased, such as in an individual with cataracts or even one in whom the pupil size is changed.[13] This again is a case where glaucoma was diag-

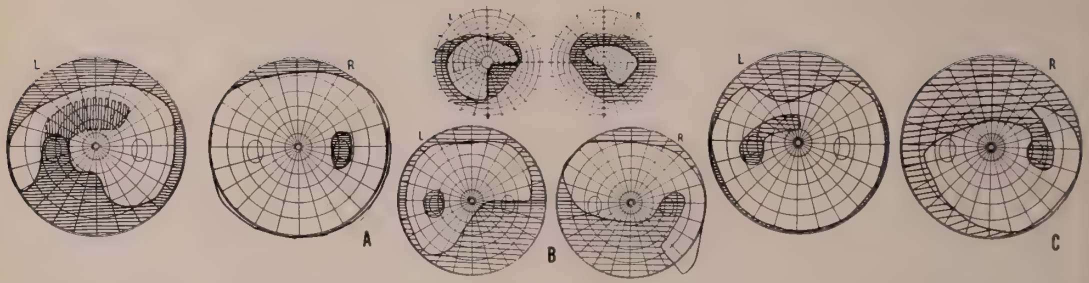

FIGURE 4. (A) Central fields of case of pituitary tumor showing nerve fiber bundle defect breaking through to periphery. (B) Peripheral and central fields of case of syphilitic optic atrophy with nerve fiber bundle defect breaking into periphery. (C) Central fields of case of calcification of internal carotids showing altitudinal and nerve fiber bundle defects. (Reproduced with permission of authors and publishers.[8])

nosed in an individual with a cataract, and after the cataract was removed the field defect disappeared.

Summary

The various errors in diagnostic technics which can lead to the diagnosis of glaucoma in a patient in whom glaucoma does not exist have been reviewed. With the Schiotz tonometer, these include errors in instrumentation, in the use of a correct calibration scale, and in the reproducibility of a Schiotz reading. The failure to recognize normative high ocular tensions and increased ocular rigidity also will lead to misdiagnosis. Changes of the disk as well as changes of the visual fields, which may be typical of glaucoma but which may be due to other clinical entities, will also lead to errors in diagnosis.

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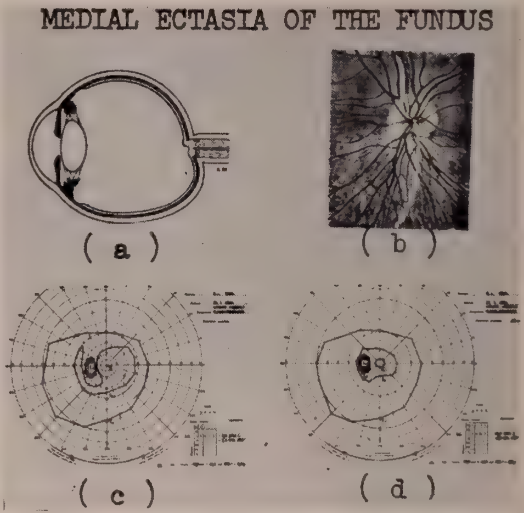

FIGURE 5. Medial ectasia of fundus. (A) Cross section of eye. (B) Slit lamp appearance of fundus. (C) Relative Bjerrum scotoma before correction. (D) Disappearance of scotoma with correction. (Reproduced with permission of authors and publishers.[10])

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Discussion

Elizabeth P. Olmsted, M.D., *Buffalo, New York.* Dr. Schwartz has made an interesting summary of the errors which can

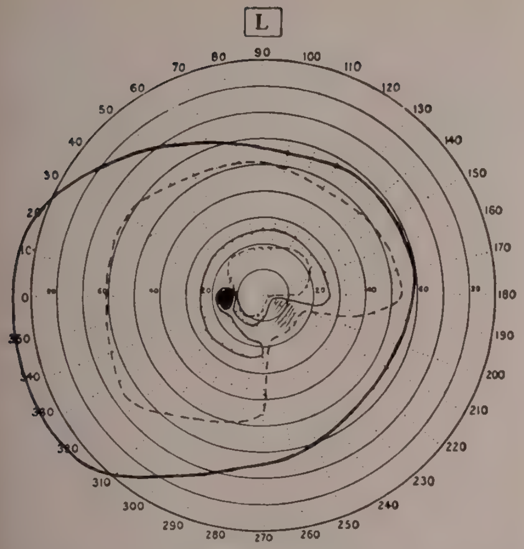

FIGURE 6. Nerve fiber bundle defect breaking through to periphery in unilateral retrobulbar neuritis. (Reproduced with permission of publisher, Henry Kimpton, London, England.[11])

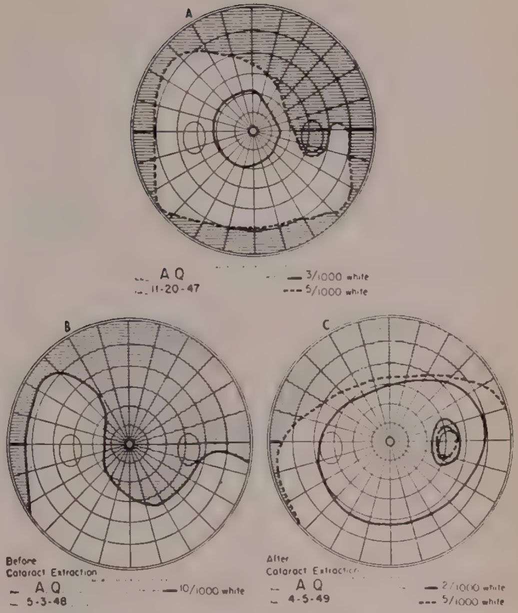

FIGURE 7. (A and B) Central fields of patient with cataract indicating defect easily imitating glaucoma. (C) Field defect disappears when cataract removed. (Reproduced with permission of authors and publishers.[13])

lead one to diagnose falsely as glaucoma normal deviations of the eye from average or abnormalities associated with other causes. I applaud his admonition that the tonometer be standardized at reasonable intervals and used with care and his warning against calibration scales older than that of 1955. I am a little afraid, however, that by dwelling on the errors of tonometry he may have created an impression of its unreliability. For example he points out that only 25 per cent of glaucoma referrals from the combined surveys were proved subsequently to be afflicted. To me this is rather an encouraging ratio to be obtained from the cursory single reading of a mass survey and only tends to emphasize the need for repeated readings over the period of time necessary to a glaucoma work-up.

Dr. Schwartz has concerned himself entirely with the misdiagnosis as glaucoma of a normal elevated pressure or other abnormalities. This can lead to false medication or even in the extreme cases cited, unnecessary surgery. In my experience the missed diagnosis of true glaucoma is by far the more common error and one of tragic consequence. While I am not engaging in semantic exercise with Dr. Schwartz, whose subject does not include this latter group, I am disturbed lest he leave the impression that one may discount too easily the physical signs of pressure rise, optic atrophy, or field changes.

By way of illustration, if the criteria of pressure, outflow, and so forth have been set to include a 2-sigma deviation from the norm, 25 out of 1,000 normal eyes might superficially be diagnosed erroneously as glaucomatous. If more severe criteria of pressure, outflow, and so forth are selected, only 1.5 normal eyes in 1,000 might be improperly suspected of glaucoma. The possibility of misdiagnosis has been reduced. However, the tests first mentioned in each case pick up 50 per cent more of the truly glaucomatous eyes than do the more restrictive limits. To me the retrievable error in improperly suspecting 2.5 eyes in 100 is relatively unimportant and will correct itself in clinical course as contrasted with detection and intervention in 95 out of 100 glaucomatous eyes which otherwise would suffer irretrievable loss of vision.

Turner's Syndrome

Review of Literature and Report of Case in Newborn Infant

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TURNER'S SYNDROME or gonadal dysgenesis is a congenital disease in which approximately 80 per cent of patients have an X-O (chromatin-negative or abnormal) pattern. The finding of 45 chromosomes with an X-O pattern and external abnormalities enable diagnosis at birth. Short stature is the most common characteristic of gonadal dysgenesis; cubitus valgus and webbed neck are the two anomalies most often found. Other skeletal defects, associated anomalies, mental retardation, and endocrinologic defects may be present. Plastic surgery, surgery to correct cardiovascular and renal anomalies, and hormonal and psychologic therapy are helpful although the affected individual can never assume all the functions of a female. An analogy between Turner's syndrome and some kind of gonadal "blight" during early embryologic differentiation is apparent, although other etiologic factors have been suggested also.

TURNER'S SYNDROME has been variously designated as gonadal dysgenesis, gonadal dysplasia, ovarian agenesis, gonadal aplasia, ovarian dwarfism, status Bonnevie-Ullrich, and primary ovarian insufficiency with decreased stature. In the light of recent findings, the word "gonadal" has come to be substituted for "ovarian"; "dysgenesis" rather than "agenesis" is favored by some because the gonads are rudimentary rather than absent.

The incidence of this interesting syndrome varies with different observers. In a recent personal communication Grumbach[1] states that it occurs in probably fewer than 1 in 2,500 births. Ferguson-Smith[2] reports that although no accurate figures are available for the frequency of gonadal aplasia in the general population, it is clearly not as common as chromatin-positive Klinefelter's syndrome.

In the past, unless exploratory laparotomy or peritoneoscopy was performed, it was not possible to prove the diagnosis of gonadal dysgenesis before puberty, at which time a high titer of urinary gonadotrophins could be detected. Now, findings of a chromatin-negative (male) pattern in a suspected case, irrespective of age, is considered strong presumptive evidence of the diagnosis. Approximately 80 per cent of patients with gonadal dysgenesis have a chromatin-negative (or abnormal) pattern.[3] The diagnosis can be substantiated by the finding of 45 chromosomes with an X-O pattern.

The purpose of this article is to review the literature and to report the earliest case of gonadal dysgenesis which according to our knowledge has been studied completely from the genetic and chromosomal points of view. The diagnosis was suspected when the child entered the nursery and was confirmed shortly thereafter.

Case Report

A newborn white female infant was delivered spontaneously at term, at Beth Israel Hospital, New York City, on September 14, 1960. The birth weight was 6 pounds, 11 ounces, and length $18^1/_2$ inches. The head circumference was $12^1/_4$ inches and the chest 12 inches. This was the mother's second child, the older sibling being alive and well. The pregnancy was uneventful

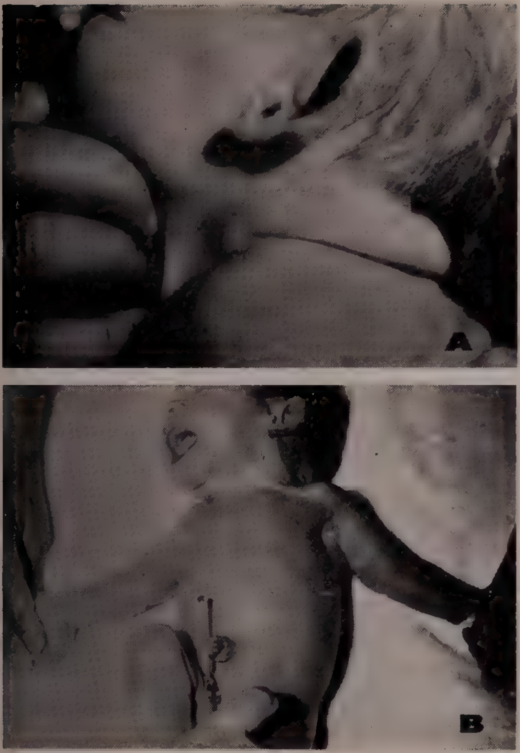


FIGURE 1. Views showing (A) Bonnevie-Ullrich type neck, posterior redundant folds, in addition to (B) the anterior triangular folds or classical webbed neck of Turner's syndrome.

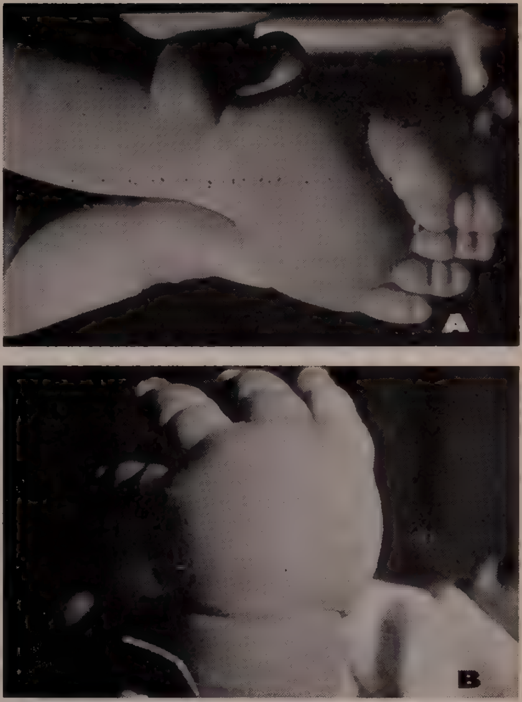


FIGURE 2. (A) Marked lymphedema of foot. (B) Lymphedema of hand.

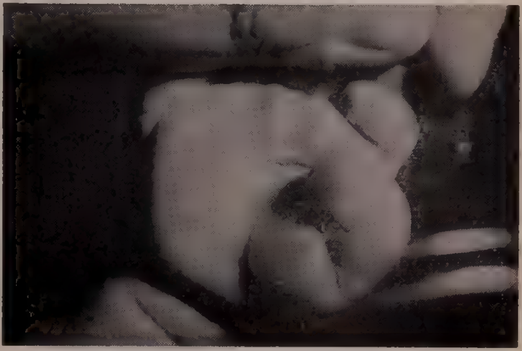


FIGURE 3. Simian line on palm.

with no history of steroid or other hormone therapy, no illness, and no unusual drug ingestion. Both parents are of average height.

An examination at birth revealed the following abnormalities: webbed neck, redundant folds at the base of the neck posteriorly (Fig. 1), low-set ears with a left lop ear, high-arched palate, low hair line, shield breast, hypoplastic nipples, and lymphedema of both hands and feet (Fig. 2). In addition there were found cubitus valgus, simian lines on the palms (Fig. 3), hypoplastic toenails, lax skin, and poorly palpable femoral arteries. The external genitalia appeared normal.

The hemoglobin was 16 Gm. per 100 ml., white blood count 11,500, lymphocytes 19 per cent, polymorphonuclear leukocytes 69 per cent, eosinophils 5 per cent, monocytes 5 per cent, and basophils 2 per cent. The reticulocytes numbered 0.6 per cent. The blood urea nitrogen was 11 mg. per 100 ml. and the alkaline phosphatase 16.5 Bodansky units. The blood calcium was 11.4 mg. per 100 ml. (5.7 mEq. per liter), and the phosphorus was 6.4 mg. per 100 ml. The total protein was 6.4 Gm., albumin 4.24 Gm., and globulin 2.16 Gm. per 100 ml. The albumin-globulin ratio was 1.96.

The urinary 17-ketosteroids showed negative findings. Smears from cells of the buccal mucosa revealed a chromatin-negative (male) pattern. Chromosome studies revealed cells containing 45 chromosomes, and the karyotype was consistent with a single sex chromsome X-O.

X-ray studies of the spine gave negative results. The proximal center of calcification of the tibia, which is usually present at birth, was absent.

Intravenous pyelograms showed faint visualization of both urinary tracts which proved to be inadequate for a definite diagnostic statement.

The clinical course in the hospital was uneventful, and the infant was discharged to be followed at home.

Characteristics of the syndrome of gonadal dysgenesis

Short stature is the most common characteristic of gonadal dysgenesis. In a series of 55 patients with the diagnosis of gonadal aplasia 100 per cent were of short stature.[4] In those cases in whom growth had ceased the height varied from 135 to 152 cm., with an average of 142 cm. In only 9 cases was there a history of conspicuously short individuals in the family. A slow rate of growth was generally noted throughout childhood, and 19 cases had birth weights of less than 2,500 Gm.

The literature does, however, show occasional cases of patients with body heights of 176 cm. and taller.[5] Grumbach[3] mentions that retardation of growth may not be apparent during the first six to twelve months of life, while Del Castillo, De La Balze, and Argonz[6] believe that growth retardation starts during "the school age."

Cubitus valgus and webbed neck are the two anomalies most often found in gonadal dysgenesis, the latter occurring in one third to one half of all cases.[7]

Other skeletal defects that may be present include "shield-like" chest, pes cavus, vertebral chondrodystrophy, spina bifida, Madelung's deformity, fusion of cervical vertebrae, abnormal rib development, shortened phalanges, and short neck; also, highly arched palate, hypoplasia of the mandible, asymmetry of the gums, syndactylism, and abnormal epiphyses.[8] Osteochondritis (aseptic necrosis) of the medial tibial tubercle has recently been observed in 12 patients with Turner's syndrome.[9]

Associated anomalies noted in gonadal dysgenesis include occular defects (ptosis, cataracts, exophthalmos, strabismus, and coloboma), congenital deafness, vascular anomalies (coarctation of aorta), hypertension, renal anomalies, azygos lobe of the lung, lymphangiectatic edema, and telangiectasis.

Mental retardation is not uncommon. Haddad and Wilkins[4] performed psychometric evaluations on 20 patients with gonadal aplasia and found that 5 patients had intelligence quotients below 79 per cent. Oberman[8] believes that the mental retardation in this syndrome is unusual, for as these children grow older, many seem to "catch up" and eventually have normal or near-normal intelligence.

The basic endocrinologic defect in the syndrome is exemplified by the finding of rudimentary gonads represented by fibrotic streaks or oval bodies with rudimentary gonadal elements[10,11] and the subsequent primary amenorrhea. Related findings are an infantile uterus and vagina, mammary hypoplasia, pinpoint nipples, scanty pubic and axillary hair, late epiphyseal union, increased urinary gonadotrophins, decreased urinary 17-ketosteroids, and normal or slightly retarded bone age.

A mild form of osteoporosis is often seen. Albright, Smith, and Fraser[12] and other workers have ascribed this to an estrogen deficiency, while Elliott, Sandler, and Rabinowitz[13] suggest that the bony changes constitute an incomplete form of osteogenesis imperfecta. Hoffenberg and Jackson[14] have noted the presence of blue scleras in certain of their cases of gonadal dysgenesis, indicating perhaps a relationship with this mesenchymal disease.

Laboratory features

CHROMATIN PATTERN. It has been well established that 80 per cent of subjects with gonadal dysgenesis are "chromatin-negative" in contrast to the normal female who is "chromatin-positive".[3,4,15–17] Nuclei of females may differ from those of males in having a chromatin mass that is usually located against the inner surface of the nuclear membrane. This "sex chromatin" is approximately 1 micron in diameter and can be demonstrated in 60 to 80 per cent of normal female nuclei. The sex chromatin is basophilic and shows positive Feulgen test results as chromocenters generally do. It is best studied in the large vesicular nuclei of neurons in certain female animals. Clinical application in determining the "chromatin sex" requires only an easily obtainable source of cells. The skin biopsy method was the first to be introduced.[16] It has been replaced largely by methods which avoid any surgical procedure, and the simplicity of the buccal smear has resulted in its extensive use. The sex chromatin is more prominent in the nuclei of vaginal than in oral smears.

Davidson and Smith in 1954[18] demonstrated a different kind of sexual dimorphism peculiar to polymorphonuclear leukocytes. A small proportion (1 to 10 per cent) of the neutrophils of normal females contain an accessory nuclear lobule. This lobule is encountered only rarely, if at all, in neutrophils of normal males. Frequently "small dubs," or smaller nuclear projections of similar shape, are observed in normal males and may make interpretation difficult.

While nuclear sexual dimorphism is an established fact, the derivation of the sex chromatin remains unexplained. Recent information concerning human chromosomal morphology has leaned to the viewpoint that the sex chromatin represents heterochromatic regions of homologous chromosomes in somatic pairing, that is, that the sex chromatin is an XX chromatin derivative and a visible consequence of the proximity of two X chromosomes in the female somatic cell. This implies that the property of heterochromaticity is less developed in the XY complex of somatic cells as compared with the XX complex. In other words, because of the small size of the Y chromosome the XY complex fails to form a conspicuous chromocenter.

The recent work by Ford *et al.*,[19] following Tjio and Levan's work[20] establishing the human diploid chromosomal number of 46, leads us to anticipate the finding of 45 chromosomes and an X-O pattern in subjects with physical characteristics of gonadal dysgenesis, and this has been the case.

If the sex chromatin mass is due to the presence of XX, then the X-O pattern and chromatin negativity in the female somatotype of Turner's syndrome are quite compatible. Similarly, the findings of 47 chromosomes and an XXY pattern and chromatin positivity in the male somatotype of Klinefelter's syndrome encourage this theory.[16]

FOLLICLE-STIMULATING HORMONE. The diminished ovarian function found in Turner's syndrome was originally thought to be due to hypopituitary function.[21] Albright, Smith, and Fraser[12] and others, however, found increased urinary gonadotrophins and correlating this with surgical explorations described the condition as a primary gonadal deficiency with increased follicle-stimulating hormone titers as an integral part of the syndrome in adolescents and adults. It was formerly believed that an increase in urinary gonadotrophin is the most important single clinical or laboratory finding in making the diagnosis of ovarian agenesis.[7]

The presently available information on chromatin pattern and chromosomal counts has altered the picture considerably, and only recently has it been possible to prove, except by exploratory laparotomy, that there was a gonadal defect before the ages of from nine to thirteen years.[10]

It is of interest to note the commonly held opinion that gonadotrophic production does not begin until the end of the first decade and that urinary gonadotrophins are not found before the age of ten to eleven years.[10] Talbot,[22] however, has shown that gonadotrophins and estrogen are produced in small amounts considerably before puberty; furthermore, reports reveal a patient with gonadal dysgenesis at the age of two years and eight months with a gonadotrophin level of 15 mouse units (the normal for children 5) and elevated levels in young children with Turner's syndrome.[7,23] Large amounts of primary gonadotrophins are excreted in the urine of postpuberal subjects, and levels of 96 to 576 mouse units per twenty-four hours have been reported in gonadal dysgenesis[10] (normal for adults 6.52 mouse units), although notable exceptions have been recorded.[14]

17-KETOSTEROIDS. The great majority of cases of gonadal dysgenesis show normal 17-ketosteroid excretions and no evidence of masculinization. There are, however, some cases reported which manifest masculinization and increased 17-ketosteroids[24-26] and others showing masculinization without increased 17-ketosteroids.[27] One of the former appears to be an example of adrenal virilism, with heavy musculature, thick growth of axillary hair, and accelerated skeletal age.[24]

In the latter and other cases characterized primarily by hypertrophy of the clitoris, the lack of axillary hair, absence of masculine distribution of pubic hair, and the failure of 17-ketosteroid output to increase after the administration of chorionic gonadotrophins when they are administered indicate that the androgen elaborated is not testosterone. Further evidence indicates that it is not of adrenal origin but may be secreted by epithelial cells of the ovarian anlagen (Leydig cells).[27] At any rate, virilism in gonadal dysplasia is uncommon and the typical findings of gonadal dysgenesis such as male chromatin patterns, basic female somatotype, and internal genitalia (tubes, uterus, and "streaks" replacing the ovaries) are unaltered in these patients, except for increased numbers of Leydig cells in the tissue resembling the ovarian stroma. It should be noted, however, that small and occasionally large clumps of Leydig cells are found in the genital ridges of cases showing no phallic enlargement.

The hemogram, electrolyte picture, and other blood studies of gonadal dysgenesis, do not reveal abnormalities, although Elliott, Sandler, and Rabinowitz[13] have recently reported phosphatase elevations in chromatin-positive patients with gonadal dysgenesis.

Differential diagnosis

The following disease entities should be considered in the differential diagnosis of gonadal dysgenesis:

1. Congenital heart disease (history, lack of associated defects and anomalies)
2. Congenital hemihypertrophy (bilateral bone measurements)
3. Sickle cell anemia with lymphedema (electrophoretic hemoglobin studies, sickle cell preparation, x-ray studies)[28]
4. Childhood diabetes mellitus (fasting blood sugar, glucose tolerance test, urinalysis, history)
5. Malnutrition (history, response to dietary therapy)
6. Hypothyroidism (protein-bound iodine, basal metabolic rate, radioactive iodine uptake, serum cholesterol, physical features)
7. Panhypopituitarism (precocious senility, dwarfism, normal mentality, basal metabolic rate, fasting blood sugar, x-ray films of skull)
8. Anorexia nervosa (age group, amenorrhea-anorexia time relationship, history of psychiatric condition)
9. Mongolism (facies, skull shape, epicanthus, rudimentary second phalanx on fifth finger, chromosome count)
10. Renal rickets
11. Pseudohypoparathyroidism
12. Primordial dwarfism
13. Pterygium syndrome (bilateral Ullrich syndrome, dystrophia brevicollis congenita, unilateral Ullrich syndrome, pterygoarthromyodysplasia congenita)
14. Selective deficiency of gonadotrophic hormones of the anterior pituitary gland
15. Eunuchoidism due to gonadal ablation
16. Premenarchal menopause praecox.

Therapy

Patients with gonadal dysgenesis have a number of serious handicaps to overcome in psychologic adjustment. It is often wise not to inform the patients and their families of the results of the determination of "cytologic sex," to avoid adverse psychologic effects which may result from this information. Plastic surgery, to correct the neck, ears, or other cosmetic defects, is important.

Surgery is also used to correct cardiovascular and renal anomalies. Hormonal therapy should not be given before the age of puberty, because it may hasten epiphyseal fusion and stunt growth still more. However, it should be instituted by the age of thirteen or fourteen years. Haddad and Wilkins[4] recommend diethylstilbestrol (1 mg. daily) or Premarin (1.25 mg. daily) given continuously for a period of from six to twelve months, followed by cyclic withdrawal, omitting therapy for seven consecutive days each month.

Comment

In the past two decades, a considerable amount of work on embryologic development and differentiation has led to some sound theories on abnormal sex differentiation.

History of gonad. A brief summary of the embryologic differentiation stressing the bipotential state of the internal and external genitalia is helpful in understanding them. The primitive gonad appears identical in both sexes up to about the 16-mm. stage (seven weeks). It is the balance between male determiners and female determiners in the genotype (XX female and XY male normally) that decides the fate of the indifferent gonad.

In the gonad destined to become female,

the cortical component develops and the müllerian duct forms the upper part of the vagina, the uterus, and the fallopian tubes during the third month. The medullary component and its wolffian ducts degenerate (vestiges are epoophoron, para-oophoron, and Gartner's duct).

When the gonad begins to develop as a testis, the medullary components proliferate, the cortical components regress, and the wolffian duct develops into the vas deferens, seminal vesicles, and epididymis during the third month. This bipotential character is shared by the external genitalia. Since the crucial step of differentiation (proliferation of medullary or cortical elements of the primary gonad) is somewhere in the ninth week, interference at the end of the second month of embryologic life can conceivably lead to a sexual abnormality.

Jost's[29] enlightening work showed that gonadectomy of female rabbit embryos at any stage, or of males before the twentieth day (corresponding to the end of second month in human embryos), is followed by the development and maturation of female elements and the repression of the male elements. This suggests that in the absence of testicular tissue some fetal or maternal element causes female sexual differentiation and that fetal testis suppresses müllerian duct development. Unilateral gonadal castration in male embryos results in homolateral müllerian duct development and contralateral wolffian duct development.

This work was repeated in rat and mouse embryos which were returned to their maternal uteri after castration.[29,30] A case has been reported which on laparotomy revealed a hypoplastic müllerian duct development on the side of a fibrotic aplastic gonad and a hypoplastic wolffian duct development on the side of a gonad with poorly developed seminiferous tubules.[10]

Thus, the analogy with Turner's syndrome and some manner of gonadal "blight" during the early embryologic differentiation is apparent. The indifferent gonad (perhaps originally destined to be male or at least usually of a chromatin-negative individual) fails to develop normally and possibly, as in the rabbit, rat, and mouse, the subject fails to develop male genitalia and emerges with a female somatotype.

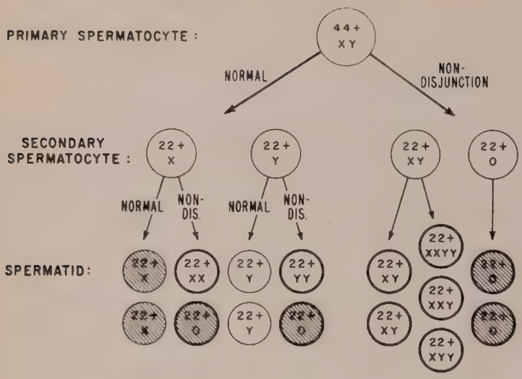
Other workers have contributed to the elucidation of the etiology of gonadal dysgenesis and the resulting syndrome. Fanconi and Wallgren[31] explained the external manifestations as a result of the abnormality of a single gene producing hydrocephalus and eventually an extrusion of liquor through the occipital gap at the fourth ventricle. This may produce migratory encapsulated collections of liquor and result in congenital lymphedema of the neck, hands, and feet.

Etiologic factors other than genetic have been suggested, such as a noxious agent of maternal origin[32] and fertilization of an over-ripe ovum with failure of the primordial germ cells to reach the gonadal ridges of the extraembryonic entoderm and subsequent hypogonadism.[33]

GENETIC EXPLANATION OF X-O CHROMOSOME. One of the most pertinent of recent developments is the work of Tjio and Levan[20] showing that man's diploid number of chromosomes is 46. The formerly accepted number, determined interestingly and perhaps significantly by Painter[34] on subjects in mental institutions, was 48. Other workers have confirmed the number at 46.[20]

Current technics utilize cellular cultures (marrow aspirations and blood) exposed to minute doses of colchicine which arrests and accumulates cells in a suitable stage of mitosis for separation and counting of the chromosomes. An idiogram, a diagram representing the human karyotype or chromosomal constitution of an individual, can be constructed by arranging the autosomes in order of decreasing total length and relative centromere (clear region where the arms of a chromosome meet) position. The sex chromosomes, X and Y, are placed at the end. Abnormalities (additions or subtractions) have been found in certain states, such as Klinefelter's syndrome and mongolism,[2] and Ford *et al.* in 1959[19] presented a case of Turner's syndrome with 45 chromosomes and no Y. Thus, instead of the usual 46 (22 pairs plus two sex chromosomes XX female or XY male), 44 autosomes and only one X were shown to be present in gonadal dysgenesis. This has been confirmed by other observers.[35-37]

When this is interpreted in terms of



BY THE PROCESS OF NON-DISJUNCTION DURING THE FIRST MATURATION DIVISION ↓ OR SECOND MATURATION DIVISION ↓ A SPERMATID OR OÖTID WITH AN ABNORMAL NUMBER OR TOTAL ABSENCE OF XY (SEX) CHROMOSOMES RESULTS ○

FERTILIZATION BETWEEN AN O AND AN X CONTAINING CELL ▨ MAY THEN EXPLAIN THE 44 XO CHROMOSOMAL PATTERN IN GONADAL DYSGENESIS AS CONTRASTED WITH THE NORMAL 44 XX FEMALE OR 44 XY MALE.

FIGURE 4. Nondisjunction in spermatogenesis. The process may also occur in oögenesis.[39]

Bridges'[38] work on Drosophila, demonstrating flies with atypical characteristics, including intersex, and abnormal chromosome numbers produced by nondisjunction (nonseparation of the chromosomes in mitosis in consequence of which both chromosomes pass to one daughter cell and none to the other instead of one to each), an insight into the etiology of gonadal dysgenesis is apparent. Primary spermatocytes and oocytes undergo two maturation divisions to form the haploid number of 23 chromosomes. The first division of the 46 chromosomes is reductional, and 22 autosomes plus one sex chromosome are found in the secondary spermatocyte.

The second division is essentially a reproduction producing a 23-chromosome spermatid or ootid, each normally containing an X or a Y. If for some reason nondisjunction should occur in either of the maturation processes, the spermatid or ootid could conceivably have no sex chromosome, two X's and two Y's, or any other combination (Fig. 4).[39]

A patient with an X-O pattern then could result from the union of an X ovum (normal) with an O sperm (abnormal) or an O ovum (abnormal) with an X sperm (normal). These findings are compatible with the previously outlined theory based on Jost's[29] work, that is, in the absence of a Y chromosome the fetal testis fails to develop, and the androgenic substances causing wolffian duct development being absent, müllerian duct elements and female phenotype then predominate. Finally, it is also pertinent to consider mosaicism, a term used to describe a combination of cells in the same individual which contain a different number of chromosomes. If during the cleavage of an already abnormal X-O zygote nondisjunction again occurs, an individual with an X-O/XX pattern could emerge. This has been postulated by Ford,[17] and patients suggestive of this mosaic pattern have been described.

Summary

Turner's syndrome is a congenital disease with protean signs and varying degrees of severity. Although there is no "cure" for this disease whereby the affected individual can assume all the functions of a female, nevertheless, with proper psychologic and hormonal therapy and plastic surgery where indicated, a very adequate subject can emerge.

The disease can be diagnosed at birth when the external abnormalities permit. This is important for psychologic reasons as well as for the anticipation of visceral anomalies that may occur with the disease. We believe the work-up of every diagnosed case should include careful elucidation of the femoral pulses, careful cardiac auscultation, and intravenous pyelograms.

The recent work showing that these subjects are chromatin-negative (in 80 per cent) and have an X-O (or X-O/XX mosaic) pattern has helped in our understanding of their sexual underdevelopment and has made definite diagnosis without surgical intervention possible.

The literature has been reviewed, and to our knowledge, our patient is the earliest case to be reported who has been studied completely utilizing chromosomal counts and patterns.

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Radioactive Phosphorus for Carcinoma of the Breast with Diffuse Metastatic Bone Disease

FOURTEEN PATIENTS *with diffuse bone metastasis from breast carcinoma without significant soft tissue involvement were treated with aqueous testosterone and intravenous radioactive phosphorus or* P^{32}. *Eighty-seven per cent had significant relief of pain, and 18 per cent had radiographic evidence of bone repair. Progressive relief of pain usually was evident one month after treatment, reached a maximum in three to four months, and lasted from two to eighteen months. The therapeutic response was not directly proportional to the dose of* P^{32} *given. Further improvement could often be obtained when symptoms recurred by a repeat course of therapy. When the total of* P^{32} *given was under 12 millicuries, the degree of bone marrow depression was minimal, but cases given greater doses did not necessarily show alarming depression of hematopoiesis.*

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A SYSTEMIC THERAPEUTIC modality appears to offer the patient with diffuse bone metastasis from breast carcinoma the most reasonable chance for improvement. The various approaches that are available are hormonal, chemotherapeutic, and radioisotopes.

The utilization of P^{32} or radioactive phosphorus in the treatment of breast carcinoma metastasis to bone has been under active investigation for over a quarter of a century.

Historical development

As early as 1935, Lawrence and Tobias[1] explored the possibility of treating carcinoma of the breast using cyclotron-produced radioactive phosphorus. From this time, various contributions to the growing pool of knowledge appeared in the literature. The distribution and metabolism of radioactive phosphorus in tumors has been studied by Forssberg,[2,3] Marshak,[4] Hertz,[5] DeOme *et al.*,[6] and Kaplan *et al.*[7]

Clinical therapeutic approaches have been evaluated by Bell and Low-Beer,[8] Friedell and Storaasli,[9] Maxfield, Maxfield, and Maxfield,[10] Taber,[11] and Storaasli *et al.*[12]

Maxfield's investigations, starting in 1941 and encompassing the largest series of patients, have indicated the proper dosage and technic of combined P^{32} and testosterone administration as well as the apparent specificity of action on breast and prostate metastases to the bone. This technic, which is now in wide use, is sometimes referred to as the "Maxfield technic." He gave 100 mg. of aqueous testosterone intramuscularly daily for five days before the P^{32} was started and continued this dose during the use of radioactive phosphorus and for five days thereafter. Intravenous P^{32} was given in divided doses of 1.5 millicuries daily until a total dose of 7.5 to 20 millicuries had been administered (the average dose was 12 to 15 millicuries). Maxfield treated 137 cases. Ninety-four per cent had significant relief, and 17 per cent had evidence of bone repair.

TABLE I. Carcinoma of the breast with diffuse metastatic bone disease in 14 patients treated with P^{32}

Case	Age (Years)	Sites of Metastases from Carcinoma of the Breast	Intravenous Dose of P^{32} (Millicuries)	Bone Marrow Depression	Degree of Bone Pain		Ambulatory Ability		Post-treatment Roentgenographic Changes	Survival
					Pre-treatment	Post-treatment	Pretreatment	Post-treatment		
1	44	Pelvis and lumbar spine	9	Minimal	Severe	Minimal	Walked with difficulty	Walked without difficulty	None	Expired after 2 months
2	62	Generalized	9 1.5 (orally)	Minimal	Severe	Minimal	Walked with marked difficulty	Walked with slightly less difficulty	None	Expired after 2 months
3	45	Cervical and lumbar spine	9	Minimal	Severe	Moderate	Bedridden	Walked with difficulty	Moderate osteoblastic repair	Expired after 3$^1/_2$ months
4	63	Generalized except extremities	9	Minimal	Severe	No pain	Bedridden	Walked with slight difficulty	Moderate osteoblastic repair	Expired after 4 months
5	45	Skull, right tibia, left femur, cervical nodes	10.5	Minimal	Minimal	Unchanged	Walked with slight difficulty	No change	No follow-up; x-ray films obtained	Expired after 5 months
6	67	Generalized excluding extremities	9	Minimal	Moderate	Unchanged	Walked without difficulty	No change	No follow-up; x-ray films obtained	Expired after 9 months
7	63	Dorsolumbar spine	14	Moderate to marked	Severe	Minimal	Walked with extreme difficulty	No change yet	No follow-up; x-ray films obtained	Alive after 4 months
8 (Fig. 1)	58	Ribs, spine, pelvis	12	Severe, required 13 pints of blood	Moderate to marked	Minimal	Walked with difficulty	Walking without difficulty	Very marked osteoblastic repair	Alive after 7 months
9	61	Lumbar spine, pelvis, left pleural effusion	9	Minimal	Inconclusive owing to previous x-ray therapy		Inconclusive owing to previous x-ray therapy		Inconclusive	Alive after 11 months
10 (Fig. 2)	54	Entire spine and pelvis	9	Minimal	Severe	Minimal	Walked with difficulty	Walking without difficulty	Marked osteoblastic repair	Alive after 11 months
11 (Fig. 3)	37	Generalized except extremities	9 6	Minimal	Severe	Minimal	Walked with difficulty	Walking with slight difficulty	Marked osteoblastic repair; no new lesion	Alive after 1 year, 2 months
			(4 months later)	Minimal	Minimal	No pain	Walked with slight difficulty	Walking without difficulty; returned to work		
12 (Fig. 4)	44	Generalized except peripheral extremities	9	Minimal to moderate	Severe	Minimal	Confined to wheel chair; could barely stand	Walking without difficulty	Osteoblastic repair; new lesions at 1$^1/_2$ years	Alive after 1 year, 7 months
13	80	Dorsolumbar spine	9	Minimal	Severe	No pain	Hemiplegia; not ambulatory	No change	None	Alive after 7 months
14	60	Generalized except extremities	14	Minimal	Severe	No pain	Confined to wheelchair; could barely stand	Ambulatory	Marked osteoblastic repair	Alive after 6 months

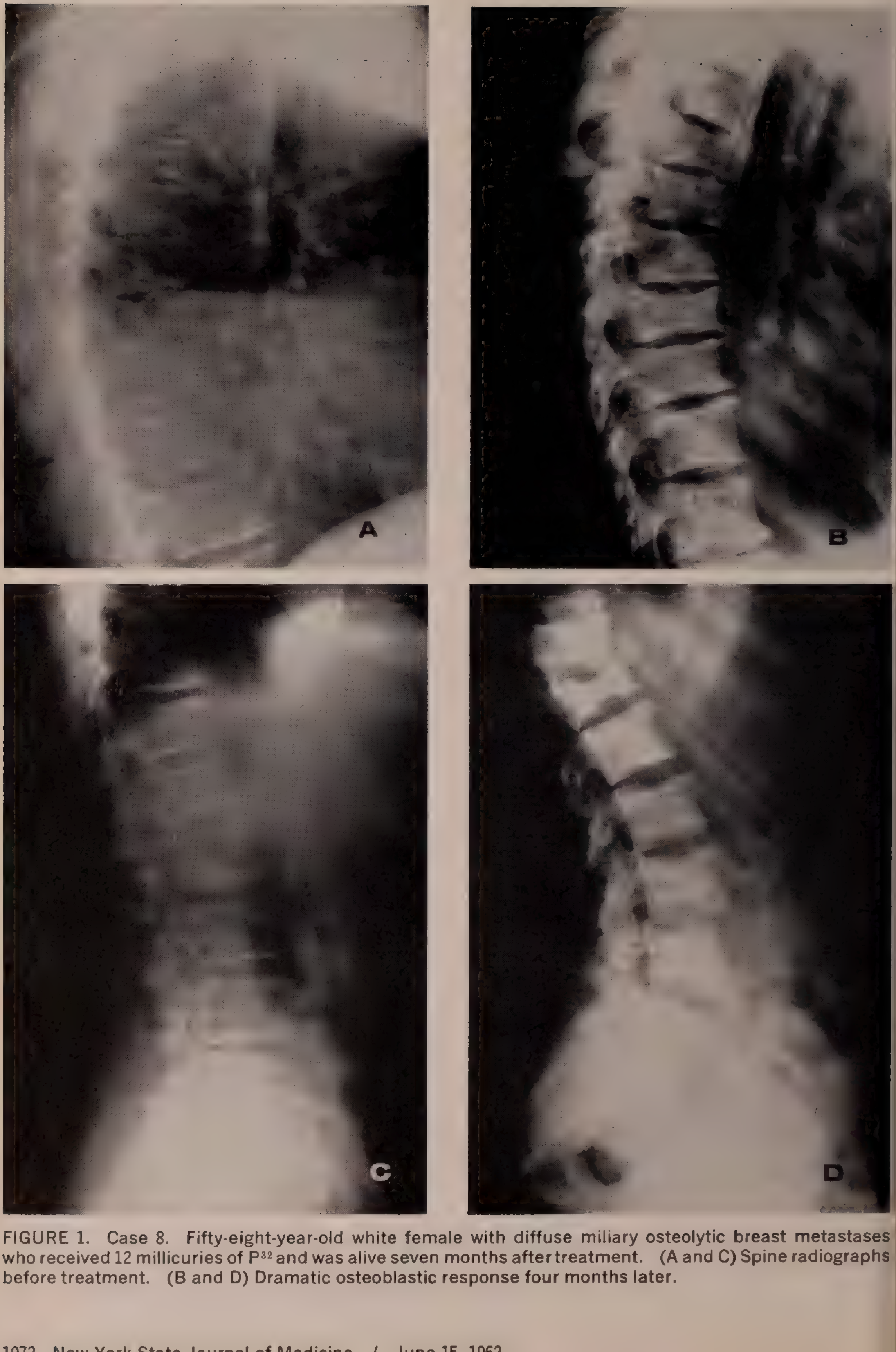

FIGURE 1. Case 8. Fifty-eight-year-old white female with diffuse miliary osteolytic breast metastases who received 12 millicuries of P^{32} and was alive seven months after treatment. (A and C) Spine radiographs before treatment. (B and D) Dramatic osteoblastic response four months later.

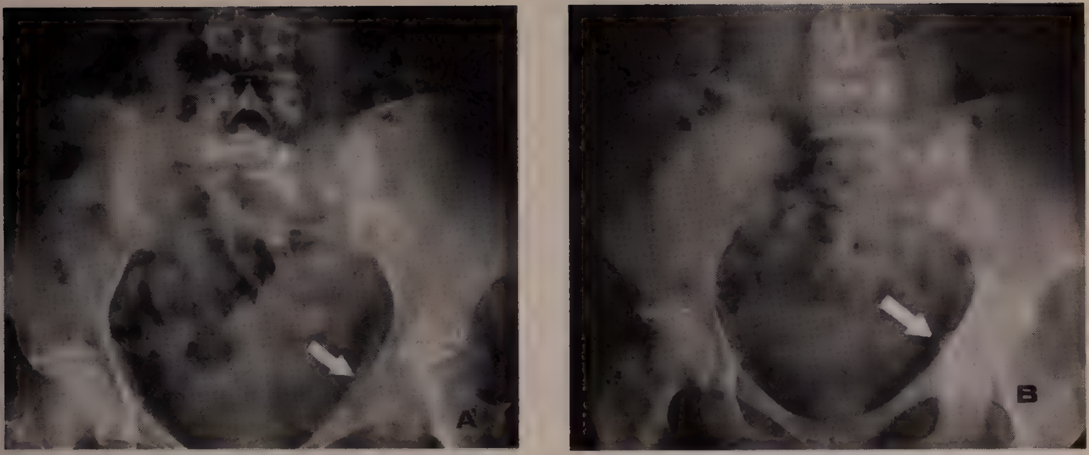

FIGURE 2. Case 10. Fifty-four-year-old white female treated with 9 millicuries of P^{32} who was alive eleven months after treatment. (A) Osteolytic metastases involving left ischium, pubis, and sacral wing. (B) Bone repair of metastases four months after treatment.

Taber,[11] utilizing the same treatment technic as Maxfield, treated 50 cases and reported 70 per cent with symptomatic improvement and 15 per cent with radiographic improvement.

Friedell and Storaasli[9] and Storaasli *et al.*[12] gave P^{32} alone and following bilateral adrenalectomy. Two millicuries were given intraveneously at five- to six-day intervals. The total doses ranged from 16 to 22 millicuries administered over a five- to six-week period. Of 42 cases who were treated with P^{32} alone, objective improvement was found in 26 per cent. Fifteen of the 22 patients (68 per cent) showed good results when radioactive phosphorus was given after bilateral adrenalectomy.

Method

Previous studies[9–11,13] indicated that the best results were obtained in cases having diffuse bone metastasis from breast carcinoma without significant soft tissue involvement. An attempt was made to limit our cases accordingly. A technic of administering P^{32} was selected similar to Maxfield's,[10] utilizing the enhancing action of testosterone.

Our patients were given intramuscular aqueous testosterone (100 mg. daily) for three weeks. During the second week 1.5 millicurie of intravenous radioactive phosphorus was given daily until a total dose of 9 to 14 millicuries was reached. P^{32} was administered orally only if the intravenous route was not feasible. The dose was then increased by one-third. Infiltration of radioactive sodium phosphate ($Na_2HP^{32}0_4$) at the site of intravenous injection, incidentally, is not a real hazard as it is cleared rapidly from the tissues. Blood counts including platelets were obtained at least once a week until recovery from bone marrow depression was apparent. This usually occurred by the fourth post-treatment month. Thereafter, blood counts were obtained as deemed necessary. Radiographic bone surveys were taken every few months.

Results

Our 14 patients (Table I) brought the total number of cases reported to date to 201. Of these, 87 per cent had significant relief of pain, and 18 per cent had radiographic evidence of bone repair (Table II). Our greater incidence of radiographic improvement (50 per cent) is noteworthy but does not appear to be statistically significant in relation to the over-all reported total. Progressive relief of pain usually was evident one month after treatment and reached a maximum in three to four months. Occasional cases took longer to reach full improvement because of associated marked musculoskeletal deformities. The palliation

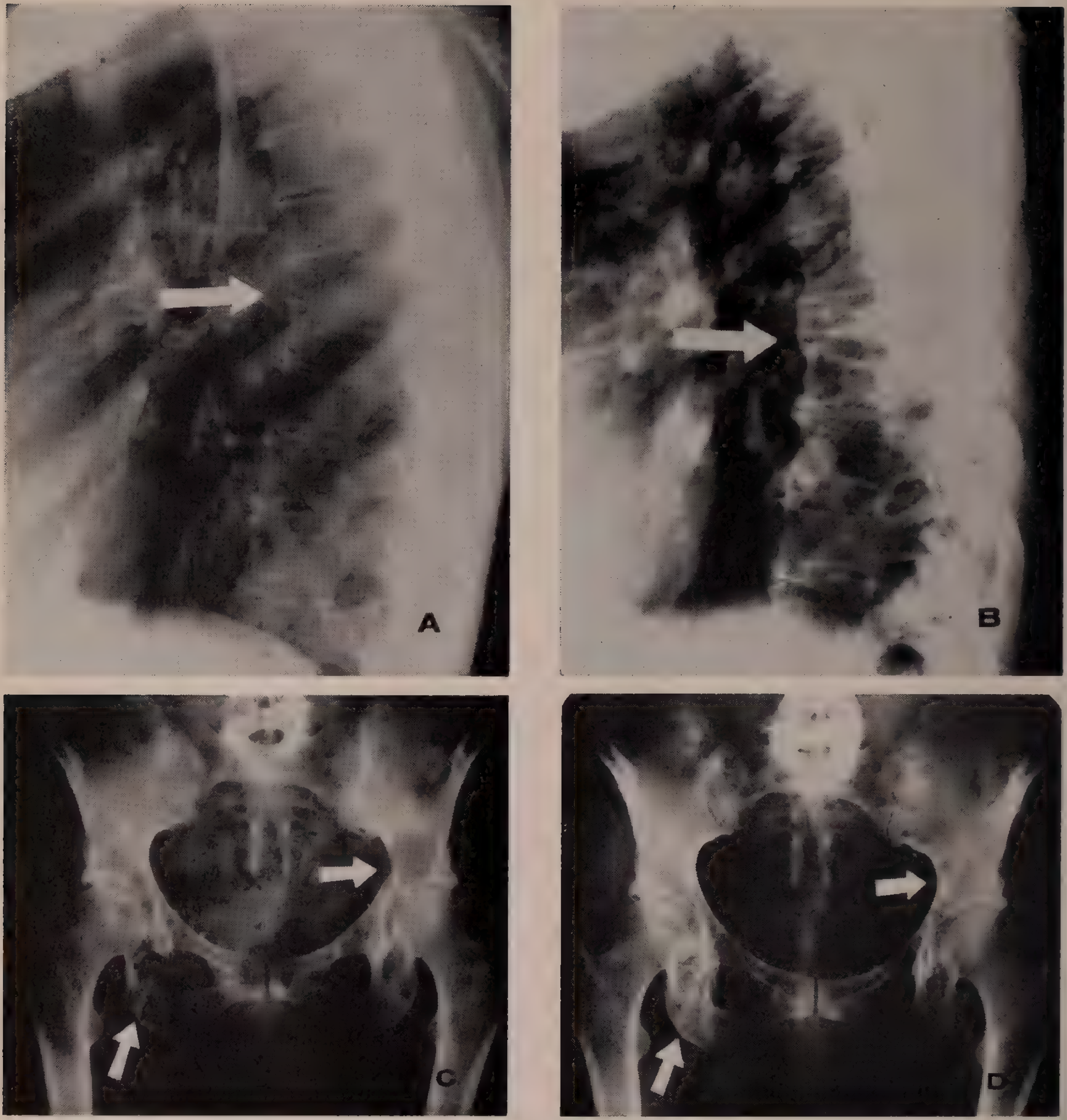

FIGURE 3. Case 11. Thirty-seven-year-old white female treated with 9 millicuries of P^{32}, followed by 6 millicuries four months later, who was alive fourteen months after treatment. (A and C) Osteolytic metastases before treatment. (B and D) Response to treatment eight months after second dose of P^{32}.

resulting from initial treatment has lasted from two to eighteen months. The therapeutic response was not directly proportional to the dose of P^{32} given. Further improvement could often be obtained when symptoms recurred, by a repeat course of therapy. The dose was then dependent on the hematologic status and the previous amount of P^{32} administered.

The physical capabilities and appearance of patients before and after treatment were often startling. Patients who were bedridden or hardly able to stand could walk without significant discomfort or even return to work after treatment. Loss of height, which was noted in some cases, varied from 3 to 6 inches (Case 12, Fig. 4). This was due to vertebral collapse which was not apparent prior to treatment in patients who were bedridden or unable to stand. Further vertebral collapse often occurred after treatment, which added to the decrease in height

TABLE II. Summary of reported cases of carcinoma of the breast with diffuse bone metastasis treated with radioactive phosphorus and testosterone

Author	Technic	Number of Cases	Significant Relief of Pain Number	Significant Relief of Pain Per Cent	Radiographic Evidence of Bone Repair Number	Radiographic Evidence of Bone Repair Per Cent
Taber, 1955[11]	P^{32} plus testosterone	50	35	70	7	15
Maxfield, Maxfield, and Maxfield, 1958[10]	P^{32} plus testosterone	137	129	94	23	17
Mandel and Chiat	P^{32} plus testosterone	14	11	78	7	50
TOTALS	P^{32} plus testosterone	201	175	87	37	18

noted when the patient was finally measured. Obviously this was of considerable concern to the patient.

When the total dose of P^{32} given was under 12 millicuries, the degree of bone depression was minimal. In 1 case who received 12 millicuries (Case 8, Fig. 1), severe bone marrow depression occurred necessitating multiple blood transfusions. However, cases given greater doses did not necessarily show alarming depression of hematopoiesis (Cases 7 and 14).

Comment

It has been well established that when P^{32} is administered systemically there is generally a higher concentration in tumor tissue as compared with normal tissue.

When P^{32} alone is given to a patient with osseous metastatic breast carcinoma, favorable results may be obtained.[12] Giving testosterone or performing an adrenalectomy appears to potentiate the therapeutic effect.

It has been noted[7,9,13,14] that the concentration of P^{32} is highest in the shell of regenerating bone surrounding the metastatic foci, with smaller amounts in the tumor and much less in normal bone, indicating that regenerating bone increases the local concentration and radiation effect of P^{32} on the metastatic lesion. Therefore it is not surprising to note the enhancing action of testosterone or adrenalectomy or

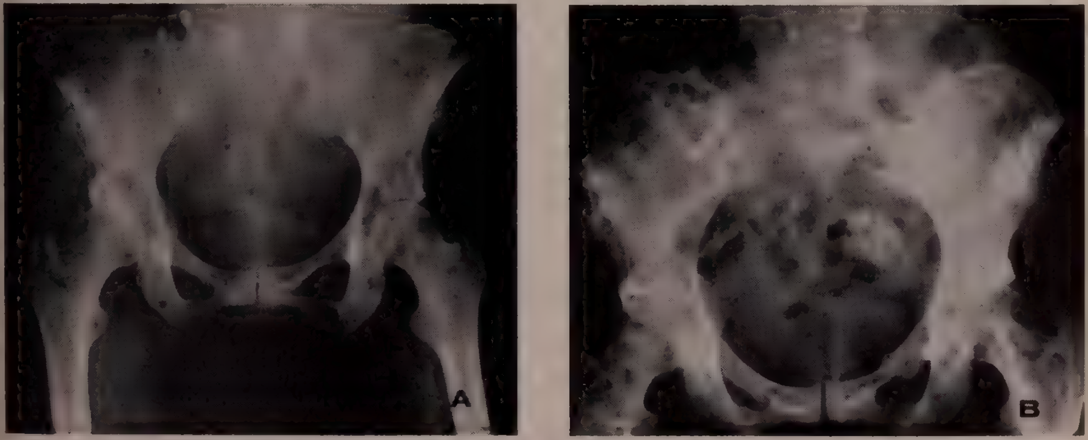

FIGURE 4. Case 12. Forty-four-year-old white female treated with 9 millicuries of P^{32} who was alive nineteen months after treatment. (A) Diffuse lytic lesions throughout pelvis. (B) Five months after treatment, both repair of older lesions and development of newer ones. (It is of interest that this patient lost 6 inches in height because of vertebral collapse.)

the uniform failure of soft tissue metastasis to respond.

Summary

Our experience with P^{32} and testosterone in the treatment of osseous metastasis from breast carcinoma has been reported. The results of other authors using similar technics have been reviewed. Sufficient clinical data exist to indicate that this technic is worthy of broader use in properly selected cases.

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Population gains in 1961

Large population gains were recorded in both the United States and Canada last year, according to statisticians of the Metropolitan Life Insurance Company. The combined population of the two countries at the end of 1961 reached 203,600,000.

The total population of the United States, including all armed forces personnel domiciled here and abroad, was 185,210,000, an increase of more than 2,950,000 during 1961. This represents a rise of 1.6 per cent, which compares with an average annual increase of 1.7 per cent during the ten-year period from 1950 to 1960.

Canada added about 350,000 inhabitants during 1961, raising its population to 18,390,000. This increase of 1.9 per cent, however, was considerably below the Canadian annual average rate of 2.7 per cent in the preceding decade.

Most of the population growth in the United States during recent years has resulted from the unprecedented number of births. There were 4,300,000 registered live births in 1961, corresponding to a rate of 23.5 per 1,000 population. The population under age twenty-one in the United States has increased by 39 per cent—from 53.7 million in 1950 to 74.4 million at the end of last year.

During the same period the population at ages sixty-five and over increased from 12.3 million to 17.2 million. While this relative growth was 40 per cent or slightly greater than that for the population under twenty-one, the number of elders added to the population totaled less than one fourth the increment in the number of youths.

Correspondingly, the large population at the main working ages of twenty-one to sixty-four years increased only moderately, from 85.8 million in 1950 to 93.6 million at the end of 1961.

Every geographic division of the country gained population in 1961. The trend of earlier years continued, with the Pacific states experiencing the most rapid rate of growth, about 3.1 per cent. The mountain states also grew rapidly during 1961, with the highest gains in Arizona and Nevada. Other states with above average rates of population growth were Florida, Maryland, Delaware, Virginia, Connecticut, and New Jersey.

Canada's population growth during 1961 was due almost entirely to its excess of births over deaths. There were about 478,000 births last year, a rate of 26.3 per 1,000 population. About 139,000 deaths were recorded.

Ontario and Quebec again were the fastest growing provinces, accounting for almost two thirds of Canada's total population increase. Ontario added about 120,000 to raise its population to nearly 6,290,000 by the end of the year, while Quebec's population increased by more than 100,000 to 5,280,000.

Hospital Management of Adolescent Patients*

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WITH THE INCREASING demand by the community to improve the treatment and rehabilitation of those adolescents who have emotional illness, studies are being made at the New York Hospital (Westchester Division), the aim of which is to acquire an increased understanding of the problem in all its ramifications.

In a brief review of some of the background which aids us in understanding the adolescent and the problems that confront him, it is recalled that an infant's security is dependent on the all-round nurturing he receives from the mother figure.[1] This security should occur in a sound marriage, with parents accepting the role of parenthood. If these conditions prevail, the infant's dependency needs are met. He then is able to move to the next period of development when separation from the mother occurs. If he is a secure child, he will view the world as friendly and begin the process of growing more independent. With wise parental guidance, his infantile fears will disappear. He will give up his dependencies and seem more willing and eager to begin to learn the technics demanded by the process of growing up. If, in moving toward the school years, the child does not have a mother who is accepting her role, the male child's notion of a real feminine woman whom he might later want to love and capture for himself, may be upset. If the male child does not have a father he can admire and emulate, yet dares to regard as a rival for his mother's affection, he may not be able to move ahead in his development. The reverse is true for the girl. Having worked through these problems which have been referred to as the oedipal period, the child is now ready to give his attention to the insecurities of the world outside the family. The secure child leaves home, goes to school, and begins to test out things and people. For a number of years now he is spared the increased inner and outer stresses of puberty, and he is free to use his energy, intellect, and senses to explore his fascinating world. He incorporates the mores of his home and community. He makes judgments concerning people, situations, and events. During this period and until the beginning of adolescence, he is like a sponge absorbing all that is required for the development of a personality which can successfully meet the stresses of the next stage of development, that of adolescence.

Defining adolescence

Adolescence begins in the early teens or before and gradually tapers off in the early and midtwenties. It is a period that defies definition. It is a period of surprises for the individual who is going through it and for those who are nearby, observing or reacting to it. It has been referred to by some as a disease which, hopefully, will run its course as quickly as possible.

There are only a few standards or rules which can be applied to the adolescent, and one of these is a tendency to upset all standards and rules. The adolescent is confronted with marked psychologic and biologic changes which he comprehends poorly. Despite his many anxieties and uncertainties, he no longer allows himself to be directed by the adults in his life. He

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* Presented at the Monday Evening Seminar, New York Hospital (Westchester Division), November 7, 1960.

is so intensely preoccupied with the changes within him that the world around him generally is not realistically appraised. He has rapid changes in his feelings and thinking which lead him one moment to the depths of despair and the next moment to the heights of self-confidence and egotism. He is a rebel in turmoil or without cause one moment and in religious ecstasy the next. He seems to be itching to sacrifice everything in love and war. The relatively settled, mature, and stable adult sees the adolescent's behavior as more or less unsound. The adult does not allow himself to remember his own turbulent adolescence and finds it difficult to respond to the adolescent's need to be taken seriously. With his intense feelings, sensitivities, and introspections, it is difficult for the adolescent to believe that his contemporaries are having the same difficulties. He tends to think that he is different from others. He and his parents cannot understand the variations in physical, intellectual, and growth rates that occur during adolescence. He wonders why some of his friends are sexually overmature and others immature; why some of them have jumped ahead intellectually, while he is only average; and why others have developed "personality plus," and he still is shy, backward, and awkward. Certainly another rule that might be set for the adolescent is that there is a wide range within which physical, intellectual, and personality attributes are quite normal.

Even this sketchy description of adolescence provokes wonder that anyone is able to move through this difficult period of adjustment and growth without real illness. Nevertheless, it would seem that in the nature of things this difficult period of turmoil and stress is necessary to prepare the individual for adulthood.

Purposes and tasks of adolescence

What are the purposes and tasks confronting the adolescent which we are able to discern from his turmoil, rebellion, and erratic drives and desires?

The first task of the adolescent is to find a solution to the struggle that he has between urges for emancipation and dependency.[2] Heretofore the individual has looked to his parents as his guide and protector in relation to his own impulses and the actions of others. Propelled by his drive for independence and despite his anxieties and insecurities, he moves away from his parents. He begins to place other people in the same role as his parents who now are devaluated. It is not difficult to see the vulnerability of the adolescent, in his state of insecurity, to the seductive voice of a leader or group with a false ideology or intent. This movement toward independence is the first crucial step taken by the adolescent.

The second task confronting the adolescent is his need to find standards of morality and of right and wrong that are acceptable and appropriate to the adult society in which he will live. This task, in essence, is the effort the adolescent makes toward some inner control of the instinctual side of himself. Not only is he in need of control in his sexual behavior, but also he must learn the rightness and wrongness of acts and all the various roles he must play in his relationships with others. In an effort to obtain this, he indulges in asceticism, philosophical intellectualizations, religiosity, and so forth, depending on the models he has available for identification. He continues to search until he has found and incorporated into his personality the standards that are acceptable to him.

The third task, and one which generates the most serious conflict in the adolescent, is the search for identification with the sex role for which he or she is biologically determined. This not only means the sexual role, but all the roles that society expects of the mature adult male and female. One can see the importance of the early parental relationships in the solution of this problem.

The fourth task of adolescents involves progress toward permanent decisions and choices that the adolescent must make as to his educational and vocational future. There is much struggle, experimentation, and trial and error in reaching these goals. Final choices are usually not made in adolescence and seem to depend on the individual's unconscious needs, the solution of other conflicts of adolescence, and pressures and value ratings attached to occupations which arise from cultural influences and peer groups.

Group study

Studies were made of the life histories of 100 young males between the ages of fourteen and nineteen years, admitted to the New York Hospital (Westchester Division).[3] They represented the consecutive admissions of this age group from 1946 to 1956, and many of these youngsters had serious and deep-seated difficulties acting to block normal maturation in addition to the more common and more usual adolescent problems outlined previously.

The average age of this group at the time of admission was seventeen years. Most of the patients came from small family units. Sixty-three or almost two thirds, were the first male children in their families. The pressure to succeed was extraordinary and a source of paralyzing anxiety for many of the patients. The families were well-to-do, with better-than-average educational and cultural opportunities. There were 54 patients who showed psychotic reactions in the family history. Twenty-five had parents who were hospitalized for psychoses. These patients were impressed by the disturbance created in the home and by the separation from the parent. There were only 10 patients from homes broken by divorce, separation, or death of one of the parents, but over 90 per cent showed a lack of harmony between the parents. The father frequently failed to set a healthy example for identification and to exert firm leadership. The fact that fathers were away in military service during the infancy and early childhood of these patients was most traumatic. While the father was away, the mother commonly went to live with her parents and the early home environment was predominantly female. On returning from war service where masculine virtues were emphasized, the fathers often gained the impression that the sons were spoiled and effeminate. They tended to enforce a Spartan discipline, sometimes of a cruel nature. Fathers who had no contact with their sons during the first few years of their offsprings' lives had not developed any real relationship with them. Many fathers commented that they had never felt close to their child, and some even doubted the paternity of the child. Patients who grew up in this situation felt rejected and reacted with a variety of psychopathologic patterns, depending on their temperaments. Feminine identification, with exaggerated passive-dependent needs, was a frequent finding. On reaching adolescence, this was a source of great conflict. Hostile, rebellious, and even delinquent behavior was often displayed by the patients in an attempt to compensate for doubts concerning their masculinity.

Of significant importance was the type of mother who was immature and inclined to be indulgent and even seductive in her attitude toward the patient. This was manifested in two thirds of the mothers by prolonging infantile dependence and by too much fondling. The psychotic symptoms precipitating the hospitalization of many patients were alternating periods of hostility and erotic advances toward the mothers. Five of these mothers, conscious of their own incestuous feelings, became psychotic and required hospital treatment.

Infancy and early childhood were commonly marked by serious physical difficulties, including birth injuries, repeated upper respiratory infections, allergies, feeding problems, and operations. These difficulties appeared to interfere with normal physical growth and to retard the development of normal, healthy relationships with members of the family and with playmates. Over 75 per cent of the adolescents were shy, isolated, poorly coordinated, and lacking in strong spontaneous feelings. The group as a whole found it difficult to invest interest in their surroundings, school work, and group activities.

There was a noticeable unevenness in personality development of these patients. Being isolated, they did not feel secure in the family group or in school. Overcompensation and preoccupation with unhealthy and impractical intellectual activities, along with philosophical, religious, and mystical rumination were common. Many of them became absorbed in solitary hobbies. Failure in emotional maturing and socialization led to increased withdrawal and a tendency to act out aggressively against parents, teachers, and, less commonly, playmates.

In this group the average duration of

difficulty in the patients prior to admission was two and one-half years. The stress of adolescence was an important precipitating factor. At this time there was a strong drive to be independent. The patients were unable to feel close to anyone and were preoccupied with sexual matters. The illness was precipitated by attempting to adjust to the first year of preparatory school or college in 30 patients. In 10 patients the illness was closely associated with a serious sickness of one of the parents. The first sign of abnormal behavior followed severe virus infections or operations in 15 patients. Ten were disturbed by a move to a new environment to which one or both parents were also reacting with signs of stress. One third of the patients showed worries about homosexuality, such as believing that others considered them homosexual or fearing that they could not control these homosexual feelings in themselves. In their state of insecurity, 40 patients became involved in stealing from their families and in minor pilfering in the neighborhood, this being an attempt to gain a sense of status or to "rent" friends, as 1 patient so aptly declared. Only 10 patients had come to the attention of the law, and in all of these patients there was close cooperation with the courts and probation officers.

The mental picture at the time of admission was largely that of adolescent turmoil. Eighty-one patients were diagnosed as schizophrenic; of these, 66 were catatonic, 8 were simple, 6 were paranoid, and 1 was hebephrenic. Ten patients were diagnosed as psychopathic personalities with asocial trends. These differed from those diagnosed as schizophrenic in their impulsive acting-out. They were more aggressive and straightforward in their acts of stealing and aggression, whereas those diagnosed as schizophrenic showed more fumbling and disorganized forms of stealing or impulsive actions. Depressive and suicidal trends were encountered in 35 patients. Usually this was associated with ideas of guilt and preoccupation with a sick religiosity closely related to concerns over masturbation, homosexuality, sadistic heterosexual fantasies, or fears of losing control. The schizophrenic reactions were always associated with trends involving projection of homosexuality and delusional thinking. Eight patients were diagnosed as having manic-depressive reactions, and 1 was diagnosed as psychoneurotic.

Physically, the group was interesting. At the time of admission, 50 per cent of the patients were poorly coordinated and awkward. Thirty patients showed some form of allergy, and 25 were undernourished. Of interest was the appearance of myopia in one half of the patients. An equal number had acne, dilated pupils, and vasomotor symptoms, such as cold, clammy hands, and excessive and odorous perspiration, associated with exertion. Only 9 patients showed abnormal electroencephalographic tracings, and these patients were not associated with any particular diagnostic grouping. Two patients were so abnormal, with clinical findings suggesting epileptic equivalence, that anticonvulsive medication was administered and proved helpful. The average hospital residence for the group was nine months.

The difficulties of the group were varied and included disturbances of mood, uncontrolled and uncontrollable behavior, withdrawal reactions, peculiarities of thought leading to personality disorganization, neurotic reactions, antisocial tendencies, sexual perversions, and frequently a lack of commitment to life in general. In spite of the variability of the presenting problems, certain generalizations can be made about the group as a whole to convey a treatment philosophy.

Treatment

An effective management of the adolescent begins even before the patient arrives at the hospital, and much can be done then which facilitates matters later on. The parents are supported in the move they are about to make, with particular reference to guilt feelings for their part in the patient's illness. This effort continues throughout the period of hospitalization. It is well to point out to the parents that if they purposely set out to do so, they could not bring about the type of situation which confronts them. They may further be told that the presence of serious emotional problems in a child will bring to the surface emotional troubles in those charged with his care.

The situation of a passive boy sired by an aggressive father is an example of this type of interplay. The father may be disappointed in the timidity and lack of energy of his son whose sensitive nature causes him to have difficulty making his way in the hurly-burly of modern society. A lack of closeness ensues which may be heightened by the father's absence from the home on business or in the service. It is not unnatural then that the child should drift into the orbit of his mother and even develop a feminine orientation. This is frequently further exaggerated when the mother unwittingly begins to fulfill some of her own emotional needs through the son. In the end the patient becomes the center of argument between the parents. The parents then begin to relate to each other primarily through the patient, an impossible situation for all.

Initially, on arrival at the hospital, the parents are met with a confident attitude and are shown the facilities of the hospital and given an explanation of the therapeutic philosophy. They are assured that all factors, including possible organic influences, will be investigated thoroughly. They are informed that the presenting symptom in the patient is but a part of a larger problem of faulty adjustment which prevents normal movement toward adulthood. This is particularly important when dealing with such alarming symptoms as homosexuality and unbridled, aggressive behavior. Many parents are reassured on learning that the hospital will employ a rounded approach which includes socialization, re-education, help with difficult interpersonal relationships through psychotherapy, and useful occupation. They are further informed that self-knowledge through competitive games, opportunities to develop special interest in music and reading, organic therapies when indicated, and, above all, the opportunity to identify with stable individuals will be provided. For their own problems parents are told that there will be help both from the psychiatrist and from the social service department.

Before admission, the adolescent should be dealt with honestly. Once hospitalization has been decided on, the patient should be informed of the plan and the reasons for it. This is frequently sufficient and, more often than not, the patient comes willingly and voluntarily to the hospital. No deals or trickery should be used, however, and it is far preferable to utilize the police or some other determined show of force than to threaten, persuade, cajole, or bribe the patient. He will almost always, at a later date, appreciate the fact that others have had the good sense to act for him when he was unable to act for himself. A number of youngsters get involved with the law and are placed on probation while they receive treatment. This is often a good thing for it usually ensures an adequate time of treatment, since it prevents panicky parents and those parents whose own deep needs cloud their judgment from removing the patient prematurely. It also helps the patient to understand the reality in the world about him. Note should be taken here of the enlightened attitude of the judiciary and probation officials in regard to the acting-out adolescent. They realize that treatment does not consist of an attempt to whitewash the adolescent. They fully appreciate the need to understand and treat the various problems which underlie antisocial behavior. Every effort is made to keep the lines of communication open between the hospital and the legal authorities, and such close cooperation has led to mutual understanding and respect.

Patients under eighteen years are admitted as voluntary minors, that is, the parents sign for their admission voluntarily. Those who have reached the age of eighteen years may sign voluntary applications on their own or may, in certain cases, require certification to the hospital.

The patient is first seen in the admitting room by the admitting physician where a brief history is taken from the patient and he is given a straightforward explanation of what to expect. His personality is often found to be undifferentiated, and he is confused and fearful of the complicated forces which have been at work. The first task, therefore, is to place the patient in an environment where visible and consistent external controls will serve him until his improvement allows development of his capacity for internal self-control. The environment is simple and well regulated, and here the patient's disordered patterns of reaction can be isolated and observed.

Initially the patient is not permitted to see relatives since premature visits produce a type of artifact which can prevent the patient from focusing on his own problems. This period of from two to four weeks gives both parents and patient adequate time to initiate a solution of their own problems. The parent-adolescent relationship has usually been so turbulent or of such a clinging variety that neither one of them can move into a new direction without such a separation. They need this time so they can look at each other more objectively. In addition, time is provided for the physician and the social service worker to evaluate ways in which parental attitudes may have influenced the course of the adolescent's illness. For instance, it is often learned that the adolescent boy has had difficulties in areas of identification with his father, and regular visits by the father are consequently planned. The mother will be excluded from visiting or only allowed to visit rarely, and then only in the presence of the father. The reverse may be true of the adolescent girl. It is obvious that such a course of action creates a touchy situation, but if the family can be brought to the realization that the response of the patient because of his illness indicates such a course, it can be done. However, if those responsible for the patient's treatment believe that the illness has been caused only by the manipulations and ineptitude of the parents, it cannot be carried out effectively because this attitude will be communicated to the parents. Furthermore, one will unconsciously be giving comfort to and re-enforcing the patient's tendency to blame his parents for all of his difficulties. Sooner or later the adolescent must learn to act responsibly for himself. He must, to some extent, understand his parents, their problems, and their actions. His tendency to blame them prevents such an understanding and at the same time helps him deny responsibility for his own responses to life.

In the controlled environment of the hospital various thinking and behavior patterns will emerge which are a reflection of the patient's problem. It is the task of the psychiatrist to attempt to evaluate these patterns and to assess their meaning. This is not an easy task since adolescents, at least initially and sometimes throughout their whole hospital stay, may not feel any great need for hospitalization. In the beginning conscious efforts on the part of the psychiatrist to form a so-called therapeutic relationship or to get the patient to reveal his problems are prone to be unsuccessful. In fact, such efforts are often scorned or, at best, tolerated politely.

Behavior patterns which emerge are, for the most part, rather infantile, although they are often disguised to give them a cloak of what might be called pseudomaturity. Their purpose is to avoid the inevitable anxieties encountered in assuming responsibility for one's self. One patient will handle these anxieties by an overbearing and condescending attitude, indicating an unwillingness to participate in what he views as childish games. Another patient will develop some somatic complaint or will elaborate on some already existing defect such as myopia, flat feet, sinus headaches, and so forth. Still another patient might project difficulties and feel that others are critical of him, perhaps even talking about him. A number of patients may overintellectualize. The symptoms vary considerably from patient to patient and change sometimes with remarkable rapidity in any particular patient.

From what has been said, it is obvious that there can be no standard approach to the adolescent. Energy which has been taken up with symptoms needs to be diverted to pathways which favor maturation. Tranquilizing medication and electric shock treatment may be required, as well as other treatment modalities, including hydrotherapy. No form of physical treatment is regarded as curative. However, physical treatment that is necessary is used without apology since it can provide a way to keep symptoms under control to a point where the patient can begin to learn about himself through introspective analysis, interpersonal relationships, and practical experiences. These experiences are centered in three areas: (1) the physician and the staff, (2) the hall and hospital social structure, and (3) the activities in the physical education and occupational therapy departments and other program activities. If one were asked which of these areas is the most important, the question could not be answered. The therapeutic team is kept well informed, and all the department heads meet with the medical staff each morning to consider problems individually. The understanding of the psychiatrist, as he gains information about the patient from the family, the patient himself, and the staff, serves as a basis for management, and he assumes the leadership of the treatment team.

The program orientation of the patient is from the simple activities to the more complex ones. In the physical education department the patient's individual capacities are evaluated, and he is given special instruction in appropriate sports. It is required that he gain experience in teamwork and in situations where he does not excel. He learns to accept his own abilities and limitations in relation to others through active participation. This knowledge gained through experience is reviewed and expanded in psychotherapeutic sessions, as indicated. A flexible schedule of psychotherapeutic sessions is maintained, the needs of the patient being the determining factor. Often short, frequent sessions are the most effective, since examples of maladaptations are constantly cropping up. Prompt attention to these maladaptations, either when they happen or very shortly thereafter, has proved beneficial, whereas discussions a few days later may have little meaning to the adolescent. Members of the program team and nursing staff participate in this on-the-spot type of psychotherapy.

Most of the adolescents that we see are fearful and insecure and have small tolerance for their own mistakes. In fact, their fear of making themselves look silly often takes many months to overcome. Perfectionistic tendencies are common to many and are a favorable prognostic sign. These tendencies are dealt with rather directly and helped particularly in the Occupational Therapy Department by assigning a certain amount of time for each project rather than permitting an endless refinement of any particular work. The patient is then encouraged to accept what he produces within the time limit and thereby learns to tolerate and find less threatening the limitations that the world imposes. The emphasis is on the here and the now. Attention to such details as dress, eating habits, hygiene, social habits, religious needs, and appropriate relationships with members of the opposite sex through dances and dancing instruction are all important, and guidance in these areas is necessary.

As improvement becomes evident, as much is demanded of the patient as his level of maturation will allow. Some very sensitive and withdrawn youngsters need a great deal of encouragement before they will participate in the various activities. Most adolescents, however, participate rather willingly and eagerly, although sometimes only because they know it is the way they can get out of the hospital. A period of adequate functioning at a less demanding level should precede the introduction of greater responsibilities. Except in rare instances, it is vain to hope that increased responsibilities and privileges will stimulate a youngster to do better when he is not functioning well at a lower level. To expose those who are unready to this kind of stimulation is all too often merely a repetition of what has happened prior to hospitalization. This rather simple and commonsense concept is often difficult for both parent and patient to comprehend, particularly over the many months required for treatment. The very nature of the patient's difficulty causes him to see this gradual, unhurried approach as unreasonable. Those dealing with this must have confidence in their judgment since much is done that will be perceived as arbitrary. Lengthy explanation will avail little, but much is gained by a consistent and supportive approach, and sooner or later repeated, constructive experiences will enable the patient to move forward.

In the treatment of the adolescent a great deal of time is spent planning for the period following discharge. The relationship between parents and the adolescent may have developed sufficiently to permit his return to the home. Schools which are prepared to handle youths with emotional problems may be a next logical step in rehabilitation. Preparatory schools may be indicated.

Often the older adolescent will secure a job, working at first from the hospital and later either living at home or at an acceptable youth residence.

In the normal course of adolescent development the individual begins to test the various attitudes and traits he has incorporated during the process of identification. If most of these traits prove useful, he will make an orderly transition into adulthood. He will have a sense of continuity between himself and his background and because of this will feel supported in the efforts he is making. He will also derive from this a sense of trust and confidence not only in himself but in other people as well. He can then see himself as part of an evolutionary process and not as if he were the first person ever born.

Lacking healthy identifications, the adolescent has little choice but to be distrustful of almost everything and to see the world as a very frightening place indeed. In the course of treatment the patient has the opportunity to make new identifications. Although the mechanism of identification is a factor in the treatment of all mental illnesses, it is nowhere as important as when dealing with adolescents. The implication of this for those treating the young is obvious. The adolescent is quickly aware of sham insincerity and disinterest. He is impressed by how a person behaves and by what a person says. He observes and is influenced by staff conduct in the major and minor crises which occur. Over and above all, the adolescent expects, and I believe he has a right to expect, that those about him will have a point of view, a set of values, and a mature philosophy of life. The adolescent is incapable of growing in a void. He need not accept these values, but as he observes the individuals around him in action, he can learn to take what suits him and reject what does not, without having this disturb his relationships with these individuals.

In the establishment of a therapeutic relationship, the first task is to structure and simplify the environment to a point where the patient can begin to function successfully at some level. When this has been achieved, his anxieties will be reduced and he will develop an awareness of what he can expect from his environment and those in it. Healthy new identifications and with them a deep and meaningful therapeutic relationship with the physician become possible. The patient can then explore his problems in depth. Nothing new is added, but the relationship provides an additional framework within which he can view himself realistically and learn to make such choices and adaptations as his capacities will allow.

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Proton radiation in cancer treatment

Proton radiation—the so-called "atomic knife"—has been used against uterine cancer in a series of experiments at the University of Uppsala, Sweden. Fifteen women have been so treated in the last few years.

Most of the cases were already regarded as hopeless when treatment started, and the women treated in the beginning of the series are now dead. However, it was said that all cancer cells had been destroyed by the proton beam and that the women had died of other causes.

The leader of the group that conducted the experiments, Prof. John Naeslund, said that proton radiation might have good clinical results with uterine cancer.

A brain operation with the proton beam was performed in Uppsala in November, 1958.—*The New York Times, May 9, 1962*

Methocarbamol Injectable in Treatment of Acute and Chronic Muscle Spasm

A STUDY WAS MADE *of the effectiveness of methocarbamol (Robaxin) in relief of muscle spasm in 60 patients. Of 32 patients with acute conditions, 40.6 per cent showed excellent results, 43.8 per cent good results, and 15.6 fair results. In 28 patients with chronic neuromuscular and arthritic conditions, 10.7 per cent obtained excellent relief, 21.4 per cent good relief, 32.1 per cent fair relief, and 35.7 no improvement. The results in patients with chronic conditions were influenced unfavorably by the poor results in patients with residual spastic hemiplegia following cerebrovascular accidents. The principal improvements noted were improved range of motion of the involved joints, relief of stiffness, and resolution of pain. The side-effects were dizziness and lightheadedness of short duration.*

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THE OBJECTIVE IN the search for skeletal muscle relaxants has been to obtain drugs which abolish spasticity, tremor, and similar excessive motor activity without interfering with normal tone and movement. Methocarbamol (Robaxin)* apparently fulfills this requirement. This study was undertaken to assess the parenteral form of methocarbamol in the Department of Physical Medicine and Rehabilitation in the Coney Island Hospital.

Methocarbamol is an organic compound available in both the oral and parenteral forms. The parenteral form is a solution of 1 Gm. methocarbamol in 50 per cent aqueous polyethylene glycol-300 and is furnished in 10-cc. single dose ampuls. It may be administered either intravenously or intramuscularly. Methocarbamol exerts a superior relaxant action on the skeletal muscle through a depression of the multisynaptic pathways in the spinal cord without producing any effect on the monosynaptic pathways.[1,2] The drug has no action on the motor end plate, muscle fiber, or monosynaptic arc.[3]

Schaubel[4] found the injectable form of methocarbamol most useful in patients with acute muscle spasm. Rather consistently his patients, who had had a spastic muscle problem for only a few days, responded rapidly to intravenous injections of methocarbamol. Spastic torticollis or "wryneck" was resolved especially well by injectable methocarbamol, with most of the patients recovering markedly in twenty-four hours.[4]

One of the complications of fractures is severe muscle spasm. It is not unusual to find a flaccid paralysis or paresis of the extremities accompanying fractures of the spinal column. O'Doherty and Shields[5] found methocarbamol valuable in muscle spasm and severe flexor spasms accompanying cord disease, and Leventen and Vaccarino[6] noted a beneficial effect in postfracture spasm.

Procedure

Sixty patients hospitalized in Coney Island Hospital or admitted to the outpatient clinic over a period of a year were selected for treat-

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* Supplied by A. H. Robins Company, Inc., Richmond, Virginia.

TABLE I. Efficacy of injectable methocarbamol in acute muscle spasm (32 patients)

Number of Patients	Diagnosis	Response to Medication*	Side-Effects
10	Skeletal muscle spasm secondary to diverse fractures	Excellent (1) Good (6) Fair (3)	Dizziness (3) Headache (1)
6	Low back derangement with muscular and ligamentous strain	Excellent (3) Good (3)	Euphoria (1) Metallic taste (1)
2	Torticollis	Excellent (2)	Dizziness (1)
3	Dislocated shoulder	Excellent (2)	Metallic taste (1) Dizziness (1) Euphoria (2)
2	Dislocated elbow	Good (1) Fair (1)	Euphoria (1)
1	Fracture with fragments overriding	Excellent (1)	None
2	Spasm following laminectomy	Excellent (1) Fair (1)	None
1	Herniated lumbar disk	Good (1)	None
1	Spasm after hip fusion	Excellent (1)	None
2	Acute bursitis	Excellent (1) Good (1)	Dizziness (1)
1	Sciatica	Good (1)	None
1	Muscle spasm, left groin	Excellent (1)	None

* Excellent, 42 per cent; good, 42 per cent; fair, 16 per cent.

ment with injectable methocarbamol. Approximately half of these patients were suffering from acute conditions including fractures, backsprains, torticollis, dislocations, and so forth, while the remaining 28 patients had chronic spasticity or muscle spasms associated with cerebrovascular accidents, spinal injuries, multiple sclerosis, osteoarthritis, and others. These patients ranged in age from ten to seventy-nine years. Their complaints were of a few hours duration in the acute cases up to many years in some of the chronic conditions. Except for the dislocations and an overriding fracture case, all patients were examined completely for strength, reflexes, pain, muscle spasm, and range of motion before treatment with methocarbamol was started. Blood counts, urinalysis, liver profile, blood pressure and pulse rate were all checked both prior to and after the discontinuance of the medication.

Method of administration. In 20 cases one ampule (1 Gm. methocarbamol in 50 per cent aqueous polyethylene glycol-300) added to 20 cc. of 5 per cent glucose in water was injected intravenously three times daily for three to four days. Several patients received intramuscular injections of one ampule without dilution, and the remaining patients received from 10 to 20 cc. intravenously, generally three times daily. For comparative purposes, a placebo containing 30 cc. of 5 per cent dextrose in water was administered intravenously to 13 patients. A double-blind study was intended, but since none of these patients obtained any relief of spasm nor complained of side-effects, the double-blind feature was discontinued.

The therapeutic effect of methocarbamol was graded in four categories. If relief of pain due to muscle spasm was prompt, the response was considered "excellent." If response was obvious, but not as prompt as in the first category, it was graded as "good." "Fair" relief was less pronounced than in the first two groups. "Poor" or "negative" indicated no noticeable response.

Results in acute muscle spasm

Spasm associated with fractures.* Patients with acute muscle spasm responded in an outstanding manner to methocarbamol (Table I). All 32 patients obtained some relief of pain and spasm. Thirteen patients reported prompt relief, often within fifteen to thirty minutes, and the effect was evident for from four to six hours. Occasionally relief for twelve hours was obtained by only one injection. Fourteen patients had moderate or good results, with pain and muscle spasm almost completely relieved in from three to four days. The remaining 5 patients reported moderate therapeutic effectiveness and improved comfort.

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* These patients were observed on the Surgical Services (John E. Hammett, M.D., Director of Surgical Services).

Eleven patients complained of side-effects, primarily of dizziness and lightheadedness immediately following the injection. This usually disappeared within a few minutes. One patient discontinued medication because of dizziness and headache. This patient's response to an injection of sterile glucose solution was similar.

The spasms associated with fracture of the hip, tibia and fibula, intertrochanteric femur, humerus, patella, and trimalleolar were included in this group. These patients, as a whole, did not respond as rapidly as patients with other conditions included in this group; however, the pain and spasm subsided usually in from two to three days. Complete relief was obtained within a week by more than half of these patients, and they were able to walk around on crutches and to start active exercises. A nineteen-year-old man was admitted with complaints of a very annoying "spasm" in his lower extremities and paresis of the upper extremities as a result of fractures at the fifth and sixth cervical vertebrae. This patient with traumatic paraplegia had forceful and very disturbing movements. He was started on intravenous injections of methocarbamol twice daily. After several injections, involuntary movements were reduced markedly in number and force. Within three days, the patient was comfortable and the dosage was reduced to one injection daily.

LOW BACK DERANGEMENT. All 6 patients with low back derangement responded satisfactorily to intravenous methocarbamol. The severe spasm was relieved in from two to three days, and return to work within a week was possible. One patient with acute back sprain (posterior cervical musculature) obtained complete relief of pain and spasm after only six injections of methocarbamol.

TORTICOLLIS. Within thirty minutes following injection, both patients with torticollis were almost symptom free. Stiffness and soreness in the neck were greatly relieved.

DISLOCATIONS AND OVERRIDING FRACTURES. In the patients with dislocations, three of the shoulder and two of the elbow, one and two ampules of methocarbamol were given intravenously simultaneously with 50 mg. of meperidine hydrochloride. In less than five minutes appreciable muscle relaxation was noted, and after fifteen to twenty minutes with minimal traction and almost no pain the dislocations were reduced. One patient with overriding fracture of the left radius had severe muscle spasm and pain. Fifteen minutes after the injection of 20 cc. of methocarbamol, pain and spasm were resolved, and a closed reduction was performed without difficulty and with minimal traction.

MISCELLANEOUS. A thirty-two-year-old woman with a diagnosis of herniated disk at the fifth lumbar vertebra had had recurrent episodes of pain and spasm of her left hip for two years. The episode that prompted her admission was of two weeks duration and consisted of pain in the hip radiating to the lower extremities, with numbness. Motion was limited and the patient was unable to walk. After three days of treatment with physiotherapy and methocarbamol (10 cc. three times a day), pain still persisted and the dosage was increased to four times daily. With the addition of the fourth dose to the regimen, she was very much improved in less than twenty-four hours. After several weeks of treatment, she was able to walk unassisted. Two patients with acute spasm following laminectomy reported greater comfort as soon as treatment with methocarbamol was started. Similar results were obtained following hip fusion. Good to excellent results were observed in patients with acute bursitis, sciatica, and muscle spasm in the left groin.

Results in chronic muscle spasm

The results of methocarbamol in patients with chronic muscle spasm are presented in Table II. The clinical efficacy in these patients is not as outstanding, on first inspection, as in patients with acute muscle spasm. In 18 of the 28 patients there was a positive therapeutic effect, with three "excellent" ratings, six "good," and nine "fair." Twelve patients complained of side-effects.

TABLE II. Efficacy of injectable methocarbamol in chronic muscle spasm (28 patients)

Number of Patients	Diagnosis	Response to Medication	Side-Effects
14	Cerebrovascular accident with residual spastic hemiplegia	Good (1) Fair (4) Poor (9)	Dizziness (4) Euphoria (2)
5	Osteoarthritis	Good (3) Fair (2)	Dizziness and nausea (1)
2	Chronic bursitis	Good (1) Fair (1)	Dizziness (1) Euphoria (1)
2	Multiple sclerosis	Excellent (1) Fair (1)	None
1	Comminuted fracture	Fair (1)	None
1	Postamputation spasm	Poor (1)	Dizziness and hypotension (1)
1	Hemiparesis	Excellent (1)	Dizziness (1)
1	Myofascitis	Good (1)	Dizziness (1)
1	Myositis	Excellent (1)	None

Here again the primary complaint was transient lightheadedness or dizziness following each injection.

The results in patients with residual spastic hemiplegia following cerebrovascular accidents influence the over-all results of methocarbamol unfavorably in chronic conditions. Thirteen of the 14 patients had fair to poor results. Only minimal relief of spasticity may be expected in this group of patients.

Excluding the patients with hemiplegia, the efficacy of the drug in the 14 remaining patients is readily apparent. An excellent therapeutic response was observed in 3 patients (21.4 per cent); a good response was observed in 5 patients (35.7 per cent), and a fair response was observed in 5 patients (35.7 per cent). The one poor response was in a patient following amputation due to arteriosclerosis and diabetes mellitus. This patient had a marked psychologic overlay and did not respond to treatment at all. The patient suffering with hemiparesis from an old spinal injury obtained excellent results after several injections. A noticeable reduction in spasm began within ten minutes after ininjection and lasted for from five to six hours.

The side-effects encountered in this group were similar to those in the acute conditions. One patient with osteroarthritis of the spine discontinued the injections because of severe dizziness and nausea. Medication was continued in the oral form without noticeable side-effects and with a fair amount of relief.

Summary

Sixty patients with muscle spasm were treated at Coney Island Hospital with intravenous methocarbamol (Robaxin). Of this number, 32 had acute conditions, such as fractures (1 with fragments overriding), dislocations, back sprain, a pathologic condition of the disk, torticollis, postoperative spasm, and myositis. In this group there were 40.6 per cent excellent results, 43.8 per cent good results, and 15.6 per cent fair results. In the second category (28 patients), consisting of chronic conditions such as hemiplegia, multiple sclerosis, osteoarthritis, chronic bursitis, and hemiparesis, 10.7 per cent of the patients obtained excellent relief of symptoms, 21.4 per cent obtained good relief, 32.1 per cent fair relief, and the remaining 35.7 per cent showed no improvement.

Methocarbamol is an excellent and worthwhile medication in the treatment of conditions characterized by acute or chronic muscle spasm. With and without meperidine hydrochloride it is a valuable adjunct in the reduction of dislocations and overriding fractures. Patients with hemiplegia secondary to cerebrovascular accidents achieved only minimum relief. Symptomatic improvement was noted in most of the patients treated. The most notable achievements were an improved range of motion of the involved joints, a relief of stiffness, and a resolution of pain.

Methocarbamol shows very little toxicity

in human beings. The primary complaint was dizziness and euphoria of short duration, usually clearing within five to ten minutes. Blood, liver, and urine profiles obtained before and after therapy showed no significant changes.

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Antibacterial drugs prevent travelers' bane

A sulfa drug has proved effective in preventing so-called "travelers' diarrhea" in a significant number of persons, according to an article by B.H. Kean, M.D., William Schaffner, B.S., Robert W. Brennan, A.B., and Somerset R. Waters, B.E., in the May 5, 1962 issue of the *Journal of the American Medical Association*.

In a study involving 473 college students newly arrived in Mexico City, phthalylsulfathiazole reduced the incidence of this common tourists' bane by 50 per cent. Another antibacterial drug, neomycin sulfate, tested among college students, also reduced the incidence of the disease. The combined effects of the drugs reduced the incidence of the more incapacitating variety of the syndrome by two-thirds.

Mexico was selected as the site for the investigation because of the prevalence of tourist diarrhea among visiting students and because educational and governmental officials cooperated completely.

Two studies were conducted, one in the summer of 1960, the other in the winter of 1960 to 1961. Among 168 students taking the placebo, 23.8 per cent suffered the illness. Of 137 taking neomycin sulfate, 16.1 per cent became ill, and of 168 taking phthalylsulfathiazole, 11.9 per cent became ill.

The effectiveness of the antibacterials in preventing moderate and severe forms of the syndrome also was ascertained. Of 168 students receiving the placebo, 17.3 per cent suffered more severe symptoms. Of the 137 receiving neomycin sulfate, 5.1 per cent were more seriously affected, and of the 168 students receiving phthalylsulfathiazole, 6.6 per cent fell into the more severe category.

No harmful side-effects were observed with either drug during the study. However, those taking the drugs were young, healthy, and free from any drug allergy and were subject to daily scrutiny while the drug was administered in low doses for only two weeks.

Effect of Isocarboxazid on Relief of Anginal Pain

A STUDY WAS UNDERTAKEN *to determine the effectiveness of the monoamine oxidase inhibitor, isocarboxazid (Marplan) for relief of pain in 15 patients with arteriosclerotic heart disease and angina pectoris. Isocarboxazid was given in doses varying from 10 to 30 mg. a day over a period of from several weeks to several months. The results were excellent in 9 patients, good in 4, and unsatisfactory in 2. Nitroglycerin needs were eliminated or reduced in the successful cases. Except for 1 case side-effects noted were controlled and subsided quickly with dosage adjustment. Beneficial effects included blood pressure reduction in hypertensive patients and the emotional benefit of mood elevation.*

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THE FORTUITOUS FINDING several years ago of a beneficial effect on anginal pain in patients under treatment with iproniazid (Marsilid) for depression, was followed by the use of this first monoamine oxidase inhibitor in clinical studies on patients with angina pectoris. Early reports on the results of these trials with iproniazid have varied from very enthusiastic[1-3] (tempered by the possible hepatotoxic effect of the drug), to favorable,[4] and finally to unfavorable, particularly by the British workers.[5-7] The following report is a study of the effect of an analog of iproniazid, isocarboxazid (Marplan), on the pain of angina pectoris.

Materials and methods

The Adult Cardiac Clinic at Montefiore Hospital consists of patients who have been discharged from the hospital and require follow-up care. A single folder contains both their hospital and clinic records, enabling one to choose cases for study with reliable, documented histories and diagnoses. We have chosen carefully a small but select group of confirmed cases of arteriosclerotic heart disease with electrocardiographic evidence of either old myocardial infarct, or coronary insufficiency, or both. All these patients had anginal pain as their major presenting symptom.

Our plan has been to evaluate the total clinical effect of the drug as well as its specific antianginal activity, with these closely observed patients serving as their own controls. By this we mean that the selected patients had a fixed pattern of pain and medication, with minor seasonal variations, and any sudden change in the pain frequency or intensity, or in their use of nitroglycerin and nitrates, would be noted immediately by the patient, his family, and his physician. Nevertheless, placebo trials were employed at strategic periods. More than half of the cases chosen had had previous trials on different sedatives and tranquilizers, as well as on frequent analgesics, for the amelioration of anginal attacks, and several required restricted diets, digitalis, and oral or parenteral diuretics to keep them free of edema and dyspnea.

After the rigid screening of a total of 52 clinic patients only 15 were chosen for a study in depth, sacrificing numbers for a

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greater degree of reliability in the results in the individual cases. The associated findings of hypertension were present in 5, diabetes in 2, and recent or old cerebrovascular accident in 2 patients.

The frequency of anginal pain, as well as its intensity and duration, varied widely in these patients from none to 25 times daily. The pain came on mild exertion in some, on walking or on any form of emotional excitement in others, and even spontaneously, or apparently so, in 2 patients. Other stimuli for anginal pain were the sudden awakening from a sound sleep with bad dreams, and new work or responsibility causing anxiety and producing angina. A few patients used 10 to 20 nitroglycerin tablets daily. Several used both nitroglycerin and PETN (penta-erythritol tetranitrate) daily. In 1 patient no nitroglycerin had been used for three years because of its excessive hypotensive effect on her, causing syncope and weakness.

Before the trial all 15 clinic patients were preoccupied and perhaps obsessed continuously with their attacks of chest pain, although these were relieved temporarily much of the time with the medications employed, whether vasodilators or tranquilizer sedatives. The patients were, as a group, far from satisfied with the management and medication for the control of their chest pain, although they were resigned to it as the best and most modern treatment available. A sense of futility, combined with skepticism, would describe their attitude toward therapeutic innovations. In this atmosphere, with anxiety and fear constantly present and always contributing to the distress of angina pectoris, the beneficial results from any new drug designed to relieve anginal pain would be expected to include relief from anxiety as well, and any improvement in mood and morale also would be welcomed heartily. The results to be described furnish a good basis for hope that this goal may be obtained, partially at first, but, as Master[3] has stated, with encouragement to researchers to find the perfect product in this field.

The patients chosen were re-examined before starting the program and questioned for any new conditions that might interfere with or modify the results of the test, such as nonanginal chest or back pain or gastrointestinal disturbances. The onset, duration, frequency, and severity of anginal pain were determined for each patient during the previous six months, together with the number of nitroglycerin tablets used daily or weekly, as well as all other medication required, for comparison with future data. Electrocardiograms and SGOT (serum glutamic oxaloacetic transaminase) tests were ordered on each patient at the outset. The transaminase later was repeated monthly for two months and then every two months for the duration of the study. A final electrocardiogram also was obtained where possible.

Each patient was started on isocarboxazid [1 - benzyl - 2 - (5 - methyl - 3 - isoxazolylcarbonyl) hydrazine], a monoamine oxidase inhibitor, an analog of iproniazid, related in its mode of action to the latter drug, and with no known toxic effects in human beings or experimental animals. The dose was one tablet of 10 mg. twice a day for two weeks, then increased to 10 mg. three times a day, and thereafter maintained at that level until the drug either was decreased or discontinued for reasons to be discussed later. The patients were re-examined at two-, four-, six-, and eight-week periods and thereafter monthly. A careful notation was made of any changes in the number of nitroglycerin tablets required, and in the frequency, intensity, and duration of the anginal pain. In addition, an attempt was made in each case to discontinue other longer-acting vasodilators or sedatives slowly and gradually where possible, particularly PETN, Compazine, meprobamate, and phenobarbital. Thereafter, when the full effect of isocarboxazid was achieved, over a period varying from six weeks to several months in different cases, a placebo supplied by the manufacturer was given in identical dosage. Again the patients were re-examined at two-, four-, and six-week intervals, and any spontaneously reported changes in symptoms were noted. Again they resumed their dose of isocarboxazid and were seen at two-, four-, and six-week intervals to report. Table I gives a summary of patients, dosage, and results with side-effects where they were noted, as well as the results of placebo trials followed by a resumption of isocarboxazid.

TABLE 1. The effect of isocarboxazid on nitroglycerin and PETN requirements

Case	Age (Years)	Nitroglycerin Before Trial	PETN Before Trial	Marplan Dosage (Final)	Nitroglycerin After Trial	PETN After Trial	Side-Effects	Nitroglycerin Requirements on Placebo	Nitroglycerin Requirements When Marplan Resumed	Results
1	75	1 to 6 daily	20 mg. t.i.d.	10 mg. t.i.d.	None	20 mg. t.i.d.	None	2 or 3 daily	None	Excellent
2	75	8 to 12 daily	None	10 mg. b.i.d.	2 daily	None	5-day rash subsided completely on diminished dosage	14 to 16 daily	1 or 2 daily	Excellent
3	70	10 to 15 daily	None	10 mg. t.i.d.	1 or 2 daily	None	Intermittent ankle edema, easily controlled	10 daily	2 or 3 daily	Excellent
4	69	3 daily	None	10 mg. b.i.d.	1 daily	None	None	3 or 4 daily	1 weekly	Good
5	67	1 or 2 weekly or occasionally	10 mg. t.i.d.	10 mg. b.i.d.	None	None	None	1 or 2 weekly	None	Excellent
6	65	2 or 3 weekly	10 mg. q.i.d.	10 mg. b.i.d.	None	None	None	3 weekly	1 in 3 or 4 weeks	Excellent
7	73	2 or 3 weekly	10 mg. t.i.d.	5 mg. b.i.d.	None or very rare	None	Faint chest rash subsided quickly on diminished dosage	5 weekly	Occasionally or 1 weekly	Excellent
8	81	2 weekly	10 mg. q.i.d.	10 mg. b.i.d.	1 or 2 weekly	10 mg. b.i.d.	Vertigo, discontinued drug	. . .	. . .	Unsatisfactory
9	71	1 to 3 daily	None	10 mg. t.i.d.	1 in 3 weeks	None	None	1 daily	None	Excellent
10	54	6 to 8 weekly	None	5 mg. b.i.d.	1 or 2 weekly	None	Mild diarrhea, 2 or 3 days, subsided on reduced dosage	No placebo trial		Good
11	64	4 weekly	20 mg. t.i.d.	10 mg. b.i.d.	None	None	None	1 daily	None	Excellent
12	63	None	None	10 mg. t.i.d.	None	None	Dryness of mouth, slight pruritis	No placebo trial		Good
13	73	5 to 7 daily	None	5 mg. b.i.d.	2 daily	None	Mild headache, completely subsided	No placebo trial		Good
14	60	1 or 2 weekly	None	10 mg. b.i.d.	1 in 7 weeks	None	None	1 or 2 weekly	None	Excellent
15	56	2 or 3 weekly	None	10 mg. b.i.d.	3 in 4 weeks	None	None	1 or 2 monthly	No change	Unsatisfactory

Results

In evaluating the effect of the trial drug on anginal pain, an "excellent" result would be total relief from pain or better than a 75 per cent reduction in the need for nitroglycerin or other vasodilators. A "good" result would be at least a 50 per cent reduction, and an "unsatisfactory" result would be anything less than a 50 per cent reduction. These standards should be sufficiently rigid for any observer. In every patient there was a favorable effect on the chest pain within a few days of starting the isocarboxazid therapy, and in only 1 case was the drug discontinued completely because of side-effects or sensitivity.

In 9 patients (Cases 1, 2, 3, 5, 6, 7, 9, 11, and 14) the effect was unmistakably excellent, and in 4 of these nitroglycerin and PETN were discontinued entirely while the patients were taking isocarboxazid. In a fifth patient nitroglycerin was eliminated although he continued taking PETN. Excellent results also were obtained in 4 other patients, with reductions in nitroglycerin requirements from a high level of 10 to 15 nitroglycerin tablets daily to 1 or 2 a day, from 1 to 3 a day to 1 in three weeks, from 1 or 2 a week to 1 in seven weeks, and from 8 to 12 daily to 2 daily.

A good result was achieved in 3 cases with decreases of from 5 to 7 nitroglycerin tablets daily to 2 daily (Case 13), from 6 to 8 per week to 1 or 2 a week (Case 10), and from 3 daily to 1 daily (Case 4). A thirteenth patient, whom we should like to refer to as a probably good result also, clearly showed a remarkable diminution in chest pain from several times daily to only a rare anginal chest discomfort while taking isocarboxazid 10 mg. three times a day, and then only when walking long distances (Case 12). However, she was the patient who was unable to take nitroglycerin because of its marked hypotensive effect on her, and we have no objective measurement of her improvement as we do with the others. In another case, where the anginal pain was relieved considerably, the drug could not be continued because of vertigo, headache, and some ankle edema that were not prevented by a lower dosage, and we call this an unsatisfactory result. One man, who certainly fitted into a well-recognized class of "placebo-dependent," did very well on isocarboxazid 10 mg. twice a day with a sharp reduction in his need for nitroglycerin. He also did well on placebo therapy and must be put in the unsatisfactory group (Case 8).

Ten patients, all of whom were grateful and much improved with isocarboxazid, received placebo tablets and quickly reverted within three or four days to their previous levels of nitroglycerin need and chest pain frequency and intensity. In 3 patients this was to an extent somewhat greater than their prior needs. When isocarboxazid was resumed, all again were greatly relieved of chest pain, and their nitroglycerin dependency dropped to the status reported before the placebo medication. There were no elevated SGOT levels as a result of treatment with isocarboxazid.

Isocarboxazid, although impressive in its antianginal action, must join the host of useful medications with side-effects. However, these are both good and bad. Fortunately, the side-reactions of an undesirable nature either disappear with the continued use of the drug or are effectively eliminated by dosage reduction. The latter was true in all our cases but one. Side-effects, which may well include a specific sensitivity to the drug, were found to be nausea, vertigo, headache, dryness of the mouth, lightheadedness, mild diarrhea, heartburn, peripheral edema, and maculoerythematous and pruritic rash. These were not associated with any gross changes on physical examination. The patients themselves, in most instances, were eager to continue the medication, for the relief from anginal pain outweighed the disturbances of the side-effects. The rash appeared in 2 cases. In 1 patient it appeared on the chest and was mild and intermittent, fading away after one week while the patient was taking the drug. In the other patient the rash was more diffuse and pruritic, lasting four or five days, subsiding rapidly on the cessation of isocarboxazid, and not reappearing when the dosage was cut from 20 to 5 mg. a day, nor after a subsequent increase to 15 mg. a day. The ankle edema was seen in 2 cases: in the patient who discontinued the drug and in another in whom it appeared after one month on isocarboxazid, 10 mg. three times a day, and subsided after the dosage was cut to 10 mg. twice a day.

The additional side-effects of isocarboxazid were of a beneficial nature. An inescapable observation was its hypotensive effect in all of the 5 hypertensive patients. Blood pressure reductions of 188/104 to 136/88 and 170/104 to 138/90 serve as examples of this action. A striking hypotensive reaction was found in Case 3, a seventy-year-old woman with a blood pressure range over several years of 160 to 210/100. She had a blood pressure of 110/80 after three months of this drug. In the normotensive patients, slight or no hypotensive effects were recorded. Those patients whose blood pressures had dropped markedly were advised to lie down whenever possible when taking nitroglycerin. One patient was able to discontinue reserpine while taking isocarboxazid, and another stopped taking meprobamate.

The most dramatic and favorable side-effect of isocarboxazid from the standpoint of our cardiac interest (although this is accepted as a primary and not a side-effect by psychiatrists using monoamine oxidases) is the elevation in mood and the cheerful, euphoric state that it produces. This emotional benefit probably serves as a distraction from the worries and anxieties in angina pectoris and may well avert the anticipation of pain. Such distraction through mood elevation, and such diminished anticipation of pain, could well lead to a sense of freedom from invalidism, and indeed this appeared to be so in our patients. In 3 cases this side-effect of isocarboxazid led to greatly increased physical activity without the production of angina, and this, we believe, was a false sense of security, for in 1 of these 3 cases the patient developed dyspnea and weakness which required rest and sedation. Consequently, all patients taking isocarboxazid are well advised to refrain from any unusual activity or exertion.

Three short summaries of patients with excellent results from isocarboxazid therapy follow.

Case reports

CASE 1. A seventy-five-year-old man, with a history of anginal pain on any exertion for the past seventeen years, had suffered a myocardial infarction in 1941. There was no hypertension or diabetes. He had been using PETN, 20 mg. three times a day for the past six months and up to 6 nitroglycerin tablets daily for the past seventeen years. He was free of chest pain only when he sat quietly in a chair or in bed. An electrocardiogram before the isocarboxazid therapy showed regular sinus rhythm, left axis deviation, interventricular conduction defect, and S-T changes indicative of coronary disease. The SGOT was 8 units. On November 30, 1959, isocarboxazid was begun, 10 mg. twice a day, and on December 7, 1959, 10 mg. three times a day was begun. On January 4, 1960, he reported that he had been able to discontinue nitroglycerin for the first time in seventeen years. Any chest pain that did appear was milder, and his left arm, which previously had been painful, gave him no further trouble. He was most enthusiastic and cheerful over this new therapy, particularly because he was able to walk several blocks without pain. Although he has remained off nitroglycerin, we were unable to wean him off PETN. There were no side-reactions to isocarboxazid. On May 23, 1960, he was started on a placebo, and on June 20, 1960, he reported that he required up to 3 or 4 nitroglycerin tablets daily for the first time since the previous January. Also, he developed chest pain on walking one or two blocks. On the resumption on July 11 of isocarboxazid, 10 mg. three times a day, he again reported a marked relief in the chest pain, both in frequency and severity, and again he required no nitroglycerin. During this trial his blood pressure, pulse rate, and general examination and transaminase findings showed no essential changes. The final electrocardiogram findings were unchanged.

CASE 2. A seventy-five-year-old man with a five-year history of anginal chest pain had had a prostatectomy three years previously. He used 8 to 12 nitroglycerin tablets daily for an average of four to six attacks of chest pain daily. An electrocardiogram revealed a depressed S-T segment in leads I, aVl, and V_4 to V_6, and left ventricular hypertrophy. He was taking digoxin 0.5 mg. daily, Hydrodiuril 50 mg. for five days a week, and required an occasional Mercuhydrin injection. The SGOT was 50 units. He was started on isocarboxazid 10 mg. twice a day on December 28, 1959, and on January 18, 1960, he reported only one attack of chest pain daily requiring 2 nitroglycerin tablets a day. One month later the drug was discontinued because of a maculoerythematous pruritic rash on the neck and anterior chest, which lasted for five days. The physical examination showed otherwise unchanged findings, and the SGOT level was 9 units. A few weeks later he was again using 10 nitroglycerin tablets daily, and isocarboxazid was resumed at slowly increasing dosages from 5 to 15 mg. a day. No rash or other side-effects appeared on this new dosage, and by May, 1960, his chest pain was so infrequent and mild that he required nitroglycerin only if he walked more than three blocks. Previously his son had to drive him to and from the clinic, but now he came alone with considerable confidence and vigor. In June he was started on a placebo, and in three weeks he reported an increased need of nitroglycerin to from 14 to 16 tablets a day and 2 or 3 at night. However, a general examination revealed no changes in the circulatory or pulmonary status. Isocarboxazid therapy was resumed on July 11, 1960, with 10 mg. twice a day, and he subsequently reported a marked improvement again with his nitroglycerin need back to 1 or 2 tablets daily on prolonged walking only. The SGOT level was normal, and an electrocardiogram taken at the end of the study also showed unchanged findings.

Case 3. A seventy-year-old woman with chest pain on exertion for ten years and a history of hypertension of 170 to 210/100 to 110 for several years, had been using 10 to 15 nitroglycerin tablets daily for frequent, severe anginal pain on mild to moderate exertion. In January, 1960, isocarboxazid 10 mg. twice a day was started and was increased to 10 mg. three times a day. By February 15 she reported marked relief of the chest pain with a rare need for nitroglycerin, down to none or 1 tablet daily. She was cheerful, had more strength, and there was a drop in her blood pressure to 146/94. A mild peripheral edema led to a decrease in isocarboxazid dosage to 10 mg. twice a day that remained very effective. She did housework, walked much longer distances than ever before, and used nitroglycerin only rarely, or on unusual exertion. She was put on an oral diuretic two days a week that kept her free of edema. A placebo was started on June 13, 1960, and in a few weeks she was back on 10 nitroglycerin tablets daily and in great distress again from chest pain. On the resumption of isocarboxazid 10 mg. three times a day she felt much improved within a week, and thereafter she used nitroglycerin rarely or up to 2 or 3 tablets a day, compared with her original requirement of 10 to 15 tablets daily. The SGOT level was normal throughout, and the final electrocardiogram showed unchanged findings.

Comment

The observed relief of anginal pain by the use of monoamine oxidase inhibitors has not yet received a firm and certain pharmacologic or physiologic basis. Extensive reviews of this important subject are now available.[8,9] The role of serotonin[10-12] and the two catecholamines, epinephrine and norepinephrine,[13-17] in the total problem of ischemic heart disease are discussed fully elsewhere. Other workers have had good results with isocarboxazid in angina pectoris,[18-20] and our observations confirm their findings.

There is no evidence that the natural history or pathologic condition of angina pectoris is altered by isocarboxazid. Nevertheless, from the data presented it appears that another treatment for angina pectoris is available, at least for pain, and that the monoamine oxidase inhibitors may join nitroglycerin and the long-acting nitrates in this important function.

Summary

Fifteen cases of arteriosclerotic heart disease and angina pectoris were selected carefully for study. All except 1 patient used either nitroglycerin or long-acting nitrates for the relief of anginal attacks which varied in frequency from one or two weekly to twenty or more daily. The monoamine oxidase inhibitor, isocarboxazid (Marplan) [1 - benzyl - 2 - (5 - methyl-3-isoxazolyl carbonyl) hydrazine], was given in doses varying from 10 to 30 mg. a day over a period of from several weeks to several months.

The results indicated a strikingly beneficial effect on the pain of anginal pectoris, with 9 patients reporting complete freedom from or a 75 per cent reduction in the frequency of pain and an associated marked reduction in the need for nitroglycerin. Four patients showed a good result, with a 50 per cent reduction in the frequency of pain and in their need for nitroglycerin. Two cases reported unsatisfactory results. There were no changes in the SGOT levels during the study as a result of taking isocarboxazid, and the final electrocardiograms, where available, showed unaltered findings. Except for 1 case, all the side-effects noted were controlled and subsided quickly with dosage adjustment.

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Partially hydrogenated fats and cholesterol

Some partially hydrogenated vegetable oils widely consumed in the American diet have been shown to create blood cholesterol responses equivalent to unhydrogenated vegetable oil, according to an article by Don E. McOsker, Ph.D., Fred H. Mattson, Ph.D., H. Bruce Sweringen, B.Ch.E., and Albert M. Kligman, M.D., in the May 5, 1962, issue of the *Journal of the American Medical Association.*

The study indicated that dietary fats containing 25 per cent or less of saturated fatty acids and a polyunsaturated to saturated ratio of greater than 0.5 created blood cholesterol responses equivalent to unhydrogenated cottonseed oil.

Seven different dietary fats with saturated fatty acid content ranging from 14 to 64 per cent were studied. The fats were included in a liquid formula diet with egg white, dextrose, salt, and water.

The fats with the highest percentage of saturated fatty acids were unsalted butterfat (64 per cent saturated) and a blend of animal and vegetable fats representing all fats present in the average American diet (40 per cent saturated).

Butterfat produced significantly higher cholesterol levels than all of the other fats. The blend representing the average American diet produces a cholesterol level significantly higher than that obtained with four partially hydrogenated fats and oils containing 25 per cent or less of saturated fatty acids.

It appears that partially hydrogenated vegetable fats are no different from unhydrogenated fats in their effect on blood cholesterol level. However, it might be expected that consumption of a fat that had been more extensively hydrogenated than those used in the study would result in an elevation of blood cholesterol.

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Hazards of Abdominal Paracentesis in the Cirrhotic Patient

Part II

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PART I OF THIS article appeared in the June 1, 1962, issue of the NEW YORK STATE JOURNAL OF MEDICINE. This is a review of some of the more important advances in the field of abdominal paracentesis. Part I included sections on varix rupture and abdominal wall and peritoneal suppuration in cirrhotic patients.

Hemorrhage within abdominal wall; peritoneal cavity

Hemorrhagic ascites is most commonly associated with disorders of the liver or of its extrinsic blood supply. The general causes are as follows:

- Trauma
  - External to abdominal wall
  - Trocar paracentesis
- Neoplasm—intra-abdominal; primary or metastatic
  - Necrosis of hepatoma nodule
  - Tumor thrombosis of portal vein
  - Rupture splanchnic vessel invaded by tumor
  - Peritoneal neoplastic implants
- Inflammation
  - Tuberculosis
  - Pancreatitis
- Hemorrhagic diathesis; coagulation defects in cirrhosis
- Acute portal vein thrombosis
  - Spontaneous—bland
  - Following steroid therapy
  - Polycythemia vera, phlebitis migrans, post-splenectomy
- Rupture of mesenteric varix
- Hepatic vein thrombosis (Chiari syndrome)

Hemorrhagic ascites occurred in 2.5 per cent of patients with uncomplicated post-necrotic cirrhosis (3.6 per cent of such patients with ascites) and in 23 per cent of those with primary hepatic carcinoma (26 per cent of such patients with ascites) as reported by Macdonald and Mallory.[8] The most common etiology, however, is associated with the mechanical drainage of a peritoneal effusion.

Abdominal paracentesis is a commonplace diagnostic and therapeutic procedure and usually is accomplished without accident. A traumatic, occasionally fatal hemorrhage may complicate such a maneuver, and many instances have been documented in the literature.[8-14] It is probable that the catastrophe has occurred on other occasions but has not been placed on record. The potential danger of such a mishap is further emphasized by the following cases.

CASE REPORTS. *Case 8.* Four abdominal paracenteses were performed over a period of ten weeks in a fifty-eight-year-old cirrhotic patient. She had a mild icterus with a prothrombin time of 26 seconds (normal, 17 seconds), and the superficial abdominal veins were dilated moderately. The site of the puncture was the midline below the umbilicus in the first and second paracenteses, one third of the distance from the navel to the pubis and 1.5 cm. to the right of the midline in the third, and 7 cm. below the umbilicus and to the right of the rectus muscle in the fourth. The observations of the house officer who performed the paracentesis may be quoted profitably.

> Immediately on partial penetration of the abdominal wall blood emitted from the trocar, but once the latter had entered the peritoneal cavity bleeding ceased, and clear ascitic fluid was obtained. The trocar had multiple openings at its lower portion and on its partial withdrawal serosanguineous fluid prevailed. When it was advanced again into the peritoneal cavity, clear yellow fluid resulted, but this became bloody with a hemoglobin content of 10 Gm. per 100 ml. when it was once more incompletely removed. During these maneuvers there was no evidence of bleeding on the external surface of the abdomen about the periphery of the trocar. The latter was withdrawn completely, and the estimated total blood loss approximated 250 cc. Manual pressure was applied at the puncture site with no evidence of overt external bleeding. Soon afterward the pulse became rapid, the blood pressure was unobtainable, the eyes deviated to the right, and the patient became completely unresponsive. Plasma, whole blood, and Levophed were without effect. The abdominal wound was opened and examined but no evidence of bleeding was noted. Cardiac massage through an incision in the left side of the chest similarly proved to be of no avail, and the patient expired two hours and forty-five minutes from the time of the paracentetic puncture.

At necropsy the peritoneal cavity contained about 4,000 cc. of bloody fluid. A perforation, surrounded by hemorrhage, was present in the peritoneal sheath in the region of the skin incision. On dissection of this area a large gaping wound measuring 4 mm. in diameter was seen in the inferior epigastric vein. The accompanying epigastric artery was undisturbed. Otherwise the peritoneal surfaces were smooth and glistening. Laennec's cirrhosis, congestive splenomegaly, and esophageal varices were additional findings.

The direct cause of death was massive bleeding into the peritoneal cavity due to perforation of the right inferior epigastric vein in the region of the final paracentetic site of entry. The free bleeding, rather than discharging onto the external surface of the abdomen, flowed along the paracentetic tract into the abdominal cavity. Unfortunately, the house officer failed to appreciate the significance of the phenomena attending the alternate advancement and withdrawal of the trocar. Ordinarily, the inferior epigastric vein is diminutive, but because of the underlying portal hypertension, this vessel, participating as an avenue of collateral flow, becomes dilated and hypertrophied to several times its normal size, thus rendering it more susceptible to injury.

Case 9. The first and only paracentesis was performed in a sixty-one-year-old alcoholic male with marked ascites. The scleras were mildly icteric, and dilated veins were visible over the abdominal wall and the upper part of the chest. The site of the puncture was 2 cm. to the right of the midline at a point midway between the umbilicus and the symphysis pubis. There were 4,720 cm. of clear yellow fluid recovered. Two hours thereafter the patient became unresponsive with a rapid, thready pulse and a precipitous drop in blood pressure. Convulsive seizures soon appeared, and he expired exactly four and three-quarter hours after the drainage procedure. At necropsy the peritoneal cavity contained approximately 3,000 cc. of grossly bloody fluid. A large hematoma was present on the peritoneal surface of the trocar tract of the recent paracentesis. Dissection of the hematoma established that the instrument had passed through a coterie of dilated veins. The liver was the seat of a portal cirrhosis and weighed 950 Gm. The spleen weighed 120 Gm. Esophageal varices were not present on gross examination.

Case 10. An uneventful paracentesis in the midline 2 cm. below the umbilicus was performed in a forty-two-year-old cirrhotic patient with moderate jaundice and a prominent superficial abdominal collateral circulation. The procedure was repeated two weeks subsequently at a site of entry 1 cm. below the previous puncture wound. Signs and symptoms of circulatory collapse soon became evident, and four hours following profound shock the patient expired. At necropsy about 500 cc. of clear yellow fluid were present in the upper part of the abdomen which was walled off from the lower half by fibrous and fibrinous adhesions and partly organized blood clots. Large clots of blood, partly adherent to the serosa, filled the rectouterine space. No gross vessel injury could be demonstrated by a study of the trocar tract wound. However, a microscopic examination of a segment of ileum revealed a huge subserosal blood clot and another attached to the serosa proper that was also the site of granulation tissue formation (Fig. 3). The liver was cirrhotic, and esophageal varices, as well as splenomegaly, were apparent. The shocklike episode following the last paracentesis must be explained on the basis of traumatic hemorrhage.

Case 11. In this patient traumatic paracentesis, as well as thoracentesis, was responsible for grossly sanguineous fluid that was aspirated respectively from the chest and abdominal cavities but fortunately without a fatal issue. This forty-nine-year-old cirrhotic female manifested moderate jaundice, fluid in the pleural cavities, ascites, petechiae over the lower

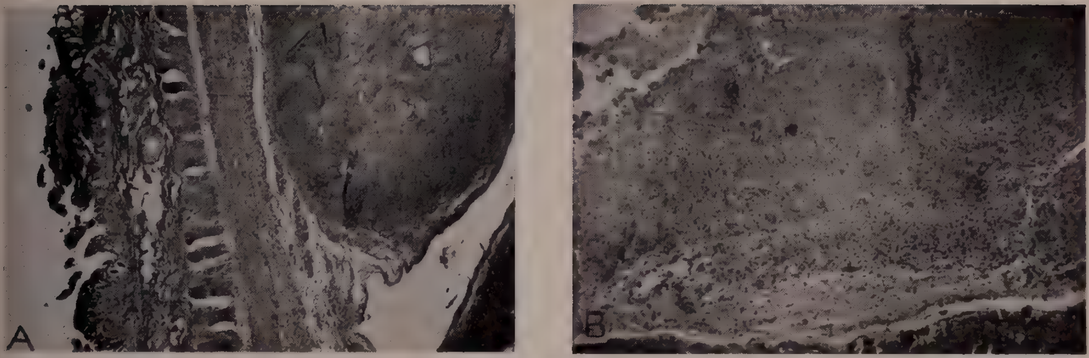

FIGURE 3. (A) Case 10. Huge subserosal hematoma of intestinal ileum caused by paracentetic trocar. (B) Diffuse hemorrhage with early organization within abdominal wall, site of paracentetic puncture. (Hematoxylin and Eosin Stain)

extremities, epistaxis, a highly positive Rumpel-Leede sign, and a prolonged prothrombin time. Thoracentesis initially yielded a clear, yellow fluid that merged in the latter half of the drainage into a uniformly reddish color. The procedure was terminated as the fluid became grossly bloody. The following day an abdominal tap just below the umbilicus in the midline recovered 5,800 cc. of grossly sanguineous fluid with a specific gravity of 1.017 and a hemoglobin concentration of 2 Gm. per 100 ml. A diagnostic puncture was performed twelve days subsequently. Fifty cc. of uniformly yellow fluid were withdrawn, indicating that the peritoneal bleeding had ceased.

Thrombophlebitis of the right thigh occurred but subsided spontaneously under simple palliative treatment. Paracentesis on three additional occasions again was performed in the succeeding three months from respective sites on either side of the umbilicus and midway between the latter and the symphysis pubis. In each instance clear yellow fluid was removed. Within twenty-four hours after the last drainage massive and fatal hematemesis occurred. At necropsy the peritoneal cavity contained about 5 L. of straw-colored fluid and a pronounced network of collateral venous channels. Multiple fibrous adhesions occupied both pleural cavities. Esophageal varices were evident, one of which revealed a perforation just above the level of the cardia of the stomach. The liver was cirrhotic, the spleen congested, and the entire alimentary tract filled with blood.

It is very likely that the sanguineous thoracentesis and paracentesis were traumatic in nature due to the injury of a vascular adhesion in the former instance and a collateral venous channel in the latter. Subsequent abdominal paracentesis from different sites presumably avoided an underlying vulnerable compensatory vein and in each instance recovered yellow nonbloody fluid. If the bleeding tendency of the patient were etiologic, the fluid should have been consistently hemorrhagic on each occasion. It also may be pointed out that a thrombophlebitis occurred despite prolongation of the prothrombin time. Of interest, too, is the onset of esophageal varix rupture within a short time after the final paracentesis.

Site of trauma

The location of the traumatized blood vessel may be within the abdominal wall or the intraperitoneal cavity. In the former site the vessel is generally the deep epigastric or one of its major tributaries. However, fatal cases of traumatic perforation of the deep epigastric artery or one of its branches in the substance of the rectus muscle has been recorded.[12]

The simultaneous and lethal perforation of a branch of the deep epigastric artery and also of the epigastric vein has been documented by Rolleston and McNee. On the withdrawal of the trocar, blood may spill freely onto the external abdominal wall. However, visible evidence of free hemorrhage may not be apparent, since the trocar acts as a tampon against the damaged vessel, and only after this device is completely withdrawn does the blood extravasate throughout the substance of the muscle coats and trickle through the paracentetic tract into the free peritoneal cavity. In fatal cases clotted blood may be found along this path and may terminate in a hematoma on the peritoneal side of the puncture wound.

In Macdonald's[9] case, paracentesis was performed in both the right and left lower quadrants of the abdomen respectively about one month apart and yielded bloody fluid in each instance. At necropsy a partly organized hematoma was present in the left rectus muscle, the site of the first paracentesis, and attached to the peritoneal surface in the left lower quadrant of the abdomen at the site of the needle puncture was a spherical organizing mass of blood clot enveloped by omentum. In the right lower quadrant of the abdomen, the site of the fatal paracentesis, extensive hemorrhage infiltrated widely among the bundles of the right rectus muscle, filled the paracentetic tract, and terminated in a clotted mass on the peritoneal side. Five L. of bloody fluid with a hemoglobin content of 5 Gm. per 100 ml. filled the abdominal cavity.

In the case reported by Serbin[10] an engorged collateral abdominal vein was similarly torn by the trocar which was inserted in the midline 4 cm. below the umbilicus. Five L. of clear amber fluid were removed. When the trocar was removed, blood gushed profusely onto the abdominal wall. The external bleeding was controlled by pressure, but the patient soon lapsed into shock from which he did not recover. By an injection technic, marked distention of the abdominal collateral veins was delineated, in addition to a patent umbilical vein designating this case as one belonging to the Cruveilhier-Baumgarten syndrome.

On the other hand, the trocar may pass safely through the abdominal parietes but may traumatize an ectatic vein or vascular adhesion within the peritoneal cavity proper. At an exploratory laparotomy for suspected hemorrhage following paracentesis in a patient reported by Hakim, Hasbrouck, and Spiro,[15] a perforation of an omental varix surrounded by a large collection of clotted blood was found immediately beneath the site of puncture. This injured vessel was especially vulnerable, since it was adherent to the peritoneal sheath as a result of previous surgery. Weber[16] additionally cites an instance of a trocar wound of the omental vessels which was ligated, and the patient survived. Unfortunately, a large branch of the portal vein also may be punctured, and this may result in profuse bleeding. The hazard of trocar penetration is emphasized by the series of postnecrotic cirrhotic patients studied by Macdonald and Mallory.[8] Only 4 patients without hepatic carcinoma had bloody ascites at necropsy, and of these, 3 had been subjected to paracentesis during the terminal admission. Blood-tinged fluid may be obtained even on repeated occasions, but necropsy nevertheless may fail to establish a focal source of bleeding.[11]

Frank hemorrhage resulting from a trocar wound of a vascular channel is facilitated by the hemorrhagic diathesis commonly found in patients with liver disease. Following injury, the degree and rapidity of bleeding will depend to a large extent on the efficacy of intravascular factors which include platelet massing, fibrin deposition, and hardening of the platelet fibrin clot. This hemostatic mechanism is defective in those patients with parenchymal hepatic disease due to abnormalities of one or generally many coagulation factors, such as platelets, accelerator-globulin, prothrombin, proconvertin, Christmas factor, and other unidentified serum and plasma thromboplastic agents. Some of these are proteins which are synthesized imperfectly because of impaired liver cell function. Prothrombin migrates electrophoretically with the serum albumin fraction and is reduced when the titer of the latter is low. Hence, bleeding from an organic lesion may be excessive and persistent under these circumstances. For example, hypothrombinemia is a major cause for continuous seepage from a ruptured esophageal varix.[2] Moreover, the onset of hemorrhagic shock causes a further decline in plasma prothrombin activity and implements the tendency for the persistence of hemorrhage once it has started. "A vicious cycle becomes established in virtue of which bleeding creates optimal conditions for more bleeding."[2]

Macdonald[9] is of the opinion that a defect in the clotting mechanism was a contributory factor in the case of fatal exsanguination following paracentesis that was reported by him. Besides direct damage by the trocar to the abdominal collateral veins already engorged with blood due to a tardy portal circulation, the patient manifested abnormalities in the prothrombin and Lee-White coagulation times. Support for this conviction was furnished by the presence of an old hematoma in the upper left rectus muscle that appeared spontaneously after the patient had "bumped himself" and which on needling contained old altered blood. An identical vascular vulnerability also was present in a personally observed decompensated cirrhotic patient who likewise developed a spontaneous hematoma within the muscle coats of the left lower quadrant of the abdomen. In the succeeding days the overlying skin became ecchymotic, and this bluish discoloration progressively extended to involve the entire left side of the abdomen, upwards to the subcostal margin, around to the left lumbar region to the midline, and ultimately to the right supra-inguinal area. Clinically, the patient also manifested bleeding from the nose and gums with the prothrombin and bleeding times twice those of normal. The application of a pressure bandage over the abdominal wall and the administration of fresh blood transfusions did not arrest the active bleeding. At necropsy a large hematoma containing approximately 2 L. of clotted blood was present between the peritoneum and the muscular coats of the described areas of the abdominal wall. The peritoneal cavity contained about 4 L. of clear, straw-colored fluid.

A hemostatic defect as the prime cause of hemorrhagic ascites is exemplified by the case reported by Mandel and Remenchik.[11] Nine paracenteses performed over a period of one and one-half years yielded bloody fluid on each occasion. At the time of an early appendectomy, many petechiae were seen within the abdominal cavity, and similar lesions were present in the skin during the patient's life. An autopsy disclosed hepatic cirrhosis, a spleen weighing 400 Gm., and petechiae in the mesentery. Specific bleeding sites were sought but were not found. Paracentetic trauma clearly played no etiologic role, since the fluid was blood-tinged at the time of the initial drainage and all those that followed. Moreover, the fluids withdrawn at the beginning and at the end of the paracenteses were of the same color and had the same hemoglobin content. The prothrombin time was consistently prolonged. Portal hypertension and portal stasis promote the development of an expanded splanchnic vascular bed that conceivably could encourage increased permeability and therefore a greater opportunity for diapedesis of fluid and formed elements in addition to the possibility of spontaneous rupture of tiny blood vessels.[2]

Because of an increased resistance to portal inflow in cirrhosis, the distal venous tree dilates and engages in the formation of a manifold tortuous maze of collateral communications. While homeostatically their development may be looked on with favor, they may be located in such vulnerable sites as to imperil the life of the patient. This is especially true in the case of cardio-esophageal diversionary pathways that promote the development of varicosities in this zone and to a lesser but significant degree in the case of a luxurious anterior abdominal wall collateral circulation. The superficial and deep anterior abdominal vessels generally are diminutive, but under the impact of portal hypertension and increased volume flow they become dilated and more numerous; previously bloodless areas now are pervaded by vascular channels. Phlebectases are found beneath the skin, which in pronounced cases form a vascular tresswork—the "geflecht" or caput medusae.

When the collateral abdominal channels are transporting a major load of recirculated blood, it can be transformed into a huge venous network capable of accommodating the major portal flow with little evidence of collateral dilatation elsewhere.[2] This is especially true of those cases with a patent umbilical vein and belonging to the group designated as the Cruveilhier-Baumgarten syndrome. A profusion of interlacing collateral venous networks similarly evolve inside the abdomen proper. Bridging communications between the portal and systemic systems are established in part by veins of the peritoneum, mesenteries, and ligaments, but mainly by larger vessels across the areolar intervals in areas of direct contact of the viscera with parietal structures. New portasystemic affiliations also develop in recently formed adhesions between the viscera and the abdominal wall.[2]

Altered hemodynamics in the portal hypertensive syndrome additionally promote hemorrhage from a traumatized vessel once it has started. Visceral circulatory velocity slows distinctly, and the retrograde stasis of blood within the vast splanchnic basin, which may be demonstrated objectively by various modalities, ensues.[2] The massiveness and recurrent character of varix bleeding, for example, often is due to the fact that a breached varix taps this large, stagnant vascular basin. Moreover, the pressure in a superficial abdominal vein is elevated and may be within the same range as in the portal venous trunk with a gradient extending from the periumbilical zone to the periphery. A tense ascites also stretches the abdominal wall with the development of lineae albicantes. The abdominal muscles become lax, atrophied, and atonic, thus precluding good constrictive action on the embodied bleeding vessel. Moreover, failure of neurogenic venomotor responses (reflex vasoconstriction) in patients with advanced cirrhosis is a factor in free bleeding.[17] For example, in cirrhotic patients hemorrhaging from esophageal varices the peripheral veins may be inappropriately large and soft in the face of severe bleeding.

Hence, it is readily apparent that the plexuses of engorged veins present within the anterior abdominal wall or intraperitoneal cavity, resting in the path of the paracentetic trocar, are exposed to injury and subject to unconstrained bleeding that may have lethal effects. The vessels in the former location also are susceptible to spontaneous hemorrhage. This interesting event was observed in a fifty-eight-year-old cirrhotic patient with rapidly accumulating ascites that required repeated paracenteses. A rather large umbilical hernia developed. The skin on its dorsolateral aspect revealed a thin, weeping, bare area. Deeper extension of this excoriating process resulted in ulceration into one of the large collateral veins with a blood loss of about 200 cc. that finally was controlled by surgical ligature.

Treatment

Abdominal paracentesis must be performed with caution and care to avoid complications. The presence of engorged and distended veins in the low midline, the usual site of trocar insertion, and generally considered a bloodless area, is "frightening." Certain precautionary measures can be practiced to appreciate their distribution and magnitude and to determine the safest puncture site. The presence of a palpable thrill or auscultatory venous hum indicates an underlying Cruveilhier-Baumgarten syndrome and therefore a patent umbilical vein signifying a rich superficial collateral circulation. The latter stands out remarkably when the patient is subjected to a Valsalva maneuver. A pictorial exposure of the compensatory vascular network is achieved easily by an infrared film of the abdominal wall.[2] The inspection of such a photograph enables the operator to so plan the paracentesis site as to avoid any major venous trunk. An abdominal phlebogram, after the method of Celis, will serve the same purpose, but entails a surgical, although minor, procedure (Fig. 4).[18] The latter is particularly valuable preliminary to an operative shunt procedure, since the resultant information permits the surgeon to so modify the abdominal incision as to preserve the useful collateral abdominal veins.

The midline between the umbilicus and the symphysis pubis is the safest site for tapping. As already indicated, a sizable blood vessel in this location may nevertheless be traumatized. Alternate sites include the linea semilunaris on one or the other side and the center of a line joining the umbilicus and the anterior superior spine. Fatal hemorrhage from a wound of the deep epigastric artery has occurred in the latter location, and it appears that the former site is equally hazardous. A very satisfactory location is a point midway between the rib margin and the pelvis in the left anterior axillary line. Any sector of the abdominal wall that contains a surgical scar is expressly avoided. The bowel may be adherent to its inner border, or vascular adhesions that carry bridging collaterals in the immediate subjacent area can exist under these circumstances.

The preliminary administration of opiates is interdicted. Such agents are poorly detoxified by the cirrhotic liver, and even a small dose may make the patient extremely stuporous or induce a state of coma. Darvon 65 mg. is an efficient and harmless analgesic. Since both venous tension and diastolic and systolic pressures fall progressively as the ascitic fluid drains, it is recommended that after the trocar is passed with the patient in a sitting position that he then be

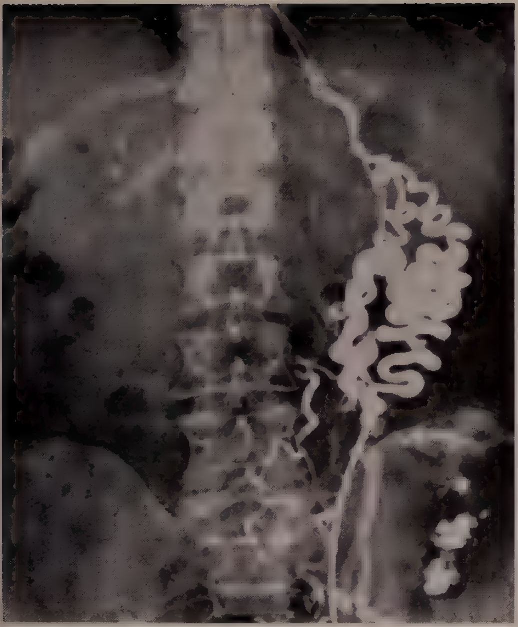

FIGURE 4. Superficial venography achieved by injection of radiopaque medium into a superficial abdominal wall vein. A markedly tortuous collateral circulation is demonstrated within the abdominal parietes. Courtesy George E. Wantz, M.D.

made recumbent to avoid a syncopal reaction.[19] The skin is draped and prepared with a suitable antiseptic solution. A wheal is raised with a 1 per cent procaine solution, and the smallest possible skin incision is made with a triangular-tipped scalpel to allow for the introduction of the trocar. Large incisions encourage a prolonged leaking peritoneal fistula. The incision is carried down to the peritoneum only. If a traumatic hemorrhage should ensue, it will always occur to the exterior where it can be controlled easily rather than into the peritoneal cavity where it is initially masked and not appreciated. Since the trocar may act as a tampon against an injured vessel in the abdominal wall, it should be partially withdrawn so that the perforations in its distal end lie within the parietes. In this way free bleeding may be detected readily. Once fully inserted, the cannula is removed, and a polyethylene tube is threaded into the peritoneal cavity through the trocar, which is then removed, and continuous drainage is established. Only sufficient fluid is drained to relieve discomfort and respiratory distress, and this generally should not exceed 5 or 6 L. Repeated small paracenteses are better tolerated than are single large ones. In exceptional instances, when large volumes of fluid must be removed, it may be preferable to do so gradually over a one- or two-day period. When clinical signs herald an impending hepatic coma, or the blood pressure is initially low, it is imperative not to exceed the 5 L. figure. Under these circumstances it may be more judicious to postpone or forego paracentesis entirely. Because of the presence of peritoneal or omental adhesions, the ascitic fluid may become loculated or encysted, and little or none effuses. Alternate sites may be tried. Since such adhesions usually are quite vascular and adherent to the peritoneal lining, they are predisposed to injury. In the event of a dry tap, an internal hemorrhage always should be suspected. Bleeding is nevertheless a possibility despite the fact that the patient has been subjected to a number of previous harmless paracenteses.

The clinical symptomatology will depend on the extent of the intraperitoneal hemorrhage. If pronounced, signs and symptoms of peripheral vascular collapse will be evident that may terminate in a picture of frank shock. It should be emphasized that if the rate of bleeding is slow, the characteristic symptoms may be postponed for several hours. At this time, too, the puncture site may be more tender than otherwise, or the free bleeding and clots may induce peritoneal irritation with signs indicative of an acute surgical abdominal condition. On the other hand, impending or frank hepatic coma may dominate the clinical picture. The liver participates in the preservation of vascular homeostasis, and this organ may be penalized severely in the sequence attending gross blood loss. The consequent decrease in oxygen saturation of the portal venous blood and the reduction in transhepatic circulatory flow jeopardize the integrity of the parenchymal cells and predispose the patient to centrilobular degeneration and ultimate organ failure.[2]

The arrest of active bleeding from the depths of the paracentetic wound by suture approximation of the skin edges does not preclude subsequent free oozing along the trocar tract and into the peritoneal cavity. Should there be a sudden change in the patient's vital signs despite an apparently uneventful drainage of clear fluid and no external bleeding, traumatic intraperitoneal hemorrhage nevertheless must be considered. This may be confirmed by a simple diagnostic needle puncture of the abdomen. The determination of hemoglobinemia and hemoglobinuria may be a useful diagnostic tool in the detection of intraperitoneal hemorrhage.[20] After such extravasation there is a rapid absorption of intact red blood cells through the diaphragmatic peritoneum with a return into the systemic circulation via the mediastinal and paramediastinal lymphatics. Any delay in their usually rapid absorption after gross hemorrhage into the peritoneal cavity predisposes the patient to hemolysis of this blood that is then reflected by a rise in plasma hemoglobin or the appearance of frank hemoglobinuria. Intra- and extrahepatic lymphatic decompensation that characterizes the cirrhotic patient with portal hypertension can account for such a delay. Dumont and Mulholland[21] have demonstrated that the pressure in the thoracic duct is elevated in such a patient.

The treatment will depend on the location of the traumatized vessel and the extent of the hemorrhage. If within the abdominal wall, it can easily be secured by surgical ligature. If intraperitoneal, then laparotomy must be considered. The stability of the hematocrit and vital signs following an initial drop may suggest a policy of watchful waiting. During this time it is advisable to replace the lost blood and sustain the circulation, principally to protect the sick liver by the use of fresh blood. The superiority of fresh blood over bank blood in correcting plasma coagulation defects in the cirrhotic patient is to a large extent due to a richer concentration of accelerator globulin and a greater viability of the platelets in the former. Should laboratory and clinical data indicate continued free bleeding, then open surgery is undertaken. After the control of the traumatic hemorrhage an ultimate side-to-side portacaval shunt may be considered if the ascites is of the recurrent or intractable type, to avoid a second and perhaps lethal hemorrhage at a subsequent paracentesis.

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Clinicopathologic Conference

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Conducted by RULON W. RAWSON, M.D.

Discussed by ROBERT D. GITTLER, M.D.

Hypoglycemia and an Intrathoracic Mass

Case history

Charles Tashima, M.D.: A twenty-year-old white female was first admitted to the Memorial Center in February, 1960. She had a total of seven admissions prior to her death in July, 1961.

Her present illness began insidiously about July, 1958, when she first noted difficulty in rising in the morning. She described this as a form of lethargy and stated that this symptom was relieved by orange juice. She also had amnesia with these lethargic episodes. The episodes began to recur two to four times a month. A glucose tolerance test done by her family physician revealed a fasting blood sugar of 65 mg. per 100 ml., 110 mg. at thirty minutes, 120 mg. at one hour, 132 mg. at two hours, and 100 mg. at three hours. By March, 1959, these attacks were recurring three to four times a week; it became extremely difficult to rouse the patient in the morning. She also developed attacks of extreme weakness, tremulousness, sweating, and cold extremities occurring three to four hours after meals, relieved in five minutes by sugar and orange juice.

In July, 1959, chest x-ray films revealed a mass (Fig. 1) in the posterior mediastinum 6 cm. in diameter, which was said to explain a five-month history of dysesthesia along the right side of the thoracic spine. The

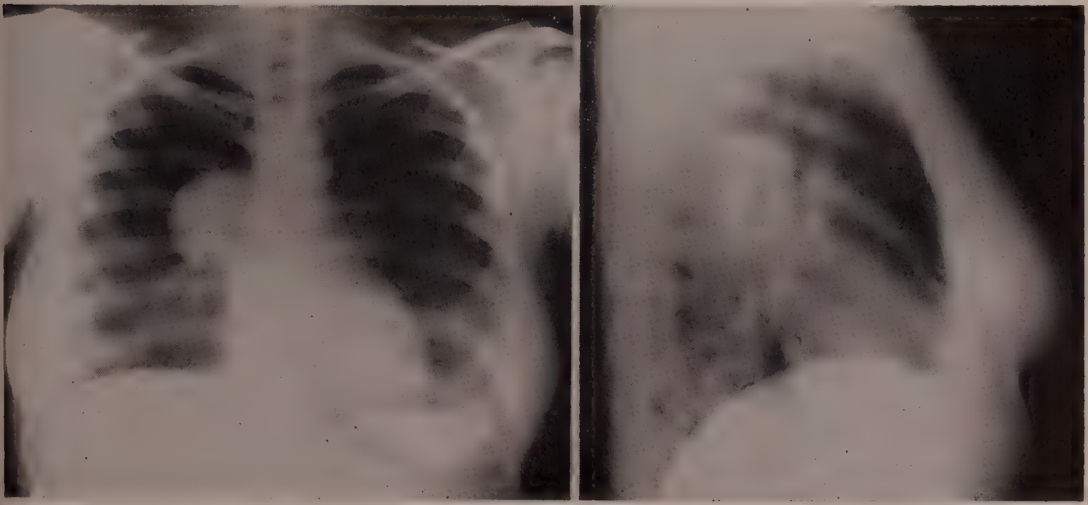
FIGURE 1. Anterior and lateral chest roentgenograms showing mass in posterior mediastinum.

blood sugar levels at this time were 18 mg. and 31 mg. per 100 ml. An intravenous glucose tolerance test revealed a blood level of 184 mg. per 100 ml. after ten minutes, gradually declining to 109 mg. per 100 ml. at one hour. A thoracotomy at another hospital revealed the mass to be attached to the fifth right intercostal nerve. It was partially excised, and the pathologist's diagnosis was neuroblastoma. When reviewed at Memorial Center, the question of a rare malignant peripheral neural tumor was raised. There was some relief of the hypoglycemic symptoms following an operation; the fasting blood sugars were recorded as 69, 43, and 44 mg. per 100 ml. The patient received 4,050 r through a posterior mediastinal port.

In December, 1959, left frontal headache developed, and in January, 1960, the patient was readmitted with fever and vomiting of two days duration and some nuchal rigidity. A spinal fluid contained protein 83 mg. and sugar 47 mg. per 100 ml. A chest x-ray film showed a right pleural effusion, and x-ray films of the skull showed a 4-cm. lytic area in the left frontal bone and a 2-cm. lytic area in the right occipital region.

The past history was not remarkable except for a history of a nephrotic syndrome at the age of eleven years without apparent sequelae and a weight gain of 20 pounds from July, 1958, to February, 1960, ascribed to increased hunger.

First admission. She was admitted to Memorial Center from February 18 to April 21, 1960, for therapy of metastatic disease. The principal complaints were a recurrence of hypoglycemic attacks, severe headache, mild fever, and vomiting for over one month. On admission the temperature was 98 F., pulse 120, and blood pressure 100/60. There was a 2-cm. hard, nontender, bony swelling over the left temporal area. The thoracotomy scar was well healed. Dullness, decreased breath sounds, and limited diaphragmatic excursion were present at the base of the right lung. The heart was normal. The liver was felt 4 cm. below the right costal margin, but no other organs or masses were felt. There was no peripheral edema. There was generalized hyperreflexia, but no abnormal reflexes were elicited. A psychologic examination disclosed a dependent personality; abstractions and serial 7's were performed poorly.

A urinalysis produced normal findings. The hemoglobin was 11.2 Gm. per 100 ml. The white blood cell count was 9,000 with a normal differential count. The stool contained no occult blood. The fasting blood sugar was 39 mg., blood urea nitrogen 9.5 mg., serum calcium 10.6 mg., and serum phosphorus 4 mg. per 100 ml. The total protein was 8.1 Gm. per 100 ml. with 5.1 Gm. albumin and 3 Gm. globulin. The serum glutamic oxalacetic transaminase was 41 units. The protein-bound iodine was 5.5 micrograms, and radioactive iodine uptake was 43 per cent in twenty-four hours. Urinary 17-hydroxysteroids were 8.4 mg., and 17-ketosteroids were 6.9 mg. per twenty-four hours. Several blood cultures were negative, and sputum cultures were negative for acid-fast organisms. An electrocardiogram showed normal findings.

Roentgenograms of the chest revealed a 5-cm. round mass in the right cardiophrenic angle. An esophagram showed the esophagus to be deviated to the right. An excretory urogram showed duplication of the left renal pelvis and ureters. A barium enema was unrevealing. X-ray films of the skull revealed a 5-cm. lytic lesion in the left frontal bone associated with a soft tissue mass and some new bone formation. There was also a 2-cm. lytic lesion in the right occipital area. The sixth thoracic vertebra contained both blastic and lytic lesions.

A right thoracentesis yielded 15 cc. of bloody fluid which contained malignant cells consistent with a neuroblastoma. A lumbar puncture revealed an initial pressure of 180 mm. The spinal fluid contained 8 mononuclear cells per cubic millimeter and protein 50 mg. per 100 ml. An electroencephalogram revealed a seizure pattern with a possible right-sided focus.

A number of tests of glucose metabolism were performed. These are summarized in Table I.

On March 25 the patient experienced a spontaneous hypoglycemic reaction with a blood sugar of 29 mg. per 100 ml. which responded immediately to the injection of 50 per cent glucose. In April she was treated

TABLE I. Glucose tests*

Study	Fasting	10 Minutes	Time in Hours							
			$^1/_2$	1	$1^1/_2$	2	3	4	5	6
Oral glucose tolerance	32	...	...	176	...	208	...	246	..	101
Oral glucose tolerance	30	...	102	136	...	188	196	...	..	...
Intravenous glucose tolerance	42	224	159	120	102	77	...	...	..	...
Epinephrine stimulation	33	...	75	80	...	98	30	...	..	...
Insulin sensitivity (glucose tolerance test with insulin)	30	...	117	131	...	147	91	25	..	...
Glucose tolerance test (after high carbohydrate diet for two weeks)	30	...	102	136	...	188	196	149	45	40
Insulin (micro-units per milliliter)	90	...	198	154	...	112	154	117	..	...
L. Leucine stimulation	50	...	45	43	...	...	...	...	..	...
Insulin (micro-units per milliliter)	28	...	42	34	...	...	...	...	..	...
Tolbutamide stimulation	49	...	22	...	...	...	...	...	..	...

* Values for glucose are given in mg. per 100 ml.

with radiation to the right lower portion of the chest of 1 mev to a tumor dose of 3,018 r with an apparent decrease in the size of the mass in that area. Occasionally during this period she would have an abrupt rise in temperature to 104 F. with no evidence of infection.

Second admission. The second admission was from April 30 to May 17, 1960, for nausea, vomiting, fever, and headache of five days duration. The bony protuberance in the left side of the forehead appeared larger; a hemorrhage appeared in the left ocular fundus, and there was nuchal rigidity. A neurologic examination revealed weakness of the conjugate upward gaze, nystagmus on lateral gaze, and mild bilateral papilledema. A lumbar puncture yielded spinal fluid under an initial pressure of 190 mm. with a protein of 45 mg. and a glucose of 89 mg. per 100 ml. She received intravenous nitrogen mustard 0.4 mg. per kilogram and a skull irradiation with a midplane total dose of 3,140 r. She was treated for increased intracranial pressure with Urevert for three days. She responded favorably to this therapy and was discharged with a clear chest film and a fasting blood sugar of 33 mg. per 100 ml.

Third admission. She was readmitted on June 30 for pains in both thighs of four days duration. The neurologic signs had disappeared; except for alopecia and mild fever, the physical examination was not remarkable. A chest film revealed hazy infiltration at the base of the right lung. X-ray films of the lumbar spine, pelvis, and legs showed no lesions. The fasting blood sugar was 39 mg. per 100 ml. The leg pains disappeared spontaneously, and she was discharged on July 5 without therapy.

She was followed in the outpatient clinic. In December, 1960, x-ray films revealed a 4-cm. lytic lesion in the right iliac bone and a separate smaller lesion adjacent to it. She was given radiation to the right side of the pelvis to a 2,000-r air dose.

Fourth admission. The patient was rehospitalized from February 10 to March 3, 1961, with a recurrence of headache and pain in the left ankle. The bony protuberance in the left side of the forehead was now tender. There was also tenderness in the right occipital area. Ptosis of the left eyelid and diplopia on right lateral and right upward gaze were present. The deep tendon reflexes and peripheral motor and sensory functions were normal.

X-ray films of the left ankle were unrevealing. A chest x-ray film still revealed infiltration at the base of the right lung. The lytic lesion in the right iliac bone measured 6 by 6 cm., and there was a questionable lytic lesion in the greater trochanter of the left femur. Skull x-ray films showed no change, and an excretory urogram was unrevealing. A lumbar puncture revealed an initial pressure of 170 mm., protein of 60 mg., and glucose of 46 mg. per 100 ml. The blood sugar at this time was 56 mg. per 100 ml.

She was treated with penicillin for a presumptive pneumonitis of the lower lobe of the right lung. During the second week of her stay she developed a mild right hemiparesis with hyperreflexia, nystagmus, diplopia, and weakness of the upward gaze, weakness of the left thumb, and difficulty in straight leg raising. The neurologic diagnosis was a tumor mass in the pretectum as well as a vertebral lesion at the level of the fourth and fifth lumbar vertebrae. An electroencephalogram revealed an abnormal focus in the left motor area. She was given irradiation to the hypothalamic area, 2,700 r through the right port, 2,550 r through the left port on 250 RV., as well as cobalt therapy to 220 r in air to the left side of the pelvis.

Fifth admission. The patient was readmitted on April 6, 1961, with a weight loss of 20 pounds in two months as well as persistent and progressive neurologic signs. The hemoglobin was 7.2 Gm. per 100 ml. The white blood cell count was 6,200, platelets 468,000, and reticulocytes 4.8 per cent. The fasting blood sugar was 87 mg. per 100 ml., and other chemical studies of the blood were within normal limits. A chest x-ray film showed a 5-cm. nodule in the lower lobe of the right lung. Skeletal x-ray films revealed lytic lesions in the left frontal bone, left acetabulum; left third, sixth, seventh, and eighth ribs; both femoral trochanters; and compression of the sixth, ninth, and eleventh thoracic vertebrae. She was treated with Methotrexate, chlorambucil, and actinomycin D. Oral lesions, hematologic depression, and fevers up to 105 F. developed. On April 19 she experienced an attack of hunger with a blood sugar of 58 mg. per 100 ml., her first attack in over a year. The fasting blood sugar fell progressively to 38 mg. per 100 ml. by May 26. Skeletal x-ray films taken a week later showed progression of most of the bony metastases. On June 15 a tolbutamide test lowered the blood sugar from 49 mg. to 22 mg. in thirty minutes, almost precipitating hypoglycemic shock. She was discharged on June 19, 1961.

When seen two weeks later in the outpatient clinic, she had developed several scalp nodules, and the anemia had progressed.

Sixth admission. She was admitted briefly on July 20 for increasing nausea, vomiting, weakness, dyspnea, and pain in the abdomen and back, but she was signed out, against advice, by her mother.

Seventh admission. Her final admission was on July 22, 1961, when she was admitted as an emergency case in a moribund state and in shock which did not respond to intravenous Aramine, glucose, and oxygen. She was pronounced dead one-half hour after admission.

Discussion

ROBERT D. GITTLER, M.D.*: I believe I saw this patient with Dr. Rawson about two years prior to her demise. The moment of truth has now arrived, and I will attempt to reconstruct my former reasoning and possibly elaborate on the basis of her subsequent course. The problem we are confronted with concerns a twenty-one-year-old woman who had a malignant tumor, the pathologic nature of which seems to be in controversy, but who had a relentless progression of her neoplastic disease and died with widespread metastases. The patient's illness began at the age of eighteen years when she first manifested undoubted symptoms of fasting hypoglycemia. This important discovery was documented by an alert physician who found the fasting blood sugar to be 65 mg. per 100 ml. If this value is a Folin-Wu determination, it is true hypoglycemia; by the Somogyi-Nelson method, it lies within the low normal range.

The occurrence of fasting hypoglycemia in a patient of this age raises immediate diagnostic possibilities. We must consider first those lesions within the pancreas that produce organic hyperinsulinism. These are islet cell adenoma, islet cell hyperplasia, or rarely islet cell carcinoma. Alternatively, we also must consider the possibility of disease of the adrenal cortex, the anterior hypophysis, or far-advanced liver dysfunction. Such lesions also may produce blood sugar depression which is predominant in the fasting state. The hypoglycemic episodes increased in severity and frequency over the next nine months. This is not unusual; as the causative disease progresses, so does the episodic hypoglycemia. However, an important additional component of the hypoglycemia is now apparent. Attacks occurred not only in the fasting state but from three to four hours after meals. This implies a stimulative component to the hypoglycemia; presumably the challenge of the carbohydrate of ingested food results in the stimulation of insulin secretion and further hypoglycemia. The presence of this stimulative component combined with fasting hypoglycemia suggests most strongly that the abnormality resides in the islet cells; I would not expect postprandial hypoglycemia with disease of the adrenal cortex, hypophysis, or liver.

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Nevertheless, no further investigations were performed until four months later when we are told that an x-ray film of the chest revealed a large mass within the posterior mediastinum. At that time the blood sugar determinations confirmed the increasing severity of the hypoglycemia; the intravenous glucose tolerance test does not further clarify the problem. The mediastinal tumor was excised only partially. Subsequently, the patient was given irradiation therapy. The statement that the patient obtained relief of her hypoglycemic episodes following the partial removal of the tumor is of great significance. One is led to the strong suspicion that there may exist a cause-and-effect relationship between this tumor and the production of hypoglycemia. Nevertheless, it is important to note that the hypoglycemia was by no means cured, for we have objective evidence of the persistence of low blood sugar values, although not of the severity that was noted prior to surgery.

Five months later the patient was readmitted to the hospital showing signs and symptoms of meningeal irritation. Whether this was due to bleeding, infection, or tumor spread was not readily determined. However, we are told that the spinal fluid sugar was 47 mg. per 100 ml. If we estimate the blood sugar at about 25 per cent higher than the spinal fluid value, this is further evidence of the amelioration of the hypoglycemia. The chest film at this time gave evidence of a persistent tumor, and the skull x-ray films indicated bony metastases; there is no reason to doubt that the neoplasm was progressing.

The patient's past history is of no assistance; I know of no relationship between hypoglycemia and a nephrotic syndrome. Let us now turn to the findings on admission to Memorial Hospital where the patient spent over six of the last seventeen months of her life. The physical signs in the right side of the chest were consistent with the presence of fluid or pleural thickening. We also are told that the liver was enlarged, the first intimation of hepatic disease. The occurrence of hypoglycemia in hepatic disease is of great interest chiefly because it is so uncommon. Indeed, when one considers the wide variety and frequency of liver disease which may give rise to hypoglycemia, it is surprising that we do not encounter it more often. It has been suggested recently that perhaps hepatogenic hypoglycemia does occur more frequently but that we are overlooking its existence; that is, the symptoms have been interpreted as being caused by drug intoxication or protein encephalopathy. The observation that the patient was having difficulty with mentation, specifically in forming abstractions and in performing serial 7's, may well be related to the intracerebral spread of disease, but it also may be a manifestation of the effects of severe recurrent hypoglycemia on the cerebral cortex.

The presence of normal urinary 17-hydroxysteroids helps to exclude anterior hypophyseal or adrenocortical insufficiency. However, one may have sufficient integrity of the pituitary-adrenal axis to maintain normal plasma and urine cortisol levels in a basal state but be unable to respond to a stress stimulus. However, I think the clinical assumption that adrenocortical disease can be eliminated from consideration is sound. When we then combine the evidence of normal adrenocortical function with tests indicating normal thyroid function, the possibility of significant hypophyseal insufficiency becomes remote. I am aware, however, of those patients who demonstrate persistent thyroidal function following surgical ablation of the pituitary body.

At the time of her first Memorial Hospital admission there was ample roentgenographic evidence of recurrent neoplasm in the right cardiophrenic angle. The deviation of the esophagus may indicate the effects of contracting fibrosis from previous irradiation or displacement from a tumor lying to the left of the esophagus. The skeletal x-ray films revealed further progression of osseous metastases; the sixth thoracic vertebra was now involved. The electroencephalogram showed intracerebral disease, but whether or not there was metastasis within the brain substance or impingement from without cannot be deduced.

Now, let us consider the very elegant studies performed during this hospitalization on the mechanism of hypoglycemia. The first oral glucose tolerance test demonstrated the existence of fasting hypoglycemia, but in addition the curve showed a hyperglycemic plateau. This is entirely consistent with hepatogenic hypoglycemia in which the liver is unable to deposit administered carbohydrate in the form of glycogen, and in the fasting state the diminution of hepatic glycogenolysis results in the depression of the blood sugar. The glucose tolerance test also was consistent with a lesion which is producing excess insulin or an insulin-like substance. It is entirely possible for such a lesion to suppress the function of the normal islet tissue. If one challenges such a patient with a carbohydrate load, and the primary lesion, be it pancreatic or extrapancreatic, does not respond with increased insulin discharge, and in addition the residual islet tissue is functionally depressed, we may encounter a glucose tolerance curve with a diabetic plateau.

This phenomenon can be duplicated easily in a normal person by administering exogenous insulin for several days and then performing a glucose tolerance test. A factitious diabetic curve will be produced. When such a phenomenon is encountered, one may restore normal islet cell responsiveness by a high carbohydrate diet which stimulates the functionally depressed islets. A second glucose tolerance curve will lack the hyperglycemic plateau. Such a maneuver was performed in this patient. If we compare the values of the second oral glucose tolerance test with those obtained on the first test, it is evident that there was some improvement in carbohydrate tolerance, although it had not yet returned to normal. The two glucose tolerance tests thus are consistent with the view that the patient harbored an intra- or extrapancreatic lesion which produced either insulin or an insulin-like substance.

The intravenous glucose tolerance test does not help solve our problem. The epinephrine stimulation test indicated that there were adequate stores of hepatic glycogen and that these stores could be mobilized. This is evidence against the presence of hepatogenic hypoglycemia, but it does not exclude the possibility completely. The insulin sensitivity test performed with a glucose load merely showed that there was no apparent resistance to insulin activity at a peripheral level. Now we come to the studies of plasma insulin, and we see that the fasting levels were elevated. Yalow and Berson[1] have reported that in both normal individuals and in stable middle-aged diabetic patients the fasting plasma insulin level does not exceed 65 micro-units per milliliter by their immunoassay. A level of 90 micro-units is higher than normal, but it furnishes no clue as to whether the source of the insulin is intrapancreatic or extrapancreatic.

At the time of the performance of the glucose tolerance tests the plasma levels of insulin were within the limits of normal response. In the nondiabetic patient one expects to find the major elevation of plasma insulin by one-half to one hour after carbohydrate ingestion. In contrast, the plasma insulin peak in a stable diabetic patient is delayed to over one hour. We can infer that the normal values obtained during the glucose tolerance test indicate that high carbohydrate feeding has restored normal sensitivity of the islet tissue.

The leucine stimulation test is based on the demonstration by Cochrane *et al.*[2] of leucine sensitivity in some patients with infantile idiopathic hypoglycemia. They showed that about two thirds of such patients will respond to the administration of leucine by precipitant hypoglycemia. Subsequent studies have shown that the mechanism of the hypoglycemia is insulin stimulation and that leucine is pancreaticotropic. Flanagan, Schwartz, and Ryan[3] have shown that some islet cell tumors also are sensitive to leucine stimulation. We have no information whether or not this is true of extrapancreatic tumors that produce hypoglycemia. Regardless, this patient was not sensitive to leucine; the blood sugar depression was only minimal. However, concomitantly, we now obtain some confusing information about the plasma insulin level, which appeared to be within normal limits. I cannot resolve this discrepancy.

The tolbutamide stimulation test is based on the study by Fajans *et al.*[4] and attempts to aid us in distinguishing among the several causes of hypoglycemia. They demonstrated that islet cell adenomas, or at least a reasonable percentage of them, are sensitive to the administration of tolbutamide and that the drug appears to cause a release of insulin. Unfortunately, it is not so much the magnitude of depression of the blood sugar that is significant as the duration of the depression. The administration of a sulfonylurea drug to a normal person produces a depression of the blood sugar that may be as much as 65 per cent of the fasting level. However, in a normal person the blood sugar returns to fasting levels in from ninety to one hundred twenty minutes. In a patient with an islet cell tumor, the depression of the blood sugar is maintained for a much longer period. Not all islet cell tumors are responsive to tolbutamide; I have had such an experience with a surgically proved tolbutamide-resistant case very recently. The particular values obtained on this test, unfortunately curtailed because of the danger of hypoglycemic shock, are of little help. Depression to this degree may occur in a normal individual, and we have no idea how long this patient would have maintained her depressed blood sugar.

The conclusion I must draw from all these studies of carbohydrate metabolism is that the patient had a lesion that was producing increased amounts of insulin. But whether this lesion was located within the pancreas or elsewhere I cannot say.

After these studies were completed the patient was given irradiation therapy to the right side of the chest, and we are told that she developed spiking fevers, the cause of which is not known. Possibly the fever was related to necrosis within the tumor or to a disturbance of the hypothalamic regulatory centers. One week after her discharge the patient was readmitted to this hospital showing evidence of progressive intracranial disease. The neurologic examination suggested a space-occupying lesion in the middle or posterior fossa, but it would be important to know the permanency of the neurologic findings to exclude causation by hypoglycemia. On this admission the patient was treated with nitrogen mustard and evidently had an excellent response, for the statement is made that the chest film was clear. Nonetheless, hypoglycemia was still present. A month later there was roentgenographic evidence of a recurrence of the chest lesion, but the skeletal metastases seemed to have improved under treatment. She did not show progression of her osseous lesions for a period of five months. Two months later she was readmitted with additional neurologic signs indicating more widespread intracranial disease than on her previous admission. The blood sugar was 56 mg. per 100 ml.; although hypoglycemia persisted, it was not as severe as it was originally.

One month later she was again readmitted with signs and symptoms of further progression of her intracranial disease. A severe anemia was present for the first time. I am hard-pressed to explain the cause of this anemia, since the high platelet level and the reticulocyte count were not entirely consistent with myelophthisic anemia due to the replacement of marrow by a tumor. There was no overt blood loss. A hemolytic component may have been present. We are told that at that time she experienced her first attack of hypoglycemia in over a year. I think that all one may conclude is that the various tumoricidal agents were effective in relieving the severity of the hypoglycemia, but the numerous blood sugar determinations indicate that hypoglycemia was still present to some degree. Following this admission, the patient went rapidly downhill and expired.

We are left, therefore, with the possibility that the patient had hypoglycemia in association with an intra- or extrapancreatic neoplasm which was producing insulin or an insulin-like substance. The literature contains about 30 examples of extrapancreatic tumors associated with hypoglycemia, all collected since the early 1930's when the first case was reported. Most of these tumors have been intrathoracic or retroperitoneal, and they are notable for their large size, averaging over 2,000 Gm. The removal of the tumors is associated with amelioration of the hypoglycemia; the recurrence of hypoglycemia heralds tumor recurrence or metastatic spread.

Histologically, there has been considerable debate regarding the classification of such growths. For the most part, pathologists have classified them as fibromas, fibrosarcomas, neurofibrosarcomas, and so forth. They seem to arise from mesodermal anlagen, or at least one comes to that conclusion from the pathologic diagnoses. Certainly the finding of a neurosarcoma would not be inconsistent with our previous knowledge of these tumors.

Several possible mechanisms have been proposed to account for the production of hypoglycemia by these neoplasms. Only two concepts need to be discussed. First, the tumors produce hypoglycemia because of the consumption of large amounts of glucose due to their great size; second, the tumors elaborate a hypoglycemic agent, insulin or an insulin-like substance. The controversy is not settled. The most we can say is that there are now 4 reported cases in which various investigators have been able to demonstrate the presence of a hypoglycemic substance, either in the plasma of the patient or in extracts of the tumor.[5]

I cannot rigorously exclude the possibility that this patient had two tumors, one the neural growth that was partially resected at thoracotomy and which gave rise to the widespread metastases, and the other a small insulin-producing islet cell adenoma of the pancreas. However, I shall not make this double diagnosis because the therapy of the obvious malignancy appeared to result in a definite amelioration of the hypoglycemic attacks, and one would have to assume that the islet cell tumor that was not treated was functioning at a very low level of hormonal activity.

Recently, the idea has been set forth that some of these patients with extrapancreatic neoplasms actually may have an islet-cell carcinoma which appears as a spindle-cell lesion in its metastases. This is a definite possibility which I cannot exclude, but it borders on the exotic. Therefore, I believe that this patient had a malignant neuroblastoma with widespread intracranial and osseous metastases which produced hypoglycemia. I cannot definitely exclude the presence of an islet cell adenoma or carcinoma.

A Physician: Have you ever seen a similar situation in a patient who had been receiving glucose infusions steadily for month after month, and who developed hypoglycemia after the glucose infusion was stopped?

Dr. Gittler: The situation you describe is not quite analogous. It is fairly well established that the normal stimulus for insulin secretion is the elevation of pancreatic arterial glucose which occurs after carbohydrate feeding. If so, the repetitive administration of glucose should act as a repetitive stimulus. Conversely, carbohydrate withdrawal acts as a depressant, producing so-called starvation diabetes. I doubt if the continuous use of glucose could cause this picture.

A Physician: I was speaking of the discontinuance of the continuous glucose.

Dr. Gittler: No. Although under such circumstances one probably would have achieved maximum stimulation of islet tissue, the removal of the stimulus should prevent further insulin elaboration.

A Physician: Could an islet-cell tumor have responded to the irradiation?

Dr. Gittler: Unfortunately, our experience with malignant islet-cell tumors is limited to about 30 reported cases in the literature. Many of these were reported before the use of current-day radiation therapy, and I do not think I can make any valid statement about the radiation sensitivity of islet-cell tumors. However, if such a tumor did respond to radiation, I would expect some degree of improvement in the hypoglycemia.

A Physician: Has anyone ever given alloxan to a patient with an insulin-producing tumor to see what happened?

Dr. Gittler: Yes, it has been given to 2 patients with islet-cell carcinoma, once by Conn and Hinerman[6] and once by Brunschwig, *et al.*[7] In neither instance did the tumor appear sensitive to alloxan.

A Physician: In this patient the steroid levels were reported as normal. Have you seen any cases in which they might have been altered?

Dr. Gittler: I do not know of any detailed studies of steroid metabolism in the presence of islet-cell tumors. I would not expect any great alteration.

A Physician: Hypoglycemia recently has been reported in association with an occasional case of hepatoma.[8] Have you ever seen this combination?

Dr. Gittler: No, I have not, although I am well aware of these reports.

A Physician: Are the tumors which produce hypoglycemia at all responsive to adrenocortical steroids?

Dr. Gittler: I have observed 1 case of extrapancreatic hypoglycemia-producing neoplasms that has been treated with cortisone or its analogs with partial success. Cortisone also has been used in the management of islet-cell tumors in patients who, for one reason or another, have been treated without surgery. In these patients one can produce some degree of amelioration of the hypoglycemia by large doses of the steroid, but by no means does one cure the hypoglycemia. The effects of insulin production eventually overwhelm the counterregulatory mechanism of the glucocorticoids. Certainly, this patient was exposed to many stresses, both spontaneous and iatrogenic, and one might anticipate some degree of amelioration. However, I do not think one could postulate that the stress was of sufficient time and severity to give amelioration for a twelve-month period.

A Physician: You suggested two mechanisms by which such a tumor may act: one by producing insulin, the other by increased glucose utilization. I don't think you committed yourself as to which mechanism was operative. But looking at the plasma insulin levels, I wondered whether this really was an insulin-secreting tumor.

Dr. Gittler: You are quite right. I did not commit myself. I did that specifically because I did not want to be put on the spot, since we had two different values for fasting plasma insulin. However, as a general rule, I do not believe that such umors are producing insulin or a substance hat stimulates insulin release. However, the rate of production and release need not be uniform; hence, the discrepancy between plasma insulin levels.

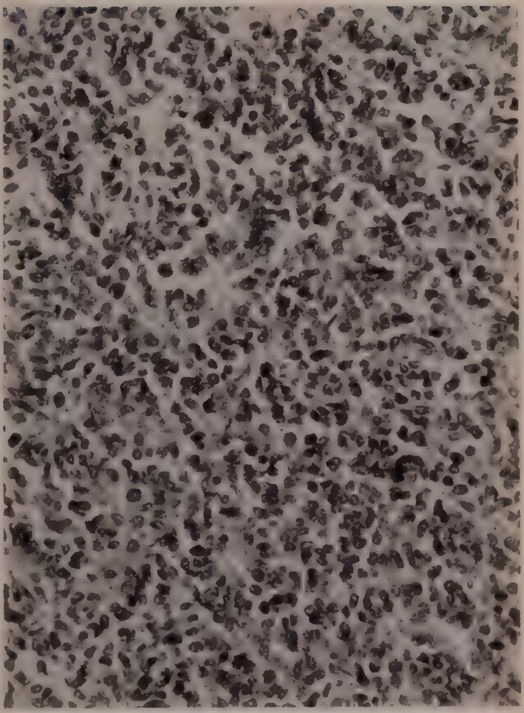

FIGURE 2. Neuroblastoma in lung forming pseudorosettes.

A Physician: How often have assays of insulin activity shown an elevation in cases with hypoglycemia associated with an expancreatic tumor?

Dr. Gittler: The first reported case with convincing evidence for the production of an insulin-like substance was by August and Hiatt.[9] These investigators were able to demonstrate a level of insulin activity in extracts of tumor tissue over three times the magnitude of normal pancreatic tissue. Other investigators have confirmed this using a variety of methods. However, the methods involved have been bio-assays, and these do not discriminate between insulin as such and a substance with insulin-like activity. However, the immuno-assay method of Yalow and Berson[1] does distinguish insulin from other possible substances, and that is the case here. I am confident that in the present case we are dealing with a true insulin-secreting tumor. However, there have been some very elaborate studies by other investigators in which

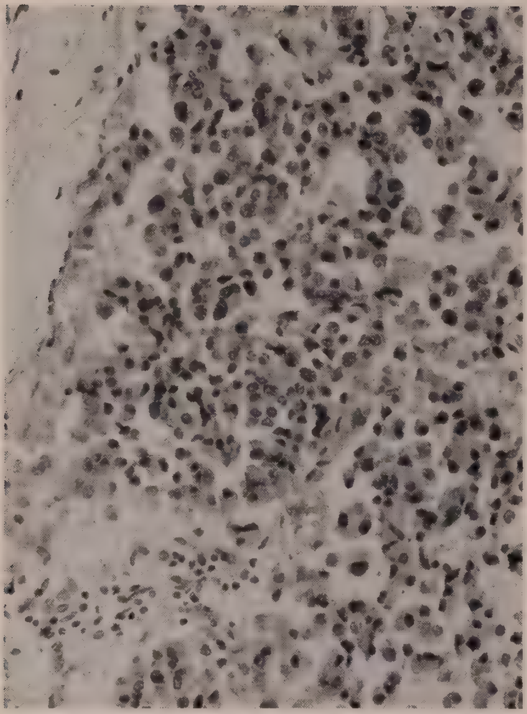

FIGURE 3. Islet-cell tumor of pancreas; the margin is sharply demarcated.

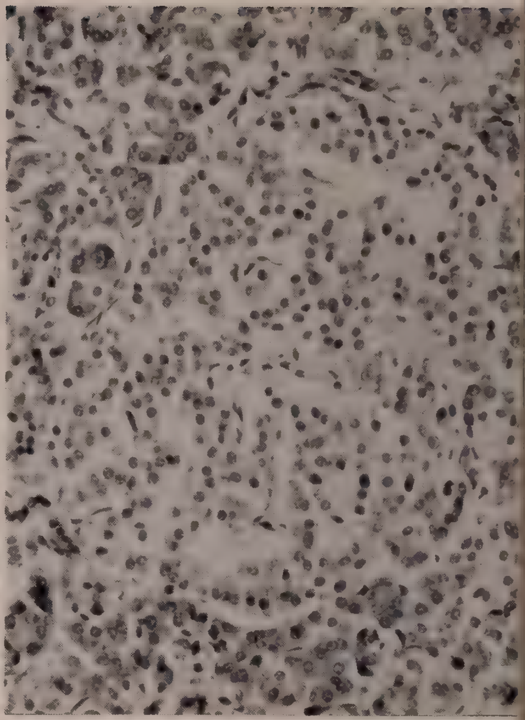

FIGURE 4. Normal islet of Langerhans.

they have failed to demonstrate insulin activity in either the tumor or the patient's serum, so this remains a point which requires resolution by the accumulation of further data.

A PHYSICIAN: Has anyone tried to treat an insulin-secreting tumor by hypophysectomy?

DR. GITTLER: Not to my knowledge, although Conn[10] has demonstrated that growth hormone intensified the hypoglycemia in 1 case of organic hyperinsulinism.

Clinical diagnoses

1. Malignant tumor of fifth intercostal nerve with local persistence and metastases to skeleton and brain

2. Hypoglycemia, secondary to above

Dr. Gittler's diagnoses

1. Malignant neuroblastoma with intracranial and osseous metastases (extrapancreatic insulin-secreting tumor)

2. Hypoglycemia, secondary to above

3. ??Islet cell adenoma or carcinoma, pancreas

Pathologic report

H. CLARKE ANDERSON, M.D.: At autopsy the body was that of an emaciated twenty-one-year-old female. The presence of emaciation in a patient subject to attacks of hypoglycemia is somewhat unusual, since these patients often ingest large amounts of sugar in various forms and become obese.

An examination of the chest revealed a large posterior mediastinal tumor involving the lower lobe of the right lung by direct extension. Yellow metastatic lesions penetrated the entire thickness of the cranium, to the dura, and were seen scattered throughout the vertebrae, ribs, pelvis, and left femur. Only bony metastases were identified, and all other tissues examined were free of metastatic tumor.

Microscopic sections of the posterior mediastinal tumor and of the bony metastases revealed typical neuroblastoma (Fig. 2) with the characteristic small, uniformly shaped cells with scant cytoplasm. Here the cells are arranged radially to form pseudorosettes.

The brain and spinal cord were free of metastases and showed no other gross or

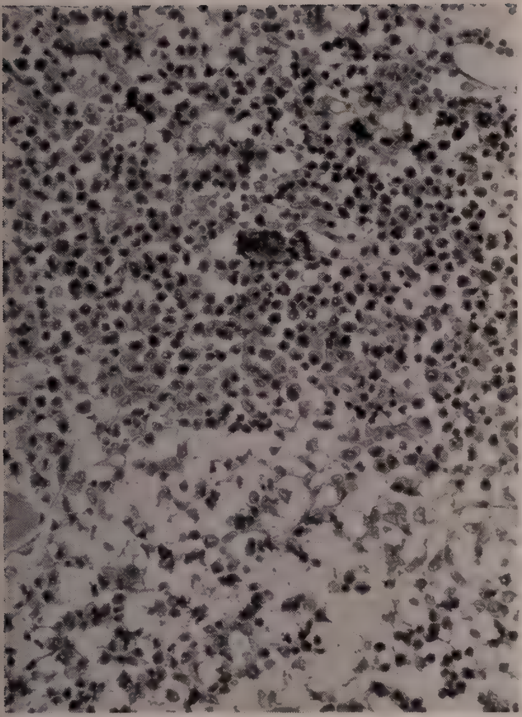

FIGURE 5. Metastatic neuroblastoma is seen in the lower portion and hyperplastic bone marrow in the upper portion of the photograph.

microscopic abnormalities. Thus, the patient's neurologic signs and symptoms may have been due to hypoglycemia.

The pancreas was externally unremarkable, but a careful examination revealed a well-demarcated tumor within the head of the pancreas. It measured 1.4 cm. in maximum dimension, was yellow-pink in color, and had the typical microscopic appearance of an islet-cell adenoma.

The islet-cell tumor (Fig. 3) was histologically readily distinguishable from the posterior mediastinal neuroblastoma and bore a striking architectural resemblance to normal islets of Langerhans (Fig. 4). In both we see uniform cells with a moderate amount of eosinophilic cytoplasm arranged in anastomosing trabeculae.

Gomori's aldehyde fuchsin method was applied to the islet-cell adenoma and to normal islets of Langerhans in the surrounding pancreas but failed to stain either. Autolysis may be the reason for the failure of these tissues to stain, because the autopsy was performed nineteen hours after the patient's death.

All other endocrine organs examined were normal, that is, pituitary, adrenals, thyroid, ovaries, and two parathyroids.

Microscopically the bone marrow showed extensive replacement by metastatic neuroblastoma. The marrow between metastatic deposits was markedly hyperplastic (Fig. 5), and the spleen showed active hematopoiesis. This is the picture of a myelophthisic anemia with compensatory extramedullary hematopoiesis.

Thus the patient was harboring two independent primary tumors: a neuroblastoma with extensive metastasis to bone and an islet cell adenoma which was probably insulin producing. She died in shock, probably from severe terminal hypoglycemia.

Anatomic diagnoses

1. *Islet cell adenoma, head of pancreas*
2. *Neuroblastoma, arising in posterior mediastinum, metastatic to cranium, vertebrae, pelvis, ribs, and left femur*
3. *Hyperplasia, bone marrow*
4. *Extramedullary hematopoiesis, spleen*
5. *Emaciation*

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Clinical Rehabilitation Conference

Prepared by the Department of Rehabilitation Medicine,
The Albert Einstein College of Medicine,
Bronx Municipal Hospital Center, New York City

EDWARD F. DELAGI, M.D., and
HEINZ I. LIPPMANN, M.D., Editors

Multiple Sclerosis

Heinz I. Lippmann, M.D.: Today a patient with multiple sclerosis is presented who demonstrated a multitude of problems. Will the student kindly present the case.

Case history

This thirty-eight-year-old white female patient has had multiple sclerosis for twelve years. The first symptoms were blurred vision twelve years ago, poor balance, and some increasing weakness of the lower extremities which progressed over a period of several years to spastic paraplegia. There has been a constant progression of the disease and few if any periods of remission. Until a year before admission she was able to get about with some difficulty. Her present problems started a year ago when she suffered an episode of a febrile illness of unknown nature, for which she was treated with bed rest and antibiotics for a period of two to three weeks. During this period of bed rest she developed a sacral decubitus ulcer. When she became afebrile she noted marked difficulty in ambulation because of spasticity. Five months prior to this present hospitalization she was admitted for two weeks to a private hospital for the treatment of her decubitus ulcer. No surgery was performed at that time, and an indwelling catheter was inserted into her bladder.

Her subsequent course was downhill; more decubitus ulcers developed over her lower back and her buttocks, and the sacral ulcer grew very large. She also developed hip and knee contractures and was at home in bed for four months. When the patient entered the hospital on April 3, 1961, an examination revealed a well-developed woman in no acute distress, with normal vital signs and a normal blood pressure. She had deep necrotic decubitus ulcers on the left buttock, the right buttock, and the sacrum. Her temperature was 102.4 F. She had a 70-degree flexion contracture of both knees and bilateral hip flexion contractures of the same degree. She showed spasticity and hyperreflexia of both lower extremities. There was mild ataxia and fairly good strength of both upper extremities. There was impairment to touch, 2-point discrimination, vibration, and pinprick over various areas in the upper part of her body and all these modalities were abolished nearly completely below the first lumbar segment on the right and the third lumbar segment on the left. There was temporal pallor of the optic disks bilaterally and horizontal nystagmus on the left lateral gaze. Her speech was normal, and no intention tremor was present.

There was a leukocytosis of 14,500 and a hematocrit of 33, with hypochromia and anisocytosis. The urine showed positive findings for albumin (2 plus) and negative findings for sugar. Many red blood cells and white blood cells were reported on microscopic examination. The urine culture was positive for proteus and Staphylococcus albus. A culture of a decubitus ulcer was positive for a Staphylococcus which was sensitive to Terramycin and a proteus which was sensitive to chloramphenicol (Chloromycetin) and kanamycin sulfate. There was no growth on the blood culture. The blood chemistry showed no abnormality. Ten days after admission, an examination showed a bladder capacity of 250 cc. with diffuse cystitis and no obstructive changes. Her bladder was classified as "automatic" at that time.

The Department of Plastic Surgery indicated that the control of spasticity was essential before the plastic closure of the decubitus ulcers could be accomplished. Twenty-four days after her admission, a neurosurgical procedure consisting of a longitudinal cordotomy from the ninth thoracic to the second lumbar vertebrae was performed. This resulted in areflexia of both lower extremities and hypotonia. The reduction of spasticity permitted better preoperative care of her decubitus ulcers. Her fever continued owing to a genitourinary infection which was treated with chloramphenicol and Gantrisin.

On June 12, 1961, the first plastic surgical procedure was performed: a first-stage delay of lumbar and right thigh pedicle flaps. On June 23, 1961, the second stage was performed. On July 10, 1961, the bony prominence of the sacrum was excised, the previously delayed flap was rotated into the defect, and the area of defect left by the flap was covered by split-thickness grafts. On September 1, 1961, the decubitus ulcer was closed by rotation of the thigh flap of the right trochanter, and the area of defect left by rotation of the flap was closed with split-thickness grafts from the left thigh.

The patient was permitted to sit up on September 12, 1961. About that time it was noted that the patient's hemoglobin had fallen to 7.6 Gm. per 100 ml., and the patient was febrile; an ecchymotic discoloration of the right trochantic flap and an indurated swelling on the right buttock were noted. The reported aspiration yield every other day was 40 to 70 cc. of blood each time for five weeks. The total blood aspirated in this fashion amounted to about 1,200 cc. A roentgenogram revealed that the patient had a right femoral neck fracture.

An examination today shows that all skin grafts are healing. A flaccid paralysis of both lower extremities is present. The patient has good strength in both upper extremities. There is no major sensory deficit in the upper part of her body down to the first lumbar dermatome. On the right side there is some patchy sensation in distribution of the second and third lumbar segments, but absent vibratory and position sense of both lower extremities. There is some impairment in the finger-to-nose test and rapid alternating movements. All tendon reflexes are absent in the lower extremities and normal in the upper extremities. There is a bilateral temporal pallor of the optic disks and some nystagmus on gaze to the left.

Dr. Lippmann: Thank you. I would welcome a supplementary statement concerning the history of this patient's admission because it throws some light on a problem which is of great concern to us.

History of admission

Edward F. Delagi, M.D.: This patient came to our attention through one of our medical students after he had spent a two-week clinical clerkship on our service. The student, after learning about the integrated multidisciplinary approach to patients with complex problems practiced on a rehabilitation ward, asked that we see the patient who was a neighbor of his. He said that there had been many attempts to solve the patient's numerous problems, but these were all made in a piecemeal fashion. The patient had been hospitalized at various times by the plastic surgeon, the urologist, and the family physician, but very little was accomplished. Her attending physicians told the husband that they knew of only one hospital in the area geared to manage such a problem, and that was the Spinal Cord Injury Center in the Veterans Administration Hospital.

On the preadmission examination, the physical findings were as described by the medical student, and I decided that the patient was an excellent candidate for our rehabilitation ward service and advised immediate admission. I estimated that the patient's hospital stay would be about one year.

Dr. Lippmann: May we see the patient now. (The patient enters in a prone position, on a low stretcher, wheeling herself.

It is demonstrated that her decubitus ulcers are granulating in. She has an indwelling catheter. The right leg is $1^1/_2$ inches shorter than the left. Both lower extremities are flaccid and moderately atrophic. There is an ecchymotic discoloration over the right hip.) How do you feel?

PATIENT: I feel all right. I have no pain as you see. I am lying on my stomach with my legs stretched out, which is certainly a relief.

VISITING PHYSICIAN: Do you have any sensation in your legs?

PATIENT: No.

VISITING PHYSICIAN: Do you feel when you have to urinate?

PATIENT: No.

VISITING PHYSICIAN: Did you feel when you had to urinate before the operation on your spine?

PATIENT: Well, I had some feeling, not normal I would say, but some feeling. I could tell when I had to urinate. It was not always possible for me to urinate though, but I had some feeling, and I don't have any now.

DR. LIPPMANN: Thank you. Does anyone else want to ask this patient any questions? If not, thank you. (The patient wheels herself out on wheeled stretcher.) Perhaps we should start by discussing the management of the combination of marked spasticity, decubitus ulcers, and recurring urinary infection. This pernicious combination threatens the lives of many of our patients with spastic paraplegia.

Management of spasticity, decubitus ulcers, and recurring urinary infection

DR. DELAGI: In our patient, as in other patients of similar condition, the progressing deeply infected bed sores with undermined edges and draining sinuses were unmanageable as long as the patient's hips and knees were in a state of flexion owing to marked spasticity. It was impossible to manage her catheter properly because of the marked adductor spasticity. The vicious cycle set up by these conditions could be interrupted only by a surgical procedure aimed at reducing the patient's spasticity.

RESIDENT: With mechanical debridement, wet dressings, the establishment of adequate drainage and enzymatic debridement, and antibiotics, there was some abating of the spasticity, but never to an extent that plastic surgery was feasible.

ALFRED EBEL, M.D.: We have to watch out for at least three complications in severe spasticity of the lower extremities. The first is the deforming flexion of both hips and knees. This is progressive and disabling; edema of the legs due to compression of the popliteal space may lead to thrombophlebitis and secondary ulceration. The second is decubitus ulceration of the medial aspect of both knees which may progress to osteomyelitis and destruction of the joint. The third is, in the male, decubitus ulceration of the scrotum and the genital organs as the result of adductor spasticity. Because these complications are practically inevitable in severe spasticity, early surgical intervention is indicated.

DR. LIPPMANN: What would you consider the surgical procedure of choice to control spasticity in this patient, and what is the basis of your choice?

DR. EBEL: One hesitates to use an irreversible destructive procedure such as rhizotomy in a patient with multiple sclerosis of short duration, where all experience indicates that it is possible to have a remission. However, this patient has had multiple sclerosis for twelve years, and there has been no known episode of true remission. In fact, there has been a slow progression up to the present point. I believe, therefore, that a definitive procedure is indicated since the spasticity and its sequelae threaten the patient's life.

DR. LIPPMANN: I would like some indication as to what procedures are available when we have some hope of remission.

Surgical procedures to alleviate spasticity

GABRIELLA MOLNAR, M.D.: Surgical procedures to alleviate spasticity in such patients may include neural crush instead of neurectomy or tenotomy. We have seen patients with similar conditions who had successful tenotomies about the affected joints so that at least for some time spasticity was relieved. Of course, the tendons became reattached, and spasticity and contracture recurred, although not to the same degree. In patients in whom we do not expect a remission, good results are obtained from peripheral neurectomies. Of course, such a procedure results in sensory loss. The obturator nerve is the one most frequently attacked because of the tendency for the adductor muscles to become spastic and produce scissoring of gait and difficulty in toileting. Fortunately, this nerve does not have a significant sensory component. A more definitive procedure is an anterior rhizotomy which will abolish all motor activity in the involved roots. Posterior rhizotomy has been proposed but would only be indicated where all sensation was lost. This procedure has not been effective as far as I know.

Richard Herman, M.D.: The procedure applied to this patient was new to us. It consists of a longitudinal severing of the spinal cord in a frontal plane bilaterally between the twelfth thoracic and the second lumbar vertebrae. This produced marked decrease of muscle tone and complete loss of all residual sensory modalities. We have not seen the amount of atrophy following this operation which we usually see in anterior rhizotomies. Peter Nathan, M.D., from Queens Square Hospital in London, who saw this patient with us after the operation, pointed out that the loss of bladder and bowel sensation was a significant disadvantage of this procedure even although muscle bulk was maintained and spasticity was reduced. We are presently investigating a method of reducing spasticity without developing disabling sensory loss or compromising the strength of muscle. This method utilizes differential nerve fiber blocks to interfere with the servo loop. This work originated with Rushworth[1] and Nathan[2] and seems to hold some prospect for success.

Dr. Ebel: I think that the results in this case are no different from what could have been achieved with an anterior rhizotomy.

Dr. Delagi: I would like to point out that the maintenance of muscle bulk was considered to be of importance in this case, and we feel that this was achieved while anterior rhizotomy might have resulted in more atrophy.

Dr. Herman: Longitudinal destruction in the frontal plane in this area involves fibers which are important to bladder function. Nathan has devised a procedure using low concentrations of phenol which he injects intrathecally, adjusting the level by means of a tilt table, so that impairment of bladder sensation does not occur.

Dr. Delagi: In the treatment of spasticity, we follow Abramson's[3] concept that a certain amount of muscular contraction inherent in spasticity is desirable. We are seeking methods to reduce excessive spasticity to moderate levels, maintaining some of the metabolic benefits of muscle contraction. That is why this operation appears preferable to anterior rhizotomy.

Visiting Physician: Would you sacrifice an automatic bladder in a patient with excessive spasticity? Are you justified in sacrificing sensation to control spasticity?

Dr. Delagi: A patient who has marked spasticity of the lower extremities requiring such intervention most likely does not have an automatic bladder. Although we would like to maintain bladder sensation whenever possible, the spasticity may represent an immediate danger, and we are forced to choose a procedure which might compromise the bladder. We are continuing to search for better methods to deal with spasticity without compromising the function of the bladder or interfering with residual motor or sensory function.

Dr. Herman: If we succeed in blocking the gamma fibers of the peripheral nervous system, an important factor in spasticity will be removed. We have been able to do this in some cases with specific dilutions of procaine. However, the effect is too short to be of any practical benefit.

Chief Resident: We sacrificed very little in this patient since bladder function and sensation were both seriously impaired preoperatively. The change in this patient's general condition after the operation has been striking.

Dr. Lippmann: Let us move on to discussing the patient's hip fracture. Dr. Ebel, would you like to comment?

Management of hip fracture

Dr. Ebel: In our Spinal Cord Injury Center we have seen fractures of the femoral neck on the basis of severe osteoporosis. These fractures occur without apparent trauma and most frequently while the patient is on bed rest. Previous attempts to treat these fractures with intramedullar nailing or traction resulted in nonunion or osteomyelitis in many cases. At present, it is our policy to continue bed rest for a short period of time to protect against excessive hematoma. Thereafter, the patient is mobilized in a wheel chair, and the usual transfer activities are permitted. In later stages, those patients who are able to stand are permitted to do so.

Treatment goals

Dr. Lippmann: What are our goals for this patient? What is the present program of treatment?

Chief Resident: Our early goal, hopefully, was that of complete independence in self-care and homemaking activities. We still think that this is possible and our program is as follows:

Bladder care. The patient will need permanent bladder drainage by an indwelling catheter; the details involved in such care were discussed on a previous occasion.[4]

Activities of daily living. At present, the patient is in a prone position because of the healing decubitus ulcers. This limits the activities she can participate in to range-of-motion and general conditioning exercises as well as occupational therapy activities to maintain strength and coordination of her upper extremities. As soon as she is permitted to sit up, other more meaningful activities can be added to her program, for example, dressing, washing, cooking, and other homemaking activities. All these will have to be done from a wheel chair. Also, she will be trained in transfer activities to bed and toilet.

Psychosocial factors. Our social worker has maintained close contact with the patient's family. Members of the rehabilitation team, including the physiatrist, the occupational therapist, and the physical therapist, have actually visited the patient's home to evaluate it for wheel-chair living.

Further care. The patient is returning to the care of her private physician to whom will be forwarded a detailed report of her hospital course and our recommendations for further management.

Dr. Lippmann: Thank you. May we have a follow-up report in a few weeks on this patient.

Follow-up

Dr. Lippmann: The chief resident has a follow-up report on the patient with multiple sclerosis whom we saw seven weeks ago.

Chief Resident: The patient was discharged home last week where she assumed her place in the family as a housewife caring for her husband and children. At that time, all her decubitus ulcers were healed, her urinary status was stabilized on catheter drainage, and she was capable of complete self-care. She was resuming all those homemaking activities which were possible from a wheel chair.

Dr. Lippmann: The house staff should be complimented for obtaining a fine result in such a complicated case. I think we have all learned that the only approach that holds any promise of success in this type of complex problem is an integrated one.

The coordinating physiatrist, the neurosurgeon, the plastic surgeon and the urologist all contributed equally essential services to produce an excellent result.

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Number seven in a series of Clinical Rehabilitation Conferences

Maternal Welfare

Prepared by the Subcommittee on Maternal and Child Welfare, Committee on Public Health and Education, Medical Society of the State of New York

EDWARD C. HUGHES, M.D., Syracuse, Editor

Routine Oxytocic Induction of Labor

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ROUTINE INDUCTION of labor, for nonmedical reasons, continues to be a controversial issue. The dangers of the use of oxytocic agents as contributory factors to both maternal and fetal mortalities and morbidities have been brought to the attention of the Chairman of the Subcommittee on Maternal and Child Welfare.

Use of oxytocic agents

There is no question that large series of cases in which labor has been induced routinely with oxytocics have been reported, with no statistical evidence of increase in maternal or newborn mortality rates. However, it would appear that in each patient in which oxytocics are used for either induction or stimulation of labor there is a calculated risk of encountering the dangerous reactions that are well understood by experienced obstetricians.

There can be little doubt that certain patients will react to oxytocics in a dramatic manner, such as experiencing a sustained tetanic contraction of the uterine musculature. There are probably many reasons for unusual reactions, but there could be a basic reason, since it is pointed out by Van den Driessche and Reygaerts* that the sensitivity of the pregnant uterus to oxytocin increases considerably during the last month of pregnancy and especially during the last ten days.

The judicious use of oxytocics for medical indications is a valuable obstetric tool. It would seem reasonable to expect those physicians who choose to employ oxytocics for nonmedical reasons to observe the same precautions as are required for medical indications.

The Manual of Standards in obstetric and gynecologic practice, prepared by The American College of Obstetricians and Gynecologists, is used by many hospitals as a guide for maintaining high standards of maternity and newborn care. This manual deals with the general subject of oxytocics in the following manner:

> Oxytocin: Pitocin and Syntocinon are valuable drugs under certain definite fixed precautions. Otherwise they are dangerous by any mode of administration. They should be given only upon written order of the physician, in specified dosage and dilution.
>
> (a) When oxytocin is administered by hypodermic injection, the patient should be observed for at least 30 minutes thereafter by her physician.
>
> (b) When oxytocin is administered by intravenous drip, the patient should be under constant observation. This means that a

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* Secretary of the Subcommittee on Maternal and Child Welfare.

* Van den Driessche, R., and Reygaerts, J.: Test de sensibilité à l'ocytocine; I. Appréciation de l'imminence du travail. II. Conséquences au point de vue de la provocation, Bull. Soc. roy. belge gynec. et obste. **28**: 227 (1958).

physician must be in the room with the patient at all times. If it becomes necessary to leave the patient alone, the drip should be stopped before the observer leaves the room, to be resumed on his or her return.

The following should be checked regularly by routine technique: fetal heart sounds, frequency and character of contractions, blood pressure, rate of intravenous Pitocin flow, stability of the intravenous insertion and other vital signs.

There seem to be borderline decisions as to what is and what is not a medical indication for induction of labor. Patients, especially multiparas at or near term sometimes present a clinical situation where it seems obvious that labor is imminent and will be very short. The physician must then decide the relative merits of inducing labor under controlled conditions or awaiting the spontaneous onset of labor, with a good chance that the patient may precipitate before she reaches the delivery room and may have to be delivered without the benefit of professionally trained personnel.

The apparent dangers of the use of predelivery oxytocics are sufficiently important so that some hospitals have set up staff requirements of a rather drastic regulatory nature. A hospital could deal with the situation by adopting a regulation somewhat as follows:

> In view of the doubtful medical, medicolegal, and teaching status of the induction of labor in the absence of clearcut medical and surgical complications, a written consultation will be necessary, prior to the induction of labor.
>
> Thus the same procedure for consultation will be required prior to the induction of labor for medical and/or surgical and nonmedical induction.
>
> A written consultation will be necessary prior to the induction of labor in the________ Hospital henceforth.
>
> Furthermore, the consultant will be required to see and examine the patient.

Comment

Induction of labor for the personal convenience of the patient or physician is controversial and no official organization can be expected to endorse such a policy. It is suggested therefore that the same precautionary procedures on the matter of induction of labor should be used for cases in which there is a bonafidé medical indication and for those cases in which the induction might be for nonmedical reasons. Thus, the indication itself is seen in proper perspective, the advisability of actually inducing labor is clarified, the contraindications can be considered, the best method of inducing labor in accordance with the obstetric condition of the patient can be evaluated, and, seemingly, the untoward effects of the occasional unusual reaction to oxytocics is kept to a minimum.

It is suggested, finally, that the physician give due consideration to the patient as an individual expectant mother before inducing labor for nonmedical reasons. He can justify the method by verified statistics as much as he likes, but he cannot escape the fact that, on occasion, the life and the health of the mother or the baby could be jeopardized. If, after due consideration, the physician elects to assume this responsibility, he should be additionally willing to assume the responsibility of taking every known precautionary measure to safeguard the mother and the baby.

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Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Burns and the Airway

A Challenge in Anesthesia

THE ANESTHETIC MANAGEMENT of patients burned about the head, face, and neck presents a problem in airway maintenance which may become apparent only when such patients are anesthetized. After exposure to smoke poisoning and asphyxia, such patients may be asymptomatic until they are rendered unconscious by anesthetic drugs. The following case report points up some of the problems.

Case report

A twenty-three-year-old white female was admitted to the hospital with 35 per cent of her body surface involved in third-degree burns. The involved areas were predominantly about the head, neck, face, and thorax.

The patient had been treated for three days at another institution where she was given open-air therapy and intravenous fluids of about 2,000 cc. daily, in addition to oral fluids. She also had received penicillin, cortisone, and ACTH. The urinary output during this time had been adequate.

On admission her blood pressure taken at the left thigh was 190/110 mm. Hg, pulse 80 per minute, and respirations 24 per minute. The hematocrit was 48, and the specific gravity was 10.010. The electrolytes were within normal range. The plasma volume measured with I^{131}-labeled albumin was 52.9 cc. per kilogram, slightly above normal. The patient received a transfusion of 500 cc. of blood.

Because the patient appeared to be in good physical condition, she was taken to the operating room on the day following admission for excision of burn scars and grafting. The patient received pentobarbital sodium, 200 mg. and atropine, 0.4 mg. for premedication.

Before anesthesia induction, the patient was instructed to open her mouth and to take several deep breaths. Ventilation with a mask was then performed to ascertain if there were any obvious indications of airway obstruction. Since there was no apparent obstruction, anesthesia was induced with 125 mg. of thiopental sodium in divided doses, and after 40 mg. of intravenous succinylcholine was given intravenously, hyperventilation with oxygen was performed to facilitate orotracheal intubation. On the insertion of the laryngoscope the anesthetist noted that the posterior pharynx and sub- and supraglottic tissues appeared swollen and crusty. An attempt was made to introduce an endotracheal tube through the glottis, but it could not be advanced although it seemed to be of appropriate size. The patient again received oxygen ventilation, and an additional dose of 20 mg. of succinylcholine was given intravenously. At no time did the patient appear cyanotic, and the pulse did not fluctuate. The second attempt at intubation appeared to be successful. However, as the tube was being passed, the assistant who was monitoring the patient's radial pulse

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noticed that the pulse disappeared. Closed chest cardiac massage was begun immediately. At this time the patient was cyanotic. The anesthetist continued the ventilation and had no difficulty in elevating the patient's chest, although there was some dissatisfaction with his ability to inflate the cuff of the endotracheal tube and secure a tight fit. Extubation and reintubation were performed by an attending anesthesiologist, and external massage was continued. Twenty minutes after the cessation of a spontaneous heart beat, T waves were first noticed on the electrocardiogram. Ten minutes later a normal sinus rhythm with an adequate peripheral pulse was present. However, the patient had not resumed spontaneous respirations.

She was removed to the recovery room and placed on a Bird respirator. The blood pressure taken on the thigh was 130/110 mm. Hg, and the pulse was 110 per minute. Her course deteriorated gradually over the next twelve hours until she expired.

The autopsy findings revealed edema of the mucosa of the larynx and trachea as well as of the pharyngeal tissues.

Comment

The observation of edematous upper airway structures always must be considered to be of grave significance, and the anesthetic management of patients with these findings requires extreme care and expert clinical judgment.

Flame injury to the respiratory tract may produce first- or second-degree burns and findings similar to those of acute infectious tracheobronchitis. All the structures of the tracheobronchial tree may be involved, but the anesthetist is particularly concerned with the supraglottic and subglottic regions of the larynx. Congestion and edema can obstruct the airway partially and raise the negative intrathoracic pressure. Increased negativity causes added congestion, transudation, and capillary damage. Infection and local circulatory changes may add to the exudate. Atelectasis and emphysema may further complicate the picture and tend to embarrass cardiac output.

Shannon in 1957* described the alterations in the respiratory apparatus which may result from burns or the inhalation of hot noxious gases.

Respiratory obstruction may result from edema of the air passages following the inhalation of noxious gases, from pressure on the trachea by accumulated edema fluid in the neck, or from crusted secretions within the vestibule of the nose. Shannon also noted that nasal crusting is particularly common with facial burns. It not only causes mouth breathing but also the accumulation of thick, viscid, postnasal secretions, which ooze on the larynx and lead to exhausting bouts of coughing.

The respiratory center may be depressed from over-sedation or stimulated from anxiety or pain, the latter causing rapid, shallow, and ineffective respiration.

The respiratory muscles may be damaged directly or their movements may be interfered with by skin burns of the thorax or abdomen.

In this case, when the anesthetist found this patient's glottic area was compromised by swelling, edema, and crustation, he should have discontinued anesthesia immediately and induced ventilation until the patient's resumed her own respiratory activity. At this point he might have elected to re-evaluate the management of this case in consultation with an expert laryngologist, advised tracheostomy, or suggested that the operative procedure be performed under regional anesthesia. A second look or second attempt at laryngoscopy should be reserved for a more expert anesthetist.

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Number one hundred twenty-three in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
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Naphthalene Poisoning

The following incidents were reported recently to the New York City Poison Control Center.

Incident 1

Substance Ingested	*Age*	*Sex*
Naphthalene	23 months	Female

This twenty-three-month-old female child was admitted to the Jewish Hospital of Brooklyn with a history of progressive lethargy, anorexia, vomiting, fever, and pallor. According to the parent, the child was perfectly well until the sudden onset of these symptoms. On inquiry, it also was found that the child had a history of pica of some duration. The mother, however, related that prior to the acute onset she saw the child playing with an empty box labeled "pure moth balls—100 per cent naphthalene." However, she did not observe the child actually ingesting any of the moth balls.

The past history, according to the report obtained from the Jewish Hospital of Brooklyn, showed essentially negative findings. The child was admitted to the inpatient service with a temperature of 100.8 F., pulse 120 per minute, extreme pallor, slightly protruding eyeballs, a Grade II systolic murmur, the liver 2 fingerbreadths below the costal margin, and the spleen not palpable. The patient was stuporous with moderate neck rigidity and a questionable Kernig's sign.

The laboratory examination revealed the hematocrit to be 9, and the white blood cell count 16,000 (60 per cent polymorphonuclear leukocytes). The cerebrospinal fluid showed a slight rise in pressure, the urine was strongly positive for coproporphyrin, there were no sickle cells (×2), the serum bilirubin was 1.7 mg. per 100 ml. (35 per cent direct), the serum lead was not detectable, the bone marrow showed erythroid hyperplasia, peripheral reticulocytes were 10 per cent, and the blood urea nitrogen was 11 mg. per 100 ml.

The x-ray films showed negative findings except for a slight heart enlargement. There was no definite "lead line" in the long bones.

On admission the patient was transfused immediately with packed cells, and her hematocrit climbed to 22 but soon thereafter dropped several points. This was associated with a fever spike. She was transfused several times after this, but hemolysis persisted, associated with a temperature rise from 101 to 103 F. The hospital's hematology department did a work-up for malaria. An analysis of the patient's blood revealed Rh sensitization (the patient is Rh positive) but the indirect Coombs' tests initially showed positive findings, and the direct Coombs' test showed faintly positive findings.

The patient also was placed on antibiotic therapy immediately following admission, but this was discontinued after three days. At the time of the report, which was about one month following admission, the patient's only medication was prednisone 12.5 mg.

every six hours. It was hoped that her hematocrit could be maintained on this, enabling all donor cells to be lost from circulation so that glucose-6-phosphatase dehydrogenase studies could be carried out.

No splenomegaly was noted as of the date of this report. The physician also stated that in view of this prolonged and repeated lysis of red cells, the incrimination of naphthalene as the cause seemed more and more remote.

Three months following the report from the hospital, the Director of Pediatrics of the Jewish Hospital of Brooklyn, Joseph Pincus, M.D., sent a supplementary report as follows:

> The patient was last seen in the pediatric hematology department on August 18. Her hemoglobin was 11 Gm. per 100 ml., reticulocytes 0.8, platelets 2 plus, white blood cell count 3,900, polymorphonuclear leukocytes 48 per cent, and lymphocytes 51 per cent. A Coombs' test showed negative findings. She is generally feeling well. Her appetite is poor, but the mother seems satisfied with her progress. Her general condition on physical examination is that of a fairly well-nourished and well-developed child. Neither the spleen nor the liver is enlarged, and there is no generalized lymphadenopathy. She is being seen in the pediatric hematology department about every two weeks.
>
> The final diagnosis is still that of an acute hemolytic anemia, probably initiated by the ingestion of naphthalene. Whether or not this is so, we cannot say with any assurance.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Naphthalene	2 years	Male

This patient, a two-year-old child, and his three-year-old sibling, who were supposedly taking a nap while the mother was busily engaged in the kitchen, obtained some camphor balls from the pocket of an apron which they found in a drawer in the mother's bedroom. Apparently, the younger child only ingested some of the balls. The mother found the patient convulsing, and the child was taken to a hospital emergency room where the stomach was lavaged with tap water. The patient was then admitted to the inpatient service, and the pertinent symptoms were abdominal pains and convulsions.

After three days of hospitalization and intensive symptomatic and supportive therapy, the patient was reported to have made a full recovery.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
"Kopper's" Moth Balls (Naphthalene)	9 months	Female

A report on a naphthalene poisoning was received from a mother from Riverside, New Jersey. There were moth balls in the chairs, under the cushions. Another child, two-and-one-half years old, removed a few and proceeded to throw them about. The baby picked one up, presumably, and began to chew it. She was found sitting in her playpen with a chunk of one in her mouth. How much she swallowed was not known. The Poison Control Center was called, and the mother was advised to take the child to the local hospital emergency room. There they pumped her stomach. They could not tell if any pieces of the ball actually came up. The parents were warned to watch for symptoms of pneumonia and toxic poisoning. The child was taken home, and she never developed any further troubles. She is fine at the time of this writing.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Naphthalene	11 days	Female

This incident was reported from Flower and Fifth Avenue Hospitals and probably will be reported in full by members of the hospital staff.

We believe, however, that knowledge of the mode of occurrence and a brief review of the symptomatology and treatment warrant wide dissemination. This was an eleven-day-old female child who was brought into the hospital because the mother noted that the child had appeared jaundiced for the last three days and that the jaundice was getting progressively worse. Also, she related that the urine had become like "dark tea," but she did not observe the color of the stools.

The child was a full-term infant, weighing 7 pounds, 8 ounces at birth, and was delivered by cesarean section. The prenatal course also was said to be normal. On discharge from the hospital, seven days following birth and four days prior to readmission, the child was not jaundiced, and according to the mother, the infant's appetite was excellent. There was no vomiting or fever or any other signs or symptoms of illness. According to the hospital report, there was no family history of jaundice or anemia. However, 2 siblings had died, 1 of pneumonia and 1 of an undetermined cause. However, neither of these had jaundice, nor were they anemic.

The hospital called the Poison Control Center, and the possibility of a naphthalene exposure was raised. The mother reported that she had placed the infant on the day following her initial discharge from the newborn nursery in the other siblings' clothes which had been kept in 100 per cent pure naphthalene.

On admission the infant was adequately nourished and well developed and presented "moderate yellow-orange" color of the skin with pallor. The liver was enlarged and soft to the level of the umbilicus. The spleen was 3 cm. below the costal margin and was soft. The mucous membranes of the mouth were moderately "yellow-orange."

The differential diagnosis was hemolytic anemia and obstructive jaundice, the etiology of both to be determined.

The laboratory data revealed that the mother's blood was type O, Rh positive, and the serology showed negative findings. The infant's blood was type O, Rh positive with a negative Coombs' test result. The urine was negative for urobilinogen and stercobilinogen on several occasions, as were the stools. The blood chemistry, which was done five days following admission, showed a direct bilirubin of 1.3 mg. per 100 ml. and a total bilirubin of 20.2 mg. per 100 ml. The icteric index was 12.5. Two days later the bilirubin total was 17.2 mg. per 100 ml. The bilirubin decreased progressively, and three weeks later the total was 0.4 mg. per 100 ml., and direct 0.15 mg. per 100 ml.

The hemoglobin on admission was 8.65 Gm. per 100 ml. and on discharge was 8.8 Gm. per 100 ml. The red blood cells (per cubic millimeter) on admission were 2,560 and on discharge were 2,420. The reticulocytes on admission were 1.2 per cent and on discharge 3.3 per cent. The platelets per cubic millimeter on admission were 574,000 and were 330,000 on discharge. The white blood cell count was 22,550 on admission and 5,800 on discharge.

During the entire hospital stay the patient was afebrile, and the urine intake and output both were reported as excellent. Bernard Nicora, M.D., of the hospital, reported that special studies to determine the etiology of the hemolytic process were performed. The initial glutathione stability test showed normal results, but repeat blood was sent for additional studies. The infant was transfused with 60 cc. of compatible whole blood on October 4, 1961. At the time of discharge the infant was asymptomatic, and there was no evidence of jaundice. The probable etiology of the jaundice was explained to the mother, and she was cautioned as to the continued use of the moth balls. The infant is to have outpatient follow-up care by the pediatric hematology service.

Comment

Although the hazard of naphthalene poisoning to newborn infants has been reported in the literature, this important point apparently has not been emphasized sufficiently. During the period of prenatal care the physician should remember to discuss the hazards of storing children's apparel and bed clothes with naphthalene flakes or balls. This probability is increased if siblings are in the household and there are "hand-me-downs." The mother should be advised that such clothes should be aired, laundered, or dry cleaned thoroughly to remove all vestiges of naphthalene. In addition, the use of naphthalene in a child's nursery should be discouraged because the vapor pressure of naphthalene, especially in a warm room, may add a significant contamination to the nursery air. Where there are young children in the home and a moth remedy is desired, paradichlorobenzene should be chosen in preference to naphthalene because of the much greater hazard of naphthalene. It is worth emphasizing again that such incidents are referred to chiefly as "camphor" ingestions by both mothers and physicians. Experience has shown that the physician never should accept the incident as a "camphor" ingestion until he has made sure that the mother is not referring to naphthalene or paradichlorobenzene. This situation has become routine in the operation of our Poison Control Center.

It might be mentioned again that in spite of the numerous naphthalene ingestions, only a few serious complications have been reported, and the outcome nearly always has been favorable.

Number ninety-two in a series of Accidental Chemical Poisonings

Wallet-size lung roentgenogram

A wallet-size x-ray film has been devised for the future reference of physicians treating patients with lung disease whose occupation requires moves to different locations, according to an article by Robert B. Stonehill, MC, USAF, and Frank A. Johnson. M.D., in the May 5, 1962, issue of the *Journal of the American Medical Association*. It is frequently desirable and often essential for a physician to review previous x-ray films of patients with lung disease. Obtaining earlier roentgenograms is frequently time-consuming, especially in a migrating population, such as the armed forces personnel and their dependents. This frequently delays diagnosis and therapy. Occasionally the patient is submitted to surgical, diagnostic procedures which could have been avoided if previous x-ray films had been available.

Consequently a patient with x-ray abnormalities, when he is discharged from USAF Hospital Lackland, is given a film of his x-ray negative trimmed to $2^1/_4$ by $2^1/_2$ inches which can be carried easily in his wallet. When a patient's occupation or situation necessitates movement to new locations, the delay experienced in obtaining previous x-ray films might well be avoided by this simple procedure.

Case Reports

Hypokalemic Alkalosis

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THE ASSOCIATION of hypokalemia with alkalosis has been recognized in the past. For example, in a study by Lans, Stein, and Meyer[1] of 404 surgical patients with hypokalemia, 64 were found to be alkalotic. Recent work revealing the permanent renal tubular damage resulting from the prolonged hypokalemic state has prompted this report to emphasize once again the necessity for prompt recognition and early treatment of this condition.

Case report

A sixty-year-old female was admitted to the Roosevelt Hospital in July, 1960, with the chief complaint of vomiting blood for an entire week. Her history revealed a heavy alcoholic intake that had increased recently. During the five weeks prior to admission, she had vomited two or three times a day and the week prior to admission had had two or three episodes of hematemesis. Hypertension, diabetes, increased hirsutism, previous renal disease, diarrhea, chills, and fever were all denied by the patient. A review of systems revealed that the patient had bronchitis and bronchial asthma of undetermined duration.

The patient was obese, and physical examination revealed her to be lethargic, disoriented, hallucinating, and incontinent. Her pulse rate was 80 per minute and regular; blood pressure, 100/70 mm. Hg; and respirations, 22. Pertinent findings included poor tissue turgor, a liver edge palpable 3 cm. below the right costal margin, and lungs that were clear to percussion and auscultation. A neurologic examination showed the condition of the patient to be within normal limits except for an abnormal sensorium and bilateral Babinski reflexes.

Pertinent laboratory data included the following: hemoglobin, 9.3 Gm. per 100 ml.; hematocrit, 34.5; white blood count, 10,700, with 86 per cent polymorphonuclear cells, 11 per cent lymphocytes, and 3 per cent mononuclear cells. The urine was amber, cloudy, and with a specific gravity of 1.004, pH of 5, and from 3 to 5 white blood cells per high-power field. The blood urea nitrogen was 96 mg. per 100 ml.; creatinine, 1.3 mg. per 100 ml.; blood sugar, 180 mg. per 100 ml.; sodium, 129 mEq. per liter; chlorine, 58 mEq. per liter; potassium, 2.7 mEq. per liter; carbon dioxide, 63 mEq. per liter; blood pH, 7.43; calcium, 95 mEq. per liter; and magnesium, 3.4 mEq. per liter. Electrocardiograms revealed changes consistent with marked hypokalemia (U waves and low T waves). The blood amonia was 83 mg. per 100 ml. and the stool guaiac test showed 3 plus.

CLINICAL COURSE. With the administration of intravenous dextrose, normal saline, and potassium (a total of 200 mEq. of potassium chloride over seventy-two hours), chemistry results were recorded as follows: sodium, 138 mEq. per liter; chlorine, 88 mEq. per liter; potassium, 5.2 mEq. per liter; carbon dioxide, 30 mEq. per liter; and blood urea nitrogen, 24 mg. per 100 ml.

The patient became oriented after twenty-four hours, although occasional brief periods of confusion were noted over the first four days. By the second day, the Babinski reflexes were no longer present. Her course was complicated by the development of pneumonia in the lower lobe of the right lung which responded to treatment with antibiotics, the Bennett respirator, Isuprel, and alevaire. Because of recurrent 4 plus stool guaiac test results, a gastrointestinal investigation was begun, but the patient signed out against advice on her fourteenth hospital day, and the studies could not be completed.

Comment[2–8]

The causes of hypokalemia are numerous. Among the causes encountered most frequently are the following: dietary inadequacies; losses from the gastrointestinal tract due to vomiting and diarrhea (often a result of excessive use of laxatives and gastric suctioning); renal loss due to "salt-losing nephritis," diuretics, and hyperadrenocorticism (spontaneous or iatrogenic); and inadequate replacement of potassium, such as occurs in the postoperative and recovery phases of diabetic acidosis.

The signs and symptoms of hypokalemia include: (1) muscle weakness (frequently of the respiratory muscles and, less often, of the cranial nerve muscles) and ileus; (2) a decrease in the reflexes of the deep tendons; (3) listlessness and mental depression (rarely coma); (4) anorexia; (5) electrocardiographic changes (prolonged Q-T intervals and low T waves); and (6) cardiac arrhythmias.

The clinical manifestations of metabolic alkalosis include increased neuromuscular excitability and a decreased respiratory rate, along with the signs and symptoms of the underlying disease. Because of the antagonistic action of potassium and hydrogen ions on muscular irritability (that is, muscular irritability is directly proportional to potassium ion concentration and inversely proportional to hydrogen ion concentration), the alkalotic state may mitigate the manifestations of potassium depletion. Thus, a direct correlation between serum potassium and the symptoms of hypokalemia does not necessarily exist in hypokalemic alkalosis.

The alkalosis frequently associated with hypokalemia is the result of the replacement of intracellular potassium ions by sodium and hydrogen ions from the extracellular fluid, in a ratio of 2 sodium ions and one hydrogen ion for every 3 potassium ions. This shift produces an extracellular alkalosis simultaneously with an intracellular acidosis. In the present case of hypokalemia secondary to prolonged vomiting, the alkalosis was augmented by the loss of a fixed anion, in excess of fixed cation in the gastric juices.

The paradoxical persistence of acid urine in the presence of extracellular alkalosis has been explained in various ways. The two most acceptable explanations are, first, that the kidney may be responding to its own intracellular acidotic environment, and second, that the tubular excretion of hydrogen and of potassium share a common mechanism that produces an increased hydrogen ion concentration in the urine when the kidney attempts to conserve potassium. Because of this inability of the kidneys to excrete an alkaline urine, spontaneous correction of a hypokalemic alkalosis must depend on respiratory mechanisms.

The therapy of hypokalemic alkalosis depends simply on the replacement of potassium. The intracellular and extracellular ion shifts that result from potassium administration increase the extracellular hydrogen ion concentration. A reduction of free extracellular bicarbonate radical concentration follows, as a result of the formation of carbonic acid, which may then be excreted by the lungs in the form of carbon dioxide and water.

Attempts to correct hypokalemic alkalosis through the therapeutic measures usually employed in treating metabolic alkalosis (sodium chloride or acid salts administered intravenously) have proved ineffective. In fact, it is believed that they may actually intensify the underlying distrubance by a further replacement of intracellular potassium and its subsequent urinary excretion in the osmotic diuresis following such fluid administration.

Conclusion

In conclusion, it cannot be emphasized too often that an early recognition of hypokalemic alkalosis and a knowledge of its most effective therapy have become increasingly important. The mounting evidence of the permanent renal tubular damage that results from a prolonged hypokalemic state has lent considerable weight to this conclusion.[9]

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Neurologic manifestations of pinworms

According to an article by Leo Litter, M.D., in the November, 1961, issue of *Archives of Pediatrics*, an awareness of the varied symptoms of pinworm infestation may often result in the identification of this entity as the cause of otherwise puzzling clinical phenomena. Like syphilis, parasitic infestation can imitate almost any disease and may affect any system of the body, including the central nervous system, eye, veins, skin, gastrointestinal tract, and genitourinary system. Of 150 proved cases of oxyurias infection in children, electroencephalograms in 63 (42 per cent) showed occipital dysrhythmias. Repeat tracings taken about one to two months after successful antihelminthic therapy showed either diminution or disappearance of the occipital dysrhythmia in 30 cases (48 per cent). During the last ten years a number of children with neurologic symptoms suggesting brain tumor, epilepsy, chorea, diffuse encephalopathy, and other diseases were found to be infested with pinworms. In many instances, the electroencephalogram appeared to corroborate the presence of an organic lesion but reverted to normal after treatment for pinworms.

Xanthofibroma of Stomach

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THE CLINICAL DIAGNOSIS of benign tumors of the stomach is frequently difficult to establish. Surgical exploration and microscopic examination of the tumor mass is necessary. The purpose of this report is to present an unusual tumor of the stomach which presented clinical symptoms of a malignant neoplasm.

Case report

A forty-two-year-old white divorced woman was admitted to the Jewish Hospital of Brooklyn for the third time on November 14, 1960, for fever, fatigue, and anemia. Her first admission had been on March 1, 1960, for vaginal bleeding secondary to a fibroid uterus. At that time she underwent a total abdominal hysterectomy, a bilateral salpingo-oophorectomy, and an appendectomy, complicated by a postoperative wound infection. However, she was afebrile and had a hematocrit of 38 when she was discharged on March 15, 1960.

On September 26, 1960, the patient was readmitted comatose, following the ingestion of 20 phenobarbital tablets. She had an aspiration pneumonia, and during her course she developed a urinary tract infection, both due to Aerobacter organisms. A thyroid nodule; weakness of her left arm and hand; and a microcytic, hypochromic anemia were noted during this admission. She was treated with antibiotics, oral iron, and blood transfusions. Her reticulocytes rose to 4.5 per cent, but there was no hematocrit response. Protein-bound iodine, radioactive iodine uptake, and a thyroid scan were normal.

At the time of discharge on October 20, 1960, her chest film showed an almost complete resolution of the left lower lobe pneumonia. The urine culture was sterile, and her temperature was 99.6 F. However, her hematocrit was 22; and the white blood cell count was 14,800, with 79 per cent polymorphonuclear cells.

After discharge she remained weak and ran a low-grade fever despite the administration of antibiotics and iron. Two weeks prior to her present admission, she became anorexic. There was no history of gastrointestinal symptoms, such as nausea, vomiting, diarrhea, constipation, abdominal pain, jaundice, or an abnormal stool.

A physical examination revealed a well-developed, pale, depressed woman appearing chronically ill, without signs of clubbing of the fingers, cyanosis, edema, or recent weight loss. Her temperature was 101.6 F.; pulse, 128 and regular; and blood pressure, 110/62. A 1-cm. firm nodule was palpable in the thyroid isthmus. There was no palpable lymphadenopathy. Diminished breath sounds were heard at the bases of the left lung. A cardiac examination revealed no enlargement, and there was a systolic murmur at the pulmonic area. No breast masses were palpable. There was no abdominal organomegaly or costovertebral angle tenderness. No rectal, abdominal, or pelvic masses were palpable. A stool guaiac test showed negative results. Weakness of the left elbow extension and flexion, weakness of the left hand muscles, and atrophy of the left first dorsal interosseous muscle were noted. The atrophy was thought to be due to trauma to the left elbow incurred during the patient's barbiturate intoxication.

LABORATORY DATA. The hematocrit was 26; the white blood cell count was 17,000, with 88 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes, 4 per cent

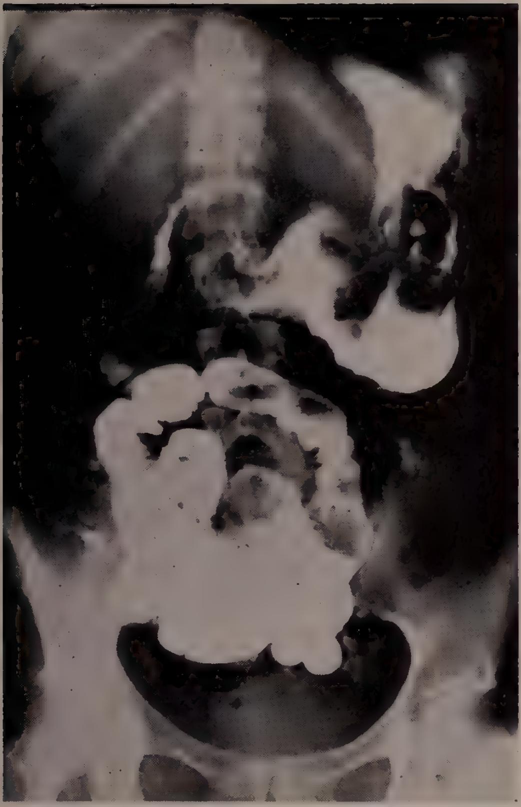

FIGURE 1. X-ray film of stomach showing tumor which is interpreted as infiltrating carcinoma or lymphosarcoma.

monocytes, and adequate platelets; marked hypochromia, moderate anisocytosis, and a slight polychromasia; 1.6 per cent reticulocytes; uric acid with no albumin, sugar, or acetone; 3 or 4 white blood cells per high-power field; blood urea nitrogen, 12 mg. per 100 ml.; sugar, 92 mg. per 100 ml.; normal electrolytes; total protein, 6.7 mg. per 100 ml., with an albumin-globulin ratio of 1.2; alkaline phosphatase, 3.3 Bodansky units; serum glutamic oxalacetic transaminase, 34 units; icterus index, 2 5; and results of the Coombs' test, negative.

An investigation for an occult neoplasm or infection was undertaken. Multiple cultures of the patient's urine, blood, stool, nose, and throat revealed no pathogens. A sigmoidoscopy revealed only hemorrhoids. Sinus films, an intravenous pyelogram, and a barium enema showed normal results. Chest films showed a left basilar pleural reaction and a further resolution of her pneumonia. A gastrointestinal series showed a large lesion of the body of the stomach (Fig. 1), thought to be an infiltrating carcinoma of a lymphosarcoma.

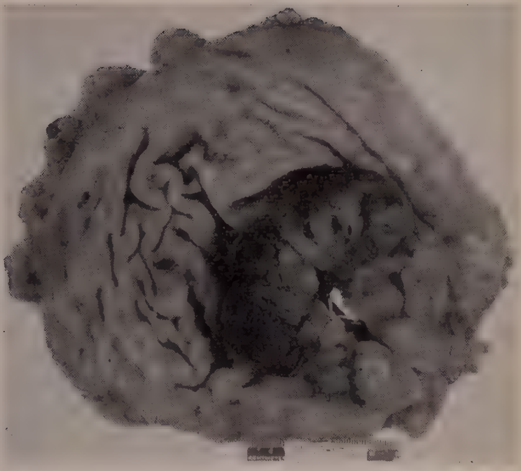

FIGURE 2. Gross photograph of tumor in stomach.

An exploratory laparotomy was performed on November 11, 1960, and a tumor was seen, involving the greater curvature and antrum of the stomach. The mucosa covering the area was normal. It was firm, not very hard, and looked like a fibrosarcoma. A subtotal gastrectomy and gastroduodenostomy were performed.

The patient received several blood transfusions before and after surgery. She did well postoperatively and was discharged on December 11, 1960, afebrile and with a hematocrit of 44. Since no ulceration of the gastric mucosa was noted on the overlying mucosa, it was thought that her anemia was due to intrinsic mechanisms.

Pathology report. The gross specimen consisted of a sleeve-shaped portion of the stomach measuring 21 cm. along the greater curvature and 14 cm. along the lesser curvature. The serosal surface was smooth and glistening except over the tumor in the posterior wall at the lesser curvature which measured 9.5 by 7 by 3 cm. The tumor was nodular, rubbery, yellow-tan, mottled with red, and moist. About 1.5 cm. of duodenum were removed with the stomach and omentum which measured 35 by 8 cm. The cut surface of the tumor was pale yellow-tan in color (Fig. 2). The lymph nodes were not enlarged, were soft, and tan grey.

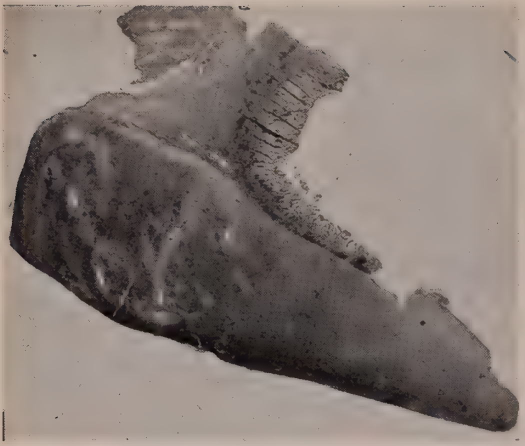

FIGURE 3. Low-power photomicrograph showing tumor of stomach with intact mucosa (Hematoxylin and Eosin Stain).

Histologically the tumor consisted of a scanty fibrous connective tissue stroma in which there were sheets of large cells with somewhat foamy and granular cytoplasm and vesicular nuclei. Some of these nuclei were eccentrically placed. The tumor infiltrated the muscular coat in places, completely obliterating the usual cytoarchitecture. The overlying mucosa appeared uninvolved (Fig. 3). The cells in some areas were polygonal, while in other areas they were more compactly arranged and spindle-shaped. The cells varied only slightly in size and nuclear staining (Fig. 4). Mitotic figures were present in a few cells. A Sudan IV stain for neutral fat revealed many orange-red granules and a positive reaction within the cytoplasm of many cells. A reticulum stain showed the presence of a great deal of reticulum fibers. Sections of the lymph nodes showed no evidence of tumor, but did show mild hyperplasia. Accordingly, a diagnosis of xanthofibroma was made. This diagnosis was confirmed by several pathologists who reviewed the sections, including A. P. Stout, M.D.

Comment

Xanthomas have been divided roughly into two groups: those tumors which are

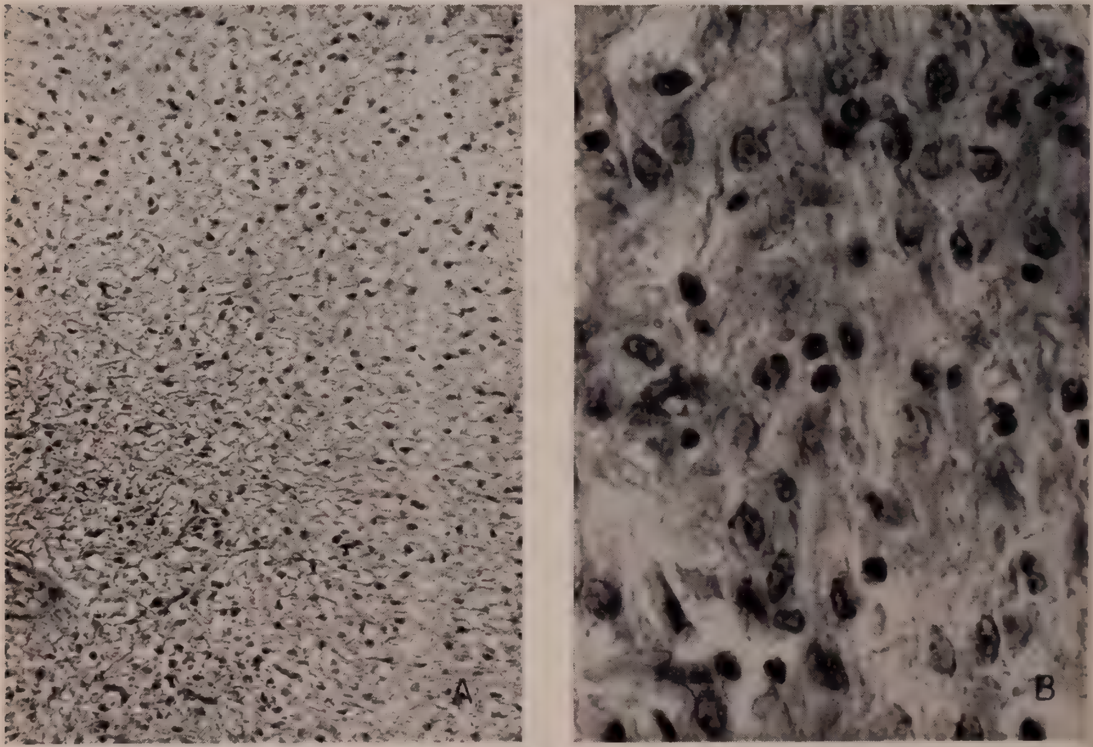

FIGURE 4. (A) Lower-power photomicrograph of tumor made up of polygonal cells with fibrous stroma. (B) High-power photomicrograph of tumor in (A), noting uniformity of cell type. (Hematoxylin and Eosin) Stain)

made up of fibrous tissue called fibroxanthomas and those with little fibrous tissue which are called histiocytomas. They are commonly located in the joints, synovia and tendon sheaths, and soft tissues. However, Brunn[1] and Bates and Hull[2] have described these tumors in the right upper lobe and right middle bronchus, respectively.

Microscopically the benign fibrous xanthomas are of two varieties.[3] One variety is made up of histiocytes that have large irregular rounded to elongated nuclei. The cytoplasm that is sometimes vacuolated has indistinct cell borders. Many of the nuclei are unusually large, and a few are multinucleated. Touton giant cells may also be found. Mitoses of about 5 to 10 per cent may be found in a 50 high-power field.

The other variety of benign fibrous xanthomas has a large number of histiocytes differentiated as fibroblasts, and these fibroblasts contain a varying amount of lipid. These facultative fibroblasts may be arranged in simple bundles which are in the more complex pattern. They rarely become malignant. Fibroxanthomas have been mistaken for fibroma, fibrosarcoma, sclerosing hemangioma, and hemangiopericytoma on gross examination.

Benign tumors of the stomach, especially symptom-producing neoplasms, are uncommon. The most common lesions are myomas, neuromas, adenomyomas, and adenomatous polyps. The commonest benign tumors of the stomach are leiomyomas. They occur in from 16 to 23 per cent of all benign gastric tumors.[4] The occasional myoma protrudes into the lumen of the stomach as a submucosal mass, frequently resulting in ulceration and hemorrhage. Other tumors which have been reported are lipomas, angiomas, and carcinoids. Heterotopic tumors made up of Brunner glands and also pancreatic adenoma made up of pancreatic acinar cells and ducts, but seldom islet cells, have been noted.

Although xanthofibroma of the stomach has apparently not been reported in the literature, Stout[4] has reported a xanthofibroma and 3 histiocytomas of the stomach. There are no apparent systemic disturbances of lipid metabolism associated with such lesions.

Summary

The first report of a benign xanthofibroma of the stomach in an adult female has been presented. Clinical considerations of differential diagnoses of gastric tumors have been briefly discussed.

ACKNOWLEDGMENT. Acknowledgment is gratefully given to D. M. Grayzel, M.D., Department of Pathology, Jewish Hospital of Brooklyn, for his invaluable assistance with this report.

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Human Anthrax

A Case of Malignant Edema with Septicemia

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HUMAN ANTHRAX is a relatively uncommon disease in the United States. About 20 cases a year have been reported, and the incidence is decreasing. The world incidence is estimated at between 20,000 and 100,000 cases per year.[1] Anthrax in man has been termed agricultural anthrax if the disease is contracted by direct contact with infected animals. In the United States the majority of the cases are of industrial anthrax, that is, they are acquired by handling animal products which are contaminated with the resistant spores of Bacillus anthracis. In many factories studies have revealed the contamination rate to be very high.[2] The striking factor always has been the relatively low infection rate.

In our area there were a number of cases reported in the late 1940's. These patients acquired their infection in a carpet factory processing imported wool. The last reported case from this source was six years ago.

The purpose of this paper is to report a sporadic case of cutaneous anthrax that had several unusual features.

Case report

A thirty-four-year-old white, married male was admitted to St. Luke's Hospital, Newburgh, New York, on January 18, 1960. He was in good general health until four days prior to his admission. At that time his wife noted a small hivelike mark just below the inner aspect of his left lower eyelid. The lesion was pink in color with a central red area. It was nonpruritic in character. Forty-eight hours later he noted some swelling in the area. By the following morning the swelling had progressed to involve the periorbital tissues, preventing the patient from opening his eye. He consulted his family physician who gave him an injection of Chlor-Trimeton maleate, feeling that this was an allergic reaction to an insect bite. The swelling progressed rapidly over the next twenty-four hours, forcing the patient's admission to the hospital. There was no pain on motion of his eye. He had no headache except in the area where the edema had become tense. He had no chills or known fever.

The patient's past medical history, review of symptoms, and family history were noncontributory.

The patient was employed cleaning the air conditioners at the United States Military Academy at West Point. The unit that he was working on flushed Hudson River water through pipes as part of the air conditioning process. The maintenance shop in which he worked was formerly a harness room when the building was used as a riding hall. The room since had been brick-floored and mortared.

As a side interest he kept farm animals around his home. At the time of his illness he had a Black Angus calf which had been inspected by the veterinarian and was well. Six months prior to his becoming ill he had six sheep. One of these was ill with a respiratory infection which was not anthrax. These sheep were slaughtered in June, 1959, and the skins and wool were disposed of in a can which he still uses. His neighbor is employed by the carpet company where anthrax had been reported ten years previously.[3]

A physical examination revealed the blood pressure to be 180/110, pulse 120 and regular, respirations 20, and temperature 101.2 F. He was a well-developed, well-nourished, white male who had a markedly swollen face but was in no acute distress. The left eye

TABLE I. Laboratory test findings

Data	Date of Tests Jan. 18	 Jan. 20	 Jan. 26	 Feb. 8
Hemoglobin (Gm. per 100 ml.)	17.2	20.2	10.6	10.2
White blood cells	11,200	35,000	16,700	8,500
Segments	71	91	67	40
Bands	4	. . .	4	1
Lymphocytes	23	9	26	44
Eosinophils	2	. . .	3	4
Monocytes	0	. . .	0	0

was closed with a hard, tense edema which involved the forehead and the left side of the face. This edema was hard and nonpitting. No definite adenopathy could be detected. Beneath the left eye the skin was slightly erythematous and wept a serous fluid. No actual lesion could be seen. The edema had extended into the oral cavity and soft tissues of the oropharynx, deviating the uvula to the left. The conjunctiva of the right eye was clear, and the funduscopic examination showed normal findings. The left eye was closed by the severe edema. The tympanic membranes were clear. The neck was supple, and the trachea was in the midline. There were no palpable glands in the cervical, axillary, inguinal, or epitrochlear areas. The lungs were clear to percussion and auscultation. There was no cardiac enlargement. No murmurs, thrills, or friction rubs were noted. There was no abdominal tenderness, and the spleen and liver were not palpable. The remainder of the physical examination, including the neurologic examination, revealed normal findings.

The laboratory data are summarized in Table I.

A urinalysis showed negative results. The fasting blood sugar on January 21, 1960, was 167 mg. per 100 ml. The blood urea nitrogen was 19.8 mg. per 100 ml., and the serum electrolytes were normal.

The scraping of the skin under the left eye in the area of the reported lesion was positive for B. anthracis (Fig. 1). A blood culture taken on January 18, 1960, was positive for B. anthracis. Both blood and skin cultures taken after the first day revealed no growth (Fig. 2). The isolated organism was lethal for guinea pigs in less than eighteen hours, and the organism was recultured from the spleen, liver, and heart blood.

The history of exposure to farm animals and an abortive early primary lesion led to the initial local culture and blood culture. The massive edema which the patient had led to the early use of antiallergic therapy. For the first twenty-four hours he was given hydrocortisone intravenously, adrenalin, and an antihistamine. A cellulitis was considered, and after the appropriate cultures chloramphenicol therapy was begun. In the next twenty-four hours the edema progressed, and the temperature rose to higher levels. A repeat blood culture and a skin culture were negative. On January 20, 1960, the laboratory reported an organism similar to Bacillus subtilis. Later that day the bacteriologic diagnosis of B. anthracis was made. The organism was found to be resistant to penicillin but sensitive to kanomycin, chloramphenicol, and erythro-

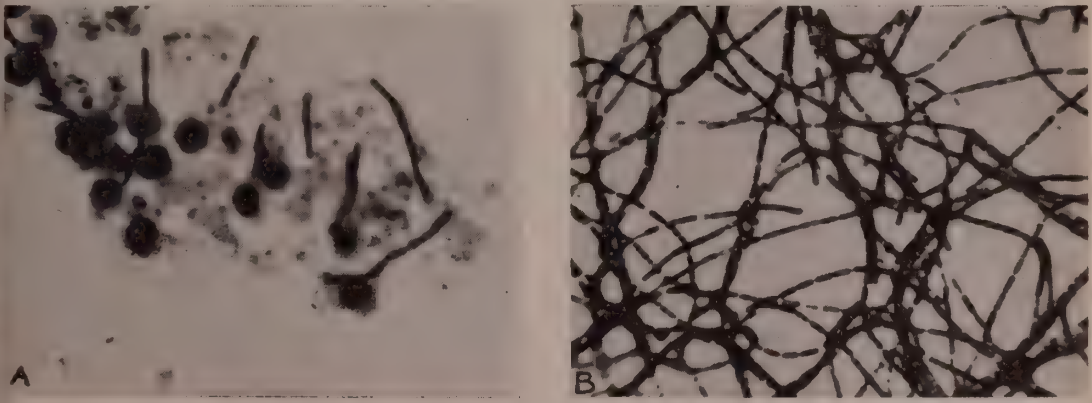

FIGURE 1. (A) Smear from below inner aspect of left eye. (B) Smear from culture.

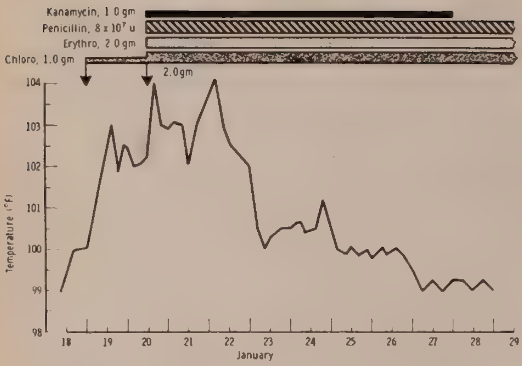

FIGURE 2. Blood and skin cultures.

mycin. The sensitivities were done by the disk method.

Because the clinical status appeared to be deteriorating, massive antibiotic therapy was begun. The patient was given 80,000,000 units of aqueous penicillin, 2 Gm. of erythromycin, and 2 Gm. of chloramphenicol daily by continuous intravenous drip. Kanamycin sulfate, 0.5 Gm., was given intramuscularly twice a day for five days. Over the next forty-eight hours the edema spread, the temperature reached 104 F., and the white blood cell count reached 35,000. On January 21, 1960, airway obstruction developed at the level of the oropharynx, requiring a tracheotomy (Fig. 3). After this the temperature fell by lysis, reaching normal and remaining normal thereafter. The patient received chloramphenicol and erythromycin for twelve days and penicillin in decreasing quantities for eighteen days. The edema gradually subsided (Fig. 4). The tracheotomy was removed, and the patient was discharged from the hospital on February 13, 1960. The edema continued to subside over the next few months (Fig. 5).

Comment

Anthrax is an infectious disease primarily of domestic animals that is contracted by man in his occupational handling of contaminated animals or their byproducts.

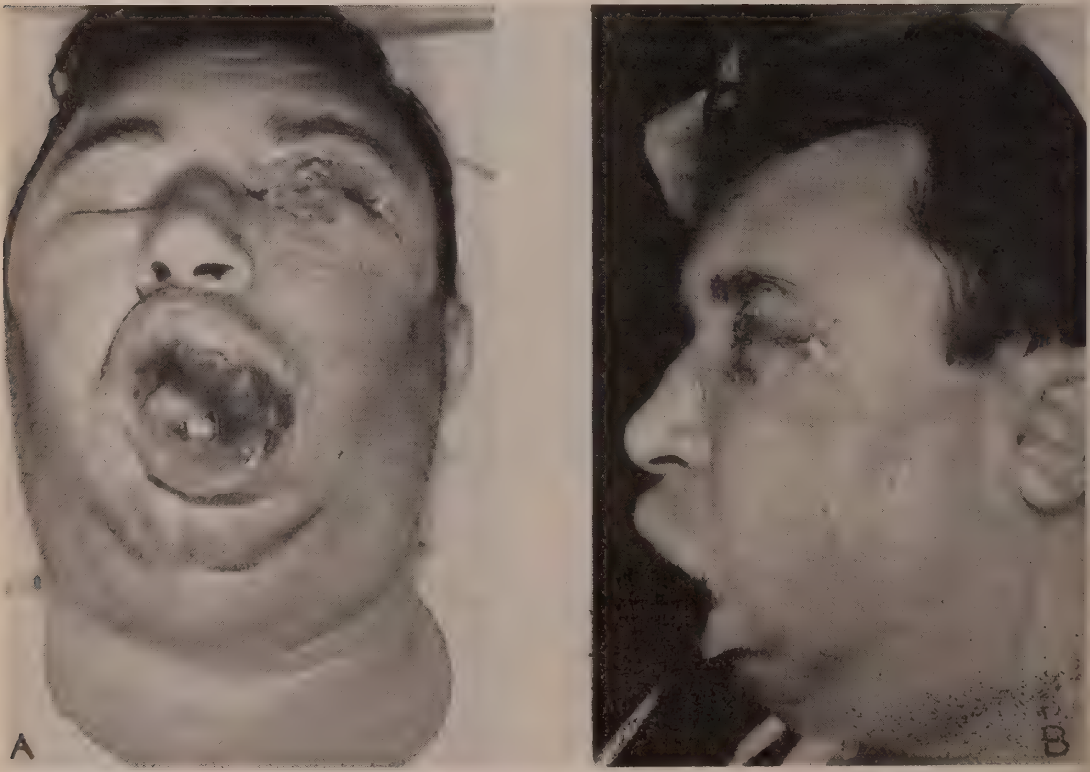

FIGURE 3. Photographs taken January 21, 1960, show (A) edema and lesions in left eye and mouth and (B) facial edema on left.

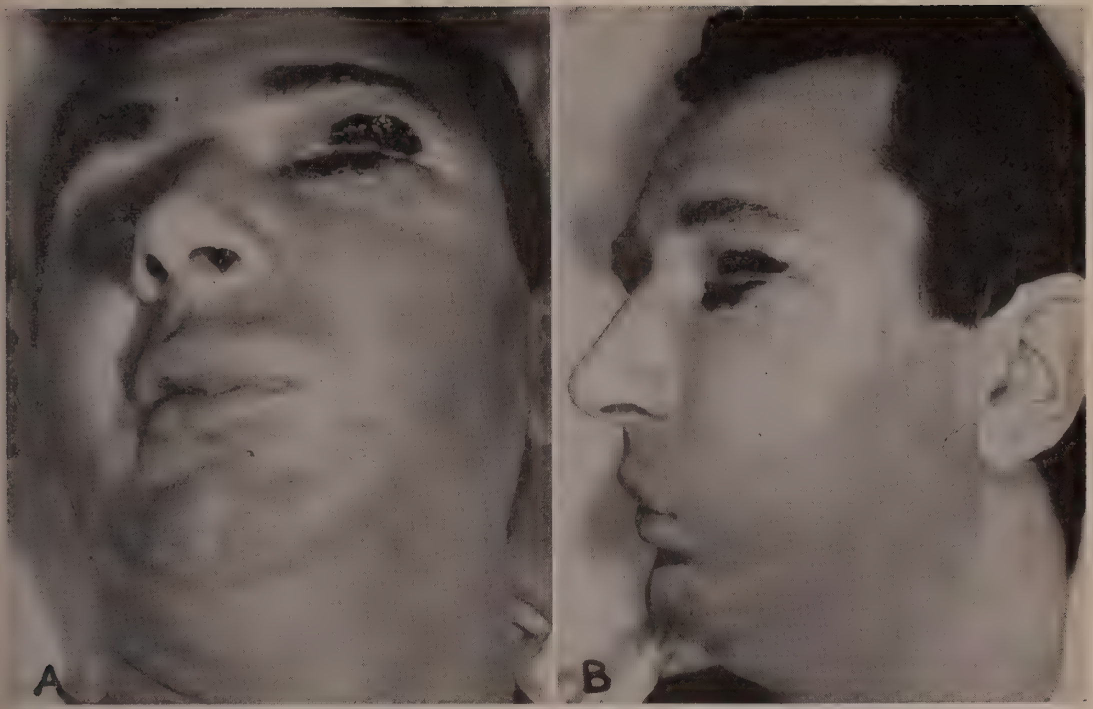

FIGURE 4. (A) Gradual subsiding of edema and lesions and (B) swelling on left side of face. Black areas are secondary to pressure necrosis caused by edema.

The causative organism is a large (1 to 1.5 by 4 to 8 microns), gram-positive, nonmotile, spore-forming organism. B. anthracis grows well on nutrient agar. The colonies, when grown from actively infected tissue under aerobic conditions, are rough and have the appearance of a "medusa head."[4] The method most commonly used to differentiate B. anthracis from B. subtilis, Bacillus megaterium, and Bacillus oereus is the pathogenicity for mice and guinea pigs. As was done in this case, the organism is injected into the animals and then reisolated at autopsy from the spleen, liver, and heart's blood. Other technics that were not used here but can be used for identification are the slow fermentation of salicin, the slow reduction of methylene blue, and the slow liquefaction of gelatin.[4] Supporting evidence is obtained by the patient's sensitivity to 10 units of penicillin per milliliter. The reported resistance in this case was to a disk which contained 2 units of penicillin. More specific identification can be obtained by gamma-bacteriophage typing.[5]

Clinically, cutaneous anthrax is the most common form encountered in the United States. The pulmonary form (wool sorters' disease) has been reported rarely.[6,7] The intestinal form has not been reported in this country. Anthrax meningitis has been reported, but this is secondary to the progressive cutaneous form.[8]

In cutaneous anthrax the spore is inoculated into the host through some break in the skin. Cases have been reported that may have been secondary to insect bites.[2,9,10] Indeed, the organism was isolated from the mouth and inner parts of the fly in an epidemic in South Dakota in 1937.[2] The typical skin lesion develops after an incubation period of from one to three days. A systemic reaction (not present in this case) of headache, myalgias, and arthralgias was present in 90 per cent of the cases reported by Ellingson *et al.*[11] The papule forms and enlarges over the next twenty-four hours. The top of the papule becomes brown in color and is surrounded by an erythematous base. Edema develops that is firm, woody in consistency, and nonpitting. This lesion is differentiated from cellulitis by the absence of pain and the relative absence of erythema. Regional nodes are enlarged but

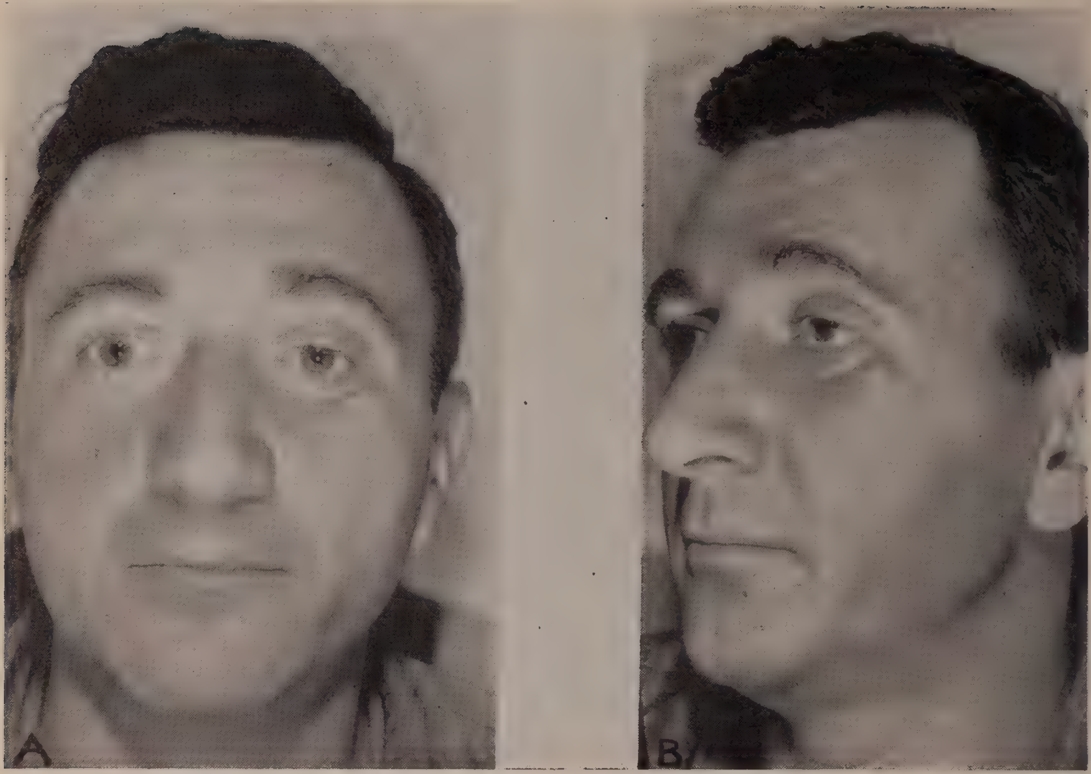

FIGURE 5. (A) Edema subsiding. Scar above and below left eye residual of pressure necrosis. (B) Same findings on left side of face.

may be obscured by the severity of the edema. In the most severe forms in the cervicofacial area the papulovesicular stage may be absent, and the edema may be extreme.[12,13]

The edema may spread during the first twenty-four hours of therapy.[14] In the case presented the edema was so severe as almost to occlude the oropharynx, requiring a tracheotomy to maintain an airway. In this case, at a time when the temperature remained elevated and the edema was spreading, the organism could not be recultured from either the blood or the skin. This reaction may have been secondary to the release of intracellular antigens that were edema-producing.

Because a positive blood culture occurred in association with high fever, leukocytosis, mental confusion, and severe edema, the clinical status appeared critical. Ellingson and his associates[11] pointed out that prior to the advent of antibiotics bacteremia was associated with a grave prognosis. Recently, in a re-evaluation of the pathogenesis of cutaneous anthrax, Nikiforov[15] of the Soviet Union described bacteremia as occurring shortly after inoculation as well as after lymphangitis. The mortality rate of untreated cutaneous anthrax is about 20 per cent. Since the advent of penicillin the mortality rate of the cutaneous form has been given at 0.8 per cent, and in many large series no deaths have been reported.[6] Penicillin is the drug of choice. The lack of sensitivity by the disk method using a disk that contains 2 units of penicillin is not a deterrent to the use of the drug. In mild cases of a simple lesion 600,000 units of procaine penicillin daily for six or seven days has been advocated.[5] Higher doses of aqueous penicillin have been reported effective in more severe cases. The tetracyclines have been reported to be effective in doses of 3 to 4 Gm. per day.[6] The decision to treat with massive antibiotic therapy was dictated by the severity of the illness and the reported resistance of the organism to penicillin.

The resistance of this organism to penicillin brings up a very important question in antibiotic therapy. The use of the in vitro sensitivity test as a guide to therapeusis has rightfully gained a favored position. In interpreting the results of these tests we must reflect on the type of test used and the system we are setting up. The dry disk technic consists in placing a disk impregnated with a given amount of antibiotic (2 units of penicillin) on an agar plate streaked with the bacteria. This rapid, easily performed technic is by its very nature qualitative. The more accurate test, "tube dilution" technic, defines the lowest concentration of antibiotic that will inhibit growth. As was pointed out earlier, most anthrax are susceptible to 10 units per milliliter of penicillin. Surrounding the disk there may be far less than 10 units per milliliter of penicillin. It must be remembered that many factors existing in an in vivo system are not considered in vitro. Tending to decrease the effectiveness of antibacterial agents in vivo are such things as protein binding, accessibility of the organism, and so forth, while tending to assist the destruction of the pathogen are the host's own immune mechanisms. Antibiotics that will not prevent growth in the test tube may be effective systemically and vice versa.[16] One cannot say, therefore, that because this anthrax bacillus was resistant on one disk-sensitivity test that it was truly a resistant organism.

Summary

A case of a patient with severe cutaneous anthrax is reported. The case is of interest from several points of view: First, no history of contact or direct exposure was found, although several possibilities presented themselves. Second, no primary lesion developed, and the symptoms were those of malignant edema. Third, septicemia was present on admission. Last, the organism was reported resistant to penicillin by the disk method.

ACKNOWLEDGMENT. I would like to thank Lewis Resnikoff, M.D., of Pine Bush, New York, for referring the patient. Torrence Payne, M.D., of the Department of Pathology, St. Luke's Hospital, Newburgh, took the pictures, and it was in his laboratory that Mrs. Robert Devitt did the bacteriology work leading to the definitive diagnosis. Paul Traub, M.D., did the tracheotomy. John A. Degen, Jr., M.D., of the New York State Department of Health did the epidemiologic survey.

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Special Articles

Proceedings of the Pediatric Advisory Committee Meeting*

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From the City of New York Department of Health

A MEETING of the Pediatric Advisory Committee of the City of New York Department of Health was held on February 20, 1962, with Samuel Karelitz, M.D., presiding as Chairman.

Sex ratio of fetal deaths

Carl Erhardt, Director of the Bureau of Statistics, reported on the sex ratio of fetal deaths, pointing out that for many years the Department of Health has observed from reported fetal deaths that the sex ratio decreases from a high of over 200 males to 100 females to the usual ratio of 105 or 106 males to 100 females which is observed at term. Different reporting methods have been tried to eliminate possible artifacts. Nevertheless, the high ratios among early fetal deaths persist. These observations from the routine reports by physicians are now being confirmed by nuclear chromatin studies both here and abroad. Further investigations will be made to ascertain the validity of the information on fetal death certificates.

Pediatric policies in the State Aid Program

Margaret A. Losty explained pediatric policies in the State Aid Program. The Department of Health administers this State Aid Program which provides funds for families with miscellaneous pediatric problems, primarily congenital in origin, which are amenable to surgical therapy. The policies are established by the State of New York Department of Health. The Bureau for Handicapped Children in New York City may influence policies or attain change in policies through the advice of various advisory committees. Most of the emphasis to date has been on the various specialty services, for example, orthopedics, epilepsy, cardiac, and so forth.

The problem presented at the present meeting is related to the inclusion of hernias. Miriam Lending, M.D., discussed the current policies, which are as follows: Inguinal hernias are eligible for care under the program only in children under three years of age. They are eligible in older children only if there is also a hydrocele and surgery is necessary to correct the hydrocele. Umbilical hernias had been routinely eligible in persons up to twenty-one years of age. However, recently the policy has been altered by the State Department of Health as follows: Umbilical hernias are eligible only if there is a history of transient incarceration or if there is mesentery or gut in the hernia.

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* The membership of the Pediatric Advisory Committee includes the following: Samuel Karelitz, M.D., Committee Chairman, Chief, Pediatrics, Long Island Jewish Hospital; Edward D. Curnen, M.D., Professor and Chairman, Department of Pediatrics, Columbia-Presbyterian Medical Center; Joseph Dancis, M.D., Professor of Pediatrics, New York University Medical Center, New York University School of Medicine; Lewis Fraad, M.D., Professor of Child Health, Department of Pediatrics, Albert Einstein College of Medicine, Bronx Municipal Hospital Center; Horace L. Hodes, M.D., Pediatrician-in-Chief, The Mount Sinai Hospital; William S. Langford, M.D., Director of Children's Psychiatric Services, Presbyterian Hospital; Jonathan T. Lanman, M.D., Professor and Chairman, Department of Pediatrics, State University of New York Downstate Medical Center, Kings County Hospital; Samuel Z. Levine, M.D., Department of Pediatrics, New York Hospital; Wallace M. McCrory, M.D., Pediatrician-in-Chief, New York Hospital; Rustin McIntosh, M.D., Special Consultant, City of New York Department of Health; Charles D. May, M.D., Professor of Pediatrics, New York University School of Medicine, Bellevue Hospital; Charles O'Regan, M.D., Director of Pediatrics, Lenox Hill Hospital; Joseph B. Pincus, M.D., Director of Pediatrics, Jewish Hospital of Brooklyn; Carl Smith, M.D., Professor of Clinical Pediatrics, Cornell University Medical College, New York Hospital; Oscar McClellan Race, M.D., Attending Pediatrician, State Island Hospital; Lawrence Slobody, M.D., Chairman and Professor, Department of Pediatrics, Flower and Fifth Avenue Hospitals; and Blandina Worcester, M.D., Director of Pediatrics, New York Infirmary, New York University Medical Center.

In various discussions between the Bureau of Handicapped children and the State Department of Health, the State indicated that assistance from the Advisory Committee in establishing a definite policy would be helpful. Rustin McIntosh, M.D., suggested that this information should come from pediatric surgeons. The members of the Pediatric Advisory Committee indicated that they would seek advice from the qualified pediatric surgeons in their institutions. This will be obtained, and then final policies established. Dr. Karelitz suggested that the committee again recommend that all general pediatric conditions be included, particularly diseases such as nephrosis. Miss Losty indicated that there are currently attempts to change the legislation in New York State. The present law is essentially a broad one but has been interpreted very tightly by the Comptroller.

Testing for phenylketonuria in the newborn infant

Harold Jacobziner, M.D., related that until very recently the ferric chloride test in its various modifications has been the universal screening test for detecting phenylketonuria in spite of its limitations such as its failure to obtain a positive reaction until about six weeks following birth and when blood phenylalanine levels are below 10 mg. per 100 ml., although brain damage may have already begun by this time.

New York City has been utilizing the diaper test since 1958 for examining all newly registered infants and preschool children under two years of age. Over 100,000 children have thus been tested in the child health stations, but no cases with positive reactions have been identified thus far. This is probably owing to the fact that a large proportion of the population under supervision is Negro and Puerto Rican in whom the incidence of phenylketonuria is very rare. Testing in the child health stations will continue.

Recently Robert Guthrie, M.D., Research Associate and Professor of Pediatrics, University of Buffalo School of Medicine, developed a simplified method for detecting elevated blood phenylalanine levels by the inhibition assay method by employing small filter paper disks impregnated with the patient's blood serum on an agar surface. A small amount of fresh blood is obtained from the infant's heel by skin puncture and applied immediately to a piece of thick filter paper. The papers are steamed to coagulate blood proteins, and a disk is punched out from each blood spot. The disks are marked and placed in rows on surfaces of large agar dishes.

Five control blood paper disks are prepared on filter paper with normal blood to which 2, 4, 8, 12, and 20 mg. per 100 ml. of phenylalanine have been added. After overnight incubation, the zones of growth surrounding the paper disks are observed. Any response comparable to that of either the 8, 12, or 20 mg. per 100 ml. phenylalanine is considered positive but should be retested and confirmed by the quantitative blood assay for phenylalanine.

According to Dr. Guthrie, one trained technician could test about 200 specimens daily.

What is actually measured in this screening test is the growth of cultures of bacteria. Bacteria (Bacillus subtilis) are mixed with thienylalanine, which normally inhibits their growth. To this mixture is added the patient's blood specimen. It has been found previously that bacterial growth is prevented in the presence of B-2-thienylalanine. This growth inhibition, however, will be prevented in the presence of proline, phenylalanine, phenylpyruvic acid, and phenyl-lactic acid. Thus, if the infant's blood serves as an antagonist to the inhibitor and growth progresses, the test shows positive results since phenylalanine acts as an antagonist to the inhibitor. This simple blood phenylalanine screening test may be done in the first week of life as early as the fifth day, and it is considered by Dr. Guthrie as a reliable screening test for newborn infants, although it yields a high percentage of false positive results (50 per cent) and hence requires confirmation by the quantitative method.

The Guthrie simplified screening test was evaluated recently in determining blood phenylalanine levels in 16 patients during phenylalanine diet treatment at the Buffalo State Hospital and more recently at the Newark State School, Newark, New York, where 3,118 blood filter paper specimens were obtained from residents at that school. The same population was tested with the ferric chloride test. At least 2 confirmed cases of phenylketonuria were detected by the Guthrie method which were missed by the ferric chloride test, and another was detected by the Guthrie method, although the patient gave negative reactions to three tests by the urine ferric chloride method. All the cases which gave positive reactions by the ferric chloride test were also identified by the Guthrie test.

The Children's Bureau has become interested in this test, and with its aid many laboratories and hospitals will participate in a national program to test 400,000 infants during a twelve-month period in newborn nurseries. Dr. Jacobziner met Dr. Guthrie last November and indicated a willingness to participate in this study, although a communication from Dr. Guthrie on February 2, 1962, stated that the Children's Bureau had yet to take any definite action on this proposal. Dr. Jacobziner requested that the Committee give its approval for the Department of Health to request certain selected hospitals to participate on a voluntary basis in this national screening testing program.

Wallace W. McCrory, M.D., moved "that the Pediatric Advisory Committee indicate its approval for the Department of Health to approach the heads of the departments of pediatrics in certain voluntary and municipal hospitals to enlist their voluntary cooperation in a projected study to test the usefulness of routine measurements of blood levels of phenylalanine in newborns as a case-finding device of value in the control of phenylketonuria." The motion was seconded by Joseph B. Pincus, M.D.

In the discussion which preceded the vote on the motion, Joseph Dancis, M.D., raised an important point. He felt that the information about the reliability of the test and its specificity should be made available to each of the department heads when they are requested to participate. The recommendation for the Department of Health to participate in the national screening program was approved by the Committee.

Prevention of staphylococcus infections in nurseries for newborn infants

Dr. Jacobziner reported on the results of the studies at Palo Alto-Stanford Hospital Center and the Yale-New Haven Medical Center as published in the December 14, 1961, issue of the *New England Journal of Medicine*.[1,2] Both papers highlighted the hypothesis that proper antiseptic skin care is perhaps the most important single factor in the prevention of staphylococcal nasal colonization in newborn infants.

The technic used is as follows: All infants are washed with a 3 per cent solution of hexachlorophene in the delivery room as soon after birth as possible, the skin and cord being washed thoroughly. All visible blood is first washed off. The skin is not dried. After the initial washing the infant is wrapped in a sterile double wrapper. The outer wrapper is retained in the delivery room. On admission to the nursery, the infant is again washed thoroughly with particular care given to the cord and umbilicus.

A thorough wash is given daily thereafter with special attention being paid to the umbilicus, especially as the cord dries, to cleanse the trough created by the skin cord margin. A sterile cotton-tipped applicator is used for this purpose.

Physicians and nurses also wash their hands in such a solution before handling each child. No other changes in personnel, housekeeping, or other technics have been instituted. Nasal and umbilical cultures were taken at the time of discharge. During the twenty-month study period at Stanford, nasal colonization with coagulase-positive staphylococci in newborn infants was virtually eliminated by means of skin care alone. Coliform microorganism and coagulase-negative staphylococci were readily recoverable from the infants. The incidence of infant staphylococcal morbidity was negligible. In a personal communication S. J. Yaffe, M.D., of Stanford indicated that follow-up examinations, which were felt to be fairly good because of the close rapport with the physicians in the surrounding community, revealed very few infections that could be attributed to coagulase-positive staphylococci. The major criticism of the report, however, is that it lacks a suitable set of control observations. The study at Yale did include a control group.

Using the same technic as at Stanford, the Yale investigators found a 51 per cent over-all colonization incidence in the control group of 500 unwashed infants as compared with an incidence of 3 per cent in 965 infants in the washed group. The investigators feel that the prevention of skin and cord colonization by means of antiseptic skin care could virtually eliminate infant nasal colonization with coagulase-positive staphylococci. They also feel that if such colonization could be prevented, maternal mastitis attributable to hospital-acquired staphylococci should disappear.

In view of the simplicity of the technic and the excellent results reported, Dr. Jacobziner inquired whether or not the Committee felt that a recommendation should be made to maternity and newborn services in New York City to institute a similar regimen.

After a brief discussion, Dr. McIntosh suggested that in view of the widely differing staphylococcal morbidity in individual institutions, the matter of control be left to the several hospitals. No action was taken.

New business

For the information of the Committee, Dr. Jacobziner demonstrated a new record, "Permanent Record of Immunization and Tests," which was prepared recently by the Department of Health at the request of the Special Committee on Child Welfare of the Medical Society of the County of New York. This card will be mailed together with the birth certificate whenever a child is born. The card provides space for the recording of dates and types of immunizations given, other tests, illnesses, anomalies and handicapping conditions, operations, defects of special senses, and special tests. The mother will be requested to keep it as a permanent record and to bring it with her whenever a visit is made to a doctor.

This card will also be made available to pediatric clinics where the medical information could be recorded and given to the parent of the child.

The Committee felt that it was a move in the right direction and would probably eliminate duplication of effort.

Carl Smith, M.D., suggested that in addition the Department of Health ought to circularize a schedule of immunizations for the guidance of physicians. Dr. Jacobziner indicated that this has been done on periodic occasions through the various county medical society bulletins.

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The Principle of Parsimony in Medical Treatment

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THE WRITER[1] previously has stressed the importance of the principle of parsimony in medical diagnosis. The purpose here is to point out its equal importance in medical treatment.

First formulated by William of Occam, a fourteenth century Franciscan monk, the principle of parsimony sometimes is referred to as "Occam's razor" because it shaves away the unnecessary. Occam stated his principle thus: "It is vain to do with more what can be done with fewer."

The physician who applies the principle in diagnosis places his main reliance in sound and tested tradition and in the cumulative knowledge and wisdom of medical science. This means that he always starts with a well-taken history and a careful physical examination, both critically evaluated. Only if these fail to reveal the diagnosis should laboratory tests be undertaken, and even then the tests should be held to a minimum.

Overtreatment

In medical treatment a similar restraint should be exercised, but examples of the overtreatment of patients are not hard to find. Vitamins, for example, are widely consumed in unnecessary quantities, at times on the advice of physicians. The reason behind this extraordinary consumption may be that if a little is good, a great deal should be much better.

The practice is not only wasteful but often positively harmful. The prolonged administration of vitamin A, for instance, may increase intracranial pressure with papilledema (pseudotumor cerebri or hypertensive meningeal hydrops).[2]

At times the prescription of vitamins or of other types of medication is in response to the patient's demand or merely to his manifest expectation of tangibly evident treatment by the physician. But using medication for a simple tension headache, for example, is a questionable practice when, as is often true, relaxation may be induced by such simple measures as swimming or other forms of exercise or recreation.

Many patients come to us in desperate need of nothing more than encouragement, reassurance, and hope. In such cases patient and doctor alike get more satisfaction if the fears can be quieted and the anguish relieved by sincere kindness and sympathy or by a simple explanation of disease that displaces despair and leaves hope in its place. Giving a pill or a hypodermic needle instead and then rushing off is not an adequate substitute for such treatment. Hit-and-run therapy of this kind is not in the best tradition of medicine. It contributes little, in Francis Bacon's phrase, to "the benefit and use of life," which is the object of good medicine.

Medication given out of sheer good will and blind hope is no better. An illustration of its fruitlessness occurred recently. The writer was asked to see a patient suffering from headache and papilledema. A pneumoencephalogram and cerebral angiography showed normal findings. A brain tumor thereby was excluded as the cause of the illness, which probably was due to hypertensive meningeal hydrops (pseudotumor cerebri). Usually this ailment tends to subside without special treatment, although at times repeated lumbar puncture is used to reduce the intracranial hypertension. Occasionally, subtemporal decompression is necessary if papilledema advances.

In this case, however, the papilledema was at a standstill, the visual acuity was essentially unimpaired, and the headache

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had subsided, although the spinal fluid pressure remained elevated at 300 to 350 mm. of water. The physician in charge of the case pressed for the use of cortisone "to see if it would help."

Suppose cortisone were used in such a case. It would be difficult to evaluate the therapy in a patient who showed improvement before it began. Even if the intracranial hypertension lessened after cortisone was administered, it would be hard to tell how much credit to give the drug, because the ailment often improves and disappears spontaneously. A physician interested in determining the effect of cortisone on intracranial pressure would be better advised to make a controlled laboratory investigation than to rely on uncontrolled clinical observation. "The error of the omitted control," wrote Cannon,[3] "is a frequent and inexcusable scientific demeanor"—it accounts for the fact that pharmacopeias are loaded with so-called cures.

A striking illustration of over-treatment occurred not long ago when a child was admitted to a hospital after a head injury. The boy, who had sustained a compound depressed skull fracture, had been unconscious momentarily. The pulse was rather rapid and the blood pressure somewhat fluctuating but not alarming.

The admitting physician plunged into a course of lively treatment, in which he inserted tubes into most of the patient's orifices. One measure was a tracheotomy, clearly necessary in some cases but used much too often when all that is necessary is a conscientious nurse who is trained to apply suction to remove nasopharyngeal secretions and maintain an open airway. Other measures were to pass a stomach tube for feeding and the introduction of a urethral catheter.

When the neurosurgeon examined the patient he humanely ordered the removal of the battery of tubes, elevated the depressed skull fracture, and repaired the wound. The operation was in the evening. The next morning the patient ate like a normally hungry boy and made an uneventful recovery, but he had both youth and good luck working for him. The unnecessary procedures he had been subjected to might have resulted in infection. Moreover, if a patient is seriously ill and has received extensive treatment, one more procedure, surgical or not, may be the straw that breaks the back of his resistance. It is bad enough in such a case when the procedure is necessary. When it is unnecessary, it is unforgivable.

Most patients suffering from intervertebral disk syndromes get well without surgical therapy. Given time, these patients get either temporary or permanent relief from bed rest, exercises, and, if necessary, measures to control their weight. If the pain is not too great, a policy of watchful waiting may be preferable to drastic therapy.

Delay

Waiting too long, of course, may be harmful. For instance, to wait until foot drop appears in a patient suffering from a lumbar herniated intervertebral disk may jeopardize his chance of recovery. Many patients with complete foot drop fail to recover from their paralysis even after the removal of the disk. On the other hand, removing the disk before the foot drop has become complete invariably is followed by recovery, often within a few days or weeks. An operation in such cases obviously is necessary and desirable, delay undesirable.

Too great a delay also was undesirable in the following poignant case of a herniated intervertebral disk in the cervical region. A middle-aged man was admitted to the hospital one morning with a history of Landry's ascending paralysis of about ten hours duration. For some months the patient had had neck pain radiating into his shoulder. The night before his admission he had complained of weakness in his lower limbs, then within a few hours, of weakness in his upper limbs. On admission he was quadriplegic and had entirely lost sensory and motor function of all his extremities. He died within an hour of his admission. An autopsy revealed an intervertebral disk extruded from between the fourth and fifth cervical vertebrae. The piece of fibrocartilage lay under the fourth cervical vertebra spinal cord segment which had been compressed severely.

Here, again, an operation was urgently necessary and therefore desirable. If weakness of a considerable degree develops in patients with herniated disks, simple conservative treatment should end, and an operation should be done. It is important to emphasize this here, lest the general caveat against purposeless and unnecessary operations and medication be misinterpreted. The point is that the physician always must be guided by practical judgment, sound reason, and experience. He should hold Occam's razor in his hand at all times but not the surgeon's knife or the pharmacopeia.

When he must use the knife or the pharmacopeia he should use it as sparingly as possible in the circumstances. Experience has shown, for example, that patients suffering from malignant brain tumors, such as glioblastoma multiforme of the cerebrum and medulloblastoma of the cerebellum, do as well after the removal of small amounts of tumor (essentially just enough for the histologic diagnosis) followed by deep roentgenotherapy as they do after extensive tumor removals. Why put these patients, then, to the greater ordeal and risk of prolonged and unnecessary operation?

Comment

In view of the writer's special medical interest, it is understandable that his examples of violations of the principle of parsimony in treatment are all from the field of neurosurgery. The final example is from the same field.

Physicians often ask whether or not a subdural tap should be done in an infant who is not doing well and who shows slight fullness of the anterior fontanelle. The writer has always been reluctant to do a subdural tap unless there is fairly clear-cut evidence of hydrocephalus or of a subdural hematoma. Doing a subdural tap in an infant with a normally narrow subdural space risks having the needle traverse the space and perforate the cortex. Such a cortical perforation, with or without hemorrhage, could lay the cicatricial basis for later epilepsy.

Therefore, there is good and sufficient reason here for using Occam's razor instead of the needle. But such neurosurgical cases as this one and the others that have been given doubtless can be duplicated in all fields of medical practice, and the principle of parsimony is equally applicable to them all, as well as to the preparation of reports for publication. No field holds the patent on Occam's razor, and there is no restriction on its use. It has another virtue, also; it never grows dull with use, but gets sharper and sharper with every shave.

References

1. Tarlov, I. M.: The principle of parsimony in medical practice, NEW YORK STATE J. MED. **59:** 2050 (May 15) 1959.

2. Morrice, G., Jr., Havener, W. H., and Kapetansky, F.: Vitamin A intoxication as a cause of pseudotumor cerebri, J.A.M.A. **173:** 1802 (Aug. 20) 1959.

3. Cannon, W.: The Way of an Investigator, New York, W. W. Norton Company, Inc., 1945, p. 122.

A matter of taste

Among the stories the French like to tell American visitors is the one about the waiter on trial for killing a customer. The victim—naturally an American—had ordered a steak. He and the waiter had had an earnest discussion about how it was to be prepared. The proprietor himself, who was also the chef, had come out of the kitchen with a tray of prime beef, from which the American had selected a well-aged Chateaubriand. The chef had bowed and departed. A short time thereafter the waiter proudly served the steak. The American looked at it, nodded approvingly and asked for some ketchup. "And then . . .?" the judge prompted. "Yes, Your Honor," the waiter said, "I slew him." Verdict, justifiable homicide.—*The New York Times, May 8, 1962*

Necrology

John Hans Benda, M.D., of Wassaic, died on March 29 at the age of sixty-nine. Dr. Benda received his medical degree from the University of Wurzburg in 1920. He was supervising psychiatrist at Wassaic State School. Dr. Benda was a Member of the American Psychiatric Association and belonged also to the American Association on Mental Deficiency.

E. Leo Berger, M.D., of Brooklyn, died on March 25 at the age of seventy-five. Dr. Berger graduated in 1909 from Cornell University Medical College. He was a consulting otolaryngologist at Jewish Hospital of Brooklyn. Dr. Berger was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Otorhinologic Society for Plastic Surgery, the Kings County Medical Society, and the Medical Society of the State of New York.

Frank Gibson Calder, M.D., of Johnstown, died on April 2 at Glynn Memorial Hospital, Brunswick, Georgia, at the age of seventy-seven. Dr. Calder graduated in 1910 from Albany Medical College and interned at Albany Hospital. He was an attending surgeon at Nathan Littauer Hospital in Gloversville and had been Fulton County coroner since 1933. Dr. Calder was a member of the Fulton County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas W. Connors, M.D., of Buffalo, died on January 18 at the age of eighty-six. Dr. Connors graduated in 1905 from the University of Buffalo School of Medicine.

Edward Thomas Dowling, M.D., of Central Islip, died on February 25 at his home at the age of fifty-six. Dr. Dowling graduated in 1930 from Georgetown University School of Medicine. He was on the medical staff of Southside Hospital, Bay Shore. Dr. Dowling was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Jacob Epstein, M.D., of Rochester, died on April 2 at Strong Memorial Hospital at the age of sixty-six. Dr. Epstein graduated in 1919 from Albany Medical College and interned at Albany, Lying-In, and Sloane Hospitals. He was an associate attending obstetrician and gynecologist at Strong Memorial Hospital, an attending obstetrician and gynecologist at Highland Hospital of Rochester, and a consulting obstetrician and gynecologist at Rochester General and Genesee Hospitals. Dr. Epstein was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Obstetricians and Gynecologists, and a member of the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John G. Gordon, M.D., of Ovid, died on April 10 at Strong Memorial Hospital, Rochester, at the age of seventy-nine. Dr. Gordon graduated in 1908 from Syracuse University College of Medicine and had practiced in Ovid for fifty-four years until his recent retirement. He was a member of the Seneca County Medical Society and the Medical Society of the State of New York.

Max Gruenthal, M.D., of New York City, died on April 28 at the age of seventy. Dr. Gruenthal received his medical degree from the University of Berlin in 1916. He was a Diplomate of the American Board of Psychiatry and Neurology, a Fellow of the American Psychiatric Association, and a member of the American Academy of Neurology, the Association for the Advancement of Psychotherapy, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Jacob G. Jacobson, M.D., of New York City, died on April 29 at French Hospital at the age of seventy-five. Dr. Jacobson received his medical degree from the University of Paris in 1919. He was the discoverer of a therapeutic agent known as Jacobson's solution. Dr. Jacobson was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Pincus Marlowe, M.D., of the Bronx, died on March 18 at the age of seventy-eight. Dr. Marlowe graduated in 1907 from the Eclectic Medical College of the City of New York. He was a member of the Bronx County Medical Society, the Medical Society of the State of

New York, and the American Medical Association.

Frank Baldwin Maynard, M.D., of Rochester, died on April 8 at the age of ninety. Dr. Maynard graduated in 1896 from Albany Medical College. Semiretired in September, 1961, Dr. Maynard was a member of the Rochester Academy of Medicine, the Rochester Pathological Society, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas Mathew O'Grady, M.D., of Woodside, died on January 1 at the age of forty. Dr. O'Grady graduated in 1946 from New York Medical College and interned at Kings County Hospital Center and Presbyterian and Francis Delafield Hospitals. Dr. O'Grady was a Diplomate of the American Board of Radiology, a Member of the American College of Radiology, and belonged also to the Kings County Medical Society and the Medical Society of the State of New York.

Deming Sarles Payne, M.D., of Liberty, died on March 15 while playing golf in Fort Lauderdale, Florida, at the age of fifty-seven. Dr. Payne graduated in 1931 from the University of Buffalo School of Medicine. He was attending physician at Liberty Maimonides Hospital. President-elect of the Sullivan County Medical Society, Dr. Payne was a member also of the Medical Society of the State of New York and the American Medical Association.

Frederick Redlich, M.D., of Olean, died on March 16 at his home at the age of sixty-eight. Dr. Redlich received his medical degree from the University of Vienna in 1919. He was an attending cardiologist at St. Francis Hospital and an honorary attending cardiologist at Olean General Hospital. Dr. Redlich was a member of the Cattaraugus County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Paul William Rogers, M.D., of New York City, died on November 18, 1961, at the age of thirty-nine. Dr. Rogers graduated in 1946 from New York University Medical College. He was a Member of the American Psychiatric Association and belonged also to the New York County Medical Society and the Medical Society of the State of New York.

Julius Rothschild, M.D., of New York City, died on March 15 at the age of eighty. Dr. Rothschild received his medical degree from the University of Munich in 1906. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Bertram Sachs, M.D., of New York City, died on May 7 at his home at the age of seventy-seven. Dr. Sachs graduated in 1906 from New York University and Bellevue Hospital Medical College and interned at Sydenham Hospital. He was a consulting pediatrician at Grand Central Hospital. Dr. Sachs was a member of the Association of Military Surgeons of the United States, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Albert Schweich, M.D., of the Bronx and Hastings-on-Hudson, died on April 28 at Montefiore Hospital at the age of fifty-six. Dr. Schweich received his medical degree from the University of Freiburg in 1929. He was an associate attending physician at Jewish Memorial Hospital and an adjunct physician in neoplastic diseases at Montefiore Hospital. Dr. Schweich was a Diplomate of the American Board of Internal Medicine and a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Stork, M.D., of Poughquag, died on May 5 at the age of eighty-three. Dr. Stork graduated in 1903 from Columbia University College of Physicians and Surgeons. Retired, he had formerly been chief surgeon at Norwegian Lutheran Deaconess Home and Hospital (Brooklyn). Dr. Stork was a Fellow of the American College of Surgeons and a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Roger Surber, M.D., of New York City, died on January 13 at the age of fifty-six. Dr. Surber graduated in 1934 from Indiana University School of Medicine and interned at St. Luke's and Manhattan Eye, Ear and Throat Hospitals. He was an associate attending surgeon in otolaryngology at Manhattan Eye, Ear and Throat and St. Clare's Hospitals. Dr. Surber was a Diplomate of the American Board of Otolaryngology and a member of the American Academy of Ophthalmology and Otolaryngology, the American Otorhinologic Society for Plastic Surgery, the New York Rhino-Otolaryngological Society, the New York Academy of Medicine, the New York County Medical Society, and the Medical Society of the State of New York.

Nelly Szilagyi, M.D., of New York City, died on March 31 at University Hospital at the age of sixty-seven. Dr. Szilagyi received her medical degree from the University of Vienna in 1923. She was a research associate cardiologist at the Brooklyn Hebrew Home and Hospital for the Aged.

Benjamin M. Volk, M.D., of Albany, died on April 4 at his home at the age of sixty. Dr. Volk graduated in 1929 from Albany Medical College. He was an attending otolaryngologist at Child's and Albany Hospitals and Albany Hospital Outpatient Department, a consulting otolaryngologist at Veterans Administration Hospital, and an associate professor at Albany Medical College. Dr. Volk was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the American Laryngological, Rhinological and Otological Society, the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Lester David Volk, M.D., of Brooklyn, died on March 31 at his home at the age of seventy-seven. Dr. Volk graduated in 1906 from Long Island College Hospital Medical School. He was a practicing lawyer and a former Republican representative from the Tenth Congressional District of Brooklyn.

Jerome Weiss, M.D., of Brooklyn, died on May 1 at Adelphi Hospital at the age of sixty-four. Dr. Weiss graduated in 1921 from New York University and Bellevue Hospital Medical College. He was a consultant physician in physical medicine and rehabilitation at the Hospital for Joint Diseases and Long Island College Hospital and an attending physician in physical medicine and rehabilitation at Beth Abraham Home (Bronx). Dr. Weiss was a Diplomate of the American Board of Physical Medicine and Rehabilitation and a member of the American Congress of Physical Medical and Rehabilitation, the American Academy of Physical Medicine and Rehabilitation, the New York Society for Physical Medicine and Rehabilitation, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Abraham Zies, M.D., of the Bronx, died on February 8 at the age of forty-seven. Dr. Zies graduated in 1941 from the Medical College of Virginia. He was an assistant attending roentgenologist at Metropolitan Hospital, executive director of roentgenology at Bird S. Coler Memorial Hospital and Home, and an attending radiologist at the Home and Hospital of the Daughters of Jacob. Dr. Zies was a Diplomate of the American Board of Radiology (Diagnostic Roentgenology and Therapeutic Radiology), a Member of the American College of Radiology, and belonged also to the American Geriatrics Society, the Radiological Society of New York State, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical Meetings

American Geriatrics Society

The nineteenth annual meeting of the American Geriatrics Society will be held June 18 through 20 at the Palmer House in Chicago.

A special session for laymen, "Partnership for Progress in Geriatrics" will open the two-day meeting. Major areas for discussion will be geriatric medicine, geriatric surgery, geriatric cancer control, and geriatric socioeconomics.

All physicians are invited to attend. There is no registration charge. For information contact: Mr. Henry Blanchard, Executive Director, American Geriatrics Society, 10 Columbus Circle, New York 19, New York.

American Cancer Society

The scientific session of the American Cancer Society will be held at the Biltmore Hotel in New York City on October 22 and 23. The title of the program is "The Clinical Impact of a Quarter Century of Cancer Research."

For further information write to: Director of Professional Education, American Cancer Society, 521 West 57th Street, New York 19, New York.

Abstracts

Howland, W. S., Schweizer, O., and La Due, J. S.: Evaluation of routine postoperative electrocardiography, New York State J. Med. **62:** 1941 (June 15) 1962.

Routine postoperative electrocardiograms were taken on 782 patients, of whom 321 (41 per cent) had normal recordings. The electrocardiograms of the remaining 461 patients revealed either abnormalities of rate, rhythm, or conduction or myocardial changes suggestive of disease. Of these, 56 would have been detected by applying criteria representing the major cardiovascular problems encountered in the recovery room, 48 were detected by a preoperative electrocardiogram, and 167 were not detected prior to operation. However, in all but 2 of the latter the abnormalities of the electrocardiogram resulted from chronic heart disease. It appears that changes that occur as the result of operative and postoperative medical and physiologic phenomena can be detected by recording a postoperative electrocardiogram on patients showing marked bradycardia or arrhythmia, sudden unexplained tachycardia, hypoxia, or hypotension not amenable to the restoration of circulating fluid volume. However, a routine preoperative electrocardiogram is indicated for every patient scheduled for operation.

Aroesty, J. M., and Furth, F. W.: Infection and chronic lymphocytic leukemia; a review of 61 cases, New York State J. Med. **62:** 1946 (June 15) 1962.

The hospital records of 61 patients with chronic lymphocytic leukemia, or CLL, were studied. Infection and anemia were the principal causes of hospital admissions. Thirty-seven patients (61 per cent) had a total of 84 clinically evident infections: 33 episodes of pneumonia, 18 skin infections, 10 genitourinary infections, 8 bacteremia infections, and 26 other infections. There appeared to be no correlation between use of adrenal corticosteroids, radiation, or cytotoxic agents and the occurrence of infections. The frequency of infection and the incidence of acquired hemolytic anemia suggest that the immune response is distorted and inadequate in chronic lymphocytic leukemia, but the exact cause has not been determined.

Schwartz, B.: The misdiagnosis of glaucoma, New York State J. Med. **62:** 1953 (June 15) 1962.

False diagnosis of glaucoma may be made in patients in whom the disease does not exist and the patient subjected erroneously to medical or surgical therapy. Correct diagnosis with the use of a Schiotz tonometer depends on reliability of the instrument, use of a correct calibration scale, and recognition of the error of reproducibility of tonometer readings. Misdiagnosis may be made on the basis of misinterpretation of the following: high normative ocular tensions, high ocular rigidity, changes of the disk and visual fields caused by other conditions, and visual fields with normal disks.

Schneck, H., Sukoff, M. H., and Sherman, H. H.: Turner's syndrome; review of literature and report of case in newborn infant, New York State J. Med. **62:** 1962 (June 15) 1962.

Turner's syndrome or gonadal dysgenesis is a congenital disease in which approximately 80 per cent of patients have X-O (chromatin-negative or abnormal) pattern. The finding of 45 chromosomes with an X-O pattern and external abnormalities enable diagnosis at birth. Short stature is the most common characteristic of gonadal dysgenesis; cubitus valgus and webbed neck are the two anomalies most often found. Other skeletal defects, associated anomalies, mental retardation, and endocrinologic defects may be present. Plastic surgery, surgery to correct cardiovascular and renal anomalies, and hormonal and psychologic therapy are helpful although the affected individual can never assume all the functions of a female. An analogy between Turner's syndrome and some kind of gonadal "blight" during early embryologic differentiation is apparent, although other etiologic factors have been suggested also.

Mandel, P. R., and Chiat, H.: Radioactive phosphorus for carcinoma of the breast with diffuse metastatic bone disease, New York State J. Med. **62:** 1970 (June 15) 1962.

Fourteen patients with diffuse bone metastasis from breast carcinoma without significant soft tissue involvement were treated with aqueous testosterone and intravenous radioactive phosphorus or P^{32}. Eighty-seven per cent had significant relief of pain, and 18 per cent had radiographic evidence of bone repair. Progressive relief of pain usually was evident one month after treatment, reached a maximum in three to four months, and lasted from two to eighteen months. The therapeutic response was not directly proportional to the dose of P^{32}

given. Further improvement could often be obtained when symptoms recurred by a repeat course of therapy. When the total of P^{32} given was under 12 millicuries, the degree of bone marrow depression was minimal, but cases given greater doses did not necessarily show alarming depression of hematopoiesis.

Feuer, S. G., Rosenbaum, I., and Baranowska, H.: Methocarbamol injectable in treatment of acute and chronic muscle spasm, New York State J. Med. **62:** 1985 (June 15) 1962.

A study was made of the effectiveness of methocarbamol (Robaxin) in relief of muscle spasm in 60 patients. Of 32 patients with acute conditions, 40.6 per cent showed excellent results, 43.8 per cent good results, and 15.6 fair results. In 28 patients with chronic neuromuscular and arthritic conditions, 10.7 per cent obtained excellent relief, 21.4 per cent good relief, 34.1 per cent fair relief, and 35.7 no improvement. The results in patients with chronic conditions were influenced unfavorably by the poor results in patients with residual spastic hemiplegia following cerebrovascular accidents. The principal improvements noted were improved range of motion of the involved joints, relief of stiffness, and resolution of pain. The side-effects were dizziness and lightheadedness of short duration.

Friedman, L. D., and Goldberger, E.: Effect of isocarboxazid on relief of anginal pain, New York State J. Med. **62:** 1990 (June 15) 1962.

A study was undertaken to determine the effectiveness of the monoamine oxidase inhibitor, isocarboxazid (Marplan) for relief of pain in 15 patients with arteriosclerotic heart disease and angina pectoris. Isocarboxazid was given in doses varying from 10 to 30 mg. a day over a period of from several weeks to several months. The results were excellent in 9 patients, good in 4, and unsatisfactory in 2. Nitroglycerin needs were eliminated or reduced in the successful cases. Except for 1 case side-effects noted were controlled and subsided quickly with dosage adjustment. Beneficial effects included blood pressure reduction in hypertensive patients and the emotional benefit of mood elevation.

Status of Chagas' disease in the United States

According to an article by Dr. Robert G. Yaeger in the November, 1961, issue of *The Bulletin of the Tulane University Medical Faculty*, by conservative estimate 35 million persons in Latin American countries are exposed to Chagas' disease. The number actually infected, based on a rate of 20 per cent determined by surveys, would be at least 7 million. In the United States, human infections are apparently very few, but many cases may be overlooked. On the other hand, the infecting organism, Trypanosoma cruzi, is widely dispersed in the southern half of the United States and may project farther north in some areas. The disease is maintained in nature by certain mammals and triatomid bugs. In the United States, Chagas' disease is rarely considered in a diagnosis. Because manifestations are varied and, in low-grade cases, subclinical, the disease is often difficult to detect. Further investigation may reveal a higher prevalence in human beings than currently supposed. No cure has been reported.

Medical News

Free book on syphilis

Leona Baumgartner, M.D., Commissioner of Health of the City of New York, has announced that there is available to physicians a free, hard cover book entitled *Syphilis, Modern Diagnosis and Management.* The volume was prepared by the United States Public Health Service with the assistance of Sidney Olansky, M.D., and Evan W. Thomas, M.D.

Requests for the book should be addressed to: Division of Social Hygiene, The City of New York Department of Health, 125 Worth Street, New York 13, New York, or the Division of Chronic Disease Services, State of New York Department of Health, 84 Holland Avenue, Albany 8, New York.

Ruling curbs nutritional quackery

According to the Food and Drug Administration, one of the country's leading sources of nutritional quackery has been curbed by Federal Court action. The F.D.A. said that sentencing of Royal Lee, president of the Vitamin Products Company, Milwaukee, Wisconsin, will stop the distribution of more than 115 special dietary products promoted by false claims for treating over 500 different diseases and conditions.

Federal Judge Robert Tehan sentenced Lee to a one-year suspended prison term with three years probation and fined the Vitamin Products Co. $7,000 on charges of interstate shipment of misbranded vitamins and proprietary remedies. Lee also consented to a permanent injunction covering all of his enterprises which prohibits the false claims for his products.

Course on rheumatic diseases

A postgraduate course on the rheumatic diseases, sponsored by the Chicago Rheumatism Society and the American Rheumatism Association, will be held June 23 and 24 at the Edgewater Beach Hotel, Chicago. The course will be acceptable for ten hours of category two credit by the American Academy of General Practice.

Information center on radioactive fallout

The State Health Department, at the request of Governor Nelson A. Rockefeller, has established an information center to provide data and handle all inquiries concerning radioactive fallout.

Herman E. Hilleboe, M.D., State Health Commissioner, said that the activities of the center, to be located in the State Health Department's Office of Public Health Education, will include:

1. Handling all press and personal inquiries promptly and fully.
2. Promptly disseminating accurate and thorough information as to what the fallout picture is.
3. Releasing general information and education about the nature of the fallout problem.
4. Providing local health departments throughout the State with data so that a uniform pattern of information is made available to the public.

Course in laryngology and bronchoesophagology

The Department of Otolaryngology, University of Illinois College of Medicine, will conduct a postgraduate course in laryngology and bronchoesophagology from September 24 through October 6, under the direction of Paul H. Holinger, M.D.

Registration will be limited to 15 physicians who will receive instruction by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures.

For information write to: Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

Women physicians invited to brunch

The American Medical Women's Association extends an invitation to all women physicians attending the A.M.A. annual meeting in Chicago, to be their guests at a brunch on Sunday, June 24, at 11:00 A.M., at the Essex Inn.

Those wishing to attend should write to: American Medical Women's Association, 1790 Broadway, New York 19, New York.

Atomic power laboratory found safe

Levels of radioactivity from waste discharged from the Knolls Atomic Power Laboratory, Niskayuna, Schenectady County, and its West Milton Facility in Saratoga County, were well within safe public health limits during 1961, according to the 1961 annual report from the

Schenectady Office of the United States Atomic Energy Commission to the State Health Department. The report also indicated there had been no adverse effect on the radioactivity levels in the area surrounding the facilities.

Unique scanning device for brain

The John A. Hartford Foundation, Inc., has awarded a $336,200 three-year grant to Presbyterian Hospital at Columbia-Presbyterian Medical Center to develop a unique scanning device which improves the method of diagnosing and localizing brain tumors and makes possible for the first time adequate appraisal of rapidly changing events within the brain.

Edward B. Schlesinger, M.D., New York City, attending neurologic surgeon at Presbyterian and associate professor of clinical neurologic surgery at Columbia University's College of Physicians and Surgeons, and his associates designed the highly complex apparatus and will direct the project.

According to Dr. Schlesinger the scanner has 63 detecting units for each side of the head which will transmit information to an electronic memory machine, providing a wealth of information about the dynamics of the brain and brain tumor circulation.

The scanning process consists in the intravenous injection of gamma-emitting isotopes, transported via the blood stream to the brain. The dispersed pattern of the gamma rays is picked up outside the skull by a radiation detection device. The local concentration of the isotope may indicate a tumor, discernible against the surrounding normal brain. Present scanning takes forty minutes, and only a single pair of symmetrical areas can be compared. This time lag and other variables can diminish the value of the information provided by the scan.

The time factor is of critical importance since each type of tumor concentrates isotope at specific times after its injection. Elimination of the time variation from point to point on the brain would allow the collection of comparable data for all areas from the time of injection throughout the period of presence of isotope in the brain.

Workshop in clinical hypnosis

A workshop in clinical hypnosis, sponsored by the American Society of Clinical Hypnosis, Education and Research Foundation, will be held June 30 and July 1 at the Sheraton-Chicago Hotel, in Chicago.

For further information write to: The American Society of Clinical Hypnosis, Education and Research Foundation, 4206 West Irving Park Road, Chicago 41, Illinois.

Personalities

Honored. Samuel Wagreich, M.D., Bronx, by the Medical Society of the State of New York, with the title "Outstanding General Practitioner of New York State for 1962."

Elected. John L. S. Holloman, Jr., New York City, as chairman of the board of trustees of Virginia Union University. . .Frederick Reiss, M.D., New York City, as an honorary member of the Indian Society of Dermatology and Venereology. . .John Romano, M.D., Rochester, to the American Academy of Arts and Sciences.

Awarded. Lawrence C. Kolb, M.D., New York City, a Henry Wisner Award from The Manhattan Society for Mental Health for his "distinguished professional service in the field of mental health". . .Doris Spector Rome, M.D., Albany, an honorary Doctor of Human Letters degree from Skidmore College. . .Louis A. Susca, M.D., Queens Village, a $500 award from the National Geriatric Society for an essay on the subject of geriatrics.

Speakers. Milton Helpern, M.D., New York City, at the twenty-sixth annual conference of the Public Health Association of New York City. . . Phelps P. Luria, M.D., Lawrence, before the staff of Peninsula General Hospital, Edgemere, on May 5 on the topic "Plastic Surgery". . . Arthur W. Pense, M.D., Albany, before the seventh annual conference of the New York State Association of Community Mental Health Boards on May 1 in Albany.

Abstracts in Interlingua

Howland, W. S., Schweizer, O., e La Due, J. S.: Evalutation del routinari electrocardiographia post-operatori (*anglese*), New York State J. Med. **62:** 1941 (15 de junio) 1962.

Routinari electrocardiogrammas post-operatori esseva obtenite ab 782 patientes. In 321 (41 pro cento) le registrationes esseva normal. In le remanente 461 patientes, le electrocardiogrammas revelava anormalitates de frequentia, rhythmo, o conduction o alterationes myocardial suggerente le presentia de morbiditate. In 56 de iste 461 casos, le information fornite per le electrocardiogramma haberea essite detegite per applicar criterios coperiente le major problemas cardiovascular incontrate in le sala de recovramento post-operatori. In 48 casos le condition habeva essite notate in un electrocardiogramma pre-operatori. In 167 casos le condition non esseva detegite ante le operation. Tamen, in omne iste casos, con duo exceptiones, le anormalitates del electrocardiogramma post-operatori esseva le resultato de chronic morbo cardiac. Il pare que alterationes que occurre como resultato de operatori o post-operatori phenomenos medical e physiologic pote esser detegite per medio de un electrocardiogramma post-operatori in patientes qui monstra marcate bradycardia o arrhythmia, subite non-explicate tachycardia, hypoxia, o hypotension non corrigibile per le restauration del circulante volumine de liquido. Tamen, un routinari electrocardiogramma preoperatori es indicate pro omne patiente destinate al operation.

Aroesty, J. M., e Furth, F. W.: Infection e chronic leucemia lymphocytic; un revista de 61 casos (*anglese*), New York State J. Med. **62:** 1946 (15 de junio) 1962.

Esseva studiate le protocollos hospitalari de 61 patientes con chronic leucemia lymphocytic (CLL). Infection e anemia esseva le causas principal del hospitalisation. Trenta-septe patientes (61 pro cento) habeva un total de 84 clinicamente evidente infectiones. Istos includeva 33 episodios de pneumonia, 18 infectiones cutanee, 10 infectiones genitourinari, 8 infectiones bacteremic, e 26 altere infectiones. Esseva apparente nulle correlation inter le uso de corticosteroides adrenal, de radiation, o de agentes cytotoxic e le occurrentia de infectiones. Le frequentia de infectiones e le incidentia de acquirite anemia hemolytic suggere que le responsa immun es perturbate e inadequate in CLL, sed le exacte causa de iste phenomeno ha non ancora essite determinate.

Schwartz, B.: Le misdiagnose de glaucoma (*anglese*), New York State J. Med. **62:** 1953 (15 de junio) 1962.

Il pote occurrer que un diagnose erronee de glaucoma es facite in patientes in qui le morbo non existe, con le consequentia que illes es subjicite innecessarimente a therapia medical o chirurgic. Le correcte diagnose con le uso del tonometro de Schiøtz depende del fidelitate del instrumento e del recognition del error de reproducibilitate in le lecturas tonometric. Misdiagnoses pote occurrer a base de erronee interpretationes del sequente observationes: Alte tension ocular normative, alte rigiditate ocular, alterationes de disco e de campo visual causate per altere conditiones, e campo visual con disco normal.

Schneck, H., Sukoff, M. H., e Sherman, H. H.: Syndrome de Turner; revista del litteratura e reporto de un caso in un infante neonate (*anglese*), New York State J. Med. **62:** 1962 (15 de junio) 1962.

Le syndrome de Turner, o dysgenese gonadal, es un disordine congenite in que approximativemente 80 pro cento del patientes exhibi un configuration X-O (con negativitate o anormalitate de chromatina). Le constatation de 45 chromosomas con le configuration X-O e externe anormalitates permitte le diagnose al tempore del nascentia. Un basse statura es le characteristica le plus commun de dysgenese gonadal. Cubito valge e cervice palmate es le duo anormalitates trovate le plus frequentemente. Altere defectos skeletic, associate anormalitates, retardation mental, e defectos endocrinologic pote esser presente. Chirurgia plastic, chirurgia pro corriger le anormalitates cardiovascular e renal, e therapia hormonal e psychologic es utile, sed le afficite individuo va nunquam executar omne le functiones de feminina. Un analogia inter le syndrome de Turner e le un o le altere typo de "derailamento" gonadal in le precoce differentiation embryologic es apparente, sed altere factores etiologic ha etiam essite proponite.

Mandel, P. R., e Chiat, H.: Phosphoro radioactive in le tractamento de carcinoma mammari con diffuse morbo metastatic de osso (*anglese*), New York State J. Med. **62:** 1970 (15 de junio) 1962.

Dece-quatro patientes con diffuse metastases ossee ab carcinoma mammari sed sin significative affectiones metastatic de tissu molle esseva tractate con testosterona aquose e posphoro radioactive (P^{32}) per via intravenose. Octantasepte pro cento del patientes experientiava un alleviamento significative del dolores, e in 18 pro cento le radiogrammas monstrava evidentia de reparo ossee. Un progressive alleviamento del dolores esseva usualmente evidente un mense post le tractamento, attingeva su maximo intra tres a quatro menses, e persisteva durante un periodo de inter duo e dece-octo menses. Le responsa therapeutic non esseva directemente proportional al dose de P^{32} usate. In casos in que le symptomas recurreva, il esseva frequentemente possibile reinfortiar le melioration per repetition del curso de tractamento. Quando le total del P^{32} administrate correspondeva a minus que 12 millicurie, le grado de depression del medulla ossee esseva minime, sed in le casos in que plus grande doses total esseva usate, le depression del hematopoiese non attingeva necessarimente un magnitude alarmante.

Feuer, S. G., Rosenbaum, I., e Baranowska, H.: Methocarbamol injicibile, in le tractamento de acute e chronic spasmos muscular (*anglese*), New York State J. Med. **62**: 1985 (15 de junio) 1962.

Esseva executate un studio del efficacia de methocarbamol (Robaxina) in le alleviamento de spasmo muscular. Le numero del patientes in le studio esseva 60. Ex 32 con conditiones acute, 40,6 pro cento monstrava resultatos excellente, 43,8 pro cento bon resultatos, e 15,6 pro cento resultatos satis bon. Ex 28 patientes con chronic conditiones neuromuscular e arthritic, 10,7 pro cento monstrava resultatos excellente, 21,4 pro cento bon resultatos, 34,1 pro cento resultatos satis bon, e 35,7 nulle alleviamento. Le resultatos in le gruppo de patientes con conditiones chronic esseva influentiate adversemente per le presentia in ille gruppo de patientes con residue hemiplegia spastic post accidente cerebrovascular. Le major meliorationes notate esseva extension del mobilitate del afficite articulationes, alleviamento del rigiditate, e resolution del dolores. Le adverse effectos secundari esseva vertigine e deliriositate de breve duration.

Friedman, L. D., e Goldberger, E.: Effecto de isocarboxazido in le alleviamento de dolores anginal (*anglese*), New York State J. Med. **62**: 1990 (15 de junio) 1962.

Esseva interprendite un studio pro determinar le efficacia del inhibitor de oxydase de monoamina, isocarboxazido (Marplan), in le alleviamento de dolores de morbo cardiac arteriosclerotic e angina de pectore. Le numero del patientes includite esseva 15. Le droga esseva administrate in doses de inter 10 e 30 mg per die durante periodos de inter plure septimanas e plure menses. Le resultatos esseva excellente in 9 patientes, bon in 4, e non satisfacente in 2. In le casos a bon successo, le requirimentos de nitroglycerina esseva eliminate o reducite. Le adverse effectos secundari esseva regulate e subsideva rapidemente post adjustation del dosage in omne le casos con un exception. Le effectos benefic includeva le reduction del tension de sanguine in patientes hypertensive e elevation del stato de anima.

Factors affecting prognosis in bacterial endocarditis

Histories of 85 cases of bacterial endocarditis admitted over a period of ten years were analyzed, in an article by Morton Lee Pearce, M.D., and Lucien B. Guze, M.D., in the August, 1961, issue of *Annals of Internal Medicine*, to discover, if possible, factors affecting prognosis. The results indicated that a poor prognosis is associated with advanced age, aortic valve involvement, congestive heart failure, infectious organisms other than streptococci, severe alcoholism or portal cirrhosis or both, and all electrocardiographic abnormalities except left ventricular hypertrophy and P mitrale. The duration of symptoms prior to treatment apparently did not affect the prognosis. If the patient survived the immediate effects of cerebral embolism and ruptured mycotic aneurysms, the prognosis was good.

Letters to the Editor

Cancer as second symptom

To the Editor: I have observed a number of cases in which clinical manifestations of malignant disease were preceded by a year or by several years by certain symptoms of a nonmalignant nature. In most of these there seemed no reason to consider a relationship between the nonmalignant and the malignant occurrences. But in others, some of which shall be described here, a possible relationship between the malignant disorder and its forerunner is difficult to dismiss even though malignant and nonmalignant disease in each of the cases is separated not only in time but also in space so that the malignant disease and its forerunner appear as affections of different organs.

Case 1. In a man fifty-eight years of age, during a routine examination and with no past history of illness, a white blood count of 17,200 was found. A recheck one week later showed a similar result. The examinations, which included bone marrow studies, showed no blood abnormalities. One month later the white blood count returned to 10,000, and he remained in good health until six years later when he came with painful lumps on both sides of the neck. Biopsies showed malignant lymphoma of the reticulum cell type.

Case 2. A man sixty years of age complained of blurred vision. His past medical history, family history, and a review of the systems were noncontributory to the present illness. On ophthalmologic examination hemorrhages, atrophy of the optic nerve, and papilledema of the left eye were found. The eyeground improved in one week, and all changes disappeared in less than four weeks. He remained in good health for three and one-half years when a hypernephroma of the left kidney was found.

Case 3. A man fifty-two years of age complained of having had severe pains for several hours the day before in his throat, in the left side of the chest, and in the left shoulder. His past history was noncontributory. The pulse rate varied from 96 to 104, and the blood pressure was 90/70 mm. with otherwise normal findings. The S-T segment of the electrocardiogram was elevated in leads II, III, Vf, V_4, V_5, and V_6, with normal upright T waves and no Q waves. Forty-eight hours later the S-T segments became isoelectric while the amplitude of the T waves diminished in all leads. The sedimentation rate was elevated (60 mm.) and remained so on repeated examinations. The findings were interpreted as being compatible with acute pericarditis. He had no further complaints until fifteen months later, when a lung cancer was found.

Case 4. A man, age sixty-three, had had for the last four months pains in various parts of the chest lasting for a few seconds and appearing independently of effort. An electrocardiogram at the onset of the illness showed an inverted T wave in lead II, with no other changes. The inverted T in lead II became isoelectric after fourteen days and finally upright in another fourteen days. With the exception of a relative lymphocytosis (white blood count 7,300, and lymphocytes 52 per cent) and elevated sedimentation rate (41 mm.), the findings were normal. Coronary disease had to be considered, but in the absence of typical clinical and electrocardiographic changes it was assumed that the disease was due to an acute myocarditis. Subsequently he was in good health and was working until three and one-half years later when he became ill and the diagnosis of lung cancer was established.

Before the possibility of a relationship between the malignant conditions in these cases and their forerunners can be considered, the nature of the latter ought to be examined. In all 4 cases the symptoms which preceded the development of cancer were ephemeral and of an undisclosed etiology and appeared in an organ other than that of the eventual malignant disease. They were compatible with the assumption that they were caused by an infectious disease. In the absence of the classic symptoms of bacterial infection, however, they might have been caused by virus infection. Virus infection may lead to the leukocytosis, pericarditis, myocarditis, and eyeground changes which were observed in these cases.

The admission of the probability that the nonmalignant forerunners were due to virus infection does not in itself reveal any information as to their relationship to the subsequent malignant conditions. Yet, in the present instances it is difficult to escape the suspicion of a link between the two occurrences. Because of the characteristic changes of the eyeground in certain kidney diseases the suspicion is particularly strong in Case 2 in which cancer of the kidney developed several years after the manifestation of a disease of the retina and the optic nerve. Similarly, because of the close relationship between the hemopoietic organs and the lymph system it is difficult to dismiss a relationship between the unexplained leukocytosis in Case 1 and the subsequent malignant lymphoma even though the latter appeared years after the former. In the other 2 patients clinical signs of heart disease, probably due to pericarditis (Case 3) and myocarditis (Case 4), were followed by lung cancer. In these it is the topographic closeness between the two organs and thus the ease with which the infectious process might have spread from the lung to the adjacent heart, which suggests a relationship between the cancer and its precursor.

If the probability of the viral nature of the primary disease and the probability of a relationship between the malignant conditions and their nonmalignant forerunners is admitted, the following picture might be drawn of the etiology and pathogenesis of cancer in these cases.

In Case 1 a virus infection of the lymph system might have taken place at the time when the leukocytosis was found. While leukocytosis was found repeatedly during one week it was absent one month later so that the acute phase of the postulated virus infection seems to have subsided in a few weeks. It is assumed, however, that a chronic phase of irritation of the lymph system persisted and while it remained asymptomatic for six years, eventually the outcome of the chronic irritation appeared as a malignant lymphoma. In Case 2 it is assumed that a virus infection of the left kidney took place at the time of the appearance of the eye symptoms. Other than the changes of the eyeground which lasted for four weeks, the postulated kidney infection was subclinical and remained asymptomatic for three and one-half years when cancer of the left kidney manifested itself, possibly as a result of chronic irritation induced by the virus. In Cases 3 and 4 a subclinical virus infection of a lung might have occurred at the time of the clinical and electrocardiographic manifestations of heart disease. These manifestations lasted no longer than weeks, but the irritation caused by the virus might have persisted, becoming apparent in the form of cancer of the lung after a period of fifteen months in Case 3 and after a period of three and one-half years in Case 4.

With reference to the concept, which is in obvious need of substantiation, attention is called to widely accepted observations derived from animal experiments. Accordingly, some cancer viruses of animals also cause short-term noncancerous acute diseases in properly susceptible animals. Often the development of cancer is a later manifestation of a disease occurring months, perhaps even years, afterward in an animal that has already survived the first effects of the virus. These observations made in animals correspond to the observations and their interpretations as described herein, except, of course, for the fact that the presence of cancer-causing viruses in human beings has yet to be demonstrated. The difficulties which are inherent in demonstrating the presence of cancer-causing viruses in human beings are made clear by the observations in animals, and, as here assumed, also in human beings, according to which there is a time lag between the original infection, when the virus may be present and may be found if a search is made for it, and the subsequent cancer, when the virus may no longer be demonstrable. In other words, in the acute illness when the search may be fruitful, no search is made because the need for it is not appreciated, and in the subsequent cancer when the need for investigation is felt, the investigation can no longer be successful.

To overcome these difficulties in demonstrating cancer-causing viruses in human beings it will be necessary to be on a sharp lookout for transitory, unexplained illness, not inconsistent with the presence of virus infection, keeping in clear focus at the same time the possibility of a subsequent development of a malignant condition. If an illness of this kind is found it will be necessary to search for laboratory evidence of a virus infection, perhaps of a specific type or of specific types. As pointed out before, attention will have to be paid to the possibility that laboratory evidence may be found in the acute phase of the infection only. Should the search for virus be successful, it will then be necessary to keep such patients under close supervision, alert to the possible development of malignant disease of the type which because of certain characteristics can be brought into etiologic relationship with its virus infection precursor. If this program with its various steps can be carried out successfully, the field will be open for the clinical evaluation of the virus theory of cancer which at present is based almost exclusively on animal experiments.

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Month in Washington

Top officials of the American Medical Association at a White House conference with President Kennedy stood pat in support of the Kerr-Mills program and in opposition to providing health care for the aged under Social Security.

President Kennedy also maintained his position that the Social Security mechanism should be used.

Using Boisfeuillet Jones, special assistant to the Secretary of Health, Education, and Welfare as an intermediary, Kennedy invited the A.M.A. officials to the White House just before the Administration started an all-out effort to get Congressional approval of legislation that would provide limited hospitalization and some other health care to older persons under Social Security.

The House Ways and Means Committee, which rejected the Social Security approach in 1960, is expected to vote on similar legislation again this year.

In its campaign for the King-Anderson bill, which utilizes the Social Security system, the Administration and its allies called rallies of aged persons, exerted pressures through a White House "lobby" office, published a propaganda pamphlet at the taxpayer's expense, and had Federal employes drumming up support for the proposal.

Following the forty-five-minute White House session with Kennedy, Leonard W. Larson, M.D., Bismarck, N.D., A.M.A. president, said the A.M.A. representatives made clear that the great majority of the nation's physicians oppose the King-Anderson bill or similar legislation. Dr. Larson also said the Administration is wrong in its statements that such legislation will be approved by Congress.

"We have a very good line of communication with the grass roots and the support of the old people for the Administration plan is decreasing now that they realize what it will mean to them," Dr. Larson said.

Dr. Larson charged that the Kennedy Administration is "trying to create a bandwagon" for its medical care for the aged program. He said "the propaganda indicates the Administration is not getting the support it needs for its bill, and we are convinced the trend is the other way."

In addition to Dr. Larson, A.M.A. officials at the White House were: Hugh H. Hussey, Jr., M.D., Washington, D.C., chairman, A.M.A. Board of Trustees; Percy E. Hopkins, M.D. Chicago, vice-chairman, A.M.A. Board of Trustees; Norman Welch, M.D., Boston, speaker, A.M.A. House of Delegates; Edward R. Annis, M.D., Miami, chairman, A.M.A. National Speakers Bureau; F. J. L. Blasingame, M.D., Chicago, A.M.A. executive vice-president; and Earnest B. Howard, M.D., Chicago, A.M.A. assistant executive vice-president.

Dr. Annis said the meeting "was an honest interchange of divergent views on the method of providing medical care for the senior citizens of our country." He said the A.M.A. position was that when the government provided for people in need, this was "a proper manifestation of the Christian-Judaic consideration for fellow man."

But when the government provides for everyone under a system of forced contributions this amounts to socialized medicine, Dr. Annis said.

On other health matters, Kennedy expressed interest in the A.M.A.-sponsored First National Congress on Mental Health this fall. He said he hoped to be able to accept an A.M.A. invitation to address it. He also noted several legislative and other items in which there was substantial agreement between the A.M.A. and the Administration, including aid for construction of medical schools and establishment of the health resources advisory committee.

Shortly after the White House meeting, Republican senators met and agreed to hold firm in support of the Kerr-Mills bill and against King-Anderson. They refused to endorse any substitute.

One of the prime tactics of the Administration has been to give the impression that the King-Anderson bill enjoys wide public support. However, congressional polls of more than 450,000 voters revealed just the opposite with increasing public opposition evident toward the disputed plan. Of 43 polls taken during the current Congress 28 showed strong popular sentiment against the bill. The latest 16 polls ran 12 to 4 against it.

The American Dental Association reiterated opposition to the King-Anderson bill. An editorial in the A.D.A. Journal stated "participation in a government-sponsored program of health care should be voluntary." A.D.A. secretary Dr. Harold Hillenbrand called the bill "election time propaganda."

The campaign against the medical profession for its opposition to the King-Anderson bill has become "downright vicious," Rep. Don Short (R., N.D.) said in a Congressional Record statement.

Prepared by the Washington office of the American Medical Association.

Books Received

*The following books were received during the month of April, 1962**

Tumors of the Breast. By Max Cutler, M.D. Quarto of 482 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1962. Cloth, $22.50.

Early Detection and Diagnosis of Cancer. By Walter E. O'Donnell, M.D., Emerson Day, M.D., and Louis Venet, M.D. Octavo of 286 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $12.

Clinical Pathology. By Benjamin B. Wells, M.D. Third edition. Octavo of 541 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $9.00.

Progress in Hematology. Volume III. Edited by Leandro M. Tocantins, M.D. Quarto of 384 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $16.50.

Shock—Pathogenesis and Therapy. An international symposium sponsored by Ciba. Edited by K. D. Bock. Octavo of 387 pages, illustrated. Berlin, Springer, 1962. Cloth, $13.

Ciba Foundation Symposium on Renal Biopsy. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Margaret P. Cameron, M.A. With 134 illustrations. Octavo of 395 pages. Boston, Little, Brown and Company, 1962. Cloth, $10.50.

The Future of Psychiatry. Edited by Paul H. Hoch, M.D., and Joseph Zubin, Ph.D. Octavo of 271 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $8.75.

Current Diagnosis & Treatment. By Henry Brainerd, M.D., Sheldon Margen, M.D., and Milton J. Chatton, M.D. Octavo of 758 pages, illustrated. Los Altos, Calif., Lange Medical Publications, 1962. Fabrikoid, $8.50.

Vector Electrocardiography. By Herman N. Uhley, M.D. Octavo of 339 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1962. Cloth, $8.50.

Radioactive Isotopes in Medicine and Biology—Medicine. By Solomon Silver, M.D. Second Edition. Octavo of 347 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $8.00.

Physical Diagnosis. By Ralph H. Major, M.D., and Mahlon H. Delp, M.D. Sixth edition. Quarto of 355 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $7.50.

Medical Department, United States Army. Internal Medicine in World War II. Volume I. Activities of Medical Consultants. Editor in Chief, Colonel John Boyd Coates, Jr., MC. Editor for Internal Medicine, W. Paul Havens, Jr., M.D. Octavo of 880 pages, illustrated. Washington, D.C., Office of the Surgeon General, Department of the Army, 1961. Cloth, $7.50.

Alcoholism and Society. By Morris E. Chafetz, M.D., and Harold W. Demone, Jr. Octavo of 319 pages. New York, Oxford University Press, 1962. Cloth, $6.95.

Schizophrenia as a Human Process. By Harry Stack Sullivan, M.D. Octavo of 363 pages. New York, W. W. Norton & Company, Inc., 1962. Cloth, $6.50.

The Dismissal. The Last Days of Ferdinand Sauerbruch. By Jürgen Thorwald. Translated from the German by Richard and Clara Winston. Octavo of 256 pages, illustrated. New York, Pantheon Books, 1962. Cloth, $5.50.

Martini's Principles and Practice of Physical Diagnosis. Revised by Yale Kneeland, Jr., M.D., and Robert F. Loeb, M.D. Third edition. Duodecimo of 275 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1962. Cloth, $4.75.

Problems of Psychiatry and Neuropathology. Volume One and Volume Two. English edition of Voprosy Psikhiatrii i Nevropatologii. Translated by Israel Program for Scientific Translations, Jerusalem, 1961. Available from The Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Cloth, volume I, $3.75; volume II, $3.00.

The Biochemistry of Intracellular Parasitism. By James W. Moulder. Octavo of 172 pages, illustrated. Chicago, The University of Chicago Press, 1962. Cloth, $6.00.

A Study of Psychophysical Methods For Relief of Childbirth Pain. By C. Lee Buxton, M.D. Octavo of 116 pages. Philadelphia, W. B. Saunders Company, 1962. Cloth, $4.75.

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* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

Officers / County Medical Societies / 1962

TOTAL MEMBERSHIP AS OF JANUARY 1, 1962—25,351

County	*President*		*Secretary*		*Treasurer*	
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Cattaraugus	B. John Toth	Olean	Frank T. Frost	Olean	Ruth R. Knoblock	Little Valley
Cayuga	Frank E. Barnes	Auburn	Henry J. Romano	Auburn	Robert J. Schaffer	Auburn
Chautauqua	Ernest Homokay	Silver Creek	Joseph V. Karnes	Dunkirk	C. Otto Lindbeck	Jamestown
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Chenango	Paul McLeod	Norwich	Arland D. Ryan	Norwich	Arland D. Ryan	Norwich
Clinton	John Menustik, Jr.	Plattsburgh	Harold Singer	Plattsburgh	William L. Ladue	Plattsburgh
Columbia	LeRoy J. Holbert	Kinderhook	Edward P. Ginouves	Hudson	Edward P. Ginouves	Hudson
Cortland	William J. McAuliffe	Cortland	Donald R. Gibbs	Cortland	Lewis H. Berk	Cortland
Delaware	David G. Doane	Walton	Marvin L. Huyck	Walton	Marvin L. Huyck	Walton
Dutchess	Sidney N. Miller	Poughkeepsie	Joseph E. Gioia	Poughkeepsie	Philip V. Buckley	Poughkeepsie
Erie	Clarence A. Straubinger	Buffalo	K. Elizabeth P. Olmsted	Buffalo	Francis W. O'Donnell	Buffalo
Essex	Onslow A. Gordon	Westport	George G. Hart	Lake Placid	George G. Hart	Lake Placid
Franklin	C. Bradley Sageman	Saranac Lake	Leon Passino	Malone	Leon Passino	Malone
Fulton	Armand J. D'Errico	Gloversville	Samuel Schoenberg	Gloversville	William H. Raymond	Johnstown
Genesee	David B. Johnson	Batavia	Sawyer A. Glidden	Batavia	Emil Kimaid	LeRoy
Greene	Edmund Frede	Athens	John A. Vosburgh	Coxsackie	Mahlon A. Atkinson	Catskill
Herkimer	Arthur H. Mulligan	Herkimer	Oscar J. Muller	Little Falls	Timothy J. Howard	Newport
Jefferson	Lawrence Withington	Watertown	James L. Harrington	Watertown	James L. Harrington	Watertown
Kings	Leslie H. Tisdall	Brooklyn	Vincent J. Tesoriero	Brooklyn	James L. O'Leary	Brooklyn
Lewis	Louis A. Avallone	Lowville	Alfred Englander	Lyons Falls	Alfred Englander	Lyons Falls
Livingston	Stanley J. Jackson	Mount Morris	G. Emerson Learn	Mount Morris	G. Emerson Learn	Mount Morris
Madison	William A. Bramley	Oneida	Felix Ottaviano	Oneida	Robert F. Schramm	Cazenovia
Monroe	Charles R. Mathews	Rochester	A. Gordon Ide	Rochester	Charles D. Sherman, Jr.	Rochester
Montgomery	David W. Childs	Amsterdam	Helen M. Blanchard	Amsterdam	Robert W. Dunlap, Jr.	Amsterdam
Nassau	Wendell L. Hughes	Hempstead	Lyon Steine	Valley Stream	Louis Bush	Baldwin
New York	Milton Helpern	New York	William L. Wheeler, Jr.	New York	C. Joseph Delaney	New York
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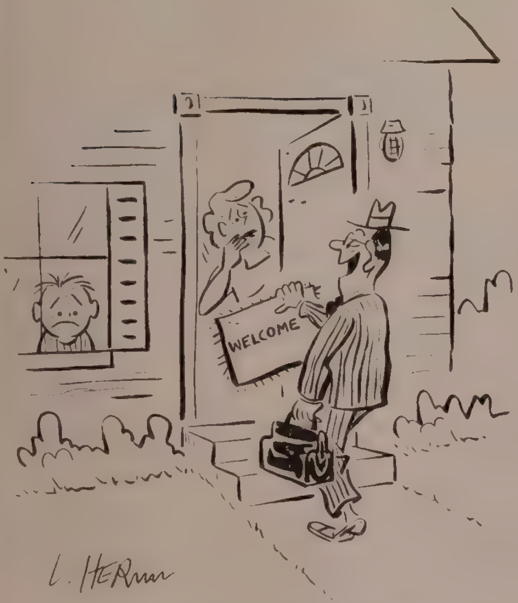

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Basic psychiatry for general practitioners, internists and medical specialists
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Differential diagnosis in gastro-intestinal radiology
Oct. 9 to Dec. 11: Tue., 5 to 6 P.M.

Electrocardiography
Oct. 15 to Oct. 26: Mon. to Fri., 9 to 12 Noon

Clinical cardiology
Oct. 16 to Dec. 18: Tue., 2 to 4 P.M.

Differential diagnosis in radiology of the chest
Oct. 22 to Jan. 28: Mon., 4:45 to 6:15 P.M.

Office proctology
Nov. 1 & Nov. 2: Thur. & Fri., 10 to 4 P.M.

Clinical hematology
Nov. 5 to Nov. 7: Mon. Tue. & Wed., 9 to 5 P.M.

Diseases of the liver
Nov. 12 to Nov. 16: Mon. to Fri., 9 to 5 P.M.

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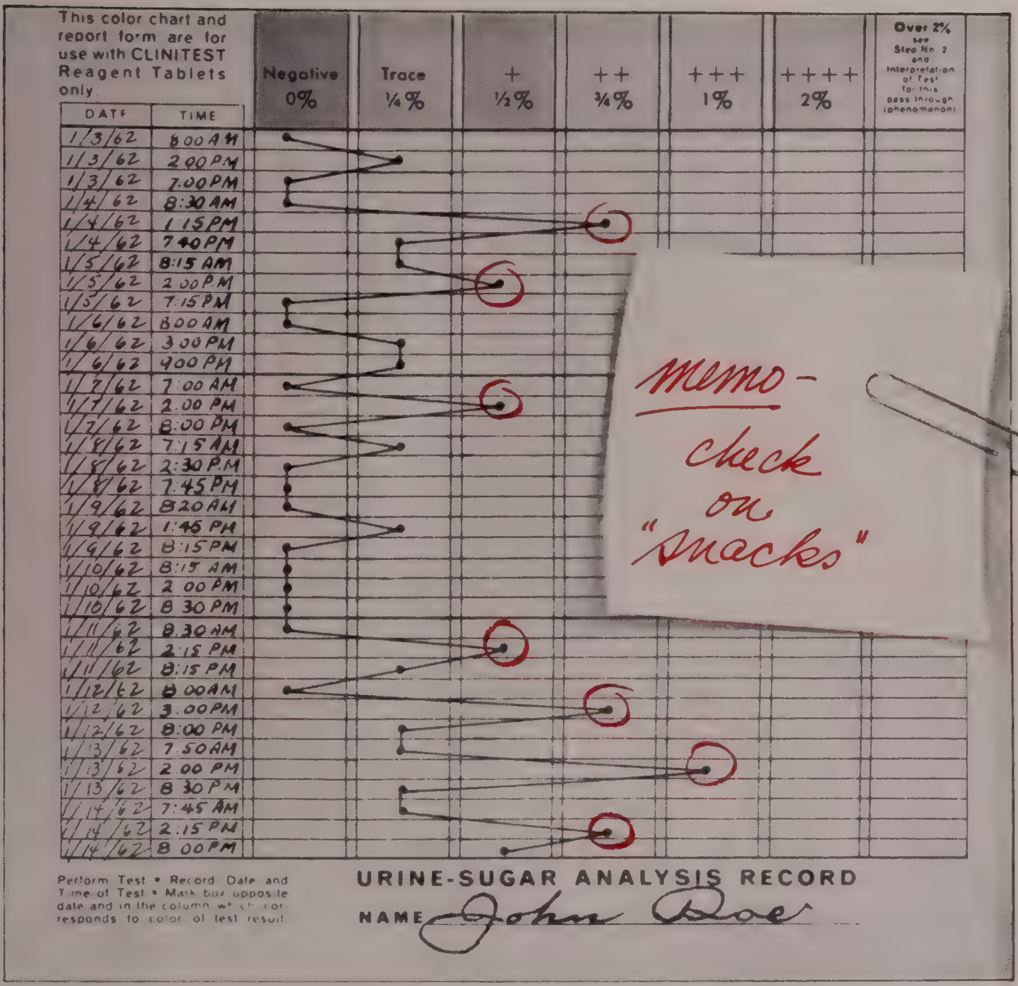

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1/4/62	8:30 AM	●						
1/4/62	1:15 PM				●			
1/4/62	7:40 PM		●					
1/5/62	8:15 AM		●					
1/5/62	2:00 P.M			●				
1/5/62	7:15 PM	●						
1/6/62	8:00 AM	●						
1/6/62	3:00 PM		●					
1/6/62	4:00 PM		●					
1/7/62	7:00 AM	●						
1/7/62	2.00 PM			●				
1/7/62	8:00 PM	●						
1/8/62	7:15 AM		●					
1/8/62	2:30 P.M	●						
1/8/62	7:45 PM	●						
1/9/62	8:20 AM	●						
1/9/62	1:45 PM		●					
1/9/62	8:15 PM	●						
1/10/62	8:15 AM	●						
1/10/62	2:00 PM	●						
1/10/62	8:30 PM	●						
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1/12/62	3:00 PM				●			
1/12/62	8:00 PM		●					
1/13/62	7:50 AM		●					
1/13/62	2:00 PM					●		
1/13/62	8:30 PM		●					
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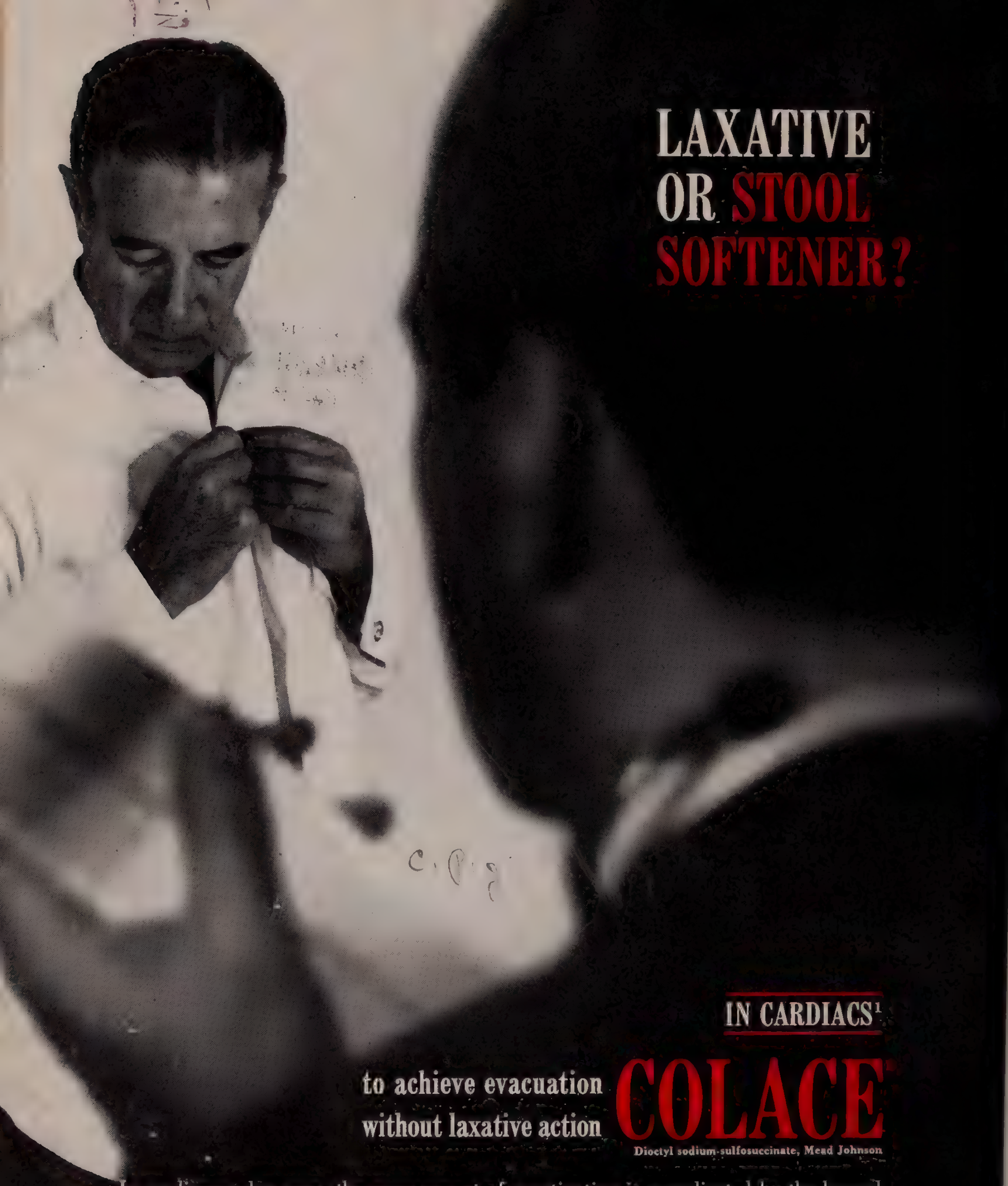

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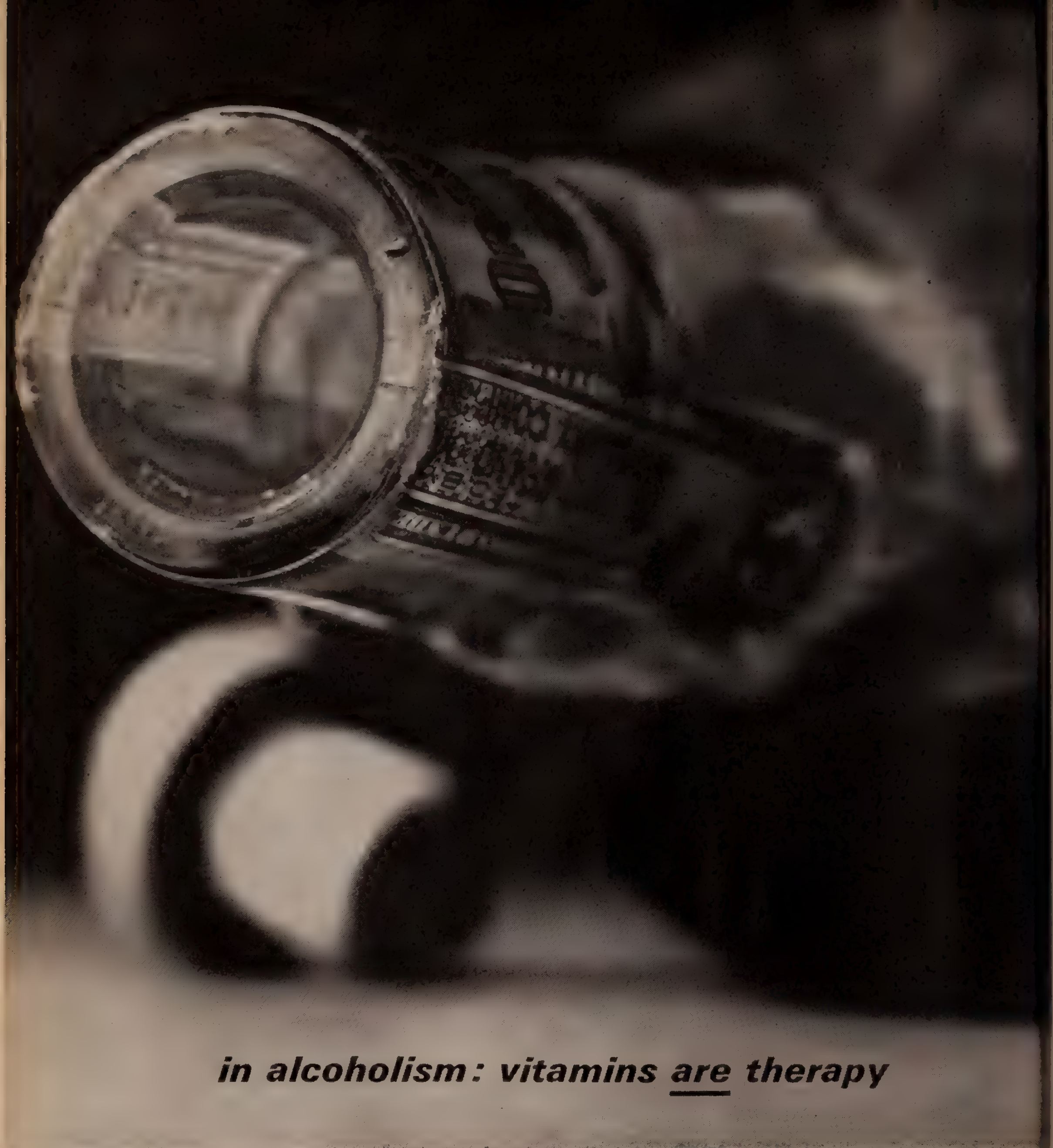

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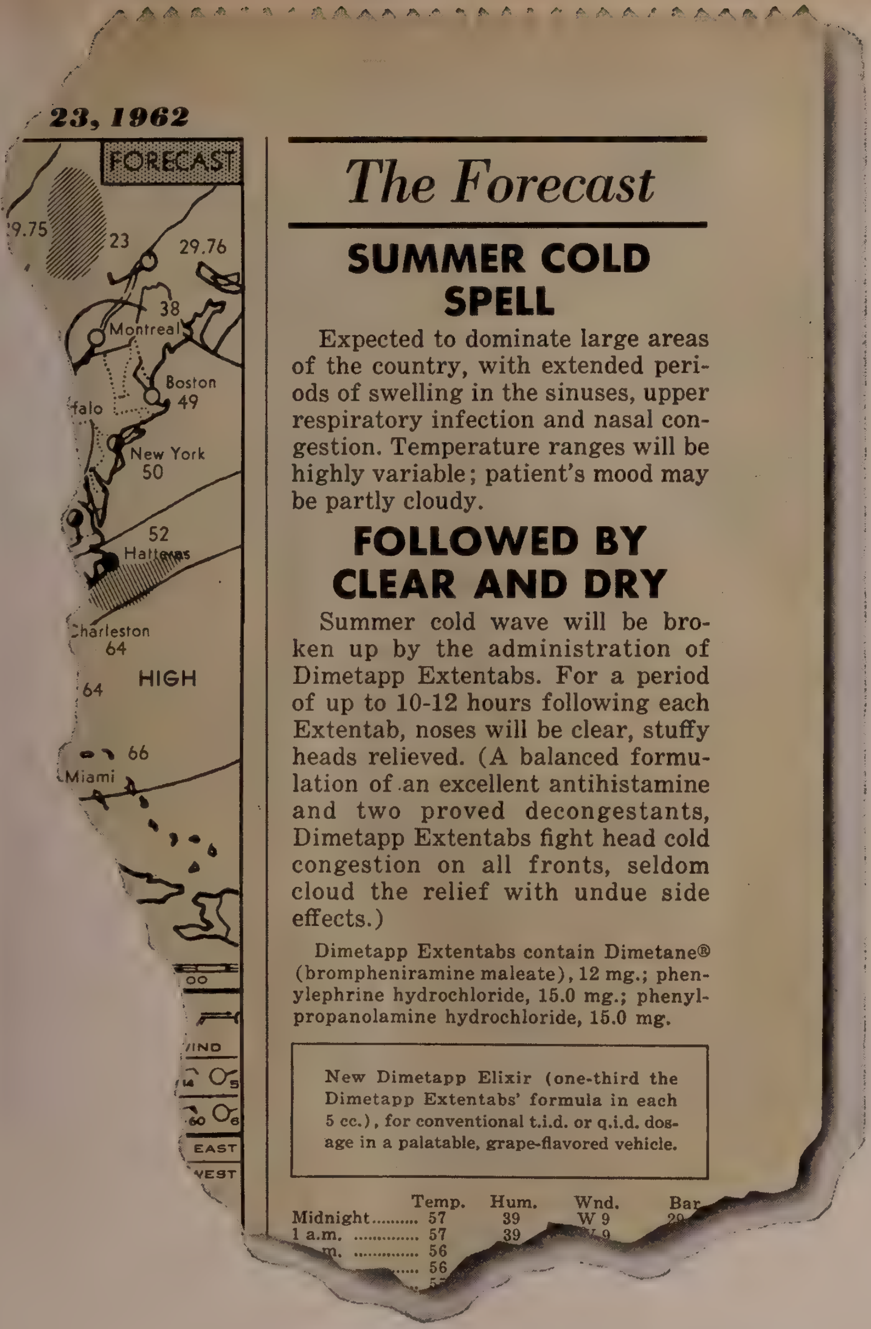

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m.	56			
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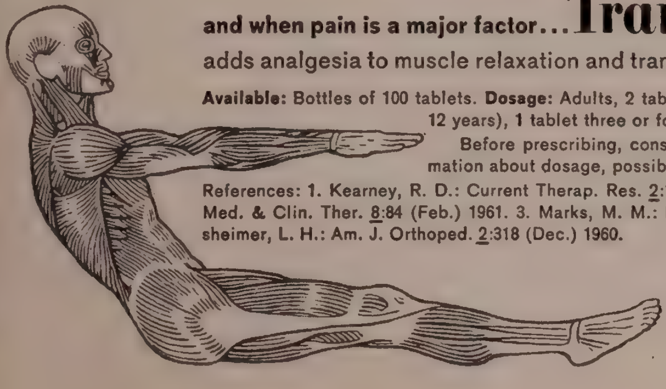

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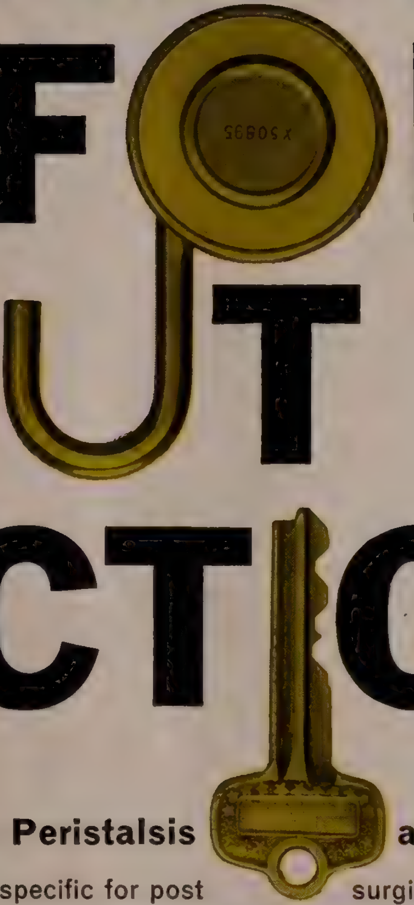

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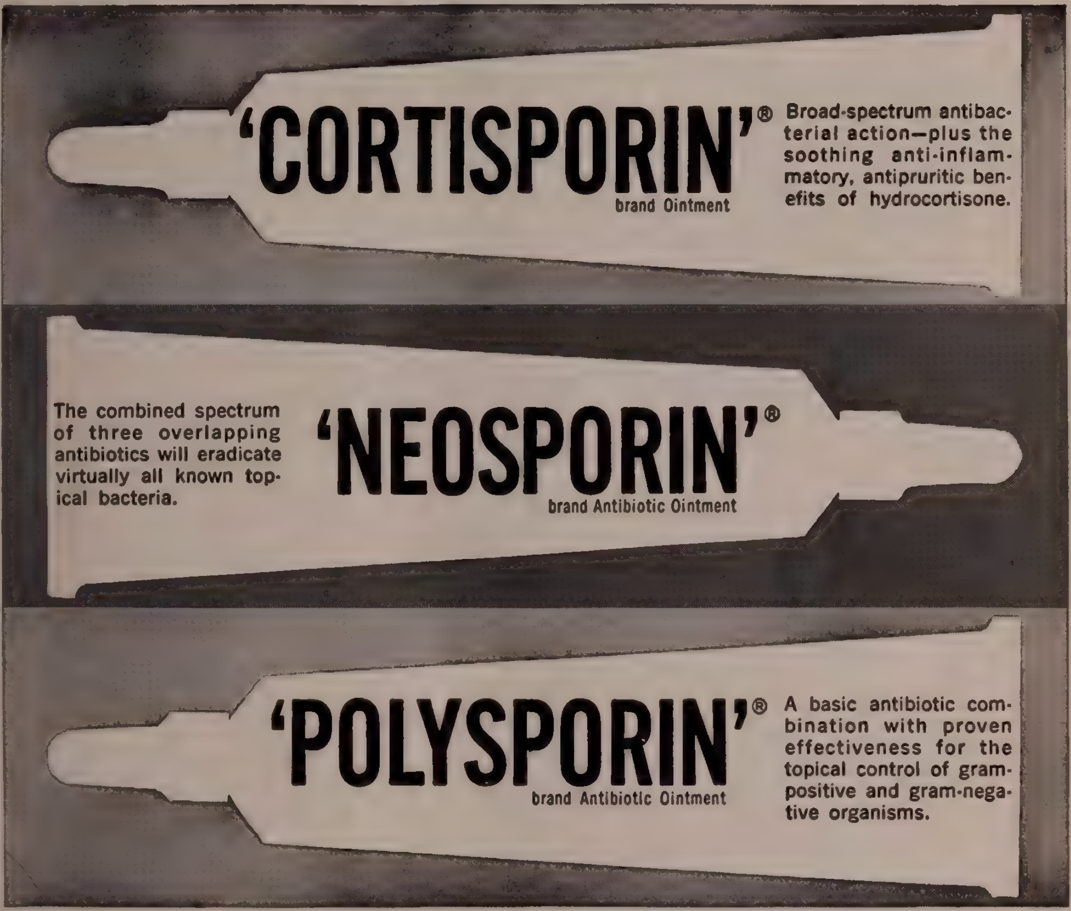

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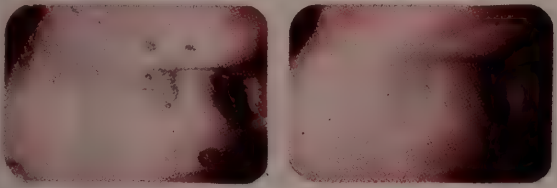
Marked success in treating psoriasis—especially in intertriginous areas—is reported with new Alphosyl Lubricating Cream.[1] In a study of 96 psoriatics, 73 patients experienced 75% to 100% clearing—15 showed 50% to 75% clearing.[1] Alphosyl Lubricating Cream not only helps remove scales and reduce erythema, but a new cream base affords added lubrication between the skin folds.



Patient E. C. Treatment started Jan. 14. On Feb. 18 clearing is almost complete.

Thus, it prevents the painful irritation that results from the rubbing of lesion against lesion. The base enhances moisture retention and, containing squalane, dissolves a cement substance in psoriatic scale.

Active Ingredients: Allantoin 2% and special coal tar extract (Tarbonis®) 5%.
Supplied: In tubes of 60 Gm.
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Reference: 1. Bleiberg, J.: Clin. Med. 8:1724 (Sept.) 1961.

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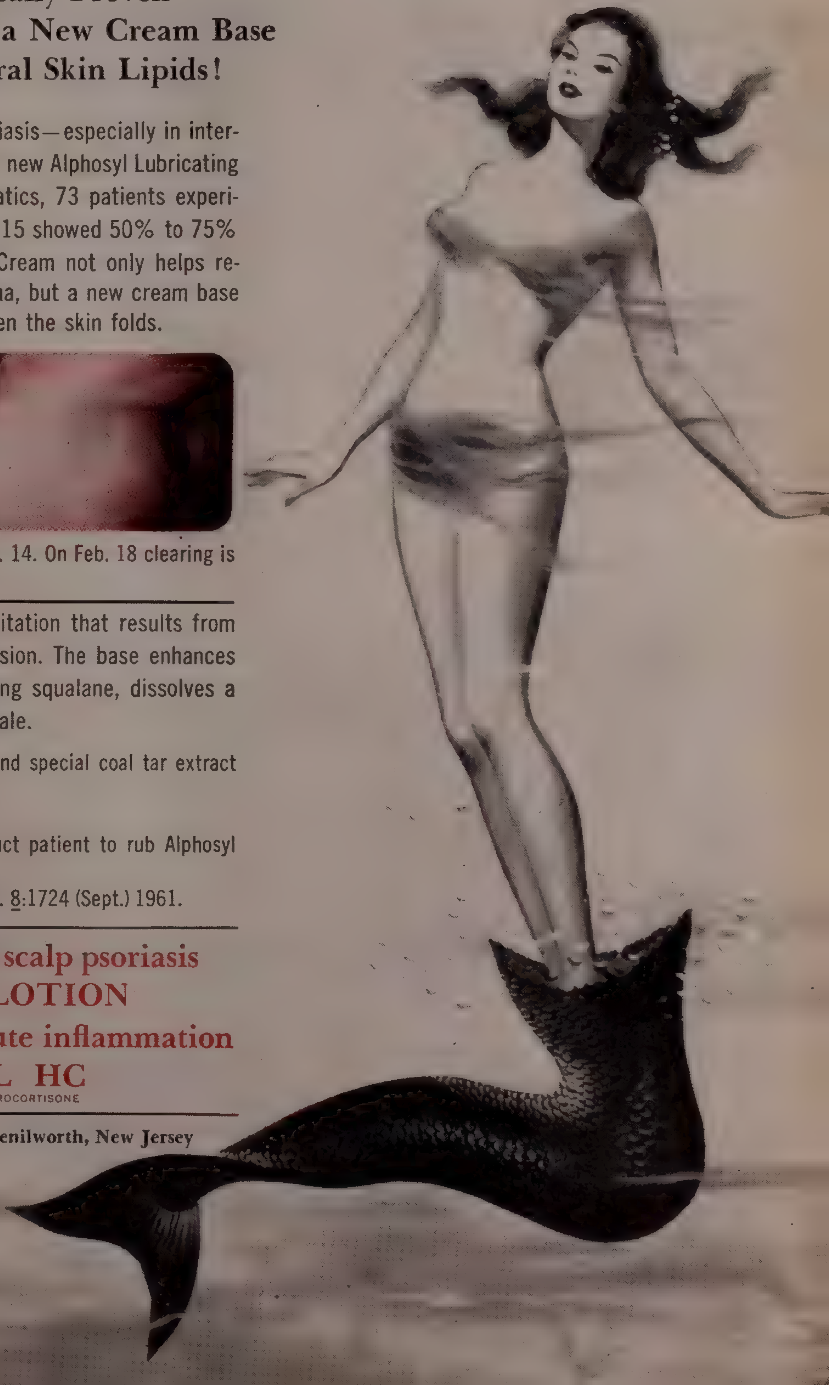
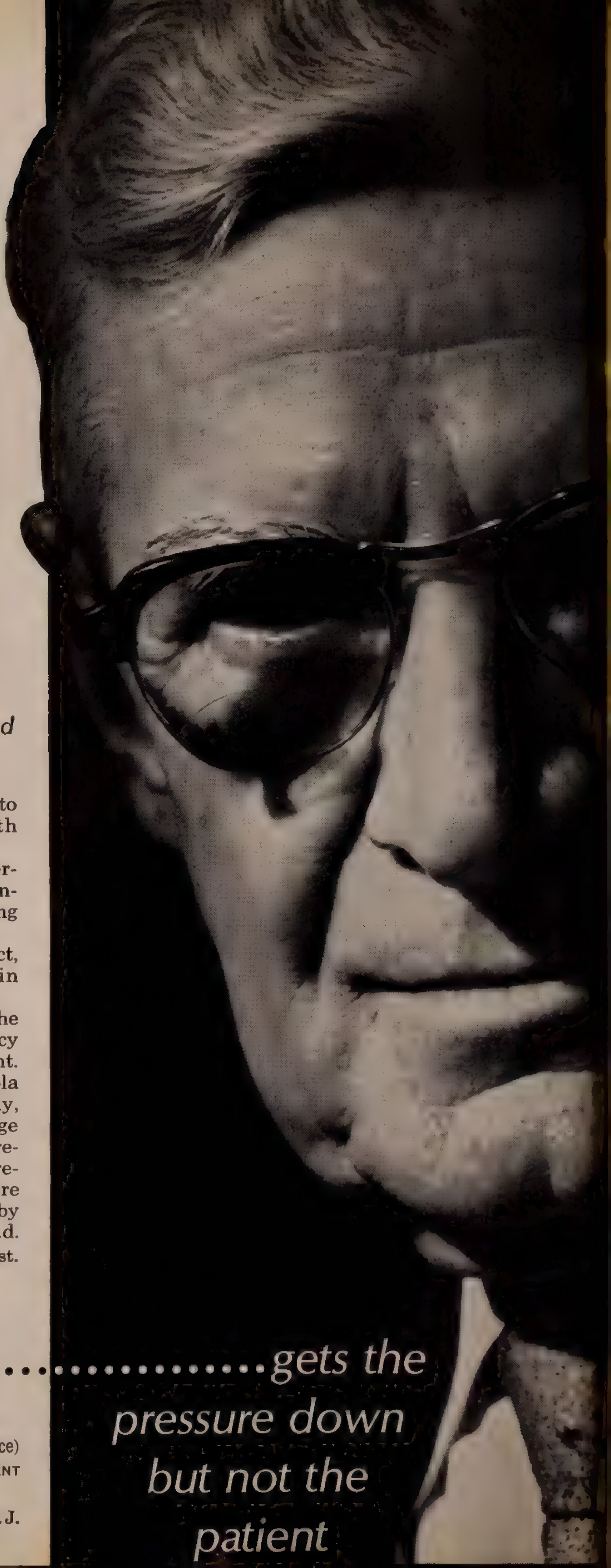
ALPHOSYL LOTION
For psoriasis—with acute inflammation
ALPHOSYL HC
LOTION WITH 0.25% HYDROCORTISONE

REED & CARNRICK / Kenilworth, New Jersey



Now–lower blood pressure with greater safety… and without serious side effects

In 755 hypertensive patients treated with Capla, no postural hypotension, depression, electrolyte imbalance or other serious side reactions were reported



Capla is a new drug that acts centrally to lower blood pressure smoothly and with greater safety.

Capla is indicated for the control of hypertension, either alone in mild cases, or in conjunction with diuretics or peripherally acting hypotensive agents in more severe cases.

In addition to its antihypertensive effect, Capla exerts a mild calming influence in many patients.

Capla is virtually free of side effects. The sole side effect occurring with any frequency is mild drowsiness, which is usually transient.

Dosage: The recommended dose of Capla is one 300 mg. tablet three or four times daily, before meals and at bedtime. The dosage should be adjusted to individual requirements; for example, older patients may require lower dosage. Where lower dosages are indicated, frequency should be maintained by giving 150 mg. (one-half tablet) q.i.d. or t.i.d.

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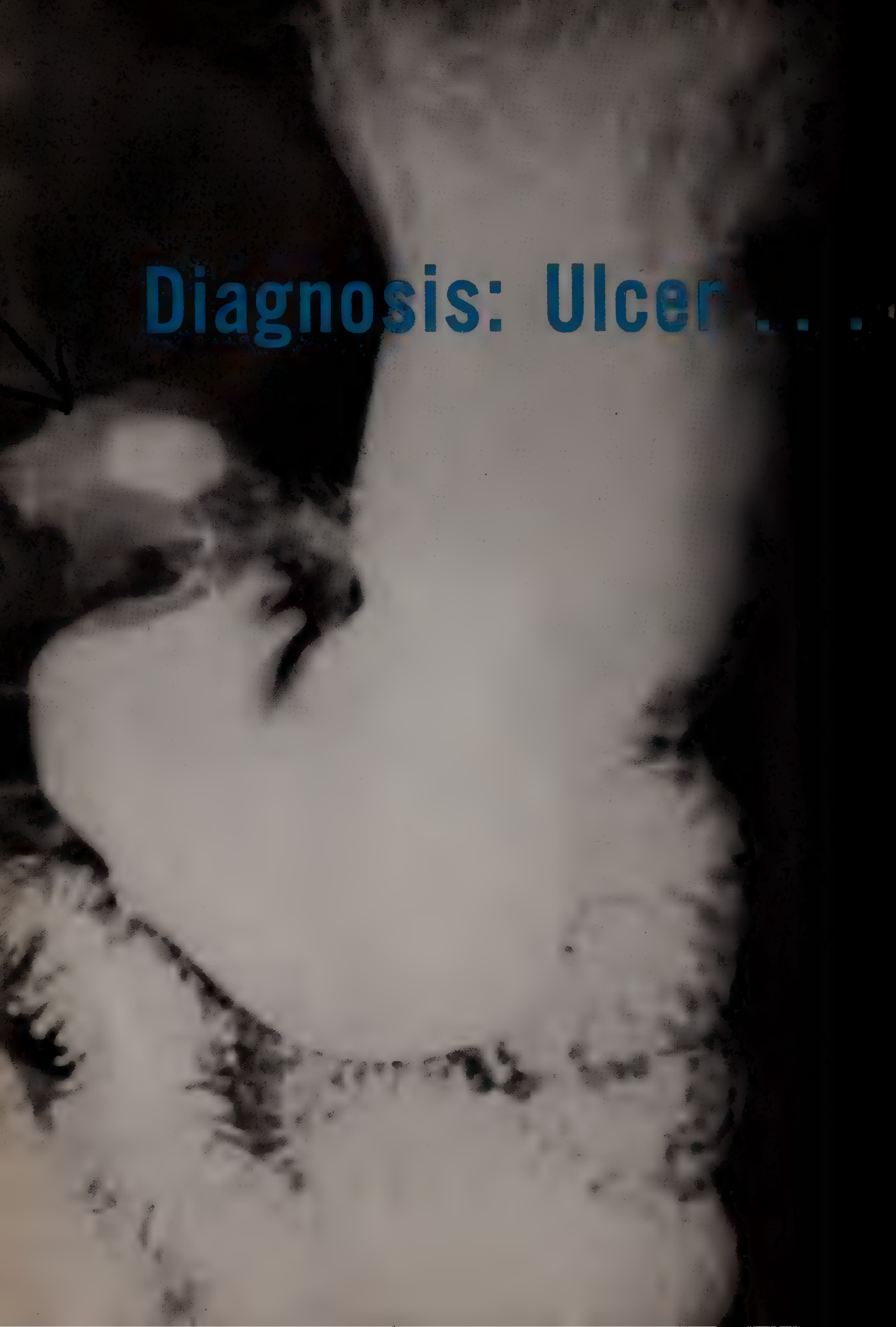

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Fair	0.9%
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Additional studies, involving another 27 investigators and approximately 500 patients, confirmed the above results.

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25 mg	Orphenadrine* hydrochloride	25 mg
25 mg	Bismuth aluminate	50 mg
45 mg	Magnesium oxide	
500 mg	Co-precipitate of aluminum hydroxide and magnesium carbonate	918 mg

Physicians' brochure available on request.

CAUTION: Federal law prohibits dispensing without prescription.

†Kirsner, J. B., J.A.M.A., 166:1727, 1958.

*Patent Nos. 2,567,351; 2,991,225.

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Niedelman, M.L.: Am. Pract. & Digest Treat., 10:1001, 1959.

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AND DEPTH TO ORAL ANALGESIA

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fills the gap between mild oral and potent parenteral analgesics

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in bronchial
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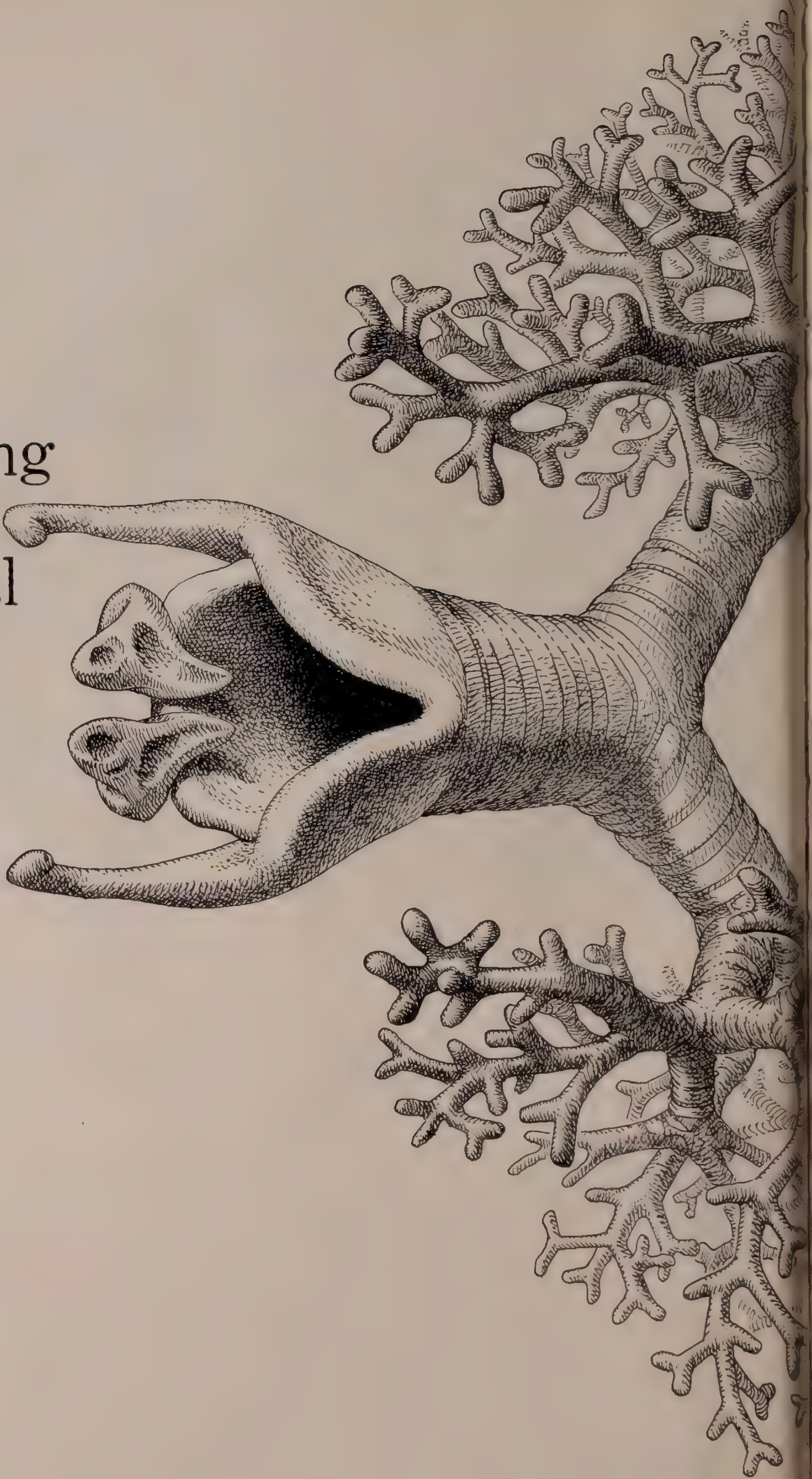

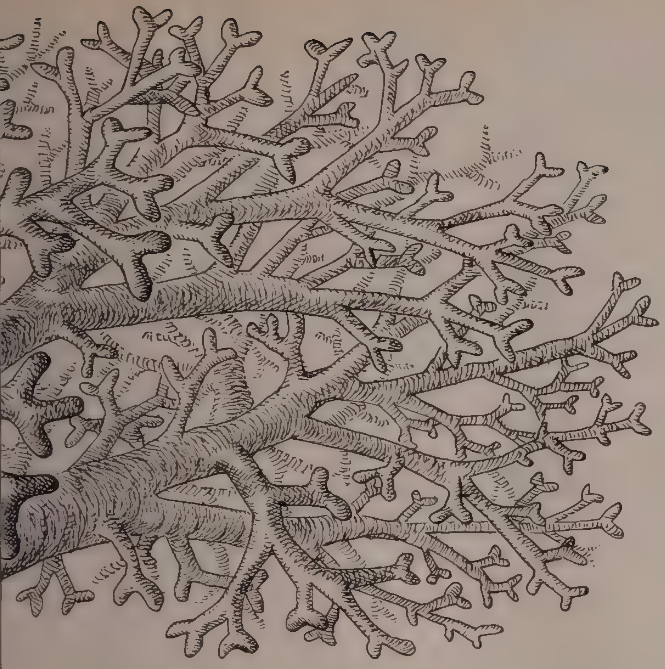

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With ARISTOCORT, asthmatic patients obtain sustained relief of wheezing, dyspnea, and spasmodic coughing. It is of particular value in ameliorating severe attacks that may have serious sequelae. With ARISTOCORT, many patients who might otherwise be invalids are able to continue their customary livelihoods or maintain their regular household activities. Yet this symptomatic relief is not often accompanied by the hormonal collateral effects —sodium retention, edema, emotional disturbance, insomnia, voracious appetite— that so often have been a deterrent to steroid therapy.

SUPPLIED: Scored tablets (three strengths), syrup and parenteral. Request complete information on indications, dosage, precautions and contraindications from your Lederle representative, or write to Medical Advisory Department.

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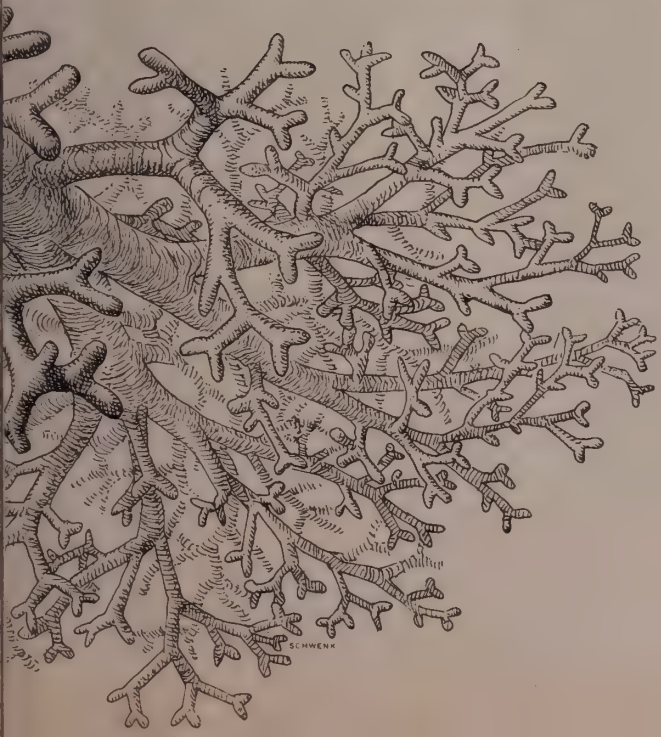

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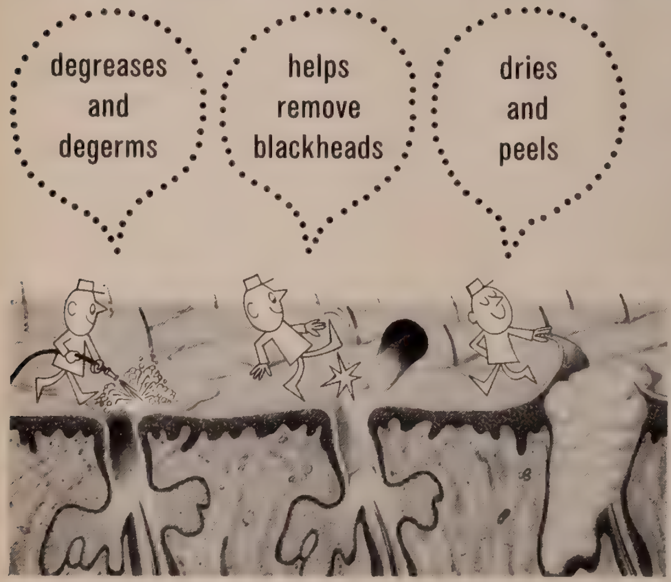
you get these results with **Fostex** to clear acne lesions faster



Fostex is a more complete acne prescription because it contains 6 anti-acne agents* . . . not just 1 or 2. These 6 agents, working together, provide essential actions necessary for the local treatment of acne.

Fostex degreases, dries, peels, and degerms acne skin. It helps remove blackheads, unblock pores, prevent pustules and scar-producing cysts, and rids the skin of bacteria.

Patients like Fostex because it's so easy to use. Instead of using soap, they simply wash acne skin with Fostex Cream or Cake 2 to 3 times daily.

***Only Fostex contains this unique combination of anti-acne agents:** Sebulytic® (3 surface-active agents—sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, sodium dioctyl sulfosuccinate), micropulverized sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

Supplied—Fostex Cake, bar form. Fostex Cream, 4.5 oz. jars. Also used as a therapeutic shampoo in dandruff and oily scalp which often accompanies and aggravates acne.

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Fostex® treats pimples • blackheads • acne while patients wash

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IN ACUTE OTITIS MEDIA • SAFE AURALGESIC
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BROAD-SPECTRUM THERAPY IN
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BIO-TOSMOSAN® **HC**
(WITH HYDROCORTISONE ALC.)

IN ACUTE EXACERBATION (EXTERNAL
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THROAT SPRAY • GARGLE • SWAB

FOR RELIEF OF SORE THROAT

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Acts with predictable safety—In 20 years of clinical use, no toxic or side actions have been reported with KOAGAMIN. Bleeding is arrested without danger of thrombosis, and because KOAGAMIN contains no protein or alkaloid, it can be administered without danger of sensitization or untoward reactions.

Acts effectively in a broad range of indications—Because of its *unparalleled safety* and *outstanding effectiveness,* KOAGAMIN has been successfully employed in...hemorrhagic diseases, abnormal bleeding, blood disorders, surgical cases and trauma.

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BEFORE, DURING AND AFTER SURGERY

KOAGAMIN®

(parenteral hemostat)

controls bleeding with minimal dosage and maximum safety

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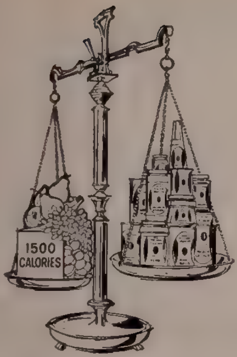

A new answer to one of America's leading health problems

60 DELICIOUS FOODS THAT MAKE WEIGHT CONTROL EASIER!

Here is a practical and down-to-earth method to help overcome obesity, the nation's No. 1 diet problem—and prime stealer of doctor's consultation time. Now a new group of 60 delicious Mott's Figure Control Food products uses the best of nutrition knowledge to create quality dishes, lower in calories by an average of 50%. Indicated calorie savings can be made pleasantly and accurately while eating normal-size portions by using these calorie-controlled foods in place of higher calorie dishes. Protein, vitamin and mineral food values are retained.

Low carbohydrate, low fat: Fats are largely extracted from meats and poultry in a way that cannot be done at home. Sauces and dressings are prepared with a high proportion of non-fat milk solids, vegetable colloids; all are delectably "natural" and tempting in flavor. Fruits, juices, desserts and sauces are prepared where indicated with non-caloric sweeteners—natural fruit values are intact, extra sugars reduced. The carbohydrate, protein and fat content appears on all labels along with the calorie count. Useful for diabetic diets, too.

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New Mott's Figure Control® Foods offer Good Eating at Half the Usual Calories

	Quantity	Figure Control Calories	"Regular" Food Calories
Apple-Grape Drink	½ cup	20	52
Five-Fruit Juice Breakfast Drink	½ cup	20	52
Braised Beef and Vegetables	6½ oz.	184	380
Meat Balls in Brown Gravy	3½ oz.	84	280
Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
Cherry Pie Filling	1 oz.	20	60
Chocolate Topping	1 tbsp.	8	63
Preserves (Peach, Strawberry)	1 tbsp.	9	55
"Maplette" Syrup	1 tbsp.	9	55
Liquid or Powder Sweetener	(to equal 1 tbsp. sugar)	0	16

Complete menus, recipes, calorie chart available for professional distribution, with weight control guides you can distribute with confidence: all menus meet N.R.C. Recommended Daily Allowances. **Use this handy order form:**

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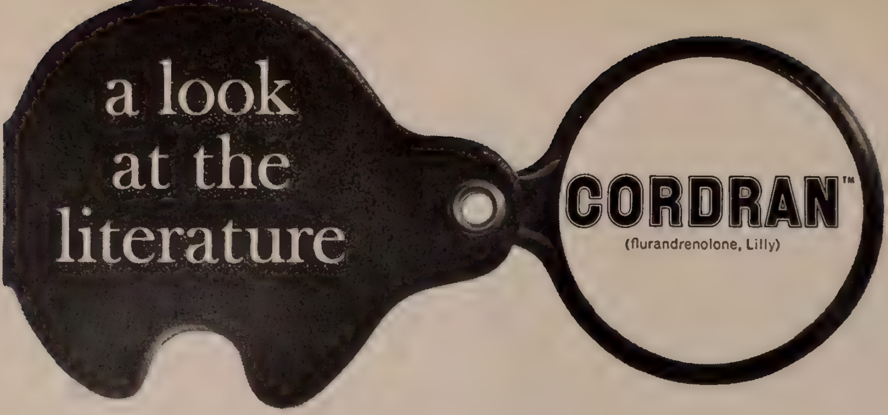

“Treatment results were good, and in many cases a dramatic response was noted. Many of the cases had previously failed to respond to various types of therapy including, in some instances, other topical corticosteroid preparations.”

—Gray, H. R., Wolf, R. L., and Doneff, R. H.: Evaluation of Flurandrenolone, a New Topical Corticosteroid, Arch. Dermat., *84:*18, 1961.

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All forms are supplied in 7.5 and 15-Gm. tubes.

Cordran™-N (flurandrenolone with neomycin sulfate, Lilly)

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New York State Journal of Medicine

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Editorials

The art and joy of reading*

The art of writing is often expounded in professional journals, and the joy of authorship is widely recognized, if not advertised. Health science practitioners, however, spend much more time consuming "literature" than producing it. Yet how-to-do-it articles on reading rarely appear, and extolling the joy of professional reading seems almost inappropriate. How can attempting to keep one's head above mounting floods of printed matter be, in any sense, a joy? Most practitioners consider it a chore; and a chore is, at best, tedious and more often frankly painful, especially when it can never be finished. A less loaded wording of the same basic question allows a more constructive answer—How can one keep abreast of progress most efficiently? Efficiency requires skill, and mastery of the art of reading is the essential first step in transforming what is to many a chore into a joy. Although not sufficient in itself, this skill opens the door to the possibility of one's professional reading becoming a source of pleasurable satisfaction rather than an onerous task.

What are the secrets of practitioners who are accomplished in the art of reading? The few analyses available[1] and personal observation suggest that these secrets are not magical. They can be used by any practitioner wishing to make the printed word his tool rather than his trial.

Speed

The first characteristic of all skillful readers is something rarely mentioned after school years—speed. Obviously, reading must be a chore to anyone who hobbles along at 100 words a minute, a slow speaking rate. Precise information on the reading rates of health science practitioners is surprisingly scarce, but watching numerous colleagues suggests that many are hopeless hobblers. The ability to read 200 to 300 words of scientific material is common among practitioners who are on top of the "literature" rather than under it. The tendency is to overestimate one's reading speed. A simple test will provide a more accurate assessment. Self-instruction[2] or the adult classes now available in most communities is the only answer for those whose reading is too pedestrian for the jet age.

Selectivity

The second ingredient for success is the selectivity practiced by the masters of the art. This selectivity begins with the sorting of the printed material that arrives in their office—the journals, brochures, booklets, fliers, and form letters. This mail they separate, figuratively or literally, into three piles—one that requires only a quick glance before discarding, the second of items that deserve at most five or ten minutes of rapid scanning, and the third that merits more extended study. They are ruthless and ask themselves constantly, "How much have I gotten out of a particular type of item in the past, and how much of my time is it worth?" The next level of selectivity comes chiefly with the third pile—the material chosen for extended study. Here they make their time count by reading only those parts of each item that promise maximal returns. For a journal this means first thumbing through the pages, scanning the titles. Where a title gives promise, they turn immediately to the summary, which in more and more journals is thoughtfully being placed immediately after the title. If the article concerns a subject somewhat peripheral to their main interests, the summary alone should give all the information needed.

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* Reprinted with permission from The New York Journal of Dentistry 32: 66 (Feb.) 1962.

If after reading the summary the decision is that the article is meaty and of direct interest then, and only then, they read the entire paper, or selected parts of it. This method gives titles and summaries great weight, but in the better journals editors are concentrating on improving the informativeness of these two most-read parts of scientific papers.[3]

Optimal use of time

The third secret of the artful reader is optimal use of time available for reading. Selective sorting is a necessary preliminary. Every practitioner has scattered free moments throughout his day—when he is waiting for a patient, an assistant, a report, or a phone call. The first pile, the glance-and-throw-away category of mail, these master readers keep handy and dispose of easily in this otherwise wasted time. Longer breaks during the working day, planned or unplanned, are utilized for the second pile, the quick-scan items. The third pile—the peruse-at-leisure material—is taken home unless the practitioner has found that scheduling specific hours for reading at his office is more efficient than reading at home.

Regularity

The fourth characteristic of the master is regularity. He designates definite periods in his weekly schedule exclusively for sustained reading under conditions allowing concentration. No serious backlog is allowed to accumulate. Each day takes care of the glance-and-discard material that arrives; items in the quick-scan category are covered within the week; and the peruse-at-length pile is kept to manageable size by giving periodicals priority in order of frequency of publication—weeklies first, then biweeklies, monthlies, and so forth. If despite his most efficient efforts, the backlog insidiously increases and he cannot schedule more reading time, he either becomes more rigidly discriminating in his sorting or carefully culls his list of subscriptions.

All this undoubtedly increases one's efficiency, but where does the pleasure or joy of reading come in? Before any pleasure is possible, the chore of professional reading must be eliminated; and many practitioners have proved that, with such a system, they can painlessly not only keep up with the essentials of progress in their major fields but also inform themselves broadly in an expanding range of related subjects.

To introduce pleasure, or perhaps some joy, into professional reading, however, no similar single prescription will suffice. For certain individuals the satisfaction of knowing they are constantly improving their professional competence is a source of so much satisfaction as to qualify as a true pleasure. No longer do they have that sinking, guilty feeling engendered by a mountain of unread journals. No longer do they suffer from the informational indigestion that seems to be an occupational disease today. For others, however, something more is necessary. Freed from the press of "must" reading, they can savor the luxury of exploring the many possibilities of what may be called reading for growth—reading not essential to practice but contributing generally to professional and personal development. Some, after routine reading is out of the way, immerse themselves in the history or philosophy of their profession; others delve into the fascinating diseases of animals, play detective by diagnosing the ills of famous personalities from biographies, range widely into the physical and social sciences, or make up for a youth misspent in narrow, technical studies by sampling the new and old in fiction. The doors to the joy of reading are many, and each must choose his own. "Reading maketh a full man," and even practitioners enjoy being completely human.

—Richard H. Orr, M.D.

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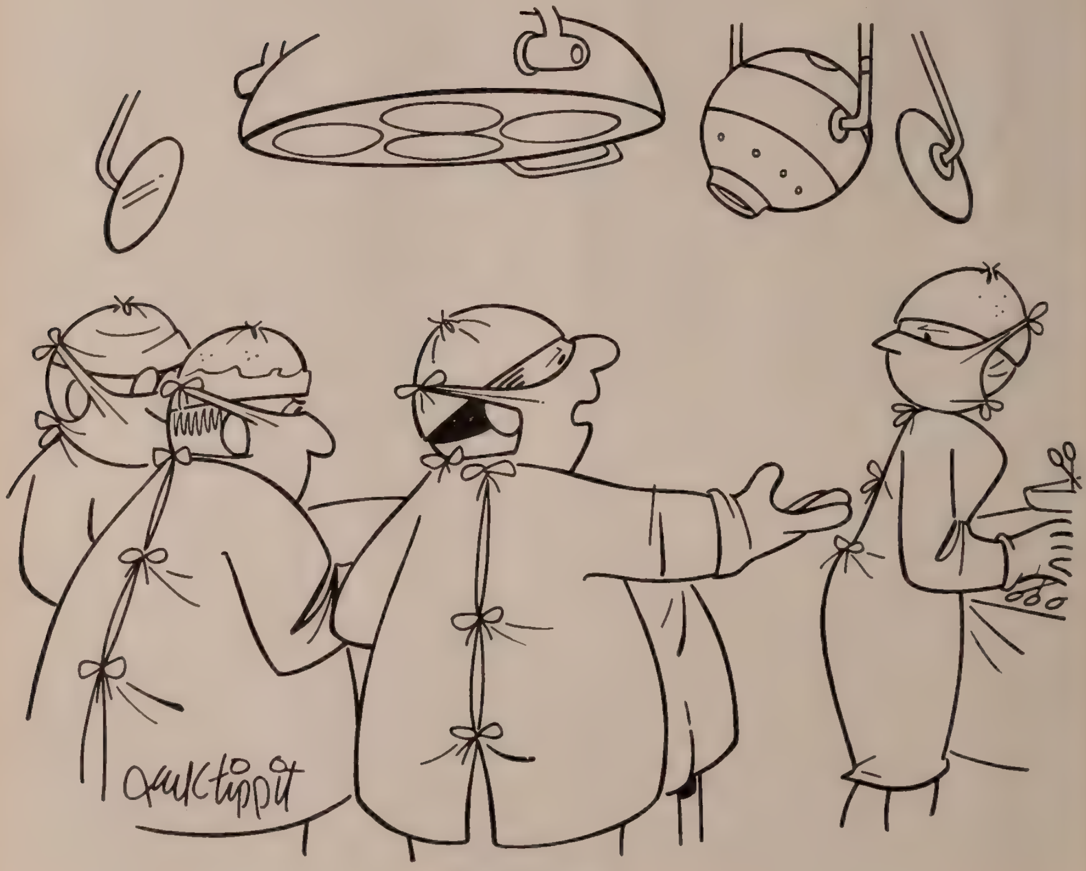
Partnership for progress

Medicine moves forward on many fronts; those of research, education, and economics are well publicized in both the specialized and the general press. There is one, however, which is little known to the public; the high quality of its accomplishments is not fully known and recognized even by the participants themselves. We refer to the important collaboration of the medical profession with the public agencies of welfare and vocational rehabilitation. This cooperative effort literally remakes lives; it turns despair to hope, disability to ability, and dependency to independence. We are privileged to publish elsewhere in this issue* two cases from a public welfare agency which demonstrate the character of this work. These are only two of many hundreds which could be documented.

At a time when both medicine and welfare are beset by criticism, well intentioned and not, we offer these results. Res ipsa loquitur.

* Page 2257.



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Scientific Articles

Repository Treatment of Grass and Ragweed Pollinosis (1961)

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Rockville Centre, New York

IN 1961 72 PATIENTS *were treated with grass emulsion and 101 patients with ragweed emulsion. Both emulsions, prepared by a private laboratory and not reemulsified before administration, were given in one to four injections in total doses ranging from 1,000 to 20,000 PNU (protein nitrogen units) before the pollinating season. The clinical results were satisfactory in 77 per cent of the grass-sensitive and 76 per cent of the ragweed-sensitive patients, and they appeared unrelated to dose and pretreatment skin tests. Slight systemic reactions occurred in 6 per cent of the grass-treated patients and moderately severe reactions in 1 per cent. Slight systemic reactions occurred in 7 per cent of ragweed-treated patients, but no severe reactions occurred. Delayed nodule formation occurred in 7 per cent of the grass-treated patients and in 8 per cent of the ragweed-treated patients.*

FREUND[1] in the late 1930's, found that the combination of Falba, paraffin oil, killed Mycobacterium, and antigen, gave markedly elevated and prolonged antibody response in animals. In 1947 Loveless[2] adapted this technic but omitted the killed Mycobacterium in the treatment of ragweed hay fever. Since the 1950's, Brown[3–6] has reported on the repository treatment of pollinosis in thousands of patients with over 90 per cent excellent results and has been largely responsible for attracting attention to this new technic.

In 1960, I reported on my first year of repository treatment with grass and ragweed.[7,8] As a result of experiences gained in the first season, modifications were made the following year. This paper is a report on the second year of repository treatment of grass and ragweed pollinosis in 1961 with the use of emulsions prepared by a commercial laboratory* and not re-emulsified before use.

Preparation and macroscopic and microscopic description of grass and ragweed emulsions

The emulsions consisted of one part emulsifier (Arlacel), six parts of mineral oil (Atreol), and five parts of aqueous antigen. They were packaged in 5 cc. vials in concentrations varying from 500 to 20,000 PNU (protein nitrogen units) per cubic centimeter. The vials were sent through the mail, stored in the refrigerator, and administered within one to four weeks later without further re-emulsification. Macroscopic and microscopic examinations were made every few days for the possible detection of breakdown of the emulsion. None of the grass emulsions even at the present time of writing, twelve months later, have shown macroscopic evidence of cracking. On aging the microscopic examination revealed a slow and gradual enlargement of the droplets. When the emulsions were first received, a microscopic examination showed an over-all droplet distribution of 1 micron in size with occasional larger droplets (3 microns in size) every fifth high-power field. After several weeks, there was a gradual increase in the number and size of some of the droplets, that is, about 5 larger droplets (4 microns in size) every second high-power field.

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* Hollister-Stier Laboratories, Spokane, Washington.

There were four shipments of ragweed emulsion received in May and June of 1961. The first batch of ragweed emulsion was not as excellent macroscopically and microscopically as the grass emulsion. On gross examination it was noted that the viscosity was decreased. Immediately after the material was prepared, microscopic examination was reported to show the average droplet to be 0.5 micron and none larger in size. Several days later, after delivery to me, microscopic examination showed the average droplet about 0.8 micron in size, with approximately 10 larger droplets (5 microns in size) in every fifth high-power field. After two weeks of storage in the refrigerator, there was a further increase in the microscopic size of the droplets. While the over-all distribution remained 1 micron in size, there were 15 larger droplets (7 microns in size) every second high-power field.

Two weeks after the delivery of the first batch of ragweed, a second shipment of emulsion was received. The preparation was identical to the first except that the ragweed antigen came from another source. Microscopic examination at the commercial laboratory immediately after preparation showed the average droplet to be 0.5 micron in size. On receipt of this second batch several days later, several of the 20,000 PNU-per cubic centimeter emulsions showed separation and cracking. In the 10,000 PNU-per cubic centimeter emulsions the over-all droplet distribution was 1 micron in size, but in addition there were 30 droplets (20 microns in size) every high-power field. The less concentrated emulsions (that is, 1,000 PNU- per cubic centimeter) did not show as many of the larger droplets. A third batch was prepared a few days later with identical macroscopic and microscopic findings. A fourth batch of emulsion was prepared with glyceryl monooleate. The microscopic examinations were essentially the same with only slight decrease in the number and size of the larger droplets. While it was desirable to administer an emulsion with the smallest uniform droplet size, this was not obtainable with the last three shipments of ragweed emulsion. The previous year, in 1960, a hand-pumped emulsion was used without causing constitutional reactions. On microscopic examination this latter emulsion had contained more of the larger droplets than the 1961 ragweed emulsion. Since a finer ragweed emulsion could not be prepared, it was decided to use this emulsion.

Preliminary testing of patients

There were 72 patients in the rose fever study and 101 patients in the ragweed-hay fever study. Preliminary to the repository treatment, each patient was tested by the puncture, intracutaneous, conjunctival threshold, and serial dilution intracutaneous threshold tests.

Dosage

The total therapeutic dose varied between 1,000 to 20,000 PNU per cubic centimeter injected subcutaneously in volumes of from 0.5 to 1 cc., and given approximately two to three months before the onset of the pollinating season. It was given in from one to four injections approximately two weeks apart. No single test but all four preliminary tests were used as criteria for determining dosage. The patients who reacted most sensitively on preliminary skin and conjunctival testing received lower doses in divided injections. The patients who were less reactive on preliminary testing received higher doses in single injections. Table I shows the dosage schedule used in this study.

Clinical results

The clinical results were evaluated as satisfactory (65 to 100 per cent relief of symptoms) and as unsatisfactory (0 to 65 per cent relief of symptoms). There were 72 patients who were given grass emulsion treatment in 1961. Satisfactory results were obtained in 77 per cent and unsatisfactory in 23 per cent of the patients. Out of a total of 72 patients given grass repository

TABLE I. Dosage schedule for repository treatment of grass and ragweed pollinosis, 1961

Pretreatment Conjunctival Threshold Test (Protein Nitrogen Units Per Cubic Centimeter)	Injections (Number)	Total Dose (Protein Nitrogen Units Per Cubic Centimeter)
10 to 320	2 to 3	1,000 to 5,000
640 to 10,240	1 to 3	5,000 to 10,000
>10,240	1	7,500 to 20,000

treatment in 1961, 31 patients received it for the first time and 41 patients were second-year repository-treated patients. Those patients who had received repository treatment for the second year had 73 per cent satisfactory results. Patients who had received repository treatment for the first time in 1961 had 81 per cent satisfactory results. The clinical results of patients treated with repository therapy for the second year showed that 41 per cent did better, 39 per cent did the same, and 20 per cent did more poorly than after the first year of emulsion treatment in 1960.

There were 101 patients who were given ragweed emulsion treatment in 1961. Satisfactory results were obtained in 76 per cent and unsatisfactory results in 24 per cent of the patients. Out of a total of 101 patients given ragweed repository treatment in 1961, 40 patients received it for the first time, and 61 patients were second-year repository-treated patients. Those patients who had received repository treatment for the second year had 74 per cent satisfactory results. Patients who had received repository treatment for the first time in 1961 had 80 per cent satisfactory results. The clinical results of patients treated with repository therapy for the second year showed that 41 per cent did better, 34 per cent did the same, and 25 per cent did more poorly than after the first year of emulsion treatment.

An attempt was made to note the relationship of dose to clinical results. In the grass studies satisfactory results were obtained in 60 per cent of the patients who received between 1,000 and 2,500 PNU; 78 per cent of those who received between 2,500 and 5,000 PNU; 65 per cent of those who received between 5,000 and 7,500 PNU; 100 per cent of those who received between 7,500 and 10,000 PNU; and 80 per cent of those who received between 10,000 and 20,000 PNU.

A similar analysis was made to note the possible relationship of dose to clinical results in the ragweed-treated group. Satisfactory results were obtained in 67 per cent of the patients who received between 1,000 and 2,500 PNU; 81 per cent of those who received between 2,500 and 5,000 PNU; 81 per cent of those who received between 5,000 and 7,500 PNU; 83 per cent of those who received between 7,500 and 10,000 PNU; and 70 per cent of those who received between 10,000 and 20,000 PNU.

Patients were classified according to pretreatment conjunctival threshold tests in an effort to note the relationship between this and clinical improvement following emulsion therapy. In the grass study, satisfactory results were obtained in 82 per cent of the patients with a pretreatment conjunctival threshold level of between 10 and 320 PNU per cubic centimeter; 75 per cent of those with a level of between 640 and 10,240 PNU per cubic centimeter; and 73 per cent of those with a level of more than 10,240 PNU per cubic centimeter.

In the ragweed study, satisfactory results were obtained in 82 per cent of the patients with a pretreatment conjunctival threshold level of between 10 and 320 PNU per cubic centimeter; 79 per cent of those with a level of between 640 and 10,240 PNU per cubic centimeter; and 76 per cent of those with a level of greater than 10,240 PNU per cubic centimeter.

Table II shows an analysis of the clinical results of repository treatment of grass and ragweed pollinosis in 1961.

Constitutional reactions

There were 6 per cent slight and 1 per cent moderately severe systemic reactions following the grass repository injections in 1961. The one moderately severe reaction occurred in a patient who tested exquisitely sensitive on all four preliminary tests and who had a previous history of constitutional reactions following multiple visit aqueous and previous repository treatments. This patient had received three injections of emulsion

TABLE II. Clinical results of grass and ragweed repository treatment in 1961

	Number of Patients		Per Cent Satisfactory (65 to 100 Per Cent Relief of Symptoms)		Per Cent Unsatisfactory (0 to 65 Per Cent Relief of Symptoms)	
Conditions	Grass	Ragweed	Grass	Ragweed	Grass	Ragweed
Pretreatment conjunctival threshold test (protein nitrogen units per cubic centimeter)						
Grass						
10 to 240	27	...	82	...	18	...
360 to 10,240	16	...	75	...	25	...
>10,240	29	...	73	...	27	...
Ragweed						
10 to 320	...	17	...	82	...	18
640 to 10,240	...	42	...	79	...	21
>10,240	...	42	...	76	...	24
Total dose (protein nitrogen units per cubic centimeter)						
1,000 to 2,500	5	3	60	67	40	33
2,500 to 5,000	22	26	78	81	22	19
5,000 to 7,500	17	16	65	81	35	19
7,500 to 10,000	6	23	100	83	...	17
10,000 to 20,000	20	33	80	70	20	30
Results						
One year of repository treatment (1961)	31	40	81	80	19	20
Two years of repository treatment (1961 and 1960)	41	61	73	74	27	26
TOTALS	72	101	77	76	23	24

spaced two weeks apart: The first injection consisted of 200 PNU, the second of 900 PNU, and the third of 2,400 PNU. Three hours after the third injection, the patient had generalized urticaria and wheezing.

There were no moderate or severe constitutional reactions following ragweed emulsion injections in 1961. There were 7 per cent extremely slight reactions, that is, sneezing, lacrimation, and slight cough, which were of very little or no consequence to the patient.

Scratch testing with emulsion

Each patient was scratch tested with the emulsion prior to treatment. In the grass study 17 patients (24 per cent) gave positive scratch test reactions. The only patient who had a moderately severe systemic reaction had a positive scratch test result with the emulsion. However, most of the patients who had slight systemic reactions following injection, did not have positive scratch reactions to the treatment emulsion. Further, most of the patients with positive scratch reactions to the emulsion did not have systemic reactions.

In the ragweed study, 5 per cent of the patients gave positive scratch reactions and the remaining gave negative reactions. There was no correlation between a positive scratch emulsion reaction and the occurrence of the slight systemic reactions.

Local reactions at site of injection

In one fourth of the patients, there was some local reaction at the site of injection following grass and ragweed emulsion administration. The local reactions varied from immediate local swelling to more pronounced swelling lasting for several days. Patients occasionally complained of moderate to marked tenderness lasting for several days.

Twelve months following the administration of repository treatment, there was a

7 per cent incidence of local delayed nodule formation. These nodules are firm and vary from 1 to 5 cm. in size. In some patients the overlying skin is slightly bluish red in color. One patient with persistent nodules of 5 cm. in size following grass and ragweed emulsions had further egg-sized enlargement of both sites seven months after the injections. Following conservative therapy, these swellings receded. Persistent nodules appear to be more frequent in children and in patients who are less reactive on preliminary testing.

Comment

The clinical results in 1961 following repository therapy showed satisfactory results in 77 per cent of the grass-sensitive patients and 76 per cent of the ragweed-sensitive patients. The clinical results following repository injections in 1960 showed satisfactory results in 67 per cent of the grass-sensitive patients and 65 per cent of the ragweed-sensitive patients. An analysis of multiple visit aqueous treatment in 1959 showed 67 per cent satisfactory results. Many of the patients who had poor therapeutic results following repository therapy in 1960 returned to multiple-visit aqueous treatments in 1961. This may possibly explain why the results were better in 1961 than in 1960.

An analysis of the relationship of dosage to clinical results following grass-repository injections in 1960 showed that patients who had higher doses appeared to have slightly better results. Clinical results seemed unrelated to dosage in the 1961 series although the poorest records came from the small group who received less than 2,500 PNU.

The repository ragweed dosage in 1960 varied from 2,000 to 5,000 PNU. There was no correlation between dosage and clinical results within this range. Nor was there any relationship between dosage and clinical results in 1961 even though the dosage range was from 1,750 to 20,000 PNU.

A study of preliminary conjunctival threshold sensitivity levels as related to clinical results following grass-emulsion injections showed slightly better therapeutic results in the group that reacted less sensitively in 1960. However, in 1961 clinical results following grass-emulsion injections appeared to be independent of pretreatment conjunctival testing levels.

TABLE III. Review of clinical results following grass repository treatment in 1961 and 1960

	Per Cent Satisfactory Results (65 to 100 Per Cent Relief of Symptoms)	
Conditions	1961	1960
Pretreatment conjunctival threshold test (protein nitrogen units per cubic centimeter)		
10 to 240	82	55
360 to 10,240	75	65
>10,240	73	73
Total dose (protein nitrogen units per cubic centimeter)		
1,000 to 5,000	74	67
5,000 to 10,000	73	69
10,000 to 20,000	80	..
Over-all results	77	67

The clinical results following ragweed repository treatment in 1960 and 1961 appeared to be independent of pretreatment conjunctival testing levels.

Tables III and IV show a summation of the clinical results of repository treatment of grass and ragweed pollinosis in 1960 and 1961.

In the present year no control studies have been done with multiple-visit aqueous or placebo injections. Because of the wide interest in this field, other workers throughout the entire United States are participating with these necessary controls. Contributions from various sources and time will eventually help to establish the value of the repository technic in pollinosis.

The incidence and intensity of severe constitutional reactions were decreased in this year's treatment. In the grass studies there was a 1 per cent incidence of moderately severe reactions whereas in the previous year there was a 5 per cent incidence. There were no moderate or severe constitutional reactions noted in the 1961 ragweed repository studies, only 7 per cent very slight and minimal reactions. In 1960, there was a total of 16 per cent reactions, of which 3 per cent were moderately severe, and 13 per cent were mild. In 1960 most of the pa-

TABLE IV. Review of clinical results following ragweed repository treatment in 1961 and 1960

Conditions	Per Cent Satisfactory Results (65 to 100 Per Cent Relief of Symptoms) 1961	1960
Pretreatment conjunctival threshold test (protein nitrogen units per cubic centimeter)		
10 to 320	81.5	64
640 to 10,240	78.5	73
>10,240	76.2	62
Total dose (protein nitrogen units per cubic centimeter)		
1,000 to 2,500	67.0	64
2,500 to 5,000	81.0	67
5,000 to 7,500	81.0	...
7,500 to 10,000	83.0	...
10,000 to 20,000	70.0	...
Over-all results	76.2	65

tients received repository injections in one single dose. In 1961, the patients who reacted most sensitively to preliminary puncture, intracutaneous, and conjunctival threshold testing were given divided doses, which probably explains the decrease in systemic reactions.

Twelve months after injection, residual nodules were still present at the site of the injection in 7 per cent of the grass-sensitive and 8 per cent of the ragweed-sensitive patients. Most of these nodules were pea-sized, although a few were twice that size with bluish discoloration of the overlying skin.

There have been various explanations for the occurrence of nodules, such as, faulty technic of administration, injection given too superficially, or leakage into the dermis. Whatever the reason, delayed nodule formation is a factor to be concerned with in the administration of these emulsions.

Unforeseen difficulties were encountered in the commercial preparation of some of the batches of the ragweed emulsion. Despite identical procedures, the same quality of emulsion macroscopically and microscopically could not be obtained. There appeared to be enzymes present in some of the ragweed pollen which were capable of breaking down some of the emulsions. In the 1960 grass and ragweed repository studies[7,8] four different types of emulsions were employed. The results of this study showed that the emulsions that contained the smallest and most uniform droplets did not necessarily provide the safety from constitutional reactions that had been theoretically anticipated. Many of the handmade emulsions which were used without occurrence of systemic reaction in 1960 contained a greater number of larger droplets than were present in some of the 1961 ragweed emulsion. Despite the occurrence of some droplets larger than 1 micron in size in the 1961 ragweed emulsions, no severe or moderately severe systemic reactions were encountered.

Time and experience will eventually prove or disprove the merit of emulsion therapy. Many facets of this problem need further clarification. At the present in the repository therapy of pollinosis, most of the workers make their own emulsions and re-emulsify immediately before use. In this study, the emulsions were prepared in a private laboratory and used without further re-emulsification. The results and safety were comparable with other studies[9] using custom-made emulsions with additional re-emulsification before administration.

Summary

Seventy-two patients were treated with grass emulsion, and 101 patients were treated with ragweed emulsion in 1961. The emulsions were prepared by a private laboratory and not re-emulsified before administration. They were given in one to four injections in total doses ranging from 1,000 to 20,000 PNU two to three months before the pollinating season. The clinical results were satisfactory for 77 per cent of the grass-sensitive and 76 per cent of the ragweed-sensitive patients. The clinical results appeared to be unrelated to dose and pretreatment skin tests. Slight systemic reactions occurred in 6 per cent, and moderately severe reactions in 1 per cent of the grass-treated patients. Slight systemic reactions occurred in 7 per cent of the patients who received ragweed repository injections, but there were no severe reactions. Delayed nodule forma-

tion occurred in 7 per cent of the grass-treated patients and in 8 per cent of the ragweed-treated patients.

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Estimate of alcoholism in teen-agers

It is estimated that 1 out of every 15 teen-agers is likely to become an alcoholic person, according to an interview with Marvin A. Block, M.D., reported in the June, 1962, issue of *Today's Health*. Unless there is broadening of our educational program, greater action, and more understanding of the subject of alcoholism, it is estimated that about 6 per cent of teen-agers may become alcoholic individuals sometime in the future. "Improvement of the home environment, understanding of the factors which contribute to alcoholism, suitable guidance, and proper education can materially modify this estimate. A person's inherent characteristics may play a part in his susceptibility to alcoholism, but these can also be considerably modified."

The primary responsibility for education about alcohol rests in the home, and the best way to teach youth is by example. "Too often, children drink to conform to what other teen-agers are doing; otherwise they feel self-conscious. An understanding, however, of why retaining independence in this area will give them stature in the eyes of their fellow teen-agers if they have good reasons for not drinking, provides the confidence they need."

On the other hand, children will drink as nonconformists because it makes them feel grown-up. If standards of responsibility are used for characterizing the term "grown-up" rather than the superficial ones, such as drinking, this situation might be corrected.

"Kiddy cocktails"—soft drink served to children in cocktail glasses—are a "dangerous procedure. Children are not little adults, and it is a mistake to encourage a child to imitate an adult. There are certain parts of an adult's world to which a child is introduced only when he is ready for such activity."

Drinking in the home should be exclusively an adult activity. However, this rule does not include ceremonial drinking or drinking with meals. "As a matter of fact, in such homes where drinking is done regularly with meals, we see very little alcoholism, since children look on such drinking as part of their home life, and rarely indulge in alcohol in excess later in life. Of special importance, however, is for parents never to drink excessively."

The general trend in our culture in the last several years has been toward an overemphasis on drinking. "The tolerance in this country for drunken behavior and the social pressure for drinking are perhaps the two greatest factors which have lead to this overemphasis on drinking. We should teach our young people that not to drink does not affect them socially, that alcohol is not a necessity of life, and that some people may drink if they wish but that to others it will bring harm. If we could teach people that the real sophisticate never drinks excessively and that to do so means social ostracism, we'd find less and less alcoholism."

SYMPOSIUM
AND PANEL
DISCUSSION

Present Status of Cancer Chemotherapy

Chairman
WILLIAM F. LIPP, M.D., Buffalo, New York
Moderator
GEORGE E. MOORE, M.D., PH.D., Buffalo, New York
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Introduction

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THERE ARE a great many agents being tossed about, more or less seriously, as anticancer drugs. Some of them are swamp water, some of them are nothing more than mineral oil, and some of them are as bad as the numerous letters that we all get from interested and sincere people, saying: "In my family, we have always taken a teaspoon of kerosene, every morning and night, and no one has gotten cancer."

On the other hand, we have the National Cancer Chemotherapy Service Center, which is testing approximately 45,000 new compounds each year. Out of these 45,000 new compounds tested in animals with tumors, approximately one out of every hundred shows some activity, and one out of every thousand shows enough antitumor activity so that we think it worth going into pharmacologic research, such as checking it for toxicity in monkeys, gastrointestinal tract toxicity in dogs, central nervous system toxicity in cats, and so on, and finally taking it up to the human level for initial clinical trials.

Each year there are several dozen new compounds available for anticancer therapy. Most of these compounds are very toxic; in fact I know of no exception to this. If someone says that an anticancer drug is nontoxic, it is ineffective, at least to date. The anticancer drugs are difficult to use. Some of them are attended with severe side-reactions, and indeed mortality, and must be used very carefully.

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, General Session, May 10, 1961.

The Use of Human Tumors in Experimental Chemotherapy*

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FOR MANY YEARS various types of animal cancers have been used in experimental chemotherapy. Various private and governmental agencies have supported the use of transplantable animal tumors to screen a large number of crude culture filtrates in search of novel antibiotics with carcinostatic properties. Other efforts have been directed toward using these same animal tumor systems to screen large numbers of chemicals. With various transplantable human tumors being available in more recent years, it was conceived that the use of such transplantable human tumors in experimental animals would somewhat bridge the gap between the testing of various potential chemotherapeutic agents against animal tumors in animals and human tumors in human beings. To be sure, the tumors are of human origin, and they retain their human characteristics even though they are grown in experimental hosts. Conditioned rodents were used for the majority of the chemotherapy studies utilizing human tumors in free-living forms.[1-4]

This report deals primarily with chemotherapy studies of human tumors grown in a nonconditioned host, the chick embryo. The human tumor-egg host system has been used rather extensively to evaluate a wide variety of chemotherapeutic agents. Numerous results of such evaluations are to be found in the literature. Dagg *et al.*[5-6] and Harris[7] have reported impressive results using various alkylating agents. When compounds of microbial origin were explored, Harris[8-10] and Harris *et al.*[11] reported that some of the agents were effective in inhibiting the growth of various human tumors grown in the egg. The exploration of hormones and related agents revealed that some of them inhibited effectively the growth of various human tumors grown on the chorioallantoic membrane (CAM) of chick embryos.[12-14] Beyond the evaluation of various agents to determine their antitumor potentials, another significant finding emerged: the qualitative and quantitative differences in sensitivities among the tumor types. This report presents findings which attest to these differences, and the implications for the practical application of this knowledge in the control of tumors in man are discussed.

Materials and methods

The types of human tumors used in these studies were H.Ep. 3 (Toolan's epidermoid carcinoma), H.S. 1 (sarcoma), H.Ad. 1 (adenocarcinoma), and A-42 (Skiff's bronchogenic carcinoma). Detailed descriptions of the procedures followed in these studies have already been published elsewhere.[9] For purposes of orientation, the salient features of the procedures are presented here. Each egg received a single tumor fragment implanted on the chorioallantoic membrane at nine days of incubation. With appropriate illumination, the tumor growth was determined four days after implantation, and the tumor-bearing eggs received a single dose of the test agent injected into the yolk sac. Six days after the injection of the test agent, the embryos were sacrificed, and the evaluations were made. The parameters used for evaluation were the comparison of mean tumor weights between the treated embryos and the controls or their ratios and the histologic examination of the tumors; in some cases bio-assays were done on the treated tumors.

Experimental findings

There is not a great difference between the tumor types in their response to TEM (triethylene melamine) (Table I). This suggests that the sensitivities of the various

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TABLE I. Effect of TEM, fumagillin, and hexestrol on human tumors in eggs

Agent and Tumor	Dose (Mg. per Egg)	Number of Embryos T*	Number of Embryos C*	Average Tumor Weight (Mg.) T	Average Tumor Weight (Mg.) C	Inhibition Results (Per Cent)
TEM						
H.Ep. 3	0.035	12	24	63	282	78
H.S. 1	0.035	21	20	59	356	84
H.Ad. 1	0.035	17	22	136	502	73
A-42	0.035	20	23	128	956	87
Fumagillin						
H.Ep. 3	2.50	24	25	103	493	79
H.S. 1	2.50	19	18	101	462	78
H.Ad. 1	2.00	19	18	194	407	52
A-42	2.00	22	23	77	1,214	94
Hexestrol						
A-42	4	11	13	612	1,420	57
H.Ep. 3	4	10	16	441	541	18
H.S. 1	4	10	14	617	932	34
H.Ad. 1	4	15	28	1,167	1,267	8

* T = treated embryos; C = controls.

tumor types are somewhat comparable to each other with respect to this particular agent. From this, it is suggestive that TEM acts on certain metabolic phenomena common to all of the tumor types in question, which could be either directly against the tumors themselves or mediated through the host.

A slightly different situation is encountered when we compare the effects of fumagillin on the various types of tumors (Table I). It is clearly shown that fumagillin inhibits the growth of all of the tumor types listed; however, there is a definite indication of quantitative differences among the tumor types in their sensitivities to this agent. The greatest contrast to be noted is between H.Ad. 1 and A-42. Here it is quite evident that the sensitivity of A-42 to fumagillin is nearly twice that of H.Ad. 1. If one were to evaluate the effectiveness of fumagillin as a carcinostatic agent using H.Ad. 1 as the test object, one would be much less impressed with the potentials of this agent than one would be if A-42 were used as the test object. If we were to examine the results purely on the basis of drug evaluation, a valid question is: Which result is more meaningful: that obtained with A-42 or that obtained with H.Ad. 1? When the results are examined, the answer to this question does not seem obvious. On the other hand, if one were to disregard attempts to evaluate the agent per se, but consider which of the tumor types proves to be a more sensitive target for fumagillin, an examination of the results proves to be more meaningful. From this, it is quite clear that whether or not experimental results give us the answers we seek depends largely on the types of questions we ask and the experimental design which is set up to provide the answers.

Differences between the tumor types in their sensitivities to hormones and related agents are illustrated in a comparative study of the effect of hexestrol on human tumors in eggs (Table I). An inspection of the table reveals nothing dramatic in terms of antitumor potential; however, the differences in sensitivities among the tumor types are clearly indicated. When one considers the denominators which are common to all of the tumors in this study, namely, the same host and the same dose level of hexestrol, it becomes quite obvious that the differences which are noted in the result column can be attributed only to the differences in the types of tumors and their sensitivities to the agent in question.

The results presented here of the effects of various agents on human tumors grown in embryonated eggs do not warrant any conclusions that the same agents would be equally effective against these types of tumors in the patient as they have been shown to be experimentally; rather it is highly suggestive that these and similar experimental results may serve as helpful guides in selecting sensitive tumor targets for the available chemotherapeutic agents. Recognizing the existence of subtle differences among the tumors of different patients whose tumors belong to the same general classification as to type, it is conceivable that more effective chemotherapy may be made possible by tumor sensitivity determinations prior to treatment. The evidence presented here is in agreement with the concept that the critical selection of the sensitive tumor target for a given agent may be more important in achieving effective chemotherapy than the use of broad spectrum chemotherapeutic agents without considerations for tumor sensitivities.

Summary

Comparative studies, using various types of chemotherapeutic agents, have been made on four types of transplantable human tumors: H.Ep. 3, H.S. 1, H.Ad. 1, and A-42, which were grown on the chorioallantoic membrane of chick embryos.

The results of the effects of TEM, fumagillin, and hexestrol on the tumor types mentioned have been presented to illustrate the existence of differences among the tumors in their sensitivities to these agents which have been chosen as representatives of alkylating agents, antibiotics, and hormonal agents, respectively.

It has been inferred that the critical selection of the sensitive tumor target for a given agent may be more important in achieving effective chemotherapy than the use of broad spectrum chemotherapeutic agents without considerations for tumor sensitivities.

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In Vitro Assessment of Chemotherapeutic Activity in Cancer*

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BIOCHEMICAL VARIABILITY among individual cancer tissues having the same structural organization or cytologic features has been reported by many investigators. Furthermore, many forms of neoplasm respond differently to different chemotherapy, and neoplasms which are identical morphologically and clinically respond differently to the same chemotherapy.

The rate of glycolysis is generally elevated in neoplasms, and consequently dehydro-

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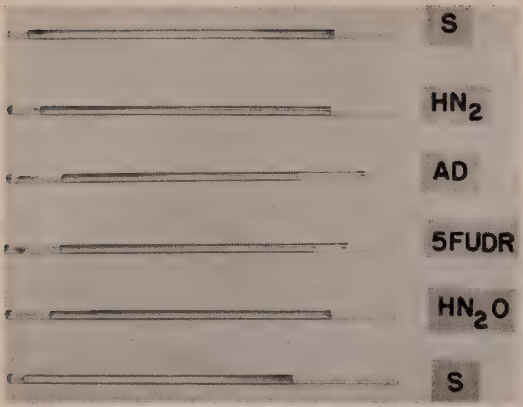

FIGURE 1. Micro-assay technic; clear area in center of capillaries with saline (S) indicates no inhibition when compared with capillaries containing nitrogen mustard (HN_2), actinomycin D (AD), 5-fluorodeoxyuridine (5-FUDR), and nitrogen mustard N-oxide (HN_2O).

genases associated with the glycolytic process are present in significant quantities. Ascites tumor cells in vitro have been used to determine dehydrogenase inhibition and possibly general cell toxicity of potential cancer chemotherapeutic agents.[1–3] This report deals with the feasibility of selecting cancer chemotherapeutic agents for patients on an individual basis by means of an agar disk-assay technic.

Materials and methods

The materials and methods involved in the agar disk-assay technic used in the present study were described in detail previously.[4,5] Cellular activity is determined by using a 0.05 per cent methylene blue solution as a redox agent. Fresh sterile human tissue is obtained directly from the operating room. Usually the laboratory is notified as the tissue is being removed from the patient.

Quite often the amount of tissue is limited, and the number of cells which can be obtained from it is too small to permit placing the cells in a Petri dish. In such cases, capillary tubes are used. The drug, cells, indicator, and nutrients are mixed together, and the capillary is then filled. The capillaries shown in Figure 1 were made with 100,000 cells per milliliter of material, and the results were obtained in approximately six hours. Although they correlate fairly well with the agar pour plates, it is not yet known whether the pour plates can be replaced by this test.

Results

Table I lists the drugs used in these experiments, together with their in vitro and in vivo effectiveness on Ehrlich ascites tumors. Since most of the compounds tested were known to have carcinostatic activity, it is not surprising that both in vivo and in vitro tests indicated the compounds as effective. 5-MU (5-mercaptouracil) showed inhibitory effectiveness in the in vitro test but not in the reported in vivo tests. 6-Mercaptopurine, which was reported as having very little dehydrogenase-inhibition activity, gave doubtful results in this test. Otherwise, the results of the two tests correlate fairly well.

It is not to be inferred that this test will indicate the effectiveness of all carcinostatic compounds. Obviously, compounds which fail to inhibit dehydrogenases or cause cytotoxicity will not be discerned. Correlation has been obtained with 17 of 25 compounds which had been tested by Creech *et al.*[6] using the EF or ELD lines of Ehrlich ascites in vivo. For some compounds which were not previously known to be effective against mouse Ehrlich ascites but were sometimes found effective with the agar pour plate tests using fresh autopsy material, our agar pour plate tests were performed also, using mouse Ehrlich ascites. The results obtained to date suggest that this system might be useful to find new drugs for human cancer chemotherapy.

The reproducibility of the method has been demonstrated using both animal tumor cells and human tumor cells. An analysis was made of the zones of inhibition produced by the same drug replicated on the same plate as well as on different plates. An analysis of the variation in the zones of inhibition for disks on the same plate as well as for disks on different plates indicates that the results of the drugs which were tested on different plates do not vary from the results of the same drug on the same plate.

Obviously, the ideal drug would be one which is inhibitory to malignant cells but which has no effect on normal cells. In

TABLE I. Results of in vitro and in vivo tests of inhibition of mouse Ehrlich ascites, using known cancer chemotherapeutic compounds

Code	Chemical	In Vitro Zone of Inhibition (Mm.) Mean	Standard Error	In Vivo
HN_2	Methylbis(β-chloroethyl)amine hydrochloride	25.8	±1.3	+*
TSPA	N,N′,N′′-Triethylene thiophosphoramide	16.0	±1.0	+
AM	Methotrexate (amethopterin)	17.6	±1.3	+
AD	Actinomycin D	18.6	±1.6	+
HN_2O	Nitrogen mustard N-oxide	18.0	±1.8	+
6-MP	6-Mercaptopurine	12.0	±0.9	+
F	Fumagillin	16.2	±0.4	+
5-FUDR	5-Fluorodeoxyuridine	14.6	±0.4	+
AB-103	Benzyl[bis(1-aziridinyl)phosphinyl]-carbamate	14.0	±0.6	+
5-MU	5-Mercaptouracil	22.6	±1.8	−
5-MU + 5-FUDR	5-Mercaptouracil + 5-fluorodeoxyuridine	25.0†		+

* Indicates significant tumor inhibition as reported in the literature.
† Single measurement only.

TABLE II. Comparison of in vitro test results on "normal" and tumor tissue from 59 patients

	Effectiveness on		
Drug	Normal and Tumor	Normal Only	Tumor Only
HN_2	4	3	6
TSPA	1	1	2
AM	9	7	6
AD	9	7	13
HN_2O	4	2	4
6-MP	2	3	6
F	0	3	4
5-FUDR	8	6	9
5-MU	7	8	6

many instances it was possible to obtain not only a malignant surgical specimen, but also a specimen from an adjacent area which was considered to be "normal" (Table II). The drugs were tested on the homogenates prepared from both the normal and the tumor tissues. The most potent drugs, which inhibited the highest number of tumors, were also the most effective against the normal tissues.

It is apparent that none of the compounds shows selective toxicity to the tumor cells; a comparison of cases in which the drug is inhibitory to tumor with cases in which the drug is inhibitory to "normal" cells shows only a slight departure from a 1:1 ratio, indicating no significant differences. This reaffirms the lack of selectivity of known cancer chemotherapeutic agents.

Although most of these drugs are known as cancer chemotherapeutic agents, many had an effect on very few tissues from the various sources tested. 5-FUDR (5-fluorodeoxyuridine) was most effective in the largest percentage of the cases, followed by methotrexate (formerly known as amethopterin), actinomycin D, HN_2O (nitrogen mustard N-oxide), and HN_2 (mechlorethamine hydrochloride); all of these show little differentiation in over-all effects.

An attempt was made to demonstrate primary site specificity of the drugs. It was noted that methotrexate was more effective on breast tissue and TSPA (triethylene thiophosphoramide) was more effective on hemopoietic and lymphatic tissue than would have been expected on the basis of over-all effectiveness. This interpretation must be made with caution, since such interaction would be expected to occur at least three times in the number of cases in this situation. Therefore, it cannot be said for certain that there is no site-specific action.

Since all the compounds which are being used here have some known carcinostatic activity, it is interesting to realize that on the basis of over 200 cases tested, 17 per cent of the tissues were not affected by any tested drug in the in vitro system. Furthermore, most tissues responded to only one or two drugs. No tissue has ever responded to all 10 drugs, and only 3 have responded to 9 of the 10 drugs. Since the tissues which responded to 5 through 10 drugs are small in

TABLE III. Number of drugs effective on each tissue, classified by drugs used

Drug	Total Number Tissues on Which Compound Effective*	Number of Drugs Effective on Each Tissue		
		1	2	3 or More
HN_2	52	8 (4)	11 (13)	33 (35)
TSPA	23	1 (2)	0 (8)	22 (13)
AM	55	14 (5)	15 (15)	26 (35)
AD	54	9 (5)	10 (15)	35 (34)
HN_2O	52	10 (5)	10 (13)	32 (34)
6-MP	31	4 (2)	7 (9)	20 (20)
F	34	5 (3)	1 (8)	28 (23)
5-FUDR	64	12 (6)	13 (16)	39 (41)
AB-103	22	2 (2)	8 (5)	12 (15)
2,4,6-TAP	18	0 (2)	0 (4)	18 (12)
5-MU	25	2 (2)	10 (6)	13 (17)
TOTALS	169	66 (38)	42 (56)	61 (95)

* None of the drugs was effective on 34 tissue specimens.
( ) Expected number, assuming no drug-tissue specificity.

number, they have been grouped together.

Table III gives the number of drugs which were effective on each tissue, classified by primary site of tumor. The fact that 71 per cent of the tissues were affected by no more than 2 drugs at a time indicates drug-tissue specificity, that is, a single compound or a small group of compounds has specific action for certain tissues. The effectiveness of methotrexate and 5-FUDR was found to be related in part to site. Methotrexate exceeds its expectations for single effectiveness on breast tissues and falls significantly short of its expected single effectiveness on female genital tissue. 5-FUDR exceeds its expectation for single effectiveness on tissue from other sites. A further examination with 5-FUDR shows it to be singly effective on 4 of the 5 tissue specimens from oral cavity tumors which were classified as miscellaneous because of the small number of specimens. Like methotrexate, 5-FUDR fell short of its expectation for single effectiveness on female genital tissue, which, as pointed out, might be generally regarded as a resistant site.

An advantage of testing at least 10 compounds simultaneously on a single tissue specimen is that similarity of response can be examined directly. Drugs can be said to be similar in response, for example, if two are effective and noneffective on a larger group of tissues than would be expected on the basis of their separate effectivenesses. One example of this concept could be the selection of drugs which might be considered members of the same family. It should be possible to choose a representative of the most effective drug of a series belonging to the same family to be used in this test. This means that subsequent to the preliminary studies some drugs could be dropped and other drugs added to the test system because a series of different representatives would be used in the same trial.

TABLE IV. Demonstration of effectiveness of selected compounds

	HN_2		
2,4,6-TAP	Not Effective	Effective	Totals
Not effective	49	17	66
Effective	4	14	18
Totals	53	31	84

Therefore, it should be possible to demonstrate whether two drugs are completely or partially independent of one another or whether one drug dominates the other. This means that the dominated drug may be dropped without losing much so far as the test is concerned. For example (Table IV), HN_2 is effective on 17 tissues in which 2,4,6-TAP (2,4,6-triaminopyrimidine) is not, but 2,4,6-TAP is effective in only 4 cases where HN_2 is not; thus, dropping 2,4,6-TAP would decrease the response spectrum by only 4 tissues, whereas dropping HN_2 would decrease the response spectrum from 35 tissues to one-half this number.

This system is being proposed in an attempt to determine the drug of choice to be

TABLE V. Relationship between effectiveness of drug as predicted by agar pour plate method and observed clinical impressions on 76 cases

Objective Clinical Impression	Agar Pour Plate Test Non-effective	Effective	Totals
Noneffective	34	32	66
Effective	0	10	10
Totals	34	42	76

administered to a patient with cancer. The drug to be selected is from compounds of interest to the clinician. This concept of individual tumor sensitivity was tested in 76 patients who had been referred to the cancer chemotherapy service. A four-square table (Table V) was made to indicate those situations in which the agar pour plate test selected a drug as being effective or noneffective and situations in which it was possible to determine by objective clinical impressions whether the clinical therapy was effective or noneffective. Of the 42 patients considered as having tumors sensitive to chemotherapy by the in vitro system, 10 showed objective clinical improvement, indicated by a decrease in tumor size or the disappearance of ascites. Thirty-four patients did not respond to any drug in the in vitro test. In 18 of these patients no recommendation could be made since the tissues were insensitive to all the drugs currently being tested, while in the remaining 16 patients some drug other than the recommended chemotherapy was given. No objective improvement was noted in any of the 34 patients.

The variety of drugs and tissues which responded clinically is demonstrated in Table VI. It can be noted that most of these cases are actually carcinomas. In the 10 cases in which there was objective clinical improvement, it would appear that the test is highly specific for drug selection. In the 3 instances in which actinomycin D was selected, no other antibiotic or drug was selected. In 2 cases in which HN_2O (Nitromin) had been indicated, that was the only alkylating agent selected. In the colon carcinoma case, two alkylating agents were selected by the test: nitrogen mustard, which was the drug of choice, and a second, less effective, drug, TSPA. The remaining cases were affected by not more than two drugs.

To see if tissues from the 10 patients on whom a compound showed clinical effectiveness showed more sensitivity to chemotherapy than did tissue specimens from 32 patients who showed no clinical improvement, the frequencies with which 1, 2, 3, or more compounds were effective on tissues from each of the two series were compared (Fig. 2). No difference in the distribution was observed, indicating that the tissues of those responding to chemotherapy were no more sensitive, as defined in this paper, than were the tissues from those not responding to chemotherapy.

The percentages of tissue on which a drug was effective for the 10 cases in which objective improvement was noted and the 32 cases in which objective improvement was not noted were compared for each of the drugs used. Figure 3 presents the in vitro results obtained by the agar disk-assay technic. On the basis of the small series involved and the distribution noted, it cannot be said that any one drug was more

TABLE VI. Compounds used in cases which subsequently showed improvement by objective criteria

Drug	Malignant Condition Diagnosis	Tissue Obtained
AD	Stomach carcinoma	Abdominal wall metastases
AD	Liposarcoma	Chest wall biopsy
AD	Fibroadipose carcinoma	Abdominal biopsy
HN_2O	Rectum adenocarcinoma	Vaginal biopsy
HN_2O	Melanoma, left eye	Abdomen skin biopsy
HN_2	Colon carcinoma	Ascites from abdomen tested
AB-103	Mesothelioma peritoneal	Umbilical wall
AB-103	Metastatic leiomyosarcoma, left spermatic cord	Leiomyosarcoma, right chest wall
5-FUDR	Rectum carcinoma	Perineal mass
5-FUDR + 5-MU	Rectum carcinoma	Perineal mass

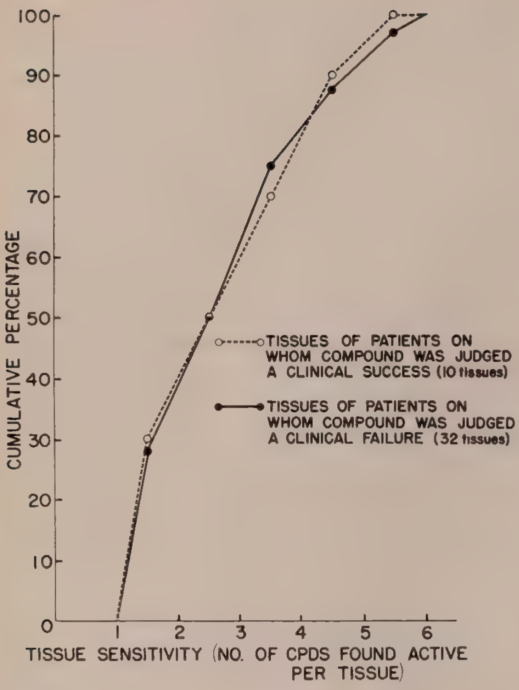

FIGURE 2. Tissue sensitivity of patients who responded to chemotherapy compared with tissue sensitivity of patients who failed to respond to chemotherapy.

effective in those cases in whom objective improvement was noted.

Comment

This in vitro system is based on the hypothesis that variation in the biologic behavior in response to therapy is actually an indication of individual tumor differences. It is proposed that cancer actually consists of many diseases varying from individual to individual determined by environmental, genetic, and environmental factors plus familial predisposition. Additional factors include the age and sex of the individual. A rational approach to the selection of the drug to be used in cancer chemotherapy has many obvious advantages to the patient.

The dehydrogenase activity of tissue of diverse forms of human cancer in tissue culture and on tissue slices, as well as in the patient, has been determined by means of reducing agents. The inhibition of dehydrogenase activity is an indication of interference with the Embden-Myerhof scheme of glycolysis. This assay technic differs from the ordinary microbial assay technic in that the cells are not multiplying. Therefore, the inhibition of dehydrogenase is only presumptive evidence of cell inhibition since the technic employs a static rather than a dynamic cell population. It is conceivable to inhibit dehydrogenase without having a

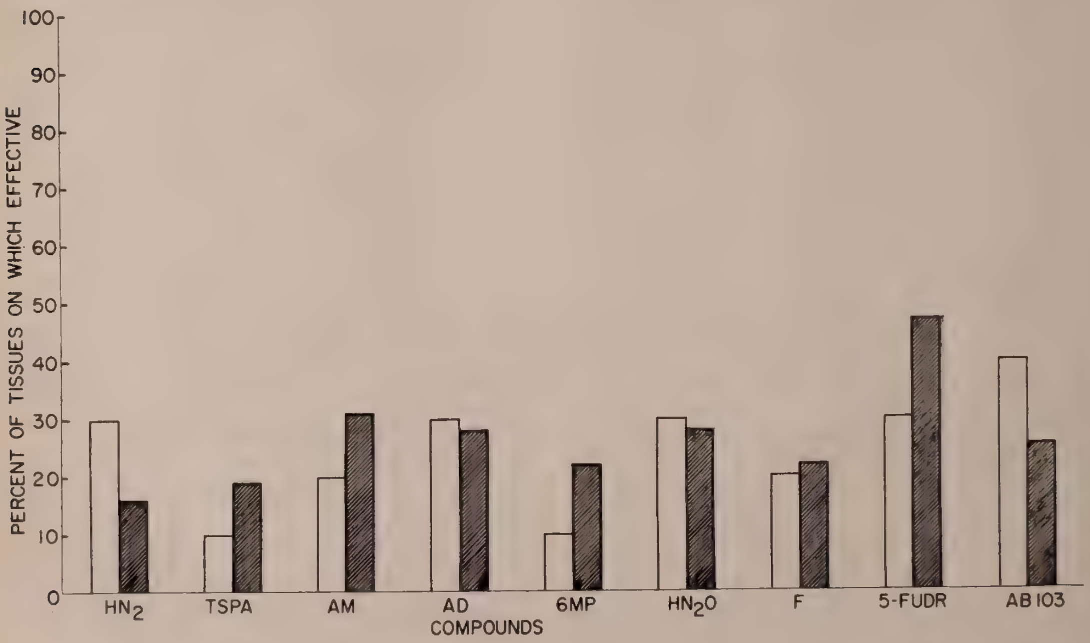

FIGURE 3. Effectiveness of drugs for cases in which improvement was noted (open bars) compared with cases in which improvement was not noted (shaded bars).

significant effect on cell growth. It is also known that the inhibition of cell proliferation can occur without damage to that part of the cell's physiology which is not concerned directly with cell division, for example, thymineless death. The application of this technic appears to be complicated further by serious limitations of drugs currently in use in cancer chemotherapy. Nevertheless, the data indicate that certain tissues tend to be more drug-resistant or drug-sensitive than others. This technic for measuring the response of tumor cells to various drugs might serve as a guide to clinical chemotherapy.

The simplicity and rapidity of this test make it very interesting; however, it shares with other in vitro tests a shortcoming, namely, the possibility of the occurrence of a metabolic transformation, insofar as the drug and host are concerned, which is not revealed by the test. There is a possibility that a drug which is inactive in the in vitro test will actually be transformed into a metabolically active drug so far as chemotherapy is concerned or that a drug which is active in vitro will be transformed into an inactive one in vivo, resulting in a false test.

Conclusion

This test is of interest, and its application may be of value in clinical chemotherapy in giving some indication as to the drug of choice for clinical chemotherapeutic use as well as in determining which cases will not respond to chemotherapy.

Acknowledgment. Gratitude is expressed to the clinical staff of Roswell Park Memorial Institute for making available surgical specimens and to George E. Moore, M.D., and Alvin Watne, M.D., for valuable objective clinical evaluation of chemotherapy.

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Summary of Present Trials of Anticancer Agents

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In 1957 a large group of surgeons and their associated hospitals throughout the nation joined together to evaluate the efficacy of various anticancer agents used as adjuvant treatment immediately following curative surgery for patients with cancer.

The tumors that were investigated were carcinoma of the stomach, carcinoma of the colon and rectum, carcinoma of the breast and lung, and carcinoma of the ovary.

Triethylene thiophosphoramide, commonly known as TSPA or Thio-TEPA, was used as an adjuvant for patients undergoing surgery for carcinoma of the stomach, colon and rectum, and breast. Nitrogen mustard was chosen as the drug for patients with carcinoma of the lung, and cyclophosphamide was chosen as the drug for patients with carcinoma of the ovary.

To date, it appears that nitrogen mustard given immediately following the curative surgery for carcinoma of the lung has not resulted in any increased survival in the treated patients.

The patients with carcinoma of the stomach and carcinoma of the colon and rectum may well have derived some value from the use of the drug; however, it is too early to evaluate completely. There are too few patients in this series of patients with carcinoma of the ovary for evaluation at this time.

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* By invitation.

The preliminary studies conducted on the patients with carcinoma of the breast appear to show some signs of increased value.

Methods and materials

The study consisted of two basic groups. Group 1 consisted of 108 patients who were treated between April 1 and October 1, 1958. Group 2 consisted of 718 patients, with more being added, who have been treated from October, 1958, to the present. The study was carried out on a double-blind basis so that neither the surgeon nor the hospital dispensary knew whether the patient received the adjuvant chemotherapy drug or the control drug.

In the first group of patients, the drug was administered as 0.4 mg. per kilogram of body weight on the day of surgery and 0.2 mg. per kilogram of body weight given intravenously on the following two days, for a total of 0.8 mg. per kilogram of body weight.

In October, 1958, the dosage schedule was changed so that a total of 0.6 mg. per kilogram of body weight was administered intravenously: 0.2 mg. per kilogram of body weight on the day of surgery and 0.2 mg. per kilogram of body weight intravenously on the subsequent two days.

Selection of patients

The eligibility of the patients for consideration in a study of this type was determined essentially by whether or not a curative surgical procedure could be carried out. The tumor must be removable. The metastases must not indicate incurability. If necessary, a biopsy was performed on adjacent nodes, and if these were involved with cancer, the patient was not placed in the study.

The following conditions are those under which a patient would be excluded from the study: Any previous treatment would invalidate any results. A concurrent or previous or subsequent malignant condition removed the patient from consideration in this study. If the bone marrow and the blood count were depressed, it was obvious that we could not administer the anticancer agent. If the tumors of the breast were sarcomas or other than the carcinomas, they were not included. Of course, the patients who were very debilitated were not included in this study because it was found out readily that the combination of the anticancer drug plus the surgery was more difficult for the patient. The drugs themselves are generally quite toxic.

If a biopsy was done on the tumor more than seven days before the surgery, the patient was excluded from this study. The condition of the tumor site at that time then is relatively unknown. If the patients were pregnant or actively lactating, they were not included in this study.

Procedure

This, then, was essentially the procedure followed on these patients: A frozen section was performed; then if the diagnosis was carcinoma, the patient underwent the usual classical radical mastectomy with the administration of the anticancer agent at the termination of the surgery. The surgeon did not know whether he was administering TSPA or the control drug.

The surgeon then kept a detailed record on the patient, the pathologist made a detailed report of the subsequent findings on the pathology specimen, and the patient entered a follow-up which included a chest x-ray film, blood count, and clinical evaluation every three months for five years. Obviously, these patients are still undergoing the five-year follow-up period.

Age of patients

The use of the double-blind study and its value are made obvious by the age distribution. The patients' age varied from twenty to ninety-four years, and the treated and the control patients in both groups were so distributed that it was obvious that no single age group received only the treatment or the control drug.

The majority of the patients undergoing surgery were postmenopausal. Of the 108 patients in Group 1, there were slightly more patients receiving the drug who were postmenopausal.

In Group 2, which now includes 718 patients, the distribution between treated and control patients was more nearly equal.

Lymph node metastases

The problem of lymph node metastases was evaluated, and it was found that approximately half of the patients had lymph node metastases. As the majority of the patients were postmenopausal, the distribution between the postmenopausal patients with nodes or without nodes was approximately equal for the patients in both groups.

When consideration was made for the patients who received TSPA or who received the control drug, it was found that the distribution of those with nodes receiving treatment or not receiving treatment was approximately the same for both groups.

The evaluation of the pathology specimen was made in some detail. Approximately 50 per cent of all the patients had lymph node metastases.

The specific distribution of large breast cancers was approximately the same in both groups, although it was slightly lower in the control patients of Group 2.

The histologic types of tumor indicating good prognosis were lobular or medullated rather than scirrhus type. Slightly fewer of the treated patients in both groups had lobular or medullated tumors; they had more of the scirrhus carcinomas.

Tumors with expansion borders showed compression of the adjacent breast tissue, and, in this case, there were slightly more treated patients in Group 1 who had this type of border to their carcinoma, in contradistinction to those with the so-called root border in which there is infiltration into the adjacent breast tissue.

Blood vessel invasion was found in only 2 per cent of the treated patients and 10 per cent of the control patients in Group 1; it is approximately equal in the 718 and more patients in Group 2.

Complications

The complications from the administration of the chemotherapeutic drugs in addition to the surgery resulted in the interesting finding of somewhat more local complications in the patients who received treatment as compared with more systemic complications in the control patients. The local complications in Group 1 were essentially hematomas, while major necrosis of the wound was more common in the control patients not receiving the drug.

In the patients in Group 2, the local complications were predominantly hematoma and infection, whereas minor necrosis of the skin flap occurred more commonly in the control patients.

Recurrence rate

Approximately 43 per cent of the control patients in Group 1 now show recurrent cancer; approximately 24 per cent of the treated patients of this group show recurrent cancer or recurrent tumor after approximately two years.

Of the patients in Group 2 who are still, of course, undergoing their follow-up (and there are more patients being added to this group continually), we find that after about twenty-one months, the control patients show a recurrence rate of slightly over 20 per cent, while the treated patients show a recurrence rate of about 12 per cent.

In correlating the recurrence of tumor in these patients according to the site and treatment, we find that in the patients in Group 1 receiving the higher dose of anticancer drug, there was less recurrence of tumor in the local area, while the treated patients showed a slightly higher incidence of distant metastases; but the over-all results were 22 per cent of recurrence in the treated patients, as compared with 44 per cent in the patients not receiving the adjuvant drug.

In Group 2, again we see a lower incidence of local recurrence, as compared with distant metastases in the treated patients, with some difference appearing between the over-all recurrence of 7 per cent for the treated patients as compared with 10 per cent recurrence in the untreated patients.

An evaluation was made of the patients in this study who have subsequently died either of their recurrent tumor or of other causes. In the treated patients in Group 1, 10 per cent showed recurrent tumor, as compared with 24 per cent in the controls. There is very little difference at this time in the patients included in Group 2.

The recurrence of tumors was compared with the occurrence of lymph node metastases at the time of surgery. As you would suspect, there is an increase in recurrent tumor in the patients who showed positive nodes in the original surveys. However, when the patients were the ones receiving treatment, there was a lower incidence of recurrent tumor in those patients. Of the patients with negative nodes, the treated patients have had a lower incidence of recurrence than the controls. However, in Group 2, there is very little difference at this time.

Summary

In conclusion, a cooperative study is being carried out on the use of chemotherapeutic drugs as an adjuvant to curative cancer surgery. To date, in a preliminary evaluation, it appears that nitrogen mustard is relatively ineffective in increasing the survival of patients with carcinoma of the lung. There may be some improvement with the use of TSPA for patients undergoing surgery with carcinoma of the stomach, colon, and rectum. The group is too small for any evaluation of the adjuvant chemotherapy in patients with carcinoma of the ovary; and in the preliminary studies of patients with carcinoma of the breast, it appears that TSPA may be of benefit in the prevention of recurrent cancer in these patients.

Question and Answer Period

Dr. Moore: I would like to ask Dr. Harris if he has additional tumors that he is using now in his work. Do all of these grow in the conditioned hamsters, and do they grow in culture?

Dr. Harris: So far, there are only two additional tumors.

Dr. Moore: The colon and the bronchiogenic?

Dr. Harris: Yes, the colon and the bronchiogenic. They will grow in the hamster.

Dr. Moore: We are aware of the studies in which volunteer prisoners in Ohio State were given human tumors carried in culture, and I believe that in most instances they failed to grow in such people, whereas they did grow in cancer patients.

I would like to know whether or not this has also been tested subsequently in patients who were equally seriously ill but not with malignant conditions.

Dr. Harris: I don't know; those were Dr. Southam's studies, and I am not aware of any such studies under other conditions.

Dr. Moore: It would seem that patients who are severely spent probably are, just as are animals, in a better position to grow malignant conditions than patients who are not in good health with the intact host system, and this point is of interest to us. We think that we have observed some kind of malignant condition speeding up in growth in patients who have been given cortisone, for example, which is another effect of stress; and actually, as surgeons, we are all interested in the effect of the stress of surgery and anesthesia on the rate of growth.

Dr. Harris: That is a good point. Stress and factors which would interfere with the immune response, such as the corticoids, would definitely aid the tumor at the expense of the patient, should the immune responses play a role in checking tumor growth.

Dr. Moore: Dr. DiPaolo, what about cyclophosphamide (Cytoxan) in your system? Cyclophosphamide is a drug that presumably is inactive until it reaches a tumor site or a similar site at which point enzymes liberate the active part of the molecule. Did you find it of any value in your system? I would presume that it would be negative.

Dr. DiPaolo: Our limited studies indicate that it is negative. Another drug concerning the metabolism of which very little is known is fumagillin. Fumagillin does inhibit some transplantable tumors but turns out to be extremely poor with our human cases.

Question: Dr. Moore, how do you explain the spontaneous cure of cancer in some patients? I have a patient who had carcinoma of the kidney with involvement of the deep vessels; this was over twenty-five years ago, and she is now perfectly well.

Dr. Moore: Well, I think that all of us wish we could explain it, and, by the way, we would love to get some serum from such a patient for testing. In fact, I can't tell you how much we would like it, in almost any shape that you will give it to us, just clotted blood and as much as possible, of course, for testing. We are very interested in such a patient.

I believe, Dr. Watne, your group at Illinois studied several hundred patients with spontaneous remission?

Dr. Watne: Yes, Dr. Everson and Dr. Cole reviewed over 600 cases of possible tumor regression of which 42 were found to have adequate documentation. Something had changed in the patient's make-up and resistance to the tumor. We would be very interested in trying to evaluate whatever that is.

Dr. Moore: Actually, we see something similar to this in some of our patients, such as those with cancer of the breast. Some of these women may go ten or fifteen years; the longest, the world's record as far as I know, is a woman in England who went forty-four years after having a radical mastectomy, with no metastasis and no evidence of disease for all this period of time until she developed fulminating cancer. Obviously, those cells had been there and were latent for that whole period of time. We do not know how they stayed; nor do we know how they get lighted up. But if we did know, it would be terrific because these are the things that we should know to aid the control of some kinds of malignant conditions. What these host factors are, we don't know. We think that they probably are not identical with the so-called immunologic systems that are effective in other kinds of infection.

Question: You just said that you do not believe that this is an immunologic process.

Dr. Moore: It is not the ordinary orthodox kind of immunity. In other words, to my knowledge, except for very weak titers under very unusual circumstances, no true anticancer antibodies have been demonstrated.

Question: Would you comment on the nebulous terms, such as host resistance and biologic immunity, which we often hear?

Dr. Moore: Well, that last one is a dirty word as far as I am concerned, but host resistance is a good legal word because we don't know anything better; we shouldn't call it immunity because we don't know that it is orthodox immunity.

Question: Would you consider blood vessel invasion one of your criteria for inoperability or incurability?

Dr. Watne: No, I don't think so. We see that in relatively few of the pathology specimens. A good number of these patients in our study had the tumor cells identified in the blood.

Question: That's what I meant. I didn't mean blood vessel invasion, but the isolation of tumor cells in the blood is not an indication of inoperability.

Dr. Moore: No, we do not use that as an indication of inoperability because there is no question that from the number of cancer cells that we find disseminated throughout the blood stream, the patient kills 99 out of 100, or more.

Now, what this mechanism of cytotoxicity within the patient against these disseminated cells is we don't know, but there is no question that the majority of those circulating tumor cells are killed.

Question: In inoperable carcinoma of the stomach, namely prepyloric disease in which it is impossible to remove the carcinoma surgically, is there any hope for using any of the so-called anticancer drugs for such a patient for objective or subjective reasons? What is your feeling? How are you doing it?

Dr. Watne: We are administering various anticancer drugs to these patients with advanced carcinoma, including those of the stomach. Unfortunately, our results with carcinoma of the stomach with the various drugs that we have tried when the tumor was in the advanced stage have been relatively poor. I am afraid that we do not have any anticancer drug that is really effective against the large carcinoma of the stomach.

Now, in this adjuvant program, the effectiveness of these drugs was first shown experimentally. They are much more effective against the tumor cells before they become established as a definite metastasis or as a larger growth. But there is a great deal of difference between their activity at that early stage and at a later stage when the patient has a large tumor.

Dr. Moore: We probably would use Dr. DiPaolo's technic to try to find out which drug would be most effective or which several drugs would be most effective. Then, since most of them are even in effectiveness, we would probably use the one that we are most interested in evaluating at the time.

One patient with carcinoma of the stomach had a thoracotomy, and surgery could not be done because of liver metastasis. This patient was given large amounts of TSPA. The patient continued to do extremely well, and at the end of one year we re-explored that patient and found only scars at the site of metastasis. The primary region was resected, and that patient is still alive. But, this is a very rare instance. Such cases are very exciting and very encouraging, but rare.

For the gastrointestinal regions, we have 5-FU (5-fluorouracil) and 5-FUDR. For colon lesions they are of some value in this particular kind of lesion, but not in the stomach.

Question: How long do the toxic effects last? Do the patients appreciate what you do?

Dr. Watne: These drugs are very toxic, and since most of the drugs either are antimetabolites or inhibit mitosis, they affect the actively dividing cells in the body, namely the bone marrow and the gastrointestinal tract mucosa, so that when the toxicity begins to develop, first you'll see nausea, vomiting, and loss of appetite. We try to control this with Thorazine and other types of sedation. The patients appreciate what is being done for them; the majority of them realize that they have an advanced tumor and that they are being treated with a very strong medicine. We tell them that the medicine is strong so that as the treatment progresses, we take them to the point of toxicity at which they are beginning to show bone marrow depression.

This generally develops within eight days to two weeks after the onset of vigorous therapy, depending a bit on the drug and the dosage that is being used. Since the white cell turnover occurs somewhere in that time, it often arises first in the white blood cell count.

Later on, you may see effects on the platelets. We have not had as much trouble with the erythrocyte depression.

The treatment is all conducted in the hospital; very little of it is in outpatients because of these toxic symptoms and because if the bone marrow depression is severe enough, then it is necessary to treat the patient with fresh blood transfusions, isolation, and protection against any subsequent infection.

Dr. Moore: I have a few more remarks. I will tell you about the hopes and significant disappointments in using drugs. We have a whole series of drugs called the AB series by two Hungarian scientists, very brilliant young men who have now synthesized 132 compounds which have been brought into the clinical level, and AB-103 (benzcarbine) and AB-132 (ethylcarbamine) have been somewhat effective. AB-132, however, also affects the central nervous system. Dr. Watne and I had a seventeen-year-old Cornell student recently with huge hepatic metastases; this young man responded beautifully to the drug, that is, in the time that his metastases decreased I would guess that at least a kilogram of tumor was actively destroyed by the drug. However, the remission lasted only two weeks, after which time the tumor grew back very rapidly.

The second patient, whom we have in our service today, is a manufacturer and a very well-known man in our community who has an inoperable, far-advanced carcinoma of the colon with metastases to the liver. His liver has been down to the iliac crest.

He was started on 5-FU in January mainly because I did not think he was going to make it through Christmas; he responded beautifully, and his liver has gone down considerably. He went down to Miami for a vacation; when he came back, his liver was somewhat enlarged again, and we put him on maintenance therapy again, which seems to be controlling him fairly well.

His only toxic symptoms were diarrhea when we first started, some vomiting, and bone marrow depression to about 2,000. And this is the sort of thing which occurs. These are investigative drugs. We are working with them, but it is difficult.

Question: In which primary lesions or metastases of the lung is it surgically acceptable to do thoracotomies?

Dr. Moore: Well, you could say lung or liver. There are not too many instances. There are certain kinds of malignant conditions which may metastasize and form isolated metastases which are worth following to the end of the road.

For example, some carcinomas of the kidney may have multiple metastases, in the lung and in a lobe or even in two lobes; they are generally peripheral in site. You can take those out with very little trouble for the patient, and many times these patients will survive for long periods of time. I believe that after thoracotomy the average survival of all of such patients, even those who we know had an unfavorable biologic characteristic, was something like eleven months, which means some of them are still alive after three years, but only a few.

We have one young man to illustrate that and dramatize it. This young man was from north of Albany. He was first operated on in 1951 for choriocarcinoma and carcinoma of the testis. I saw him in 1953 when I first joined the Buffalo community. He was comatose from brain metastases and lung metastases in the left chest. He had been irradiated and had a resection of the left iliac vessel, lymph node.

We then removed a 205-Gm. brain metastasis; six weeks later we took out his left lung, which had five metastases.

He came back in a year with a recurrence of brain metastasis. He had another regrowth of some 100 Gm., which we took out. He came back two years later and again had evidence of a recurrence of brain metastasis. We explored the chest for the third time. It showed negative findings. We had made a diagnostic error. He had an obstructing lesion of the duodenum, another metastasis. This was removed surgically and treated by x-ray. Since then, he has been hospitalized once for abdominal obstruction from adhesion, but he has had no evidence of the disease in the last five years.

He is now thirty-eight or thirty-nine years old. He has had one child since. He drives. He drove to Buffalo the other week. We won't allow him to have a license, but he drives illegally, and there isn't much we can do about it. And he gets around very well; but then again, this is rare.

But if you understand the tumor with which you are dealing and know what you are doing, then you can make these choices, and sometimes you can do very well. Trying to do it for a carcinoma of the pancreas is a different matter; I would say it was a sort of malpractice to try to take out a dozen metastases from the liver, pancreas, or stomach, which are different kinds of diseases altogether.

Question: I would like to say that this whole problem is one which raised a problem for us. People write to Buffalo that they have seen certain results in the paper, and they write us for our opinions. I wondered just what we should do about these cases. All the larger cities have form letters for these people. Every one of them has to be answered. One of these letters concerned a carcinoma of the pancreas, diagnosed on the basis of exploration, which we thought was not a case for a written procedure.

Dr. Moore: That is perfectly correct, and, of course, as you might expect, we receive a tremendous number of letters, that come from all over the country, from Thailand, from Egypt, from everywhere. We had two letters from Egypt last week.

I don't know what you can do. We write back and tell them to pay attention to what their doctors tell them: If it is a drug that can be used in their case, their doctor already knows about it, and if they have any question, their doctors can certainly write to us.

Our purpose is to investigate new compounds and not to treat wholesale lots of patients, because we do not have the facilities for them. In some instances, we do see patients who have been thought inoperable by their physicians but who actually were not inoperable. We had one such patient last week who had already gone home. On the other hand, we have some sent in who are said to be curable, but who actually are not. So, we get it both ways. If the doctors are sincere and write to us, we always try to take care of them and help with their problems of cancer chemotherapy.

These are problems which you can't slough off; otherwise, the patients go spend their money on quack potions. Every time a person is lost to such a racket, it just keeps all the groups that are putting out these swamp waters going.

QUESTION: Did you perform perfusion with metastases?

DR. WATNE: Yes, we have performed regional perfusions; which reminds me, there is one thing that you can help even with these toxic drugs and that is their use in the control of effusions. There are several drugs that are excellent in controlling pleural or peritoneal effusions, and you can do this much less expensively than with radioactive colloids, and you can do it yourself. The toxicity is low because much of the drug does not get into the systemic circulation.

Regional perfusion again is an experimental thing. It is mainly for palliation; as you could well expect, if there are lesions on the leg, there is little reason why you should not do an amputation for that leg. Otherwise, if you are doing perfusion, you are already saying that this is something that cannot be cured and you are going to try to use perfusion for palliation; and yet there have been some good results, although not many.

QUESTION: First of all, this is a tremendously complicated problem not only among the patients but among the profession too. Of all these drugs that you talk about, there are only a few, actually just one or two, that are available commercially.

DR. MOORE: TSPA, nitrogen mustard, TEM (triethylene melamine), chlorambucil, and cyclophosphamide are all available.

QUESTION: Yes, but the point comes up that most physicians do not know enough about them.

DR. MOORE: That is right.

QUESTION: They are afraid to use them.

DR. MOORE: Yes, they are.

QUESTION: We all agree that great things are being done. We know that it is a step in the right direction compared with some of the older methods. Then the point comes up, shall we send the patient to Buffalo? It's really complicated at times. Do you ever come to the surrounding areas to look at patients and decide whether or not the patient should go up to Buffalo and whether or not it is safe to do a lot of traveling?

DR. MOORE: If you have a patient with carcinoma of the breast who is now not responding to hormonal therapy and so on and you write in, that letter comes to me. I usually send it to Dr. Dao, who is head of the Breast Clinic, and if it is thought that it can be controlled locally by the use of a compound which is not too toxic, we always recommend that the patient be taken care of in the community.

We try to tell the physician what to use and how much. I would recommend asking for advice because we see these crazy, stupid things that sometimes happen. We'll say, as Dr. Watne said, that the specific dosage is 0.8 mg. per kilogram. So someone has a patient who weighs 350 pounds; if he gives her 0.1 mg. per kilogram, she probably would die, because she can't stand that much of a dose.

On the other hand, if he has a 70-pound woman and he gives her 0.8 mg. per kilogram, it wouldn't even ruffle her hair; and so we try to tell them about the advantage of using ideal body weight, how to give the drug, and what our experience has been.

QUESTION: The x-ray therapy department in your hospital or medical center is concerned in this problem in a much higher per cent, you might say, than you people would be with your chemotherapy; therefore, is there not a tremendous amount of friction going on between these different parties?

DR. WATNE: X-ray treatment is a therapy much like surgery. It is generally limited to the care of local or regional lesions. It is not a systemic kind of therapy; when you have a breast patient with a single metastasis to the spine, that patient should be treated by x-ray.

On the other hand, if she has multiple lesions all over the body, then it is a systemic disease which is best cared for by systemic means such as adrenal resection, hormone therapy, or, finally, the alkylating agents.

So, the final care depends on the medical judgment of the physician in charge. There is bound to be conflict. I do not know when there hasn't been conflict between therapists of all different kinds as to how best to treat patients.

QUESTION: The problem of the latent toxicity is a difficulty I have had.

DR. MOORE: This is a problem. In other words, a long-acting drug, such as chlorambucil, is given for ten days, and then all of a sudden the toxicity appears.

You have to know the characteristics of the drug. You give the ordinary dose, and then you start spacing the therapy until you see how that patient is going to respond; primarily, in all bone marrow depressant drugs, the rate at which the depression takes place is probably more important than the degree. Some people go along with 3,000 for a long time, but if they drop from 5,000 to 3,000 in one day, that is the time to discontinue therapy so that the depression won't proceed. You just have to be careful.

Question: In deep carcinomas of the breast with systemic manifestations, do you do anything about oophorectomy?

Dr. Moore: Yes, we certainly do. If the patient is premenopausal, as far as we're concerned we think prophylactic castration is indicated if there are metastases. If she has not been castrated at the time and comes back with metastatic lesions, we think that that is the first thing that should be done, either by x-ray treatment or by surgery.

And then as the next step, we think she should be treated by hormones, preferably male hormones rather than female; once the hormones run out, if she has responded to that, she is probably a good candidate for adrenalectomy. Forty-four per cent of all patients subjected to adrenalectomy respond for an average duration of eleven months. After adrenalectomy runs out, then we usually go to TSPA, cyclopyrazate, cyclophosphamide, or a similar drug, which sometimes gives beautiful results but which gives primarily an average remission of about three months.

Question: When you say metastases, are you including the regional, ancillary metastatic lesions?

Dr. Moore: No, they are regional or local, as I indicated before. I think the best treatment is by x-rays, at first; but for any adenoid, even a regional one, if the patient were premenopausal, I would still do the castration procedure. I think that is recommended

Dr. Watne, have you anything to add?

Dr. Watne: Dr. Moore, if I might, on this whole general problem, I think that in general we tend to use the conventional types of treatment for the benefit of the patient as much as possible. If there are metastases with bone pain, if there are local lesions, if there is a carcinoma of the breast with local recurrence in the neck or in the lung, we will try x-ray treatment first, and then we will try the subsequent hormone treatments before the patient comes to treatment with the chemotherapeutic drugs.

The chemotherapeutic drugs are in general to be reserved for those patients for whom there is no other possible treatment.

Question: Dr. Moore, a few years ago and before then, there were reports of the use of so-called "immune serums." I think there was one from Toronto. Has that all gone by the board, or are there continuing investigations?

Dr. Moore: There are continuing investigations on immune serum and vaccines at quite a few places. Dr. Harris is actually related to some studies at Sloane-Kettering. We have at least three groups actively studying vaccines and immune processing. There are very good ones going on, but I would just say that they are all investigative, and, to my knowledge, there are no results that make immune serum and vaccines worthy of consideration clinically. It is of interest scientifically, but it is of no value clinically. I am sorry that we cannot talk about some of the things because of civic reasons, but they are going on all the time. They are done very carefully, with due regard for the patients, and we do hope that they will be advantageous.

Question: I have one other minor question for Dr. Watne. When you are using an agent of such toxicity, how long does the basically double-blind study remain blind?

Dr. Watne: Until the time of the first recurrence. Actually, in the study with nitrogen mustard, someone did figure it out. There was a little red-headed secretary in Pittsburgh who watched the ampules as they were dissolving. She noticed the difference, and she tested out the code numbers for two weeks and broke the code.

Considerations of Medical Shock of Unknown Origin

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MEDICAL SHOCK *may be caused by numerous diseases. The correct diagnosis is necessary to the prompt, specific, and supportive therapy which is essential to sustain the life of a patient admitted to a medical service in a profound state of shock. The most common cause of medical shock is myocardial infarction; other cardiac causes include the arrhythmias, pericarditis, myocarditis, cardiac rupture and tamponade, rupture of valve cusps, chordae tendineae, and papillary muscles, septal perforation, and necrotizing angiitis. Bacteremia is also a very common cause of shock. Hypovolemic states which may cause shock include acute internal blood loss, acute pancreatitis, diabetic acidosis, and adrenal insufficiency. An acute allergic condition may cause shock. Impediment to blood flow, such as sudden embolic phenomena and dissecting aneurysm of the aorta, is another cause of shock. Neurogenic causes of shock include all forms of cerebral vascular accidents, "hypoglycemic shock," and effect of drugs on the central nervous system.*

LIKE FEVER of unknown origin, the problem of medical shock of unknown origin presents many diagnostic possibilities for consideration. The patient who is admitted to a medical service in a profound state of shock demands prompt, specific, and supportive therapy if his life is to be sustained.

Before reporting the following perplexing case of sustained medical shock, a definition is in order. We have chosen the concept of shock depicted by Weil: "Shock is a descriptive term used by clinicians to denote a syndrome that is characterized by protracted prostration and hypotension and usually accompanied by pallor, coldness, and moisture of the skin, collapse of the superficial veins, alteration of mental state, and suppression of the formation of urine."[1] A more precise definition, according to Weil, limits the usefulness of the term which is "to indicate the clinical state of the patient without specific implications as to the underlying cause." By the term medical shock, we are arbitrarily excluding trauma, surgery, and anesthesia as causes.

Case report

The patient was a seventy-seven-year-old white female seen originally five months prior to her last admission because of symptoms of intestinal obstruction. X-ray films showed an incomplete volvulus of the cecum, multiple diverticula of the colon, a nonfunctioning gallbladder, and essentially clear lung fields. An electrocardiogram showed S waves in leads I and II and T inversion in leads V_1 through V_4. The treatment consisted of intubation, and the patient did well. She was readmitted ten weeks prior to her last admission with abdominal colicky pains, nausea, and vomiting. Her blood pressure was 150/90. The initial hemogram and electrolytes showed normal findings, and the patient underwent surgery. Cholecystitis, cholelithiasis, choledocholithiasis, and diverticulitis were found. The gallbladder was removed; the common duct explored; and a transverse colostomy performed because of a dense, matted area of diverticulitis. Postoperatively she did well except for a wound abscess until pain in the right side of the chest was noted, which was worse with deep breathing. No rub was heard. X-ray films did not clearly demonstrate a pulmonary infarction although it was suggested at one examination, and an electrocardiogram showed essentially the same pattern. The patient was not given anticoagulation therapy. The blood loss at surgery was estimated at 700 cc. and was replaced with 500 cc. of blood. The hematocrit at the time of the patient's discharge was 37 per cent, and she appeared to be clinically much improved. In the interim at home she did quite well. Seven hours prior to her final admission she suddenly became weak and perspired profusely. Her physician noted a blood pressure of 90/60 and a tachycardia, and she was readmitted.

The examination disclosed an obese, pale, white female in shock and in acute distress and

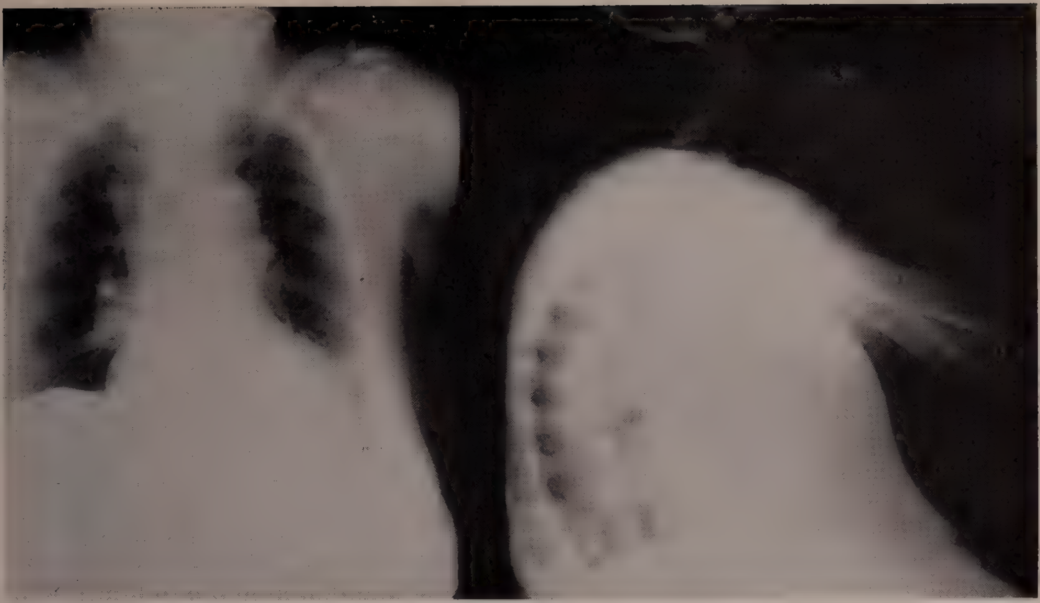

FIGURE 1. Slight increase in heart size.

appearing chronically ill. Her blood pressure was 90/60, pulse 120, and temperature 99.8 F. Her neck veins were not distended, and the lungs were clear to percussion and auscultation. There was no cardiac enlargement, the aortic second sound equaled the pulmonic second sound, and a harsh systolic murmur of moderate intensity was heard at the apex. The colostomy was functioning well. There was an oblong mass in the right lower quadrant of the abdomen which was mildly tender and which was not present at a follow-up examination. The patient was alert and oriented, and except for symmetrical hypoactive reflexes the neurologic examination was unremarkable.

Her white blood cell counts were slightly elevated throughout her hospital course, except for 43,900 terminally. The hematocrits ranged from 38 to 42 consistently. The blood urea nitrogen and electrolytes varied within broad normal ranges except for low sodium and chloride at one point. The total protein was 5.2 Gm. with 3.3 Gm. of albumin. The bilirubin was 1.2 mg. per 100 ml. total with 0.8 direct at the highest level. The SGOT (serum glutamic oxalacetic transaminase) was 56, 56, 23, 20, and 10 units, and the SGPT (serum glutamic pyruvic transaminase) was 150, 22, 42, 20, and 6 units at approximately two-day intervals. A urinalysis showed persistent traces of albuminuria and pyuria. Chest films showed a slight increase in the heart size, and a later film demonstrated evidence of pulmonary infarction in the lower lobe of the right lung (Figs. 1 and 2). A consolidation in the lower lobe of the left lung, which cleared with treatment was demonstrated one week prior to the patient's demise. Electrocardiograms (Fig. 3) showed a changing pattern compatible with pulmonary circuit obstruction. Two blood volume determinations were done which showed the total volume to be 66 per cent of the predicted normal, the plasma volume was 70 per cent of the predicted normal, and the red blood cell volume was 62 per cent of the predicted normal. The total plasma 17-OH corticosteroids was 15 micrograms.

The patient was treated with intravenous metaraminol bitartrate and then through a right femoral vein cutdown with levarterenol to maintain her blood pressure adequately at 110 to 130/70 to 90. A gallop rhythm with increasing hypotension was noted, and the patient was digitalized. Penicillin and streptomycin were added without affecting the course. Hydrocortisone was tried without any effect on the hypotension after blood for 17-OH corticosteroids was drawn. Anticoagulation was begun six days after admission. While she was receiving anticoagulation therapy, the patient developed pain in the right side of the chest, and a pleural friction rub was heard for the first time. Vitamin K had to be administered once when the patient lost an estimated 400 cc. of blood from a crack in the colostomy. Atropine and ephedrine were started in an effort to wean her from the pressor agent. A sudden asymptomatic drop in her blood pressure which required 8 ampules of levarterenol per liter to maintain her pressure at the 120/80 level made it necessary to reinstate anticoagulation therapy. Contracted blood volumes and low sodium and chloride prompted the administration of hypertonic saline plus 2 units of whole blood. After nineteen days on continuous levarterenol she finally maintained her blood pressure, and the femoral catheter was removed. One week prior

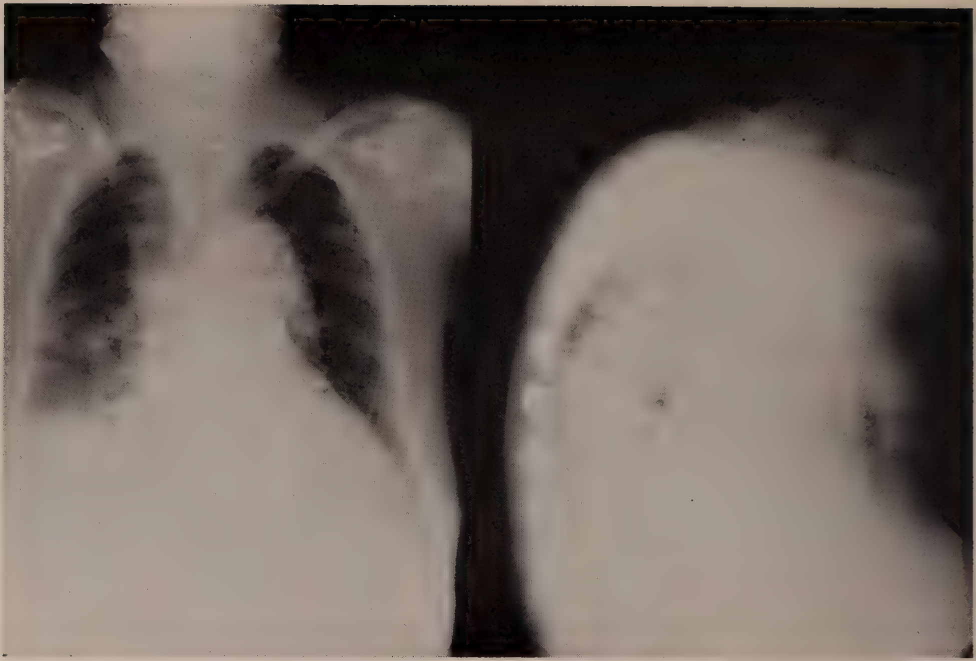

FIGURE 2. Pulmonary infarction in lower lobe of right lung.

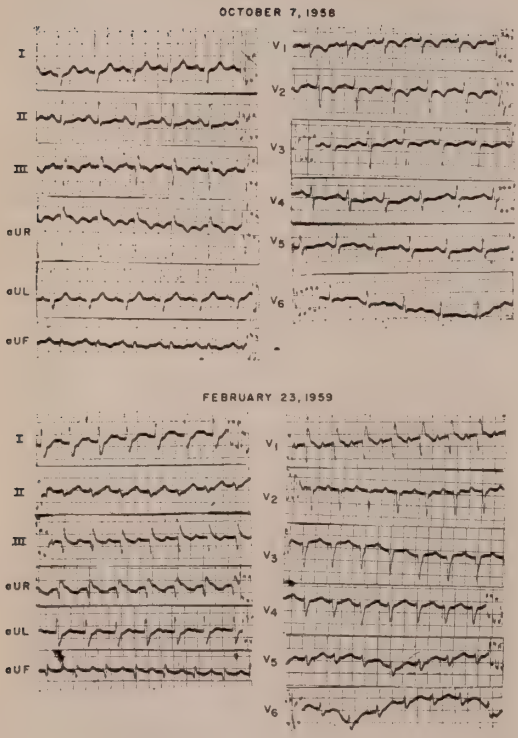

FIGURE 3. Electrocardiogram showing changing pattern compatible with pulmonary circuit obstruction.

to her death she developed pneumonia in the lower lobe of the left lung from which pneumococci were cultured and which responded to antibiotics with almost complete clearing. Anticoagulants were stopped again. However, she again developed severe hypotension, her temperature rose to 106 F., and she expired. Terminal blood cultures were positive for Escherichia coli.

At autopsy the gross findings included thrombophlebitis of the deep femoral and external iliac veins on the right side with massive right pulmonary arterial embolism. Old infarctions in the lower lobe of the right lung were present. There was right ventricular hypertrophy and dilatation, plus 5,000 cc. of pleural effusion on the right side. Fifteen cc. of pus were found in a small multiloculated pocket along the descending colon. It was felt that the old pulmonary infarctions were of the same age as the existing embolism and that the small fragments had broken off the main embolism during her course. Hypocellularity of the bone marrow of a slight degree was listed as possibly contributing to the contracted total blood volume.

Comment

It is our purpose in this paper to provide a reasonably complete list of the causes of medical shock and to comment briefly on the rational approach to patients with undiagnosed disorders who have this syndrome. We do not propose to discuss all the various diagnostic features of each disease. Weil's[1] classification lists the subdivisions of medical shock based on the broad etiologic classification:

1. Cardiac
2. Toxic products
3. Hypovolemia
4. Hypersensitivity
5. Impediment to blood flow
6. Neurogenic factors
7. Miscellaneous.

Cardiac

The most common causes of medical shock fall in the cardiac group, and the major entities include myocardial infarction, the arrhythmias, pericarditis, myocarditis, cardiac rupture and tamponade, rupture of the valve cusps, chordae tendineae and papillary muscles, septal perforation, and necrotizing angiitis.[2–4]

Myocardial infarction is unquestionably the most common cause of medical shock. Precordial pain, which is usually an important aid in establishing this diagnosis, is not always present. This appears to be true, particularly in older patients and in those patients sustaining a myocardial infarction during or just after surgery.[5] The accuracy of the electrocardiogram in diagnosing myocardial infarction varies in autopsy studies from 62 to 94 per cent.[6,7] Other studies would suggest that approximately 20 per cent of acute myocardial infarctions are missed by the electrocardiogram.[8,9] The work of Myers *et al.*,[10–16] while not easily lending itself to simple comparisons of infarctions diagnosed and infarctions missed by the electrocardiogram, would indicate that approximately 20 per cent of myocardial infarctions are missed by the electrocardiogram. The assumption that myocardial infarction appears mainly in the elderly and later-middle-aged patients is not nearly as reliable as once was thought because the entity is being reported in younger individuals with increasing frequency.

Cardiac arrhythmias occasionally are accompanied by the shock syndrome. Paroxysmal arrhythmias in otherwise normal individuals usually are not associated with any evidence of circulatory insufficiency except in very rare cases. However, if an arrhythmia develops in a patient already very sick with an underlying illness, sudden collapse may occur. Auscultation of the heart and the electrocardiogram will establish the diagnosis of the great majority of arrhythmias.

In cardiac shock from any of the listed causes, the mechanism is that of a decreased cardiac output due to failure of the pump which is frequently coupled with a failure of the total peripheral resistance either to maintain its level or increase to maintain its circulation.[1–3,17,18]

Toxic

The importance of bacteremia as a cause of shock can be emphasized by the fact that it has become the commonest single cause of shock, other than that due to myocardial infarction, now being treated on the medical services of the University of Minnesota Hospitals.[19]

When presented with a patient in shock that presumably is due to an infection, certain clinical considerations often are helpful in establishing the presence and the etiologic background of the organism. Most authors agree that the genitourinary tract is the most common portal of entry, and all too frequently, sudden fever, bacteremia, and shock are seen following manipulation in this area.[20–22] It should be borne in mind that while gram-negative organisms and their endotoxins frequently are implicated in the "gram-negative shock" syndrome, gram-positive organisms, as well as rickettsia, can produce the identical clinical picture.[22] The warm shock or pink shock associated with gram-negative infection also is a variable finding, and its absence should not eliminate the possibility of a gram-negative organism.[20]

Bacteremic shock is more common in the elderly debilitated patient or in patients with debilitating systemic diseases, such as carcinomatosis, agranulocytosis, diabetes, and liver or renal disease. Weil and Spink[19] state that the clinical features of bacteremic shock rarely are distinctive enough to allow for an unequivocal and prompt diagnosis. An awareness of the existence of a source of infection and a prompt analysis of the clinical events that occurred in the period of twelve hours preceding the onset of shock are most helpful. Signs of sepsis, including fever, polymorphonuclear leukocytosis, nausea, vomiting, diarrhea, and/or abdominal pain occurred in the majority of Weil's patients. Because of the frequency with which electrocardiogram changes and especially evidence of myocardial ischemia are detected in elderly patients with shock, the differentiation between myocardial infarction and bacteremic shock may be difficult. The absence of chest pain, the presence of gastrointestinal signs, the pronounced vasodilatation, and a consideration of historical features may aid in this differential diagnosis.

In discussing shock due to infection, contaminated blood or other infusions should be mentioned, since this source of infection frequently is overlooked.[23] The staphylococcus deserves mention because any serious staphylococcal infection can be complicated by hypotension. Occasionally the patient with a staphylococcal bacteremia can die in from twelve to twenty-four hours with the shock syndrome. Whether or not staphylococcal infections are increasing is still being debated, but the entity, pseudomembranous enterocolitis, apparently has been increasing in occurrence during the recent years and is often accompanied by shock. In a recent autopsy review of 21 such cases, shock was found to be a prominent feature in 15 cases.[24]

The work of Weil and Spink and others has done much to clarify the mechanism of shock associated with endotoxins from various organisms. Briefly, there is a great pooling of blood on the venous side without affecting arteriolar tone; the portal pressure increases, and the cardiac output decreases markedly secondary to the decreased venous return.[19,20,25,26] In the Waterhouse-Friderichsen syndrome the adrenals are involved acutely with the overwhelming septicemia, and an acutely insufficient adrenal state is superimposed on the effects of the endotoxins. The meningococcus has been responsible for the majority of cases, but again it should be noted that other organisms, including the pneumococcus, hemophilus influenza, and staphylococcus also can reproduce the syndrome.

Hypovolemic states

Illnesses which deplete the blood volume directly or which cause loss and changes of the extracellular and intracellular fluid volume, which in turn deplete the blood volumes, are considered under this heading.

Internal hemorrhage as a manifestation of a bleeding peptic ulcer, esophageal varices, ruptured ectopic pregnancy, ruptured spleen, and many other causes may lead to a patient's admittance to a medical ward in a state of shock. The differential diagnosis between a bleeding peptic ulcer and bleeding esophageal varices can be quite difficult because known cirrhotic patients with proved esophageal varices are said to have more peptic ulcers than the general population.[27] Often a gastrointestinal series and/or esophagoscopy are the only definitive diagnostic means, and they are by no means certain.

Next to acute internal blood loss, acute pancreatitis should be mentioned, since the shock seen in this condition often is a combination of internal hemorrhage into the retroperitoneal spaces, plus vomiting, dehydration, and loss of exudative fluid. Abdominal pain with elevated amylase and lipase determinations should alert one to this condition.

Two special conditions which can cause shock are diabetic acidosis and adrenal insufficiency. In diabetic acidosis the defect is that of severe dehydration, and fluid and electrolyte replacement usually will correct the shock syndrome. The Kussmaul respirations, dehydrated appearance, and acetone odor to the breath, plus the demonstration of glycosuria, acetonuria, hyperglycemia, and acidosis confirm such a diagnosis. An absolute or relative lack of adrenal cortical hormones during an acute stress may result in an adrenal crisis characterized by the shock syndrome, among others. The acute condition with shock can be superimposed on clinically apparent or latent chronic adrenal insufficiency secondary to hemorrhage, infection, thrombosis, and other causes. The shock also can be due to adrenal insufficiency resulting from a state of panhypopituitarism. The prolonged administration of ACTH or an adrenal cortical steroid to an individual with normal adrenals results in a suppression of the response of the pituitary-adrenal mechanism to stress. A quite simplified explanation of the shock in adrenal insufficiency is that it results from an acute loss of extracellular fluids superimposed on a decreased blood volume. The combination of fatigue, weight loss, and pigmentation should arouse the suspicion of adrenal insufficiency.

Generally, any condition, acute or chronic, which involves dehydration, with or without associated electrolyte loss, can produce circulatory collapse if the process has been severe enough.

Allergic

The diagnosis of the acute allergic reaction is usually not so difficult because of the preceding history of contact with an allergen, either by injection or ingestion. These reactions may result from treatment with penicillin, foreign serum used as antitoxin, desensitization treatments with allergenic materials, oral ingestion of certain drugs including penicillin, and an insect sting in certain sensitized individuals. Patterson[28] states that the symptoms of severe constitutional reaction may vary but include dyspnea, cyanosis, fall in blood pressure, collapse, and death. The reaction may be immediate, occurring at the instant of the injection, but usually it occurs within thirty minutes. Thus, when presented with an allergy patient who developed sudden peripheral circulatory collapse within minutes of an injection of penicillin or other allergenic substance, the diagnosis of anaphylactic shock should be considered quickly. The mechanism of shock in allergic reactions is related to the antigen-antibody reaction with the liberation of histamine, serotonin, or similar substances.

Impediment to blood flow

Strictly speaking, the category of impediment to blood flow should include only sudden embolic phenomena, but we feel that a dissecting aneurysm of the aorta is reasonably similar to justify its inclusion here. To dwell briefly on the subject of dissecting aneurysms of the aorta, an entity which often is accompanied by shock, we would like to point out some features that might make one suspicious of this disease. A patient with arachnodactyly (Marfan's syndrome), pregnancy, hypertension, coarctation, idiopathic kyphoscoliosis, or a known luetic or arteriosclerotic aneurysm would be a candidate for the dissection. If one had the benefit of a history of sudden onset of severe, almost indescribable pain in the chest or epigastrium which may extend along the course of the ribs to the back and then up into the neck and shoulders or down into the abdomen, one might be inclined to think of this diagnosis.[29]

The most common entity thought of as impeding blood flow is the pulmonary embolus. That this entity often is complicated by shock is well known. In Israel and Goldstein's[30] series of 90 patients with pulmonary embolism, hypotension was encountered in a total of 25 patients. Both Israel and Short[31] state that pulmonary embolism is the most common acute pulmonary disease, outnumbering in a given length of time pneumonia and bronchogenic carcinoma. It is distressing that in this relatively common disease the classic symptoms, signs, and laboratory findings often are absent. Hemoptysis and a pleural friction rub, two of the clinical findings which are regarded as most characteristic of pulmonary embolism, were both relatively uncommon in Israel's series (28.9 and 24.4 per cent respectively). Likewise, pulmonary embolism and infarction do not always result in pathognomonic chest x-ray findings. In Israel's series the radiologists suggested pulmonary embolus among other possibilities in 55.2 per cent of the chest films in that series. In an additional 28.4 per cent of those x-ray films there were, in retrospect, significant radiologic findings for pulmonary embolus, but they were not reported by the radiologists. The electrocardiogram was noted to be helpful in 70.7 per cent of the patients on whom tracings were done in the previously mentioned series. They were in the form of rather transient and characteristic abnormalities, such as the appearance of Q waves in aVf, S-T segment depressions, and T-wave inversion over the right precordial levels. Thus, these electrocardiogram abnormalities can be quite variable and can be confused easily with those of acute myocardial infarction at times. As is true of the chest x-ray abnormalities where follow-up films are important for the sake of comparison, serial electrocardiograms often are very helpful in establishing the diagnosis of pulmonary infarction. Our case presentation illustrates this concept very well.

In Selzer and Bradley's[32] discussion of the origin of shock in pulmonary embolism it was noted that initially there was a decrease in the cardiac output along with a compensatory increase in peripheral resistance. Then suddenly, further hypotension occurred which the authors ascribed to a neurogenic peripheral mechanism and not to further strain or failure of the right ventricle. It is speculated that a similar neurogenic mechanism may be operative in a dissecting aortic aneurysm where blood loss is not a factor.

Neurogenic

All forms of cerebral vascular accidents, including subarachnoid hemorrhage, meningitis, and encephalitis, characteristically produce the comatose rather than the hypotensive state in patients except in the terminal event. That shock can occur with central nervous system damage is well known, and attention toward the appropriate neurologic tests will aid in the diagnosis. The vasovagal reflex, commonly associated with a syncopal episode, may persist for long periods of time because of severe pain. It is not uncommon for a patient with severe precordial pain from a myocardial infarction to obtain relief from his hypotension as the chest pain is relieved. Presumably, the vasovagal reflex is broken, and the normal compensatory mechanisms come into play.

The term "insulin shock" or "hypoglycemic shock" deserves comment. As hypoglycemia develops, a patient often goes through a phase of epinephrine release, and his blood pressure actually can rise. Only in the later stages of "hypoglycemic shock," when the cerebrum has long since ceased to function, and the vasomotor center in the medulla is deprived of nutrients, does the true hypotensive state occur. In their book on this method of treatment in psychiatric disorders, Kalinowsky and Hoch[33] state that when systolic blood pressures reach low levels, the treatment is terminated rapidly. Hence, the term "shock" does not refer to hypotension, and it would be wise to substitute the term "coma" for "shock" when used in this context.

Frequently, drugs affecting the central nervous system must be considered. An overdose of barbiturates not uncommonly produces a hypotensive as well as a comatose patient. The wide use of phenothiazine drugs which have weak ganglionic-blocking properties of their own has occasioned the shock syndrome. It is not unusual to see patients on chlorpromazine hydrochloride doses in the 400- to 800-mg. per day range with systolic blood pressures in the 90- to 100-mm. Hg range.

Miscellaneous

It should be apparent that there are numerous diseases and mechanisms whereby a patient can become hypotensive. A few fail to fit easily into the classifications we have adopted. Scheinberg *et al.*[34] noted that patients with myxedema can have a reduction of their cardiac output up to 47 per cent of the normal, and this may well explain why some patients with this condition can develop the shock syndrome. Three observations on patients with emphysema and increased carbon dioxide tension are pertinent to a discussion of hypotension. First, these patients often maintain a significantly lower blood pressure than their pre-emphysema level. Second, they are frequently more susceptible to the hypotensive effects of morphine. Third, they occasionally will become quite hypotensive during or after their carbon dioxide pressure is decreased toward normal by the use of a positive pressure breathing apparatus. Recent data on these phenomena would indicate that hypercapnia alone can cause an increased cardiac output. Patients with borderline cor pumonale or failure from any other cause might be unable to increase their outputs and decompensate with hypotension as one of the signs. Morphine, as a respiratory depressant, can cause a sudden hypercapnia with the hypotensive result. The patient on the positive pressure apparatus may be becoming hypotensive on the basis of a rapid reduction of carbon dioxide pressure analogous to the normal patient who is hyperventilated, and has decreased carbon dioxide pressure, vasodilation, and decreased blood pressure.[35,36] Also, the increased filling of the alveoli by the positive pressure may decrease the blood flow through the lungs, and, hence, the left ventricular output.

It should be obvious that one cannot consider all the causes of medical shock. An endeavor has been made to classify the various mechanisms so that a rapid and decisive method of handling the medical patient in unexplained shock can be facilitated.

Summary

A case of a seventy-seven-year-old female with unexplained medical shock is presented. The case illustrates pulmonary embolism as one cause of medical shock. A discussion follows on the various clinical, diagnostic, and pathologic aspects of shock.

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Current Neurosurgical Researches and Treatment Referable to the Hyperkinetic Disorders

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DURING THE PAST DECADE a busy interest in the treatment of the hyperkinetic disorders has characterized neurosurgical endeavor throughout the world. The impetus for this is traceable to the pre-World War II period, 1931 to 1941, during which surgical extirpation of the motor cortex, first performed in 1899 by Horsley,[1] was exploited further by Bucy and his collaborators,[2-4] and two new procedures in the form of Putnam's[5,6] antero- and posterolateral cervical cordotomies and the present writer's[7-9] interruptions and extirpations of several structures in the basal ganglia, including the ansa lenticularis, were devised and successfully implemented. Surgical investigations in this area were suspended during World War II.

Between 1946 and 1951 the development of human stereotaxic apparatus[10,11] and human brain coordinates[12,13] opened the way for attacking certain structures in the basal ganglia and thalamus with degrees of safety and accuracy of lesion placement not theretofore attainable. Toward the end of this five-year period, lateral[14,15] and intermediate[16,17] midbrain pedunculotomies and subcortical interruption of the U-fibers between the precentral and premotor gyri,[18] all executed by the then conventional surgical methods, were performed successfully in selected cases of ballism, athetosis, and alternating tremor.

During the decade since 1951, a number of additional valuable contributions from several sources have been made. These may be regarded as being in the nature of technical advances, providing increasingly greater safety and facility of execution and more consistently predictable therapeutic results, rather than operations invoking novel pathophysiologic principles. Briefly, they encompass improvements in stereotaxic devices and atlases,[19-27] in the manner of producing nondiscriminating cerebral lesions by special leukotomes,[28-30] electro- and thermocoagulation,[31-35] chemocoagulation,[36-41] nuclear energy,[42-45] and tissue-discriminating, high-frequency, focused ultrasound.[46]

The present vogue of surgical attack, then, consists largely of placing lesions in the basal ganglia, ansa lenticularis, dorsal thalamus, and closely related pretectal and tegmental structures. Such placements may be preceded by stimulation and/or the deliberate production of transient, reversible dysfunction(s) with procaine, and so forth, the purpose of which is to minimize postoperative complications and to achieve the desired therapeutic result as regularly and fully as modern methods permit.[47-51]

The remarks to follow should be prefaced by the observations that (1) the surgery of hyperkinesia is limited in application to a relatively small fraction of the rather considerable population, estimated at a million in the United States, suffering from the hyperkinetic disorders; (2) surgery in this area, far from having been standardized, is as yet decidedly in the developmental phase; (3) such surgery is always alleviatory in nature, rather than curative; and (4) it is nonspecific, in that the surgeon does not attack the "seat of disease," as in operations for cerebral tumors, cysts, abscesses, cicatrices and atrophic or dysplastic lesions, but

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aims at interrupting one or more neural pathways or circuits, the integrity of which appears essential to the development and/or perpetuation of certain abnormal movement disorders.

Current surgical endeavors in this area exhibit two broad aims: to contrive symptomatic relief and to illuminate understanding of the pertinent healthy neuro-chemo-humoral mechanisms and the manner(s) in which they may become deranged.

Hyperkinetic disorders currently known to be susceptible of central surgical intervention

Up to the present, it has been shown possible to alleviate and/or abolish by surgical measures the following varieties of abnormal movements:

Patterned hyperkinesias—tremors
1. Resting type, for example, parkinsonian, with or without a background of hypertonus (rigidity) and/or akinesia
2. Posture-attaining type, for example, senile intention tremor and congenital "rubral" tremor
3. Posture-maintaining type, for example, spasmus nutans
4. Ataxic type, for example, dyssynergia cerebellaris progressiva.

The electromyograms obtained in these disorders largely honor Sherrington's law of reciprocal innervation and thus closely simulate those of the purposive and nonpurposive phasic movements exhibited by normal subjects.

Nonpatterned hyperkinesias
1. In which the phasic movements take off from a eutonic or hypotonic background of muscle tonus
    - Choreatic type (dominantly, the distal members of appendages)
    - Ballistic type (dominantly, the proximal members of appendages)
    - Myoclonic and tic twitching types (local, regional or general, involving facial, nuchal, truncal, and appendicular members)
2. In which the phasic movements take off from a hypertonic background of muscle tonus of fluctuating or relatively enduring character
    - Athetosic type
    - Dystonic type

SURGERY FOR HYPERKINESIA *is limited, alleviatory rather than curative, and nonspecific. It consists largely of placing lesions in the basal ganglia, ansa lenticularis, dorsal thalamus, and closely related pretectal and tegmental structures and is directed to contriving symptomatic relief and illuminating understanding of the pertinent healthy neuro-chemo-humoral mechanisms and the manner in which they may become deranged. The disorders may be divided into two categories: patterned hyperkinesias or tremors of the resting, posture-attaining, posture-maintaining, or ataxic type; and nonpatterned hyperkinesias in which the phasic movements take off from a eutonic or hypotonic background of muscle tonus or in which they take off from a hypertonic background of muscle tonus of fluctuating or relatively enduring character. A sound general theory of the manner in which pertinent neurohumoral mechanisms become so deranged that clinical hyperkinesia appears is lacking; there are failures in the structure-bound, system-bound, and relational theories and combinations of these. The components of a propositional function of hyperkinesia include: the pallido-pallidofugal complex, the integrity of which seems to be a precondition of hyperkinesia, and the concept of somatotopic arrangements. The concept of a facilitation-inhibition ratio and that of synchronous firing of the FCP (final common pathway) lack empiric verification but may well receive it in the near future. There is reason to anticipate that a multiple convergence hypothesis in which disturbed dynamic relationships, rather than damage to particular agents, will provide the basis of an explanation of hyperkinesia.*

The electromyograms obtained in the disorders listed largely violate Sherrington's law of reciprocal innervation and in this respect do not constitute simulacra of those of the purposive and nonpurposive movements exhibited by normal subjects.

Clinical observations amply document the circumstance that in some patients each of the special varieties of patterned and nonpatterned hyperkinesias may remain delimited over the course of years, even a lifetime, to particular members and regions of the body, for example, the thumb of one side, the face, neck, and so forth. In others, they spread by irregularly advancing stages to implicate additional and not necessarily adjacent parts. In still others, they progress steadily and inexorably, often at an increasing pace. Such observations provide the student of the pathogeneses of these disorders with an important clue: Somatotopic representation somehow abides in the neural mechanisms deranged in the hyperkinesias.

Moreover, the several varieties of abnormal movements not infrequently run their courses for years in what amounts to "pure culture," uncontaminated by other varieties, altered myotonic states, and/or additional neurologic and psychologic disabilities. This circumstance provides a second important pathogenetic clue: Whatever the pathophysiologic mechanisms corresponding to the several clinical forms of hyperkinesia may be, they probably differ from one another in spatial and perhaps other relational ways in at least some portions of their structures.

Surgical data bearing on attendant phenomena

While observations indicate that the several hyperkinetic disorders may exhibit themselves for protracted periods in "pure culture," nothing in the clinical or pathophysiologic circumstances compels them to do so. For example, while it is true that alternating tremors exhibited in some forms of parkinsonism are typically present during repose and are visibly dampened, even abolished, during the execution of "voluntary" movement (in consequence of which highly skilled acts often can be performed with essentially normal facility), clinical observations in other instances reveal that the resting tremors persist and may even become augmented in vigor and amplitude during the attainment of a new posture of the limb and/or the maintenance of a posture newly assumed; and that if, at any given period, the resting tremors happen to be in abeyance, the acts of assuming and/or maintaining a new posture often evoke observable alternating tremors. In brief: "Voluntary" movement may have the effect in some cases of suppressing, and in others of augmenting alternating tremors. In the latter case eupraxia is, of course, severely compromised.

Similarly, the athetosic movements that afflict a given bodily member during repose often are attended by ataxic movements which supervene whenever posture-attaining and posture-maintaining efforts involving the same and/or other limbs are made. That athetosic and ataxic movements are mediated by neural mechanisms which differ in at least some parts of their respective courses in the central nervous system is apparent from two substantial observations: (1) that ataxic movements may be and often are unattended by athetosic movements, and (2) that ataxic movements which appear on "voluntary" effort persist postoperatively despite surgical alleviation of the athetosic movements exhibited preoperatively during repose.

Furthermore, although the combination in any given patient of a patterned hyperkinesia, for example, parkinsonian tremor, in one limb and a nonpatterned hyperkinesia, for example, choreatic, in the contralateral fellow is unusual, such instances have been documented,[52] and the coexistence of tremors and choreoathetosic movements in the same limb has been recorded recently.[53] These circumstances offer us a fourth pathogenetic clue: While the particular neural mechanisms deranged in the various hyperkinetic disorders are presumably separate in at least certain portions of their spatial configurations, it is probable that they are closely proximate in other portions. Consistent with this postulate, extensions of lesions beyond their original sites may and, depending on their locus, often do invoke additional hyperkinetic manifestations.

Just as the several clinical varieties of hyperkinesia may exist singly or in combination, so may they exist independently of or in combination with clinically observable alterations in muscle tonus, that is, hyper- and/or hypotonus. For example, alternating tremors in some instances may precede and in others follow by considerable periods of time the onset of rigidity, or they may develop pari passu with rigidity.

Jackson asserted in 1896[54] that rigidity is merely tremor run together. However, clinical observations, animal experimentation, and the results of neurosurgical procedures since his day have combined to make clear that the peripheral and central pathophysiologic mechanisms that subtend tremors, on the one hand, and rigidity, on the other, are separable. Nevertheless, it is evident from surgical investigations in which tremors and rigidity have been alleviated or abolished by a single procedure, that in at least some portions of their central courses, the structural configurations of their respective neural agents must course in close proximity to or intimately intermingled with one another.

Unlike alternating tremors, choreatic and ballistic movements are rarely, if ever, attended by hypertonus. On the contrary, they appear to take off from a prevailing background of muscular activity which is either eutonic or hypotonic.

Ataxic hyperkinesias are more often than not attended by hypotonus, whereas myoclonic jerkings and tic twitchings usually are attended by eutonus.

It is of pathogenetic interest that hypotonus, when present preoperatively, persists essentially unaltered postoperatively, despite the alleviation of choreatic, ballistic, or ataxic movements by surgical intervention. Here again, an inference appears warranted that in at least some portions of their configurations, the neural mechanisms subserving choreatic, ballistic, ataxic, and myoclonic hyperkinesias are separate, although presumably spatially proximate to one another.

Athetosic and dystonic hyperkinesias may be distinguished from choreatic, ballistic, ataxic, and myoclonic movements in virtue of qualitative differences in the prevailing muscle tonus. In the first two disorders, which appear to differ from each other only in degree,[55] the phasic movements take off from an unstabile myotonic background. It is as if the arrival of neural impulses provocative of phasic abnormal movements finds the FCP (final common pathway) and/or its related internuncial pools already preempted by impulses that incite hypertonus. In consequence, athetosic and dystonic movements are, when compared with choreatic, ballistic, ataxic, and myoclonic movements, relatively sluggish.

The term, choreoathetosis, is familiar in the jargon of current-day neurology. In accord with the popular concept, exemplified in Bucy's[56] theory of choreoathetosis, in which the derangement of a single neural mechanism is conceived to underlie this hyperkinesia, choreatic and athetosic movements are merely quantitative variants of the one abnormal process. However, a consideration of the differences in backgrounds of myotonus referred to previously suggests that it would be more appropriate to associate choreatic and ballistic movements, on the one hand, and athetosic and dystonic movements, on the other, than choreatic and athetosic movements.[57]

The various signs and symptoms subsumed by the term akinesia are characterized by asthenia and a sluggishness of intentional movements "off the mark," during execution and in termination.[58] Additional manifestations by which akinesia is expressed clinically include fatigability, petit pas, festination, pro-, retro-, and lateropulsions, masked facies, reptilian stare, defects in automatic associated movement, and low, monotonous, dysarthric speech.

As with myotonic disorders, the hyperkinesias may exist independently of or associated with akinesia; conversely, akinesia may occur independently of or associated with abnormal movements and disorders of muscle tonus.

The therapeutically disappointing fact is that, with one exception,* surgical procedures of every variety thus far usefully employed against tremors and rigidity have proved largely incapable of alleviating akinesia. In view of this, the available clinical and neurosurgical data warrant an inference regarding the neurohumoral correlates of akinesia: Whatever their details, their spatial configuration must be largely independent of and, as compared with those of tremor and rigidity, relatively remote from the latter.

Presumptive sites of surgical lesions effective against hyperkinesia

The data accumulated during the past quarter century bearing on the presumptive loci* of surgical lesions that have proved effective against hyperkinetic and hypertonic disorders may be summarized under two headings.

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* The exception was a sufferer from postencephalitic tremors who exhibited no rigidity but several conspicuous akinetic manifestations. He was subjected to ultrasonic irradiation directed at Forel's field H, just caudal to the zona incerta, following which a gratifying improvement in alacrity of movement and intelligibility of speech was noted.

Lesion sites which, while alleviating hyperkinesia, regularly invoke paresis, dyspraxia, "disregard" of limb and/or spastic phenomena

1. Precentral gyrus (Brodmann's "Area 4")
2. Precentral and "premotor" cortex (Brodmann's "Areas 4 and 6")
3. White matter subjacent to precentral and "premotor" cortex
4. Internal capsule (anterior limb; posterior limb)
5. Midbrain crus (intermediate three-fifths, with or without the later-almost fifth)
6. Spinal cord
    - (*a*) Anterolateral segment
    - (*b*) Dorsolateral segment ("pyramidotomy")
    - (*c*) Lateral funiculus and lateral portion of anterior funiculus.

Lesions at sites 1 through 5, and 6 (*a*) and (*c*) have been for many years considered essentially those of the pyramidal system.[59] The implication is that the interruption of the pyramidal component and of that alone provides the therapeutically effective surgical maneuver against tremors. Both notions are based on a fictional dichotomy between pyramidal and extrapyramidal systems for which embryologic, phylogenetic, anatomic, physiologic, pathologic, clinical, and logical support are lacking.[60,61] In characterizing the sites of lesions as being pyramidal and extrapyramidal, we seriously compromise our efforts to clarify pathogenetic obscurities.

Lesion sites which, while alleviating hyperkinesia, do not regularly invoke paresis, dyspraxia, "disregard" of limb and/or spastic phenomena

1. Globus pallidus
2. Ansa lenticularis (ventral, intermediate, and dorsal components)
3. Tissues constituting the border zone between the tegmentum and substantia nigra at the lateral half of the dorsal margin of the substantia nigra
4. Pretectal Forel's fields H_1 and H_2
5. Tegmental field H of Forel just caudal to the zona incerta
6. Tissues constituting the mesial-inferior borders of the nucleus ventrolateralis of the dorsal thalamus
7. Nucleus ventrolateralis of the dorsal thalamus.

Because lesions at these sites do not necessarily impose additional neurologic deficits in the form of paresis, and so forth, neurosurgical endeavors of the current day are for the most part directed at one or another of these structures. And inasmuch as these procedures interrupt the pallido-pallidofugal complex at some portion of its origin, course, or destination(s), the inference may be tentatively drawn that the ansa lenticularis is one the integrity of which appears to be essential to the onset and perpetuation of hyperkinesia. This is not to say that other structures are not incidentally damaged, much less that their interruption is inconsequential to therapeutic relief. The ansa lenticularis simply appears to constitute the one common, readily identifiable denominator that brings unity to what otherwise might be considered unrelated surgical procedures.

Progress in illuminating the neurohumoral mechanisms pertinent to the hyperkinesias

A growing need exists in both academic and clinical realms for a sound general theory of the manner in which pertinent neurohumoral mechanisms become so deranged that clinical hyperkinesia appears. To the writer's knowledge, no general theory of hyperkinesis thus far has been proposed. If and when it is formulated, a sound general theory may be expected to suggest new or accommodate current special theories by which the familiar clinical disorders may be better understood.

It may be contended that, considering the current dearth of knowledge as to how voluntary and involuntary postural and phasic movements are normally produced, it is at present premature to theorize about the pathogenesis of movements. Against this, it may be urged that in the history of the biologic sciences enhancement of understanding of normal processes has been accomplished most conspicuously by studying the abnormal processes encountered in the accidents of disease and the designs of experiment.

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* Up to the present time, histologic confirmation of the precise sites, spatial distributions, and remote neural changes of lesions considered to have proved effective in relieving hyperkinesia and/or hypertonus has been meager and, wherever described, equivocated by its incompleteness. It is highly improbable that any surgical lesion thus far produced has destroyed all, but no more and no less, of the intended neural target. Hence, present discourses must be limited to remarks about presumptive lesions. This circumstance almost certainly will be emended within the next year or two.

The endeavor to fashion a sound general theory from which special theories may emerge is but one strategy. The antithetic strategy aims to develop sound special theories from which a general theory may be inferred. Happily, we are not forced to an either-orish choice; there is ample room for workers engaged in analytic and synthetic types of tasks.

The adoption of either strategy requires the adoption of at least three tactics: (1) critical scrutiny of the prevailing neurologic theories, with a view to clearing the field of those (or parts thereof) which appear to constitute impediments to progress and retaining those which appear substantial; (2) itemization of all factual phenomena and substantial postulates that demand incorporation in a sound theory; and (3) demonstration of a construct-by-analogy such as will provide a satisfying economical framework of neuro-physico-chemical relationships within which each fact and postulate will find an appropriate, noncontradictory place; serve dependably as an instrument of prediction for diagnostic, prognostic, and therapeutic purposes; and indicate the directions that future investigators might advantageously explore.

To blueprint the details of a sound general theory does not at the moment appear realizable. Nevertheless, some of its essential components and certain portions of its over-all structure appear sufficiently clear to permit envisioning, even if but dimly, its shape. In view of this, the writer ventures to exercise the tactics previously cited as far as current information permits.

CRITICAL EXAMINATION OF PREVAILING THEORIES. In retrospect, the numerous pathogenic accounts proffered during the past century appear to fall into four classes: (1) structure-bound theories, (2) system-bound theories, (3) theories in part structure and/or system-bound and in part relational, and (4) relational theories.

Structure-bound theories. Examples of structure-bound theories are the contentions that disease of the corpus luysi produces ballism[62-64]; of the globus pallidus, alternating tremor[65-67]; of the caudate nucleus, chorea[65,68-70]; of the putamen, athetosis[65,68,70]; of the reticular portion of the thalamus, choreoathetosis and ataxia[71]; and of the reticular portion of the substantia nigra, poverty of movement, rigidity, and defects of automatic associated acts.[71] The list is in no sense complete. Kleist's[71] doctrines, published in 1934, constitute the ultimum ultimorum of such theories.

Cooper[72] has envisioned the abnormal movement and tonic disorders as expressions of "irritative" phenomena, and other authors[65,73-76] have seen them as phenomena of "release" in the classical jacksonian tradition.

All the theories mentioned are characterized by naïve realism, that is, they implicitly assume the notion of a one-to-one correspondence existing between a healthy neural structure on the one hand, and its function on the other; and, as a logical corollary, between damage to that structure and derangement of the function expressed as a particular clinical manifestation. For this reason, the writer has chosen to designate them as structure-bound.

It is, of course, true that one-to-one correspondences are empirically demonstrable in neurology: Cutting across an optic nerve produces ipsilateral blindness; extirpation of an occipital pole, contralateral hemianopsia; and interruption of the lateral spinothalamic tract, contralateral hemianalgesia and thermanesthesia in the dermatomes below the level of section. The question pertinent to the present inquiry is not whether one-to-one pathogenetic correspondences do obtain, but whether they constitute the one and only pattern by which a neural derangement may be expressed.

A serious deterrent to accepting any naïvely realistic theory as a cogent account for the hyperkinetic and myotonic disorders arises from empiric considerations alone. As abundantly revealed in the literature, damage to a given neural structure is asserted by some authors to be responsible for a particular clinical sign; by some, for a different sign; by others, for several different signs; and by still others, as incompetent to explain any of the signs so claimed. To take a single example, that of damage to the globus pallidus, some[65–67,77–79] hold that this results in alternating tremors; some[71,80,81] that it results in athetosis and dystonia; others[66,71,73,77–79,82] that it results in rigidity; and still others[65,66,71,77–79] that it results in akinesia.

Conversely, a given sign is asserted by some authors to be regularly imputable to damage to a particular structure; by others, to a different structure; and by yet others, to a combination of structures. For example, alternating tremor has been imputed to damage of the globus pallidus,[65–67,77,78] the caudate nucleus,[71] the putamen,[71,79] the substantia nigra,[66,71,77,78] and combinations of globus pallidus and substantia nigra.[80]

These contradictory assertions necessarily raise doubts as to the veracity of all such and, in addition, raise an embarrassing question as to whether some or all of the described lesions can be regarded properly as causally related in any way to the clinical manifestations. Until other and more convincing data are adduced, the logical alternative possibility must be entertained, that all such lesions are merely epiphenomenal, neither necessary to nor sufficient per se for a cogent account.

Further difficulties, this time of a logical nature, confront the structure-bound doctrines. For, to establish on logical grounds that damage to a given structure, A, is both a necessary and sufficient explanation of a clinical sign, P, the following conditions have to be met:[83]

1. In every case in which A is shown to be damaged at autopsy, or damaged beyond some arbitrarily designated degree, P and not Q, R, S, or T must have been present during life.

2. Conversely, in every case in which A is shown to be undamaged at autopsy, or damaged less than some arbitrarily designated degree, P must have been absent during life.

3. In every case in which P is known to have occurred during life, it must be shown at autopsy that A and not B, C, D, or E is damaged, or damaged beyond some arbitrarily designated degree, and

4. Conversely, in every case in which clinical manifestation P is known to have been absent during life, it must be shown at autopsy that A rather than B, C, D, or E is undamaged, or damaged less than some arbitrarily designated degree.

In brief, the construction of a sound theory demands as rigorous consideration of negative as of positive cases. Inasmuch as it is possible to exhibit a negative histologic specimen which contradicts every positive claim regarding damage to structures A, B, C, and so forth, variously asserted to be responsible for a particular clinical sign[84]; and inasmuch as a negative clinical case can be cited for every positive claim that P, Q, R, and so forth, are imputable to a particular local damage of the brain,[84] one is logically and empirically justified in dismissing the structure-bound theories as inept.

The pathologic evidence so far accumulated reveals that a wide distribution of cerebral lesions, occurring singly or combined, has been encountered in the hyperkinesias. Lesions have been found in various parts of the neocortex, caudate nucleus, putamen, globus pallidus, amygdala, zona incerta, Forel's fields, dorsal thalamus, hypothalamus, nucleus ruber, substantia nigra, corpus luysi, mammillary bodies, midbrain tegmentum, pons, medullary tegmentum, and inferior olives.[8] In short, as each doctrine thus far advanced has its contradictions, it may be inferred that the pathologic changes of the hyperkinesias are, in fact, currently unknown and that pathogenetic accounts cast in structure-bound terms appear to proffer little.

System-bound theories. Examples of system-bound doctrines are that disease of the extrapyramidal system produces tremors, rigidity, and flexor-dominated postures[67]; of the pyramidal system, paresis and spasticity[59]; of the cerebello-mesencephalo-thalamo-cortical system, choreoathetosis[76,85]; of the neostriatal system, a release of the paleostriatal system, such as to produce tremors and choreoathetosis[73,79,82]; and of the paleostriatal system, a release of the neostriatal system or other mechanisms, such as to produce tremors and hypertonic postural abnormalities.[77–79]

The system-bound theories are not limited, as are the structure-bound, to the envisionment of any one locus of lesion as being responsible for and/or necessary to the emergence of a particular clinical manifestation. However, they do envision that the lesion(s) be located somewhere within a particular system.

A critical inquiry into these doctrines reveals that they, like the structure-bound theories, are posited on the notion of a one-to-one correspondence. For this reason they lie open to many of the empiric and logical objections leveled at the structure-bound theories. They are further vulnerable in that they presuppose that the anatomic, physiologic, and pathologic components of the invoked "systems" are operationally delineable and universally recognized. Neither of these presuppositions is warrantable.[86]

The survival of the system-bound theories in the face of the rather formidable antithetic empiric data depends wholly on the uncertainty of the delineation of the systems. In a very obvious sense, then, the system-bound theories constitute logical tautologies of a type elsewhere characterized as self-sealing doctrines. As such, they proffer little beyond the structure-bound theories.

Theories in part structure and/or system-bound and in part relational. Examples of combinations of theories are the pathogenetic theories of tremor proposed by Rioch[74] and Bucy and Case,[4] the theories of choreoathetosis by Spiegel and Wycis[87] and Bucy,[56] that of ballism by Meyers,[88] that of the extrapyramidal disorders by Hassler,[89] and that of dystonic movements by Denny-Brown.[65] These resemble the two classes of theories just discussed in that they invoke lesions of particular structures and/or systems; however, they take leave of the untenable notion of one-to-one correspondences as applied to the hyperkinesias and introduce a perceptibly more sophisticated concept, namely, that disturbed relationships between or among structures and/or systems constitute the essential pathogenetic agencies of the hyperkinesias.

For purposes of illustration, a typical example of the class, namely, the oft-cited theory of alternating tremor by Bucy, will be considered. This theory envisages a tremorogenic propensity inherent in the healthy pyramidal cortex, Area 4, potentially mediated via the pyramidal system to the lower motor neurons. It holds that, in normal circumstances, a reverberating extrapyramidal circuit, consisting of Area 4-s, the "suppressor strip," caudate nucleus, globus pallidus, ansa lenticularis, ventrolateral nucleus of the thalamus, thalamocortical radiations, and precentral cortex, inhibits the appearance of tremors. When, in virtue of disease, any part of the circuit, for example, the globus pallidus, is "gone," the pyramidal component is immediately released from inhibitory control by the extrapyramidal circuit, and tremors develop. Bucy held that the integrity of the pyramidal tract is a sine qua non of the appearance of tremor and, as a corollary, that the surgical relief of tremor requires damage to the corticospinal (pyramidal) tract in some part of its course. An estimate as to how much pyramidal damage must be produced to provide surgical relief has not been ventured by Bucy, but it is apparent from his recent defenses that he considers damage of such small magnitude as to be unattended by the Babinski, Chaddock, and other "upper motor neuron signs" to be sufficient.[90] The untenability of this position will be brought out later.

The outstanding weaknesses of Bucy's theory consist in its axioms regarding the dichotomy of pyramidal and extrapyramidal systems and the existence of cortical suppressor strips. Both notions have been undermined seriously by recent studies.[91,92] Furthermore, evidence indicating that surgical damage to the pallido-ansal-dorsal thalamic complex abolishes tremor rather than enhances it, as assumed by Bucy, is now abundant. Finally, Bucy's contention that when surgical lesions prove therapeutically effective they do so because and to the extent that the pyramidal tract is inadvertently damaged, appears to be vitiated by the recent demonstration of Spiegel *et al.*[93] that lesions in the midbrain tegmentum of the monkey, spatially remote from the pyramidal tract, alleviate alternating tremors.

The limitations of space preclude attempts at a critical analysis of other theories of this class. We should note, however, that considerable merit inheres in their introduction of the notion of disturbed relations among structures and systems. As will be brought out later, this notion accommodates the circumstance that cerebral lesions associated with the hyperkinetic disorders appear to be inconstant from case to case and, in a particular case, often multiple and seemingly irreconcilable with one another.

Relational theories. Theories which deemphasize the notion that damage to particular structures and systems is prerequisite to the development of particular clinical disorders and which lay major emphasis on the notion of disturbances of relationships among structures and systems may be designated as relational. Those advanced up to now constitute special rather than general accounts of hyperkinesia and are exemplified by Jung's[94] phylogenetic release theory, the theory invoking synchronous firing of motoneurons as proposed by Magoun,[95] and Austin and Sata's[96] theory of deranged ratios of facilitation-inhibition, the reticular tremorogenic-center theories of Ward and Jenkner[97] and Spiegel and Wycis,[98] Denny-Brown's[65] theory of physiologic dissolution, and the amplification of the Jenkner-Ward and Hassler theories proposed by Stern and Ward.[99]

Time permits citation of only one of these, and since Ward's[100] 1958 revision of a theory proposed in 1953 by Jenkner and Ward typifies the class, it will be synopsized here for purposes of evaluation. Ward contended that the bulbar reticular formation constitutes a primitive motor center which harbors, among other things, spontaneously oscillating neural circuits. The latter regularly tend to produce alternating movements. In normal circumstances this tremorogenic region is held clinically silent by dynamically suppressive neural impulses transmitted to the bulbar cells via fibers that originate in cephalically situated structures. Disease processes which diminish the output of the cephalic structures are thought to produce partial denervation of the tremorogenic circuits. In consequence, a denervation sensitivity is thought to develop. Whether the latter is due to an excess of acetylcholine, release of inhibition, or some other factor(s) appears to be of less importance than that sensitivity does somehow develop and that it is responsible for an unwonted play of impulses via reticulospinal pathways on the motor apparatus of the spinal cord. Ward holds that any circumstance in which the spinal cord receives subliminal "tonic" bombardment from the pyramidal tract enhances the ability of oscillating bulbar circuits to trigger the FCPs and thus produce tremor. In the circumstance of maximal excitation of the pyramidal tract, for example, during voluntary activity, the internuncial pools of the spinal cord are captured by the pyramidal impulses and, for the time being, smooth phasic activity prevails. When, on the other hand, the motor cortex and/or pyramidal tract are paralyzed, the threshold of excitability of the internuncial pools of the spinal cord rises. The bulbar tremorogenic impulses are considered insufficient in themselves to activate the pool. Hence, without the summation made possible by the normal concomitant play of pyramidal impulses, they are incapable of firing the FCPs, and tremor is absent.

The origin and function of the cephalic structures envisioned in Ward's theory are acknowledged to be obscurely known. The forebrain, basal ganglia, and cerebellum are presumed to constitute such agents, the chief mediator of whose impulses is presumed to be the ansa lenticularis. But whatever the structural details may be, such impulses appear to funnel through the medial and midbrain tegmental reticular formation at the level of the red nucleus.[100] Unless unduly large, electrolytic lesions made at this site in the cat and monkey result in alternating tremors in 50 to 60 per cent of the attempts.[101–104]

To the extent that Ward's theory resorts to systemic agencies, for example, the pyramidal system, it lies open to the attacks leveled at the system-bound theories. The theory also poses a tautology, in that it envisions an inherent, spontaneously-acting, bulbar tremorogenic region by means of which the phenomenon of tremor it purports to explain is hypostasized and postponed by one step. Moreover, since the implied predictions of the theory regarding the locus of the tremorogenic circuits cannot be put to experimental test, for the reason that destruction of the bulbar reticular formation is incompatible with survival, the theory must remain, at least for the present, a self-sealing doctrine. More serious than any of the foregoing, however, is the criticism that if the theory were accepted in principle as a sufficient account for tremors, it would lead to more rather than fewer difficulties, for, in the endeavor to use it as a model for the fashioning of a more general hyperkinetic theory, the student of pathogenesis would find himself under the awkward necessity of postulating analogously inherent choreogenic, ballistogenic, athetogenic, dystonogenic, and myoclonogenic centers in the brain. Last, a serious empiric difficulty is posed by the circumstance that small ultrasonic lesions, presumably placed in Forel's tegmental field H just caudal to the zona incerta, are highly effective in abolishing parkinsonian tremors in the human being.[105] This site is comparable to that which, when coagulated in experimental animals, is asserted to be followed by tremors.[101–104] This empiric criticism, derived from human data, cannot, of course, be leveled seriously at Ward's theory until the human geometric target can be shown by histologic study to correspond closely to the anatomic target.

But beyond the objections just mentioned, much merit appears to inhere in this and all other relational theories, for, in contrast to structure and system-bound theories, they comfortably accommodate positive and negative cases exemplified in the diverse sites, types, and degrees of lesions demonstrable by necropsy studies. This advantage invites full exploitation.

Building blocks of a general theory of hyperkinesia

A necessary preliminary to fashioning a sound general theory in this area is to itemize as completely as possible the numerous empiric observations that unequivocally demand accommodation and all inferences and postulates that currently appear to be warranted. To this task we now turn.

Empiric observations regarding hyperkinetic disorders

1. The several clinical varieties of hyperkinesia can and do exist independently of each other and of the myotonic disorders and akinesia.
2. They are absent during natural and induced sleep, general anesthesia, and coma, but not necessarily during merely lethargic, stuporous and confusional states.
3. They are present during the wakeful state but, in a given member, never constantly so. Characteristically, they wax and wane and, for varying and irregular periods of time, come to an apparently spontaneous halt. Thus, they appear clinically reversible.
4. Variations in frequency, amplitude, duration, and pattern occur from patient to patient, from time to time within a given patient, and in respect of any bodily member.
5. Hyperkinesia may afflict one or more bodily members on right and/or left sides of the body to the exclusion of others.
6. When two or more bodily members are afflicted in a given patient, they may, but do not necessarily (and, in fact, uncommonly) exhibit action-in-concert. Still less often do they exhibit pari passu phasing, frequency, amplitude, duration, and patterning.
7. The hyperkinesias are regularly augmented by emotion-evoking circumstances and often, but not necessarily, by fatigue, attention, and efforts on the part of the sufferer to control them.
8. Whatever the prevailing state of hyperkinesia may be at a given time, that is, relatively quiescent or manifest, active and passively imposed postural changes most commonly evoke a change therein.
9. During periods when overt abnormal movements are in process, voluntary movements always can be initiated. Their adaptiveness may or may not be compromised. If they cannot be initiated, the deficit must be ascribed to concomitant akinesia and/or rigidity.
10. The hyperkinesias are often, but not necessarily, progressive over the course of months or years in intensity, extensity, duration, and degree of attendant disability.
11. The apparent etiologic and pathologic factors may differ from patient to patient. Hence, similar etiologic and pathologic processes may be attended by different clinical manifestations in different patients; conversely, similar clinical manifestations may attend apparently different etiologic and pathologic processes in different patients.
12. In hyperkinesia, multiple macro- and/or microscopic pathologic cerebral changes are the rule. It is rare to encounter in human beings the con-

dition of unit-factor lesions, such as can be produced at selected sites in experimental animals.

13. Hemiplegia of the upper motoneuron type regularly abolishes alternating tremor and much reduces rigidity. However, as can be documented amply, hemiparesis of such degree as to be attended by Babinski and Babinski-confirmatory signs, hyperactive tendon reflexes, and clonus does not necessarily preclude the exhibition of alternating parkinsonian tremors. The failure to specify the degree of corticofugal damage essential to abolishing tremors appears to be responsible for much fruitless disputation in this area.
14. The solanaceous alkaloids and their synthetic counterparts relieve in some measure certain but not all patterned tremors. They are uniformly ineffective against the nonpatterned hyperkinesias.
15. Surgical interruption of the deep-lying structures related to the origin, course, and/or destination of the ansa lenticularis alleviates or abolishes contralateral hyperkinesia. To a much less but perceptible degree, it often appears to alleviate ipsilateral hyperkinesia.
16. Incidental to such surgery, contralateral rigidity is often alleviated to greater or lesser degrees depending on the site and size of the lesion(s). Ipsilateral rigidity also may be slightly reduced thereby.
17. Akinesia and spasticity remain essentially unaltered by such surgery, as do also dysarthria, monotony, low volume of speech, and defects in equilibrium and ambulation.
18. As to the various surgical procedures thus far employed, some accomplish amelioration of tremors and/or rigidity with lesions appreciably smaller in size than those required by others. Some are manifestly more effective against tremors than rigidity, and vice versa. Thus, among the writer's 30 most recent ultrasonic cases, the abolition of tremor and rigidity required larger (by a factor of 3 to 8) lesions directed at the pallido-pallidofugal site than at either Forel's fields H_1 and H_2 or Forel's tegmental field H. Small lesions, (1.5 by 3 by 3 mm.,) directed at Forel's tegmental field H just posterior to the zona incerta appear to alleviate tremor promptly and with far greater consistency than when directed elsewhere. On the other hand, comparably small lesions intended for the base of the ventrolateral thalamic nucleus appear more effective against rigidity than do lesions aimed elsewhere.
19. Alleviation and abolition of hyperkinesia by surgery of the deep-lying structures can be but temporary or long-enduring. The longest follow-up period of a successful case, that of a patient reported on in 1941,[8] is now nineteen years. Many similar cases followed for eight, ten, and twelve years are now on record at our own and other neurosurgical clinics.[72]

Inferences and postulates

1. Neural mechanisms are but special cases of physicochemical mechanisms.
2. Neurologic signs and symptoms appear as they do in virtue of derangement of one or more neuro-physico-chemical mechanisms.
3. The neural components of such mechanisms are usually more extensive in spatial disposition than many students of neurology are accustomed to envision.
4. Derangements of these neuro-physicochemical mechanisms result in similar signs and symptoms, regardless of the etiopathologic processes which produce them.
5. Patients are clinically similar or dissimilar to one another to the extent that similar or dissimilar mechanisms are deranged.
6. Responsible lesions need not be limited to macro- and microscopically demonstrable changes; they may be so subtle as to require electron microscopy and/or other biophysical and biochemical procedures for their demonstration.
7. The mere disclosure by a particular technic of a cerebral lesion at a given site, even if oft-encountered, constitutes no certain index that such is necessarily related to a particular clinical sign or symptom. To validate any asserted causal relationship, the postulates cited in our critical analysis of structure-bound theories, as mentioned previously, require to be fully honored.
8. The absence of demonstrable cerebral lesions does not per se warrant the conclusion that a given disorder is functional, that is, psychogenic. The disregard of this rubric underlies the ineptness of many pathogenetic accounts of the past and present, for example, that athetosis and paralysis agitans are psychoneuroses.
9. The time at which a cerebral lesion is established in the course of the

growth and maturation of the individual is an important determinant of the clinical picture which results from the derangement of a particular neuro-physico-chemical mechanism.

10. The quantum of damage done to a neuro-physico-chemical mechanism or complex of such mechanisms, expressed in terms of intensity, extensity, and duration, is an important determinant of whether or not clinically discernible manifestations develop, and, in the event of their development, of their character.
11. The assumption that a given nucleus of the central nervous system subserves one function and that alone is unwarranted. This naïveté, often exercised in regard to neurologic matters, is not exercised in respect of, for example, the liver, despite the fact that, from part to part, the latter appears structurally more homogenous than any brain nucleus we might select for examination.
12. The central derangements that subtend the several clinical varieties of hyperkinesia differ from one another as well as from those of hypotonus, hypertonus (rigidity and spasticity), and akinesia.
13. Spatially, the deranged central mechanisms subtending hyperkinesia are closer, in at least some parts of their courses, to those subtending myotonic aberrations than to those subtending akinesia.
14. Somatotopic representation abides in the neuro-physico-chemical mechanisms deranged in the hyperkinesias.
15. Since the hyperkinesias characteristically ebb and flow in a given bodily member, the neuro-physico-chemical mechanisms subtending them are dynamic, relatively unstabile, and subject to modification by a wide variety of evanescent organismic influences. Their spontaneous clinical reversibility warrants confidence that enduring therapeutic reversibility is achievable by medical and/or surgical endeavor. In this connection, our investigative tasks consist in identifying and contriving to simulate the critical neuro-physico-chemical factors of the organism that foster spontaneous, transient, clinical abeyance of hyperkinesia.
16. Neurosurgery currently directed against the hyperkinetic disorders is nonspecific, that is, it does not attempt to remove the seat of disease or reconstitute damaged tissues but to find the optimal site or sites at which one or more neural pathways, as parts of reverberating neuro-physico-chemical circuits, whose integrity is seemingly essential to the perpetuation of hyperkinesia, may be relatively safely interrupted.
17. The origin, course, and at least some destinations of the ansa lenticularis appear to constitute one such pathway. There may be and probably are others.

Toward a general theory of hyperkinesia

In broad terms, any theory that purports to encompass the empiric observations, inferences, and postulates itemized in the foregoing, must invoke the notion of a convergence of a multiplicity of factors—central and peripheral, physicochemical, and neural—on the internuncial pools of the FCPs. It also must conceive of this convergence as exhibiting a dynamically unstabile character such that, if hyperkinesia is to appear from time to time, certain factors must be present, and others must be absent. Similarly, if no hyperkinesia is to appear, certain factors must be present and others absent.

These conditions correspond to those of a transitive relationship familiar to students of modern symbolic logic as the conjunction of an assertion with a negation. The equation for this is as follows:

$$C \supset A.\bar{B}$$

Where C symbolizes "any event occurring at a given time"; $\supset$ means "implies"; A symbolizes "an event occurring prior to"; the dot means "and"; a bar over any symbol means "not"; and B symbolizes some event other than A. Translated, the equation reads, "The appearance of C at a given time implies that A occurred and B did not occur at a prior time."

This shorthand may be altered to serve our present purposes as follows:

$$H \supset \Sigma A.\bar{B}$$

Where H symbolizes hyperkinesia; Σ means "an aggregate of"; and $\bar{B}$ symbolizes events such that, if H is to appear, they must not concur with A.

In this mathematicological expression we possess a matrix in the form of which a sound pathogenetic theory conceivably may be cast. Since the equation is highly abstract, that is, exhibits form devoid of content, it constitutes a propositional function rather than a proposition or theory. Its chief virtue is that it guides us in searching for the kinds of analogies that may be explored profitably in the endeavor to identify the neuro-physico-chemical contents by means of which the propositional function may metamorphose and become a general theory of the pathogenesis of hyperkinesia.

Our next task is that of exploring for promising analogies by means of which the unknown may be related to the already familiar. A certain amount of trial-and-error spadework is necessary at this point.

One such analogy exhibiting a familiar oscillator occurs to us—a coiled spring suspended from the ceiling and hanging free at one end. Here the observer can readily identify prime activating factors, for example, gravity, inertia, momentum, and perhaps an electrical input which makes the spring oscillate in the direction of its long axis; dampening factors, for example, downward-acting weights and/or upward-acting agents; and adventitious sensitizing factors, for example, changing temperatures of the surround, winds, and similar promptings to oscillation in the direction of the long axis of the spring and/or in a pendular or circular manner. This model immediately suggests ways in which certain phenomena germane to hyperkinesia may be categorized and evaluated. However, it falls short of our recognized need for a model with abiding dynamic instability. Such is furnished by a plate spinning gyroscopically in dynamic equilibrium on a pivot and maintaining a smooth, horizontal plane. The term, smooth, must be taken in a relative sense, for as close examination soon reveals, a vertical oscillation, best discernible at the edge of the plate, actually abides. This oscillation we evaluate as trivial, as we do physiologic tremors and ataxias, and accept the finding as normal, without feeling under any compulsion to account for it.

Let us suppose that on yet closer examination a number of agents are found to be attached to the upper surface of the plate. At first encounter, they appear to be distributed at random. However, a little reflection leads us to suspect that the distribution must be such that the components of forces of the various agents related to the upward thrust of the pivot effect a balance. At some later time this suspicion proves justified by empiric testing.

Each of the agents may be as dynamically active in its intrinsic and external aspects as, for example, a reverberating electronic or neuro-physico-chemical circuit. For the sake of simplifying our imaginative exercise, however, let us regard the agents as objects exhibiting differences in size, shape, material, and weight.

Now let one of the agents be removed. An abnormal oscillation of the edge of the plate at once ensues. If the initial condition be restored and another of the agents removed, a similar, but not identical abnormality ensues. Repeated experimentation of this sort reveals that the ablation of certain agents results in negligible perturbations of the plate and that of others, in abnormal states of greater or lesser degree.

We now try a series of experiments with combinations of ablated agents in two's, three's, and so forth. These studies reveal, among other things, that when we effect ablation of two or more of those agents which, when singly ablated, regularly resulted in negligible perturbation of the plate, unequivocally abnormal oscillations ensue.

Four useful inferences, three of them negative and one positive, now may be drawn: (1) The agents are not equipotential; (2) the potential for producing abnormal oscillations is not uniquely imputable to any one agent or combination, regardless of how often postmortem examination reveals involvement of that particular to the exclusion of another or others; (3) while ablation of a certain agent or combination is observed regularly to be followed by an abnormal state, it is not warranted to conclude that the normal function of that particular is inhibitory, specifically, to inhibit development of that state; and (4) when abnormal oscillations appear, they do so in consequence of a disturbance in relationships among the agents which yet remain on the plate. They are obliquely connected with the ablated agent; hence, scrutiny of the latter, however intensive, is unlikely to yield crucial information regarding the mechanism which produces the abnormality.

By analogy, the various agents attached to the plate and the pivot beneath it correspond to the dynamic neuro-physico-chemical agents that play on the FCP, the nil-point of the various components of forces corresponds to the FCP, the edge of the plate corresponds to the muscle effectors, and the relatively steadily maintained horizontal plane corresponds to the normal state of no-hyperkinesia. The removal of an agent is comparable to establishing a lesion, and its examination apart from the original apparatus is analogous to histologic, cytologic, biophysical, and chemical study.

In the endeavor to rectify an abnormal oscillation, three general alternatives or combinations of them lie open to us: (1) to restore the original relationship by fashioning an agent similar to that ablated and secure it to the site previously occupied by the original, (2) to modify the prevailing relationship by such redistribution of the remaining agents as to simulate the healthy state, and (3) to modify the prevailing relationship by removing one or more of the remaining agents such that a better balance, simulating the healthy state, is achieved. By analogy, human neurosurgery works within the frame of reference of the third alternative.

Turning closer attention to the relationships that obtain among the agents acting on the plate, we may imagine any number of disparate objects, say, four, as analogous to different neural and other physicochemical agents. With them a number of relationships, for example, spatial, may be contrived, for example, rectilinear, curvilinear, triangular, quadrilateral, tetrahedronal, and so forth. Assume, then, that the dynamic relationships of quadrilaterality and tetrahedronality correspond to healthy states and that, wherever encountered and however produced, triangularity corresponds to hyperkinesia.

Let one of the four agents entering into the relationship of quadrilaterality be ablated. A relationship of triangularity immediately ensues.

If we are overly naïve, we are in danger of concluding that the property of quadrilaterality normally inheres in this particular agent, perhaps this alone. However, a more sophisticated view, backed by familiarity with relationships, warns us that damage to any other one of the four original agents would prove equally capable of converting a relationship of quadrilaterality to one of triangularity, and so we avoid serious error.

A similar circumstance may be imagined in which some particular one of four agents entering into a relationship of tetrahedronality is ablated. Again, a relationship of triangularity ensues.

These two experiments impress us that a new relationship, for example, triangularity, may appear in consequence of derangement of pre-existing disparate relationships, for example, quadrilaterality and tetrahedronality. These result from the ablation of agents at different loci. Indeed, even with such simple configurations as the two figures here adopted, eight separate loci of agents prove capable of producing triangularity.

A final analogy, this from topical geometry, will suffice to indicate what must be encompassed by a cogent pathogenetic theory of hyperkinesia. The empiric counting of the features of a rectangular solid, for example, a cube, reveals six faces, eight vertices, and twelve edges. These constitute special cases of relational circumstances that prevail among all so-called spheroid solid figures, in contrast, for example, to doughnut-like figures. This relationship is expressed by the equation:

$$F + V = E + 2$$

F equals the number of faces; V, the number of vertices; and E, the number of edges.

Let us now imagine that this broad relationship corresponds to a living, dynamic state of the organism; that the special relationships demonstrable in the rectangular solid correspond to some pertinent neuro-physico-chemical complex within the organism; and that the number of faces, F, in this case six, is a necessary condition of no hyperkinesia.

Consider, now, that when the rectangular solid is singly truncated, that is, one vertex is sliced off, a circumstance analogous to the establishment of a pathologic lesion is accomplished. Since truncation may effect ablations ranging in size from infinitesimally small to very large, we allow that not all such lesions actually result in abnormal clinical manifestations; that to produce the latter, some critical quantum of damage must be exceeded. In consideration of this, we may assume arbitrarily that lesions less extensive than those in which truncation reaches as far as the diagonals which connect the three vertices closest to a vertex selected for truncation are incapable of producing an abnormal clinical manifestation.

Regardless of which of the eight vertices we select for ablation, single truncation results in but one type of figure, each particular instance of which exhibits 7 F's, 7 V's, and 12 E's. The broad relationship, $F + V = E + 2$, is preserved, but relational changes on a less grand scale are now discernible, for example, an increase of F from 6 to 7 and a decrease in V from 8 to 7.

Double truncation produces two types of figures, manifestly different from both the parental and grandparental antecedents. One type results from the ablation of two adjacent vertices; the other, from ablation of two diagonally opposite vertices. Here again, our broad relationship is preserved. But we now observe further relational changes in that all instances of the former type of double truncation exhibit 5 F's, whereas those of the latter type exhibit 8 F's. If we now suppose that hyperkinesia appears whenever $F = {<}6$, and that no hyperkinesia but some other abnormality, for example, rigidity, appears whenever $F = {>}6$, it is clear that the abnormal clinical picture actually produced depends not only on accomplishing two lesions, but also on which of two possible typical spatial relationships results from double truncation.

It remains to explain how it happens that, when hyperkinesia prevails, that is, $F = {<}6$, the advent of yet another lesion (in consequence of disease or surgical intent) in some instances succeeds and in others fails to ameliorate abnormal movements. For this purpose, we turn to the analogy of triple truncation. On the ablation of a third vertex, four types of figures emerge. The type differences depend, as in double truncation, on the particular spatial relationships of the vertices we select for ablation. Three of the types exhibit 5 F's, a condition which perpetuates hyperkinesia; one exhibits 6 F's, the condition of no hyperkinesia.

By exploring the possibilities of certain analogies in this way, we begin to envision how factual, inferential, and postulational data might be accommodated by a general theory of the pathogenesis of hyperkinesia. Other models, of course, may be explored similarly.

It remains for us and future investigators to fill in as best we can the contents of the propositional function previously referred to. One palpable component appears to be the pallido-pallidofugal complex, the integrity of which seems to be a precondition of hyperkinesia. Another component, that relative to somatotopic arrangements, is almost within our grasp. The concept of a facilitation-inhibition ratio, recently proposed by Austin and Sata[96] and that of synchronous firing of the FCP, proposed by Magoun,[95] lack empiric verification as of the present, but may well receive it in the near future.

Information in this area has been increasing at an accelerating pace during the past decade and may reasonably be expected to continue so to do. There is good reason to anticipate that, holding to a multiple convergence hypothesis in which disturbed dynamic relationships, rather than damage to particular agents, are envisioned as the sine qua non of hyperkinesia, we shall eventually expose to view the innermost pathogenetic secrets of these fascinating disorders and derive therefrom ever more effective means of control.

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Discussion

Edgar M. Housepian, M.D., *New York City.* Dr. Meyers' proposed classification of the hyperkinetic disorders into patterned and nonpatterned hypotonic and hypertonic types is an extremely important one, for it groups three conditions, some of which have superficial similarities, into a meaningful framework based on observable clinicophysiologic differences. It is precisely these differences which should provide a first clue to understanding pathophysiology and thereby direct the advances in therapy. Indeed, we already see a specific differentiation in the symptomatic surgical treatment of parkinsonian and ataxic tremor on the one hand, and the nonpatterned dyskinesias on the other. This is entirely related to such differences in pathophysiologic mechanisms.

Dr. Meyers also has presented a scholarly summary of past propositions relating to pathogenesis, pathophysiology, and empiric attempts at drug and surgical therapy of the various motor disorders. By placing each in its proper perspective he clearly devastates one after another for a common reason, simply, the lack of supporting data.

I would like to elaborate on two points which Dr. Meyers has discussed and to raise one general argument.

The constellation of autonomic, mental, and motor symptoms usually included in the broad definition of the term "akinesia" reflects a diffuse involvement of several central organizations or systems. I would like to stress the usefulness of limiting the definition of akinesia to mean "difficulty in initiation and maintenance of volitional activity," and to separate masked facies, oily skin, and other vegetative symptoms from this entity.

Dr. Meyers has alluded to the ansa lenticularis as a common pathway for a variety of subcortical organizations and implicates lesions of this structure in the relief of tremor and rigidity. Optimal lesions of the ansa lenticularis are effective in abolishing rigidity, and certain nonpatterned hyperkinesias, particularly in dystonia, but do little to influence alternating tremor. It has been shown by a number of clinical investigators including Hassler and Riechert,[23] Spiegel and Wycis,[13] Cooper,[38] and, I had thought, Dr. Meyers also, that tremor can be lastingly eliminated only by implicating the nucleus ventralis oralis posterior (posterior part of nucleus ventralis lateralis), the area which receives the dentate projection via the brachium conjunctivum and relays this activity to the premotor cortex through the capsule.

Although one cannot deny that much has been learned about normal physiology by the study of deranged mechanisms, it does not seem realistic to hope that we can make significant strides in understanding these pathophysiologic processes by patiently waiting to study postmortem material from surgically treated cases. Dr. Meyers already has intimated that there are basic defects inherent in this approach. First, it is impossible to produce functionally complete yet anatomically exclusive lesions, and it is not possible by the study of histopathologic material to assess this. Second, the errors inherent in human stereotaxic methods related to variations in the location and size of subcortical structures, particularly in disease states, have not heretofore been compensated successfully. Only following the development of methods of localization by identification of subcortical structures either by an analysis of evoked electrocortical potentials, by characterizing the clinical manifestations resulting from electrical stimulation, or by other physiologic means will there be a significant correction of this problem. It has been shown clearly in our laboratory that defunctionalizing lesions can be localized and evaluated as to completeness only by such means. Therefore, we have been quite concerned with the development of physiologic methods for the identification of subcortical regions.

A variety of evoked cortical responses differing in latency, configuration, and distribution have been used to identify intralaminar and specific thalamic systems in laboratory animals. With similar technics we have been able to supplement our stereotaxic methods to achieve greater accuracy of lesion placement first in the laboratory and now in man. However, the application of methods of electrophysiologic testing for the completeness of defunctionalization following the creation of such lesions has shown a greater degree of error than we could hope to find by histologic examination alone.

These considerations make it doubtful that we can make great headway in understanding the anatomy, physiology, and pathogenesis of the dyskinesias by close adherence to traditional methods of investigation.

Nevertheless, as Dr. Meyers has stated, by stressing the developmental nature of this type of surgery, we are obtaining useful physiologic data on central motor organization, and by the application of technics of histochemistry and electron microscopy, we may hope to make some headway in understanding pathogenesis while offering this form of symptomatic treatment as a clinical service.

PANEL DISCUSSION

PROCEEDINGS

Special Committee on Infant Mortality
Medical Society of the County of New York

Perinatal Mortality in Elective Cesarean Section

HAROLD ABRAMSON, M.D., Editor
Chairman
CARL GOLDMARK, Jr., M.D., New York City
Moderator
EDWIN M. GOLD, M.D., Director, Department of Obstetrics and Gynecology, Jewish Hospital of Brooklyn
Panelists
FRANK MOYA, M.D., Assistant Professor of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York City
MARVIN CORNBLATH, M.D.,* Assistant Chairman, Michael Reese Hospital and Medical Center, Chicago, Illinois
CARL ERHARDT, Director, Bureau of Records and Statistics, City of New York Department of Health

Harold Abramson, M.D.: *Since earliest times, men of medicine have pondered the many problems of cesarean section: its use and misuse; the definition of the terms elective, repeat, and indicated; the optimal time for operative intervention; the technics involved; the safest type of anesthesia; and the differences on various hospital services in perinatal mortality among babies delivered by cesarean section as compared with those delivered vaginally. These problems are discussed in detail in this provocative panel discussion.*

Introduction

Edwin M. Gold, M.D.: The subject tonight reflects the tremendous interest in the perinatal loss which we are still experiencing. Not only has there been an increase in the incidence of cesarean sections in recent years, but also concurrently there has been no dramatic fall in perinatal loss; in fact perinatal loss in general, at least in New York City, has been on the increase during the past three years. This is indeed of concern to all of us.

As a result of this concern and because our interest in perinatal loss has always been a multidisciplined affair, the Program Committee of the Special Committee on Infant Mortality has developed a panel which takes into consideration varied specialties: namely, an obstetrician (myself), an obstetric anesthesiologist, a pediatrician, and a biostatistician.

There are a number of urgent questions which I hope will be answered this evening by the panelists. (1) Do we or do we not dispel the clinical opinion that babies who are delivered vaginally do better than those who are delivered by cesarean section, particularly when they are premature? (2) There is the question of the relationship of prematurity to repeat elective cesarean section. What, if anything, can be done about this? (3) There is the question: Is there or is there not a basic perinatal mortality rate

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Presented at the open meeting of December 7, 1960, of the Special Committee on Infant Mortality of the Medical Society of the County of New York, Carl Goldmark, Jr., M.D., Chairman, and Harold Abramson, M.D., Secretary, Coliseum Building, 10 Columbus Circle, New York 19, New York.

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that we should expect from elective cesarean section?

Before I call on the panelists, I would like to call for a definition. What do we mean by elective cesarean section? Is it the cesarean section that is done electively, whether primary or otherwise, in the absence of stress factors, that is, with no relation to a pathologic condition of the placenta, to placental complications, to fetal distress, or to abnormalities of labor? Or, do we confine the term only to the repeat elective cesarean section? This is something that I hope each panelist will make clear at the outset of his discussion.

With this introduction, I should like to call on Frank Moya, M.D.

Relationship of anesthesia to mortality in elective cesarean section

Frank Moya, M.D.: Eastman has stated over and over again that an analysis of infant deaths associated with cesarean section will usually reveal that they were not attributable to the method of delivery, but to the presence of either prematurity or the obstetric complications for which the operation was done in the first place. He states in addition that "the anesthesia used for cesarean section, other than local infiltration, is always a potential threat to the infant and doubtless accounts for a certain fraction of these deaths."[1]

What I would like to do is to review briefly the results of recent studies that have appeared in the literature and also to cite some of our own work dealing with the association of anesthesia and perinatal mortality and morbidity. We want to see whether or not anesthesia does account for some of these deaths, and if it does, in what manner.

Hingson and Hellman[2] studied the total fetal loss in 3,886 cesarean sections. These were analyzed according to the method of anesthesia and whether the birth was full-term or premature. There were all types of cesarean section, the majority being elective. The investigators concluded that when regional anesthesia was compared with a combination of local and general anesthesia, usually thiopental sodium (Pentothal sodium), there was no difference in mortality in the full-term group of babies according to the type of anesthesia. The same held true when types of anesthesia were compared in the group of premature babies. However, in terms of what we are looking for tonight, that is, mortality and morbidity in well-defined elective cesarean section, these figures do not enable us to reach any decision.

Several years ago Apgar[3] reviewed our experience at Sloane Hospital for Women. She studied 233 elective cesarean sections. The women met the criteria that Dr. Gold outlined. None of these women were in labor when they came to section. Their babies were therefore not subject to the stress of labor. The babies were divided into those whose mothers received either spinal or cyclopropane anesthesia. Only the neonatal deaths were studied. There was one death in the spinal series and one in the cyclopropane anesthesia series.

Of course, the few cases prevent a valid statistical analysis of the data. As a matter of fact, this is the objection that we can raise to any statistical series in which we try to see the effects of anesthesia on the perinatal mortality. We deal with so very few deaths. If we try to draw conclusions from these data, they would be very misleading.

Instead of trying to compare spinal versus cyclopropane anesthesias, the ideal comparison would be with a series of mothers who have undergone cesarean section in which no anesthesia was used. This group is hard to obtain in our present society. Rather than use a crude measure of mortality in studying the influence of anesthesia, Apgar[4] analyzed a series of babies in terms of their condition at birth, using two clinical standards; first, the Apgar score, with which I am sure you are familiar, and second, the time sustained respiration was achieved, that is, the number of seconds it takes the infant after birth to establish well-sustained respiration. She found that there is an inverse relationship between the incidence of neonatal deaths and the Apgar score in babies weighing 500 Gm. or more (Fig. 1). The lower the score, the higher the incidence of neonatal death. Note particularly that there is a fairly marked drop between the 6- and 7-score category. We are going to make

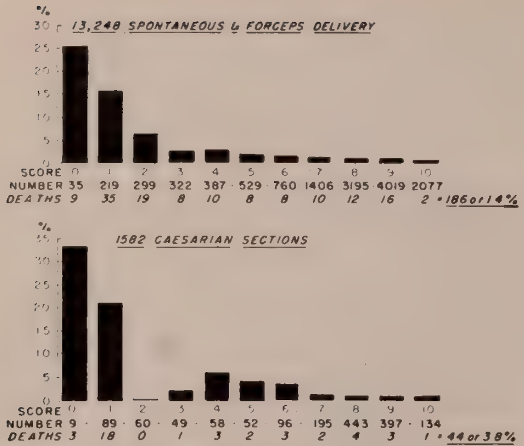

FIGURE 1. Relationship between frequency of neonatal deaths and Apgar score in babies weighing 500 Gm. and over, according to type of delivery.[3]

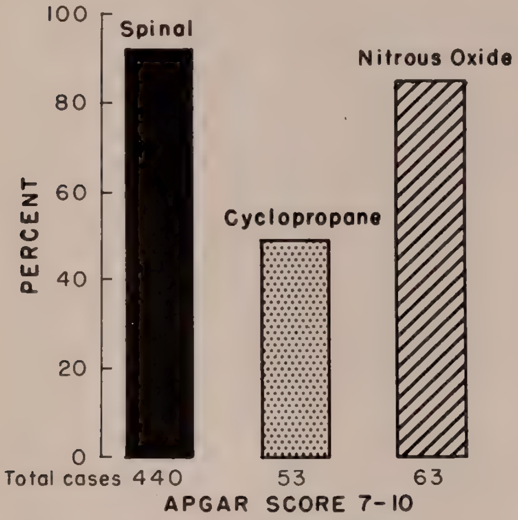

FIGURE 2. Analysis of Apgar scores in babies who were delivered by elective cesarean section, according to type of anesthesia.

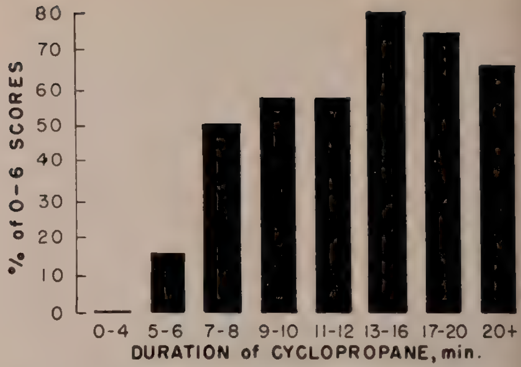

FIGURE 3. Analysis of Apgar scores in babies who were delivered by elective cesarean section and whose mothers received cyclopropane anesthesia, according to duration of anesthesia.

use of the group of babies scoring 7 to 10 to compare the various types of anesthesia.

Apgar analysis. Figure 2 illustrates an analysis of babies with Apgar scores of 7, 8, 9, or 10, according to whether they were born by spinal, cyclopropane, or nitrous oxide anesthesia. In these elective cesarean sections, approximately 94 per cent of the babies born with the aid of spinal anesthesia fell into the high Apgar score group. On the other hand, of the cyclopropane babies, only 50 per cent fell into this group; or, looking at it from the poor side of things, 50 per cent of these cyclopropane babies were either moderately or severely depressed, with scores below 7 one minute after birth. The difference is statistically significant.

Now, we should not draw the immediate conclusion that these data indicate that all general anesthesia is potentially dangerous. We have left out two very important variables, namely, the depth of anesthesia and the duration of administration of anesthesia prior to the birth of the baby.

Depth. With cyclopropane it would be difficult or impossible, especially in a retrospective study, to have any idea at all as to how deep a particular patient was at the time the baby was born. However, we can apply the measure of the duration of anesthesia prior to the birth of the baby and appraise the condition of the baby in terms of the Apgar score.

Duration. There is a positive correlation between the incidence of the moderate-to-severely depressed score group (0 to 6 scores) and the duration of cyclopropane prior to birth. As is seen in Figure 3, if the mother has received cyclopropane for only five or six minutes before delivery, the babies generally do very well. Beyond this time there is a rapid increase in the number of babies falling into the moderate-to-severely depressed score group. Most of these babies were born in the earlier years of this study. During that time we were not completely aware of the inherent danger of this potent anesthetic cyclopropane. The longer you expose the baby, the worse is the condition of the baby. However, if the baby is delivered within five to six minutes, there is little or no untoward effect resulting from cyclopropane.

Technic

In recent years we have been investigating a technic through which we hope to do away with the use of cyclopropane for cesarean section. Instead, we substitute a very light form of general anesthesia. The simplest way to do this is by means of nitrous oxide and oxygen anesthesia, using little premedication, such as Demerol hydrochloride 50 mg., and scopolamine 0.4 mg. These are combined with a muscle relaxant such as succinylcholine chloride. This is an effective technic. It will keep the mother completely paralyzed and cooperative throughout the entire procedure of cesarean section.

Of course, our first thought might be, "Well, does the succinylcholine chloride get across the placenta and will the baby come out paralyzed, too?" We have investigated this thoroughly and find that succinylcholine chloride, as we use it clinically, does not get across in any significant concentration when measured in terms of baby response. We also measured it by means of a bio-assay method and could not find a significant concentration in the baby's blood when the dose of succinylcholine hydrochloride was used in the usual clinical range.

With this technic of light general anesthesia plus muscle relaxation, the induction can be performed by means of a small amount of thiopentol sodium. However, we have recently been using 80 per cent nitrous oxide in oxygen following a 100 per cent oxygen washout for three minutes, then succinylcholine chloride intravenously. The mother is intubated immediately, and maintenance levels of 75 per cent nitrous oxide in oxygen and a continuous succinylcholine chloride drip are used. Shortly before the baby is born we reduce the concentration of nitrous oxide to 50 per cent and continue with the succinylcholine chloride.

The obstetricians on our service quickly became used to this technic and relied on it so much that, unlike cyclopropane, where the idea was to proceed as rapidly as possible to deliver the baby, they took their time. From the time that they started until the time the baby emerged varied anywhere from a few minutes up to one and one-quarter hours, the latter in one instance. I see many raised eyebrows. I would like to defend our obstetricians on this particular one-and-one-quarter-hours baby. The mother was an immense individual. She was so big it took forty-five minutes just to find the uterus, and then another thirty minutes to deliver the baby.

The critical question is: What is the condition of the babies at delivery? Figure 2 illustrates the clinical condition of 63 strictly comparable babies born with the aid of this technic. The patients were healthy mothers who were chosen for elective section. They were not in labor, and all had exactly the same premedication. As you can see, about 84 per cent of the babies born with the nitrous oxide-succinylcholine technic fell into the Apgar scores of 7, 8, 9, and 10. There was no significant difference between the succinylcholine chloride-nitrous oxide and the regional anesthesia groups. As far as the time of administration was concerned, there was no correlation between how long this technic was employed before the baby was born and the baby's Apgar score.

As I mentioned before, we also use the clinical indicator of how long the baby takes to establish sustained respirations. Correlating the time of sustained respirations of ninety seconds or less in spinal, cyclopropane, and nitrous oxide-succinylcholine chloride anesthesia, there was a marked difference between the cyclopropane anesthesia and the other two but very little difference between the spinal and the nitrous oxide groups.

SUMMARY. If we use the clinical condition of the infant at birth as a criterion, we find that the babies born in the regional anesthesia group are significantly better off at birth than those born after a potent, deep general anesthesia, especially if the latter is prolonged beyond six minutes. However, when we use a light form of general anesthesia, there is either very little difference or no significant difference whatsoever between regional and light general anesthesia.

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Dr. Gold: Thank you very much, Dr. Moya. Our next speaker will be Marvin Cornblath, M.D.

Factors influencing perinatal mortality in elective cesarean section

Marvin Cornblath, M.D.: In recent years, the over-all perinatal mortality of infants delivered by uncomplicated elective cesarean section has not differed significantly from that of infants delivered vaginally.[1–6] However, the infants delivered by cesarean section have an increased incidence of respiratory distress, often transient,[7] and hyaline membrane disease.[1,2,4,5,8] This is true for premature[8] as well as for full-term[1,2,4,5] babies. In an attempt to understand this qualitative difference in morbidity and mortality, a variety of metabolic parameters have been studied and the results of the two groups compared. Significant differences have been found in levels of hemoglobin and hematocrit,[9] calcium,[10] and 17-hydroxycorticosteroids[11] in blood. The purpose of this paper is to present a summary of studies in our laboratory of carbohydrate metabolism* in the newborn child which illustrate perinatal factors that influence fluctuations of blood sugar and hyperglycemic responses to glucagon during the first hours of life.[12–14] It was found that hyperglycemia was influenced not only by the mode of delivery and exposure to labor, but also the administration of hydrocortisone to the mother, the maturity and age of the infant in hours, and the amount of glucagon given.[12–15]

Course of blood sugar. When mothers were given parenteral glucose prior to or during cesarean section, significantly higher levels of sugar in umbilical venous blood were found than when parenteral saline was administered. This occurred whether or not labor had begun prior to surgery. Following birth, a decrease in blood sugar levels was observed in all infants except those delivered by elective section from mothers given saline. In the latter group, the mean level of sugar actually rose. By four hours of age, the levels of blood sugar were within a range of 50 to 63 mg. per 100 ml. and by six hours, 47 to 57 mg. per 100 ml. This was independent of the administration of glucose or any fluid to the mother, labor, or mode of delivery, such as vaginal or cesarean section.

Effect of age in hours on response to glucagon (30 micrograms per kilogram). Ten full-term, vaginally delivered infants were given glucagon within three hours of birth. They responded in one hour with a mean rise in blood sugar of 36 mg. per 100 ml. (Table I). Nine infants, given glucagon after six hours of age, had a mean rise of 56 mg. per 100 ml. sixty minutes later, significantly higher than that in the younger infants ($p<0.05$).[12] These differences in response indicated clearly the need for the precise timing of metabolic studies and the rapidity of some of the homeostatic changes which occur in the full-term infant.

Effect of glucagon (30 micrograms per kilogram) in infants delivered by cesarean section. Glucagon was given to 9 infants within three hours after delivery by cesarean section. Their mothers had received parenteral glucose, but labor had not begun. The mean hyperglycemic response sixty minutes after glucagon administration was 16 mg. per 100 ml.[12] This rise was significantly lower than the one obtained in infants delivered vaginally. This poor response was not affected by giving saline rather than glucose prior to cesarean section, since the mean rise in blood sugar of 7 infants whose mothers were so treated was only 15 mg. per 100 ml. at sixty minutes.[12] In addition, giving parenteral glucose to mothers before vaginal delivery did not diminish their infants' hyperglycemic responses to glucagon (the response at sixty minutes was 38 mg. per 100 ml.). It was concluded, therefore, that fluid administered to the mother had little influence on the re-

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* These studies were done at Michael Reese Hospital and Sinai Hospital of Baltimore in collaboration with G. S. Baens, M.D., W. Oh, M.D., E. Y. Levin, M.D., D. Nicolopoulos, M.D., A. F. Ganzon, M.D., R. J. Hollander, M.D., H. H. Gordon, M.D., and M. H. Gordon, Ph.D.

TABLE I. The effect of labor or hydrocortisone on zero to sixty-minute change in blood sugar after glucagon administration*

Group	Number of Infants	Mode of Delivery	Labor	Hydrocortisone	True Blood Sugar (Mg. per 100 Ml.)† 0	True Blood Sugar (Mg. per 100 Ml.)† 60′Δ
I	16	Cesarean	No	No	54 ± 5.2	15 ± 4.0
II	7	Cesarean	Yes	No	82 ± 14.0	35 ± 6.2
III	6	Cesarean	No	Yes	60 ± 8.6	36 ± 4.0
IV	10	Vaginal	Yes	No	55 ± 4.0	36 ± 3.2

* 60′Δ = mean hyperglycemic response sixty minutes after glucagon administration. $t = \frac{M_1 - M_2}{\sqrt{SE_1^2 + SE_2^2}}$; p = probability.

60′Δ	t	p
I vs. II	2.7	<0.02
I vs. III	3.75	<0.01
I vs. IV	4.06	<0.01

† Mean plus S.E.

sponse of her newborn infant to glucagon.[12]

Seven infants delivered by cesarean section after a trial of labor were given glucagon within three hours of birth. Their mean rise in blood sugar at one hour was 35 mg. per 100 ml. which was significantly higher than that in 16 infants delivered by cesarean section with no exposure to labor (Group I vs. Group II, Table I). Thus it appears that exposure to labor is an important influence on the response of the newborn to glucagon.

Since 17-hydroxycorticosteroids are elevated by labor[11] and can augment the effect of glucagon, it was decided to determine the effect of hydrocortisone* administered to mothers prior to elective cesarean section with no labor. The infants were given glucagon (30 micrograms per kilogram) two hours after birth, and the hyperglycemic response was measured. The mean increase in blood sugar after sixty minutes was 36 mg. per 100 ml., significantly greater than that seen in similar infants with no exposure to labor or hydrocortisone (Group I vs. Group III, Table I). It is concluded that hydrocortisone is an important factor in the varied responses to glucagon.

EFFECT OF LARGE DOSES OF GLUCAGON (300 MICROGRAMS PER KILOGRAM). All of the differences observed with maturity,[15] mode of delivery, and labor can be obliterated by giving 300 micrograms per kilogram of glucagon. With this dose comparable hyperglycemia occurred in infants delivered vaginally or by cesarean section and ranged from mean rises of true sugar of 40 to 51 mg. per 100 ml. at one hour to 44 to 59 mg. per 100 ml. at two hours after glucagon.[12] It was of some interest that the hyperglycemic response in newborn infants of diabetic mothers was related to an exposure to labor and the dose of glucagon rather than to the maternal illness (Figure 1).[13]

COMMENT. The high perinatal mortality in cesarean section, in most instances, is attributable to prematurity, placental abnormalities, accidents of labor, fetal distress, or maternal illness.[1–6] To delineate the effect of operative delivery alone, it is necessary to consider those elective cesarean sections in which optimal anesthetic and operative technics existed and no abnormal factors were present. By considering all these parameters, it readily becomes apparent that the operative mode of delivery alone has little effect on the perinatal mortality rate.[1,3,5] On the other hand, infants delivered by elective cesarean section have an inordinately high incidence of respiratory distress and hyaline membrane disease.[1,2,4,5,8] It would be of interest to consider what perinatal factors influence the neonate during the first hours of life.

The initial level and subsequent changes of blood sugar in the infant were affected not only by fluids administered to the mother but also by the mode of delivery. Despite higher levels of sugar at birth and a more rapid fall during the first two hours, all of the infants were able to stabilize their blood sugar level by from four to six hours of age.[12] The necessity for considering maternal fluid

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* Cortef generously supplied by S. S. Stubbs, M.D., The Upjohn Co., Kalamazoo, Michigan.

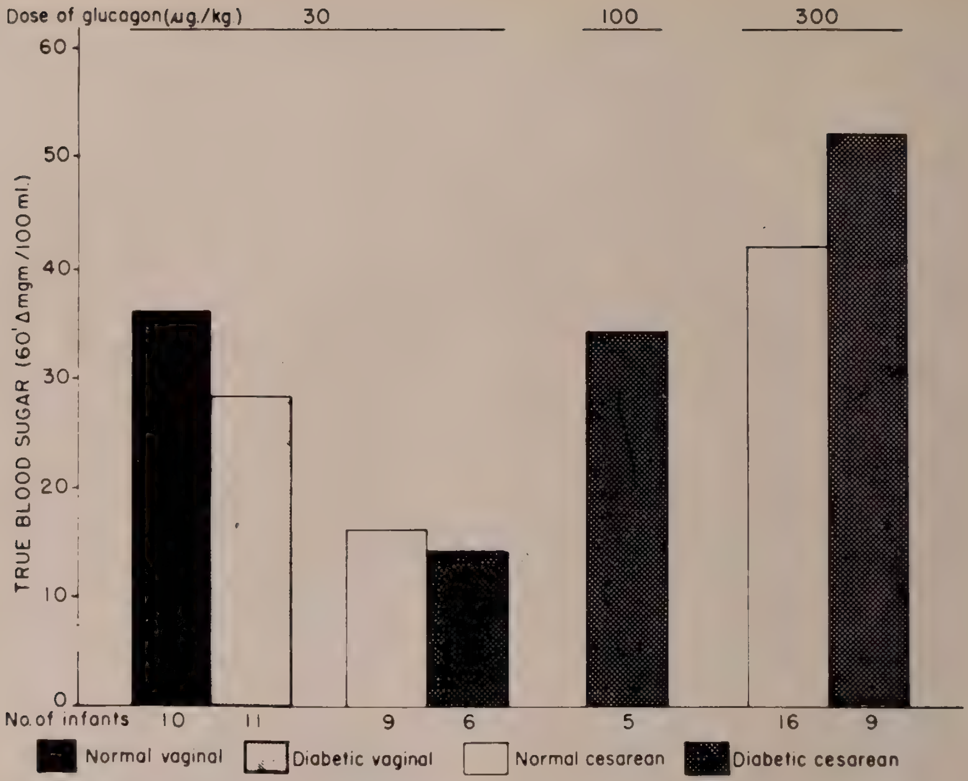

FIGURE 1. Effect of varying doses of glucagon according to type of delivery. Diabetic vaginal is column 11.

administration as well as the mode of delivery before evaluating such data is emphasized. These factors would be important in evaluating differences in hematocrits and hemoglobins which have been found to be lower in infants following cesarean section.[9]

The difference in hyperglycemic response to glucagon in infants under three hours of age as compared with infants over six hours old indicated the necessity for defining the precise age of infants in metabolic studies during the first days of life. Similarly, the calcium level in blood tends to fall over the first thirty-six to forty-eight hours of life before feedings are initiated.[16] Although Gittleman *et al.*[10] found a significantly lower level of calcium in infants delivered by cesarean section, he grouped all the first-day values for calcium levels without regard to age in hours.

Although the type of fluids administered to the mother prior to delivery did not affect her infant's blood sugar response to glucagon, a trial of labor certainly did. An exposure to labor has been shown to elevate the level of 17-hydroxycorticosteroids in the blood of the mother and infant,[11] and to augment the infant's hyperglycemic reaction to glucagon (30 micrograms per kilogram) regardless of the mode of delivery. Furthermore 17-hydroxycorticosteroids increased gluconeogenesis, phosphorylase, and glucose-6-phosphatase activity in animals, which would increase the hyperglycemic effect of glucagon. When hydrocortisone was given to mothers prior to elective cesarean section, their infants showed a significantly greater rise in blood sugar after glucagon.[14]

Since some of the differences between infants delivered by elective cesarean section and those delivered vaginally are related to an exposure to labor, the influence of labor on perinatal morbidity and mortality would be of considerable importance. Unfortunately, in most reported series, it is not possible to assess the role of labor. However, King, King, and Pitt[2] divide their 1,003 elective cesarean sections into two groups, 767 who labored less than four hours and 236 with more than four hours of labor or ruptured membranes. There were 14 neonatal deaths in the former group and none in the latter compared with 14 neonatal deaths and 13 stillbirths in 216 nonelective cesarean sections.[2] Pedowitz, Schwartz, and Goldberg[4] correlated the duration of labor with perinatal mortality in primary cesarean section, both elective and nonelective. In 369 babies whose mothers did not labor, the perinatal mortality was 7.6 per cent. If the mothers labored zero to nine, ten to nineteen, or twenty or more hours before surgery, the total fetal loss was 3.5, 0.0, and 2.2 per cent of 199, 155, and 138 babies. These studies do not consider many other factors relating to perinatal mortality and are therefore certainly not conclusive. However, the results might suggest some relationship between a short trial of labor and perinatal mortality in cesarean section and the need for much more data analyzed in a similar manner. Neonatal morbidity was not considered in either study.

Furthermore, oxygen saturations have been reported to be lower in heel capillary blood one-third to four hours after delivery by cesarean section.[17] More detailed studies on umbilical arterial blood at birth, as well as on left auricular samples during the first twenty-four hours of life, clearly indicate that the mode of delivery has little influence on the oxygen saturation, pH, partial pressure of carbon dioxide, carbon dioxide content, or buffer base capacity of the blood.[18] On the other hand, intra- or extra-uterine asphyxia has a profound effect on the acid-base balance, regardless of the type of delivery.[19]

Conclusion. It is apparent that morbidity and mortality in infants delivered by elective cesarean section are influenced by many factors. Some of these include exposure to labor, pretreatment of mother, circumstances which compromise the infant's condition during or after birth, and maturity. All of these variables must be recorded and considered to evaluate the effect of elective cesarean section on the newborn infant.

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Dr. Gold: Thank you very much, Dr. Cornblath. No doubt we will hear more about what you said during the question and answer period. The next panelist is Mr. Carl Erhardt, the biostatistician of the team.

Statistical report of experience

Carl Erhardt: Each obstetrician knows the experiences of his own patients who have undergone cesarean section, whether primary or repeat. Reports also appear in the literature on various hospital series. Our contribution to this panel discussion consists of a statistical report on the experience of an entire large community with some emphasis on differences between geographic and medical care segments of the community.

The New York City data cited here are derived from answers to items on birth and fetal death certificates regarding (1) instrumental or operative procedures used for delivery and (2) the indications therefor. "Elective sections" are those for which that is the reported indication; "repeat sections" are estimated from the number for which the indication was stated as "previous section." It was recognized that a clear indication for surgical intervention might exist apart from the fact that a previous section had been performed, but there was no way of identifying the "repeat with indication" for the 1959 series presented here.

On 1960 certificates a question has been specifically included asking whether a section, if done, was primary or repeat. Among the 132,122 live births during the first nine months of the year 7,003 cesarean sections were reported. Of this number 3,873, or 55.3 per cent, were reported as primary. This proportion does not vary much by borough, being highest in Queens (57.6 per cent) and lowest in Richmond (53.3 per cent).

In evaluating the 1959 data on cesarean sections it is useful to know that more than 97 per cent of the reported repeat and elective sections in 1960 would be selected for study if they were selected on the same basis as those for 1959. In other words, the 1959 statistics probably understate the true number of repeat or elective sections by less than 3 per cent. It seems unlikely that this small proportion would influence substantially the findings related here.

The frequency of repeat cesarean section naturally depends on the liberality of obstetric opinion regarding appropriate indications for primary sections coupled with the current preferences for family size. If obstetricians become more inclined to resort to section, then the primary section rate will rise. If at the same time, pregnancies of higher order increase, and the "once a section always a section" philosophy prevails, then the repeat section rate must also rise and the total section rate has a double impetus. In little more than twenty years the birth rate in New York City has risen from its depression-years low of 13.6 to a high of 22 per 1,000 population in 1957, declining but little since then. Of later years, the birth rate has continued high because of the increasing numbers of births of higher order. At the same time, the frequency of cesarean section since 1943 has almost doubled, as indicated in Table I, from 30 per 1,000 deliveries in 1943 to 56 in 1959.

Although adequate data to document the conjecture are not available, it seems likely that both more widespread resort to cesarean section and increasing births of higher order have contributed to the advancing incidence of section. We can say that the incidence of primary sections has increased from 30.4 to 32.6 (about 7 per cent) in the past five years, while the incidence of sections reported as done because of a previous section rose from 19.9 to 23.9 (20 per cent).

It may be of some interest to know that the incidence of cesarean section for the delivery of live infants and for stillborn fetuses have been equivalent throughout this period. The significance of these and other factors relating to sections in general have been discussed in a previous paper.[1] A brief exposition of the general situation in the city may, however, serve as useful background for a discussion of elective and repeat sections.

Frequency of section, by borough. For the three-year period, 1956 to 1959, the incidence of all sections in the city was 53.6 per 1,000 deliveries at twenty weeks gestation or more. Their incidence varies considerably by borough, from 46.8 to 59.7, the highest rate holding in Manhattan and the lowest in Richmond (Table II). However, the disparity between boroughs is diminishing. In the 1950 to 1955 period, the Manhattan incidence was practically the same as currently, 60.2, but that in Richmond was then 33.4. The frequency of section has increased by 40 per cent in the

TABLE I. Frequency of cesarean section associated with live births and with fetal deaths, by years

Year	Total Sections		Live Births		Fetal Death	
	Number	Rate*	Number	Rate†	Number	Rate**
1943	4,117	29.7	4,001	29.7	116	29.7
1944	4,195	33.2	4,090	33.3	105	28.5
1945	4,795	36.2	4,654	36.1	141	37.6
1946	5,753	36.6	5,583	36.6	170	38.5
1947	6,729	38.3	6,536	38.2	193	42.1
1948	6,873	42.4	6,689	42.3	184	43.8
1949	7,093	44.1	6,901	44.0	192	48.6
1950	7,404	46.4	7,253	46.5	151	41.2
1951	7,821	47.0	7,632	46.9	189	49.8
1952	8,206	48.8	8,007	48.8	199	51.9
1953	8,186	49.6	8,015	49.6	171	48.0
1954	8,408	50.1	8,233	50.2	175	46.3
1955	8,541	50.6	8,358	50.6	183	49.2
1956	8,535	50.4	8,345	50.4	190	52.2
1957	9,145	53.5	8,934	53.5	211	52.7
1958	9,455	55.0	9,260	55.2	195	45.9
1959	9,567	55.5	9,357	55.7	210	47.9

* Per 1,000 live births, plus fetal deaths of twenty weeks gestation or more.
† Per 1,000 live births.
** Per 1,000 fetal deaths of twenty weeks gestation or more.
Bureau of Records and Statistics, Department of Health, City of New York.

TABLE II. Frequency of cesarean section and perinatal mortality associated with section, by borough, New York City, 1956 to 1959

Borough	Total Sections		Live Births		Fetal Deaths		Perinatal Mortality
	Number	Rate*	Number	Rate†	Number	Rate**	Rate**
New York City	36,702	53.6	35,896	53.7	806	49.5	52.7
Manhattan	12,684	59.7	12,423	60.0	261	48.1	50.3
Bronx	4,789	53.7	4,679	53.8	110	48.4	55.3
Brooklyn	12,129	51.5	11,850	51.6	279	50.5	52.7
Queens	6,220	48.2	6,087	48.2	133	49.4	54.8
Richmond	880	46.8	857	46.5	23	63.2	59.1

* Per 1,000 live births plus fetal deaths of twenty weeks gestation or more.
† Per 1,000 live births.
** Per 1,000 fetal deaths of twenty weeks gestation or more.
Bureau of Records and Statistics, Department of Health, City of New York.

latter borough, and increments ranging from 16 to 19 per cent have been recorded for the other three boroughs also. The position of the boroughs in order of magnitude of their rates has remained the same.

The relative frequency with which section is associated with live births or fetal deaths shows considerable variation by borough, but inferences beyond the simple observations themselves would be hazardous. The gross perinatal mortality associated with section is lowest in New York County, but it would seem self-delusory to claim satisfaction from this fact without a detailed clinical survey of the cases involved.

HOSPITAL AUSPICES AND TYPES OF SERVICE. The rise in frequency of sections is shared by each type of hospital group and service. For example, the incidence in municipal hospitals in 1954 to 1955 was 35.4, while in 1959, as shown in Table III, it was 42, an increase of 18.6 per cent. The present frequency in the proprietary hospitals is 16.5 per cent above that for 1954 to 1955, while the voluntary hospital rate has risen but 6.3 per cent. Again, as with borough variations, the disparities among hospital care groups is diminishing, but the frequency of section remains highest among private patients in voluntary hospitals.

The similarity of the incidence among ward patients in the voluntary and municipal hospitals is striking, as is the similarity of perinatal mortality associated with section.

TABLE III. Frequency of cesarean section and perinatal mortality associated with section by hospital auspices and service, New York City, 1959

Auspices and Service	Number	Section Rate per 1,000 Deliveries*	Perinatal Mortality Rate*
New York City†	9,567	55.5	53.3
Proprietary hospitals**	1,594	58.5	55.2
Voluntary hospitals	6,395	60.8	48.9
Private service	5,022	67.0	42.6
General service	1,373	45.3	72.1
Municipal hospitals††	1,514	42.0	68.7

* Live births plus fetal deaths of twenty weeks gestation or more.
† Includes 64 deliveries which occurred in State and Federal institutions.
** All private patients.
†† All general service (ward) patients.
Bureau of Records and Statistics, Department of Health, City of New York.

TABLE IV. Elective and repeat cesarean sections and sections with specific indications, by hospital auspices and service, New York City, 1959

Auspices and Service	Elective and Repeat Sections			Sections with Specific Indications		
	Number	Per Cent of Total Sections	Rate*	Number	Per Cent of Total Sections	Rate*
New York City	4,235†	44.3	24.6	5,332**	55.7	30.9
Proprietary hospitals	634	39.8	23.3	960	60.2	35.2
Voluntary hospitals	2,801	43.8	26.6	3,594	56.2	34.2
Private service	2,293	45.7	30.6	2,729	54.3	36.4
General service	508	37.0	16.8	865	63.0	28.6
Municipal hospitals	759	50.1	21.0	755	49.9	21.0

* Per 1,000 live births plus fetal deaths of twenty weeks gestation or more.
† Includes 41 deliveries which occurred in State or Federal institutions.
** Includes 23 deliveries which occurred in State or Federal institutions.
Bureau of Records and Statistics, Department of Health, City of New York.

The lowest perinatal mortality occurs among the voluntary hospital private patients. These mortality rates in 1959 are lower than in 1954 to 1955 among ward patients in both voluntary and municipal hospitals, but higher in the others. The changes are not statistically significant, however, nor, despite the apparent wide variation, are the differences between the rates. However, the constancy with which perinatal loss is highest among ward patients lends credence to the belief that a real difference exists.

INCIDENCE OF ELECTIVE AND REPEAT SECTIONS. As indicated previously, the frequency of repeat sections is understated by about 3 per cent because of the manner of compiling the data. The repeat sections omitted will be those for which a medical or obstetric indication was reported rather than "previous section." Although it seems probable that perinatal loss may be higher among those repeats for which a specific indication was cited,[2] their small proportion seems unlikely to affect the conclusions markedly.

Elective and repeat sections together comprised 44.3 per cent of all sections in 1959, according to the raw data. Correcting for the estimated underidentification, this proportion becomes 45.6. No further attempt at adjustment will be made, however. The assumption is made that relationships between groups would not be altered. The incidence of elective and repeat sections is 24.6 per 1,000 deliveries (Table IV).

Substantial proportions of current sections are elective or repeat in each hospital service group, even exceeding slightly 50 per cent in the municipal hospitals, with nearly 46 per cent among private patients in the voluntary hospitals. However, the incidence rates show a reverse relationship. These apparently anomalous observations are quite understandable. It appears in-

TABLE V. Perinatal mortality associated with elective and repeat cesarean sections and with sections with specific indications, by hospital auspices and service, New York City, 1959*

Auspices and Service	Elective and Repeat Sections		Sections with Specific Indications		Total Perinatal Mortality Rate†
	Number of Deaths	Rate†	Number of Deaths	Rate†	
New York City	116**	27.4	394††	73.9	43.0
Proprietary hospitals	17	26.8	71	74.0	32.3
Voluntary hospitals	75	26.8	230	66.2	36.3
Private service	54	23.5	160	58.6	33.0
General service	21	41.3	78	90.2	44.6
Municipal hospitals	21	27.7	83	109.9	71.9

* Infant deaths under seven days plus fetal deaths of twenty weeks gestation or more.
† Per 1,000 live births plus fetal deaths of twenty weeks gestation or more.
** Includes 3 deliveries in State or Federal institutions.
†† Includes 2 deliveries in State or Federal institutions.
Bureau of Records and Statistics, Department of Health, City of New York.

evitable that the high primary section rate among the voluntary hospital private patients will produce a high repeat rate. But since births of a high order are likely to be relatively infrequent among this group of women, the proportion of repeat sections will be comparatively small. On the other hand, a low primary rate in the municipal hospitals produces a low repeat rate. But since the clientele of these hospitals are likely to produce more children, repeat sections will form a larger proportion of the total in any one year.

As would be expected, repeat sections increase constantly with the age of the mother, from 5.7 per 1,000 deliveries among women under twenty to 59.5 at ages forty and more. The parity picture is somewhat different, with a rate of 2.6 for para 1 women and a sharp rise to 37.1 for those who are para 2. The rate declines slightly for higher parities.

PERINATAL MORTALITY IN ELECTIVE AND REPEAT SECTIONS. The nub of our discussion is how perinatal mortality associated with elective and repeat section compares with that for primary section and with perinatal mortality in general. Klein[2] has stated a belief that there is no reason to expect any lower rate for repeat surgery because the indication for the primary section will continue to exist. However, this cannot always be true, because some conditions, such as pathologic conditions of the placenta, fetal distress, prolonged labor, or an abnormal presentation, may have been peculiar to the pregnancy requiring the original intervention. Even disproportion that does not represent true contracted pelvis could fall into this category. Since perinatal loss associated with some of these conditions is relatively high[3] their even partial exclusion among repeat sections would tend to lower the risk to the fetus.

It is obvious from Table V that elective and repeat section is accompanied by considerably lower perinatal loss than is primary section in the city's experience. The mortality rate associated with primary section approaches treble that of elective and repeat sections, 73.9 versus 27.4 per 1,000 deliveries of each character. The rate associated with elective and repeat sections is 36 per cent below the gross perinatal mortality of the community. Apparently the operative procedure does not carry exceptional risk to the fetus. This comparison should not be interpreted further, however, since the women undergoing elective or repeat sections are a very selected group.

The consistency of perinatal loss between the several hospital service groups, except for the voluntary general service segment, is remarkable. It must be remembered, however, that small numbers are involved, and the rates are subject to a rather large sampling variation These rates, however, are uniformly lower than for primary sections as well as for gross perinatal mortality in each of the hospital service segments.

The point that Klein[2] made, that the indication for the original intervention continues to exist, undoubtedly does operate in a substantial number of instances. It cannot be expected, therefore, that perinatal loss will, or should necessarily, disappear entirely in repeat sections. Schwartz, Pedowitz, and Goldberg[3] state that 6 per cent of their repeat sections with indications such as maternal diabetes mellitus, antepartum hemorrhage, toxemia, and the like were responsible for 39 per cent of the losses, even though they represented only 6 per cent of the total indications.

Infant deaths. Of the 116 perinatal losses associated with elective or repeat sections, 89 were infant deaths. It may shed some light on the problem to look at the reported causes of death for these infants. They were classified as follows:

Postnatal asphyxia and atelectasis (with immaturity—20)	37
Immaturity, unqualified	17
Congenital malformations	12
Birth injury (with immaturity—3)	7
Ill-defined causes (with immaturity—5)	7
Erythroblastosis	3
Pneumonia of newborn (with immaturity—1)	3
Maternal disease	2
Sepsis of newborn	1

Congenital malformations accounted for 12 of the deaths. Perhaps these could not have been salvaged. Otherwise, the most notable factor is that the physician mentioned prematurity specifically in 46 of the cases. If postnatal asphyxia and atelectasis, without reported immaturity, are included as possible evidences of immaturity, the total connected with that condition rises to 63. Erythroblastosis, it seems, should also be controllable with exchange transfusion, while with good pediatric attention pneumonia of the newborn, without immaturity, may be avoidable. These 5 deaths increase to 68 the total that seem essentially preventable. In other words, a clinical study of these deaths should be extremely profitable; the reduction of at least the hebdomadal infant losses associated with elective or repeat cesarean section to nearly zero (except for congenital malformations incompatible with life) appears distinctly within the realm of possibility.

The age of the infant at death is also revealing. This distribution is:

Under 12 hours	26
12 to 24 hours	16
1 day	19
2 days	22
3 days	3
4 days	0
5 days	1
6 days	2

Practically all the losses occur within seventy-two hours of delivery. If the infant can be sustained through this period, the probability of death is very small.

Weight at birth. Additional evidence of the important role of properly timed intervention is contained in the weight distribution of the infants delivered electively or in a repeat operation. In this community experience 12.8 per cent of all deliveries by cesarean section produced infants (dead and alive) less than 2,501 Gm. in birthweight; even the exclusion of 31 fetuses of less than 1,001 Gm. only reduces the proportion of prematures to 12.4 per cent. The corresponding proportions for all liveborn infants are 9.4 and 8.7. Clinical investigators have made similar observations.[2–5] It must be recognized, of course, that choice in timing is not always the privilege of the obstetrician who is often faced with a situation requiring immediate intervention.

As might be expected, repeat and elective sections appear to be timed somewhat better than primary sections, since the proportion of infants under 2,501 Gm. is only 10.3, a figure which becomes 10.2 if 4 deliveries at less than 1,001 Gm. are excluded. However, among this 10 per cent of the deliveries, nearly 60 per cent of the perinatal deaths occur. In view of the high mortality (15.6 per cent) among the infants premature by weight compared with that among those 2,500 Gm. or more (1.1 per cent), it is obvious that a delay of intervention until the fetus developed further would improve perinatal mortality associated with elective and repeat cesarean section.

SUMMARY. 1. Both primary and repeat sections are increasing in frequency in New York City. These facts are functions of a widening liberality in resorting to surgical intervention and increased numbers of births of a higher order.

2. There are variations in the incidence of sections by borough and by hospital auspices and service, but these differences are diminishing.

3. Perinatal loss associated with elective and repeat sections in 1959 was 27.4 per 1,000 deliveries, compared with 73.9 for all

other sections and 43 for all deliveries regardless of mode.

4. Despite the probability that adverse medical or obstetric conditions evoking the primary intervention continue to exist in some women undergoing a repeat procedure, an examination of the reported causes of death leads to the conclusion that fastidious obstetric and pediatric care might well avoid the major proportion of the infant deaths that occur in the first week.

5. The timing of the intervention is of extreme importance. A larger proportion of infants delivered by section weigh less than 2,501 Gm. than is true of all liveborn infants, whether primary or repeat sections are considered. Despite this fact perinatal mortality among deliveries in elective and repeat sections is substantially less than the general city rate for all deliveries. Improvement, however, seems quite feasible of accomplishment.

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Summary

Dr. Gold: Thank you Mr. Erhardt. Now, having heard three facets of the question, let us see whether we have answered some of the basic questions which were originally posed.

It would appear from Dr. Moya's presentation that there is a relation between the type of anesthesia and perinatal mortality in cesarean section and that there is a significant difference between modes of anesthesia, namely, spinal and the newer method of light, general anesthesia, supplemented by muscle relaxants, which is more beneficial than cyclopropane anesthesia.

From the point of view of the pediatrician, Dr. Cornblath has told us that while in general the mode of death differs between the vaginally delivered and the cesarean section-delivered baby, that of hyaline membrane disease is more frequent in the cesarean section-delivered than in the vaginally delivered baby. He also stated that metabolic differences, such as in hyperglycemic responses, calcium levels, the corticosteroids, and oxygen saturation of the umbilical vein and arterial blood, are more or less equivocal at the present time. More research will be necessary to make a more definitive statement about these factors. However, there is a significant observation on the influence of labor, namely, that the baby who has had some labor even although it is delivered by cesarean section, does better than the baby delivered by elective cesarean section.

Finally, Mr. Erhardt made the point that there is an obviously lower perinatal mortality in the elective and repeat cesarean section baby than in the indicated cesarean section baby or in the vaginally delivered baby of all types. It was also stressed that the modes of death in these babies, namely, prematurity, asphyxial diseases, erythroblastosis, and pneumonia of the newborn infant have a marked preventable component both obstetrically and pediatrically.

In summation, he stated that if we could eliminate prematurity we might also eliminate some of the perinatal loss associated with elective cesarean section, particularly if the obstetrician would utilize better judgment as to the time of doing the elective cesarean section and the pediatrician would render more definite and timely postnatal care.

Question and answer period

What the basic perinatal mortality should be in the nonstress, elective cesarean section still remains to be answered. I hope that the questions and discussion from the floor may give us more definite information. I see Paul Pedowitz, M.D., and Ralph M. Schwartz, M.D., in the audience, both of whom have been quoted liberally since they came up with a "basic perinatal rate for the elective cesarean section" in the neighborhood of 2 per thousand. I wonder if either Dr. Pedowitz or Dr. Schwartz or both would like to comment.

Paul Pedowitz, M.D.: It is gratifying to hear that my papers are well read in Chicago, but it is disquieting to realize that the data on the relationship of labor to perinatal mortality in primary cesarean sections were being misquoted. As quoted these figures were utilized to demonstrate that labor has a beneficial effect on the baby, an impression that we all share, and that its absence is associated with a high perinatal mortality. However, the data in the original table and text of the papers reveal that the length of labor, unless it exceeds twenty-four hours, has very little effect on fetal mortality. When cesarean section was performed prior to the onset of labor or with labor of less than ten hours duration, the high fetal mortality was due to the indication for cesarean section and not to the duration of labor. These indications in themselves have a deleterious effect on the fetus, whether it be diabetes mellitus, abruptio placenta, placenta previa, or fetal distress. These are the patients who form the vast majority of the group in whom abdominal delivery is performed with little or no labor. Basically, then, the reason for the high fetal mortality in this group is not the length of labor but rather the condition for which the cesarean section was performed.

As regards hyaline membrane disease, an incidence of 12 per cent in full-term babies is rather high. But, if one looks a little further, one will note quickly that the majority of these infants were from diabetic mothers. They were full-term by size and not by gestational age. They were not elective cesarean sections. The indication was diabetes mellitus. In other words, the actual incidence of full-time babies with hyaline membrane disease would probably be less than 1 per cent of all babies; only 2 full-term-sized babies succumbed to hyaline membrane disease when the indication for the primary or repeat cesarean section was truly elective.

Now, as regards a fatal outcome, the reason we believe that the fetal mortality inherent in cesarean section per se is in the neighborhood of 0.2 per cent is that the vast majority of deaths are not related to the mode of delivery but to the indication for this approach and to errors in management, prior to and following delivery. Unfortunately, when we gather statistics on cesarean sections, we include all fetal deaths whether they occur antepartum or neonatally. Certainly the mode of delivery is not responsible for the antepartum fetal death in utero.

Now, why do many of these deaths occur in the neonatal period? You can divide these deaths into four different categories. Part of them are due to people like myself, obstetricians. Another group is due to anesthesiologists, a factor that was not stressed tonight and incidentally is not related to the type of anesthesia. We found that anesthesia played no role in fetal mortality in our study.

The third group, I guess we can say, is due to pediatricians and the fourth to nursery personnel. Each is well represented here tonight.

The greatest fault of the obstetrician is to perform elective cesarean section too early. At this point, we must clarify terminology. An elective cesarean section, primary or repeat, indicates the absence of labor and of medical or obstetric complications. A primary cesarean section is truly elective only when performed prior to the onset of labor because of a previous gynecologic operation or for a viable baby. It is obvious that cesarean sections which are performed because of diabetes mellitus, toxemia, placenta previa, a previous cesarean section, or premature labor, and so forth, are not truly elective. The fetal risk in this group is much greater than in the former.

Good obstetric judgment dictates that if the fetus is estimated to be less than 3,000 Gm. it is far safer to wait until labor commences. Even though uterine scars may be defective, they will rarely rupture symptomatically during the course of prodromal labor. Adherence to this principle will minimize the incidence of prematurity due to errors in judgment.

Then there are errors in operative technic resulting in fetal deaths. There have been cases, fortunately not too frequent, wherein the scalpel went a little deeper than it should, or great difficulty was encountered in extracting the baby because of an inadequate incision. Such deaths are credited to the mode of delivery, when actually it is not the mode of delivery but the operator who is responsible.

Thus, the obstetric contributions to fetal wastage are due to errors of judgment and technic. The fetal loss in each instance is preventable.

The fourth factor, namely, adequate well-trained nursery personnel is a problem common to all institutions today. Inadequate staffing and poorly trained personnel are responsible for some of the neonatal deaths. These nursery accidents are preventable, and it is our task to see that the nurseries are adequately staffed. In addition to the preventable fetal deaths, there are many that are nonpreventable, regardless of the mode of delivery, namely, congenital defects incompatible with life, antepartum fetal death in utero, and the patient with a previous cesarean section who goes into premature labor. In these instances labor generally commences at a period in gestation wherein fetal salvage is poor, whether the delivery is abdominal or vaginal. Probably, some of these fetuses in the lower-weight group, under 1,500 or 1,700 Gm., would be better off if they were delivered from below. When labor occurs earlier than anticipated, in the presence of other complications of maternal or fetal origin, this accounts for more than 99 per cent of the total mortality as seen in the repeat cesarean section. Thus, the fetal risk inherent in the mode of delivery is approximately 0.2 per cent.

The anesthesiologist's role in minimizing fetal loss is to perform adequate resuscitation of the newborn in the delivery room. In many hospitals it is usually done by the most inexperienced junior assistant resident or intern on the pediatric service. I believe that it should be done only by an obstetric anesthesiologist. Unfortunately, when it is done by the junior man one finds only too often that aspiration is not properly accomplished, and the fetal death is generally attributed to hyaline membrane disease. However, postmortem examination readily reveals the true cause of the fetal death. The other problem is trauma from too-vigorous attempts at resuscitation, producing hemothorax and hemopericardium. This accounts for the loss of one or two babies every five years or so. True, it is not much, but they all add up.

Fetal deaths due to errors in pediatric judgment are preventable. At times, there is too long an interval between the onset of symptoms and adequate therapy. This is well exemplified in a recent case wherein the marked anemia of the newborn infant was recognized immediately following delivery. Despite this, a blood transfusion was not attempted until many hours later.

DR. GOLD: Thank you very much, Dr. Pedowitz. Are there any other comments or discussion or questions?

HAROLD JACOBZINER, M.D.: First I want to make a minor correction with regard to infant mortality. For 1960 there has been a 1.5 per cent reduction in infant mortality. We are rather happy about it.

Now I would like to ask a few questions of Mr. Erhardt. In Table III, I see that the rate for municipal hospitals is 68.7, while for general services of voluntary hospitals, which also means ward services, it is 72.1. I would like to ask whether the difference is statistically significant. I do not believe so. But I would like it stated that it is not statistically significant.

MR. ERHARDT: It is not; nor is the difference between those rates and the others of significance.

DR. JACOBZINER: I realize that, but I wanted to get your reply to it. Then on Table IV the rates for both elective and repeat sections are considerably higher for the private than for ward patients. Now, is the ward patient so much healthier than the private patient? And, if cesarean sections are good for private patients, why are they bad for ward patients?

DR. GOLD: Dr. Jacobziner, I presume, is referring to the figure of 30.6 in the elective repeat group, and 36.4 for all other sections, versus the respective rates of 21 and 21 for the patients delivered in municipal hospitals.

Mr. Erhardt: These are frequency rates and the differences between private and service patients are significant. Why do we do more cesarean sections on private services than we do on ward services? If it is a salutary procedure then let us not deprive the ward patients of its benefits.

Dr. Gold: Dr. Jacobziner, I think that this is the best way I could answer the question you pose. In the past ten years, at least on the services of voluntary hospitals, the gap or the disparity between the incidence of cesarean section on the private service versus the ward service of the same hospital has narrowed. In most of the teaching voluntary hospitals today the rates are approximately the same for the ward as for the private patient.

Dr. Jacobziner: We have to do a job in the places where the gap has not narrowed.

Dr. Gold: Let us say the gap is narrowing. I think that there are many considerations that enter into the disparity of cesarean incidence between ward and private patients. I think that this was most aptly put, as I recall, back about 1950, when out West a symposium was held on cesarean section. As you know, the West Coast is known particularly for its inordinately high incidence of cesarean section. In the course of the discussion, a most pithy remark was made, that if there could be an elimination of the fee differential between a vaginally delivered and an abdominally delivered baby, then and only then would parity be reached between the cesarean section incidence of private and nonprivate patients. I leave that to you to consider.

Myron Gordon, Ph.D.: I am not sure the staff patient at the voluntary hospital would be better off being delivered by cesarean section according to the statistics in Table V. Do I take it correctly that the rate expressed there is a perinatal mortality rate? The perinatal mortality rate for staff patients on a general service is 41.3 per 1,000 compared with 23.5 per 1,000 for private patients. They may be better off not having cesarean sections.

Mr. Erhardt: The difference between these rates for elective and repeat section is only of borderline significance. The rates for both the ward patients in the voluntary hospitals and the municipal hospitals are based on 21 deaths. Such rates are subject to a fairly wide sampling variation. The difference between the rates for private and general service patients with primary section, however, is highly significant.

Dr. Jacobziner: But in one case you have 21 deaths in each category; 21 patients for the private and 21 deaths for the ward, and there is a difference in frequency rate. So you do have statistical differences. You have 21 deaths in each group—the number is 21 in each group—and yet you have such a difference in rate.

Mr. Erhardt: It does not mean the difference is significant, Dr. Jacobziner. It depends on how many deliveries are involved.

Dr. Cornblath: In answer to Dr. Pedowitz, his data as reported are subject to a variety of interpretations. Indeed, this summarizes the point of my discussion, namely, the lack of detail in most published reports can lead to many different conclusions. It is necessary to know all the contributing factors before any conclusions are justified. For example, the level of sugar in blood in infants delivered by cesarean section depends on the type of fluid that the mother was given. In evaluating the infant's response to glucagon it is necessary to know whether the mother labored or not. In discussing morbidity in these babies, their Apgar rating, the type of anesthesia and analgesia given to the mother, and the indication for the section are all pertinent. Certainly, all of these factors and many more must be considered and be available if we hope to resolve the questions raised.

Alfred Fischer, M.D.: First I would make a plea for better coordination between the obstetrician and the pediatrician. In some hospitals there is still a debate as to whether or not the baby is under the care of the obstetrician or the pediatrician. Some obstetricians say, "I will not let a pediatrician get hold of the baby that I deliver." The answer is that unqualified pediatricians may be taking care of his babies. This is his answer: "If that is so, it is a sad thing." One might also say there may be unqualified obstetricians delivering babies too!

Second, it is perfectly evident that nursing care is a tremendous factor in this thing. Even in good hospitals there are the problems of vacations and of personnel. During the night shifts there is a shortage of trained personnel, and this is so even in excellent hospitals. If the baby is delivered by cesarean section at 8:00 or 9:00 o'clock in the morning, or at 10:00 or 11:00 o'clock at night, or at 1:00 or 2:00 o'clock in the morning, a resident may not be available, or he may not be called because the nurse is not aware of trouble.

I think that personal observation and care of these infants by intelligent residents or graduate residents and the rest of us can save babies. I know they can. I think that mortality rates can be improved just by having experienced personnel around, knowing what is going on and being aware of the dangers that can befall babies. You have heard the possible causes of death. These are sometimes reversible.

Edward Wasserman, M.D.: I think from a pediatric point of view, I can only agree wholeheartedly with what Dr. Fischer said. I think that with adequate care and attention by all those involved the number of babies who could be saved is far greater than is generally thought, whether the babies are delivered by cesarean section or vaginally. This same problem comes up with anesthesia. I think it depends more on the person behind the machine than the type of anesthesia. I think all of these factors really are much more important and are probably the reasons you did not get your answer.

Dr. Gordon: I should like to ask Dr. Moya as an anesthesiologist what his preference is for anesthesia for cesarean section, either in elective cesarean section for a patient who is not in labor or for one who is in labor?

Dr. Moya: For most mothers, whenever possible we still prefer, and this is also my own preference, the regional type of anesthesia, either spinal or lumbo-epidural. However, there are others when this is not feasible. A very common example is fetal distress; when this occurs you have no time to do such a procedure. Severe hemorrhages are not uncommon in situations in which a mother refuses to have a spinal anesthesia. Under such circumstances, we have been using cyclopropane anesthesia.

In recent years we have come to realize its great limitations, especially the greater length of time it takes us to deliver the baby. This is why we have been trying, as a possible substitute for cyclopropane in situations where we cannot use regional anesthesia, the combination of light, general anesthesia, nitrous oxide, and a muscle relaxant. But our preference in general, whenever possible, is spinal anesthesia.

Dr. Gold: I think from the discussion it is obvious that this approach to the problem of cesarean sections must be multidisciplined. The obstetrician, the pediatrician, the biostatistican, the anesthesiologist, certainly the pathologist, and the public health workers have almost equal responsibilities to investigate the reasons why we lose babies, whether in the course of vaginal delivery or of cesarean section. Possibly the best modality to employ is the examination of the clinical case when the mortality occurs. By that I mean the perinatal mortality conference at both the hospital and the community levels. I think that the crystallization of opinion within the institution or within the community is what eventually is going to give us the answer, together with research along such metabolic and biochemical lines as were suggested to us tonight by Dr. Cornblath.

Dr. Goldmark: If there are no further questions, the meeting is adjourned. I want to thank the members of the Panel and all who participated for a most interesting evening.

Transverse Lie and Perinatal Mortality

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TRANSVERSE LIE OF THE fetus is not a frequently encountered presentation, occurring in only about 0.2 to 0.3 per cent of all pregnancies. However, this type of presentation poses special problems both for the fetus and the mother. The infrequent occurrence of transverse lie does not give any single individual sufficient experience to pass judgment on the correct method of handling the various problems nonnected with this complication of pregcancy. Therefore, it is necessary to obtain large numbers of cases from many areas to have a sufficient number to arrive at significant conclusions.

The greater availability of good obstetric services today, coupled with the use of antibiotics and the availability of blood, has removed some of the dangers associated previously with this complication of pregnancy. Therefore, it was thought advisable to survey a large number of transverse lie presentations which have occurred in recent years to assay the problem in the light of modern obstetrics.

Survey of transverse lie presentations

The material for this study was obtained from the records of 11 hospitals which sent in their information to the Obstetrical Statistical Cooperative. The years surveyed were from 1951 to 1958, inclusive. The patients of these hospitals were from all types of socioeconomic levels, both Negro and white. The total number surveyed was 169,457 single pregnancies. Of these pregnancies, 426 or 0.26 per cent were cases of transverse lie. Only fetuses alive on admission to the hospital and weighing 1,000 Gm. or more at the time of delivery were included.

Two hundred and eighty-four patients or 66.6 per cent were white and 142 or 33.4 per cent were Negro. Transverse lie is known to occur more frequently in the multiparous individual, and this was well illustrated in the present series since 42 or 10 per cent were primigravidas and 384 or 90 per cent were multiparas (Table I).

The birth weights, according to 500-Gm. increments, are shown in Table II. Two hundred and eighty-eight or 67.6 per cent of all transverse lie presentations were mature infants, and 137 or 32.2 per cent were premature infants. This illustrates dramatically the high incidence of prematurity associated with this entity and is one of the important factors for its increased perinatal loss.

The two most frequent maternal complications were placenta previa and a prolapse of the umbilical cord. There were 78 or 18.2 per cent of the mothers who had

TABLE I. Parity and race

	White		Negro		Total	
Patients	Number	Per Cent	Number	Per Cent	Number	Per Cent
Primigravidas	33	7.7	9	2.2	42	10
Multiparas	251	58.9	133	31.2	384	90
TOTALS	284	66.6	142	33.4	426	100

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TABLE II. Birth weight

Grams	Number	Per Cent*
1,001 to 1,500	30	7.0
1,501 to 2,000	44	10.4
2,001 to 2,500	63	14.8
Over 2,500	288	67.6
Unknown	1	0.2
TOTALS	426	100.0

* Incidence of prematurity, 32.2 per cent.

TABLE III. Maternal complications

Complications	Number	Per Cent
Placenta previa	78	18.2
Prolapse of umbilical cord	30	7.0
Abruptio placentae	28	6.5
Rupture of uterus	2	0.5

A STUDY WAS MADE *of 426 cases of transverse lie, 0.26 per cent of the total number of pregnancies surveyed. Ninety per cent of the patients were multiparas, and 32.2 per cent of the transverse lies which occurred were associated with prematurity. Placenta previa, prolapse of the umbilical cord, and contracted pelvis were associated with the entity in a high incidence. Perinatal loss in patients delivered by cesarean section was 10.2 per cent, whereas in vaginal delivery it was 35.4 per cent. The patient with an uncomplicated term transverse lie may be allowed to go into spontaneous labor to determine whether or not a spontaneous conversion to a longitudinal presentation will occur. If conversion does not occur at once, a cesarean section should be performed. A scout roentgenogram should be done in all cases to determine the position of the fetus.*

associated placenta previa. This is 18 times the incidence of placenta previa in the population as a whole. A prolapse of the umbilical cord occurred thirty times, in 7 per cent of the patients, which is approximately 10 times the incidence of this complication in the entire group (Table III).

There were 2 cases of rupture of the uterus, both associated with mature infants. One case occurred at term and involved a previous cesarean section scar. The mother was delivered of a living infant weighing over 3,500 Gm. The second case occurred in an individual again at term, with an infant that weighed 3,500 Gm. which was delivered as a stillbirth after the mother had been in labor for approximately five hours.

The perinatal loss, according to weight, is shown in Table IV. It is clearly evident that the total perinatal loss of 15.7 per cent is high, and in analyzing this loss it is obvious that the big bulk of it occurred in the premature group. The mature loss was only 4.5 per cent. There were twice as many neonatal deaths as stillbirths. The causes of the deaths that occurred during labor are shown in Table V. The incidence of prematurity in these stillbirths was 62.5 per cent. The two most frequent causes of death of those infants who died during labor were prematurity and a prolapse of the umbilical cord. These two conditions accounted for 20 of the 24 stillbirths.

The analysis of the causes of the neonatal deaths is listed in Table VI. The incidence of prematurity in this group was 90.7 per cent, and the two most frequently found causes were prematurity and atelectasis, the latter undoubtedly associated with prematurity. These two entities accounted for 32 of the 43 neonatal deaths.

TABLE IV. Perinatal loss according to weight

		Died During Labor		Neonatal Deaths		Total Perinatal Loss	
Weight (Grams)	Total Cases	Number	Per Cent	Number	Per Cent	Number	Per Cent
1,001 to 1,500	30	6	20.0	15	50.0	21	70.0
1,501 to 2,000	44	5	11.4	11	25.0	16	36.4
2,001 to 2,500	63	4	6.3	12	19.0	16	25.3
Over 2,500	288	9	3.1	4	1.4	13	4.5
Unknown	1	..	...	1	...	1	100.0
TOTALS	426	24	5.6	43	10.1	67	15.7

TABLE V. Causes of death during labor

Cause of Death	Number of Cases
Prematurity	10
Prolapse of umbilical cord	10
Atelectasis	2
Placenta previa	1
Ruptured uterus	1

TABLE VI. Causes of neonatal deaths

Causes	Number of Patients
Prematurity	22
Atelectasis	10
Pneumonia	3
Anoxia	2
Central nervous system hemorrhage	2
Congenital heart disease	1
Multiple anomalies	1
Hemolytic disease	1
Unknown	1

The manner in which it is advisable to deliver patients with transverse lie will be discussed in detail later, but in Table VII the perinatal loss is listed according to abdominal and vaginal delivery and as to premature and mature infants. It can be seen that the number of infants lost by either method of delivery is about the same, but the percentage is very different since more patients were delivered by cesarean section than by vaginal delivery, 330 and 96 respectively. Thus, the total percentage lost by cesarean section was 10.2 per cent, whereas in vaginal delivery 35.4 per cent of all infants succumbed.

The vaginal delivery of a transverse lie is usually accomplished either by version and extraction or by the conversion of the transverse lie to a longitudinal presentation. These two methods of delivery have been analyzed in greater detail in Table VIII. There were 96 infants delivered vaginally, and of these 60 were delivered by version and extraction, with a total perinatal mortality of 36.7 per cent. Of those infants delivered by version and extraction, 45 per cent were premature with a perinatal loss of 59.3 per cent, and 55 per cent were mature with an 18.1 per cent perinatal loss. The majority of the mature infants who were delivered by version and extraction were associated with a prolapse of the umbilical cord or with patients who entered the hospital in advanced labor. The second part of Table VIII is of considerable interest, for here are listed the vaginal deliveries that occurred after the transverse lie had converted to a longitudinal presentation. Five of these infants were delivered as breech presentations and 31 were delivered as vertex presentations. All five breech presentations were premature, weighing under 2,000 Gm. Of these, 3 babies were lost as stillbirths. Twenty of the 31 vertex vaginal deliveries were mature infants, and of these only 1 infant was lost for a perinatal loss of 5 per cent. This one loss was a stillbirth associated with a prolapsed cord. The mother had entered the hospital in advanced labor.

It would seem from the figures presented that it is advisable for patients with transverse lie presentations to be allowed to go into spontaneous labor rather than perform an elective section, if no complication is present. Some of these patients, 36 out of 426, converted spontaneously to a longitudinal type of presentation.

There were 330 patients delivered by cesarean section. The types of cesarean section and the associated perinatal losses are listed in Table IX. The low-segment section was used in the majority of the cases, apparently indicating that today most operators prefer this type of section and do not believe that the classic type is mandatory for the delivery of a transverse lie. It is interesting that the perinatal loss in primary cesarean section is almost double when the

TABLE VII. Perinatal loss according to type of delivery

Type of Delivery	Premature		Mature		Total	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Cesarean	27	28.3	6	2.6	33	10.0
Vaginal	27	62.8	7	13.2	34	34.4

TABLE VIII. Vaginal deliveries

Deliveries	Total Cases Number	Total Cases Per Cent	Perinatal Mortality Number	Perinatal Mortality Per Cent
Version and extraction				
Premature infants	27	45.0	16	59.3
Mature infants	33	55.0	6	18.1
TOTALS	60	100.0	22	36.7
Other deliveries				
Premature infants	16	44.4	11	68.7
Mature infants	20	55.6	1	5.0
TOTALS	36	100.0	12	33.3

TABLE IX. Cesarean sections

			Perinatal Loss			
	Total Cases		Primary		Repeat	
Types	Primary	Repeat	Number	Per Cent	Number	Per Cent
Low cervical	166	36	12	7.2	2	5.5
Classical	97	18	13	13.5	1	5.5
Cesarean hysterectomy	10	2	3	30.0	1	50.0
Extraperitoneal	. . .	1	. .	. . .	1	100.0
TOTALS	273	57	28	10.3	5	8.6

classic type is employed in comparison with the low-segment operation. However, it must be appreciated that some of these presentations were complicated by placenta previa in which the classic section is employed by many operators.

A cesarean hysterectomy was employed 12 times, and the indications for the hysterectomies were as follows: 9 cases had the procedure performed for sterilization, 2 cases because of multiparity and associated myomata uteri, and 1 case because of a rupture of the uterus. It is of interest that no cesarean hysterectomy was performed because of sepsis.

It has been stated that possibly 1 of the etiologic factors for the causation of transverse lie is a contracted pelvis. Three hundred and twenty-eight of these pelves were classified. Forty-one or 12.5 per cent of these pelves were known to be contracted. This incidence of contraction is several times greater than anticipated in this population as a whole. Thirty-eight of the 41 cases of contracted pelves were delivered by cesarean section, and 3 were delivered by version and extraction associated with premature infants. There were no maternal deaths in the entire series.

Comment

Transverse lie is a condition almost always associated with multiparity. The explanation for this may be the relaxed abdominal wall which does not support the uterus, a condition found also in the primigravida, and therefore allows for a greater mobility of the fetus with a decreased tendency to adapt to the longitudinal presentation.

Placenta previa is associated with this entity in a great percentage of the cases, 18 per cent in our own series. Therefore, with the knowledge of a transverse lie, one should always be on the alert for the possibility of placenta previa and be prepared to treat the patient accordingly.

The high incidence of prematurity, almost one third of all the cases, is a big contribution to the high perinatal loss in this entity. The number of neonatal deaths is about double those during labor, and this, to a large degree, is due to the high incidence of prematurity. Thus, 90 per cent of the neonatal deaths were associated with prematurity.

In cases of transverse lie the most favorable type of delivery for the welfare of the baby, as well as the mother, is cesarean section. The over-all perinatal loss from vaginal delivery is three and one-half times that obtained by cesarean section. Although cesarean section has a much better over-all perinatal survival than vaginal delivery, it must be appreciated that there are certain cases that rightly can be delivered vaginally. The small premature infant, particularly associated with advanced labor and a prolapsed cord that may not be pulsating, could well be delivered vaginally. Moreover, even in the mature group that enter the hospital in advanced labor and with intact membranes, there is a place for vaginal delivery by means of version and extraction. However, these cases are relatively few, and one must realize that even in the mature group delivered by version and extraction there is a high perinatal mortality, almost 30 per cent.

The question of doing an elective cesarean section on a known term transverse lie prior to the onset of labor has not been answered definitely. It would appear from our report that it is advisable to allow the uncomplicated case of transverse lie to enter labor spontaneously to ascertain whether or not spontaneous conversion to a longitudinal presentation will occur. If spontaneous conversion does take place, then one can anticipate in the mature infant a very satisfactory perinatal survival. On the other hand, if the patient does not convert the presentation immediately after the onset of labor, procrastination should not take place, but an abdominal delivery should be performed. However, spontaneous conversion of a transverse lie of a term infant to a longitudinal presentation is very rare. Therefore, there can be little disagreement with those who would perform an elective cesarean section on all cases of transverse lie at term.

It would appear that most operators today prefer the low-segment section in the uncomplicated case of transverse lie. However, one should caution that if the fetal back is directed downward, it may be difficult to deliver the infant through this type of incision. The position of the transverse lie should be known prior to the cesarean section so that the most advantageous uterine incision will be used. Therefore, a scout roentgenogram of the abdomen is indicated in every case of suspected or known transverse lie.

Summary

1. A series of 426 cases of transverse lie of the fetus have been presented.

2. Placenta previa, prolapse of the umbilical cord, and contracted pelvis are associated with this entity in a markedly increased incidence.

3. Prematurity, present in 32.2 per cent of the infants, was the greatest single cause of the perinatal loss.

4. Cesarean section should be the method of delivery in most cases. However, vaginal delivery may be performed in a few properly selected cases.

5. The patient with an uncomplicated term transverse lie may be allowed to go into spontaneous labor to determine whether or not a spontaneous conversion to a longitudinal presentation will occur. If conversion does not occur at once, a cesarean section should be performed.

6. A scout roentgenogram of the abdomen should be done in all cases to determine the position of the fetus.

ACKNOWLEDGMENT. We acknowledge and appreciate the cooperation of the following physicians who helped to make this study possible: Irving Cushner, M.D., Baltimore City Hospital; William Levine, M.D., Beth-El Hospital; Duncan Reid, M.D., Boston Lying-In Hospital; E. Stewart Taylor, M.D., Colorado General Hospital; C. Lee Buxton, M.D., Grace-New Haven Community Hospital; Alexander Rosenthal, M.D., Long Island Jewish Hospital; Edward Solomons, M.D., Maimonides Hospital of Brooklyn; Alan Guttmacher, M.D., The Mt. Sinai Hospital; Isadore Siegel, M.D., Sinai Hospital of Baltimore; Arthur Haskins, M.D., University of Maryland; and Louis Hellman, M.D., Kings County Hospital.

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Effectiveness of Aerosol Administration of Ergotamine Tartrate in Migraine Headache[*]

FORTY-EIGHT PATIENTS *with migraine headache and 2 patients with headache of vascular origin were treated with aerosol administration of ergotamine tartrate. Of a total of 261 headaches treated, 82 per cent were relieved, 65 per cent completely. Relief was obtained in from fifteen to thirty minutes—more rapidly than with either rectal or oral administration and as quickly as with the parenteral method. Side-effects were noted in 10 per cent but necessitated discontinuance of the medication in only 1 case. Convenience of administration, rapidity of results, and degree of relief obtained made this the method of choice of 72 per cent of the patients studied.*

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THE RELIEF OF migraine headache has always presented the practitioner with a difficult problem. In 1883, Eulenburg[1] first described the value of ergotamine tartrate in the treatment of migraine headache. Subsequently, its use has been reported by many observers and is well documented by Friedman, Von Storch, and Araki.[2] During the past twenty-five years this medication has been accepted as the drug of choice in the treatment of hemicrania (migraine headache). It is generally conceded that to date the mode of administration has been the major problem in the use of ergotamine tartrate. In an effort to find an effective and more practical method of administration, aerosol inhalation has been developed. The current study reports our experience with this new method of administration: aerosolized ergotamine tartrate delivered across the epithelium of the respiratory tract.

Methods of administration

PARENTERAL INJECTION. Parenteral injection is undoubtedly the most effective mode at present. The subcutaneous route is the most practical, but it is accompanied by all the hazards of injection and by the highest incidence of side-effects associated with the drug.

ORAL AND SUBLINGUAL. The major drawbacks to oral and sublingual administration are the relatively long time required for relief (from one to five hours),[3] the frequent failure in severe attacks, the unpredictability of absorption, and the local and central nervous system effects that produce nausea and vomiting. In a summary of the literature, Friedman, Von Storch, and Araki[2] give the incidence of side-effects as 10 per cent. However, Goodman and Gilman[5] state that side-effects occur "in a large number of patients," and in our experience we have found the percentage more than double that given by Friedman.

RECTAL SUPPOSITORIES. The rectal suppository mode of administration is also accompanied by an unpredictability of absorption plus its inconvenience and esthetic unacceptability. In general, this has been the most practical method of administration until now.

AEROSOL ADMINISTRATION. By the aerosol administration method the ergotamine tartrate is delivered per os to the respiratory tract epithelium, and apparently is absorbed rapidly into the systemic circulation. The

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[*] This study was supported by a grant from the Riker Laboratories, Inc., Northridge, California.

TABLE I. Frequency distribution of cases and headaches

Number of Headaches per Month	Number of Cases Treated	Per Cent of Cases	Number of Headaches Treated	Per Cent of Headaches
1 to 2	34	68	171	65.5
2 to 3	7	14	48	18.4
4 to 6	4	8	20	7.7
6 to 8	2	4	11	4.2
8 to 12	2	4	7	2.7
Other	1	2	4	1.5
TOTALS	50	100	261	100.0

aerosol inhaler* is a simple plastic device using Freon as a propellent to deliver micronized ergotamine tartrate. This propellent has been studied carefully, and its toxicity is reportedly less than that of carbon dioxide. Each depression of the metering valve delivers a dose of 0.36 mg. of ergotamine tartrate at the orifice of the adapter.

The ergotamine tartrate is micronized with 90 per cent of the entire mass in particles less than 7 microns in diameter and a mass median diameter of 3.5 microns.[4] The small particle size allows the ergotamine to be presented readily to the respiratory tract membranes and then carried by the circulation to its point of action. The patient is instructed to: (1) place the long end of the adapter deep inside the mouth and on the extended tongue, the vial being above the adapter. Close the lips around the mouthpiece; (2) after a slightly forced expiration and at the onset of a deep inspiration, the fingers press the vial against the adapter, releasing the metered dose; (3) the breath is held in deep inspiration for as long as is comfortable, and then exhaled slowly. This method undoubtedly requires an intelligent patient or absorption will not be achieved. This is illustrated in our study.

Pharmacophysiology of ergotamine tartrate

The beneficial effects of ergotamine tartrate are apparently produced by a vasoconstriction of the extra- and intracranial branches of the external carotid artery. The site of action appears to be on the smooth musculature of the vessels. The contractile effect is exerted on all smooth musculature and accounts for many of the side-effects when ergotamine tartrate is used. Among the side-effects are: nausea and vomiting, intestinal and uterine spasm, muscle spasm, numbness and tingling of the extremities, as well as substernal pain due to coronary vasoconstriction. These reactions are merely lesser manifestations of the toxic effects, which are thromboses in vessels, gangrene of the extremities (so-called ergotism), and reportedly coronary occlusion.[5] Therefore the use of ergotamine tartrate would be contraindicated in the presence of peripheral vascular disease, coronary artery disease, impaired hepatic function, thyrotoxicosis, asthma, and pregnancy.

Results

This study reports the results of the use of aerosolized ergotamine tartrate in the treatment of 48 patients with well documented cases of migraine headache and 2 patients with headaches of vascular origin. A total of 261 headaches were treated, and Table I shows their frequency of occurrence.

Table II summarizes the degree of relief obtained. The data by the number of headaches relieved are more accurate than are those by the number of cases because several patients fell into more than one category, and in these instances they were always included in the lower degree of relief.

Comment

Despite the fact that all patients were given adequate instruction (a demonstration

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* Medihaler supplied by Riker Laboratories, Inc., Northridge, California.

TABLE II. Incidence and degree of relief obtained

Degree of Relief	Number of Cases	Per Cent of Total	Number of Headaches	Per Cent of Total
Complete*	29	58	170	65.1
Partial†	9	18	44	16.9
None	12	24	47	18.0
TOTALS	50	100	261	100.0

* Complete—total relief obtained within thirty minutes.
† Partial—marked decrease in frequency and/or severity of pulsations.

and written directions), 2 patients did not use the instrument correctly and are included among the failures. One patient eventually used the device properly, and then obtained relief; the other had previously been relieved by ergotamine tartrate via other methods of administration. Although some patients required three inhalations, the majority found that two were sufficient to obtain relief, and 2 isolated cases were relieved by a single inhalation.

As with all other modes of ergotamine therapy, the best results were obtained when the drug was administered at the onset of the headache. In all cases where relief was obtained, the patients reported that the headache subsided in from fifteen to thirty minutes. This equals the results obtained with the parenterally administered agent and is much more rapid than that obtained by either oral or rectal erogtamine tartrate. Of the 41 patients relieved by using the aerosol inhaler, 36 reported that the results were far superior to those obtained from the oral or rectal routes. The headaches were alleviated completely with only 2 inhalations of the aerosol in 1 patient who previously had responded only to the parenteral route.

Side-effects in this series were observed in 5 of the patients treated. The most serious was vomiting in 1 case, and after three trials, the patient refused further use of the medication. Three subjects reported mild nausea which did not necessitate discontinuance of the drug, and 1 complained of a slight vertigo which was transient. It should be noted that in this study, ergotamine tartrate was used without any adjuvant drugs such as caffeine, belladonna, alkaloids, or barbiturates.

Summary

Fifty patients with migraine or vascular headaches were treated with ergotamine tartrate by a new method: aerosol administration.

Of the 261 headaches treated, 82 per cent were relieved, 65 per cent completely.

Relief was obtained more rapidly than with either rectal or oral administration, and as quickly as with the parenteral method.

The convenience of administration, the rapidity of results, and the degree of relief obtained made this the method of choice of 72 per cent of the patients studied.

Side-effects were noted in 10 per cent, and in all instances they were minimal.

The results of this study indicate that aerosol inhalation is both a practical and an effective method for the administration of ergotamine tartrate.

ACKNOWLEDGMENT. We are indebted to Miss Ruth Raisly for her invaluable help in the preparation of this manuscript.

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Carcinoma of the Endometrium*

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In the ten years 1951 to 1960 inclusive 82 women with cancer of the endometrium were seen at Bellevue Hospital. This is too small a number to give statistically significant figures, but an analysis of these cases can serve as a text to point out some of the interesting observations made by us and by others bearing on the etiology of this disease.

Ratio of carcinoma of the endometrium to carcinoma of the cervix

During the same ten-year period there have been 482 women at Bellevue suffering from carcinoma of the cervix uteri. This is a ratio of 1 to 5.9. Comparison with the figures at the University Hospital only a few city blocks distant is interesting. Here 245 cases of carcinoma of the endometrium and 229 cases of carcinoma of the cervix were seen in ten years, a ratio of 1 to 0.93. The obvious difference in the two institutions is one of economic status, Bellevue serving the poorest and most destitute while a large proportion of the patients at the University Hospital are private. The financial difference between the patients at the two hospitals may be irrelevant, however, covering up the really significant ones of color and race.

To get a truer picture of the incidence of carcinoma of the endometrium compared with that of the cervix we have turned to the 1959 Annual Report of the New York State Bureau of Cancer Control.[1] Cancer is a reportable disease in New York State outside New York City. In 1959, 1,287 cases of carcinoma of the cervix and 714 cases of carcinoma of the endometrium were reported, or 1 case of carcinoma of the endometrium to every 1.8 cases of carcinoma of the cervix. If we examine the age-standardized cancer incidence rates, we find that the incidence of cancer of the cervix in 1942 was 25.22 per 100,000, of carcinoma of the endometrium 14.19, giving a ratio of 1:1.78. In 1959 the figures were for cervix 29.78 per 100,000, for endometrium 16.63, giving a ratio of 1:1.79.

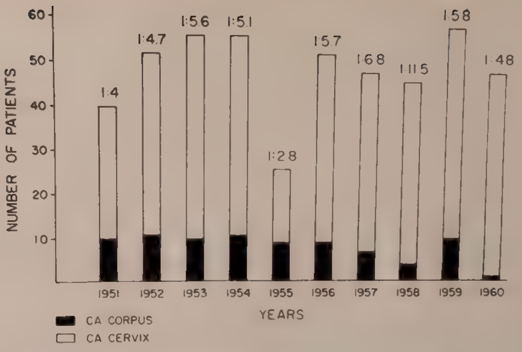

FIGURE 1. Incidence of carcinoma of the corpus and of carcinoma of the cervix at Bellevue Hospital.

Two things are obvious from these figures; first, that it is unsafe and misleading to draw inferences about the over-all occurrence of cancer of the cervix and endometrium using the clinic population of large city hospitals where a great deal of selection of patients may have taken place by the very nature of the institutions. The second conclusion is that the increasing incidence of carcinoma of the endometrium, which has been rather generally mentioned, does not seem to be very marked in New York State.

In Figure 1 the cases of carcinoma of the endometrium and of carcinoma of the cervix seen at Bellevue each year since 1951 are diagrammed to illustrate the fact that while some years ago there were usually more than 10 cases a year of endometrial cancer and 40 to 55 cases of cancer of the cervix, in the last three years there have been only 15 cancers of the endometrium even though the number of cancers of the cervix remained high, 152.

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Obstetrics and Gynecology, May 12, 1961.

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TABLE I. Incidence of carcinoma of the endometrium at Bellevue Hospital

Group	Number of Patients	Per Cent
Jewish	12	14.6
Other white	56	68.3
Negro	10	12.2
Puerto Rican	4	4.9
Totals	82	100.0

Relationship of carcinoma of the endometrium to race and color

In noting the fall off in cases of carcinoma of the endometrium in the last three years, we speculated about possible causes for this change. The most obvious shift in the hospital population on the Gynecological Service at Bellevue is the recent increase in the number of Puerto Rican women as compared with Jewish, "other white," or Negro women. No exact figures are available, but recent casual observations on the wards indicate that over 50 per cent of the patients are Puerto Rican.

A study of the birthplaces of the 82 women with endometrial carcinoma showed that only 4 or 4.9 per cent were born in Puerto Rico. This compares with 31 per cent of the 482 cervix cases. Twelve of the 82 or 15 per cent were Jewish, 10 or 12 per cent were Negro, and 56 or 68 per cent were "other white" (Table I).

A search for confirmation of this possible observation that cervical cancer is common and endometrial cancer rare in Puerto Ricans revealed a study done by Haenszel and Hillhouse[2] on uterine cancer morbidity in New York City in 1952. These authors through the cooperation of all the hospitals of the city were able to get almost complete figures. Some of their results, shown in Table II, are quite startling. Notice, for instance, that in age-adjusted incidence rates cancer of the endometrium is only about half as frequent in Puerto Ricans as it is in Jewesses, whereas cancer of the cervix occurs 27 times as frequently in Puerto Ricans as it does in Jewesses.

FROM 1951 TO 1960 82 WOMEN *with cancer of the endometrium were seen at Bellevue Hospital, as compared with 482 women with carcinoma of the cervix, a ratio of 1 to 5.9. New York State statistics showed a ratio of 1 to 1.8. The difference is attributed to the large proportion of Puerto Ricans admitted to Bellevue in whom the incidence of carcinoma of the endometrium is low and that of carcinoma of the cervix high. The average age of the patients was 62.6. Although 48.8 per cent of the patients were admitted within six months of the first symptoms, 26 per cent waited over a year. The age at the menopause had no effect on causation of endometrial carcinoma. There was a lack of fertility in the patients. The majority were obese, suggesting that estrogens might be stored in the body fat, smoothing out the normal peaks of estrogen excretion. Obese women were shown to excrete less isotopically labeled estradiol in three days than thin women. Experimentally 4 of 20 rabbits implanted with 25-mg. pellets of estradiol developed carcinoma of the endometrium in two hundred nineteen to five hundred ninety-seven days—the mechanism of this is not clearly understood.*

TABLE II. Age-adjusted incidence rates per 100,000 females, New York City, 1952[2]

Group	Cervix	Endometrium	Ratio
Jewish	3.6	15.2	0.23
Other white	13.5	12.6	1.07
Puerto Rican	97.6	7.8	12.5
Negro	47.8	9.2	5.19

Cintrón-Rivera[3] of Puerto Rico says that in the period 1949 to 1958, 3,227 new cases of cancer of the cervix uteri were reported in Puerto Rico. This represents 24.1 per cent of all cancers in females. During the same period of time 229 cases of carcinoma of the corpus uteri were reported or 1.7 per cent. The ratio in Puerto Rico of endometrial carcinoma to cervix carcinoma is 1:14.1.

The conclusion seems justified, therefore, that the incidence of carcinoma of the endometrium is high in Jewesses and low in Puerto Ricans and that the reverse is true for cancer of the cervix. The occurrence rate of either of these diseases in a given hospital will depend to some extent on the racial backgrounds of the people from which it draws its clientele.

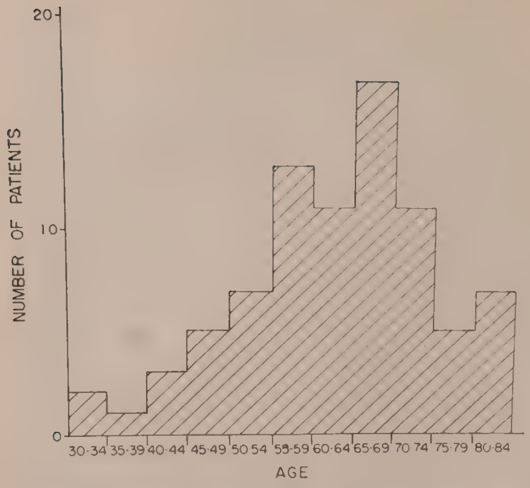

FIGURE 2. Age distribution of patients with carcinoma of the corpus, Bellevue Hospital.

Age

Figure 2 shows the ages of the 82 patients with carcinoma of the endometrium. The average was 62.6. A study of 201 cases at the Sloane Hospital for Women showed an average age there of fifty-seven years.[4] The average for the State of New York for 1958 was 61.4.[5] Perhaps the older and poorer patients have a tendency to go to the large city hospital.

The youngest patient in the present group was thirty-two, the oldest was eighty-four years.

Diagnosis and delay in diagnosis

Table III gives the delay between the onset of symptoms and admission to Bellevue Hospital. Forty (48.8 per cent) were admitted within six months of the appearance of the first symptom. What is always disturbing is to see the large numbers of patients who delay unusually long through ignorance, fear, neglect, or bad medical advice. In the present group 21 or 26 per cent waited over a year from the onset of bleeding to admission to the hospital.

This statistic allows us to emphasize once again our firm conviction that endometrial biopsy with such an instrument as the Novak curet is an easy and practical office procedure which in the majority of cases will confirm the diagnosis at the time of the patient's first visit. An endometrial biopsy curet should be among the sterile supplies of doctors carrying on general physical examinations in women over the age of thirty-five. Carcinoma of the endometrium is quite curable in its early stages. Doctors who take the trouble to make early diagnoses can save the lives of thousands while advances in radical surgery or chemotherapy are saving or prolonging the lives of tens.

TABLE III. Delay from onset of symptoms to hospital admission

Months of Delay	Number of Patients
Less than 1	27
1 to 6	13
6 to 12	12
Over 12	21 (26 per cent)
Not recorded	9
	—
TOTAL	82

Evidence for a hormone factor in the etiology of carcinoma of the endometrium

CLINICAL ASPECTS. Studying the records of financially destitute patients, many of whom were senile or psychotic, when no protocol aimed at uncovering a hormonal role has been followed by those who have taken the histories, leaves much to be desired if one is looking for possible evidences of endocrine stimulation ten years or more prior to the onset of uterine cancer. For instance, 2 patients gave histories of previous ovariectomies in other hospitals, but the nature of the tumor removed was unknown by the patient and untraceable. Two other patients were said to have been operated on for "tumors of the womb" twenty-two and thirty-four years before admission. It is possible that hidden in these 4 cases there may be a granulosa cell or theca cell tumor. We are aware of no proved case in our material, however, in spite of all that has been written on the apparent etiologic relationship of the one to the other.

If one searches for menstrual irregularities, again the results are disappointing. The onset of menstruation averaged 13.5 years (median thirteen). The duration was from three to five days in 72 per cent, less than

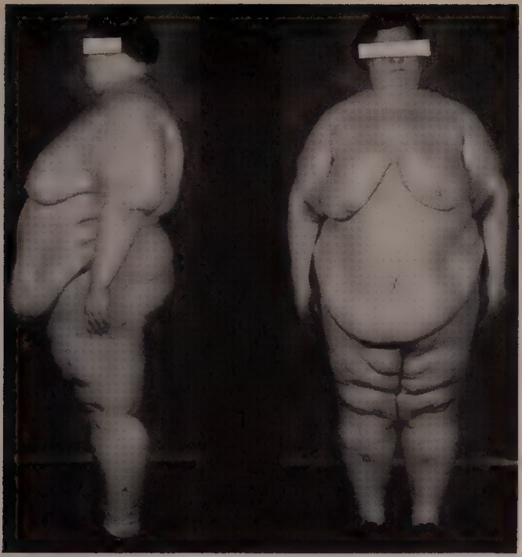

FIGURE 3. An obese patient who suffered from carcinoma of the endometrium; cured successfully by hysterectomy over seven years ago.

five days in 9 per cent, and more than five days in 19 per cent. The interval was from twenty-six to thirty days in 91 per cent, less than twenty-six days in 5 per cent, and irregular in only 2 patients.

Menopause. The age at the menopause was thought by Corscaden and Gusberg[6] to be later in women who subsequently developed carcinoma of the endometrium than in the general population (fifty-three versus forty-eight years) and indeed this was also our clinical impression. However, in the present study there were 57 women who had passed the menopause when they were admitted for uterine cancer, of whom 29 had the menopause before the age of fifty and 28 at fifty or over. The average age at the menopause of all was 48.4 years.

It occurred to us that if anovulatory cycles at or near the menopause played a role in the causation of endometrial carcinoma, the women with early menopause might show their cancers earlier than those who ceased menstruating later. Consequently, we examined the 29 who stopped their periods before the age of fifty and found that they waited an average of twenty-two years (median twenty-one) to develop their cancers. Their average age when they came to the hospital was 65.4. Patients who had their menopause at fifty or over numbered 28,

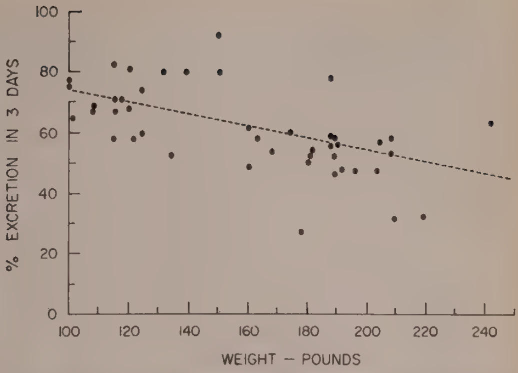

FIGURE 4. Excretion of C^{14}-labeled estradiol by women.[9]

and they waited an average of 13.1 years to develop clinical carcinoma (median twelve). Their average age when they came to the hospital was sixty-six. At least in our material the menopause seems to play no causative role.

It has been mentioned frequently that patients with carcinoma of the endometrium are more apt to be single, or, if married, sterile, than women who do not develop this disease. Of 82 women 10 or 12 per cent were single. Of 74 women giving reliable data, 21 or 28 per cent had never borne children. These same 74 women gave birth to 150 children or 2.03 children per patient. The lack of fertility in this group is confirmed by these observations, but neither the single state nor the sterility is as great as has been recorded by many other authors.

Twelve patients or 14.6 per cent had diabetes.

Obesity

Patients with carcinoma of the endometrium tend to be obese. Of our 82 patients, weights were recorded on 34. The average weight was 169 pounds. One patient, who was successfully operated on, weighed 357 pounds (Fig. 3). In 14 additional cases the notation was made that the patient was "obese," but her weight was not recorded.

In contemplating the relationship of obesity to carcinoma of the endometrium and particularly after reading a paper by Davis and Plotz[7] recording their studies of the metabolism of C^{14}-labeled progesterone, it occurred to us that estrogens might be stored in the body fat and that this storage might smooth out the normal peaks of estrogen excretion, making an obese patient more continuously stimulated by her own estrogens than a thin woman. If it is long-continued low-level estrogenic stimulation which causes carcinoma of the endometrium to develop, then a fat patient may store her own estrogens in her own fat during times of high production by her ovaries and feed it out again into her blood stream when estrogenic production is low.

A recent communication from Liebelt[8] on this matter is of interest. Experimentally he has made some mice obese with gold thioglucose. Such obese females when castrated and starved go into a state of constant estrus as their fat is broken up and metabolized.

Pursuing this idea further, we have injected C^{14}-labeled estradiol in tracer amounts into 52 women and collected seventy-two-hour urines thereafter and measured the excreted radioactive material.[9] If the amount of radioactivity is plotted against weight, we find that there is a significant difference in excretion rate between fat and thin women (Fig. 4). The thinner the woman, the more of the metabolites of the injected estrogen does she excrete in three days.

In 2 preoperative patients who were moderately obese, radioactive estradiol was injected. At operation small quantities of fat were removed from the edges of the abdominal wounds. Appreciable amounts of radioactivity were found in these samples indicating fat storage.

Animal experiments

In 1938 Greene and Saxton[10] reported that Dutch rabbits in their colony developed carcinoma of the endometrium after being afflicted by a pregnancy toxemia which produced cirrhosis of the liver. The picture found on autopsy in these animals was one of chronic low-grade estrogenic stimulation, apparently the result of the failure of the rabbits to detoxify and excrete their own estrogens through their damaged livers.

In 1957 Meissner, Sommers, and Sherman[11] reported the production of six carcinomas of the endometrium in 18 rabbits injected repeatedly with diethylstilbestrol. The animals received 5 mg. of the drug in oil by subcutaneous injection once every three weeks for as long as forty-five weeks. Cancers appeared in from three hundred fifteen to six hundred sixteen days, the average being four hundred eighteen days.

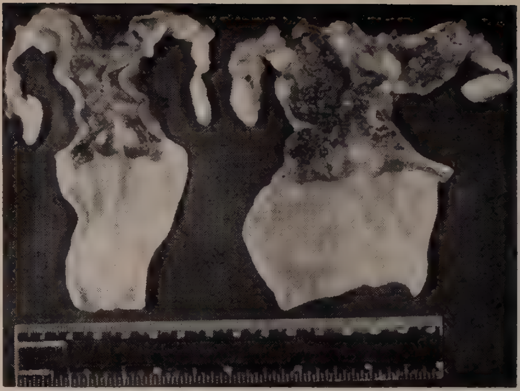

FIGURE 5. Two rabbit uteri from animals implanted with pellets of estradiol, 25 mg., two hundred nineteen days previously. Uterus on left shows hyperplasia of endometrium and polyp formation. Uterus on right shows carcinoma of endometrium which has metastasized to regional lymph node.

Our hypothesis was that the implantation of pellets of estradiol would provide a steadier dose level and perhaps would imitate our concept of possible estrogenic production of carcinoma of the endometrium in women better than repeated injections.

Female Dutch rabbits two to three months old were implanted with 25-mg. pellets of estradiol.* Of 20 rabbits which survived two hundred nineteen or more days, 4 showed carcinomas of the endometrium (Fig. 5), the slowest appearing after five hundred ninety-seven days. Two of these metastasized, one to a regional lymph node (Fig. 6A) and one to the peritoneum of the abdominal wall, the intestine, and the omentum (Fig. 6B).

While we had undoubtedly produced carcinoma of the endometrium by long-continued steady stimulation with a potent estrogen, the exact mechanism is not as clear-cut as one could wish. First, only 4 out of 20 animals showed cancer and, second, all animals implanted with the estogren pellet

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* The pellets were supplied by the Schering Corporation, Bloomfield, New Jersey, through the kindness of Edward Henderson, M.D.

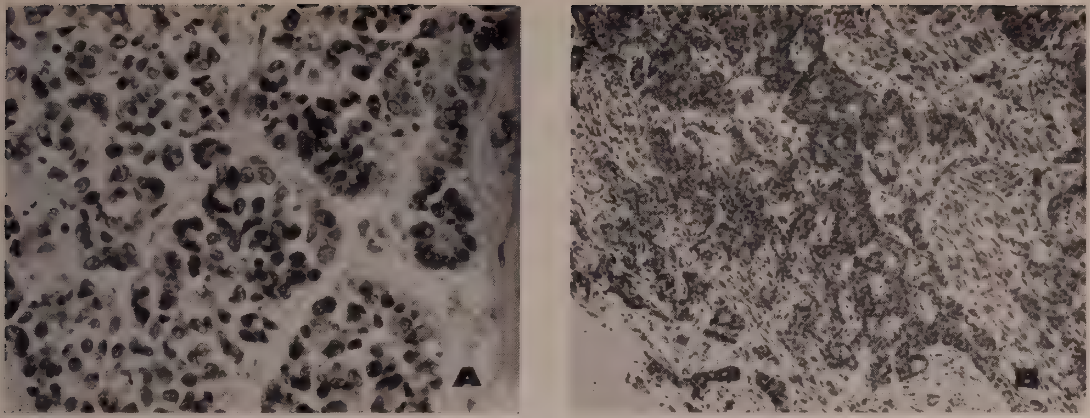

FIGURE 6. Rabbit implanted with pellet of estradiol, 25 mg. (A) Metastases to a regional lymph node. (B) Metastases to peritoneum of abdominal wall.

showed tremendous stimulation of their uteri accompanied by pyometra in some cases, polypoid endometritis, uterine horns distended with fluid , or even calcification of the uterine walls. Therefore it is impossible to be sure that the cancer is a direct result of the hormone stimulation rather than a secondary outcome of the abnormal changes in structure of the uterus produced by the hormone.

Summary

1. There have been 82 cases of carcinoma of the endometrium seen at Bellevue Hospital in the last ten years. During the same period there have been 482 patients with carcinoma of the cervix, a ratio of 1:5.9.

2. The number of cases of carcinoma of the endometrium seen annually seems to be decreasing. This may be because of the increasing proportion of Puerto Rican women in the city hospital population, since this study and others suggest that carcinoma of the endometrium is relatively rare among Puerto Ricans.

3. Twenty-one of the 82 cases had delayed a year or longer from the onset of symptoms to admission to the hospital. Our principal means of improving results in carcinoma of the endometrium is to try in every way to eliminate this delay.

4. A lowered fertility rate suggests an endocrine etiology for carcinoma of the endometrium. However, whether the menopause occurs early or late, women develop cancers at the same average ages.

5. Carcinoma of the endometrium occurs in obese women, the average weight recorded for our patients being 169 pounds. This may be because fat women store their own endogenous estrogens in their own fat, thus flattening out peaks and depressions in blood estrogens and so substituting steady for intermittent stimulation of their uteri.

Experimentally, fat women have been shown to excrete less isotopically labeled estradiol in three days than do thin women.

6. Four of 20 rabbits implanted with 25-mg. pellets of estradiol developed carcinoma of the endometrium in two hundred nineteen to five hundred ninety-seven days.

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Flank Cutaneous Ureterostomy and Ureteroureteral Cutaneous Neostomy

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CUTANEOUS URETEROSTOMY is recognized as a useful procedure for urinary diversion in selected cases. Abeshouse[1] has written a comprehensive review of this operation regarding the historical background, the advantages, the disadvantages, the indications, and the various technics up to 1948.

Various means to prevent the constriction and retraction of the cutaneous ureteral stoma by the use of skin flaps have been proposed by Abeshouse,[1] McDonald and Heckel,[2] Hudson, Wolan, and Marden,[3] Schinagel,[4,5] Obrant,[6] and others. In a review of 174 cases of cutaneous ureterostomy, Humphreys[7] stated that the end result did not seem to correlate with any type of stoma. He concluded that the neostomies with pliable mucosal lining offered a better functional prognosis than those with a lining of skin and that a ureter with ample length usually gave satisfactory postoperative results, regardless of the method of neostomy formation. Our experience supports the views of Humphreys. The excision of a disk of the entire abdominal wall at the site where the end of the ureter is brought to the skin surface appears to be an additional aid in the procurement of good function.

The end of the average-length ureter will not reach to the anterior abdominal wall without too much tension even when it is divided as close as possible to the bladder. When it is allowed to lie without tension and to conform to the retroperitoneal space, it will come adequately beyond the skin surface only in the anterior flank between the tip of the tenth or eleventh rib and the iliac crest.

Method of flank cutaneous ureterostomy

Such flank cutaneous ureterostomies have been performed on 10 patients by the following method (Fig. 1). An incision is made from a point midway between the tip of the twelfth rib and the iliac crest parallel to the fibers of the external oblique muscle and extending to the anterior midline. The anterior rectus sheath is transected, but it is usually unnecessary to divide the rectus muscle. The retroperitoneal space is entered, and the peritoneum is retracted medially. There is little difficulty in exposing and transecting the ureter well below the brim of the bony pelvis. The ureter with all possible surrounding adventitial tissue is dissected free from the peritoneum and psoas muscle. The dissection is carried superiorly to a point opposite the lower pole of the kidney. When it is allowed to conform to the curvature of the retroperitoneal space, a transected end of the ureter will reach to the surface near the posterior end of the skin incision with 2 to 4 cm. of its length beyond the skin level, at a point usually between the tip of the tenth or eleventh rib and the iliac crest. A disk of muscle, fascia, and skin about 2 cm. in diameter is excised from the abdominal wall at this point. The adventitia of the ureter is attached to the skin with 2 to 4 interrupted

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sutures of 000 chromic catgut. If the ureter has been distended, a number 6 or number 7 ureteral catheter is left in place for drainage. If the ureter appears normal or is relatively thick-walled from a long-standing obstruction and an adequate blood supply is in evidence by bleeding from the cut end, no catheter is inserted. The incision is closed in layers.

Indications for flank cutaneous ureterostomy

At the time of the preparation of this manuscript, 10 patients had been subjected to the procedure of flank cutaneous ureterostomy. Seven of the 10 patients developed healthy epithelialized stomas which arose from 0.5 to 1.5 cm. above the level of the skin surface, from three to eighteen months postoperatively. The remaining 3 patients were elderly and had advanced carcinomatosis of the bladder. The end of the ureter in each of these patients sloughed and retracted.

TEN PATIENTS *were subjected to flank cutaneous ureterostomy; 7 patients developed healthy epithelialized stomas from three to eighteen months postoperatively. The remaining 3 were elderly with advanced carcinomatosis of the bladder, and the end of the ureter in each of these patients sloughed and retracted. Indications for the procedure were: Pseudomonas pyocyanea infection, tuberculosis of the urinary tract, certain neurologic deficits, and inoperable cancer of the bladder. Ureteroureteral cutaneous neostomy was performed on 6 patients with cancer of the bladder and 2 patients with neurogenic bladders. The procedures provided a satisfactory means of total urinary diversion in 4 of 8 patients. The remaining 4 died of carcinomatosis too soon after operation to evaluate the procedure. Both procedures are useful methods of catheter-free urinary diversion with a low incidence of stricture and retraction of the ureteral stoma.*

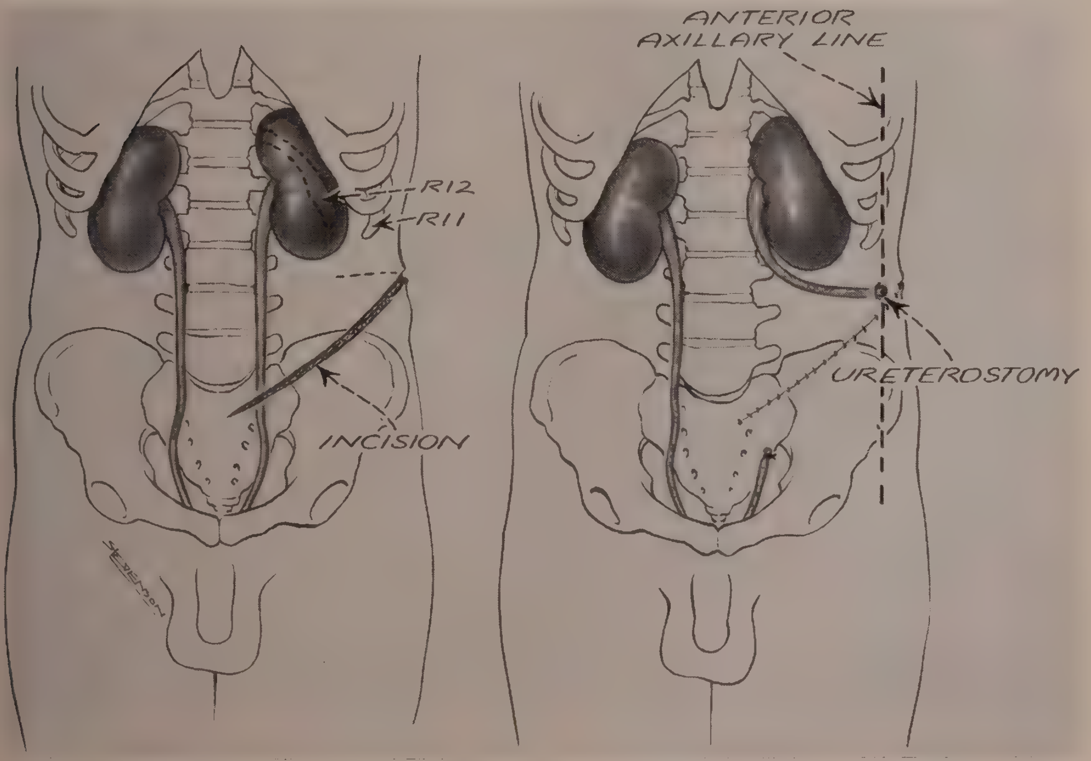

FIGURE 1. Incision and position of stoma for left flank cutaneous ureterostomy.

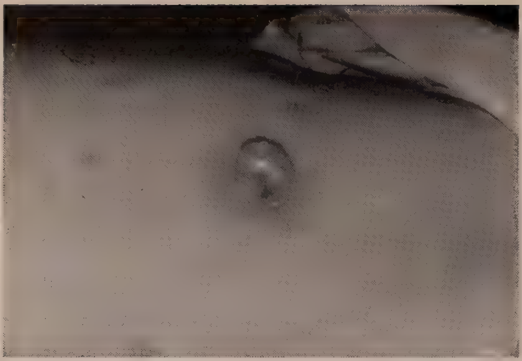

FIGURE 2. Position of ureterostomy on right flank with patient lying supine.

The procedure was first performed on a thirty-nine-year-old woman with a chronic Pseudomonas pyocyanea infection in a solitary right kidney resulting in marked contraction of the bladder and a stricture of the lower third of the ureter. The location and appearance of the stoma eighteen months following operation is shown in Figure 2.

Tuberculosis of the urinary tract of twelve years duration was considered an indication for a left flank cutaneous ureterostomy in a twenty-seven-year-old man who had undergone a right nephrectomy, developed a marked contracture of the bladder, and had left vesicoureteral reflux (Fig. 3A). The excretory urogram one month after operation is shown in Figure 3B. The appearance of the ureterostomy stoma with a Lapides apparatus in place fifteen months postoperatively is shown in Figure 3C. This patient has remained entirely symptom-free and has returned to full-time employment.

This type of urinary diversion has been found useful in selected patients with neurologic deficits. A nine-year-old child with a right nephrectomy and lumbar paraplegia as a result of an automobile accident had reflux into duplicated ureters of his remaining left kidney and was incontinent. The ends of the duplicated left ureters were brought to the skin surface of the left flank. The recurrent urinary infection subsided. An excretory urogram one year following the flank cutaneous ureterostomy was normal (Fig. 4). The stomas of the bifid ureters appeared healthy and almost completely epithelialized one year following operation (Fig. 5).

There is need for a simpler procedure than isolated ureteroileostomy and a less complicated procedure than ureterosigmoidostomy for palliative urinary diversion in the often poor-risk patient with inoperable cancer of the bladder. An example was a forty-year-old patient with inoperable bladder cancer whose right upper urinary tract did

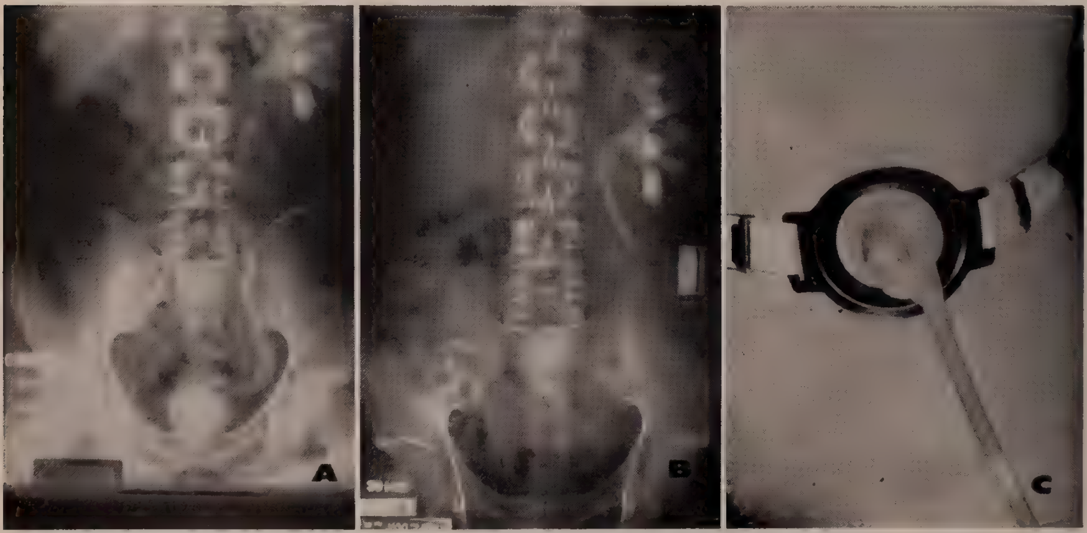

FIGURE 3. (A) Cystogram showing contracted bladder with left vesicoureteral reflux. (B) Intravenous pyelogram one month after left flank cutaneous ureterostomy. (C) Lapides drainage apparatus in place over ureterostomy.

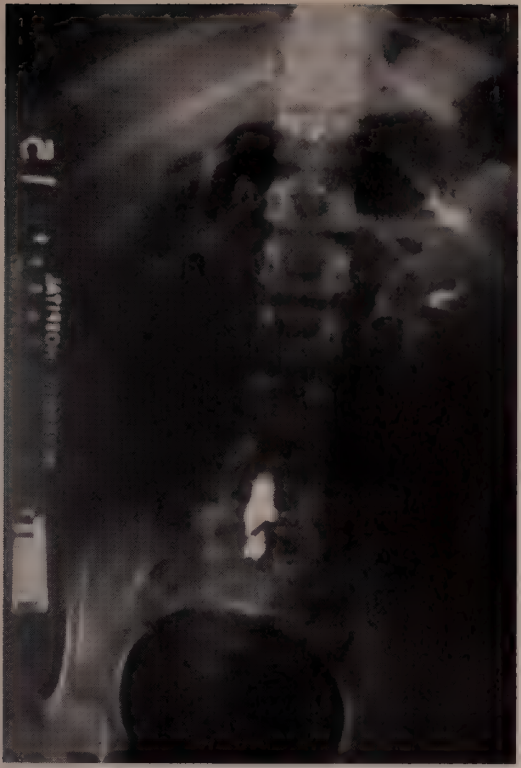

FIGURE 4. Intravenous pyelogram one year after left flank ureterostomy (fifteen-minute film).

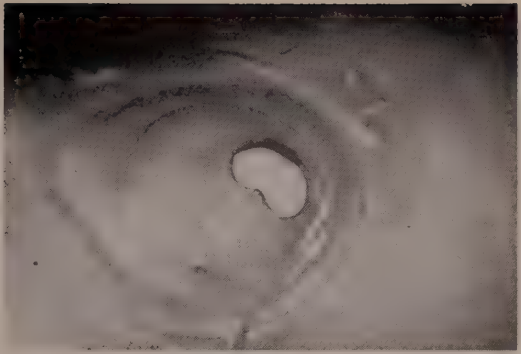

FIGURE 5. Ureterostomy of bifid left ureter one year after operation. End of incisional scar just inferior to end of eleventh rib.

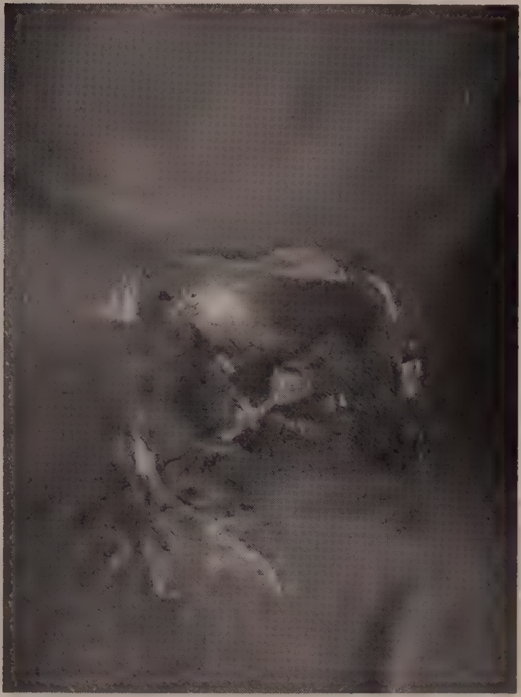

FIGURE 6. Left ureterostomy stoma five months after operation.

not visualize on excretory urography. The right ureter was ligated to prevent any drainage into the bladder from this side, and the end of the left ureter was brought to the flank. The stoma appeared healthy five months postoperatively (Fig. 6). In a similar manner, the left ureter was ligated in a seventy-five-year-old woman who had a vesicovaginal rectal fistula following treatment for cancer of the cervix, and the right ureter was brought through the right flank. The ureterostomy stoma was healthy and draining well three months postoperatively (Fig. 7).

The merit of this procedure would seem to be its relative simplicity in providing catheter-free drainage without the hazards of intestinal surgery and the complications which are encountered frequently when loops of bowel are used in urinary diversion. There is an additional advantage of having the renal pelvis readily available to catheterization if and when the necessity arises. The method is perhaps most useful when urinary diversion is indicated in the case of a single kidney. The application of a collection device has been no problem since the stoma is in the belt line, and any of the apparatuses used for ileal loop drainage have proved satisfactory.

Method of ureteroureteral cutaneous neostomy

After an apparent degree of success with the flank cutaneous ureterostomy, the

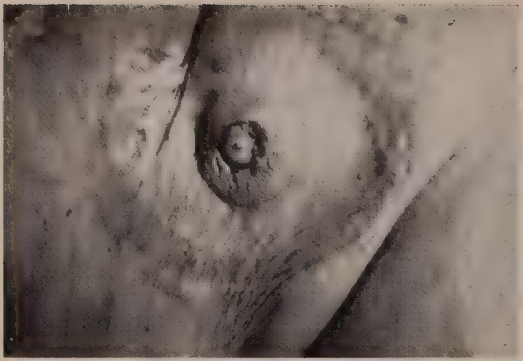

FIGURE 7. Ureterostomy of right flank three months after operation. Patient lying supine.

procedure was supplemented by bringing the opposite ureter across the midline to form a ureteroureteral cutaneous neostomy as first reported by Obrant in 1957.[6] This operation is performed through a transverse abdominal incision which is made above the level of the umbilicus (Fig. 8). The peritoneum is opened to facilitate retraction and exposure. Each end of the transverse incision will lie just below the end of the respective twelfth rib. The peritoneum is grasped at each corner of the wound and reflected medially so that the retroperitoneal space can be entered and one ureter brought to the skin surface according to the method described previously (Fig. 9). This can be done on either side. If one ureter is larger than the other, the end of the larger ureter is usually brought out as the cutaneous ureterostomy. A line of cleavage between the anterior surfaces of the aorta and vena cava and the posterior peritoneum is easily developed at a point between the inferior mesenteric artery and the gonadal vessels (Fig. 10). This is approximately anterior to the body of the third lumbar vertebra. After the end of the ureter is brought through this retroperitoneal space, an end-to-side single layer anastomosis is performed with 00000 chromic catgut making sure that a very slight amount of tissue has been included in the suture. No catheter is inserted into either ureter. A Penrose drain is left in the retroperitoneal space on

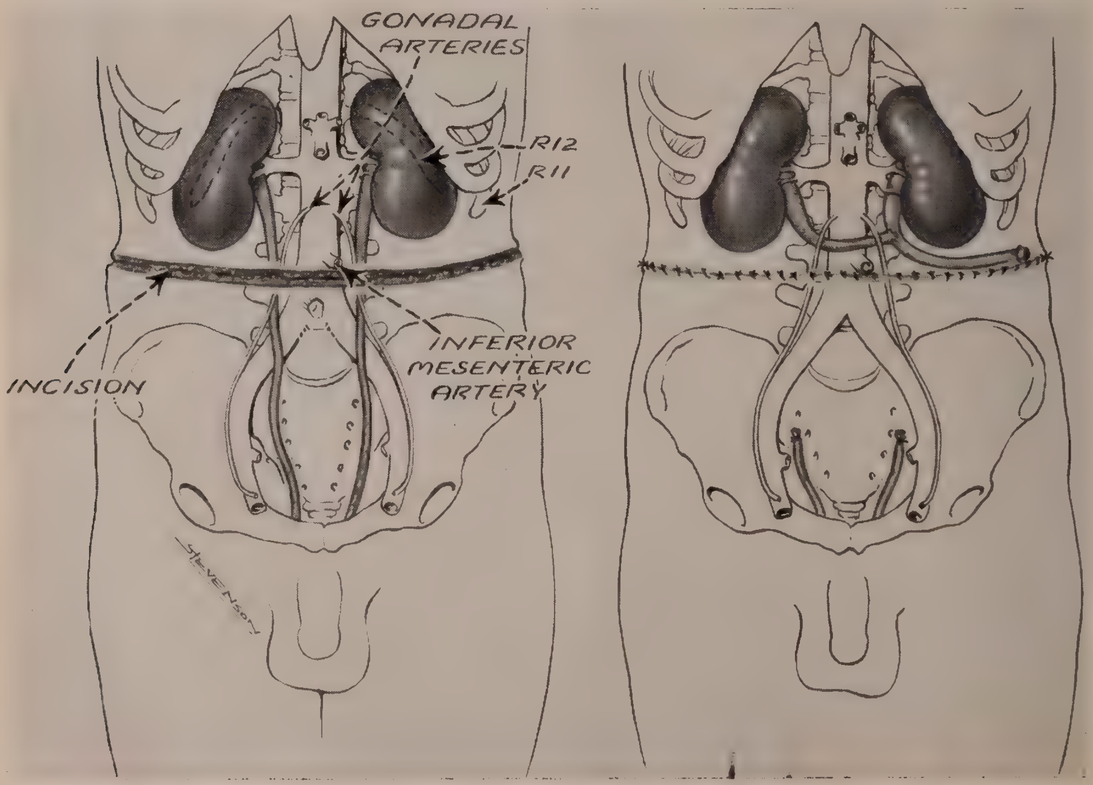

FIGURE 8. Incision and location of stoma for left ureteroureteral cutaneous neostomy.

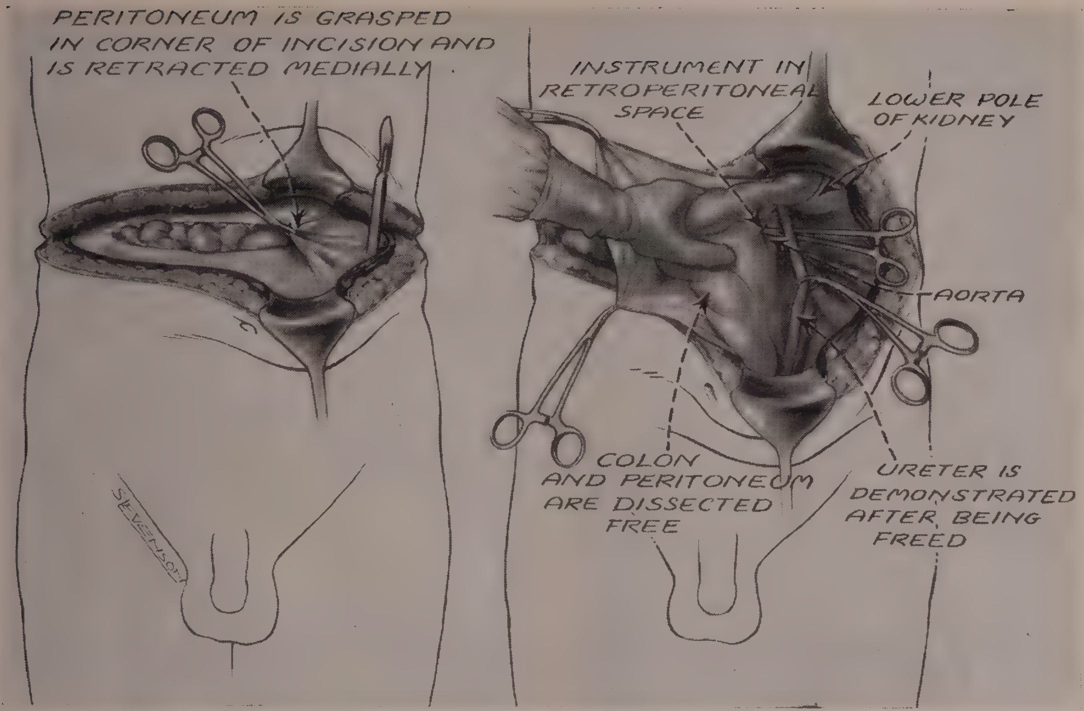
PERITONEUM IS GRASPED IN CORNER OF INCISION AND IS RETRACTED MEDIALLY
STEVENSON
INSTRUMENT IN RETROPERITONEAL SPACE
LOWER POLE OF KIDNEY
AORTA
COLON AND PERITONEUM ARE DISSECTED FREE
URETER IS DEMONSTRATED AFTER BEING FREED

FIGURE 9. Retracting peritoneum and descending colon to expose left ureter.

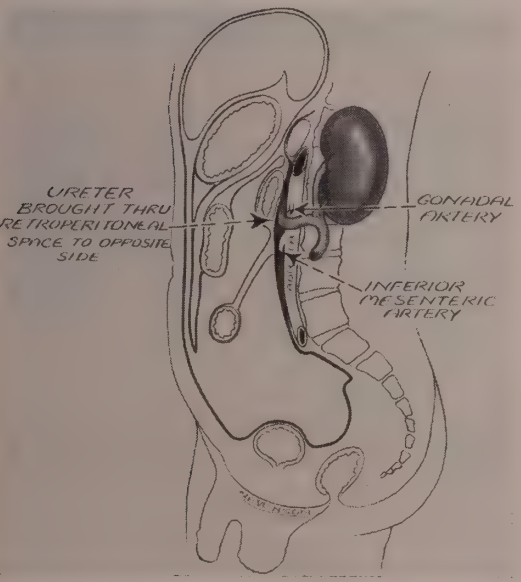
URETER BROUGHT THRU RETROPERITONEAL SPACE TO OPPOSITE SIDE
GONADAL ARTERY
INFERIOR MESENTERIC ARTERY
STEVENSON

FIGURE 10. Right ureter brought across midline anterior to great vessels in retroperitoneal space.

the side of the anastomosis and brought out through a stab wound about 2 cm. from the cutaneous neostomy. A Coloplast bag is applied to collect the urine.

Indications for ureteroureteral cutaneous neostomy

Ureteroureteral cutaneous neostomy was performed on 6 patients with inoperable cancer of the bladder and on 2 patients with neurogenic bladders as a result of permanent neurologic deficit with incontinence and vesicoureteral reflux.

This method of urinary diversion was first used on a fifty-nine-year-old man who had marked urinary symptoms with hematuria secondary to a large inoperable cancer of the bladder. He withstood the procedure quite well. His ureterostomy was draining satisfactorily, and his blood urea nitrogen was 10 mg. per 100 ml. on the fourth postoperative day when he died from bronchopneumonia. A second patient with a large inoperable cancer of the bladder withstood the procedure well but died with a massive coronary occlusion on the ninth postoperative day.

Ureteroureteral cutaneous neostomy was thought to be a suitable means of urinary diversion in a seventy-five-year-old man again with a massive inoperable cancer

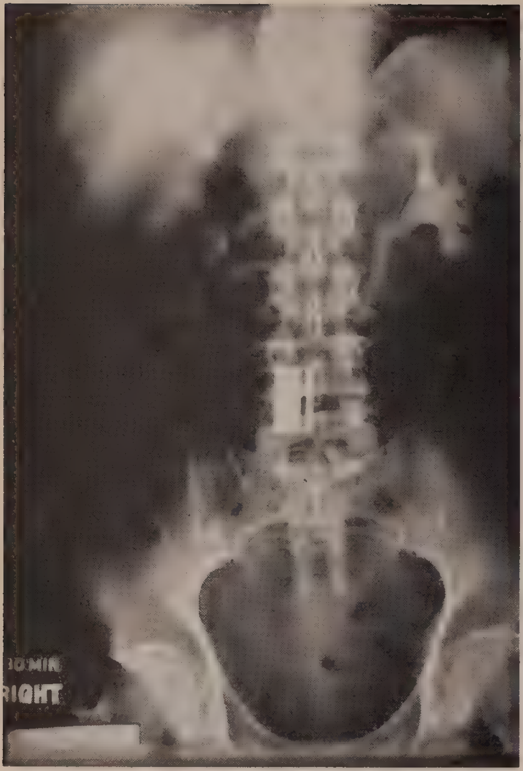

FIGURE 11. Thirty-minute film of intravenous pyelogram three weeks after right ureteroureteral cutaneous neostomy.

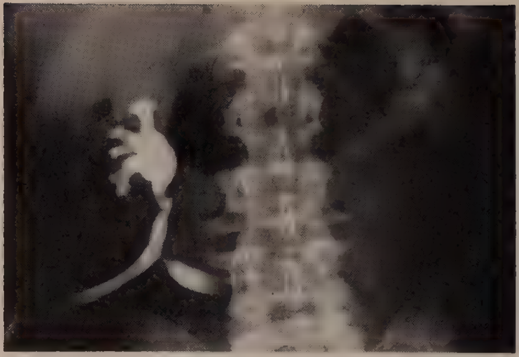

FIGURE 12. Retrograde urogram showing constriction at ureteroureteral anastomosis, but some of opaque medium can be seen in left kidney.

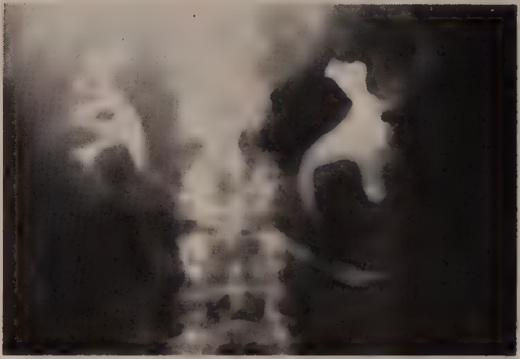

FIGURE 13. Retrograde urogram through neostomy showing relatively normal pelves and ureters.

of the bladder associated with marked urinary symptoms and gross hematuria. The right upper urinary tract did not visualize on an excretory urogram prior to operation. The procedure was performed on June 20, 1958. The ureteral catheters were removed on July 1, 1958. An excretory urogram on July 12, 1958, showed a mild dilatation of the left upper urinary tract and a moderate dilatation of the right renal pelvis (Fig. 11). The patient used a Lapides drainage apparatus. Five months following the operation a retrograde pyeloureterogram showed a minimal dilatation of the upper urinary tract and some constriction of the left ureter at the anastomosis (Fig. 12).

Again, because of inoperable bladder cancer with a vesicovaginal fistula, the urine was diverted by this method in a forty-four-year-old woman. The procedure was tolerated well and was technically satisfactory. Urine drainage from the site of the anastomosis persisted for about seven weeks. A retrograde urogram through the cutaneous neostomy showed a relatively normal upper urinary tract three months postoperatively (Fig. 13). She remained quite comfortable from this aspect until the time of her death from metastatic cancer six months after the operation.

Our first attempt at this procedure in a patient with no malignant disease was in a forty-four-year-old man who had a permanent neurogenic condition of the bladder following a transverse myelitis. The rehabilitation of his bladder was unsuccessful after several procedures. He had developed bilateral vesicoureteral reflux, bilateral hydroureteronephrosis, and a contracted hypotonic bladder (Fig. 14A). In addition to this disease, he was found to have ulcerative colitis, cholelithiasis, chronic cholecystitis, and an esophageal hiatal hernia. Because it appeared indicated to avoid the use of the

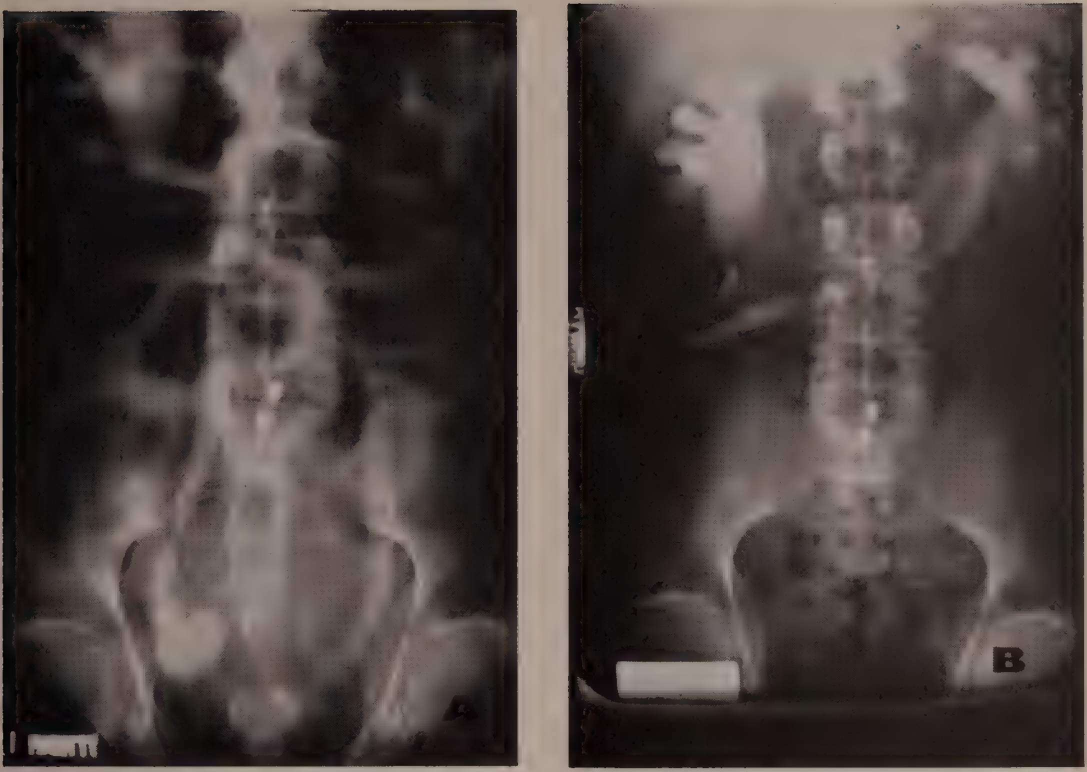

FIGURE 14. (A) Cystogram showing contracted bladder and bilateral vesicoureteral reflux. (B) Retrograde urogram at time of stoma revision.

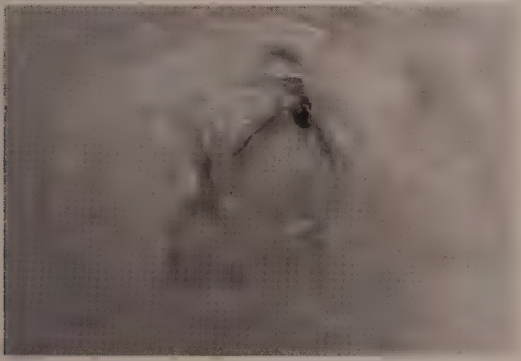

FIGURE 15. Cutaneous neostomy after revision with skin flaps.

intestinal tract for urinary diversion in this type of patient, ureteroureteral cutaneous neostomy was performed on the right side on June 22, 1959. The ureteroureteral anastomosis leaked but gradually closed. A stricture developed of the ureteral stoma. The stoma was revised with skin flaps on January 1, 1960 (Fig. 15). A Perma-type bag is used by the patient, and the cutaneous neostomy now drains well. A retrograde ureteropyelogram at the time of the stoma revision is shown (Fig. 14B).

A seven-year-old girl with a neurogenic condition of the bladder as a result of multiple congenital malformations including absence of the lower spine, large hydroureters, and paraplegia was completely incontinent with infected residual urine (Fig. 16). The transplantation of this type of ureter to segments of bowel has had a high incidence of complications. It was thought inadvisable to bring the ends of these dilated ureters to the surface of the lower abdomen as proposed by Swenson and Smyth[8] because of the deformed pelvis. A double cutaneous ureterostomy was performed on the left flank. The stoma to the right ureter retracted and strictured because the length was inadequate to reach this point. The right ureter was subsequently anastomosed to the left in the retroperitoneal space. The stoma has remained healthy and functioned well (Fig. 17A). A retrograde pyelo-

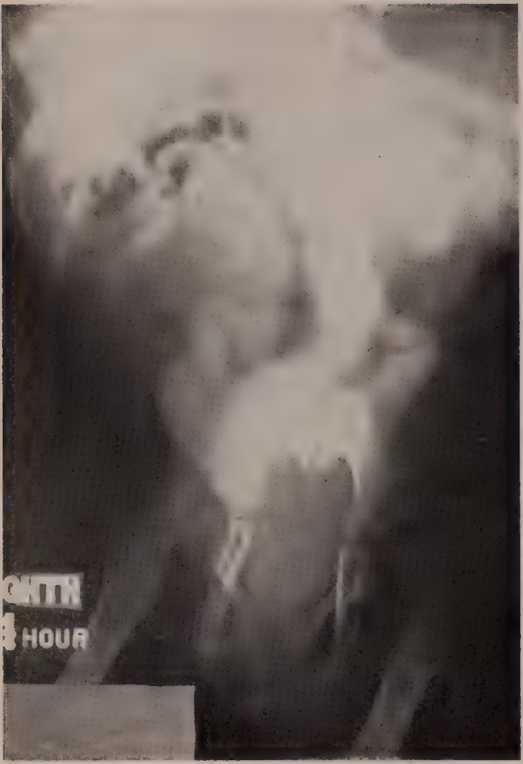

FIGURE 16. One-hour film of intravenous urogram showing marked hydroureteronephrosis.

gram two months after the ureteroureteral anastomosis showed improvement in the hydroureteronephrosis (Fig. 17B).

Summary

Bringing the end of the ureter to the skin surface of the anterior flank allowed the ureter to lie in the retroperitoneal space without tension and resulted in a ureterostomy with a good functioning stoma in 7 of 10 patients.

Ureteroureteral cutaneous neostomy provided a satisfactory means of total urinary diversion in 4 of 8 patients. The remaining 4 died of carcinomatosis too soon after operation to evaulate the procedure. One stoma required revision and has functioned well since. Urine leakage from the ureteroureteral anastomosis persisted up to seven weeks in 1 patient and for a shorter time in 3 others. The drainage subsided spontaneously in each case.

Flank cutaneous ureterostomy and ureteroureteral cutaneous neostomy are useful methods of catheter-free urinary diversion with a low incidence of stricture and retraction of the ureteral stoma.

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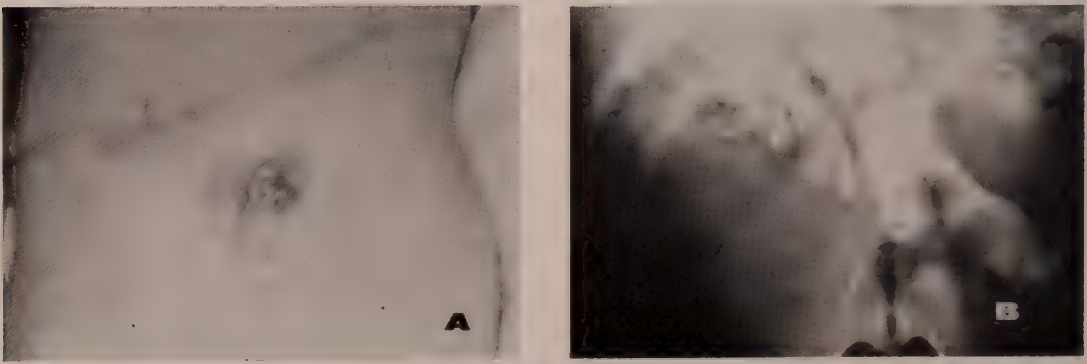

FIGURE 17. (A) Stoma of left ureteroureteral cutaneous neostomy two months after anastomosis of right ureter to it and ten months after original ureterostomy. (B) Retrograde pyeloureterogram two months after anastomosing right ureter to left.

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Discussion

Gustavus A. Humphreys, M.D., *New York City.* I want to thank Dr. Young for an excellent and timely discussion of urinary diversion which is both stimulating and informative. He has emphasized the importance of the most simple procedure with the lowest morbidity and mortality despite current trends to more complicated forms of diversion now in vogue. We are aware of the vicissitudes of patients with any cutaneous ureterostomy, dependent in many ways on gadgets for dryness; we realize that those with intubated ureterostomies are afflicted with the complications associated with foreign bodies while those who are dependent on cups avoid these complications, only to incur a different statistical incidence of complications based on a deteriorating drainage system, secondary to distal ureteral obstruction.

The fact remains clearly defined that those who are good operative risks with good upper urinary tracts are candidates for other types of diversion and are seldom included in the group which is subjected to cutaneous ureterostomy. Our interest in this has been revitalized by reviewing cases who were subjected to cutaneous ureterostomy on the side where the "kidney was worthless" and in whom some other form of diversion has been done on the "better" side. A few years postoperatively, we find some of them living with an improved "worthless" kidney while the good kidney with a more acceptable and exotic form of ureteral diversion has become functionless. This reinforces the truth behind the old adage that more patients are alive and wish they were dead because of cutaneous ureterostomies while more are dead and wish they were alive because they didn't have cutaneous ureterostomies.

The use of the flank as a drainage site of such ureterostomies has advantages as demonstrated by Dr. Young and admittedly many of the usual disadvantages. Although I am intrigued by his ureteroureteral cutaneous neostomies, I have never performed such a procedure and am not qualified to judge. This is partly because I have never wanted to compromise the drainage of a "better" kidney by anastomosing the ureter to a poorer one, based on the doubtful advantage that one wet area is better than two. This deserves evaluation on the basis of experience as does the entire problem of cutaneous ureterostomy. The final answer has not been arrived at. Dr. Young is to be congratulated on stimulating thought on such fundamental problems. We need more variations on the old theme.

Varying tolerance to alcohol

Two persons of the same weight who drink the same amount of alcohol may not appear to tolerate it equally as well for a number of reasons, according to a statement of the AMA Subcommittee on Alcoholism in the May 19, 1962, issue of the *Journal of the American Medical Association.* "An experienced drinker has learned how to counteract some of the adverse effects of alcohol, whereas a novice, faced with the same situation, would be less capable of compensating for the alcohol-imposed handicap. Habitual drinkers absorb their alcohol more slowly and oxidize it more rapidly than do persons who rarely take a drink. Also, the presence of food in the upper gastrointestinal tract tends to retard the rate of alcohol absorption and thus ameliorates the effect of a given dose."

However, there is little difference among individuals in the ability of brain tissue to resist the effect of a given tissue concentration of alcohol. "All persons show some impairment in driving ability at a blood alcohol concentration of 0.10 per cent, and in some this ability is impaired at a level as low as 0.02 per cent. Regardless of tolerance, the fatal concentration is 0.6 to 0.8 per cent."

Scientific session held at the
Hotel Beekman Tower,
New York City,
November 29, 1961
JOSEPH FRIES, M.D.,
President, Chairman

PROCEEDINGS

New York Allergy Society

SHEPPARD SIEGAL, M.D., AND MURRAY DWORETZKY, M.D.,
Editors

Impressions of Allergy in Asia

HORACE BALDWIN, M.D.
New York City

Consultant in Medicine, New York Hospital,
Chairman, Allergy Foundation of America

TODAY THERE IS rising interest in improving the welfare of peoples in those parts of the world where medical progress has been slow, as compared with the great developments in our own country. In particular, interest has been centering on Asia where underdeveloped countries are now seeking ways and means of solving their problems. The work of the Rockefeller Foundation is an outstanding example of real interest from the United States seeking to aid in this development through its support of medical research and education in those countries.

On a recent trip to Japan, Hong Kong, India, and Turkey I visited various medical centers to gain an impression of the prevalence of allergic diseases in those countries and the various methods of diagnosis and treatment used, as compared with those in the United States. John Maier, M.D., of the Rockefeller Foundation, and Henry Pratt, M.D., of The New York Hospital, were helpful in telling me the places to visit and in arranging introductions.

Japanese centers

In Japan my hospital visits were confined to St. Lukes International Hospital and the University Medical School and Hospital in Tokyo. St. Lukes Hospital is a large general hospital of high standards supported by lay gifts, a large percentage of which come from the United States. My guide at this hospital was Ryosaku Tanida, M.D., a young physician trained in Japan who completed his graduate work in New York City and at Oak Ridge, Tennessee, where he was interested in radioisotopes. Dr. Tanida is in charge of medical patients chiefly in the outpatient department, and his observations on the allergic illnesses were those of an internist. It was his opinion that asthma is very prevalent in adults and children and comprises the same percentage of total patients as in the New York City hospitals. He is not aware of much hay fever. There is considerable eczema and urticaria. In St. Lukes Hospital there are no special allergy clinics and no staff doctors particularly interested in allergy. Most of the asthmatic patients are seen in the Pulmonary Clinic where there is also much tuberculosis, emphysema, silicosis, and lung carcinoma. No special testing is done to determine sensitivities. This is attributed to lack of confidence in skin testing and skin-testing diagnostic materials. Emphasis in asthma is placed on the control of respiratory infection. Psychosomatic factors are considered of secondary importance. For the most part, the treatment of asthma is entirely symptomatic, consisting of bronchial dilators, inhalational therapy, antibiotics, iodides, and corticosteroids.

At the Tokyo University Medical School and Hospital I met with Yoshio Oshima, M. D., who is in charge of the allergy patients and whose title is Professor of Physical Therapy and Medicine in the University. Dr. Oshima is particularly interested in drug allergy. He is also very much interested in hypersensitivity factors in asthma and in other allergic illnesses. He is very eager to secure adequate materials for skin testing and immunization. These materials are very limited at present, and scarcely any skin testing or immunization with specific allergens is attempted. This situation may be improved as soon as the Torii Pharmaceutical Company develops the materials. Dr. Oshima estimated that there were at least 1 million sufferers from asthma in Japan. Hay fever is not common. Urticaria is prevalent and attributed to the large consumption of sea food. Drug allergy to penicillin is not uncommon. Ragweed grows in Japan. I saw plants of low ragweed growing in the fields adjacent to the hospital, and in Kyoto I also observed ragweed.

There is a Japanese Allergy Society of 700 members. I was given several reprints representative of research work now being published. Two of these reports, by Hidenari Araki, M.D., were of particular interest to American allergists. One is titled "Pollen Survey in Tokyo and Its Neighboring District," published in 1960. It is the first report on atmospheric pollen counts in Japan. Dr. Araki concluded the following:

> There were three pollen seasons in this area like in U.S.A. Pollination period of trees ranged from February or March to June. Japan Cedar and Pine were prevalent. Marked peaks of Pine were found in late April and early May with a maximum count of 144 in Tokyo.
>
> Pollination of grasses begins in April and continues till October, their pollen counts were considerably low especially in June and July (rainy season). Predominant pollens of the grass curve were Dactylis Glomerata, Alopecurus, Equalis and Miscanthus sinensis.
>
> The weed season ranged from August to October. The prevalent pollen was short ragweed. (Ambrosia Artemiiafolia var. elatior) The peaks were observed in late August and early September with a maximum count of 95 in Narashino. Giant ragweed was very few (sic) and no other ragweed in this area.
>
> Comparing with the results of some surveys in U.S.A. the present study seemed to indicate that in Tokyo and its vicinity the pollen concentrations especially of short ragweed were generally lower but not so extremely lower than those in U.S.A.

In the second report, "Sensitization with Pollens in Japan," Dr. Araki reported:

> Positive skin reactions to short ragweed pollen in 36% of asthmatic patients, 32% of patients with nasal allergy including bacterial allergy, 52% of patients with nasal allergy expecting bacterial allergy, and 19% of normal control persons, whereas positive skin reactions to house dust in these four groups were 69%, 51%, 65% and 23% respectively.
>
> But positive skin reactions to Japanese red pine and Japanese cedar pollens were observed far less frequently than to ragweed pollen and only a very few cases reacted to Japanese pine and Japanese hop pollens.

Dr. Oshima introduced me to a number of Japanese doctors interested in immunology and allergy. From them I gathered that there is a great demand for opportunities to study in the United States. The chief sources of grants are Fulbright fellowships and Rockefeller Foundation grants. Young doctors who want to secure further training here have difficulty in finding an institution that offers facilities and then having the institution accept them.

Chinese centers

In Hong Kong I visited Queen Mary's Hospital which is the teaching hospital of the Hong Kong University Medical College. Beautifully situated outside Victoria and overlooking the water, this is a 600-bed hospital, government-supported by the British people. It is the main hospital facility for over 1 million people who live on Hong Kong Island. C. T. Lee, M.D., the superintendent, spoke sadly about the severe tax on the hospital's facilities in taking care of the many thousands of refugees who have come from Red China. Tuberculosis, syphilis, leprosy, cholera, heroin addiction, and malnutrition are great problems in Hong Kong that absorb most of the available medical facilities. The staff of the hospital is, for the most part, made up of Hong Kong-trained physicians. They often go to the British Isles for special training.

Asthma is prevalent. The hospital takes care of only the status cases. These cases are most often said to be complicated with infection. Treatment consists primarily of antibiotics and bronchodilators and corticosteroids, if needed. There is no skin testing and no immunization with specific allergens. There have been no pollen or mold surveys. Hay fever is not a problem. Urticaria is frequent and is attributed to sea food.

Indian centers

In Calcutta I visited the Calcutta University Medical College which is so familiar to many physicians in the United States because of its famous School of Tropical Medicine. Sarbad Hikary, M.D., the Principal of the Medical College, arranged for me to meet with J. C. Banerjea, M.D., Professor of Medicine and Director of the Department. Dr. Banerjea indicated that asthma was the most important and prevalent allergic disease in the Calcutta area. In the hospital patient admissions for allergic diseases in 1960 constituted 1.7 per cent of the total, of which asthma made up 86.4 per cent. Several deaths from penicillin allergy have occurred. Infection is the most important consideration in asthma, but there have been no pollen or other inhalant extracts for testing or immunization. In the Calcutta area no pollen or mold surveys have been made.

At a meeting of the Calcutta Branch of the Indian Medical Association I presented a report on the over-all management of asthma to an interested audience of over 100 Indian physicians. In the discussion which followed it was emphasized that the chief gap in the management of allergic problems in Calcutta had to do with the lack of materials for testing and immunization, as well as a lack of knowledge of common airborne allergens, such as pollens and molds. Here, as in Tokyo, there is a desire for training in allergy in the United States, provided funds and facilities can be obtained.

The All India Institute of Medical Sciences in New Delhi represents great progress in the development of ways and means for India to attack its problem of disease. I met with Lucien Gregg, M.D., Associate Director of the Rockefeller Foundation. He is stationed there to assist the Indian faculty in the formative stages of development in the education and training of medical scientists not only for India but also for other parts of Asia. This Institute was chartered by the Government of India in 1956 under an Act of Parliament. It is operating now as a medical school and hospital, with incomplete facilities which will be completed in from one to three years. Dr. Gregg indicated that bronchial asthma is a serious problem in India. A great deal remains to be done as far as other allergies are concerned. On the other hand, the control of cholera, tuberculosis, typhoid, smallpox, leprosy, and malnutrition are the main problems which preventive medicine must solve and where, for the present, emphasis must be placed.

Turkish centers

In Istanbul my guide was Kenan Binak, M.D., of the First Medical Clinic of the Gerrepasa Hospital. Dr. Binak had recently completed a fellowship in cardiovascular disease in the United States under the auspices of the Rockefeller Foundation. Through Dr. Binak I met Osman Barlas, M.D., Chief of Medicine at the Gerrepasa Hospital and Professor of Medicine at the Istanbul University School of Medicine. I also met Osman Yemini, M.D., Chief of the Dermatology Hospital of the Medical College. In discussing the problems of allergy in Turkey chief emphasis was once again placed on the lack of extracts for testing and immunization and the absence of anyone trained in allergy research and practice. A great need is a survey of pollens and molds. Basically the problem is lack of funds for training in the United States. It would seem that unless funds are provided, the status of allergy practice, teaching, and research in Turkey will remain in its present state of inadequacy.

Comment

In the United States great advances have been made in the field of allergic disease extending over the past thirty years. Large government funds are available for research and training through the National Institute of Allergy and Infectious Diseases. The Allergy Foundation of America, a voluntary health organization founded by joint action of the American Academy of Allergy and the American College of Allergists, is doing much to educate the public in the nature of the allergic diseases and the importance of early diagnosis and treatment. It also fosters research and medical education in this field. American allergy has much to contribute to other countries, especially in Asia. On the other hand, even here in

America many problems remain unsolved. It is not too much to hope that, in addition to the humanitarian aspects of our assistance, we may also stimulate ideas and discoveries from new points of view, unconditioned by traditional methods and practice.

The Heart in Human Anaphylaxis

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FATAL AND NEAR-FATAL anaphylactic shock reactions persist as a significant danger in drug therapy today. Penicillin remains the outstanding hazard in this respect, but other therapeutic agents have been incriminated. Among them are aspirin, chymotrypsin, trypsin, and penicillinase. It is probable that most enzyme therapy carries some hazard of this type.

Anaphylactic threats

ASPIRIN. Aspirin asthma, particularly as it may seriously involve the heart, is illustrated by the 1957 case of Rosenfeld, Silverblatt, and Grishman.[1] In their case, a thirty-one-year-old man almost succumbed to an acute myocardial reaction induced by 10 grains of aspirin. This patient had aspirin allergy which frequently caused severe asthma. The electrocardiographic changes, Q-wave changes, and lowered T waves approximated changes of acute myocardial infarction induced by the allergic reaction.

DIAGNOSTIC TESTS. Two diagnostic tests commonly in current use also pose a definite hazard of anaphylaxis, especially in allergic and, above all, in asthmatic patients. The intravenous Bromsulphalein test of liver function has caused several serious and even fatal anaphylactic reactions in recent years. Even more troublesome, because it is more frequently indicated, is intravenous pyelography. Acute allergic reactions to the various organic iodide materials used in this diagnostic procedure are fairly frequent and quite unpredictable. Many of these reactions are minor but occasional instances of shock and even fatalities have been reported. Unfortunately, preliminary skin tests are of no value. Even small preliminary trial doses are not always an accurate index of tolerance. Intravenous pyelograms should be done with caution in asthmatic subjects. Repeated pyelograms should be avoided as repetition invites anaphylaxis.

INSECT STINGS. Another major anaphylactic threat is that due to insect stings. Every summer the front pages of the daily press report deaths of this kind. Shaffer[2] recently called attention once again to this ever-present danger. He emphasized the necessity for the patient to have a suitably equipped emergency kit should he be stung before desensitization can be accomplished. Parrish,[3] in a survey of deaths in the United States due to venomous animals and insects for the five-year period from 1950 to 1954, found, to his evident surprise, that 86 deaths, or 40 per cent of all fatalities recorded, were due to insect stings. He was convinced that most if not all of these deaths were due to anaphylaxis. It is our responsibility as allergists to alert the profession to the urgent need for such patients to undertake desensitization. Although there may be differences of opinion as to the best materials or methods, it is without question an effective method of preventing recurrence of shock due to stings.

PENICILLIN. In a 1953[4] report on fatal and near-fatal penicillin anaphylaxis I included electrocardiographic tracings during and following recovery from anaphylactic shock, as observed in a twenty-seven-year-old male. The T-wave alterations were definite, indicating transient myocardial damage. More dramatic are the findings in the 1959 case of Bernreiter[5] in which atrial fibrillation, multifocal ventricular premature contractions, intraventricular conduction defect, and probable acute myocardial damage were induced by a single dose of procaine penicillin. This patient was a seventy-four-year-old male. Since older patients are at least as prone to anaphylaxis as young ones, one may anticipate that cardiac anaphylaxis will often be superimposed on an abnormal arteriosclerotic coronary circulation, presumably with even more disastrous effect.

Importance of heart

The recognition of the crucial role which the heart may play in anaphylactic shock is the particular point of this discussion. In the past this role appears to have been underemphasized or ignored. Attention has largely centered on peripheral collapse or overinflation of the lungs as the cause of death. That the experimental animal heart responds to the sensitizing antigen has been demonstrated repeatedly. The isolated animal heart reacts just as certainly to the addition of antigen as does the uterine muscle or the ileum in the classic Schultz-Dale experiment. The 1960 report of Feigen, Vaughan Williams, Peterson, and Neilsen[6] demonstrated once again that the anaphylactic reaction with the release of histamine takes place in the myocardium itself, as represented by the isolated atrial strip. It is thus not dependent on the response of the coronary arteries, although a reduction in the coronary flow is also a usual concomitant of anaphylaxis. There is, therefore, repeatedly confirmed extensive experimental evidence of the occurrence of a specific acute allergic or anaphylactic reaction in the heart itself. It is highly probable that in man also the myocardium, as well as the coronary vessels, may be the site of an acute allergic shock reaction.

Treatment of anaphylaxis

The perusal of the history of fatal acute anaphylactic reactions to penicillin and other agents reveals that the patient may collapse within a matter of seconds. On examination he may be found without heart sounds and may then be pronounced dead. Emergency aid in such cases ought not to be limited to the administration of epinephrine or measures for countering peripheral shock. It is not sufficient at this crucial moment to inject intracardiac epinephrine, supplemented by artificial respiration. Such attempts ought to be supplemented by external cardiac massage as advocated by Kouwenhoven, Jude, and Knickerbocker.[7] This technic offers the possibility of resuscitation without opening the chest. By means of regular repeated pressure over the lower end of the sternum, it has been possible to maintain the circulation of the blood. This has been sufficient, when coupled with mouth-to-mouth artificial respiration, for the critical requirements of cerebral oxygenation until the spontaneous mechanism of the heart may again become active. This treatment has been maintained for as long as one hour or more. According to the reports of these observers, 100 of 150 patients thus treated have been restored to health with an intact central nervous system. Jude, in a personal communication, states that 3 out of 4 patients with cardiac arrest due to anaphylaxis also responded to this method.

Summary

As allergists, it is important that we recognize the role of the heart in human anaphylaxis and, accordingly, emphasize the value of this new technic of external cardiac massage as a necessary measure in the emergency treatment of anaphylactic shock when there is cardiac arrest. In anaphylaxis where there is no cardiac arrest, the usual methods hitherto employed are sufficient. By prompt application of this new method some patients might be saved who would otherwise succumb. With closed-chest massage we will enable patients with hearts often otherwise structurally normal to be salvaged from the danger of sudden death due to anaphylaxis.

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Diverticulum of the Female Urethra

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THE DIAGNOSIS *of a urethral diverticulum should be suspected in any woman with symptoms of chronic urethritis. The palpation of a pulpaceous mass in the anterior vaginal septum and a panendoscopic examination of the urethra are usually diagnostic. Over a seven-year period 23 patients were treated by simple excision, which is the treatment of choice in uncomplicated cases. The complications were urgency and frequency with one of stress incontinence, all resolving with conservative office management. In diverticuli containing tumors, simple excision suffices if the urethra is not involved; if it is, more radical procedures are indicated with or without adjunctive radiation therapy.*

DURING THE PAST ten years numerous reports concerning urethral diverticula and their complications have appeared in the literature. Prior to this time the entity was known, but relatively few cases were recorded. More recently recognition has been given to the not-too-infrequent presence of carcinoma contained within a diverticulum. These facts have been pointed out by Wishard, Nourse, and Mertz,[1] who stated that it took one hundred forty years for the entity of urethral diverticulum to become well recognized, but only during the last ten years has the importance of carcinoma contained therein been well established. At this writing 12 cases of the latter have been recorded.

The frequency of new reports concerning this problem attests to the fact that both urologists and gynecologists are becoming more aware of its existence and are making a more careful study in any female patient with chronic urethral symptoms. This is corroborated by the fact that Wharton and Te Linde's report in 1956[2] of 66 patients demonstrated that 33 per cent had symptoms for longer than five years, as contrasted to the reports of Faulkner[3] and Wishard and Nourse[4] which revealed symptoms of less than eighteen months duration in 46 per cent of the cases.

The etiology of these lesions generally has been accepted to be on an acquired basis resulting from an inflammation of the periurethral submucosa which may lead to abscess formation and subsequent rupture into the urethral lumen with the development of a diverticulum. This promotes stasis and infection in most cases with consequent symptoms. It is also thought that urethral trauma, such as endoscopy and the passage of calculi, may result in the formation of diverticula.

In a review of the literature it is found that most diverticula are uncomplicated. Wharton and Kearns,[5] however, reported that 10 per cent of these lesions contained calculi, and Kirby and Reynolds[6] reported on 44 cases complicated with stones. Hamilton and Leach in 1951[7] reported the first case of diverticular carcinoma in a fifty-three-year-old woman complaining of stress incontinence and vaginal bleeding. Since then, 11 additional cases have been recorded, 3 containing adenocarcinoma, 5 containing transitional cells, 2 containing epidermoid, and 2 containing undifferentiated cell types, 1 probably of Wolffian duct origin.[8] The ages of these women ranged between thirty-five and sixty years. Statistics on the incidence of diverticular carcinoma are unavailable, but from the

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TABLE I. Summary of 23 cases treated by excision

Case	Age (Years)	Symptoms in Order of Frequency or Severity	Duration (Months)	Complications
1	53	Frequency, burning with urination, pressure at end of urination	36	Frequency, urgency
2	50	Nocturia	6	Urgency
3	41	Hematuria, nocturia, frequency, dripping after voiding	4	None
4	70	Pain in vagina, burning with urination	17	None
5	29	Asymptomatic, discovered during postpartum examination	6	None
6	18	Pain in vagina, mass in vagina (parous)	6 weeks	None
7	40	Frequency, burning, dyspareunia (postpartum)	18	None
8	42	Pressure in lower part of abdomen, frequency, hesitancy	12	None
9	47	Painful urination, burning, urgency, frequency, incontinence	24	Urgency
10	56	Spasms in urethra, hematuria	24	None
11	41	Frequency, burning with urination	7	None
12	34	Pain in vagina and vulva, frequency, brown urine	8	None
13	38	Chills and fever, burning, hematuria	10	None
14	47	Pain in vulva, urethral bleeding, frequency, stress incontinence	48	None
15	47	Burning with urination, urgency, incontinence	12	None
16	38	Burning with urination, pressure at end of urination	18	None
17	41	Pain in urethra, dyspareunia	14	None
18	44	Frequency, hematuria	8	None
19	51	Burning with urination, frequency, nocturia	3	None
20	43	Bleeding from urethra, frequency, and burning with urination	4	None
21	47	Dyspareunia, frequency	5	Burning with urination, frequency
22	51	Stress incontinence, urgency	10	None
23	34	Asymptomatic, discovered during postpartum examination	6	Urgency, stress incontinence

cases reported, it ranged from 4 to 6 per cent. This is undoubtedly high.

The diagnosis of a urethral diverticulum should be suspected in any woman with symptoms of chronic urethritis. The physical findings of a suburethral pulpaceous mass palpated along the anterior wall of the vagina with or without the expression of purulent material or urine is almost diagnostic. A panendoscopic examination associated with palpation may afford visualization of the mouth of the lesion, especially if purulent material is extruded. This is of especial value if carcinoma is present, since the tumor may be partially expressed from the diverticulum and visualized. Cystourethrography is a valuable adjunct to determine the location of the tumor prior to surgery and also to observe filling defects.

The purpose of this paper is to report 23 cases occurring over a seven-year period and to review 2 typical cases (Table I).

The youngest patient in this group of women was eighteen years old and pregnant who complained of pain in the vagina and noted a bulge protruding from the vaginal outlet. This lesion was removed later and proved to be a true diverticulum. The eldest woman was seventy years old. Two women, twenty-nine and thirty-four years respectively, were completely asymptomatic. Both were postpartum, and the lesions were discovered during postnatal examinations by their obstetricians. The mean age was forty-five years with 75 per cent under fifty years of age.

In this group, the most prominent symptoms in order of frequency were:

1. Pain, either in the vagina, vulva, urethra, or bladder
2. Burning with urination
3. Urgency
4. Frequency
5. Dyspareunia
6. Bleeding from the urethra
7. Pressure in the lower abdomen
8. Nocturia
9. Decrease in force of urinary stream
10. Leakage of urine after voiding
11. Stress incontinence
12. Chills and fever.

This list of symptoms is not set down as a criterion for diagnosis, for they certainly overlap and appear differently in each patient. However, they point up the fact that suspicion and a careful examination are paramount in establishing the correct diagnosis in any woman with chronic symptoms. This is, of course, more significant in view of the evidence that carcinoma can exist within the lesion.

The duration of symptoms varied from six weeks to forty-eight months.

Examinations of all our patients revealed an easily palpable suburethral mass and in most instances, by a combined endoscopic examination with counterpressure on the urethra, demonstrated purulent matter extruding from the lesion. Cystourethrography was performed in 16 patients.

The lesions were excised surgically, and the postoperative complications consisted mainly of urgency, frequency, and burning with urination and 1 case of stress incontinence. All were amenable to conservative office management.

Operative technic

Under general anesthesia the patient is placed in the exaggerated lithotomy position using the perineal table. A number 18 or 20 Foley catheter is anchored in the bladder. An incision is made along the anterior vaginal wall for a distance of approximately 3 or 4 cm. and is carried through the vaginal mucosa. Frequently it is necessary to incise the pubocervical fascia to expose the lesion adequately. The vaginal flaps are developed and elevated laterally, exposing the dome of the diverticulum which is then grasped with an Allis clamp for traction. By sharp dissection it is freed from the fascia circumferentially. The dissection is carried down to the urethra at which point the floor of the urethra adjacent to the neck is incised sharply on the catheter. The closure is in layers using interrupted 0000 atraumatic catgut sutures to approximate the urethral mucosa and fascia. These layers are staggered to prevent superimposition. Almost always the vaginal mucosa is redundant, and therefore it is partially excised on one side so that the closure lies lateral to the fascial suture lines. The Foley catheter is left indwelling, and a vaginal pack is placed. The pack is removed in twenty-four hours and the catheter in from six to eight days.

Case reports

Case 1. A fifty-three-year-old white housewife was first seen by her family physician because of frequency, burning with urination, and severe pressure at the termination of urination of three years duration. She was treated with antibiotics for five days, and because the symptoms persisted she was referred for more specific study. Her past medical history did not disclose any significant illnesses other than a chronic dermatophytosis of the feet and legs, and the family history showed negative findings. She had four normal pregnancies the last eighteen years prior to her admission.

Physical findings confined to the genitourinary system revealed a firm mass measuring 2 by 3 by 2 cm. along the anterior vaginal septum. Palpation of this mass caused severe pain and expressed a thick, milky fluid from the urethral meatus. The cervix, uterus, and adnexa were normal.

Laboratory studies disclosed normal hemogram findings. The urine was a cloudy yellowish color with a pH of 6.5 per cent with a specific gravity of 1.022. There was no sugar or acetone present, but there was a trace of protein. A microscopic examination revealed 15 to 20 white blood cells per high-power field. A urine culture was sterile, and an intravenous urogram showed normal upper urinary tracts. Three days after admission cystoscopic and panendoscopic examinations were performed. The bladder was completely normal. Visualization of the urethra showed a moderate hyperemia on the left side just

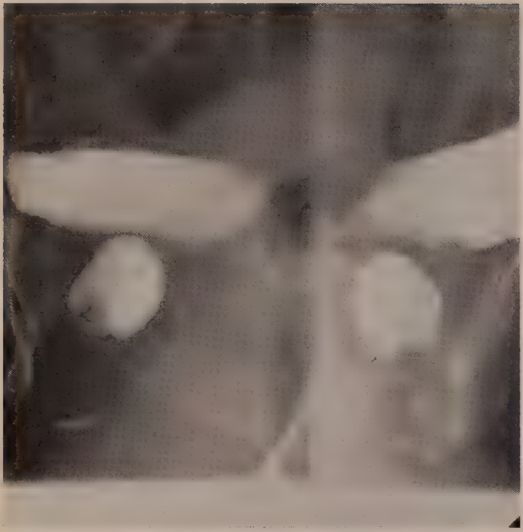

FIGURE 1. Case 1. Cystourethrogram with Skiodan solution showing diverticulum.

outside the sphincteral region. Palpation of the urethra with counter-pressure over the scope extruded a thick milky fluid from a slitlike area in the midurethra on the left side. A careful examination along with palpation enabled visualization of the mouth of the lesion. It measured approximately 3 or 4 mm. in diameter. A cystourethrogram was then made using a 20 per cent Skiodan solution, and it confirmed the diagnosis of diverticulum (Fig. 1). The lesion was subsequently excised.

On removal of the catheter eight days later, the patient was able to void satisfactorily with the exception of frequency and urgency. Other than this her course was uneventful, and she was discharged on the twelfth postoperative day. The pathology report showed that the lesion was lined with stratified squamous epithelium, and the walls were made up chiefly of connective tissue.

She was seen periodically for a number of months postoperatively, and after a few urethral dilatations she became asymptomatic.

Case 2. A fifty-year-old white woman was first seen by her family physician because of nervousness. A routine urinalysis revealed pyuria, and she was referred to a urologist. The genitourinary history revealed no significant symptoms with the exception of nocturia four or five times for the past six months. She could not relate any associated symptoms. A urinalysis disclosed cloudy, amber urine with a pH of 7.5. There was no sugar, acetone, or protein. Microscopically it was loaded with pus cells.

A physical examination revealed the blood pressure to be 130/65 with a pulse of 86. The pertinent findings were confined to the pelvic region which disclosed a large, saccular, pulpaceous mass measuring 4 by 3 by 3 cm. anteriorly almost protruding from the vagina. It was tender, and pressure on it caused an extreme desire to void. The cervix, uterus, and adnexa were normal. A presumptive diagnosis of a diverticulum was made, and the patient was admitted to the hospital for further study. Laboratory studies disclosed normal hemogram findings. A two-hour postprandial blood sugar showed normal findings. The urine was cloudy, yellow, and contained 80 to 100 white blood cells per high-power field. It cultured Pseudomonas aeruginosa resistant to all chemotherapeutic agents and antibiotics. An intravenous urogram showed normal findings.

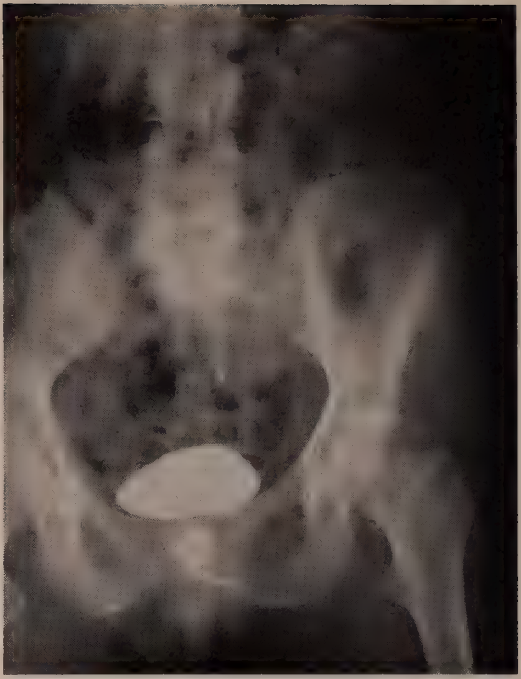

FIGURE 2. Case 2. Cystourethrogram showing urethral diverticulum with mouth close to vesical neck.

A panendoscopic examination revealed a normal-appearing bladder and urethra. Palpation of the anterior vagina over the instrument revealed a large, boggy sacculation which was quite tender. No fluid or tissue could be seen extruding from the lesion. A cystourethrogram confirmed the diagnosis of a urethral diverticulum which was of a fairly large size and with the mouth situated close to the vesical neck (Fig. 2). It was excised surgically.

Her postoperative course was uneventful. The catheter was removed on the tenth postoperative day to diminish the possible complication of fistula formation. She was discharged on the fourteenth postoperative day on urinary antiseptics and was voiding with good control, although she had some urgency.

The pathology report disclosed marked, chronic, nonspecific inflammation and sections showing mostly fibrous tissue with a few cystic areas lined by papillary transitional epithelium. No malignant condition was noted.

She was followed in the office for seven months because of urgency which subsequently disappeared after conservative management. Her urine became normal, and the cultures became sterile.

Summary

Diverticula of the urethra should be suspected in any woman with chronic urethral symptoms. The palpation of a pulpaceous mass in the anterior vaginal septum and a panendoscopic examination of the urethra usually will establish the diagnosis. An awareness of the possibility of tumor formation contained within the lesion should be kept in mind. Carcinoma in this location is best discovered by an endoscopic examination associated with counterpressure on the urethra which frequently will express the tumor into view. Cystourethrography is helpful in establishing the exact location and extent of the lesion.

In uncomplicated cases simple excision is the treatment of choice. In those containing a tumor simple excision usually suffices if the urethra is not involved. If it is, more radical procedures are indicated with or without adjunctive radiation therapy.

Twenty-three cases have been summarized briefly, and 2 typical cases are presented. The treatment in all was simple excision. The complications were urgency and frequency with one of stress incontinence, all resolving with conservative office management. No strictures of true incontinence developed.

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Serendipity in drug research

Everybody who talks about the products of the future should admit from the outset that he doesn't know what he's talking about. Because we literally don't know—and in some ways can't even imagine—what will turn up. . . . Drug research today doesn't proceed in a logical straightforward line from the discovery of the cause of a disease to the discovery of a treatment for that disease. Instead, scientists experiment with a broad range of chemicals, related chemicals, and chemicals related to the related chemicals. Some of the greatest breakthroughs in the industry were found while working on something else. The new diuretics, for example, came while looking for a way to keep the kidneys from excreting penicillin too rapidly.—*Walter A. Munns, President, Smith Kline & French Laboratories, to New York Society of Security Analysts*

Value of Paramedical Services to Patients in Nursing Homes and Homes for the Aged

Report of Study

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In the spring of 1957 a small group of interested individuals in the city of Buffalo formed a Community League on Aging. The active participation of the various community health and social agencies was encouraged.

The objectives of the group were to investigate the needs of the geriatric patient, to determine what steps might be taken to stimulate programs to provide restorative services for patients confined to nursing homes and homes for the aged, and to train the staffs to assist with restorative services.

It was obvious that none of the homes had sufficient bed capacity to make it economically practical to employ the ancillary disciplines required in a rehabilitation program on a full-time basis.

As a practical approach to this problem, it was proposed that a pool of therapists be engaged on a part-time basis and made available to nursing homes.

On the recommendation of the group, a request was made to the State of New York Department of Health for a three-year grant to pay for these services. When the grant of $2,000 per year for a three-year period was approved, the Community League on Aging agreed to disband to permit the Western New York Geriatrics Society to incorporate, a requirement for receiving State funds.

Method

The community was canvassed to secure a list of the various therapists (physical, occupational, speech, and nutritional) who could be interested and willing to participate in the program. The Society felt that this would demonstrate to the operators of these facilities the value and importance of instituting restorative services to round out the medical care program for their patients.

The homes were required to request the services of the therapist, obtain clearance from attending physicians, and agree to have at least one member of the staff assigned to the therapist while he was at the home, to receive instruction to follow through on the procedures between the visits of the therapist. This was necessary because the funds available were not sufficient to permit complete service by the therapist. Furthermore, the program was designed to train the staff in the technics and demonstrate the value of the procedures.

Problems

Since this was the first attempt with such a program, it was obvious that several problems would arise. The following are some of the difficulties encountered:

1. Since all the therapists were currently employed, their services were available only on weekends. This proved to be an inconvenient time for the operators of the homes and posed a difficult administrative problem of scheduling visits of the therapists.

2. The initial enthusiasm of the operators subsided during the lapse of time from the date of application for the grant and the final approval of funds. This delay may be unavoidable.

3. Because of the rapid turnover of personnel in the nursing homes, it was impossible to attain the goal of training the staff to do follow-up work. The new person-

TABLE I. Nursing home utilization of rehabilitation personnel

Area	Number of Homes	Physiatrists	Physical Therapists	Occupational Therapists	Speech Therapists	Nutritionists
Buffalo	18	3	11	3	3	2
Erie County	13	2	7	3	2	2
TOTALS	31	5	18	6	5	4

TABLE II. Did you request and receive services of consultants?*

Area	Yes	No
Buffalo		
Physical therapist	10	8
Occupational therapist	3	15
Speech therapist	3	15
Nutritionist	3	15

*Erie County: No response.

TABLE III. Did this service fill a need in your nursing home?

Area	Number Requested	Need Filled
Buffalo		
Physical therapist	10	9
Occupational therapist	3	2
Speech therapist	3	3
Nutritionist	3	3
Erie County		
Physical therapist	5	0
Occupational therapist	3	1
Speech therapist	0	0
Nutritionist	0	0

TABLE IV. Do you plan to continue this program on your own?

Area	Yes	No
Buffalo	8	10
Erie County	5	3

nel were not oriented about the program, and this resulted in unfavorable attitudes toward the study. Some of the personnel felt that this was an extra chore not stipulated at the time of employment.

4. This group is difficult to assemble for educational purposes because of minimal staff; workers are on three shifts, and the available space is limited.

5. The process of payment presented difficulties since the contract called for payments or reimbursements on a quarterly basis, and the Western New York Geriatrics Society, Inc., did not have sufficient funds in the treasury to cover this period. This process was later amended to permit reimbursement on a monthly basis.

Results

In Table I, there is a summary of the number of homes requesting the various categories of therapists. It should be noted that a total of 121 visits were made by the physiotherapists in 18 of the 31 nursing homes in the area. In 6 of the homes, 53 visits were made by the occupational therapist, and in 5 homes, 31 visits were made by the speech therapist. Only 4 homes requested single calls by the nutritionist.

At the close of the project on March 31, 1961, a questionnaire was sent out to the operators, with the following questions:

1. Did you request and receive the services of consultants?
2. Did this service fill a need in your nursing home?
3. Do you plan to continue this program on your own?
4. Please check the reaction of your staff members as sympathetic or not.
5. Would you recommend continuance of this service by the County of Erie Department of Health?

Tables II to VI summarize the answers.

Some of the comments are quite noteworthy. Although there were some homes which were noncommittal about the use of paramedical services in general, most of them emphasized, according to the figures, the importance of physical therapy; next was occupational therapy; and to a very minimal extent, speech therapy. Four homes utilized nutritional therapy.

Three of the homes for the aged reported that they had all the available services. One institution recommended more frequent medical supervision by the attending physicians during the time physical therapy

TABLE V. Please check reaction of your staff members as sympathetic or not (figures shown indicate a positive reaction).

Area	Physical Therapist	Occupational Therapist	Speech Therapist	Nutritionist
Erie County				
Nursing staff	6	3	2	2
Housekeeping staff	4	3	1	2
Kitchen staff	2	2	1	2
Buffalo				
Nursing staff	9	4	2	3
Housekeeping staff	2	1	3	3
Kitchen staff	4	2	3	3

TABLE VI. Would you recommend continuance of this service by the County of Erie Department of Health?

	Yes	No
Buffalo	15	3
Erie County	7	1

is being instituted. It would be profitable if the therapist received orientation with the various aspects of aging as it affects the aged patient. The remark from one home was that all the patients were beyond any possible rehabilitation. Another institution claimed that as soon as new modern facilities were completed, all types of therapy, especially physical therapy, would be started by competent personnel.

The most encouraging remark coming from a nursing home operator was:

> The complete staff was antagonistic to the complete program at first. They seemed to think we were just trying to make them more duties. After seeing the results six months later, and discussing the complete program with them, they agreed their duties were less than before. In 1960 we were able to send patients home as they were able to do for themselves. As a result of this we had a greater turnover in patients. We were surprised to see in our report for the social welfare that our patients' length of stay in the nursing home had decreased.
>
> I especially found it easier to sell our nursing home to people looking for accommodations for their relatives, as I stressed rehabilitation and that our job was to be able to return the patient to his home or society, not just to give custodial care and keep the patient forever—thus decreasing the cost.
>
> The patients who have been in the home over a period of years we were not as successful with. Often the relatives interfered and thought making them walk or feed themselves was being unkind or that we were not doing our work.
>
> The new patients admitted to the home after our program started, accepted it; the relatives and visitors cooperated and are content we are doing something for them.
>
> We have hired one practical nurse and she does nothing but the rehabilitation and therapy; when the patients are busy with therapy we have tried to have group therapy, as this seems to stimulate conversation and a friendly atmosphere. In cerebrovascular accident cases that are recent we have been very successful.
>
> I feel we could use a "rehabilitation counselor." I have employed one for three months. She taught us a much better way to suggest this work to the patient and to the relatives. She was able to break down the antagonism of the staff; the approach is so important.
>
> Our greatest problem seems to be to keep after the staff continually to continue the program. I find if I don't push them, they become slack. I feel they should show as much interest in this program as I do.

In conclusion, it would appear that some success was obtained in achieving the goals set up for the project, in spite of the many difficulties which were encountered.

It is noteworthy that 22 of the 31 homes expressed a desire to have their county health departments continue this service.

It is our opinion that if this service could be furnished by full-time personnel and the visits scheduled at the convenience of the operators, it should be easy to resell the program, and, as a result of this, an important addition to the medical care of the elderly patient could be attained. The larger homes should be expected eventually to provide this service themselves.

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Hazards of Abdominal Paracentesis in the Cirrhotic Patient

Part III

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Parts I and II of this article appeared in the June 1 and June 15 issues of the New York State Journal of Medicine. Part I included sections on varix rupture and abdominal wall and peritoneal suppuration in cirrhotic patients. Part II dealt with hemorrhage within the abdominal wall and peritoneal cavity, site of trauma, and treatment.

Low-salt syndrome

A low-salt syndrome complex may supervene in paracentesis, characterized by thirst, weakness, headache, nausea, painful muscle cramps, muscular tremor, drowsiness, mental confusion, vascular collapse, and impending or deep irreversible coma. Hyponatremia, hypotension, oliguria, and azotemia often are demonstrable. The mechanism is postulated to be an acute hyponatremia prompted by a rapid loss of serum sodium and the transudation of fluid from the circulating plasma to the reforming ascites. Approximately 700 mEq. of sodium are lost with every 5 L. of ascitic fluid that are removed. The syndrome occurs especially if the salt intake has been restricted and the patient has been allowed to satisfy his thirst at will, since paracentesis is a dehydrating procedure. Water retention (antidiuresis) results in the dilution of extracellular fluid and thus acute hyponatremia; therefore, sodium is not being retained isotonically. Striking clinical improvement following intravenous hypertonic saline has been reported in individual patients.[22,23]

A presumed low-salt syndrome should not be diagnosed merely on the basis of a reduced serum sodium for two reasons. First, the enthusiastic correction of the depressed sodium level by salt administration can be hazardous. Second, the hyponatremia may be misleading, since such a reduced serum concentration is commonly and paradoxically present in cirrhotic patients whose total body exchangeable sodium is often increased as measured by isotope dilution technics using sodium[24] and deuterium oxide (heavy water) as tracer substances.[25,26] Such cases of hyponatremia fall into the so-called "new steady state" category, bespeaking a relative inefficiency of homeostatic mechanisms.[27] The osmoreceptor systems appear to be set at a lower level of osmolality with redistribution of water and sodium, the latter shifting from the extracellular to the intracellular compartment because of an alteration in cell membrane metabolism. The patient becomes adapted to this new, steady hypotonicity state, and the condition is virtually symptomless, unaffected by water restriction or salt administration which only aggravates

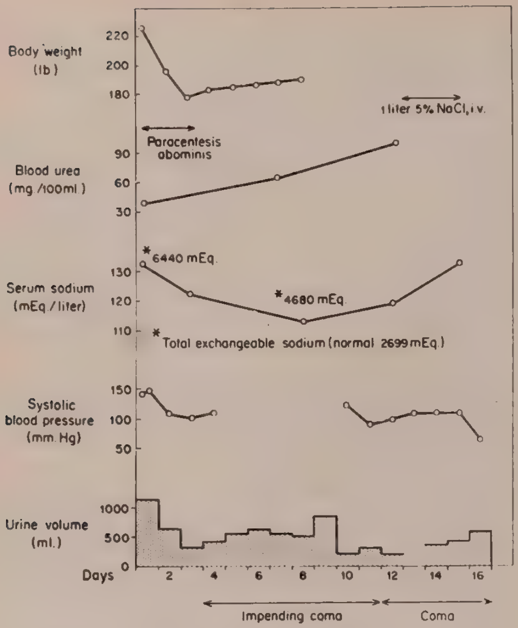

FIGURE 5. Terminal hypotension, oliguria, hyponatremia, uremia, and coma following paracentesis abdominis. No response to conservative treatment or hypertonic saline infusion. Note "paradoxic" hyponatremia.[26]

the edema or ascites. This was illustrated strikingly in a mildly edematous cirrhotic patient with a serum sodium of 117 mEq. which was altered little by intravenous saline that merely exaggerated the fluid retention with the appearance of moist rales throughout both lung fields.

Hepatic failure

It is not an unusual clinical experience for paracentesis to initiate the terminal phase of hepatocellular disease.[26,28,29] A falling serum sodium, diminished kidney output, and icterus betoken a fatal issue. Summerskill[26] applies the term "hypotensive oliguria" to an analogous group of patients (Fig. 5). The initial clinical similarity to a low-salt syndrome is evident. However, intravenous saline is completely without benefit and often aggravates the fluid retention or precipitates pulmonary edema.

Kidney failure

Renal insufficiency may be the outstanding feature in the clinical decline of the cirrhotic patient following paracentesis. Within a few days to a week after the peritoneal tap, lethargy, oliguria, falling blood pressure, and a rise in nonprotein nitrogen make their appearance but without any significant change in the bilirubin concentration. This sequence transpires despite the fact that the patient is still able to elaborate a concentrated urine and that prior to paracentesis the glomerular filtration rate and the phenolsulfonphthalein excretion were normal. The serum sodium may or may not be reduced simultaneously. The cause of the renal failure is obscure since the kidneys are normal histologically. "Certainly greater degrees of renal failure are perfectly compatible not only with life but with an active productive existence in many patients with primary renal disease."[30] Hyponatremia per se cannot be etiologic inasmuch as comparably reduced sodium titers are not unusual in cirrhotic patients without an impairment of kidney function, the sodium may be no lower than before paracentesis, azotemia may be apparent prior to a drop in the sodium level, and finally the administration of saline is without benefit. According to Papper, Belsky, and Bleifer,[30] the cause must be sought among circumstances that can produce acute or subacute renal dysfunction without any change in the anatomic integrity of the kidney. They suggest the possibility that a decrease in the extracellular fluid volume or what is termed the "effective circulating volume" may be responsible for the diminished renal plasma flow. However, attempts to expand the circulation with dextran or whole-blood transfusions are fruitless. A continuous intravenous drip of noradrenalin is of transient benefit.[28] It is most probable that the renal failure represents one facet of widespread disintegration of the organism wrought by some inexplicable influence or noxious agent liberated by the diseased liver.

Ammonia encephalopathy

An increase in blood ammonia associated with disorders of consciousness has been observed following abdominal paracentesis due to one or a combination of causes.[31–33] Improved respiratory excursions following the decompression of the peritoneal cavity enhance the venous return of blood pooled in the splanchnic portal basin that has a high ammonia content, thereby raising the titer in the peripheral circulation; the potentiation of normal renal formation of ammonia by the concurrent use of diuretics, such as Diamox, chlorothiazide, and so forth; and the retention of various nitrogenous substances due to renal insufficiency in the cirrhotic patient. The latter act as substrates on which gastrointestinal amino acid oxidase and urease enzymes elaborate more ammonia.

It is well established that patients with liver disease are intolerant to exogenous ammonia loads, whether such loads be a high-protein diet or free blood in the alimentary tract, with a resultant encephalopathic clinical picture.[1] Apparently endogenous urea, secondary to uremia, follows a similar catabolic pattern, since gastrointestinal ammonia production increases roughly in proportion to blood urea levels.[32] Antibiotics reduce intestinal and gastric ammonia production in patients with severe uremia. Chlortetracycline is the agent of choice under these circumstances since, in contrast to other antibiotics, its serum half-life is little affected by impaired kidney function.[32] Stahl, Roger, and Witz[33] have demonstrated that under certain circumstances the central nervous system symptoms subsequent to paracentesis may be prevented by pretreatment with antibiotics. In one personally observed case, encephalopathic symptoms following paracentesis and associated with hyperammoniemia subsided with the administration of both oral and intravenous chlortetracycline. In another patient, L-arginine may have effected a similar benefit under the same circumstances.

Hypokalemia

A negative potassium balance can follow paracentesis, and the sudden depletion of this element may be one factor in the precipitation of coma in the cirrhotic patient.[34,35] However, if thiazide diuretics have been administered, it should be borne in mind that such agents likewise can cause a potassium deficit and so contribute to the development of a comatose state. The elevation of blood ammonia concentrations by these drugs may be more responsible in this regard. The often nonspecific nature of the clinical manifestations of hypokalemia in the seriously ill and mentally beclouded patient emphasizes the importance of laboratory aids in diagnosis and electrocardiographic monitoring. On the other hand, with the development of diminished glomerular filtration and azotemia in hepatic failure with ascites, hyperkalemia may be noted. Such change is not due to the retention of potassium, since isotope assay indicates that there is little change in the total body exchangeable potassium values. Hence, the hyperkalemia appears to result from an alteration in cell membrane metabolism which permits the redistribution of potassium between the intra- and extracellular compartments.[25]

Hemodynamic derangements

A sudden decrease of a tense intra-abdominal pressure effected by rapid paracentesis incurs many hemodynamic changes in the decompensated cirrhotic patient. The venous pressure declines early during drainage and may continue to drop as more fluid is removed.[19] This decrement appears to be due principally to an improvement in respiratory excursions which become deeper as the fluid is progressively withdrawn. The mechanism for the venous pressure drop may be the increased aspiration of blood into the thorax accompanying improved respiratory movements. Systolic and diastolic pressures simultaneously fall, and this sometimes results in faintness or collapse. This sequence prevails especially if the blood pressure is initially low, or even when it is normal but with the tap performed with the patient in a sitting rather than a supine position.[19] Such a reaction represents a failure of neurogenic venomotor adaptation to intra-abdominal fluid decompression. Duggan, Albright, and Murphy,[17] for example, have demonstrated the failure of normal reflex venoconstriction in response to the immersion of the opposite hand in ice water in patients with advanced portal cirrhosis. While shifts in body water and extracellular fluid seemingly might influence cardiac output, the resting level, which initially may be normal or even elevated, generally remains unchanged.[36] Occasionally, the output may rise temporarily, soon to return to resting values.[37]

Protein depletion

Paracentesis incurs the loss of large amounts of protein contained in ascitic fluid which is generally present in a concentration of 1 or 2 Gm. per 100 ml. in cirrhotic patients. The albumin fraction is slightly higher than in the plasma, and that of the alpha, beta, and gamma globulins a bit lower because of an increased permeability that permits more rapid diffusion of proteins of low molecular size into the peritoneal cavity.[38] I^{131}-labeled albumin studies reveal that the total body albumin is reduced in cirrhotic patients; that its rate of exchange between intra- and extravascular compartments is, however, similar to that in a normal subject; and that the total exchangeable albumin is between 230 and 510 Gm., of which 30 to 170 Gm. are present in the ascitic collection.[39] Hence, the proportion of the total albumin pool of the body lost by paracentetic drainage can be substantial and will depend on the quantity of fluid removed and the frequency of tapping. The normal liver synthesizes about 18 Gm. of albumin per day in contrast to the liver of patients with hepatic disease who generally cannot manufacture more than 9 or 10 Gm. in the same period of time.[40] As established by tritium-labeled water studies, the ascitic pool is not a stagnant body but a rapid circulating medium with a continuous exchange of protein, electrolytes, and fluid between the peritoneal cavity and the blood.[41] Hence, it is apparent that with repeated paracenteses the body albumin deficit will become more pronounced, the ascitic and plasma protein will decline progressively, and the accumulation of peritoneal fluid will be accelerated. Such a sequence is hastened when basic amino acids necessary for the synthesis of protein are not freely available by virtue of a reduced dietary intake. Then extracatabolism of body tissues will occur to provide this substrate with the natural result of body wasting.

Colon bacillus bacteremia

The invasion of the blood stream by colon bacillus microorganisms uniquely and not uncommonly occurs in cirrhotic patients and may be precipitated by abdominal paracentesis.[42–44] The clinical onset, several hours to days after the tap, is sudden with shaking chills, spiking fever, and sometimes vasomotor collapse. Profuse gastrointestinal bleeding may ensue, arising from disseminated erosions in the mucosa. The latter allegedly are produced by a systemic Schwartzman phenomenon provoked by the gram-negative endotoxins.[43]

Several causes underlie the pathogenesis of the bacteremia. The flora of the duodenum and upper jejunum of cirrhotic patients contain an abnormally large number of coliform organisms.[45] Bacterial invasion across the intact mucosal barrier of the gastrointestinal tract into the lymphatics and so into the general circulation is facilitated by paracentetic sterile peritonitis and also by congestion and mucosal inflammation that characterize the stagnant vascular splanchnic basin of the portal hypertensive patient. Furthermore, bacteria are shunted via collateral circulatory pathways into the systemic circulation and thus away from the liver where they are customarily destroyed. Also, the cirrhotic liver is less proficient in synthesizing or elaborating the protein complexes that are necessary for antibacterial defense mechanisms. The observation also has been made that the high ammonia content of tissue fluids commonly found in cirrhotic patients may under certain circumstances invalidate bactericidal cellular and humoral mechanisms.[43] Recovery often follows the use of appropriate antibiotics and supportive treatment.

Perforation of peptic ulcer

The onset of abdominal pain, physical signs of a surgical condition in the abdomen, or evidence of clinical shock need not necessarily signify a contaminated paracentesis and peritonitis or gross intra-abdominal hemorrhage. Koide, Texter, and Borden[46] report 2 cases of acute perforation of a duodenal ulcer and also 1 of rectosigmoid carcinoma following paracentetic drainage. All the patients expired. The development of a boardlike surgical condition in the abdomen is often masked by the residual ascitic fluid. Their explanation for the mechanism of perforation is of interest. The high positive pressure differential of approximately 72 cm. of water between the intestinal lumen and the peritoneal cavity is canceled out as the ascitic fluid accumulates and ultimately achieves a state of equilibrium when the ascites is profuse. However, a sudden drop in intra-abdominal tension following tapping coupled with vigorous peristaltic contractions greatly increases the differential pressure gradient between the bowel lumen and the abdominal cavity and would be sufficient to perforate the thin base of an active ulcerative lesion. This observation is significant, since gastroduodenal ulcers exist more frequently in patients with cirrhosis, exceeding its rate of expectancy as regards the general population. Among my own material, a rupture of the varices of the cecum with consequent hemoperitoneum transpired in a cirrhotic patient following a hot colonic irrigation. A partially obstructive rectosigmoid carcinoma was simultaneously present. It is probable that the hyperperistaltic activity of the colon incidental to the obstruction by the neoplasm at the rectosigmoid junction, enhanced by the strong colonic contractions induced by the enema (and a probable competent ileocecal valve), precipitated the rupture of the cecal varicosities. In the case records of the Massachusetts General Hospital is documented an instance of a ruptured acutely inflamed appendix which was necrotic in its central portion and had a 1-cm. longitudinal tear in the wall.[47] Paracentesis had been performed in this ascitic cirrhotic patient four days prior to the acute abdominal catastrophe. An example of fatal rupture of a mesenteric varix with hemoperitoneum immediately following paracentesis has been mentioned elsewhere.

Summary

Abdominal paracentesis is undertaken in the cirrhotic patient with ascites for a number of reasons:

1. For the relief of dyspnea and orthopnea. The adverse effects of massive ascites on pulmonary mechanical efficiency has been discussed. Moreover, a low arterial oxygen tension characterizes cirrhotic patients due to a hypoventilation of the basal segments of the lung because of the elevation of the diaphragm and to increased venous admixture via portal to pulmonary communications which bypass the alveolar capillary bed. The former is corrected by paracentesis and the arterial oxygen tension is increased.[48]
2. For the relief of discomfort of a taut abdomen.
3. To increase alimentary tract capacity and overcome anorexia.
4. To facilitate abdominal examination.
5. As a preliminary to liver biopsy, percutaneous trans-splenic venography, assay of splenic pulp pressure, and peritoneoscopy.
6. As a protective measure against the development of an umbilical hernia or of its rupture with spontaneous drainage of ascitic fluid that may initiate peritonitis or hepatic failure.[49]
7. Bradley[50] has shown that when the intra-abdominal pressure is increased, blood flow through the liver is curtailed. Moreover, abdominal compression reduces renal plasma flow, glomerular filtration, and urine flow.[51]
8. One of the functions of the lymphatics of the diaphragm is to drain off free peritoneal fluid up to a liter or more per day. Such absorption is aided by movements and changes in pressure associated with the respiratory cycle, especially diaphragmatic excursions. Immobilization of the diaphragm by tense ascites impairs this function.[52] The rapid reduction of the ascitic accumulation follows cannulation drainage of the thoracic duct in the neck in man.[21]
9. The hydrostatic pressure effect of a tense ascites causes a rise in the wedged hepatic vein, intrasinusoidal and therefore portal tension. The suggestion has been made that when ascites is associated with portal hypertension and bleeding esophageal varices, cautious abdominal paracentesis may be a useful therapeutic measure, since it reduces the intra-abdominal pressure and thereby lowers the portal tension.[53] Such an approach is circumspect, especially

since certain pharmacologic agents accomplish this effect more expeditiously.

However, a variety of complications may be associated with the paracentetic procedure. Among these are disorders of water and electrolyte metabolism, hemodynamic derangements, mental and neurologic symptoms, and signs of specific organ failure, principally that of the liver and kidney. Several of these symptom complexes may occur simultaneously. Hence, clinical and laboratory data must be interpreted cautiously else inappropriate treatment may be instituted with deleterious consequences. For example, a low serum sodium does not oblige the administration of intravenous saline. The hyponatremia is more frequently one facet of the widespread failure of body cell function in the cirrhotic patient. The integrity of the liver cells and ultimate hepatic reserve are the most important factors in determining the onset and progression of these metabolic and homeostatic complications. Recovery, therefore, depends more on the capacity of the hepatic cells toward recompensation than on the ministrations of the physician who must strictly observe the principle of "primum non nocere." On the other hand, gross hemorrhage and suppuration within the abdominal wall and peritoneal cavity, in addition to the precipitation of varix bleeding, are more ominous complications that require prompt and accurate treatment.

Fortunately, with progress in the understanding of the pathologic physiology of the genesis of ascites, the trend has been away from paracentesis, long the standard method of treatment, and this has been replaced by efficient diuretic programs that embrace the use of a low-sodium diet, steroids, aldosterone antagonists, and osmotic agents. Hence, routine instrumentation should not be instituted until these conservative measures have been given an adequate trial, unless the ascites is so massive as to impair seriously the respiration and general comfort of the patient, or as a necessary preliminary to certain diagnostic studies. Accordingly, general and technical precautions are outlined that help make abdominal paracentesis a safer procedure.

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Number one hundred twelve in a series of Recent Advances in Medicine and Surgery. Parts I and II appeared in the June 1 and June 15, 1962 issues of the JOURNAL.

Progress toward vaccine against common cold

There is now enough accumulated knowledge on viruses that cause colds and respiratory disease to attempt the development of vaccines to protect both adults and children, according to a report by Hilleman *et al.* in the May 12, 1962, issue of the *Journal of the American Medical Association.* A study involving more than 200 industrial workers at Rahway, New Jersey, revealed the presence of coryzavirus in 14 per cent of 141 volunteers suffering colds. Coryzavirus was found in 20 persons with cold symptoms, but no coryzavirus was found among 49 persons without colds. This virus was the most prevalent in the adult study designed to determine the relative importance of 11 different viruses or virus families.

According to other studies of the causes of respiratory illness in adults in the general population, three types of viruses appear to be the most important causes of respiratory illness in this group: coryzaviruses, rhinoviruses, and Eaton agent. Previous studies have implicated rhinoviruses in 15 to 32 per cent of colds in adults and Eaton agent in 24 per cent of atypical pneumonia cases.

In a study of 667 cases of acute respiratory illness in Philadelphia children under eight years of age, the RS (respiratory syncytial) virus was the most prevalent, occurring in 17 per cent. Other studies of respiratory illness in children have showed that RS virus, some adenovirus and parainfluenza viruses, and Eaton agent are the predominant causes of this syndrome.

For children a vaccine containing certain adenoviruses and parainfluenza viruses, RS virus, and Eaton agent may well be indicated. For adults, a vaccine providing coverage against coryzavirus, rhinovirus, and Eaton agent would be worthy of development.

The development of cold vaccines might require extensive tests because of the multiplicity of viral strains. A continuous survey to determine the susceptibility of the population to certain strains at given times might also be needed as a guide to the development of such vaccines.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
January 31, 1962

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by ABRAHAM SUNSHINE, M.D.

Cough, Weight Loss, and Pulmonary Lesions with Air-Fluid Levels

Case history

SALVATORE BALDINO, M.D.: A fifty-six-year-old Negro male was admitted to Knickerbocker Hospital for the first time on September 9, 1961, because of cough, weakness, and weight loss of four weeks duration. The patient's past history was unremarkable except that one to two years prior to his admission he had had a chest x-ray film taken by a mobile unit and was subsequently advised to report to a health center for an examination. Since he was completely asymptomatic, he failed to do so.

Approximately four weeks prior to his admission the patient developed anorexia, weight loss, and weakness which became progressive. It was impossible to determine the exact amount of weight loss, but according to his family it was considerable. In addition, the patient developed a cough which was productive of moderate amounts of thick, yellowish sputum and was associated with intermittent feverishness. He denied hemoptysis, although his family noted "red streaks" in his sputum on several occasions. Shortly before admission the patient was noted to be forgetful and irritable. His anorexia and weakness became severe, and he was brought to the hospital.

There was no history of nausea, vomiting, diarrhea, chills, sweats, fainting, or dizziness. The stools were normal in color. He had no chest pain. A review of his systems yielded no additional information of significance. The patient never had been hospitalized and was not under a physician's care. He denied having diabetes, tuberculosis, venereal disease, heart disease, or hypertension.

The patient worked as a plumber until the onset of the present illness. He admitted to being a moderate binge drinker but denied smoking. The family history revealed no contagious or familial disease.

On physical examination the patient was a well-developed, poorly nourished, elderly male appearing acutely and chronically ill. He was conscious and cooperative but confused as to time and place. His blood pressure was 100/70, pulse 112 per minute and regular, respirations 24 per minute, and temperature 102 F. There was no sign of head trauma. The pupils were equal and reacted to light. His tongue was dry and coated. The neck was supple, and the neck veins were flat. There were no deformities of the chest, and the respiratory excursions were equal bilaterally. In the midfield of the right lung there was an area of dullness to percussion. Harsh, bronchial breath sounds were heard in the right axilla and in the midfield of the right lung posteriorly with a few crackling rales in the same area. The heart was not enlarged to percussion, and the heart sounds were of good quality with no audible murmurs. No abdominal organs or masses were palpable. There was marked clubbing of the fingers and toes, but no cyanosis or edema was present. A neurologic examination produced findings within normal limits, and the deep tendon reflexes were hypoactive throughout.

The initial laboratory data revealed a hemoglobin of 8.8 Gm. per 100 ml. and a white blood cell count of 7,300 with 72 per cent polymorphonuclear leukocytes and 28 per cent lymphocytes. The erythrocyte sedimentation rate was 130 mm. per hour. The reticulocyte count was 0.5 per cent. The urine had a specific gravity of 1.020, showed no sugar, acetone, or albumin, and contained only 1 to 3 white blood cells per high power field. The fasting blood sugar was 78 mg., nonprotein nitrogen 37 mg., and cholesterol 83 mg. per 100 ml. with 66 per cent esterified. The serum albumin was 3.2 Gm. and the globulin 4.4 Gm. per 100 ml. The serum bilirubin was 0.45 mg. per 100 ml., transaminase 280 units, and prothrombin time 23 seconds with a control of 13 seconds. A VDRL test produced positive findings. A sickle-cell preparation showed negative results. A purified protein derivative first strength gave negative results.

Chest x-ray studies revealed a homogeneous infiltrate involving the upper and middle lobes of the right lung. There was a large, irregular radiolucency without pulmonary markings at the right apex. There were several loculated areas of radiolucency with fluid levels in the upper field of the right lung. The mediastinum was not displaced. The left lung was clear except for what appeared to be an area of platelike atelectasis in the midfield. The skull roentgenograms revealed unremarkable findings.

A lumbar puncture done shortly after admission produced unremarkable results. Gram-positive diplococci were seen on a sputum smear, and pneumococci were cultured subsequently. The patient was started on penicillin in large doses. There was no improvement. The addition of broad-spectrum antibiotics in full dosage failed to alter the clinical picture. He continued to look toxic with a temperature ranging between 100 and 102 F. A bronchoscopy revealed a normal tracheobronchial tree except for some hyperemia and a slight bloody discharge from the upper lobe orifice of the right lung. An examination of bronchial washings for cell block, fungi, and acid-fast bacilli produced negative findings.

On the sixth hospital day repeat chest x-ray studies showed the same infiltrate, radiolucencies, and air-fluid levels on the right. In addition, there was a large "cavity" with an air-fluid level in the midfield of the left lung where previously an area of platelike atelectasis had been described. On the ninth hospital day a closed thoracotomy was performed in the right first intercostal space, and air, but no fluid or pus, was obtained from the area.

The patient's physical findings did not change. He continued to be febrile and had a persistent cough, raising thick, greenish-brown sputum. Three sputum specimens were examined for fungi and acid-fast bacilli, but none were found. On the twelfth hospital day a fourth sputum specimen was found to contain a few acid-fast organisms. All cultures still were negative. The patient was started on isoniazid, PAS (para-aminosalicylic acid), and streptomycin. Other antibiotics were discontinued.

At this time the patient complained of pain and paresthesias in the left lower extremity. Over the next few days a left hemiparesis gradually developed. A neurologic examination revealed a cooperative but confused patient. The carotid pulsations were good. The cranial nerve function was intact. There was marked weakness of the left arm and leg. The joint position sense was impaired in the left hand and foot. A repeat spinal tap revealed clear fluid with a pressure of 200 mm., protein 20 mg., and sugar 65 mg. per 100 ml. No organisms were seen.

The patient pulled out his chest tube which was not reinserted. Subsequently, a foul discharge was noted from the chest wound. This grew Aerobacter aerogenes as did a sputum culture at this time. The wound was irrigated and dressed frequently but continued to drain.

Over the next two weeks the patient continued to appear toxic. His temperature remained around 100 F. A physical examination of the chest showed no additional findings. The left hemiparesis remained about the same or, perhaps, became slightly worse. The patient was about to have a carotid arteriogram when he suddenly expired on the thirteenth hospital day.

Discussion

ABRAHAM SUNSHINE, M.D.*: This is the problem of a fifty-six-year-old male admitted to Knickerbocker Hospital with a four-week history of cough, weakness, and weight loss. We know that two years ago on a routine photofluorogram the x-ray film showed abnormal findings and that he was advised to report to the Health Center. It is very difficult to know what this means; at best I can say that there was some finding in his chest which may or may not have been significant. We know that he had been sick before, manifested by anorexia, weight loss, fever, weakness, and a cough productive of a moderate amount of yellowish, blood-streaked sputum. He also had mental symptoms indicative of an organic mental syndrome, including forgetfulness and irritability at the time of the onset of his illness. From a negative standpoint, there was no nausea, vomiting, chills, sweats, fainting, or dizziness, and no chest pain. We do know this man was a binge drinker, and I think that this is quite important as we try to develop the story into a coherent one.

On physical examination, he was a poorly-nourished, elderly patient both acutely and chronically ill. He was conscious but confused as to time and place. The blood pressure was normal, but tachycardia, tachypnea, and fever were present. There was no evidence of head trauma. We are missing information that I would like to have to aid in making a diagnosis of the pathologic condition in his lung. I think Dr. Moynahan can help us. Did this man have teeth, or did he not? I think he did have teeth. One of the diagnoses I would like to entertain is that of a putrid lung abscess. This would be excluded by the absence of teeth, since these do not occur in individuals who are edentulous because the organisms found in the mouth are located about the teeth. I have looked at the skull films this morning with Dr. Moynahan, and although I don't qualify as a radiologist, we both agreed that he did have teeth. This permits us to include in the diagnostic possibilities a putrid lung abscess. There are no meningeal signs. The examination of the chest is most important, and I will go over that in detail. There were no deformities of the chest, and the respiratory excursions were equal and bilateral. In the midfield of the right lung there was an area of dullness. Harsh bronchial breath sounds were heard in the right axilla and in the midfield of the right lung posteriorly with a few crackling rales in the same area. It is interesting that there were no wheezes heard either. The heart was not enlarged, and there were no murmurs. An examination of the abdomen showed unremarkable findings. Now we see that this patient had clubbing of the fingers. This, too, I think is extremely important in attempting to arrive at an etiologic diagnosis. As you know, clubbing is a most unusual finding in uncomplicated tuberculosis. Clubbing brings to mind carcinoma or a pyogenic infection of the lung. I think we can say on the basis of this physical finding that this man had more than tuberculosis. If tuberculosis is a feature, it does not explain the whole problem. The initial neurologic examination showed normal findings, and this is extremely important, because later on he developed neurologic complications.

Let us review the laboratory findings: The patient was anemic. He did not have a leukocytosis, although the differential count revealed an increase in the polymorphonuclear leukocytes. The sedimentation rate was rapid. There was no evidence of hemolysis, and the urine examination was within normal limits. The cholesterol of 83 mg. per 100 ml. gives a real insight into this patient. He probably was chronically malnourished. He was not jaundiced. He had a slightly elevated transaminase; the prothrombin time was 23 seconds with a control of 13 seconds. We do not know if this responded to vitamin K. I am at a little bit of a loss to explain this prothrombin time. The serology showed positive findings. The tuberculin test gave negative findings

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This in itself has very little meaning. The patient would have to have been tested with the intermediate or second-strength tuberculin before we could assume that he did not have tuberculosis. So, from this skin test alone, we cannot draw any definite conclusions. I will leave the descriptions of the skull films and chest x-ray films to Dr. Moynahan. A lumbar puncture was performed and gave normal results. We will discuss this a little later when we discuss the cerebral pathologic condition. Sputum cultures revealed pneumococci and no other organisms. A bronchoscopy revealed a normal tracheal-bronchial tree except for some hyperemia and a slight bloody discharge from the upper lobe orifice of the right lung. An examination of bronchial washings for fungi, acid-fast bacilli, and tumor cells showed negative findings. The patient's course continued to be febrile. He complained of a persistent cough and produced greenish-brown sputum. One sputum specimen revealed a few acid-fast organisms on smear. The patient was started on PAS, streptomycin, and isoniazid, and all other antibiotics were discontinued. He developed weakness of his left arm and left leg with an impairment of his position sense. A spinal tap at this time was unrevealing. This weakness developed over a period of a few days. He continued to be toxic and febrile with a temperature of 100 F. He suddenly expired on the thirteenth hospital day.

Let us now consider the possibilities which led to the cerebral pathologic condition. There are four categories which should be considered: tumor, abscess, hematoma, or a vascular lesion. The lesion was in the distribution of the middle cerebral artery, and it came on very slowly, progressed gradually, and then led to death. I think that an occlusion of the middle cerebral artery would be very unlikely because of the slowness of the onset and then the sudden catastrophic event. A hemorrhagic episode also would be unlikely because of the slowness of the onset. A brain tumor can present symptoms in this manner. However, this would require two diagnoses to explain both the lung and cerebral pathologic conditions. Of course, if we considered a primary malignant condition of the lung with metastasis to the brain, this could be a likely possibility. However, as we will see in a moment, I do not believe that this patient had a bronchogenic carcinoma. Consequently, I will not give this matter serious consideration. A subdural hematoma always must be mentioned and certainly could be the diagnosis. It would not then fit in with the pulmonary pathologic condition except to say that this was a man who was a binge drinker and may have been hit on the head at the same time that he developed some problem in his chest. It has to be mentioned, and there is really no way of excluding it on the basis of what we know about this patient.

We then come to the problem of a brain abscess which I think is the real consideration. One could consider a pyogenic brain abscess, or, as was probably considered by the house staff, the possibility of tuberculosis. Tuberculomas are rare, but the course of the patient from the standpoint of his central nervous system from what I was able to determine about tuberculomas, is quite compatible. The absence of spinal fluid findings is not inconsistent with an abscess provided the abscess was deep-seated. In the preantibiotic era, the most common cause of a brain abscess was a mastoid infection. Recently Loeser and Scheinberg* reviewed the etiology of brain abscesses. Prior to the antibiotic era 60 per cent of brain abscesses were the result of mastoid infections; for the postantibiotic era about 13 per cent were from mastoid infections. Lesions about the face also can give rise to brain abscesses. About 12 per cent of brain abscesses were metastatic from inflammatory lesions in the lung. In this same series the primary site was undetermined in about 26 per cent of the patients who had a brain abscess. The organisms found in brain abscesses were staphylococcus, streptococcus viridans, pneumococcus, and mixed infections by both gram-negative and gram-positive organisms. A group of cases were sterile at the time of surgery or autopsy. The time from the onset of the symptoms to the time of death in the antibiotic era combined with surgical treatment was anywhere from three to thirteen

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* Loeser, E., Jr., and Scheinberg, L.: Brain abscesses; a review of ninety-nine cases, Neurology 7: 601 (Sept.) 1957.

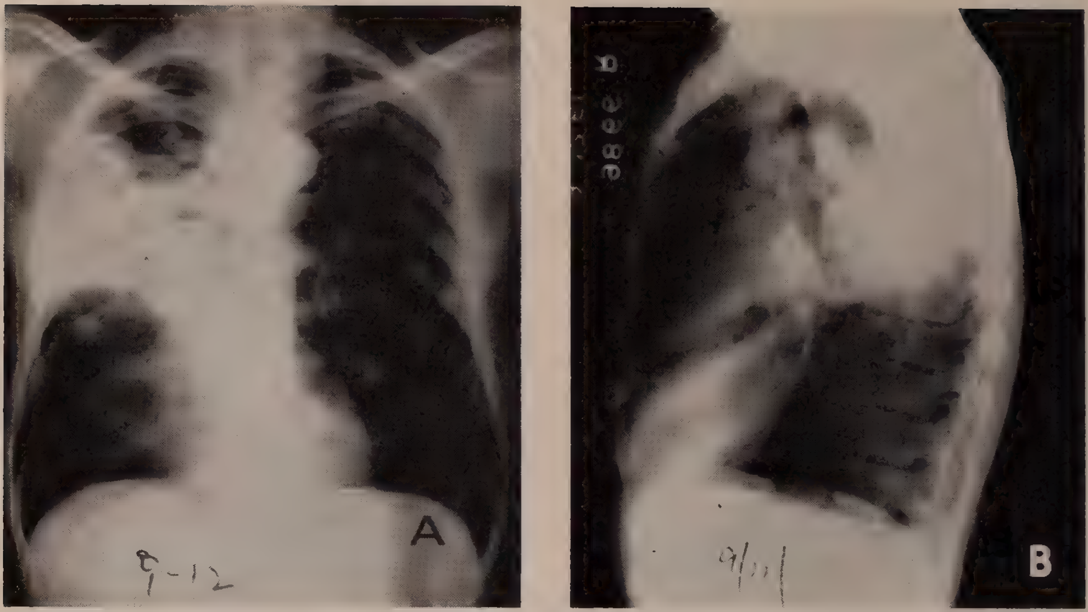

FIGURE 1. Chest roentgenograms. (A) Shortly after entry showing consolidation of the right upper lobe with poorly visualized foci of radiolucency. There is a large zone of radiolucency at the right apex. Adjacent to the mediastinum just to the right of the ascending aorta is an air-fluid level. A medium-sized emphysematous bulla is outlined near the left hilum. (B) In lateral projection at the same time as (A) shows that the radiolucency with the air-fluid level is located anteriorly, away from the area of consolidation.

days. Occasionally these cases will survive for two months. Our patient expired suddenly on the thirteenth day. It is interesting to note that the authors stated that the time from symptoms to death had not changed from the preantibiotic to the postantibiotic era. We cannot say that surgery and antibiotics have not helped, but rather that statistically, from the onset of symptoms to the average time of death, there has been no change. They do believe that the time from the primary infection to the onset of symptoms has been prolonged. Many patients who developed infections have been treated, and this seems to delay the appearance of the neurologic symptoms. I believe that this patient had an abscess in the brain. The clinical setting of this patient's neurologic disorder is most compatible with the diagnosis.

Let us now go back to the pulmonary problem and discuss the pathologic conditions that will give rise to a brain abscess. I think that tuberculosis is entirely compatible with the findings on x-ray examination. I am being influenced against this diagnosis by two factors. First, the presence of clubbing is most unusual in uncomplicated tuberculosis. Second, there is the paucity of tubercle bacilli. Carcinoma has to be considered, and I have no way of excluding it fully. However, I am more inclined to tie the whole case together with one diagnosis, so I would like to go on to the consideration of a lung abscess. The portal of entry into the lung usually is through aspiration. It would not be unlikely for our patient to have been on a binge, and this could have been the beginning of his lung problem. The ready recovery of pneumococci from his sputum is consistent with this. We certainly would expect to find such organisms on culture. We have mentioned that the portal of entry of the organism into the lung is aspiration. There is also the hematogenic route, but this patient gave no indication of this. Finally, it should mention a penetrating chest wound which he also did not have.

Joseph M. Moynahan, M.D.: An examination of the chest on admission (Fig. 1) revealed a large radiolucent area occupying the entire right apical region and a smaller radiolucent area

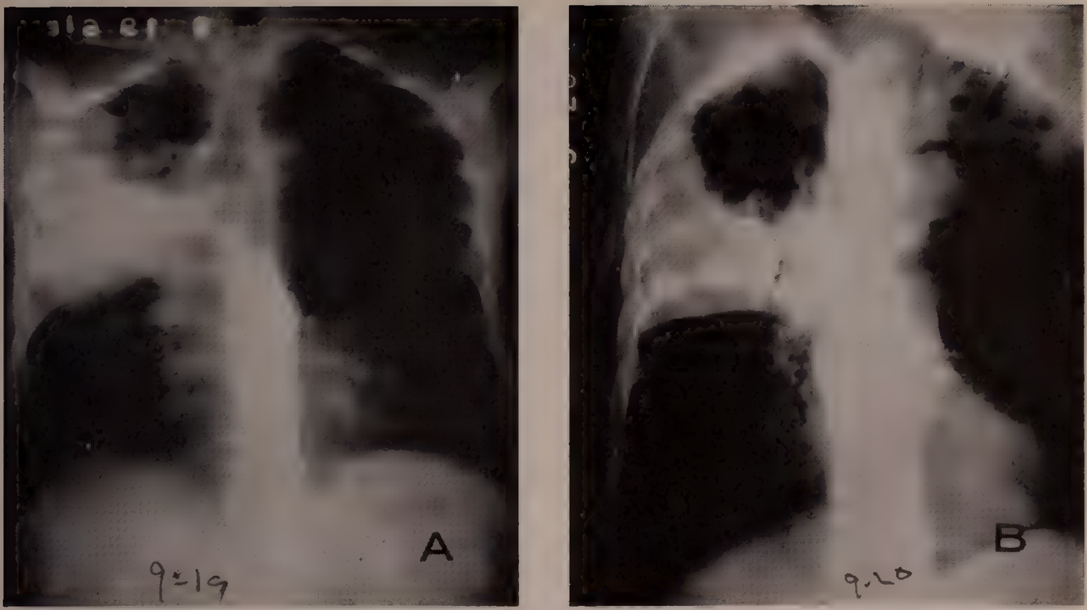

FIGURE 2. Chest roentgenograms. (A) One week later the chest roentgenogram shows an increase in size of the emphysematous bulla on the left, which now contains a small fluid level. The findings in the right lung are essentially unchanged. (B) X-ray film in the decubitus position shows a large fluid level in the radiolucent area at the right apex and nearby areas of nonaerated lung parenchyma similar to that seen in pneumothorax.

located anteriorly. Both of these spaces contained fluid levels. In addition, there was a consolidation of the posterior segment of the upper lobe of the right lung and to a lesser extent of the anterior segment. A portion of the middle lobe also appeared consolidated. One can differentiate this from the roentgenographic appearance of loculated fluid by observing that there were air-filled bronchi traversing this zone of consolidation. Several of the radiolucent areas appeared larger than normal bronchi, suggesting the possibility of small cavitations. There was a medium-sized radiolucent area in the left hilum, suggesting an emphysematous bulla.

The radiolucent areas in the upper field of the right lung may represent either loculated hydropneumothorax, abscess cavity, or infected emphysematous bullae containing fluid. I feel that the most likely possibility is a loculated hydropneumothorax, since the small radiolucent area is located at a distance from the consolidation rather than within it, as would be more common in an abscess. In addition, in one film less dense parenchyma are noted simulating the hypoaerated lung seen in severe pneumothorax. In infected bullae the radiolucent area tends to be smooth and rounded, and there is usually other evidence of emphysema.

A re-examination several days later (Fig. 2) revealed similar findings on the right, but the bulla at the left hilum has increased considerably in size, and it now contains a fluid level.

In summary we have an area of consolidation of the upper lobe of the right lung with possible small cavities, a loculated hydropneumothorax, and a progressively enlarging bulla on the left. This is a rather unusual picture, and several possibilities must be considered. Necrotizing pneumonitis with a bronchopleural fistula could give this picture. In view of the upper-lobe distribution of the lesion and possible cavitation, tuberculosis must also be considered. Finally, pneumonia distal to a bronchogenic carcinoma is also possible. The relationship of the bulla at the left hilum is not apparent, but it may represent aspiration of material from the right with partial obstruction of a segmental bronchus.

Dr. Sunshine: I don't know that a radiologist or clinician, except for the points that Dr. Moynahan has already mentioned, can really differentiate the two types. I think then that on what Dr. Moynahan says that this is probably an acquired lung cyst.

I thing this man's main problem was a lung abscess with metastatic spread of the abscess to his brain giving him the brain abscess that caused his death. I do not have the explanation for the pain in his leg, but I doubt that he had any spinal cord involvement. With a normal albumin, I really am not too anxious to make a diagnosis of cirrhosis of the liver. I think the liver problem was probably related to an overwhelming sepsis as was the anemia.

Clinical diagnoses

1. *Pulmonary tuberculosis, right upper lobe, with pyopneumothorax, secondary to bronchopleural fistula, and bronchogenic dissemination to left lung with infected bulla*
2. *Tuberculoma of brain*

Dr. Sunshine's diagnoses

1. *Lung abscess, right upper lobe, with secondary brain abscess*
2. *Hydropneumothorax, right*
3. *Emphysematous bulla, left lung, infected*

Pathologic report

Perry Berg, M.D.: The major findings at autopsy were in the lung and brain. The apical portion of the upper lobe of the right lung contained a large tuberculous cavity, and there was a bronchopleural fistula through it which had created a loculated hydropneumothorax. The inferior portions of the upper and the middle lobes of the right lung contained multiple areas of tuberculosis, some with small central cavities about 2 to 3 mm. in diameter. I think these correspond to the radiolucent areas which were seen on the x-ray examination. Microscopically, there was extensive caseation with minimal fibrosis and only a scant inflammatory reaction with few collars of epithelioid cells and very few giant cells. This probably indicates very little resistance to the tubercle bacillus and is what used to be called "galloping consumption."

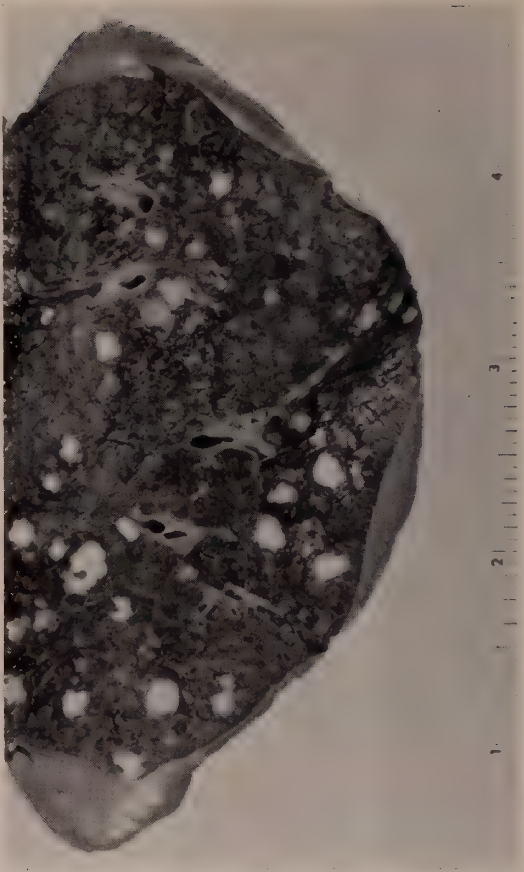

FIGURE 3. Cut surface of the spleen is studded with many miliary tubercles 1 to 3 mm. in size.

As predicted, the large air-filled space in the left lung was a huge emphysematous bulla. It was very thin-walled and ruptured at the autopsy table, spilling a small amount of dirty, yellowish-brown fluid. We could not establish its connection with the left bronchial tree. However, its wall was composed of a thin layer of fibrous tissue and compressed pulmonary parenchyma. It showed no evidence of tuberculous infection. There were scattered small foci of acute tuberculous caseation elsewhere in the left lung, but these were minor and probably represent miliary intrapulmonic spread. In both lower lobes there was nontuberculous pneumonia. The exudate was composed entirely of polymorphonuclear leukocytes and fibrin; it probably represents a terminal

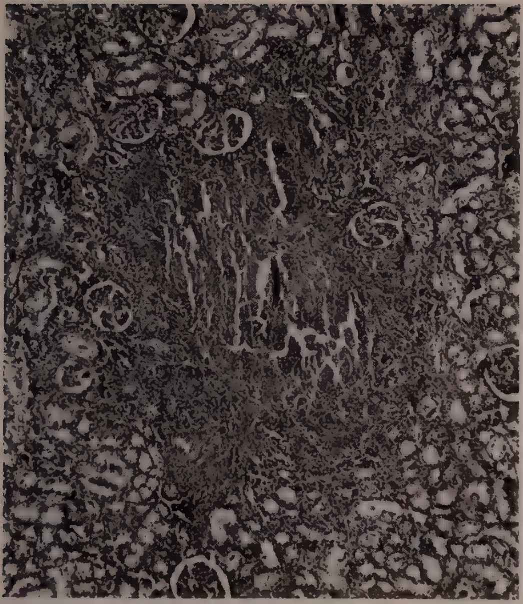

FIGURE 4. A focus of acute caseation in the renal cortex.

infection. There was considerable acute caseation in the mediastinal lymph nodes.

The cerebral lesion was located in the right internal capsule. It was an area of nonspecific encephalomalacia with no evidence of infection, tuberculous or otherwise, and it is interpreted as a banal cerebral infarct. There was no evidence of meningitis. There was a moderately advanced degree of cerebral arteriosclerosis as well as aortic and coronary arteriosclerosis. Apparently, the presence of arteriosclerosis was not affected by the patient's low serum cholesterol and strenuous, if involuntary, weight reduction.

Miliary tuberculosis was detected in the spleen (Fig. 3) where it was extensive, and focally in the kidneys (Fig. 4) and adrenal glands.

Anatomic diagnoses

1. *Pulmonary tuberculosis with cavitation and bronchopleural fistula, upper lobe, of right lung, with loculated hydropneumothorax*
2. *Miliary tuberculosis, left lung, mediastinal lymph nodes, spleen, kidneys, and adrenal glands*
3. *Emphysematous bulla, infected, left lung, nontuberculous*
4. *Subcutaneous emphysema, right chest and arm*
5. *Bronchopneumonia, both lower lobes, terminal*
6. *Cerebral infarct, right internal capsule*
7. *Cerebral, aortic, and coronary arteriosclerosis*

Blow to chest restarts arrested heart

A heart that had stopped beating was restarted by a sharp blow to the chest, according to an article by Felix Feraru, M.D., in the May 19, 1962, issue of the *Journal of the American Medical Association*. When a sharp blow with the side of a clenched fist was struck to the chest of a patient whose heart stopped beating during abdominal surgery, the heartbeat resumed immediately, but subsequently it stopped again and was restarted by two similar blows to the chest. When the patient's heart stopped beating a third time, the chest was opened and the heart massaged by hand. However, the heartbeat could not be restarted, and the sixty-seven-year-old man died. An examination showed that the patient had advanced coronary heart disease.

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

VALENTINO D. B. MAZZIA, M.D., Chairman
LEE S. BINDER, M.D.
ELIZABETH J. CRAWFORD, M.D.
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GERTIE F. MARX, M.D.
ROBERT I. SCHRIER, M.D.

Blindness and Anesthesia

COMPLAINTS REFERABLE to vision and the eyes are not uncommon following anesthesia. The following case illustrates an unusual cause.

Case report

A thirty-one-year-old Negro female was admitted to the hospital with the chief complaints of pain in the lower part of the abdomen and vomiting of three days duration. She was intoxicated at the time of admission.

Her last menstrual period had been seven months previous. She was pregnant.

There were eleven pregnancies in the past with nine living children and two stillborn. The last delivery was nine months before this admission. There was no history of surgical or medical illnesses.

Her husband, who had been a narcotic addict, died seven years before and left her with five children. She had been living in a common-law relationship with one man for the past six years. For the previous four years she had been drinking heavily.

The significant findings in the admission physical examination were a temperature of 97 F., pulse 130 per minute, respirations 26 per minute, and blood pressure 130/90 mm. Hg. The lips were dry and cracked, and the tongue was dry. There was an alcoholic odor to the breath.

The fundus of the uterus was palpated 2 fingerbreadths below the xiphoid. The vertex was down and floating. The fetal heart was beating at 136 per minute. On vaginal examination the membranes were intact.

The admission hemoglobin was 13 Gm. per 100 ml., and on admission the urine contained albumin and acetone. The patient was not thought to be in labor on admission. She received hydration therapy.

Twenty-four hours after her admission she precipitously passed a fetus, although no contractions had been felt. This infant had an Apgar score of one and died within a few hours of birth. An autopsy revealed a respiratory distress syndrome.

After appropriate consultation the patient was scheduled for a tubal ligation which was performed ten days after admission by which time her physical condition was good.

She was made to fast from midnight on the day of surgery. At 11:40 A.M. meperidine hydrochloride 50 mg. and atropine sulfate 0.4 mg. were administered intramuscularly. The preanesthetic vital signs were a blood pressure of 120/80 mm. Hg, and a pulse of 100 per minute.

At 12:10 P.M. anesthesia induction was begun with 125 mg. of 2.5 per cent thiopental sodium intravenously, and cyclopropane-oxygen by face mask was administered for maintenance by a closed circle system. An additional 0.4 mg. of atropine sulfate was administered subcutaneously at 12:15 P.M. A succinylcholine 0.2 per cent intravenous infusion was administered during the laparotomy which required fifty minutes. The vital signs remained stable throughout the procedure and were unchanged from the preanesthetic level. The total anesthesia time was one hour, and the patient was awake at the conclusion of the surgery.

Presented and discussed at a conference held at Bellevue Hospital, New York City, March 5, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

She arrived in the recovery room at 1:15 P.M. where she remained until 5:00 P.M. The vital signs still were unchanged.

Soon after her arrival in the recovery room she complained that she was blind and could not see from both eyes. Her eyes were irrigated by the nurses with a physiologic solution which did not seem to help.

An ophthalmology consultation was requested, and she was seen in the recovery room at 4:00 P.M. The ophthalmologist noted that the patient was lying quietly in bed with her eyes open, but her lids were not excessively separated. He said to the patient, "I am the eye doctor. They tell me that you cannot see. Is that right?"

She replied, "Yes."

He asked, "Can you see me?"

She said, "No."

When asked to look up, down, right, and left, her eyes roamed about in an irregular fashion. They did not follow a flashlight.

On examination her lids, conjunctivas, cornea, anterior chamber, and iris showed no unusual findings. Her pupils were round, regular, and equal, and reacted directly and consensually to light.

A funduscopic examination revealed no abnormal findings in the disk or vessels. There were no foveal reflexes. Global pressure elicited arterial pulsations.

The position of the eyes was straight by corneal reflexes. The eye movements were full with no nystagmus. No increase in tension was noted on finger pressure.

The ophthalmologist's feeling was that the blindness was of a hysterical nature, and a psychiatric consultation was requested.

By the time the patient was seen that evening her vision had returned, and the psychiatrist felt she had suffered a conversion reaction.

The remainder of her hospital course was uneventful, and she was discharged well on the seventh postoperative day.

Comment

Anesthesia can be associated with many types of eye injuries. Blindness can result from central retinal artery occlusion which could be produced by prolonged and excessive pressure on the eyeballs. Such pressure could be produced by a face mask and would be more likely to occur if the patient experienced a bout of hypotension. It is related simply to exerting a higher pressure on the eyeball than the systemic blood pressure which thus prevents blood flow to the retina through the retinal artery, an end artery. This condition is not often bilateral.

Cortical blindness may be the result of hypoxia or anoxia associated with respiratory or circulatory embarrassment. In this condition light often can be perceived, but objects are not recognized.

The clues to the diagnosis of hysteria were the patient's unusual lack of concern over her sudden complete blindness and the inability to look in a particular direction when asked to do so. She could not see, therefore she would not look.

Another test that could have been performed is that of optokinetic nystagmus. Moving alternate vertical strips on a sheet of heavy lined paper in a horizontal direction before the eyes would have produced involuntary nystagmus.

ACKNOWLEDGMENT. We wish to thank Newton B. Chin, M.D., chief resident on the Ophthalmology Service of Goodwin Breinin, M.D., Bellevue Hospital Center, for assisting us with this discussion.

Number one hundred twenty-four in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
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Scorpion Bite Poisoning

A PHYSICIAN from St. Michael's Hospital in Toronto, Canada, called the Poison Control Center for help and advice regarding the management of a scorpion bite.

On the afternoon of January 17, 1962, a thirty-five-year-old inspector of the Canadian Division of Fruits and Vegetables of the Department of Agriculture appeared at the Emergency Department of St. Michael's Hospital and related that he had been bitten at the base of the thumb by a scorpion while opening a crate of tomatoes imported from Mexico. On admission he complained of a throbbing pain and an electrical sensation at the site of the bite. According to the inspector, the insect was about 1 inch long, and from his description it conformed to the characteristics of a scorpion. The insect was not caught.

An examination of the patient revealed a tiny puncture wound surrounded by an area of erythema less than 1 mm. in diameter; otherwise, the physical examination gave entirely negative findings. A tourniquet was immediately applied above the elbow and released every fifteen minutes, and the hand was immersed in cracked ice. Procaine-epinephrine 5 cc. and Chlor-Trimeton maleate 10 mg. then were injected above the site of the bite.

The Poison Control Centre in Toronto then was called for assistance. Through its facilities a search was made for specific antiserum, but none was available in Canada. The hospital was informed that the City of New York Department of Health might have some in stock, and contact thus was made with the Poison Control Center in New York City. The Canadian Armed Forces also were contacted, but none was stocked by them either. In the interim, on the advice of the Canadian Poison Control Centre, 10 cc. of snake antivenin was administered intramuscularly and locally, as the literature suggests should be done whenever specific antiserum is not available, in the hope of obtaining some nonspecific action.

A request was made from the New York City Poison Control Center for a scorpion antivenin. We informed the physician from St. Michael's Hospital that this Center does not have any supply available on hand but that we would make an effort to procure antivenin for this patient.

The following sources were solicited without success: Local zoos and museums; pharmaceutical suppliers; armed forces installations; the national clearinghouse for poison control centers; the Public Health Service (Biological Division); Findlay E. Russell, M.D., Director of Laboratory and Neurological Research, College of Medical Evangelists, Los Angeles County Hospital, Los Angeles, California; and Dr. Herbert Stahnke, Director of Poisonous Animals Laboratory in Arizona State College at Tempe, Arizona.

We were informed that none was available in the United States and that the nearest source was in Mexico City manufactured by Laboratorius Myn, Coyoacan 1707, Mexico City 12, D.F. We also were informed that no specific antivenin was available in Canada.

The patient was admitted to the hospital for observation. A small, foreign body was observed in the region of the sting, and this was removed easily. It had a nondescript appearance, and the Pathology Department could not identify it as part of an insect. The general physical examination revealed no abnormalities, except for an area of hypoesthesia involving the whole thumb and the base of the thumb. The patient complained of pain in the elbow region, but there were no physical findings noted. There were absolutely no systemic signs. The hemoglobin was 100 Gm. per 100 ml., and the white blood cell count was 7,400. The sedimentation rate was 16 mm. in one hour. The blood smear and differential count showed normal findings. The blood urea nitrogen was 15 mg. per 100 ml. There was no evidence of hemolysis. A urinalysis revealed no abnormal findings. The blood pressure was 190/110 on admission, but fell quickly to a normal level of 120/70 where it remained over the next twenty-four hours.

The New York City Poison Control Center kept in constant touch with St. Michael's Hospital's physicians in Canada, relaying to them the information which was gathered painstakingly from various authorities. On the advice of Dr. Stahnke, whom we contacted several hours after the onset of the incident, the patient was treated as follows:

The hand was immersed and kept in cracked ice. If convulsions developed, Dr. Stahnke advised administering phenobarbital in dosages necessary to control the convulsions. The hospital, therefore, discontinued all therapy except keeping the patient's hand in cracked ice and observing him for forty-eight hours. The following day, January 18, 1962, the thumb still had some degree of hypoesthesia, but this eventually disappeared. The patient was discharged after forty-eight hours of hospitalization and observation and returned to his usual work on January 19, 1962.

Three days following his discharge, on January 24, the patient was re-examined, and the following findings were noted: There was hypoesthesia of the skin for 2 or 3 cm. around the site of the sting. There also was an area of itching and redness at the base of the thumb to the wrist and a similar area in the posterior aspect of the right arm. These latter areas were not sites of the injection of antivenom. This may have been early serum sickness, but there were no other signs or symptoms to suggest this. The patient was to phone the hospital in one week to report on his condition.

Symptoms

As reported in this case, there is a minimum of local evidence at the site of the bite. At first, there is a tingling and burning sensation locally which extends rapidly upward in the extremity. Later, there may be generalized muscular spasms, pains, nausea, vomiting, abdominal cramps, convulsions, restlessness, incontinence, and generalized involvement of the central nervous system. There also may be respiratory and circulatory distress. When death occurs, it usually is due to a failure of respiration or circulatory collapse. Symptoms usually last for from twenty-four to forty-eight hours. However, longer periods also have been observed in some cases.

Treatment

The specific antivenom is, of course, the most effective mode of therapy, but if none is available, the cold treatment is recommended. Calcium gluconate is recommended if absorption has occurred. If convulsions occur, sedation with phenobarbital is indicated. Supportive measures also should be instituted. Some authorities have recommended the use of corticosteroids, such as ACTH. Because of the rarity of incidents of various poisonous bites in this area, there frequently has been observed an unusual amount of unnecessary alarm and hysteria on the part of both patients and physicians. This incident, however, in spite of its infrequent occurrence, points out the need for a central repository of antivenoms of an unusual nature. It is most surprising that this step has not been taken already.

TABLE I. Incidents reported to the Poison Control Center during a recent weekend

Substance Ingested	Patients	
	Age (Years)	Sex
After-shave lotion	2	M
Air-Wick	$10^1/_2$	M
Alcohol (highball)	2	Unknown
Alcohol (isopropyl)	16	M
Anacin	17	F
Anacin	5	M
Aspirin (baby)	3	M
Aspirin (baby)	$2^1/_2$	M
Aspirin	2 and 3	M & F
Baby ointment	1	F
Bacitracin	2	M
Barbiturate	51	F
Bath oil	4	F
Bubble bath	$2^1/_2$	M
Bubble bath	2	F
Camphor balls	1	M
Cement (tile)	$1^1/_2$	F
Chap ice	2	Unknown
Cleanser	2	M
Cleanser	Unknown	Unknown
Cleanser	3	M
Cleanser	4	M
Chalk (tailors)	14	M
Cobalt chloride	12	M
Bleach	1	F
Antihistamine	$2^1/_2$	F
Cosmetics	$2^1/_2$	M
Cough medicine	2	M
Vitamin tablets	3 and $4^1/_2$	M
Deodorant	$1^1/_2$	M
Detergent	Adult	M
Detergent	$1^1/_2$	Unknown
D.D.T. (roach powder)	15	F
Dye	$1^1/_2$	F
Oven cleaner	Unknown	Unknown
Meprobamate	32	M
Flashlight battery	1	Unknown
Floor wax	$2^1/_2$	M
Flower (poinsettia)	Unknown	F
Furniture polish	$1^1/_2$	M
Furniture polish	1	M
Hand lotion	1	F
Insect repellant	2	F
Insecticide	Child	M
Lactrin	$1^2/_3$	M
Liver pills	2	Unknown
Disinfectant	Adult	F
Disinfectant	$1^1/_2$	M
Matches (book)	1	F
Matches	$1^2/_3$	M
Menthollatum	$1^1/_2$	M
Mercurochrome	5	F
Mercury (from thermometer)	$1^1/_2$	M
Metrecal	$2^1/_2$	F
Midol (tablets)	Unknown	Unknown
Moth balls	$2^1/_2$	F
Mr. Clean (detergent)	2	M
Nail polish remover (Cutex)	2	M
Nail polish remover (Cutex)	3	M
Nail polish (Swish)	$10^1/_2$	M
Nair lotion (hair remover)	Adult	F
Nitroglycerin tablets	$1^1/_2$	F
Sleeping tablets	2	F
Nose drops	2	M
Nytol (antihistamine)	36	F
Oil of wintergreen	20	F
Oil of wintergreen	$2^1/_2$	M
Paint remover	Unknown	Unknown
Paint thinner	1	M
Paregoric	5 months	M
Pedatone (foot care)	1 month	M
Pencil (indelible)	2	M
Perfume	$2^1/_2$	Unknown
Perfume	2	M
Phenotoxiazine	2	F
Photo developer	2	F
Powder, baby	$1^1/_2$	F
Pyridine	62	M
Quinine	2	Unknown
Seconal	25	F
Scopolamine	Unknown	Unknown
Shampoo	2	M
Stamyl	Adult	F
Starch	Unknown	Unknown
Sulfamethizole	3 and 2	F
Tranquilizer	21	F
Toy (Tinker Bell)	1	M
Sedative	49	F
Turpentine	1	Unknown
Turpentine	$1^1/_2$	M
Vitamins	3	Unknown
Warfarin	1	F
Water paint color	2	M

In Mexico, as was stated previously, there is a specific antivenom and also a polyvalent preparation which presumably is effective against all types of Mexican scorpions.

This incident also brings up the interesting question of whether or not a foreign medication would get rapid Federal clearance if it were not an accepted drug.

Modern transportation has increased the

danger of the transmission of disease. Airplanes must be treated for mosquitoes and other insects which may have been living a few hours ago in the tropics. Imported vehicles must be treated for snails. Occasional local incidents occur in which snakes are discovered in bananas. Such snakes have been of the constrictor type. The large, horrendous, hairy "spiders" not infrequently transported in banana stalks are not venomous.

Although most calls for help can be handled expeditiously, an inquiry such as the one reported here requires an unusual expenditure of time and funds.

The New York City Poison Control Center spent three hours calling various authorities all over the United States from New York City to Arizona and Los Angeles and constantly relaying the information obtained to the physician at St. Michael's Hospital who was at the bedside of the patient.

Comment

Poisonous scorpion bites in the United States generally occur in the Southwest and are practically unknown in the Northeast and Canada. The varieties involved are Centruroides gertschii and Sculpturatus.

It has been reported that in Arizona alone approximately 2,500 persons are bitten each year by scorpions. Although there are many varieties of scorpions in the South and Southwestern parts of the Unites States, only the previously mentioned varieties are said to be dangerous.

While the toxicity of scorpion venom is reportedly greater than that of the snake venom, fortunately the scorpion injects a smaller amount of the toxic material.

The mortality rate from scorpion bites is much higher in children than in adults. It is said to be between 1 and 2 per cent in children under five years but much lower in individuals over six years of age.

Number ninety-three in a series of Accidental Chemical Poisonings

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Need for improved communications

The public, the health professions, government, and indeed all segments of our society—I regret to say—are substantially unaware of the nature of our business. They know little of the contributions we make and have made, the problems we face, and the steps we are taking to meet these problems on our own initiative. We are to blame for this communications failure. For years we have directed our message almost exclusively to physicians and pharmacists, and the events of the recent past suggest that we have not done even that with any substantial degree of effectiveness. But we have been forced to recognize the need for improved communications, and we are beginning to learn its particular language. I hold this to be one of the most pressing problems we face in the decade ahead. It should make abundantly clear the interrelationships and interdependence of all components of the health team. These are not issues for the pharmaceutical industry alone. They are for all of us, and for society itself.—*John T. Connor, President, Merck & Company, Inc., to New Hampshire State Medical Society*

Case Reports

Perforated Peptic Ulcer Complicating Sulfonylurea Therapy

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SULFONYLUREA DRUGS have now been established as effective and relatively safe in the treatment of mild cases of diabetes mellitus, generally of the stable maturity-onset type. Toxic reactions of varying severity—hematologic, dermatologic, and hepatic—have been described and usually disappear with the discontinuance or interruption of the drug. Nausea and vomiting have also been noted but have rarely necessitated the interruption of therapy. However, Beaser[1] recorded an aggravation of symptoms of a duodenal ulcer in 1 patient and the perforation of a peptic ulcer in a second patient in whom no previous history of gastric disease was noted. Both patients were on tolbutamide therapy. Gelfand[2] reported 2 cases of gastric bleeding in patients on tolbutamide therapy, with a known history of peptic ulcer. To this small number of relatively severe gastric complications we now add 2 cases of perforated peptic ulcer in patients without previous history of gastric disease, 1 on tolbutamide therapy and the other on chlorpropamide therapy.

Case reports

CASE 1. A sixty-one-year-old male gave a history of diabetes beginning in 1943. He was controlled initially by dietary measures alone. Subsequently, because of a deterioration in the control, he was started on tolbutamide therapy in April, 1958. On this regimen, blood sugars ranged from 145 to 240 mg. per 100 ml. Chlorpropamide therapy was started in March, 1959. With this change, there was some improvement in control, as reflected in the range of the levels of blood sugars from 130 to 198 mg. per 100 ml. Urine examinations generally indicated negative findings except after dietary indiscretions. On October 3, 1960, the patient complained of nausea. Two days later he developed classic symptoms of a perforated peptic ulcer which was repaired at a private hospital. His recovery was uneventful. The chlorpropamide was continued without untoward symptoms but was later completely withdrawn, and control was maintained effectively by a strict dietary regimen.

CASE 2. A forty-two-year-old man gave a history of diabetes beginning in 1946. He was maintained on a dietary regimen without insulin until May, 1958, when tolbutamide treatment was started. His maintenance dosage was 1 Gm. per day. The response to this drug was not spectacular. Effective control was achieved as long as rigid dietary discipline was maintained. Chlorpropamide therapy was started in April, 1959, but was stopped because of complaints of vertigo and nausea and the failure to achieve satisfactory control. Tolbutamide treatment was resumed on February 2, 1960. The control improved chiefly because of better dietary discipline. On October 10, 1960, the patient suddenly developed symptoms of a perforated peptic ulcer which was repaired within a few hours after the onset of symptoms. His recovery was uneventful, and since the operation tolbutamide has been continued without untoward symptoms.

Comment

In both of these cases the drugs were used for a relatively long period of time. In both patients there was no suggestion of previous gastric disease. The drug dosage was not excessive in either case. It is difficult to establish causal relationship between the employment of the drugs and the gastric complications. Any such conclusion is precluded by the normal high incidence of peptic ulcer estimated by some to be as much as 10 per cent of the general population.[3] Among the 300 patients treated in our diabetic clinic, an incidence of 6 per cent was noted.

In pursuing the subject further, gastric analyses were done on a total of 16 cases on sulfonylurea therapy. Of these, 12 were given tolbutamide (1 Gm. per day) and 4 were given chlorpropamide (250 mg. per day). The test meal was 7 per cent alcohol. The usual sulfonylurea drug was taken several hours before the gastric extraction. Normal figures for the gastric concentration of hydrochloric acid in this laboratory range to about 40 degrees. Of the total number examined, 6 of the tolbutamide-treated and 2 of the chlorpropamide-treated cases showed distinct hyperchlorhydria. Two of the cases reached levels of 100 degrees.

The figures thus cited are too small to be significant statistically. They do suggest, however, that tolbutamide and chlorpropamide may have hypersecretory gastric effects in some individuals. The paucity of case reports of clinically significant gastric complications among the many thousands of cases now under oral treatment certainly would indicate that the existing potential danger is small. Therefore, there is no reason, on the basis of our present knowledge, to be deterred in the use of these valuable drugs. It may be wise, however, to exercise caution and perhaps use antacid and/or antisecretory drugs in patients known to have gastric disease and those who require the use of antidiabetic agents.

Summary

Two cases of perforated peptic ulcer have been reported in patients treated with oral antidiabetic agents, 1 with chlorpropamide and the other with tolbutamide. Causal relationship of the drugs to the gastric complication has not been definitely established. Gastric analyses of 16 cases receiving sulfonylurea therapy revealed hyperchlorhydria in 8 of them. This finding, although by no means conclusive, together with other reports in the literature of gastric complications, suggests the need for caution in the use of oral antidiabetic drugs in the presence of overt gastric disease.

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Acknowledgment. I wish to express my deep appreciation for the contribution made by Mr. Louis E. Wagshol, M.S., Chief Technologist, Laboratory Service, New York Regional Office, Veterans Administration, in the performance of the gastric analyses noted in this report.

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Renal Hypertension

Unilateral Kidney Disease in Patient with Massive Kidney Tumor

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In 1934 Goldblatt[1] described his classic experiment of compression of the blood supply to the kidney with a resultant elevation of the blood pressure which persisted until the interference to the circulation was removed. The explanation of the mechanism, which incidently is not accepted by everyone,[2] is that renal ischemia causes the kidney to secrete a proteolytic enzyme (renin) which combines with a plasma globulin (hypertensinogen), producing an active pressor polypeptide (angiotensin) which raises the blood pressure, both systolic and diastolic. Pyelonephritis and various vascular lesions are the two main causes of this hypertension. Tumor is also reported as the cause. According to all the authorities, as long as there is interference with the circulation in the one kidney, there will be an elevation of the blood pressure. If the renal pedicle is involved early in the disease when there is still functional kidney tissue to react, hypertension will result; if the cortex is involved first and the renal pedicle is involved later, involvement of the kidney can no longer produce hypertension.

In 1939 Graef and Page[3] described a type of experimental renal hypertension in dogs which was incident to a cellophane perinephritis. He noted that the hypertension in dogs occurred after two or three weeks and before an actual compression took place, but that afterward there was a gradual constriction, including the pedicle, which resulted in permanent hypertension until it was relieved by nephrectomy or by some other means. Clinically, this is rare, but it should be expected in patients who have sustained renal injury. Engel and Page[4] emphasize that the lesion should be subcapsular so that it results in renal compression because otherwise the looseness of the perirenal tissues precludes the development of a renal constriction force. Dustan, Page, and Poutasse[5] have reported 2 cases of hemorrhage about the kidney in adolescents due to football injuries which resulted in hypertension. A case of hypertension due to a retroperitoneal lymphosarcoma involving both kidneys, ureters, adrenals, abdominal aorta, and inferior vena cava has been reported.[6]

Kidney tumors in adults as a cause of hypertension are comparatively rare aside from those such as pheochromocytoma which elevate the blood pressure by their own secretions. In 101 cases of urinary tract pathologic conditions associated with hypertension reported by Abeshouse,[6] only 2 cases of renal tumor were found. Smithwick, Porell, and Whitelaw[7] state that hypertension of renal and adrenal origin is rarer than the essential or malignant types. They reported 54 cases of which 22 were pheochromocytomas or paragangliomas, 15 had unilateral disease, 10 had primary aldosteronism, and 7 had Cushing's disease. In Abeshouse's[6] report it was stated that hypertension is of little prognostic significance in renal tumors.

Diagnosis

In the literature the following reasons are given for being suspicious of the Goldblatt type of renal hypertension: (1) a recent history of trauma of the abdomen or flank, (2) recent abdominal or flank pain which may mimic almost any type of abdominal disease and which may be indicative of a vascular lesion in a kidney, (3) a known source of emboli, (4) a history of pyelonephritis, (5) malignant hypertension in patients over sixty years, (6) sudden malignant hypertension in a patient who has been normotensive prior to this time, and (7) hypertension of unknown cause in patients under thirty-five years. Wilms' tumor is a common cause in children.

The presence of an atrophic kidney or a nonfunctioning kidney in any hypertensive case does not necessarily indicate that removal of this kidney or a correction of the constrictive condition of the vessels will result in a cure. This has been demonstrated by the fact that after the initial experiments of Goldblatt[1] there was a tremendous amount of surgery done, mainly nephrectomies, the results of which were so poor that this was gradually given up.[2] In recent years the use of various tests such as an intravenous pyelogram, the Howard test, the renogram, and the most important, as considered by recent authorities,[5] the use of aortograms, have accurately demonstrated the interference with the arterial blood supply to the kidney. As a result, late reports indicate increased interest in the surgery of renal hypertension and improved results with both nephrectomy and with the various vascular and plastic procedures to correct the ischemia.[2]

The review that has been done, especially the studies of Page[3-5] and the case report cited in Abeshouse's[6] article has encouraged us to report a case which embodies many of the points indicated in the diagnosis of renal hypertension. The time and length of the symptoms and the tremendous size of the tumor mass when first seen and when symptoms of renal hypertension were present were not encountered in any of the cases in the literature reviewed by us.

Case report

A sixty-one-year-old white farmer was admitted to Lourdes Hospital on November 24, 1957. He stated that he had had an attack of pain in the right kidney area at the age of ten years which had lasted about two or three days. The patient then was free from any trouble until thirteen years later when he suffered a similar recurrence also lasting for two or three days. Similar attacks, mild in character, had been present on and off since then. For the last six months he had noticed that his abdomen was becoming much larger. He also noticed that he had been having intense headaches and marked swelling of his feet and legs. He denied any unusual urinary symptoms and stated that he only got up once at night. Aside from this complaint, his health had been excellent. Two months ago he consulted a physician who put him on diuretics under the impression that the edema might be due to some cardiac condition, and he lost 20 pounds. The physician noted at this time that his blood pressure ranged between 230/130 and 220/130. The patient stated that the swelling of his abdomen which had been prominent at all times had been much more marked in the last few months. On admission the blood pressure was 220/130. An examination demonstrated the presence of a large, firm tumor mass extending from the right costal margin down to the pubis and to the umbilicus laterally. At the umbilicus the mass in the form of an L was present also on the left side of the abdomen as far as the anterior superior spine. Aside from being obese, the abdomen did not seem to be distended by fluid or air exclusive of the mass. There was also a marked swelling of both ankles and legs. An examination of the fundi showed a narrowing of the arterioles, but there was no exudate present. Examinations (Dr. Mazar) on several occasions on the days prior to surgery showed that the blood pressure ranged between 190/120 and 180/110. The patient was on bed rest during the entire period. An intravenous pyelogram showed hydronephrosis with no function on the right side, and a retrograde cystoscopy also showed no dye excretion after forty-five minutes (Fig. 1). The left kidney was perfectly normal in all respects. A barium enema showed the presence of a large retroperitoneal mass on the right side, pushing the colon toward the medial side. The electrocardiogram was essentially normal; there were few changes that could be interpreted as hypertensive cardiovascular disease. The chest x-ray film showed essentially normal findings. The urine specimen, which was

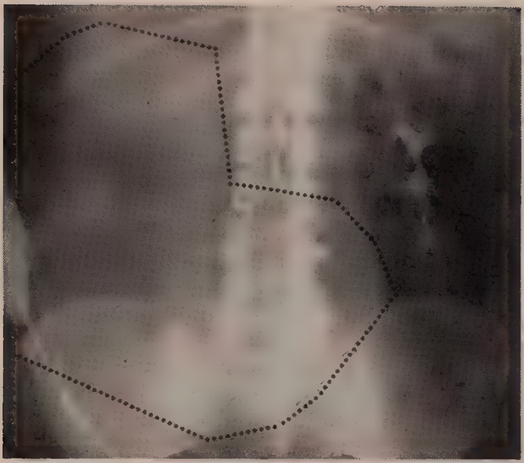

FIGURE 1. Composite picture of separate pyelograms showing normal pelvis and calyces on left and pyelonephritis on right. Unfortunately right kidney area is not shown on film in its entirety. Outline of tumor mass is shown by dotted lines.

slightly cloudy, showed 10 mg. albumin. The pH was 5.5 and the specific gravity was 1.018. The sediment contained from 4 to 6 red blood cells and from 10 to 15 white blood cells per high-power field. There were occasional squamous epithelial and renal cells and occasional coarse, fine, and hyaline-cast pellagra preventive factor. A urine microscopic examination from the left and right kidneys indicated the following: the left kidney had occasional white blood cell moderate renal and epithelial cells in clumps; the right kidney had full-field red blood cells, from 3 to 5 white blood cells, with occasional clumps of from 4 to 6 red blood cells. The blood hemoglobin was 11.6 Gm. per 100 ml. The white blood cell count was 7,800, with a differential count of 60 per cent neutrophils, 37 per cent lymphocytes, 2 per cent monocytes, and 1 per cent basophils. The nonprotein nitrogen was 46.5, the blood sugar was 79, and the blood cholesterol was 160. The serum total protein was 5.29 Gm., the serum albumin was 3.88, the serum globulin was 1.41 Gm., and the albumin-globulin ratio was 2.7. The bilirubin was as follows: in one minute, 0; in fifteen minutes, 0.25; in thirty minutes, 0.5; total bilirubin, 0.5, and indirect bilirubin, 0. The Regitine test for pheochromocytoma indicated negative results. The urine from both kidneys on culture showed no growth after forty-eight hours. The possibility of a Goldblatt type of renal hypertension was suggested by Dr. Mazar. On December 15, 1957, it was considered that the patient was in as good condition as possible and surgery was performed, primarily for the tumor rather than for the hypertension. A large incision was made from the right costal margin down to the pubis. The fascia was cut, the muscle was retracted, and the peritoneum was opened. The mass extended from the costal margin down to the public area and was firm and smooth throughout and adherent toward the medial portion. The colon was now reflected medially over to the midline and even then it was impossible to determine where the tumor mass ended. By careful manual dissection this mass was freed and was found to be densely encapsulated and adherent to what seemed to be the kidney pedicle. Below the umbilicus this mass swung over to the left, extending to the other side, and this could also be freed. Due to the adherence to the pedicle, it could not be determined completely what vessels were involved in the tumor mass. Because of the fear that blind grasping might result in injury to the aorta and vena cava, the capsule was incised medially over the pedicle area and the entire mass was raised very carefully with the idea of trying to clamp the pedicle from behind as soon as it could be outlined. No kidney tissue as such was noted at this time. With great care the tumor was lifted to the level of the abdominal wall, so that the pedicle could be seen. At this point the entire mass became detached. There was a sudden gush of blood which filled the wound and which was corrected by immediate clamping. The patient went into deep shock but responded to stimulation and blood. On examination it was found that the inferior vena cava had been torn out for about two thirds of the lateral wall and had also completely severed the renal artery. It was noted that the renal artery was tremendously enlarged and thick and almost corrugated in type. The renal artery and the clamped edges of the vena cava were tied off with 0 chromic catgut. It was felt that the lumen of the vena cava which was left, about one third, would be adequate for circulation. For two days the patient's condition remained serious.

On the third day his blood pressure was 120/76, his pulse was slow, and his general condition was excellent. On the tenth postoperative day the wound was entirely healed and clean and the patient was discharged.

The laboratory report of the gross specimen was as follows (J. S. Grewal, M.D.):

> The specimen consists of a large well-encapsulated mass measuring 40 cm. in length, 28 cm. in width, and 20 cm. in thickness and weighing 4,000 Gm. One end of the specimen has been torn during removal and presents a soft, hemorrhagic cystic appearance. This area is devoid of the capsule. On sectioning, this portion contains a small partly atrophic kidney wedged firmly in the tumor tissue. The kidney appears to be entirely separate from the tumor except at its hilum and toward one of its poles where the tumor presents a cystic appearance and seems to be incorporated with the renal tissue. The recognizable portion of the kidney presents a well-formed pelvis and ureter. The cut surface of the tumor presents well-defined, large and small discrete nodules presenting pale gray solid and cystic areas. The cystic areas in some places appear to be foci of necrosis. In other areas the wall of the cystic spaces seems to be lined with smooth membrane. These areas contain clear to turbid and blood-stained fluid.

The diagnosis was liposarcoma. A supplementary report on slides and tissues submitted to the Division of Laboratories and Research of the Department of Health of the State of New York stated "retroperitoneal leiomyosarcoma and chronic pyelonephritis." A similar supplementary report from the Armed Forces Institute of Pathology stated "it is still difficult to make an unequivocal diagnosis on the tumor from the pararenal tumor in the case of . . . . Based on the available material and information we believe that it is probably a diffuse (malignant) mesothelioma." After consultation with the pathology and x-ray departments, it was decided that x-ray therapy would not be of benefit and therefore none was given. Since discharge, the patient has remained well. He has had no abnormal urinary symptoms, is ambulant, and is working. He has, however, gained a great deal of weight. The blood pressure on December 30, 1959, was 110/79. On December 22, 1960, it was 116/80, and on January 16, 1961, it was 124/78. He has had no signs or symptoms referable to abnormal blood pressure.

Comment

In the discussion of their case, two workers mentioned that the exact mechanism was impossible to determine as to when compression occurred causing the symptoms, when the circulatory disturbance began, and which of these was the prime factor.[6] In our case a similar situation exists.

> Beside the capsule of the kidney proper, the kidney and its vessels are imbedded in a mass of fatty tissue termed the adipose capsule or perirenal fat. This is fixed at the margin of the kidney and is prolonged through the hilum into the renal sinus. The kidney and the adipose capsule together are enclosed in a specialized lamination of the subserous fascia called the renal fascia.

In our case the entire tumor mass and kidney were enclosed in this capsule with constriction of the kidney, as noted previously. The tumor which replaced or displaced the fatty tissue originated in the kidney itself, according to the pathologist. Exactly when the tumor started to form cannot be stated, but it does not seem possible that the mass could have existed for so long without causing compression sufficient to interfere with the circulation. It is a fact, however, that no symptoms referable to such a condition were noted prior to six months before admission to the hospital. It is possible that the patient may have been running a hypertension prior to that time but not enough to cause symptoms. The swelling of the feet and ankles may have been due to a cardiac decompensation which apparently was corrected by rest in bed prior to surgery and which has not recurred since then. On the other hand, the history of recurring insults to the kidney area over a fifty-year period suggests that this could have caused the condition exclusive of the tumor. The pyelonephritis and arteriosclerosis of the renal area corresponds to the usual picture in renal hypertension.

Summary

A case of unilateral disease with hypertension of six months duration (estimated)

in the presence of a massive tumor has been presented. The history is typical of renal hypertension, and the symptoms suggesting this entity had been present for fifty years. The position of the tumor, which was essentially perirenal, would indicate that constriction similar to that described by Page[3-5] was the prime factor. However, the finding of chronic pyelonephritis and marked arteriosclerosis of the right renal artery and the extreme length of the symptoms and size of the mass before hypertension occurred seem to contradict this. Whatever the cause, nephrectomy has resulted in a revision to normal, below 140/90, for three years, indicating that this is a case of true renal hypertension.

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Stomach freezing for duodenal ulcer

Cooling the stomach to near zero has been shown to be a successful method of treating persons with duodenal ulcer, according to an article by Wangensteen *et al.* in the May 12, 1962, issue of the *Journal of the American Medical Association.*

Freezing the stomach inhibits its secretion of the digestive juice containing hydrochloric acid which is believed to be an irritant to the duodenum.

No harm has resulted from this method of stomach freezing in a series of 24 patients. The study suggests that stomach freezing is the best way to relieve pain and other symptoms of duodenal ulcers and to heal the ulcers.

A balloon is passed into the patient's stomach, and a mixture of alcohol and ice water is allowed to flow through the balloon by means of inflow and outflow tubes until the temperature of the stomach is reduced to about one above to four below zero. The stomach is kept frozen for about an hour.

Patients treated in this manner are allowed a general diet. The only dietary restriction is advice to partake sparingly of alcoholic and caffeine beverages.

One patient in the series was not hospitalized after the procedure.

Although there is evidence of significant decreases in gastric secretory reponses attending gastric freezing, only further observations can determine how long this decrease will last after the procedure is performed. Stomach freezing could be repeated should this secretion return and cause a recurrence of symptoms.

Successful Resection of an Aneurysm of the Left Ventricle Utilizing Cardiopulmonary Bypass

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ANEURYSM OF THE left ventricle is one of the most common complications of myocardial infarction, causing a significant increase in the work load of the heart while reducing its efficiency. Congestive heart failure, mural thrombosis, and peripheral embolization are common late sequelae of left ventricular aneurysm.

The purposes of this presentation are:

1. To describe the characteristic clinical course and findings in a patient with a postinfarction aneurysm of the heart.
2. To show that, despite prolonged anticoagulant therapy, clotting within the aneurysm remains a hazard.
3. To indicate that age is no contraindication to operative intervention if surgery is otherwise advisable.
4. To describe the surgical technic of aneurysmectomy.

Case report

A sixty-three-year-old machinist was admitted to Jewish Chronic Disease Hospital on March 27, 1961. Twenty-nine months previously he was hospitalized elsewhere for treatment of an acute anterior wall myocardial infarction following a coronary occlusion. Anticoagulant therapy with Dicumarol was instituted at that time and was continued thereafter. Following a two-month convalescence, he returned to his former occupation. Eight months later a small aneurysm of the left ventricle appeared. Although this gradually increased in size, it caused no difficulty until one week prior to admission, when he developed signs of a basal pneumonia on the left side. In spite of the administration of antibiotics, this precipitated a bout of early left ventricular decompensation, and hospitalization was advised.

An examination revealed an apprehensive, well-developed, and well-nourished white male in no acute distress. The blood pressure was 130/80 mm. of mercury. An examination of the head, neck, lungs, abdomen, and extremities showed negative findings. A funduscopic examination revealed moderate angiosclerosis. The cardiac apex was at the anterior axillary line in the fifth interspace; there was a heaving impulse at the apex, but there were no shocks, thrills, or thrusts. The second aortic sound was accentuated. The rate and rhythm were normal, and no murmurs were heard.

Roentgenograms of the thorax (Fig. 1) showed marked cardiac enlargement with a boot-shaped configuration and prominence of the left border of the heart consistent with aneurysm formation. The aorta was sclerotic and elongated. The barium-filled esophagus showed a slight posterior displacement. Roentgenkymograms revealed a well-demarcated area of decreased motion along the left ventricular border. Fluoroscopy, which demonstrated

This study was partially supported by Grant H-6617 from the National Institutes of Health, Bethesda, Maryland.

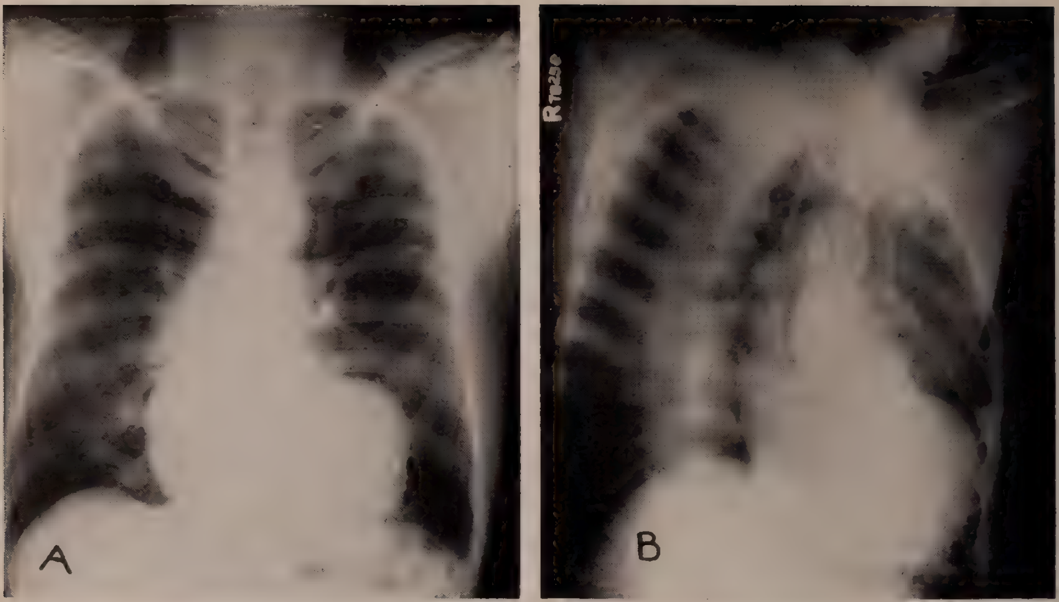

FIGURE 1. (A) Preoperative roentgenogram reveals boot-shaped configuration of heart, increase in its transverse diameter, and apical bulge consistent with aneurysm. (B) Right anterior oblique roentgenogram reveals marked bulge over anterior and lower aspect of heart.

paradoxic motion at this site, also suggested aneurysm formation.

Electrocardiograms (Fig. 2) revealed negative T waves in leads I, II, aVl, and V_1 through V_6. There were small Q waves in leads I and aVl and deep Q waves in V_1 through V_5. Precordial leads also showed persistent elevation of the S-T segments, and there was a persistent R wave in aVr. These findings also were indicative of a ventricular aneurysm.

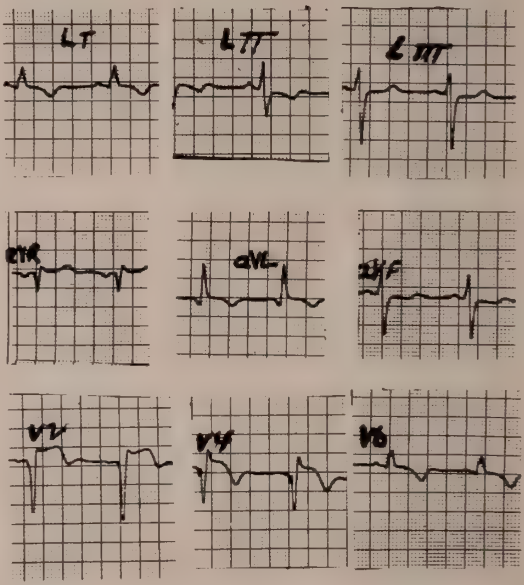

FIGURE 2. Electrocardiogram on November 28, 1960, reveals negative T waves in leads I, II, and aVl, and in precordial leads. There is persistent elevation of the S-T segments and persistent R wave in aVr.

The blood cholesterol was 188 mg. and dextrose 84 mg. per 100 ml.; SGOT (serum glutamic oxalacetic transaminase) 27 units; C-reactive protein was negative; carbon dioxide-combining power 52.5 volumes per cent; chlorides 90 mEq., potassium 5.7 mEq., and sodium 131 mEq. per liter; urea nitrogen 15.3 mg. per 100 ml.; fibrinogen 561; and serum albumin 3.4 Gm. and globulin 3.2 Gm. per 100 ml. A urinalysis showed negative findings. The hemoglobin was 14.5 Gm. per 100 ml., and the white blood cell count was 5,000 per cubic millimeter with 50 polymorphonuclear leukocytes, 45 lymphocytes, 2 eosinophils, and 3 mononuclear leukocytes. The corrected sedimentation rate was 14 mm. per hour. The blood volume was 6,125 cu. mm. (94.8 ml. per kilogram of body weight), the red blood cell volume 3,883 cu. cm.

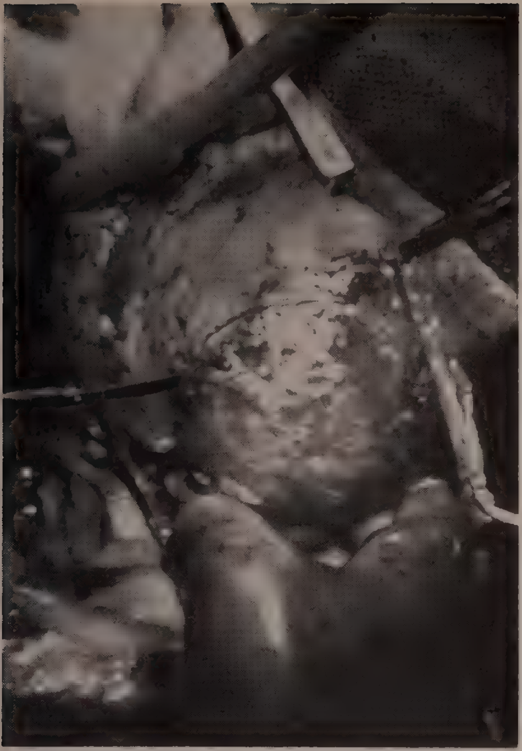

FIGURE 3. Aneurysm of left ventricle exposed at operation.

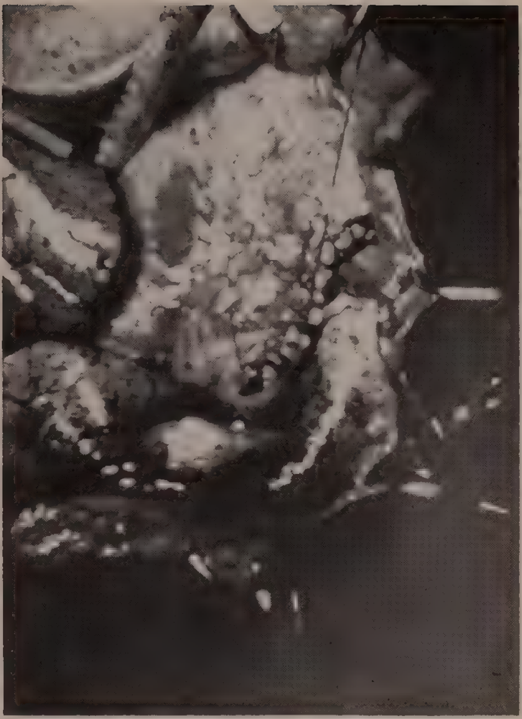

FIGURE 4. Aneurysm has been removed, and left ventricular wall has been reconstituted.

(60 ml. per kilogram of body weight), and plasma volume 2,242 cu. cm. (34.8 ml. per kilogram of body weight). The venous pressure was 7.5 cm. of water, and the circulation time was 15 seconds.

Course in hospital. The symptoms of congestive heart failure, which appeared on the second hospital day, responded promptly to the institution of digitoxin, mercurial injections, and oxygen. Because this patient had an enlarging aneurysm of the anterolateral wall of the heart in association with congestive failure, it was decided that an aneurysmectomy was indicated. Following the appropriate preparation, the operative correction was undertaken on April 13, 1961, utilizing the heart-lung machine.

An incision was made across the anterior part of the chest through the fourth interspace on either side with a transection of the sternum. The anterolateral wall of the left ventricle was found to be the site of a paradoxically pulsating aneurysm which measured approximately 11 cm. in its greatest diameter (Fig. 3). The parietal pericardium was densely adherent to the aneurysm. Before this was separated the remainder of the pericardium was opened widely anterior to the phrenic nerve. The pulmonary artery and aorta individually were encircled with umbilical tapes. The right auricular appendage was encircled with a purse-string suture of number 2 silk, and the patient was given 1.5 mg. of heparin per kilogram of body weight. The right common femoral artery and the right atrium were cannulated, the pulmonary artery was clamped, and the patient was placed on cardiopulmonary bypass. The flow rate was 2.2 L. per square meter of body surface area. Intermittently, to avoid excessive blood loss through the ventriculotomy incision, the ascending aorta was clamped. When cardiac arrest seemed imminent, the aortic clamp was opened, and the coronary vessels were retroperfused with arterial blood.

The adherent pericardium was dissected off the heart, and the left ventricle was opened widely along either side of the

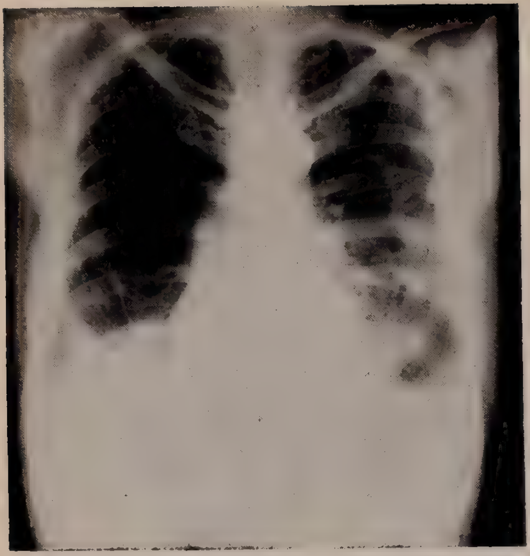

FIGURE 5. Postoperative roentgenogram demonstrates bilateral pleural reaction and some residual subcutaneous emphysema. Cardiac contour normal.

aneurysm, which was then removed. A soft and adherent clot filled most of its cavity. The wall of the left ventricle was reconstituted with two layers of sutures, a deep one of number 2 silk mattress sutures, and a superficial layer of interrupted atraumatic number 2-0 silk (Fig. 4). A strip of reinforcing Teflon felt of $^1/_8$-inch thickness was sutured over the wound in the left ventricle, which was approximately 12 cm. in length. Before the final suture was placed the pulmonary arterial and aortic clamps were removed, and the left ventricle was tilted upward and permitted to fill with blood to replace the remaining air. Care was taken during the closure to incorporate the most peripheral portion of the wall of the aneurysm into the suture line, since this was composed of dense fibromuscular tissue and lent itself well to suturing. In addition, care was taken to avoid the major branches of the coronary arterial system, the papillary muscles, and attachments of the mitral valve. On completion of the repair the heart action was satisfactory, and the cardiopulmonary bypass was terminated. The patient had been on extracorporeal circulation for thirty minutes.

Postoperatively, perhaps because of a rupture of a pulmonary bleb, he developed a bilateral pneumothorax and subcutaneous emphysema. On the second postoperative day a tracheotomy was performed. Tube drainage of both pleural spaces was continued for ten days, when the air leakage spontaneously subsided. The tubes were removed, and the patient was ambulated. He was discharged as improved on April 30, 1961. A roentgenogram of the thorax (Fig. 5) at that time showed a normal cardiac contour. Repeat electrocardiograms (Fig. 6) showed upright T waves in lead II; Q waves in lead I and in aVl persisted.

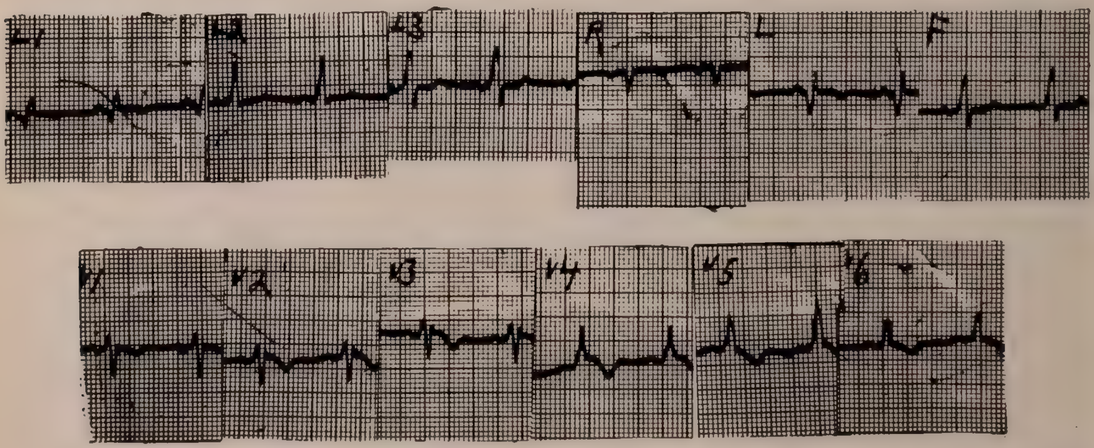

FIGURE 6. Electrocardiogram of April 26, 1961, demonstrates that T wave in lead II is upright. There are Q waves in leads I and aVl. R wave in aVr is no longer present, and S-T segments in leads V_1 V_4, and V_5, are now isoelectric.

The R wave in aVr was no longer present. The S-T segments in leads V_1, V_4, and V_5 had returned to normal.

PATHOLOGIC REPORT. The specimen was a slightly curved piece of ventricular wall, 7 by 8 cm. in size. The epicardium was ragged because of attached fibrous tags. The myocardium was replaced mainly by grey-white fibrous tissue. A larger portion was thinned out to 0.3 cm., while a smaller portion was up to 1 cm. thick. Included were firm clots separated from the lesion. The largest was 6 by 7 by 1.5 cm. On sectioning, this showed lamination of a yellow-grey to deep red material.

On microscopic examination the myocardium was markedly thinned and extensively replaced by fibrous tissue largely undergoing hyalinization. There were occasional foci showing endothelial and fibroelastic proliferation as well as accumulations of plasma cells and eosinophils. The endocardium was thickened by loose fibrous tissue and collections of foamy cells. There was a closely attached thrombus made up of abundant hyalinizing fibrin clots and collections of red blood cells. The epicardium was thickened with fibrous tissue and showed some vascular proliferation.

The pathologic diagnoses were (1) fibrosis of the myocardium (healed infarction), (2) mural thrombosis, and (3) fibrous pericarditis.

Comment

Ventricular aneurysms may be either congenital or acquired, but they occur most often after myocardial infarction.[1,2] The incidence of aneurysm subsequent to myocardial infarction varies from 5 to 38 per cent, with a sex ratio of 3.6 males to 1 female.[3] Douglas, Sferrazza, and Marici[4] reviewed 4,427 consecutive autopsies, of whom 524 had died of myocardial infarctions. Of these, 45, or 8.7 per cent, had a ventricular aneurysm. They point out that when cardiomegaly with or without a localized bulge develops following a transmural myocardial infarction, the presence of an aneurysm must be considered.

An aneurysm which forms rapidly is made up of necrotic muscle. When it develops over a longer period of time, its walls are composed of varying quantities of fibrous tissue. Its size varies from less than 3 cm. to one greater than the remainder of the heart, depending on the extent of the necrosis of the heart muscle.[3] An aneurysm is more likely to develop in patients who do not rest adequately after a myocardial infarction[5] or in those with hypertension. Usually the wall is markedly thinned, and in a substantial number the cavity of the aneurysm is filled with old, adherent, and fresh friable clot. When eggshell calcification occurs in its wall, the prognosis is more favorable, possibly because this type of aneurysm cannot pulsate paradoxically.

In a series of 102 patients with ventricular aneurysm the apex was involved in 49, the anterior wall in 45, the posterior wall in 29, and the interventricular septum in 17.[3] The right ventricle was involved only four times. Thromboembolic phenomena were twice as common in patients with myocardial infarction and aneurysm as in those with infarction but no aneurysm. Eighty-eight per cent of 66 patients analyzed died within five years, indicating that the prognosis is probably twice as unfavorable in patients with postinfarction aneurysm as in those with infarction but no aneurysm. Death usually was due to congestive heart failure and never to rupture. Sixty per cent of the patients had thromboembolic phenomena which caused death in 35 per cent.

Congestive heart failure probably is due to interference with the ejectile force of the left ventricle and the reduction of left ventricular output.[5] The stroke volume of the left ventricle is reduced because its contractile force is partially dissipated by the nonexpansile or paradoxically pulsating aneurysmal chamber. These patients develop pulmonary congestion, particularly with exercise, because of stasis in the left atrium and the pulmonary circuit. In diastole, the sac empties itself into the main chamber, interfering with left atrial emptying. As a consequence of these abnormal forces, the left ventricle dilates and shows signs of hypertrophy.

The indications for surgery are congestive failure, thromboembolism, and rapid enlargement of the aneurysm. Beck, in 1944,[6] was probably the first to attempt surgical correction by covering an aneurysm with a fascia lata stent. Bailey *et al.*[7] reported 9 patients with aneurysms, six of them acquired. All the patients were treated by a closed surgical technic with 8 survivals. Surgical fatality usually is due to embolization during surgery or congestive failure at a later date. The latter may be caused by the inclusion of an important coronary arterial branch in the suture line, or more likely by a significant reduction in the capacity of the left ventricle.

Cooley *et al.*[5] reported on 10 patients operated on under cardiopulmonary bypass, with 8 survivals. The 2 patients who died were sixty-three years of age, and he was of the opinion that their age acted against a successful result. Our patient, however, demonstrates that age should be no barrier to the removal of a symptomatic, enlarging postinfarction aneurysm. We agree that an open technic, permitting the deliberate excision of the aneurysm, the avoidance of vital structures, and the evacuation of the clot is preferable to a closed procedure. Because the fibromuscular wall at the periphery of the sac holds suture material better than the normal heart wall, and to ensure an adequate residual capacity to the left ventricle, the incision is repaired by approximating the edges of the aneurysm close to its junction with normal cardiac muscle.

Summary

We have presented a patient with an aneurysm of the anterolateral wall of the left ventricle which developed after an extensive myocardial infarction. Despite anticoagulant therapy, which was continued for two and one-half years, the aneurysm at surgery was found to be filled with clot. The aneurysm and its contents were removed successfully utilizing a cardiopulmonary bypass.

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New approach to acne therapy

A drug chemically related to estrogen has been found to suppress oiliness in the skin and alleviate acne, according to an article by Walter C. Herold, M.D., in the May, 1962, issue of *Archives of Dermatology*. In a preliminary study involving 27 acne patients the drug, 16-epiestriol-3-allyl ether, was found capable of decreasing sebaceous gland activity.

As anticipated, a definite correlation between the amount of oil and the degree of acne was found. As the oil decreased, the acne decreased.

The treatment of acne has been directed mainly toward removing or covering up excessive amounts of oil, but it is much more satisfactory to decrease or eliminate the formation of excessive oil in the first place.

Of 17 men and 10 women studied, most were under treatment for several months. Only 3 patients failed to show any improvement; 10 showed marked improvement and 10 moderate improvement. The observed complications were minimal.

Disability to Ability

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From the State of New York Department of Social Welfare

Two cases are presented which illustrate the collaboration of the medical profession and the public agencies of welfare and vocational rehabilitation.

Aid to Dependent Children (ADC)

A thirty-year-old mother of two daughters ages eleven and seven applied to a county welfare department in September, 1958, because of her husband's desertion and refusal to support the family.

The caseworker noted early in his contacts with this young mother that she did not appear in good health. She frequently had to remain in bed and was unable to care adequately for her home or her children. Her husband's family were very concerned about her and helped her as much as they could with the housework and the care of the young children.

The initial reports from her attending physician indicated only the diagnosis of a cardiac condition. At one point there was a reference to a possible rheumatic heart condition. The client continued to receive regular medical supervision as needed until six months following the opening of her case on public assistance when she was referred to a hospital specializing in cardiac work for a complete evaluation. This was done on March 2, 1959. The diagnosis of patent ductus arteriosus was established, and the hospital recommended that cardiac surgery be done as soon as possible.

The public welfare department referred the client to the Division of Vocational Rehabilitation for consultation prior to her hospitalization for cardiac surgery. The Division in turn reviewed the medical situation and concurred with the hospital's recommendation for cardiac surgery. The welfare department helped the client to make her own personal plans for admission to the hospital as she wished to maintain her independence in her own home. Her parents-in-law were able to care for the children so that a source of potential anxiety was removed. On March 24, 1959, the patient was admitted to the hospital for surgery and was discharged on June 10, 1959.

She returned home for a day or two to visit with her children and then was admitted to a cardiac rest home in Yonkers where she remained until July 21, 1959. With the exception of the diagnostic work-up which the welfare department paid for, the hospitalization for surgery and subsequent convalescence at the rest home were paid for by the Division of Vocational Rehabilitation. Following her discharge from the convalescent home on July 21, 1959, the Division of Vocational Rehabilitation was ready to begin vocational rehabilitation. In view of this client's strong desire to maintain both her independence and her own home, it was felt that she would need vocational retraining of some kind as she had not finished high school (married at the age of sixteen) and had never been employed.

The client was sponsored by the Division of Vocational Rehabilitation at a beauty school for forty weeks from September, 1959, to June, 1960, a course which she attended conscientiously. Throughout her hospitalization, convalescent care, and training period, the welfare department participated by providing for the care of the children as well as for the client's maintenance. The Division of Vocational Rehabilitation paid for all costs pursuant to her vocational retraining. On completion of her course at the beauty school, the client promptly became employed. Following one month's employment in July, 1960, she reported to her caseworker that she wanted to have her welfare check reduced since she was receiving some income from her employment. Apparently her first month of employment as a beautician was on a trial basis or as a continuation of her training. The welfare department continued to supplement her earnings, and her health remained good. She reported at one time to the case-worker that she was happy because she felt better physically than she ever had before in her life. This case is now closed, and she has achieved financial independence and is capable of caring for her family.

Aid to Dependent Children and Aid to the Disabled (AD)

This is the case of a couple and their two young sons whose application for Aid to Dependent Children was made by the wife because of the prolonged hospitalization at a local sanatorium of her husband, age forty, for pulmonary tuberculosis. At the time of application in August, 1957, the wife was at home with her two-year-old son (the younger son, age one year, was hospitalized at a state tuberculosis hospital for pulmonary tuberculosis). Her husband's family was assisting by providing a home on their farm, but they were unable to support fully the mother and son.

The couple were born and reared in Holland and were married in New York State where the husband worked as a self-employed farmer. The woman met her husband in Holland and came to the United States in 1954 to marry him. He worked until May, 1957, when he was diagnosed as having pulmonary tuberculosis and was admitted to a local sanatorium. On the opening of the case for public assistance, the mother and her son were provided for adequately by the county welfare department, which also provided for regular x-ray follow-up through the public health nurse who visited the home regularly. The client visited her husband several times a week and her one-year-old son once a month while both were in the sanatoriums.

During the course of her husband's hospitalization, he was transferred to a state tuberculosis hospital in April, 1958, for surgery (resection of the apical posterior and anterior segments, block resection of the lingula, apicolysis on the left, and extrapleural plombage). During April, 1958, the couple's young son was discharged home from the state tuberculosis hospital. In June, 1958, the husband was readmitted to the local sanatorium for chemotherapy and convalescence and was discharged in January, 1959, on chemotherapy and outpatient department follow-up. On discharge he was medically approved for limited activities and was advised not to attempt work for at least five to six months. Needless to say the family was very happy to be together again.

In view of the husband's being unemployable, he was included on the family's Aid to Dependent Children budget. In April, 1959, the husband was hospitalized for eight days for an emergency appendectomy. Following a chest re-examination, he was advised that he would not be able to return to farm work as it was too strenuous. He continued to recuperate from his recent appendectomy and from pulmonary tuberculosis. In September, 1959, he was transferred to the Aid to the Disabled program as it was clear that with his pulmonary disability and limited employment potential vocational rehabilitation would be required to fit this man for suitable employment. He had no other skills aside from farming.

The county welfare department continued to afford this family excellent medical supervision and follow-up, and their health was described as being good. The husband continued to be very anxious to return to work, but all medical reports of follow-up examinations indicated that he could only work four to five hours daily and would have to be able to lie down whenever he was fatigued. This case was reviewed by the agency and referred to the Division of Vocational Rehabilitation by the caseworker in October, 1959. The client was interviewed by the vocational rehabilitation counselor in December, 1959, and he was sent to the Williamsport Technical Institute in Pennsylvania for one month's vocational diagnostic evaluation. As a result of testing and shop trials, it was recommended that the client be given training in office machine servicing. In May, 1960, he began a two-year training course with the Division of Vocational Rehabilitation assuming the responsibility for the cost of tuition fees, books, tools, and transportation and the welfare department providing maintenance for the client away from home and continued maintenance for his family in the community. During his absence from home, the welfare department continued to support his family. Dental care for the mother and children was authorized, and a special food allowance for tuberculosis contacts and arrested tuberculosis cases was included in the budget to enrich this family's diet.

Although this was a two-year vocational rehabilitation training course for the husband, a job opportunity in a city near his home occurred in a typewriter repair shop, and as the client had done very well in school, he was advised by the instructor at the school to accept this position. The salary was such that he was able to support his family fully, and the case was closed by the welfare department in September, 1961.

270 Broadway

Measles immunity and reexposure

The persistence of immunity to measles after an individual has had the disease apparently does not depend on repeated exposure to the measles virus, according to an article by Samuel Karelitz, M.D., Floyd S. Markham, Ph.D., and James M. Ruegsegger, M.D., in the May, 1962, issue of the *American Journal of Diseases of Children.*

The level of immunity to measles was determined among 25 pediatricians who had been exposed repeatedly to measles-infected children and among 27 other adults, none of whom was known to have been exposed to measles during the preceding five years. When the degree of immunity between the two groups was compared, there was no significant difference. This suggests that a single vaccination with live measles virus vaccine may provide lifetime immunity.

BILLSBORD

It is our privilege each Wednesday to be one of a small group of masculine gender who meet for dinner, preceded by the usual liquid suppression of inhibitions and followed by joint activity, which while it requires sitting around a table and the holding of hands and produces occasional table rappings has nothing to do with spiritualism.

Over the years there are few subjects, be they personal, economic, or political, that escape discussion. A few weeks ago one of the group announced his intent to retire. He was sixty-three and could see an assured income of $600 a month besides what he would receive from Social Security. He was challenged immediately by one of the group who insisted that the income was insufficient and that to retire an annual income of $12,000 was necessary. At the time this argument seemed to me to have all the social significance of Marie Antoinette's alleged "Let them eat cake" attitude and was quickly forgotten.

The other day "B" came to see me and said his retirement was now an accomplished fact; that he was on his way to Fort Lauderdale, Florida, and just came in to say good bye. His visit recalled the previous discussion, so I asked about his Social Security. He stated he would receive about $113 a month which was pretty good inasmuch as he had paid only about $3,000 into the system over a period of thirteen years. After the usual amenities and what passes for humor on such occasions he left, and about then I suddenly realized that under the proposed King-Anderson legislation he would also receive free medical care except for token payments. Over $700 a month and he gets free medical care and who pays for it? Payment would be extorted weekly from my office girl, the grocery clerk, the gas station attendant, and others in similar circumstances.

What could be more unfair? How can anyone be he doctor, lawyer, or Indian chief, justify it? By what logic, by what concept, be it common sense or common decency, can one support and foster a program that will, week in and week out, for years to come take monies (however small) to pay the medical expenses of someone who has an income greater than they will ever earn.

And, don't tell me "B" is an isolated case. I'll wager that everyone reading this knows someone in similar circumstance. There isn't a responsible person in this country that wants any individual whether old or young to go without necessary medical care even if he can't pay for it. Our profession has given free medical service for over 2,000 years and will continue to do so. We are happy to cooperate with any religious, voluntary, or governmental group who wish to assume a share of the task. Certainly if what we all want is to make sure that any person needing medical care will receive it, then we could work out a method to ensure it without inequity. Actually there is a method available which provides for medical expenses without deduction, exception, or token contribution, and which is paid jointly by the state and Federal governments. Thus in the event an older citizen needs medical care he can't pay he receives it—and who pays for it? Not only my office girl, the grocery clerk, and the gas station attendant but also Mr. "B" and me.

This method can do the job but only if it is properly implemented and intelligently administered. This, in turn, requires the cooperation of all of us with a common objective to make sure no one is deprived of necessary medical attention.

With such cooperation Kerr—Mills will work. Without such cooperation no method will work.

WRC

Necrology

Henry Lambert Bibby, M.D., of Kingston, died on April 16 at his home at the age of seventy-six. Dr. Bibby graduated in 1910 from Columbia University College of Physicians and Surgeons. He was a consulting pediatrician at Kingston Hospital and medical director of Wiltwyck School for Boys, Esopus. From 1950 to 1959 he was president of United Cerebral Palsy of Ulster County and directed the well-baby clinic founded and sponsored by the Junior League of Kingston. During World War II he conducted the child health and nine other clinics. Dr. Bibby was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the American Public Health Association, the New York Academy of Medicine, the Ulster County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David Treadwell Bishop, M.D., of Kings Park, died on March 24 at the age of eighty. Dr. Bishop graduated in 1905 from Long Island College Hospital School of Medicine. He was a senior attending ophthalmologic surgeon at Brooklyn Eye and Ear Hospital. Dr. Bishop was a Diplomate of the American Board of Ophthalmology and a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Isidor Dicker, M.D., of Freeport, died on April 13 at the age of ninety. Dr. Dicker graduated in 1908 from New York University and Bellevue Hospital Medical College. He was a consulting dermatologist at Stuyvesant Polyclinic. Dr. Dicker was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James F. Hoffman, M.D., of Olean, died on April 27 at his home at the age of forty-five. Dr. Hoffman graduated in 1942 from the University of Buffalo School of Medicine. He was director of anesthesiology at St. Francis Hospital. Dr. Hoffman was a Diplomate of the American Board of Anesthesiology and a member of the American Society of Anesthesiologists, Inc., the Cattaraugus County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Leo Jacobs, M.D., of Brooklyn, died on April 12 at the age of sixty-nine. Dr. Jacobs graduated in 1915 from Long Island College Hospital Medical School. He was an adjunct in ophthalmology at Brooklyn Eye and Ear Hospital and an associate attending ophthalmologist (Off Service) at Maimonides Hospital of Brooklyn. Dr. Jacobs was a Diplomate of the American Board of Ophthalmology and a member of the Brooklyn Ophthalmological Society, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Robert Murray, M.D., of Binghamton, died on May 10 at Wilson Memorial Hospital at the age of sixty-six. Dr. Murray graduated in 1924 from Syracuse University School of Medicine. He was an attending obstetrician at Wilson Memorial Hospital. Dr. Murray was a member of the Binghamton Academy of Medicine, the Broome County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Michael Paley, M.D., of Forest Hills, died on May 10 at The Mount Sinai Hospital at the age of forty-nine. Dr. Paley received his medical degree from the University of Bologna in 1937 and interned at the Hospital for Joint Diseases and the Queens General Hospital. He was an assistant attending orthopedic surgeon at Queens Hospital Center and an assistant adjunct orthopedic surgeon at the Hospital for Joint Diseases. Dr. Paley was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Clara H. Pierce, M.D., of Syracuse, died on April 24 at Memorial Hospital at the age of seventy-one. Dr. Pierce graduated in 1921 from Syracuse University School of Medicine. She was a retired director of the Bureau of Child Hygiene, Syracuse Public Health Service. Dr. Pierce was a member of the Syracuse Academy of Medicine, the Onondaga County Medical Society, and the Medical Society of the State of New York.

John Frederick Neander, M.D., of New York City, Nanuet, and Pearl River, died on April 25 at the age of forty-five. Dr. Neander graduated in 1943 from the University of Minnesota Medical School. He was an attending psychiatrist at the Postgraduate Center for Psychotherapy and at Grasslands Hospital, Valhalla. Dr. Neander was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Member of the American Psychiatric Association, and belonged also to the Rockland County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry Rudolph Rado, M.D., of Mount Vernon and Candelwood Isle, Connecticut, died on May 15 at the age of sixty-nine. Dr. Rado graduated in 1918 from Columbia University College of Physicians and Surgeons and interned at St. Francis Hospital, The Bronx. He was a consulting surgeon at Fordham Hospital. Dr. Rado was a Fellow of the American College of Surgeons and a member of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas Milton Rivers, M.D., of New York City, died on May 12 at New York Hospital at the age of seventy-three. Dr. Rivers graduated in 1915 from Johns Hopkins University School of Medicine. He was a vice-president for medical affairs of the National Foundation—March of Dimes, vice-president and director of the Rockefeller Institute and its affiliated hospital until retiring in 1955, continuing as director emeritus and a member emeritus. He was among the first to establish the importance of viruses as a distinct group of infective agents and spent much of his professional life helping to establish virology as a specialty within the field of microbiology; during the 1930's he made significant and original contributions to an understanding of psittacosis, lymphocytic choriomeningitis, and allergic encephalitis. Dr. Rivers was a member of the Association of American Physicians, the American Pediatric Society, the American Association of Immunologists, the American Association of Pathologists and Bacteriologists, the Society of American Bacteriologists, the American Society for Clinical Investigation, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Romeo Roberto, M.D., of Yonkers, died on April 10 at St. John's Riverside Hospital at the age of seventy-eight. Dr. Roberto graduated in 1910 from Cornell University Medical College. He was emeritus physician, emeritus radiologist, and consultant at the Chest Tumor Clinic at St. John's Riverside Hospital, a former director of the tuberculosis division of the Yonkers Health Department, and vice-president of the Yonkers Tuberculosis and Health Association from 1937 to 1959. A former president of the Yonkers Academy of Medicine, Dr. Roberto was a Diplomate of the American Board of Radiology (Diagnostic Roentgenology), a Fellow of the American College of Chest Physicians, and a member of the American Trudeau Society, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Meyer Silberman, M.D., of Forest Hills, died on April 15 at the age of seventy-five. Dr. Silberman graduated in 1913 from Long Island College Hospital Medical School and interned at Beth Israel Hospital. He was a consulting otolaryngologist at Cumberland Hospital and an attending otorhinolaryngologist (Off Service) at Maimonides Hospital of Brooklyn. Dr. Silberman was a Diplomate of the American Board of Otolaryngology and a member of the American Academy of Ophthalmology and Otolaryngology, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Oscar Hayen Stover, M.D., of Buffalo, died on April 22 at Deaconess Hospital at the age of sixty-two. Dr. Stover graduated in 1922 from the University of Buffalo School of Medicine. He was chief anesthesiologist at Deaconess Hospital and an associate consulting anesthesiologist at Buffalo Eye and Ear Hospital. An assistant professor of anesthesiology at the University of Buffalo School of Medicine, Dr. Stover was a Diplomate of the American Board of Anesthesiology and a member of the American Society of Anesthesiologists, Inc., the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Bernard Zaglin, M.D., of New York City, died on May 12 at Beth Israel Hospital at the age of seventy-one. Dr. Zaglin graduated in 1915 from New York Homeopathic Medical College and Flower Hospital. He was chairman of the health committee and director of the East Side Torah Center. Dr. Zaglin was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Felice Zaino, M.D., of Long Island City, died on May 12 at the age of sixty-six. Dr. Zaino received his medical degree from the University of Naples in 1923. He was an associate attending physician in general practice at Columbus Hospital. Dr. Zaino was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

Bronx Pediatric Society elects officers

The Bronx Pediatric Society has announced the election of the following officers for the year 1962–1963: David Milliken, M.D., president; Charles Abler, M.D., vice-president; Lawrence T. Taft, M.D., secretary-treasurer; and Murray Davidson, M.D., member of the executive council.

Cancer experts get grants

The first Alfred P. Sloan Awards in Cancer Research have been conferred on four scientists from Memorial Sloan-Kettering Cancer Center, New York City, in recognition of their contributions to cancer research.

The awards of $10,000 each were recently established by the Alfred P. Sloan Foundation.

The recipients are: Oscar Bodansky, M.D., chairman, Department of Biochemistry, and Felix Wróblewski, M.D., associate attending physician, Memorial Hospital for Cancer and Allied Diseases; and Charlotte Friend, Ph.D., associate member, and Lloyd J. Old, M.D., associate, Sloan-Kettering Institute for Cancer Research.

To qualify for awards candidates must have made a significant contribution to basic scientific knowledge relating to cancer, have advanced the treatment of cancer, or have shown unusual promise of future noteworthy accomplishments in this field.

Early success of new type of medical welfare service

The first findings in a five-year experimental project for improving quality and reducing costs of medical care to families on relief have been encouraging, according to Charles H. Goodrich, M.D., director of the experiment at New York Hospital.

The project, which began in July of 1961, has been established to test the practicality of giving complete medical care to welfare families under the auspices of a single medical center rather than sending the patients to various clinics for their illnesses. The purpose of the project is to study the cost, utilization of services, and quality of this care.

It was thought that the patients might refuse to cooperate with the new type of service but this has proved to be untrue; over 80 per cent did. The fear that the service might lead to an excessive number of home visits also proved to be foundless since the close medical follow-up provided by the service has helped to eliminate emergency situations.

Selective Service calls for physicians

Because of a decrease in the number of physician-volunteers for the Armed Forces it was necessary during 1961 to issue three Selective Service calls for physicians. The number of physicians required by the Service was obtained by: discontinuing the acceptance of resignation of regular officers; denying the release of those reserve officers who had voluntarily extended active duty for an indefinite time; issuing a Selective Service call for up to 1,025 physicians; and calling to active duty the National Guard and Reserve Units with medical officers attached.

The physicians called up by Selective Service were those in the youngest age group who had completed their internships. This group included almost exclusively first-year residents and physicians just beginning private practice. Since the call was based on age it was not evenly distributed and some hospital training programs suffered a depletion of their first-year residents while others were untouched.

The American Medical Association has prepared a brief summary of the present status of Selective Service as it relates to physicians. Those who would like to know the steps they should take to help alleviate this situation should write to: Council on National Security, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Course in emotional and psychiatric problems

The New York Academy of Medicine will present the fourth in an annual series of courses on "Emotional and Psychiatric Problems in Medical Practice," starting Monday, October 22, and ending February 8, 1963. The course, which is open to all physicians in specialty and general practice, will consist of basic and advanced sections meeting at weekly intervals for 14 one-and-one-half-hour sessions at the Academy building, 2 East 103rd Street, New York 29, New York.

The objective of the course is to help physicians to comprehend more fully the continuous interaction of psychologic, social, and medical factors encountered in clinical practice. The course will be divided into basic sections for the benefit of those who have not participated previously and advanced sections for those who have already taken the basic course. The American Academy of General Practice, cosponsor of the course, will allow 21 hours of category 1 credit for its completion.

For information write to: Executive Secretary for Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

New York State Medical Assistants Association

The third annual convention of the New York State Medical Assistants Association was held in Syracuse, April 27 through 29.

Designed to acquaint the medical assistant with the latest advances in health care, discussions at the meeting covered the fields of rehabilitative medicine, psychology, hypnotism, economics, and legislation. Speakers included: Leo Jivoff, M.D., medical director of the Rehabilitation Center of Syracuse University Hospital and chairman of the Department of Rehabilitative Medicine of the State University of New York College of Medicine at Syracuse; Chalmers L. Stacey, Ph.D., professor of psychology, Syracuse University, and associate clinical psychologist, Syracuse State School; and Raymond J. Pieri, M.D., emeritus professor, State University of New York College of Medicine at Syracuse.

New officers of the Association are: Mrs. Loretta Davern, Onondaga County, president; Miss Mary McNulty, Broome County, vice-president; Mrs. Rae Capizzi, Erie County, president-elect; Mrs. Elsie Adams, Nassau County, recording secretary; Miss Barbara Brandt, Albany County, treasurer; and Miss Lina Fernandez, Onondaga County, corresponding secretary.

Fulton Society formed

During the recent International Congress of Neurology in Rome, Italy, a meeting was held in memory of John Farquhar Fulton, M.D., famous neurophysiologist and medical biographer.

As a result of the meeting the Fulton Society was formed and it was decided that a symposium should be held every two years so that recent advances in the contributions that Dr. Fulton made to the field of neurology could be discussed.

The first symposium will be held at the same time and place as the 1963 meeting of the American Neurological Association. The subject of the symposium will be "Motor and Premotor Areas."

Interested physicians should write to: Dr. Victor Soriano, M.D., Editor, Revista Internacional de Neurologica, Calle Buenos Aires 363, Montevideo, Uruguay.

Medical publications urgently needed

The doctors of the United States are being asked to pass their medical journals on to colleagues overseas (Asia, Latin America, and Africa) who wish to have access to current medical literature but who, either because of currency regulations or actual cost involved, cannot subscribe to medical periodicals. The name, address, and medical specialty of doctors interested in receiving these journals will be supplied on request to: United States Committee, The World Medical Association, 10 Columbus Circle, New York 19, New York. When writing please state the journals which you wish to contribute.

Research support applications invited by American Heart Association

Applications from research investigators for support of studies to be conducted during the fiscal year beginning July 1, 1963, are now being accepted by the American Heart Association.

The deadline for submitting applications for advanced research fellowships and established investigatorships is September 15, 1962. Applications in the grant-in-aid category must be received by November 1, 1962.

Awards will be made as follows: Established Investigatorships: Established investigatorships for five years, in amounts ranging from $8,500 to $12,500 yearly plus dependency allowances, are usually awarded to scientists of proved ability who have developed their research careers to the point where they are independent investigators. The awards are subject to annual review.

Advanced Research Fellowships: Advanced research fellowships are awarded for a one- or two-year period to postdoctoral applicants with some research training and experience who are not yet clearly qualified to conduct their own independent research. Stipends range from $6,500 to $8,600 annually, plus a dependency allowance.

Grants-in-Aid: Grants-in-aid are made to experienced investigators to help underwrite the costs of specified projects, such as equipment, technical assistance, and supplies.

Further information and application forms may be obtained from: John H. Peters, M.D., Associate Medical Director for Research, American Heart Association, 44 East 23rd Street, New York 10, New York.

Course on cardiopulmonary problems in children

The American College of Chest Physicians in cooperation with the American Academy of Pediatrics will hold a postgraduate course on cardiopulmonary problems in children, July 23 through 27, at the Edgewater Beach Hotel, Chicago.

For further information write to: American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Occupancy Tax due

Hilda G. Schwartz, Treasurer of the City of New York, has announced that an amendment to the Occupancy Tax Law enacted on May 18 changes the rates of the Occupancy Tax for the tax year beginning July 16, 1961, and ending July 15, 1962. The amendment also changes the due date of the tax from July 15 to June 5.

The Occupancy Tax is payable by persons who occupy space for gainful purposes for a period of one month and fifteen days or more prior to July 15, 1962. A title owner of premises who occupies space in such premises is exempt from the payment of the tax. The amount of the tax due is based on the rental value of each separate premises so occupied. A grace period of July 5 has been established to provide taxpayers with time to make out their returns.

Assistance to taxpayers and answers to inquiries are available at all the borough offices of the Bureau of City Collections, Department of Finance.

Worthless devices banned

The Food and Drug Administration has announced that shipments of seven types of worthless devices to health practitioners throughout the country have been permanently banned by a Federal Court.

The Court prohibited distribution of new, used, or repaired devices known as Neurolinometer, Radioclast Model 40, Radioclast Model P, Radioclast Treating Unit, Electron-O-Ray 46, Electron-O-Ray Model 51, and Quto-Electronic Instrument Model 0-20-1 P.

The FDA said the devices vary in size and shape but in general have an impressive appearance with panels of lights, rows of switches, control knobs, and electrodes. Some are supposed to measure electrical frequencies emanating from diseased areas of the body although such frequencies do not exist.

Rhinologic courses scheduled for 1963

Two courses in rhinology will be presented at Leiden University, Holland, in July, 1963.

A "Boerhaave" course in rhinology will be held July 4 through 6 and will be followed by the fifth international course in "Reconstructive Surgery of the Nasal Septum and External Pyramid," July 7 through 19. The courses will be presented with the cooperation of the American Rhinologic Society.

For further information write to: American Rhinologic Society, 530 Hawthorne Place, Chicago 13, Illinois.

Personalities

Honored. Arthur A. Knapp, M.D., New York City, at a dinner on April 30 given by the U.S. Naval Reserve Medical Company 3-2 of Manhattan at which he was presented with an engraved silver bowl.

Installed. Milton Helpern, M.D., New York City, as president of the Medical Society of the County of New York.

Appointed. Harold Meiselas, M.D., Hempstead, as director of the narcotics addiction program of the State of New York Department of Mental Hygiene.

Awarded. Maxwell H. Poppel, M.D., New York City, the Alumni Meritorious Service Medallion from the New York University Alumni Federation for his work in the field of radiology.

Elected. Leo S. Drexler, M.D., Brooklyn, as president of the Medical Society of the County of Kings. . . George Himler, M.D., New York City, as president-elect of the Medical Society of the County of New York. . . Robert Moore, M.D., and Julius E. Stolfi, M.D., Brooklyn, as vice-president and president-elect respectively, of the Medical Society of the County of Kings.

Speakers. Murray B. Bornstein, M.D., New York City, in June at a meeting of the Tissue Culture Association. . . Clarence C. Hare, M.D., White Plains, on May 14, in New York City at a meeting of The Society of Medical Jurisprudence. . . George James, M.D., New York City, First Deputy Health Commissioner of the Department of Health of the City of New York, before a meeting of fire prevention experts on May 11. . . Bernard O. Marbach, M.D., White Plains, and John G. Muccigrosso, M.D., Yonkers, at a meeting of The Society of Medical Jurisprudence on May 14 in New York City. . . George T. Pack, M.D., the Austin M. Curtis Memorial Lecture at Howard University, Washington, D.C., on May 7, on the subject "The Clinical Aspects of Cancer Immunity and Cancer Susceptibility". . . Henry N. Pratt, M.D., New York City, on May 23 in Atlantic City at the annual meeting of the Middle Atlantic Hospital Assembly. . . Thomas S. Szasz, M.D., Syracuse, on June 5, at the commencement exercises of the Postgraduate Center for Psychotherapy.

Abstracts

Sobel, G.: Respository treatment of grass and ragweed pollinosis (1961), New York State J. Med. **62:** 2117 (July 1) 1962.

In 1961 72 patients were treated with grass emulsion and 101 patients with ragweed emulsion. Both emulsions, prepared by a private laboratory and not reemulsified before administration, were given in one to four injections in total doses ranging from 1,000 to 20,000 PNU (protein nitrogen units) before the pollinating season. The clinical results were satisfactory in 77 per cent of the grass-sensitive and 76 per cent of the ragweed-sensitive patients, and they appeared unrelated to dose and pretreatment skin tests. Slight systemic reactions occurred in 6 per cent of the grass-treated patients and moderately severe reactions in 1 per cent. Slight systemic reactions occurred in 7 per cent of ragweed-treated patients, but no severe reactions occurred. Delayed nodule formation occurred in 7 per cent of the grass-treated patients and in 8 per cent of the ragweed-treated patients.

Dadey, J. L., and Stafford, R. M.: Considerations of medical shock of unknown origin, New York State J. Med. **62:** 2143 (July 1) 1962.

Medical shock may be caused by numerous diseases. The correct diagnosis is necessary to the prompt, specific, and supportive therapy which is essential to sustain the life of a patient admitted to a medical service in a profound state of shock. The most common cause of medical shock is myocardial infarction; other cardiac causes include the arrhythmias, pericarditis, myocarditis, cardiac rupture and tamponade, rupture of valve cusps, chordae tendineae, and papillary muscles, septal perforation, and necrotizing angiitis. Bacteremia is also a very common cause of shock. Hypovolemic states which may cause shock include acute internal blood loss, acute pancreatitis, diabetic acidosis, and adrenal insufficiency. An acute allergic condition may cause shock. Impediment to blood flow, such as sudden embolic phenomena and dissecting aneurysm of the aorta, is another cause of shock. Neurogenic causes of shock include all forms of cerebral vascular accidents, "hypoglycemic shock," and effect of drugs on the central nervous system.

Meyers, R.: Current neurosurgical researches and treatment referable to the hyperkinetic disorders, New York State J. Med. **62:** 2151 (July 1) 1962.

Surgery for hyperkinesia is limited, alleviatory rather than curative, and nonspecific. It consists largely of placing lesions in the basal ganglia, ansa lenticularis, dorsal thalamus, and closely related pretectal and tegmental structures and is directed to contriving symptomatic relief and illuminating understanding of the pertinent healthy neuro-chemo-humoral mechanisms and the manner in which they may become deranged. The disorders may be divided into two categories: patterned hyperkinesias or tremors of the resting, posture-attaining, posture-maintaining, or ataxic type; and nonpatterned hyperkinesias in which the phasic movements take off from a eutonic or hypotonic background of muscle tonus or in which they take off from a hypertonic background of muscle tonus of fluctuating or relatively enduring character. A sound general theory of the manner in which pertinent neurohumoral mechanisms become so deranged that clinical hyperkinesia appears is lacking; there are failures in the structure-bound, system-bound, and relational theories and combinations of these. The components of a propositional function of hyperkinesia include: the pallido-pallidofugal complex, the integrity of which seems to be a precondition of hyperkinesia, and the concept of somatotopic arrangements. The concept of a facilitation-inhibition ratio and that of synchronous firing of the FCP (final common pathway) lack empiric verification but may well receive it in the near future. There is reason to anticipate that a multiple convergence hypothesis in which disturbed dynamic relationships, rather than damage to particular agents, will provide the basis of an explanation of hyperkinesia.

Hall, J. E., Kohl, S. G., and Kavaler, F.: Transverse lie and perinatal mortality, New York State J. Med. **62:** 2187 (July 1) 1962.

A study was made of 426 cases of transverse lie, 0.26 per cent of the total number of pregnancies surveyed. Ninety per cent of the patients were multiparas, and 32.2 per cent of the transverse lies which occurred were associated with prematurity. Placenta previa, prolapse of the umbilical cord, and contracted pelvis were associated with the entity in a high incidence. Perinatal loss in patients delivered by cesarean section was 10.2 per cent, whereas in vaginal delivery it was 35.4 per cent. The patient with an uncomplicated term transverse lie may be allowed to go into spontaneous labor to determine whether or not a spontaneous conversion to a longitudinal presentation will occur. If conversion does not occur at once, a cesarean section should be performed. A scout roentgenogram should be done in all cases to determine the position of the fetus.

Meyers, L., and Craft, G. S.: Effectiveness of aerosol administration of ergotamine tartrate in migraine headache, NEW YORK STATE J. MED. **62:** 2192 (July 1) 1962.

Forty-eight patients with migraine headache and 2 patients with headache of vascular origin were treated with aerosol administration of ergotamine tartrate. Of a total of 261 headaches treated, 82 per cent were relieved, 65 per cent completely. Relief was obtained in from fifteen to thirty minutes—more rapidly than with either rectal or oral administration and as quickly as with the parenteral method. Side-effects were noted in 10 per cent but necessitated discontinuance of the medication in only 1 case. Convenience of administration, rapidity of results, and degree of relief obtained made this the method of choice of 72 per cent of the patients studied.

Twombly, G. H., and Jacobowitz, W. E.: Carcinoma of the endometrium, NEW YORK STATE J. MED. **62:** 2195 (July 1) 1962.

From 1951 to 1960 82 women with cancer of the endometrium were seen at Bellevue Hospital, as compared with 482 women with carcinoma of the cervix, a ratio of 1 to 5.9. New York State statistics showed a ratio of 1 to 1.8. The difference is attributed to the large proportion of Puerto Ricans admitted to Bellevue in whom the incidence of carcinoma of the endometrium is low and that of carcinoma of the cervix high. The average age of the patients was 62.6. Although 48.8 per cent of the patients were admitted within six months of the first symptoms, 26 per cent waited over a year. The age at the menopause had no effect on causation of endometrial carcinoma. There was a lack of fertility in the patients. The majority were obese, suggesting that estrogens might be stored in the body fat, smoothing out the normal peaks of estrogen excretion. Obese women were shown to excrete less isotopically labeled estradiol in three days than thin women. Experimentally 4 of 20 rabbits implanted with 25-mg. pellets of estradiol developed carcinoma of the endometrium in two hundred nineteen to five hundred ninety-seven days—the mechanism of this is not clearly understood.

Young, J. D., Jr., and Powder, J. R.: Flank cutaneous ureterostomy and ureteroureteral cutaneous neostomy, NEW YORK STATE J. MED. **62:** 2201 (July 1) 1962.

Ten patients were subjected to flank cutaneous ureterostomy; 7 patients developed healthy epithelialized stomas from three to eighteen months postoperatively. The remaining 3 were elderly with advanced carcinomatosis of the bladder, and the end of the ureter in each of these patients sloughed and retracted. Indications for the procedure were: Pseudomonas pyocyanea infection, tuberculosis of the urinary tract, certain neurologic deficits, and inoperable cancer of the bladder. Ureteroureteral cutaneous neostomy was performed on 6 patients with cancer of the bladder and 2 patients with neurogenic bladders. The procedures provided a satisfactory means of total urinary diversion in 4 of 8 patients. The remaining 4 died of carcinomatosis too soon after operation to evaluate the procedure. Both procedures are useful methods of catheter-free urinary diversion with a low incidence of stricture and retraction of the ureteral stoma.

Talarico, L. H.: Diverticulum of the female urethra, NEW YORK STATE J. MED. **62:** 2216 (July 1) 1962.

The diagnosis of a urethral diverticulum should be suspected in any woman with symptoms of chronic urethritis. The palpation of a pulpaceous mass in the anterior vaginal septum and a panendoscopic examination of the urethra are usually diagnostic. Over a seven-year period 23 patients were treated by simple excision, which is the treatment of choice in uncomplicated cases. The complications were urgency and frequency with one of stress incontinence, all resolving with conservative office management. In diverticuli containing tumors, simple excision suffices if the urethra is not involved; if it is, more radical procedures are indicated with or without adjunctive radiation therapy.

Medical Meetings

West Virginia State Medical Association

The West Virginia State Medical Association will hold its ninety-fifth annual meeting at the Greenbriar Hotel, White Sulphur Springs, West Virginia, August 23 through 25. For further information contact: Mr. William Lively, Executive Secretary, West Virginia State Medical Association, Box 1031, Charleston 24, West Virginia.

American Congress of Physical Medicine and Rehabilitation

The American Congress of Physical Medicine and Rehabilitation will hold its fortieth annual session, August 27 through 31, at the Hotel Commodore, New York City. Nonmember physicians are invited to attend the scientific sessions.

For further information write to: Glenn Gullickson, Jr., M.D., Executive Director, American Congress of Physical Medicine and Rehabilitation, 30 North Michigan Avenue, Chicago 2, Illinois.

Utah State Medical Association

The Utah State Medical Association will hold its sixty-seventh annual scientific meeting in Salt Lake City, Utah, September 11 through 14 at the Hotel Utah Motor Lodge. Paul I. Robinson, M.D., of New York City will be among the guest speakers.

For further information write to: Utah State Medical Association, 42 South 5th East, Salt Lake City, Utah.

American Rhinologic Society

The eighth annual meeting of the American Rhinologic Society will be held at the Statler Hilton Hotel, Los Angeles, November 1 and 2. The meeting will be preceded by a three-day course in "Expanded Surgery of the Nasal Septum" to be presented at the Loma Linda University in cooperation with the American Rhinologic Society.

For further information write to: American Rhinologic Society, 530 Hawthorne Place, Chicago 13, Illinois.

Academy of Psychosomatic Medicine

The ninth annual meeting of The Academy of Psychosomatic Medicine will be held in Minneapolis, November 1 through 3, at the Radisson Hotel.

For information write to: Bertram B. Moss, M.D., Executive Secretary, 55 East Washington Street, Chicago 2, Illinois.

American Society of Cytology

The American Society of Cytology (formerly the Inter-Society Cytology Council) will hold its tenth annual scientific meeting at the Chase-Park Plaza Hotel, St. Louis, Missouri, November 8 through 10. For further information write to: Paul A. Younge, M.D., Secretary-Treasurer, American Society of Cytology, 1101 Beacon Street, Brookline 46, Massachusetts.

National Society for Crippled Children and Adults

The National Society for Crippled Children and Adults will hold its annual convention at the Hotel Fontainebleau, Miami Beach, Florida, November 16 through 20.

For further information write to: National Society for Crippled Children and Adults, 2023 West Ogden Avenue, Chicago 12, Illinois.

Letters to the Editor

Employment of unlicensed nurses

To the Editor: As you know, it is a misdemeanor in New York State for anyone to practice nursing who is not a Registered Nurse or a Licensed Practical Nurse. It has been reported to us that in some cases, however, families are employing women who call themselves "practical nurses" but who are not licensed by the State of New York Department of Education.

We should appreciate it if you could have this situation called to the attention of your members through the NEW YORK STATE JOURNAL OF MEDICINE. It will be helpful if physicians are on guard against the employment of so-called nurses who are not licensed.

RHODA E. BESWICK, L.P.N., President
Licensed Practical Nurses of New York, Inc.

250 West 57 th Street
New York 19, New York

Excessive number of medical meetings

To the Editor: The plethora of medical meetings which one must attend is a source of annoyance and embarrassment. In most instances, the number of local meetings could be reduced by two-thirds and the number of meetings of national groups and their regional and state offspring halved. The duplication of meetings is a ridiculous waste of time for the several men who are obligated to attend the meeting because they are on the committee for arrangements or are personal friends of the speaker or for the young physician who hopes to further his acquaintance with his fellow practitioners. This situation is equally ridiculous for the "nationally known speaker" who has traveled 500 miles with notes and slides for a formal lecture only to find 6 to 10 tired, sleepy practitioners, and several retired physicians who have finished cocktails and a heavy meal and are desperately trying to appear interested and awake. Many of the younger members attended the dinner then swiftly disappeared on emergency calls. This comedy occurs every day in thousands of medical communities.

It is time for a moratorium on such meetings. The following rules should be considered:

1. If the "scientific portion" of three consecutive meetings are attended by fewer than 12 practicing physicians, the lectures should be discontinued.
2. If less than 25 are in attendance, only speakers from the group or immediate medical community (25 miles) should be invited.
3. If there are from 25 to 50 members, no speaker should be invited who must travel over 50 miles or make special travel arrangements. A group of this size is well suited for informal lectures with adequate time for discussions.
4. If there are from 50 to 100 members or over, such an audience may warrant a prominent speaker from a distant city, particularly if it is a topic suitable for the particular group and occasion. (An excellent but obtuse dissertation on the thermodynamic relationship of alligator erythrocytes may be exquisite torture for a group of practicing physicians).

G. EUGENE MCCRAE, M.D.

Dangers of destructive criticism

To the Editor: In clinical reports and at medical meetings, there seems to be an increasing tendency to belittle a new thesis, plan of diagnosis, or therapy—or even an established mode of treatment—merely by a forceful expression of personal opinion. The dangers of this practice are evident. Thoughtful studies are being dismissed by such pompous expressions as "Each patient must be treated separately," or "You can't forget the whole man." A distressing number of physicians are making thinly veiled insinuations that valid, properly controlled studies are inhuman. A new drug may be given to thousands of patients without real evidence of its value. Thus, the family physician is in effect conducting an initial human pharmacologic experiment, administering the drug without proper knowledge of its toxicity and without satisfactory means for assessing its value. I would highly recommend that incipient wordy arguments be interrupted and future debates be conducted according to Bross's rule, "Do unto your proponent as you would have him do"*; that is, only contrary valid clinical or statistical findings should be used to criticize a presentation, not personal polemics.

GEORGE E. MOORE, M.D.

Roswell Park Memorial Institute
Buffalo 3, New York

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* Bross, D.: Statistical criticism, Cancer **13**: 394 (Mar.-Apr.) 1960.

Abstracts in Interlingua

Sobel, G.: Tractamento per injection de emulsion repositori contra pollinosis de gramine e ambrosia (1961) (*anglese*), New York State J. Med. **62:** 2117 (1 de julio) 1962.

In 1961, 72 patientes esseva tractate con emulsion de gramine e 101 con emulsion de ambrosia. Ambe le preparatos esseva le producto de un laboratorio private. Illos esseva administrate, sin re-emulsification, in inter un e quatro injectiones in un dosage total de inter 1.000 e 20.000 unitates de nitrogeno proteinic ante le comenciamento del saison de pollination. Le resultatos esseva clinicamente satisfacente in 77 pro cento del subjectos con sensibilitate pro gramine e in 76 pro cento del subjectos con sensibilitate pro ambrosia. Il pareva que iste resultatos non esseva relationate con le magnitude del doses o con tests cutanee de effectuation ante le tractamento. Leve reactiones constitutional occurreva in 7 pro cento del patientes tractate a ambrosia. Occurreva nulle reaction sever. Formation tardive de nodulos esseva constatate in 7 pro cento del patientes tractate a gramine e in 8 pro cento del patientes tractate a ambrosia.

Dadey, J. L., e Stafford, R. M.: Considerationes in re choc medical de origine non cognoscite (*anglese*), New York State J. Med. **62:** 2143 (1 de julio) 1962.

Choc medical pote esser causate per numerose morbos. Le correcte diagnose es indispensabile pro le prompte initiation de un therapia specific e supportative le qual es essential pro mantener le vita del patiente admittite a un servicio medical in un stato de choc profunde. Le causa le plus commun de choc medical es infarcimento myocardial. Altere causas cardiac es arrhythmias, pericarditis, myocarditis, ruptura e tamponage cardiac, ruptura de cuspides valvular e de chordas de tendine o musculos papillari, perforation de septo, e angiitis necrotisante. Etiam bacteremia es un causa communissime de choc. Statos hypovolemic que pote esser le causa de choc es acute perdita interne de sanguine, acute pancreatitis, acidosis diabetic, e insufficientia adrenal. Un acute condition allergic pote esser le causa de choc. Impedimentos in le fluxo de sanguine es etiam possibile causas de choc. Tales es subite phenomenos embolic e aneurysmo dissecante del aorta. Causas neurogenic de choc include omne le formas de accidente cerebrovascular, hypoglycemia ("choc hyperglycemic"), e le effectos de certe drogas in le systema nervose central.

Meyers, R.: Currente recercas neurochirurgic e lor signification pro le tractamento de disordines hypercinetic (*anglese*), New York State J. Med. **62:** 2151 (1 de julio) 1962.

Le uso de chirurgia in hypercinese es restringite; illo es alleviatori plus tosto que curative; e illo es nonspecific. Illo consiste in grande mesura in effectuar lesiones in le gangliones basal, in le ansa lenticular, in le thalamo dorsal, e in intimemente connexe structuras pretectal e tegmental. Su objectivo es obtener alleviamento symptomatic e promover nostre comprension del pertinente mechanismos neurochimo-humoral in stato normal e del maniera in que illos pote devenir disrangiate. Le disordines pote esser dividite in duo categorias: (1) hypercinese de comportamento specialisate, i.e. tremores in reposo, in transition in postura, in mantenimento de postura, o de typo ataxic e (2) hypercinese de comportamento non specialisate, in que le movimentos phasic parti ab un fundo eutonic o hypotonic del tono muscular o in que illos parti ab un fundo de hypotonia muscular de character fluctuante o relativemente stabile. Il non existe un bon theoria general in re le maniera in que pertinente mechanismos neuro-humoral es disrangiate de maniera que il occurre hypercinese clinic. Il ha debilitates in omne le varie theorias, illos a base structural, illos connexe con systemas, illos de typo relational, e illos que es combinationes del mentionate tres typos. Le componentes de un function propositional de hypercinese es le complexo pallido-pallidofugal (le integritate del qual pare esser un precondition de hypercinese) e le concepto del arrangiamento somatotopic. Le notion de un proportion significative inter facilitation e inhibition e le notion de un activation synchrone del final circuito commun es disproviste de verification empiric, sed il es possibile que tal verification va esser obtenite in le proxime futuro. Es a previder le disveloppamento de un theoria de convergentia multiple in que disturbate relationes dynamic plus tosto que damnificate agentes particular providera le base pro le explication de hypercinese.

Hall, J. E., Kohl, S. G., e Kavaler, F.: Position transverse e mortalitate perinatal (*anglese*), New York State J. Med. **62:** 2187 (1 de julio) 1962.

Esseva studiate 426 casos de pregnantia a position transverse. Isto correspondeva a 0,26 pro cento del numero total de pregnantias revistate. Novanta pro cento del patientes esseva multiparas, e 32,2 pro cento del casos de position transverse esseva associate con prematuritate. Placenta previe, prolapso del cordon umbilical, e contraction del pelve esseva associate con le condition in un alte procentage del incidentia. Perdita perinatal in patientes a parturition per section cesaree amontava a 10,2 pro cento, sed in le gruppo a parturition vaginal le perditas perinatal constitueva 35,4 pro cento. In le caso del patiente con position transverse del feto sed sin altere complication al termino, le progresso spontanee del labores pote esser permittite pro vider si o non un conversion spontanee al presentation longitudinal va occurrer. In caso que nulle tal supervini immediatemente, section cesaree debe esser effectuate. Un roentgenogramma exploratori debe esser obtenite in omne casos pro determinar le position del feto.

Meyers, L., e Craft, G. S.: Efficacia del administration per aerosol, de tartrato de ergotamina in cephalalgia de migraine (*anglese*), NEW YORK STATE J. MED. **62:** 2192 (1 de julio) 1962.

Quaranta-octo patientes con cephalalgia de migraine e 2 patientes con cephalalgia de origine vascular esseva tractate con tartrato de ergotamina administrate per aerosol. In un total de 261 episodios de cephalalgia tractate, 82 pro cento esseva alleviate; in 65 pro cento, le alleviamento esseva complete. Le effecto esseva obtenite intra inter dece-cinque e trenta minutas—i.e. plus rapidemente que con administration rectal o con administration oral e tanto rapidemente como con administration parenteral. Adverse effectos secundari esseva notate in 10 pro cento, sed suspension del medication esseva necessari in 1 caso solmente. Le facilitate del administration, le rapiditate del resultatos e le grado de alleviamento obtenite faceva de iste methodo le methodo de election in 72 pro cento del patientes studiate.

Twombly, G. H., e Jacobowitz, W. E.: Carcinoma del endometrio (*anglese*), NEW YORK STATE J. MED. **62**: 2195 (1 de julio) 1962.

Ab 1951 ad 1960, 82 feminas con cancere del endometrio esseva vidite al Hospital Bellevue. Durante le mesme intervallo, 482 casos de carcinoma del cervice esseva vidite. Le proportion inter le duo esseva 1 a 5,9. Le statisticas pro le Stato de New York monstrava un proportion correspondente de 1 a 1,8. Le differentia es attribuite al alte procentage de portoricanas admittite a Bellevue. In iste population le incidentia de carcinoma del endometrio es basse e illo de carcinoma del cervice es alte. Le etate medie del patientes esseva 62,6 annos. Ben que 48,8 pro cento del patientes esseva admittite al hospital intra sex menses post le prime symptomas, 26 pro cento attendeva plus que un anno. Le etate al tempore del menopause habeva nulle effecto in le causation de carcinoma del endometrio. Esseva notate un manco de fertilitate in le patientes. Le majoritate de iste feminas esseva obese, lo que suggere que estrogenos esseva possibilemente thesaurisate in le grassia del corpore, con le resultato de un applattamento del normal extremos in le excretion de estrogenos. Esseva monstrate que feminas obese excerne minus isotopicamente marcate estradiol intra tres dies que feminas tenue. Esseva trovate experimentalmente que in 4 ex 20 conilios in que glomerulos de 25 mg de estradiol habeva essite implantate, carcinoma del endometrio se disveloppava intra inter duo centos decenovem e cinque centos novanta-septe dies. Le mechanismo de iste phenomeno non es clarmente comprendite.

Young, J. D., Jr., e Powder, J. R.: Ureterostomia cutanee al flanco e neostomia cutanee uretero-ureteral (*anglese*), NEW YORK STATE J. MED. **62:** 2201 (1 de julio) 1962.

Dece patientes esseva subjicite a ureterostomia cutanee al flanco. Septe de illes disveloppava ben-epitheliisate stomas a inter tres e dece-octo menses post le operation. Le remanente 3 esseva subjectos de alte etate con avantiate carcinomatosis del vesica. In omne iste 3, le termino del ureter se mortificava e esseva retrahite. Indicationes pro le operation esseva infection per *Pseudomonas pyocyanea*, tuberculosis del vias urinari, certe deficits neurologic, e inoperabile cancere del vesica. Neostomia cutanee uretero-ureteral esseva effectuate in 6 patientes con cancere del vesica e in 2 con vesicas neurogene. In 4 de iste 8 patientes, le operation provideva un satisfacente medio pro le diversion total del urina. Le altere 4 patientes moriva de carcinomatosis troppo tosto post le operation pro permitter un evalutation del resultatos. Le duo hic discutite operationes es utile methodos pro le effectuation—sin le uso de catheteres—de diversion urinari, con un basse incidentia de strictura e retraction del stoma ureteral.

Talarico, L. H.: Diverticulo del urethra feminin (*anglese*), NEW YORK STATE J. MED. **62:** 2216 (1 de julio) 1962.

Le diagnose de diverticulo urethral deberea esser suspicite in omne femina con symptomas de urethritis chronic. Le palpation de un massa pulpacee in le septo antero-vaginal e le examine panendoscopic del urethra es usualmente diagnostic. In le curso de un periodo de septe annos, 23 patientes esseva tractate per simple excision, lo que es le tractamento de election in casos non complicate. Le complicationes esseva urgentia e frequentia del micturition e—in un caso—incontinentia sub stress. Omne iste complicationes se resolveva in le curso de un tractamento conservatori al sala de consulta. Quando un diverticulo contine tumores, un simple excision suffice si le urethra non es afficite. Si illo lo es, interventiones plus radical es indicate con o sin adjunctive therapia radiatori.

Books Reviewed

The Premature Baby. By V. Mary Crosse, M.D. Fifth edition. Octavo of 266 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $7.

Dr. Crosse began in 1946 to try to reduce the death rate of premature infants at Sorrento Maternity Hospital in the neighborhood of Birmingham, England. Over the years she has built up a valuable fund of knowledge of the requirements for the proper care of premature babies, and in this volume she expounds on the subject in considerable detail, starting with the definition of a premature infant and advancing by logical steps through the characteristics of these small babies, their hospital and home care, the complications to be expected, and their feeding and clothing.

The subject matter is fortified by a wealth of statistical data in tables.

The book will be of great value to medical students, nurses, physicians, and pediatricians in the smaller towns and rural areas. In the larger cities the development of premature centers takes the premature babies out of the hands of even the experienced smaller hospital pediatricians and puts them into the hands of an extremely small group, usually of resident physicians, so that the subject is of lessening interest among the larger city pediatricians.

The text is excellent, well organized, and well indexed.—KENNETH G. JENNINGS, M.D.

Cardiac Disease in Pregnancy. By Curtis Lester Mendelson, M.D. Octavo of 385 pages, illustrated. Philadelphia, F. A. Davis Company, 1960. Cloth, $13.50.

Dr. Mendelson has had the advantage of seeing a great number of cardiac patients during their pregnancies at one of the large centers in New York. As a result, he is well qualified to discuss the problems involved.

Practically every category of cardiac disease is covered, some of these so rare as to be almost a medical curiosity. The author goes into considerable detail on the physiologic changes of pregnancy as they apply to the circulatory and respiratory systems and then treats general problems of cardiac disease in pregnancy. He takes up specific cardiac conditions as they affect pregnancy or as pregnancy affects them. In this area of the book, there begins to be repetition, for the same course of treatment may apply to several diseases. In following a sort of outline for each condition, the author tends to repeat.

The book will appeal to obstetricians who are affiliated with services which have a large number of medical cases under their direction. The author is to be congratulated on his thoroughness.—SANFORD KAMINESTER, M.D.

Poliomyelitis. Papers and Discussions Presented at the Fifth International Poliomyelitis Conference, Copenhagen, Denmark, July 26–28, 1960. Compiled and edited for the International Poliomyelitis Congress. Quarto of 435 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $7.50.

The information conveyed by this collection of articles and discussions is now more than one year old, and the important points have become general knowledge throughout the medical profession. Nevertheless, a leisurely reading of this book is enjoyable and enlightening.

In contrast to the content of earlier conferences one notes an absence of articles concerning the disease and its treatment. One finds a discussion only of prophylactic vaccines—their safety and efficacy.

Part one comprises a group of essays describing advances in our knowledge of the results of the activities of poliomyelitis viruses in the cells of the tissue culture media.

Part two is divided into a section analyzing the success of the inactivated vaccine of Salk and a section presenting formal papers on field studies of the attenuated live vaccines of Sabin and of Cox and of Koprowski.

The efficacy of the Salk vaccine is not questioned. Three disadvantages are brought forward; first, the necessity for multiple injections; second, the prohibitive cost of the vaccine itself to the underprivileged nations; and third, the lack of assurance that a purely humeral immunity will endure for life and eliminate the disease, paralytic poliomyelitis, for good.

Dr. Salk answers that it should be possible to prepare a one-dose vaccine, thereby eliminating the first two disadvantages, and that the study of the duration of immunity as result of each vaccine is still incomplete.

With regard to the attenuated live virus vaccine, essays from all parts of the world except Asia are presented, and there is no report of a return to virulent neurotropic mutants in any of the vaccines despite the inclusion of about 10 million human beings in whom vaccine was implanted in the various field studies. The cost of preparation of the vaccine is said to be reasonable, and if it is implanted in a substantial percentage of the population of a community, it will spread by fecal contamination to a further substantial percentage of the people in close proximity, thereby increasing the number of immune persons. The effectiveness of these vaccines has been found to be markedly reduced if they are given during an epidemic of another enteropathogenic virus disease. The Russians have incorporated the vaccine into a candy for use in children.

Very interesting is the attempt to monitor changes in the virulence of the excreted vaccine virus by use of the so-called acid-overlay tissue culture test—the so-called "d" test and the temperature differential or "T" test to reduce the number of monkeys required.

The book abounds in tables to fortify the conclusions reached in all subjects. The discussions following each subdivision are excellent. There is an adequate index.

While this is primarily a book of reference, interested physicians and public health workers will want to read it from cover to cover.—KENNETH G. JENNINGS, M.D.

Progress in Medical Genetics. Volume I. Edited by Arthur G. Steinberg, Ph.D. Octavo of 341 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $9.75.

The publication of this, the first of a projected series of volumes, was stimulated by the burgeoning interest in human genetics in recent years. Like its smaller counterpart, *Recent Advances in Human Genetics*, edited by L. S. Penrose and published in England, it contains chapters on such topics as mutation in man, the chromosomes, and the hemoglobinopathies. Unlike the British book, however, this volume devotes two chapters to the blood groups. Unfortunately, however, instead of discussing the important recent advances in the knowledge of Rh-Hr serology and genetics, as many as 40 pages are wasted on a discussion of certain recent papers on blood groups in disease. The chapter in question pretends to demonstrate associations between particular A-B-O blood groups and such diverse diseases as gastric and duodenal ulcers, pernicious anemia, carcinoma of the stomach, colon, rectum, and cervix of the uterus, salivary tumors, cholelithiasis, portal cirrhosis, diabetes mellitus, hypertension, toxemia of pregnancy, and others. The author of this chapter was apparently unaware of the similar claims regarding associations between particular Rh-Hr types and peptic ulcer, ulcerative colitis, Dupuytren's contracture, and so forth. After spending much effort wading through more than 40 pages of meaningless statistics, the reader is left completely bewildered. Since this volume wastes fully one eighth of its valuable space on sheer nonsense, it cannot be recommended. This necessarily slights the other more satisfactory chapters that the volume contains by authors unfortunate enough to have their work included in a volume containing a chapter devoted to blood group mythology.—A. S. WIENER, M.D.

Essentials of Histology. By Gerrit Bevelander, Ph.D. Fourth edition. Octavo of 288 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $5.75.

In this edition of a text designed especially for students, several new illustrations have been added and many chapters rewritten. Emphasis is directed to the relationship between cell structure, chemical composition, and function of cell components.

This publication should be especially helpful to students, for were they to wade through our very detailed histology books they would find it extremely time consuming. It should be used as a classroom guide only, and as such it has accomplished its goal.—NATHAN REIBSTEIN, M.D.

Clinical Obstetrics and Gynecology, Volume 3, Number 4. December 1960. Fetal Physiology and Distress. Edited by Thaddeus L. Montgomery, M.D. **Endocrinology.** Edited by Robert B. Greenblatt, M.D. Octavo of 328 pages, illustrated. New York, Paul B. Hoeber, Inc., 1960. Published quarterly (four numbers a year). Cloth, $18 per year.

Endocrinology, edited by Robert B. Greenblatt, M.D., presents a rather clear and concise summary of the present status of gynecologic endocrinology. The author has enlisted the aid of some of the outstanding authorities in this country as well as such world-known figures as Hubert DeWatteville of Geneva, Bernhard Zondeck of Jerusalem, and Peter M. F. Bishop of London. Each subject is handled by an expert in his particular field. This amazing collection of talent has resulted in a really worthwhile book.

Perhaps the one weak spot in the book is the chapter on the hormone control of lactation. The author simply gives his experience with one particular modality without mention of many other methods which are used widely with much success.

In general, the book deserves high praise. It is recommended not only to gynecologists but also to general practitioners and to all physicians interested in endocrinology.—SEYMOUR H. LIVINGSTON, M.D.

Progress in Clinical Medicine. Edited by Raymond Daley, M.D., and Henry Miller, M.D. Fourth edition. Octavo of 345 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $12.50.

This fourth edition of a standard British review of medicine has been thoroughly revised by its editors. Chapters on radioisotopes and space medicine bring the review up to 1961. Bibliographies, attached to each chapter or its subdivisions, are short but well chosen and indicate the literature's key articles.—MILTON PLOTZ, M.D.

Symposium on Anticoagulant Therapy. Edited by Professor Sir G. W. Pickering, M.D. Octavo of 284 pages, illustrated. London, Harvey & Blythe Limited, 1961. Cloth, 21s.

This symposium was held at the Royal Society of Medicine in England in November, 1960. The physicians who were invited to participate represented the outstanding clinicians of the British Commonwealth. In addition two outsiders were invited: Professor Owren from Sweden and Dr. Millikan from the Mayo Clinic.

The objectives of this symposium were to summarize the knowledge of the following questions: 1. How does anticoagulant therapy work? 2. How is this form of therapy best controlled? 3. In what illnesses does anticoagulant therapy prolong life and reduce complications?

In addition many other problems were discussed, for example: 1. Should anticoagulants be continued for life in the patient with coronary artery disease? For how long should they be continued in the patient with cerebrovascular insufficiency? 2. Are the indications for anticoagulants the same for men and women? 3. What effect does the age of the patient have in making a decision as to the use of anticoagulants?

All these questions and many more were answered. The surprising thing was that there was almost complete agreement on the answers. The only area of limited controversy lay in the merit of the Quick method for testing prothrombin as opposed to the Owren method. The consensus seemed to be that the Owren method was more exact but that the Quick method was very adequate in experienced hands. Most places seemed to be using the Quick method.

This is a most stimulating and informative volume. The discussions are lively and even humorous The fact that there was no great disagreement among the discussants is only a minor criticism.

I heartily recommend this volume. Since the indications for using anticoagulants are so broad and bridge so many different specialties, there is something in this volume for every physician who is responsible for patient care and management.—FELIX TAUBMAN, M.D.

Classics in Psychology. Edited by Thorne Shipley. Octavo of 1,342 pages, illustrated. New York, Philosophical Library, 1961. Cloth, $20.

This prodigious work was compiled and edited by a well-known psychologist who has long been interested in "firsts" in psychology. He has taken the trouble to examine the original article whenever possible to get the meaning intended by the authors. This has meant a great deal of intensive searching, and it must have been a work of love for the editor to have completed this volume.

It is the sort of a book one takes along on a vacation for leisure reading when one can digest the contents of each chapter with enjoyment. It brings our present knowledge in proper focus with the original founders of psychology and psychiatry—Wundt, von Hemholtz, Pinel, James, Bleuler, Charcot, Kraepelin, and Freud among many others.

It has been a delight for this reviewer to skip from chapter to chapter as it struck his fancy. At the end of each chapter there is a short biography of the author of the article which enchances the pleasure of book.—JOSEPH L. ABRAMSON, M.D.

Therapeutic Exercise. Edited by Sidney Licht, M.D. Second edition. Octavo of 959 pages, illustrated. New Haven, Elizabeth Licht, Publisher, 1961. Cloth, $16.

The editor and publisher have produced five volumes in a physical medicine library. *Therapeutic Exercise* was well covered in their third volume published in 1958 and is very well done again with more illustrations, the latest literature, and the addition of two chapters on posture analysis and gait analysis and training. This latest edition contains 37 chapters written by 35 authors, all eminently qualified to present their respective topics.

Therapeutic exercise is the single most important modality in any rehabilitation program and has thus received much attention. There are many volumes, but none as extensive as this. The basic science chapters are thorough, well written, and very informative. The practical and clinical chapters are presented regionally and by clinical entities; of necessity, therefore, they are repetitious in some instances. As in the previous edition, it is extremely difficult to judge which aspects merit stress at the expense of others. However, the goal of presenting exercise thoroughly is achieved. The subject index and the author references are extensive and deserve special commendation.

Therapeutic Exercise does not present any new data, but it does present all the data applicable to health and disease. It is a reference work which readily presents the known and the most recent advances. It rightfully belongs on the shelves of those utilizing this modality and in libraries for digestible and accessible reference.—EUGENE J. ROGERS, M.D.

Psychoanalysis and Social Process. Edited by Jules H. Masserman, M.D. Octavo of 196 pages, illustrated. New York, Grune & Stratton, 1961. (Science and Psychoanalysis. Volume IV). Cloth, $6.75.

This is the fourth volume emanating from the Academy of Psychoanalysis and edited by Dr. Masserman, professor of neurology and psychiatry at Northwestern University Medical School.

Previous volumes have dealt with the relationship of psychoanalysis and other aspects of human values. The present volume explores its relationship to social processes as it reflects the thinking of psychiatrists, psychologists, and sociologists who are well qualified in their respective fields.

This reviewer has always found these volumes of considerable value and refreshing and provocative in the manner of presentation.—JOSEPH L. ABRAMSON, M.D.

Pathologic Physiology, Mechanisms of Disease. Edited by William A. Sodeman, M.D. Third edition. Octavo of 1,182 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $15.

The third edition of Sodeman's *Pathologic Physiology* is welcome. The editor, confronted with the rapid advances in our knowledge of the mechanisms of disease, has brought his volume up to date. The contributors, carefully chosen, are all able. Their contributions, while not exhaustive, are comprehensive enough for medical students, house officers, general practitioners, and many specialists.—MILTON PLOTZ, M.D.

Medical Pharmacology: Principles and Concepts. By Andres Goth, M.D. Octavo of 551 pages illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $11.

The intention of the author is to emphasize principles and concepts in pharmacology, rather than to limit this text to a recital of facts. This is highly desirable in many disciplines for a knowledge of principles and concepts allows the reader to apply them in a larger scope or in various situations and therewith enables him to understand facts better. Conversely, the presentation of facts alone imparts the knowledge of the fact but does not necessarily give an understanding of principles. Most books on pharmacology—except the much abbreviated versions—discuss principles in greater or lesser measure.

Principles and concepts are commendably presented in this book. Some aspects are only touched on, but its extensiveness makes it reasonably comprehensive. The emphasis is pharmacologic, as expected, but there is a distinct clinical orientation. The text does not unduly take much knowledge for granted on the part of the student, yet it is not patronizing. The structural formulas are illustrative and tighten up the presentation. For those who wish to have a more intensive aspect, the bibliography is by-and-large well chosen. In spots the text can be considered oversimplified, yet this is a trait of an approach that is extensive rather than intensive.

An example of the approach to principles regarding vasodilators follows: ". . .little meaning merely to state that a drug dilates or constricts coronary vessels. . .clinically useful coronary vasodilators. . .increase coronary blood flow without simultaneously increasing the work of the heart." Such reminders are highly useful.

In that fashion there are chapters on drugs divided into pharmacologic classes, as effects on the nervous system and neuroeffectors, cardiovascular disease, endocrine functions, anesthetics, chemotherapy, and so forth.

This text, intermediate between the large pharmacology texts and the abbreviated "quickies," is a very good choice for the student and the practitioner. The text that most closely resembles it is Beckman's *Pharmacology*.—ERWIN DI CYAN, PH.D.

Nursing Home Administration. By John D. Gerletti, Ed.D., C. C. Crawford, Ph.D., and Donovan J. Perkins, M.S. Octavo of 472 pages, illustrated. Downey, Calif., published by the Attending Staff Association, 1961. Cloth, $6.50.

This book presents a distillation of wisdom, technics and methods of practitioners in the field of nursing home administration—doctors, nurses, administrators, and public health personnel.

The writers differ from the usual authoritarians. They are educators, expert in utilizing a specific technic for building a body of content or curriculum material where none existed before—the slip technic. A total of 26,000 ideas, each on a separate sheet of paper, was elicited in workshops first—a difficulty analysis, next a method analysis, and last "how-to" formulas.

The result is more than a discourse on nursing home administration. Interwoven are on-the-job training, group work, and class- and self-instruction suggestions and methods. Also do not expect the usual dry, serious, pedantic textbook. This one has charm, humor, and a simplicity that disguises profound wisdom. It is written in the language of its intended audience—nursing home operators. Those accustomed to the altruistic language of the usual medical, nursing, and health field literature may find their risibilities rising at such a revolutionary idea as "Let's try to fit our more humanitarian patterns of thinking into the standard commercial vocabulary," and the ensuing phrases such as "selling the customer." These same people, however, will be hard put to deny the practical wisdom contained within the terminology.

While the book is primarily meant to be a how-to-do-it manual and textbook for nursing home operators, personnel in regulatory agencies, doctors, and nurses working with nursing homes will also find it informative.—Mary Annice Miller, R.N.

The Cry for Help. Edited by Norman L. Farberow, Ph.D., and Edwin S. Shneidman, Ph.D. Octavo of 398 pages. New York, The Blakiston Division, McGraw-Hill Book Company, Inc., 1961. Cloth, $9.95.

The Cry for Help is a compendium of previously unpublished articles about suicide, written by practitioners of different professional disciplines and varying philosophic orientation. The editors, who have also contributed to the content, speak from concentrated experience in this field as codirectors of the Suicide Prevention Center in Los Angeles, investigators at the Centeral Research Unit, Veterans Administration Center, Los Angeles, and clinical associate professors of psychiatry (psychology) at the School of Medicine, University of Southern California.

The organization of the book heightens its effectiveness and helpfulness to an even wider group of potential readers than the "theoreticians and practitioners in the broad range of human psychology" for whom it is purportedly intended. In particular, the first section, "The Community Response to the Cry for Help," offers badly needed guidance for the many professional, semiprofessional, and lay consultants to whom distraught people commonly turn—physicians, lawyers, teachers, and school guidance counselors, for example. These people, whose daily work includes guidance functions incidental to a central responsibility other than that of "practitioners of. . .human psychology," often have to decide whether or not a person appealing for help is close enough to suicidal action to warrant emergency intercession to preserve life, and they may thus make possible treatment and recovery.

The direct help to be found in this book differs from much in the literature in that it is based on substantial and carefully evaluated experience with many persons who were close to suicidal action. The research findings at the Suicide Prevention Center are evaluated and described, including a study of available sociologic data about completed and attempted suicides in Los Angeles County in 1957, as well as analysis of the Center's own experience. Hypotheses based on this material are presented to point to factors which, in constellation, are likely, to indicate an immediate risk of suicide.

It might have been clarifying to add that although some constellations sound an alarm, their absence by no means guarantees that there is no cause for alarm, because of the well-known refusal of individuals in our society to conform consistently to statistical tables. Despite this omission, a counsellor confronted with a potentially suicidal confidant can make his decision about protective intercession with the immensely reassuring knowledge that he is following the best guides that study, research, and experience can afford.

The second section of the book, "The Psychotherapeutic Response to the Cry for Help," presents eight analyses of the same case by different therapists, each representing his own therapeutic school, that is, Freudian, Jungian, Adlerian, Sullivanian, and so forth, with its philosophy and its diagnostic and treatment approach. There is also a pithy summary of the eight papers and the theoretic constructs they present, by Faberow, one of the author-editors.

There is frequent mention of the vital importance of family support in the treatment of the potentially suicidal patient and reference as well to the social worker's role in evaluating a family's capacity to provide such support. It is puzzling, therefore, that this section lacks any reference to the work which is being done by social workers in many treatment settings to enable conflicted ambivalent families to muster their positive feelings for the patient so that they can provide the support he needs so badly.

The final section is a bibliography of the literature on suicide published in various languages from 1897 through 1957. This lists and classifies material for a student and research use, as well as for interested readers in general.

The Cry for Help is a book of value to all who carry responsibility, professional or otherwise, for response to people in trouble. It should be helpful in increasing their sensitivity to the desperate, often veiled appeal for understanding and rescue which the authors believe is often characteristic of a prodromal phase preceding suicide.—Ruth Michaels

Ciba Foundation Symposium on the Nature of Sleep. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M. B., and Maeve O'Connor, B.A. With 101 illustrations. Octavo of 416 pages. Boston, Little, Brown and Company, 1961. Cloth, $10.

The wonder is not so much that an animal falls asleep but that it awakens and observes the rhythmicity between sleep and waking with the regularity that it does.

There is an abundance of data on hypnotics, tranquilizers, and sedatives and a fair amount on the psychic and neurologic mechanisms by which these pharmacologic agents exert their effect. These are directed predominantly to sleep. Moreover, psychoanalytic schools place a great importance on the diagnostic and prognostic importance of dreams—which occur only during sleep. It is strange, therefore, that there are comparatively few studies on sleep which is the objective of hypnotic drugs and the framework within which dreams take place.

While this symposium on sleep does not

answer the numerous questions on sleep—for want of data—it explores the fundamental happenings relating to it. Also, it reports certain responses of the sleeping animal and gives an account of the methods used in studying sleep. Thus for example, while the book is not clinically oriented, it enters into the basic studies that eventually may find clinical extrapolation. Among neurophysical studies it presents electroencephalographic measurements, other electrical potentials, and data and discourses on the mechanism of arousal. There are chapters on hibernation wherein the relationship with sleep is probed, on sleep in pathologic states, and on change in brain metabolism during sleep.

A chapter on sleep deprivation related to muscle tension which, while it is rather oversimplified, is well modified by Kety's chapter on sleep and energy metabolism of the brain in which he reports that hypercapnia—not a fall of cerebral blood flow—occurs during sleep which is associated with an increase of carbon dioxide. It may be profitable to speculate on the increase of carbon dioxide pressure for the induction of sleep. In fact, carbon dioxide can depress the respiratory center to the point of coma.

This symposium will be found useful by clinicians and research workers in the psychoneurologic sciences as well as by psychologists.—Erwin Di Cyan, Ph.D.

A Textbook of Pathology. By William Boyd, M.D. Seventh edition, thoroughly revised. Quarto of 1,370 pages, illustrated. Philadelphia, Lea & Febiger, 1961. Cloth, $18.

The seventh edition of Dr. Boyd's well-known *Textbook of Pathology* has been extensively rewritten. The author has placed increased emphasis on physiopathology in relation to disease processes. Almost every chapter includes a discussion of the physiologic and biochemical aspects of the disease process that is being considered. This expansion of pathology beyond the confines of "morbid anatomy" has been long recognized, of course, and it is good to have it so presented in a textbook designed primarily for students of medicine.

The book is printed in a restful double-columned page format and is profusely illustrated. There are several colored plates. Each chapter includes an outline of the subject matter covered and a limited bibliography.

Although the textbook is intended primarily for the medical student, it is recommended as an excellent reference book for the graduate as well.—Philip G. Cabaud, M.D.

Abdominal Operations. By Rodney Maingot, F.R.C.S. Fourth edition. Quarto of 1,402 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $29.50.

This excellent book presents a detailed consideration of abdominal surgery. It deals with the choice of operative procedure, technic, and dangers that arise during and after the operation. Pre- and postoperative care are discussed in detail. Considerable attention is given to clinical and pathophysiologic aspects of intra-abdominal disease.

Great advances in abdominal surgery are being made. It was necessary, therefore, to revise the previous third edition. There is important new information on anesthesia, water balance, and transfusion.

This work should appeal to the abdominal and general surgeon. It gives reference to the surgeons who are interested in newer developments in the management of intra-abdominal surgical diseases.

A high standard of workmanship is manifest in the organization of the text. The authors represent a cross section of the great teachers of surgery from the United States and England.

This book is recommended to surgeons and residents in surgery.—Alan A. Kane, M.D.

Clinical Methods of Neuro-Ophthalmologic Examination. By Alfred Kestenbaum. Second edition. Quarto of 577 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $16.75.

This excellent book of neuro-ophthalmology was written by one of the great teachers of the subject. It was written with a thoroughness one can expect of the author. It will not replace the book on the same subject by Frank Walsh, M.D., but it contains many original ideas and valuable information.

It should be in every ophthalmologist's office. —Daniel Kravitz, M.D.

A Synopsis of Ophthalmology. By J. L. C. Martin-Doyle, D.O. Second edition. Duodecimo of 249 pages, illustrated. Bristol, John Wright and Sons Ltd., 1961. Cloth, $6.50.

This book, written by the senior surgeon of the Worcester Eye Hospital in England, is a detailed, comprehensive summary of the practical points in clinical ophthalmology. It will be useful to both the specialist and the general practitioner. Recent advances in ophthalmic medicine and surgery are included also. It should fulfil an important purpose for the busy practitioner. There is a good index so that it is possible to locate any subject easily.—Norris C. Elvin, M.D.

Medical-Surgical Nursing. By Kathleen Newton Shafer, R.N., Janet R. Sawyer, R.N., Audrey M. McCluskey, R.N., and Edna Lifgren Beck, R.N. Second edition. Octavo of 876 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $8.75.

This book written by expert practitioners of nursing can serve as a source book for the practitioner of nursing and as a textbook for the nursing student. If focuses primarily on the nursing needs of patients and the nursing care for patients having specific medical and surgical treatment.

The introduction to the first edition perhaps best describes the second edition:

> To give a broad general background in the nursing care of patients who require medical and surgical treatment. Details of physical care for some common conditions are included as a guide for the nurse in making adaptations for individual patients. To equip the nurse to give comprehensive care, the cause, prevention, medical care, principles of nursing care, and the significance of the disease to the patient, his family, the community and the nation are considered.

The format is two-columned with large readable type, making it seemingly easier to read and handle, for it is a large book. New material, procedures, and so forth, have been added, and the rearrangement of some sections makes it more meaningful.

The study questions placed at the beginning of each chapter should assist the practitioner of nursing to review basic preclinical subject matter not always repeated in the text; the questions might be too broad for student review.

The references are excellent and easily available in most nursing and/or medical libraries, and those more suitable for nursing students have been so designated.

The book makes no attempt to encompass all aspects of medical-surgical nursing in detail but rather encourages the professional nurse to do more intensive reading of the more detailed aspects of medical and surgical care.

Physicians might be interested in this text as it concentrates on the role of the nurse in providing comprehensive nursing care to their patients and may give an understanding of the role the professional nurse is attempting to play in the care of all patients.—Edith M. Augustson

Correction

The reader's attention is called to the following authors' correction in Fogel, R. L., Epstein, J. A., Stopak, J. H., and Kupperman, H. S.: Achilles tendon reflex test (photomotogram) as a measure of thyroid function, New York State J. Med. **62**: 1159 (Apr. 15) 1962. The height of the reflex curve in Figure 6B should be approximately half that of 6A as illustrated here, not the same height as was mistakenly shown earlier.

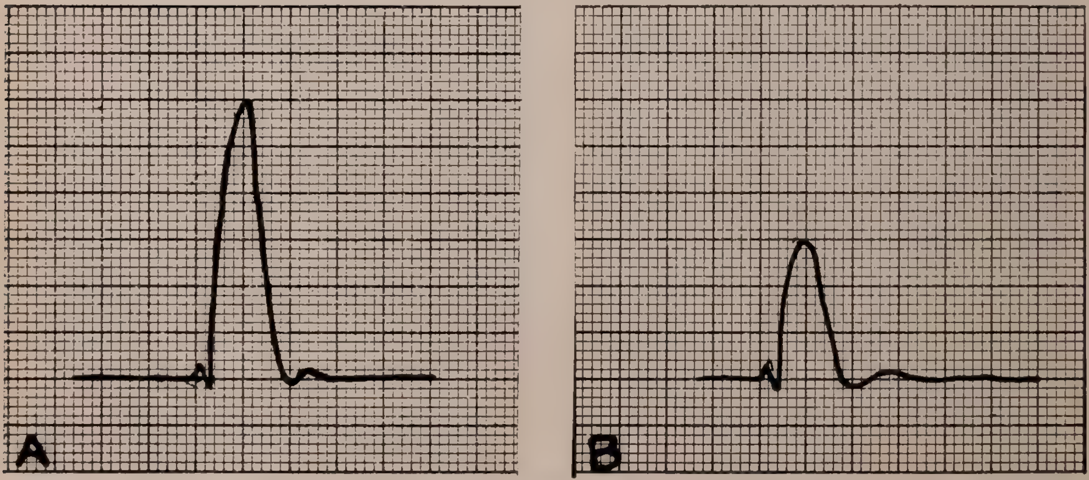

FIGURE 6. Achilles tendon responses of (A) right foot (0.28 second) and (B) left foot (0.28 second) in a euthyroid patient with a herniated nucleus pulposus. Note the differences in the height of the reflex curves, while the duration remains the same.

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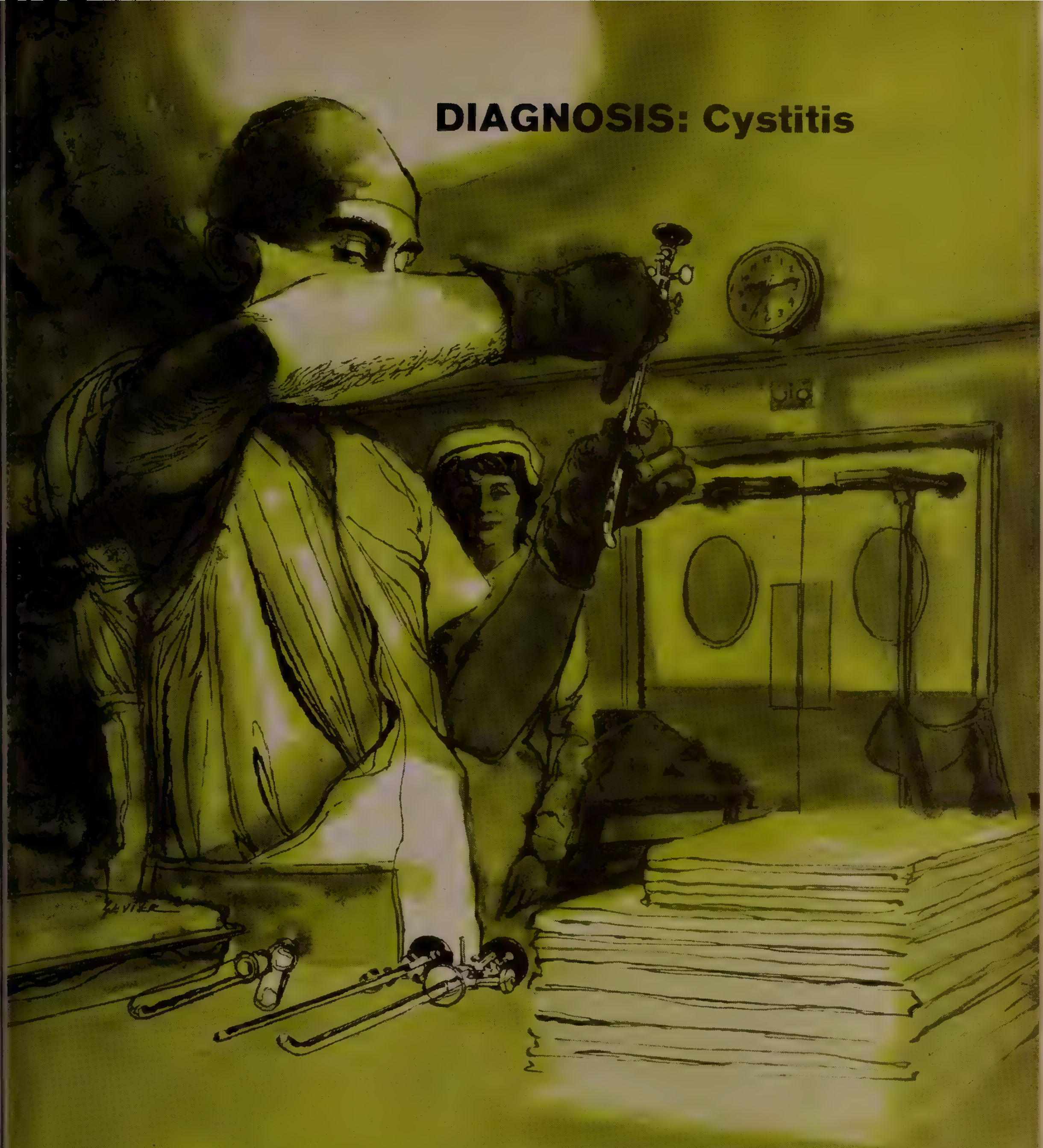

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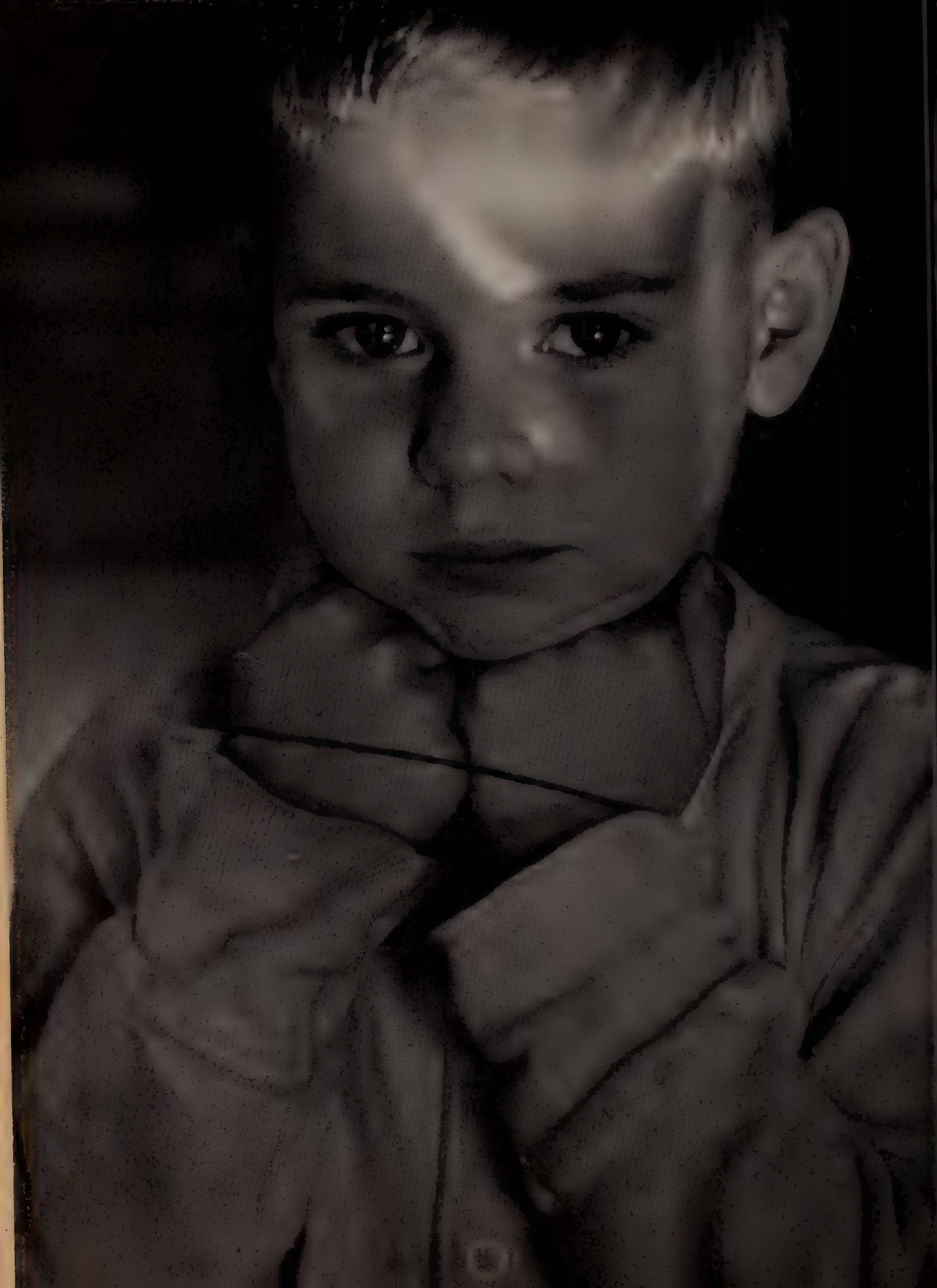

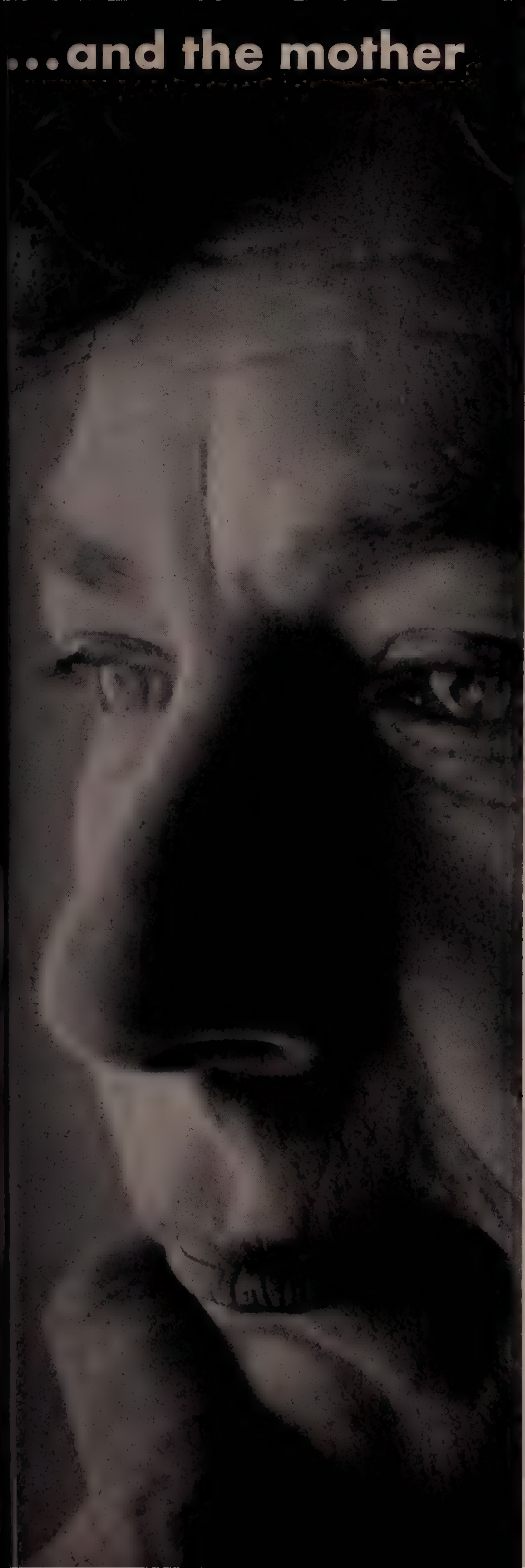

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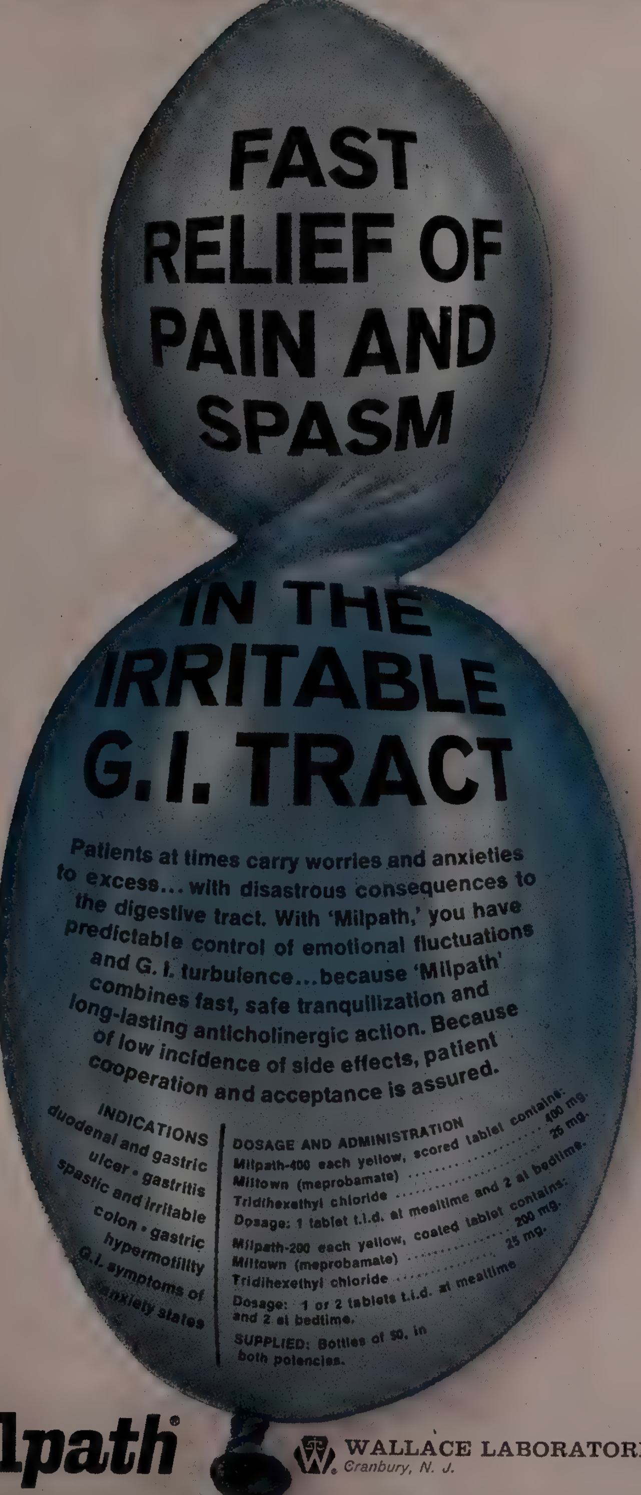
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1. Ford, R. V.: Clin. Res. Notes 2:1 (Dec.) 1959. 2. Ford, R. V.: Cur. Therap. Res. 2:92 (Mar.) 1960. 3. Elliott, J. P., Jr., and Goldman, A. M.: South. M.J. 54:794 (July) 1961.

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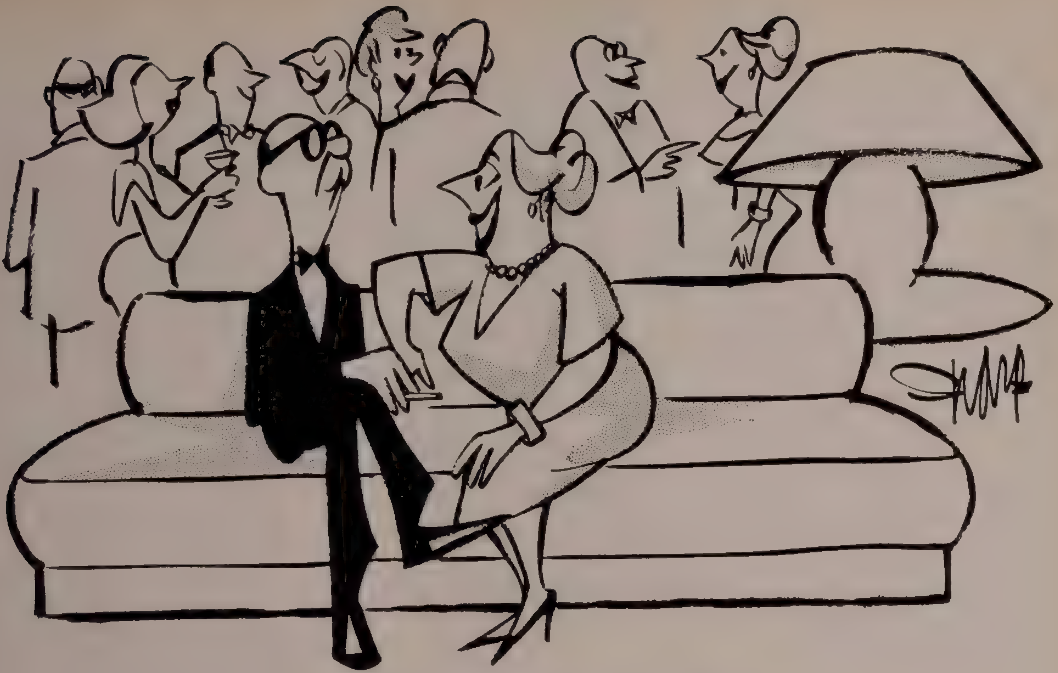

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1. Cohen, B. M.: M. Times 88:855 (July) 1960. 2. Cohen, B. M.: Méd. et Hyg. (Genève) #494, p. 210 (Mar. 15) 1961.

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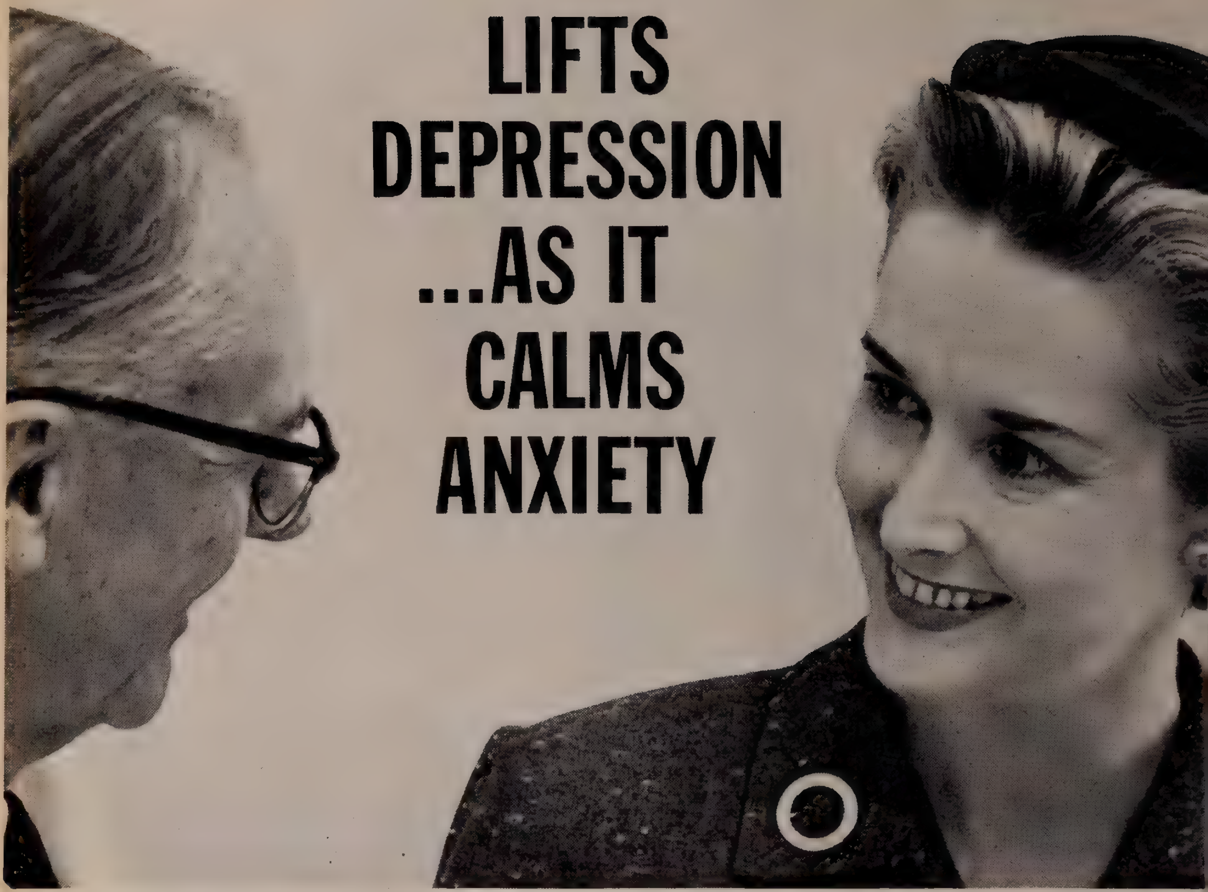

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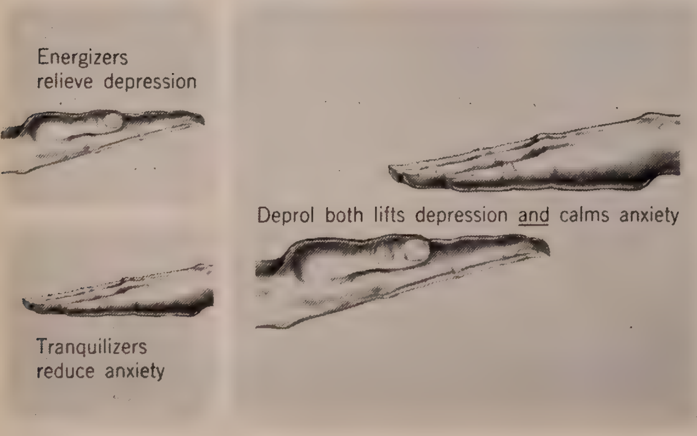
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References: (1) Minchew, B. H., & Cluff, L. E.: *J. Chron. Dis.* **13**:354, 1961. (2) Wallmark, G., & Finland, M.: *Am. J. M. Sc.* **242**:279, 1961. (3) Wallmark, G., & Finland, M.: *J.A.M.A.* **175**:886, 1961. (4) Welch, H., in Welch, H., & Finland, M.: Antibiotic Therapy for Staphylococcal Diseases, New York, Medical Encyclopedia, Inc., 1959, p. 14 (5) Hodgman, J. E.: *Pediat. Clin. North America* **8**:1027, 1961. (6) Bauer, A. W.; Perry, D. M., & Kirby, W. M. M.: *J.A.M.A.* **173**:475, 1960. (7) Petersdorf, R. G., *et al.*: *Arch. Int. Med.* **105**:398, 1960. (8) Goodier, T. E. W., & Parry, W. R.: *Lancet* **1**:356, 1959.

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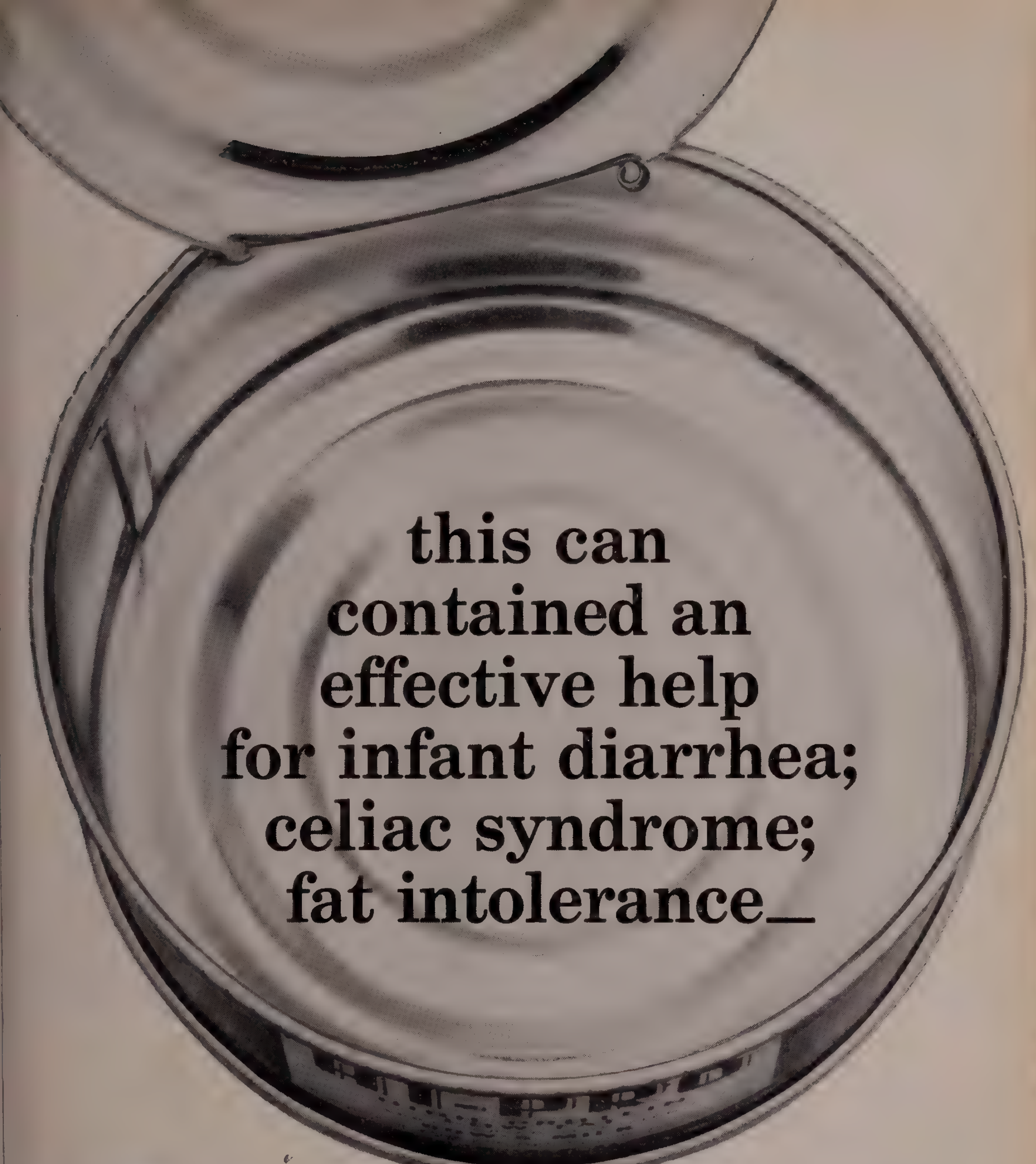
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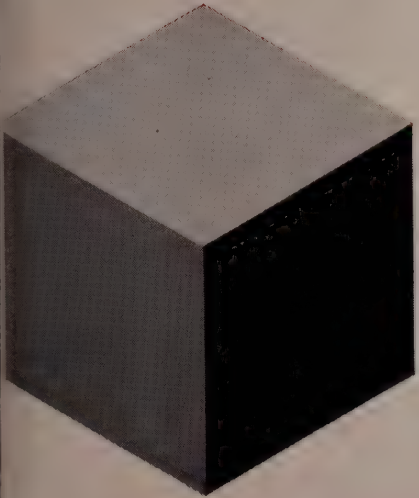

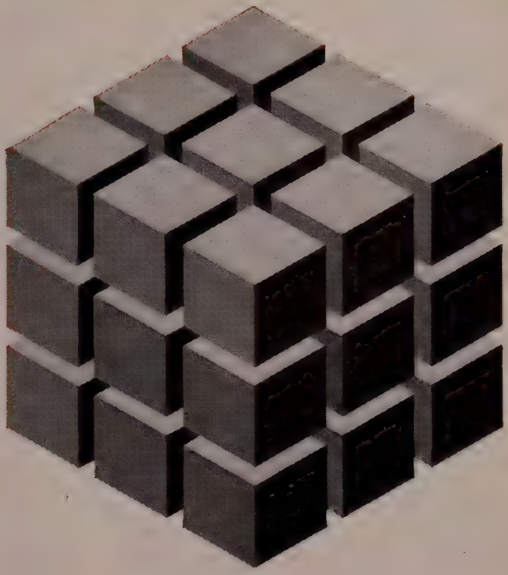

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* Feinblatt, T.M., and Ferguson, E.A., Jr., Phenobarbital idosyncrasy, avoidance by use of phenobarbital-niacin, *N. Y. State J. Med.* 62:221-3, Jan. 15, 1962.

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Here is a practical and down-to-earth method to help overcome obesity, the nation's No. 1 diet problem—and prime stealer of doctor's consultation time. Now a new group of 60 delicious Mott's Figure Control Food products uses the best of nutrition knowledge to create quality dishes, lower in calories by an average of 50%. Indicated calorie savings can be made pleasantly and accurately while eating normal-size portions by using these calorie-controlled foods in place of higher calorie dishes. Protein, vitamin and mineral food values are retained.

Low carbohydrate, low fat: Fats are largely extracted from meats and poultry in a way that cannot be done at home. Sauces and dressings are prepared with a high proportion of non-fat milk solids, vegetable colloids; all are delectably "natural" and tempting in flavor. Fruits, juices, desserts and sauces are prepared where indicated with non-caloric sweeteners—natural fruit values are intact, extra sugars reduced. The carbohydrate, protein and fat content appears on all labels along with the calorie count. Useful for diabetic diets, too.

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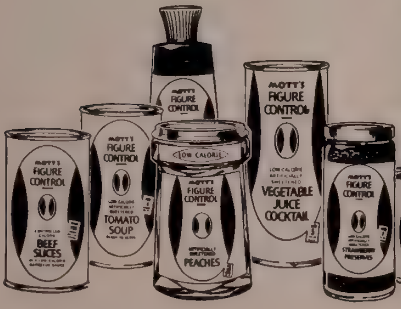
New Mott's Figure Control® Foods offer Good Eating at Half the Usual Calories

	Quantity	Figure Control Calories	"Regular" Food Calories
Apple-Grape Drink	½ cup	20	52
Five-Fruit Juice Breakfast Drink	½ cup	20	52
Braised Beef and Vegetables	6½ oz.	184	380
Meat Balls in Brown Gravy	3½ oz.	84	280
Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
Cherry Pie Filling	1 oz.	20	60
Chocolate Topping	1 tbsp.	8	63
Preserves (Peach, Strawberry)	1 tbsp.	9	55
"Maplette" Syrup	1 tbsp.	9	55
Liquid or Powder Sweetener	(to equal 1 tbsp. sugar)	0	16



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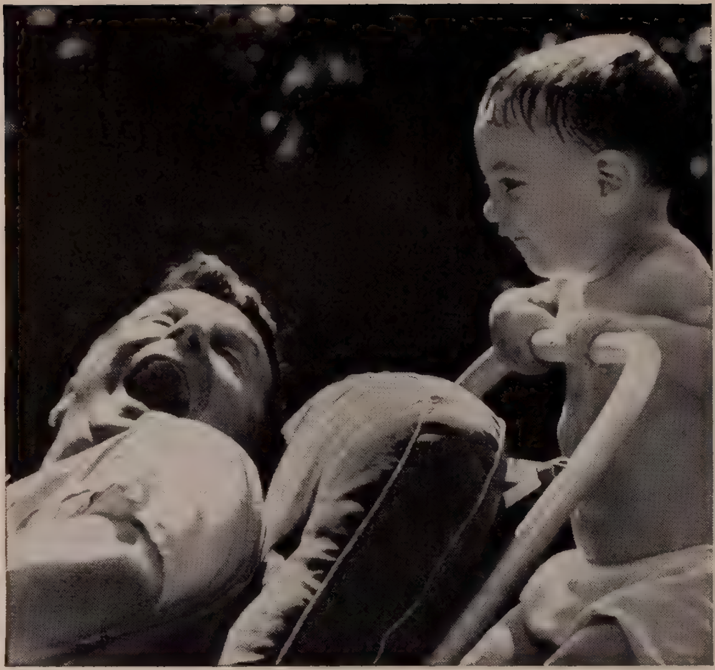

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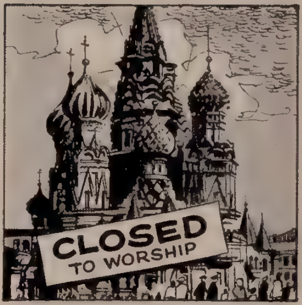

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FORMULA SUPPLIES 45 MG. OF IRON — AT NO EXTRA COST

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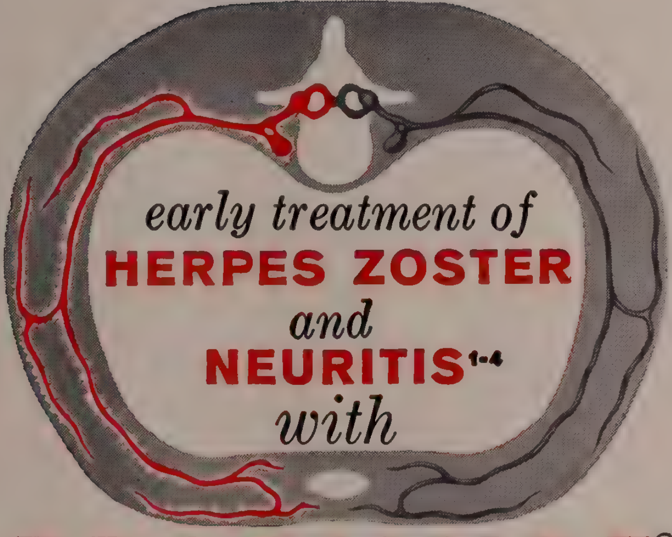

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HERPES ZOSTER
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Relief of inflammatory radicular pain, including herpes zoster, is prompt when Protamide is administered early[1-4] in the course of the disease. More important, recovery usually follows in three to six days, with prompt response even in ophthalmic herpes zoster.[5]

Published studies suggest that Protamide acts as a direct suppressant of neuritis due to acute inflammation of the nerve root. In such disorders, the response to early treatment with Protamide is sufficient to be diagnostic in inflammatory neuritis.[3,4]

Protamide—an exclusive denatured colloidal enzyme preparation, virtually safe and painless—not foreign protein therapy. One ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early.

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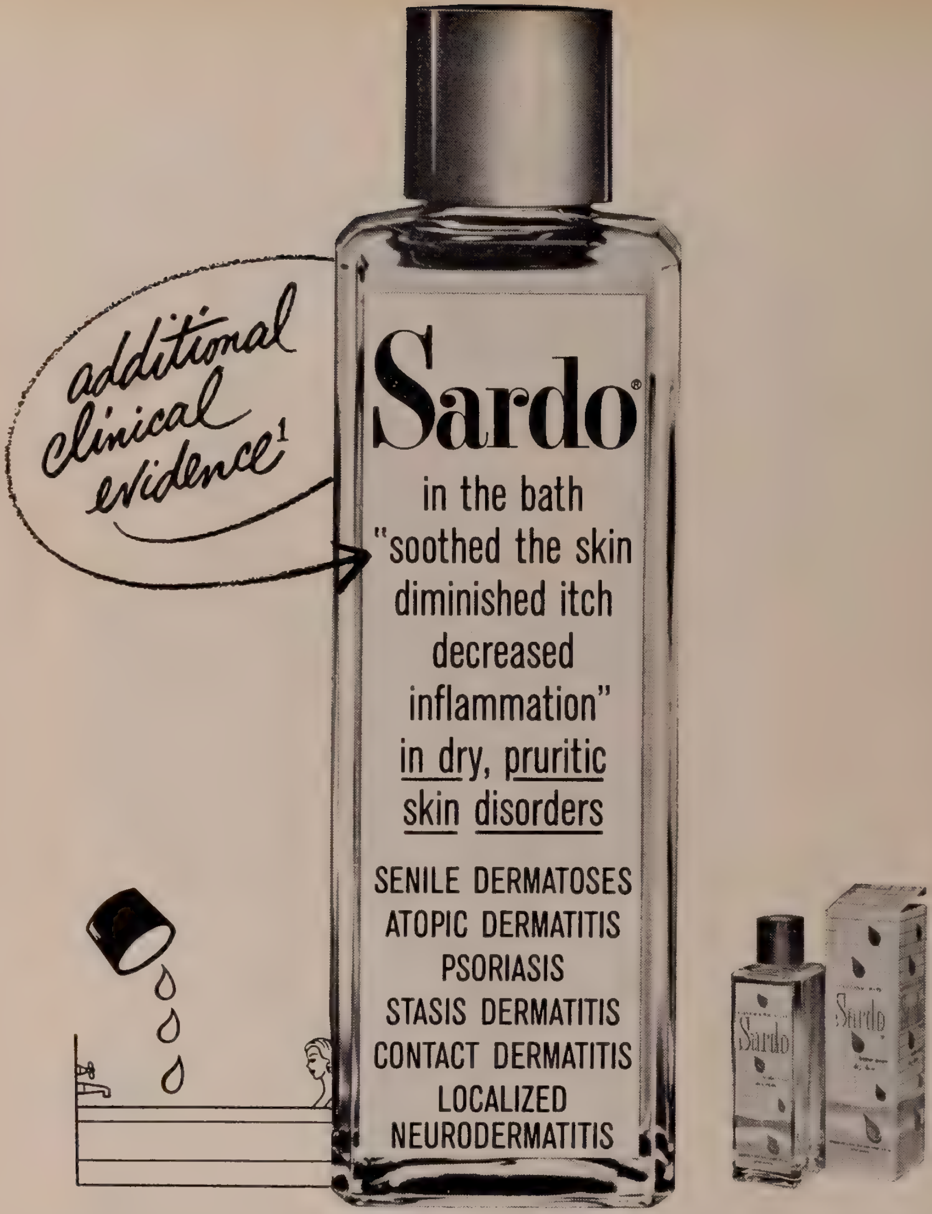

additional clinical evidence[1]
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"soothed the skin
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Pleasant, easy-to-use SARDO releases millions of microfine water-dispersible globules* in the bath. Bottles of 4, 8 and 16 oz.

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1. Borota, A., and Grinell, R. N.: J. Amer. Geriatrics Soc., 10:413, 1962.
2. Spoor, H. J.: N. Y. State J. M. 58:3292, 1958.
3. Lubowe, I. I.: Western Med. 1:45, 1960.
4. Weissberg, G.: Clin. Med. 7:1161, 1960.

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when abortion threatens, habitually…

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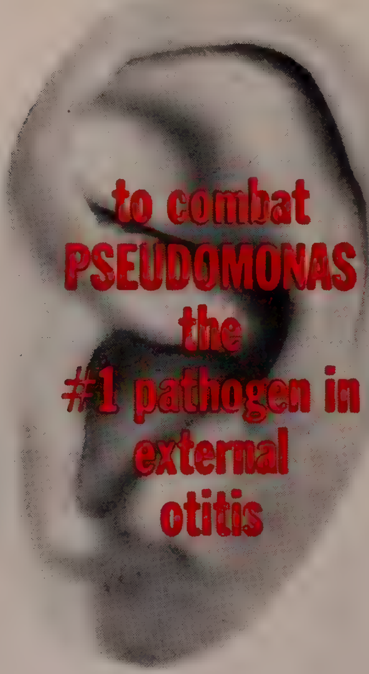
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PSEUDOMONAS
the
#1 pathogen in
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'CORTISPORIN'® brand

OTIC DROPS (sterile)

the #1 therapy for inflamed, infected ears

Because it provides Polymyxin B for the eradication of Pseudomonas, the prime cause of external otitis, 'Cortisporin' is the logical choice of treatment for inflamed, infected ears. Polymyxin B is the antibiotic specific for *Pseudomonas aeruginosa* infections, and is, for this pathogen, the standard of effectiveness against which other antibacterials are measured.

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5 cc
CORTISPORIN
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BURROUGHS WELLCOME

Each cc. contains:

'Aerosporin'® brand Polymyxin B sulfate	10,000 units
Neomycin Sulfate (Equivalent to 3.5 mg. Neomycin Base)	5 mg.
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Bottles of 5 cc. with sterile dropper.

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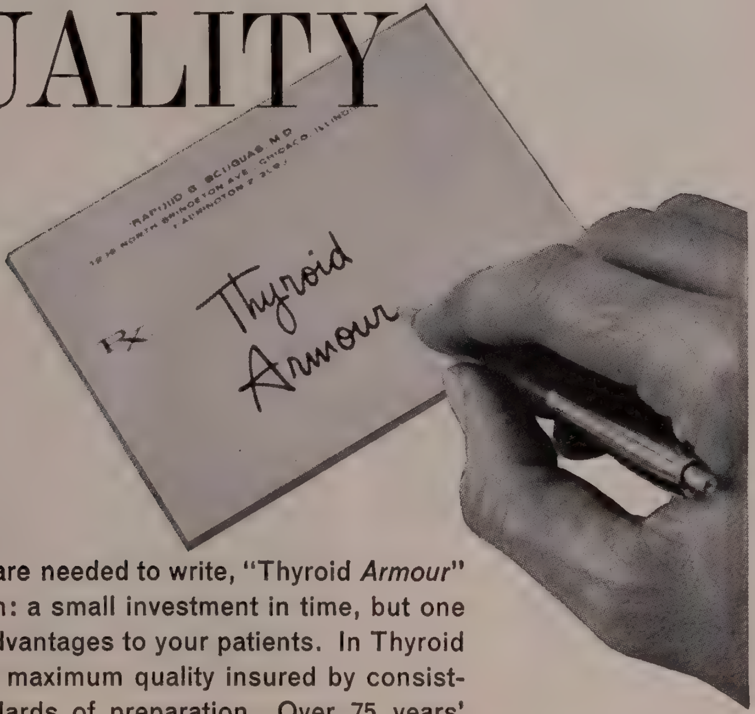

Only 2 seconds are needed to write, "Thyroid *Armour*" on a prescription: a small investment in time, but one that offers big advantages to your patients. In Thyroid *Armour* you get maximum quality insured by consistently high standards of preparation. Over 75 years' experience is behind the Armour brand.

THYROID U. S. P.

Thyroid Tablets (Armour) are prepared from fresh selected glands, desiccated and standardized by official U.S.P. method to contain 0.2 per cent of iodine in thyroid combination. Thyroid Powder U.S.P. (Armour) is standardized and of uniform potency. USES: Thyroid deficiencies, cretinism, myxedema, nodular goiter (nontoxic), non-nodular goiter. A variety of clinical conditions will respond to the use of Thyroid (Armour) when subclinical hypothyroidism is involved. DOSAGE: ¼ to 5 grains daily as required by clinical condition. Therapeutic effect develops slowly and lasts for two months or longer. Thus the daily dose may be given as a single dose (preferably in the morning) rather than several times daily. Patients treated with thyroid should be continuously under the physician's observation. CONTRAINDICATIONS: Heart disease and hypertension, unless the metabolic rate is low. SUPPLIED: Tablets—bottles of 100, 1000 and larger; potencies of ¼, ½, 1, 2 and 5 grains. Powder—1 oz., 4 oz. and 1 lb. bottles.

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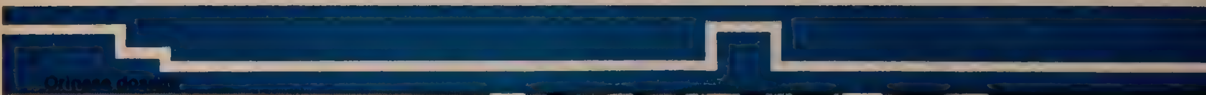
Orinase Case History



When Mrs. F. G., an actress, was first seen in October, 1956, her diabetes was poorly controlled on diet —symptoms classic, glycosuria 4 plus, fasting blood sugar 170. Control was achieved in 2-3 months on Orinase, 3 and then 1.5 Gm. daily. By January, 1957, fasting blood sugar was 100. Since then, dosage of 1 Gm. a day has routinely maintained control.

THE NIGHT OF THE IGUANA
TENNESSEE WILLIAMS
The Affair
RONALD MILLAR
C. P. SNOW
THE PREMISE
NO STRINGS

On occasion, Mrs. G's Orinase requirement may rise temporarily under certain stresses of the theater. For example, the patient has needed a two-month increase to 3 Gm. daily because of anxiety over a career decision (two roles were offered at the same time).

Indecision once resolved, the control-maintaining Orinase dosage reverts to 1 Gm. daily. This suffices to carry the patient smoothly and comfortably through a fairly energetic program of activity. Besides acting, Mrs. G. directs and produces plays; she looks after the domestic chores of her household and attends classes in the dramatic arts.

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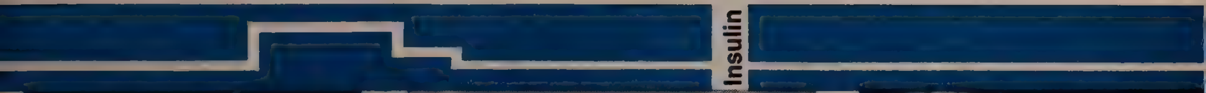
*TRADEMARK, REG. U.S. PAT. OFF. — TOLBUTAMIDE, UPJOHN

5 years of control



During an extended trip in 1959, the patient reacted adversely to a severe sunburn. On returning home, Mrs. G. (shown as her husband helps her from their car), required increased Orinase (3 and then 2 Gm. daily) for several months.

When the patient underwent surgery that same year, she was given insulin, 30 units, 2 days preoperatively and 8 days postoperatively. After this 10-day interval, she resumed her usual level of 1 Gm. Orinase daily, and has since then been consistently well managed on that dosage.

Mrs. G. has now been Orinase-treated for 5½ years, living a busy life, with her diabetes controlled and without untoward developments.

Orinase* (tolbutamide) stands in a unique position; it alone, among oral antidiabetes agents, has had five years or more of day-to-day routine clinical use in the hands of thousands of physicians throughout the country. Accordingly, there are by now a considerable number of truly long-term Orinase-treated patients. A series of Orinase five-year case histories has been prepared to illustrate and exemplify some aspects of actual experience in management. Patient data, made available to us by the respective physicians, have been factually incorporated; however, patients' identities have been concealed. Any inquiries regarding this Orinase case history series should be addressed to: Medical Department, The Upjohn Company, Kalamazoo, Michigan.

Orinase is supplied in bottles of 50 and 200 tablets.
Each tablet contains: Tolbutamide ... 0.5 Gm.

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The Upjohn Company, Kalamazoo, Michigan **Upjohn**

a look at the literature
CORDRAN™
(flurandrenolone, Lilly)

> “Treatment results were good, and in many cases a dramatic response was noted. Many of the cases had previously failed to respond to various types of therapy including, in some instances, other topical corticosteroid preparations.”

—Gray, H. R., Wolf, R. L., and Doneff, R. H.: Evaluation of Flurandrenolone, a New Topical Corticosteroid, Arch. Dermat., *84:*18, 1961.

A look at the products—Cordran cream and ointment are new corticosteroid preparations especially formulated for the skin. Each Gm. contains 0.5 mg. Cordran.

Cordran™-N cream and ointment combine Cordran and the wide-spectrum antibiotic, neomycin. Each Gm. contains 0.5 mg. Cordran and 5 mg. neomycin sulfate (equivalent to 3.5 mg. base). Cordran-N is particularly useful in steroid-responsive dermatoses complicated by potential or actual skin infections.

All forms are supplied in 7.5 and 15-Gm. tubes.

Cordran™-N (flurandrenolone with neomycin sulfate, Lilly)

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New York State Journal of Medicine

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Editorials

The Redway Medal

LAURANCE D. REDWAY AWARD FOR MEDICAL WRITING

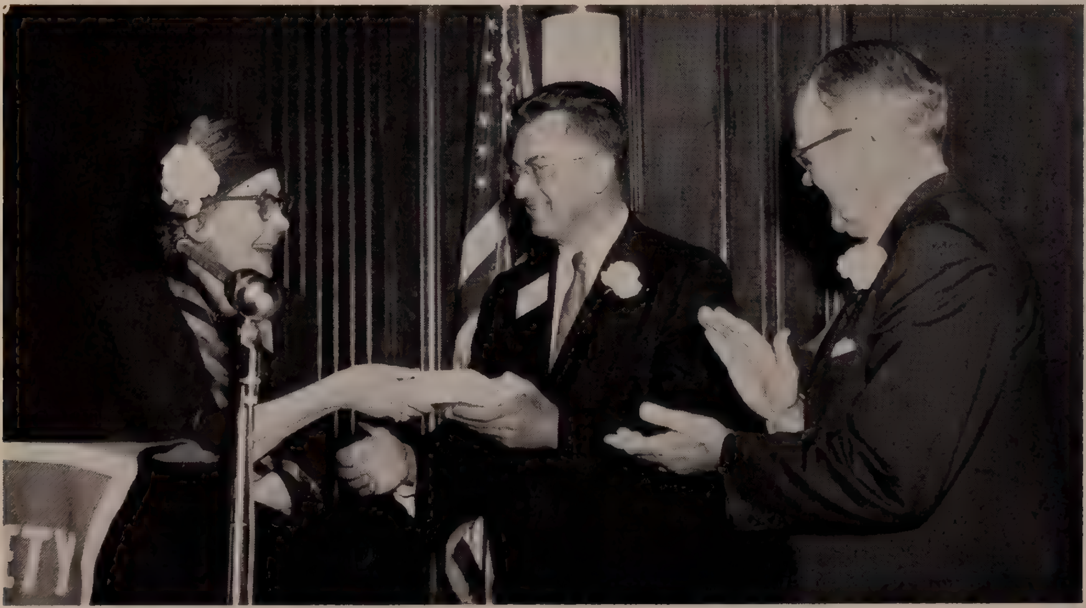
REDWAY MEDAL

The first annual award of the Redway Medal which took place at the Annual Meeting of the House of Delegates on May 14, 1962, established a new tradition. It is altogether fitting that both the man memorialized and the recipient so honored be described.

Four years before his death Laurance D. Redway, M.D., Editor of the JOURNAL, wrote as a year-end greeting: "The JOURNAL is a collective enterprise now in its fifty-sixth year of continuous publication. It is the product of men's minds and hearts, of their toil and ingenuity throughout those years. To what end? That knowledge and scientific truth shall flow continuously from its source to our readers. In its small way the JOURNAL seeks to aid the great advance of learning, to present the picture in vignettes, of the procession of medical history of the State, to further the peaceful arts of healing to the comfort of mankind.

"Surely there is here in our privilege to write and publish freely much to be thankful for, much to gladden the heart and uplift the spirit. To have a part, however small, in the great purpose of the Creator is a joyful thing. So to you all wherever you may be, seasons greetings."

No added word is needed to portray Dr. Redway's high aims for the JOURNAL nor the beauty of his character.



John M. Galbraith, M.D., State Society President, applauds presentation of the Redway Medal to Jerome A. Urban, M.D., by Mrs. Laurance D. Redway.

The award, decided on by an impartial jury of three, from among recommendations made by the readers and the Associate Editorial Board, went to Jerome A. Urban, M.D., for his three-part article on "Current Treatment of Breast Cancer," which appeared in the JOURNAL, September 15 through October 15, 1961.

Both the development of the subject matter and the clarity and lucidity of the writing met the judges' high standards for excellence.

Dr. Urban is a graduate of Columbia University College of Physicians and Surgeons in the class of 1938, Diplomate of the American Board of Surgery, Fellow of the American College of Surgeons, Associate Attending Surgeon at Memorial Hospital, and Clinical Assistant Professor of Surgery at Cornell University Medical School.

Within the plethora of reading material presented to doctors today only medical writing of the highest quality can survive. It is the hope of the JOURNAL and of the Society for which it stands that the award of the Redway Medal this year and in the years to come will further this end.

Allergic reactions to insect sting

The peak season for allergic reaction to insect sting is from May to October, with August the month of highest incidence. According to a report from the Registry for Insect Sting Reactors of the American Academy of Allergy, bees, yellow jackets, and wasps, in that order, were responsible for the allergy reaction. Of 517 individuals reported with systemic reactions, 26 per cent had a personal history of atopy, and 26 per cent had a family history of atopy. It is interesting to note, however, that 78 persons in the Registry, who had no personal or family history of atopy, had severe generalized reactions. Over 10 per cent of the entire group showed intolerance to penicillin, and 20 per cent showed intolerance to one or more drugs.

Advance warning before the occurrence of systemic reaction to insect sting often is not present. There is little relationship between the local reactions and the severity of general reactions. If anything, there is a slight tendency for persons with severe general reactions to have relatively smaller local reactions at the site of the sting than those reporting milder sting reactions. In 75 per cent of the group, no unusual local reactions prior to the general reactions were reported. Of 174 persons having a severe generalized reaction, in many cases with some period of unconsciousness, 130 reported no unusual reactions from previous stings. The rate of progression of the sensitive state to insect sting is unpredictable. Severe general reaction may occur without fatal outcome, even after eight episodes in which the patient became unconscious. Of 625 incidents on file, 195 persons reported two or more generalized reactions, one reported 20 to 25 severe reactions, and one reported 50 mild reactions. Of 258 persons reporting repeated stings, 160 became progressively worse, 73 reported their reactions unchanged in intensity, and 25 believed that their reactions were decreasing in intensity. Insect identification, depth, and site of injection were uncontrolled factors in the report.

Treatment by hyposensitization appears of benefit. Of 94 persons with generalized reactions who were treated and subsequently stung, 76 reported lessened reactions. However, occasional persons continued to have severe reactions after what would appear to be an adequate course of treatment. Persons highly allergic to insect venom should protect themselves by having readily available an emergency kit which should contain a tourniquet, several ampules of epinephrine 1 : 1,000, and an injectable antihistamine, and they should be instructed in how to use these immediately at the time of the sting. Hospitalization and continued emergency treatment is often necessary and should be within reach at all times of anyone in this condition.

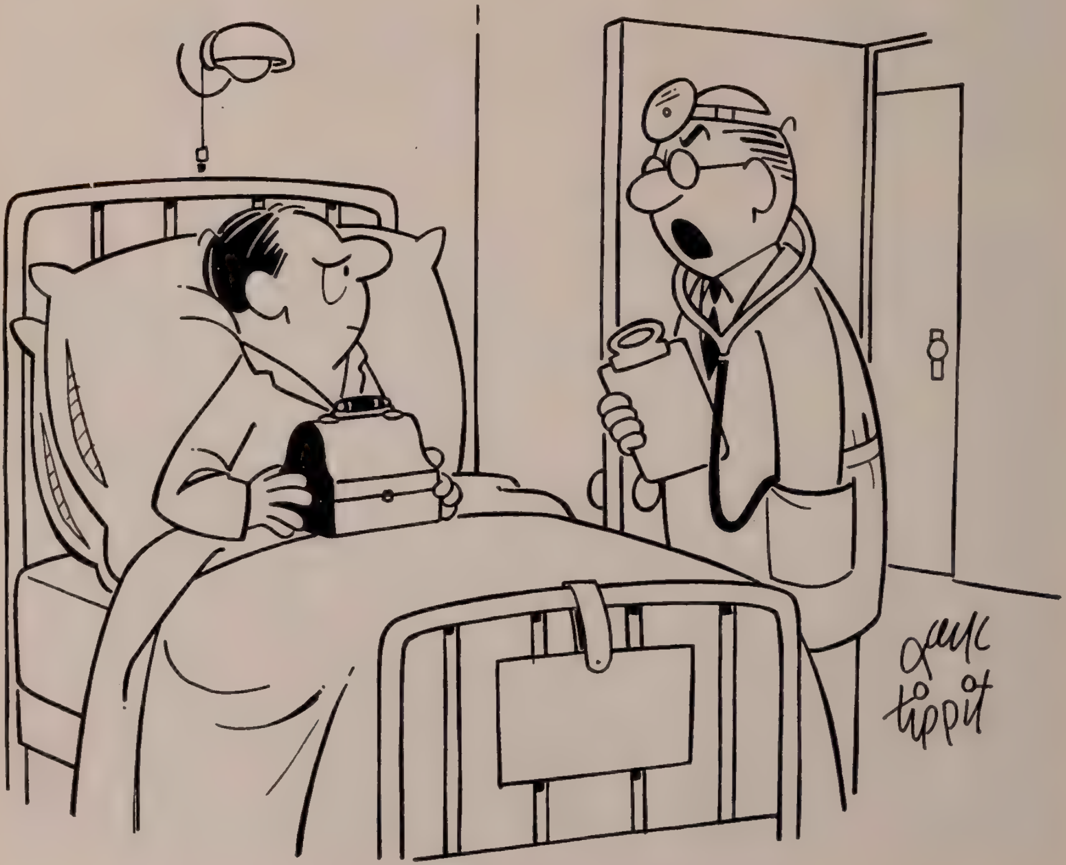
Patterns of study

The results of a recent sampling by questionnaire of 4,668 physicians as to postgraduate study patterns, published by Parke, Davis & Company in *Patterns of Disease*, re-emphasize the important position of the scientific journals. The reading of books and journals held a commanding lead over the next most effective method, attendance at postgraduate courses.

This state of affairs imposes a heavy responsibility on the editors and editorial boards of the 542 scientific periodicals indexed by the *Index Medicus*. These periodicals publish material which is considered worthy to be added to the record, and we are happy to state that this JOURNAL is numbered among them.

An almost clairvoyant perceptivity in selection is required. The editors and their boards are fallible, but they persist in trying to bring to their readers those things which are new and stand a good chance of being sustained, fresh approaches that breathe new life into established concepts, and critical reviews that are constructive and bring matters up to the minute. They try to write editorials that will evoke thinking; they try to publish case reports and teaching conferences that carry a lesson.

The learned professions were founded on study and reflection. It is a sad commentary on our present society that he who reads must run. The art of writing and the habit of reading fight a stiff battle against the electronic age, but it need not be a losing one. Time can be apportioned in a busy schedule for enrichment other than that of the market place.



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1. Guttmacher, A. F. (Chairman and Moderator): Clinical Experience with and Practical Techniques for the Use of Enovid in Ovulation Control, Transcript of a Closed Circuit Television Symposium, Chicago, G. D. Searle & Co., Jan. 18, 1961, pp. 26-28. 2. For references and review of laboratory and clinical studies, Physicians' Product Brochure No. 67 is available on request.

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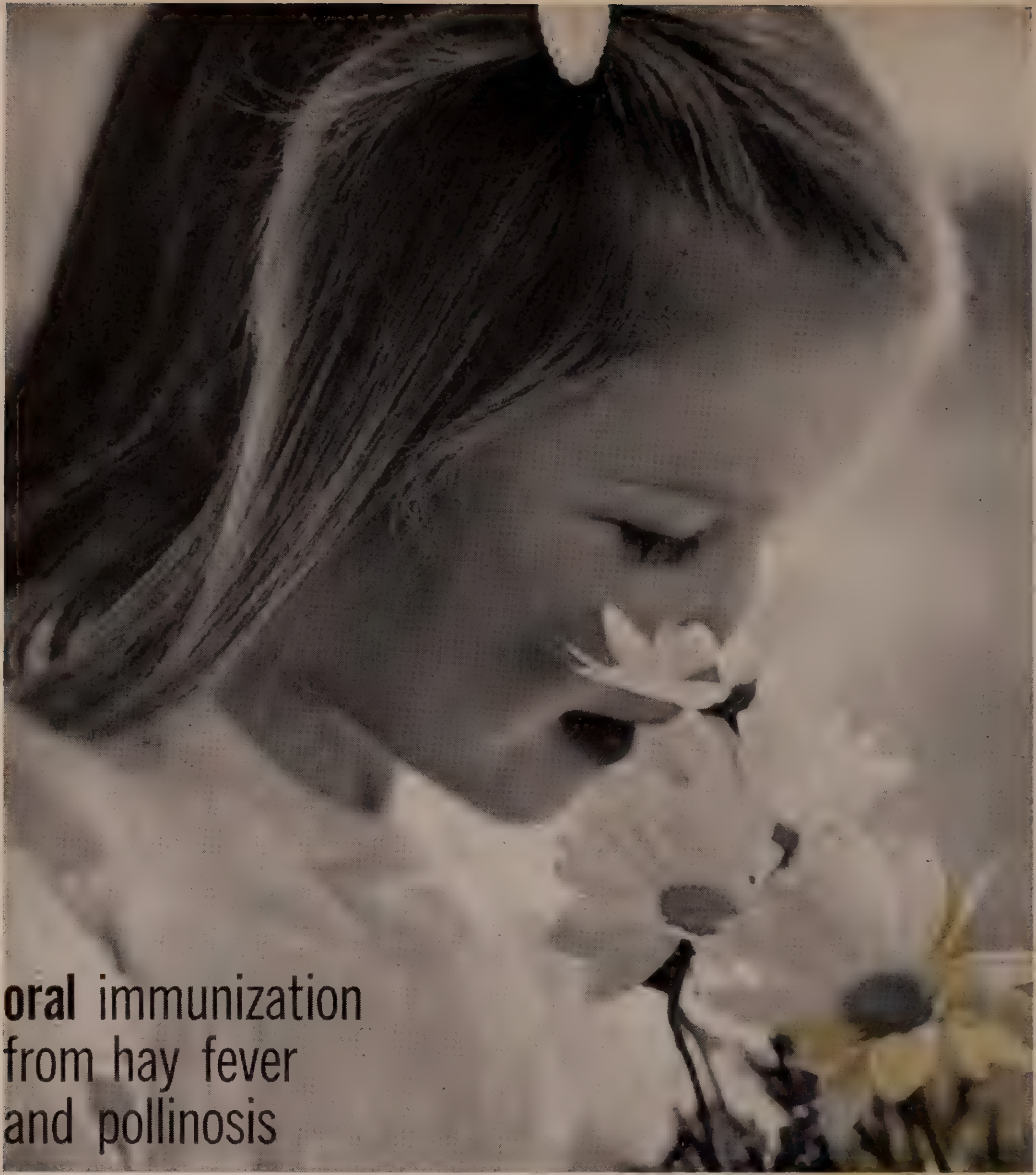

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Cardiac Rupture in Myocardial Infarction

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THE INCIDENCE *of cardiac rupture following myocardial infarction as reported in three different series varies from 4.7 to 73 per cent. The underlying factors are: recent coronary artery closure occurring with an acute infarction; dissecting hematoma; hypertension of long duration; age and sex—rupture appears to be more frequent in women than in men and rarely occurs in young patients; physical effort and emotional strain; and anticoagulant therapy. Rupture is most frequent at the site of a massive myocardial infarction and most frequently involves the left ventricle and anterior wall. Aspiration of the accumulated blood may be lifesaving in some cases. Rupture probably is caused by bulging of the infarcted area during systole and contraction of the adjacent healthy muscle against the devitalized area which produces tears in the arteriosinusoidal as well as in the arterioluminal vessels that initiate the dissection of blood through the myocardium, especially if a transmural infarct or intramural thrombus is present.*

CARDIAC RUPTURE with hemopericardium has long been recognized as a sudden and rapidly fatal complication of myocardial infarction. Clinicians have studied the condition since it was described originally by Harvey in 1647.[1] The incidence is especially high after acute myocardial infarction,[1–4] and the frequency of cardiac rupture has risen[1] as the incidence of myocardial infarction has increased, but the incidence statistically of cardiac rupture is still a matter of conjecture because, in the absence of specific diagnostic tests, the differential diagnosis of the condition remains a challenge to the clinical acuity of the physician. This is evidenced by the fact that it is very difficult to diagnose perforation antemortem, and there is a relative paucity of postmortem examinations where a diagnosis of myocardial infarction has been made clinically.

Despite an extensive literature, the exact cause of cardiac rupture is still not clear. The term myocardial rupture usually denotes an acquired defect through the complete muscular wall of one or more cardiac chambers. It includes perforations of the interventricular or interauricular septum but does not refer to incomplete myocardial tear or rupture of the coronary arteries, veins, cardiac valves, papillary muscles, chordae tendineae, or aorta. Krumbhaar and Crowell[5] emphasized that the condition usually occurs in an acute infarct of the anterior wall of the left ventricle. Instances of rupture in myocardial infarction have been observed in patients who died suddenly without any history of acute infarction. In the absence of extracardiac causes rupture is regarded as spontaneous.[6] Rupture of the heart also may occur, rarely, as a result of gumma, bacterial endocarditis, tuberculosis of the myocardium, ecchinococcus cyst, or malignant growth; also, as a result of trauma to the chest wall.

Some authors[7-10] have reported diagnosing this catastrophic condition antemortem.

The incidence of rupture following myocardial infarction varies from 4.7 to 73 per cent. The incidence is higher among females.[4,11-15]

Large series of cases were published describing this condition.[1,16-20] Recently, other authors published cases in compilations of series.[2,3,6,21-24]

Acute fatal myocardial infarction is complicated by cardiac rupture in 8 to 9 per cent of cases,[4,19,25] and rupture occurs even more frequently in acute massive myocardial infarctions. The rupture may occur as early as one day and as late as four weeks after the onset of the infarction.[13] Most commonly it occurs at the end of the first week.[26] If rupture occurs three or four weeks after the infarction, it is likely that a complication is present, such as another acute infarct.

Site and size of rupture

The site of the rupture in all cases was within the area of the infarction. It occurred in the anterior wall of the left ventricle in 61 per cent, in the posterolateral wall of the left ventricle in 22 per cent, in the posterior wall of the left ventricle in 1 per cent, in the anterior wall of the right ventricle in 1 per cent, and in the interventricular septum in 2 per cent. Usually rupture of the left ventricle was near the apex; in other cases it was close to the interventricular septum, which in that event also was involved. Rarely, it occurs in the interventricular septum alone,[27-31] and, more rarely, rupture may be confined to the papillary muscle.[32]

Rupture of the anterior wall is about three times as frequent as rupture of the posterior wall. The size of the perforation varies from a pinpoint opening barely permitting a small probe[6] to a coin-size opening or a linear, ragged tear up to 4 cm. in length. The endocardial tear may be difficult to detect,[33] whereas the epicardial tears, either one or more, were found easily and varied in length from 3 to 40 mm. Left and right ventricular rupture occurred at approximately the same ratio as the occurrence of left and right ventricular infarction. Rupture of the interventricular septum, of the atrial walls, and of the papillary muscles represents less than 10 per cent of the total number of ruptures,[14] and over 90 per cent are through the ventricular wall. Krumbhaar and Crowell[5] listed the order of frequency of rupture as the left ventricle, the right ventricle, the right auricle, the left auricle, the septum, and the papillary muscle. They observed unusual patterns of perforations. One patient had two ragged openings through the anterior surface of the left ventricle, and a second patient had a perforation through the left ventricle, splitting the base of one of the papillary muscles of the mitral valve. Jetter and White[15] found both the left ventricular wall and the interventricular septum ruptured in 1 patient. Edmondson and Hoxie[1] described a patient with numerous small perforations. Large perforations invariably are associated with large amounts of blood in the pericardial cavity but, regardless of the size of the perforation, the pericardial sac in most instances will contain several hundred cubic centimeters of blood.

Pathogenesis

The myocardial alterations leading to rupture depend on the degree of coronary sclerosis, thrombosis, and the degree of infarction. A single precipitating cause of the perforation is usually not demonstrable. The production of the initial tear may result either from increased or sustained intraventricular pressure or from force on the contracting heart muscle directed to the infarcted area. The tensile pull of the contracting muscles on the area of softened muscle may produce the initial tear and, subsequently, each systole conceivably could widen the aperture because of unusual stress due to the divergent action of the muscle bands.[33] The heart usually ruptures through an acutely diseased myocardium, or occasionally by extension through a healthy part of the myocardium, but only very rarely through a fibrosed area.[1,6,21] Old scar tissue in the region of a fresh infarction may lessen the chance of perforation because of the presence in the scarred areas of increased collateral circulation, greater resistance of the fibrous tissue to ischemia, and the support that the fibrous tissue gives to the necrotic area.[1]

It is possible that more than one mechanism may be involved in the origin of cardiac rupture.[34] During systole the healthy muscle pulls on the involved wall which, because of its difference of elasticity from normal muscle, may produce a paradoxic pulsation in the infarcted area, resulting in stretching of the infarcted area which then tends to become thinner. At the junction of the healthy and infarcted muscle the infarcted fibers are twisted and bent and may fracture during the paradoxic movement; in addition, a high concentration of leukocytes, proteolytic enzymes, and debris is found which weakens the collateral structure of the muscle wall. In the absence of normal cell metabolism and in the absence of factors acting to repair any plastic deformation, stresses concentrated at this junction of normal and infarcted muscle tend to produce a rupture at this point. The extent of the rupture appears to depend on the tension in the wall at the time of the rupture, and once it is started it is completed by the pull of the contracting muscle and dissection from the spurting blood. The majority of cardiac ruptures occur by dissection, and frequently a subepicardial hematoma is found. The commonest site of a rupture is the lower third of the anterior wall of the left ventricle.[13] Anderson[35] considered a heavy leukocyte infiltration in the area of infarction an important factor in the etiology of rupture.

It has been noted that only a few cases of external rupture of the heart have been diagnosed antemortem because specific signs are few and evanescent.[7,9,10,27] A rupture of the infarcted interventricular septum, however, gives specific findings. An antemortem diagnosis of this condition has been reported in medical literature in nearly 140 cases.[1,6,8,36–38] The characteristic murmur and thrill associated with shunt and progressive right-sided heart failure will establish the diagnosis.[36] Septal rupture may be confused easily with a rupture of a papillary muscle.[39] Septal rupture usually arises after massive necrosis of the infarcted septum. It is believed that the presence of hypertension, which may be obscured by an associated drop in blood pressure, contributes to the production of septal rupture.[35]

The gross appearance of the myocardium in the affected area of the rupture depends largely on the duration of the infarct.[40] The muscle is usually mottled, yellowish-grey, frequently infiltrated with extravasated blood, and partly necrotic. In some cases the heart muscle in the involved area is reduced to a thin membrane; sometimes an intramural thrombus is found. Considerable hypertrophy of the heart resulting from long-standing hypertension is usually present. Coronary sclerosis is evident in all instances, associated with partial or complete occlusion of the affected arteries.

Disagreement exists as to the relative value and the added hazard of anticoagulant therapy in acute myocardial infarction. While it is fairly well established that the judicious administration of anticoagulants increases the survival rate in myocardial infarction, it must not be forgotten that anticoagulants increase the risk of hemorrhage and the frequency of cardiac rupture and hemopericardium.[19,41] The beneficial effects of anticoagulant therapy in decreasing the thromboembolic complications which frequently follow myocardial infarction have been described in numerous papers.[22,42–45]

Anticoagulants may increase the frequency and severity of hemorrhage, particularly intracardiac hemorrhage, and may increase the risk of myocardial rupture and hemopericardium with cardiac tamponade.[22]

A total of 796 cases with autopsies were reported in three American series of cases.[19,22,46] Of this group, 557 were not receiving anticoagulant therapy, and 239 were treated with anticoagulants. In the untreated group, rupture occurred in 3.9 per cent; in the treated group, rupture occurred in 12.1 per cent. Thus, rupture was found more than three times as often in the group that received anticoagulants. It is interesting to note that this ratio was fairly constant in each individual series.

In a series of 1,303 cases of fatal cardiac infarction, of which 94 per cent were examined postmortem, there were 89 instances of hemopericardium, 3 had a rupture of the aorta, and 5 had no demonstrable cause of death.[41] These 5 cases occurred among 33 patients receiving anticoagulant therapy. A dissecting hematoma in the ventricle could be an important factor in the pathogenesis of cardiac rupture.[47] The greater tendency to intramural hemorrhage could account for the greater incidence of myocardial rupture reported in cases of myocardial infarction treated with anticoagulants.[19]

The diagnosis of myocardial infarction is subject to a varying amount of error electrocardiographically.[22,46,48-54] It is conceivable that errors in diagnosis by the electrocardiogram may occur in cases of trauma to the chest wall leading to cardiac rupture. The resiliency of the chest may permit traumatic compression of the heart between the sternum and vertebral column, resulting in endocardial or epicardial tears and hemopericardium.[55] Sometimes myocardial infarction and rupture of the heart may ensue. No relationship between the degree of chest trauma and the development of cardiac pathologic conditions could be shown in the reported cases; however, with pre-existing heart disease the possibility of extensive damage or even cardiac rupture as a result of chest trauma is greater.

Cause of death

Death from myocardial infarction results from congestive failure, shock, or abrupt cardiac cessation due to fatal ectopic rhythm, cardiac standstill, thrombo-embolism, or rupture of cardiac muscle with tamponade.[56] Once rupture has occurred, death is inevitable and except in a very few instances usually occurs within a very few minutes. There may be three types of death: (1) sudden death, similar to that of cardiac standstill or ventricular fibrillation[5,23,33]; (2) death within a few minutes or hours due to tamponade with a failure of diastolic filling and the production of fatal cerebral anoxia[5,23,33] (death may be postponed, rarely, by an organizing epicardial clot which seals the opening, or when the perforation is very small; or (3) death may then occur from congestive failure. Prolonged survival more often accompanies atrial rupture or rupture of the interventricular septum.[37] In 90 per cent of 400 instances of cardiac rupture, the time of survival was twelve hours or less after the onset of the rupture.[5] In the case of ventricular septal rupture, survival is often longer, varying from several hours to days. Myocardial rupture as a cause of death in patients with acute myocardial infarction has been reported as varying from 3.3 per cent in one series[57] to 6.3 per cent in another series of cases.[58]

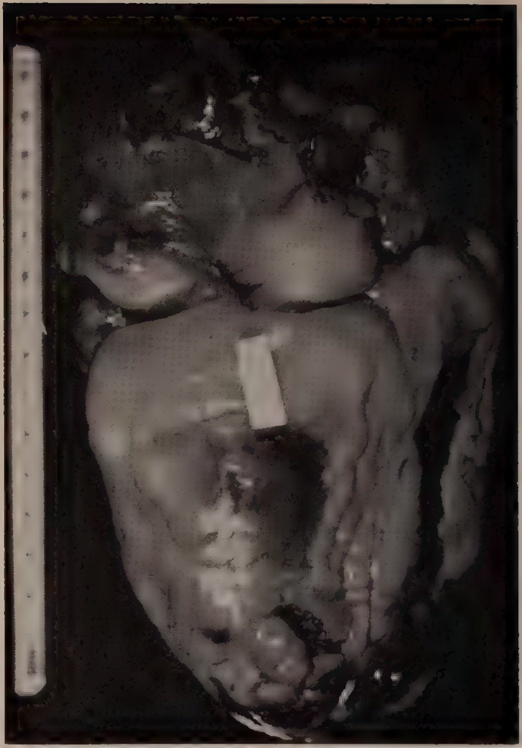

FIGURE 1. Case 1. Gross specimen of heart. Irregular rent on anterior surface of left ventricle. Surrounding this area at apex is hemorrhagic extravasation into pericardium. Above tear is hemorrhagic area on pericardium which represents site of massive infarction.

Case reports

CASE 1. A sixty-six-year-old white female was admitted to the hospital on January 14, 1959. Her chief complaint was severe chest pain radiating to both arms. Vomiting started on the night previous to her admission. Her past history included diabetes mellitus for eleven years. She had had carcinoma of the right breast, which was removed by radical mastectomy in 1954. A cataract of the left eye was removed in 1958. On physical examination the patient was unconscious with cold, clammy extremities. Crepitant rales were heard bilaterally. The liver was not enlarged. The pulse was 100. The temperature was 100 F. No blood pressure was detected. An electrocardiogram showed an elevated S-T segment in leads II, III, aVf, and V_4; inverted T waves in leads I, II, III, aVl, aVf, V_4, and V_6; Q waves in leads II, III, and aVf; and small Q waves in V_4 and V_6. The diagnosis was acute postero-

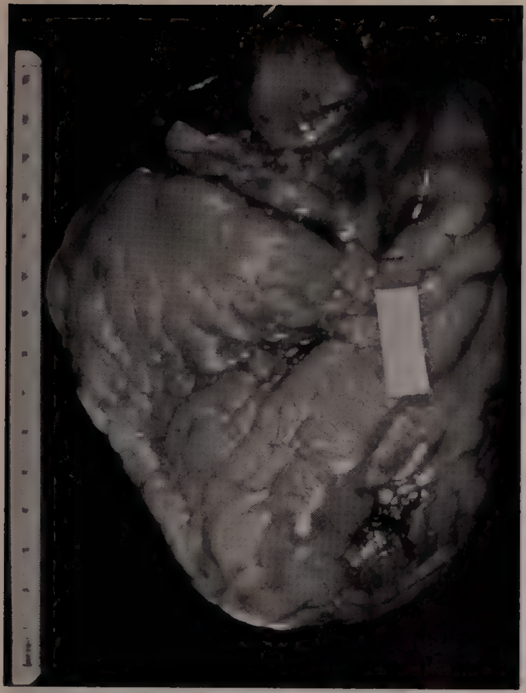

FIGURE 2. Case 2. Gross specimen of heart showing irregular rent in epicardium through which blood poured into pericardial cavity.

lateral myocardial infarction. The urine showed glucose 4 plus, acetone 4 plus, and albumin 4 plus. Oxygen and heroic measures failed, and the patient expired after ninety minutes.

At autopsy the pericardium contained 400 cc. of blood. The heart weighed 400 Gm. and was of average size and shape. An area around the apex measuring 6 by 4 cm. revealed an hemorrhagic infiltration into the visceral pericardium. On the posterior aspect of the left ventricle, 0.5 cm. above the base of the infiltrated area, there was noted a laceration of the myocardium measuring 2 by 0.4 cm. (Fig. 1). This laceration extended deeply into the myocardium and could be followed easily in its oblique direction. The heart was of regular consistency except in the region of the apex where it appeared softer than normal. The tricuspid valve measured 10.5 cm. in circumference. The pulmonic and aortic valves measured 7.5 cm. The mitral valve was 10 cm. The cusps appeared unremarkable. The left ventricular wall was 2 cm. thick and, in its apical region, blood which was partially clotted infiltrated the myocardium.

On removal of this blood, a laceration of the endocardium and of the myocardium was noted. This corresponded to the laceration seen on the posterior external surface. On section the myocardium revealed an area of discoloration surrounded by a hemorrhagic infiltration. This was soft in consistency, measured 4 by 3 cm., and was located in the apical region of the posterior wall. The coronary ostia were closed nearly completely. A serial section of the coronary vessels revealed them to be markedly sclerosed but patent. The thoracic portion of the aorta showed several atheromatous plaques. On microscopic examination the pericardium revealed an extravasation of blood with necrosis. The coronary vessels were very markedly atherosclerotic with extremely small lumina. The myocardium showed myolysis with acute inflammatory cell infiltration. Old areas of myofibrosis cordis also were noted.

Case 2. A seventy-six-year-old female was admitted to the hospital on January 14, 1959, with severe pain in the pericardium, a choking sensation, and shortness of breath. She had a history of previous hypertension. Her symptoms began four days prior to her admission. She vomited once. On admission the patient was in acute distress. She was orthopneic and restless with cold, clammy perspiration. The pulse rate was 120. The temperature was 101 F. Crepitant rales were heard bilaterally in the lungs. The heart sounds were barely audible. The blood pressure was 80/40 mm. Hg. The abdomen showed negative findings. She was given 2 cc. of levarterenol bitartrate (Levophed) in 1,000 cc. of 5 per cent dextrose, and the blood pressure rose to 120/90 mm. Hg but then dropped, and she died three hours later. An electrocardiogram had showed Q_1 and V_1 through V_3. There was an elevated ST in I, aVl, V_1, V_2, and V_3, and this was diagnosed as an acute anteroseptal infarction.

At autopsy the pericardium appeared normal externally, but on opening was found full of unclotted and clotted blood. On the anterior wall of the left ventricle, approximately midway between the apex and the base, 1.5 cm. to the left of the interventricular septum, there was a "V"-shaped rupture, each limb of which measured 0.5 cm. This rupture opened the left ventricular cavity to the pericardial cavity (Fig. 2). The heart weighed 400 Gm. It showed normal chambers, valves, cusps, and chordae tendineae. Almost the whole anterior myocardial wall, including the interventricular septum, showed hemorrhagic points with necrotic, soft, pale areas indicating massive infarction (Fig. 3). About 2.5 cm. from its origin the anterior descending branch of the left coronary artery showed complete closure. The remaining branches of the coronary system were sclerotic but not occluded. The great vessels were essentially normal. A microscopic examination of the heart revealed a massive area of acute myocardial infarction. Toward the periphery of the infarction the myocardium, endocardium, and epicardium were necrosed, denoting the area of rupture. Areas of normal myocardium and areas of myofibrosis also were present. The vessels showed sclerotic changes with diminished lumina. Also seen was an area of antemortem thrombus on the endocardium.

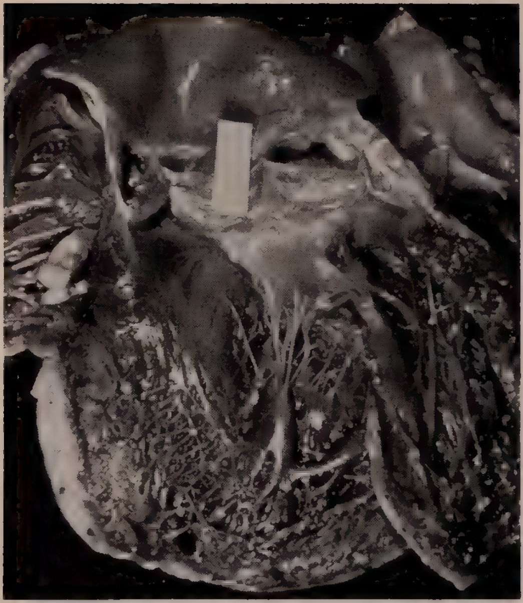

FIGURE 3. Case 2. Left ventricle opened to show at left a pale grey area of recent infarction. In this area there is hemorrhagic extravasation into myocardium, toward the heart. Below this area pericardium is considerably thinned and shows same changes of pallor as seen above. In addition, there is small oval opening in this area which is site of complete rupture and is continuous with irregular rent seen in Figure 2. Also noted is adherent recent thrombus at apex which is seen on cut surface on right.

Case 3. A seventy-year-old female was unconscious and cyanotic when she was admitted to the hospital on March 8, 1959. On the day previous to admission she complained of joint pains. The next day she was found unconscious. The blood pressure was unobtainable. The pulse rate was 120, the temperature 100.6, and the respiratory rate 28. The heart sounds were indistinct. The lungs presented crepitant and bubbling rales. An electrocardiogram showed S-T elevations in leads II, III, aVf, V_4, V_5, and V_6, and indicated recent posterolateral myocardial infarction. Treatment consisted of morphine sulfate, oxygen, and levarterenol bitartrate. However, these measures were of no avail, and she expired three hours later. Autopsy findings included a hemopericardium, ruptured myocardium, and acute posterior myocardial infarction (Fig. 4). There was a thrombosis of the left common coronary artery. The aorta had lost its elasticity, and the intima contained a few atheromatous plaques. The lungs showed pulmonary edema. Chronic passive congestion and fatty infiltration of the liver were present. The urinary bladder showed evidence of chronic cystitis. On microscopic examination sections of the heart showed acute infarction with the area of rupture surrounded by hemorrhage, degeneration of the heart muscle fibers, and infiltration by acute inflammatory cells.

Comment

The underlying factors in cardiac rupture in myocardial infarction are:

1. A recent coronary artery closure occurs with an acute infarction. Rupture occurs in areas of fresh infarction usually on the seventh or eighth day, although it may occur within ten to thirty-five hours after the onset of the infarction. Two of our cases apparently ruptured within thirty hours from the onset of the acute infarction. In a series of 165 cases of old infarction none showed rupture at autopsy.[25] Rupture rarely occurs in areas of organized infarction.

2. The infarction leading to rupture is usually transmural, and a dissecting hematoma may be an important factor in the causation of rupture in many cases.

3. Hypertension of long duration is an underlying cause in most cases. Rupture occurs with much greater frequency if the blood pressure remains higher than normal after the onset of infarction. Segall[59] reported rupture in 4 patients with normal or low blood pressure while they were at bed rest and not under strain or effort.

4. Age and sex may have some relationship to rupture. It very rarely occurs in young patients. Our cases were females in the sixth and seventh decades of life. Rupture appears to be more frequent in women than in men. At this time there is no adequate explanation for the greater tendency to rupture in women or for the rarity of rupture in the younger-age group.

5. Physical effort and emotional strain increase the incidence of cardiac rupture. This is demonstrated by Jetter and White's[15] very high incidence in a mental institution where the control of activity was impossible. A compromise between the dangers of too little activity (thromboembolism) and too much activity (failure, rupture, and so forth) should be followed.

6. Rupture is most frequent at the site of a massive myocardial infarction. It most frequently involves the left ventricle, usually close to the apical region where the musculature is thinnest. The anterior wall is

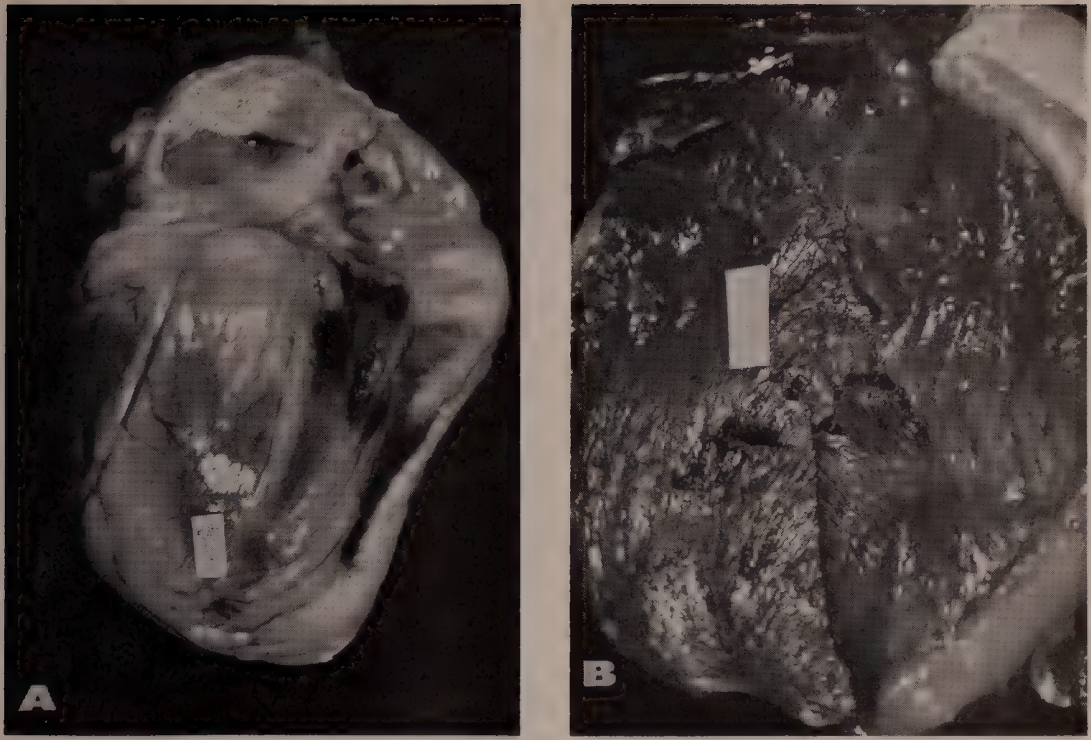

FIGURE 4. Case 3. Gross specimen (A) Closed showing linear rent in epicardium surrounded by hemorrhagic extravasation into surrounding fat. (B) Open showing myocardium of left ventricle opened in middle from apex to base. Note rent in myocardium surrounded by hemorrhage. This is noted in both halves of sectioned myocardium. Adjacent areas of pallor reveal extent of infarction.

the site of rupture only twice as often as the posterior wall. Occasionally, the interventricular septum or the papillary muscle may be involved.

7. Hemopericardium or rupture of the heart in myocardial infarction appears to occur about three times as often in patients treated with anticoagulants as in those patients who are not treated with anticoagulants.

8. If the autopsy rate in myocardial infarction were greater, the incidence of myocardial rupture in infarction also would be greater.

Treatment

In patients with myocardial infarction and associated rupture the escape of blood into the pericardial cavity may be so slow that an impending cardiac tamponade may be diagnosed clinically, and in that event aspiration of the accumulated blood may be lifesaving.[60]

Rupture of the interventricular septum following myocardial infarction has been repaired surgically.[61,62] Ravitch[63] recently reported on the effectiveness and immediate safety of the aspiration treatment in cardiac tamponade after myocardial rupture due to penetrating wounds of the heart in patients who reach the hospital emergency room alive. Those with massive wounds of the heart usually succumb to external hemorrhage or to insupportable tamponade. The patients reaching the hospital alive with tamponade usually are those who have relatively small wounds of the ventricles or atria so that fatal compression of the heart does not occur for some time. Such wounds are sufficiently small and, if the patients can be tided over the tamponade, the myocardial wounds will heal without surgical intervention. Of 31 patients treated solely by aspiration, none died. Survivals of patients with recognized cardiac tamponade reaching the hospital alive with penetrating wounds of the myocardium were 39 out of

40. Usually, however, all cases of spontaneous rupture die suddenly and there is little besides rest and care that can influence the occurrence of a rupture of a cardiac muscle. Hypertension seems to increase the hazard, but it decidedly is not amenable to treatment during the acute myocardial infarction.

Since most cases of cardiac rupture can be ascribed to atherosclerosis, preventive measures would involve the treatment of that condition.

Summary

A review of the literature as well as a report of 3 validated cases of rupture of the heart in myocardial infarction are presented. Rupture occurs with greater frequency in women than in men, usually in patients over fifty years of age where the normal histologic pattern of the myocardium is altered because of the effect of the acute infarction and its concomitant leukocyte infiltration, with local enzymatic destruction of myocardial fibers. Rupture almost never occurs in the younger-age group. The lesion probably is caused by bulging of the infarcted area during systole and contraction of the adjacent healthy muscle against the devitalized area. This produces tears in the arteriosinusoidal as well as in the arterioluminal vessels that initiate the dissection of blood through the myocardium, especially if a transmural infarct or intramural thrombus is present.

Rupture usually develops between the second and eleventh day, most commonly the eighth day, of an acute myocardial infarction in a hypertensive patient with no previous history of infarction or congestive heart failure. The hypertension in these patients usually persists during the period of infarction, and there may be a history of unusual or sudden physical effort or emotional stress within twenty-four hours of the rupture. Fever, leukocytosis, and the cardiac drugs generally used during the acute infarction, except anticoagulants, bear no relation to the occurrence of myocardial rupture. It was found that rupture occurred more than three times as often in patients who received anticoagulant therapy than in patients not receiving anticoagulants.

Rupture is rare in areas of organized infarction, but it does occur in areas of fresh myocardial infarction. The usual location of occlusion is in the anterior descending branch of the left coronary artery. The rupture generally is in the anterolateral region of the left ventricle near the apex. Cases of ventricular aneurysm generally do not rupture; these patients die of congestive heart failure.

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Sex Differences in Acute Myocardial Infarction

IN A STUDY *of 77 patients with fatal acute myocardial infarction on whom autopsies were performed from 1955 to 1960, 67.5 per cent were men and 32.4 per cent women. Only 8.4 per cent of the women were under the age of sixty in comparison with 28.8 per cent of the men. Over 20.7 per cent of the patients had diabetes mellitus: 15.3 per cent of the males and 24 per cent of the females. Hypertension was noted in 25 per cent of the males and in 60 per cent of the females. The study failed to reveal any significant shift away from the greater incidence of acute myocardial infarction in the male sex, and it would support the commonly accepted contention that estrogenic factors provide relative immunity to coronary heart disease.*

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PHYSICIANS GENERALLY agree that acute myocardial infarction is encountered with greater frequency among men than among women. Several studies made prior to 1940 support the contention that there is a decreased incidence of coronary atherosclerosis among women. Levy and Boas in 1936[1] reported a male-female ratio of 4.9 to 1. Master, Dack, and Jaffe in 1939[2] reported an incidence of 3.4 to 1.

More recent epidemiologic studies report a shift in the relative incidence of this disease in the sexes. Lee and Thomas[3] report that prior to 1940 the incidence of acute myocardial infarction at the Barnes Hospital in St. Louis, Missouri, was twice as high among men as among women, and during the period from 1940 to 1954 the incidence was as high among women as among men. Brown[4] recently reported 2 cases of myocardial infarction associated with pregnancy. Dock[5] reported a similar trend: "The sex incidence of coronary disease however, has markedly changed in the past fifty years, the incidence in Caucasian women has risen from 3 per cent to nearly 20 per cent, and in Negroes in Atlanta, Georgia, deaths from coronary disease occur in women earlier in life than in men."

Subjects

The purpose of this study is to present our experience relative to the sex incidence and allied aspects of acute myocardial infarction as observed on the medical service of a general county hospital during the years from 1955 to 1960. Our report is based on 77 cases of patients with fatal acute myocardial infarction who were hospitalized and on whom autopsies were performed at the Meadowbrook Hospital during this period. Cases were selected for this study solely on the basis of autopsy findings of acute myocardial infarction. Studies which deal with autopsy material are unavoidably selective. The assumption naturally is made that these are cases which present the most extensive pathologic conditions and are most apt to show poor results with therapeutic effort. There is, however, one major advantage in dealing with autopsy material: The diagnosis is no longer in doubt. The importance of error in diagnosis is emphasized by Capeci and Levy[6] in a recent article where they state, "Among the fifty

TABLE I. Age and sex incidence of acute myocardial infarction

Age (Years)	Females	Per Cent	Males	Per Cent
40 to 49	1	4	5	9.6
50 to 59	2	8	10	19.2
60 to 69	8	32	15	28.8
70 and over	14	56	22	42.3
TOTALS	25		52	

untreated patients, recent myocardial infarction was not recognized ante mortem in ten instances, an error of 20 per cent."

Results

Our study revealed a decreased incidence of acute myocardial infarction in females. Of the 77 patients, 52 cases, or 67.5 per cent were men, and 25 cases, or 32.4 per cent of the total were women (Table I). These findings confirm those of Master, Dack, and Jaffe[2] who noted in their studies of myocardial infarction that 77.4 per cent of their patients were men, and 22.6 per cent were women.

With reference to age, it is important to note that in our series only 8.4 per cent of the women who experienced fatal myocardial infarction were under the age of sixty years, whereas 28.8 per cent of the men had their fatal episode before sixty years of age. Robinson, Higano, and Cohen[7] in a recent article noted the rarity of this disease in women under forty years of age. In their study they noted the increased incidence of coronary heart disease in women who were castrated prior to the menopause which suggests that estrogens exercise a protective influence.

Both diabetes mellitus and hypertension are said to predispose the patient to the development of myocardial infarction. In our series over 20.7 per cent of the patients had diabetes mellitus. The incidence of diabetes was noted in 15.3 per cent of the males and in 24 per cent of the females (Table II). Our finding indicating the greater incidence of diabetes in the female also was noted by the statistical department of a large insurance company.[8] They reported the results of a survey showing that known cases of diabetes are about one and one-third times as frequent among women as among men. They report further that three fourths of all deaths among diabetic patients were due to cardiovascular diseases. Hypertension, which often has been considered an etiologic factor in coronary occlusion, was noted in 25 per cent of the males and in 60 per cent of the females.

TABLE II. Patients with diabetes

Condition	Male	Female	Total
Diabetic	8	7	15
Nondiabetic	44	18	62
TOTAL	52	25	77

Comment

This report of 77 cases of acute myocardial infarction on whom autopsies were performed during the years from 1955 to 1960 failed to reveal any significant shift away from the greater incidence of this disease in the male sex. The commonly accepted contention that estrogenic factors provide relative immunity to coronary heart disease is supported. As the span of life is lengthened and more women survive to the postmenopausal age group, a greater increase in hospital admissions for this disease in the older segment of the female population can be expected.

Maxcy[9] observes, "... as a cause of death, the cardiovascular diseases appear to have advanced sharply in recent years .... When correction is made for the age changes in the population, it is evident that the death rate from the cardiovascular renal diseases (age adjusted) is actually declining."

This points up the difficulty of interpreting a trend in the incidence of a disease when a specific hospital population is studied. Numerous socioeconomic, geographic, racial, religious, and health insurance factors influence the sample of the population admitted to any one hospital. In a study of sex differences the sex ratio of hospital admissions is an important consideration. The ratio of female to male admissions has remained remarkably constant at Meadowbrook Hospital in the two sample years of 1936 and 1960. In 1936, 2,099 patients or 47.8 per cent of the total admissions of 4,387 were females. In 1960, 7,832 or 47 per cent of the total admissions of 16,659 were females. These totals are exclusive of the newborn service.

Conclusions

1. Our series revealed no significant change in the predominant incidence of acute myocardial infarction in the male.
2. Acute myocardial infarction is more apt to strike the male in the younger-age brackets, but the incidence for the female increases markedly after the age of sixty years.
3. A high incidence of diabetes and hypertension is noted in this group of cases of acute myocardial infarction.

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Physician population increased by 4,500

The physician population of the United States and its possessions increased by about 4,500 in 1961, according to a report by the A.M.A. Council on Medical Education and Hospitals, published in the June 9, 1962, issue of the *Journal of the American Medical Association.*

A total of 8,023 first licenses to practice medicine and surgery were issued in 1961. Since approximately 3,500 physicians died during the year, the physician population increased by about 4,500, compared with a net gain of about 4,330 in 1960.

Of 8,714 applicants for licensure by written examination, 7,650 passed while 1,064 (12.2 per cent) failed. However, the rate of failure in approved medical schools was 2.8 per cent. Twenty-six approved schools had no failures among their graduates. The greatest number of graduates from any one school to be examined was 214 from the University of Tennessee College of Medicine.

Statistics also were reported by the ECFMG (Educational Council for Foreign Medical Graduates), founded in 1957 to certify that foreign-trained physicians entering the United States had an education equivalent to that of graduates of approved medical schools in this country.

The Council, which has held eight qualification examinations for foreign medical graduates, said that the net effect of the ECFMG certification plan has been not to restrict but rather to increase both the number and the quality of foreign medical graduates coming to the United States for graduate training in hospitals.

In 1961 more than 3,600 foreign medical graduates were qualified directly from abroad by the ECFMG. The number of foreign medical graduates taking the ECFMG examination abroad is now greater than the number taking it in the United States.

Recent Advances in Cerebrovascular Disease

THE RANGE AND ACCURACY *of diagnosis in cerebrovascular disease have been extended since the introduction of cerebral angiography. Strokes commonly are caused by internal carotid artery occlusion, basilar artery insufficiency, hemodynamic crisis, and unusual causes. The treatment of occlusive vascular disease has not been established definitively; experiments with vasodilators, anticoagulants, fibrinolytic enzymes, and steroids continue, but all of these have drawbacks. Surgery has been successful in some cases. In the treatment of cerebral hemorrhage, surgical treatment is helpful in hematoma but not in acute fulminating hemorrhage.*

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IN THE PAST, the management of a stroke was relatively simple. There was no preventive or curative treatment. All that could be done was to try and save the patient's life and reduce the ensuing disability as far as possible. An accurate anatomic and pathologic diagnosis was relatively unimportant because it did not make a great deal of difference to the treatment. Now all this has changed. In the last twenty years there has been an immense literature on the cerebral blood supply and its disorders. Treatment, as well as becoming more complex, has become more specific, so that an exact diagnosis has become more and more important. It is sometimes possible to avert or at least to postpone an incipient stroke. The hopelessness and inertia that used to surround cerebrovascular disease are disappearing, and the whole field is being subjected to an intense scrutiny which promises further advances in the future.

Advances in diagnosis

The range and accuracy of diagnosis in cerebrovascular disease have been extended since the introduction of cerebral angiography.[1] Entities, such as thrombosis of the internal carotid artery, which formerly were hardly considered as diagnostic possibilities, are now found to be common. Many strokes are found to be due to occlusive disease of the great vessels of the neck at sites which are accessible to surgery. Angiography has permitted berry aneurysms to be localized with an accuracy which was impossible on clinical grounds; it also has demonstrated that causes other than aneurysm must be considered for subarachnoid hemorrhage, and in particular that angioma is not as rare as was once thought.[2] The risks of cerebral angiography are considered slight by those who have occasion to use it frequently.

Internal carotid artery occlusion

The occurrence of massive occlusion of the internal carotid artery has been known for many years. The recognition and diagnosis of insufficiency of the internal carotid circulation has been common only in the past decade and has followed a diffusion of knowledge as to the variations in the clinical picture and the increased use of angiography. The commonest site of obstruction of the artery is shortly above its origin from the common carotid. Stenosis also may occur in the siphon, near the origin of the ophthalmic artery, and at the lower end of the common carotid or innominate arteries.

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The complete occlusion of the internal carotid artery is compatible with normal neurologic function. This is especially so in young patients. Surgeons sometimes have to tie off this vessel as a therapeutic measure, and the procedure usually results in no, or at most temporary, neurologic dysfunction. Whether or not a defect appears depends in large measure on the adequacy of the collateral circulation which, in turn, depends on such congenital factors as the completeness of the circle of Willis and the presence or absence of degenerative changes of the vessels comprising or feeding the circle. The occlusion of the internal carotid artery may result from many causes: atherosclerosis is commonest; syphilis, embolus, giant cell arteritis, blood diseases, and tumor in the neck or skull or within the cranial cavity all have been incriminated; trauma to the head is an occasional cause.

There is a wide variation in the results of internal carotid artery occlusion. There may be no defect or there may be an unheralded sudden hemiplegia of a type suggesting thrombosis of the middle cerebral artery. It frequently manifests itself with recurring headaches, or with transient, recurrent neurologic defects, or with both. The headaches may be unilateral or generalized. The pattern of the neurologic disease tends to be the same in each attack. Patients may have recurring episodes of weakness or numbness or paresthesia in a hand or a limb or on one side of the body; there may be recurring mental confusion, or if the dominant hemisphere is affected, there may be transitory dysphasia. Epilepsy, either focal or generalized, may occur. Papilledema is sometimes seen. Ischemia in the territory of the ophthalmic artery may lead to recurring amaurosis. The combination of recurring blindness in one eye and episodes of numbness or weakness on the opposite side of the body is pathognomonic of internal carotid artery insufficiency. The occurrence of intermittent headaches in association with papilledema will suggest the possibility of a cerebral tumor; the combination of recurring visual disturbances with unilateral headache will suggest migraine. After a time the neurologic defects tend to extend and persist.

The diagnosis may be strengthened by the finding of impaired pulsation in the internal carotid artery in the neck, a test, however, which is fraught with difficulty because of the proximity of the external carotid pulse. A bruit may be heard over the obstructed artery. Retinal artery studies provide an ancillary but, in many hands, unsatisfactory method of diagnosis.

Basilar artery insufficiency

Complete occlusion of the basilar artery is hardly compatible with life. Insufficiency of the basilar artery circulation may be difficult to distinguish from similar insufficiency of the internal carotid. Here again there may be recurring episodes of neurologic disease and headaches. In that the vertebral-basilar system supplies the brain stem and parts of the occipital and temporal lobes, the disordered function will involve these regions. Thus, a patient may have episodes of numbness or weakness affecting the arms and the legs or the legs alone on one or both sides of the body. There may be episodes of dysphagia or dysarthria; of tinnitus or vertigo; of numbness or pain in the face, mouth, and tongue; of diplopia, hemianopsia and rarely bilateral blindness. Episodes of disturbed consciousness are of special interest in view of the recent work on the part played by the brain stem in the function of consciousness. Abdominal disturbances, presumably associated with ischemia of the vagal nuclei, may be experienced.[2]

Hemodynamic crisis

These recurring stereotyped attacks of focal brain dysfunction have been ascribed in the past to an arterial spasm. The cerebral blood vessels are known to go into spasm on occasion, but this spasm appears to require a direct trauma to the vessel wall as in needling or other manipulation. Local bleeding or the impaction of emboli also would appear capable of inducing spasm, but such an explanation would not appear tenable in most of the patients under discussion. It has been claimed that emboli are dispatched from atheromatous and thrombotic lesions in the carotid sinus. It seems unlikely, however, that an embolism could explain episodes which are transitory, recurrent, and of the same pattern. The most satisfactory explanation would appear to be the "hemodynamic crisis." These recurrent attacks have been explained by Denny-Brown[3] on the basis of ischemia. He postulates a critical reduction in the cerebral circulation; these patients are usually able to get along; the blood supply is adequate and no more. Under physiologic stress compensation fails, and ischemia develops. The failure of the circulation may result from many causes: failure of postural control of the blood pressure, as in aged patients; postoperative shock or coronary thrombosis; attacks of paroxysmal tachycardia; dehydration from vomiting or diarrhea or mercury diuretics; blood loss; or the administration of hypotensive drugs. The clinical picture will vary with the distribution of the arterial narrowing. Thus, a patient with insufficiency of the internal carotid artery also may have local involvement of the middle cerebral artery with resulting ischemia in its territory during a hemodynamic crisis.

Unusual causes of stroke

The stroke is more and more seen to be but the neurologic manifestation of diseases which are generalized, such as atheroma, arteriosclerosis, hypertension, or thromboembolic proclivity. In the understanding of strokes, both a general disease of this type and the local impairment of the blood supply must be considered. Sometimes the general factors are more important, such as when a disease of the heart leads to cerebral emboli; sometimes local factors are more important, such as when a trauma to the head or neck in a patient in middle life leads to insufficiency of the internal carotid artery, or cervical spondylosis compromises the circulation of the vertebral artery. Competence in neurology predicates a certain competence in internal medicine.

The process of thrombosis is far from simple. For the conversion of fibrinogen to fibrin, a highly complicated chain of reactions involving at each stage inhibitors as well as activators has been found to be necessary. Changes in the viscosity and electric charges of the particles of the blood and changes in the platelets and in the level of the hydrophilic colloids all play a role and may be modified by such processes as surgical operation, the presence of a malignant tumor, or a primary disorder of the blood. The factors leading to local changes in the vessel wall are even more obscure and much work still has to be done to determine the effects of the cholesterol level of the blood, of diet generally, and of exercise.

Thus the neurologist, confronted with an atypical stroke, may find himself searching for evidence of such diverse disease processes as polycythemia vera; sickle cell anemia; collagen disease, such as acute disseminated lupus and polyarteritis nodosa; giant cell arteritis; myxedema; Buerger's disease; and leukemia, as well as such old enemies as diabetes and syphilis. And in the presence of the apparently transient stroke he will be alert to such differential diagnoses as postepileptic paralysis, migraine, the hypertensive crisis, the congestive attack of general paresis, hypoglycemia, acute multiple sclerosis of the hemiplegic type, as well as a metastatic tumor of the brain.

Treatment of occlusive vascular disease

Despite advances on a broad front, the treatment of occlusive and thromboembolic disease continues to offer many problems.

VASODILATORS. The search continues for the ideal vasodilator. The big disadvantage of most of them is that they cause general vasodilatation which may have the paradoxic effect of reducing the blood supply to the brain with the aggravation of the cerebral difficulties they seek to overcome. Papaverine hydrochloride, tolazoline hydrochloride, and histamine have had their proponents, but they have not proved to be useful generally. The inhalation of 5 per cent carbon dioxide in oxygen has been advocated; it increases the cerebral blood flow, and unlike other vasodilators, tends to maintain the level of the blood pressure by stimulating the pressor centers. But its action is temporary, it tends to raise the intracranial pressure, its effect on coagulating factors is unknown, and it is already present in a high concentration in the ischemic tissue. Alcohol is a weak vasodilator and may have some value in increasing the cerebral blood flow.

On the supposition that a vascular spasm plays an important role in many cases of stroke, stellate ganglion block has been used widely, but the procedure has proved generally disappointing as has surgical section of the cervical sympathetic trunk.

ANTICOAGULANTS. Although the value of anticoagulants[4] in preventing and lessening the incidence of embolic strokes in patients with rheumatic or arteriosclerotic heart disease is accepted, relatively little has been learned about the treatment of an embolic infarct of the brain once it has formed, and no particular method of treatment can be recommended.

The value of anticoagulants in the treatment of cerebral thrombosis has not been decided. In the first place, it is often a matter of great difficulty to decide whether a patient has a thrombosis or a hemorrhage. Even where there has been an infarction, there is the danger of subsequent bleeding into it. The walls of the small blood vessels in the infarct are bereft of their own blood supply and undergo necrosis. Should the blood flow be restored, as may happen if the shock responsible for the infarct is overcome, or an embolus breaks up and moves onward, or a clot becomes recanalized, or a vascular spasm relaxes, hemorrhage may occur. Such a hemorrhage would be rendered more dangerous by anticoagulants. The most plausible argument for anticoagulants is in patients with a normal blood pressure who have had recurring hemodynamic crises, but in whom the complete occlusion of the compromised vessel has not yet occurred. However, the administration of anticoagulants is never free from risk, and the practical day-to-day management of these patients is frequently difficult.

FIBRINOLYTIC ENZYMES. Whereas the use of anticoagulants is to prevent thrombi from forming, the use of fibrinolytic enzymes is to remove thrombi once they are formed.[5] Much work is going on in assessing the value of these enzymes in the treatment of strokes. In the absence of a potential source of bleeding, such as a peptic ulcer, they appear to be safe, but they are still in the experimental stage, and there is not strong evidence of their value in even a recent stroke where there inevitably must be a time lag between the onset of the thrombosis and the beginning of treatment.

STEROIDS. Cortisone has been used in the immediate treatment of strokes, and striking claims have been made for its value.[6] However, the studies have not been well controlled, and the dramatic improvement which frequently can occur in a mild stroke without the benefit of any special treatment appears to have been overlooked. It is reasonable to suppose that the cerebral edema accompanying an infarction is lessened by cortisone, but whether or not this has any long-term advantage has not been proved, and cortisone therapy carries the potential danger of further thrombosis.

SURGICAL TREATMENT. Thrombosis of the internal carotid artery in the neck has been treated successfully by thrombectomy and by resection and anastomosis of the affected vessel when the occlusion is well localized and the artery proximal and distal to the occlusion is relatively normal.[7] When the lesion is more extensive, the occlusion may be bypassed with a graft. The surgical approach would appear to be especially valuable in the young where there may be a solitary atheromatous plaque.[8] Such procedures have been facilitated by the introduction of controlled hypothermia and controlled hypotension.

Cerebral hemorrhages are not necessarily fatal, as was once commonly believed, and attention is now being directed at reducing their consequences by evacuating them surgically. A cerebral hemorrhage generally must be regarded as an episode in the natural history of hypertensive cardiovascular disease. In their treatment, therefore, attention should be directed at the general as well as at the local disease. Hypertensive encephalopathy also occurs in association with severe degrees of hypertension from whatever cause, such as essential hypertension, unilateral kidney disease, toxemia of pregnancy, pheochromocytoma, porphyria, or coarctation of the aorta. The relative merits of thoracolumbar sympathectomy, hypotensive drugs, salt-free diets, and total adrenalectomy still have to be decided. In severe hypertension it seems axiomatic that any measure that will reduce the pressure will lessen the chance of cerebral hemorrhage occurring or recurring. Against the danger of hemorrhage must be weighed the risk of thrombosis if the blood pressure is reduced too far.

Treatment of cerebral hemorrhage

Since it has been realized that intracerebral hemorrhages are not inevitably fatal, it has been contended that the evacuation of the clot might permit the patient to recover more quickly and more fully than if it were left in situ. The immediate evacuation of a recent clot would lead to further bleeding; consequently, there is little hope of surgical help in acute fulminating hemorrhage. The hope lies in the more slowly evolving hematoma, which, however, may be difficult to recognize or differentiate from an ischemic softening. Although the mode of onset of the stroke and the associated circumstances, such as the degree of hypertension, may be of value, radiologic studies usually are essential for the differentiation. Arteriography may demonstrate a deviation of the midline vessels toward the hemiplegic side, and pneumography may show a distortion of the ventricular system. These findings in a patient who continues to deteriorate at a stage when if he had a thrombosis he might be expected to improve, would point to an increasing intracerebral hemorrhage and justify an operation to evacuate the clot.

Conclusion

The fatalism which used to surround the patient with a stroke is no longer justified. The treatment of cerebrovascular disease is in a stage of rapid evolution, and every patient with a stroke must be scrutinized closely if the best treatment is to be applied.

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Discussion

Abraham M. Rabiner, M.D., *Brooklyn, New York*. Until recently, once the diagnosis of a vascular lesion in the brain was made, the interest in the patient waned from the scientific point of view. He was regarded usually as a problem only in custodial care. Because this is still so to a considerable degree, we should continue to stress the importance of more and more interest and study of these clinical syndromes. Dr. Smith's paper, therefore, is a timely and important contribution.

The advent of cerebral angiography has explained many perplexing problems and has been of great value in localizing intracranial aneurysms. The importance of extracranial arteries in the neck as the site of the pathologic condition affecting irrigation of the brain is now appreciated.

Hemiplegia developing gradually, or convulsive seizures in the patient with a stroke, usually justified the diagnosis of a space-occupying intracranial lesion, but angiography has demonstrated that carotid artery insufficiency is associated also with such clinical manifestations.

Moreover, by angiography we now find that the symptoms in many patients with so-called migraine are due to spasm of the carotid artery.

In 2 patients diagnosed as having multiple sclerosis, transient visual impairment was caused by interference with the blood flow due to carotid artery spasm.

In discussing anticoagulants, Dr. Smith emphasizes, "It is often a matter of great difficulty to decide whether a patient has a thrombosis or a hemorrhage."

We have found red blood cells in the cerebrospinal fluid of patients who have had a cerebral thrombosis, and anticoagulants are, in my opinion, contraindicated in any case where there is a sizable infarct. In minute infarcts, such as occur in the so-called "small strokes" in the brain stem due to occlusion of perforating branches of the basilar artery, the use of anticoagulants is not as jeopardizing as in supratentorial infarcts.

Steroids are of no value in cerebral vascular disease and are contraindicated. Surgery in cerebral vascular disease has been a most important form of therapy, especially in those cases where the sequence of events of the clinical picture warrants suspicion that the symptoms are not typical of the occlusion of an artery by thrombosis, embolus, or hemorrhage and thus justifies either air studies or angiography.

In brief, the patient with the typical occlusive lesion of an artery irrigating the brain should present maximum symptomatology at the onset. Thereafter there should be either a stationary picture or improvement. If at the onset there is only partial symptomatology, such as a monoplegia or aphasia, going on then to hemiplegia, or if there are convulsions at any time in the course of the clinical picture, or if after the acute onset there is later increasing somnolence and stupor, every facility should be utilized to make certain that a space-occupying lesion is not overlooked. In such instances angiography may reveal thrombosis of the carotid artery or a space-occupying lesion. In any event, this type of patient then becomes a surgical problem and can be salvaged.

The patient with a spontaneous cerebral hemorrhage is unconscious at the onset, remains unconscious, and dies within a matter of hours or days. With such a prognosis inevitable, angiography should be instituted immediately. The evacuation of a clot may save a life.

H. W. GILLEN, M.D., *Buffalo, New York*. The recent changes in diagnostic methods and therapeutic ideas are considerable. Although many of the technics have been available for almost a quarter of a century, their recent application to the problems of cerebrovascular disease has renewed clinical interest in the stroke patient among the nonneurologic members of our profession.

Dr. Smith has described the value of cerebral angiography in diagnosis. The search for a surgical resectable lesion in the proximal positions of the carotid and vertebral arteries has greatly advanced the use of angiography. Partial occlusions of the great vessels may impair the blood flow to the brain, and in periods of vascular stress they apparently result in inadequate blood flow, yielding regional or focal ischemic infarcts. Occasionally the potentiality of such a partial impairment of blood flow can be evaluated through the combined use of a tilt-table and electroencephalography. The patient's orientation with respect to gravity is suddenly altered, reducing the effective cardiac output. This decreases the focal cerebral blood flow and will produce a temporary insult to the brain tissue. Reflections of the tissue embarrassment may be seen on the electroencephalogram as focal slow waves. Similar effects may be produced by substituting nitrogen or low oxygen concentrations for air during normal respiration. Recently there have been attempts made to measure by impedance methods deviations from normal cerebral blood flow in various disease states. Gastaut* has described observations made in his clinic demonstrating the utility of this technic in instances of ischemic infarct of the brain.

Dr. Smith also has discussed the concept of the hemodynamic crisis and its relation to the diagnosis of a stroke. He quoted Denny-Brown who postulated a critical reduction in cerebral circulation, without occlusions, producing ischemia in patients who previously had been able to compensate. There is another mechanism of this type that needs further emphasis—the clinically silent myocardial infarction. The myocardial infarct may be silent to the physician either because the patient is speechless and cannot relate the classical cardiac symptomatology, or because in many instances the infarct is truly silent. At the E. J. Meyer Memorial Hospital we have been able to study 14 definite examples of this clinical combination and 6 additional probable examples. Only 1 patient presented any classical signs or symptoms of acute myocardial infarction at admission, yet each developed definite electrocardiogram alterations considered to be diagnostic, and all who had serial transaminase studies demonstrated the typical transient elevation of the glutamic oxalacetic transaminases only. These patients have a higher mortality rate than the patient with classical myocardial or cerebral infarct. Their care by the physician must be tempered by the knowledge of the double pathologic process. Heroic measures to reconstitute the patency of the cerebral vessels is misplaced. In those instances when autopsies were obtained, confirmation of the diagnosis was made. In one instance a new complete occlusion of the internal carotid artery was present. In this case we believe that the carotid occlusion occurred as a consequence, although proof was unobtainable. It is now part of the admission studies of each stroke patient to initiate the evaluation of cardiac function and health in an attempt to diagnose those instances of silent myocardial infarction that exist.

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* Gastaut, H., and Poirer, F.: The electroencephalogram in cerebrovascular disease, Neurology 2: 110 (Apr.) 1961.

Dr. Smith gave us a list of causes of atypical stroke. I shall take the liberty of adding an unusual cause that may become less rare. A considerable number of people are skin diving, either with or without underwater breathing equipment. Those who use breathing equipment are susceptible to a rare but dangerous incident called air embolism. If the diver abandons his breathing device and ascends to the surface of the water without forcibly and continuously exhaling the expanding gas in his lungs, he may rupture the pulmonary tissues, and real bubbles will enter the pulmonary circulation, traverse the heart, and ascend into the cerebral circulation. When this occurs, unconsciousness almost always follows immediately, and many focal neurologic syndromes may be seen, as after any other type of cerebral embolism. This variety of atypical stroke usually happens during ascent or shortly after the diver reaches the surface. Treatment consists of immediate recompression in an appropriate chamber and the accepted supportive measures. Without treatment most patients die, although survival in mild cases is possible. The residua among survivors can cover the total scope of neurology and are indistinguishable from any other cerebral embolism.

Dr. Smith is to be congratulated for his thorough review of the recent advances in the diagnosis and treatment of one of our most prominent crippling disorders, cerebrovascular disease. The current period is one of hope and accomplishment. The future appears to be very bright.

Emotional problems in university students

Emotional problems ranked third behind respiratory and skin diseases among university students, according to a ten-year study reported by Alfred S. Evans, M.D., and Jeffrey Warren, B.S., in the June, 1962, issue of *Archives of Environmental Health*. Respiratory infections, not including influenza, far outnumbered all other causes of illness. Respiratory ills, skin eruptions, psychiatric problems, and gastrointestinal upsets were termed the "Big Four" among the 10 most common diagnoses in the young adult student population.

The availability and low cost of counseling and psychiatric services might be a factor in the relative frequency of emotional problems seen at the student health facilities. Another factor is the greater likelihood of emotional problems emerging in university students than in those in a more stable working environment.

The findings point up the need for psychiatrists and dermatologists, at least on a consultant basis, in university health departments.

Gaucher's Disease Without Splenomegaly

Oldest Patient on Record, with Review

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In 1882 GAUCHER[1] described the first instance of the disease which now bears his name. He was of the opinion that the large pale cells he saw in the spleen represented a neoplasm which was primary to that organ. It was not until thirteen years later that Picou and Ramond,[2] as well as Collier,[3] described the finding of similar cells in the lymph nodes. In 1900 Bovaird[4] commented on the familial incidence of what he considered a toxic disease and found the characteristic cells in the liver. Five years later Brill, Mandlebaum, and Libman[5] first described Gaucher cells in the bone marrow. That the disease was a result of the deposition of a "foreign" substance was suggested by Marchand.[6] Brill and Mandlebaum[7] described additional cases and suggested that the entity be called "Gaucher's disease." Mandlebaum and Downey[8] proved that the origin of the Gaucher cell was the reticulum of the lymph-hemopoietic organs and suggested that the disease was due to a disturbance of lipid metabolism. In 1924 Epstein[9] and Lieb[10] found that the substance deposited in the cells was a cerebroside.

At present Gaucher's disease is defined as a familial disorder, characterized by the accumulation and retention of cerebrosides in the reticular cells and histiocytes of the involved organs. The exact metabolic defect responsible for the abnormal deposition of cerebrosides has not been elucidated. The demonstration of increased serum acid phosphatase in patients with Gaucher's disease by Tuchman, Suna, and Carr in 1956[11] has been confirmed and is of some interest.

After reviewing more than 350 cases of Gaucher's disease, it seemed that the case to be presented might be of interest for several reasons. It represents the oldest reported patient with this malady, and it is only the ninth reported case of Gaucher's disease diagnosed in the absence of splenomegaly,[12-19] although others undoubtedly have been noted. It also represents a patient with a minimum of symptoms and signs referable to his disease, characteristic of the group of cases to be discussed.

Case report

An eighty-six-year-old Jewish male was admitted to The Mt. Sinai Hospital for the first time on March 30, 1960. He had been transferred from a home for the aged because of jaundice of one month's duration. During this period he had also complained of weakness and loss of appetite.

Several months prior to admission he had been given chlorpropamide for diabetes mellitus, a condition that had been present for forty years and previously had been controlled by diet. In 1937 he had a cholecystectomy at another hospital for "gallstones," but there was no history of any previous jaundice. Otherwise, his past medical history indicated completely negative findings, as did his family history.

On physical examination, the patient was a thin, jaundiced, listless white male. His temperature was 101.2 F.; pulse, 104; and respirations, 18. The blood pressure was 110/70 mm. Hg. The skin and mucous membranes were dry. The optic fundi showed some sclerotic changes but no diabetic retinopathy. The scleras were icteric, but otherwise they showed negative findings. The neck was supple. There were no enlarged lymph nodes. The chest was emphysematous in configuration, with a slight degree of kyphoscoliosis. There were bibasal coarse rales; the bases were hyporesonant to percussion. The heart was not enlarged and there were no murmurs. The liver and spleen were not felt and were not enlarged to percussion. There was an old surgical scar in the right upper quadrant. The rectal examination indicated negative findings, and it was also noted that the stool was of normal color. The lower extremities had linear pigment streaks of a bluish-brown hue from the knees to the ankles.

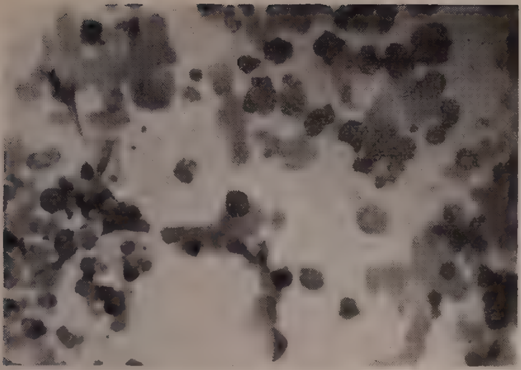

FIGURE 1. Typical large Gaucher cell in sternal marrow aspirate.

GAUCHER'S DISEASE *is a familial disorder, characterized by the accumulation and retention of cerebrosides in the reticular cells and histiocytes of the involved organs. The case of an eighty-six-year-old man with Gaucher's disease is presented. Like the other cases of asplenomegalic Gaucher's disease in the literature, the patient did not show most of the usual signs and symptoms and did not have splenomegaly. This group of cases may represent a milder type of the disease, probably owing to a quantitative difference in the enzyme disturbance. Clinical signs of the disease include marked splenomegaly, hepatomegaly, absence of signs of hepatic decompensation, skin pigmentation, and pingueculas. Bone-marrow aspiration, bone biopsy, splenic puncture, liver biopsy, and radiographic examination are helpful in diagnosis. Treatment is merely symptomatic and supportive.*

A urinalysis showed a specific gravity of 1.018, 2 plus sugar, 2 plus bile, and 1:40 urobilinogen. The hemoglobin was 10.9 Gm. per 100 ml. The white blood count was 8,100 per cubic millimeter, and a differential count revealed 55 segmented forms, 15 band forms, 20 lymphocytes, 2 eosinophils, 1 basophil, and 7 monocytes. The platelet count was 60,000 per cubic millimeter. There were 0.8 per cent reticulocytes. The erythrocyte sedimentation rate was 58 mm. per hour (Westergren method). The initial blood chemistries were as follows: urea nitrogen 11 mg.; fasting sugar, 117 mg.; total bilirubin, 11.6 mg.; direct reacting bilirubin, 7 mg.; total cholesterol, 236 mg.; and esterified cholesterol, 166 mg., all per 100 ml. The serum total protein was 5.8 Gm.; the albumin, 3.5 Gm.; and the globulin, 2.3 Gm. per 100 ml. Serum electrophoresis showed a low albumin and alpha-one globulin, with a slightly increased gamma globulin. The patient had a prothrombin time of 22 seconds, with a control of 12.5 seconds. The cephalin flocculation test was 2 plus in forty-eight hours. The serum glutamic oxalacetic transaminase was 23 units per cubic centimeter. The serum alkaline phosphatase was 28 King-Armstrong units, and the acid phosphatase was 4.2 King-Armstrong units. The amylase was 35 Somogyi units. The Coombs' direct antiglobulin test indicated negative findings.

Initially the patient was considered to have bronchopneumonia and, in addition, jaundice secondary to chlorpropamide. He was treated with penicillin which resulted in the subsidence of fever and the disappearance of rales. His jaundice diminished gradually in a three-week period. An intravenous cholangiogram at this time demonstrated a bile duct of normal caliber, without any evidence of calculi. A Bromsulphalein test showed a 6 per cent retention after forty-five minutes when the patient was no longer icteric.

Because of the persistence of anemia and thrombocytopenia, a bone-marrow aspiration was performed. The marrow was infiltrated with 5 per cent Gaucher cells (Fig. 1). A bone-marrow biopsy (performed by Stanley Bauer, M.D.) confirmed the diagnosis of Gaucher's disease. A liver biopsy revealed subsiding cholestasis but no Gaucher cells.

Incidence

Gaucher's disease has occurred in all ethnic groups, although a relatively large percentage of reported cases involved Jewish patients. The majority of reported cases are members of the white race, but there have been cases in Orientals[20] and Negroes.[21-23] There is undoubtedly a familial incidence to the disease, approximately one third of reported cases being familial. Two or more cases of Gaucher's disease often occur in the same generation of an affected family. The illness has been reported in a set of identical twins[24] and in as many as five members of the same generation of a family.[25] Cases in succeeding generations have been observed,[26] but these are not as common as multiple cases in the same generation.[27] Hsia, Naylor, and Bigler[28] and others believe that most familial cases are transmitted by a recessive mechanism. Groen[29] has postulated that the trait is transmitted as a simple dominant.

SEX. There is no significant difference in the sex incidence of Gaucher's disease. The diagnosis has been established as early as the first few days of life and, prior to our case, up until the age of seventy-nine years.[17]

AGE. An analysis of the cases studied shows the following age incidence:

Years	Per Cent
Up to 10	41
10 to 20	15
20 to 30	16
30 to 40	11
40 to 50	9
50 to 60	4
60 to 70	3

Pathology

The characteristic Gaucher cell is usually found in the spleen, liver, lymph nodes, and throughout the bone marrow in adult cases. Instances of kidney[30] and lung[31] involvement have been the subject of isolated case reports. A biopsy of a typical pinguecula revealed cells resembling Gaucher cells.[32] Although the skin of a patient may be pigmented, this is due to melanin pigmentation and not to Gaucher cells in the skin.[33] Nervous system involvement is rare in adult cases, but it is common in the infantile form of the disease. In the infantile type the Gaucher cells may be found in the adrenals, ovaries, pituitary, hypothalamus, superficial lymph nodes, thymus, lungs, kidneys, and cerebral cortex. The cortex reveals a proliferation of glial cells and degenerative changes in the pyramidal cells.[21] Although the superficial lymph nodes are usually not enlarged in adult cases, the intrathoracic and abdominal nodes are commonly larger than normal.

SPLEEN. The spleen is usually enlarged and has been reported to weigh as much as 8,100 Gm. The average weight of the spleen in reported cases seems to increase with age. The spleen retains its normal contour and is firm in consistency. The cut surface shows a fine network of greyish material. Histologically, the splenic pulp is almost completely replaced by the pale-staining Gaucher cells. Brownish pigment which gives the iron stain is found in the trabeculas and in the sinusoidal walls.

LIVER. The liver is not as greatly enlarged as the spleen, nor is liver enlargement as consistently found as splenomegaly. In the reported cases without splenomegaly there was usually no clinical evidence of hepatic enlargement. The cut surface of the liver reveals greyish streaks against a brownish-pink background. Cirrhosis due to Gaucher infiltration has not been reported, although there is an increase in interlobular connective tissue. Large numbers of Gaucher cells are found in the portal spaces and sinusoids. Increased iron pigment is found in Glisson's capsule and in the walls of the large vessels.

LYMPH NODES. In adult cases enlarged nodes are found in the thorax and the abdomen. In infants and children the superficial lymph nodes may also be involved. The lymph node, as the spleen, is largely replaced by Gaucher cells. Hemosiderin pigment is found in the lymph nodes, and the capsule is thickened.

BONE. It would seem from the 9 cases presented in Table I that bone marrow involvement is the single clinical sine qua non for the diagnosis of Gaucher's disease. The marrow has been described as soft in consistency, red or pink in color, and mottled with small whitish or grey areas. The Gaucher cell is found in all parts of the marrow and represents the most convenient way to establish the diagnosis. The Gaucher cell in the marrow is similar to the cells found in other organs, but they may be spindle-shaped.[12,34] The proliferating cells may lead to the loss of osseous tissue, this being due to the loading and expansion of the marrow with deposited Gaucher cells. This causes a flaring of the ends of long bones and gives rise to the characteristic "Erlenmeyer flask" deformity of the distal femur. The rarefaction may also lead to a vertebral collapse and spontaneous fractures. The periosteum may be elevated by hemorrhage, but it is not primarily involved. The cartilages are not infiltrated but may be destroyed by collapse of the adjacent bone.

GAUCHER CELL. The pathognomonic cell is a large, pale, round, or polyhedral cell, 20 to 40 microns in diameter. The cytoplasm is clear and has many parallel wavy lines. The likeness to tissue paper has been mentioned. The nuclei are small, with a finely granular chromatin structure, eccentric in position, and with oxyphilic nucleoli. From 10 to 12 nuclei may be present in a given cell. The cytoplasm does not stain with any of the lipid stains, such

TABLE I. Nine cases of Gaucher's disease without splenomegaly*

Reference	Age (Years)	Sex	Spleen	Liver	Bone X-ray Findings	Nodes	Blood	Bone Marrow Findings	Miscellaneous
Block and Jacobson[12]	49	F	0	0	Negative	0	Anemia	Positive	Gastrointestinal complaints
Erf,[13] (Case 5)	59	M	0	0	Positive	. . .	Normal	Positive	Bone pain
Feinberg and Quigley[14]	20	M	0	0	Negative	0	Anemia	Positive	Bone pain
Levine and Solis-Cohen[15]	29	F	0	0	Positive	0	Slight anemia	Positive	. . .
Morgans[16]	67	M	0	1 to 2 fingerbreadths enlarged	Positive	0	Slight anemia	Positive	Bone pain, pingueculas
Petit and Schleicher[17]	79	M	0	0	Negative	0	Anemia	Positive	Spleen and liver had Gaucher cells at autopsy
Reich, Seife, and Kessler[18]	49	F	0	0	Positive	0	Anemia	Positive	Bone pain
Snapper and Goldberg[19]	65	F	0	0	Positive	0	Normal	Positive	Back pain, osteoporosis, and compression of vertebrae
Authors' case	86	M	0	0	Positive	0	Anemia and thrombopenia	Positive	Cholestatic jaundice

* 0 = not enlarged; — = not mentioned.

as Sudan III.[35] Gaucher cells do stain with periodic acid-Schiff stain because of their carbohydrate content. This latter reaction helps in the differentiation from other lipidoses, such as Niemann-Pick's disease.

Pathogenesis

Numerous theories of pathogenesis have been offered. Gaucher's belief that it represented a primary neoplasm of the spleen has already been mentioned and represented the earliest attempt at explanation. Pick[36] proposed that Gaucher's disease was due to a disturbance in intermediary metabolism with excess production of cerebroside which is carried in the serum to be deposited in the histiocytes of the involved organs.[37] It was Thannhauser[38] who maintained that the disturbance takes place entirely within the cell, leading to an increased synthesis and the storage of cerebroside. The fact that cerebrosides are not detectable in the serum of affected patients lends support to the latter theory. Moreover, Ottenstein, Schmidt, and Thannhauser[39] measured red cell cerebroside in both normal subjects and patients with Gaucher's disease and were unable to demonstrate any abnormal amounts or varieties of cerebroside. Aghion,[40] on the other hand, demonstrated that the increased cerebroside in Gaucher spleens was mainly glucosidocerebroside and not the physiologically usual galactose-containing variety, although the galactosidocerebroside was also present in increased amounts.

Gaucher's disease may be classified more properly as belonging to the "inborn errors of metabolism." The exact site of the defect has not yet been elucidated. The recent finding of elevated serum acid phosphatase in most cases of Gaucher's disease has led to further work, showing that this acid phosphatase is different from phosphatases originating in such sites as the liver, spleen, prostate, and bone marrow.[11,41,42] The serum enzyme concentration is elevated, as determined by using the substrate disodium phenylphosphate, the King-Armstrong method. The Bodansky method, using beta-glycerophosphate as a substrate, may give normal results despite the elevation noted using the King-Armstrong method (as modified by Gutman). The serum acid phosphatase in Gaucher's disease is not inhibited by L-tartrate, as is prostatic acid phosphatase. Whereas copper and formaldehyde inhibit red blood cell acid phosphatase, only formaldehyde has any effect on Gaucher acid phosphatase and only slightly inhibits it. Saline homogenates of Gaucher spleens show activity on glycerophosphate three times that of spleens from patients with Niemann-Pick's disease. This activity is inhibited by fluoride and tartrate. After splenectomy in Gaucher patients, there is a 40 to 75 per cent decline in serum acid phosphatase[43] which is usually temporary. The excess serum enzyme appears to arise from the spillage of tissue accumulations, probably with some modification of the phosphatase before spillage. It is proposed by Sobotka, Goldstein, and Weissbarth[44] that the abnormally elevated enzyme has some primacy in the disease. By making available more lignoceryl sphingosine and other sphingosines, from hydrolysis of sphingomyelin, more cerebrosides are synthesized in the presence of glucose and galactose. If this explanation were true, Gaucher's disease would be a unique instance where excess of an enzyme could lead to "overproduction" of a body constituent. However, proof is lacking for this latter theory. It is more likely that the elevated acid phosphatase is symptomatic of a more elusive enzyme disturbance. The type and concentration of the glycosidases in Gaucher's disease remain to be described.

Kerasin on acid hydrolysis yields sphingosine, lignoceric acid, and carbohydrate. Recent work on the structure of cerebroside in Gaucher's disease has shown that the sugar moiety is attached to the primary hydroxyl group of sphingosine. The sugar is mainly glucose. Fatty acid analysis by gas and paper chromatography shows, in addition to lignoceric acid (24 carbons), behenic acid (22 carbons) and palmitic acid (16 carbons) as well as small amounts of arachidic acid (20 carbons) and stearic acid (18 carbons). The site of attachment and transconfiguration of the sphingosine are similar in both glucosido- and galactosido-cerebroside.[45]

Clinical course

Gaucher's disease may last for decades, have no effect on life expectancy, and produce only the mildest symptoms. At the opposite extreme, it may lead to death in a matter of days or weeks. Within this broad range there are general types of Gaucher's disease.

The infantile or neurologic type of Gaucher's disease was first described by Reuben[46] and in 1927 by Oberling and Woringer.[25] Reuben noted the relation between the age of onset and the duration of disease, an earlier onset meaning a more rapid course. The neurologic form usually begins in the first six months of life. The signs and symptoms are rather striking.[47, 48] There may be a failure of the infant to gain weight, with a retardation in development. Dyspeptic manifestations are noted. Hepatosplenomegaly is outstanding, and so are severe neurologic disturbances, such as muscular spasm, strabismus, and dysphagia. There may be anemia and pallor with a febrile course. Leukopenia is also frequently demonstrated. Death usually results in a few months from intercurrent infection, cachexia, or laryngeal spasm. When the disease appears after six months of age, there is generally an absence of neurologic symptoms. The disease then resembles the "adult" form, although the course of the disease is usually rapid, leading to early death. Infants with Gaucher's disease are unlikely to have roentgenographic evidence of the disease,[49] skin pigmentation, or pingueculas, all of which are frequently seen in adults.[50] On the other hand, neurologic involvement, with rare exceptions, is found only in infants.[51]

The adult variety of Gaucher's disease is the most commonly encountered form. It is compatible with long life, although death may occur from intercurrent illness or from the results of hypersplenism. There seems to be a relation between the age at onset of the disease and the duration. Even aside from the acute infantile form, an earlier onset, particularly in the first decade, seems to be associated with a more virulent form of illness. The prognosis in adolescents is fair,[52] and when symptoms manifest themselves beyond the third decade the prognosis is good.

Splenomegaly is an almost constant finding in Gaucher's disease. The absence of splenomegaly in our case led us to search the literature for other instances. The spleen may attain tremendous proportions and fill the entire side of the abdomen. Hepatomegaly is a frequent finding, but the liver is not as massively enlarged as the spleen. Superficial lymph node enlargement can occur, but it is unusual.

There may be gastrointestinal symptomatology. Many authors have noted an increased incidence of cholelithiasis in adult Gaucher cases. Whether the symptoms are due to gallstones or to a large spleen may be difficult to decide. Anorexia, nausea, regurgitation, frequent belching, a sense of fullness, vague indigestion, and diarrhea are usually attributable to pressure symptoms of the remarkable hepatosplenomegaly. Anemic symptoms, such as dyspnea, orthopnea, fatigue, or fainting spells may be the presenting complaints. The anemia has been found in the majority of cases and is usually attributable to splenic mechanisms. However, there may be anemia in the absence of splenomegaly. This is probably due to marrow replacement by Gaucher cells or, where blood loss is considerable, anemia may be due to this cause. Epistaxes, melena, petechias, and ecchymoses occur owing to thrombocytopenia.[53] Marrow replacement or hypersplenism can be invoked to explain the low platelet count.[34,54] Leukopenia predisposes the patient to infection.

Another frequent complaint is bone pain and tenderness. This occurs mostly in the lower extremities.[55] The bone pain may or may not be accompanied by an x-ray evidence of bone involvement. However, at times pathologic fractures are noted. The pain is presumably a result of pressure of Gaucher cells which infiltrate the marrow and expand the marrow cavity. The bone pain may be accompanied by redness and when associated with certain x-ray findings, it has resulted in a number of operations for osteomyelitis. Mild jaundice is often noted, but mostly it is subclinical. Surprisingly, liver function tests are usually normal despite an extensive hepatic infiltration with Gaucher cells.

A brownish pigmentation of the exposed parts of the body is not uncommon, and the finding of pigmentation of the leg from the knee to the ankle is characteristic.[33] Pingueculas are seen in a minority of cases. Diabetes mellitus and cholelithiasis have been noted in a number of cases, but are probably no more common than in the population which gave rise to the Gaucher cases.

A third clinical form of the disease seems to be a variety without splenomegaly. In a review of the literature for cases without splenomegaly we were able to find only 8 in addition to our own (Table I). These cases were found in a somewhat older age range than that usually encountered in Gaucher's disease. Only 2 patients were below the age of forty-nine years, twenty and twenty-nine years respectively. The oldest case on record is the patient in this report who was eighty-six years old at the time of diagnosis. As in the typical adult case, lymph nodes were not felt in those cases where mention was made of that fact. In a sixty-seven-year-old man a 1- to 2-fingerbreadth liver was palpated. In the remainder of the cases no liver enlargement was noted. X-ray films showed that 6 of 9 cases had evidence of bone disease. This is a somewhat higher percentage than is found in the more "typical" cases with enlarged spleens. Anemia was present in 7 of the cases, validating other mechanisms than hypersplenism in the anemia of Gaucher's disease. The bone-marrow aspiration revealed the pathognomonic cells in each case. Bone pain was noted in 5 cases. One case was examined at autopsy and had a normal spleen grossly, but microscopic evidence of Gaucher cells was found.[17]

It would seem that the "asplenomegalic" form of Gaucher's disease is probably a milder form of the malady, compatible with long life and relative freedom from the incapacitating symptoms of splenic enlargement. It may represent a milder enzyme defect than the classic variety.

Radiologic aspects

The radiographic findings are quite varied in Gaucher's disease. With infants and children a bone survey may show entirely negative findings.[56] Osteoporosis is commonly seen.[19] There may be destruction of the finer bone trabeculas, with a distortion and irregularity of the remaining trabeculas. This leads to a "moth-eaten" or a "soap bubble" appearance of the bones. Localized osteolytic lesions due to the destruction of bone trabeculas by proliferating Gaucher cells are seen.[49]

An expansion of the medullary cavity is a frequent finding, often with a thinning of the cortex. The inner border of the cortex may show irregular notching, "endosteal scalloping." Endosteal scalloping is not specific in Gaucher's disease, since it is seen in a number of other conditions affecting the marrow cavity, like multiple myeloma. Due to the infiltration of the medullary cavity, Erlenmeyer flask expansion of the lower femur is often noted. The expansion is often first noted along the medial aspect of the lower femur, causing a loss of the normal concavity above the medial condyle (Fischer's sign).[56-58] The flask deformity has been seen in hyperthyroidism, Pyle's disease, marble bones, and leukemia.[49] Expansion may occur in the humerus, tibia, fibula, radius, ulna, or clavicle. The skull rarely manifests roentgen changes, but Reed and Sosman[57] reported a case where the skull showed a fine punctate appearance.

Intermingled with areas of rarefaction may be irregular sclerotic changes. Bands of new ossification may form in the medullary cavity, paralleling the inner aspect of the cortex but separated from it by a thin translucent zone. This has been called "bone within bone."[59] Periosteal reaction is uncommon but occurs and does not appear to represent periostitis.[49] Gaucher cells do not invade the periosteum. Pathologic fractures are found frequently and most often in weight-bearing bones. A collapse of several vertebrae may lead to a gibbous deformity, and hip fractures may also lead to deformity.[60,61]

Aseptic necrosis can occur in the heads of the femur and humerus, presumably owing to such a massive infiltration of capillaries and small arteries as to lead to a considerable reduction in the blood flow.[60,61] In children the changes in the femoral head may resemble those of Legg-Calvé-Perthe's syndrome.[60-62] A mushrooming of the femoral heads, a widening and shortening of the femoral necks, a coxa vara deformity, sclerosis, and areas of lucency can occur in both conditions. In later life severe osteoarthritis may result. Findings in the lungs have been described and may resemble a large area of pneumonic infiltration or have a miliary appearance.[63] However, lung infiltration by Gaucher cells is extremely rare.

Radiographic findings in our case included a moderate degree of osteoporosis with a slight distortion of the bony trabeculas. No lytic or sclerotic changes were seen. The medullary cavities were expanded, especially in the femurs and the short bones of the hand. There was a slight endosteal scalloping of the femurs. In the midthoracic spine there were several partially collapsed vertebrae. The lineae aspera in both femurs were very prominent (Fig. 2).

Diagnosis

Since the onset of Gaucher's disease may be mild and insidious, the disease may be undetected for a considerable time. In a patient with marked splenomegaly, hepatomegaly, absence of signs of hepatic decompensation, skin pigmentation, and pingueculas the diagnosis is evident clinically. Bone-marrow aspiration and bone biopsy are the simplest and surest ways of demonstrating the Gaucher cells. However, several cases have been reported where bone marrow aspirations were unsuccessful in establishing the diagnosis. A splenic puncture may give diagnostic tissue but is not without danger in thrombocytopenic patients. Liver biopsy has been successful at times in demonstrating Gaucher cells.

In a patient with bone pain, a radiographic examination may give the first clue to the diagnosis. The Erlenmeyer flask deformity and the other bone changes may suggest the presence of Gaucher's disease.

Differential diagnosis

The symptoms and signs in Gaucher's disease can simulate many different clinical entities. Gaucher's disease should be considered in the differential diagnosis of: (1) hepatosplenomegaly, (2) bone pain with fever, (3) diffuse osteoporosis,[19] (4) pancytopenia, (5) lymph node enlargement, and (6) skin pigmentation. The infantile form of the disease with neurologic manifestations must be differentiated from Tay-Sach's disease and Niemann-Pick's disease.

Treatment

There is no specific therapy for Gaucher's disease. Treatment is merely symptomatic and supportive. Hypersplenism and the mechanical effect of a huge spleen may necessitate splenectomy.[64,65] The blood count usually returns toward normal following the removal of the large spleen. Anemia has

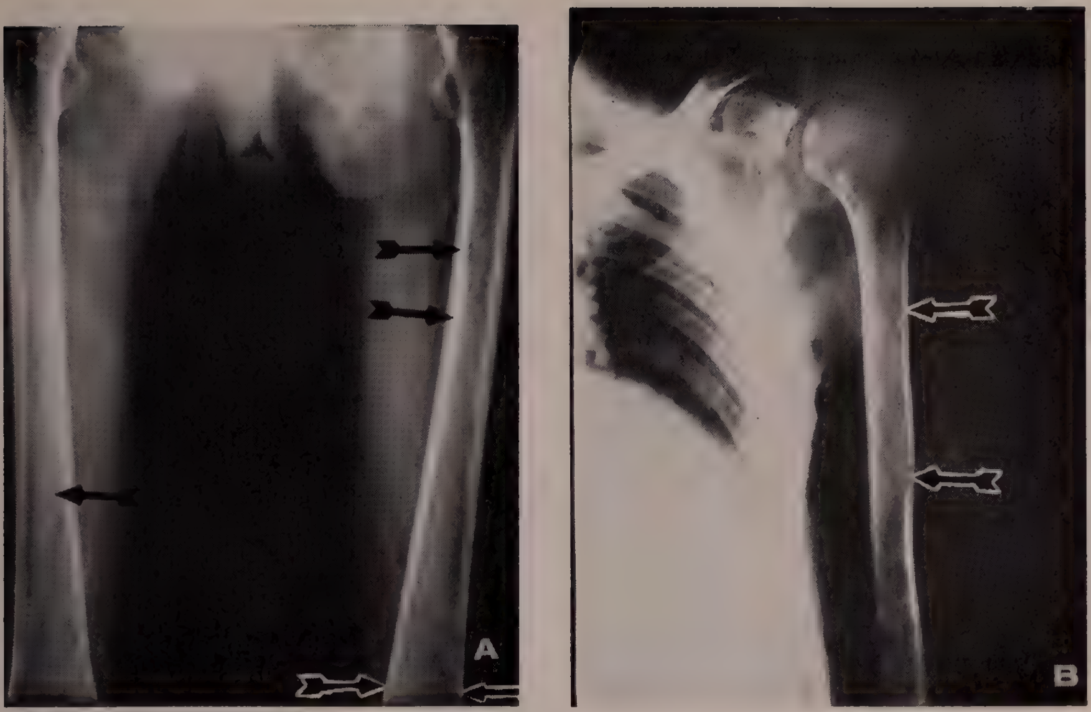

FIGURE 2. (A) Views of both femurs showing osteoporosis with loss of trabeculas. There is widening of medullary cavity with thinning of cortex (lowest arrows). Slight endosteal scalloping is evident (upper arrows). Linea aspera (arrow at right) is more prominent than usual due to osteoporosis and should not be confused with "bone within bone" appearance which is actual sclerosis within marrow cavity. (B) Humerus showing osteoporosis with widening of medullary cavity and thinning of cortex.

been reported to recur following the initial improvement after splenectomy in some cases. The white blood count and the platelet count usually remain at normal levels following splenectomy.[65] X-ray therapy has been successful in relieving excruciating bone pain, but it is of little value in the treatment of hypersplenism. Steroids have proved of some use in the treatment of bone pain but have no influence on the basic disease process. Anemia may be treated by transfusions when necessary.

Summary

We have presented a case of an eighty-six-year-old man with Gaucher's disease, the oldest reported case in the literature. The case was of interest in that the patient did not show most of the usual signs and symptoms and did not have splenomegaly.

Only 8 other cases of asplenomegalic Gaucher's disease were revealed by an intensive review of the literature. These patients had a milder course and were older than most Gaucher's disease patients. This group of cases may represent a milder type of Gaucher's disease, probably owing to a quantitative difference in the enzyme disturbance. In addition, the literature has been reviewed and summarized from historic, clinical, pathologic, radiologic, and pathogenetic aspects.

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Emergency Care of Digital Injuries

IN THE EMERGENCY CARE *of digital injuries an accurate assessment of the extent of damage and sound wound management are essential. Extensor tendon lacerations usually can be treated successfully with a primary suture; however, flexor tendon repair is best accomplished as a delayed procedure. Nerve and tendon repairs are delayed until the fracture is healed. Fractures are splinted with the finger in flexion to avoid permanent stiffness.*

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INJURIES OF THE FINGERS are among the most frequently encountered traumatic problems that come under the care of the physician. Such injuries may range from minor lacerations to extensive wounds involving skin, tendon, nerve, and bone. An accurate evaluation of the extent of the damage and adequate emergency treatment is essential in all instances. Poorly conducted emergency care may lead to unnecessary permanent disability in the hand.

The purpose of this paper is to outline the basic principles of emergency care of finger injuries. Stress will be laid on technics that can be utilized sucessfully by the individual whose primary interest does not lie in surgery of the hand. More advanced methods of tendon and nerve suture will not be considered.

Evaluation of the extent of damage

All digital injuries deserve a thorough examination. Small lacerations may produce great functional damage, severing a nerve, artery, or tendon. Large skin wounds may be accompanied by remarkably little or no injury to vital structures.[1]

A thorough examination of a digital injury requires an evaluation of the nerve and blood supply of the finger in addition to tendon function and skeletal integrity. The examination is carried out before anesthesia is given. Arteries and nerves are closely related in the digits (Fig. 1). Each digit has two digital arteries and two nerves. These course volarward on either side of the skeleton of the finger. The nerve function is checked by testing for the ability to perceive a pinprick on both the radial and the ulnar aspects of the volar surface of the finger.

The blood supply to the finger is evaluated by observing color return after compressing the pulp of the finger. The severance of one digital artery will not compromise the function of the finger. Laceration of both digital arteries, however, is catastrophic and should be confirmed by an exploration of the wound. If both vessels are interrupted, the digit is best amputated.

Tendon function in the digit is checked by two simple tests. The patient is asked to flex voluntarily the distal phalanx to evaluate the flexor tendon complex. An inability to flex the distal phalanx identifies an interruption of the profundus tendon. If distal phalanx flexion is absent, the voluntary flexion of the proximal interphalangeal joint is next examined to determine if the sublimis tendon is intact.

Although finger extension is the result of a complicated interplay between the long extensor tendon and the intrinsic muscles, severance of the extensor complex in the finger may be recognized by the inability of the

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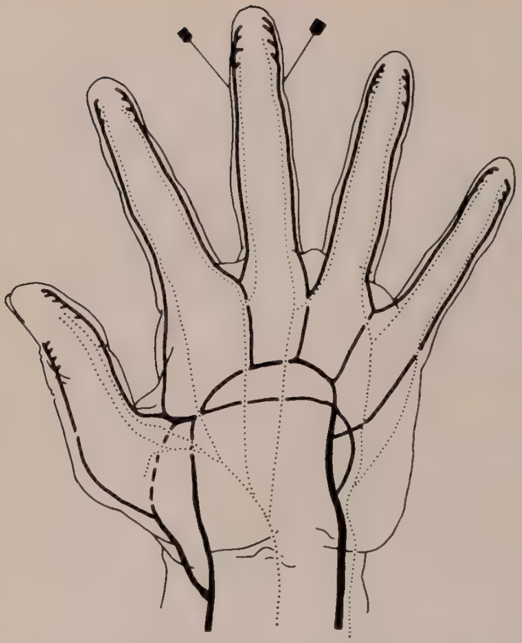

FIGURE 1. This schematic drawing depicts the basic pattern of digital vascular and nerve supply. Digital arteries are represented as solid black lines, digital nerves as dotted black lines. Each digit has two nerves and two arteries. Two needles are drawn touching ulnar and radial aspects of the long finger to stress the necessity for a complete sensory check to evaluate digital nerve integrity. Note that the digital artery and nerve are closely related. A laceration of one usually involves the other.

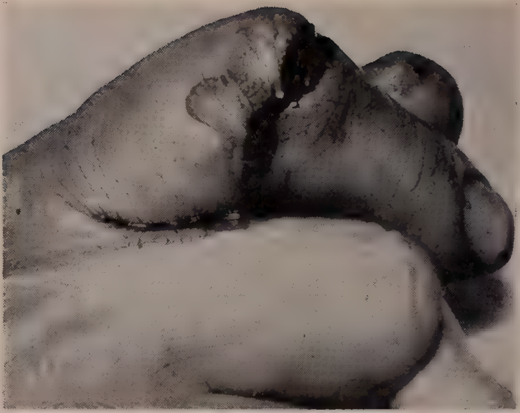

FIGURE 2. The extensor tendon mechanism of the index finger of this thirty-five-year-old male was lacerated with a band saw. The patient was unable to extend the proximal interphalangeal joint. Inability to extend a finger joint completely signifies damage to the extensor complex. Intermetacarpal block anesthesia permitted a single tendon suture in the operating room. After three weeks of immobilization with the finger slightly flexed, tendon union was sound, and full function was regained rapidly.

patient to extend the finger joint immediately distal to the wound[2] (Fig. 2).

Skeletal damage to a digit can be properly evaluated only with x-ray studies. Minor fractures may easily be overlooked clinically. The careful physician obtains a radiograph of every injured finger.

Wound management

Good wound care requires adequate anesthesia. The type of anesthesia to be employed varies with the patient and the wound. In general, the author uses general anesthesia in severe injuries in children and adults and when definitive tendon or nerve surgery is contemplated. The great majority of digital injuries, however, are not so extensive and can be managed in a highly satisfactory manner with an intrametacarpal nerve block.

The intrametacarpal block can be performed easily with a minimum of experience (Fig. 3). After the back of the hand has been scrubbed and then painted with antiseptic solution, a long number 22 needle is introduced under the skin of the dorsum of the hand over the distal third of the metacarpal. Two cc. of 2 per cent lidocaine hydrochloride (Xylocaine hydrochloride) or procaine hydrochloride is deposited as a subcutaneous wheal. The needle is then passed palmward to one side of the metacarpal of the involved finger. A small amount of anesthetic agent is injected as the needle passes through the intermetacarpal space. When the needle point can be felt just under the skin of the palm, an additional 2 cc. of anesthetic agent is deposited. The needle is then withdrawn, and the injection is repeated on the other side of the metacarpal. Using a 2 per cent anesthetic solution, a profound anesthesia of the finger will be obtained in about ten minutes.

The ten-minute time interval from the injection to the development of anesthesia is employed to prepare and drape the hand. The entire hand is washed thoroughly with hexachlorophene soap (pHisoHex) and running tap water, or, if the patient is reclining,

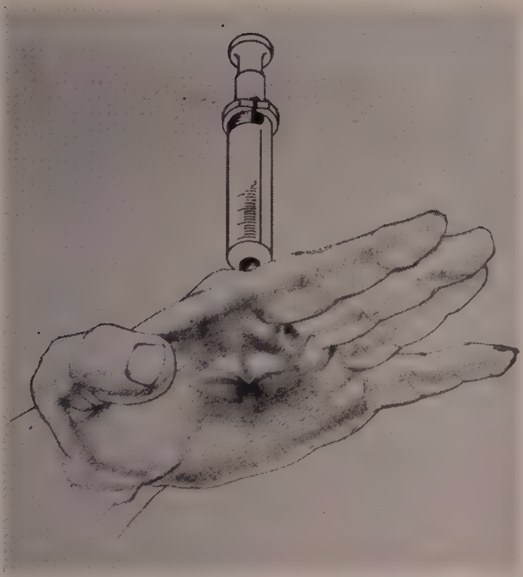

FIGURE 3. The intermetacarpal block is a highly satisfactory form of anesthesia for digital surgery. A wheal of 2 per cent lidocaine hydrochloride or Novocain is raised over the dorsum of the hand. A number 22 hypodermic needle is then passed to one side of the metacarpal of the involved finger. As the needle advances toward the palm, a small amount of anesthetic agent is injected. When the needle can be felt to protrude under the palmar skin, an additional 2 cc. of anesthetic solution is deposited. The needle is then withdrawn and the injection repeated to the other side of the metacarpal. The use of a 2 per cent concentration of anesthetic agent produces profound digital anesthesia in about ten minutes.

with normal saline and hexachlorophene soap. Tetanus prophylaxis and antibiotics are given at this time when they are indicated.

The hand is then draped, and the wound is explored for foreign material and flushed with normal saline. Grossly contaminated or devitalized tissue is removed. Hemostasis is secured with free ties of 4-0 plain catgut. Badly contaminated wounds are left open, and closure is carried out four to five days later.

If the wound is not grossly contaminated, primary closure is performed. The skin is approximated with interrupted sutures of 4-0 black silk. If the wound edges cannot be approximated, some form of skin graft is necessary. If bone, tendon, or nerve are not exposed, a split-thickness graft is adequate. In digital wounds one usually can obtain enough skin from the volar surface of the forearm with a long, single-edged razor blade. The graft can be taken with general or local anesthesia. The technic is not hard to master if one is careful to exert light pressure on the blade which is kept flat against the skin surface.

The exposure of nerve, tendon, or bone requires a full-thickness pedicle skin graft. Cross-finger, thenar, or abdominal pedicle flaps require considerable experience to employ and in the author's experience are rarely indicated. A local rotation pedicle, on the other hand, is simpler to perform and gives highly satisfactory results. An example of this procedure is shown in Figure 4. A sharp knife blade produced the injury to the ulnar aspect of the little finger. Skin, soft tissue, and digital nerve were sliced away, leaving the flexor tendon mechanism and digital nerve ends exposed. The wound was closed by elevating a flap of skin from the dorsum of the finger and rotating it around to cover the wound. The defect created over the dorsum of the finger was closed with a split-thickness graft obtained from the forearm. Wound healing occurred promptly. Three weeks later a free nerve graft was used to bridge the two nerve ends. The ultimate end result was excellent.

While the majority of digital injuries deserve an attempt at surgical repair, an occasional finger will have both digital arteries severed or be so extensively damaged as to require amputation. As a general rule, the surgeon should preserve as much digital length as will permit skin closure over the end of the stump (Fig. 5). Conservatism is especially warranted if multiple fingers are involved. In such instances a badly damaged finger may serve as a priceless source of skin or nerve in the later reconstruction of a companion digit.

Fingertip injuries

The fingertip is primarily an organ of sensation. The management of injuries to the fingertip should have as its goal the preservation of as much sensitive volar skin as possible. If the entire volar pad of skin is lost, the finger is simply amputated proximally enough to allow skin closure over the stump.

If sensitive volar skin remains over the tip,

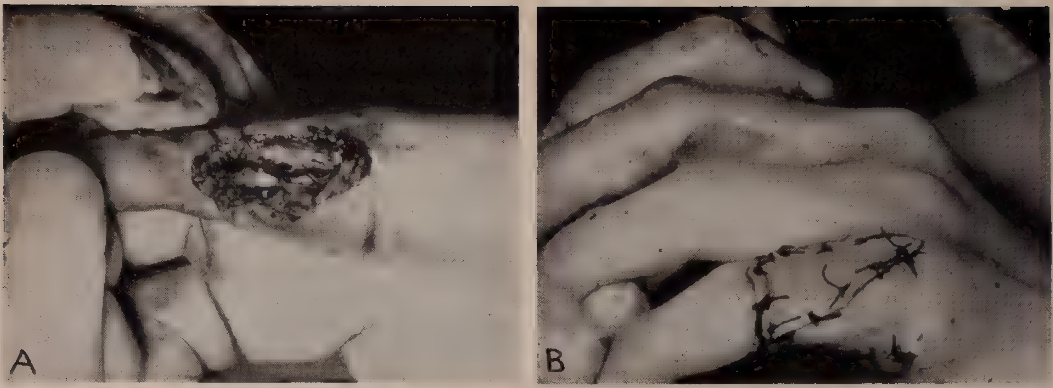

FIGURE 4. (A) Careless use of a sharp knife by this sixteen-year-old male resulted in a block excision of skin, soft tissue, and a segment of the digital nerve along the ulnar border of the little finger. The flexor tendon mechanism is evident in the depths of the wound. A split-thickness graft would not be adequate for coverage and would not allow later nerve repair. (B) The wound defect was covered by elevating a full-thickness pedicle flap from the dorsum of the finger and rotating it around the side of the digit. The surgically created defect on the dorsum of the finger was covered with a split-thickness graft. Known as a local rotation pedicle flap, this procedure is much easier to carry out than a cross-finger or abdominal flap, and, in the author's experience, is more satisfactory.

it should be preserved. Wound closure frequently may be accomplished by a simple closure of the wound edges or by the application of a small split-thickness skin graft (Fig. 5). If the bone of the distal phalanx is exposed in the wound, it is resected proximally enough to allow the closure of soft tissue over the end, and the graft is then applied. Pedicle flaps for fingertip injuries are rarely indicated and are probably best reserved for the hand surgeon.

Fractures of the distal phalanx frequently accompany fingertip wounds and are adequately splinted with a firm dressing. After the dressing is removed, a small aluminum splint is applied to protect the fingertip for three weeks after the injury.

Before leaving the subject of fingertip injuries, some reference should be made to the management of such problems in small children. Skin grafting rarely is necessary, and a conservative approach to surgery is strongly recommended. A simple suture or two and a firm dressing will produce remarkable results in many of the most severe injuries.

Tendon and nerve injuries

Experienced hand surgeons are reluctant to perform a primary suture of severed flexor tendons in the fingers.[3] Efforts to do so almost invariably are unsuccessful and may seriously handicap secondary repair.

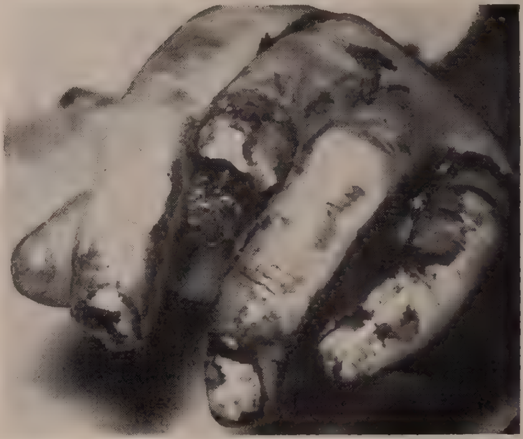

FIGURE 5. This forty-year-old carpenter caught his left hand in a milling machine. The index fingertip has been partly amputated. The long finger has been amputated at the proximal interphalangeal joint, and there are compound fractures of ring and little fingers. The index fingertip was closed with a small split-thickness graft obtained from the forearm with a razor blade. The bony stump of the long finger was resected a slight amount to permit skin closure. The compound fractures of ring and little fingers were managed by cleansing and primary closure of the wounds. After closed reduction of the fractures, the digits were immobilized in flexion with aluminum splints incorporated into a short arm plaster cast.

A much higher percentage of satisfactory results can be obtained by initial simple wound closure. After the skin and underlying soft tissues are healed, secondary repair of the tendon may be carried out with greatly increased chances for success.

In the adult patient, severance of both the profundus and the sublimis tendons is best managed by resecting the sublimis and replacing the lacerated segment of the profundus tendon with a free tendon graft that extends from the palm to the fingertip. By inserting the graft, the necessity for tendon suture within the tendon sheath is obviated, and incapacitating adhesions are avoided. In those instances in which the laceration of the profundus tendon occurs distal to the midportion of the middle phalanx, a free graft is not necessary, and the proximal stump of the tendon can be advanced to insert into the distal phalanx. If the profundus only is injured and the sublimis tendon is intact, experienced surgeons usually do not attempt profundus tendon repair but elect to fuse the distal joint of the finger or to suture the distal stump of the profundus to the middle phalanx to provide stability to the fingertip.

Free tendon grafts in children are not as successful as those in adults, and injuries to flexor tendons are best treated by primary wound closure to be followed by delayed tendon suture several weeks after. When delayed suture is carried out, the sublimis and a portion of the flexor tendon sheath are resected to minimize adhesion formation.

Extensor tendon injuries, in contrast to those of flexor tendons, give good results with primary repair. On the other hand, primary suture should be done only in the clean wound that may be expected to heal without incident. If primary healing is doubtful, tendon suture is delayed. In most instances surgical repair is best accomplished in the operating room. The tendon ends are brought together with 3-0 black silk. In the usual case only one horizontal mattress suture is necessary. Postoperatively the digit is splinted for three weeks in a position of slight flexion of all of the joints of the finger. A volar aluminum splint incorporated into a short plaster cast on the arm gives satisfactory immobilization (Fig. 5).

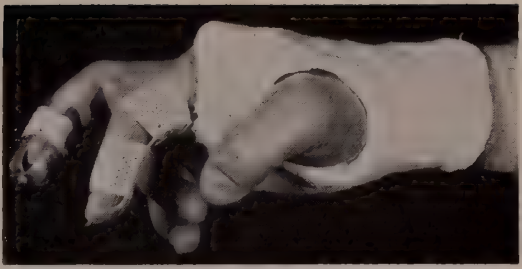

FIGURE 6. Two technics are illustrated here. The index finger has been immobilized on an aluminum splint which has been incorporated into a short cast for fixation. Note the flexed position of the finger which is essential to prevent stiffness. The finger is held to the splint with two Band-Aids. A small aluminum splint has been applied over the tip of the long finger and is held in place with adhesive. This splint provides satisfactory immobilization for a fracture of the distal phalanx.

The primary suture of digital nerves may be highly successful if the wound heals by first intention and if the suture is done with skill. In the average case of digital nerve injury, however, the safest course is to perform nerve suture several weeks after the initial wound has healed to minimize the risk of a complicating wound infection. Neither a tendon nor a nerve suture should be considered until fractures have healed or until good skin coverage has been gained. If nerve and tendons are both severed, nerve suture should be delayed until the time of definitive tendon repair.

Fractures and dislocations

Compound fractures and dislocations are managed by the usual technics of wound closure followed by an adequate period of immobilization. Nerve and tendon repairs are delayed until the fracture is healed.

An intermetacarpal block is a highly satisfactory anesthetic for the reduction of fractures or dislocations. After the reduction check x-ray films are obtained, and the digit is immobilized for three weeks on an aluminum splint corporated into a short plaster cast on the arm (Fig. 6). It is essential that the finger be immobilized in a flexed position to avoid prolonged joint stiffness. Traction to the finger in the splint is rarely necessary, and when employed, may produce considerable stiffness.

Multiple finger fractures may be managed with several aluminum finger splints incorporated into a cast or by immobilizing the entire hand with a molded plaster splint. The hand and fingers are placed in the position they would assume in grasping a large orange.

Summary

Good emergency care to digital injuries requires an accurate assessment of the extent of the damage and sound wound management.

While extensor tendon lacerations usually can be treated successfully with a primary suture, flexor tendon repair is best accomplished as a delayed procedure.

Both tendon and nerve repair must await fracture healing. Fractures are splinted with the finger in flexion to avoid permanent stiffness to the finger.

150 MARSHALL STREET

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Some children resist respiratory bacteria

A significant number of children are able to resist some respiratory germs they are exposed to in their homes, according to a study by Henry Stimson Harvey, M.D., and Marjorie Bodwell Dunlap, M.A., reported in the June, 1962, issue of the *American Journal of Diseases of Children.* The finding indicates that other factors besides exposure are involved in the acquisition of respiratory organisms.

A total of 351 children from 94 healthy families living in rural communities were studied for periods of from one to two years to determine the incidence of three bacteria: hemolytic streptococcus, hemophilus influenzae, and pneumococcus.

Between birth and one or two years, children carried large amounts of the influenza and pneumonia germs but very little streptococcus. Children entering the two- to six-year-old period frequently carried all three organisms. The peak incidence of streptococcal infections came in the early school period, while all three organisms gradually decreased after the age of twelve years.

Within this general pattern, there were wide individual differences, particularly in the occurrence of streptococcus, which was not found in all individuals in the susceptible age period, between babyhood and the twelfth birthday.

Thirty-six per cent of the children from one to six years old and 26 per cent of those from six to twelve did not acquire the hemolytic streptococcus even though it was present in their homes. Of those who did acquire it, 60 per cent in the susceptible age groups had it less frequently than would be anticipated from the exposure rates.

More than one third of 910 streptococcal infections were not shared by members of the same family at the same time. Whether this resistance was due to a previously acquired immunity to the particular type involved, to some genetic characteristic of the individual, or to some temporary condition cannot be explained without further investigation.

Operative and Nonoperative Treatment of Bleeding Esophageal Varices*

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IN 21 PATIENTS *with cirrhosis and major bleeding from esophageal varices who were treated by a shunting operation, 76.1 per cent were alive after one year, 57.1 per cent after two years, and 47.6 per cent after three years. Of 21 comparable patients who were treated medically, 38 per cent were alive after one year, 28.5 per cent after two years, and 14.3 per cent after three years. An additional experience with 4 patients suggests that prophylactic shunts may reduce the incidence of early death due to hemorrhage secondary to esophageal varices.*

HEMORRHAGE is the direct cause of death in a high percentage of patients with cirrhosis and varices. Even in the cases in which bleeding is controlled by tamponade and transfusions, liver failure, caused by the hemorrhage, often results in the death of the patient.

In a review of the records of 97 patients admitted to our hospital with bleeding esophageal varices, it was found that 40 (41.2 per cent) died as the result of the patient's first major hemorrhage. It is important to note, however, that if the patients are divided into two groups, one with ascites and the other without ascites, there is a striking difference in the mortality rate. With ascites, 65.7 per cent of the 35 patients died with the first major hemorrhage, while only 27.4 per cent of the 62 patients who did not have ascites succumbed. In both groups the mortality with bleeding is such that some procedure to reduce the incidence of hemorrhage is needed.

Proponents of shunting operations believe that a fistula which reduces the portal pressure to a nearly normal level gives a high degree of protection against future hemorrhage and hence increases a patient's life expectancy.[2-9] Voorhees,[10] in reporting on the large experience at Presbyterian Hospital in New York City, states that 90 per cent of those patients who recover from a portacaval shunt should survive more than one year and that 60 per cent should still be alive for as long as six years after a successful operation.

However, there are skeptics[11,12] who doubt that the prognosis of a patient with cirrhosis and portal hypertension is altered by an operation which shunts blood around the liver. This point of view has recently been presented by Baker, Smith, and Lieberman.[13] In a study of 115 cirrhotic patients in whom varices were diagnosed prior to bleeding, they noted that only 9.5 per cent died with the first hemorrhage. Therefore it was concluded that, since this figure approximated the reported operative mortality, there was nothing to be gained by a prophylactic shunt. Cohn and Blaisdell[14] reported a study of 40 patients with cirrhosis who had recovered from a major hemorrhage and were acceptable for portacaval anastomosis but, who were not operated on. They concluded that 30 per cent of such patients will survive five years on medical therapy alone.

It is difficult to find reports of comparable

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[*] Based on an article published previously,[1] with an additional follow-up.

cases treated by shunts or by medical therapy and followed for a significant period of time. It is for this reason that we report our experience with 42 patients. They represent less than 50 per cent of a total group of 97 patients with cirrhosis and major bleeding from esophageal varices, who were seen over a period of twelve years at St. Luke's Hospital in New York City. Subsequent to the serious hemorrhage, each of the 42 patients was evaluated and declared to be a satisfactory risk for operation. Each patient had a serum albumin level of 3 Gm. or more per 100 ml., a bilirubin of less than 1.5 mg. per 100 ml., a bromsulphalein retention of under 20 per cent in forty-five minutes, a prothrombin time of 60 per cent or more, and a cephalin flocculation of not more than 2 plus.

Insofar as it was possible to determine, the patients were comparable for the purposes of evaluating different types of treatment. One half of the patients were subjected to a venous shunt, and one half were treated conservatively. The remaining 55 patients were not included in this evaluation because: (1) they died before hemorrhage could be controlled (40 patients); (2) they were poor operative risks by the criteria stated previously (10 patients); or (3) they were lost to follow-up study (5 patients).

Nonoperative treatment

Because of skepticism regarding the value of a shunt, 21 of the 42 patients were continued on a medical regimen. The results of this nonoperative treatment are shown in Figure 1. Thirteen of the 21 patients died within one year of the first major hemorrhage. Thus, only 8 (38 per cent) of the 21 patients survived more than one year. Another 2 patients died in the second year, leaving 6 (28.5 per cent) two-year survivors. In the third year, 3 more patients died. Thus, the three-year survivors numbered 3 (14.3 per cent).

Operative treatment

Nineteen patients were treated by a portacaval shunt and 2 by a splenorenal anastomosis, with the hope that operation would give protection against another hemorrhage and thus prolong life. There were 2 operative deaths, and another 3 patients died within one year of operation. As illustrated in Figure 1, 16 (76.1 per cent) of the 21 patients survived more than one year. Four patients died in the second postoperative year, leaving 12 (57.1 per cent) of the 21 patients alive at the end of two years. In the third year, 1 patient died, and another was lost to follow-up. Thus, the three-year survivors numbered 10 (47.6 per cent).

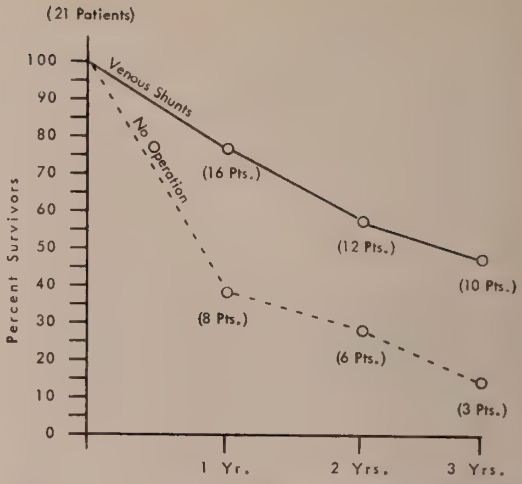

FIGURE 1. Results of venous shunts and medical therapy in comparable cases of cirrhosis with bleeding varices.

Prophylactic shunts

In addition to the recorded 21 patients who were treated by a shunt after their recovery from hemorrhage, we have had the opportunity to establish shunts in 4 relatively good-risk patients with demonstrable varices, but no history of bleeding. In these patients the shunt was made in an attempt to prevent, or at least delay, death by hemorrhage. All have remained well: 1 patient for five years, 2 patients for three years, and 1 patient for two years.

Summary

Forty-seven per cent of 21 patients with cirrhosis and bleeding esophageal varices, who were treated by a shunting operation, survived three or more years, while only 14 per cent of 21 comparable cases, who were treated

medically, were alive at the end of three years.

An experience with 4 patients suggests that prophylactic shunts may reduce the incidence of early death due to hemorrhage secondary to esophageal varices.

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Electroencephalographic patterns in allergic children

Although electroencephalographic deviations have been reported in allergic children since 1944 by some investigators, others have found tracings in such children within normal limits, according to an article by William M. Fowler, M.D., and associates, in the January, 1962, issue of *Annals of Allergy*. Except in a single instance, no attempt apparently has been made to establish a causal relationship between allergy and convulsive seizures by deliberate challenge of the subject with an allergen.

This study was undertaken (1) to compare the electroencephalograms of children with respiratory allergy with those of children with behavior problems as well as with a control group with chronic disease alone and (2) to record electroencephalograms in children with respiratory allergy plus seizures and children with respiratory allergy alone when challenged with their offending inhalant allergen.

All of the experimental groups had an incidence of electroencephalograms with abnormal findings significantly higher than the controls (children with congenital heart disease) and higher than estimates of the incidence in the general population.

Among the children challenged with their offending allergen during electroencephalogram recordings, the allergy plus seizure group did not demonstrate any electroencephalographic response to such challenge, although 2 showed exacerbations to saline challenge and 5 to allergen challenge. In the group with allergy alone (23 children), 14 showed exacerbations of allergic symptoms on allergen challenge.

Experience with Fluorinated Pyrimidines in Adenocarcinoma of the Lower Intestinal Tract*

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THE CLINICAL EFFECTS of the fluorinated pyrimidines have been investigated extensively since the synthesis of 5-FU (5-fluorouracil) by Heidelberger *et al.*[1] and Duschinsky, Pleven, and Heidelberger.[2] The initial clinical trials of this compound by McIver *et al.*[3] followed a demonstration of the antitumor and antileukemic effect of 5-FU in mice.[1,4] Although there has been further study of the effects of 5-FU as well as of three related pyrimidine analogs, FO (5-fluoro-orotic acid), FUR (5-fluorouridine), and FUDR (5-fluoro 2′-deoxyuridine) in animal tumors, only 5-FU[3,5-15] and FUDR[12,16-27] have had extensive clinical trial.

Mechanism of action of 5-FU and FUDR

5-FU is an antimetabolite which is thought to affect cell metabolism in at least three ways: (1) by preventing the methylation reaction mediated by thymidylate synthetase which converts deoxyuridylic acid to thymidylic acid, thus interfering with the synthesis of DNA (deoxyribose nucleic acid), (2) by incorporation to a small extent into RNA (ribose nucleic acid) to produce a fraudulent RNA, and (3) by the inhibition of the synthesis of RNA.[28-32] The first of these three actions may be the most important in producing the antitumor effect, since it is the only demonstrable direct inhibitory action of FUDR, the deoxyriboside of 5-FU.[31,32]

Although FUDR has been shown to be much more potent than 5-FU in isolated systems, such as the chick embryo,[33] the sand-dollar embryo,[33-35] human tumor cells in vitro,[36] and some bacteria,[31] this difference has not been noted in experimental animals.[13] In addition, little difference has been found between the dose of 5-FU and FUDR in man on a molar basis.[16-27] When FUDR is given as a single intravenous dose, it is probably rapidly cleaved to 5-FU,[37] accounting for the similarity in action of the two drugs. When the method of administration of the two drugs is changed to a continuous intravenous drip twenty-four hours a day for several days, a dosage difference between the two has been observed.[38] There is a considerable decrease in the toxicity of 5-FU with 15 mg. per kilogram per day tolerated for as long as thirty-seven days (instead of the usual five to seven days) and 35 mg. per kilogram per day for nine days. On the other hand, when FUDR is administered in this fashion, toxicity increases, with doses of 0.75 to 3 mg. per kilogram per day producing toxicity in seven days.

Dose

The dose of 5-FU is based on the patient's actual weight with the ideal weight used, however, if the patient is obese. Ansfield and Curreri and their associates[5,6,8,9] have divided their patients into categories of "average risk" and "poor risk," and the

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dose depends on the type of patient. The average-risk patients are those with reasonably good nutrition, adequate marrow function, and relatively adequate liver function. In these patients the course of therapy recommended consists of 15 mg. per kilogram intravenously daily for five successive days. They also recommend that the dose of 5-FU used not exceed 1 Gm. per day. If no toxicity is then observed after forty-eight hours of observation, 7.5 mg. per kilogram may be given on alternate days until toxicity is manifest. The poorer-risk patients as defined by Ansfield and Curreri are those with any one or more of the following: a poor nutritional state, cachexia, marked protein loss, a history of wide pelvic irradiation, a history of therapy with alkylating agents, widespread involvement of bone marrow by metastatic tumor, extensive liver impairment with jaundice, or major surgery within the past thirty days. In this situation the daily dose of 15 mg. per kilogram is given for only three successive days followed by a single dose of 7.5 mg. per kilogram on the fifth day. In both types of patients a course of therapy may be repeated thirty days after the last dose.

We have noted a similar rough division of patients into average- and poor-risk groups.[12,24,27] However, we have seen a wide range of tolerated doses (range of toxic dose from 30 to 150 mg. per kilogram; average 90 mg. per kilogram), and there are occasional exceptions to the division into average and poor risk with some of the first group tolerating less of the drug and some of the second tolerating a longer course of therapy. At the present time, therefore, we have reduced our standard dose of 5-FU to 15 mg. per kilogram daily for only three successive days, followed by 7.5 mg. per kilogram given on alternate days to the point of toxicity. The dosage has to be watched quite carefully and must be individualized with daily checks on the white blood cell count and twice-weekly checks on the platelet count, as well as a daily examination of the patient's mouth and queries as to the occurrence of diarrhea.

The course of therapy with FUDR has been found to be like that outlined for 5-FU except that the daily dose is doubled, that is 30 mg. per kilogram daily for five days followed by 15 mg. per kilogram on alternate days until toxicity occurs.[16–27] Ansfield and Curreri again warn of the need to characterize the patients as good or poor risks and recommend giving the poor-risk patient only four doses of 30 mg. per kilogram with one or two additional doses of 15 mg. per kilogram. Again, however, we have noted a wide variation in the sensitivity of the patient to medication, with this variation not always related to the patient's general status, previous therapy, and so forth. In our experience, toxicity to FUDR has followed a total dose of from 120 to 345 mg. per kilogram (average 190 mg. per kilogram).

WHEN *5-FU (5-fluorouracil) and FUDR (5-fluoro 2′-deoxyuridine) are used in the treatment of adenocarcinoma of the lower intestinal tract, the dose is based on the patient's weight and the classification of the patient as average or poor risk. The chief drug effects are noted in the hematopoietic and gastrointestinal systems. The severity of these two types of toxicity is not necessarily correlated. Approximately 5 per cent of patients with various solid tumors treated with 5-FU or FUDR died of causes directly attributable to severe drug toxicity, and 5 to 10 per cent developed life-threatening toxicity from which they recovered. Tumors which appeared most responsive to therapy were those of the colon and rectum in which occasional responses lasted for from four to eight months. However, improvement was obtained at the expense of some degree of toxicity, and a significant prolongation of life has not been demonstrated as a result of the use of these drugs. The response to therapy is related to primary site of the disease, morphologic type of cancer, extent of the tumor, and rate of progression of the disease. Patients with carcinoma of the colon or rectum with primarily local spread and those with intra-abdominal involvement appear to do better than those with obvious hepatic metastases.*

Toxicity

The chief drug effects are noted in the hematopoietic and gastrointestinal systems.

The earliest signs of toxicity are often anorexia and stomatitis. Anorexia, nausea, and occasional vomiting can be tolerated and usually are not limiting side-effects. Stomatitis must be considered as a more serious evidence of toxicity and should occasion the cessation of the course of therapy. The stomatitis may consist only of oral mucosal erythema or may also include ulceration, especially on the inner margin of the lip. Diarrhea may occur either with stomatitis or occasionally without it. This diarrhea can become quite severe, and fluid replacement therapy may be required. While anorexia, vomiting, and nausea occur in about half the patients, stomatitis and diarrhea occur in about three-quarters. The 5-FU or FUDR administration should be stopped if stomatitis or diarrhea develops.

Leukocyte and platelet depression may start during the outlined course of therapy, or the onset may be delayed with maximum depression occurring about two weeks or more after the start of the drug administration. Abnormalities in the erythroid and granulocyte precursors have been seen in the marrow with megaloblastic changes in the nuclear pattern of the erythroid elements. An increase of the myeloid-erythroid ratios in the marrow has been noted.[28] The degree of such an increase appears to correlate well with the subsequent degree of leukopenia. The degree of the depression of the white blood cell count usually parallels that of the platelets.

The severity of the two types of toxicity are not necessarily correlated with one another. Both the gastrointestinal irritation and the hematopoietic depression seem to occur after smaller total doses in patients who receive repeated courses of therapy at brief intervals. If there is a month between the courses of therapy, the drug usually is tolerated to the same degree on the second course as on the first. Other less limiting toxic symptoms include occasional severe alopecia and dermatitis.

When patients with far-advanced cancer die during the course of therapy with toxic agents, it is often difficult to assess the role the drug has played in the death of the patient. The steps leading to the patient's death often involve the derangement of several organ systems, but occasionally at least the initial abnormality can be traced to drug administration. In one series of 155 patients with a variety of types of cancer treated with 5-FU there were 15 fatalities reported.[11] Nine of these occurred among 82 patients who had been rated as poor risks, and 6 occurred in 73 good-risk patients. It was noted that 10 of these instances were in patients with ulcerative neoplastic lesions of the skin or mucosa, obstructive uropathies, or blockage of the respiratory or intestinal passages, that is, in patients with increased portals of entry for infection. Of these 15 patients, 10 died with septicemia, 3 with acute bacterial pneumonia, and 2 with gastrointestinal hemorrhage. Among a group of patients with colon carcinoma studied at Memorial Hospital for Cancer and Allied Diseases, approximately the same incidence of patients died during a phase of life-threatening toxicity, although the over-all incidence of fatal toxicity in all types of patients treated was lower.[24] Approximately 5 per cent of the patients with various solid tumors treated by us with 5-FU or FUDR died of causes directly attributable to severe drug toxicity. Another 5 to 10 per cent of the patients treated by us developed life-threatening toxicity from which, however, they recovered.

Response to treatment

Objective evidence of improvement following the use of 5-FU or FUDR has been reported for a variety of tumors. Among the tumors which appeared most responsive was carcinoma of the colon and rectum. Some of the reported responses are summarized in Table I. When repeated courses of therapy were not given, the duration of improvement often was less than two months. With treatment repeated every month, however, occasional responses lasting for from four to eight months, or rarely longer, were noted. Despite the clinical benefit noted during the period of response, most observers do not feel that a significant prolongation of life has been demonstrated as a result of the use of these drugs.

Almost all of the improvement noted by

TABLE I. Summary of selected clinical reports on the response to 5-FU (5-fluorouracil) and FUDR (5-fluoro-2′-deoxyuridine) in carcinoma of the colon and rectum

Investigators	Therapy	Total Patients Treated	Adequate Therapy (Patients)	Number Improved
Ansfield and Curreri[8,21,26]	5-FU	115	. . .	18
	FUDR	39	. . .	18
Brennan and Vaitkevicius[11]	5-FU	45	. . .	3
Hurley and Ellison[15]	5-FU	29	20	12
Olson and Greene[14]	5-FU	12	. . .	1
Memorial Center and affiliates*	5-FU	107	87	10
	FUDR	47	43	3

* Includes cases treated at Memorial Hospital for Cancer and Allied Diseases, James Ewing, and Veterans Administration Hospitals, New York City; Kings County Hospital Center, Brooklyn, New York; and Albert Einstein Medical Center, Philadelphia, Pennsylvania.

TABLE II. FUDR (5-fluoro-2′-deoxyuridine) in carcinoma of colon and rectum; relationship of pattern and stage of disease to response

Stage	Pattern	Total Patients*	Number Improved
Clinical Stage 2	Local	9	2
	Hepatic	4	1
	Intra-abdominal	7	0
	Generalized	7	0
Clinical Stage 3		16	0

* Includes cases treated at Memorial Hospital for Cancer and Allied Diseases, James Ewing, and Veterans Administration Hospitals, New York City; and Kings County Hospital Center, Brooklyn, New York.

the various investigators was obtained at the expense of some degree of toxicity. The percentage of fatal toxic reactions as well as other severe reactions is high. It remains to be seen whether or not similar series of patients treated more conservatively in an attempt to avoid severe toxicity will respond comparably.

The reported response rate of carcinoma of the colon and rectum to 5-FU ranged from 8 per cent[14] to 41 per cent.[15] The evaluation of the effects of treatment may be extremely difficult, but this probably plays only a small role in explaining the difference. While the variation in results might reflect a lack of uniformity in the method of evaluation of the responses, this, too, may not be a major factor. All of the groups cited defined improvement as the objective regression of the disease accompanied by subjective benefit and increase in the performance status. In all instances this improvement had to persist for periods of from one to three months, that is, at least until another course of the drug could be given.

A larger portion of the variability probably depends on differences in the clinical status of the patients at the time they were treated. The response to therapy is undoubtedly related not only to the primary site of the disease and the morphologic type of cancer, but also to the extent of the tumor and the rate of progression of the disease.

Attempts have been made to delineate various clinical patterns of carcinoma of the large intestine.[24] A study of the records of a series of patients who had been seen for chemotherapy between 1952 and 1960 showed that each patient fell into one of four clinical patterns of progressive disease. The patterns of disease were described as local or pelvic, hepatic, intra-abdominal, and generalized. The clinical course within each pattern was then further subdivided into three stages of disease: early (Stage 1,) progressive compensated (Stage 2), and progressive decompensated (Stage 3).

We have applied this division into patterns as well as stages of the disease to evaluate the chemotherapeutic agents. This is illustrated by the results of FUDR (Table II).

It is our impression that patients with carcinoma of the colon or rectum with primarily local spread and those with intra-abdominal involvement do better than those with obvious hepatic metastases. The least responsive group included those patients with a generalized spread of the disease. In addition, the responses were noted only in patients with early or "progressive but compensated" disease, whereas those with "progressive decompensated" disease had no responses thought to be of therapeutic benefit. It seems possible that such an analysis of the patient material used for drug evaluation might explain the great difference between our results with

FUDR and those reported by Ansfield.[26] We have not seen a difference between the therapeutic effectiveness of 5-FU and FUDR such as they report.

The results to date definitely indicate that 5-FU and FUDR are active compounds able to suppress temporarily the growth of certain human neoplasms, notably adenocarcinomas of the intestinal tract, as well as those of the breast and ovary. However, the drugs apparently have a low therapeutic index, being regularly toxic at effective doses. Also, they appear to be of less value in the management of widespread, rapidly growing metastatic disease both because these patients seem to be benefited less and because they are apt to fall into the "poor risk" category and tolerate less drug. There are several approaches currently being studied which might make these agents more useful clinically. It is necessary to attempt systematic treatment with smaller, more slowly administered courses of therapy to see whether or not improvement will occur with tolerated doses of 5-FU. As noted earlier, we have reduced the standard dose of 5-FU given to 15 mg. per kilogram intravenously daily for only three successive days, followed by 7.5 mg. per kilogram on alternate days until the point of toxicity, and we are not treating patients with generalized rapidly progressive disease, impaired hematopoietic function, or debilitation. The use of oral 5-FU may add to the flexibility of treatment by giving a source of less rapidly accessible drug, similar to the slow intravenous drip, but the therapeutic effectiveness of this method of treatment is not yet known.[38] A preliminary clinical trial suggests, however, that there is great variation in tolerated doses, presumably due to variable absorption and/or intraintestinal destruction of the drug. Second, although the use of continuous intravenous administration of 5-FU or FUDR might not be expected to affect the therapeutic index, this variation is being studied. Studies on the combination of 5-FU and FUDR intra-arterially with the use of potentiating compounds regionally or antagonizing compounds systemically are under way.[39] Finally, carefully controlled studies of the effects of 5-FU combined with irradiation therapy must be continued to investigate the possibility of a synergistic effect.[40-42]

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Questionable value of round hospitals

Round hospitals may not be as efficient or practical as some designers have claimed, according to an article by Anthony J. J. Rourke, M.D., in the April 1, 1962, issue of *Hospitals*.

Two advantages are commonly cited for round hospitals: They are cheaper to construct, operate, heat, and ventilate because the exterior wall is shorter than that of a comparable square or rectangular hospital, and they are more efficient for nurses because of reduced walking distances and increased visual control of the patients' rooms.

Concerning construction costs, Dr. Rourke said it is impossible to determine whether or not costs are different, since the method of bidding, the question of profit, and the timing of construction for each hospital varies. "However, many would agree that it is more costly to build a round hospital because of the need for special items and the labor of fitting." Practically all prefabricated, fixed, and movable equipment is either square or rectangular, which means "additional labor in trying to put square pegs into round holes."

As to nursing stations in the center of all activities, Dr. Rourke pointed out that "nursing care is a problem of bedside work in the room and that nursing administration, rather than nursing care, comes from the center." This is equally applicable to every nursing station, regardless of the geometric design of the hospital.

He also questioned whether circular units really save steps, since the corridor can only be "single-loaded" with rooms along only one side, whereas the rectangular single-corridor hospital may have "double-loaded corridors" with rooms on both sides of the hall, thus reducing the travel distance to the same number of beds.

Some other problems of circular hospitals cited by Dr. Rourke include: day room location, orientation, greater mixing of supplies, patients, and visitors in the circular corridor from core elevators than there is in the rectangular hospital, and expansion difficulties.

"Whether or not it is wise to rush into building circular hospitals will certainly remain a large question for all planners," Dr. Rourke said, urging that consideration be given to the viewpoints of physicians and nurses who will be using the hospitals.

Clinical Effectiveness of Potent Trichomonacide, Metronidazole

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THE EFFECTIVENESS *of a new trichomonacide, metronidazole (Flagyl), in the treatment of Trichomonas vaginalis was studied in 39 patients. Treatment consisted of one 250-mg. oral tablet twice daily and one 500-mg. vaginal insert daily for ten days. Thirty-seven patients were cured after the first course of therapy, 1 was cured after a second course of therapy, and the remaining patient still had symptoms after one course of therapy but was unavailable for a second course. Metronidazole appears to be specific in its action against T. vaginalis. Side-effects occurred in only 2 patients and consisted of rather severe nausea and vomiting and slight sedation.*

THE INCIDENCE OF trichomonal vaginitis has increased considerably in the United States during the past fifteen years. This is primarily owing to the fact that the normal acid reaction of the vagina is constantly being altered by contraceptive devices, by douching with a wide variety of agents, and by the more prevalent use of vaginal tampons to absorb menstrual fluid.

To control trichomonal infections a wide variety of powders, tablets, suppositories, salves, ointments, and creams and jellies for oral, vaginal, parenteral, and topical application, as well as various mechanical devices, have been placed at the disposal of the physician. That such a wide variety of preparations is available is unquestionably a reflection of the fact that no single product or device has been found entirely satisfactory by physicians for the control of Trichomonas vaginalis. As a matter of fact, every gynecologist is or has been faced with the problem of a patient who has been infected with the trichomonal organism for a number of years and who does not respond satisfactorily to any therapy.

Recently, however, reports from several investigators in France and England have shown that a new compound, a nitroimidazole, metronidazole (Flagyl),* has been developed which is highly trichomonacidal, orally active, safe to use, well tolerated by patients, and highly effective on a short course of therapy.[1,2] This compound was presented to me for clinical evaluation in August, 1960. I am pleased to offer the results of my observations.

Methods and procedures

Data are presented on 39 consecutive female patients from my private practice whose diagnoses of trichomonal infections were established by wet smears. These patients ranged in age from eighteen to sixty-six years, the mean age being 39.5 years. In each case, when the presence of the trichomonal organism had been confirmed, metronidazole therapy was instituted immediately. Without exception, each patient was instructed to employ one 250-mg. oral tablet twice daily and one 500-mg. vaginal insert daily for ten days. Following this therapy, the presence or absence of trichomonas was again confirmed by a wet smear, and a second course of metronidazole was given, if indicated.

These patients, except 2 who were asymptomatic, presented complaints of vaginal discharge, odor, itching, pain, bleeding, or a combination of these symptoms and had apparently been infected for periods of from five days to more than five years. Twelve of these 39 patients had been treated intravaginally prior to the institution of metronidazole therapy without success.

Patients were advised to avoid coitus as long as any discharge persisted and, of course,

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* Supplied by G. D. Searle & Co., Skokie, Illinois.

TABLE I. Data on treatment with metronidazole of 39 patients

Patient Number	Age (Years)	Results of First Course of Treatment	Number of Recurrences	Side-Effects
1	36	Cured	None	None
2	53	Cured	None	None
3	43	Cured	None	None
4	38	Not cured*	?	None
5	22	Cured	None	None
6	27	Cured	None	None
7	61	Cured	None	None
8	41	Cured	None	None
9	55	Cured	None	None
10	53	Cured	None	None
11	39	Not cured†	None	Nausea and vomiting
12	28	Cured	None	None
13	27	Cured	None	None
14	43	Cured	None	None
15	23	Cured	None	None
16	50	Cured	None	None
17	20	Cured	None	None
18	53	Cured	None	None
19	32	Cured	None	None
20	52	Cured	None	None
21	44	Cured	None	None
22	42	Cured	None	None
23	24	Cured	None	None
24	42	Cured	None	None
25	49	Cured	None	None
26	54	Cured	None	None
27	41	Cured	None	None
28	38	Cured	None	None
29	18	Cured	None	None
30	66	Cured	None	None
31	30	Cured	None	None
32	43	Cured	None	None
33	39	Cured	None	Slight sedation
34	38	Cured	None	None
35	43	Cured	None	None
36	36	Cured	None	None
37	36	Cured	None	None
38	40	Cured	None	None
39	23	Cured	None	None

* Patient had no second course of treatment.
† Patient cured on second course of treatment.

during the ten-day course of treatment. The clinical course of all patients was followed whenever possible at intervals of from several weeks to several months following the cessation of therapy.

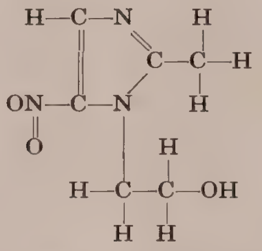
Results

Thirty-seven of the 39 patients (Table I) were cured after ten days of metronidazole therapy, as indicated by the cessation of symptoms and by an absence of the trichomonal organism in a wet smear. Of the remaining 2 patients, 1 (Patient 11) was cured following a second course of therapy, and the remaining patient (Patient 4) still had symptoms after one course of therapy but was not available for a second course. Thus, 38 of 39 patients were definitely asymptomatic and cured and, to date, none of them have had recurrences of the infection. Many of these patients were free of symptoms after from four or five days of therapy. Since those patients with other vaginal infections were not relieved of the symptoms of the associated infection, it would appear that metronidazole is specific in its action against T. vaginalis.

Comment

The potent trichomonacidal properties of metronidazole are readily seen from the fact that one part of metronidazole in 400,000 is the minimal concentration of the drug which will destroy 99 per cent of a standard culture of T. vaginalis within twenty-four hours. This indicates that metronidazole, in vitro, is considerably more potent than the best currently available trichomonacides. It is also to be noted that, although metronidazole is extremely potent, a concentration as high as 1:300 does not inhibit the growth of Döderlein bacilli in a glucose yeast extract medium.

Metronidazole has the descriptive formula, 1-(-hydroxyethyl)-2-methyl-5-nitroimidazole, and has the following structural formula:



Only 2 (5 per cent) of the 39 patients exhibited any side-effects. One of these patients had rather severe nausea and vomiting and apparently could not retain enough to build up trichomonacidal concentrations of the drug, since a wet smear following her first ten-day course of therapy indicated that T. vaginalis was still present. However, a second course of therapy resulted in a cure. The other patient was slightly sedated.

It is well known that males infected with this protozoan are usually asymptomatic and notoriously difficult to treat. The male sexual partners of the patients in this series were referred to a urologist for treatment, but it is often difficult to establish a diagnosis of trichomoniasis in a male and very few of these men actually received metronidazole. Males, however, should be treated whenever possible and empirically, if necessary, since failure to effect a cure in the male will very likely result in the reinfection of the female, necessitating another period of treatment.

The disappearance of the symptoms of trichomoniasis does not necessarily indicate a cure. If one is to be certain that the trichomonal organism has been eradicated, it is essential that the physician use microscopic technics, since, as has been noted, trichomonal infection can persist without causing symptoms.

Subsequent to the time this study was initiated, additional reports from various European investigators have indicated that a dosage of three 250-mg. oral tablets per day for ten days may be as satisfactory as combined oral and vaginal therapy to eliminate a trichomonal infection. This, of course, would be highly advantageous, in that vaginal therapy would no longer be required. We have now embarked on a study employing this particular dosage regimen, and the results of this study may be the subject of a future report.

Summary

Data have been presented on 39 adult female patients with Trichomonas vaginalis infections who were given a potent new orally active trichomonacide metronidazole (Flagyl). Thirty-eight of these patients were proved cured by a wet smear and by clearing of all symptoms, with only 2 patients reporting side-effects. On the basis of this study, metronidazole appears to be a safe and potent new trichomonacide which may well replace all other forms of medication in the treatment of this common and distressing condition.

Addendum

Thirty new cases have been treated by the oral route only with equally good results.

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Clinical Investigation of Antitussive Properties of Pholcodine

A CLINICAL STUDY *was made of the effectiveness of pholcodine (Ethnine), a morphine derivative, as an antitussive. Twenty-three patients with chronic cough resulting from inflammatory irritation and bronchial secretions associated with pulmonary tuberculosis were given 10 to 20 mg. of pholcodine, codeine sulfate, or a placebo for from one to twenty-nine days. A second group of 26 patients received the three preparations alternately within a one-week period. Eighty per cent of the patients experienced relief after the administration of pholcodine. Pholcodine was found superior to codeine sulfate as an oral antitussive agent without the side-effects often associated with codeine administration. Its effectiveness did not diminish after daily use over a two-week period, and it was not habituating.*

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A SEARCH FOR NEW antitussive agents involves the use of a number of tests leading stepwise to the determination of a degree of clinical efficacy. The three pathways to a successful search are: (1) a primary screening assay on animals; (2) a secondary trial on human subjects under strict experimental conditions of induced cough; and (3) a clinical study on patients with cough due to various causes, through the use of both negative (placebo) and positive (codeine) agents as controls against the action of the test drug.

Pholcodine* is a 3-[2-(4-morpholinyl)-ethyl] morphine: $C_{23}H_{30}N_2O_4$. It is an odorless, bitter white powder, soluble in 54.1 parts of water at 20 C. Green and Ward,[1] Chabrier, Giudicelli, and Thuillier,[2] and Cheymol *et al.*[3] found that pholcodine was about one fifth or less as toxic as codeine, while respiratory depression was about equal. Toxic doses of codeine cause convulsions, but pholcodine results only in sedation.

The threefold investigation of pholcodine, a morphine derivative, was made by separate investigators who undertook the study on a cooperative basis. The laboratory assay was performed by Mulinos[4] who reported that in the cat anesthetized with pentobarbital and prepared for the induction of the cough reflex with both chemical and mechanical stimuli pholcodine was superior to codeine sulfate as an antitussive agent, corroborating the experience of Green and Ward.[1]

Simultaneously, Bickerman and Itkin[5] assayed pholcodine on trained human subjects, using the method of Bickerman and Barach.[6] The frequency of cough induced by an irritant spray over a four-hour period was decreased about equally by an oral dose of 15 mg. of codeine, while a dose of 10 mg. of pholcodine was twice as effective.

Clinical studies

A group of 28 adult patients with chronic cough due to asthma or upper respiratory infection were treated with pholcodine in the Columbia Research Division of Goldwater Memorial Hospital.[7] One 10-mg. capsule

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* Supplied as Ethnine by the Purdue Frederick Company, New York City.

TABLE I. Antitussive properties of pholcodine in asthma and respiratory infections (28 subjects)*

			Cause of Cough		Degree of Relief			
					Complete			
Sex	Number	Average Age (Years)	Asthma	Infection	Number	Per Cent	Marked	Slight to None
F	9	48 (22 to 73)	10	18	23	82	3	2
M	19	57 (24 to 78)						

* Studies carried out in the Columbia Research Division of Goldwater Memorial Hospital.[7]

of pholcodine was given every four hours. Usually relief was prompt, the cough severity and frequency diminishing within twenty minutes to one-half hour. Twenty-six subjects were markedly improved, most of them experiencing a relief of cough which was considered over and above any relief which had been obtained with the placebo. No side-effects were reported, and it was concluded that the dosage used in these subjects was antitussive and nontoxic (Table I).

Procedure used in present study

Hospitalized patients from the Chest Service of the Metropolitan Hospital in New York City were used. They had chronic cough resulting from inflammatory irritation and bronchial secretions associated with pulmonary tuberculosis. Each cough was persistent and yielded to treatment with difficulty, and therefore it was considered a better assay medium than a cough due to more transient causes.

Care was taken to observe and record the frequency of the cough, its severity, when it occurred in relation to the time of day and position of the subject, and its degree of disturbance to nocturnal sleep. A comparative study on the same subjects was made with a placebo or codeine sulfate, given in equivalent dosage units, frequency, and form by the methods described previously by Nair and Haar[8] and Snell and Armitage.[9]

The physicians who graded the degree of effectiveness of each preparation in allaying cough were unaware of the contents of each tablet. The patients' responses to the remedies were recorded daily as "none to slight," "marked," or "complete." The establishment of a pattern in the sequence of the administration was minimized by giving each preparation first to every third subject, followed by a rest period of at least one day before the next preparation was given. The antitussive effects of each coded preparation were recorded on a chart, from which they were collated by a physician who had had no contact with the patients.

Results

The first group of 23 patients under our care received 10 to 20 mg. of either pholcodine or codeine sulfate, two to four times a day or every four hours, for from one to twenty-nine days (Table II). Although the day-to-day responses were not always uniform, the superiority of pholcodine and codeine sulfate over the placebo was immediately evident. The low incidence of favorable responses from the placebo is attributable to the chronicity of the cough and the critical attitude of the subjects toward cough medications.

The second group of 26 patients (Table III) received the three preparations alternately within a one-week period. This rapid alternation enabled the ward physician to judge the antitussive effects of each preparation, based on any expression of preference by the patients themselves. This method had been found effective by Boyd, Gittinger, and Schwimmer[10] and Boyd *et al.*[11] in the evaluation of hypnotic compounds. The assay value of frequent comparison of the three preparations was enhanced further by the use of cough due to tuberculosis because its course is not altered by short-term antitussive treatment. The

TABLE II. Antitussive properties of pholcodine in pulmonary tuberculosis (23 subjects)*

Medication†	Number of Subjects	Days on Medication: Average	Days on Medication: Range	Relief Marked to Complete: Number	Relief Marked to Complete: Per Cent
Pholcodine	16	9.6	5 to 14	16	100
Codeine sulfate	17	9.1	1 to 29	12	70
Placebo	18	7.6	3 to 14	4	23

* Seven female and 16 male subjects, twenty-five to seventy-one years of age (average, forty-six years).

† One or two 10-mg. tablets, two to four times a day.

TABLE III. Comparative single-dose data on cough alleviation in pulmonary tuberculosis (26 subjects)*

Medication	Dose: Mg.	Dose: Number of Administrations	Degree of Relief: Complete: Number	Degree of Relief: Complete: Per Cent	Degree of Relief: Marked	Degree of Relief: Slight to None
Pholcodine	10	23	7	30	8	8
	20	22	14	63	7	1
Codeine sulfate	10	24	5	21	15	4
	20	22	8	36	14	0
Placebo	..	25	3	12	10	12
	..	22	0	0	11	11

* Ten female and 16 male subjects, twenty-one to sixty-five years of age (average, forty-four years).

drugs were administered only once a day, in the evening, thus allowing time for their effects to disappear by the following evening. On the morning following each administration data on the frequency and severity of cough, the occurrence of side-effects, and other pertinent information were immediately recorded on the chart (Table III).

An expression of preference for pholcodine over codeine sulfate was made by 14 subjects (67 per cent). Not one voiced a preference for the placebo, whatever the order of administration. The data in Table III also show a positive dose-related gradation of antitussive response to the two active preparations and usually no response, with a return of the cough, after the administration of the placebo.

These clinical data support those of Bickerman and Itkin,[7] reported earlier, and of Chabrier, Giudicelli, and Thuillier[2] who found that pholcodine was effective and well tolerated by children with whooping cough or cough due to tracheobronchitis. Infants given 10 to 40 mg. daily in divided doses were included in these studies.

Our patients slept better following both pholcodine and codeine sulfate, but this was ascribed to the alleviation of the cough. No attempt was made to assay the hypnotic effect of pholcodine in patients without cough who were in need of sedation. However, Chabrier, Giudicelli, and Thuillier[2] reported that pholcodine did have a hypnotic action which was more marked than that from codeine.

Pholcodine is not analgesic agent

Chabrier, Giudicelli, and Thuillier,[2] using the method of Bovet,[12] reported that pholcodine, administered to rabbits, had analgesic properties equal to codeine. However, Cheymol *et al.*,[3] using the method of Sivadjian,[13] reported that pholcodine had no analgesic properties.

Mersheimer[14] corroborated the lack of analgesia from pholcodine on 15 male and 10 female subjects with postoperative pain who required sedation. No special choice of patient was made, other than their need for analgesia. The criterion of effectiveness was the patient's voluntary expression of relief of the pain after an intramuscular injection of pholcodine, compared with the effect of a 5 per cent glucose solution or the analgesic agent usually used by the staff physicians for the treatment of this type of pain.

Pholcodine was injected in doses of 1 to 3 ml. of a 1.5 per cent concentration (1 ml. = 15 mg.) in a 5 per cent dextrose solution. The identity of the test solutions was not known to the physicians in charge who were under the impression that they were comparing the relative potency of two analgesic agents. Each patient received one or the other of the solutions in rotation, as needed. If adequate relief of the pain had not been obtained within one-half hour of the first injection, the second injection was always a similar dose of the other preparation. On subsequent injections, the dose was increased at the discretion of the physician.

As in the antitussive studies, an analysis of the data on analgesic effectiveness of the two coded preparations was made by a physician who had had no contact with the patients. The analgesia response scores were equally poor for both pholcodine and glucose, compared with morphine or other analgesics. Mersheimer[14] concluded that pholcodine, in doses of 15 to 45 mg. injected intramuscularly, had no analgesic utility in postoperative pain. There were no side-effects such as sensations of dizziness, floating, euphoria, or clouded mentality, so commonly encountered following the use of opiates or barbiturates under similar circumstances.

Side-effects

Few side-effects were observed during the administration of pholcodine or codeine sulfate for their antitussive effects in patients with bronchial asthma or pulmonary tuberculosis. Symptoms usually associated with the long-term administration of morphine derivatives, such as constipation, nausea, anorexia, euphoria, or habituation, were looked for but none were found.

When codeine sulfate was substituted for pholcodine or vice versa, or when the placebo was substituted for either of these drugs, there was no desire shown for the previous medication, nor were there any withdrawal symptoms. However, the cough returned within twenty-four hours after switching to the placebo, disturbing the patients and frequently interfering with their sleep. All patients reported more satisfactory sleep during codeine sulfate administration than with pholcodine, although they were unaware which preparation they were receiving.

There was no apparent harm from the suppression of cough associated with tuberculosis. Prior to the administration of pholcodine or codeine sulfate, it had been determined that the cough was irritative rather than productive because the patients were receiving adequate antituberculous therapy, such as isoniazid and cycloserine or cycloserine alone. When bronchial secretion was present, the patients had no difficulty in expectorating it.

Comment

The antitussive effects of pholcodine have been reported by Snell and Armitage.[9] In a clinical assay study, using the method of sequential analysis, comparing pholcodine with diacetylmorphine and a placebo, they found no difference between the two active preparations, while both were better than the placebo. Unfortunately, pholcodine was given in combination with antazoline hydrochloride and extract of ipecac, either or both of which may have altered the ultimate effectiveness of the pholcodine.

In pholcodine we have a derivative of morphine which possesses the antitussive action of morphine to the virtual exclusion of all other opiate effects. In contrast to the convulsant action of morphine and codeine, Cahen, Groskinsky, and Parisek[15] found that pholcodine had an anticonvulsant effect in animals. This challenges the theories of many chemoneurotherapists and physiologists who lean toward the explanation of brain function and response to drugs on a quantitative rather than a qualitative basis or who ascribe an alteration in an action to the rate of an elaboration of a common chemomediator.

Conclusion

1. Pholcodine, the morpholinethyl derivative of morphine, has been investigated clinically by three independent groups to determine its antitussive and analgesic properties.

2. Pholcodine has been found superior to codeine sulfate as an oral antitussive agent

without the side-effects often associated with codeine administration. Pholcodine's effectiveness against cough did not diminish after daily use over a two-week period.

3. Pholcodine has no analgesic powers in postoperative pain in doses of up to 45 mg. given intramuscularly. Its effects were indistinguishable from a placebo administered similarly.

4. Pholcodine is much less toxic than codeine. The significance of its specificity for the cough centers and lack of action on various brain centers affected by other morphine derivatives have been discussed.

Summary

Data have been presented from two sources which show that pholcodine, the 3-[2-(4-morpholinyl)-ethyl] derivative of morphine, administered orally to patients with a cough in tablets containing 10 mg. had antitussive properties which were superior to those seen from the use of an equal dose of codeine sulfate. Eighty per cent of the patients experienced relief of their cough after the administration of 10 to 20 mg. of pholcodine daily. The long-term administration did not cause habituation, and it was not necessary to withdraw the drug gradually. No side-effects were seen in patients suffering from cough due to tuberculosis, bronchial asthma, or other respiratory tract infections treated with pholcodine for varying periods.

In another investigation pholcodine, injected intramuscularly, was found to have no value in the relief of postoperative pain when compared with codeine. None of the side-effects so often seen from the use of the opiates or barbiturates were seen in any of the patients to whom pholcodine was given either by the oral or intramuscular route.

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A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

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The Present Status of Shock or Somatic Treatment

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THE TERM SHOCK treatment has been replaced by the term somatic treatment. This enables us to include in this survey modes of treatment procedures in psychiatry that can be classed as organic treatment. The history of somatic treatment procedures in psychiatry has not been one of logical development. There is also no connection between the development of the various individual treatments. All of these organic methods have one point in common, namely, that they are based on the belief that psychiatric conditions can be influenced therapeutically by nonpsychologic methods.

The great strides made during the last few decades in the active treatment of mental illness were all made by the psychiatrists in psychiatric hospitals who used clinical observations for their therapeutic attempts.

The first successful step in somatic therapy of mental illness was based on the observations of clinical improvement in psychotic patients during intercurrent infections. This led Von Wagner in 1917[1] to introduce malaria treatment into the treatment of general paresis. The failure of this method in other psychoses indicated that it acted against the infecting agent of general paresis and not against the psychotic symptoms. This became more obvious when penicillin became the chief method of treating general paresis.

As a predecessor of shock treatments we must mention the important step of Klaesi in 1922[2] when he used barbiturates for prolonged narcosis in the treatment first of schizophrenia and later of depressions.

The almost simultaneous and independent discovery of a treatment for hypoglycemic coma and of pharmacologic convulsive therapy ushered in the new era of shock treatments. Steck[3] introduced insulin treatment into psychiatry for the purpose of increasing the patient's weight and influencing excitement in the treatment of morphine addiction. Sakel[4] made the decisive step from symptomatic use to a curative treatment when he observed that deep hypoglycemic coma, which had occurred unintentionally during symptomatic treatment of psychotic patients, actually benefited the psychosis itself. This work done at the University Clinic of Vienna was reported by Sakel in 1933. This valuable technic was speedily disseminated and avidly adopted.

Von Meduna,[5] having observed that epilepsy and schizophrenia are usually antagonistic to each other and that schizophrenic symptoms disappear temporarily after spontaneous convulsions, attempted, in 1935, to treat schizophrenia with artificially induced convulsions. Historical surveys show that several similar attempts to use convulsive therapy had preceded Von Meduna's systematic work. Oliver in 1785[6] reported the first successful use of camphor in the treatment of a case of mania.

In 1938 Cerletti and Bini[7] demonstrated a new "electroshock" therapy. This was developed largely as a replacement for pharmacologic convulsive treatment. With the recognition of the value of convulsive therapy in the affective disorders, electric shock treatment became the most widely used organic therapy in psychiatry.

In 1936 Moniz[8] reported a surgical approach to the treatment of mental illness. His knowledge of the function of the frontal lobes enabled him to develop the procedure of prefrontal leukotomy. This work became more widely accepted as a result of the work of Freeman and Watts.[9] The advent of the neuroleptic drugs has replaced psychosurgery in the majority of chronic schizophrenic cases.

Therapies

At this point it seems advisable to give a more detailed account of the therapies mentioned.

INSULIN COMA THERAPY. Many will recall the enthusiasm with which Sakel's[10] insulin coma therapy was greeted on its introduction into this country in 1938. Its difficulty in application was its main drawback from more extensive use. Insulin coma treatment is a hospital procedure and requires a special setup for proper execution. Most psychiatrists familiar with its administration agree that it is preferable to give the treatment on a separate psychiatric ward. A well-trained staff must be present throughout the entire procedure to administer to the needs of the patient. Because of the lack of personnel as well as funds, it is not entirely fulfilling its initial expectations; its use has been curtailed sharply in mental hospitals. In spite of these difficult technical demands which necessitate a large and highly trained staff, insulin coma treatment in the total treatment program of a hospital results in actual dollar savings as well as in salvaged human minds.

Insulin was used in psychiatry before Sakel. It was used as a sedative for excited patients and in cases of delirium tremens. It was also used to overcome refusal of food and to build up run-down patients, but the dosage used was small, and only a mild hypoglycemia was produced. Insulin shock treatment is like an operative procedure and necessitates careful observations by the physician and nurse of the physical and mental changes that occur during and after hypoglycemia.

SELECTION OF PATIENTS FOR TREATMENT. From a psychiatric point of view the selection of patients for treatment is relatively simple. Since this treatment was introduced for the cure of schizophrenia, acute cases should have preference, and later the chronic patients who respond less well should also be treated. Before treatment is instituted all patients should be tested for allergic reactions, hypersensitivity, and especially for insulin resistance, which is much more common.

TECHNIC OF INSULIN COMA TREATMENT. Sakel divided the treatment into four phases: (1) Phase I or the preparatory phase. Starting with an initial dose of 10 to 15 units, progressively larger doses of insulin are given once a day, increased by 10 to 15 units daily until signs of hypoglycemia are observed. This preparatory phase lasts until the shock dose is reached. (2) Phase II. The second phase consists of the production of severe hypoglycemic shocks which may be expressed as coma or epileptic seizures. This phase is continued until satisfactory improvement is obtained, or it is discontinued after about 50 to 60 shocks if no improvement occurs. (3) Phase III. After a series of shocks, one or more rest days are advisable. On these days the patient receives either no insulin or only small doses, the usual coma doses being given on the intervening days. (4) Phase IV. In the terminal or polarization phase 40 units of insulin are administered, and the hypoglycemia is terminated after two hours.

In the first phase the symptoms of the patient's psychosis are intermingled with mental symptoms of hypoglycemia during the first two hours of treatment and again after awakening. The symptoms during the first hour include feelings of lassitude, somnolence, increased perspiration, and increased salivation; after this, there are complaints about hunger and thirst. These symptoms become more marked in the second hour. Consciousness becomes clouded, and the patient is drowsy and frequently falls asleep. Other patients become restless, try to get up, turn and toss around, shout and yell, and demand food. Some show an alteration in perception, spatial and time sense are impaired; illusions and hallucinations are common. Emotional outbursts of laughing, crying, and aggressive behavior are observed as is a disorientation and impairment of recent memory, reaching a true confusional state.

The second or shock phase is reached when the hypoglycemia is so marked that it produces loss of consciousness or an epileptic fit reaction. In this state of real coma there is no response to outside stimuli. At first this coma should be kept for about fifteen minutes. Later the comas may be extended to an hour or longer. The average coma dose is about 100 to 150 units of insulin. In patients who are able to drink the comas are terminated orally. Those patients who are in a semicomatose or comatose state should have their comas terminated with glucagon or with glucose by tube or intravenously. In cases that do not respond readily an intravenous injection of glucose is given. Shortly after termination of the coma, the patient should receive a substantial breakfast.

Insulin treatment is given six times a week with one rest day. The treatment should be continued as long as the patient shows improvement. Most cases require between fifty and sixty coma days. A minimum of 20 comas should be given regardless of cases of rapid recovery, to prevent a relapse. The patient should be observed for a period of four weeks after the treatment has been discontinued to guard against the occurrence of a relapse. In case of a relapse treatment is resumed immediately. Many variations have evolved since insulin shock treatment was introduced.

SUBCOMA. The use of hypoglycemia without producing coma was used by Sargant and Craske[11] in the treatment of war neuroses prior to Sakel. Polatin, Spotnitz, and Wiesel[12] introduced this treatment in schizophrenic patients and claimed favorable results. Today subcoma treatment is used widely in physically run-down psychoneurotic patients but is unsuitable in other psychoneurotic patients.

THE CONVULSIVE THERAPIES. Von Meduna introduced convulsive therapy, choosing the pharmacologic provocation of convulsions. His primary object was to utilize the effect which convulsive seizures may have on the schizophrenic disease process. Cerletti and Bini[7] tried to replace chemical convulsive agents with the electric current. The latest development is the discovery of indokon, a pharmacologic convulsant, which is mostly used by inhalation.

PHARMACOLOGIC CONVULSIVE TREATMENT. Although pharmacologic convulsive treatment has taken a secondary place since the electric method was introduced, knowledge of this pharmacologic technic remains important. Von Meduna in his first group of patients used 25 per cent camphor in oil injected intramuscularly. The initial dose was 10 cc. This could be increased to a single dose as high as 40 cc. The injection was given before breakfast. The production of nausea and vomiting as a frequent complication caused Von Meduna to choose a soluble synthetic camphor preparation, pentamethylentetrazol (Metrazol). It was injected intravenously in a 10 per cent solution. The convulsion occurs from three to thirty seconds after the injection of the drug. If the convulsion does not occur, the patient remains conscious and has a feeling of impending death and sudden annihilation.

A few seconds after the injection the patient becomes pale and rigid, makes a few clonic movements or escape movements, loses consciousness, and goes into a tonic spasm. At the end of the tonic phase slight twitchings take place which initiate the clonic part of the convulsion. The tonic phase lasts about ten seconds, the clonic phase forty to forty-five seconds. A comatose sleep of not more than five to ten minutes duration is followed by a period of confusion lasting half an hour or longer. Postconvulsive excitement states occur. The patient has an amnesia for the convulsion but unfortunately he remembers the feeling of deadly fear which he experienced between the injection and convulsion.

INHALATION CONVULSIVE TREATMENT WITH INDOKON. In 1957 a pharmacologist, Krantz, and his coworkers,[13] while studying an anesthetic, Fluoromar, found a very similar compound, hexafluorodiethyl ether, which was a convulsant in addition to being an anesthetic. This drug, which produced convulsions in small concentrations of 29 or

30 parts to a million in the inspired air, and named indokon, was used for convulsive therapy by Esquibel *et al.* in 1958.[14]

This colorless, noninflammable liquid is not metabolized in the body and leaves unchanged. A mask and vaporizer with gauze is saturated with the liquid and applied over the mouth, and from fifteen to thirty seconds after inhalation a convulsion occurs. The patient loses consciousness, myoclonic movements occur, and these are followed slowly by a tonic phase which passes into the clonic phase of a convulsion.

Patients after this treatment feel more comfortable; confusion is less pronounced, and they show a slight euphoria without the development of fear. They wake up in a more relaxed and cheerful manner.

Krantz has developed indokon for intravenous administration. Since the solvent is excreted through the kidneys, patients with renal insufficiency should not be treated by this method.

Clinical evidence has shown that this type of convulsive therapy is as efficient as pentylenetetrazol and electrically induced convulsions.

ELECTRIC CONVULSIVE THERAPY. Cerletti's and Bini's[7] electrically induced convulsions rapidly replaced the pharmacologic method. Its advantages were: (1) The method is simpler and cleaner and can be repeated without the danger of thrombosis from intravenous injections, (2) the loss of consciousness is immediate, and (3) failure to respond with the desired convulsion can be avoided.

The simplest model of Bini's design seems to be best for it is not complicated and can be used on electric light circuits having a frequency of 50 to 60 cycles. Electrodes adaptable to the shape of the patient's head are used, and sufficient current is allowed to flow to produce a convulsion. Because many of these patients are prone to fractures, a muscular relaxant is used.

Brief stimuli technics have been used, but the opinion is that these patients do not show typical improvement such as is seen after the higher currents of the standard methods are used.

ELECTRIC NARCOSIS. Electric narcosis was a logical development in an attempt to replace convulsive therapy. Unconsciousness without muscular phenomena was induced by applying subconvulsive stimuli with the usual electric shock technic, but therapeutic results were disappointing.

ELECTRIC SLEEP. Electric sleep treatment was introduced by Giljarowsky and his coworkers[15] in Russia. It is little used in Russia but has attracted great interest in the United States. The technic consists of applying an electrode to the occipital region and another to the root of the nose. The patient is placed in a dark room and told that he will fall asleep shortly. The current may be left on for two hours and then turned off. The patient continues to sleep. This treatment has found its main use not in psychoses but in neurotic conditions.

COMBINED INSULIN-CONVULSIVE TREATMENT. The object of combining the two methods of insulin and convulsive shock treatments is the hope of achieving an aggregate of the effect of the two methods. The classical method of "summation" recommended by Georgi[16] consists in effecting a convulsion during the second hour of hypoglycemia when the lowest blood sugar values have been reached; it is at this point that most spontaneous hypoglycemic convulsions occur. No difficulties have been encountered, and the results appear satisfactory.

Various ways of combining insulin and convulsive therapies have been recommended. The most practical way to administer this combined treatment is to remove the most disturbing psychotic symptoms with electric convulsive treatment after or during which insulin treatment is instituted; more convulsive treatments may be given at certain regular intervals or when clinical improvement under hypoglycemia therapy alone has reached a stalemate.

Ambulatory electric convulsive therapy has been widely accepted and applied as an office procedure. Office treatment should be given only where the patient can rest for hours if necessary. Postconvulsive excitement is the greatest problem, so that these patients should be accompanied to the office. Long courses of treatment, such as are needed by schizophrenic and involutional paranoid patients, are difficult or impossible of application in office practice. While depressive patients are suitable patients for office treatment, there is the danger of suicidal risk, and they need constant supervision from their relatives.

INDICATIONS AND RESULTS: THE AFFECTIVE DISORDERS. While convulsive therapy is no longer the only treatment in the affective disorder states, it is still the most reliable treatment for depressions. It is the only method that can remove the depressive as well as the manic phase of a manic depressive psychosis. It is equally effective in agitated depressions. The responses of the various types of depression are so similar that it is safe to assume a close relationship exists in the underlying process in manic depressive, involutional, senile, and even psychoneurotic depressions. The total number of treatments vary between five and ten. Treatments are usually given three times a week.

In schizophrenic patients, the depressive and other acute symptoms previously overshadowed become more recognizable.

MANIC DEPRESSIVE PSYCHOSIS. The remission rate of depressions in the manic depressive disorder varies between 80 and 100 per cent. The duration of the illness has no bearing on the outcome. The institution of treatment markedly cuts short the hospital stay of these patients. It has been suggested that patients with two or more episodes should receive, as a prophylactic, single treatments at monthly intervals for the purpose of preventing recurrences.

INVOLUTIONAL PSYCHOSIS. Involutional psychosis in its pure form offers the most spectacular results in convulsive therapy. The remission rate is similar to that reached by the manic depressive depressions. The number of treatments is the same as for other depressions, five to ten. The results are equally good in deeply retarded and in agitated depressions. Failures usually are due to an admixture of paranoid or other schizophrenic symptoms. The duration of the illness does not influence the prognosis. The detection of such cases in the chronic wards of mental institutions produces gratifying results and is a valuable means of decreasing the hospital population.

Senile and presenile depressions respond equally well to convulsive treatment. The results in these old patients will depend on how far arteriosclerotic or senile brain changes have determined the depressive symptoms. The presence of some arteriosclerotic brain changes does not exclude the possibility of a favorable result.

Paranoid involutions show a much less favorable response to convulsive therapy. The rate of recovery is about one half that obtained in involutional melancholia. The belief is that the paranoid type of involutional psychosis is more closely related to schizophrenia than to the affective disorders. Here the duration of the illness plays an important part, and twenty shock treatments are necessary.

SCHIZOPHRENIA. Convulsive therapy was introduced as a treatment for schizophrenia and for several years was used exclusively for this disease. Long and adequate treatment is required by all forms of convulsive therapy. Prolonged treatment is dangerous with pentylenetetrazol while with electric convulsive therapy such intense treatment can be applied more readily, fifteen to forty convulsions being necessary. It is believed that schizophrenic patients respond to electric shock better than to pentylenetetrazol but not as well as to insulin treatment.

PSYCHONEUROSES. The application of electric convulsive therapy in these diseases is on the whole disappointing. Patients with anxiety hysteria are least amenable to electric convulsive therapy; most of them remain unimproved. Cases of conversion hysteria show an equally unsatisfactory result. The only effect is similar to that of any suggestive method. Hysterical paralysis responds readily to shock treatment, but here too the result was suggestive, for a quick response can be obtained if one utilizes the patient's ability to move the extremities while in the awakening period, in the presence of witnesses. Psychoneurotic depression offers the best results and clears up after a few treatments.

In obsessive compulsive neurotic patients the results are uncertain. They show some temporary benefit which fails to be lasting. The only result seems to be a temporary lessening of emotional tension.

PSYCHOSURGERY. Surgical treatment of mental illness over the years has changed in two important aspects: restricted operations largely reduced the undesirable side-effects of the patient's personality, and the selection of candidates for brain surgery has changed radically. If properly applied, psychosurgery continues to be a valuable and indispensable therapeutic method in psychiatry as evidenced by favorable surveys from English and American reports.

Systematic work in this field started when Moniz conceived the idea of frontal lobe surgery on mental patients. Historically, psychosurgery goes back to the Swiss psychiatrist Burckhardt[17] who on December 29, 1888, performed the first brain operation on a psychotic patient. Burckhardt's aim was to change a very assaultive patient into a quiet, harmless individual. He believed that sensory stimuli of abnormal quality and intensity reaching the motor area caused the patient's impulsiveness. Therefore, he cut the connections between the motor and sensory areas in the parietal lobe. The operation caused a definite improvement, but three additional operations, including one on the left hemisphere were necessary before the patient became quiet and cooperative. In this second case, an interruption of the fibers between the central area and the frontal lobe, actually the first case of frontal lobotomy, was necessary before the patient lost his aggressiveness entirely.

Several decades later Moniz in Lisbon, Portugal, unaware of Burckhardt's work, did experimental work based on physiologic and clinical observations by injecting alcohol into the frontal lobes. Rizzatti[18] of Italy took up this work and intensively pursued it. In the United States Freeman and Watts on September 14, 1936,[9] performed their first operation. After strong opposition this method has found acceptance, especially in England. It has been proved that a modified operation for well-selected cases is of beneficial value.

Various surgical technics have been attempted, but most of these standard operations were a "blind" procedure performed through small lateral burr holes. Originally Moniz injected alcohol for the destruction of brain tissue, and later on a leukotome was inserted. Moniz[8] with his wire loop made scores of cuts of various depths in the white matter in both hemispheres. In the standard operation landmarks are used to find the sphenoidal ridge, here a leukotome is introduced, and sweeping movements of from 30 to 40 degrees with a radius of 4.5 cm. are made. This same procedure is done on both hemispheres. More radical operations were used on chronically ill patients who had failed under a standard lobotomy.

Modified lobotomies have been performed with varying success; their goal was to arrive at a therapeutic effect with minimal damage. Unilateral prefrontal lobotomy, complete and partial lobotomies, and bimedial lobotomy all give varying results, but the bimedial lobotomies seem to give the best results. Chemical lobotomies have been tried by injecting a 0.5 per cent uroselectan as a necrotizing solution. Mandl[19] used a 6 per cent phenol solution. Myers *et al.*[20] injected procaine. Electrocoagulation for the destruction of the ventromedial quadrants of both frontal lobes was introduced by Grantham in 1951,[21] for the relief of intractable pain and other psychiatric symptoms. Some relief was obtained, and fatalities were very few. Lindstrom[22] and Fry[23] have used ultrasonic waves to produce local necrosis.

The cortical substance has undergone a concentrated assault to obtain the desired relief for these chronically suffering psychiatric patients. Peyton, Noran, and Miller[24] excised the frontal areas, while Penfield *et al.*,[25] in hopes of sparing parts of the frontal cortex, used a limited cortical excision and later carried out a bilateral symmetrical removal of the cortex, calling it a "bilateral frontal gyrectomy." The difficulty of the procedure and the conclusion that it had no greater value than lobotomy led to its abandonment. Topectomy, a selected partial ablation of the frontal cortex, performed by workers of the Columbia-Graystone Associates in 1948,[26] at first produced good results, but later it was found that the results did not depend on a specific area but rather that the amount of brain substance removed was the decisive factor in the therapeutic outcome. Anterior cingulectomy was another method of cortical extirpation, but it has proved relatively ineffective. Selective cortical undercutting, a method by which certain areas of the frontal cortex were detached, had a vogue. A suction tip and spatula were used to interrupt the long association fibers of the overlying cortex. The anterior-superior undercutting was least effective and produced undesirable personality changes, while the best results were obtained with orbital undercutting.

Transorbital lobotomy, an approach to the frontal lobes, has surpassed the results of the standard lobotomy. Freeman[27] initiates his operation by the administration of two electrical convulsions for the production of anesthesia. This is repeated when the opposite side is operated on.

Parietal, temporal, and occipital lobotomies have been attempted, but the results, even if more convincing than psychosurgery of the frontal areas, show that the "mute" areas still seem to be the site of choice for this form of therapy.

PHARMACOTHERAPY. The advent of the "tranquilizers" seemingly has produced a revolution in psychiatry as has the development of the antidepressant drugs. Their most important effect lies in the more hopeful attitude toward therapy and the prognosis in mental illness, especially the psychoses. The response of many chronic psychotic patients previously regarded as unamenable to treatment, to such a drug as phenothiazine, led to greater interest in other forms of therapy and produced an attitude of therapeutic optimism. Their value in controlling states of acute excitement created an entirely different atmosphere in the wards of many hospitals and enabled a larger proportion of these patients to participate in social events and benefit from other hospital facilities.

The early claims for the new drugs have not been fulfilled. It is realized that they improve symptoms only, rarely producing a deep-seated effect on the fundamental aspects of the illness. The main value of the tranquilizers appears to be threefold: (1) they benefit the acutely disturbed patients, otherwise uncontrollable, particularly those suffering from schizophrenia, manic excitement, or toxic psychoses; (2) they produce a symptomatic improvement in chronic patients, enabling them to have more freedom and to participate in activities, and (3) they provide a greater stimulus to new fields of research.

The number of terms applied to the new group of drugs is confusing, since many of them do not adequately describe either the characteristic effects of the drug or the factors which differentiate them from each other, from the earlier sedatives, such as the barbiturates, or from the stimulants, such as the amphetamines. Since their mode of action is unknown, it is impossible to use this as a basis for classification. The most satisfactory method seems to be that which groups together those drugs with a similar chemical structure and differentiates those which have a sedative action and those which are mainly mood elevators.

The term "tranquilizer" was first applied to chlorpromazine, which calmed disturbed behavior without the hypnotic effect. The term "ataraxic," meaning the production of emotional equilibrium, is used to describe the characteristic effect of a large group of varied drugs which have been developed recently. These terms do not distinguish between those drugs that have a pronounced effect on the psychoses and the milder sedatives whose action is mainly on anxiety and tension and whose danger of addiction and withdrawal symptoms place them close to the barbiturates.

In Paris in 1954 Delay, Deniker, and Fourment[28] proposed the following classification of the new drugs based on their predominant action:

Psycholeptics or sedatives. These sedatives depress mental tonus, slow mental activity, diminish alertness, sometimes produce somnolence, and effect indifference. This group may be subdivided into hypnotics, such as barbiturates, which cause sleep; the neuroleptics, such as phenothiazines and reserpine, which cause psychomotor inhibition and changes in the neurovegetative system and disturbances in tonus with a reduction of psychotic manifestations; and the tranquilizers, which have a sedative action on anxiety and agitation. They influence the psychotic processes only mildly. This group contains such drugs as the meprobamates.

Psychoanaleptics. These drugs elevate mental tonus, increase intellectual activity or alertness, and elevate emotional tonus. This group of drugs are the "psychic energizers" which alleviate psychotic depression and which includes Tofranil and the amino-oxidase inhibitors. These have a true antidepressive effect beyond mere stimulation and euphorization.

Psychodysleptics or psychotomimetics. These drugs can produce the so-called "model psychoses" and have characteristically hallucinogenic and mild stimulant properties. Lysergic acid, Ditran and Sernyl have been used in therapy with some success.

Chlorpromazine hydrochloride (Thorazine, Largactil, Megophen, Aminazine) was synthesized by French workers who were attempting to find a substance with more potent effects than those of promethazine. Laborit in 1951[29] used the term "artificial hibernation" to describe the state which the drug produced in patients. The first psychiatric reports appeared in 1952 when Hamon, Paraire, and Velluz[30] reported on a case of manic excitement which subsided after twenty days of treatment with chlorpromazine and pethidine hydrochloride. The typical response to the drug was one of apparent indifference to external stimuli with emotional neutrality and decreased initiative, but without the impairment of intellectual facilities or consciousness. Their results were spectacular in violent excitement but inconclusive in depressions.

Clinically on administration the drug causes a fall in the blood pressure of from 20 to 40 mm. systolic pressure and from 10 to 30 mm. diastolic pressure which varies with the dosage and individual response. The appetite improves, and weight is gained. With large doses there is listlessness and a reduction of the voluntary muscle power. A catatonic attitude was assumed in bed in some cases, and the patient would remain immobile for long periods. As complications there may develop a hemolytic anemia and jaundice, but these usually are of a mild nature.

The psychologic effect of chlorpromazine may be a short period of drowsiness, and as this disappears a state of calm and indifference to the surroundings and to symptoms develops. Intellectual faculties and awareness are not diminished; the distress caused by hallucinations, delusions, or tension decreases; but there is no loss of contact with the environment.

Chlorpromazine can be given orally, intramuscularly, or intravenously, diluted as an injection or usually by drip. Some patients show little response to oral doses as high as 1,200 mg. but will respond to small intramuscular injections of 25 mg. three times daily. Artificial hibernation as produced by Deschamps in 1952[31] producing narcosis for two weeks used chlorpromazine to potentiate the effects of small quantities of barbiturates with the addition of Phenergan and Diparcol. The dosage used in treatment varies, and the exact amount depends on the individual reaction to the drug. In schizophrenia the dosage has varied from 75 to 3,600 mg. Females require a higher dose than males. Treatment usually is commenced with doses of from 25 to 50 mg. three times daily which are increased rapidly to obtain the desired result. In the acute illness the drug may be withdrawn within a month; patients with a chronic condition with many paranoid or obsessive features should have the daily maintenance dose progressively reduced, while those with fixed paranoid or obsessive features require a maintenance dose for an indefinite time.

PSYCHIATRIC INDICATIONS. Schizophrenia is the disorder in which chlorpromazine and other neuroleptic drugs have had their widest application. The best results were found to occur in the paranoid form, even in patients resistant to insulin and electric convulsive therapy. These results were obtained no matter how long the duration of the illness. In the catatonic and hebephrenic forms the prognosis worsens with the duration of the psychosis; the worse results were had with the hebephrenic group. In the acute schizophrenic conditions there is a complete disappearance of delusions and hallucinations, while in chronic conditions the only change is in the patients' emotional response to these symptoms. There seems to be a greater improvement in female over the male patients. The drug seems to have little effect in depressions. In manic syndromes all neuroleptic drugs have a calming effect and render the patient less toxic, drowsy, or inaccessible. However, the symptoms usually return when the drug is withdrawn.

SYMPTOMATIC PSYCHOSES. These symptomatic psychoses due to various causes are highly responsive to the effect of chlorpromazine. The cause of the psychosis must be treated primarily wherever possible, but, regardless of the cause, the symptomatology of these acute psychotic reactions responds well to the drug. Good results have been reported in acute posttraumatic psychoses, epileptic clouded states, eclamptic psychoses, delirium tremens, withdrawal psychoses in barbiturate addicts, psychoses consequent on thyrotoxicosis and cardiovascular disturbances, and toxic and infectious conditions producing mental manifestations. Organic confusional states, such as arteriosclerotic brain disease and senile dementia with agitation and disturbed behavior are helped symptomatically.

ALCOHOLISM; WITHDRAWAL FROM DRUGS. Favorable results have been reported in delirium tremens when chlorpromazine was given by slow intravenous injection in a warm saline solution combined with a barbiturate.

PSYCHONEUROSES. Chlorpromazine and other neuroleptic drugs have been used extensively on neurotic patients receiving psychotherapy. The drugs can relieve anxiety symptoms and tension, but the results are not good if there are depressive or hysterical features. Obsessional patients as well as those with conversion hysteria showed no improvement. It is agreed that the action of chlorpromazine in the neuroses is slight and that its main role is one of the symptomatic relief of tension, with no effect on the underlying neurotic mechanism.

CONTRAINDICATIONS. Contraindications are few, such as infections for fear of aggravating the condition. In tuberculosis it may increase weakness and loss of weight. Liver damage, extrapyramidal diseases, and circulatory debility are mentioned as contraindications. In cases of coma due to alcohol or the barbiturates or in cases of previous agranulocytosis chlorpromazine should not be given. Many investigators warn against its use in ambulatory patients with vascular conditions, such as coronary disease, severe generalized arteriosclerosis, and arterial hypertension.

Comparisons of treatments

Insulin coma is believed to be far superior and brings about a more lasting and basic psychotherapeutic accessibility than that obtained with drugs. In chronic schizophrenic patients who fail to respond to insulin, chlorpromazine is helpful. It is evident that neither insulin nor any of the drugs at present available is curative in schizophrenia. Chlorpromazine covers up symptoms which could not be lastingly influenced by insulin in chronic paranoid patients. Undoubtedly insulin is more apt to produce better and lasting remissions in patients whose condition is still reversible. Neuroleptic drugs are successful only in suppressing symptoms, while insulin coma can produce a complete resolution of the disease process.

Electric convulsive therapy or the antidepressant drugs are the treatment of choice for psychotic depression. Chlorpromazine may relieve the agitation but rarely produces a complete remission of the illness. In mania, acute schizophrenia, and delirious psychoses the drugs are as effective as electric convulsive therapy. Their advantage lies in not producing the confusion caused by electric convulsive therapy. In patients with chronic illness, drug therapy, since it can be used more easily to maintain the patient, is the treatment of choice.

PSYCHOSURGERY AND PHARMACOTHERAPY. The difference in personality changes produced by chlorpromazine hydrochloride compared with those found in postpsychosurgery is most marked. Both treatments may have the same effect on mental illness, but the brain operation produces an irreversible condition. The obvious difference between lobotomy and drug treatment is that only the latter tends to bring the patient to more normal behavior patterns without personality changes.

COMPARISON OF CHLORPROMAZINE AND RESERPINE. Results indicate that chlorpromazine hydrochloride is superior to reserpine and is the drug of choice because the degree of improvement was greater and the toxic and side-effects were less troublesome.

TRANQUILIZERS. Meprobamate (Miltown, Equanil, Mepavlon), a muscle relaxant, was first introduced in 1946 and was found to be too rapidly oxidized and its action of short duration. By 1951 Ludwig and Berger[32] reported on meprobamate, which had a pronounced muscle relaxing power and anticonvulsive action.

Clinical effects. Meprobamate has a sedative action, relieving anxiety and producing muscle relaxation. It also has some sleep-producing effects. In doses of 400 mg. it produces some impairment of performance in driving a car, but this is less intense than that with chlorpromazine hydrochloride. The drug is administered orally as a tablet. Neurotic symptoms may be controlled by 400 to 800 mg. three times a day, and the dose can be increased rapidly if there are no untoward symptoms. Where high dosage has been used the drug should be withdrawn slowly because of the risk of producing a withdrawal psychosis and convulsions.

Meprobamate is used mainly in the treatment of the neuroses. It particularly relieves insomnia, irritability, and mild depressions. Treatment by this drug should be confined to fairly short periods of time and never should be used indefinitely because of the danger of habituation. The drug is most beneficial to patients who have an illness of recent onset and moderate severity, accompanied by acute symptoms. Patients with anxiety states, reactive depressions, and obsessional neuroses were helped by the drug, but patients with hysteria did not respond.

Meprobamate has little effect in the psychoses and is less effective than the phenothiazines or reserpine. It is of little use in controlling the withdrawal symptoms in alcoholism. Its only use lies in the neuroses, and it has the same disadvantages of habituation and withdrawal symptoms that the barbiturates have. Meprobamate should be used preferably for short periods of treatment in acute cases to help the patients over a crisis.

Present trend

Many observers have noted the reduction of the hospital population since the introduction of effective somatic treatment methods in psychiatry. The effect of these treatment methods have made it possible to shorten the duration of many otherwise long-term, if not chronic conditions.

Before the advent of the somatic therapies the state mental hospitals, unable to control effectively psychotic symptoms, were really places for custodial care. Up to this time the outlook for schizophrenia, the main source of the long-term accumulation of patients in state hospitals, seemed hopeless. The schizophrenic patient had a one-in-five chance of spontaneous remission without systematic treatment. The introduction of the somatic treatment about twenty-five years ago began a new era in mental hospital practice. The schizophrenic patient was found to respond to insulin therapy, and the remission rate increased to three-in-five. The gradual addition of the other forms of somatic treatment, including the introduction of pharmotherapy, has continually raised the remission rate. The outlook has been improved further by the introduction of proper psychologic and social treatment. All these factors have led to a gradual emptying of the large state mental hospitals. Convulsive treatments helped to solve the state mental hospitals' problem in relation to all types of depressive patients and still further helped to empty these hospitals. Pharmotherapy and psychosurgery, with their ability to control the disturbed patient, helped further to reduce the state hospital population.

The quick and dramatic results of these treatments, while they did not cure, enabled the patients to be returned readily to the home environment within a short time where they could receive the necessary psychotherapy. The admiration of our culture for quick definite action has stimulated the demand for these treatments to be given closer to home. Therefore, the demand was made for office ambulatory treatment and later for beds in a general hospital.

The general hospitals are beginning to welcome these patients. As a result, a certain number of hospital beds are being set aside for this specific purpose. This has caused the evolution of the neuropsychiatric section of the general hospital. It seems that this change is expressive of a nationwide trend. I do not wish to imply that the establishment of the psychiatric unit in a general hospital will mean the demise of our state mental hospitals, but it does seem that these units now can be built to house fewer patients. While the somatic therapies provided the initial impetus, other methods have helped further it. Some of the new patterns of patient care have been the establishment of night and day psychiatric treatment in a general hospital. The first Day Center was established by the psychiatric department of the Montreal General Hospital. It was established in 1950 as an extension of its inpatient and outpatient services. These beds in the Day Center are available for three different groups of patients during each twenty-four hours as follows: From 8 : 30 to 11 A.M. for the day patients who will undergo subcoma insulin therapy; from 1 to 3 P.M. for patients who attend the Day Center for electroshock therapy; and from 6 P.M. to the following morning the beds are available for night patients.

Individual and group psychotherapy is given to selected patients. Occupational therapy also is utilized, as is educational diversional social therapy by nonprofessional people. Rehabilitation and vocational training are given by qualified personnel, and therapy also is given to the patient's family by competent social workers.

In 1954 there were established similar facilities for the night hospital, but here the treatment is given only to individuals who are still able to carry on with their employment and who can be treated without having to take time off from their occupation.

This new knowledge and its treatment potentials have stimulated a more balanced program for the mentally ill. The indications are that the majority of the acutely mentally ill will receive intensive treatment in community facilities. To this end mental health clinics are being established, such as mentioned in the above description of the day and night hospital, to fill these needs.

Inpatient services

These services are based on the belief that all mentally ill patients are entitled to intensive treatment in a facility which is easily accessible to them. No distinction is to be made between the acute and chronic mental illness. This treatment can best be given in small hospitals providing both inpatient and outpatient care in the heart of the community. The inpatient services are integrated with the community services, particularly to aid in the rehabilitation and after-care of the patient.

Another outgrowth of the increased remission rate in psychotic patients caused by the use of somatic therapies has been the development of foster homes and boarding homes as an in-between stopping place in preparation for the patient's return to his home. These foster or boarding homes are associated closely with the hospital or clinic in which the patient was treated and received regular visits from the psychiatric social worker.

The results of a survey by a Commission, a nongovernment body authorized by Congress in 1955, were published in 1962.[33] Governor Rockefeller presented his proposals to the State Legislature a short time ago from a plan prepared by Paul H. Hoch, M.D., New York State Commissioner of Mental Hygiene.[34] This program has two main objectives: The utilization to the full of our present-day knowledge about the treatment of all types of mental illness, and the organization and support of a comprehensive program of research into the causes of all the forms of mental abnormalities, so as to lead to a better method of treatment.

While it is evident that the present types of somatic therapy do not cure the mental illnesses, they do enable the patient, in his remission state, to be returned to society and lead a more normal social existence. They also prepare him to further his treatment by various known psychotherapeutic means, so necessary to perpetuate and improve the patient's more normal status.

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Roentgenologic aspects of the black eye

There is nothing particularly comical about a black eye, according to an article by Leonard C. Doubleday, M.D., in the January 6, 1962, issue of the *Journal of the American Medical Association*. In this era of frequent automotive injury, the possibility of fracture of the floor of the orbit should be considered in all patients with a black eye and excluded only after adequate x-ray examination. If this complication is present and goes unrecognized and untreated, enophthalmos and diplopia follow, either because of the abnormal axis of the globe or defective mechanics of the inferior extraocular muscles. A direct blow to the orbit of sufficient force causes the orbital cavity to fracture at its weakest point, the floor. At the same time the thin medial wall limiting the ethmoid cells may be ruptured also.

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
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Oil of Wintergreen, Potassium Permanganate, and Analgesic Tablet Poisonings

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Japanese Wonder Flowers	2 years	Male

A mother called to inquire about possible injury to a two-year-old male who had swallowed a glass of water containing a Japanese Wonder Flower. The "flowers" are imported compressed paper novelties which expand, when immersed in water, to realistic, full-bloom colored "flowers." The father had purchased three of these flowers. He had placed two in a bowl containing goldfish and had put the other in a glass of water.

While the specific nature of the "flowers" was not known here, the father had conveniently provided the Center with the answer, since goldfish are very sensitive to toxic substances. Several of our briefs have noted previously that chemicals used in the maintenance of fish tanks and for treatment of tank fish are harmless.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Artificial Snow-Liquid Paperweight	19 months	Female

The patient's father, a physician, contacted the Poison Control Center in reference to this episode. The father's report to the Health Department was as follows:

> My daughter, aged nineteen months, accidentally ingested about two tablespoonfuls of the fluid contained in a plastic ball "snow scene" on the date mentioned. About twenty minutes later she began to vomit and appeared nauseated. She was brought to the Emergency Room at Meadowbrook Hospital, in East Meadow, New York, where a gastric lavage was done with a saline solution. A chemical analysis of the material ingested was carried out by me and by E. B. Bien, M.D. The fluid ingested consisted of a solvent made of water and methyl-ethyl-ketone and a solute of strontium chloride. My daughter was not admitted to the hospital and recovery was prompt, complete, and spontaneous.

The composition of this particular paperweight is a little surprising to us because incidents that have been reported previously to this Department consisted of water as a solvent, and the "snow" was cal-

TABLE 1. Incidents reported to Poison Control Center during recent weekend

Type of Poison	Age (Years)	Sex
Tetracycline hydrochloride	2	M
Tetracycline hydrochloride	$2^{1}/_{3}$	M
Scouring powder	45	M
Scouring powder and ammonia	$3^{1}/_{2}$	M
Ammonia	40	F
Ammonia water	2	F
Analgesic tablets	16	F
Apiol and ergot	27	F
Aromatic spirits of ammonia	$2^{1}/_{2}$	F
Analgesic tablets	2	M
Analgesic tablets	22	F
Analgesic tablet	4	M
	$1^{5}/_{6}$	F
Analgesic tablet	3	F
Analgesic tablet (baby)	$2^{1}/_{2}$	M
Analgesic tablet (baby)	2	M
Analgesic tablet (baby)	3	F
Analgesic tablet (baby)	2	F
Analgesic tablet (baby)	2	M
Analgesic tablet (baby)	2	M
Belladonna	36	F
Benzene	20 (?)	M
Insecticide	Adult	F
Powder hand soap	$1^{1}/_{3}$	M
Boric acid	$3^{1}/_{2}$	M
Chloral bromide	51	M
Button (metal)	3	M
Tranquilizer	46	M
Corn remover (liquid)	2	F
Kerosene	2	M
Liniment	$1^{1}/_{12}$	M
Hair tonic	3	F
Teething medicine	$^{5}/_{6}$	M
Ice melting material	3	M
Oil	Unknown	Unknown
Iodine	36	F
Detergent (liquid)	$1^{1}/_{2}$	M
Tranquilizer	15	F
Baby lotion	6	Unknown
Matches	$1^{1}/_{2}$	M
Matches	Unknown	Unknown
Methapyrilene hydrochloride tablets	Adult	F
Moth balls	$^{6}/_{7}$	M
Tranquilizer	Child	Unknown
Tranquilizer and phenobarbital	24	F
Glyceryl trinitrate tablets	$2^{1}/_{2}$	F
Paint	Unknown	Unknown
Paint remover and lacquer thinner	72	M
Pine oil	25	F
Plastic cement	2	M
Chewable vitamins (2 children)	Unknown	M and F
Powder (aluminum)	2	M
Battery fluid	3	M
Quinine sulfate	2	M
Rat poison	19	F
Cleanser	$1^{1}/_{4}$	M
Liver pills	3	M
Camphorated oil	56	F
Chalk	1	M
Cigaret	$^{2}/_{3}$	F
Cleaner	2	M
Bleach	12	F
Bleach	2	M
Bleach	2	M
Bleach	26	F
Disinfectant	Unknown	Unknown
Carbon monoxide	29	F
Cologne (2 children)	3	M
	2	M
Tranquilizer	8	F
Decongestant tablets	2	F
Crayon	2	M
Crayon	1	F
Ointment	2	M
Detergent	3	M
Appetite depressant	3	M
Insect repellent	4	F
Dilantin sodium	$1^{1}/_{12}$	M
Antihistamine tablets	Unknown	M
Antiemetic	$1^{5}/_{6}$	M
Cleanser	2	M
Sleeping pills	57	M
Cold syrup	3	M
Shampoo	1	F
Shoe polish	$1^{1}/_{2}$	M
Sleeping pills	Unknown	Unknown
Cough drops	$2^{1}/_{2}$	M
Sulfuric acid	Adult	M
Antidepressant drug	Unknown	Unknown
Tranquilizer	36	M
Thermometer fluid	6	F
Thyroid tablets	2	M
Tincture of iodine	65	F
Dye	$2^{1}/_{2}$	M
Toilet water	$2^{1}/_{2}$	M
Triamunic syrup	$2^{1}/_{2}$	M
Trichlorethylene	Adult	M
Vegetable dye	$1^{1}/_{4}$	F
Suppositories	$8^{1}/_{2}$	F
Vinyl wall finish	2	M
Water color	Unknown	M
Water color	3	M
Analgesic tablet	2	F
Overdose of drug (unknown)	30	M
Overdose unknown	48	F

cium carbonate. Since there does not seem to be any logical reason for using any harmful ingredients in this type of novelty toy, it would seem that the manufacturers are not sufficiently prophetic with what happens with these products.

It is a matter of continued wonder to us what prompts children to pull the rubber plug and drink the contents of these toys. Where a manufacturer has a choice of using the universal, unique, and safe solvent, which is water, the substitution of any other product is incomprehensible. In addition, the failure to state somewhere on toys and household products that water is the substance present has repeatedly resulted in incidents causing unnecessary alarm and anxiety to the patient, the parent, and the doctor and, frequently, prompted an overtreatment of the patient.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
Oil of Wintergreen	3 years	Female

The attending physician reported as follows:

> This child was found in the bathroom with a bottle of oil of wintergreen, some of which she had swallowed. After she was given universal antidote, this was removed by a repeated lavage until the fluid was clear. The child was perfectly well at all times, but a purpura of the face and chest appeared during lavage and persisted for four to five days after her discharge. The only other specific therapy was vitamin K, 2.5 mg.

It is known that the salicylate had a lower plasma prothrombin by interfering with the vitamin K utilization of the liver. Gastric bleeding following the ingestion of a salicylate is reported commonly. Hemorrhagic states, which may be encountered following salicylate ingestion and overdosages, are usually petechias in the skin and mucous membranes, in addition to the gastric hemorrhages mentioned previously. Reports of confirmed purpura cases have not come to our attention thus far.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Potassium Permanganate	29 years	Female

This patient swallowed 16 tablets of potassium permanganate with suicidal intent. She was taken to a hospital emergency room where her stomach was lavaged. No symptoms were manifested within forty-five minutes following the ingestion. In addition, catharsis was also used. Since there were no symptoms, the patient was observed for several hours and discharged from the emergency room. The absence of symptoms was notable. The same cannot be said about sequelae which might follow, particularly strictures of the esophagus and throat.

INCIDENT 5

Substance Ingested	*Age*	*Sex*
Analgesic Tablet	26 years	Female

This patient swallowed 90 analgesic tablets with suicidal intent. The patient vomited spontaneously and was taken to the Kings County Hospital where her stomach was lavaged with normal saline later. No abnormal findings were noted on physical examination and in the laboratory tests. The treatment was entirely supportive, and after twenty-six hours of hospitalization the patient was discharged. The absence of symptoms and laboratory findings on the ingestion of this massive dose are noteworthy and puzzling.

Number ninety-four in a series of Accidental Chemical Poisonings

Staphylococcal Infection Following Closed Mitral Commissurotomy

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THE GROWING INCIDENCE of life-threatening invasion by the Staphylococcus aureus in postoperative patients is evidenced by the increasing number of published reports. Because of the very nature of cardiovascular surgery and the spectacular developments in this field,[1] the complication of Staph. aureus infections becomes potentially more menacing than in other areas of surgery. This is particularly so because the ever-widening emergence of antibiotic-resistant strains of this organism has brought about an alarming increase in the incidence of bacteremia with drug-fast staphylococci.

The actual number of patients who become infected with staphylococci following mitral commissurotomy is difficult to estimate. From the very nature of the operative procedure, this complication would appear to be more frequent than the dearth of published reports would indicate.[2] To document this, it seemed advisable to present 2 such instances.

Case reports

CASE 1. A thirty-four-year-old white female was admitted to the hospital with the chief complaints of progressive exertional dyspnea and palpitation. She had experienced an attack of rheumatic fever at the age of ten years. Three years prior to admission she first noted the onset of her presenting symptoms. Her symptoms had progressed rapidly within the past year.

A physical examination was noncontributory except for the cardiac findings. A regular sinus rhythm was present. The mitral first sound was loud and snapping. A rumbling presystolic murmur was heard over the mitral area. The pulmonic second sound was accentuated. No other murmurs were present.

Laboratory studies revealed a normal blood count and urinalysis. The cholesterol was 158 mg. per 100 ml.; the protein was 7.8 Gm. per 100 ml., with an albumin-globulin ratio of 5.5 to 2.3. The sodium was from 130 to 140, the potassium 4 to 5, the chlorides 88 to 100, and the carbon dioxide content was 25 mEq. per liter. The serology and the C-reactive protein showed negative findings. An electrocardiogram revealed a right ventricular hypertrophy. An x-ray film of the heart demonstrated the typical findings of mitral stenosis.

A mitral commissurotomy for valvular and subvalvular stenosis was performed. The mitral valve which barely admitted a finger tip was opened so that two fingers could be accommodated without any resultant regurgitation. For the first three to five days postoperatively, the patient received daily a million units of procaine penicillin and 1 Gm. of streptomycin intramuscularly. However, she developed a temperature of 102 F. and appeared extremely ill and toxic. At this time her white blood cell count was 30,000 per cubic millimeter. On the third postoperative day a thoracentesis was performed, and 400 cc. of sanguinous effusion were removed. A second thoracentesis performed on the fourth postoperative day resulted in the evacuation of 250 cc. of similar material. Cultures of the blood and fluid were sterile.

A program consisting of prednisone (Meticorten) and 2 Gm. of Mysteclin-F daily was begun on the fifth postoperative day, after which the temperature fell to 101 F. For the next two weeks the temperature hovered between 100 and 101 F. During this period the patient developed atrial-flutter fibrillation but looked well and was ambulatory. On the seventh postoperative day, 1 Gm. of tetracycline hydrochloride (Achromycin) daily was substituted as the antibiotic of choice. Chest x-ray films presented the typical cardiac silhouette of a pericardial effusion. This effusion increased gradually over the first two postoperative weeks despite the continued use of prednisone. Antibiotics were discontinued on the thirteenth postoperative day, with a prompt recrudescence of the temperature to 102 F. The white blood cell count, which had dropped to 9,000 per cubic millimeter while the patient was receiving antibiotics, rose to 15,000 per cubic millimeter. On the fifteenth postoperative day a pericardicentesis was performed, yielding thick purulent material from which Staph. aureus was cultured. This later proved sensitive to erythromycin and Chloramphenicol. The blood cultures remained sterile. Penicillin, streptomycin, and Varidase were instilled into the pericardiac sac. The next day the patient appeared to be developing pericardial tamponade, and consequently a pericardiostomy and a partial pericardiectomy were performed. Immediately after the drainage of the purulent material, the patient's pulse and blood pressure reverted to normal. Six hundred cc. of brownish, purulent material were removed from the pericardial sac at this time. Following the pericardial drainage, erythromycin therapy was instituted. The temperature gradually receded to 99 to 100 F., and the white blood cell count fell to 13,000 per cubic millimeter. A small pocket of air in the anterior left pleural cavity required forty-eight hours of tube thoracotomy and underwater drainage. Following the procedure, the patient did extremely well. She was placed on postural drainage, with a gradual obliteration of the pericardial sac. She remained well, with a daily dressing and neomycin irrigations and was ambulatory until the eighteenth day after pericardial drainage. On her thirty-fourth postoperative day she suddenly developed a temperature of 101 F. For the following three days her temperature remained between 101 and 103 F. During this time her white blood cell count remained normal. The patient had all the signs of an upper respiratory infection, including headache, running nose, sore throat, and a cough. Therefore, no antibiotics were given, and the patient was treated symptomatically. Her temperature gradually fell to 100 F. during the next week, and she again felt well. On the thirty-fifth postoperative day she experienced a chill and a temperature elevation to 104 F. She complained of a right flank pain, with urinary symptoms of frequency and dysuria. A blood culture taken at this time showed negative results. However, a catheterized urine was loaded with pus cells. She received Furadantin, with a rapid subsidence of her temperature within the next four days. Subsequently she was maintained on Gantrisin. Five days before the patient left the hospital, a secondary suture of the wound was performed. Four days later she developed a temperature of 104 F. with a chill. She complained of tenderness over the closed wound. The wound was opened. and a few cubic centimeters of purulent material were expressed. This was followed by a rapid subsidence of her temperature to normal. She was discharged on her sixty-first postoperative day, feeling well and afebrile.

Comment. Fortunately, in this case the resistant staphylococcus did not erupt from the thorax into the blood stream despite the use of steroids without adequate antibiotic coverage. Because the initial thoracic fluid cultures were sterile, the possibility of a postcardiotomy syndrome was considered. It was not until fifteen days after the operation that the infecting organism was cultured from the pericardial fluid. Radical measures for the evacuation of the pus (pericardiectomy) along with a more specific antimicrobial regimen enabled the patient to surmount her infection. This patient was fortunate in that successful surgical intervention and an effective chemotherapeutic program assisted her in overcoming a refractory type of purulent pericarditis.[3]

CASE 2. A twenty-eight-year-old white male was admitted to the hospital for the second time, complaining of increasing exertional dyspnea, orthopnea, and ease of fatigability. Two months previously he had been institutionalized for treatment of pneumonia. Since the age of fifteen he had experienced several attacks of rheumatic fever.

A physical examination was noncontributory except for the cardiac findings. A regular sinus rhythm was present. The mitral first sound was loud, snapping, and accentuated. A rumbling presystolic murmur was heard over the mitral area. The pulmonic second sound was markedly accentuated and snapping in character. No other murmurs were heard.

Laboratory studies revealed a normal urinalysis and blood count except for a white blood cell count of 14,000 per cubic millimeter. The urea nitrogen was 15 mg. per 100 ml.; the blood sugar was 61 mg. per 100 ml.; and the total protein was 7 Gm. per 100 ml., with an albumin-globulin ratio of 4.2 to 2.8. The carbon dioxide was 28.5, the sodium 136, the potassium 4.35, and the chlorides were 97 mEq. per liter. The electrocardiogram revealed a right ventricular and atrial hypertrophy. An x-ray film of the chest demonstrated an enlargement of the right side of the heart and the left atrium consistent with a diagnosis of mitral stenosis.

A mitral commissurotomy was performed which the patient tolerated without incident. For several days preoperatively, the patient received a million units of intramuscular penicillin daily. Following surgery, a daily dose of 1 Gm. of streptomycin was added. However, on the second postoperative day his temperature rose to 102 and then to 103 F. He developed phlebitis of the right arm. On the third postoperative day rales were audible at the right base posteriorly, and a diagnosis of a right basilar pneumonitis was made. Blood cultures drawn at that time were sterile. Tetracycline hydrochloride was introduced, and the daily doses of penicillin and streptomycin were increased. Two days later the patient's temperature spiked to 103 F. Blood cultures drawn at this time were subsequently reported positive for Staph. aureus (coagulase positive), sensitive only to erythromycin and novobiocin sodium. A thoracentesis performed on the sixth postoperative day yielded only a small amount of serous fluid. Therefore, prednisone therapy was started. Pericardicentesis was performed on the seventh postoperative day, at which time some purulent material was aspirated. Blood cultures at this time were markedly positive for coagulase-positive, penicillin-resistant Staph. aureus. Accordingly, the patient was returned to the operating room, at which time an anterior thoracotomy was done, and a drainage of the pyopericardium and pyothorax was effectuated. Approximately 500 cc. of purulent material were aspirated from the pericardial sac, and a partial pericardiotomy was performed. Erythromycin was added to massive doses of intravenous penicillin and intramuscular penicillin and streptomycin. On the following morning the patient became markedly toxic and appeared to be in shock. His blood pressure fell steadily, and he expired on the eighth postoperative day.

Comment. In this instance too much reliance was placed on routine antibiotic coverage which obviously did not control the infection. Because the fever did not abate by the sixth postoperative day despite the utilization of penicillin, streptomycin, and tetracycline hydrochloride, and because the paracentesis of the thorax and pericardium was nonproductive, the possibility of a postcardiotomy syndrome was considered. Thus, the patient was started on steroid therapy. Unfortunately, it was not until the next day that pus was evacuated from the chest and pericardial sac. About this time the blood culture yielded the resistant Staph. aureus (coagulase-positive) which proved sensitive to erythromycin and novobiocin sodium. Erythromycin was thereupon introduced into the treatment program. In retrospect one might speculate as to whether or not (1) the steroid therapy exacerbated the infection, (2) the prompt employment of erythromycin and novobiocin sodium, to which the organism was sensitive, might have contained the infection, and (3) earlier postoperative surgical intervention might have been lifesaving.

Comment

The 2 cases which are the subject of this report fulfilled all the criteria for a successful and uneventful mitral commissurotomy. Complications arose which were due to staphylococcal infection presumably introduced during or shortly after surgery. Unfortunately, the persistence of fever despite the administration of conventional pre- and postoperative chemotherapeutic programs in both cases led to a suspicion of a postcardiotomy syndrome. Accordingly, steroid therapy was employed which not only was of no avail but also may well have been detrimental. Ultimately, the staphylococcal infection was recognized, and rigorous antibiotic programs were instituted.

Whether or not Case 2 could have been saved under any circumstances is debatable. However, a valuable lesson can be learned from this experience. It is imperative to have a high index of suspicion of the presence of staphylococci in patients undergoing cardiovascular surgery when there is a persistence of fever despite the conventional prophylactic use of antibiotics. Treatment with an optimum antibiotic program should be inaugurated even before bacteriologic studies are completed. The aim is rapid destruction of the invading staphylococci before the patient develops ominous signs of infection.[4] This calls for a drug or, better yet, a combination of drugs which is rapidly bactericidal for the etiologic organism. Often markedly toxic antimicrobial agents must be employed. The risk of serious toxic side-effects must be weighed against the hazard of treatment failure in a disease which could be fatal unless the infection can be eradicated. Again, one might stress the fact that antibiotic programs to combat staphylococcal infection postsurgically can in no way replace the ever-necessary need for perfection and aseptic technic in the operating room. A program to assist in the prevention of postoperative infection has been presented in detail in a previous publication.[5]

Summary

1. The need for a high index of suspicion of staphylococcus infection in the presence of postoperative fever has been demonstrated in 2 patients following mitral commissurotomy.
2. The etiologic organisms must be eradicated by prompt optimum antimicrobial agents before they cause critical complications such as pyothorax, pyopericardium, and endocarditis.
3. Immediate surgical intervention is imperative, should localization of pus occur.
4. The routine prophylactic use of antibiotics pre- and postoperatively should be re-evaluated.
5. Rigorous measures for the prevention of infection following cardiovascular surgery are of paramount importance.

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Hemorrhagic Pancreatitis Complicating Anticoagulant Therapy

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New potent oral anticoagulants have greatly simplified anticoagulant therapy for both the clinician and the patient. Not only is the administration easier by the oral method, but also it is easier to maintain effectively constant levels of anticoagulation, resulting in a decrease in the frequency of prothrombin tests necessary for control. However, complications in anticoagulant therapy are still possible, and the simplified means of administration may give both the clinician and the patient a false sense of security.

The clinician must become increasingly aware of certain medications and diseases which may affect the action of these newer anticoagulants. It is well established that aspirin and Butazolidin may potentiate certain anticoagulants.[1] Liver disease may also produce an additive effect on anticoagulants, as may pancreatitis. The purpose of this report is to present a heretofore unreported complication of anticoagulant therapy and to discuss the possible mechanism involved as well as the treatment and prognosis.

Case reports

Case 1. A forty-nine-year-old white female was admitted to Presbyterian Hospital on July 22, 1961, with the chief complaints of malaise and increasingly severe abdominal pain of two days duration. The pain was localized to the right upper quadrant and radiated to the back. Also, on the day of admission there was an onset of watery diarrhea, nausea, and vomiting. There had been no jaundice and no previous symptoms referable to the liver or biliary system. The patient had been on warfarin sodium, hydrochlorothiazide, and digoxin therapy for six years following a mitral commissurotomy for severe rheumatic mitral stenosis. The patient was not alcoholic but usually had at least one drink daily.

A physical examination revealed auricular fibrillation and right upper quadrant tenderness, guarding, and rigidity. The admission chest and abdominal x-ray films showed normal findings. The prothrombin time was 32 per cent. The hemoglobin and hematocrit were normal, and the white blood count was 10,800 with a normal differential. Since mesenteric thrombosis was seriously considered on the basis of an embolus from auricular fibrillation, the patient was given 125 mg. of Lipo-Hepin subcutaneously on the second hospital day. Twelve hours later the Lee-White coagulation time was forty-three minutes, and the patient became worse clinically.

It was believed that the patient probably had acute cholecystitis. She was given 90 mg. of protamine sulfate and 5 mg. of Mephyton intravenously and taken to surgery the evening of the third hospital day. At surgery the gallbladder was found to be normal, but the pancreas appeared to be inflamed with marked pancreatic hemorrhage. However, there was no fat necrosis or calcification. There was a large retroperitoneal hematoma and considerable free blood in the peritoneal cavity. The abdomen was drained with two $^1/_2$-inch Penrose drains and a cholecystostomy with a Pezzar catheter was effected. The patient's prognosis was considered poor.

Postoperatively she was given penicillin, hydrocortisone succinate (Solu-Cortef), and 50 mg. of additional protamine sulfate, as

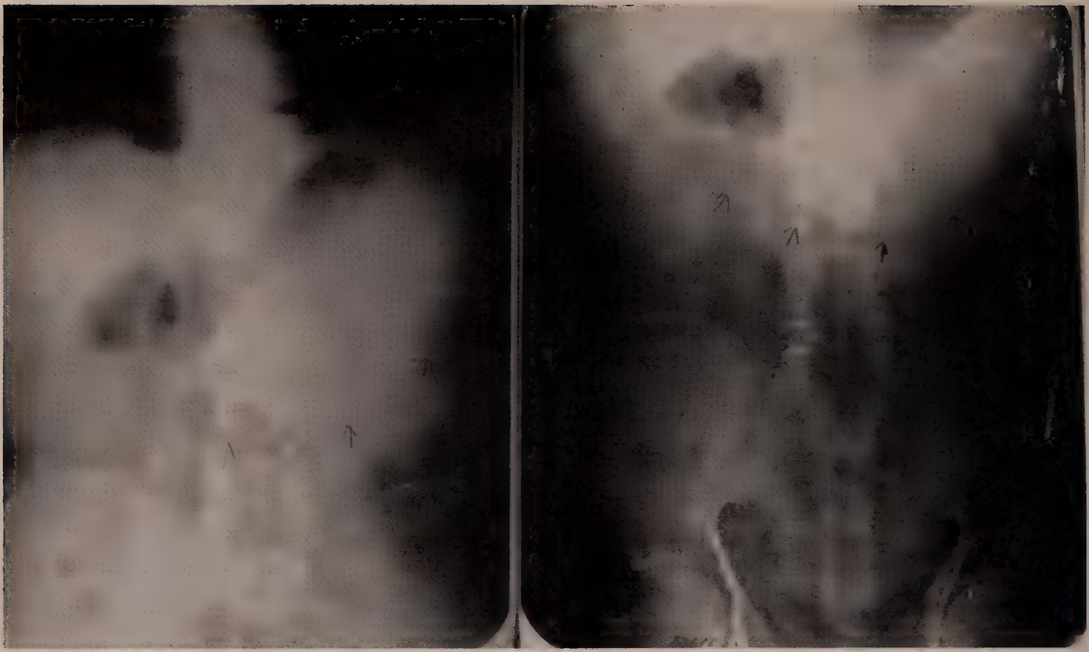

FIGURE 1. Case 2. Abdominal roentgenograms revealing large radiopaque shadow in left upper quadrant.

the Lee-White time was still elevated. The peritoneal fluid amylase was 524 units, and the serum amylase was 129 units. However, the patient did amazingly well. She was almost pain-free the day following surgery and began taking oral fluids on the fifth postoperative day. Anticoagulant therapy was reinstituted on the eighth postoperative day. On the twelfth postoperative day a cholangiogram through the catheter was normal, and so the catheter was removed and the patient discharged. She has had no subsequent difficulty.

Case 2. A sixty-one-year-old white male was admitted to Presbyterian Hospital on February 10, 1962, with the chief complaint of diarrhea and mild abdominal cramping pain for two days. The diarrhea had become quite severe, with 20 to 30 stools, the evening before his admission. There had been no nausea or vomiting, but the patient seemed quite weak and confused. He also had urinary urgency, with an empty bladder, and was quite shaky and nervous. The patient had a history of severe pulmonary emphysema and had undergone an appendectomy. He usually had from one to four drinks daily. His medications included aminophylline, isoproterenol inhalor, chlorothiazide with potassium, meprobamate, digoxin, and warfarin sodium.

At admission, the physical examination revealed a blood pressure of 80/60 and a pulse rate of 144. The patient's hands were cold and clammy. There was tenderness, with voluntary guarding and no rigidity in the right upper quadrant. Bowel sounds were present but hypoactive, with moderate distention. The hemoglobin and hematocrit were normal. The white blood count was 21,000; the prothrombin time was 14.5 per cent. The serum electrolytes were all slightly lower than normal. The serum amylase was 159 units (normal, 160 units).

Later on the day of admission, the hemoglobin fell from 14 Gm. to 12.6 Gm. per 100 ml. The white blood count went up to 27,150 and the serum amylase to 189 units. Abdominal x-ray films revealed a large radiopaque shadow in the left upper quadrant (Fig. 1). Levophed became necessary to maintain the blood pressure.

On the evening of admission the patient was taken to surgery. A large retroperitoneal hematoma was found, and the lesser peritoneal sac was filled with blood (which accounted for the shadow on the x-ray film). The surgeon described the pancreas as "looking like raw hamburger," with considerable hemorrhage, clots, and fat necrosis. Gastrostomy, abdominal drainage with multiple Penrose drains, and tracheotomy (because of the severe emphysema) were done, and the patient was returned to the recovery room with a poor prognosis.

Postoperatively he was given blood, hydrocortisone succinate, and antibiotics and did much better than had been expected by any of his physicians. By the fifth postoperative day the gastrostomy tube was clamped, and he received oral liquids. On the fourteenth postoperative day he developed acute thrombophlebitis in the left leg, but this responded promptly and favorably when anticoagulant therapy was reinstituted. His hospital stay was prolonged because of his marked emphysema.

Comment

These 2 cases are of particular interest because (1) a careful search of the literature reveals no previous report dealing with this complication of anticoagulant therapy; and (2) this represents a type of acute hemorrhagic pancreatitis far different from the kind of hemorrhagic pancreatitis we have known up to this time.

The exact etiology of the problem presented by these 2 patients is far from obvious, but there are some possibilities that should be considered. There may have been developing an early, low-grade pancreatitis which complicated the anticoagulant therapy. It is well established that there is an antithrombin substance released in acute pancreatitis, and that acute pancreatitis may be accompanied by hemorrhagic diathesis.[2] Thus, it could be that early inflammation in the pancreas, plus the associated antithrombin substance and the anticoagulant therapy, resulted in the severe pancreatic hemorrhage with shock and the gross appearance of acute hemorrhagic pancreatitis. The other possible explanation is that bleeding, as a result of anticoagulant overdosage, began in the pancreas as a matter of chance and this initiated a low-grade pancreatitis. It is our opinion that the latter is the more likely explanation.

It is difficult to say what is the best treatment for this condition, but surely restoring normal volume and coagulation of the blood and putting the pancreas at rest are desirable. Possibly the latter is not necessary. Both cases presented symptoms of acute surgical conditions in the abdomen, and it appears that there was no way to avoid laparotomy. Even though peritoneal needle taps were done, it still was not possible to rule out a mesenteric thrombosis or strangulated small-bowel obstruction. Nevertheless, as in other types of pancreatitis, it seemed wisest to do only minimal surgery.

Judging from the good prognosis in these 2 cases, it seems that they represented an entirely different problem from acute hemorrhagic pancreatitis as previously known. The recovery in these cases was rapid and complete, with very little therapy, while acute hemorrhagic pancreatitis carries a poor prognosis and is frequently fatal.

Summary

Two cases of acute hemorrhagic pancreatitis in patients on anticoagulant therapy are reported. Both cases presented symptoms of acute surgical conditions in the abdomen, and the diagnosis was made at laparotomy. The possible etiology of the disease in this circumstance is discussed. Both patients recovered speedily and completely from their illness, with very little treatment other than restoration of normal blood volume and coagulation and putting the pancreas at rest. It is believed that because of the apparent excellent prognosis in this condition these cases represent an entirely different disease from the usual hemorrhagic pancreatitis, and that the problem is secondary to anticoagulant overdosage which is manifested by intrapancreatic hemorrhage with subsequent inflammation of the gland.

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Cardiac Arrest Following Massive Transfusion

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CARDIAC ARREST DURING massive blood replacement has been ascribed variously to hyperkalemia,[1] hypothermia,[2,3] citrate intoxication,[4,5] and hypocalcemia.[6] In the vast majority of cases the diagnosis was made in retrospect or by a review of charts and operative records some weeks or even years following the surgical procedure.[7] Electrocardiographic changes, variations in electrolyte concentration, and an elevation of the blood citric acid levels were reported in only a small number of cases of actual arrest.[3,4,8] Similarly, a body temperature was reported in only 1 of the documented cases.[3]

It is at least controversial whether or not variations in the serum potassium levels cause cardiac arrest.[9] The effects of hypothermia on cardiac rhythm are well documented.[10] It has long been suspected that a comparable reduction in the body temperature, which occurs as the result of the rapid infusion of cold blood, would have a similar effect on the myocardium, but confirmatory clinical evidence is lacking. The binding of ionized calcium by citrated blood can, no doubt, cause abnormalities in the cardiac rhythm and contractility. Because serum calcium levels equilibrate with the large calcium stores in bone rather rapidly,[2] a decrease in the calcium concentration is said to be an uncommon cause of cardiac asystole during transfusion. Commonly employed methods for the determination of serum calcium include that fraction which is bound as calcium citrate.[11] Data based on calcium blood levels must be interpreted with caution unless ionized calcium levels are determined or calculated. Elevations of blood citric acid levels following transfusion are well documented.[3–5] Dangerous levels are seldom reached in normal human beings because citrate is metabolized rapidly and infusion is usually slow.[12,13] In some instances, however, the ability to clear the plasma of citrate may be so impaired as to make abnormally high citrate levels a real danger.[3] We recently had an opportunity to observe the following case of cardiac arrest which was secondary to massive transfusion.

Case report

A sixty-nine-year-old Negro female, weighing 50 Kg. (110 pounds), was hospitalized on August 19, 1960, when she suffered a cerebral concussion as a result of a fall. Her history revealed several episodes of clouded sensorium and bizarre behavior. There had been one previous hospital admission in October, 1958. At that time the patient had complained of mild exertional dyspnea as well as of pain in the left shoulder and thorax. A large density in the left chest had been seen on x-ray examination. A scalene node biopsy and a bronchoscopic examination revealed no abnormalities.

A physical examination at the time of the current admission indicated negative findings except for dullness to percussion and diminished breath sounds over the upper two thirds of the left lung field. Peripheral pulses were recorded as being present and equal. A roentgenologic examination of the chest revealed the presence of a huge density occupying the upper two thirds of the left hemithorax. A scalene node biopsy showed

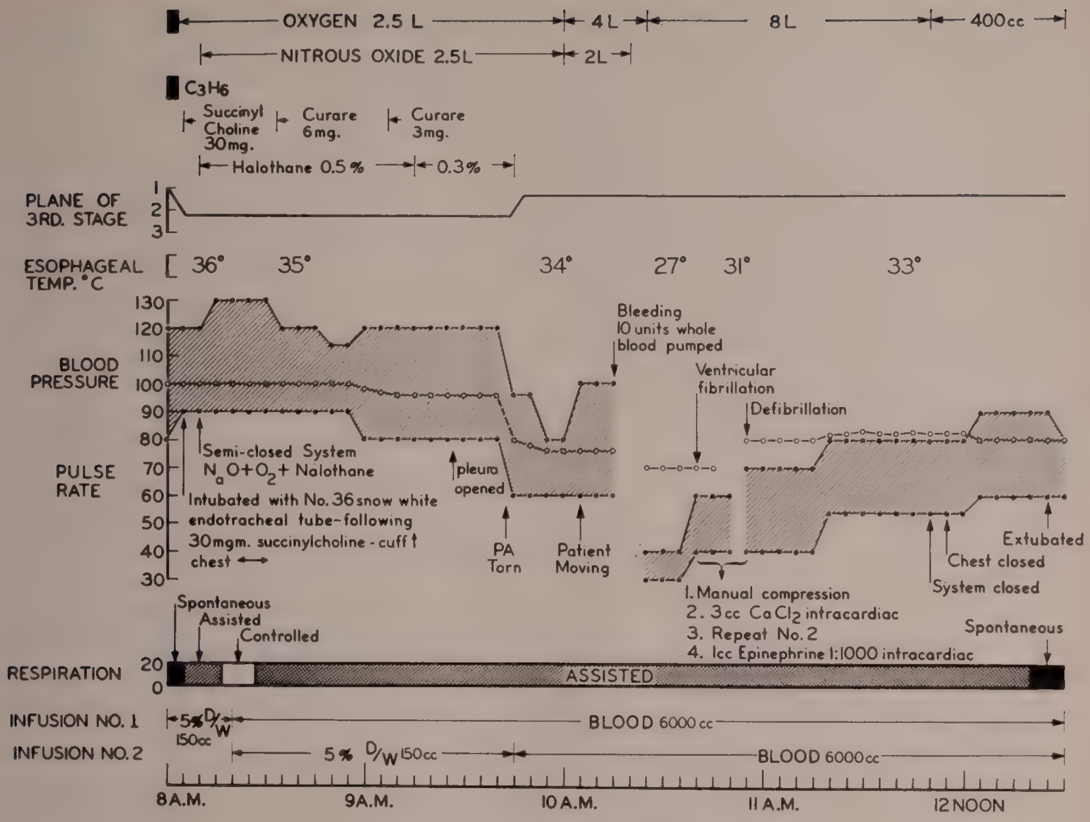

FIGURE 1. Anesthesia record.

negative results. A compression of the left main stem bronchus by an extrinsic mass was noted on endoscopic examination. A diagnosis of a tumor of neurogenic origin was made, and an exploratory thoracotomy was performed on August 29. At the time of exploration the mass proved to be a large aortic aneurysm arising in the ascending aorta and extending at least to the level of the diaphragm. The chest was closed, and the patient was returned to the ward in satisfactory condition. Except for occasional episodes of supraventricular tachycardia, the patient's course was unchanged from its preoperative state. Aortography confirmed the presence of the aneurysm which extended into the abdominal aorta to a level just above the renal arteries.

On October 17, 1960, the patient was scheduled for resection and grafting of the thoracic portion of the aneurysm, utilizing a pump-oxygenator to bypass the circulation. The physical findings at this time were the same as on admission. The hemoglobin was 11.2 Gm. per 100 ml., the hematocrit was 33, and the blood urea nitrogen was 15 mg. per 100 ml. A urinalysis was within normal limits.

The patient was medicated with pentobarbital sodium, 50 mg., and atropine sulfate, 0.3 mg., administered by the intramuscular route one hour prior to the start of anesthesia. Anesthesia was induced with a cyclopropane-oxygen mixture administered from a closed-circle absorber system. Following the establishment of a steady state of anesthesia, an intubation of the trachea was accomplished with a 36F cuffed endotracheal tube under direct vision. Relaxation had been obtained previously with 30 mg. of succinylcholine choride. The maintenance of anesthesia was with a nitrous oxide-oxygen halothane mixture administered with a semiclosed circle absorber system. The operative course was uneventful for the first seventy-five minutes. When bleeding

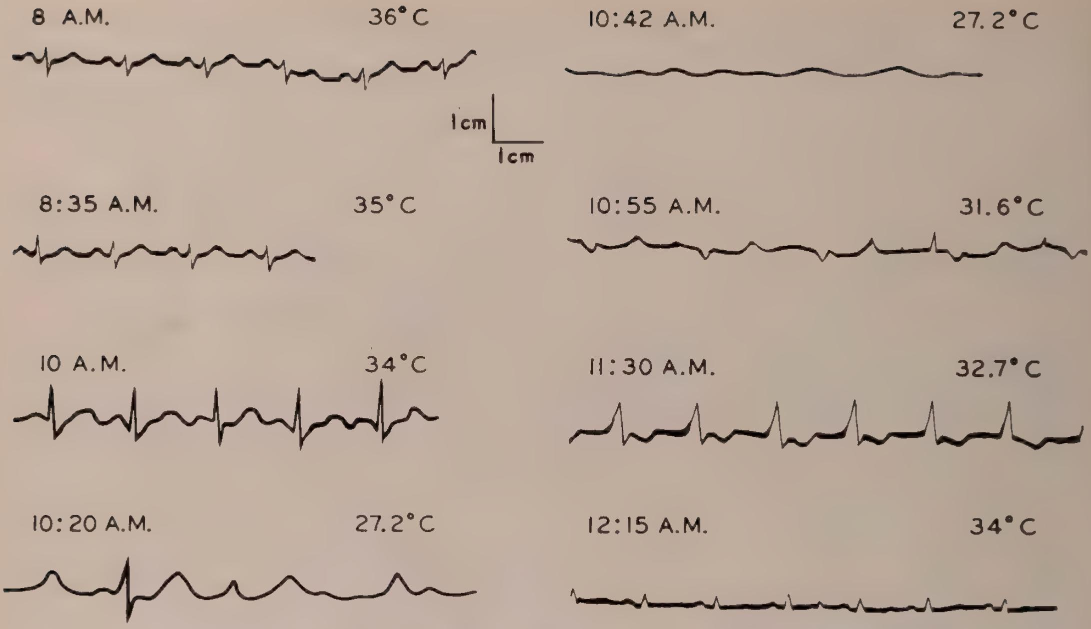

FIGURE 2. Evolution of electrocardiographic changes during course of surgery.

became excessive, the blood loss was replaced as lost. One hour and forty minutes after the start of surgery the continuity of the left pulmonary artery was disrupted. The esophageal temperature at this time was 35 C. As a result of the brisk hemorrhage which followed, the blood pressure declined from 100/70 to 80/50. The pulse rate remained stable at 90 per minute (Fig. 1). Blood was replaced, and the patient was stabilized at this level for a period of ten minutes. An attempt to mobilize and repair the torn vessel was followed by further brisk bleeding with a fall in the blood pressure to 60/50. In a period of twenty minutes the patient received 10 units of citrated blood to replace the estimated blood loss. The electrocardiogram at this time showed a widening of the QRS complex, a prolongation of the Q-T interval, and a peaking of the T waves (Fig. 2). Forty minutes after the first hemorrhagic episode, ventricular fibrillation was observed. Asystole followed quickly. At this time the esophageal temperature was 27.2 C. A manual compression of the heart was instituted immediately. Three cc. of 10 per cent calcium chloride were injected into the heart without any significant result. The dose of calcium chloride was repeated, followed by 1 cc. of 1 : 1,000 epinephrine. Ventricular fibrillation followed this combination. Esophageal temperature was now 30.5 C. Defibrillation was accomplished successfully with a single shock. The blood pressure was recorded as 70/40 and the pulse rate was 80 per minute. The torn vessel was repaired, and the chest was closed as expeditiously as possible. The vital signs remained stable, and the patient made an uneventful recovery from the immediate insult of surgery. On the fourth postoperative day digitalization was required for progressively increasing congestive heart failure. The patient did fairly well until the tenth postoperative day when she expired suddenly. An autopsy revealed a rupture of the aneurysm at the level of the iliac arteries.

Comment

With the fall in the esophageal temperature from 35 to 27.2 C., it is tempting to say that the observed cardiovascular changes were secondary to the rapid induction of the hypothermic state. It is well known that fibrillation or asystole occur at this temperature, especially when the mediastinal structures are being manipulated. The ability to defibrillate and the return of a spontaneous rhythm following the elevation of the body temperature to 31 C. are further arguments for hypothermia as the underlying cause of the arrest. However, at no time were the electrocardiographic changes characteristic of those described for this degree of hypothermia.

The rate was somewhat higher than would be expected. There was no S-T segment or T-wave depression, and the characteristic J wave was not observed. A prolongation of the Q-T interval and a peaking of the T wave are characteristic of hyperkalemia. A similar change in the configuration of the electrocardiogram is seen with hypocalcemia and has been reported with the elevation of the blood citric acid level. This is not unexpected in the latter 2 instances, since a lowering of the plasma-ionized calcium level is tantamount to an elevation of serum potassium. Under such circumstances electrocardiographic changes indicative of potassium excess may be seen in the presence of normal serum potassium levels. The average age of the blood transfused into this patient was three days. Banked, citrated blood of this age, stored under ideal conditions, should contain no more than 1.25 mEq. of potassium per unit of blood. Therefore, this patient received approximately 12.5 mEq. of potassium. At the same time, however, she lost an equal volume of blood containing a similar amount of potassium. Le Veen *et al.*[7] have pointed out that the mobilization of potassium induced by an increased circulating level of catechol amines during shock may elevate significantly the potassium levels. Hyperkalemia produced in this manner could, no doubt, have contributed to the cardiovascular status of this patient. However, Howland *et al.*[13] have been unable to demonstrate significant elevations of serum potassium following massive transfusion.

Citrate intoxication with its consequent reduction in the ionized calcium level occurs infrequently under normal clinical circumstances. When the rate of infusion of citrate is rapid or its degradation or excretion is decreased, blood levels in excess of those considered safe may occur. Citrate infusion at the rate of 1 mg. per kilogram per minute elevates the blood citrate level 12.5 mg. per 100 ml.[3] Levels in excess of 50 mg. per 100 ml. are considered unsafe, since the ionized calcium level at this blood concentration of citrate is below 0.5 mM. per kilogram of water. Each bottle of bank blood filled with 120 cc. of the Solu-B contains the equivalent of 1.43 Gm. of citric acid. This patient, therefore, received 14.3 Gm. of citrate in twenty minutes, an equivalent of 14.3 mg. per kilogram per minute. The resulting blood citrate level, calculated from Ludbrook and Wynn's data, approached 180 mg. per 100 ml., three and one-half times the level considered safe. In addition the degradation of citrate was depressed some 30 to 40 per cent by the degree of hypothermia observed in this patient. Further evidence of the role of citrate as the offending agent in this case is the restoration of cardiac function following the introduction into the circulation of 600 mg. of calcium chloride. After restoring the level of ionized calcium, it was possible to defibrillate and resuscitate the myocardium electrically.

Summary

A case of cardiac arrest following massive transfusion has been presented. The blood citrate levels in this patient reached a level well in excess of that normally considered safe. This level was brought about not only by the rapid rate of infusion of blood, but also by the decreased destruction of citrate resulting from the patient's hypothermic state. A resuscitation was made possible by the intracardiac injection of 600 mg. of calcium chloride.

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Medical use of radiation

The amount of radiation to the reproductive organs of Americans from medical uses of x-rays was estimated to be a third to a sixth of earlier presumed levels by Richard H. Chamberlain, M.D., in a report prepared for a hearing before the Joint Committee on Atomic Energy. Based on studies in other countries, an early estimate of about 150 thousandths of a rad per year is much too high. The figure is more likely to fall between 25 and 50 thousandths of a rad. The medical dose figure compares with natural background radiation of about 150 thousandths of a rad absorbed annually by people living in most parts of the United States.

Thus, the slight risk involved in medical x-rays is far outweighed by the benefits involved. The amount of radiation exposure needed to make diagnostic studies has been decreased in recent years through the development of faster films and intensifying devices which require less energy to provide clear pictures.

Besides the reproductive organs, regarded as the most critical factor in radiation exposure, the rest of the body is unlikely to get enough exposure in medical x-rays to have any significant effect on health. The possible latent effects of large doses of x-rays are offset by the fact that a large number of patients who require and receive large doses have poor life expectancies.

"The judgment with which the physician or dentist balances possible radiation hazards against vital information or other benefits to be obtained must be an educated one which gives proper weight to each relevant factor. Many of the most important technical factors in dosage reduction also depend on highly skilled application of intelligence rather than inherent characteristics of radiation apparatus. In this light, by far the most important technic for medical radiation control and reduction is educational.

"It is of interest to assess the extent of radiation exposure from medical uses and to relate it to that from other sources and to potential hazards which accompany all human radiation exposures. But it is far more important to see that we are using radiation for medical purposes with a high degree of control of dosage, without unnecessary wastage and with wise choice of indications for its use.

"Such considerations result in a progressive reduction of radiation dosage in achieving any given amount of good. The full utilization of present radiologic methods for the maximum benefit of the population is not yet achieved, and an increase in volume of many studies is a desirable goal which will and should accompany the further advance of medical care.

"It would appear almost paradoxical that we are striving to reduce radiation dosage while encouraging and welcoming large increases in it. The two objects should be sharply distinguished, however, for the first is to reduce unproductive radiation exposure, while the latter is to appreciate that medical benefits from indicated procedures, no matter how extensive, usually far outweigh the relatively small potential hazard from the radiation."

Diffuse Alopecia Following Use of Triparanol

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RECENTLY THE INTEREST of the medical profession has been directed toward triparanol (MER/29), a compound which inhibits the synthesis of cholesterol. Cooper[1] and Achor, Winkelmann, and Perry[2] have reported that alopecia may develop subsequently with the use of triparanol. We have seen a patient with a similar problem and are presenting this case report to call further attention to this side-reaction.

Case report

A seventy-eight-year-old white female was known to have hypertensive cardiovascular disease for at least five years. In 1959 she had suffered a cerebrovascular accident which resulted in a hemiparesis of the left side. When she was seen in December, 1960, by one of us (C.R.G), her blood pressure was 176/94. A physical examination at that time was not remarkable except for a left ventricular enlargement. Her cholesterol level was 337 mg. per 100 ml.

On December 23, 1960, she was placed on 250 mg. of triparanol daily. The medication was continued until May 9, 1961. During this period of four and one-half months the patient also was receiving Rauwolfia, benzydroflumethiazide (diuretic and antihypertensive), thyroid extract, secobarbital, amobarbital, and phenobarbital. A low-cholesterol diet was prescribed. On March 16, 1961, the patient's cholesterol level was 215 mg. per 100 ml.

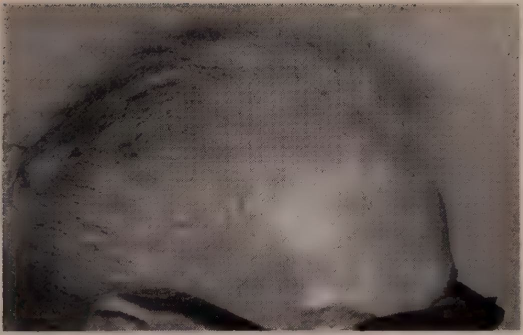

FIGURE 1. Patient with signs of diffuse alopecia.

When the patient was seen on May 9, 1961, a diffuse alopecia was easily noticeable (Fig. 1). She stated that marked hair loss had developed in the preceding two to three weeks. At this time triparanol was discontinued, but her other medications were left unchanged.

Comment

Achor, Winkelmann, and Perry[2] reported 7 cases of cutaneous side-effects to triparanol. All 7 patients had diffuse alopecia. In addition, 2 patients had a scaling of the skin resembling ichthyosis. It was their impression that the dosage required to produce this side-effect varied from patient to patient, but that it was unlikely to occur on a dosage lower than 500 mg. daily. Our patient received only 250 mg. of triparanol daily. Perhaps her advanced age played a role in this increased reactivity.

In the 7 patients noted previously, it was found that the alopecia was reversible when the medication was stopped.

Summary

A case of diffuse alopecia following the use of triparanol (MER/29) has been presented.

MEDICAL CENTER

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Denial of Due Process and Civil Rights to Aged Senile Persons Without Major Mental Impairment*

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As IS GENERALLY KNOWN, the legal and medical professions sometimes clash in areas of common interest. One of these is in the field of commitment of those who are claimed to be mentally ill. In this field the conflict is due to the doctors' lack of appreciation of the importance of civil rights and the lawyer's lack of appreciation of the importance of mental illness as a medical problem. Thus, I have had occasion to be critical of the Commissioner of Hygiene's lack of understanding of the persisting trauma to the layman when he is hospitalized in a mental hospital. On the other hand, a spokesman for the Commissioner is reported to have accused me of being "over-occupied with civil rights," an accusation which in the case of the senile aged is largely true.

However, the conflict obviously must be resolved not in the interest of either profession but in the interest of the patient, so that, ideally, neither his medical needs nor his civil rights will be denied him.

Now it is becoming increasingly clear that in the desire of the Department of Mental Health and its Commissioner to make medical attention immediately available to the mentally ill, two of the forms of involuntary admission recently enacted into law on their recommendation, namely, Sections 73 and 73a of the Mental Hygiene Law, have resulted in a denial of the basic protections of personal freedom and of the safeguards of due process, particularly as these two sections apply to aged senile persons who are without major mental impairment. So glaringly have commitment procedures under these two statutes caused a retrogression of constitutional rights that voices are currently raised either to repeal them or to modify them drastically. It is true, of course, that true mental illness requires immediate medical attention and should not be encumbered by any legal impediments which would jeopardize treatment; but in the case of the not seriously disturbed aged senile patient, whose real need is custody rather than speedy medical attention, there is no excuse whatever for the denial of the rights of due process and of freedom of person, especially at a time of his life when because of the aging process he is least capable of securing those rights for himself.

I am aware that studies are going forward whose purpose it is to evolve a plan which would blend the legal requirement of due process with the medical need for immediate care so that each will be given its respective due. I doubt, however, that any serious effort will be made to do away with the hospitalization in a mental hospital of aged persons who are not the proper subjects therefor, although I am certain that much will be done to restore to them their right to the due process of law.

In the case of the senile person who is not seriously ill mentally I must, of course, indulge in certain basic assumptions and accept little-known but established facts. These are that although mental illness is

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* Reprinted by permission from *New York State Bar Journal* **34:** 19 (Feb. 1) 1962.

becoming progressively recognized as a medical problem, society does and will in our time continue to stigmatize the patient and his family for hospitalization for a mental illness; that hospitalization against one's will still involves loss of liberty, particularly when there is no right to release, and even though hospitals are not prisons, they do affront human dignity when one's confinement is enforced among the mentally ill; that of all the persons annually admitted into mental hospitals, 26 per cent are sixty-five years or older and have no serious mental disease but are largely troubled with senility or the aging process, and one half of them die within one year of their hospitalization.

Now, how do Sections 73 and 73a of the Mental Hygiene Law violate the rights of senile persons? Why did these statutes, enacted on the urgings of the Mental Hygiene Department and its Commissioner mistakenly and wrongfully stress medical aspects to the prejudice of legal safeguards?

Section 73

Section 73 (the pink sheet) is the admission procedure for the nonobjecting patient. Under this section, a nonobjecting patient may be sent directly to a state hospital on the affidavit of one physician, who need not be a psychiatrist. I have already had occasion to point out that in the case of the aged senile patient the absence of an objection is meaningless and unrealistic (see, *Re Jones*, reported in 19 Misc. 1084, 172 N.Y.S. 2d 869):

> . . . Section 73 is a technique increasingly used by the Department of Mental Hygiene which effectively shunts seniles into involuntary confinement without awareness by them of their plight and without their actual approval or judicial surveillance. These unwanted seniles may not even hope to escape factually involuntary confinement because the possibility of private care, often provided at a judicial hearing, is denied to them and, of course, they cannot thereafter effect their own release.
>
> Moreover, the denial of judicial hearing or sanction is based on a statute of questionable constitutionality because it is grounded on a fictitious consent given by one who concededly is confused and disoriented. Even if positive objection is not required by the Mental Hygiene Department, the consent thus extracted is dubious because the senile is not likely to understand that the admitting institution is a mental institution, even if he be told that it is. Often he is chagrined and humiliated following family rejection and has neither the will nor the capacity to object even if he be carefully advised. That he is aware of his right to object or of the significance of his failure to object is doubtful. In short, the pink sheet procedure, in my view, is little less than a ruse designed to circumvent the need for judicial consideration or review of the transfer of the senile to a mental institution. Thus unknowingly certified, without opportunity to secure private custodial care, we have assembly line incarceration, depriving the aged of their liberty of person and, as was said by Judge Garrity (*Matter of Neissloss*, 9 Misc 2d 912, 913): "No matter how sweetly disguised or delicate the language, involuntary confinement is a loss of freedom."

There are other shortcomings to be found in Section 73. While a member of the patient's family signs the petition, that member is not required to respond to judicial scrutiny even when he seeks, as he frequently does, to slough off his responsibility to an aged parent or relative. The single physician who signs the certificate need not even be qualified to certify the mental illness. Since the patient either feels beaten or is uncomprehending, his passive submission during the initial sixty-day stay almost always lapses into perpetual and involuntary incarceration during the last months or days of his life when he most needs but seldom receives the strong and protecting arm of the law. The conclusion is inescapable that Section 73 (presently used in 17 per cent of all the City commitments) is not, in fact, a method for a voluntary or nonobjecting admission, but is a ruse for involuntary admission when applied, as it most frequently is, to the aged senile. Nor is there any question but that court surveillance over this form of indirect forced detention or for the purpose of safeguarding the rights of the aged senile patient who is not seriously ill mentally are wholly neglected principles under this section of the law.

Section 73a

But if Section 73 is indefensible, the more recently enacted Section 73a is even more so. Under the latter section, compulsory admission is effected for sixty days on the petition of a relative and a certification by two physicians, one of whom must be a qualified psychiatrist, and the concurrence of the hospital's psychiatrist. All these requirements are without prior notice to the patient, who is only notified after three days of his hospital admission, which notice may be dispensed with if the doctors believe it to be harmful. The patient under this section will be discharged only on his giving written notice of his desire to leave, which discharge cannot take place until after sixty days. The commitment procedure under this law, while yet in an experimental state, will, based on reliable information supplied to me, become increasingly used for aged senile patients. Obviously, the senile person will be no more capable of appreciating the significance of the belated notice under Section 73a than he is of the significance of the notice, nor of his plight in failing to object thereto under 73. Here again, if he is so heavy-hearted that he does not care, even if he does appreciate its significance, the notice becomes meaningless. Because of his passivity the initial sixty-day stay will invariably be lengthened and become involuntary hospitalization for the remainder of his life. What is more, under this statute no effort need be made, as is the case under section 73, even to inquire if the patient objects or if his right to a judicial hearing is denied to him, nor is he himself likely to make the physical effort to give the required subsequent notice of his objection.

Comment

However well formulated, any plan to protect the right of due process of law which continues to countenance a denial of the freedom of a person, arising from the hospitalization in mental hospitals of aged senile patients who do not suffer major mental impairment, cannot wholly solve the problem. Indeed such a plan might even serve to perpetuate the mischief to these unfortunate elderly people. It is my view that their rights can be secured only if Sections 73 and 73a of the Mental Hygiene Law either are repealed or are so modified as to make mandatory a judicial hearing in their behalf, to prevent the transfer to mental hospitals of those who are not actually suffering from serious mental illness. Hospitalization for such people must be truly voluntary, and it should be limited to their care and medical attention at geriatric clinics and geriatric wings of general hospitals. For, regardless of protestations as to governmental fiscal difficulty in the creation of such facilities, the law must secure personal freedom for these patients by specifically prohibiting their hospitalization in mental hospitals. Expressions of doubt about the power of the Department of Mental Health to maintain nonpsychotic hospital and clinic facilities may be discounted readily since other such nonpsychotic facilities are currently maintained by that Department without challenge for inebriated, narcotic, and for very aged patients themselves.

Finally, it must be reiterated that the concept of the need for immediate and urgent medical attention for aged senile patients who are not critically ill mentally is fallacious and inappropriate since their need is simply that of care and watchfulness. There is thus no excuse for the law to tolerate a legal twisting of the term "lack of objection" as specified in Section 73, or the callous disregard of all need for inquiry as to objection and a belated and useless notice under 73a. Most important, it is morally wrong to deny to aged senile patients afflicted with no serious mental illness the right to be free and to retain the dignity of their person, at a time when that freedom is most urgently needed yet most difficult for them to secure because of their very extreme age and physical debility.

Necrology

Ten Eyck Elmendorf, M.D., of Leonia, New Jersey, formerly of New York City, died on June 1 in Bergen Pines Hospital, Paramus, at the age of eighty-one. Dr. Elmendorf graduated in 1906 from Columbia University College of Physicians and Surgeons and interned at St. John's Guild and Bellevue Hospital. He was a consulting pediatrician at Lutheran Hospital of Manhattan. Dr. Elmendorf was a Licentiate in Pediatrics and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Guy Granger, M.D., of Mayville, died on June 7 at the age of eighty-seven. Dr. Granger graduated in 1899 from the University of Buffalo School of Medicine. He was a member of the Chautauqua County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Greenwald, M.D., of New York City, died on June 6 at Mount Vernon Hospital at the age of sixty-seven. Dr. Greenwald graduated in 1920 from New York Homeopathic Medical College and Flower Hospital. He was an attending surgeon at Columbus Hospital, an assistant attending surgeon at Flower and Fifth Avenue Hospitals and an associate attending surgeon at Metropolitan Hospital and Bird S. Coler Memorial Hospital and Home. Dr. Greenwald was a Fellow of the International College of Surgeons and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John James McGowan, M.D., of Los Angeles, California, formerly of New York City, died on June 7 at Mercy Hospital at the age of eighty-three. Dr. McGowan graduated in 1903 from New York University and Bellevue Hospital Medical School and interned at Fordham Hospital. He was a former New York City Police Department surgeon, an attending physician at St. Elizabeth's Hospital, and a consulting physician at Fordham Hospital. Dr. McGowan was a member of the American Academy of General Practice, the New York Celtic Medical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Edwyn Watkins O'Dowd, M.D., of Tappan, died on May 29 at his home at the age of sixty-one. Dr. O'Dowd graduated in 1926 from New York University and Bellevue Hospital Medical School and interned at St. Vincent's Hospital, New York City. Retired in 1961 as chief surgeon of the Nyack Hospital, he was an attending surgeon at Rockland State and Letchworth Village Hospitals and consulting surgeon and vice-president of the medical staff at Summit Park Sanatorium. Dr. O'Dowd was a Fellow of the American College of Surgeons, a Fellow of the International College of Surgeons, and a member of the New York Academy of Medicine, the Rockland County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Predisposition

The other day I was sent a pencil by the manufacturers of a hypnotic drug. It was a poor pencil, it was difficult to sharpen, its lead broke easily. I found myself trying to use the pencil when editing an article by one of my colleagues about tranquilizers. I noted with interest that the article was rather critical of the drug marketed by the pencil-givers. I found myself wondering whether the issue of poor pencils would do more to reduce sales of this drug than the review: such is the way of the world that I suspect it will.—*The Lancet, May 26, 1962, page 1120*

Abstracts

Kamil, M., Miller, M., Messeloff, C. R., and Lepow, H. I.: Cardiac rupture in myocardial infarction, New York State J. Med. **62:** 2327 (July 15) 1962.

The incidence of cardiac rupture following myocardial infarction as reported in three different series varies from 4.7 to 73 per cent. The underlying factors are: recent coronary artery closure occurring with an acute infarction; dissecting hematoma; hypertension of long duration; age and sex—rupture appears to be more frequent in women than in men and rarely occurs in young patients; physical effort and emotional strain; and anticoagulant therapy. Rupture is most frequent at the site of a massive myocardial infarction and most frequently involves the left ventricle and anterior wall. Aspiration of the accumulated blood may be lifesaving in some cases. Rupture probably is caused by bulging of the infarcted area during systole and contraction of the adjacent healthy muscle against the devitalized area which produces tears in the arteriosinusoidal as well as in the arterioluminal vessels that initiate the dissection of blood through the myocardium, especially if a transmural infarct or intramural thrombus is present.

Tabor, S. H., and Zaino, E. C.: Sex differences in acute myocardial infarction, New York State J. Med. **62:** 2336 (July 15) 1962.

In a study of 77 patients with fatal acute myocardial infarction on whom autopsies were performed from 1955 to 1960, 67.5 per cent were men and 32.4 per cent women. Only 8.4 per cent of the women were under the age of sixty in comparison with 28.8 per cent of the men. Over 20.7 per cent of the patients had diabetes mellitus: 15.3 per cent of the males and 24 per cent of the females. Hypertension was noted in 25 per cent of the males and in 60 per cent of the females. The study failed to reveal any significant shift away from the greater incidence of acute myocardial infarction in the male sex, and it would support the commonly accepted contention that estrogenic factors provide relative immunity to coronary heart disease.

Smith, B. H.: Recent advances in cerebrovascular disease, New York State J. Med. **62:** 2339 (July 15) 1962.

The range and accuracy of diagnosis in cerebrovascular disease have been extended since the introduction of cerebral angiography. Strokes commonly are caused by internal carotid artery occlusion, basilar artery insufficiency, hemodynamic crisis, and unusual causes. The treatment of occlusive vascular disease has not been established definitively; experiments with vasodilators, anticoagulants, fibrinolytic enzymes, and steroids continue, but all of these have drawbacks. Surgery has been successful in some cases. In the treatment of cerebral hemorrhage, surgical treatment is helpful in hematoma but not in acute fulminating hemorrhage.

Glabman, S., and Brinn, L.: Gaucher's disease without splenomegaly; oldest patient on record, with review, New York State J. Med. **62:** 2346 (July 15) 1962.

Gaucher's disease is a familial disorder, characterized by the accumulation and retention of cerebrosides in the reticular cells and histiocytes of the involved organs. The case of an eighty-six-year-old man with Gaucher's disease is presented. Like the other cases of asplenomegalic Gaucher's disease in the literature, the patient did not show most of the usual signs and symptoms and did not have splenomegaly. This group of cases may represent a milder type of the disease, probably owing to a quantitative difference in the enzyme disturbance. Clinical signs of the disease include marked splenomegaly, hepatomegaly, absence of signs of hepatic decompensation, skin pigmentation, and pingueculas. Bone-marrow aspiration, bone biopsy, splenic puncture, liver biopsy, and radiographic examination are helpful in diagnosis. Treatment is merely symptomatic and supportive.

Wray, J. B.: Emergency care of digital injuries, New York State J. Med. **62:** 2355 (July 15) 1962.

In the emergency care of digital injuries an accurate assessment of the extent of damage and sound wound management are essential. Extensor tendon lacerations usually can be treated successfully with a primary suture; however, flexor tendon repair is best accomplished as a delayed procedure. Nerve and tendon repairs are delayed until the fracture is healed. Fractures are splinted with the finger in flexion to avoid permanent stiffness.

Edmunds, R., and West, J. P.: Operative and nonoperative treatment of bleeding esophageal varices, New York State J. Med. **62:** 2361 (July 15) 1962.

In 21 patients with cirrhosis and major bleeding from esophageal varices who were treated by a shunting operation, 76.1 per cent were alive after one year, 57.1 per cent after two years, and 47.6 per cent after three years. Of 21 comparable patients who were treated medically, 38 per cent were alive after one year, 28.5 per cent after two years, and 14.3 per cent after three years. An additional experience with 4 patients suggests that prophylactic shunts may reduce the incidence of early death due to hemorrhage secondary to esophageal varices.

Ellison, R. R.: Experience with fluorinated pyrimidines in adenocarcinoma of the lower intestinal tract, New York State J. Med. **62:** 2364 (July 15) 1962.

When 5-FU (5-fluorouracil) and FUDR (5-fluoro-2′-deoxyuridine) are used in the treatment of adenocarcinoma of the lower intestinal tract, the dose is based on the patient's weight and the classification of the patient as average or poor risk. The chief drug effects are noted in the hematopoietic and gastrointestinal systems. The severity of these two types of toxicity is not necessarily correlated. Approximately 5 per cent of patients with various solid tumors treated with 5-FU or FUDR died of causes directly attributable to severe drug toxicity, and 5 to 10 per cent developed life-threatening toxicity from which they recovered. Tumors which appeared most responsive to therapy were those of the colon and rectum in which occasional responses lasted for from four to eight months. However, improvement was obtained at the expense of some degree of toxicity, and a significant prolongation of life has not been demonstrated as a result of the use of these drugs. The response to therapy is related to primary site of the disease, morphologic type of cancer, extent of the tumor, and rate of progression of the disease. Patients with carcinoma of the colon or rectum with primarily local spread and those with intra-abdominal involvement appear to do better than those with obvious hepatic metastases.

Jameson, W. J.: Clinical effectiveness of potent trichomonacide, metronidazole, New York State J. Med. **62:** 2370 (July 15) 1962.

The effectiveness of a new trichomonacide, metronidazole (Flagyl), in the treatment of Trichomonas vaginalis was studied in 39 patients. Treatment consisted of one 250-mg. oral tablet twice daily and one 500-mg. vaginal insert daily for ten days. Thirty-seven patients were cured after the first course of therapy, 1 was cured after a second course of therapy, and the remaining patient still had symptoms after one course of therapy but was unavailable for a second course. Metronidazole appears to be specific in its action against T. vaginalis. Side-effects occurred in only 2 patients and consisted of rather severe nausea and vomiting and slight sedation.

Mulinos, M. G., Nair, K. G. S., and Epstein, I. G.: Clinical investigation of antitussive properties of pholcodine, New York State J. Med. **62:** 2373 (July 15) 1962.

A clinical study was made of the effectiveness of pholcodine (Ethnine), a morphine derivative, as an antitussive. Twenty-three patients with chronic cough resulting from inflammatory irritation and bronchial secretions associated with pulmonary tuberculosis were given 10 to 20 mg. of pholcodine, codeine sulfate, or a placebo for from one to twenty-nine days. A second group of 26 patients received the three preparations alternately within a one-week period. Eighty per cent of the patients experienced relief after the administration of pholcodine. Pholcodine was found superior to codeine sulfate as an oral antitussive agent without the side-effects often associated with codeine administration. Its effectiveness did not diminish after daily use over a two-week period, and it was not habituating.

Letters to the Editor

Handling of professional visitors

To the Editor: Physicians and scientists in teaching hospitals are often plagued with casual visitors.

There seems to be no socially acceptable way of avoiding the visitor, announced by the secretary as Dr. Smith, who assumes a comfortable position and asks "What's new?" One must decide whether to assume the entire burden of entertaining Dr. Smith or to "dump" him on hapless colleagues (who will undoubtedly return the favor) or on a research fellow if the visitor's seniority doesn't rate "VIP" treatment.

In my opinion, a visit should be for a specific purpose and should be preceded by a definite arrangement for an appointment. When possible, technical information should be provided by subordinates; they usually are a better, more accurate source of information, anyway. The visitor should assume responsibility for concluding the interview.

Suggestions as to how others politely handle professional visitors, domestic and foreign, would be welcome.

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Simplfying the law with respect to wills

To the Editor: Slowly but surely the van of progress moves forward. Technicalities and rigamarole are disappearing, and modern business efficiency is gradually finding a place in legal procedure.

Deeds, mortgages, bills of sale, and numerous other legal documents need only be signed and acknowledged before a notary public, yet the archaic law with reference to wills, which goes back many hundreds of years, still requires many unnecessary and cumbersome formalities. These should be abolished, just as dower and courtesy and many other ancient encumbrances have been removed.

A will should merely have to be signed and acknowledged before a notary public. It should not be necessary twenty or thirty years later to conduct an exhaustive investigation to find the witnesses to a will, who may have died or disappeared long since. The signature of a notary public can be proved very easily at any time because it is always on file. The probate of a will should be an easy matter, not a trying procedure involving the services of a Sherlock Holmes to locate missing witnesses.

Let us abolish all of the rigamarole of ancient days and allow a will to be signed and acknowledged before a notary public, as is a deed or any other legal instrument. It will make it easier to probate the will and faster to close the estate and distribute to creditors and legatees. Many estates are not liquidated for many years because witnesses can not be located. This can and must be stopped. A simple amendment allowing a will to be drawn and acknowledged in the manner indicated will accomplish the needed purpose.

Meyer Kirschenbaum, Esq.

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Elimination of shortage of general practitioners

To the Editor: We, as physicians, can help to eliminate the shortage of general practitioners. Of all physicians, the general practitioner has the closest relationship with patients, thus enabling him to know the patient's needs best. During these days of difficult public relations it is necessary to have physicians better understand the socioeconomic needs of patients.

The lure of specialty practice has robbed our citizenry of many capable general practitioners. This is due, in large part, to the inadequate training programs maintained by many of our medical schools. The men are not prepared to enter general practice—many are uncertain and have not been reassured by their teachers in academic medicine.

I believe that a mandatory period of five years of general practice should be required as a prerequisite for specialty training. This plan would offer many benefits to the physicians themselves and to the public. It would provide a continuing supply of general practitioners; it would give the specialist a better understanding of the factors underlying the diseases which they are treating. Too often today the specialist who has gone from medical school to internship and residency without having experienced general practice is a cold, callous individual, who is more concerned with the disease than with the patient. It has been my observation that the specialist who has been in general practice has a better understanding of the whole patient.

For the preceding reasons I believe that mandatory five years of general practice should be required before specialty training is permitted.

KENNETH M. KRON, M.D.

Stenton Avenue at Hortter Street
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Requests for illegal abortion in Puerto Rico

To the Editor: We are constantly receiving complaints from fellow physicians in Puerto Rico to the effect that women from continental United States, predominantly from New York, continue to come to our island under the impression that abortion is a legal procedure here.

Practically every day we receive telephone calls from physicians in New York requesting that my office recommend some gynecologists to whom they should refer their patients. Even I myself, an internist, went through the displeasure of receiving a visit of one of those patients at my home, requesting such a service.

You can very well see the difficulties that such practice is creating among the medical profession in Puerto Rico.

I believe that you would do us a great service if you could inform the members of your Society, as well as all nonmember physicians in New York, that the practice of abortion is just as illegal in Puerto Rico as it is in New York. We will certainly appreciate any other measure you may be willing to undertake to eliminate the practice of recommending that people in your State come to Puerto Rico to have an abortion performed.

JOSÉ MANUEL TORRES, M.D., President
Asociación Médica de Puerto Rico

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New lead in search for cause of muscular dystrophy

An abnormality in the distribution of magnesium in the blood of persons suffering the childhood type of muscular dystrophy was reported by Harris L. Smith, M.D., Robert L. Fischer, M.D., and James N. Etteldorf, M.D., in the June, 1962, issue of the *American Journal of Diseases of Children*.

This previously unrecognized abnormality appears to involve the combining of magnesium with some as yet unidentified substance, perhaps protein, of high molecular weight.

Because of the significant roles played by magnesium and calcium individually and their apparent interrelationships in muscle contraction and relaxation, 21 patients ranging from three to twenty-nine years of age were studied to determine the levels of these two metal ions in the blood and in the residue after the blood had been processed by ultrafiltration. The results were compared with 34 normal persons. The calcium levels among the normal group did not differ significantly. On the other hand, twice as much magnesium was found in the blood of normal persons as in dystrophic patients. However, the magnesium found after ultrafiltration was about the same in both groups.

From this finding it is theorized that there is an abnormal binding of magnesium to some other substance in the blood of persons with the childhood type of muscular dystrophy. The process of ultrafiltration removes or eliminates the substance responsible for this abnormality. It appears that during ultrafiltration alterations occur which release or make available previously bound magnesium.

Since the interfering substances are not ultrafilterable they are of high molecular weight.

Although the true significance of this finding remains to be determined, it appears that the availability of magnesium to activate certain enzymes linked to muscle contraction might well be a factor in the development of muscular dystrophy.

Abstracts in Interlingua

Kamil, M., Miller, M., Messeloff, C. R., e Lepow, H. I.: Ruptura cardiac in infarcimento myocardial (*anglese*), New York State J. Med. **62:** 2327 (15 de julio) 1962.

Le incidentia de ruptura cardiac post infarcimento myocardial, secundo le reportos de tres differente series, varia inter 4,7 e 73 pro cento. Le subjacente factores es: Recente clausura de arteria coronari occurrente con infarcimento acute; hematoma dissecante; hypertension de longe duration; etate e sexo (ruptura pare esser plus frequente in feminas que in homines e occurre rarmente in patientes de etate juvene); effortio physic e stress emotional; e therapia anticoagulante. Rupturas occurre le plus frequentemente al sito de un massive infarcimento myocardial; in le majoritate del casos illos es in le ventriculo sinistre e in le pariete anterior. Aspiration del accumulate sanguine pote salvar le vita del patiente in certe casos. Il es probabile que le causa del ruptura es un extrusion del infarcite area in systole insimul con contraction del adjacente musculo normal contra le disvitalisate area. Isto produce fissuras in le vasos arteriosinusoide e etiam arterioluminal le quales initia le processo hematomato-dissecante in le myocardio, specialmente si un infarction transmural o un thrombo intramural es presente.

Tabor, S. H., e Zaino, E. C.: Differentiation inter le sexos in acute infarcimento myocardial (*anglese*), New York State J. Med. **62:** 2336 (15 de julio) 1962.

In un serie de 77 patientes con mortal acute infarcimento myocardial, in qui necropsias esseva effectuate inter 1955 e 1960, 67,5 pro cento esseva homines e 32,4 feminas. Solmente 8,4 pro cento del feminas habeva etates de minus que sexanta annos, a comparar con 28,8 pro cento in le caso del homines. Plus que 20,7 pro cento del patientes habeva diabete mellite, 15,3 pro cento del homines e 24 pro cento del feminas. Hypertension esseva notate in 25 pro cento del homines e in 60 pro cento del feminas. Le studio revelava nulle significative tendentia contra le predominantia de acute infarcimento myocardial in le sexo mascule, e illo pare supportar le communmente acceptate these que factores estrogenic provide un immunitate relative contra morbo de arteria coronari.

Smith, B. H.: Recente progressos in nostre cognoscentias in re morbo cerebrovascular (*anglese*), New York State J. Med. **62:** 2339 (15 de julio) 1962.

Le applicabilitate e le accuratia del methodos diagnostic in morbo cerebrovascular se ha extendite depost le introduction de angiographia cerebral. Accidentes cerebrovascular es usualmente causate per (1) occlusion del interne arteria carotide, (2) insufficientia de arteria basilari, (3) crises hemodynamic, o (4) factores inusual. Le tractamento de occlusive morbo vascular es non ancora definitemente establite. Experimentos con vasodilatantes, anticoagulantes, enzymas fibrinolytic, e steroides continua, sed omne ille agentes ha lor disavantages. Chirurgia ha essite successose in certe casos. In le tractamento de hemorrhagia cerebral, intervention chirurgic es utile, sed solmente si il se tracta de hematoma e non de acute hemorrhagia fulminante.

Glabman, S., e Brinn, L.: Morbo de Gaucher sin splenomegalia; le patiente le plus vetule in le litteratura; con revista (*anglese*), New York State J. Med. **62:** 2346 (15 de julio) 1962.

Morbo de Gaucher es un disordine familial, characterisate per le accumulation e retention de cerebrosidos in le cellulas reticular e in le histiocytos del afficite organos. Es presentate le caso de un masculo de octanta-sex annos de etate con morbo de Gaucher. Como le altere patientes con asplenomegalic morbo de Gaucher reportate in le litteratura, le presente patiente non monstrava le majoritate del usual signos e symptomas e non habeva splenomegalia. Iste gruppo de casos representa possibilemente un plus leve typo del morbo, probabilemente in consequentia de un differentia quantitative in le disturbation enzymatic. Signos clinic del morbo include marcate splenomegalia, hepatomegalia, absentia de signos de discompensation hepatic, pigmentation cutanee, e pinguiculas. Aspiration de medulla ossee, biopsia de osso, e examine radiographic es utile in le diagnose. Le therapia es mermente symptomatic e supportative.

Wray, J. B.: Auxilio de urgentia in vulnerationes digital (*anglese*), New York State J. Med. **62:** 2355 (15 de julio) 1962.

In le assistentia de urgentia in casos de vulneration digital, un accurate evalutation del importantia del damnos e un meticulose manipulation del vulnere mesme es essential. Lacerationes de tendine extensori es usualmente tractabile a bon successo per suturation primari. Del altere latere, le reparo de tendines flexori se face le melio como procedimento procrastinate. Reparo de nervo e de tendine es a procrastinar usque le fractura es restablite. Fracturas es harnesate con le digito in flexion pro evitar permanente rigiditate.

Edmunds, R., e West, J. P.: Tractamento operatori e non-operatori de sanguinante varices esophagee (*anglese*), NEW YORK STATE J. MED. **62:** 2361 (15 de julio) 1962.

Ex un serie de 21 patientes con cirrhosis e major formas de sanguination ab varices esophagee, tractate per shunt operatori, 76,1 pro cento esseva in vita post un anno, 57,1 pro cento post duo, e 47,6 pro cento post tres. Ex un comparabile serie de 21 patientes, tractate medicalmente, 38 pro cento esseva in vita post un anno, 28,5 pro cento post duo, e 14,3 pro cento post tres. Experientias additional in le tractamento de 4 patientes suggere que shunts prophylactic es forsan capace a reducer le incidentia de morte precoce ab hemorrhagia secundari a varices esophagee.

Ellison, R. R.: Experientias con le uso de fluorisate pyrimidinas in le tractamento de adenocarcinoma del vias infero-intestinal (*anglese*), NEW YORK STATE J. MED. **62:** 2364 (15 de julio) 1962.

Quando 5-FU (5-fluorouracil) e FUDR (5-fluoro-2′-disoxyuridina) es usate in le tractamento de adenocarcinoma del vias infero-intestinal, le dose es basate in le peso del patiente e in su classification como caso mediemente o altemente impericulate. Le major effectos del droga es manifeste in le symptomas hematopoietic e gastrointestinal. Le severitate de iste duo typos de toxicitate non es necessarimente inter-correlationate. Approximativemente 5 pro cento del patientes con varie tumores solide tractate con 5-FU o FUDR moriva de causas directemente attribuibile al toxicitate sever del droga, e 5 a 10 pro cento disveloppava grados de toxicitate impericulante le vita sed restabliva se ab illos. Le tumores que pareva responder le melio al therapia esseva illos del colon e del recto. In iste casos, le responsa durava a vices inter quatro e octo menses. Tamen, melioration esseva obtenite al expensa de un certe grado de toxicitate, e nulle significative prolongation del vita esseva demonstrate como resultato del uso de iste drogas. Le responsa al therapia es relationate con le sito primari del morbo, le typo morphologic del cancere, le extension del tumor, e le rapiditate del progresso del morbo. Il pare que patientes con carcinoma del colon o recto con dissemination predominantemente local e patientes con affectiones intra-abdominal profita plus que patientes con obvie metastases hepatic.

Jameson, W. J.: Efficacia clinic del potente trichomonacida, metronidazol (*anglese*), NEW YORK STATE J. MED. **62:** 2370 (15 de julio) 1962.

Le efficacia del nove trichomonacida, metronidazol (Flagyl) esseva studiate in le tractamento de 39 patientes con infection per *Trichomonas vaginalis*. Le tractamento consisteva in le administration oral de un tabletta de 250 mg duo vices per die e in le application diurne de un inserto vaginal de 500 mg durante dece dies. Trenta-septe del 39 patientes esseva curate post le prime curso del therapia; 1 esseva curate post un secunde curso; e le ultime, qui habeva ancora symptomas post le prime curso, non esseva accessibile pro un secunde curso. Il pare que metronidazol es specific in su action contra *T. vaginalis*. Adverse effectos secundari occurreva in solmente 2 patientes. Illos consisteva de grados satis sever de nausea e vomito e leve grados de sedation.

Mulinos, M. G., Nair, K. G. S., e Epstein, I. G.: Investigation clinic del proprietates antitussive de pholcodina (*anglese*), NEW YORK STATE J. MED. **62:** 2373 (15 de julio) 1962.

Esseva interprendite un studio clinic del efficacia del derivato de morphina pholcodina (Ethnina) como agente antitussive. Vinti-tres patientes con tusse chronic resultante ab irritation inflammatori e secretiones bronchial associate con tuberculosis pulmonari esseva tractate con 10 a 20 mg de pholcodina, de sulfato de codeina, o de un placebo durante periodos de inter un e vintinovem dies. Un secunde gruppo de 26 patientes recipeva le mesme tres preparatos in alternation in le curso de un septimana. Octanta pro cento del patientes experientiava alleviamento post le administration de pholcodina. Pholcodina se monstrava superior a sulfato de codeina como oral agente antitussive e non produceva le adverse effectos secundari que es frequentemente associate con le administration de codeina. Su efficacia non declinava post uso diurne durante un periodo de duo septimanas. Le patientes non se habituava a illo.

Medical Schools

Albany Medical College

Commencement. The 133rd commencement exercises were held on June 3. Willard C. Rappleye, M.D., president of the Josiah Macy, Jr. Foundation and dean emeritus of Columbia University College of Physicians and Surgeons gave the address and was awarded an honorary doctor of science degree. The class of 61 received their degrees from Dr. Carter Davidson, chancellor of Union University, Dr. Harold C. Wiggers, dean, administered the traditional Hippocratic Oath, and the hoods symbolic of the M.D. degree were place on the graduates shoulders by Thomas L. Hawkins, Jr., M.D., instructor in medicine, assisted by Thomas Hale, M.D., director of Albany Medical Center Hospital. Marshall for the academic procession was James Dougherty, M.D., assistant professor of orthopedic surgery.

Albert Einstein College of Medicine

Declaration of Geneva pledged by graduates. The fourth commencement exercises were held on May 31 for 88 men and women at which the Declaration of Geneva, which affirms that no questions of religion, nationality, race, party politics, or social standing may come between physician and patient, was pledged by the new doctors of medicine. Genocide was also foresworn. Dr. Philip Morrison, professor of physics, Cornell University, delivered the commencement address and discussed "The Population of the Other World," and the students were presented by Marcus D. Kogel, M.D., dean, and Samuel Belkin, M.D., president, of the College, presented the diplomas.

Clinical Center for study of acute conditions. Shock, burns, severe infections, and acute conditions arising during and after surgery will be the target of extensive clinical research in the new center being established at the College under a grant made by the National Institutes of Health. The new unit will be located in the Jacobi Hospital. Stanley M. Levenson, M.D., professor of surgery, is the program director.

Cornell University Medical College

Research career award. Gerhard H. Giebisch, M.D., associate professor of physiology, has been given a Research Career Award by the National Institutes of Health to carry on his program of study of "Ion Transport Across Renal Tubules of the Mammalian Kidney." The award has been made for a period of five years beginning July 1.

Commencement. Eighty-four seniors received their medical degrees at the commencement exercises held on June 6. Dr. W. Clarke Wescoe, Chancellor, University of Kansas, delivered the address and John E. Deitrick, M.D., dean, administered the Hippocratic Oath.

New York Medical College

Lord Mayor of Dublin, Ireland, commencement speaker. The Honorable Robert Briscoe, Lord Mayor of Dublin, Ireland, delivered the 103rd commencement address on June 6. The College conferred an honorary degree of Doctor of Humane Letters on the Lord Mayor and an honorary Doctor of Science degree on Representative John E. Fogarty (democrat, Rhode Island) in recognition of his leadership on health legislation in the House of Representatives. Music was provided by the Doctors' Orchestral Society of New York, whose president, Harvey Salomon, M.D., is an alumnus of the College. The graduating class consisted of 126 students, six of whom were women.

New York University Medical Center

Occupational health course. A full-time, five-day course in occupational health for registered professional nurses in industry will be given beginning October 15 by the Department of Industrial Medicine. The course will be given in cooperation with the American Association of Industrial Nurses and will be under the direction of David H. Goldstein, M.D., professor of industrial medicine. Applications should be sent to the dean, New York University Post-Graduate Medical School, and the course will be limited to 50 students.

President of Alumni Association. Charles E. Kossman, M.D., associate professor of medicine and president, New York Heart Association, has been elected president of the Alumni Association of New York University School of Medicine. Other officers elected are: Richard M. Hyman, M.D., vice-president; David H. Goldstein, M.D., secretary; Joseph M. Pisani, M.D., treasurer; Claude E. Heaton, M.D., re-elected historian; and Maxwell H. Poppel, M.D., re-elected to the board of directors of the Alumni Federation. A former president of the Association, Dr. Poppel has been named the recipient of this year's alumni meritorious service award. President-elect is Randolph A. Wyman, M.D.

V. H. Kazanjian visiting professorship in plastic surgery. "A Lifetime Experience in Plastic Surgery" was the title of a lecture given by V. H. Kazanjian, M.D., professor emeritus of plastic surgery, Harvard Medical School, on May 28. At that time Dr. Kazanjian was awarded the presidential citation of New York University. The lecture was the inaugural one of the V. H. Kazanjian Visiting Professorship in Plastic Surgery and has been established at the School of Medicine and Post-Graduate Medical School through a contribution from the Society for the Rehabilitation of the Facially Disfigured, Inc. Named for its first lecturer it is to be an integral part of the teaching program of the Institute of Reconstructive Plastic Surgery.

International Committee on laboratory animals. The Medical Center was the only nongovernmental organization represented at a meeting on animal caretaker education of the International Committee on Laboratory Animals, a branch of the United Nations Educational, Scientific and Cultural Organization, held May 28 and 29 in Paris. L. R. Christensen, M.D., director of scientific services at the Center's Henry W. and Albert A. Berg Institute for Experimental Physiology, Surgery and Pathology and associate professor of pathology, and Mr. Berton Hill, executive of the Institute of Laboratory Animal Resources, a division of the National Academy of Sciences, National Research Council, represented the United States.

Appointed. Clark T. Randt, M.D., a consultant to the Cleveland Vocational Guidance and Rehabilitation Service, and the Office of Life Science Programs, National Aeronautics and Space Administration, has been appointed as professor of neurology at the School of Medicine and director of the NYU third neurology division of Bellevue Hospital Center.

State University of New York Downstate Medical Center

Annual honors day. President Harry D. Gideonse, Brooklyn College, delivered the fourth Annual Honors Day address in May. Dr. Gideonse spoke on "A Nonspecialist Looks at Russia." Preceding the address six members of the June graduating class presented reports of research which they have carried out during their medical school years. Students participating were: Richard Elkort—"Acute Metabolic Acidosis and Cardiovascular Function," Stephen R. Gluck—"An Analysis of the Mechanical Properties of the Uterine Smooth Muscle," Stanley J. Goldsmith—"Enzymatic Activity During Cellular Degeneration and Regeneration," Wilfred Minkin—"Purification and Properties of a Reduced Vitamin K_1"—"Cytochrome C Reductase Isolated from Spinach," Arthur L. Rozman—"Injection Studies of the Arterial Supply of the Interventricular Septum and the Relationship of Vascular Changes to Atrioventricular Conduction," and Arthur H. Wolintz—"Method and Clinical Application of Acrylamide-Gel Electrophoresis."

The Society of the Sigma Xi. Wallace R. Brode, science adviser to the State Department and national president of The Society of the Sigma Xi delivered the annual Sigma Xi Lecture on May 28. His topic was "The Growth of Science."

State University of New York Upstate Medical Center

MEND. Leo G. Rigler, M.D., executive director, Cedars of Lebanon Hospital, Los Angeles, California, discussed "Roentgen Observations of Abdominal Trauma" at the MEND lecture in May.

Student research symposium. Robert Nemiroff, senior medical student, who received the 1962 Honors Thesis first prize, presented his paper "A Study of Psychoanalytic Practice and Opinions" at the Student Research Symposium in May. Other students who participated and their subjects were: Jerome Reich—"Fine Anatomy of the Mesangium of the Human Glomerulus," Norman H. Pearl—"Interviewing and Attitude Shift; a Semantic Differential Analysis," and Reynold S. Golden—"Studies in the Diagnosis of Urinary Tract Infection in Pediatric Patients."

Alumni reunion. The 87th annual reunion was held on May 26 with traditional events and five-year class reunions, a dinner-dance, and the annual Weiskotten Lecture. Dr. C. Wesley Eisele, associate dean in charge of postgraduate medical education, University of Colorado Medical Center, spoke on "Education for General Medical Practice" and following the lecture a panel discussion on Dr. Eisele's topic was held by Robert Persson, M.D., alumni president, Dr. Carlyle Jacobsen, president of the Medical Center and dean of the College, and Richard Bellaire, M.D., Saranac Lake. Mr. Robert Nemiroff, and a 1962 graduate, was invited to present his winning Honors Thesis paper on "A Study of Psychoanalytic Practices and Opinions" during the morning program on Alumni Day. Jehan Shah Saleh, M.D., class of 1933, and minister of Education for Iran, was the after-dinner alumni speaker.

Commencement exercises. Commencement exercises were held in Nottingham Auditorium for 71 candidates for the doctor of medicine degree. Philip B. Armstrong, M.D., professor and chairman, Department of Anatomy, gave the address on "Where Have We Been, Where

Are We and Where Are We Going?" Chief marshall was Dr. W. W. Westerfeld, professor and chairman, Department of Biochemistry and associate dean for graduate education and research, and marshalls were William H. Bergstrom, M.D., associate professor, Department of Pediatrics, C. B. Mueller, M.D., professor and chairman, Department of Surgery, and Bernard W. Asher and David R. Yates, members of the Class of 1963. Donald C. Samson, M.D., associate professor, Department of Medicine, administered the Hippocratic Oath and degrees were conferred by Dr. Carlyle Jacobsen, president of the Center and dean of the College. Richard W. Lyons, M.D., professor and chairman, Department of Medicine, announced the doctor of medicine degree candidates.

University of Rochester School of Medicine and Dentistry

International cancer congress. Charles D. Sherman, Jr., M.D., assistant professor of surgery, will take part in the International Cancer Congress in Moscow which is being held from July 23 to 28. Following the Congress, Dr. Sherman will lecture in Athens as the guest of Professor P. Chrysopathic and will then visit the Cancer Institute in Rome and the University of Montpelier in France. Dr. Sherman is sending Robert D. Brenman, a third-year student, to Montpelier to work with Dr. Claude Romieu for the summer.

Appointed. William L. Morgan, Jr., M.D., associate physician with the Division of Cardiovascular Disease, Henry Ford Hospital, Detroit, Michigan, has been appointed associate professor of medicine effective September 1. Dr. Morgan will serve as coordinator of the medical house staff training program and will supervise electrocardiography in the adult services of the Medical Center. He also will be a member of the staff of the Cardiopulmonary Unit, Department of Medicine, and will have major responsibilities for both undergraduate and postgraduate education in the Center.

Decision in bedrail case up to jury

A trial court erroneously dismissed a suit against a hospital for damages resulting from a patient's fall in the absence of bedrails, according to a case reported in the May 31, 1962, issue of *The Citation*, published by the American Medical Association. The Oklahoma Supreme Court ruled that the suit should have been submitted to the jury.

Evidence showed that the patient had been admitted to the hospital in a "state of disturbed consciousness" and in a weak condition. Her husband advised that side rails be put on the patient's bed. After consultation with the attending physician, a nurse promised that the rails would be installed. She directed a nurse's aid to get the rails, and they were placed in the hall outside the patient's room. Several hours later, a noise was heard, and the patient was found face down on the floor next to the bed. Only after the patient was lifted back into bed were the side rails installed. The evidence showed that the patient suffered injuries from the fall sufficient to warrant at least nominal damages.

The court said that, after the warning by the husband and the promise that side rails would be installed, the hospital had an obligation to exercise reasonable care and diligence in installing the rails. This was sufficient for submission of the case to the jury, the court ruled. It was not necessary to prove that, in the light of the patient's condition, the hospital had a duty to foresee that the patient might fall if side rails were not installed. [(*Sanders* v. *St. John's Hospital & School of Nursing*, 369 P. 2d 165 (Okla., Feb. 27, 1962)]

Month in Washington

The American Medical Association challenged the Kennedy Administration on the accuracy and legality of its propaganda campaign for the King-Anderson bill.

F. J. L. Blasingame, M.D., executive vice-president of the A.M.A. wired Attorney General Robert Kennedy about a booklet issued by the Department of Health, Education, and Welfare. His wire said: "This booklet lobbies for the enactment of the King-Anderson bill. This bill would raise Social Security taxes to provide limited health services to aged beneficiaries, regardless of whether they need financial help.

"The Department of Health, Education, and Welfare has used tax funds, collected from everyone, to propagandize for a bill which many people and many groups have vigorously opposed. Under law, the publishing of this kind of a booklet without Congressional authority is a criminal act, punishable by fine or imprisonment, or both, and removal from office."

A.M.A. president Leonard W. Larson, M.D., wrote President Kennedy correcting a misstatement the Chief Executive made at a news conference.

The President told his news conference that "the A.M.A. was one of the chief opponents of the Social Security system in the 30's."

Dr. Larson pointed out to Mr. Kennedy that the American Medical Association had never opposed the Social Security system, either before or after its adoption.

"The Association," Dr. Larson's letter said, "testified before Congress on only one section of the Social Security legislation, the section concerning extension of public health services. It should be noted that the A.M.A. testified in support of this section."

Dr. Blasingame also called on the Justice Department to stop Cabinet members from using taxpayers' money for lobbying purposes and to launch an investigation of "improper" lobbying activities of employes of the Department of Health, Education, and Welfare.

Dr. Blasingame in a letter to Attorney General Robert Kennedy listed more than a dozen incidents which he said violated Federal statutes prohibiting lobbying by Federal employes and officials.

"Government employes," Dr. Blasingame said, "are being sent out as speakers at public meetings to urge enactment of the Administration's bill. This, in our opinion, is a clear violation of Title 18, Section 1913, of the U.S. Code on crimes and criminal procedure which prohibits among other things the use of 'personal services' for lobbying purposes."

Dr. Blasingame said that Secretary of Commerce Luther Hodges, Secretary of Labor Arthur Goldberg, and Interior Secretary Stewart Udall were appearing at rallies concurrent with President Kennedy's appearance in Madison Square Garden in the Administration's campaign for the King-Anderson bill.

"We strongly protest the use of tax monies by these Cabinet members to lobby for a bill which is clearly not within the scope of their respective departments," Dr. Blasingame said. "I call on you to issue an injunction against this type of activity by these Cabinet members."

The A.M.A. executive vice-president also noted that between six and ten government employes "have been lobbying in the White House offices for several months" for the King-Anderson bill. He said the group occupying a four-room suite "has been writing television and radioscripts, drafting advertisements and helping with publicity releases for various organizations which are backing the King-Anderson bill."

Dr. Larson, A.M.A. president, also urged that "the American people demand an honest accounting from the Department of Health, Education, and Welfare on how much of their tax money the department is spending on lobbying for the King-Anderson bill."

Dr. Larson said that the National Council of Senior Citizens should be required to register as a lobbyist.

In a statement, Dr. Larson cited contradictory statements by two prominent advocates of President Kennedy's health-care-for-the-aged bill—Secretary of Health, Education, and Welfare Abraham Ribicoff and Rep. Cecil R. King (D., Calif.).

"Mr. Ribicoff and Mr. King may be on the same team but they are in basic disagreement as to the extent of services Social Security should provide and how much of an increase in taxes the public will tolerate to finance these services," Dr. Larson said. "This is what is happening: Secretary Ribicoff, in an effort to make the King-Anderson bill palatable to those fearing greater Federal taxes, is saying that the health care program will not be expanded because Social Security taxes have just about hit 10 per cent, his estimate of the saturation point. Meanwhile, Mr. King, in order to gain the support of those who believe in the 'Federal government playing the role of Santa Claus' is

Prepared by the Washington, D.C., office of the American Medical Association.

promising increased Social Security benefits in the future."

* * *

The American Medical Association opposed legislation that would permit beneficiaries of the Federal Employees' Compensation Act to utilize the services of chiropractors.

In a letter to the chairman of the Senate Subcommittee on Employees Compensation, Dr. Blasingame, A.M.A. executive vice-president, said: "Chiropractic is a pseudo-science which is not based on scientific methods and, therefore, should be recognized as what it is, a theory of cultism. It is premised on the theory that human illness is all related to the spinal column. It holds that the nerves that emanate from the spinal cord become impinged or pinched by the vertebrae, thereby causing malfunction and disease.

"As a result of this theory, chiropractors claim that disease and illness such as allergies, diabetes, heart trouble, and tonsillitis, to name a few, can be cured by adjusting or manipulating the spinal column. Such a theory, of course, runs counter to the established facts of medical science.

"Chiropractors are not educated or equipped by either background or training to diagnose human illness. This inability to render a diagnosis coupled with their pseudoscientific method of treatment, when taken into consideration in connection with their vociferous stand against lifesaving vaccines and wonder drugs, precludes that any consideration be given them."

One type of mental health

One type of mental health has been found among persons who are of average intelligence and feel that they have achieved their niche in life but who are somewhat lacking in ambition and creativity, according to an article by Roy R. Grinker, Sr., M.D., in the June, 1962, issue of *Archives of General Psychiatry*. This conclusion was drawn from an investigation into the personalities and background of 65 "mentally healthy" young male students attending a small college. The students, averaging eighteen years of age, came from every area of the United States and Canada, from farms and cities. All were working toward degrees in health and physical education, group work, or community recreation and had strong convictions and motivations about their career choice.

The following conditions were characteristic of the group: sound health from birth; average intelligence; relatively low socioeconomic family circumstances; affectionate relationship with both parents; parental agreement and cooperation in child-raising; definite and known limitations on behavior; punishment reasonable and consistent; sound early religious training; held a job early in life; externally oriented rather than introspective with low degree of creativity; ideals of contentment, sociability, doing good, and making friends; success sought in achieving limited goal rather than ambition to rise higher socially, earn more, or live better than parents; strong identification with father and father figures. Any one or all of these factors may be important in the development of this type of personality.

The I.Q. averaged 110. Low intelligence is not conducive to mental health, but average intelligence with a capacity for honest and accurate self-appraisal is an antidote to useless and disappointing goal-seeking. In contrast to the plight of students at many modern universities where an infinite number of goals are possible, this group had a single goal: finishing school and starting their chosen work. Furthermore, most of the students studied had become associated with this type of work in childhood and felt the college and the future career for which they were preparing was the "right place" for them.

While this type of adjustment is associated with "stability and a special type of happiness," it is also associated with narrowness and limitations of interests, ambition, creativity, and excitement.

These young men cannot be understood apart from the culture in which they were reared. Parental emphasis on early work, sound religious training, and the ideals associated with doing good as well as parental firmness and interest constitute aspects of protestant virtues and ethics acceptable without rebellion because of the sincere manifestations of love and consistency toward the child. The subjects became more interested in avoiding failure than attaining great success, and "doing the best one can" became a virtue as a way of life.

From the present study it is not possible to conclude that the benefits of "mental health" were achieved at the cost of creativity and other advantageous factors. It is difficult to determine whether some factors are a cause or an effect of the students' adjustment to life. For example, it is not known whether a lack of creativity results from their present stability or whether it is one of the factors that led to it.

Industrial Health and Workmen's Compensation

ROBERT KATZ, M.D., Director,
Bureau of Industrial Health and Workmen's Compensation

PETER J. DINATALE, M.D., Chairman,
Council Committee on Industrial Health

CARL F. FREESE, M.D., Chairman,
Council Committee on Workmen's Compensation

Medical Society of the State of New York

Clarifying Amendments to 1960 Medical Fee Schedule

THE FOLLOWING clarifying amendments to the 1960 medical fee schedule were duly filed with the Department of State of the State of New York and are reprinted for your information.

For easy referral, it is suggested that you clip and file this notice in your copy of the 1960 workmen's compensation medical fee schedule.

STATE OF NEW YORK

WORKMEN'S COMPENSATION BOARD

Clarifying Amendments to 1960 Medical Fee Schedule

SPECIALIST FEES

Code	*Item*	*Fee*
0108	Consultation or first visit at hospital when and if especially called, additional	$7.50
0109	Consultation or initial examination if called to home of patient, additional	$7.50

(Code items 0109 and 0110 have been renumbered 0110 and 0111.)

(Added to notes following Code Item 0121.)

The additional fee for consultation or initial examination is payable in instances of elective surgery or when it is incumbent upon the specialist to examine the patient in order to make a proper diagnosis, prognosis and to decide on the necessity and type of treatment to be rendered. This fee is in addition to the unit fee prescribed for the operation or treatment subsequently rendered by the specialist except that where the therapeutic procedure or treatment is of a minor character and the fee for the procedure or treatment is in excess of the fee for the office visit, the greater fee (not both fees) is payable.

Consultations may be held and referrals may be accepted by physicians with S ratings or XD ratings only.

Referral by a hospital to a physician is not to be deemed a referral for which a higher fee is payable.

MILEAGE

(Notes added to Code Item 0175.)

Mileage fees do not apply within the City of New York.

Two criteria must be met, namely:

a) Travel must be a point outside the city or village.

b) Travel must be beyond three miles from physician's place of departure, office or home.

Mileage fees are not payable to a doctor visiting a patient in a hospital if the doctor is on rounds or has other patients in the hospital at the time.

ANAESTHESIA

(Added to notes following Code Item 0310.)

Anaesthesia fees do not apply when anaesthesia is administered by the operating surgeon.

A consultation fee is not payable to an anaesthetist examining the patient prior to operation.

Intravenous therapy under Code 0310 applies to the introduction intravenously of any medication by a anaesthetist only.

No charge for anaesthesia supplies is to be made by the hospital or the anaesthetist.

PHYSIOTHERAPY

(Notes added to Code Item 0463.)

Physiotherapy rendered by a hospital:

Although the head of the department may be an SM-1, the hospital shall not be entitled to $7.50 per treatment.

The $7.50 fee applies to treatment rendered by the SM-1 or under his direct supervision. It does not apply to treatment rendered under the general supervision of a physiatrist. Code 0461 applies in such instances.

EYE

(Additional notes under "EYE.")

In instances where a foreign body is removed from the eye and a complete examination and refraction is done on the same day, the above paragraph applies. Where further examination or refraction is necessary, each such instance must be judged by the particular facts in the case and no general rule is feasible. Good medical procedure should be the guide for the physician.

EYE EXAMINATIONS*

(Notes to follow Code Item 5801.)

Code 5800 applies only to an initial examination on the first day the claimant is seen by the doctor and not to an examination on a subsequent date. Final examination or treatment, with a refraction, should be billed under Code 0110 ($5.00) plus the refraction fee under Code 5801 ($10.00) when necessary to complete Item 9 in Eye Surgeon's Report, Form C-5.

July 1, 1962. S. E. SENIOR, Chairman

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* Code item 5921 should read: "Suture of sclera for wound or injury . . . . . $100.00. The $10.00 fee appearing in the July 1, 1960, Schedule is a printing error.

N.B. Multiple ratings in major specialties are no longer granted. No applicant will be given more than one major rating, but if qualified he may be given an additional minor rating if it is closely allied to his major specialty and if he shows some special ability or has had a reasonable amount of training along the minor specialty line.

Medical Meetings

American Association of Electromyography and Electrodiagnosis

The annual meeting of the American Association of Electromyography and Electrodiagnosis, will be held on August 26 at the Commodore Hotel, New York City. For information write to: M. K. Newman, M.D., 16861 Wyoming Avenue, Detroit 21, Michigan.

Twelfth international congress of dermatology

The twelfth international congress of dermatology will be held in Washington, D.C., September 9 through 15. Sponsor for the meeting is the American Academy of Dermatology. Cosponsors are the American Dermatological Association, the American Medical Association's Section on Dermatology, the Society for Investigative Dermatology, and the Canadian Dermatological Association.

Three teams of simultaneous translators will function throughout the five-day scientific session, enabling physicians to hear most of the offerings in either English, French, German, or Spanish.

Among the participants will be three New York City physicians: Victor H. Witten, M.D., Carl T. Nelson, M.D., and Rudolf L. Baer, M.D.

Interstate Postgraduate Medical Association

The forty-seventh annual scientific assembly of the Interstate Postgraduate Medical Association will be held at the Palmer House, Chicago, October 1 through 4. The program has been especially designed for the general practitioner. Twenty and one-half hours of category 2 credit will be given by the American Academy of General Practice for attendance at the meeting.

The Interstate Postgraduate Medical Association is not a membership organization but offers an annual teaching program. For information write to: N. A. Hill, M.D., Secretary, Interstate Postgraduate Medical Association, Box 1109, Madison 1, Wisconsin.

Midwest forum on allergy

The fifth annual meeting of the Midwest forum on allergy, sponsored by the Allergy Society of Buffalo, will be held on Saturday and Sunday, October 13 and 14, at the Hotel Statler-Hilton, Buffalo. A feature of the meeting will be a symposium on the "Newer Immunologic Techniques and Allergic Aspects of Connective Tissue Disease." Ernest Witebsky, M.D., professor of immunology, and Evans Calkins, M.D., professor of medicine, University of Buffalo will be the moderators.

For information contact: Leonard Wolin, M.D., General Chairman, Midwest Forum on Allergy, P.O. Box 143, Buffalo 23, New York.

American Heart Association

The scientific sessions of the American Heart Association will be held October 26 through 28 in the Public Auditorium, Cleveland, Ohio. For further information contact: New York State Heart Assembly, Inc., 105 East 22nd Street, New York 10, New York.

New England postgraduate assembly

The Council of the New England State Medical Societies in cooperation with the New England State Chapters of the American Academy of General Practice will sponsor a New England postgraduate assembly to be held at the Statler Hilton in Boston, November 6 through 8. For information write to: Mr. Getty Page, Secretary-Treasurer, Council of the New England State Medical Societies, 128 Merchants Row, Rutland, Vermont.

Medical News

Pilot project for psychiatric patients

A three-month pilot project to improve the movement of psychiatric patients between general hospitals in New York City and State mental hospitals was inaugurated on June 15. The plan will be put into operation first at Bellevue Hospital and then at Kings County Hospital and will continue on a trial basis until September 15.

The purpose of the project is to provide treatment for patients who require state hospitalization as soon as possible after the need is recognized. This will be accomplished through the expanded use of nonjudicial admission forms and by daily transportation of patients from Bellevue Hospital to certain State institutions.

Under the plan, nonjudicial forms (voluntary and one and two physician certificates) may be processed at Bellevue and Metropolitan Hospitals and also at the following hospitals: The Mount Sinai, Presbyterian, Roosevelt, St. Clare's, St. Luke's, St. Vincent's, and Gracie Square. These hospital patients may then be sent to Bellevue for transportation to the State hospitals or brought by appointment directly to the State institution by their own families.

Clinical science course

The New York Academy of Medicine will present the third in an annual series of correlated clinical science courses on Tuesday evenings from 8:00 to 10:00 P.M., September 11 through April 30.

The objective of the course is to provide a basic review of the several human organ systems with particular emphasis on their physiology, pharmacology, and biochemistry as related to clinical disease.

The 1962–1963 course is being supported by a grant from the Josiah Macy, Jr. Foundation. No fee will be charged, but advance registration is required.

For information and registration write to: Aims C. McGuinness, M.D., Executive Secretary, Committee on Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Military service rejects to get aid

The Office of Program Planning, Research, and Evaluation of the City of New York Department of Health will participate in a national effort to help young men who are rejected for military service because of health defects.

In 1960 approximately 6,000 young men in the New York City area were rejected for military service because of medical and psychiatric causes. Starting this year certain of the young men who are rejected for military service will be referred to appropriate community facilities which will try to help them solve their medical and psychiatric problems.

Plans for the actual operation of the program are now being worked out jointly with the Public Health Service, Selective Service Headquarters in New York, and the Department of the Army.

Grant awarded for thyroid study

The role of the thyroid in mental illness is one of the basic questions which will be studied at Hillside Hospital as a result of a $36,800 three-year grant from the National Institutes of Health. The award has been made to Arnold G. Blumberg, M.D., director of medical services at the Hospital and principal investigator in other research on the function of the body in the causation and continuance of emotional disorders.

For many years it has been noted that the function of certain glands seems to correlate with particular emotional disorders. Dr. Blumberg intends to study the reaction of the thyroid to the commonly used tranquilizer type drugs administered to the psychiatric patient. By better understanding the thyroid reaction to these drugs and evaluating the effects that thyroid change has on behavior, it is hoped that more knowledge may be gained of how physical-chemical factors affect the emotions.

Action on proprietary hospitals

Ray E. Trussell, M.D., Commissioner, The City of New York Department of Hospitals, has announced the following actions with respect to proprietary hospitals in New York City which are licensed by the Department of Hospitals:

1. To improve medical staffing in certain proprietary hospitals and to assist in minimizing unnecessary surgery such as that disclosed in a medical audit just released and limited to certain hospitals, a committee of medical leaders is being formed to advise the Department.

2. The Proprietary Hospital Code which guides the licensing of such facilities by the Department has been revised by consultants and will be the subject of public hearings after staff and Board of Hospitals review.

3. Until the advisory committee has completed its work and the Code is revised, the Department will issue provisional thirty- to ninety-day licenses to proprietary hospitals

rather than an annual license with the aim of stimulating hospitals to take the corrective action required by the Department.

4. Two proprietary hospitals have been advised by the Department that their applications for expansion of bed capacity will not be approved. This action was taken because expansion of the two facilities was considered to be unnecessary in terms of community needs.

Electric toothbrushes seized by FDA

The Food and Drug Administration has announced the seizure of Vibra Dent Electric Toothbrushes and warned purchasers that the motor and cord units are not sealed and are capable of transmitting severe or fatal shock to the user after immersion in water.

The FDA particularly warned that the devices should be kept out of the hands of small children who might dip or drop them into the washbowl.

Grant for psychiatric program

A grant of $161,658 from the National Institute of Mental Health has been awarded to "The Brooklyn Project," a unique program in which Brooklyn psychiatrists, general practitioners, and nonpsychiatric specialists have been deepening the understanding of emotional problems encountered in everyday medical practice.

Since the inception of the program in 1958, more than 500 physicians have participated in the seminars, nearly 100 of whom have taken three or more of the series, each enrollment under a different psychiatrist.

The program is sponsored jointly by the Medical Society of the County of Kings, the Brooklyn Psychiatric Society, and the Brooklyn Chapter of the American Academy of General Practice.

New way to test cough suppressants

A tape recording of a cough has been used effectively as a control to assess the value of cough suppressants. This unusual way of testing the drug was reported at the annual meeting of the National Tuberculosis Association and its medical section, the American Thoracic Society.

The patient being tested was placed in a room with no other patients for a period of days. A microphone in the wall of the room was connected with a tape recording system in an adjacent room. The sounds in the patient's room were picked up around a twenty-four-hour cycle, and the time the sounds were made was automatically clocked.

On the first day no medication was given the patient. This was the "control" day when the patient's cough was recorded. On the second and third day the patient was given dummy pills without being informed what they were. The microphone continued to pick up his cough and the tape recorded it. On the fourth day, the patient was given the drug being tested.

The investigators found that the sound made by coughs is clearly distinguishable from other sounds on the tape recorder, and that two investigators listening to the same tapes gave almost identical interpretations. The number of coughs produced for each patient was noted and also the number of coughs produced for the two hours after medication. These were compared for the control day, the placebo days, and the drug days to determine whether or not the coughs on the day the drug was given differed in number and kind from the other days.

This new technic is expected to provide much additional information about placebo effect and about the cough of chronic chest disease.

Business tax can be paid in installments

Hilda G. Schwartz, Treasurer of the City of New York, has announced that an amendment to the New York City General Business and Financial Tax Law provides for the payment of the tax for the calendar year 1962 on a current basis, in installments. A declaration of estimated tax is to be filed on or before August 15. The General Business and Financial Tax rates remain unchanged.

For more complete information about this new procedure contact the Bureau of City Collections in your borough.

Will Rogers cardiopulmonary seminars

The Will Rogers Hospital and O'Donnell Memorial Research Laboratories, Saranac Lake, will sponsor a series of seminars on cardiopulmonary physiology and diseases to be held on Mondays at 1:00 P.M. in the hospital auditorium. The schedule is as follows:

July 16: "Some Factors Influencing Arterial Oxygen Saturation in Emphysema," William Briscoe, M.D., Columbia University College of Physicians and Surgeons, New York City; July 23: "Elastic Properties of the Lung and Aorta in Health and Diseases," Martin Fitzpatrick, M.D., Will Rogers Hospital and O'Donnell Memorial Research Laboratories; July 30: "Nature of Heart Failure in Cor Pulmonale," Ludwig Eichna, M.D., State University of New York Downstate Medical Center, Brooklyn; August 6: "Experimental Airborne Tuberculosis with Epidemiological Implications," Richard Riley, M.D., Johns Hopkins University School of Hygiene and Public Health, Baltimore; August 13: "Rate of Blood Gas Exchange in the Lungs," Arthur DuBois, M.D., University of Pennsylvania School of Medicine, Philadelphia; August 20: "Drug Resistant Mycobacterium," Harold Lyons, M.D., State University of New York Downstate Medical Center; and on August 27: a seminar, the title of which is to be announced, presented by James Whittenberger, M.D., Harvard University School of Public Health, Boston.

Award for medical reporting

Miss Mildred Spencer, science writer for the *Buffalo Evening News,* has been named as the winner of the third annual Empire State Award for Excellence in Medical Reporting.

Miss Spencer received the $500 award from Henry I. Fineberg, M.D., executive vice-president of the Medical Society of the State of New York, at the Annual Health Conference held in Syracuse in June.

The annual award is sponsored by the Medical Society of the State of New York and Annual Health Conference Inc., on behalf of the State of New York Department of Health. The award was established to encourage the further development of sound medical reporting in New York State and to recognize the significant contributions to public knowledge and understanding of health and medicine that are made by reporters and newspapers.

Applicants sought for bilirubin survey

To stimulate interest in the accuracy of bilirubin determinations the College of American Pathologists Standards Committee announces a national bilirubin survey, available to all physicians and hospitals.

Accurate bilirubin measurements are of great importance in decisions as to the need for exchange transfusion in newborn erythroblastosis fetalis, the differential diagnosis of the various icteric syndromes in patients of all ages, and the evaluation of prospective blood donors.

Participants in the survey will receive a set of samples. Following the survey, a critique of bilirubin standards and methods of analyses will be provided. Questions arising during the survey may be directed to the Committee.

Interested physicians should write to: Standards Committee, College of American Pathologists, Prudential Plaza, Chicago 1, Illinois. Applications should be received not later than August 1.

Folder on services for mentally retarded

A folder entitled "Community Services for the Mentally Retarded" has been published by the State of New York Department of Mental Hygiene.

Designed to stimulate the development of community services for the mentally retarded, the folder describes outpatient clinics, day training centers for children, day occupation centers for adults, inpatient services in general hospitals, and consultation and education services.

Copies of the folder may be obtained from: Office of Mental Health Education and Information, State of New York Department of Mental Hygiene, 240 State Street, Albany, New York.

Vacancies for psychiatrists in California

The Regional Office of the Veterans Administration, San Francisco, California, has announced several vacancies for psychiatrists in its Department of Medicine and Surgery.

For information concerning the benefits and requirements of these positions write to: Harry Leeb, M.D., Director, Outpatient Clinic, Regional Office, Veterans Administration, 49 Fourth Street, San Francisco 3, California.

Booklet on radiation

The State of New York Department of Health has announced the publication of a new booklet "Radiation and You" which describes radiation and the Department's program to minimize unnecessary exposure.

Copies of the booklet are available without cost to residents of New York State from city and county health departments, district health offices, and from the Office of Public Health Education, 84 Holland Avenue, Albany 8, New York.

Course in radioactive isotopes for technicians

The Queens Hospital Center, Jamaica, is offering a course in radioactive isotopes for technicians. The course will consist of 8 sessions of four hours each and will be held on Wednesday afternoons from 1:00 to 5:00 P.M. from September 26 to November 14.

Requests for applications should be sent to: Philip Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82-68 164th Street, Jamaica 32, New York.

Personalities

Honored. Frederick Reiss, M.D., New York City, with the title of "honorary member" of the Venezuelan Dermatological Society.

Awarded. Robert F. Loeb, M.D., New York City, an honorary degree from Dartmouth College in recognition of his work in the field of electrolyte and water metabolism and for his advancement of the treatment of Addison's disease and diabetes. . . Ben-Henry Rose, M.D., Miami Beach, Florida, (formerly of the Bronx) the bronze medallion of the American Heart Association for "meritorious service."

Speakers. Paul H. Hoch, M.D., New York City, Commissioner of the State of New York Department of Mental Hygiene, at a dinner on June 12 to aid the Civic Center Clinic. . . Marcus J. Kogel, M.D., Bronx, at a fund raising dinner at Albert Einstein College of Medicine of Yeshiva University. . . Howard A. Rusk, M.D., New York City, on June 15 at the dedication of the I. S. Ravdin Institute of the Hospital of the University of Pennsylvania. . .

Harley C. Shands, M.D., Brooklyn, before the members of the staff of the Veterans Administration Hospital, Northport, Long Island, on the topic "Pursuit of Dominance in Schizophrenia and Homosexuality". . . Lewis Thomas, M.D., New York City, on the subject of the treatment of heroin addiction, at the annual dinner meeting of the Health Research Council.

Appointed. Harvey Bluestone, M.D., New York City, as director of psychiatry assigned to the City of New York Department of Correction. . . .Julius A. Katzive, M.D., Brooklyn, as director of the Bureau of Hospital Review of the State of New York Department of Health. . . Harvey J. Tompkins, M.D., New York City, reappointed as a member of the New York City Community Mental Health Board.

Elected. Nathaniel B. Cole, M.D., New York City, as president of the Circus Saints and Sinners. . .Joseph K. Surls, M.D., New York City, as New York County commander of Retreads, Inc. . . .S. Jay Tepperman, M.D., as president of the Society for Experimental Biology and Medicine. . . Isaac Wolfson, M.D., Thiells, as vice-president and chairman of the section on medicine of the American Association on Mental Deficiency

Necessity of early and adequate prenatal care

Early and adequate prenatal care would reduce substantially the annual toll of perinatal deaths in the United States, according to statisticians of Metropolitan Life Insurance Company.

Perinatal deaths consist of stillbirths of twenty or more weeks gestation and deaths occurring in the first week after birth.

The somewhat over 140,000 perinatal deaths reported in 1959, the last year for which national figures are available, is certainly an understatement of the actual mortality. A large proportion of stillbirths, even those of twenty or more weeks gestation, are unreported.

The task of obstetricians and pediatricians in controlling perinatal mortality is often complicated by a lack of knowledge as to the cause of death. In the large majority of stillbirths the cause of death is undetermined, and in many cases is not determinable.

In those cases where the cause of fetal death is known, somewhat over half are attributed to abnormalities of the placenta, especially premature separation, and to conditions of the umbilical cord. An additional fourth are due to diseases of the mother, including the toxemias of pregnancy.

More is known as to the causes of early neonatal deaths. Immaturity is reported either as the cause of death or as an associated condition on the death certificates of about two thirds of the babies dying during the first week of infancy. The leading specific causes of neonatal mortality are asphyxia and other lung conditions, which account for about one fourth of all such deaths, and birth injuries, responsible for an additional one seventh of the total.

Books Received

*The following books were received during the month of May, 1962**

Treatment of Injuries to Athletes. By Don H. O'Donoghue, M.D. Octavo of 649 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $18.50.

Laboratory Medicine—Hematology. By John B. Miale, M.D. Second edition. Quarto of 918 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $17.

The Ciba Collection of Medical Illustrations. Volume 3. Digestive System. Part II—Lower Digestive Tract. Prepared by Frank H. Netter, M.D. Edited by Ernst Oppenheimer, M.D. Folio of 243 pages, illustrated. Summit, N.J., Ciba, 1962. Cloth, $15.

Surgical Anatomy of the Colon, Rectum and Anal Canal. By Harry E. Bacon, M.D., and Porfirio Mayo Recio, M.D. Quarto of 152 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1962. Cloth, $12.

Congenital Cardiac Disease: A Review of 357 Cases Studied Pathologically. By Robert S. Fontana, M.D., and Jesse E. Edwards, M.D. Octavo of 291 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $10.

Medical State Board Questions and Answers. By Harrison F. Flippin, M.D. Tenth edition. Octavo of 507 pages. Philadelphia, W. B. Saunders Company, 1962. Cloth, $9.50.

Psychoanalytic Education. Edited by Jules H. Masserman, M.D. Octavo of 332 pages. New York, Grune & Stratton, 1962. Cloth, $9.75.

The Medical Clinics of North America. Nationwide Number. May, 1962. Bedside and Office Diagnosis. LeRoy H. Sloan, M.D., and Ford K. Hick, M.D., guest editors. Octavo. Philadelphia, W. B. Saunders Company, 1962. Published bi-monthly (six numbers a year). Cloth, $18 net; paper, $15 net.

Developments in Psychoanalysis. By Leon Salzman, M.D. Octavo of 302 pages. New York, Grune & Stratton, 1962. Cloth, $7.75.

Annual Review of Medicine. David A. Rytand, editor. William P. Creger, associate editor. Volume 13. Octavo of 552 pages, illustrated. Palo Alto, Calif., Annual Reviews, Inc., 1962. Cloth, $7.00.

Psychoanalysis of Behavior—Collected Papers. Volume Two: 1956–1961. By Sandor Rado, M.D. Octavo of 196 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $6.50.

Self-Hypnosis: A Conditioned-Response Technique. By Laurance Sparks. Octavo of 255 pages, illustrated. New York, Grune & Stratton, 1962. Cloth, $5.75.

The Nature of Psychotherapy. By Walter Bromberg, M.D. Octavo of 108 pages. New York, Grune & Stratton, 1962. Cloth, $4.50.

Suicide and Mass Suicide. By Joost A. M. Meerloo, M.D. Octavo of 153 pages. New York, Grune & Stratton, Inc., 1962. Cloth $3.75.

The Nature of Ego. By Benjamin Meynard. Octavo of 211 pages, illustrated. New York, Philosophical Library, 1962. Cloth, $4.50.

Dr. Mary Walker: The Little Lady in Pants. By Charles McCool Snyder. Duodecimo of 166 pages, illustrated. New York, Vantage Press, 1962. Cloth, $3.95.

Day Hospital. A Study of Partial Hospitalization in Psychiatry. By Bernard M. Kramer, Ph.D. Duodecimo of 103 pages, illustrated. New York, Grune & Stratton, 1962. Paper.

Works of the Institute of Higher Nervous Activity. Physiological Series—Volume 3. Translation of the Russian book: Akademiya nauk SSSR Seriya fiziologicheskaya—Tom 3—Izdatel'stovo, Akademii Nauk SSSR—Moskva—1959. Octavo of 263 pages, illustrated. Jerusalem, Israel, Program for Scientific Translations, 1961. Available from The Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Paper, $2.75.

Symposium on Use of Indicator-Dilution Technics in the Study of the Circulation. Edited by Earl H. Wood, M.D. Quarto. New York, The American Heart Association, Inc., 1962. Paper, $2.50. (American Heart Association Monograph Number Four)

Cardiovascular Abstracts II-1961 Selected from World Literature. Edited by Stanford Wessler, M.D. Quarto. New York, The American Heart Association, Inc., 1962. Paper, $2.75. (American Heart Association Monograph Abstracts II-1961)

* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

Books Reviewed

Medical Physiology and Biophysics. Edited by Theodore C. Ruch, Ph.D., and John F. Fulton, M.D. Eighteenth edition. Quarto of 1,232 pages, illustrated. Philadelphia, W. B. Saunders Company, 1960. Cloth, $16.

Constant revision is an essential requisite for all textbooks which form the foundation of the art and science of medicine. This text remains an outstanding teaching and reference source in the field of medical physiology. To keep abreast of the progress being made, many of the chapters have been extensively revised or completely rewritten. Examples of this are the sections on cardiovascular, renal, and neuromuscular physiology. Two new chapters have been added: one on the biophysics of the cell membrane and the other on the neurophysiology of emotion.

The text is well illustrated and edited. The references and bibliography at the ends of sections and chapters are complete and pertinent. The text itself is well organized.

This volume is an essential reading and reference book for individuals at all levels of medical education, from the first-year medical students to the university professors.—DAVID A. TICE, M.D.

The Psychotherapy Relationship. By William U. Snyder, Ph.D., with the collaboration of B. June Snyder, M.A. Octavo of 418 pages, illustrated. New York, The Macmillan Company, 1961. Cloth, $7.50.

This book characterizes the crevasse separating the medical profession from academic psychology. The authors have been "doing psychotherapy" for years in a college psychology department environment. Their credentials or background for such undertaking are not listed. Their therapeutic method is vague and a hodgepodge. Their aim is not patient-oriented, that is, not directed towards the alleviation of suffering or illness, but rather toward the achievement of statistics. In this instance, the so-called research project, which took several years, was focused on an attempt to measure transference relationships. This was to form the basis of a scale. However, the final result is contained in a lengthy psychologic discussion and not in measurements. Moreover, the language is that of psychoanalysis or dynamic psychiatry generally, but there is little relevance to psychoanalysis in the credits. The work is undoubtedly aimed primarily at academic psychologists, and they doubtless appreciate its worth. As for psychiatrists and analysts, they will understand the significance of transference in psychologic terms without the aid of so-called statistics.—SAM PARKER, M.D.

Ciba Foundation Symposium on Quinones in Electron Transport. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Cecilia M. O'Connor, B.Sc. With 82 illustrations. Octavo of 453 pages. Boston, Little, Brown and Company, 1961. Cloth, $11.

The abstruse title of this text covers a lively subject. Commonly known as the group which includes the vitamins K, quinones have other important functions. For example, certain quinones are one of the carriers in the bucket brigade involved in electron transport between chlorophyll and a cytochrome, wherein electron loss and gain is related to energy metabolism.

The newly isolated coenzyme Q is a quinone, that is ubiquinone, probably only a member of a group of enzymes. These are involved in electron transport in plants, as well as in animals. The symposium dealing with chemical, biochemical, and biosynthetic aspects, is concerned with findings on the role and conversion of quinones in plant and animal tissues. There are chapters on the effect of mitochondria—the power units of tissues—on the quinones, the chemistry of vitamins K, and histochemical studies concerning the coenzyme Q and its relation to other enzymes in tissue. As is customary with these symposia, the discussions of the participants frequently elucidate the data the chapters present.—ERWIN DI CYAN, PH.D.

Proceedings of the Fourth National Cancer Conference, September 13 to 15, 1960. Sponsored by American Cancer Society, Inc., and National Cancer Institute, U. S. Public Health Service. Quarto of 774 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $9.00.

The presentation by Vincent Collins of the changing concepts of breast cancer highlights this conference: Early, rapid, silent growth and even metastases occur before the original cancer reaches 0.5 cm. in size and before its possible detection. The survival rates in selected cases of radical surgery pales in the face of this premise. Rigid and unbiased experimental controls are advocated by the two keynoters of the convention, as well as the National Advisory Cancer Council. "Precancerous lesions" and cancer in situ (most difficult of diagnosis) meet the same criticisms of iatrogenic disfigurement, mental and physical distress, and even death without predigested, strict, scientific methods of study.

In the same category are roentgen and anticarcinogenic therapy which also can arrest temporarily the rate of cell division and destroy cancer. In the former, the best results are reported by Peters, with a heavy load of early cases, in Hodgkin's disease. The need for restudy in all phases of cancer are stressed repeatedly. The results of the use of the newer procedures for the treatment of female genital tract diseases are incomplete; poor feminine hygiene and infection are accepted as causes of cancer without due credit being given to the increase in effective feminine hygiene as a possible cause of the decrease in the incidence of cancer of the cervix.

Favorable results are reported in chorioepithelioma. The inhibitory effects of saccharolactone and pyridoxine in bladder cancer show the value of cooperation of the many disciplines in science. Differences of opinion in regard to rectal and colonic polyps are poles apart. Hilleboe's article on the care of the advanced cancer patient requires reading. This book is for everyone interested in oncology.—BERNARD SELIGMAN, M.D.

Progress in Neurology and Psychiatry. Volume XVI. Edited by E. A. Spiegel, M.D. Octavo of 617 pages. New York, Grune & Stratton, 1961. Cloth, $12.75.

The sixteenth volume of *Progress in Neurology and Psychiatry* displays the excellence which has come to be expected of this series. Two themes recur throughout the volume: one that it is impossible to review completely the total literature on any one of the 35 subjects included within the broad domain of basic sciences, neurology, neurosurgery, and psychiatry which comprise the major headings of this work; the other that no major breakthroughs have occurred during the period reviewed. How many breakthroughs might have gone unnoticed without this excellent scholarship in view of the immensity of the work in the past few years is impossible to estimate, and herein lies one of the book's great values.

Critical examination is necessarily sacrificed in the interests of the broadness of review of the subject and seems wanting in places, particularly in the section devoted to the literature on drug therapy. Although the distinctions between basic and clinical investigation in places seems contrived, remarkably there is practically no overlapping of the work cited in the closely related fields such as pharmacology and drug therapy, and neurophysiology and neurochemistry.

While it is quite timely, this work could make even more interesting reading to the scholar of the future examining those fields of effort which proved barren and those which proved fruitful. The book is certainly of interest to those in any field of medicine, and its greatest value is probably that of a source of an enormous quantity of information extremely well organized and readily available to the expert in his particular field.—ROBERT W. KIMBALL, M.D.

Heredity in Ophthalmology. By Jules Francois. Translated from the French edition. Octavo of 731 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $23.

The aim is to study ocular pathology with referral to new concepts of genes, linkage, mutation, crossing over, and histochemical and physicochemical studies. There is a detailed study of family trees with the general idea of understanding the origin, transmission, and outcome of the developmental gene. There are interesting chapters on the inheritance of glaucoma and the abiotrophies of the retina, which permit great hopes for control.

In 1944 congenital and hereditary abnormalities were responsible for more than two thirds of the cases of blindness in England. The author indicated an important therapeutic approach through genetics which covers congenital cataract, diabetes, and many other congenital situations.

The book is highly technical and is of value to the medical and ophthalmologic specialists.—NORRIS C. ELVIN, M.D.

Progress in Liver Diseases. Volume I. Edited by Hans Popper, M.D., and Fenton Schaffner, M.D. Quarto of 363 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $13.75.

It would be easy to review this splendid work either by quoting the foreword of the editors or even by simply excerpting some of their comments.

As one looks back over a period of more than forty-six years since one's days in medical school, the accomplishments in liver diseases as presented in this volume are really staggering.

There are so many excellent chapters in this book, it would seem unfair and perhaps discriminatory to choose one or more for special mention. I could call attention to the beautiful and expressive x-ray films shown in the chapter on splenoportography. The articles on bile formation and bilirubin transport deserve special notation, as do those on diagnostic tests and the relationship between the liver and the hemopoietic system.

I would rather say that if one wants to know what is new in the study of liver disturbances, I know of no book which can provide as much sound information or is as well written as this one. It should have a niche waiting for it on the shelf of any interested student, at the college level or among postgraduate practitioners of medicine.—BENJAMIN M. BERNSTEIN, M.D.

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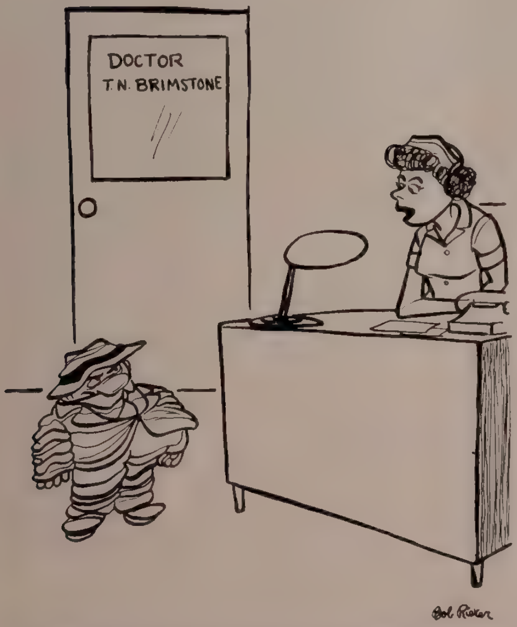

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956.
2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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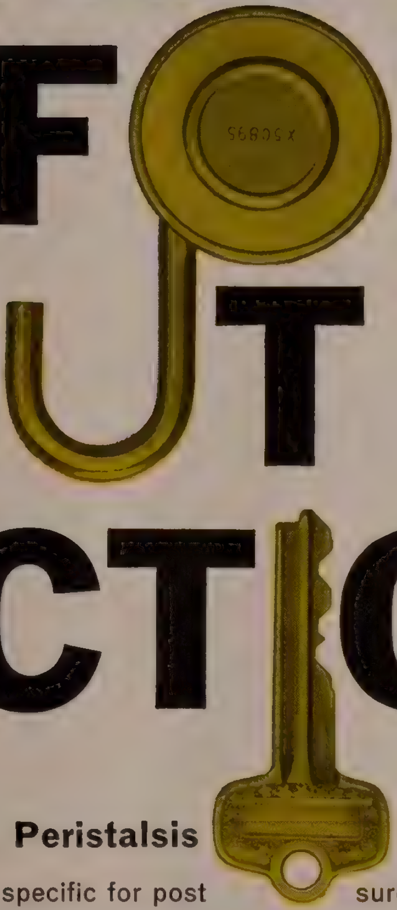

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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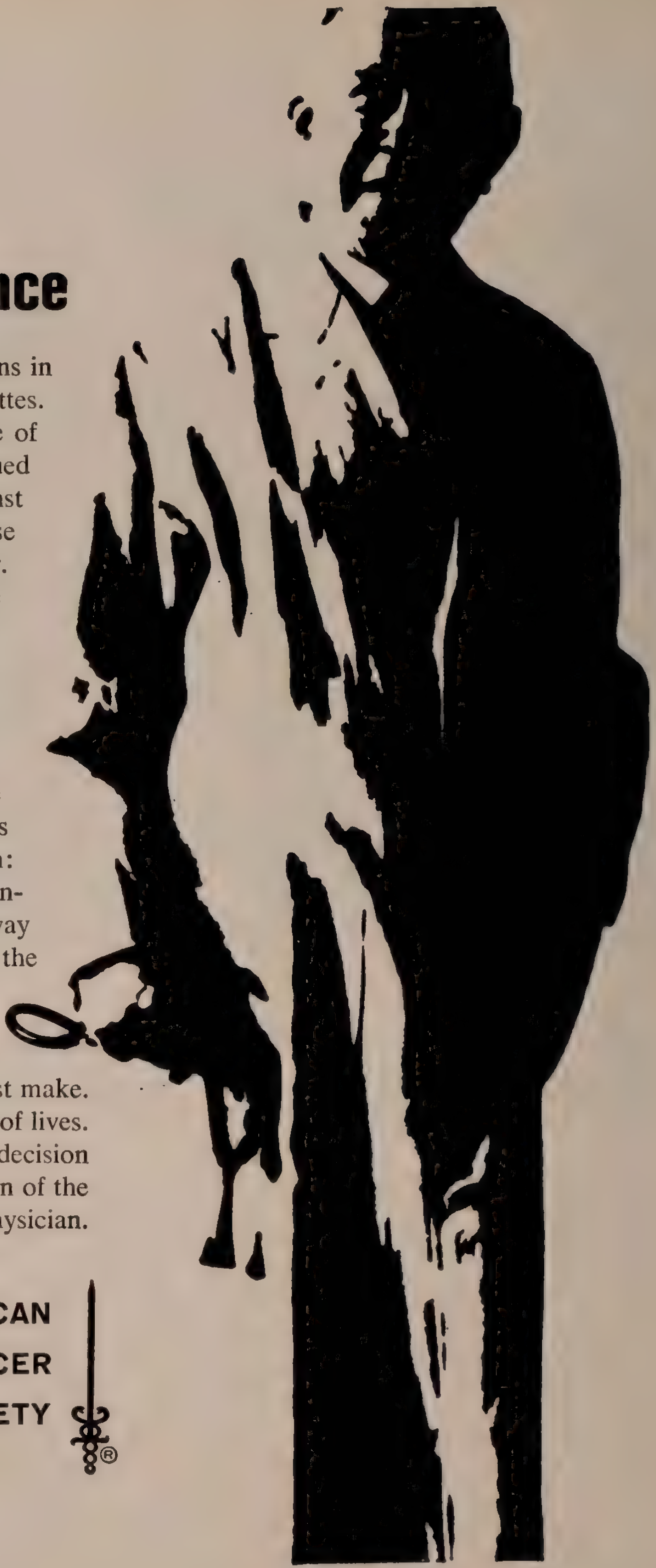

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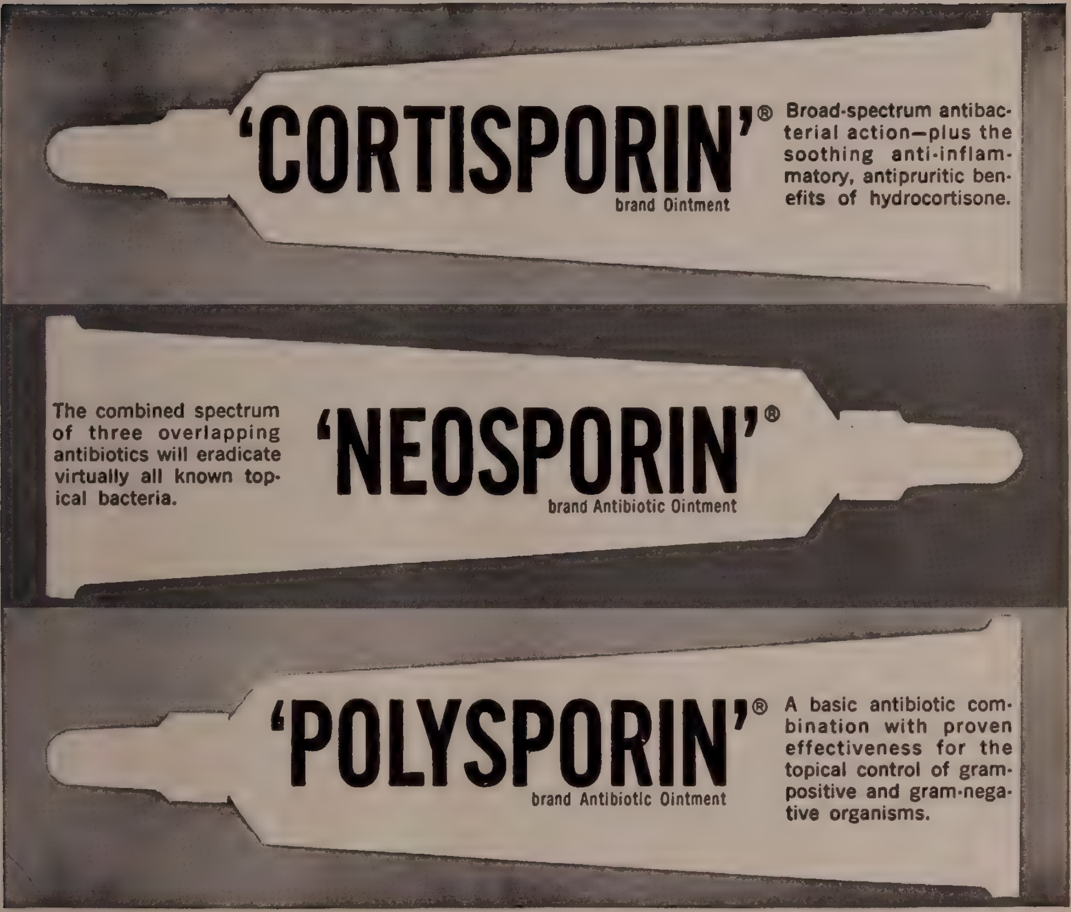
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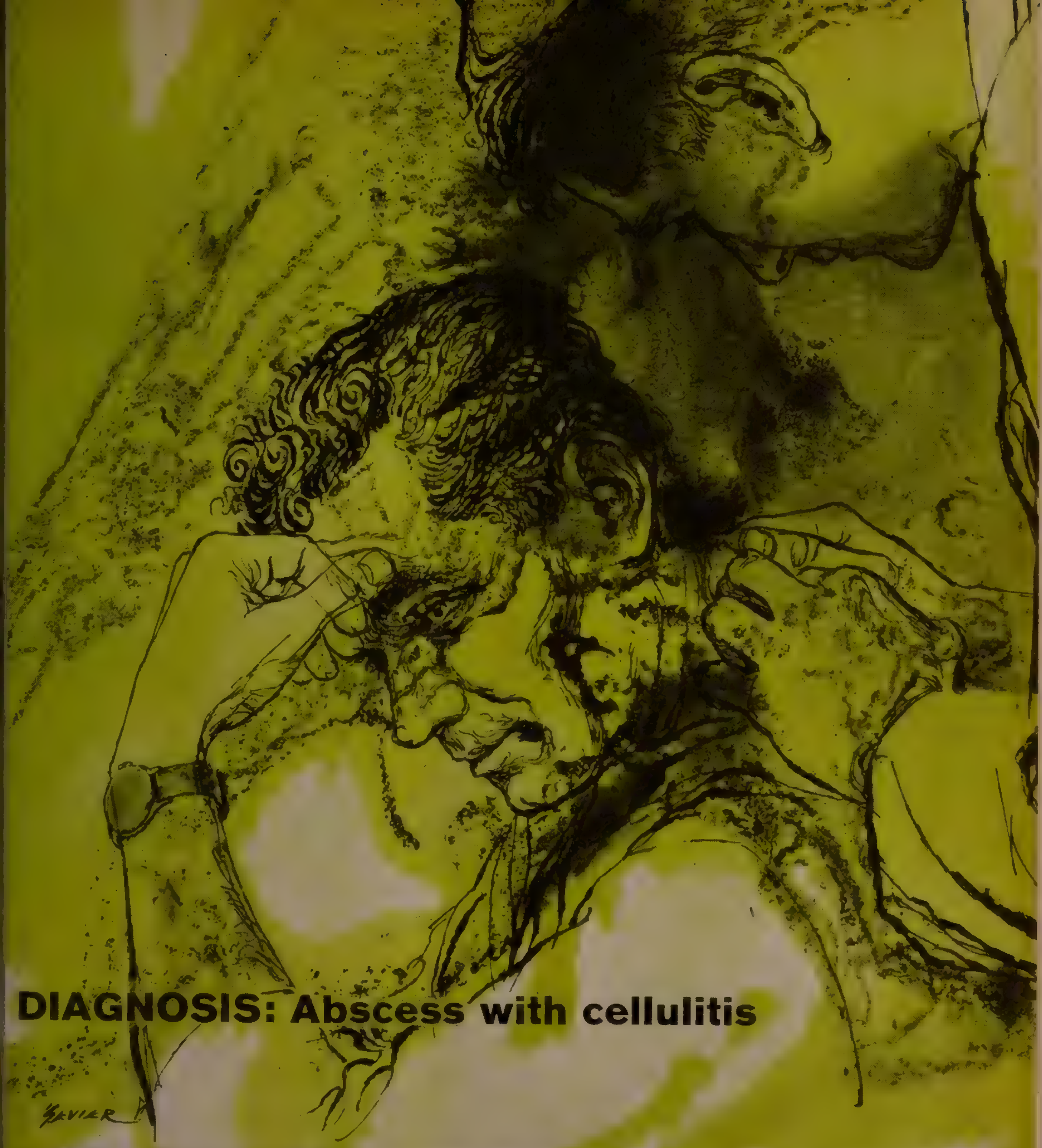

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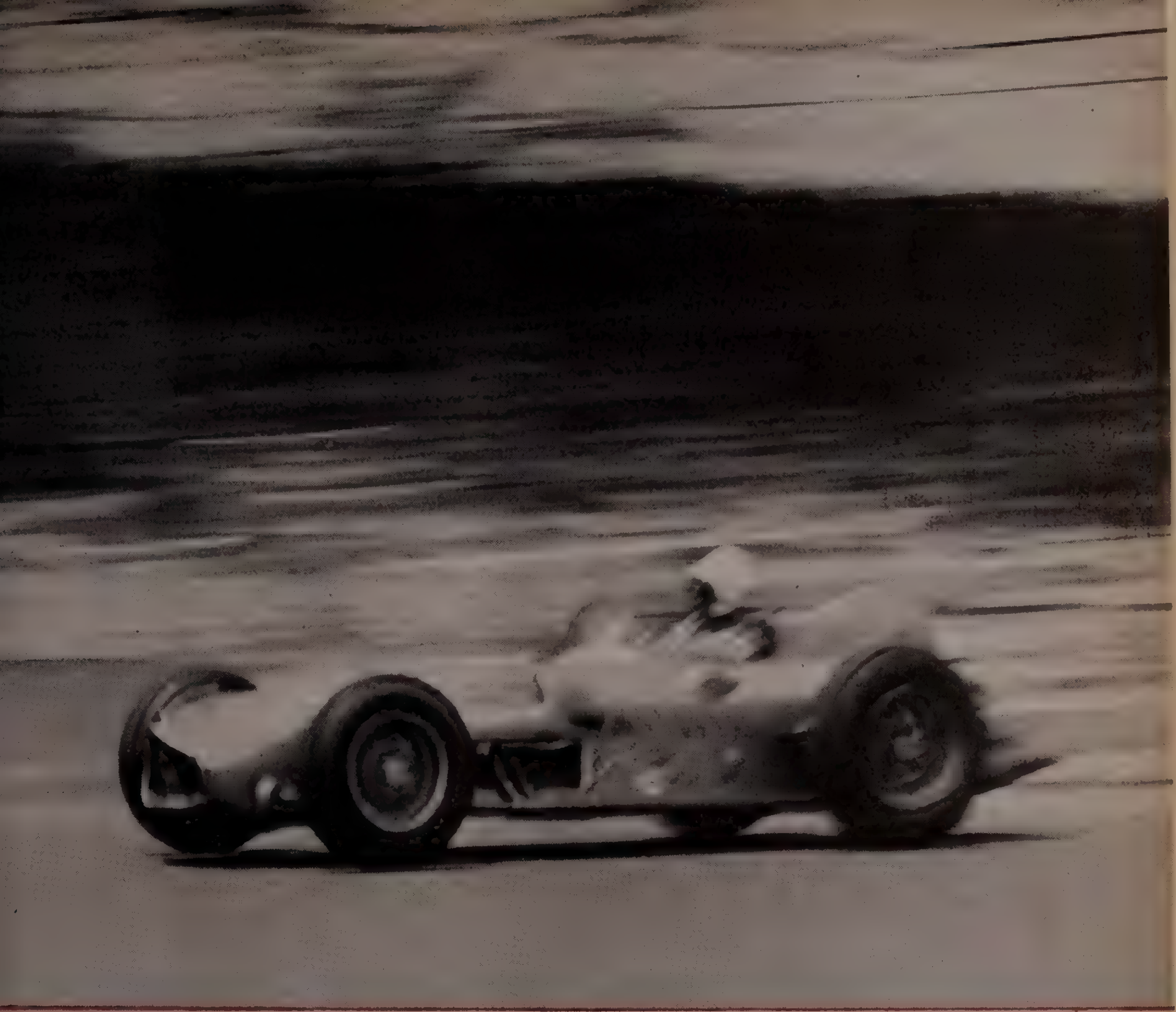

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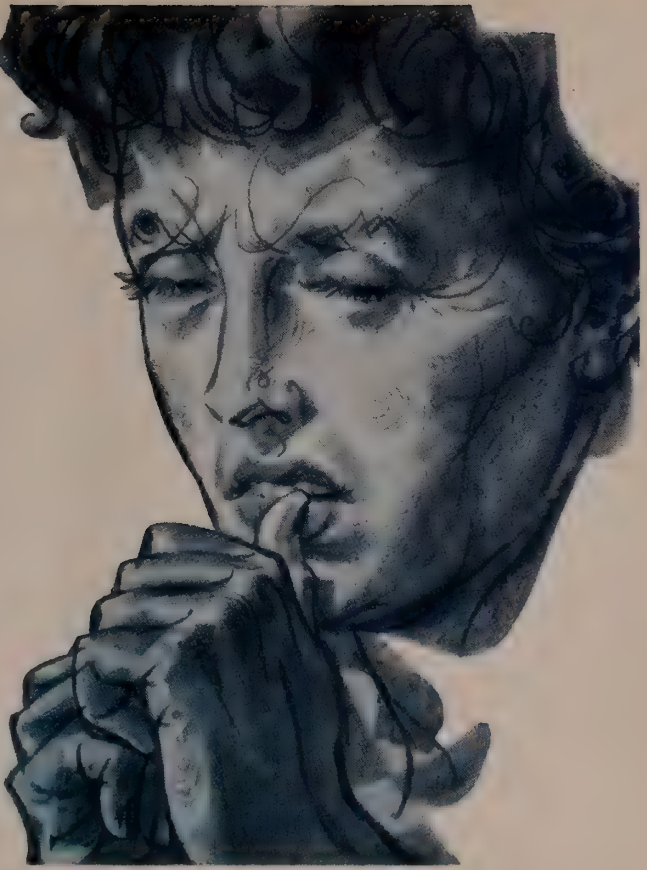

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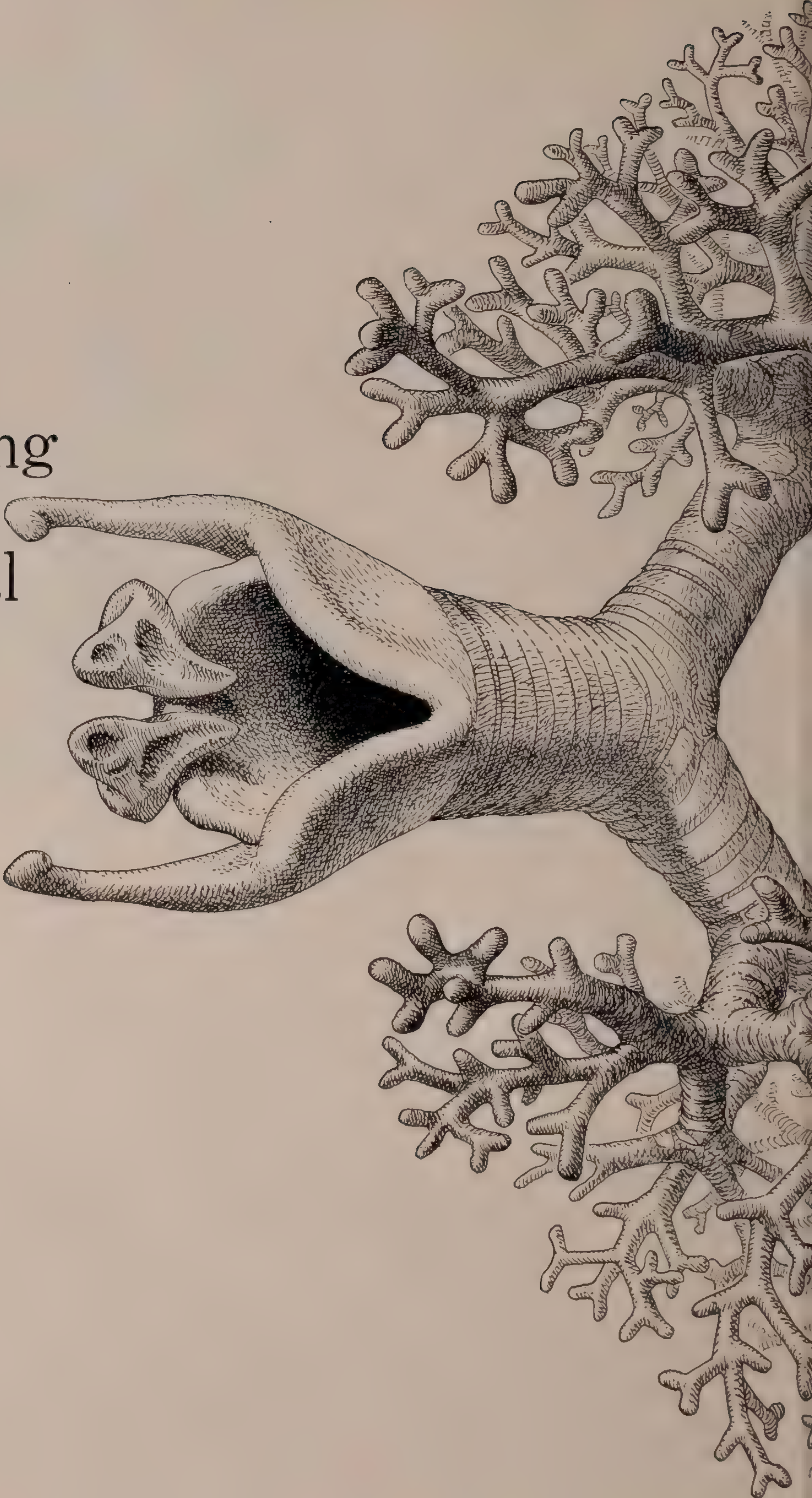

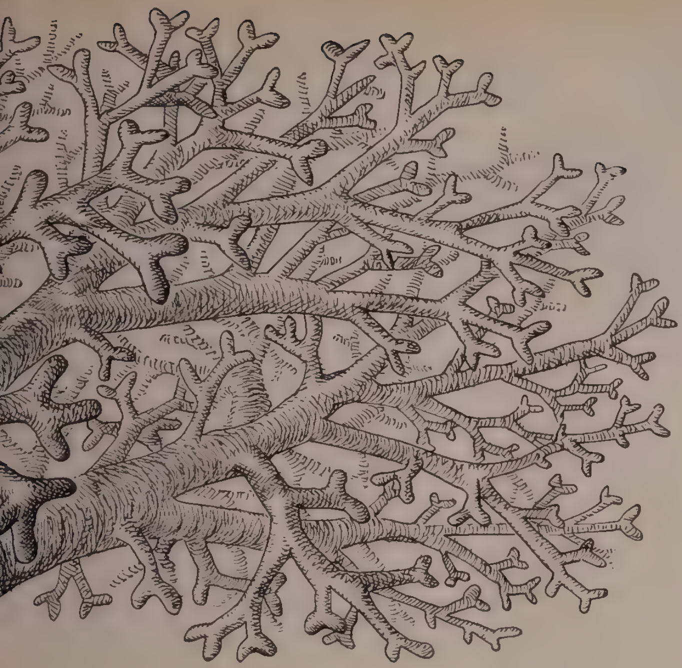

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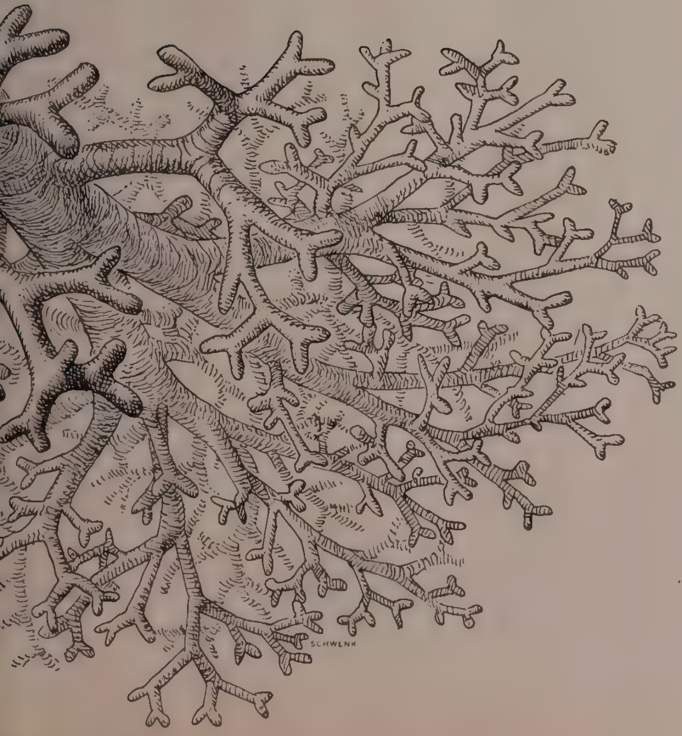

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Editorials

No vested right

New York's highest court, the Court of Appeals, in April, 1962, in affirming the decisions of lower courts held that a voluntary hospital association's constitution and the bylaws of its medical board which gave to its board of trustees the right to make annual appointments only to the staff, did not give a former staff member a vested right to the use of the hospital facilities for the care and treatment of private patients.

The majority opinion stated that the

> hospital's constitution and the by-laws of its medical board, when read in context, indisputably establish that the plaintiff, a surgeon, has no vested right to the use of the hospital's facilities for the care and treatment of his private patients. More specifically, his successive annual appointments effected no contractual relationship with the defendant (hospital) which prevented its board of trustees from terminating his membership on its medical staff. His exclusion from the staff and "off-service" privileges, incident to staff membership, including privileges to care for private patients in the hospital, rested entirely in the discretion of the board of trustees. As the Court at Special Term, aptly noted, the by-law provision granting such "off-service" privileges to doctors "of the hospital staff" "cannot derogate from the right of the board of trustees to make annual appointments only, and . . . can refer only to those physicians and surgeons whom the board . . . determines annually to reappoint to the hospital's medical staff 'off service' after they have reached the age limits" provided for by the hospital's constitution. Consequently, the denial to the plaintiff of future courtesy privileges following the termination of his annual employment constituted no legal wrong.

One judge, however, in a vigorous dissent urged that the lower courts' decisions be reversed and the hospital be compelled to grant the physician courtesy privileges.

He said that the physician

> during his many years as a member in good standing of respondent's hospital staff rendered service to the hospital in reliance upon the provisions in article IX of the by-laws of the medical staff, which secure to him the enjoyment of certain privileges upon his retirement. That article provides:
>
> > When any surgeon or physician of the Hospital Staff below the rank of Director or Attending shall have reached the age limit as provided for by the Constitution of the Board of Trustees, such surgeon or physician shall thereafter continue to retain the rank then held but without service, and shall be designated with the title, "off service." These physicians and surgeons shall enjoy the following Hospital privileges;
> >
> > 1. The care of their private patients in the Hospital.
>
> Respondent now seeks to divest appellant of his *right* to the enjoyment of these privileges; a *right* to which he became entitled in 1959, when he attained the age limit provided for one in his rank. In my opinion, the fact that the board of trustees, to whom the hospital's constitution commits the control, direction and management of all the affairs and property of the corporation, could have altered or abrogated the by-laws, or even discharged appellant on the day before he attained the stated age limit and became entitled to the privileges provided in article IX, does not mean that they may divest him of these rights *after* they vest.

He then went on to say that in his view the controlling fact was that the physician was a member in good standing of the hospital staff when he attained the stated age limit in 1959. At that moment, by virtue of the previously quoted provision of the bylaws, he became entitled to the designation "off-service" and the privileges which accrued to one in his new "off-service" category. The judge pointed out that the bylaws are couched in mandatory terms which are tantamount to a contract, and the physician's right may not be impaired.

He argued that the fact that the physician was denied reappointment as a member of the hospital staff after May 1, 1960, was irrelevant and could not affect the rights to which he became entitled in 1959. He said that he recognized the sweeping powers given the board of trustees by the hospital constitution, including the right to exercise its powers with respect to those members of the staff who have not as yet attained the retirement age, but felt that they could not "reward 10 years of service, rendered in reliance upon rights assured by article IX, with a summary abrogation of these rights" after the physician had become legally entitled to them.

Editorial comment

A look backward and a look forward. Dr. Glenn T. Seaborg, Chairman of the United States Atomic Energy Commission, in his commencement address to the graduating class at Northern Michigan College on June 3, 1962, made some interesting observations on our scientific past and future. Taking the year 1962 as an epicenter he cast back thirty years to 1932 and described what might have been predicted for the next thirty years. In the same manner he projected a forecast for what may happen in the next thirty years from 1962 to 1992.

There intervened between 1932 and 1962 a bewildering array of developments: the development of radar; wonder drugs, the introduction of new operative technics, a better understanding of viruses, the development of new drugs for the treatment of mental disease, and poliomyelitis vaccine; high energy physics; earth satellites; men circumnavigating the globe in minutes in orbits many miles above the earth; television in almost every home in the nation; synthetic rubber, foamed plastics, high fidelity sound reproduction, synthetic adhesives, synthetic gems, paints, and corrosion-resistant coatings; new methods of printing and reproduction, color, and almost instantaneous photography; titanium, tantalum, and zirconium metals, transistors, magnetic reactors, nuclear-powered submarines, and computing devices which perform calculations equivalent to thousands of man years of effort in unbelievably short time; and many, many other things.

The fact that science is ever growing is undisputed. This growth invariably has brought with it new tools by which man has been able to conquer nature in manifold forms and make nature his servant. But beyond this, the pace of scientific discovery and application has increased to a startling degree. From the time man first learned to use tools, it was six thousand years before he settled down to a more or less stable agrarian life. But only ten years elapsed between the discovery of the neutron in 1932 and the first chain reaction pile in 1942. And since then, the gap has further narrowed.

The astonishing pace of these developments could hardly have been predicted in 1932. The necessities of a war for survival, of course, accelerated the pace, the Manhattan project being the most important of these. It seems that the tempo quickens. Now we have a cold war, and the survival of our way of life is just as much at issue. Dr. Seaborg goes on to speculate about the scientific marvels of 1992.

Let me first dispose of what in some persons' minds are conventional predictions. By 1992 travel to Europe and other far places of the world will be possible in the matter of an hour or two, through either ultrahigh-speed jets or rocket transport. Travel in space to artificial satellites or the moon and the nearer planets will be possible. The telephone may evolve to the point where everyday communication is not only aural but visual, that is, through the television phone. Also communication satellites will routinely take television and radio broadcasts direct to homes on a world-wide basis. Simple radios will be made even more compact. The wrist-watch transmitter and receiver popularized in the comic strips will have become a widespread reality, with communication possible from a street corner, a golf course, or virtually anywhere else. There will also be advances in clothing material; perhaps paper will be developed to the extent that durable and fashionable clothes made inexpensively of paper will be widely worn, eliminating the need for expensive cleaning, since the clothing could be discarded after several wearings. Fuel cells, now in the developmental stage, will be in wide use wherever portable electrical power is desired. Buildings will be designed to make maximum use of solar energy to keep the occupants warm in the winter and cool in the summer.

These predictions, as I have said, are considered by some to be conventional, and to some of you they may not be new. There are, however, other scientific and technologic developments that may be foreseen, some of which are even more startling and in some ways unbelievable.

By 1992 we should know whether or not there is life on the planet Mars, and, if so, whether or not it bears any relation to that on earth. If we do not fruitfully develop Mars in the next three decades, certainly there will be a large increase in the use of Arctic and Antarctic regions, perhaps using nature's iceboxes for the long-term storage of foodstuffs.

I have heard it said that man, starting from raw chemicals, may some day be able to produce materials with the ability, given the proper environment, to reproduce themselves. Should this become possible, one of the greatest mysteries of all time, the mystery of life, would be brought into sharper focus. Certainly by 1992 we will have an even greater understanding of the life process and the role that each of the constituent complex molecules plays.

Self-lubricating metal will have been developed by 1992, reducing the maintenance now required for the lubrication of moving parts. Your car will need no 30,000-mile check-up; machines will have been perfected far beyond such nuisances. Wood, brick, and concrete are common materials today. Probably just as common thirty years from now will be newly developed materials with now-unattainable qualities of strength, insulation, and heat transmission.

Other technologic applications of scientific advances will be just as astonishing. Today's Maser and Laser will find many future applications. For example, the "Laser tower" may replace the "microwave tower" in our communications networks. Lasers also may be used to produce a source of intense, focused energy for the intricate machining of exotic materials, such as gems. Also, the unusual superior properties of very pure metals, studied today on a microscopic scale, may be applied on a larger scale to actual uses, making possible accomplishments that defy today's imagination.

In virtually every home in 1992 you may find a control center of electronic computation, for keeping budgets, planning menus, figuring income taxes, reminding the family of appointments, and even helping the family to arrive at policy decisions. Perhaps a computer will help you decide whether or not to attend your thirtieth class reunion. Business offices without doubt will make infinitely more use of computers, and so, probably, will elementary schools. Advances in the art may be of such a character and extent that national policy will be affected both directly and indirectly; computers may be making some of the most important decisions on many levels, and political scientists may suggest mechanisms for controlling the input to such machines.

Unless we solve one problem soon, you may not be able to travel to the 1992 period because mountains of papers, books, and journals will clog your path in all directions! The problem I have particularly in mind is the physical accumulation of scientific information at a rapidly accelerating rate. In the Atomic Energy Commission, the organization that I know best, the reservoir of scientific knowledge, information, and data is doubling in size about every seven years. Thus by 1992 we will require 16 times more storage space than now, unless steps are taken soon to develop and apply new concepts and technics, including automatic data processing, to the collection, organization, and dissemination of scientific and technical information.

In the year 1992 the differing languages of the world may no longer be such obstacles to communication, since it might be possible with the use of large computers to translate almost any language automatically.

Libraries as we know them now may no longer be prevalent. Instead there could be electronic devices to select and present to an individual researcher any information he desires from a central repository. You may "borrow" a book from such a library by dialing, using a closed-circuit, remote-control television system, without leaving your living room.

Pharmaceuticals which change and maintain human personality at any desired level can easily be imagined as a part of the 1992 scene. It may thus become necessary to establish new legal and moral codes to govern those who prescribe the use of these materials. Who should prescribe, for example, and under what conditions, such a drug to a person in a position of high authority when he is faced with decisions of great consequence? Under what conditions should such individuals be stimulated to energetic courses by artificial means, administered by their personal physicians?

The next thirty years should show great progress in predicting storms, earthquakes, and other natural hazards. Perhaps then some progress can be made in controlling these menaces to the well-being of mankind. Certainly as our knowledge of weather and climate grows we should be able to take steps to detect, to avoid, to divert, or possibly to deactivate disastrous storms. It may be possible to develop technics to control the weather to permit major rearrangements of the world's rainfall. Of course, climate control, even on a limited basis, will create major political problems.

The peaceful uses of nuclear explosives may include deepening the Straits of Gibraltar or opening up the Sierra Nevada passes. Current and planned experiments with these explosives could assist mankind in truly heroic projects like those, should further study prove them necessary and desirable.

Today we have a common synthetic food in the oleomargarine on our tables. By 1992 we may expect to find synthetic proteins, carbohydrates, and fats, all nourishing and palatable foods. Apart from the development of plentiful synthetic foodstuffs, it is reasonable to suppose that many new economic crops, both plant and animal, may be developed in the next thirty years.

The production of electrical power by thermonuclear devices is within the realm of possibility, and our research results within the next few years should shed further light on the feasibility of this process. All the waters of the seas and oceans are available as an energy source once this process is worked out.

In 1992 we can celebrate the one hundred and thirty-fifth anniversary of the proof of Pasteur that alcoholic fermentation is caused by yeasts and that yeasts are living cells. The last hundred years have seen biologic synthesis grow into a major industry. The next thirty years should see truly amazing advances in controlled biologic synthesis.

Industry is turning more and more to the use of microorganisms in developing new methods and processes. For example, as more becomes known about bacterial processes, the oil-producing companies may be able, with such processes, to promote oil discovery and recovery. As another example, many organic wastes, such as sewage liquids, contain large amounts of fixed nitrogen. I understand that the losses of fixed nitrogen from these sources just about equals the input from the present fertilizer industry. Perhaps biologic systems will be found in the next thirty years for the profitable extraction of this valuable material from "waste."

I should think that the oceans will serve as a great frontier in the next thirty years. Perhaps ways can be found to "farm" and "mine" the seas on a practical basis. Recent studies of the floor of the oceans indicate vast reserves of copper, manganese, nickel, and cobalt. It has also been estimated that nine tenths of all life on the earth is synthesized in the oceans and that the oceans could supply tenfold more food for man than is being produced presently if the methods for its cultivation were developed.

Perhaps, too, effective and cheap ways can be found in the next thirty years to make fresh and potable water from the oceans. As an example, perhaps someone can suggest a really effective way of combining garbage disposal, electrical energy manufacture, and desalinization of sea water into a simple fuel cell and solve all three jobs at one time.

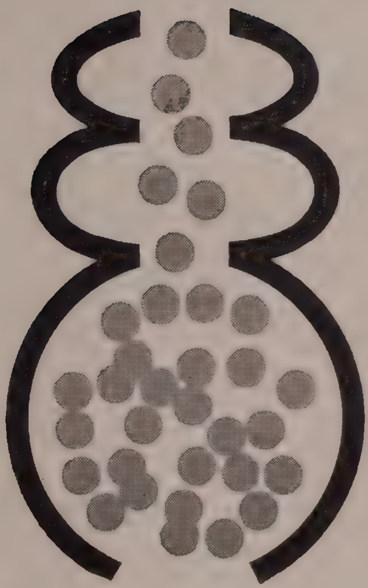
Great progress will be made in the prevention and control of infection; the treatment of sick, lame, deaf, and blind persons; the maintenance of mental health; and the general extension of useful life span. New surgical technics such as the cryogenic knife, involving extremely low temperatures, will be developed over the next thirty years, to allow even more seemingly miraculous repairs to the human machine.

All of these things that I have mentioned may come to pass. It is likely, at least, that a number of them will. And I think it certain that other wonders, yet undreamed of, will be a part of your surroundings in 1992.

Fantastic? Not any more so than what has happend between 1932 and 1962. We have lagged in political adjustment to the marvels of the past thirty years. We dare not continue this lag but must accelerate these adjustments and provide a moral climate fit for the great developments to come.

Announcement 1962 District Branch Meetings

Branch	*Date*	*Place*
FIRST	May (at time of State Society meeting)	New York City
SECOND	Sunday, Monday, Tuesday November 11, 12 13	Grossinger's Grossinger, New York
THIRD	*(to be announced)*	
FOURTH	Saturday, September 22	Queensbury Hotel, Glens Falls, New York
FIFTH	Friday, Saturday, Sunday September 7, 8, 9	Whiteface Inn, Lake Placid, New York
SIXTH	Joint meeting with Fifth District Branch	
SEVENTH	Thursday, Friday, Saturday September 20, 21, 22	Grossinger's Grossinger, New York
EIGHTH	Thursday, October 4	Bartlett Country Club Olean, New York
NINTH	May (at time of State Society meeting)	New York City



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(brand of diphenoxylate hydrochloride with atropine sulfate)

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lowers motility / relieves cramping / controls diarrhea

Roentgenographic studies by Demeulenaere[1] established that a single dose of 10 mg. of Lomotil slowed gastrointestinal transit within two hours and that it maintained its decelerating activity for more than six hours.

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Investigators have found the antidiarrheal action of Lomotil not only "excellent"[2] but "efficacious[3] where other drugs have failed. . . ."

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NOTE: Lomotil is an exempt narcotic preparation.

Descriptive literature and directions for use detailed in Physicians' Product Brochure No. 81 available from G. D. Searle & Co., P. O. Box 5110, Chicago 80, Illinois.

1. Demeulenaere, L.: Action du R 1132 sur le transit gastrointestinal, Acta Gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.
2. Kasich, A. M.: Treatment of Diarrhea in Irritable Colon, Including Preliminary Observations with a New Antidiarrheal Agent, Diphenoxylate Hydrochloride (Lomotil), Amer. J. Gastroent. 35:46-49 (Jan.) 1961.
3. Weingarten, B.: Weiss, J., and Simon, M.: A Clinical Evaluation of a New Antidiarrheal Agent, Amer. J. Gastroent. 35:628-633 (June) 1961.

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Chronic Occlusive Arterial Disease

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CHRONIC OCCLUSIVE *arterial disease includes various diseases in which chronic arterial insufficiency is a predominant manifestation. The clinical manifestations may include intermittent claudication, ischemia of the branches of the arch of the aorta, and stenosis of a renal artery. Arteriography, either percutaneous or intravenous, is the most useful method of diagnosis. Patients with occlusive arterial disease require meticulous care. They are candidates for arterial reconstruction if the occlusion is segmental, if the arterial tree distal to the occlusion is patent and adequate, and if an operation is not otherwise jeopardous because of associated or attendant conditions. The procedures include sympathectomy, endarterectomy, and grafting procedures. A successful outcome of surgery can be achieved in almost 90 per cent of the patients who meet the required surgical indication and have an adequate "run-off." The number of failures occurring months to years following an operation have been disappointingly high; however, some of the patients with late failure can be successfully operated on again.*

THE RECOGNITION of the fact that the arterial insufficiency of chronic occlusive vascular disease is frequently caused, or at least augmented, by segmental occlusion of the larger arteries has led to the recent development and application of surgical technics which have alleviated dramatically the disabling and deadly effects of ischemia not only of the extremities but also of the brain, kidneys, and other organs. Notwithstanding these observations, experience has revealed a disappointing number of both early and late failures due mostly to the characteristically generalized and progressive nature of arteriosclerosis, the almost exclusive cause of chronic occlusive vascular disease. That there are failures, however, should not cause undervaluation of surgical intervention in chronic occlusive vascular disease, because until ways are found to prevent arteriosclerosis, no other method of treatment offers such great improvement providing that a well-chosen procedure is successfully carried out and the obliterative arterial disease is chiefly segmental.

Etiology

Chronic occlusive arterial disease and other similar names are frequently substituted for any of the terms designating syndromes and disease entities in which chronic arterial insufficiency is a predominant manifestation. Greater etiologic and diagnostic specificity is impossible. A partial list of conditions embraced by such a designation includes: arteriosclerosis;

thromboangiitis obliterans and other specific and nonspecific arteritides; collagen diseases such as scleroderma; and the vasospastic diseases such as Raynaud's disease, acrocyanosis, ergotism, and erythromelalgia. That such a multitude of diseases may not be more definable is understandable in view of the ubiquitous and protean nature of arteriosclerosis, the fact that a specific arterial disease may supervene on arteriosclerosis, and the further fact that the end result of an arterial disease, regardless of its etiology, is also arteriosclerosis which lacks distinction. For example, in the absence of a typical history, an old embolic arterial occlusion could not with any certainty be distinguished clinically or histologically from an old arterial occlusion due to arteritis or atheromas. Consequently, it is not surprising that dispute exists as to whether or not the syndromes and diseases characterized by chronic ischemia due to an arterial occlusion are actually entities with a specific but unknown etiology, or are merely manifestations of arteriosclerosis. Nevertheless, the majority of those who deal with patients who have chronic arterial occlusive disease hold that it results broadly from two principal pathologic states: namely, the degenerative arterial diseases, such as arteriosclerosis obliterans, and the arteritides, of which thromboangiitis obliterans is the notable example.

ARTERIOSCLEROSIS OBLITERANS. Arteriosclerosis obliterans is not only the most common arterial disease but also it is by far the most frequent cause of segmental occlusion of medium- and large-caliber arteries. This condition predominates in men and in both sexes over the age of forty. Diabetes mellitus predisposes the individual to a particularly severe form of it. Although typically generalized and progressive, the intensity of the pathologic alteration and the degree of arterial obliteration is never uniform. Occasionally it occurs in young individuals, in which case it is localized characteristically to a segment of an artery with the arteries elsewhere remaining fairly free of arteriosclerosis.

The degenerative changes of arteriosclerosis may predominate in either the media or the intima and thereby predispose them respectively to arterial dilatation and aneurysms or to arterial obliteration. In arteriosclerosis obliterans, the type of arteriosclerosis is atherosclerosis which is confined chiefly to the intima. The principal pathologic evidence consists of intimal and subintimal deposits of cholesterol and other lipids with secondary fibrosis, hemorrhage, calcification, and endothelial ulceration. The intima becomes thickened, roughened, and susceptible to mural thromboses where it was galled. Thus, the atheromatous process gradually and ultimately occludes the lumen of arteries. Aside from the small arteries the earliest obliterative changes occur in the arteries to the lower extremities, especially at arterial origins and the first few centimeters thereafter, or in the stems of arteries wherever they are fixed and enveloped by fascia.

THROMBOANGIITIS OBLITERANS. Thromboangiitis obliterans (Buerger's disease) is a rare disease characterized, as its name implies, by thrombosis and inflammation of both the arteries and veins. It occurs in young individuals in their twenties or early thirties who have long been heavy smokers. Seldom, if ever, does it begin past the age of forty years. The etiology is unknown. Many consider that tobacco is the causative agent, but others believe that it only augments the manifestations of the disease by constricting the involved vessels and the collateral circulation. Nevertheless, patients with the disease so often are excessive smokers that the tobacco habit is a diagnostic feature of the disease and dramatic improvement almost always follows the cessation of smoking, even when the disease is in its acute phase and arterial insufficiency is not evident. The large and medium vessels to the lower extremity are involved more often than those elsewhere. The acute lesion consists of segmental, nonsuppurative, acute arteritis and acute phlebitis which frequently extends to involve the nerves in the neurovascular bundle.

Thus, in the early acute phases, the disease frequently manifests itself by superficial migratory phlebitis (40 per cent) and neuritis; only later, when the disease is chronic and the artery is occluded by thrombus and proliferated intimal cells, does chronic arterial insufficiency dominate the clinical picture.

Clinical manifestations

The clinical manifestations of chronic occlusive vascular disease vary depending on what artery is occluded; whether or not the occlusion is complete or partial, localized or extensive; and the degree of development of collateral circulation.

CLAUDICATION. In the lower extremities the first manifestation of chronic arterial insufficiency is intermittent claudication. This symptom complex consists of a cramping, squeezing pain in the muscles of the leg which is brought on by walking and promptly relieved by rest. The amount of exercise causing the symptoms, providing other things are equal, is a rough measure of the degree of arterial insufficiency. The location of the claudicating pain varies with the level of arterial occlusion. In femoral artery occlusion the pain is in the calf, while occlusion of the common iliac artery usually produces pain in the hips and thigh. Occlusion of the lower end of the aorta, which is known as Leriche's syndrome, results in bilateral hip and thigh pain and, in men, impotence. As the degree of ischemia becomes worse, the extremity begins to feel cold, and rest pain and night cramps occur. This pain has the same character as that causing intermittent claudication and is relieved by standing or dangling the legs to allow gravity to assist arterial circulation. Atrophy and contracture from disuse develop. Ultimately ischemic neuropathy produces hypesthesia, hyperesthesia, and intolerable constant pain. At any time after the onset of an arterial occlusion, ulceration and gangrene of the toes, heels, or ankle may follow trivial trauma or develop spontaneously and herald the need for amputation.

On examination the involved extremity exhibits absent or greatly diminished pulsation of the major arteries. Oscillometry provides confirmatory and more accurate information of the state of the pulses. The skin is cool, dry, shiny, and, if the ischemia is long-standing, hairless. Atrophic muscles and trophic nails are obvious. Venous filling is slow, and the elevated extremity rapidly exhibits a severe pallor which turns to an intense rubor when the extremity is made dependent.

ISCHEMIA OF THE BRANCHES OF THE ARCH OF THE AORTA. Occlusive arterial disease may also involve chiefly the branches of the arch of the aorta, and their major subdivisions. Thus the manifestations of cerebral, cerebellar, and the upper-extremity chronic ischemia may occur independently or in combination. The clinical features of chronic arterial insufficiency in the upper extremity are essentially identical to those of the lower extremity. They should not be mistaken for brachial plexus neuritis due to compression by a cervical rib or the anterior scalene muscle. It is quite likely that many patients with the so-called scalene anticus syndrome, especially those who were not benefited by scalenotomy, had instead organic obstruction of the arteries to the upper extremities in the root of the neck or superior mediastinum. In general, collateral circulation to the arm is abundant. Thus, absent wrist pulses are by no means a constant finding. The blood pressure in the arm, however, is invariably lower than that in the uninvolved extremity.

Diminished vertebral artery blood flow produces incoordination and weakness, disordered speech and vision, vertigo, and occipital headaches. That extracranial carotid artery occlusions either complete or partial are responsible for nearly a quarter of cerebral apoplexies emphasizes the clinical importance of this surgically correctable lesion. The occlusion which is at first only partial may be at either end of the common carotid artery, but usually it is found at the bifurcation of the carotid artery and in the origin of the internal carotid artery.

The typical pathognomonic signs and symptoms of internal carotid arterial insufficiency consist of attacks of monocular blindness accompanied by numbness in the opposite arm and sometimes by headaches, seizures, and short periods of unconsciousness. Usually the attacks recede and recur but finally progress to hemiplegia. When the artery is occluded in the neck, there is on the side of the lesion acrotism of the tonsillar fossa, diminished ophthalmodynamometric determination, and often an audible bruit over the carotid bifurcation. One should never compress the normal carotid artery in the neck, for this frequently advocated diagnostic test which induces syncope may

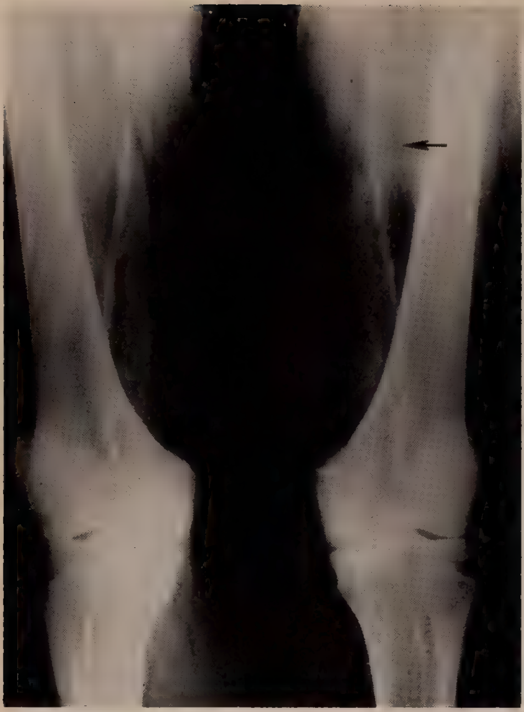

FIGURE 1. Intravenous arteriogram, a simple and safe method for radiographically opacifying the whole vascular system, clearly reveals in this fifty-year-old woman a segmental occlusion, 1 cm. in length, of the left superficial femoral artery at the beginning of the adductor canal. Note abundant collateral circulation around the arterial block and that the vessels in the right lower extremity are normal. This patient, who exhibited advanced generalized arteriosclerosis, complained of 2-block intermittent claudication for two months. She was completely relieved of symptoms by bypassing the femoral arterial occlusion with a Teflon prosthesis.

instead cause irreparable damage.

Stenosis of a renal artery. Stenosis of a renal artery has long been recognized both experimentally and clinically as a cause of hypertension. The apparent mechanism for the hypertension is the elaboration by the kidney of a proteolytic enzyme, renin, in response mainly to diminished pulse pressure rather than to reduced blood flow. Renin then reacts with an ingredient in the liver which leads to the formation of the vasopressor substance, hypertensin. Hypertensin also appears to be the principal stimulant causing the release of aldosterone from the adrenals, suggesting thereby that the entire mechanism is basically a physiologic one for maintaining homeostasis.

The only accurate way to diagnosis the lesion short of an actual pressure determination made at operation on either side of the stenosis is by arteriography. However, certain distinctive clinical and laboratory findings may provide a clue to its presence. Typically the hypertension begins abruptly and progresses rapidly, but sometimes renal artery stenosis causes a sudden augmentation of hypertension or the malignant phase of hypertension in patients who previously had only mildly elevated blood pressure. The involved kidney is smaller than the uninvolved one and exhibits delayed, reduced, and abnormal function by intravenous pyelography, by radioactive Diodrast renography, and by differential or split renal function studies. The latter studies, determined by simultaneously comparing the function of each kidney via ureteral catheters, point to the ischemic kidney when it exhibits reduced phenolsulfonphthalein excretion, urea clearance, urine volume, and urine sodium content. However, none of these typical clinical and laboratory findings are constant, and they may actually be misleading either because the renal artery stenosis may be bilateral or because, in the case of unilateral involvement, the kidney with the normal nonstenotic renal artery is literally unprotected from the hypertension and therefore ultimately becomes insufficient and ischemic from nephrosclerosis and arteriolosclerosis.

Arteriography

Arteriography is singularly the most important diagnostic examination in the evaluation of patients with chronic occlusive arterial disease (Fig. 1). By no other means can the location and extent of an arterial occlusion and the patency of the vessels distal to it be precisely and accurately determined. Such information, of course, is necessary for the selection of candidates who are suitable for surgical intervention. Among the several technics of arteriography, the simplest, but not necessarily the most desirable, is the direct percutaneous intra-arterial injection of the contrast agent via the femoral abdominal aorta, carotid, subclavian, brachial, and even the vertebral arteries (Fig. 2). How-

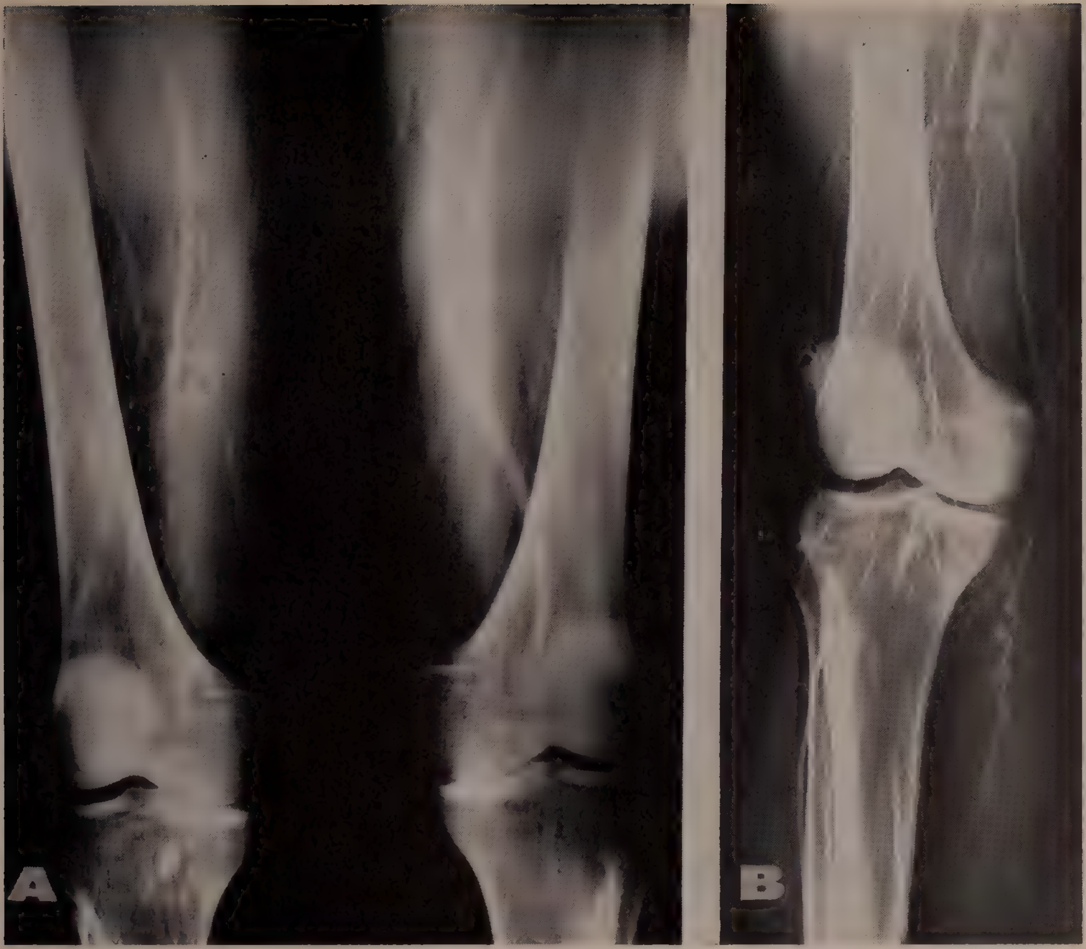

FIGURE 2. When intravenous arteriography does not reveal extent of an arterial occlusion or patency of the distal arterial tree (A) knowledge of these facts, which determine the patient's suitability for an operation, may sometimes be gained by direct-puncture arteriograms. These films are of thirty-one-year-old patient who received complete relief (B) from disabling unilateral intermittent claudication by a bypass arterial prosthesis a year after a lumbar sympathectomy which had failed to bring significant improvement. (Reproduced from Glenn, F., and Wantz, G. E.: Problems in Surgery, St. Louis, C. V. Mosby Company, in press.)

ever, complications which are sometimes serious may arise from malpositioned needles and extravasated dye and blood. With peripheral arteries, such as the femoral artery, these complications can be avoided by exposing the artery through a small incision and carefully selecting the best site for the injection. For convenience, "cut-down" arteriography is frequently incorporated with the definitive operative process.

Intravenous aortography is a safe and excellent substitute for percutaneous aortography. Because it has the additional advantage of displaying all or any part of the entire arterial tree, we now use it in the preoperative evaluation of nearly all candidates for arterial surgery.

Arteriograms can also be made via a catheter inserted percutaneously or by "cut-down" into the femoral artery (the brachial artery can also be used) and passed retrograde up the aorta and if necessary into selective aortic branches. This arteriographic technic is especially useful in demonstrating the coronary arteries, branches of the aortic arch, the renal arteries, the superior mesenteric artery, and the arteries of the celiac axis.

General treatment

All patients with occlusive arterial insufficiency, whether mild or severe, require meticulous care. They should not smoke, especially those with thromboangiitis obliterans. They should be instructed in foot and skin hygiene and in the prophylactic use of fungicidal powders and warned of the dangers of patent corn removers and improper nail trimming and callus paring.

The feet should be kept warm at all times, but external heat and extra-hot baths must be absolutely avoided. All abrasions and cuts, no matter how trivial, demand prompt medical attention if gangrene is not to follow. Exercise should be reduced to an amount less than that which induces pain. By walking slower and stopping to rest short of intermittent claudication, many can extend their distance afoot. The vasodilatory drugs in general are unsatisfactory, but there is no harm in prescribing them, since occasionally they do provide some improvement. Similarly, prolonged anticoagulant therapy in the majority of patients with chronic occlusive disease of the larger arteries is usually not warranted since it rarely leads to improvement and does not stop the disease from advancing.

Surgery

Selection of patients for arterial reconstruction. Patients with chronic occlusive arterial disease are candidates for arterial reconstruction if the occlusion is segmental, if the arterial tree distal to the occlusion is patent and adequate, and if an operation is not otherwise jeopardous because of associated or attendant conditions (Fig. 3). In patients meeting these requirements, there is an excellent chance of safely restoring arterial circulation and relieving the disabling manifestations of chronic ischemia. Generally arteriography is necessary to establish with certainty whether or not a chronic arterial occlusion is segmental, although the answer to this pathologic question is often apparent by clinical findings alone. Usually the patients with chronic segmental arterial occlusion are fairly young and have unilateral occlusions in noncalcified proximal vessels with intermittent claudication occurring in the presence of relatively good circulation. Elderly patients with calcified arteries and bilateral severe signs and symptoms of chronic arterial insufficiency unfortunately often have such advanced peripheral arteriosclerosis that arterial reconstruction is impossible and, if attempted, may even jeopardize the existing meager circulation. These patients, however, may be benefited by sympathectomy.

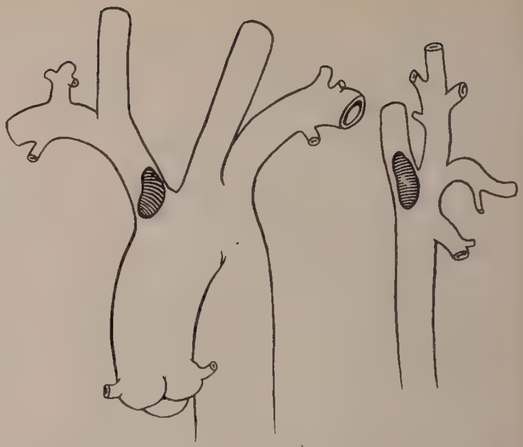

FIGURE 3. About a quarter of all cerebral apoplexies result from extracranial arterial occlusions. Occlusions involving carotid arterial bifurcation are about eight times more common than those occurring at origin of carotid arteries or in branches of aortic arch.

For a successful result blood must flow freely, under full pressure, and without impedance into and through the distal arterial tree. If it does not, thrombosis becomes inevitable despite anticoagulant therapy. Nevertheless the presence of ischemic ulceration, minimal gangrene, rest pain, ischemic neurititis, or diabetes mellitus—even when such findings occur in the elderly—are not necessarily contraindicative for possible arterial reconstruction. Moreover, arteriography does not always provide an accurate preoperative picture of the vessels distal to an occlusion. Thus in many instances, the distal arteries are evaluated better by direct exploration. For example, in patients with Leriche's syndrome, the femoral arteries may be easily and safely exposed for evaluation at the time of the proposed definitive operation. Then, if there is any question concerning the state of the distal arteries, an arteriogram by direct puncture can be made. Should the distal arteries prove inadequate for arterial reconstruction, a sympathectomy can instead be undertaken as the definitive procedure.

All patients with transient cerebral ischemia from extracranial arterial occlusion are candidates for arterial reconstruction. Extracranial carotid arterial occlusion can be dealt with easily and with minimal trauma with the aid of local anesthesia. It is particularly important that the operation not be postponed, since the intermittent attacks inevitably recur with increasing frequency until there is a major stroke or the internal carotid artery becomes completely and irreparably occluded. Even those who have sustained a major stroke are operative candidates since arterial reconstruction may prevent a recurrent and possibly fatal apoplexy. Carotid arteriography, although diagnostically useful when the results of other examinations are equivocal, should not be done in patients with recent hemiplegia due to intracranial vascular accidents since it may cause death or hinder recovery. Hemiplegia is rarely the first manifestation of extracranial arterial occlusion, and it is doubtful that an operation could be performed soon enough or before there is irreversible cerebral necrosis in such patients to insure a better result than if no operation was performed.

The selection of candidates for renal artery reconstruction is, as indicated previously, based almost solely on arteriographic and operative findings. But not all patients with hypertension due to renal artery stenosis are candidates for renal artery reconstruction; some are best treated by complete or partial nephrectomy. Nephrectomy is preferable when, in the case of unilateral lesions, the renal vein is occluded with thrombus, the kidney is irreparably damaged, or successful arterial reconstruction is technically impossible because either the renal artery is too small or there are multiple stenoses of the distal branches of the renal artery.

CHOICE OF SURGICAL PROCEDURE. There are a variety of procedures which are applicable to the therapeutic problems of chronic arterial occlusion; all have their advantages and proponents but none are universal. The surgeon dealing with these problems must be familiar with all the technics available, for successful results depend largely on the neat performance of a well-chosen procedure.

SYMPATHECTOMY. Not only does sympathectomy overcome arterial spasm but there is little doubt that it also can promote the development of collateral circulation. Thus, this procedure can often be of great value. It is the only procedure offerable to those patients with extensive and irreparably occluded arteries. Unfortunately these are the very patients in whom the effects of sympathectomy are least dramatic. Sympathectomy rarely improves intermittent claudication unless it is limited to the toes. Also it probably does not significantly augment the flow of blood to muscles nor can it prevent amputation of a gangrenous extremity. Nevertheless, it does increase the blood supply to the skin, makes the extremity warm, promotes the healing of ulcers, and will often save an extremity and relieve intolerable rest pain and ischemic numbness. We believe it is an excellent adjunct to definitive reconstruction of occluded arteries to the lower extremity whether the occluded vessel is the aorta or the femoral artery. We have never seen it make the condition of an extremity worse nor have postsympathetic neuralgias been common or persistent.

To do a sympathectomy of the leg, foot, and posterior thigh all that is required is to excise the second and third lumbar ganglia. It is impossible by the excision of higher ganglia to perform a sympathectomy of the anterior thigh because of residual sympathetic pathways in the motor nerves. The effect of lumbar sympathectomy is permanent and complete below the knee, and this is all that is necessary in the majority of patients with vascular insufficiency.

Sympathectomic denervation of the upper extremity is best accomplished by resection of the ganglionic chain from the midcervical to the third thoracic ganglion. This causes a Horner's syndrome which if it is bilateral is not disfiguring. Consequently, if sympathectomy of only one upper extremity is necessary, a symmetrical appearance of

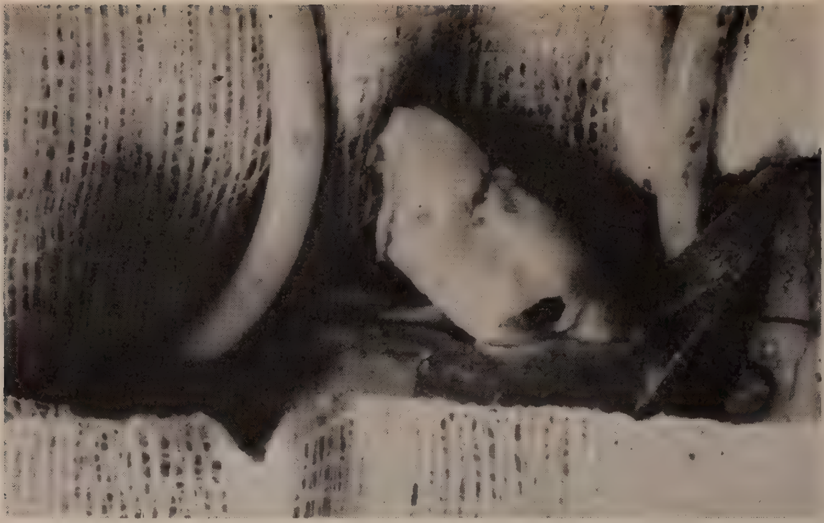

FIGURE 4. Occlusions of carotid arteries are usually short and therefore amenable to endarterectomy.

the eyes can be created simply by excision of the opposite superior cervical ganglion. Unfortunately, unlike sympathectomy of the lower extremity, sympathectomy of the whole upper extremity including the distal portion is sometimes incomplete because residual motor pathways may carry sympathetic fibers all the way to the periphery. This fact, however, should not deter the performance of an upper-extremity sympathectomy should such a procedure be indicated.

ENDARTERECTOMY. Endarterectomy has the advantage not only of preserving the patient's own vessels and existing collateral vessels but also of permitting new collateral channels to develop through arteries arising from the formerly occluded main stem artery (Fig. 4). Arteries in which there is an intense inflammatory component to the occlusion are usually unsuitable for endarterectomy since the diseased intima does not readily strip from the media. The results of endarterectomy are best if the procedure is confined to short occlusions of the larger arteries such as the aorta, and iliac and common femoral arteries. It is also particularly well suited for the short partial occlusions of the carotid and renal arteries but less so in the case of the superficial femoral arteries where the occlusive process is always more extensive than it is on first suspicion. The diseased intima may be removed through either transverse or longitudinal arteriotomies. Closure of the latter type of arteriotomy may reduce the caliber of the vessel severely. This disadvantage, however, can be overcome by closing the arteriotomy with a patch graft composed of one of the commercially available synthetic materials such as Teflon or Dacron (Fig. 5). In dealing with partially occluded arteries, when the patient can't tolerate the complete occlusion required to perform the endarterectomy, a temporary shunt consisting of plastic tubing placed in each end of the arteriotomy may be used.

The tendency toward early postoperative thrombosis of an endarterectomized artery is high if the vessel is small, impeding distal atheromas exist, the diseased intima is incompletely removed, and the distal edge of the intima is free to curl into and occlude the artery's lumen. Consequently it is not surprising that the results of long endarterectomies performed blindly with loop instruments in small arteries are not nearly as satisfactory as those achieved with a bypass graft; indeed, thrombosis of a long endarterectomized artery may lead to premature gangrene and amputation. Nevertheless, in many instances an endarterectomy is the procedure of choice.

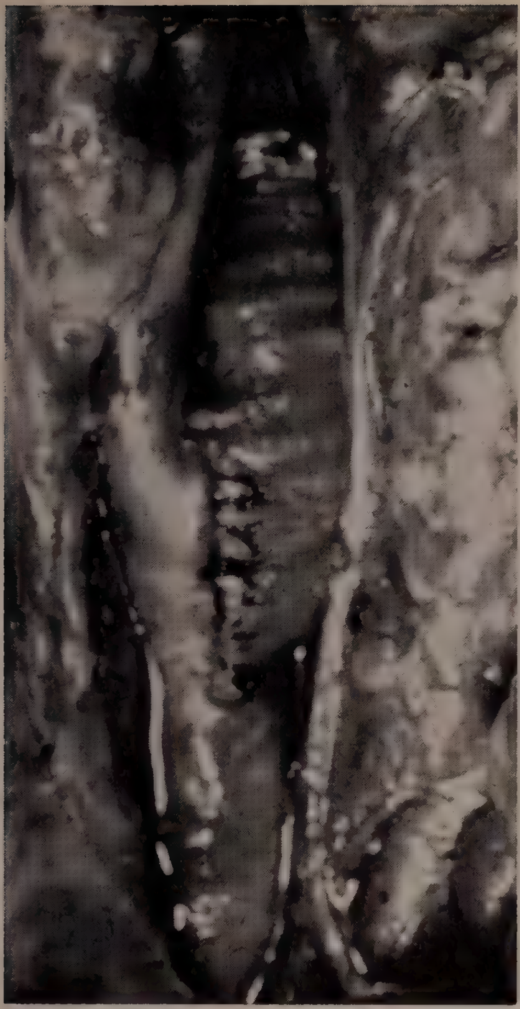

FIGURE 5. Should the closure of the arteriotomy, through which the arteriosclerotic and thrombotic debris is removed, result in arterial constriction, the arteriotomy may be widened by closing it with aid of patch graft of either synthetic material or autogenous vein.

Grafting procedures. There is as yet no agreement as to the type of arterial graft which is best. Arterial homografts, which were the first to be used, have now been in place and functioning perfectly in some patients for ten years. The difficulties in procuring and processing arterial homografts have led to their disuse. Saphenous autogenous vein grafts, inserted so that their valves do not hinder the flow of blood, also have proved satisfactory to bypass occlusions in small arteries. Crimped plastic prosthesis composed of Teflon or Dacron are currently enjoying widespread popularity not only because of their ready availability and convenience but also because they have given excellent results. We prefer Teflon arterial prostheses since in our hands this type of graft has been quite satisfactory. Bypass grafts are preferable to interpolated replacement grafts. In the former there is little risk of interruption of collateral arteries and therefore a failure of the graft to function is less likely to jeopardize the extremity. Moreover, the insertion of a bypass graft is simpler than that of interpolation, and in the event of a failure successful reoperation is possible.

Nearly every type of segmental occlusion is amenable to bypass grafts since the grafts are available in various sizes and shapes and may be tailored by adding limbs to meet a specific requirement. Sometimes, when there are segmental occlusions in both the iliac and superficial femoral arteries on one side, the graft anastomosed end-to-side to the aorta and popliteal artery can also be anastomosed side-to-side to the common femoral artery to supply blood to the deep femoral artery. With the exception of the aorta the size of a bypass graft generally should exceed the size of the artery to which it is anastomosed by about one and a half times. The anastomotic angle between the graft and the host artery should be as acute as possible so that the flow of blood is smooth and streamlined. Usually a linear incision in the artery to which the bypass graft is to be sutured suffices, but sometimes an oval or an ellipse of the vessels's wall must be excised. If a linear arteriotomy is made it should not be too long, nor should the artery in which it is made be soft and pliable because a constricted and inefficient end-to-side anastomosis, rather than one that is widely patent, may be created.

Outcome of reconstructive arterial surgery. While the outcome of arterial reconstructive procedures depends on a variety of factors, our experience and that of surgeons experienced in the problems of vascular surgery indicates that a successful outcome can be achieved in nearly 90 per cent of the patients who meet the required surgical indication and have an adequate "run-off." For an operative result to be classified as successful, the

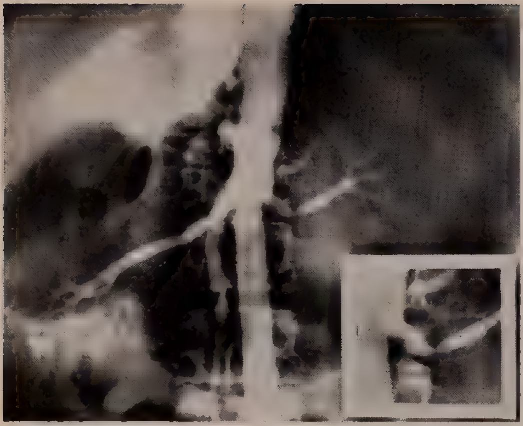

FIGURE 6. No artery is immune to segmental occlusive disease. This film from percutaneous retrograde arteriogram revealed severe stenosis of the left renal artery. Note also diminished vascularity and small size of left kidney. This seventeen-year-old boy's hypertension was not relieved until a left nephrectomy was done, primary reconstruction of the left renal artery having failed.

peripheral pulses should return. Nevertheless, the peripheral pulses of many patients do not return after the operation, yet the patients are sufficiently improved so that they are completely relieved of their ischemic symptoms. Often the extremities of patients who have a return of their pulses after arterial reconstruction of a chronic occluded vessel exhibit a reactive hyperemia. This hyperemia, which sometimes lasts several weeks, may be intense and even painful with the extremity being warm and displaying blotchy erythema. In general it is most difficult to achieve successful results when there is occlusion of the femoral and popliteal arteries because in these small arteries the underlying occlusive disease is usually very advanced.

The number of failures occurring months to years following an operation have in many instances been disappointingly high. Usually late failures are the result of the progressing nature of arteriosclerosis, but they may be inherent in the operation itself. However, some of the patients with late failure can be successfully operated on again. The fact that failures occur should not deter the performance of arterial reconstruction since the percentage of rehabilitation of these otherwise disabled patients is high (Fig. 6).

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Therapy of Iron-Deficiency Anemias

AN EVALUATION *was made of a new iron-carbohydrate complex of low toxicity (Jefron) in 26 newborn infants, 4 severely anemic infants, 17 private pediatric patients, and 35 obstetric patients with hemoglobin values of below 10 Gm. per 100 ml. Satisfactory hemoglobin responses occurred in all groups at levels of iron lower than those which are conventionally used. There were no significant side-effects, and the complex was well tolerated.*

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IRON-DEFICIENCY DISEASE was recognized and treated successfully long before other nutritional diseases, such as rickets, scurvy, and pellagra. While the specificity of iron in the treatment of deficiencies has long been recognized, the objectionable features of available therapeutic iron preparations have been sufficient to warrant a search for more effective and safer preparations. The disadvantages of various therapeutic forms of iron include unpalatability, production of gastrointestinal disturbances, staining of teeth, and, with some frequency, toxic reactions and fatalities.

In the past few years the knowledge of the metabolism, requirements, absorption, and toxicity of iron, especially with respect to premature and newborn infants, children, and pregnant women, has been increased through extensive research. This interest reflects the importance that physicians, public health workers, and others attach to iron-deficiency disease. The present report reviews the status of iron therapy and presents the results of a clinical study which was made with a new iron-carbohydrate complex.*

Hazards of iron therapy

Accidental iron poisonings, especially in young children, have been receiving increasing attention, and the importance of keeping iron preparations out of reach of infants and young children has been pointed out editorially.[1] The records of the New York City Poison Control Center show that ferrous sulfate was involved in 35 incidents during the past two and one-half years,[2] and the city's health department reports that 75 per cent of all cases of iron poisoning are due to ferrous sulfate.[3] Three fatal and 2 nonfatal cases of iron poisoning in young children have been described from the records of the National Clearing House for Poison Control Centers.[4]

A review of 40 cases of poisoning in children caused by the ingestion of from 2 to 10 Gm. of ferrous sulfate points out that the margin of safety between the therapeutic dose and the toxic dose is less than was previously thought.[5] The same report shows that in acute iron poisoning the mortality rate is approximately 50 per cent. The Committee on Toxicology of the American Medical Association has stated that "iron sulfate or other iron salts which have produced injury may ultimately be replaced by safer iron compounds provided that the substitutes are equally effective and not too expensive."[2]

Candy-coated preparations of ferrous

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Pediatrics, May 11, 1961.

* The iron-carbohydrate complex used in this study was supplied as Jefron by the Pitman-Moore Company, Indianapolis, Indiana, Division of the Dow Chemical Company.

TABLE I. Distribution of patients

Group	Total	Age Range	Males	Females
Pediatric outpatients	26	Newborn	12	14
Control infants	13	3 to 9 months	8	5
Severely anemic infants	4	9 to 20 months	3	1
Private pediatric patients	17	8 months to $10^1/_2$ years	8	9
Obstetric patients	35	. . .	. .	35
TOTALS	95		31	64

sulfate increase the dangers of accidental poisoning by offering a strong temptation to small children.

Incidence of iron-deficiency disease

The need for a safe, effective, and inexpensive iron therapy continues to concern physicians treating iron-deficiency anemia. Iron deficiency with hypochromic anemia is considered the most common nutritional deficiency of children in the United States, particularly during the last half of the first year.[6] Low iron intake is the most frequent cause of nutritional anemia in infancy, and the rapid growth rate with increased demands for hemoglobin formation results in a high incidence.[7] Iron requirements are two to three times greater than at any other period of life, and subclinical or marginal states of iron deficiency are often found.[8] Premature infants require more iron than normal ones because of more rapid growth, relatively small blood volume, and lower iron stores at birth. Before the third to fourth month after birth, iron produces little clinical response in premature infants, but it is essential and well utilized and prevents the development of hypochromic anemia after that period.[9] Rapidly growing infants, premature infants and twins, and infants born after repeated pregnancies are especially vulnerable to iron-deficiency anemia.[10]

Maternal iron deficiency also has been cited as an important etiologic factor of nutritional anemia in infancy.[11] The incidence of anemia in pregnant women can be related directly to socioeconomic levels[12]; 50 per cent or more of it was found in the lowest economic group, while private obstetric patients in the top income group had an incidence of less than 10 per cent. Infants with iron-deficiency anemia were found to be born rarely to nonanemic mothers, although occasionally anemic mothers were found to give birth to infants showing no signs of iron deficiency. Puerto Rican children from parents of low income had a high incidence of iron-deficiency anemia, with hemoglobin values as low as 5 Gm. per 100 ml.[13] The experience in our outpatient prenatal and pediatric clinics, where 95 per cent of the patients are Puerto Rican or Negro, has been similar.

While the adult male needs to absorb only 0.5 to 1 mg. of iron daily, a woman during her years of menstruation and childbearing needs twice this amount and normally maintains a rather precarious balance.[14] During the last ten weeks of pregnancy, for example, the uptake of iron is three times that of the first trimester.[15] Anemia may not be the sole criterion of iron deficiency during pregnancy; recent evidence suggests that iron therapy may be beneficial also when pregnancy is accompanied by fatigue or poor appetite, despite normal hemoglobin levels.[16]

Materials and methods

The iron-carbohydrate complex used in this study contains 45 per cent of iron, more than twice the amount in ferrous sulfate. Its stability in solution over a wide pH range (4 to 11) favors absorption after oral administration. The margin of safety is high. In comparative pharmacologic studies no evidence of toxicity occurred in mice given oral doses more than 12 times the lethal dose of ferrous sulfate, and, in marked contrast to results with ferrous sulfate, no emesis occurred in dogs given much higher doses of the iron-carbohydrate complex.[17] Other advantages of the pharmaceutical preparation include palatability, freedom from the characteristic taste of iron (the complex is virtually tasteless), and failure to stain the teeth.

Before we undertook this study, low hemoglobin values reported in our Well Baby Clinic had prompted a check of hemoglobin levels and diets of the expectant mothers. An analysis of the self-chosen diets of women attending the prenatal clinic revealed that the iron intake of the majority of pregnant women was about 6 to 8 mg. daily. Assuming that 10 per cent of this was absorbed, ordinary requirements would be met, but at least double this amount would be required to maintain body reserves in pregnancy.

This study was planned to include patients from the Prenatal and Well Baby Clinics of the Brooklyn Women's Hospital, from the Pediatric Clinic of the East New York Dispensary, and from private obstetric and pediatric practice (Table I). Patients who were treated with iron-carbohydrate complex are considered under the following four groups: (1) newborn infants, (2) severely anemic infants, (3) obstetric patients, and (4) private pediatric patients.

All hemoglobin determinations were made by the oxyhemoglobin method.

Group 1. Beginning four days after delivery, infants in the newborn group were treated prophylactically with daily doses of the iron-carbohydrate complex equivalent to 7.5 mg. of elemental iron together with a multivitamin preparation. The mothers were advised to continue giving the same dosage until the infants were returned to the Well Baby Clinic for a blood count at the end of the second month, at which time the dosage was increased to 15 mg. of iron as an iron complex with a multivitamin preparation. Additional blood counts were done at the end of the third and ninth months. Data on height, weight, and acceptability of the product, as well as the occurrence of any side-reactions such as diarrhea or constipation, were recorded. Thirteen patients in the same age group were selected at random from the Well Baby Clinic of the Brooklyn Women's Hospital and used as controls. These patients received no medication except a multivitamin preparation.

Group 2. Four severely anemic infants of Puerto Rican parentage with hemoglobin levels of less than 7 Gm. per 100 ml. were given 75 mg. daily of iron as an iron complex. Their ages varied from nine to twenty months. Data on hemoglobin levels were obtained at the first, third, sixth, and ninth weeks, and gains in weight and height were also recorded. Records were kept on the acceptability of the product and on the incidence of side-reactions.

Group 3. All of the obstetric patients in Group 3 had hemoglobin values of below 10 Gm. per 100 ml. Three different dosage levels of iron complex were used: 1, 2, and 3 teaspoonfuls per day, equivalent to 100, 200, and 300 mg. of elemental iron. Blood counts were made at three-month intervals so far as possible, with a final count being made prior to delivery or soon after. Since the pregnant patient is known to be especially susceptible to nausea, diarrhea, constipation, and other gastrointestinal disturbances, particular attention was given to the occurrence of side-reactions. The acceptability of the product to patients was noted carefully also. A control series was not used; prior to our undertaking this study we had found that hemoglobin levels before and after delivery were very similar, usually below 8 to 9 Gm. per 100 ml.

Group 4. A series of pediatric patients seen in private practice were given the iron complex at dosage levels of 7.5 or 15 mg. of iron three times daily. The patients varied in age from eight months to ten and a half years and were under treatment for a variety of conditions. Anorexia, listlessness, pallor, and underweight were common symptoms, complicated at times by upper respiratory infections, allergies, and jaundice. Conventional management was employed, and multivitamin preparations were included routinely.

Results

Group 1. Hemoglobin levels of the 26 newborn infants in Group 1 increased from an average of 10.6 Gm. per 100 ml. to 11.9 Gm. between the second and third month for a net rise of 1.3 Gm. (Table II and Fig. 1). Gains in body weight averaged 5 pounds, 6 ounces for the first three months. The continuation of the iron medication for nine months resulted in an average

TABLE II. Response of newborn infants to prophylactic amounts of iron-carbohydrate complex*

Case	Sex	Weight at Birth (Pounds Ounces)	Weight Gain in 3 Months (Pounds Ounces)	Hemoglobin (Gm. Per 100 Ml.) 2 Months	3 Months	Gain	9 Months	Total Gain
1	F	7 − 3	4 − 9	11.1	12.5	1.4	13.4	2.3
2	M	8 − 0	5 − 8	12.3	13.8	1.5	14.1	1.8
3	F	6 − 6	6 − 11	10.2	11.3	1.1	12.8	2.6
4	M	9 − 4	4 − 0	11.0	11.5	0.5	13.5	2.5
5	F	5 − 15	4 − 13	11.0	12.3	1.3	12.8	1.8
6	F	7 − 3	4 − 9	11.0	11.5	0.5	13.5	2.5
7	F	7 − 6	6 − 14	9.4	12.3	2.9	12.9	3.5
8	F	6 − 12	5 − 4	9.7	12.3	2.6	13.9	3.9
9	F	8 − 10	3 − 6	10.8	11.0	0.2	12.8	2.0
10	M	6 − 12	5 − 5	10.2	11.3	1.1	12.9	2.7
11	F	8 − 15	5 − 7	11.3	12.5	1.2	13.2	1.9
12	M	6 − 3	4 − 13	11.3	12.9	1.6	12.6	1.3
13	M	10 − 2	6 − 10	10.1	10.9	0.8	13.4	3.3
14	F	6 − 15	7 − 2	10.7	12.3	1.6	13.6	2.9
15	F	5 − 13	3 − 15	10.3	11.3	1.0	12.0	1.7
16	M	8 − 2	5 − 6	10.0	11.5	1.5	12.5	2.5
17	F	5 − 4	3 − 15	10.7	11.3	0.6	12.0	1.3
18	M	7 − 0	5 − 4	10.2	12.3	2.1	12.9	2.7
19	M	6 − 4	7 − 6	9.4	11.1	1.7	12.7	3.3
20	M	7 − 11	6 − 4	10.4	10.9	0.5	11.6	1.2
21	M	7 − 9	7 − 0	11.0	11.5	0.5	12.5	1.5
22	F	8 − 13	5 − 5	11.3	12.5	1.2	12.8	1.5
23	M	9 − 12	5 − 8	11.1	11.9	0.8	13.2	2.1
24	F	5 − 8	5 − 11	11.1	12.3	1.2	14.1	3.0
25	F	5 − 7	6 − 13	9.4	12.7	3.3	13.3	3.9
26	M	5 − 7	3 − 11	10.7	11.5	0.8	12.8	2.1
Average		7 − 3	5 − 6	10.6	11.9	1.3	13.0	2.4

* Dosage equivalent to 7.5 mg. daily for the first month and 15 mg. daily thereafter.

TABLE III. Response of severely anemic infants to iron-carbohydrate complex*

			Weight (Pounds Ounces)			Hemoglobin (Gm. Per 100 Ml.)				
Case	Sex	Age (Months)	1 Week	9 Weeks	Net Gain	1 Week	3 Weeks	6 Weeks	9 Weeks	Net Gain
1	M	18	27 − 8	30 − 12	3 − 4	6.5	11.0	11.5	11.8	5.3
2	F	9	18	21 − 8	3 − 8	5.5	7.8	11.0	. .	5.5
3	M	18	25 − 12	29	3 − 4	7.0	. .	9.2	12.5	5.5
4	M	20	28 − 8	32	3 − 8	6.2	8.5	10.0	11.8	5.6
Average		16	24 − 14	28 − 4	3 − 6	6.3	9.1	10.4	12.0	5.5

* Dosage equivalent to 75 mg. of iron per day.

level of 13 Gm. of hemoglobin for an increase of 2.4 Gm. above the second month. The control infants who received iron from dietary sources exclusively showed lower hemoglobin levels over the nine-month period; the net increase above the second month was 1.6 Gm. (Fig. 1).

Group 2. The hemoglobin levels of the 4 severely anemic Puerto Rican infants in this group increased an average of 5.5 Gm. per 100 ml. over a six- to nine-week period. The average values at the start were 6.3 Gm. per 100 ml. Gains in body weight averaged 3 pounds, 6 ounces for this period (Table III and Fig. 2).

All 30 infants in Groups 1 and 2 took the medication readily, and there were no instances of vomiting, diarrhea, constipation, or other gastrointestinal disturbances.

Group 3. The average hemoglobin levels of the 35 obstetric patients increased as follows over the last trimester: from 8.6

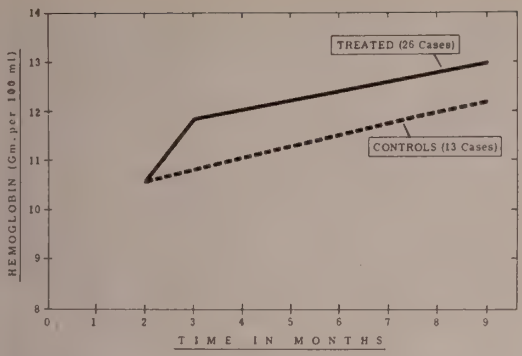

FIGURE 1. Hemoglobin response of newborn infants given iron-carbohydrate complex and multivitamin preparation.

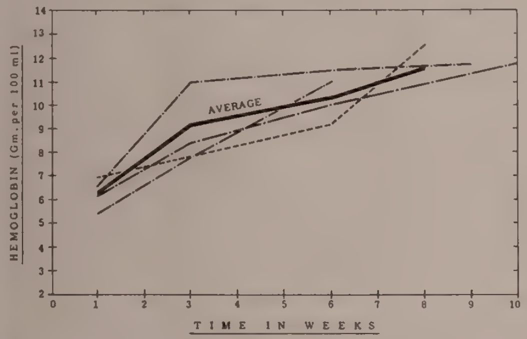

FIGURE 2. Hemoglobin response of severely anemic infants to iron-carbohydrate complex.

Gm. per 100 ml. to 11.1 Gm. in those receiving 1 teaspoonful (100 mg. iron) daily, from 9.1 to 11.3 Gm. in those receiving 2 teaspoonfuls daily, and from 10.2 to 12.3 Gm. in those receiving 3 teaspoonfuls daily. Thus the average increases were 2.5, 2.2, and 2.1 Gm. per 100 ml. respectively for the 1-, 2-, and 3-teaspoonful dosages (Table IV), which indicates that a single dose of 1 teaspoonful of the iron complex daily produced a rate of response in these patients comparable to that of 2 or 3 repeated doses. Several patients reported subjective responses of feeling better and losing their tiredness. All the women took the iron complex readily and found the flavor pleasant. Despite the fact that the preparation was taken routinely between meals, none of the patients reported any of the side-reactions which are frequently seen with iron preparations, such as cramps, nausea, upset stomach, diarrhea, and constipation. No discoloration of the teeth occurred.

Group 4. Data on the 17 private pediatric patients are presented in Table V. The duration of treatment ranged from nine to twenty-seven weeks with an average of thirteen weeks. The average levels of the 14 patients receiving 15 mg. three times daily increased 1.8 Gm., from 11.3 to 13.1. The hemoglobin levels of the 3 patients (too few for significance) receiving 7.5 mg. three times daily also increased markedly. Satisfactory gains in weight, height, and general body tone were observed in all patients; the improvement in appetite or weight was exceptional in 6.

The following 3 case reports, taken from our private patient files and clinic, are presented in detail since they are representative and provide additional information of interest to clinicians.

Case reports

Case A. This case illustrates the need for iron in infants with hemolytic anemia.

History. A male infant,* the second child in the family, weighed 5 pounds, 4 ounces when he was born prematurely August 19, 1959. Jaundice, which had been noticed shortly after birth, was more pronounced on August 21, and the baby's weight had dropped to 4 pounds, 14 ounces. (The first child, also a boy, had not had neonatal jaundice and was well.)

Laboratory report. The serum bilirubin was 17 mg. per 100 ml. (direct 1.5 and indirect 15.5). The blood picture was: hemoglobin 17 Gm. per 100 ml.; red blood count, 5,500,000; white blood count, 5,700; polymorphonuclear leukocytes, 54 per cent; lymphocytes, 42 per cent; monocytes, 3 per cent; normoblasts, 2 per cent; and reticulocytes, 0.5 per cent.

Serologic tests failed to show any abnormal antibodies from the mother's serum, and the agglutination and antiglobulin tests showed negative findings. No finialed cells were present.

Clinical progress. After a transfusion at the hospital the baby's physical progress was satisfactory. There was no further evidence of jaundice three days after the transfusion. The baby was discharged on August 26.

On October 10, 1959, a physical examination revealed the following: heart and lungs normal; abdomen, soft; no palpable enlargement of liver or spleen; weight, 8 pounds, 2 ounces; height, 20 inches; and hemoglobin, 9.4 Gm. per 100 ml. An iron complex equivalent to 7.5 mg. of ele-

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* Delivered by Charles Weitzman, M.D., at the Carson C. Peck Memorial Hospital and seen in consultation with Alexander Wiener, M.D.

TABLE IV. Hemoglobin response of obstetric patients to iron-carbohydrate complex

	Hemoglobin (Gm. Per 100 Ml.)			
Case	Initial	Final	Net Gain	Therapy (Weeks)
Schedule 1 (daily dosage, 1 teaspoonful or 100 mg. of iron)				
1	9.0	10.8	1.8	16
2	8.2	10.6	2.4	19
3	10.4	12.5	2.1	16
4	9.2	12.5	3.3	18
5	8.0	9.8	1.8	5
6	6.9	10.4	3.5	2
Average (6 cases)	8.6	11.1	2.5	12.6
Schedule 2 (daily dosage, 2 teaspoonfuls or 200 mg. of iron)				
7	8.8	10.2	1.4	20
8	8.8	11.0	2.2	8
9	9.6	11.5	1.9	14
10	9.6	10.9	1.3	26
11	9.8	11.6	1.8	19
12	9.2	12.8	3.6	22
13	9.4	11.6	2.2	6
14	8.6	11.4	2.8	8
15	9.3	11.2	1.9	9
16	8.2	10.2	2.0	9
17	8.6	11.8	3.2	3
18	8.8	10.8	2.0	6
Average (12 cases)	9.1	11.3	2.2	12.5
Schedule 3 (daily dosage, 3 teaspoonfuls or 300 mg. of iron)				
19	10.2	13.0	2.8	21
20	10.2	13.0	2.8	14
21	11.0	12.6	1.6	25
22	10.6	12.8	2.2	20
23	9.1	12.4	3.3	12
24	10.4	12.2	1.8	12
25	10.8	12.0	1.2	11
26	9.8	11.6	1.8	14
27	9.8	12.0	2.2	12
28	9.6	11.7	2.1	12
29	10.9	12.0	1.1	14
30	9.8	12.0	2.2	14
31	9.8	11.0	1.2	11
32	10.9	13.0	2.1	12
33	11.2	14.0	2.8	13
34	10.6	12.0	1.4	26
35	9.4	11.6	2.2	20
Average (17 cases)	10.2	12.3	2.1	..

mental iron was prescribed to be taken three times daily, plus a multivitamin preparation.

On October 18, 1959, the iron as iron complex was increased to 15 mg. twice daily. On November 4, 1959, the serum iron level was 110 micrograms per 100 ml.

On December 26, 1959, the blood report showed: hemoglobin, 10.5 Gm. per 100 ml.; red blood count, 3,620,000; target cells, 20 per cent; slight achromia; white blood count, 7,800; stab neutrophils, 2 per cent; segmented neutrophils, 48 per cent; and lymphocytes, 50 per cent.

On February 27, 1960, the laboratory report was: hemoglobin, 10.7 Gm. per 100 ml.; red blood count, 3,450,000; white blood count, 8,550; polymorphonuclear leukocytes, 24 per cent; bands, 1 per cent; lymphocytes, 62 per cent; large lymphocytes, 3 per cent; monocytes, 4 per cent; eosinophils, 5 per cent; and basophils, 1 per cent. The child weighed 20 pounds, 9 ounces and measured 28 inches in height. There was a moderate skin pallor, but otherwise the condition was good.

On June 4, 1960, the hemoglobin was 12.6 Gm. per 100 ml. The infant had a good appetite, took all feedings, and was very active. His bowel movements were regular. There was a marked improvement in the color of the skin.

Case B. This case illustrates the need for iron medication in children with intractable diarrhea, one of the many indications for iron replacement.

History. A nine-year-old female was seen on January 4, 1960. She had had all the routine inoculations; she had had measles at nine months of age, whooping cough at two years, and chickenpox at six years. After an upper respiratory infection, the child lost weight and had frequent loose mucous stools during the preceding two weeks. Her bowel movements were painful, and there were as many as 8 to 10 loose green stools daily. Her temperature had been between 101 and 103 F. for five days but was normal at the time of the visit. During the past year she frequently had diarrhea and gastrointestinal upsets.

Physical examination. A physical examination revealed a fairly tall, pale child, who weighed 56 pounds and was 53 inches in height. The eye pupils were equal, and the scleras were bluish-white. Other findings were: cryptic tonsils; heart regular sinus rhythm, no murmurs; lungs clear; some tenderness over the abdomen; spleen and liver not enlarged; and a moderately excoriated rectum.

Laboratory report. The blood report was: hemoglobin, 10.5 Gm. per 100 ml.; red blood count, 3,100,000; and differential count, normal. The urine examination showed negative findings for albumin and sugar. The stool examination showed negative culture and occult blood.

Clinical progress. A special constipating diet was prescribed. Medication included 1 teaspoonful daily of the iron complex (equivalent to 100 mg. of elemental iron) plus multivitamins. The patient was continued on this therapy for three and one-half months, during which time her color, appetite, and weight improved.

TABLE V. Hemoglobin response of private pediatric patients to iron-carbohydrate complex

			Hemoglobin (Gm. Per 100 Ml.)			
Case	Sex	Age	Initial	Final	Net Gain	Therapy (Weeks)
Schedule 1 (7.5 mg. of iron three times a day)						
1*	F	11 months	11.0	14.1	3.1	16
2	M	8 months	9.1	12.8	3.7	9
3	F	$2^{1}/_{2}$ years	10.9	13.6	2.7	4
Average			10.3	13.5	3.2	9.6
Schedule 2 (15 mg. of iron three times a day)						
4*	M	$10^{1}/_{2}$ years	10.5	13.5	3.0	12
5	F	7 years	11.0	12.5	1.5	9
6	F	4 years	12.2	14.0	1.8	13
7	F	8 months	12.0	13.2	1.2	9
8	M	$4^{1}/_{2}$ years	10.9	13.0	2.1	20
9*	F	3 years	12.5	13.2	0.7	27
10*	M	$4^{1}/_{2}$ years	12.0	14.6	2.6	17
11*	M	2 years	12.0	13.5	1.5	18
12	M	8 months	10.5	11.7	1.2	9
13	F	8 years	11.5	12.5	1.0	14
14*	F	$2^{1}/_{2}$ years	11.0	13.5	2.5	10
15	F	$5^{1}/_{2}$ years	10.7	13.5	2.8	8
16	M	8 months	10.5	12.8	2.3	6
17	M	16 months	10.7	12.0	1.3	9
Average			11.3	13.1	1.8	13

* **Marked improvement in appetite and/or weight.**

Except for occasional upper respiratory infection, she was well.

On April 30, 1960, her weight was $62^{1}/_{2}$ pounds, and her height was 54 inches. The blood count was: hemoglobin, 13.5 Gm. per 100 ml.; red blood count, 4,800,000; white blood count, 4,200; stab neutrophils, 36 per cent; eosinophils, 4 per cent; basophils, 1 per cent; lymphocytes, 51 per cent; and monocytes, 3 per cent.

Case C. This case is typical of iron-deficiency anemia associated with prematurity.

History. A female infant born prematurely June 26, 1958, weighed 4 pounds, 10 ounces. She attended the outpatient Pediatric Clinic of the East New York Dispensary on October 24, 1958. Her appetite was poor, and she was extremely restless.

Physical examination. The results of the physical examination were essentially negative. Her weight was 8 pounds, 12 ounces.

Laboratory report. The blood picture was normal except for a low hemoglobin, 10.5 Gm. per 100 ml.

Clinical progress. The caloric intake was increased, and 12 mg. of iron daily in the form of ferrous sulfate were advised.

On November 28, 1958, the mother reported that although the infant took more milk, she refused all other foods. There was no change in the blood picture.

On August 18, 1959, the mother stated that the infant's milk intake was less than one quart daily and that she refused all solid foods except desserts. The infant was restless and slept poorly. She had been taking a multivitamin preparation. A physical examination revealed the following: anemic appearance; ear, nose, and throat examination negative findings; heart and lungs normal; abdomen soft; spleen and liver nonpalpable; and extremities normal. Her weight was 28 pounds, and her height was $36^{1}/_{2}$ inches.

The laboratory report was as follows: hemoglobin, 10 Gm. per 100 ml.; red blood count, 3,200,000; white blood count, 6,550; stab neutrophils, 2 per cent; segmented neutrophils, 56 per cent; and lymphocytes, 42 per cent. Fifteen mg. of iron as iron complex twice daily were prescribed plus multivitamins. Feedings with egg yolk added to milk were advised.

On December 12, 1959, there was marked improvement in her color, appetite, and sleeping pattern. Her weight was 31 pounds, and her height was 37 inches. The hemoglobin was 11.5 Gm. per 100 ml.

On February 10, 1960, the infant was lively and was eating well. Her hemoglobin was 12.5 Gm. per 100 ml. She readily took the iron complex mixed in fruit juice. There were no gastrointestinal disturbances; the bowel movements were regular and normal. The sleep pattern was good with little or no restlessness.

On May 21, 1960, the patient's weight was 33 pounds and height $37^{1}/_{2}$ inches. The hemoglobin was 13.5 Gm. per 100 ml., and the remainder of the blood picture was essentially normal. The mother had no further complaints regarding the infant's progress.

Comment

Few blood diseases are limited strictly to children. Childhood presents special circumstances that do not pertain to adult life; for example, blood disorders may arise from antinatal influences and from circumstances resulting from separation from the mother. Furthermore, the blood-forming tissues of children are more labile than those in adults, and variations that would be pathologic in adults are not so in children. Relative lymphocytosis, which often occurs normally between the ages of two and five years, can be reflected in a lymphocytosis in the bone marrow in an adult sufficiently to suggest lymphatic leukemia.

One of the several factors that may influence anemia of the newborn infant is the early clamping of the cord; it is estimated that as much as 60 cc. of blood may be lost by this procedure. Although some obstetricians still milk the cord to increase the iron content, this practice is of questionable merit, and it is definitely contraindicated in hemolytic disease.

Since the average newborn infant may lose about 10 per cent of blood at birth, or 30 cc., he starts life with an initial deficit (approximately 18 mg.) of iron.[18] The iron requirements of an infant are approximately 2 mg. per kilogram of body weight per day for satisfactory tissue iron storage. However, this requirement is not always met by the diet, especially during the first few months. In the event of diarrhea, infection, celiac disease, cystic fibrosis of the pancreas, chronic infections, and surgery, the requirement for iron is higher.

Some investigations have shown that the addition of a reducing agent such as ascorbic acid increases the absorption of iron. In our studies the iron complex was frequently administered with orange juice. Since it may take as long as six to ten months to correct an iron-deficiency anemia fully, it is important to start iron therapy early in infants: at least from the first month in the premature infant and the fourth to sixth month in the normal newborn infant. This practice is consonant with the early administration of the vitamins to infants, which one author advocated in 1939.[19,20]

In our experience, the older child of from four to ten years also is found frequently to have low hemoglobin levels. For this reason we recommend complete blood examinations as a routine procedure during the period of development and growth and during times of recurrent infections in older children.

Relapses of iron-deficiency anemia are seen frequently when the administration of iron is stopped as soon as the hemoglobin returns to normal. Since a deficiency of body iron other than hemoglobin iron may be present also, it is advisable to continue iron therapy until tissue iron as well as hemoglobin iron have been replenished.

Recently, Ragen *et al.*,[21] following the technic of Bonnet, Hagedorn, and Owen[22] conducted a study to compare the rate of gastrointestinal absorption of an oral iron-dextran complex with the rate of gastrointestinal absorption of ferrous sulfate in the same subjects. Known amounts of the iron compounds labeled with radioactive iron, Fe^{59}, were given orally. The difference between the amount of iron given orally and the iron recovered in the stools, as measured with a scintillation counter, was assumed to represent the amount of iron absorbed. In the subjects, the absorption of iron from an iron-carbohydrate complex varied from 37 to 78 per cent of an oral dose of 354 micrograms, seven times the dose of ferrous sulfate. The average absorption was 51 per cent. The actual absorption ranged from 131 to 278 micrograms with an average of 180 micrograms.

Hoffman and Wilson,[23] in a clinical evaluation of this new iron-carbohydrate complex for patient tolerance and for hematopoietic effect, reported that an analysis of the number and severity of complaints reported at each of the three visits revealed that the patients receiving the organic iron complex experienced fewer and less severe gastrointestinal symptoms than did those receiving ferrous sulfate. This difference in the incidence of side-effects was statistically significant (chi-square test) in favor of the iron-carbohydrate complex. The hematopoietic changes (hemoglobin and hematocrit) which were produced by the iron-carbohydrate complex (200 mg. of elemental iron per day for eight weeks) were favorable in all but 1 patient, a pregnant woman who had undergone surgery immediately before being placed on the preparation. The hemoglobin and hematocrit changes produced by the iron-carbohydrate were statistically significant (Student's t test, $p > 0.01$ level of confidence).

Summary

A new iron-carbohydrate complex of low toxicity was evaluated clinically in 82 patients, including infants, children, and adults. Satisfactory hemoglobin responses occurred in all groups of patients at levels of iron lower than those which are conventionally used. A high degree of patient acceptability was observed in all age groups with virtual freedom from side-reactions. This new iron complex appears to fulfil the requirements for a safe, palatable, effective, and well-tolerated iron preparation.

60 PLAZA STREET

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Discussion

JACOB HALPERIN, M.D.: Iron deficiency in the newborn infant and in later life is too common and too well known to require much elaboration except to speak, also, of its relationship to the pregnant mother.

Iron is obtained by the fetus from the plasma iron of the maternal blood. Thus when the maternal plasma is deficient in the proper amount of iron, this is reflected directly in the fetus. Such deficiency may occur also in the mother's plasma because of hemorrhage; chronic infection; low iron storage in the liver, spleen, and marrow; and so forth, as well as anemia of other causes, such as poor iron intake or poor utilization of the iron intake.

According to most authors, about 40 to 50 per cent of all pregnant women show a lowered hemoglobin content of the blood in the later months of pregnancy. In my private practice, in which all the laboratory procedures on the patients are performed by the same laboratory, I have found that in only about 40 per cent of the pregnant patients was the initial hemoglobin 13 Gm. per 100 ml. or better. The rest ranged between 11 and 12 Gm. per 100 ml. or less, which places them in the class of so-called physiologic anemia of pregnancy. This is due to the hydremia and increase of the plasma in pregnancy, which dilutes the blood more and more as pregnancy advances, with its resultant lowering of the hemoglobin and iron content. I believe that in addition many of these patients actually commence the pregnancy with a lowered hemoglobin, due probably to the lack of iron intake.

Holly* of the University of Nebraska in his studies has shown that the iron reserves of pregnant women are depleted when the hemoglobin falls below 11.5 Gm. per 100 ml. of blood. In these patients the administration of an adequate iron supplement will maintain normal hematologic values throughout the pregnancy. To repeat, the fetus obtains its initial iron stores from the mother. If the mother's iron stores are deficient, an iron-deficiency anemia will develop in the infant within the first year of life.

Of the various forms of anemias of the newborn infant, iron-deficiency anemia is the most common. This may occur in many ways. We know, for instance, that maternal red blood cells can pass the placental barrier and enter the fetal circulation. It was found that, conversely, fetal bleeding may occur into the maternal circulation. The amount of such bleeding varies. The clinical picture presented by such infants varied from pallor to acute hemorrhage requiring transfusion. Some deaths ascribed to asphyxia pallida may be caused by such fetal hemorrhage into the maternal circulation or into the uterine cavity before or during labor.

Some already iron-deficient infants become more so when the obstetrician clamps the cord before pulsations cease. The blood loss sustained is then about 50 cc.

As for therapy in the iron-deficiency conditions of the mothers, infants, and children later in life, iron is by far the most efficacious, whether it is given orally or, in the more severe cases, parenterally; transfusions are reserved for emergencies. The form of iron which we found most efficacious and suitable was that mentioned in the preceding report.

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Psychic factors found in bleeding disorder

Emotional problems appear to be related to chronic purpura, in much the same way that psychologic factors have been linked to bleeding stigmata, according to an article by David P. Agle, M.D., and Oscar D. Ratnoff, M.D., in the June, 1962, issue of *Archives of Internal Medicine*. A study of 9 women with purpura revealed that all previously had experienced hysterical symptoms. The emotional background of these patients "displays similarities to that previously described in some individuals with bleeding stigmata."

Perhaps the most extensively studied stigmatized individual of this century has been Theresa Neumann of Konnersreuth. Prior to the first appearance of the stigmata, reproducing the wounds of Christ, Miss Neumann had alternating episodes of blindness, deafness, convulsions, bleeding, and paralysis.

Similar episodes have been described in Mohammedans in whom bleeding simulating the battle wounds of their prophet have appeared during times of deep contemplation. A number of case reports describe bleeding episodes unrelated to religious experience in patients with various emotional problems.

The present study suggests that "purpuric bouts" occur at times of emotional stress. Among stresses reported in the 9 patients were fear, resentment, anxiousness, despair, and anger directed outwardly and inwardly.

Eight of the group admitted that they had severe problems in their relationship to members of their family. Bleeding disappeared in 2 patients after their husbands died.

In addition to hysterical reactions, such as hallucinations, loss of speech, and paralysis, the patients also demonstrated masochistic traits, that is, an actual enjoyment of hardship.

The authors plan further investigations of the influence of emotional factors on bleeding episodes in known organic diseases, such as hemophilia.

Field Test of Simple, Foam-Producing Chemical Contraceptive

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A FIELD TRIAL *of a contraceptive foam-producing liquid used with an insertable moistened sponge (Durafoam) was carried out in Jamaica, West Indies. The study, which lasted an average period of nine months, included 640 women. There were 18 pregnancies, or 4.2 per hundred years of woman exposure, as compared with the normal rate in the population of 70 to 80 per hundred exposure years. The method is inexpensive, simple, and suited for use in women of little education and in low-income brackets.*

THE PROBLEM of family planning is one of world-wide importance. This is a problem which can no longer be ignored either by the physician or by the millions of people who have only limited access to medical advice. It is a problem which concerns not only the family physician but also public health authorities, as has been made clear by the resolution of the American Public Health Association on this subject.[1] Like many other parts of the world, Jamaica and in fact most of the countries in the Caribbean area must find some practical solution to this problem.

It was for these reasons that a search was made for a simple and effective contraceptive method which would be practical for use in a public health clinic in Jamaica and which could act as a guide in setting up public health action on this problem.

Specifications

The specifications to be met were that the method must be: (1) simple to teach, (2) simple to use, (3) one requiring a minimum of equipment, (4) inexpensive, (5) stable in areas of high heat and humidity, such as Jamaica, (6) safe, free from irritating or toxic materials, and (7) effective.

Publication approved by the Ministry of Health, Jamaica, West Indies.

Description of method

The method which was selected was a foam-producing liquid used with an insertable moistened sponge.* It was of more than passing interest to us that various modifications of the sponge and foaming material method have been used for many years. In all, a spermicide in either powder, ointment, or liquid form is applied to a moistened sponge and inserted in the vagina. Gentle manipulation before insertion produces a spermicidal foam, and the sponge then acts as a reservoir for continued spermicidal foam production during coitus, distributing the foam throughout the vaginal vault and thus providing both a mechanical and spermicidal barrier to the passage of spermatozoa into the uterus.

The active spermicide in the liquid selected is p-Triisopropylphenoxypolyethoxyethanol. This is a material of the class of safe and effective spermicides used in most of the chemical contraceptives in the United States.† The vehicles which carry this active ingredient vary widely: jelly, cream, suppositories, foaming powder, foam tablets, and a foaming liquid. Since the cheapest vehicle and one which is particularly well adapted to hot, humid climates is the liquid, this was chosen.

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* Durafoam, manufactured by Durex Products, Inc., New York City. It is listed and described officially by the Planned Parenthood Federation of America, *Methods of Contraception in the United States*, and in the official publication of the International Planned Parenthood Federation.

† These include Lactikol, Metacreme, Preceptin, Delfen, Emko, Immolin, Koromex (A), Durex foam powder, and others.

Laboratory evaluation of spermicidal power

Procedures set up by the Margaret Sanger Research Bureau and the Planned Parenthood Federation of America for the foam-producing liquid used in our tests indicated the product to be satisfactory for further field trials.[2] It is known to exclude toxins, irritants, and carcinogens. In laboratory tests in vitro it was tested in the Margaret Sanger Research Bureau by both the Brown-Gamble[3] and the Sander-Cramer[4] methods. The former showed that 0.5 cc. of the liquid gave a spermicidal power sufficient to immobilize the spermatozoa in 70 cc. of human semen in less than twenty seconds. Since the dosage to be recommended was 0.5 cc. and since the average ejaculate is in the neighborhood of 3 cc. this means a spermicidal factor of safety of approximately 23. Using the Sander-Cramer test at a dilution as low as 0.5 cc. of the liquid in 120 parts of saline, 24 parts of the spermatozoa in human semen were immobilized in less than twenty seconds. These tests were the median of 5 tests by each method.[5]

Clinical evaluation of irritation

In clinical tests which also were performed in the Margaret Sanger Research Bureau the foaming liquid and sponge method was tested to determine the effect on the genital mucosa of the recommended dosage of the foam liquid when it was used for twenty-one consecutive days. The application of the liquid to a moistened sponge was made by wiping the rod attached to the closure of the bottle containing the liquid twice on each side of the moistened sponge and working it into a foam. Twelve women participated in the study. An initial examination was performed, and all findings were recorded. Particular attention was paid to the condition of the vulval, vaginal, and cervical mucosa. The women were instructed to insert the foam-filled sponge nightly for a period of twenty-one days. A string was attached to the sponge for easy removal. The patient was instructed to make a careful note of any evidence of irritation. Vaginal examinations were made twice weekly as well as after the test period was completed, and all objective findings were recorded. There was no complaint of irritation in 11 patients. One complained of slight itching. There were no objective signs of irritation in any of the 12 subjects.[6]

It was further determined that the foam and sponge materials had been distributed to 10,000 women in 1938 by the Planned Parenthood Federation of America and have been used consistently by some doctors and clinics ever since. In the only field trial previously recorded[7] using foam-producing ointment and sponges in 145 women in a Kentucky rural and mining community, the rate of pregnancy was reduced from 80 per hundred years of woman exposure to 4. This checks very closely with the results of Eastman and Seibels[8] with foam powder and sponge who reported a pregnancy rate of 3.6 per hundred exposure years in 193 patients. However, the foam powder used by Eastman and Seibels proved irritating, probably because it used paraformaldehyde as the spermicide.

Field trial

The field trial of the liquid and sponge method was carried out at the St. Elizabeth Health Department, Black River, and the Manchester Health Department, Mandeville, Jamaica, West Indies. This service is manned by well-trained physicians and nurses. The foaming liquid was distributed to patients in small dropper bottles to make measurement easy, and the patients were instructed to bring the bottles back to be refilled. The patients were also told to return when they required additional material. They were instructed how to use the materials, that is, the sponge was to be moistened on each side with 0.25 cc. of the liquid and inserted. A small string made removal easy. Public health nurses followed the patients at regular intervals to determine the results. The experiment ran a period of eighteen months.

In the field trial of the liquid and sponge method in a population of low economic status 640 patients were given the liquid with sponge, of whom 69 discontinued the use of the liquid with sponge, leaving 571 patients using it at the end of the period.

The test lasted eighteen months, with an average period of use of nine months. The total number of pregnancies was 18.

Multiplying the figure 571 by 9 and dividing by 12 gives 428 years of woman exposure with 18 pregnancies. This is 4.2 pregnancies per hundred exposure years. The normal rate in this population is between 70 and 80 per hundred exposure years. The method therefore reduces the pregnancy rate very substantially.

Of the 69 patients who discontinued the use of the method, 18 became pregnant. Of these 18, 12 admitted irregular use, and 4 stated that their husbands objected to the use of the sponge. Fifty-one discontinued either because they were planning a pregnancy or were indifferent and did not want to be bothered with using the method.

Comment

Now that family planning is becoming more widely accepted in public health and medical practice, new problems have arisen both in developing and well-developed countries. Simple, relatively inexpensive methods which can be used with a minimum of professional supervision even by poorly educated people are of great importance. With any method, of course, the user must be sufficiently well motivated to be willing to use it regularly. It may well be that with certain groups the concept that they will benefit by using any method is a first step. But in our experience in Jamaica there are many women of little education and in low-income brackets who are eager and will use a simple inexpensive contraceptive method of the kind described herein.

The cost of the materials used in our study, especially for clinic and public health use, is quite low and well within what patients of low economic status can pay.

It seems clear that the widely used diaphragm and jelly method is too complicated for this group. Its cost is also beyond what the family or a governmental service can usually afford.

The oral contraceptive as now available also has drawbacks for this group, not only from the point of view of expense and need for close medical supervision but also because of the necessity of taking it twenty out of each twenty-eight days in a menstrual cycle. This demands a kind of discipline and responsibility which is difficult to find in such groups. It seems possible, too, that bringing the action to be taken by the user close to the time of coitus may actually be of psychologic value in maintaining its use. This question of why different groups of persons do or do not use given methods demands further study. In the meantime more experience with known simple methods is needed, particularly among low-income groups with limited education.

Summary

Some of the problems of family planning among persons of low economic status and limited educational background are discussed. The results of laboratory and clinical tests and field trials of a highly spermicidal foaming liquid and sponge in such a population using the public health services in a rural area in Jamaica, West Indies, are presented. The method was found to be acceptable, practical, and effective. The costs are very low. The usual pregnancy rate in this population is between 70 and 80 per hundred years of woman exposure. Among those using the method the rate dropped to 4.2 pregnancies per hundred exposure years.

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A Novel Test for Pregnancy

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Aschheim and Zondek perfected the modern test for pregnancy which still bears their name[1] but which has been extensively modified since its origin.

In the classic test, 0.04 cc. of the first morning urine of the supposedly pregnant woman is injected into each of five immature female white mice on six different occasions over a period of two days. One hundred hours after the first injection the animals are sacrificed, and the ovaries are examined for either hemorrhagic follicles or corpora lutea, the presence of either or both, in at least one animal, being looked on as a positive result.[2]

The method of Aschheim and Zondek is involved, to say the least, and sounds almost like an incantation when compared with the somewhat less complex present-day procedures to which we have become accustomed. It is not surprising therefore that ever since their test was introduced the search has continued for a pregnancy test which is less complicated and still does not sacrifice accuracy for simplicity.

It was originally supposed that the changes in the mouse ovaries were due to the action of estrin,[3] but we now know that the response is due to the effect of chorionic gonadotropin secreted quite early in pregnancy and apparently acting to maintain the persistence and function of the corpus luteum and its hormone.[4]

With the increasing knowledge of hormone activity and in view of the characteristic persistence of progesterone during pregnancy, it is not surprising that attempts were made to devise some method whereby this hormone might be used in testing for pregnancy.[5] Furthermore, a great deal of attention has recently been drawn to a physiologic form of uterine bleeding which results from the withdrawal of progesterone, and interest has centered on the possible use of this phenomenon as a test. The easier availability of oral progestational agents as well as their more dependable action has further stimulated work along these lines.

In the experiments to be described the withdrawal bleeding which follows the use of anhydrohydroxyprogesterone, a progestational agent, and ethinyl estradiol, an estrogen, in combination* has been used in testing for the presence of early pregnancy. The procedure will be referred to hereafter as the "PD" pregnancy test. The accuracy of this test was compared with that of the "AZ" (Aschheim-Zondek) test (Frank-Berman modification) in the same patient, both tests being carried out at the same time.

Principle of the method

If the endometrium is estrogen-primed, whether endogenously or exogenously, the exhibition of a progestational compound will produce the same characteristic secretory changes seen during the menstrual cycle. The endometrial glands become tortuous, secretory activity can be seen in their lining epithelium, and the stromal cells become larger in size. Furthermore, progesterone accentuates the effect of the estrogen on the spiral arterioles in the stroma so that there is increased coiling and growth of these vessels and, consequently, an increased blood supply to the surface of the endometrium.

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* Pro-Duosterone for these experiments was supplied through the courtesy of the Roussel Corporation, New York City.

The withdrawal of these hormones produces a set of familiar changes which end in bleeding from the endometrial surface of the uterus, generally within four days. However, if both hormones have been used, and then withdrawn, the effects are more pronounced than when only estrogen has been employed.

From the foregoing it becomes apparent that in a case of amenorrhea, during the childbearing time of life, uterine bleeding on the withdrawal of the estrogen-progesterone combination would arise from a proliferative endometrium. If the endometrium is not proliferative or if a decidua is present, withdrawal bleeding would not occur.

A STUDY WAS MADE *of the effectiveness of the PD (Pro-Duosterone) pregnancy test which has as its physiologic basis the uterine bleeding which occurs after progesterone withdrawal. Of 122 patients on whom the PD and the AZ (Aschheim-Zondek) tests (Frank-Berman modification) were performed, 66 were found to be pregnant and 56 nonpregnant. Among the pregnant cases there were 9 false results obtained with the AZ test and 1 with the PD test, an accuracy of 98.4 per cent with the latter. In the nonpregnant group 4 incorrect results were obtained with the PD test and 1 with the AZ test. No significant side-effects occurred in this group or in an additional series of 100 cases, all known to be pregnant. In the largest number of cases a negative result becomes available within three days after the last dose of the estrogen-progesterone combination.*

Method

The PD pregnancy test is carried out in the following simple manner. The hormone combination described, in the form of a tablet containing 0.03 mg. of ethinyl estradiol and 50 mg. of anhydrohydroxyprogesterone, is administered four times a day for three days. It is best given with each of the three daily meals the fourth dose being taken at bedtime. If no bleeding occurs the result of the test is positive, but if bleeding does occur then the result of the test is negative. In the largest number of cases a negative result becomes available within three days after the last dose of the estrogen-progesterone combination (Fig. 1), but in a few instances as much as ten days may elapse before a negative result is obtained. In no instance has the patient complained that the amount of blood loss is greater than that of normal menstruation.

Clinical experience

In the first group studied, when the diagnosis of pregnancy was sufficiently doubtful to warrant further investigation, both the PD test and the AZ test were used. The patients were instructed to collect the first morning urine and then to begin taking the tablets containing the estrogen-progesterone combination. They were also asked to note the exact number of days which elapsed between taking the last tablet and the onset of bleeding, if this occurred. The most frequent interval reported was three days. In other words, a negative result as evidenced by uterine hemorrhage became available within three days.

In all, there were 122 patients on whom both the PD and the AZ tests were performed. Clinically, 66 eventually were found to be pregnant and 56 nonpregnant.

Among the 66 pregnant cases there were 9 false results obtained with the AZ test whereas there was only 1 false result with the PD test, thus giving an accuracy of 98.4 per cent with the PD test. This compares favorably with an accuracy of 98 per cent in a smaller group reported elsewhere. This single failure was a twenty-year-old patient whose period was fifteen days overdue and who was bleeding slightly when first seen. In view of the fact that the bleeding did not stop within ten days after the use of the estrogen-progesterone combination the case was considered a failure. The result of the AZ test done at the same time was positive, and when the patient was seen again there was no further bleeding, and she was eleven weeks pregnant.

In the nonpregnant group 4 incorrect results were obtained with the PD test and only 1 with the AZ test. This last patient complained of intermittent spotting since her last period six weeks before. The result of the AZ test was positive, but since bleeding recurred the next day after the estrogen-progesterone combination was stopped, the result of the test was considered PD negative. Another normal period started spontaneously a month later thus clinically confirming the result of the PD test. One might ask was this a missed abortion, and was there still some active chorionic tissue at the time the AZ test was done?

Side-effects

No side-effects of any importance were encountered either in the patients already described or in any of those in an additional series of 100 cases, all known to be pregnant, in which only the PD test was done to see whether or not the hormone combination might exercise any harmful effects on the pregnancy.

In the main group, in which both tests were done, 2 women complained of slight nausea and a third of both nausea and vomiting. Since the synthetic estrogens sometimes do cause such mild symptoms as nausea and vomiting,[6] it is conceivable that ethinyl estradiol might have been responsible. However, the 3 were all early pregnancies, and it was felt unnecessary to attach any importance to these slight upsets.

The additional 100 cases were all known to be pregnant for from eighteen to thirty-eight weeks. The hormone combination was taken for three days, and then ten days later the patients were questioned regarding nausea, hemorrhage, or vomiting. In 97 of these women there was no disturbance of any sort. The other 3 cases are of interest. The first was an obese multigravida, weighing 310 pounds, who developed mild pre-eclampsia the day before the PD test was started when she was thirty-six weeks pregnant. After taking only three tablets she began to bleed profusely and was admitted to the hospital as an emergency patient. A diagnosis of placenta previa was made and confirmed at section when she was delivered of a living child weighing almost five pounds.

The second case, age forty-one, is interesting because the patient was eighteen weeks pregnant and had complained of intermittent spotting and abdominal cramps throughout her pregnancy and again the day before she started taking the hormone tablets. A diagnosis of threatened abortion was made. Her symptoms disappeared during the first two days of medication but recurred on the third day and then again nine days later. Although the fundus was at the level of twenty weeks she had as yet felt no movement, and the fetal heart could not be heard. Three weeks later she still had occasional spotting, but aside from this the pregnancy was normal.

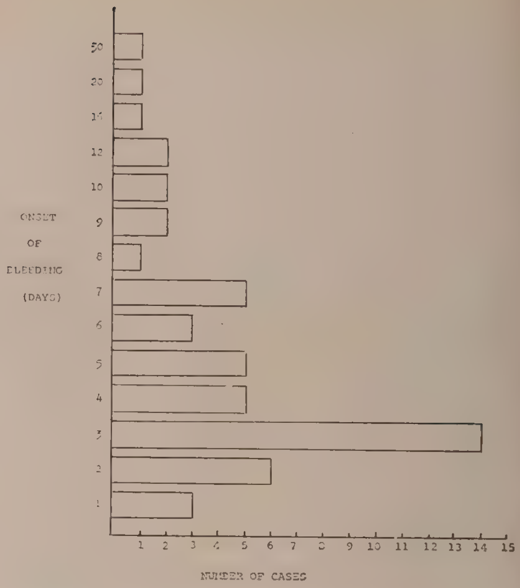

FIGURE 1. Range of onset of bleeding in patients with negative results following administration of a combination of estrogen and a synthetic progestational agent.

The third case passed some drops of blood on the second day of the estrogen-progesterone medication, after rushing to her small child who had fallen out of bed. When examined, ten days later, the cervix was found to be the site of a large erosion after a traumatic cleansing.[7] This oozed easily on touch and was diagnosed as the source of the bleeding.[8]

Comment

The PD pregnancy test appears to have a sound endocrinologic as well as physiologic basis. Progesterone withdrawal bleeding as a differential test, between amenorrhea and pregnancy, has been used by a number of clinicians[9,10] who have been impressed by the high degree of accuracy of this method.

Now that the use of oral progestational agents has become commonplace, simplicity can be added to accuracy.

This diagnostic test has been carried out with progesterone alone. Success under these circumstances postulates a proliferative endometrium, a state which may not always exist. Women who have just entered the menopause or those suffering from some genitoendocrinologic upset may not have an endometrium which is sufficiently proliferative to respond to progesterone withdrawal. In view of this, the use of an estrogen in conjunction with progesterone to ensure a proliferative phase is a rational step which would tend toward greater accuracy of differentiation between secondary amenorrhea and pregnancy.[11,12]

To date, no comparative study has been carried out, in the same patient, between this hormone test and the so-called biologic tests, none of which have total accuracy. This lack of accuracy is more pronounced the earlier the pregnancy. In the present study this comparison has been made for the first time, and the results obtained in these experiments are certainly noteworthy.

Furthermore, the great simplicity of the test is not to be overlooked. The PD test is a direct one, carried out on the patient herself without the intervention of test animals and the innumerable possibilities of error which these introduce. The doctor himself carries out the test, and the patient reports to him for an interpretation of the results. If bleeding occurs the result of the test is negative, if there is no bleeding the patient is pregnant.

Summary

The PD (Pro-Duosterone) pregnancy test has as its physiologic basis the uterine bleeding which occurs after progesterone withdrawal. The test is carried out by the administration, for three days only, of a combination of estrogen (ethinyl estradiol) and a synthetic progestational agent (anhydrohydroxyprogesterone). The simplicity and accuracy of this novel method have been discussed.

In an evaluation of toxicity in 222 patients there were only 3 cases of early pregnancy in which the combination used might have contributed to mild nausea and vomiting. In a comparison with the AZ test (the Frank-Berman modification of the Aschheim-Zondek test), the PD test was found to have a greater accuracy (98.4 per cent) in diagnosing pregnancy.

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Clinical Evaluation of 245 Ragweed-Sensitive Patients Treated with Precipitated Pyridine Ragweed Complex

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FUCHS AND STRAUSS[1] reported on the use of a new water-insoluble, whole ragweed pollen complex for the treatment of sensitive hay fever patients. The 88 highly sensitive patients were chosen because of the fact that they were unable to undergo satisfactory treatment or reach maximum dosages with the regular aqueous ragweed extracts. Good results were obtained with this new ragweed complex and no local irritation, dermatitis, or toxic effect was noted.

The extracting fluid consisted of one part of pyridine and one part of 0.3 per cent sodium bicarbonate or 0.9 per cent sodium chloride in water. Nondefatted pollen was extracted with this solution which gave a clear extract of the proteins, polysaccharides, and pollen oil. The active material from this extract was then precipitated with alum. Excess pyridine and alum were washed from the alum-precipitated complex. The advantages of this extract over the regular aqueous extracts are that it not only contains the pollen oils as well as the proteins, but also that it is absorbed slowly since it is a pyridine complex with an alum precipitate. The extracts were standardized by means of a protein-nitrogen determination which was performed on the final washed precipitated pollen complex in a saline solution and was converted into the protein nitrogen unit (P.N.U.).[2] There were 98 patients in 1959 who were treated with the alum-precipitated pyridine ragweed complex (allpyral)* (allergens, pyridine, and alum precipitated).

These patients included (1) those whose intracutaneous skin tests showed a marked reaction to 10 P.N.U. per cubic centimeter of the regular aqueous ragweed extract, (2) those patients whose skin tests were not too marked but who could not tolerate even small doses of ordinary aqueous ragweed solution, and (3) patients who were so sensitive that in previous years 5 mg. of chlorpheniramine were added to each aqueous ragweed injection in order that the injection could be administered and tolerated at all. Of the 98 patients treated, 11 were treated coseasonally and 87 were treated preseasonally.

Preseasonal treatment (1959)

There were 87 patients with a past history of late hay fever who gave positive intracutaneous test results to regular aqueous ragweed extract. These patients were given subcutaneous injections of the alum-precipitated pyridine ragweed complex once a week.

RESULTS. Excellent and/or good results were obtained in 81 out of 87 cases. There were fair or poor results in the remaining 6 cases. Therefore, 93.1 per cent good results were obtained by using the alum-precipitated pyridine ragweed extract. Although it is possible that there is a certain carry-over of the effects of one year's hyposensitization therapy into the following year, this is a much higher percentage of good results than is generally reported with the use of the regular aqueous extracts. There were 9 cases with good or excellent results who had a past history of hay fever and no previous specific therapy, so that there was no possible carry-over of past therapy in these cases.

In this group of 87 sensitive patients there were 22 who were so sensitive to the regular aqueous ragweed extract that the antihistamine chlorpheniramine was incorporated into each injection to prevent undue reactions. No antihistamine was necessary when the alum-precipitated pyridine ragweed extract was administered, and the dosages were well tolerated. Of the 87 patients, there were 47 who had been treated with the regular aqueous ragweed extract in the preceding year. The average top dosage in these 47 patients receiving regular ragweed was 435 units and in the patients receiving the alum-precipitated complex it was 1,114 units. Therefore, the dosage was more than doubled, and in most cases no attempt was made to push to the highest possible dosage.

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* The alum-precipitated pyridine ragweed used in this study was supplied by Miss Margaret B. Strauss, New York City.

Preseasonal treatment (1960)

One hundred and twelve ragweed-sensitive cases were treated with alum-precipitated pyridine ragweed in 1960. The group of hay fever patients selected for this treatment were by past experience the most sensitive and difficult cases to handle. They received an average number of 19.3 injections, and no attempt was made to reduce the number of injections over those given previously with the regular aqueous ragweed extract or the complex, but a top maximum dosage was attempted with each individual. In general, it was possible to increase greatly the protein nitrogen unit strength of the alum-precipitated pyridine ragweed over the amount administered previously with regular aqueous extract.

RESULTS. The results were 45 excellent, 55 good, 9 fair, and 3 poor; thus, 100 cases or approximately 89 per cent reported successful treatment. There were two constitutional reactions, one in a patient who had an initial injection of 10 units, and this very sensitive patient never tolerated more than 2 units thereafter. There were 2 other patients who had local reactions. Otherwise, this material was very well tolerated by the remaining patients. There were no systemic or local untoward effects following the use of allpyral ragweed in these 112 cases, with the 4 exceptions noted previously. No toxicity was noted. The high percentage of good or excellent clinical results obtained with this alum-precipitated pyridine whole pollen suspension is considerably superior to that generally obtained with the soluble aqueous extracts, and the ease of the administration is superior. Table I shows 21 of the 112 cases treated preseasonally in 1960. These cases were selected for tabulation because they had never been treated previously. Nineteen of the 21 cases (90 per cent) had excellent or good results.

ALUM-PRECIPITATED *pyridine ragweed complex was given to three groups of patients sensitive to regular aqueous ragweed extract: 87 preseasonally in 1959, 112 preseasonally in 1960, and 48 coseasonally in 1959, 1960, and 1961. In the groups treated preseasonally, from 89 to 93 per cent good or excellent results were obtained. All of the patients treated coseasonally reported good or excellent results. There were two constitutional reactions and two local reactions. Otherwise there were no systemic or local side-effects and no toxicity, and larger dosages were administered than was possible with aqueous ragweed extracts.*

Coseasonal treatment

There were 48 patients who presented themselves for treatment during the time of pollination on or after August 15 and were treated coseasonally in 1959, 1960, and 1961. Tables II, III, and IV show the pertinent data on these patients. There was 1 child of six years, and the remaining patients were adults from nineteen to forty-six years of age. They were all Class A or B sensitivity.*

In the first year (1959) 11 patients were treated coseasonally. They received an average of 10.6 injections over an average of 21.4 days. Of the 11 patients, 3 received excellent clinical results, and the remaining 8 had good results where the symptoms were minimal.

No attempt was made to decrease the number of visits in the first 11 patients of

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* Class A shows a marked test reaction to the intracutaneous injection of 0.05 cc. of 10 P.N.U. per cubic centimeter aqueous ragweed extract, and Class B shows a marked test reaction to 100 P.N.U. per cubic centimeter.

TABLE I. Preseasonal treatment with allpyral in 1960*

Case	Classification	Top Dosage in Protein Nitrogen Units	Results
1	B	2,000	Good
2	C	2,500	Excellent
3	B	2	Good
4	A	1,500	Good
5	C	1,250	Good
6	A	1,500	Fair
7	A	80	Good
8	A	4,000	Good
9	D	2	Excellent
10	A	4,000	Good
11	A	1,000	Good
12	B	100	Excellent
13	C	7	Good
14	A	3,500	Excellent
15	B	2,250	Excellent
16	C	5,000	Good
17	A	400	Good
18	A	2	Good
19	A	20	Fair
20	C	200	Good
21	B	20	Good

* Only previously untreated hay fever cases reported herewith.

this series of cases on coseasonal treatment with the alum-precipitated pyridine ragweed complex, and injections were administered in some cases on a daily basis. We now know that injections given more frequently than every third day should be eliminated in future coseasonal treatment. This would remove the possibility of overdosage which occurred during this first year of coseasonal treatment but which was absent thereafter. The one constitutional reaction resulted in an injection one day after three previous daily injections and was probably due to a cumulative effect of the slowly absorbed antigen. There were also five marked local reactions, due undoubtedly to injections given at one- to two-day intervals.

There were 23 cases which were treated coseasonally in 1960, all for the first time. All patients had hay fever during the ragweed pollen season. Treatment on all except 1 patient started with 20 units of alum-precipitated pyridine ragweed. The exception, a twelve-year-old Class A patient, was started with 10 units. The average top dosage of 255 P.N.U. was attained in an average of two and one-half weeks. The results were good or excellent, and there were no systemic reactions and no untoward side-effects. Fourteen cases were treated coseasonally in 1961. All except 1 presented himself during the hay fever season. They received an average of 6.8 injections over a three and one-half week period. Five patients had excellent results, 9 had good results, and there were no fair results or failures.

Economically, this is a very interesting statistic because the 48 patients made an average of 7.7 visits to the physician within a three-week period, constituting the entire treatment. This is in contrast to approximately 25 visits over twenty-one weeks which similar hay fever patients make with preseasonal treatment on regular aqueous extract.

Summary

Larger dosages of alum-precipitated pyridine complex were administered than was

TABLE II. Coseasonal treatment with alum-precipitated pyridine ragweed complex (1959)

Cases	Age (Years)	Injections Number	Injections Period (Weeks)	Top Dosage (Units)	Ragweed Class	Results
1	41	11	2	1,000	A	Excellent
2	28	10	3	100	A	Excellent
3	6	11	3	100	B	Excellent
4	25	9	3	200	A	Good
5	43	10	3	80	A	Good
6	19	11	$3^{2}/_{7}$	200	B to A	Good
7	26	11	3	100	B	Good
8	36	14	$4^{4}/_{7}$	1,750	A	Good
9	28	14	$4^{5}/_{7}$	4,000	B	Good
10	32	10	$2^{5}/_{7}$	300	A	Good
11	46	6	$1^{1}/_{7}$	200	B	Good

TABLE III. Coseasonal treatment with alum-precipitated pyridine ragweed complex (1960)

Cases	Age (Years)	Injections		Top Dosage (Units)	Ragweed Class	Results
		Number	Period (Weeks)			
1	38	5	2	150	A	Good
2	73	7	3	200	A	Good
3	13	6	$2^{1}/_{2}$	300	A	Good
4	77	2	1	100	C	Good
5	61	4	$1^{1}/_{2}$	70	B	Good
6	$3^{1}/_{2}$	8	$3^{1}/_{2}$	600	D	Excellent
7	13	8	$3^{1}/_{2}$	600	C	Excellent
8	42	5	$2^{1}/_{2}$	300	D	Good
9	18	4	2	200	B	Good
10	12	4	2	100	A	Good
11	32	5	2	50	A	Good
12	7	8	4	600	A	Excellent
13	11	5	3	20	B	Good
14	57	4	$1^{1}/_{2}$	50	A	Good
15	31	4	4	200	A	Good
16	14	3	$1^{1}/_{2}$	100	B	Good
17	7	10	4	1,250	C	Excellent
18	28	13	5	250	A	Excellent
19	22	3	1	100	B	Good
20	39	7	$3^{1}/_{2}$	300	B	Good
21	10	3	$3^{1}/_{2}$	70	B	Good
22	6	5	2	300	A	Good
23	24	9	4	60	B	Good

TABLE IV. Coseasonal treatment with alum-precipitated pyridine ragweed complex (1961)

Cases	Age (Years)	Injections		Top Dosage (Units)	Ragweed Class	Results
		Number	Period (Weeks)			
1	13	5	$2^{1}/_{2}$	300	A	Good
2	28	6	$2^{1}/_{2}$	700	B	Excellent
3	19	6	2	100	C	Excellent
4	42	5	2	60	C	Good
5	9	5	$3^{1}/_{2}$	300	B	Good
6	23	7	3	300	B	Good
7	12	5	2	400	C	Excellent
8	49	8	5	200	B	Excellent
9	15	8	5	200	B	Excellent
10	48	8	4	300	C	Good
11	3	8	4	300	D	Good
12	12	7	3	700	B	Good
13	34	12	$7^{1}/_{2}$	1,500	A	Good
14	11	6	4	300	A	Good

possible to give with aqueous ragweed extracts. There were no harmful side-reactions or toxicity.

From 89 to 93 per cent good or excellent results were obtained in treating a very sensitive group of 199 hay fever patients preseasonally with alum-precipitated pyridine ragweed complex.

There were 48 hay fever patients who presented themselves for treatment during the season and were treated coseasonally. All of them reported good or excellent results. Of this group, 43 patients had received no previous treatment.

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Pitfalls of Mobilization Surgery

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STAPES SURGERY has changed, is changing, and will continue to change in the months and years ahead. The obvious reason for this is that previous technics have been inadequate in solving the problem. Will our present procedures be the answer? Only a vigorous and careful follow-up and study can answer this.

Few of us have had the experience of such vast numbers of patients or procedures as reported by a few leading workers. We all know that the operations are very difficult, tedious, and time-consuming. Although this work is challenging and stimulating in many respects, there are times when we prefer the more simple procedures of otolaryngology.

There probably is no more satisfying professional experience than a follow-up visit from a patient who, having struggled through life with depressed hearing, has had his hearing restored surgically. These people have a new lease on life. Their families and friends tell them how improved they are in personality. They report how they have actually improved in physical well-being. One woman stated that her family doctor is able to control her hypertension easily since her hearing has been restored.

Technics of stapes surgery

In the last three and one-half years, I have operated on 67 otosclerotic patients. Of these, 35 hear adequately today. That is, the average of the speech frequencies is 30 decibels or less. I have performed 85 operative procedures on these 67 patients. A technic has evolved. The first 12 procedures were attempts at mobilization indirectly through manipulations on the stapes superstructure. Two of these early patients today have socially adequate hearing. The next 59 cases were variations of crurotomies and footplate procedures, using chisels. A fragmentation of the footplate, with an insertion of polyethylene prosthesis, was done in 18 cases.

The last 11 cases were stapedectomies. Nine of these cases had a vein graft, with polyethylene prosthesis inserted by the technic described by Shea.[1] In 2 of these cases a stainless steel wire prosthesis with vein plug technic was used after the procedure described by Kos.[2] Of the 30 cases done last year with recent follow-up, 22 have socially adequate hearing now. Three of the 35 successful patients have socially adequate hearing as a result of the three fenestrations for otosclerosis I have done on them. The big question is which of the various technics we should follow. The final analysis of advantages and disadvantages is not possible now.

The failures are the discouraging part of this surgery. At the beginning of this work, before I was adequately visualizing the pathologic conditions at the footplate, I used to realize failure in the operating room immediately. Something would snap as I manipulated the stapes superstructure. Sometimes there would be a dramatic hearing gain, but more often I could find no objective evidence of gain. I often hoped for improvement with time. Nearly all of these cases regressed to or beyond the preoperative level.

In recent years the otologic literature has been filled with reports on stapes surgery. There is considerable variation in even the

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latest technics, as evolved in the various parts of the country. There has been and still is considerable conservatism in many quarters toward the more vigorous and radical approaches. In general, what used to be considered extreme and radical is almost routine today. Today stapedectomy seems to be the operation which holds the hope of lasting hearing restoration. I wonder what the consensus will be a few years from now.

In a few cases the pathologic conditions are so extreme as to obliterate completely the oval window area. In these cases I abandoned stapes surgery, and at a later date I performed what is now considered the outdated Lempert novovalis fenestration of the lateral semicircular canal. If I knew that these extensive otosclerotic pathologic conditions were in my temporal bone, I would not want my labyrinth opened through the otosclerotic focus. I would prefer an opening away from this focus and accept the immediate and future disadvantages of a fenestration cavity. In the last three and a half years since I started performing stapes surgery, I have done just three fenestrations. Two of these fenestrations have been done on patients whose disease was very extensive. One was done on a patient who elected to have the fenestration procedure after the stapes reankylosed. All 3 patients have socially adequate hearing today.

I have 1 patient on whom I should have done a fenestration.

Case report. The patient is a school teacher whose worst right ear I mobilized through a crurotomy with chisels in 1958. The hearing gain lasted less than a month. In the second right ear operation a great deal of difficulty was encountered owing to the pain and bleeding about the promontory operative site. Finally, through a fragmentation of the thin central portion of the footplate and an insertion of a polyethylene prosthesis, a gain was obtained. Facial paresis followed the surgery, and it took the patient eight months to recover completely. This woman had socially adequate hearing restored for nine months when, suddenly and without explanation, the hearing gain dropped overnight.

During the third stapes operation on this same ear the polyethylene tube was found in good position, but the lenticular process had fractured and broken the ossicular chain continuity. A total stapedectomy was accomplished without technical difficulty. However, the patient's facial paresis recurred, and after eight months it was totally recovered. She has no functional hearing in the ear, and a perforation which had developed in the ear drum is slowly closing. Despite all this, this patient is eager and anxious that I try a fenestration on her ear, if I consider her an adequate candidate.

STAPES SURGERY *has progressed from the blind, remote pressure mobilization to the total removal of the stapes, including the footplate, with a vein graft, vein plug, or a gelatin filler over the oval window and either a polyethylene or a metal wire prosthesis. The technics used today are more difficult than previous technics, and the complications are much more serious. However, the results are promising although they have not been evaluated fully as yet.*

Methods and materials

Shea,[3] in a justification of stapedectomy and vein graft technic, states, "However, the mobilization operation is rarely of real value to the patient and presents the great disadvantage of increasing the likelihood of injury to the ear at subsequent surgery."

Stapes surgery has progressed from the blind, remote pressure mobilization to the total removal of the stapes, including the footplate, with a vein graft, vein plug, or a gelatin (Gelfoam) filler over the oval window and either a polyethylene or a metal wire prosthesis. There are many variations of technic between these extremes. The percentage of initial success and the duration of hearing gain thus far have not been evaluated fully. The newest method of stapedectomy with artificial prosthesis certainly shows promise.

This type of surgery is for otosclerosis, but scar deformity, as a result of childhood suppurative disease, does not rule out the possibility of otosclerosis. Otosclerosis can cause the greater part of the conductive loss, having developed and progressed much later in life. I have 3 such patients in whom scarred but intact ear drums were present but whose histories suggested otosclerosis. This was substantiated at surgery. One of these 3 patients has socially adequate hearing today as a result of surgery.

Obviously, candidates for surgery should have good cochlear reserve and an air bone gap. The ear with the greatest hearing impairment is usually the one with the most tinnitus and is usually operated first. It may not be the side of the greatest impairment audiologically. The patient who was the most disappointed at the failure of surgery was the one who had an operation on the side which was considered as having the better ear. Audiologically the hearing was not much worse, but to the patient it seemed much more impaired.

Unilateral losses have a high incidence of success. I do not encourage a patient to have surgery who is not anxious to have binaural hearing. Many patients are socially handicapped, however, because their work requires binaural hearing. I do not promise much noticeable change subjectively, although the procedures are successful audiometrically.

Difficulties at surgery are numerous. Raising the canal skin and drum, if carefully done, causes no trouble. Occasionally skin bleeding can be disconcerting until it is controlled with vasoconstrictors or electrocoagulation.

The chorda tympani branch of the facial nerve often prevents access to the footplate. It can be stretched and dissected out of the way, but frequently it is severed in the process. When injured, the patient complains postoperatively of one-sided, unusual taste, but frequently this improves in time. The patients with severed chorda tympani nerves complain less often.

A visualization of the complete circumference of the footplate usually is not possible, and frequently only a relatively small portion of the articular edge can be seen owing to a narrowing of the oval window niche. This narrowing can be caused by an overhang of the facial nerve or by a closing off from the inferior edge due to a deep-seated stapes or an active otosclerotic disease itself.

Many authors in their articles on this subject infer that there is an easy delineation of diseased bone from normal bone. Shea[3] states, "To the surgeon doing mobilization, the stapes is an iceberg. He sees only what appears on the surface, and the greatest part of the lesion is blissfully hidden from his eyes." Even the thinnest and bluest footplates removed at surgery were found invaded by otosclerotic bone, proving that the visualization obtained with the operating microscope is not enough to judge correctly the histopathology (Henner *et al.*[4]).

Comment

The trend of surgery is the total removal of the stapes and a closure of the oval window with either vein graft, vein plug, or gelatin. A continuity of the ossicular chain is established with polyethylene tubing or metal wire prosthesis. This trend has occurred because previous methods have not given satisfactory quality, quantity, consistency, or duration of hearing improvement. We certainly all hope they will stand the test of time.

A good test of time study in the literature was the article by Hilleman and Shambaugh.[5] This article reports on a follow-up of 690 fenestrations, followed for from ten to seventeen years after operation. When the reports had been tabulated solely with regard to the final level of hearing at the most recent test, 43 per cent of the patients had remained at the 30-decibel level and had been considered successful, while 57 per cent had a loss of 31 decibels or more for the speech frequencies and had been considered failures. This is certainly an impressive report. We know how difficult it is to get patients to report back faithfully for a follow-up evaluation, even when they are in the immediate vicinity.

The complication of perforation of the tympanic membrane occurs occasionally but, usually, with care, it can be closed. Otitis media has not been a problem, and this seems unusual.

On two occasions I have had difficulty in fitting the polyethylene tube prosthesis because of an unusual angle between the lenticular process and the oval window. I then fashioned a wire prosthesis to a vein plug after the Kos technic to reconnect successfully ossicular continuity. Thus wire prosthesis has more flexibility of application than polyethylene.

A further complication which has occurred on 2 of my cases, the cause of which has not been explained to my satisfaction, was as follows. On chiseling the edge of the footplate and fracturing it loose, a tremendous outpouring of clear fluid occurred. This took several minutes to subside. On the second case thick otosclerotic bone was being thinned over the center of the footplate. As a small opening occurred, fluid poured forth under considerable pressure. After twenty to thirty minutes, it was controlled with a gelatin pack in the fenestra. It has been suggested that this could have been cerebral spinal fluid and not perilymph, but this explanation does not seem to fit completely, since we know where we are anatomically with the microscopic visualization of the footplate region.

A most serious complication, of course, is a perceptive hearing loss in the ear, making it worse than it was before surgery. Many of the stapedectomy procedures cause this type of loss, but they usually recover within a few weeks. As of yet, I have not had the misfortune to cause total deafness of an ear.

Conclusion

In conclusion, the evolution and changes of technic have been manyfold in relation to stapes surgery. None of them have stood the test of time. The technics used today are much more difficult, and the potential complications are much more serious. Despite this, we have high hopes that they will succeed in accomplishing our aim. I believe that further progress will be made when we report on the difficulties encountered and when failures and their causes are emphasized as much as the successes.

Summary

Stapes surgery is difficult. It has been wonderfully successful in restoring hearing. Previous technic results have not been successful in maintaining good hearing. Present procedures hold some hope of being the remedy, but it is too early to be sure. There are technical advantages of the restoration of more normal hearing through stapes surgery over fenestration of the lateral semicircular canal. Vigorous stapes surgery is not without risk, especially when repeated procedures are carried out. Fenestration of the lateral semicircular canal has been found durable in 43 per cent of cases.

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Yogis able to make pulse inapparent

Yogis are able to accomplish "amazing tricks with their pulse rate and blood pressure," according to a letter by Albert Salisbury Hyman, M.D., in the June 16, 1962 issue of the *Journal of the American Medical Association.* Yogis are followers of yoga, a Hindu philosophy of mental discipline.

A study made thirty-five years ago showed that no pulse could be detected at the wrist of a trained yogi who "willed the pulse to stop."

Since yogi methods teach selective muscle contraction and relaxation, it is mechanically possible for them to stop or diminish the pulse. A yogi can constrict the main artery leading to the arm by contracting certain upper chest muscles.

PANEL

DISCUSSION

PROCEEDINGS

Special Committee on Infant Mortality
Medical Society of the County of New York

Is Perinatal Loss Increased as a Result of the Induction of Labor?

HAROLD ABRAMSON, M.D., Editor
Chairman
CARL GOLDMARK, JR. M.D., New York City
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LOUIS M. HELLMAN, M.D., Director, Department of Obstetrics and Gynecology, University of the State of New York College of Medicine, New York City
Panelists
MARTIN STONE, M.D., Chairman and Professor, Department of Obstetrics and Gynecology, New York Medical College, Flower and Fifth Avenue Hospitals, New York City
CHARLES H. HENDRICKS, M.D., Associate Professor of Obstetrics and Gynecology, Western Reserve University School of Medicine, University Hospitals, Cleveland, Ohio
HERBERT RICH, M.A., M.S., Senior Statistician, Bureau of Records and Statistics, Department of Health, New York City

HAROLD ABRAMSON, M.D.: *The controversy with regard to indications for the elective induction of labor and its implications relative to fetal outcome still continues. In this panel discussion cogent reasons are presented for and against the procedure of artificial initiation of the birth process. Risks to the fetus as measured by perinatal mortality rates are also given due consideration.*

Introduction

LOUIS M. HELLMAN, M.D.: The topic before us tonight, "Is Perinatal Loss Increased as a Result of the Induction of Labor?" is one of tremendous and pressing importance to modern obstetricians and pediatricians. It is one which generates a good deal of emotion and a considerable number of divergent opinions.

The practice of the elective induction of labor is almost part and parcel of the current American scene. As far as I can determine, in private practice in this country, about 10 per cent of labors, possibly double that figure, are induced for no medical reason. I believe that it is this area to which we should now devote our attention. It is obvious that if a labor is induced for toxemia, or for a host of other medical con-

Presented at the New York Academy of Medicine before the open meeting of March 22, 1961, of the Special Committee on Infant Mortality of the Medical Society of the County of New York, Carl Goldmark, Jr., M.D., Chairman, and Harold Abramson, M.D., Secretary, Coliseum Building, 10 Columbus Circle, New York 19, New York.

ditions, it is the opinion of the obstetrician that he is doing this to improve the mother's chance of survival in good health or the baby's chance of survival. I do not think that we need to get into this area of argument. The area to which we should devote our attention is that in which there exist no direct medical indications for the induction of labor. There may be indirect medical indications which should be considered, such as the patient living far from the hospital, traffic, rapid previous labor, and so forth. These patients, along with those induced merely because it is convenient to have their babies on Monday or Tuesday, constitute a whole group where we would do well to consider the effect of induction.

It is my plan tonight to have a pro, a con, some statistics, a chance for the panel to have a bit of rebuttal, and then a chance for all of you to have rebuttal or to express opinions.

I would like to introduce to you Martin Stone, M.D.

Elective induction

MARTIN STONE, M.D.: Is perinatal loss increased as a result of the induction of labor? This biased question implies that an answer unfavorable to induction will be forthcoming. I would suggest that the question read, "Is perinatal loss decreased as a result of the induction of labor?" Another problem in semantics concerns itself with agreement on the meaning of induction of labor. Do we mean all inductions, only elective inductions, only indicated inductions, unselected patients, or all methods?

To answer the original question properly or discuss the relationship of induction to perinatal outcome, we must concern ourselves with elective induction only. My answer tonight is based on our experiences with elective induction at the New York Medical College–Metropolitan Medical Center, as well as on the numerous reports in the literature.

INDICATIONS FOR INDUCTION. The need to terminate a pregnancy for a variety of medical and obstetric complications is generally accepted. Termination is often desirable for elective reasons including what is unfortunately referred to as patient and/or physician convenience. These elective inductions may be indicated for the following reasons: (1) a history of previous rapid labors, (2) to avoid possible anesthetic complications, (3) the availability of optimum personnel and facilities, (4) to provide for constant medical supervision, and (5) to relieve apprehension concerning the onset of labor.

The inherent advantages are obvious. The patient and her obstetrician are better prepared psychologically. For the many who live outside urban areas the anxiety of reaching the hospital in time is eliminated. City traffic may make this a problem even for those who live in town. Uncontrolled delivery prior to admission in patients with a history of rapid labor is obviated. Since the patient can be instructed about eating, the dangers of aspiration are minimized. Almost all hospitals suffer from shortages, and the most and best personnel are present on the day shifts. The obstetrician can be with his patient throughout labor and when he is fresh and alert enough to exercise his best skill and judgment.

INCIDENCE. Scientific and lay articles suggest that "Monday and Thursday" obstetrics are quite common. The origin of this term, "Monday and Thursday" obstetrics dates back to 1928. For this bit of historical information we are indebted to Alan Guttmacher, M.D., who reports an incident that occurred during his residency under the great J. Whitridge Williams, M.D., at Hopkins. Dr. Williams showed him a letter from a former student who stated that he was an enthusiastic golfer and had discovered that by rupturing membranes on Monday and Thursday, golf on Tuesday and Friday was much less disturbed. He had a successful series of 50 cases. Dr. Guttmacher and a junior associate, R. Gordon Douglas, M.D., were assigned this arbeit. They reported on 120 women in 1931.[1]

On our service, the incidence is 23.6 per cent for private patients and 1.8 per cent for ward patients. The incidence of other areas is shown in Table I and is probably higher in private hospitals that are not reported in the literature.

With proper selection, incidence will vary between 20 and 30 per cent. Eastman[2] reports an incidence as high as 25 to 35 per

TABLE I. Comparative percentage incidence of elective induction

Hospital	Per Cent Ward	Private
Milwaukee	0	10
University of Iowa	10	3
Memphis (University of Tennessee)	0	35
Philadelphia (7 hospitals)	1	11.7
Flower and Fifth Avenue Hospitals	1.8	23.6

TABLE II. Fetal outcome percentage in elective induction

Hospital	Per Cent Premature Infants	Perinatal Mortality
Mt. Sinai, New York City	2.6	0.2
Millard Fillmore	1.4	0.0
University of Iowa	3.1	0.6
Philadelphia	2.2	0.18
Flower and Fifth Avenue Hospitals	4.0	0.22

cent in some of the best obstetric clinics.

METHOD. For elective induction we advocate the intravenous administration of a dilute solution of oxytocin. Any technical procedure or therapeutic regimen is only as good as the training and intelligence of those applying it. This applies in the use of intravenous oxytocin. Of greatest importance is the proper choice of cases and adherence to proper technic. This necessitates good obstetric judgment.

Selection of patient. To select cases at term with mature infants, one must evaluate each case carefully at each prenatal visit. This includes the observation of uterine growth, station of the presenting part, and changes in the cervix. The expected date of confinement is only a guide, and if clinical observations are not in agreement with this date, we prefer to rely on cervical changes and fetal size. The cervix must be favorable; the criteria of a "ripe" cervix are well known. These include partial effacement, softening, 2-cm. dilatation, and an anterior position in line with the axis of the vagina.

Actual technic. Our specific technic has been described previously by us[3-5] and by others. Two or three points bear emphasis. First, all patients receive analgesia (Demerol and scopolamine) prior to the start of the infusion. We feel that this enhances the oxytocic effect perhaps by eliminating hypothalmic inhibition and allows for more coordinated uterine response. Analgesia is repeated as indicated.

Second, to avoid possible overdosage, the infusion is started without oxytocin and set to run at the slowest rate possible. The oxytocin is then added in a 1:1,000 dilution. The subsequent rate is titrated against uterine response rather than by any arbitrary number of drops per minute. Frequently a change from the initial slow rate is unnecessary.

Third, membranes are kept intact until labor is well established.

RESULTS. Over-all maternal results have been reported frequently by us and by others and are not specifically germane to the topic tonight. It suffices to say that the uterine contractions subsequent to intravenous oxytocin are indistinguishable from those of spontaneously occurring labor. There are no adverse effects on length of labor, method of delivery, or maternal morbidity and mortality. In most series prolonged labor, operative forceps, and cesarean section rates were of low incidence.

Perinatal results are our concern tonight. Our figures for 1959 are shown in Table II. Our incidence of prematurity in elective inductions was 4 per cent. Our over-all incidence of prematurity was 9.9 per cent. Of the 15 babies classified as premature on our private service, 12 weighed over 5 pounds, 5 ounces. Our perinatal mortality for elective inductions was 0.22 per cent. Comparable figures for representative institutions are shown in Table III.

COMMENT. The elective induction of labor for selected patients carries no greater risk, maternal or fetal, than does spontaneous labor. In fact, the dangers from this procedure should approach zero with proper selection and management. Just because complications can occur does not mean that they must occur. If patients are chosen carefully, a high success rate can be anticipated. Not infrequently a patient scheduled for induction goes into labor the night before. If all criteria are considered, an incidence of

TABLE III. Comparable figures for representative institutions in 1959

Conditions	Metropolitan Hospital Number of Patients	Metropolitan Hospital Per Cent	Flower and Fifth Avenue Hospitals — Ward — Number of Patients	Ward Per Cent	Private — Number of Patients	Private Per Cent	Total	Per Cent
Deliveries	4,450	100	933	100	1,437	100	6,820	100
All inductions	206	4.6	63	6.8	379	26.4	648	9.5
Elective inductions	62	1.4	35	3.7	340	23.6	437	6.4
Premature infants	2	3.2	1	2.8	15*	4.4	18	4.0
Deaths	0	0.0	0	0.0	3†	0.9	3	0.7

* Twelve of these weighed over 5 pounds, 5 ounces.
† Two congenital malformations.

up to 30 per cent would appear to be acceptable. Private services run a consistently higher indidence than do ward services.

The method of choice is the intravenous administration of a dilute solution of oxytocin. We are of the opinion that this method has many advantages over amniotomy. The latter technic, although successful in many hands, is associated with a higher perinatal mortality than is intravenous oxytocin. This is apparently related directly to the length of the latent period which is over forty-eight hours in a significant percentage of cases.

It would seem to explain the differences in perinatal mortality between inductions in Iowa where amniotomy is the technic and inductions in New York City (either The Mt. Sinai Hospital or our data) where intravenous oxytocin is the technic used. Another hazard of induction by amniotomy is the possibility of prolapse of the cord. This is not a factor where medical induction is employed.

Where amniotomy is performed the obstetrician is committed to delivery one way or another. Because of this, rupture of the membranes is not carried out as part of our inductive procedure. We prefer not to burn our bridges behind us and be compromised by rupture of the membranes if a case should not respond to oxytocin. After labor has been established, rupture of the membranes may occur spontaneously or become a relatively simple procedure with no danger of cord prolapse. Rupture of the membranes is not necessary for success with intravenous oxytocin, but once labor ensues, such a rupture will enhance the effect.

Other methods of administration of oxytocin are less satisfactory because of the difficulty in controlling the dosage and rate of absorption.

Obviously other types of induction such as bags and catheters are archaic and should be relegated to an obstetric museum.

The chief hazard to the fetus from induction is prematurity, and the responsibility must be assumed by the obstetrician. The incidence of prematurity is less in later series than in original reports. This undoubtedly reflects the use of more careful criteria and better obstetric judgment. The incidence in most recent series is lower than over-all hospital incidence, and many of the premature infants delivered following induction are of patients who deliver babies of this size even with pregnancy terminated by a spontaneous onset of labor. Prematurity can further be prevented by a proper adherence to the principles of the method advocated: careful selection of patients and intravenous oxytocin without rupture of the membranes. The technic has a built-in safety factor in that preterm the uterus will not respond to usual dosages, and the attempt at induction can be abandoned.

Irregularities of the fetal heart are no more significant than those seen in labor without oxytocin infusion. In one controlled study, this occurred in 5 per cent of cases and in 8 per cent of the controls. While perinatal mortality, prematurity, and prolapse of the cord can be analyzed, morbidity, particularly of a long-term nature, is a problem which remains unanswered. The anterospective collaborative research project on obstetric factors[6] in brain-damaged children, as well as the retrospective study of Kohl and Eastman[7] will perhaps shed some light on this most important aspect.

"I believe if this practice were to become general and widely adopted, women would be worse off eventually than had their labors been conducted by midwives." This quotation does not refer to induction of labor but to prophylactic forceps and episiotomy. It is credited to the venerable Dr. Williams in his discussion of Joseph B. De Lee, M.D.'s paper recommending these procedures. Like elective forceps, episiotomy, analgesia, and anesthesia, elective induction can no longer be considered meddlesome obstetrics but a worth-while addition to our obstetric armamentarium for making delivery safe, simple, and comfortable.

All these procedures may occasionally be associated with intrinsic dangers, but proper skill and judgment reduces hazards, and the advantages outweigh the disadvantages. In any series reporting deleterious effects, the question arises as to whether these should be charged against the procedure itself or against the obstetrician and his judgment.

Where maternal or fetal morbidity or mortality follow forceps deliveries, the responsibility is placed on the obstetrician, not the forceps. The same reasoning should apply to elective induction with intravenous oxytocin. It is not a panacea. It cannot replace good obstetrics. As with any potent tool, it must be used intelligently.

Summary. There are specific indications for elective induction. The elective induction of labor has an incidence of 23.6 per cent in our institutions, a figure in keeping with accepted standards.

The method of choice is intravenous oxytocin. Good results can be achieved by meticulous attention to patient selection and the technic recommended.

Perinatal mortality is not increased by elective induction of labor.

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Dr. Hellman: Thank you, Dr. Stone. The quotation that Dr. Stone used startled me a little bit. It was followed by Dr. De Lee's threat to resign from the American Gynecological Society. He was only persuaded from not carrying this out by a promise from the Society that if he would do more work, they would publish his paper on episiotomy and low forceps delivery.

I think the next speaker has quite a job. I asked Charles H. Hendricks, M.D., to take the opposite point of view and to try to give us some insight into the physiologic action of oxytocin by various methods and routes of administration. I do not know whether he has accepted his assignment with enthusiasm or not, but I think he will let us know that in a few minutes.

Induction versus noninduction

Charles H. Hendricks, M.D.: The question of whether or not induction of labor increases perinatal mortality is probably impossible to answer categorically. If one were to ask: "Has the induction of labor ever resulted in a perinatal mortality?" our answer would be unanimously in the affirmative. But if we ask: "Does the induction of labor itself imply some increase in perinatal mortality?" the issue must be approached far more cautiously.

To answer this last question completely, one would need to make clear the answers to a whole series of further questions, such as the following: What is an induction of labor? What methods for induction are to be included? What are the criteria for induction, and to what degree are these standards adhered to? When is an induction elective? For any proposed "therapeutic" induction, would cesarean section delivery be safer? In any given hospital what are the conditions as to equipment, nursing service, and training of obstetric attendants under which inductions can be done?

Finally, in assessing the net result of the induction of labor we would like to know what are the dangers of not doing an induction, that is, are any babies lost in utero or in labor that would have been born alive and well if induction had been done at some time prior to the onset of spontaneous labor?

Difficulties in controlled study. A statistically valid assessment of this clinical problem would require a forward-moving study wherein the method of delivery was rigidly controlled in accordance with the single criterion of the group to which the patient had been assigned in advance. The difficulties of such a scheme are readily apparent to obstetricians. The automatic induction of labor at term in an entire preassigned group, for example, would deprive the obstetrician of the advantage of exercising his clinical judgment as to whether or not the labor was easily inducible. This would undoubtedly increase the number of difficult inductions which, in turn, might affect the perinatal mortality adversely. Furthermore, the possibility of inducing the birth of premature-weight infants would be enhanced, since the apparent size and maturity of the infant always enters into the obstetrician's decision to perform an induction of labor. Many patients have a genuine fear of inductions; to start a so-called "elective induction" on such a reluctant patient, in addition to violating a cardinal rule of obstetric practice, would have the added drawback of promoting the less efficient and less satisfactory labor which seems to be the lot of the frightened patient. If the obstetrician made exceptions to the rule by declining to carry out any of the scheduled inductions, the "quality control" of the study would suffer. But if such a study were to be conducted conscientiously, it is conceivable that the very rigidity in its performance might alter the results and thus detract from the validity of such a scientifically pursued study.

I doubt that many hospitals or clinicians would be willing to initiate and carry through such a closely controlled study. In the absence of well-controlled studies, the clinician is left with only second-class methods for assessing the results of his clinical procedures.

Material and method. The present report on a small retrospective study* offers little of scientific value and certainly no scientific proof. It still may be of clinical interest and usefulness, however, to compare the observed results in a series of patients, in some of whom inductions were done, and in the remainder of whom labor was not induced. Through this device, we may be permitted to gain a general picture of what happens to the infant who is born following induction as compared with the one born to the mother whose labor is not induced.

The material for examination was taken from the delivery records of infants born at the University Hospitals of Cleveland during the years 1959 and 1960. To focus as directly as possible on the question at hand, that is, perinatal mortality as affected by the induction of labor, all inductions which were performed in the hospital during those two years and which met the following criteria were included in the study: single pregnancies of thirty-seven or more weeks gestation, wherein the infant was living at the time the induction began. There were 1,028 inductions meeting these specifications out of the total of 8,583 mothers delivered during that time. These were termed the induction group, which was further subdivided into those cases where the induction was considered "elective" (the elective induction group, 832 cases) and those where the induction was deemed indicated to avoid or to mitigate some obstetric hazard (the therapeutic induction group, 196 cases). The stated indications for the therapeutic inductions include preeclampsia and/or maternal vascular disease (52 cases), those done because of a previous unusually short labor or because the patient lived at a great distance from the hospital (45 cases), premature rupture of membranes with failure of labor to ensue (36 cases), and a wide range of miscellaneous indications (63 cases).

For purposes of comparison, another group of records were selected. For each induction of labor, a noninduction case (single pregnancy, infant living at the start of labor or delivery) was taken from the

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* The data presented are from a study supported in part by Grants RG-7200 and H-1914 (C5) from the National Institutes of Health, U.S. Public Health Service, Bethesda, Maryland.

TABLE I. Distribution of study cases by weeks of gestation

Weeks Gestation	Elective Induction	Therapeutic Induction	Noninduced	Totals
37	5	20	29	54
38	54	35	93	182
39	168	35	208	411
40	426	69	491	986
41	106	19	131	256
42	62	8	69	139
43 to 44	11	10	22	43
TOTALS	832	196	1,043	2,071

same month's deliveries in which the following characteristics were as nearly identical as possible with the induction record: weeks of gestation, sex of baby, type of service (staff or private), and racial group (white or nonwhite). The distribution of cases by weeks of gestation is summarized in Table I.* For all the groups studied, the records were equally accessible. Besides the delivery record, the infant's charts were also studied, which gave equal access in all groups to follow-up medical reports on all babies who had been readmitted to the University Hospitals for subsequent difficulties.

The two groups were compared by perinatal mortality, birth weights, and combined perinatal complications.

Perinatal mortalities. All the fetal losses are summarized in Table II. Of the total of 2,071 infants, 4 were born with congenital anomalies of such severity as to be incompatible with prolonged extrauterine survival: All of these died in the neonatal period.

Each of the remaining 4 neonatal deaths might stimulate some speculation concerning the part which induction of labor either played or might have played in preventing the death of the infant. In retrospect, the most obviously preventable of these deaths is that of the infant in the noninduced group who died shortly after an extremely difficult forceps delivery. The staff who managed this delivery agreed that this pregnancy might better have been terminated by cesarean section after an initial trial of forceps had indicated that vaginal delivery would be difficult. No one in our hospital would have suggested doing an induction of labor on this woman with the idea of delivering her before the baby grew too large for feasible vaginal delivery.

Among the deaths in the induction group, the relationship between the inductions and the neonatal deaths is more obscure. In the case of the infant who died of a perforated duodenal ulcer, induction was not begun until the membranes had been ruptured nearly thirty-six hours without labor. A positive blood culture was obtained on the fourth day of life. Shortly thereafter, surgical repair of a perforated ulcer was carried out, but the infant succumbed at the age of twenty-five days. One might wonder whether or not the induction of labor contributed to the stressful situation which resulted in the eventual death of the infant. Again, if the prolonged rupture of the membranes contributed in any degree to the development of this infant's sepsis, one might be led to speculate that this child may possibly have died not because an induction was done but because it was not done soon enough.

The other death in the therapeutic induction group raises questions equally difficult to answer. This labor was induced in a white private patient with demonstrated chronic renal disease because the patient was losing weight and the fundus, never large, had been becoming progressively smaller during the previous three weeks. The patient had received meticulous prenatal care since early in the first trimester. The preinduction diagnosis was "possible placental insufficiency." The 2,160-Gm. infant exhibited respiratory distress immediately and died on the second day after birth. In the absence of a complete pathologic examination (autopsy permission was denied), the final diagnoses were listed simply as "idiopathic respiratory difficulty and sclerema." Assuming that there was no lethal hidden anomaly, and granting that this was actually a pregnancy of thirty-nine weeks gestation—and the clinical evidence is good on this point—several questions

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* The minor discrepancies in numbers between the two groups result principally from the fact that the delivery records from which these cases had already been drawn for a separate study included a few cases which did not meet the stated criteria for the current survey. All such were excluded.

TABLE II. Perinatal (intrapartal and neonatal) deaths among 2,071 births

Causes of Death	Elective Induction Gestation (Weeks)	Elective Induction Weight (Gm.)	Therapeutic Induction Gestation (Weeks)	Therapeutic Induction Weight (Gm.)	Noninduced Gestation (Weeks)	Noninduced Weight (Gm.)
Malformations incompatible with extrauterine life						
Congenital heart disease	40	2,460	. . .	. . .	. . .	. . .
Osteogenesis imperfecta	. . .	. . .	39	2,560	. . .	. . .
Myelomeningocele	. . .	. . .	. . .	. . .	38	3,970
Hydrocephalus and meningocele	. . .	. . .	. . .	. . .	42	4,350
Other causes						
Hyaline membrane disease	39	2,540	. . .	. . .	. . .	. . .
Perforated duodenal ulcer	. . .	. . .	38 (Membranes ruptured 30 plus hours without labor)	2,970	. . .	. . .
Maternal renal disease, cause not established	. . .	. . .	39 (Induced because fundus becoming progressively smaller; no autopsy)	2,160	. . .	. . .
Birth trauma	. . .	. . .	. . .	. . .	40 (Died few minutes after difficult delivery)	3,780

come to mind: Would this infant's prognosis have been enhanced by induction a week earlier? Would the infant have been better off if the pregnancy had been allowed to proceed to term, or would there have been an increasing likelihood of fetal demise in utero before the onset of labor? Was the fetal nutritional state already so far compromised that the infant would have had a better prognosis if he had been delivered by cesarean section, rather than being subjected to labor at all? Even in retrospect, these questions seem impossible to answer.

The hyaline membrane neonatal death in the elective induction group was in an infant born to a thirty-five-year-old para 7, six days prior to the estimated date of confinement. The infant, delivered by low forceps after a twelve-hour labor, breathed and cried immediately, but soon developed respiratory distress and succumbed on the third neonatal day. It appears that this uterus was stimulated by intravenous Pitocin drip at a rate in excess of that employed in other inductions at term in our hospital. The questions one might ask concerning the management of this case should be considerably easier to answer than were the questions raised by the previous 3 cases.

Birth weights. In any discussion of inductions of labor, the question of birth weights arises sooner or later, based on the old fear that the obstetrician will mistakenly induce labor while the infant is still actually premature. To the limited extent that one may judge prematurity by birth weight alone, it would appear that the elective inductions resulted in the birth of somewhat fewer infants of premature weight than did the spontaneous labors (Table III). The same generally parallel pattern exists between the babies weighing over 4,000 Gm. which were born to the elective induction and the noninduction groups (Table IV). It might be suspected that the mothers of the 4 babies weighing over 4,000 Gm. in the therapeutic induction group might be diabetic. However, none of these mothers had been so diagnosed.

Major complications. It seemed worth while to try to determine whether or not the induction groups had more total complications than the noninduction group. A list of major complications was devised and

TABLE III. Births of infants weighing under 2,500 Gm. according to type of induction and weeks of gestation

	Elective Induction		Therapeutic Induction		Noninduced	
Weeks Gestation	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000
37	1 per 5	200.0	1 per 20	50.0	10 per 29	344.8
38	2 per 54	37.0	1 per 35	28.6	8 per 93	86.0
39	4 per 168	23.8	2 per 35	57.1	4 per 208	19.2
40	6 per 426	14.1	0 per 69	. . .	4 per 491	8.1
41 to 44	1 per 179	5.6	2 per 37	54.1	0 per 222	. . .
Totals	14 per 832	16.8	6 per 196	30.6	26 per 1,043	24.9

TABLE IV. Births of infants weighing over 4,000 Gm. according to type of induction and weeks of gestation

	Elective Induction		Therapeutic Induction		Noninduced	
Weeks Gestation	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000
37, 38	1 per 59	16.9	4 per 55	72.7	0 per 122	. . .
39	8 per 168	47.6	2 per 35	57.1	12 per 208	57.7
40	46 per 426	108.0	4 per 69	58.0	48 per 491	97.8
41	15 per 106	141.5	2 per 19	105.3	21 per 131	160.3
42 to 44	8 per 73	109.6	0 per 18	. . .	16 per 91	175.8
Totals	78 per 832	93.7	12 per 196	61.2	97 per 1,043	93.0

arranged arbitrarily more or less in descending order of severity; thus, "neonatal death," the most significant diagnosis, appears at the top of the list, while "birth weight under 2,500 Gm." was placed last, since it was considered the least significant of the diagnosed abnormalities. Each complication listed in Table V represents 1 infant only, since it was decided to score each only once, even if more than one of the complications was present in the same individual. In cases of multiple complications, the infant is listed with the highest priority category for which he could qualify.

It may be seen in Table V that the rates were quite similar, item by item, for the elective induction group and the noninduction group. Among the infants born after therapeutic inductions, the complication rate is much higher. Expressed in rates per thousand, the cumulative complication rate for the elective induction group was 37.3, while that for the noninduction group was 41.4. Among the infants born after therapeutic inductions, the complication rate is much higher (76.5), as would be expected from the fact that therapeutic inductions so often are carried out on what the obstetrician might term a "sick pregnancy" and one which he deems it wisest to terminate, either because of maternal disability or suspected fetal difficulty. While the complication rate in the therapeutic induction group was nearly twice that of the total rate of the other two groups, a substantial part of the excess can be accounted for among the severe malformations, while the higher incidence of neonatal deaths accounts for most of the rest.

Comment. The total complications of the three groups under discussion are graphed in Figure 1, from which it would appear that the complications from elective inductions versus those found in noninductions are approximately equal. The real problem is what to do with the therapeutic inductions, whose "complication rate" column looms far above those of the other two groups. This raises the question of the varying attitudes of obstetricians toward inductions in general.

The size of the columns shown in Figure 1 could easily be rearranged to fit the prejudices of almost anyone. For example, if

TABLE V. Complications encountered according to type of induction

Complications	Elective Inductions (832 Infants)		All Inductions (1,028 Infants)		Therapeutic Inductions (196 Infants)		All Except Elective Inductions (1,239 Infants)		All Noninductions (1,043 Infants)	
	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000	Number of Patients	Rate per 1,000
Intrapartal and neonatal deaths	2	2.4	5	4.9	3	15.3	6	4.8	3	2.9
Severe malformations	4	4.8	9	8.7	5	25.5	11	8.9	6	5.8
Neonatal respiratory distress	4	4.8	4	3.9	0	0.0	6	4.8	6	5.8
Neonatal infections	3	3.6	4	3.9	1	5.1	6	4.8	5	4.8
Diagnosed birth trauma	5	6.0	7	6.8	2	10.2	4	3.2	2	1.9
Central nervous system damage possibly associated with birth trauma	1	1.2	1	1.0	0	0.0	3	2.4	3	2.9
Birth weight under 2,500 Gm.	12	14.4	16	15.6	4	20.4	22	17.8	18	17.3
TOTALS	31	37.2	46	44.8	15	76.5	58	46.7	43	41.4

one felt that all inductions were pretty much alike and involved the practice of meddlesome obstetrics, he might tend to consider as a single group all the complications which occur in all induced deliveries. In this instance, the obstetrician might carry a mental image of the combined complication rate of all inductions versus all noninductions (column 2 versus column 5 in Fig. 2). At the other extreme might be the person who carried a mental image of elective inductions versus all other deliveries (column 1 versus column 4, Fig. 2). Obviously, neither device would present the picture accurately. The better way is to consider the three original groups separately, each having similarities to the other groups, but each having its own unique problems.

We should remember that the elective induction group is a highly favored group, where no abnormality is claimed or seriously suspected by the obstetrician: We should expect that the results of elective inductions should be very good indeed. Equally, we would anticipate more complications from the therapeutic induction group, inasmuch as inductions are done in these instances as a partial solution to what is considered an obstetric hazard. Finally, it should be borne in mind that the group not subjected to induction for any reason also carries some extra pathologic conditions. Two examples are those cases in which cesarean section is elected as a means for meeting an obstetric hazard and the occasional baby who dies before the onset of labor (not considered in this series).*

The little study presented here could not possibly be interpreted as indicating that induction of labor either increased or decreased the perinatal mortality in the series under discussion. The original provocative question which is the theme of this panel is not likely to be answered authoritatively in the near future.

Even though the question cannot be answered, inductions will continue to be done. The induction of labor is a valuable tool for the obstetrician, and no one would think

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* For example, in 1960, among a total of 4,278 deliveries, there were 9 deaths in utero in single pregnancies in our hospital where the infant died at thirty-seven or more weeks of gestation. The cause of death could be well established in only 3 of these cases. Would induction of labor at some earlier time have avoided any of these intrauterine deaths?

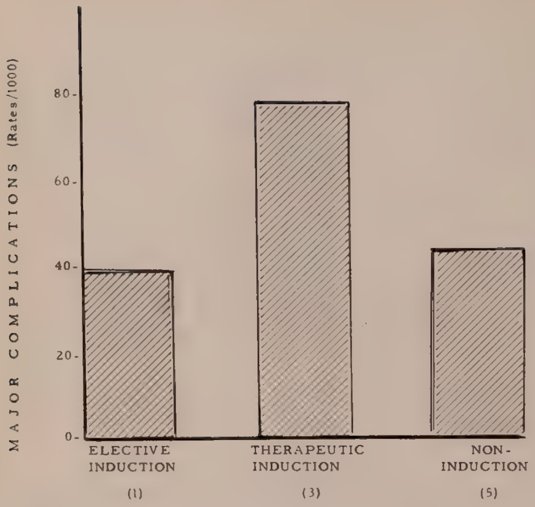

FIGURE 1. Graphic representation of complication rates according to type of induction.

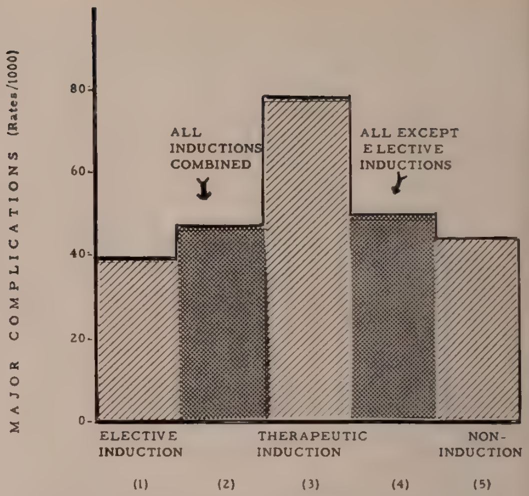

FIGURE 2. Combined complication rate of all inductions as compared with noninductions.

seriously of discarding it. Obviously induction, like cesarean section or forceps delivery, can be a dangerous process when it is misused; the occasional abuse of these procedures does not mean that any of them should be abolished, but simply that we must learn to use them more safely and effectively.

As clinicians, we would like to feel that induction, conducted thoughtfully and carefully in good obstetric surroundings, should not raise the perinatal mortality at all. Furthermore, our results should improve further as we achieve a better understanding of the physiology of labor and the methods for the measurement of potential hazards to the fetus in utero. Finally, we should remember that the safety with which induction of labor is carried out will probably rise in direct proportion to the improvement of all the obstetric standards and obstetric practices of any given community.

ACKNOWLEDGMENT. The author wishes to express his appreciation to Mrs. Jane Daley and to Mrs. Carol McKinney for their assistance in the processing of the study data.

DR. HELLMAN: Thank you Dr. Hendricks. I think, Dr. Hendricks, I agree with the "con" side very well. I think his complication factor is perhaps the crux of the matter and in the discussion I would hope to take exception to his control, because I believe that the adequate control for electively induced labors would show a complication factor of zero. I would like to amplify this in the discussion if I could. It seems to me that this is one of the most vital arguments against elective induction of labor that one could raise. I am glad that he brought this out.

We now are privileged to hear the statistician who knows all the answers and who continues to say he walks in the middle of the path and has no opinions. You can draw your own conclusions from his data. Mr. Herbert Rich.

Perinatal mortality rates

MR. HERBERT RICH: The data that I am going to discuss are being presented with no implication that induction of labor is or is not good. I leave that to the medical people. The data presented were drawn from the confidential reports submitted by physicians in conjunction with the filing of fetal deaths and live-birth certificates.

There was available a 20 per cent systematic sample of all fetal deaths, a 10 per cent systematic sample of all live births, and the complete file of all infant deaths occurring during the year. From these files the data were tabulated and rates computed after appropriate weighting. However, whenever a certificate indicated that the data for any of the subclassifications were

TABLE I. Perinatal mortality rates according to type of hospital and service and according to type of induction, New York City, 1960, per 1,000 deliveries

Stimulation or Induction	Total	Proprietary*	Voluntary		Municipal†
			Private	Ward	
Neither	28.4	21.1	25.1	28.3	39.1
Stimulated	16.9	14.5	9.1	28.2	60.6
Induced	19.9	25.8	9.5	41.8	64.6

* All cases are private service.
† All cases are ward service.

unknown, except for an indication for stimulation or induction, the case was omitted completely from tabulations to simplify the report.* This tended to lower the mortality rates, but future review, it is hoped, will indicate that the lowering was reasonably proportional in the various cells.

It is granted that there is a good deal lacking in the data as reported to the Department of Health. We have done various studies of this. In some cases certain items are fairly well reported. In the particular item of induction of labor, as far as we can tell, there is a certain amount of under-reporting. No information is available as to the extent of under-reporting of stimulation and induction. This under-reporting could have a significant bearing on the rates to be presented.

These data were tabulated for the various classifications indicated by several consultant obstetricians as being the minimum necessary for proper evaluation.

It is of importance to note that the induction of labor varied markedly between types of hospitals—the proprietary, the voluntary, and the municipal—and varied greatly within the voluntary as to whether they were private or ward service cases.

In our answers to the question on the certificates as to whether labor was or was not induced, we received a large proportion reporting stimulation of labor; and for that reason I have included those as a separate group on the theory that they are not quite comparable to those who went into a normal, uninterrupted labor or a normal start of labor that may have been interrupted but which then started again spontaneously.

In this so-called normal labor, that is nonstimulated and noninduced, we had a perinatal rate of 28.4 per thousand. In the stimulated group it was approximately 17 per thousand and in the induced group approximately 20 per thousand. This lower rate for induced labor should not be interpreted as indicating an over-all advantage of induction in all pregnancies. The noninduced, nonstimulated pregnancies could be a composite of three subpopulations of pregnancies: (1) Some were pregnancies with a normal and uncomplicated prenatal course and delivery. Actually this would be a very low-risk group from a perinatal viewpoint. (2) In the nonstimulated, noninduced group there were those who had an abnormal prenatal course or some logic which would have called for induction to protect the life of the fetus, but induction was not done. (3) There might be a group for whom stimulation or induction would not have increased the chance of survival of the fetus.

We have no way of knowing, or estimating from our data, the proportion each of these three subpopulations was of the nonstimulated, noninduced group. Thus it appears that the noninduced, nonstimulated population, as reported to a registration office, is not the best control population for the evaluation of stimulation and induction.

Hospital classification. The population of pregnant women is obviously not homogeneous on a socioeconomic level. Perinatal rates were computed on the basis of type of service and hospital classification. Possible differences in populations and/or differences in hospital policies may also be reflected by the rates presented in Table I.

For ward service cases the perinatal mortality rates are approximately 50 per cent higher for induced than for noninduced labors in both voluntary and municipal hospitals. The noncomparability of popula-

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* On the basis of this omission procedure, the following proportions of the indicated groups were included in the tabulations: live births, 90.3 per cent; fetal deaths, 63.7 per cent; and infant deaths, 91.6 per cent.

TABLE II. Perinatal mortality rates according to parity and type of induction, New York City, 1960, per 1,000 deliveries

Stimulation or Induction	Parity 1	Parity 2 or 3	Parity 4 and Over
Neither	26.6	24.5	38.0
Stimulated	18.2	15.3	18.9
Induced	17.6	14.1	33.9

TABLE III. Perinatal mortality rates according to indication for induction, New York City, 1960, per 1,000 deliveries

Stimulation or Induction	Elective	Medical
Stimulated	2.5	22.4
Induced	5.9	39.7

tion and medical service could be the factor behind the variability of rates, particularly since the rate for induced labor in proprietary hospitals is 26 per 1,000 and in the private services of voluntary hospitals is 10 per 1,000.

PARITY. Since parity plays an important part in perinatal mortality, the data were tabulated as to first pregnancy, second plus third pregnancies, and fourth and later pregnancies (Table II).

As we would expect, the pattern of second and third pregnancies having the lowest risk is evidenced for each group (induced, stimulated, or neither). By itself, parity does not appear, on a statistical basis, to be a contraindication to induction or stimulation.

INDICATIONS FOR INDUCTION. A classification of reason for induction or stimulation using the broad groupings of "elective" and "medical" does to some extent classify the pregnant woman as "healthy" or "not healthy." In attempting to compare perinatal mortality in the induced and stimulated groups for elective and medical indications the obvious relationship was evidenced (Table III).

A question might be raised as to whether or not these data are completely representative of the facts, since approximately 20 per cent of the certificates did not give an indication for the procedure used (13 per cent of the stimulated, 21.9 per cent of the induced). Thus, it is possible the rates are operating at a different level. However, it seems unlikely that the pattern would be significantly affected. It should be kept in mind that the groups are composed of inductions and stimulations not further classified by type of hospital and service. It would also be of interest to classify these data on a weight and parity basis.

FETAL WEIGHT. The weight of the fetus carries with it its own patterning of mortality. The over-ride of induction, stimulation, or neither changes the perinatal rate to a great extent, although it must be emphasized again that it should not be inferred that it is because of the intervention per se (Table IV).

The pattern by weight grouping cannot be evaluated without considering other variables: the possible underlying differences in the populations in each cell. Of prime importance possibly is the indication for intervention, but because of the proportion of "unknown indication" this cross-classification has not been prepared.

MODE OF DELIVERY. The mode of delivery subsequent to the intervention or nonintervention in the course of labor is tabulated in Table V. No inference as to the interaction of induction of labor and mode of delivery on perinatal mortality is possible. However, of interest is the high rate when a section was necessitated following the induction of labor.

TABLE IV. Perinatal mortality rates, arranged according to birth weight and type of induction, New York City, 1960, per 1,000 deliveries

Stimulation or Induction	Birth Weight (Gm.) Under 1,001	1,001 to 2,500	2,501 to 3,000	3,001 and Over
Neither	907.7	121.9	11.8	8.0
Stimulated	*	35.0	28.9	8.7
Induced	*	82.8	20.0	6.0

* Frequencies too small to compute valid rates.

TABLE V. Perinatal mortality rates arranged according to mode of delivery and type of induction, New York City, 1960, per 1,000 deliveries

Stimulation or Induction	Spontaneous, Forceps	Breech	Section
Neither	21.3	166.3	42.3
Stimulated	14.7	120.0	*
Induced	15.7	86.5	85.7

* Frequencies too small to compute valid rates.

Comment. I would like to sum this up in a very few words. These data are not presented to prove—and as a neutral I did not hope to prove with these limited data—that induction is good, bad, or indifferent.

A determination of the value of induction may best be made on the basis of a clinical experiment designed statistically with medical-statistical evaluation and interpretation of the findings. The pregnant woman whose labor is induced or stimulated may be different from her sister who goes into a normal, uninterrupted labor. The setup of a control study may not be possible when you have a medical indication. An evaluation of elective induction appears more feasible.

This report is not intended to imply that induction or stimulation of labor carries a greater or lesser danger to the fetus as measured by perinatal mortality rates. I wonder whether perinatal mortality should be the sole criterion for evaluating the value of induction. Very little has been said about morbidity in the infant and early childhood periods. This infant mortality committee may have to include morbidity in its discussions.

Dr. Hellman: Thank you, Mr. Rich. I think it quite remarkable that Table III of Mr. Rich and the tables of Dr. Stone and of Dr. Hendricks, all depicting perinatal mortality in induced inductions, show practically the same figure, namely 5 per thousand or just a little better. This is the rate of congenital malformations which are incompatible with life that one would expect in our population, plus one or two mistakes that happen in most large series of inductions. I think that the similarity of these figures among the three groups is quite remarkable. I have another group here that I will perhaps bring out in the discussion. It concerns some of the data coming from another community, but it has very similar results.

Dr. Stone, do you have any rebuttal that you want to make before we open this to general discussion?

Dr. Stone: There is nothing to rebut on what Dr. Hendricks said. I think he was put a little bit in the unexpected position of being against something that he is probably not completely against. But I have to rebut the statistician, Mr. Rich.

I think the only thing his statistics showed is the shortcomings of our birth certificates. Other than that I do not see what conclusions we can draw from the data. Today one hesitates to dispute the statistician. I do not think that the birth certificates in New York City, and probably elsewhere, can presently serve as a basis for our coming to any sound medical conclusions.

Dr. Hellman: Mr. Rich, do you have anything to add?

Mr. Rich: I have heard Dr. Stone's comment, but I emphatically do not agree with it.

Dr. Hellman: The discussion is now open to any individual here.

Question and answer period

Robert Lowrie, M.D.: I would like to pounce on Dr. Stone for a few minutes. I admired his paper very much. It was very well presented.

I would like to ask Dr. Stone to consider these questions. Were there any violent labors in your series as a result of your medications? How do you select your cases and for what reasons? I have forgotten now whether your tables showed any control series. Were there any control series? What proportion of your cases were therapeutic and what were just for convenience? In how many cases did you start your medication and then had to stop because of something that went wrong? How many cases of overdue pregnancy did you have?

Dr. Stone: Thank you, Dr. Lowrie. I will not answer them all because I think it would take another paper.

For some of the points you mention, the data are not available to me at the moment.

Some I think I have already presented. By case selection, do you mean the kinds of cases?

Dr. Lowrie: Yes.

Dr. Stone: I limited my discussion by definition to those that we considered elective but listed what we now consider indications for elective induction, namely, those with a history of previous rapid labor and presenting anesthesia complications, and so forth, but no purely medical or obstetric complications. I had a personal experience just this week with a primipara who was offered induction last Friday on the basis of an examination in the office. She called me at three o'clock in the morning to say her membranes had ruptured and she was starting labor. I told her to come to the hospital. She lives in Manhattan. At 3:16 A.M. her husband phoned that she had a baby boy. I could hear it crying in the background. We have all had this happen to multiparas. This is the first time I had it happen in a primipara.

But the case selection for tonight's talk refers to elective inductions, not to any therapeutic induction or indication, and, therefore, they do not include overdue patients by dates. But we do not consider this an indication for interruption on the basis of most of the reports that have been presented to us.

We had no control series. This is a weakness of any other reports on oxytocin. The only thing that served as a control over the period of a year was the number of good institutions using oxytocin even with strict control compared with the number of deliveries that were available to us. I think that even without control, after awhile the sheer force of numbers of accepted statistics gives us trends as to mortality and morbidity.

Let us go back to Dr. Hellman and Dr. Guttmacher and then to the people in England. If they were getting serious complications, the procedure would have been stopped long ago. This is not a statistical analysis; it is obviously in proper hands and the results have been good. Its use is increasing. That is the only control that anyone has. The ideal would be an anterospective study with controls, but I do not know how to match a control for a pregnant patient. No other woman is a control for her, and she is not a control for herself from one pregnancy to the next because the conditions are not the same.

I have no statistics here on how many inductions had to be stopped. These are not personal cases. This is a total report. I am sure there are some that were stopped for one reason or another, but this was not a significant problem.

Dr. Hendricks: Mr. Rich pointed out that in considering these problems we are concerned not only with infant mortality, but also with the morbidity rate. With this statement I am in hearty agreement. When he makes the additional implication that we will not know the complete picture until the child is five or ten years old, he is of course technically correct, although really to complete the picture we might ask to see the entire lifetime morbidity record of the individual whose birth record is being studied. It seems to me, however, that in our pursuit of truly long-range follow-up programs, important as they are, we should not lose sight of the fact that careful observation during the perinatal period and during the early childhood period should give reliable indications of the infant's fate in the overwhelming percentage of cases.

Alan Guttmacher, M.D.: I came here as a listener and I enjoyed very much what I heard. I must admit I go away neither being persuaded for or against. I suppose the data presented tonight would leave us very little choice. Certainly one cannot indict induction from the data given by any of the discussants. I have heard no mention made whether parity seems to play a role in the choice of cases. I have heard no mention made about failures in induction, but I suppose these topics are really not germane to the discussion. The discussion seems to center on perinatal mortality, and if one keeps the discussion in clear focus, from what I have heard here so far I cannot say that I have learned that induction does any harm as far as perinatal mortality is concerned. If I am wrong in taking away this idea, I wish to be corrected.

Samuel Scadron, M.D.: I am very happy and interested to hear Dr. Stone and each of the proponents for the elective induction in view of the fact that many years ago he supported me when he was a resident, when I began to use Infundin before Pituitrin was synthesized. I used the former with the philosophy that you cannot teach an old dog new tricks. Dr. Stone supported me as a resident, and I see that he went a little further. He went from the latter agent to elective induction. Having practiced obstetrics for many years, I cannot see why we should hurry. What is the hurry? Why take a woman and induce labor, except that obstetric practice is going into the suburbs and patients themselves come in. They are induced by appointment. In fact, the lay people started the demand for induction, not the doctor. The deduction I derived from Dr. Stone's paper was that the obstetrician is being individualized and not the patient. I do not think it is good for perinatal mortality to advertise or to propose a universal use of induction of elective labor, and I have been many times more sorry then successful.

Theodore R. Seidman, M.D.: I just wanted to say that I have practiced obstetrics for a number of years and I think I have been responsible for perhaps two or three elective inductions of labor. I seem to get adequate sleep and recreation. Twenty-five per cent of your patients who offer you a choice as to approximately when they will deliver do not seem to me to offer any great advantage to the obstetrician. Some day I would like to see a panel of delivery room nurses on the dais to join in the discussion of elective inductions of labor. For some reason they seem to take it a lot more seriously than many of the doctors. And I think that in many of the institutions this 25 per cent induced creates a pressure on the rest of the doctors to be equally modern. This is possibly the reason why in the proprietary hospitals where they do not have a continuously trained resident staff to watch the patients for the doctor, the perinatal mortality appears to be considerably higher.

I can see no advantage. The case is quoted where the patient is delivered spontaneously at home. It seems to me the only one who loses is the obstetrician. I have never heard of any serious complications for mother and child under those circumstances.

Edwin M. Gold, M.D.: I think the discussions tonight did a remarkable job with a very sensitive and difficult subject. I think that what has come out of the discussion, at least in my own mind, from the statistics is that elective induction of labor, as defined, is a good procedure. Whether it has more merit than not doing an induction at all or whether it has less merit than no induction at all has to do with the man behind the procedure that is being done. The selection of the case, the intelligence of the man, and the integrity of the institution are probably the crux of the entire situation. Under those circumstances, at least from the statistics, there seems to be a very favorable outcome not only for the mother, but for the infant as well.

So that all of this talk about yes and no I think has been diluted by the fact that here is a modality on the American scene which apparently seems so successful when it is used with good judgment by good qualified hands that it has been taken up by the vast numbers of practitioners perhaps in the institutions where qualified supervision perhaps is not of the best. People do get into trouble, as we read from varying reports of maternal mortality and morbidity, ruptured uteri, and also perinatal loss, and the procedure begins to get a black eye. But I think that with the very clear-cut criteria and qualifications that were set down by Dr. Stone, at least to me it seems obvious what the conclusion is as a result of tonight's discussion.

Dr. Hellman: There is a group here that we have not heard from: the pediatricians. Any pediatrician want to raise his voice?

Gilbert W. Mellin, M.D.: We were just wondering whether the low mortality rate was due to induction or noninduction or increased pediatric care? This might be the difference between some of the private hospitals and some of the voluntary hospitals, that the burden of saving the baby may be shifted from the obstetrician to the pediatrician. This is definitely true in so-called medical induction where often the burden of saving the baby is shifted from the obstetrician to the pediatrician. I do not think we have the figures really to show whether or not this is true.

Comment

DR. HELLMAN: If there is no further discussion, I would like to take the prerogative of summing up what we have heard for just a minute, if you will.

In the first place, the question before the panel is, "Is perinatal loss increased as a result of the induction of labor?" It seems to me that the data presented by Mr. Rich and by both of the pro and con essayists indicates that it is not.

I would like to support this by the study from Hartford. I have the Hartford Hospital results here. We had a very tricky but neat device for picking up all the elective inductions of labor, and I think we got them all. In this institution we had 625 inductions out of roughly 6,500 deliveries. Our perinatal mortality was 0.5 per cent which again is right in the range that we discussed. So that I think we answer our question before the panel by saying "no."

The second question that came up, and it came up continually in everybody's talk, was the question of the control. Mr. Rich made the suggestion that there be a matched control. Dr. Hendricks made a very commendable effort to supply a matched control. Dr. Stone frankly admitted he did not have any control.

It seems to me that we have a built-in control and that one does not have to look very far for this. The control ought to be those normal women at term who go into labor spontaneously and have normal labors, whose babies are alive at the onset of labor. We have made a considerable study of this very factor to obtain the basic infant mortality. This varies slightly from race to race and age to age, but over all this figure falls somewhere between 0.4 and 0.7 per cent. If the infant mortality in induction does not exceed this figure, then again I think the answer about the perinatal loss is "no."

Dr. Hendricks brought out another point, and it seems to be extremely important. It does not really come into the purview of this panel, but I hate to have us leave without thinking about it. This was the complication factor. I cannot quite match his figures on complication factors. He had 42 per thousand, roughly 4 per cent. He had some data that I cannot get from the Hartford material without a little bit more work. But I do have a complication factor of my own, and it is extremely interesting. This is from a group of obstetricians from Hartford in an excellent hospital that is not connected with the medical school. That is the reason this was chosen. As far as I know, this is an excellent group of obstetricians.

The premature factor was almost negligible. They had no babies below 2,000 Gm. and very few between 2,000 and 2,500 Gm. Interestingly enough, in spite of the fact that the method of practice in this community is to do a vaginal examination before sending the patient into the hospital, before the induction of labor, this group of expert obstetricians had a 2 per cent incidence of breech in their figures, and they had 1 transverse lie. These are errors made by the obstetricians.

In addition to this they had 11 cesarean sections in their 600 inductions. It seems to me that one could presume that if these were normal women who would have gone into labor themselves, 11 cesarean sections is high. I think that perhaps in discussing induction of labor, we had better put a little more emphasis on the complication factor which comes about, by and large, through errors made by perfectly well-trained obstetricians; in a large series these are probably unavoidable. Thank you very much for your help here.

DR. GOLDMARK: I want to thank Dr. Hellman and his panelists for their splendid presentation and the audience for their participation in the discussion. The panel again demonstrates the value of reviewing current procedures in obstetric care with the view toward lowering perinatal disability and death.

Management of Patients with Cleft Lip and Palate

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CLEFTS OF THE LIP and palate are among the most frequent major physical congenital malformations. Community resources devoted to the rehabilitation of patients with this type of deformity are well justified because their rehabilitative prognosis is better than that of any other group with congenital anomalies. The majority of these patients can be rehabilitated to normalcy and can take their places as productive members of society.

According to a 1952 report of the American Public Health Association, about 5,000 children with cleft lip and/or palate are born in the United States every year.[1] In 1957, Montana reported one such deformity in 650 births. Pennsylvania, in 1949, reported one in 762 births.[2] In New York City, in 1955, one cleft lip and/or cleft palate was reported in about 1,200 live births.[3] The incidence of clefts in Negroes is estimated at about half that among the white population. The high mortality rate in infants with clefts (close to 20 per cent, according to the 1955 figures for New York City) is due to the multiple abnormalities frequently associated with cleft lip and palate.

Many of these infants require prolonged and sustained rehabilitative efforts, which include not only surgical treatment but the combined services of a team of specialists as well. Many of these services are difficult to obtain because trained personnel are scarce, and the cost is high. Except for surgical care, almost none of these services—dental, speech training, and others—are covered by medical insurance plans. Through their Crippled Children's Bureaus, several states have developed excellent programs for the rehabilitation of these children. New York State has a comprehensive program of assistance to patients with cleft lip and palate.[4] New York City instituted a program for the care of these children in October, 1953, through the Bureau of Handicapped Children.[5]

There is a great variation in the comprehensiveness and effectiveness of many of these plans. Most of them encourage the formation of coordinated, multidiscipline teams and finance the diagnosis and treatment of these patients. The payment for hospitalization and fees for surgical operations, dental care, orthodontic treatment, dental prostheses, speech therapy, psychiatric evaluation, and counseling usually are included. Several states have a very limited program, and some have none at all.

A number of cleft palate teams or clinics have been established throughout the United States and Canada. Such teams usually include a pediatrician, plastic surgeon, otolaryngologist, general dentist or pedodontist, orthodontist, prosthodontist, speech

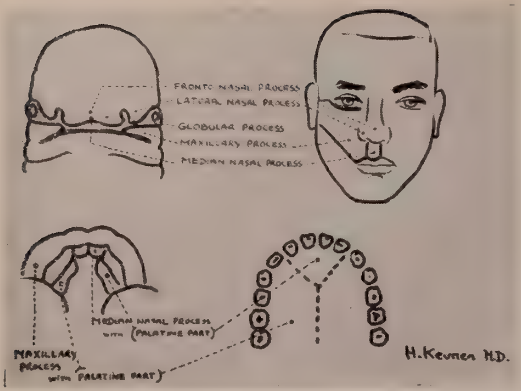

FIGURE 1. Development of face and palate. Upper sketch shows thirty-day-old embryo illustrating embryonic processes and their ultimate role in formation of the face. Lower sketch shows development of palate showing embryonic processes and their relation to adult palate.

therapist, social worker, and often a psychiatrist.

Classification

These patients can be divided into three groups: (1) cleft lip with or without cleft of the alveolus but with an intact palate, (2) cleft palate alone (postalveolar), and (3) cleft lip and palate. Clefts can be unilateral or bilateral and may vary in severity from a slight notching of the vermilion border of the lip or a simple cleft of the uvula to a severe deformity of the facial skeleton, exemplified by a bilateral cleft lip and palate. A combined cleft lip and palate occurs more frequently than the two other groups together (in about 63 per cent of the cases). A cleft palate alone occurs somewhat more often than a cleft lip (22 and 15 per cent respectively). While cleft lip and palate occurs almost twice as often in males as in females, the relationship is reversed in clefts of the palate alone.[6]

Embryologic development

It is now accepted that cleft lip and cleft palate occur at different stages of embryonic development and probably by different processes. The classic theory of the development of the face, advanced by the embryologists of the nineteenth century and described by Arey[7] as recently as 1942, attributes the formation of facial clefts to the lack of fusion of the various embryonic processes which form the embryo's face. However, according to modern theory, and recently well documented by Stark and Ehrman,[8] the development of the facial components begins with the formation of a thin epithelial wall. Normally, masses of mesoderm reinforce the epithelial layer by advancing toward the midline. The mesodermal mass is responsible for the development of muscle, bone, and cartilage, and its absence or faulty ingrowth into the early lip and alveolus leads to the tearing or separation of the thin epithelial layer and results in a cleft. The formation of the lip takes place between the fourth and seventh week of embryonic development. This theory explains the occurrence of partial clefts and the thin skin bridges occasionally present in cleft lips. Postalveolar clefts are due to a failure of the fusion of the palatal processes which form the definitive palate (Fig. 1). The development of the palate occurs during the eighth to twelfth week of prenatal life.

Causes of cleft lip and palate

"Why did this happen to us?" The question always asked by parents of children with clefts still remains unanswered, although some hereditary influence seems to be indisputable. According to Fogh-Anderson,[6] Sanders,[9] and Davis,[10] a family history of cleft lip or palate has been documented in 41 to 57 per cent of cases. Some studies support the contention that older parents, particularly if they are over thirty-five years of age, are more likely to produce infants with cleft lips and palates. However, this has not been substantiated sufficiently by others.[6,11] German measles during the first trimester of pregnancy is known to be responsible for various congenital anomalies, but it has not been established whether or not facial clefts are among them.[12] Clefts have been produced in experimental animals by a variety of agents. Dietary deficiency produces clefts in rats, according to Warkany and Nelson.[13] Fraser *et al.*[14] have induced clefts of the palate in pregnant mice by the administration of cortisone. Ionizing radiation has been shown to have a teratogenic effect.[15] In general, it is accepted that the duration, intensity, and time of action of noxious agents during pregnancy is more important in producing clefts in offspring than is the specific nature of the agent.[16]

Pediatric aspects

Aside from the emotional reaction of the parents, the first problem in the management of the infant with cleft lip and palate is feeding. These infants cannot be breast fed or bottle fed with the ordinary feeding bottle. Before repair of the lip they can be fed best with a syringe. Although this is a tedious process, the infant learns surprisingly fast to maneuver the tongue and carry the fluid into the oropharynx without spilling the fluid through the nose. Feeding is easier if the infant is held on the lap in an upright position. After repair of the lip, a nipple with a large opening can be used. A variety of devices, such as a cleft palate nipple or a Brecht feeder, are recommended for the child with a cleft palate, but they are rarely needed. If the infant does not take food, the possibility of other abnormalities should be considered. Gavaging is rarely necessary. Indeed, it is most undesirable, since it does not stimulate the sucking and swallowing reflexes and may cause aspiration pneumonia.

Close and competent pediatric care and guidance is essential during the early life of these children. They are prone to infections of the respiratory tract and to ear infections. Their feeding programs must be individualized. The parents' anxiety and distress can be handled best by the pediatrician, unless it reaches such proportions that psychiatric help is indicated.

Surgical care of cleft lip

A cleft lip deformity is not limited to the lip alone. A complete cleft lip always includes a deformity of the nostril and nasal tip. The nostril is stretched across the cleft, and the whole nasal tip is distorted and deviated. Repair of the lip must include the correction of the nostril deformity. In repair the aim is to produce a lip normal in appearance and function with an inconspicuous scar. The several procedures popular in this country and abroad all bring a flap of tissue from the lateral position into the medial portion of the cleft lip. The flap may be triangular or quadrangular in shape and can be fitted either immediately above the vermilion border, in the center of the lip or below the columella[17−21] (Fig. 2). Thus, the resulting scar on the lip can be either curved, step-ladder, or Z-shaped. Only a minimum of unusable lip tissue should be discarded during the repair, since a tight upper lip is not only unsightly but also impedes the proper development of the maxilla.

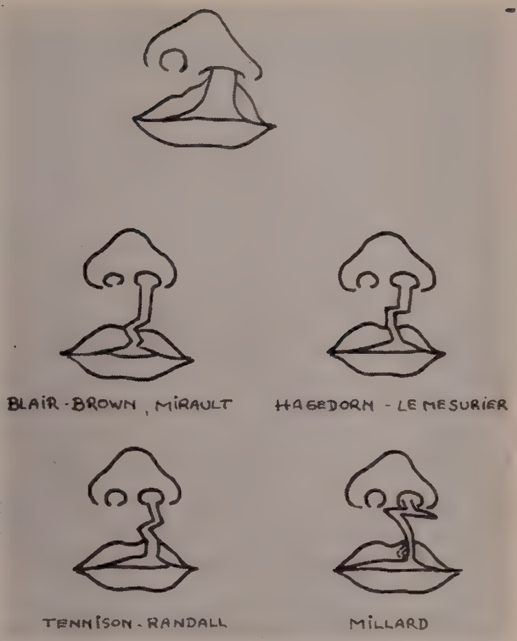

FIGURE 2. Patterns of unilateral cleft lip closure. Various patterns of technic of lip repair, all of which may produce a satisfactory result.

The repair of a bilateral cleft lip is “about twice as difficult as in a single cleft, and the results are about half as good.”[22] The difficulty is caused by the marked underdevelopment of the central part of the lip, consisting of the prolabium and the columella. The central fragment of the alveolus, the premaxilla, is often found completely out of alignment and far in front, under the nasal tip (Fig. 3). The prolabium belongs to the upper lip and not to the

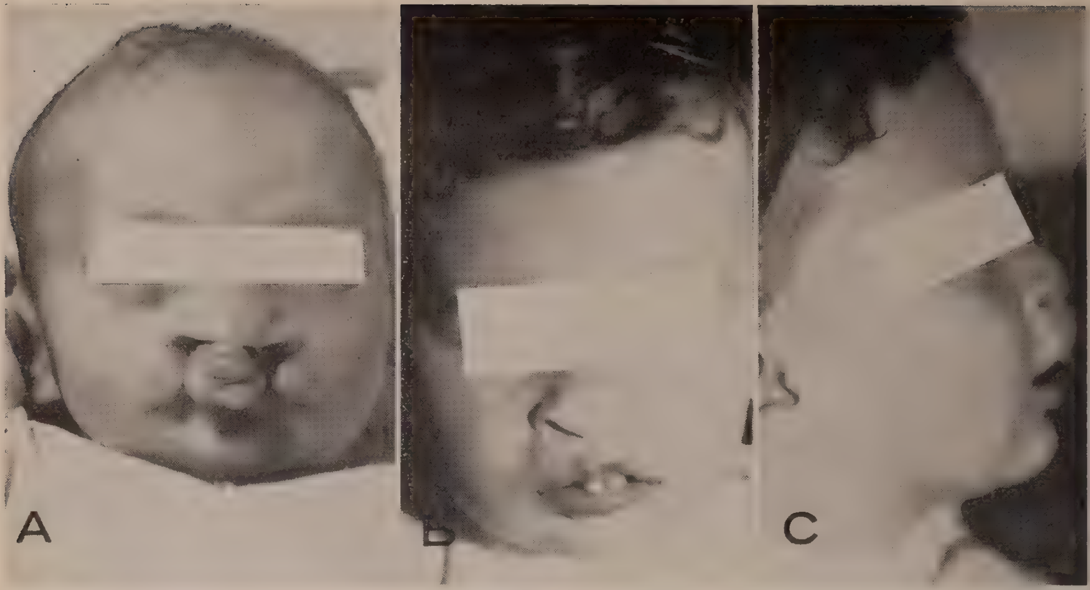

FIGURE 3. Bilateral cleft lip and palate. (A) Note position of premaxilla on tip of nose. (B, C) Collapse of lateral maxillary fragments after repair of lip prevented premaxilla from receding into its correct position. Note absence of columella.

columella (in the male it will become hairbearing in later life), and it has an extraordinary potential for growth when it is incorporated into the lip and stretched.[23] Thus, procedures which incorporate flaps from the lateral components of the lip to lengthen the prolabium are likely to result in later life in an upper lip which is too long and too tight. Many surgeons have adopted the simple, straight-line repair, stretching the prolabium and utilizing the excessive mucous membrane from the lateral component to enforce the attenuated vermilion of the central portion.[23,24] The immediate result may not be impressive, but there is spectacular improvement with growth, and the deficiency can be corrected when the child is a few years old. The columella is usually very short, resulting in a typical deformity of the nose. Lengthening of the columella is usually performed during the preschool period. A bilateral cleft lip is repaired in either one or two stages, with the operating done on each side separately.

Management of the alveolus

Attempts at forcible approximation of the cleft alveolus in unilateral cleft lip have long been abandoned. Over a period of several months the gentle, constant pressure of the repaired lip slowly brings the alveolar fragments together. However, they are rarely approximated in correct alignment; this becomes the orthodontist's task in later years.

The management of the forward displacement of the premaxilla in bilateral cleft lip is still controversial. Some surgeons recommend osteotomy or ostectomy of the vomer and retropositioning of the premaxilla, which is then fixed by pinning.[24,25] Most surgeons, however, feel that the forceful retropositioning of the premaxilla results in a fibrous union and in the eventual tilting and underdevelopment of the premaxilla. They prefer to repair the lip over the displaced premaxilla and to rely on dynamic molding by the repaired lip to force the premaxilla into the correct position gradually and slowly.[23]

Timing of lip repair

The complete cleft lip, unilateral or bilateral, is an unsightly deformity. The result of repair is usually dramatic and a morale booster for the distressed family.

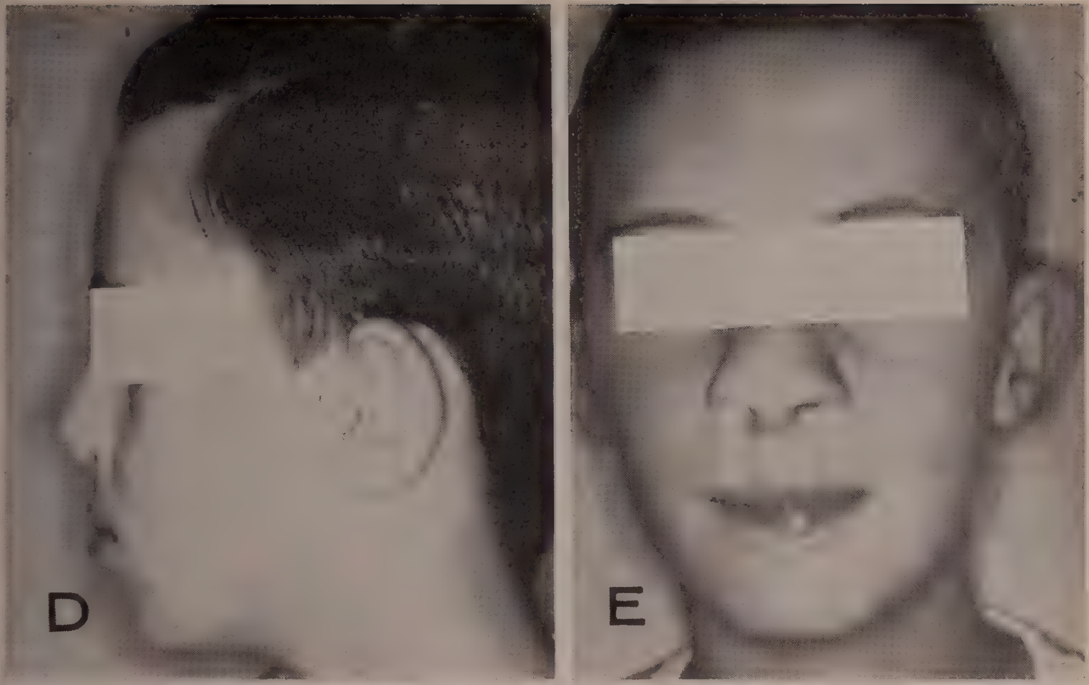

FIGURE 3. (D, E) Appearance of patient at seven years of age. Columella was lengthened, and fullness of upper lip was restored by transfer of a flap from lower lip (Abbe-Estlander flap). Scars will be revised at a later date.

Early repair is the common practice, although this may vary from a few days postpartum to as late as three or four months. Our preference is to wait until the child is in good general condition, gaining weight, and weighing close to 9 or 10 pounds. Our experience has shown that by delaying the operation until the face is larger we can perform it with full attention to details, thus substantially reducing the need for secondary corrections (Fig. 4).

Anesthesia

The majority of cleft lip operations are performed under general anesthesia. Ether insufflation is now used rarely and has been replaced by intubation technics which allow for a smooth, even anesthesia with control of the airways during the operation. Many surgeons, including ourselves, have found that they can reduce postoperative morbidity and mortality, although such mortality is very low, by performing these operations under local anesthesia supplemented by analgesia. The infants are given a rectal barbiturate supplemented by repeated small doses of Demerol hydrochloride intramuscularly or intravenously during the operation. Blocking of the infraorbital nerves and local infiltration with weak Xylocaine hydrochloride and epinephrine produce adequate anesthesia and minimize bleeding. The feeding routine is interrupted very little.

Cleft palate repair

The primary aim of cleft palate repair is to establish a mechanism which will permit the development of normal speech. A mere bridging over of the cleft usually will fall short of this purpose.

The soft palate is a muscular organ whose contracture, together with the action of the pharyngeal musculature, must create an airtight closure, preventing air from entering the nasal cavity. The column of air must be directed to the oral cavity, where it is subjected to various changes by the articulation mechanism. The absence or incompetence of the velopharyngeal valve is

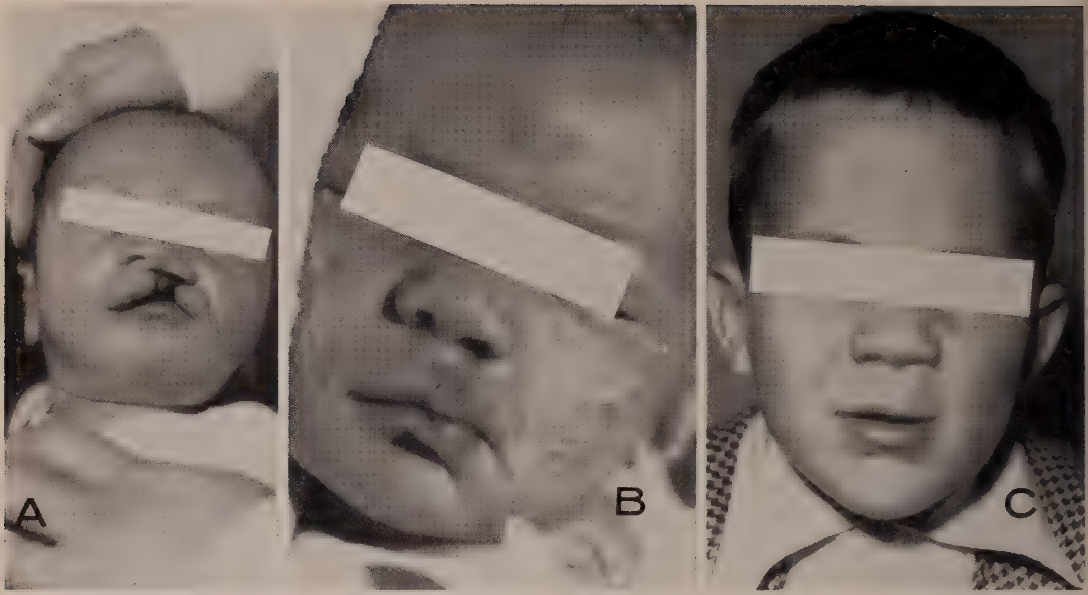

FIGURE 4. (A) Unilateral cleft lip and palate at birth. (B) Patient with unilateral cleft lip repaired at six weeks of age. (C) Appearance at four years of age.

responsible for the various degrees of nasality characteristic of cleft palate speech. The surgical restoration of a competent velopharyngeal sphincter depends on preserving the muscular contractility of the soft palate and on obtaining sufficient length so that it can reach the posterior pharyngeal wall.

There is considerable controversy among American surgeons about the timing and method of the repair of the cleft palate. The classic von Langenbeck operation, which has been in use for about one hundred years, utilizes lateral incisions to obtain relaxation and to permit mucoperiosteal flaps to be moved medially, bridging the cleft.[26] On the nasal surface the pharyngeal aponeurosis and the nasal mucosa are severed from their attachment to the palatal shelves. This creates a large, raw area on the nasal surface of the soft palate which heals by cicatrization, pulling the soft palate away from the pharyngeal wall. In the majority of cases, the von Langenbeck procedure creates a palate which is too short to reach the pharyngeal wall. This is particularly true in the postalveolar cleft where there seems to be an inherent shortness of the palate and underdevelopment of the palatal elements. Some surgeons accept this limitation and rely on secondary lengthening procedures, the "pushback" or a pharyngeal flap, to overcome this inadequacy.[27]

The most widely used procedure, both here and abroad, is one which incorporates the feature of lengthening in the primary repair. The Wardill[28] operation, with various modifications by Kilner[29] and others,[30] displaces the repaired palate posteriorly by lengthening the oral surface, utilizing the principle of V-Y advancement (Fig. 5). The viability of the triangular mucoperiosteal flaps is maintained by the preservation of the posterior palatine neurovascular bundles. They are pulled out of the bony canal, or the posterior bony wall of the canal is removed to facilitate retroposition.[31] The palatal aponeurosis is severed, but the continuity of the nasal mucosa is maintained. The latter is teased out of the floor of the nasal cavities and around the pterygoid plates. Although keeping the nasal mucosa intact limits the amount of retroposition, it avoids a raw surface on the nasal side, thus minimizing secondary contracture. Both the nasal and oral mucosa are closed by sutures, and the palatal muscles are brought into complete opposition. By fracturing the hamulus, the tensor veli

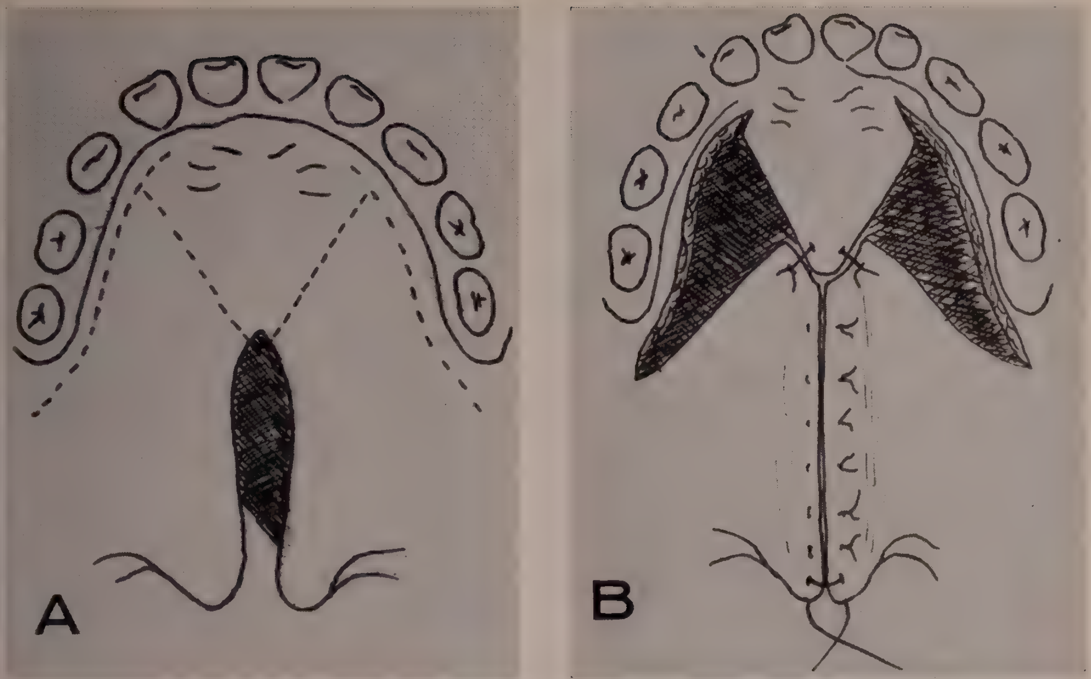

FIGURE 5. (A and B) Repair of cleft palate with retroposition. The Wardill "V-Y" advancement accomplishes lengthening along with closure of the cleft palate.

palatini muscle is converted into a levator, and the lateral tension of the palatal musculature is relaxed.[32] This method is particularly useful in the repair of the posterior cleft palate. In a complete transpalatal cleft, either unilateral or bilateral, the vomer is usually a good source of material for the repair of the anterior palate. The use of a vomeral flap to close the bony palate converts the cleft into a partial one (Fig. 6).

Most surgeons try to complete the repair of the cleft palate by the eighteenth to the twenty-fourth month so that the child can learn to speak from the very beginning, unencumbered by this handicap.

A large number of patients with cleft palate have a developmental deformity of the maxilla which becomes apparent when they are a few years old and consists mainly of a collapse of the alveolar arch, narrowing of the palate, and lack of forward development. This deformity is influenced by surgical repair of both the cleft lip and the cleft palate. Some surgeons believe that the dissection of the mucoperiosteal flaps is the primary or exclusive factor interfering with the growth centers of the maxilla and that the scarring on the palate which remains after the operation is a further hindrance to normal growth.[33] Thus, they delay the repair of the cleft palate until the child is over four years of age. At that time four fifths of the maxillary growth, as measured by the distance between the molars, is complete. Others repair the soft palate during the second year, leaving the cleft in the anterior palate untouched.[34] The dynamic force of the repaired muscular palate brings about a gradual narrowing of the bony cleft in much the same manner as the repair of the lip approximates the cleft alveolus. This permits the subsequent repair of the splitlike defect in the hard palate, with minimum dissection of the mucoperiosteal flaps.

It is not unusual, however, to observe the typical maxillary deformity in a patient with cleft palate before the palate is repaired but after the lip is closed. There is general agreement that repeated, ill-advised operations on the palate, common a few decades ago, were largely responsible for the severe distortion of the dental arches and

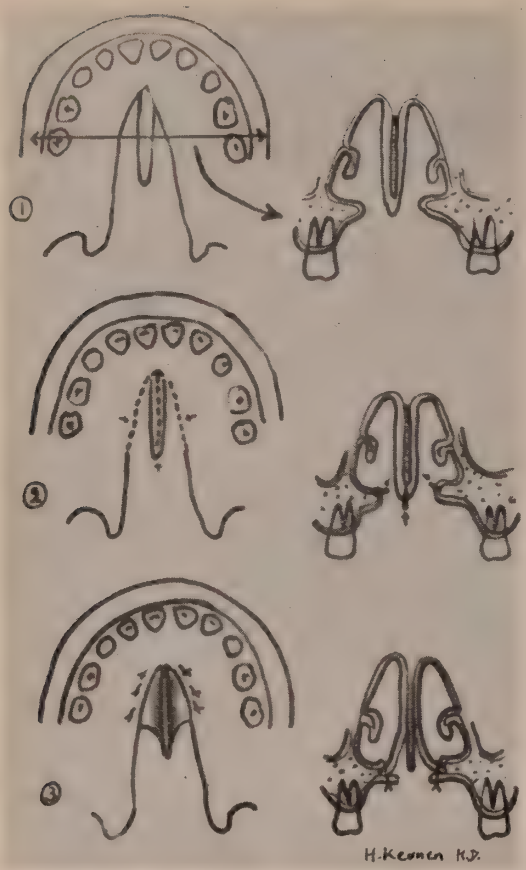

FIGURE 6. Vomer flap. Mucoperiosteal flaps are used to bridge the anterior portion of the cleft palate. These are reflected from the vomer which projects down into the anterior portion of the defect. The mucosal surface faces the nasal cavity. The palatal surface epithelializes rapidly.

the contraction and recession of the maxilla. This, however, need not be true of a well-planned, well-executed conservative operation on the palate, with full respect for the neurovascular supply and with minimum scarring. Since there is no assurance that delaying palatal repair will eliminate facial and dental deformities and make orthodontic treatment unnecessary, we prefer to repair most palates before the patient is two years of age, recognizing the need for orthodontic treatment and preferring to focus on the restoration of the speech mechanism. Delaying the repair predisposes to otologic infections, requires the construction of a temporary dental prosthesis, often hard to obtain, and calls for the continuous supervision of these children. Nevertheless, there are certain clefts in which surgical repair can be delayed advantageously until a later age.

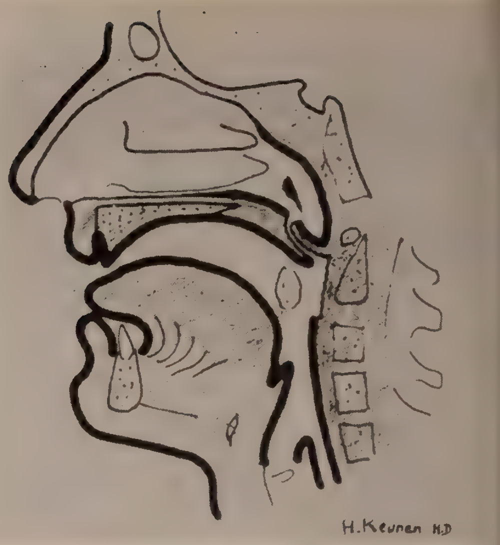

FIGURE 7. Superiorly based pharyngeal flap attached to the nasal surface of the soft palate. Pharynx is also narrowed by closure of the defect on the posterior pharyngeal wall.

Palatal insufficiency

Palatal insufficiency is a term reserved for velopharyngeal incompetence without a visible cleft palate and presents the typical nasality of speech characteristic of cleft palate. Some repaired cleft palates will exhibit signs of insufficiency due to the inability of the repaired palate to obtain velopharyngeal closure. This can be attributed either to poor mobility or to shortness of the palate in relation to the size of the nasopharynx. Palatal insufficiency is also present in cases of submucous clefts of the soft palate. These clefts often are overlooked, particularly if the examiner is not familiar with this syndrome. They are usually characterized by a bifid uvula, thinness of the palate in the midline, and contracture of two lateral muscular masses. Frequently, the shortness of the palate is conspicuous, particularly in relation to the size of the pharynx. Many of these patients are treated unsuccessfully for functional speech defects until the real physical cause of the disability is found.

Palatal insufficiency also can be present in cases of a congenitally large pharynx or shortness of the palate without submucous clefts. Palatal insufficiency also can develop in paralysis of the soft palate as a result of bulbar poliomyelitis, diphtheria, and so forth. Mild forms of palatal insufficiency can be compensated for by hyperactivity of the pharyngeal musculature. After prolonged speaking or when the patient is fatigued, the nasality of speech usually becomes apparent.

Mild forms of submucous cleft or other palatal insufficiency can be corrected by an operative retroposition of the palate mentioned in connection with the repair of cleft palate. The submucous cleft should be excised and the muscular elements brought into close approximation. Most of the severe forms of palatal insufficiency of whatever nature require some form of pharyngoplasty.

Pharyngoplasty

Pharyngoplasty is indicated in any case of repaired cleft palate in which a palatal insufficiency remains. In this country the form of pharyngoplasty most popular for the last decade is the pharyngeal flap[35] or Rosenthal pharyngoplasty.[36] This operation consists of the dissection of a wide mucomuscular flap from the posterior pharyngeal wall, leaving it attached either above or below, and the attachment of this flap to the posterior border of the soft palate (Fig. 7). Most surgeons prefer to base the pharyngeal flap superiorly, considering it more physiologic, since the palate has to contract upward. The defect on the posterior pharyngeal wall can be closed by primary suturing or can be allowed to heal by cicatrization. In either case it produces narrowing of the pharynx. The flap should occlude most of the nasopharyngeal airway, leaving a gutter on either side. These lateral openings permit the drainage of nasal secretions and allow for the escape of the air needed for certain sounds, such as M and N. Electromyographic studies suggest that the pharyngeal flap functions as a muscular element.[37] However, its effectiveness usually is considered to be due to physical obliteration of the nasopharyngeal space.

Since some forms of cleft palate are known to have poor functional postoperative results, the use of a concomitant pharyngeal flap at the time of the primary repair was suggested.[27] Some surgeons rely on the pharyngeal flap to achieve velopharyngeal competence and perform only a simple repair of the cleft palate. We believe that the pharyngeal flap should be used only when nasopharyngeal competence cannot be established by retroposition of the palate at the time of the primary repair, so that it should not be needed in more than 25 per cent of cases.

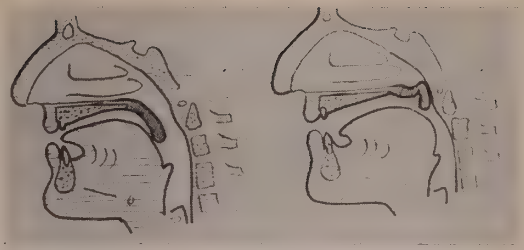

FIGURE 8. Velopharyngeal closure. Lateral projections of positions assumed by soft palate during phonation as verified by cineradiographic technics.

Technics for evaluation of palatal function

In recent years new technics have been developed which permit a better evaluation of palatal insufficiency and contribute to a better understanding of the function of the palate and oropharyngeal structures in speech and swallowing. Soft-tissue x-ray visualization and rapid picture-taking technics made it possible to demonstrate the position of the palate, the tongue, and the pharyngeal wall during the enunciation of various sounds. This led to the development of cineradiography of the functioning palate. The image intensifier has made it possible to film the functioning palate without exposing the patient to excessive radiation, which is particularly hazardous in children. From cineradiography we have learned that in the normally functioning palate the middle third of the soft palate contracts upward and backward. It approximates to the posterior pharyngeal wall, which moves forward, above the level of the hard palate. Together, the soft palate and the pharyngeal musculature

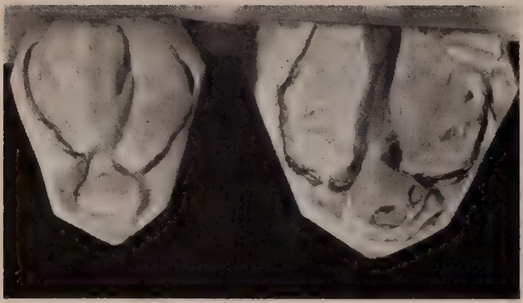

FIGURE 9. Orthodontic correction. Model at left illustrating constriction of dental arch in an infant with bilateral cleft lip and palate. This occurred a few months after repair of lip and prevented premaxilla from recessing into dental arch. At right, spreading of maxillary fragments with an expansion prosthesis, thus creating space for premaxilla.

occlude most of the nasopharynx (Fig. 8). The relative size of the nasopharynx and the ability of the palate to approximate the posterior pharyngeal wall can be demonstrated in lateral projection. However, this two-dimensional image does not take into consideration the three-dimensional pharyngeal space.

The competence of the nasopharyngeal sphincter can be evaluated better by the vital capacity test.[38] With a competent nasopharyngeal sphincter, the results of the vital capacity test will be the same with or without a clamp occluding the nares. In case of incompetence, there will be a great disparity between the results of the same test performed with and without the nasal clamp, since a large portion of the expired air will escape through the nose. In severe cases of velopharyngeal insufficiency, as much as 50 per cent of the expired air may escape through the nose if it is not occluded by a clamp.

Orthodontic treatment

The orthodontist, by introducing cephalometric measurement, focused attention on the normal and pathologic growth of the facial skeleton.[39] He also has come to play an ever-increasing role in the treatment of patients with cleft palate.

One controversial aspect of orthodontic treatment is its proper timing. Some orthodontists prefer to wait until the permanent teeth have erupted, since they have found that orthodontic correction completed at an early age requires the use of retainers for many years and additional orthodontic treatment at various times, particularly with the advent of permanent dentition. Others, however, feel that the orthodontic treatment of deciduous teeth is feasible and desirable and that the establishment of a functional occlusion will be followed by the eruption of the permanent teeth in a more favorable position.

The main challenge facing the orthodontist in treating patients with cleft palate is the constriction or collapse of the maxillary segments, particularly the short segment on the cleft side (Figs. 9 and 10). The maxillary teeth occlude on the lingual side of the mandibular dental arch, forming a "cross bite." This lingual locking of the maxillary teeth prevents normal development of the maxilla and influences unfavorably the vertical growth of the lower third of the face. The constriction of the maxilla not only results in poor occlusion but causes a noticeable deformity consisting of flatness of the middle third of the face. The high vaulted palate is likely to cause a severe buckling of the septum with obstruction and narrowing of the nasal cavities.

The early expansion of the maxillary segments at the age of three or four years seems desirable, even though orthodontic treatment in such small children is difficult. At this early age orthodontic treatment may shift not only the teeth, but also the entire maxillary segment.[40]

As soon as the first permanent teeth appear, at about six or seven years of age, the incisors and molars are treated to bring them into occlusion. The final orthodontic treatment is carried out when all the permanent teeth have erupted. At that time definitive occlusion can be established. Thus, the patient remains under orthodontic supervision from early childhood until virtual maturity. In special situations, orthodontic treatment has been used in infants before the eruption of any teeth.

Prosthodontic treatment

The trend toward conservative surgical repair of the cleft palate has stimulated the

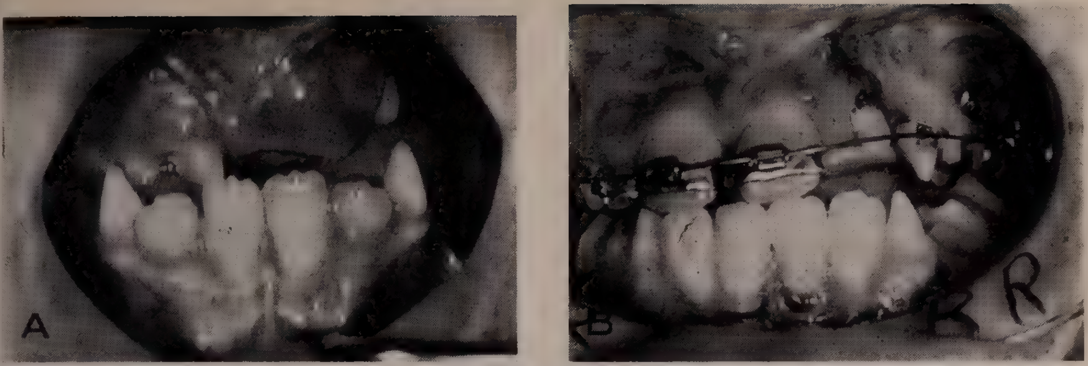

FIGURE 10. (A) Patient with unilateral complete cleft lip and palate presenting constricted maxilla, lingual tilt with displacement of maxillary teeth, and severe dental irregularities. (B) Same patient after completion of active orthodontic therapy prior to placement of retentive device. Note congenitally missing and unerupted teeth which will be dealt with after all permanent teeth are erupted. (Courtesy of A. Fingeroth, D.D.S., and M. Fingeroth, D.D.S.)

development of palatal prosthesis. The highly specialized skill of the prosthodontist is now available in many cleft palate rehabilitation programs.

Palatal prosthesis with the pharyngeal component or bulb can effectively restore near-normal speech. This is accomplished by the contraction of the pharyngeal musculature and the cleft palate around a rigid bulb, thus simulating the velopharyngeal sphincter mechanism.[41] However, this bulky oral appliance requires frequent cleansing, adjustment, and maintenance. The patient is kept aware of his disability and often resents the prosthesis. In a very wide, U-shaped posterior cleft with obvious hypoplasia of the palatal elements, such a prosthesis may be indicated permanently or temporarily. It stimulates the pharyngeal musculature to maximum performance and thus may be helpful after future repair of the palate. However, since most of these patients require a supplementary procedure, such as a pharyngeal flap, the long-term advantage of delaying the operative intervention is questionable. Moreover, facilities to construct and fit such a prosthesis, particularly for children, are not always available.

In addition to the construction of a speech prosthesis, there are other opportunities for the prosthodontist's skill in the rehabilitation of the child with a cleft palate. In severe deformities of the dental arch, for example, a partial dental prosthetic replacement often is necessary and can contribute a great deal toward a successful outcome. When the premaxilla is displaced, in cases of bilateral cleft lip and palate, prosthetic restoration of the anterior dental arch can salvage an otherwise hopeless situation.

Speech

Today, neither the surgeon nor the speech therapist is satisfied with intelligible speech alone. Intelligible speech is not enough when normal speech, without any stigmata of cleft palate, is attainable.

Normal speech depends on a multitude of interacting factors. The column of air coming from the lungs and the vibration of vocal cords are not affected in patients with cleft palate. The most important consideration is the distribution of the column of air when it enters the oral cavity. In cases of velopharyngeal incompetence the patient may be unable to develop the intra-oral pressure needed for pronouncing the explosive consonants. While this is the primary defect in a cleft palate patient, there are many secondary ones. It is within the oral cavity that the sound becomes articulated with the help of the tongue, the teeth, and the lips. Dental deformities, particularly those affecting the front teeth, rigidity of the lip, and poor motility of the tongue, thus severely affect articulation.

As the first step in the rehabilitation of these patients, the speech pathologist analyzes the speech and pinpoints the nature of the difficulty. This is essential before any corrective speech therapy is undertaken. Physical defects should be corrected before any intensive speech treatment is begun.

Many patients will speak normally after the repair of a cleft palate without intensive speech therapy. Nevertheless, each child's speech should be evaluated by a speech pathologist as early as possible, usually at about three years of age. This will permit the detection of certain weaknesses, and corrective measures can be initiated before faulty speech habits develop. The speech therapist also will aid the parents to help the child who is just beginning to talk to develop normal speech. In some instances intensive and prolonged speech therapy may be required.

Otolaryngologic aspects

Every child with a cleft palate should have an otolaryngologic evaluation and an audiometric test before he enters school. Ear infections are frequent in this group, although sometimes they are so mild that they are not detected clinically. Audiometric examinations reveal a surprisingly large number of subclinical hearing losses among these children.[42] It has been shown statistically that hearing is preserved better in children in whom the cleft palate has been repaired early than in those in whom repair has been delayed. It is not unusual to find a substantial hearing loss to explain a child's poor response to speech therapy. A progressive hearing loss may require an adenoidectomy with or without tonsillectomy. This operation should not be delayed if there is a danger of deafness. The adenoid pad in the nasopharynx usually helps to establish nasopharyngeal closure because of its space-occupying role.[43] Even if adenoidectomy is performed most carefully and consists only of cleaning the area around the eustachian openings, there may be a noticeable increase in the nasality of the speech. This usually can be overcome in time, but it may remain permanently in cases of borderline palatal insufficiency.

Psychiatric evaluation and guidance

The emotional development of the handicapped child will reflect the attitudes of his parents and family. Parents burdened with feelings of resentment and guilt can compound their child's difficulties by being either overly protective or overly rigid and demanding. The objective of parents in their handling of a youngster with a physical impediment is to help him develop enough self-assurance and self-acceptance to be able to function to his fullest capacity. Psychiatric and psychologic evaluation of the child and parents is aimed at determining realistic goals for the child's achievement and at helping the parents to resolve their conflicting emotions and to accept their role as parents of a handicapped child.

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Etiology of paronychia

Tight adherence of the eponychium to the base of the nail probably is the best natural protection against pyogenic infections in this area, according to an article by Robert B. Benjamin, M.D., in the January, 1962, issue of *Minnesota Medicine*. This conclusion is suggested by a study of 37 patients with such digital infections and 50 normal controls. In 73 per cent of the fingers of paronychia patients, it was noted that the eponychium was separated from the surface of the nail, whereas this condition prevailed in only 32 per cent of the control fingers.

Even careful manicuring, although it may not cause direct injury to the finger, tends to elevate the eponychium and interfere with its normal adherence, allowing pyogenic organisms access to the soft tissues around the nail. It was found that children are still taught to push back the cuticle by one means or another, to "show the moon." This practice is also promoted by glamor magazines by their illustrations of the "long look" achieved both by pushing back the cuticle and by allowing the nails to grow long.

Paronychia is an important disease. The average patient with this trouble is absent from work five to eight days, resulting in millions of man-hour losses in every civilized country. Yet no one up to now has considered the infection of sufficient importance to carry out a study on the etiology of the disorder.

Clinicopathologic Conference

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WILLIAM B. OBER, M.D., Editors

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Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by THOMAS SILVERBERG, M.D.

Arthritis, Anemia, and Renal Failure

Case history

Salvatore Baldino, M.D.: A thirty-eight-year-old Negro female was admitted to Knickerbocker Hospital for the fourth time in September, 1961, because of nausea, vomiting, and shortness of breath of several weeks duration. She had a long and significant past history.

At the age of thirteen years, in the British West Indies, she had had a febrile illness associated with multiple joint pains and a skin lesion consisting of pigmented and depigmented spots over the entire body. She was treated at home by a doctor. At the age of twenty-eight, following a premarital examination, she was found to have positive serologic reactions and was given a course of penicillin injections. In 1953 she was admitted to a hospital in Connecticut after the sudden onset of pain in her hands, knees, and ankles. The presumptive diagnosis of rheumatoid arthritis was made. The patient was discharged after one week with no medication. For a month she was asymptomatic; thereafter, the joint pains recurred and seemed to get progressively worse. In addition, she noted increased pigmentation of her face and ears and the loss of a considerable amount of hair. For these reasons she was first admitted to Knickerbocker Hospital in April, 1954.

A physical examination revealed a young Negro female in moderate distress who complained of joint pain. The blood pressure was 110/70 and the temperature was 101 F. There was deep pigmentation of the bridge of the nose, the upper lip, both cheeks, and the right ear. The lung fields were clear. The heart was not enlarged and an apical systolic murmur was heard. No abdominal organs or masses were palpable. The fingers, wrists, elbows, and knees were red, hot, swollen, and tender. There was no significant lymphadenopathy.

Laboratory data included a hemoglobin of 12 Gm. per 100 ml. and a white blood count of 6,200 with a normal differential count. Many specimens of urine were analyzed and revealed a trace to 3 plus albumin. An examination of the sediment revealed many white cells, occasional red cells, as well as coarse and granular casts. The specific gravity ranged from 1.010 to 1.023. The erythrocyte sedimentation rates varied from 40 to 108 mm. per hour. The VDRL was 2 plus. The nonprotein nitrogen was 36 mg. per 100 ml. The serum albumin was 2.29 Gm. and globulin 4.21 Gm. per 100 ml. Lupus erythematosus cells were seen in the peripheral blood as well as in bone marrow. X-ray films of the chest and joints showed normal findings.

The patient was treated with aspirin and cortisone. After three months in the hospital she was discharged to the outpatient clinic and advised to take 125 mg. of cortisone daily. She appeared to do well for about five months, when her joint pain recurred and she was readmitted. At this time she had swelling of her wrists, elbows, and knees. The rest of the physical examination was as before. Her urine again contained albumin, clumps of white cells, and many casts. The erythrocyte sedimentation rate was over 100 mm. per hour, and the L.E. preparation again gave positive findings. The patient was treated initially with large doses of steroids until she was symptomatically improved. A maintenance dose of 75 mg. of cortisone per day was continued on discharge.

In June, 1955, the patient was admitted to another hospital because of severe joint pain and fever. There was no change in the physical examination as reported. Multiple joints were red, swollen, and tender. Her hair was sparse, and there was a pigmented rash on the face. Her urine contained 2 plus albumin, occasional granular casts, and white cells. The hemoglobin was 8.5 Gm. per 100 ml. and the white blood count 3,400. The blood urea nitrogen was 25 mg. per 100 ml. The sedimentation rate was 68 mm. per hour. The VDRL test was 1 plus. An L.E. preparation again gave a positive reaction. A sheep cell agglutination test showed negative results, and the C-reactive protein was 4 plus. The patient was treated with steroids and chloroquine and was discharged improved on prednisone (Meticorten), 10 Gm. daily, and chloroquine, 500 mg. daily.

For the next four years the patient was followed in the clinic and received varying doses of prednisone. She had intermittent episodes of joint pain but none was severe. In September, 1959, she was admitted to the hospital for renal biopsy. Significant laboratory data included a hemoglobin of 12 Gm. per 100 ml., blood urea nitrogen 27 mg. per 100 ml., and serum albumin 3.6 and globulin 3.6 Gm. per 100 ml. Serum electrophoresis demonstrated an albumin of 43 per cent, alpha-1 globulin 6 per cent, alpha-2 globulin 15 per cent, beta globulin 14 per cent, and gamma globulin 22 per cent. A twenty-four-hour urine collection contained 1.4 Gm. of protein. The phenolsulfonphthalein excretion was 12 per cent in fifteen minutes and 54 per cent total in two hours. An L.E. preparation reacted negatively.

In April, 1961, the patient was admitted to Knickerbocker Hospital for the third time. She complained of persistent vomiting and headache of about five weeks duration. There was no relationship of vomiting to food or meals, and the vomitus did not contain blood. She had lost 25 pounds in weight during this period. The blood pressure was 180/120. The fundi showed narrowing of the arterioles with arteriovenous nicking and several flame-shaped hemorrhages bilaterally. The lungs were clear, and the heart sounds were of good quality. A neurologic examination was unremarkable.

The hemoglobin on admission was 7.3 Gm. per 100 ml. and the white blood count 9,200. The urine had a specific gravity of 1.010, contained 3 plus albumin, occasional red cells, and 5 to 7 white cells per high-power field. An L.E. preparation gave negative results. The nonprotein nitrogen was 151 mg., creatinine 12 mg., calcium 6.8 mg., and phosphorus 9.9 mg. per 100 ml. The serum albumin was 3.2 Gm. and globulin 2.3 Gm. per 100 ml. A chest x-ray film showed generalized cardiac enlargement. The serology showed negative results. The phenolsulfonphthalein excretion was markedly impaired. The patient was continued on prednisone and given supportive care. Although there was no change in her blood chemical values, she improved symptomatically.

In June, 1961, the patient was admitted to another hospital because of vomiting and shortness of breath. She was reported to be in moderate congestive heart failure, and her blood chemical values were consistent with uremia. She was given digitalis and diuretics followed by symptomatic improvement.

In September, 1961, the patient was admitted to Knickerbocker Hospital for the last time. She complained of persistent nausea, vomiting, fatigue, and weakness. The blood pressure was 190/120, temperature 98.4 F., pulse 100 and regular, and respirations 18 per minute. She appeared acutely and chronically ill with marked facial pallor. The fundi again showed hemorrhages, exudates, and arterioventricular nicking. The neck veins were distended, and there were rales in both lower lung fields. The liver was 2 fingerbreadths enlarged and tender. There was 2 plus pitting peripheral edema.

The hemoglobin was 5.5 Gm. per 100 ml. and the white cell count 18,000 with 87 per cent polymorphonuclear leukocytes. The nonprotein nitrogen was 369 mg., creatinine 16 mg., calcium 6.8 mg., and phosphorus 14 mg. per 100 ml. The serum potassium was 6.6 mEq. per liter.

The patient was transfused with packed red cells, given intravenous calcium gluconate, and was started on 75 mg. of prednisone per day. On the second hospital day she became semicomatose. Shortly after this her blood pressure fell to 100/40. In spite of emergency measures she died on the third hospital day.

Discussion

Thomas Silverberg, M.D.*: To a considerable extent, if not entirely, today's clinicopathologic subject can be discussed as an open case. For I think there is hardly room for doubt that the patient's primary disease throughout her long and intensely interesting course was well established as disseminated lupus erythematosus. As a matter of fact, if there is such a thing as a classic case of lupus, this one fits that designation. We are dealing with a disease involving multiple systems, progressive in its development, beginning in a young female at the age of thirteen and encompassing over the next twenty-five years such manifestations as fever, arthritis, skin lesions, alopecia, anemia, leukopenia, hyperglobulinemia, positive serologic test results, renal insufficiency, and terminal uremia with hypertension and severe congestive heart failure. In addition, we are told that the patient had positive L.E. cell test results on both peripheral blood and bone marrow in 1954 and again in 1955. On the basis of all this, by any set of criteria that would be accepted today, the diagnosis of systemic lupus must be made, and we ought certainly to expect that the pathologist will show us evidence to confirm it. More than that, we ought to insist that he bear out such a clear-cut clinical and laboratory picture. There seems to be no way to beg this issue; for when the L.E. test results were positive the patient was not on penicillin, or Apresoline hydrochloride, or any other drug that might have produced the L.E. phenomenon without the disease itself. Likewise, the patient rather obviously did not have scleroderma or dermatomyositis as the disease causing a positive L.E. test reaction. Finally, to try to split hairs and distinguish between systemic lupus and rheumatoid arthritis with a finding of positive L.E. preparation is little better than an exercise in scholastic logic. For there seems to be no real difference between them.

Accepting both the genuineness of the L.E. tests and the fact that the patient had systemic lupus, it might be well to review just the high points in her course as they are set out in this long and excellently prepared protocol. At thirteen years of age the patient first became ill with polyarthritis, fever, and generalized skin lesions, described as pigmented and depigmented spots. The nonspecificity of the skin changes is not in the least disturbing, since lupus is often associated with a variety of skin lesions, some of them quite different from the classic erythematous plaque-like butterfly rash. She was treated, we do not know how, and presumably went into a prolonged remission. Her disease seems to have been quiescent for the next seventeen years. However, two years before any symptoms returned, she was found to have a positive serologic test result for syphilis and was given a series of penicillin injections forthwith. Interestingly, and we might say providentially, she was not hypersensitive to the penicillin. In 1953, when the patient was thirty, she developed polyarthritis for the second time. On this occasion, what seems to have been a purely clinical diagnosis of rheumatoid arthritis was made. Accompanying the joint involvement went increased pigmentation of the face and ears and the loss of a good deal of hair. A year later she entered Knickerbocker Hospital for the first time. She presented herself with fever; objective evidence of an inflammatory polyarthritis; deeply pigmented areas over the cheeks, bridge of the nose, upper lip, and right ear; and a systolic cardiac murmur. Her liver and spleen were evidently not palpable, and no enlarged lymph nodes were found. Her blood count was normal at that time. The sedimentation rate was consistently elevated; the VDRL test was 2 plus positive; and an analysis of her serum proteins showed a slightly lowered albumin fraction and moderately elevated globulins. Although her nonprotein nitrogen was essentially normal, there were significant urinary findings: consistent proteinuria up to 3 plus, pyuria, occasional red blood cells, and coarse and granular casts. At this time L.E. cells were found on an examination of the bone marrow and peripheral blood.

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The patient was then treated with large doses of steroids and showed improvement for several months. In 1955 she was again disabled by arthritis and fever. When she was studied at another hospital her physical findings were unchanged. However, she was now found to be moderately anemic, and her white blood count was reported as 3,400. The urinary abnormalities were approximately the same, and the blood urea nitrogen was slightly elevated to 25 mg. per 100 ml. The L.E. test result was positive, the sheep cell agglutination test finding negative, and a C-reactive protein 4 plus.

On continuous steroid therapy and some treatment with chloroquine, the patient remained fairly well during the next four years. When she came back to Knickerbocker Hospital for a renal biopsy in 1959, it is interesting that anemia was not found.

Dr. Baldino: The renal biopsy was not done here; it was done at another hospital.

Dr. Silverberg: Thank you. The blood urea nitrogen was almost unchanged after the four-year interval, phenolsulfonphthalein excretion test showed a marked diminution of renal function, especially for the first fifteen-minute period. Serum electrophoresis showed a lowered albumin fraction but an almost normal globulin pattern. At this time, with the patient on prolonged prednisone medication, the L.E. preparation reaction was negative.

Two years later the patient developed signs of terminal illness. She complained of headaches, vomiting, and weight loss. She was hypertensive, had cardiac enlargement, and showed eyeground changes typical of end-stage renal or malignant hypertensive disease. The nonprotein and creatinine values had soared to grim levels, and the urine showed moderate amounts of protein, microscopic hematuria, pyuria, and a fixed specific gravity. Anemia, this time without leukopenia, was present. The serologic test for syphilis gave negative results, and so did the L.E. test. The remainder of her course took five months during which there was a steady progression of uremia and finally the appearance of congestive heart failure, very severe anemia, and hyperkalemia. In spite of desperate efforts to prolong her life, she expired quickly.

Only ten or fifteen years ago the length of this patient's life span from the onset of her disease would have raised serious doubts in most minds as to whether she could have had systemic lupus from the start. To quote a fairly recent comment by Dameshek,[1] "Some years ago, when diagnosis seemed easier than it is now, lupus was invariably thought of as a rapidly fulminating disease of perhaps a year or two in duration, characterized by fever, weight loss, facial eruption, joint involvement, non-bacterial verrucal endocarditis, splenomegaly, leukopenia, and renal disease. This picture seems to have changed and there can be no question of the relative mildness and lengthy course of many cases of the disease." Dameshek's comment expresses the time concept of lupus that now prevails, and our patient, who survived for twenty-five years, would no longer be thought of as an exceptional case.

Our picture of systemic lupus has broadened and deepened in many other respects as well. Although we are still in the dark as to its ultimate cause, we can use the experimental discoveries that in recent years have thrown so much light on its pathogenesis, and from this knowledge gain a more penetrating view of the disease.

A number of recent investigations have shown that systemic lupus is fundamentally a complex disorder of auto-immune mechanisms involving a variety of factors which are present in the serum to which one or another body tissue or particular cell type has become specifically sensitized. The factors which seem to possess antigenic properties have been tracked down and localized to the gamma globulin protein fraction. They are gamma globulins with molecular weights of about 150,000 and have been assigned to the 7-Svedberg unit fraction on ultracentrifugation. L.E. factors have been found which act on red cells (producing autoimmune hemolytic anemia), platelets (producing thrombocytopenic purpura), leukocytes, prothrombin, thromboplastin inhibitors, thyroglobulin, kidney, heart, and liver cells. These abnormal gamma globulins are responsible for the positive Coombs test results, positive serologic reactions, and finally, for the L.E. cell phenomenon itself. This last involves highly specific antinuclear factors which may react with whole nuclei, nucleoprotein, or the substituent desoxyribose nucleic acid and histone. The evidence for the immunologic nature of these reactions seems convincing. The antigenic factors are gamma globulins; gamma globulin is actually found on the target cells or tissues, and its reactions are attested by complement fixation, precipitation tests, hemagglutination tests, and even by passive cutaneous anaphylaxis.

How does all this help us understand some of the things that happened to our patient?

Most probably it explains the finding of a positive serologic test result for syphilis that persisted from 1951 until shortly before her death. Unfortunately, no further tests were done to assay her serum against the Treponema itself, so that this point cannot be proved. The appearance of anemia and leukopenia simultaneously, and at a stage when renal impairment was not yet marked, suggests strongly that both a leukoagglutinin and an antierythrocyte factor were present. Here it is interesting, although certainly a very speculative point, that at a later date, when the patient had more severe renal disease but was on steroid therapy, both the anemia and leukopenia had disappeared. Was the steroid administration suppressing an allergic reaction that had been going on a year or two earlier?

Taking the period from the beginning of the illness to the appearance of renal failure, I feel reasonably sure that the story is lupus, all lupus, and nothing but lupus. If there is a joker in the deck, I suspect we are going to find it buried in what took place when the patient's kidneys began to fail. Not that there is anything strange about a case of lupus ending in renal failure and death in uremia. At first glance it seems perfectly reasonable and, by all accounts, an acceptable and orthodox way to finish the disease. But there are a few points that make one pause a moment for thought. Soffer and his colleagues[2] very recently reviewed the renal manifestations of systemic lupus in 90 patients who had been seen on The Mount Sinai Hospital Medical Service from 1949 to 1959. They came to some interesting conclusions. One of them was that "there appeared to be an inverse correlation between the incidence of renal involvement and the age of the patient." Out of 90 patients a total of 53 showed renal involvement at the time of the initial diagnosis; 61 per cent of these were under thirty years of age. Of 34 patients who had no evidence of renal injury, 22 (or 65 per cent) were over the age of thirty.

They also noted that "those patients who had impairment of renal function generally manifested it early in the course of the illness. The longer the disease continued without the development of this complication the less likely was it to occur." This is illustrated by the observation that of the 56 patients with renal lesions, 53 already had this complication at the time of the initial hospital admission. The other 3 patients developed it within one to three years.

If these observations are significant, there may be a reason for questioning whether or not our patient simply developed a lupus kidney at the end of a very long course and at the ripe old age of thirty-eight. This would make her a little exceptional, although still part of a substantial minority.

Sifting over the progression of her renal disease, its hypertensive and cardiovascular consequences, and the physiologic observations that are detailed does not help me much. The memory of making a wrong etiologic diagnosis on a similar occasion and on another patient with end-stage kidneys still burns when it is provoked. Bright's disease is Bright's disease, and it is often perilous to try to pick out the chronic pyelonephritic kidney from the chronic glomerulonephritic kidney from the malignant hypertensive kidney, and so on.

Let me sum it up this way. My primary diagnosis is disseminated lupus erythematosus. In the interests of consistency and the neatness of a single diagnosis I hope that the kidneys, along with the spleen and perhaps other organs, will show the pathologic changes of lupus. However, I will not be astonished if Dr. Ober demonstrates for us the typical kidney of malignant nephrosclerosis, chronic pyelonephritis, or chronic glomerulonephritis. As to whether we will see a verrucous endocarditis, I would rather not guess.

MICHAEL S. BRUNO, M.D.: For some time it has been considered axiomatic that the development of nephritis in a patient with systemic lupus was ominous and unresponsive to steroid administration. It was considered a prognostic guidepost. Recently, however, with very large doses of steroids, the nephritis picture seen in some cases of systemic lupus has been reversed. It would appear to be a matter of dosage and good fortune. The development of nephritis in these patients does not necessarily augur a grim prognosis.

MARDOQUEO I. SALOMON, M.D.: Friedman *et al.*[3] have pointed out that about 30 per cent of patients with rheumatoid arthritis have positive L.E. preparation results and that this phenomenon is not modified by medication. Also, recently I have seen an article which tried to demonstrate that lupus erythematosus and chronic glomerulonephritis are one and the same disease.

DR. SILVERBERG: In the first blush of our enthusiasm for immunohistochemistry as a tool, let us not be carried away by that fact that although the tissues in a number of diseases such as lupus, rheumatoid arthritis, and a variety of glomerulonephritides share in common the capacity to bind fluorescent antibodies, the distinctions among them are still very real. I don't think we should be surprised that the L.E. phenomenon can be demonstrated with some frequency in diseases related to lupus. The value of the test lies in the fact that in most cases of untreated lupus the reaction is positive and, therefore, it is a good screening test. However, the diagnosis of lupus, like that of any other disease, does not hinge on one test alone.

I don't really know to what extent renal lesions are reversible. However, the proponents of the use of corticoids in lupus base their hopes on the idea that progressive glomerular involvement may be influenced; that is, that even if lesions are not reversed, they can be held stationary.

MAXWELL L. GELFAND, M.D.: I wonder if we are dealing with the same sort of lupus erythematosus that I was taught about some twenty years ago. The traditional concept of lupus is that it is a progressively fatal disease, the outcome being resolved in about three or four years. This patient had an abnormal urinalysis as far back as 1955, some six years ago, and her renal involvement may not have been of such recent origin. Indeed, the literature contains reports of patients surviving ten and fifteen years following the convincing establishment of a diagnosis of lupus.

DR. BRUNO: I think we are detecting many of the less aggressive cases by newer laboratory methods. Also, we have been sensitized to this diagnosis by virtue of the great strides made in our understanding of it. As for improved survival, I think that steroids have significantly improved the prognosis. Even though we must always maintain an attitude of healthy skepticism regarding the claims of any form of therapy for any disease, there are occasions when we can take a bit of credit for healing the sick.

PERRY BERG, M.D.: I have seen cases signed out by pathologists as "atypical glomerulitis," also as "atypical membranous glomerulonephritis," in which the clinical diagnosis of lupus was well established. One does not have to have a wire loop to die of lupus nephritis.

Clinical diagnosis

1. *Systemic lupus erythematosus with lupus nephritis*
2. *Hypertensive cardiovascular disease, secondary*
3. *Uremia*

Dr. Silverberg's diagnoses

1. *Systemic lupus erythematosus with lupus nephritis*
2. *Secondary hypertension with cardiac hypertrophy*
3. *Uremia*

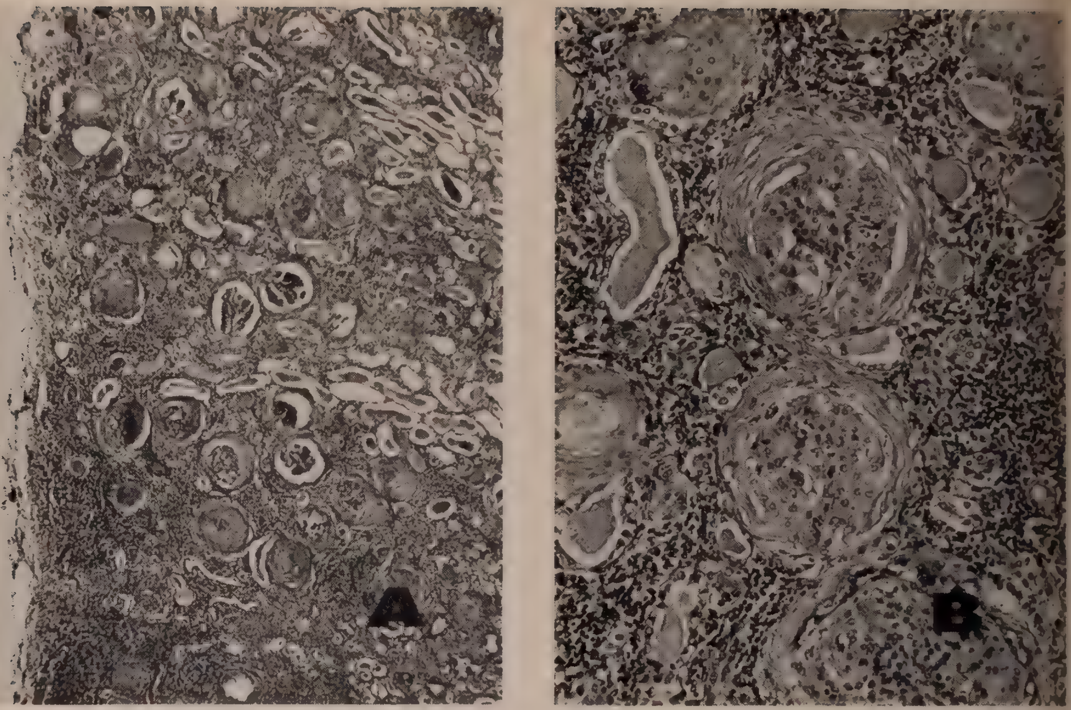

FIGURE 1. Kidney. (A) Low-power view showing diffuse scarring and lymphocytic infiltration of chronic pyelonephritis. (B) Medium-power view showing two partly scarred glomeruli with concentric lamellar periglomerular fibrosis, lymphocytic infiltration, and hyaline casts in tubules, all consistent with chronic pyelonephritis.

Pathologic report

William B. Ober, M.D.: It is perfectly true that our ideas about systemic lupus erythematosus have broadened considerably over the past generation as the technics of protein electrophoresis, fluorescent microscopy, electron microscopy, and histochemistry have contributed to the area subsumed under the general term autoimmune phenomena. Shifting concepts and their elaboration in regard to this disease are the substance of a penetrating historical chapter by Klemperer[4] who knows more about the morbid anatomy of the disease than anyone else. By way of analogy, consider what was known of pneumonia in 1862. It was a recognized disease, but the mechanisms underlying its clinical manifestations, to say nothing of its etiology, were only dimly perceived. Over the next generation the discipline of bacteriology evolved, and we gained a great deal of insight into the various causes of pulmonary infections, their morbid anatomy, their pathologic physiology, and so on. Yet even today, in such a reasonably well-defined and readily recognizable entity, clinical and experimental investigations are still furnishing us with new information and new insights. It is perfectly true that lupus isn't what it was when I was a boy. The discussion in a recent clinicopathologic conference at the Massachusetts General Hospital points out clearly that pathologists can re-evaluate old material and find that it fits into our present-day concept of lupus erythematosus and reverse the diagnoses so proudly made a generation ago.[5] The judicious application of the retrospectroscope can be one of the most rewarding experiences in pathology.

To answer the question, What is lupus?, we must first consider that old fiction, the eye of the beholder. If we classify all patients with a complex of joint pain, fever, disordered globulins, possibly a skin rash, possibly some urinary findings, and a positive L.E. preparation reaction to have lupus, we will probably trap most of such

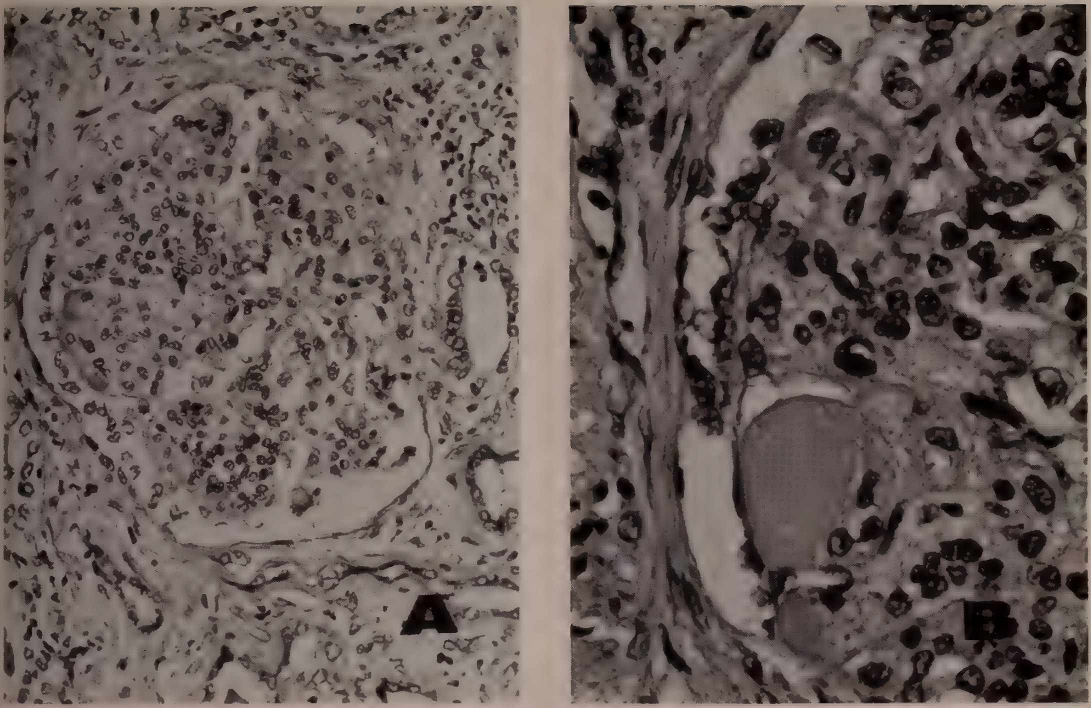

FIGURE 2. Glomerulus. (A) High-power view showing an adhesion and thickening of the periphery of one capillary loop to form a refractile, eosinophilic, wirelike structure, consistent with the renal lesion of systemic lupus. (B) Detail of another glomerulus showing a typical "wire loop" above and an amorphous blob of mucopolysaccharide-rich material below. The cellular detail of an early glomerular synechia is also seen.

cases in our net. We will also include some allied disorders which might well be distinguished from lupus when the final score is added up. However, if we limit the diagnosis of lupus to patients with a characteristic vasculitis, glomerulitis, and splenic periarterial lamellar sclerosis, we will obviously exclude a considerable number of patients who really have lupus. It is one thing to observe a patient with a fluctuating course and a host of variable symptoms related to a number of different systems for a period of years; it is quite another thing to look at a few thin slices of such a patient's entrails through a narrow tube fitted with some polished glassware. I do not think we have yet achieved a correlation of clinical phenomena with pathologic observations that would satisfy a statistician's concept of "goodness of fit"; however, as the years go on, we are getting closer to it. Operating under the limits of current knowledge, I think it is reasonable to say that, given a suitable history supported by corroborative laboratory tests (most notably a positive L.E. preparation result), pathologists can support a diagnosis of systemic lupus erythematosus. Conversely, given a set of unknown sections in which reasonably consistent lesions are present, most pathologists would consider lupus as a very likely diagnosis provided the other pieces fitted into the puzzle.

However, such security as we may have as microscopists is somewhat shaken by the well-known fact that the distribution and nature of the lesions of systemic lupus can vary widely from case to case. The vasculitis is certainly not a demonstrably specific lesion. It resembles closely the lesions of periarteritis nodosa,[6] other types of collagen disease, and allergic vasculitis of known and unknown cause. Many of the lesions we have come to associate with lupus can be modified and even abolished by prolonged steroid therapy, and it is a rare

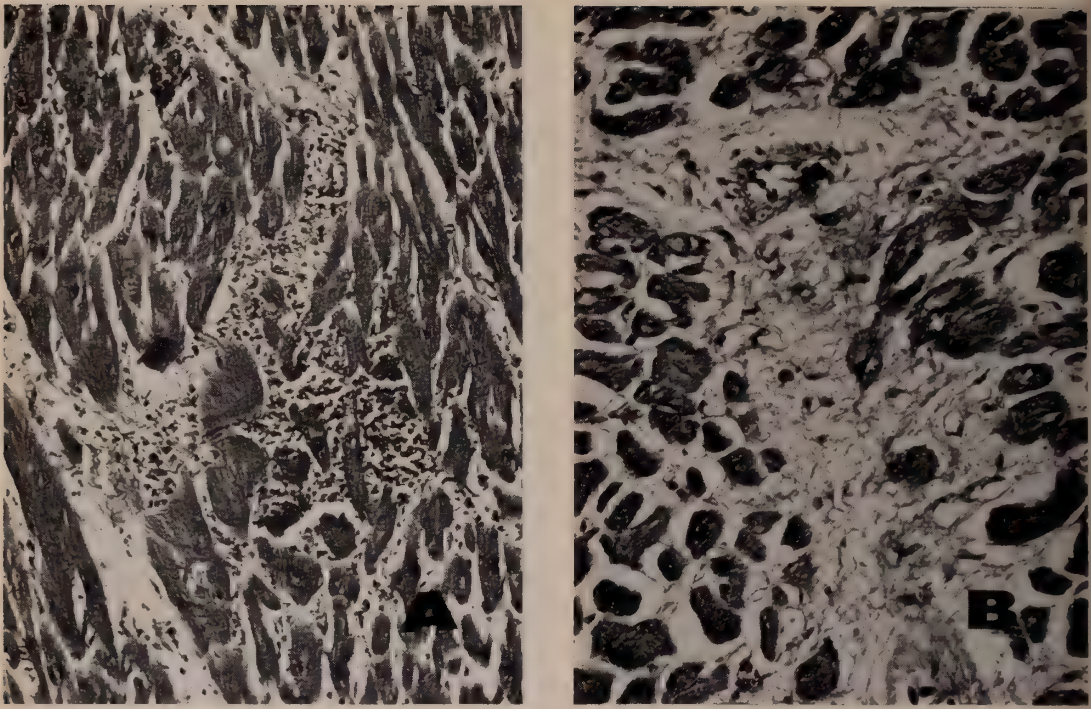

FIGURE 3. Myocardium. (A) Exhibits focal infiltration by leukocytes, interpreted as lupus myocarditis. (B) Elsewhere the myocardium shows swelling of the ground substance.

case that comes to autopsy nowadays without having had the benefit of steroid therapy.

Speaking personally, I find it extremely difficult to diagnose systemic lupus on the basis of a skin biopsy, and discussion with many of my colleagues convinces me that this is not owing to my own amblyopia. Probably the optimal material that can be sent to a pathologist in a suspected case of systemic lupus is a needle biopsy of the kidney from an untreated patient. Muehrcke *et al.*[6] have illustrated in detail the characteristics of the glomerulitis. Farquhar, Vernier, and Good[7] have demonstrated that when the glomerular lesion of systemic lupus is seen with the electron microscope, it consists of a more or less generalized thickening of the basement membrane proper, associated with a variable degree of endothelial proliferation. They suggest that an accentuation of the process of basement-membrane thickening results in the "wire loop" appearance seen by light microscopy.

In this patient we have a rather complex situation. A needle biopsy of the kidney was taken about two years before the patient's death and interpreted as consistent with chronic pyelonephritis. In the meantime, the clinicians were unswerving in their opinion, based on the history, physical findings, and laboratory studies, that the correct diagnosis was systemic lupus. I must confess that I am a bit surprised that in face of a diagnosis of chronic pyelonephritis on renal biopsy that there is no mention of a urine culture.

Dr. Baldino: In June, 1959, a urine culture at the hospital where the renal biopsy was done did show Escherichia coli.

Dr. Ober: At autopsy the left kidney weighed 150 Gm. and the right kidney 110 Gm. Both were diffusely scarred, the right more so than the left, and they most closely resembled the gross kidneys of chronic pyelonephritis. This impression was borne out by the microscopic appearance. There was extensive cortical scarring, interstitial infiltration by lymphocytes, concentric periglomerular capsular fibrosis, alternation of atrophic tubules with dilated tubules, many

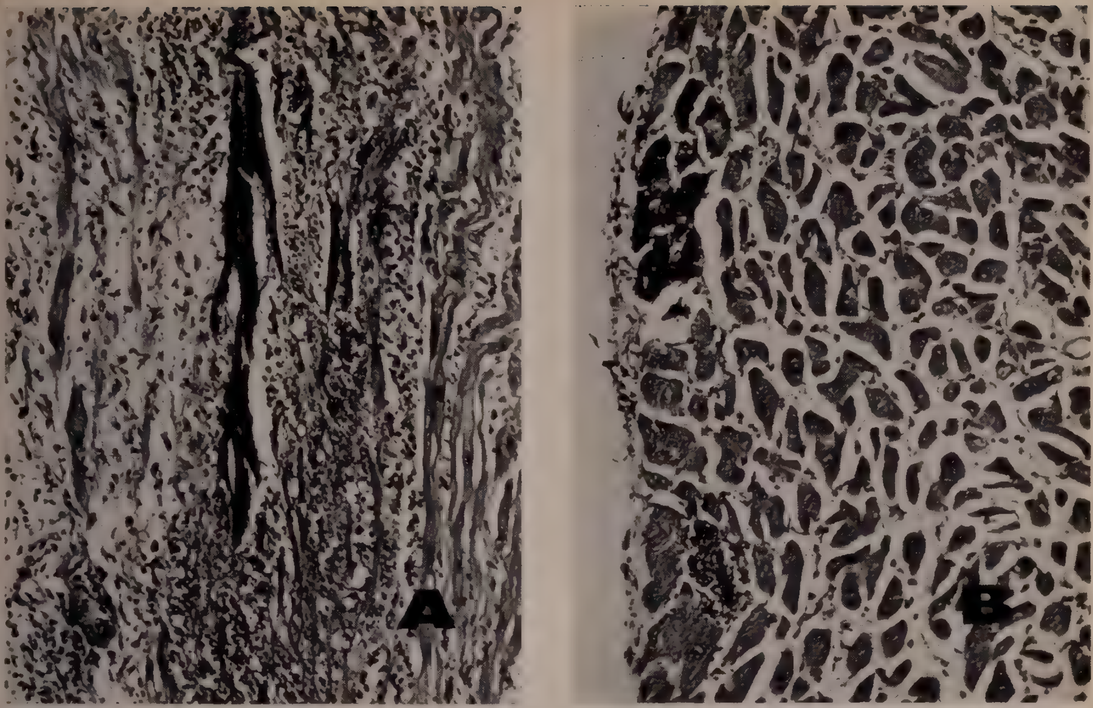

FIGURE 4. Myocardial fibers. (A) A calcified myocardial fiber lies longitudinally in a sea of polymorphonuclear leukocytic exudation. (B) Two subendocardial myocardial fibers cut transversely show calcification without nearby inflammation.

of which contained colloid-like casts (Fig. 1), and arterial hypertrophy. However, many of the partially scarred glomeruli showed increased cellularity and endothelial proliferation. In a compulsive mood, I counted 2,000 glomeruli and managed to find 2 of them in which I felt I could demonstrate the "wire loop" effect (Fig. 2). Thus, it would appear that the kidneys showed the lesions of both systemic lupus erythematosus and chronic pyelonephritis.

I was not able to find vasculitis in the kidneys or in any of the other organs. The spleen weighed 240 Gm., and its capsule was thickened. It did not show any of the supposedly characteristic periarterial lamellar sclerosis, but there was diffuse extramedullary hematopoiesis. The heart weighed 560 Gm. and showed hypertrophy consistent with hypertension of severity and long duration.

Microscopic examination of the heart revealed a focal myocarditis (Fig. 3A) and some nonspecific swelling of the ground substance (Fig. 3B) which I think is more likely part of the lupus than secondary to the uremia. Also, individual myocardial fibers were calcified. This peculiar phenomenon was seen both in areas of myocarditis (Fig. 4A) and in areas where there was no inflammatory reaction (Fig. 4B). Calcification of individual myocardial fibers is quite uncommon. One does see it adjacent to focal myocytolysis when there is concomitant uremia, and one does find similar calcification in the hearts of stillborn infants who die of a myocarditis or myocardial infarction sustained in utero. A fiber which dies abruptly of acute ischemia is unable to participate in ionic interchange and will not imbibe calcium, whereas a fiber that is slowly dying of ischemia can exchange sodium and potassium selectively for calcium, provided the extracellular equilibriums are favorable. Apparently such ionic transfer can occur in tissues of patients with uremia and in fetal tissue when blood stream clearance into the amniotic fluid is impaired by a failing fetal heart.

Heterotopic calcification was also seen in the media of hypertrophied renal interlobar

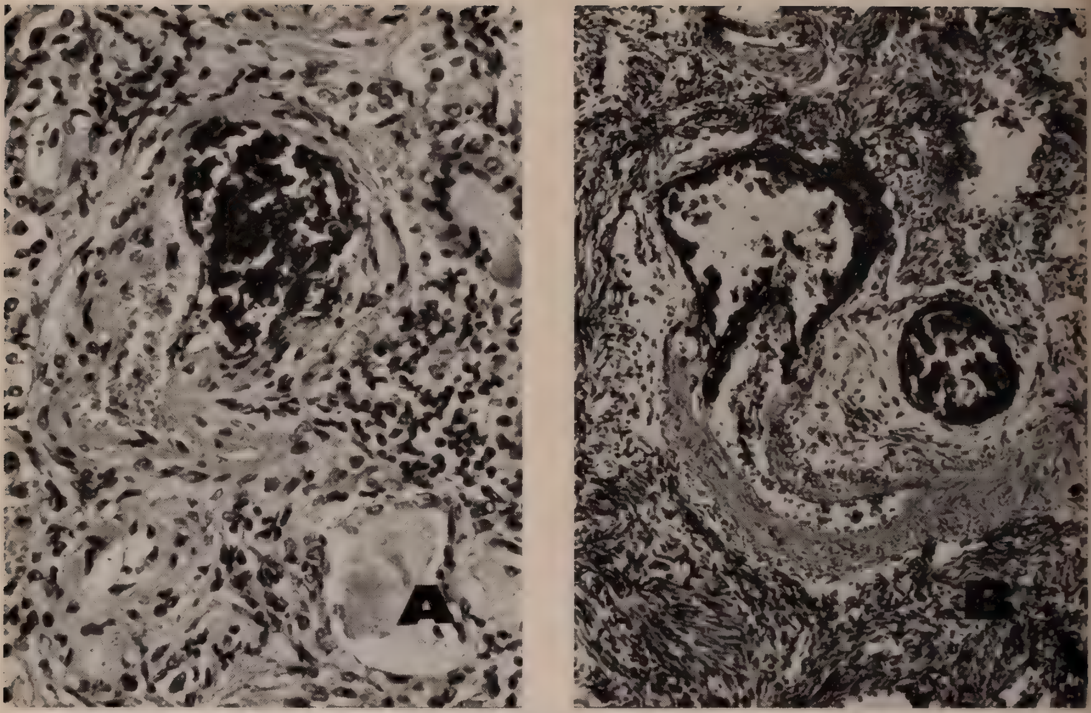

FIGURE 5. Calcification. (A) An oblique section through an interlobular renal artery shows a large plaque of calcification in the media. The endothelium is seen as a thin but well-preserved line of cells separating the calcific material from the blood-containing lumen. (B) An arteria recta of the uterus just beneath the endomyometrial junction exhibits calcification of its media.

and interlobular arteries (Fig. 5A) and in the arteriae rectae of the uterus immediately subjacent to the endomyometrial junction (Fig. 5B). I would not interpret these observations as showing a healed lupus arteritis but rather as a reflection of disordered calcium metabolism in uremia.

Anatomic diagnoses

1. *Systemic lupus erythematosus with nephritis and myocarditis*
2. *Chronic pyelonephritis, severe*
3. *(Uremia)*
4. *Cardiac hypertrophy, hypertensive type*
5. *Heterotopic calcification of myocardial fibers, renal and uterine arteries*
6. *Bronchopneumonia, terminal*

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Nutrition Excerpts

Prepared with the cooperation of the faculty
of the Graduate School of Nutrition,
Cornell University, Ithaca, New York

DAPHNE A. ROE, M.D., Editor

Nutrition and Neomycin-Induced Enteropathy

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THE OBSERVATION THAT AMMONIA formation in the intestine can be reduced and hepatic coma thereby frequently reversed or prevented by the use of orally administered neomycin[1] has been followed by observations on the nutritional and metabolic effects of this agent. These aspects of neomycin administration bear consideration in the therapy of cirrhosis and in the use of this antibiotic agent for intestinal flora reduction preoperatively.

The diarrhea which is commonly seen in patients receiving neomycin has been found to reflect a malabsorptive state similar in some respects to that seen in nontropical sprue.[2] Fecal excretions of fat, nitrogen, sodium, and potassium are increased to varying but significant degrees, and other parameters of absorption are also affected. Thus, the absorption of carotene, vitamin B_{12}, D-xylose, glucose, iron, and I^{131}-labelled trioleate is reduced, and serum cholesterol levels are lowered. Intestinal biopsies have revealed changes of the jejunal mucosa which are reminiscent of early sprue syndromes, namely clubbing of the villi, edema of the lamina propria, and round-cell infiltration.[3] A reversal of these changes occurs when the neomycin is withdrawn.

Some distinct differences between the neomycin-induced syndrome and naturally occurring sprue have also been found. The roentgenologic patterns of malabsorption have not been found, and urinary 5-hydroxyindole-acetic acid excretion is not increased when neomycin is given. The malabsorption is not reversed by the administration of hydrocortisone or the removal of gluten from the diet.[4] Protein loss into the intestinal tract, found in many sprue patients, has not been observed in subjects given neomycin as indicated by the failure of I^{131}-labelled polyvinyl-pyrrolidine to be found in excessive amounts in the stool and by the normal disappearance of I^{131}-labelled albumin from the serum.[5]

Although the studies noted have been carried out with doses of 12 Gm. of neomycin sulfate daily, the malabsorptive effect is also found with doses of 4 to 6 Gm. daily. In this more commonly used dosage the effect on fecal fat excretion may be less marked, but clear-cut reduction in absorption of carotene and D-xylose is present.[6] A reduction in serum cholesterol has also been reported using doses as low as 0.5 Gm. daily.[7] Whether or not this dosage is associated with other evidence of malabsorption is, however, not yet known.

Malabsorption: possible mechanisms

The mechanisms responsible for the malabsorption occurring during neomycin administration have not yet been clearly defined, but two possibilities seem most likely from the available evidence. The mucosal changes suggest that there may be some type of physical or chemical blockade produced by the irritative effect of neomycin. On the other hand Goldsmith, Hamilton, and Miller[8] have found increased bile acid excretion in the feces of patients receiving 2-Gm. doses of neomycin. This suggests the possibility that alteration in bile acid metabolism may impede the absorption not only of fat but also of other materials. That the lowering of serum cholesterol may occur as a result of increased conversion of cholesterol to bile acids must also be considered. If this is so, the decrease in serum cholesterol may occur independent of any malabsorptive effect of neomycin. The mechanisms that it seems possible to exclude are transit time increase and bacterial flora change.

Severe diarrhea induced by magnesium sulfate did not alter carotene absorption as did neomycin,[2] and malabsorption has not been found with increased peristaltic activity per se. Bacterial flora change seems an unlikely explanation for the absorptive alteration in that the major sites of absorption, namely the jejunum and the ileum, ordinarily do not have significant numbers of bacteria present, and the colon, which is accustomed to large numbers of bacteria and which has relatively little absorptive activity, is the site of the chief alteration in bacteria induced by agents such as neomycin. In addition, Steiner, Howard, and Akgun,[9] in studying a wide variety of antibacterial agents, found irregular cholesterol lowering with chlortetracycline and kanamycin but with no other agents except neomycin. Certainly further observations are in order to establish the mechanism of neomycin-induced malabsorption.

Considerations in use of neomycin

Regardless of mechanisms, however, certain points in the use and possible abuse of neomycin may be of practical value. In patients with severe liver disease, nutrition becomes paramount. When receiving neomycin the patient may suffer added insult to his precarious metabolic state unless he is eating well and is observed carefully. The excessive loss of potassium in the feces may lead to potassium depletion and result in a possible increase in the blood ammonia levels.[10] Therefore, close attention should be paid to potassium intake and serum potassium changes in such patients. Similar precautions would of course apply to the patient who is about to undergo, or who has recently undergone, surgery and is receiving neomycin. Malnourished patients who are eating poorly should perhaps be given vitamin supplements orally or parenterally as the occasion requires.

Comment

More information about the changes induced by neomycin is obviously needed before its use is judged. It remains a most valuable therapeutic agent, particularly in patients with hepatic coma or episodic stupor in whom it will allow ingestion of moderate amounts of protein, and its beneficial effect preceding intestinal surgery remains undiminished. In addition to the potential hazard of renal toxicity if absorbed in significant amounts and the occasional occurrence of neomycin-resistant staphylococci, the nutritional effects of neomycin must be kept in mind. On the positive side, however, this agent may lead us to new information about the physiology of intestinal absorption and about the control of serum cholesterol.

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Number twenty-nine in a new series of Nutrition Excerpts

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

VALENTINO D. B. MAZZIA, M.D., Chairman
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Blindness After Hemorrhage

Visual deficit following a sustained direct trauma to the eyeball from the pressure of a face mask or a head rest with the patient in the prone position is an occasional complication following anesthesia. Less well recognized is the possibility of partial or complete blindness as a result of hemorrhage. The following case report is an illustrative example of this phenomenon.

Case report

A sixty-two-year-old white male weighing 144 pounds with a preoperative blood pressure of 120/80 mm. Hg, pulse 90 per minute, hemoglobin 12.7 Gm. per 100 ml., of average habitus, edentulous, and with a history of a high intake of alcoholic beverages, was admitted with a carcinoma of the floor of the mouth for which a resection of the mandible and the floor of the mouth and a radical neck dissection were proposed.

Premedication consisted of secobarbital sodium, 100 mg., meperidine hydrochloride, 50 mg., and scopolamine, 0.5 mg., given intramuscularly thirty-five minutes before the induction of anesthesia. Anesthesia was accomplished through a tracheostomy performed at the outset under thiopental sodium, nitrous oxide, halothane, and oxygen anesthesia by mask. A number 32 anode tube was inserted into the stoma of the tracheostomy by the surgeon. The cuff was then inflated by the anesthesiologist, and anesthesia was continued with thiopental sodium, nitrous oxide-oxygen, and meperidine hydrochloride. In the four-and-one-half-hour period following the tracheostomy a total of 1.4 Gm. of thiopental sodium and 160 mg. of meperidine hydrochloride were administered in divided doses. Fluid therapy included 1,000 cc. of 5 per cent dextrose in water and 1,000 cc. of whole blood. The operation as planned was carried out with an uneventful anesthetic course except for one or two occasions when the patient coughed on the endotracheal tube.

A third 500-cc. bottle of whole blood was being administered as the patient was transferred to the recovery room. At the time of his admission to the recovery room in the late afternoon his blood pressure was 150/88 mm. Hg, pulse 96 per minute, and respirations 24 per minute. The vital signs remained in this range for the next few hours, during which the patient became more responsive and then became restless with increased pain. He was noted to have fairly large amounts of blood on the dressing and copious tracheobronchial secretions which were suctioned frequently and vigorously. That evening, four hours after his admission to the recovery room, there was a sudden fall of the blood pressure from 145/90 mm. Hg to 75/50 mm. Hg. For the next thirty minutes the blood pressure could not be obtained by palpation or auscultation; during this interval the heart rate was 108 to 112 per minute. After the administration of ephedrine, 25 mg. intravenously and 25 mg. intramuscularly, the blood pressure was palpated at 45 mm. Hg systolic, gradually rising

Presented and discussed at a conference held at Bellevue Hospital, New York City, May 5, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

to 60. Five hundred cc. of Albumisol followed by 1,000 cc. of whole blood effected a rise in blood pressure to 105/60 mm. Hg. The systolic blood pressure thereafter remained at 75 to 90 mm. Hg throughout the night, during which the patient also received meperidine hydrochloride, 50 mg. intramuscularly for pain, and thiosecobarbital, 25 mg. intramuscularly for sedation.

The following morning he showed marked facial edema and cyanosis with respiratory stridor despite the presence of the tracheostomy tube. It was apparent that there had been marked bleeding beneath the neck flap, and the patient was returned to the operating room. Under local anesthesia with oxygen insufflation via the tracheostomy tube the skin flap was elevated, and an estimated 1,000 cc. of blood were removed. An arterial bleeder, presumably a branch of the lingual artery, was discovered and ligated. The subsequent course was uneventful, with the blood pressures ranging from 120/80 to 140/90 mm. Hg. An additional 500 cc. of whole blood were administered in the recovery room, and the patient was discharged to his own room later that evening.

Over the next several days there was a gradual improvement in the swelling of the face with little else remarkable.

On the sixth postoperative day the patient noted the gradual onset of an inability to see and also was unable to swallow. The patient had unequal pupils, with the right larger than the left. The light reflex was absent. Extraocular movements were normal, but there was complete blindness of both eyes. An examination of the retina revealed no papilledema and an essentially normal fundus except for some retinal arteriolar constriction, for which treatment by vasodilatation with 1,000 cc. of 0.1 per cent procaine hydrochloride intravenously was suggested and carried out.

It was thought that the clinical picture was that of blindness secondary to hemorrhage, superimposed on the predisposing factors of a suspected compromise of the optic nerve fibers by the large alcohol intake and arteriosclerosis of the retinal vessels. The prognosis for the recovery of vision was guarded, and in fact the patient has continued to remain totally blind.

Comment

It has been known for centuries that unilateral or bilateral serious or even total loss of vision can occur suddenly and remain permanently after hemorrhage from a tissue or organ remote from the eyes. The loss of vision may or may not be noted immediately following massive hemorrhage and is more likely to follow a series of hemorrhages, not necessarily massive. The most frequent sources of such bleeding have been gastrointestinal and less frequently uterine. The onset of the visual deficit may occur during or immediately following a hemorrrhage in less than one quarter of the cases; it is most frequently delayed up to three to seven days following the bleeding and may in fact be delayed for as long as three weeks. The variation in the type of visual deficit from patient to patient indicates the responsible lesion to be located at times in the brain, at times in the optic nerve, and at times in the retina itself, so that there may be no changes observed in the retina, or these may be quite marked. When present, the fundal changes may begin with generalized pallor, arteriolar narrowing, and blurring of the optic disk, subsequently progressing to an appearance similar to that seen with albuminuric retinitis or hypertensive neuroretinopathy, with papilledema, marked hemorrhages, and retinal exudates. The retinal vessels remain contracted. Visual acuity varies from simple blurring to total loss. The papilledema may result in secondary optic atrophy.

The prognosis is necessarily guarded, although there is usually some degree of recovery with a residual partial permanent loss of vision. The treatment consists of a transfusion to restore the blood volume and terminate the hypoxia in the tissues. When the blood pressure has been stabilized at normal values, the treatment is geared toward the stimulation of retinal elements not yet degenerated. This may be attempted with a stellate ganglion block, intravenous procaine hydrochloride, and other vasodilators.

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Number one hundred twenty-five in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

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The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Lead Poisoning Associated with Ascariasis

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Plaster (painted)	2 years	Female

This incident was reported to the Poison Control Center as a case of lead poisoning. For about a year the mother had observed the two-year-old child eating bits of plaster but was unaware of the harmful effects which it may cause. The child was under supervision in a child health station, and because of a failure to gain weight and a history of pica, the patient was referred to the hospital for further investigation and possible treatment.

On admission to the hospital the only complaint was abdominal pains, and the presenting symptoms were anemia and underweight. The laboratory findings showed the lead blood level to be 0.07 mg. per 100 ml. and the urine lead level to be 0.06 mg. per liter. Spinal fluid and protein determinations were not done. The hemoglobin was 9.4 Gm. per 100 ml., and the red blood cell count was 3,300,000. After two weeks of hospitalization and therapy, the child was discharged.

This case was complicated by the finding in the stools of a parasitic infestation (ascariasis). In addition to ascariasis, a diagnosis of lead intoxication was made. Following her discharge from the hospital, the child was treated in the outpatient department with piperazine hydrochloride for the parasitic infestation and with iron therapy for the anemia.

Lead poisoning and parasitic infestation are not infrequent in Puerto Rican children, and their coexistence is not uncommon. A confirmed diagnosis of lead poisoning, particularly in a Puerto Rican child, should not exclude a stool examination for the determination of another condition which also may contribute to the anemia.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Prochlorperazine dimaleate, aspirin, imipramine hydrochloride	7 years	Male

A seven-year-old child, who was mentally retarded, ingested 2 prochlorperazine dimaleate, 1 aspirin, imipramine hydrochloride, and barbiturate tablets. He was brought by his father to the emergency room of a hospital which consulted the Poison Control Center. The Poison Control Center recommended the removal of the contents by means of a gastric lavage as an emergency measure to be followed by supportive treatment. The physician replied that he would use ipecac and was reminded that prochlorperazine dimaleate was an antiemetic and that gastric lavage therefore was the logical first-aid measure. The identity of drugs presently used, which have antiemetic properties, should be emphasized to those in the emergency room and to the staff providing the emergency services.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
Wisteria Buds	9 years	Male

This nine-year-old child apparently was attracted to the seeds, played with them, and then consumed about six. About three hours later he began to vomit. This continued for about five hours at twenty-minute intervals. He was admitted to the hospital. The presenting symptoms were abdominal pains and vomiting.

The mother related that she gave him a teaspoonful of ginger ale every ten minutes, presumably as an emetic, and prochlorperazine dimaleate suppositories $2^1/_2$ mg. every six hours. The following day the patient appeared normal except for epigastric tenderness.

Intoxications following the ingestion of wisteria seeds have been reported with increasing frequency. These seeds remain in pods on the vine and present an attractive hazard. The removal of such pods by the parents is a desirous safety precaution.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Elixir of Paragoric	18 days	Male

The mother related to the interviewing Public Health nurse that she awoke at 4 A.M. to give the infant his formula feeding. She had several bottles of the formula and a paragoric solution on the shelf in the refrigerator. She mistakenly picked up the paragoric solution and fed it to the infant. When the bottle was empty, the mother returned to bed and slept until 8 A.M. When the mother awoke at 8 A.M., she noticed that the baby had difficulty in breathing and could not be aroused. She then realized what had happened and immediately called the family physician who advised a coffee enema. When this emergency therapy failed, he advised hospitalization. The child was then taken to Beth-El Hospital in Brooklyn.

The paragoric solution had been prescribed for an eighteen-and-one-half-month-old sibling by the family physician because of frequent attacks of diarrhea. The medication was to be made up into a solution of $^1/_2$-ounce paragoric and $3^1/_2$ ounces of boiled water with sugar to taste, to be given $^1/_2$ ounce at a time. The mother prepared the solution as ordered and placed it in the refrigerator adjacent to the bottles of formula; hence the mixup.

Israel Miller, M.D., a pediatrician at Beth-El Hospital, reported that the patient was immediately sent to the pediatric ward of the hospital. The physical findings included drowsiness, Cheyne-Stokes respiration with crying out during the stertorous phase, cyanosis, constriction of the pupils, and a grade 3 systolic murmur over the left fourth intercostal space.

A diagnosis of morphine poisoning, and incidentally possible congenital heart disease, was made. The Poison Control Center of the City of New York Department of Health was consulted.

Nalorphine hydrochloride (Nalline hydrochloride) 0.3 mg. intravenously and oxygen were given at once, and intravenous fluid was started. Within about thirty minutes the patient's breathing became regular, and his color was better. By 1 P.M. the infant, although still lethargic, responded to stimuli, and his color was good. By the next morning the infant was active, alert, his color was good, and feedings were taken orally.

The laboratory findings included a hemoglobin of 16.8 Gm. per 100 ml. and 9,500 white blood cells with a normal differential. The urine showed a trace of albumin. An electrocardiogram showed right axis deviation, and a chest x-ray film showed some increase in pulmonary vascularity, probably related to a congenital heart lesion.

The infant was discharged in good condition on the fourth hospital day. His cardiac status was to be followed in the outpatient department.

We frequently have pointed out the danger which may result from placing containers of equal size, shape, and color adjacent to each other. Castor oil and camphorated oil, boric acid powder and Epsom salts are frequently offending pairs. Serious incidents are not uncommonly reported from such mistaken identities, and physicians should warn families against this hazard.

While the use of nalorphine hydrochloride in this case was justified, we have often noted that it is used without real necessity, as in some cough syrup ingestions. Sometimes nalorphine hydrochloride is used to differentiate between barbiturates and codeine. There is a legitimate use for nalorphine hydrochloride, however, in cases of coma of unknown origin to determine whether or not the coma is due to an opiate or its derivatives.

INCIDENT 5

Substance Ingested	*Age*	*Sex*
Nair (thioglycolate depilatory)	14 months	Female

This fourteen-month-old child chewed on a cloth on which her mother had applied a hair remover for application to her legs. The child soon began to vomit, had abdominal pains, and developed diarrhea. She also had difficulty in swallowing. After two days of symptomatic and supportive treatment the child made a full recovery.

The dysphagia reported in this case is noteworthy and indicates that the ingestion of larger amounts might lead to more serious complications with a possible later development of strictures of the esophagus.

INCIDENT 6

Substance Ingested	*Age*	*Sex*
Aminopyrine	32 years	Male

This patient was admitted for the treatment of a perforated peptic ulcer with a history of over thirty hours of bleeding. He was treated conservatively. On the eighth day following his admission the patient was given an overdose of 13 Gm. of aminopyrine rectally by mistake. Forty minutes after the initial administration the patient was given a Harris irrigation and 1,000 cc. of lactated Ringer's solution. According to the reporting physician, the patient had no ill-effects except for mild dizziness and mild confusion. The patient made a complete recovery.

Table I lists incidents reported to the New York City Poison Control Center over a recent weekend.

TABLE 1. Incidents reported to the Poison Control Center during a recent weekend*

	Age (Years)					Sex			Number of Patients
Type of Poison	0 to 4	5 to 9	10 to 19	20+	Unknown	Male	Female	Unknown	
Alcoholic beverages	2	. . .	. . .	1	. . .	3	. . .	. . .	3
Cleansing agents and bleaches	18	1	1	3	1	10	13	1	24
Cosmetics	9	. . .	. . .	. . .	1	8	1	1	10
Miscellaneous (nonedible)	25	1	1	2	1	16	13	1	30
Medicines									
Aspirin	8	. . .	. . .	1	. . .	4	4	1	9
Barbiturates	. . .	. . .	. . .	2	. . .	. . .	2	. . .	2
Cough medicine	4	. . .	. . .	1	. . .	1	4	. . .	5
Tranquilizers	1	. . .	2	2	3	2	3	3	8
Laxatives	1	. . .	. . .	. . .	. . .	. . .	1	. . .	1
Others	19	. . .	. . .	3	2	16	8	. . .	24
TOTALS	87	2	4	15	8	60	49	7	116

* Nearly 100 different products were involved in these incidents.

Number ninety-five in a series of Accidental Chemical Poisonings

Association of Benign Esophageal Tumors and Diverticula

Report of a Lipoma and Review of the Literature

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An isolated coexistence of two uncommon lesions may well be dismissed as coincidental. The repeated occurrence of similar incidents should prompt a thorough analysis in an attempt to elicit causal relationships.

The following case report is submitted to document the association of a lipoma with a large intrathoracic diverticulum of the upper esophagus. Although the authors could find no previous reports of similar cases involving lipomas, 9 instances of other benign esophageal tumors associated with diverticula were collected from seven previous publications. The common features, pathogenesis, and treatment of these cases will be discussed.

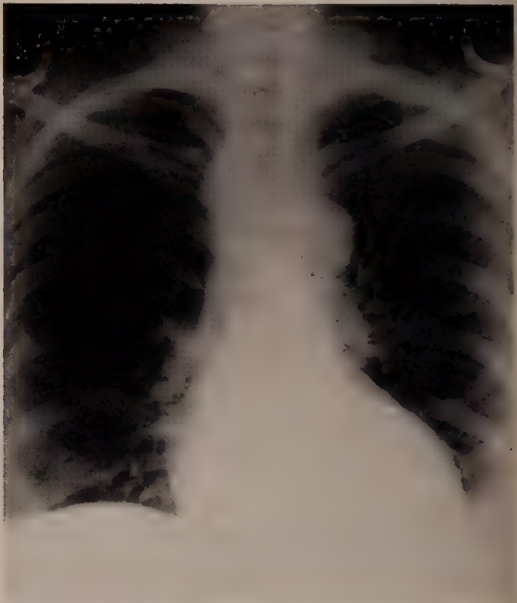

FIGURE 1. Preoperative chest x-ray film showing lesion in upper right mediastinum.

Case report

A sixty-two-year-old white woman was admitted to The Buffalo General Hospital on November 9, 1959, with the chief complaints of several years duration of choking sensations after meals and regurgitation of food on assuming the supine position. Nine months previously a routine chest x-ray film, which was taken prior to the excision of a benign cyst of the scalp, disclosed a widening of the right upper mediastinum (Fig. 1). There was no loss of weight prior to the present hospitalization. Upper abdominal pain, which the patient felt was due to nervousness, had been present for one week. She also complained of frequent upper respiratory infections and a cough productive of white sputum of four to five years duration. Her throat had been sore for the past eight to ten months.

The admission physical examination was

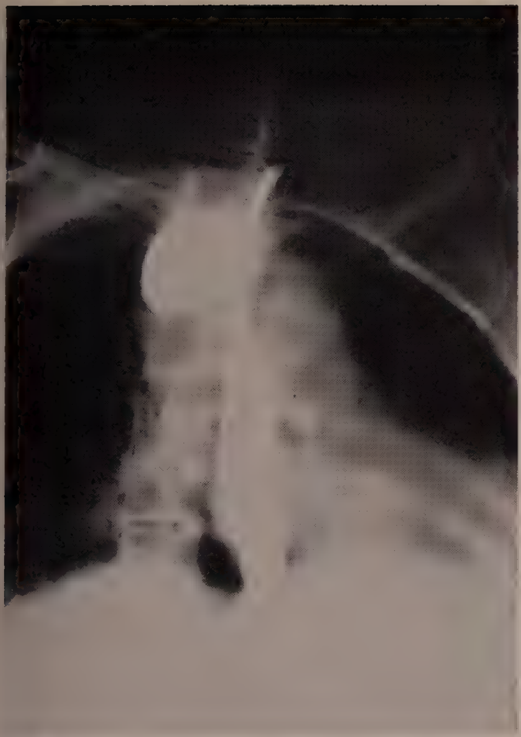

FIGURE 2. Esophageal barium study showing lesion well below usual location of pharyngoesophageal diverticula.

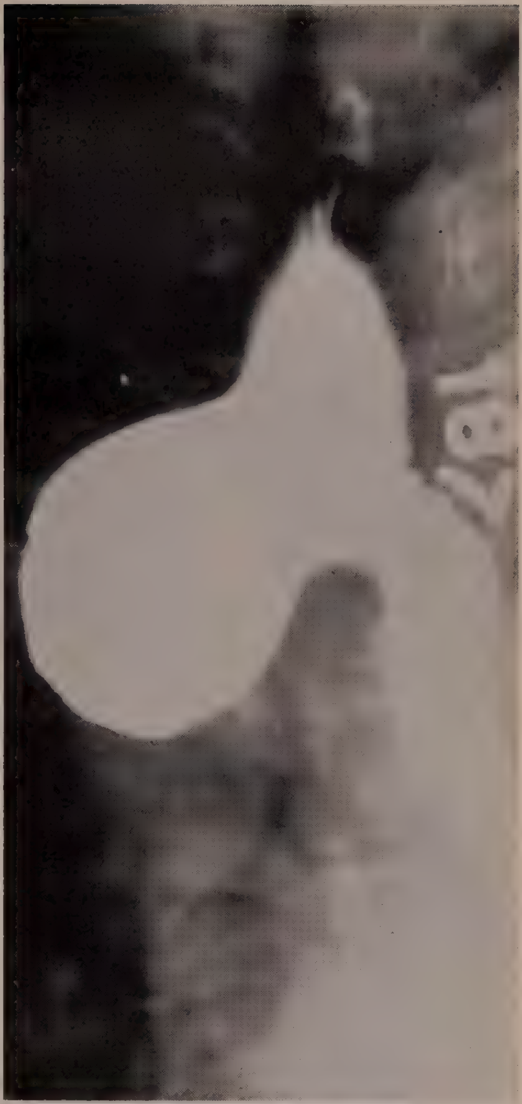

FIGURE 3. Close-up of distended diverticulum with presence of mass below diverticulum suggested in retrospect.

not remarkable, and the patient appeared to be in fair health. Routine laboratory examinations were within normal limits. Barium studies of the esophagus showed a large esophageal diverticulum on the right side near the thoracic inlet (Figs. 2 and 3). The appearance was that of a pulsion-type diverticulum, although its location was considerably below the classic pharyngoesophageal site of origin. Because of its location within the thoracic inlet, there was some concern as to whether or not a diverticulum of this size could be resected satisfactorily through a cervical approach.

On November 11, 1959, surgery was performed by John R. Paine, M.D., through a right cervical incision paralleling the sternomastoid muscle. The superior mediastinum was entered after the division of the sternomastoid muscle, and the diverticulum was visualized. As the lesion was dissected free and delivered into the wound, it was found to consist of a lipoma measuring 5 by 8 cm. overlying and intimately attached to a large esophageal diverticulum (Fig. 4). Both lesions were excised as one by transecting the broad base of the diverticulum. The esophagus was closed in two layers using fine interrupted silk sutures. The exposure through the cervical incision was better than might have been anticipated.

The postoperative course was complicated by a wound abscess which was incised and drained on the sixth postoperative day. A small fistula was confirmed by a barium swallow study on the fourteenth post-

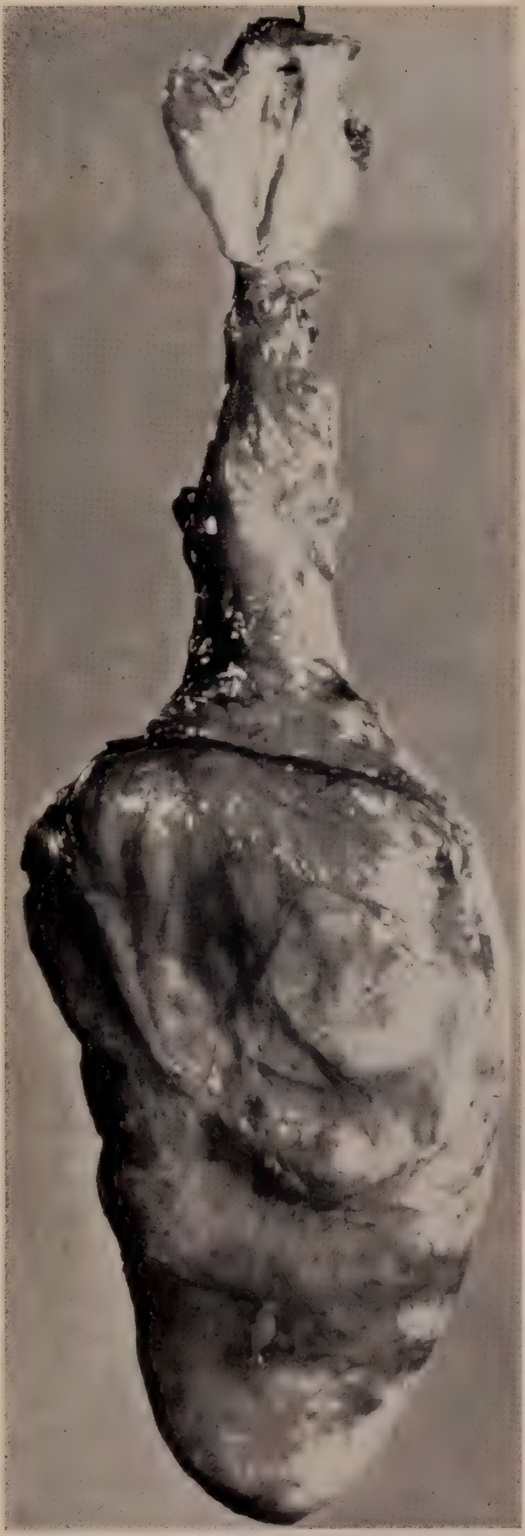

FIGURE 4. Resected specimen: diverticulum (above) markedly contracted and lipoma hanging from outer wall of diverticulum.

operative day, but this closed spontaneously five days later. In addition, transitory hoarseness with right vocal cord paralysis was noted several days after surgery which regressed spontaneously. The patient was discharged on the twentieth postoperative day in good condition, and she has had no further difficulties.

Histologically the lesion proved to be a well-circumscribed lipoma, intimately attached to the muscular layers of the esophagus. The esophageal mucosa was intact.

Comment

Benign esophageal tumors, although uncommon, have been reported with increasing frequency since Minski presented the first review of 34 cases in 1895.[1] Additional reviews have been presented since that time by Patterson in 1932,[2] Rose in 1936,[3] Adams and Hoover in 1945,[4] and Totten *et al.*[5] The latter authors were able to collect 163 cases reported up to 1953, rejecting 40 other cases because of insufficient information. Many isolated cases have probably not been reported, but an idea of the incidence of benign esophageal tumors may be obtained from Moersch and Harrington's[6] report of 15 cases diagnosed among 11,000 patients presenting symptoms of dysphagia at the Mayo Clinic up to 1944. An incidence of 11 out of 6,001 autopsies was reported by Schafer and Kittle[7] from the University Clinics of the University of Chicago. Chi and Adams[8] brought out a point of contrast by citing the occurrence of 2 benign cases with 246 malignant conditions of the esophagus seen at the same clinics between 1936 and 1947.

Traditionally benign esophageal tumors have been classified as follows: (1) intraluminal (polypoid or sessile) and (2) intramural (solid or cystic). Simple polyps predominate in the first group, and leiomyomas make up most of the second group.[5] Other benign tumors that have been described include polypoid lipomas,[9] leiomyomas and various sarcomas,[5] sessile papillomas,[10] and intramural fibromas and leiomyosarcomas.[5]

Although small, asymptomatic lipomas may be seen occasionally as submucous elevations at postmortem examination,[11]

TABLE I. Summary of cases of benign esophageal tumors associated with diverticula reported in the literature

Author	Year	Age (Years)	Sex	Symptoms	Type of Lesion	Site	Treatment and Comments
Stewart[14]	1931	32	F	Asymptomatic	Leiomyoma, 3.5 by 1.5 by 1.3 cm. surrounding diverticulum of 1 by 1.5 by 2 cm.	2.5cm. above cardia	Suicide by poison
Stewart[14]	1931	59	F	Asymptomatic	Leiomyoma, 1.2 by 1.3 cm. in wall of diverticulum of 1.5 by 1 by 0.5 cm.	3.5cm. above cardia	Died of arteriosclerotic heart disease
Pechatnikova[15]	1950	Publication not available for review					
Hoyne and Rogers[16]	1951	44	F	Occasional epigastric heaviness on overeating	Fibromyoma, 12 by 3 by 3 cm. with stalk consisting of diverticulum of 3 cm. diameter	Lower third	Excision; tumor showed mucoid degeneration
Boyd and Hill[17]	1957	40	M	Dysphagia, weight loss of 15 pounds	Leiomyoma, 2.5 cm. in diameter, in wall of diverticulum	Upper third	Excision
Nese[18]	1958	42	M	Dysphagia, weight loss, nausea, fullness on eating, substernal pressure	Neurinoma, orange-sized, in wall of large diverticulum	Lower third	Excision
Nese[18]	1958	48	M	Weight loss, nausea and vomiting, recurrent respiratory infections, cough, pain on bending forward	Leiomyoma, goose egg-sized, in apex of large diverticulum	Middle third	Excision
Martins and Arduino[19]	1959	61	M	Postprandial epigastric pain in supine position	Leiomyoma, 4 cm. in diameter, in apex of small diverticulum	Lower third	Excision; diverticulum simulated hiatal hernia on x-rays films
Nemeth[20]	1959	32	F	Dysphagia for six years	Leiomyoma	Junction of middle and lower thirds	Invagination of diverticulum followed by excision of tumor in recurrent diverticulum six months later; tumor not recognized at first operation
Razin and Adler	1961	62	F	Choking sensation on eating, epigastric pain, sore throat, cough, frequent colds	Lipoma, 5 by 8 cm. at apex of diverticulum of 5 cm. diameter	Upper third	Transcervical excision

larger ones are among the least common of esophageal tumors. Ochsner and Ochsner[9] were able to collect only 9 cases from the literature up to 1956, and they added one of their own. All of the lipomas were intraluminal, and 6 of them were pedunculated masses originating in the upper third of the esophagus. Such tumors may occasionally be regurgitated or even protrude from the mouth.[12] A case of epidermoid carcinoma overlying such a pedunculated lipoma has been described recently.[13] To the authors' knowledge, the present case represents the first reported instance of a lipoma of the esophagus that occurred as an extraluminal mass.

The association of a benign tumor with a diverticulum of the esophagus was first reported by Stewart in 1931.[14] He presented 2 cases of leiomyomas associated with small diverticula which were incidental findings at autopsy. Isolated cases of other benign tumors associated with diverticula have since been reported by Pechatnikova[15] (publication not available for review), Hoyne and Rogers,[16] Boyd and Hill,[17] Nese[18] (2 cases), Martins and Arduino,[19] and Nemeth.[20] These cases are presented in Table I.

Although the number of collected cases is admittedly too small to draw any definite conclusions, several features merit comment. The age of reported cases varied from thirty-two to sixty-two with an average of forty-seven years. The sex distribution was approximately equal. A 2-to-1 male predilection has been reported for benign esophageal tumors in general.[5]

Since Stewart[14] found islands of superficial glands suggestive of embryonal rests in the vicinity of the tumors he described, he felt that the origin of the lesions was undoubtedly congenital. He nevertheless mentioned possible mechanical factors favoring diverticulum formation such as thinning of the esophageal wall around the tumor and progressive enlargement from the act of swallowing. The reported age incidence tends to discredit congenital theories in favor of purely mechanical considerations. It is indeed tempting to consider these diverticula as traction-pulsion diverticula in the sense described by Oekonomides[21] rather than as pure traction or pulsion types as described by Rokitanski.[22] A possible mechanism may be initial thinning of the esophageal wall around the tumor with traction exerted by the relative fixation of the tumor against the more mobile rest of the esophagus. Once a small diverticulum has been formed, intraluminal pressure developed during swallowing could increase its size by a pulsatile mechanism. By means of serial sections, Stewart[14] demonstrated that the tumor is found in an angle between the esophageal wall and the diverticulum in small lesions. The fact that the tumor is found in the wall or the apex of the diverticulum in larger lesions lends some support to this theory. A similar mechanism has been advanced by Hoyne and Rogers,[16] who expressed surprise at the infrequent occurrence of this combined lesion.

The location of the lesion was in the lower esophagus in at least 5 of the 9 reported cases. Epiphrenic diverticula unassociated with tumors are usually found in this region.[23,24] In these cases one is tempted to implicate the association of a congenital weakness of the esophageal wall with the direct influence of the tumor in the formation of the combined lesion. Yet in other cases the lesion was situated in areas not usually tending to form diverticula. Here the tumor may well be the sole cause of the associated diverticulum.

Symptoms, when present, are similar to those reported for benign esophageal tumors in general.[5] They are related directly to the simultaneous presence of a slowly enlarging mediastinal mass and a disturbance of the swallowing mechanism. Dysphagia, weight loss, choking sensations, cough with frequent upper respiratory infections, and epigastric pain have been reported.

The diagnosis of the combined lesion should be entertained whenever a diverticulum is found in an unusual location. Occasionally the x-ray appearance of a thick-walled diverticulum will be suggestive. More often than not, however, the presence of the diverticulum will overshadow the preoperative recognition of an associated tumor.

Transcervical or transthoracic excision has been reported in all but 2 of the cases. Surgery certainly seems advisable for the alleviation of symptoms in all suitable-risk patients. The potential threat of a malignant condition may be a practical consideration although no cases have been described to date. The occasional presence of carcinoma in pharyngoesophageal diverticula, however, is well known,[25] and potential malignant degeneration of leiomyomas has been reported also.[26]

Summary

A case of lipoma associated with a large diverticulum of the upper intrathoracic esophagus is presented. The lesion was removed through a transcervical approach. No previous reports of a similar lesion have been found although 9 cases of other benign esophageal tumors associated with diverticula were collected from the literature. In 2 cases the lesion was an incidental finding at autopsy. In all others the combined lesion was excised successfully by the transcervical or the transthoracic route.

The pathogenesis and clinical implications of this association of benign esophageal tumors and diverticula are discussed.

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Carcinoma of the Penis

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CANCER OF THE PENIS comprises from about 1.5 to 2 per cent of all the malignant growths of the male genitourinary organs. To the ancient civilizations, cancer was known as the "stinking disease." It may appear anywhere from the second decade of life on, but actually increases in frequency up to the fifth or sixth decade. It is more prevalent in white people than in Negroes. It is more prevalent among Americans and Italo-Americans. According to the literature, cancer of the penis has been diagnosed in at least 19 nationalities. It is never found in circumcised Jews.

Jews do not develop cancer of the penis because they perform ritualistic circumcision on their male children in early infancy. However, there is a case report of carcinoma of the penis in a Jew who never was circumcised. They do not have any racial immunity to epidermoid cancer in other parts of the body. Mohammedans who practice circumcision between the ages of three to ten years of life rarely develop penile cancer. The Hindus of India, who do not practice circumcision, have a higher percentage of cancer of the penis.

Other lesions which may cause confusion in diagnosis are tuberculosis, balanitis, herpes progenitalis, gummatous ulceration, and granuloma inguinale.

Cancer of the penis very rarely occurs in people who have been circumcised in infancy, but it may and does occur even in the circumcised when the operation has been done later on in years. Chronic irritations of the glans or mucosa of the prepuce to the glans, or concealed "toad-in-a-hole penis" found in stout people are unavoidable. Hard inspissated smegma, fatty acids, and some chemicals from the urine make the anterior aspect of the penis the most common site for the development of cancer. In a series of 100 cases of cancer of the penis studied by Barney,[1] 85 per cent had definite phimosis. There seems to be little doubt that the disease is associated with irritation, both chemical and mechanical. In a series of 58 patients with carcinoma of the penis treated at a Zurich hospital, phimosis was the most frequent predisposing or contributing factor in its development, being present in 21 of the 58 patients.[2] The retained irritating secretion under an irretractable, or, at least, infrequently retracted prepuce is a strong reason for protecting completely against cancer of the penis by circumcision in infancy.

Social status

The majority of cases of carcinoma of the penis occur in persons who were never circumcised during infancy and whose personal hygiene has been poor. The medical literature points out a few exceptions to the preceding statement.[3-9] Cancer of the penis has been found in physicians, clergymen, judges, and editors.

Syphilitic or chancroidal ulcers apparently do not predispose to or aggravate cancer of the penis. Careful study and thought on this point suggests a tendency for lues to increase the susceptibility of the malignant growth. While there is no authentic case showing that cancer comes from syphilis, nevertheless, it is true that lues does lower the resistance of the individual and may make him more susceptible to the factors which cause malignant degeneration. Circumcision during infancy protects against cancer of the penis, but, as mentioned previously, it is not similarly effective when performed later in life. Early circumcision causes a thickening of the epidermis, while later on in life the glans remains relatively sensitive to the contacts of everyday life.

Location of the tumor

Most likely the tumors originate where irritation is greatest. Nearly all the early lesions grow from the proximal third of the glans penis, the coronal sulcus, close to either side of the frenum.

There are two recognized types of carcinoma of the penis: the papillary, and the flat or ulcerative forms. The former is seen more frequently. This type increases rapidly in size by active proliferation, sometimes penetrating the prepuce. As increasing growth takes place, the blood supply becomes lessened, and for that reason the tumor becomes ulcerated, necrotic, infected, and foul-smelling. The flat type of the neoplasm infiltrates the deep tissues, forming an ulcer and metastasizing earlier than the proliferative type.

Most of the neoplastic diseases are not seen by the medical man until they have existed for a considerable length of time, usually ranging from many months to a year or more. As a rule, it is difficult for a patient to state or for a doctor to determine accurately the point of origin, but they arise from the glans penis in most cases. The rapidity of growth varies greatly. It is not uncommon to see the entire end of the penis, both glans and prepuce, invaded and replaced by neoplastic disease within a few weeks or months. On the other hand, many patients live in health and comfort for as long as eleven years without treatment. Possibly the relatively slow growth of certain tumors explains why patients seek medical advice late.

As to the nature of these neoplasms, it is enough to say that both types are squamous cell carcinoma, usually grade I or II.

Symptoms

Cancer of the penis always starts as a small but definite lesion, but the patient's first symptom depends largely on the degree of phimosis present. If retraction of the prepuce is possible, the patient first sees what he describes as a sore, a pimple, a wart, a red spot, or a psoriasis-like lesion. There may exist a foul, purulent discharge, occasionally blood-tinged. Pain is sometimes severe. A lump may be felt on palpation. Phimosis, paraphimosis, or occlusion of the urethral meatus may be present. The interval between the patient's first symptom and his first visit to a physician averages about fourteen months, and it is usually two years until he is treated by a urologist. Occasionally urinary fistulas are present. Enlarged inguinal lymph nodes may be the first sign of carcinoma of the penis. This invariably indicates that the tumor cells have metastasized, even if the primary penile lesion was not noted.

Diagnosis

While the diagnosis of cancer of the penis usually may be elementary, it must be emphasized that the penile lesion also may suggest the first stage of lues. It may even be that the blood Wassermann test may show positive results. However, this does not preclude the lesion being cancerous. The "soft chancre" of chancroid, as well as the chancre, may resemble cancer of the penis, but it is even more important to remember that the reverse may be true. The lesion of carcinoma of the penis may resemble papillomatosis of the penis or granuloma inguinale. Strong chemical solutions of bichloride of mercury or the cresols may produce a neoplastic-appearing lesion. However, the diagnosis of penile cancer always should be made by microscopic examination. Just as soon as the lesion is noted, a biopsy should be taken. An unfortunate situation arises when lues coexists with carcinoma of the penis. Much valuable time may be wasted in treatment of the lues if the lesion actually is cancerous. If phimosis is present and not too easily retractable, slits are made after careful palpation of the small tumor mass to avoid cutting the tumor proper and thereby avoiding dissemination of the tumor cells.

Metastases

After examining the primary tumor, a careful search should be made for metastases. The inguinal and femoral regions should be palpated, and a pelvic examination should be made per rectum. In most cases there is adenopathy. A metastasis in a small node sometimes can be recognized by its

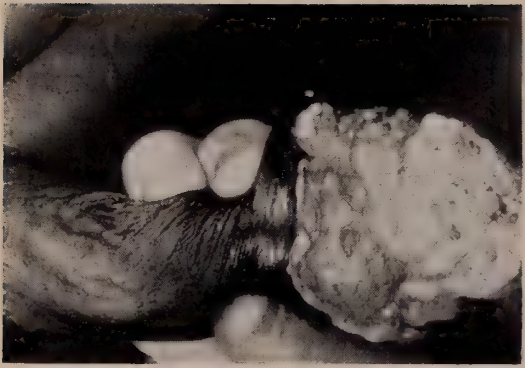

FIGURE 1. Epithelioma of penis in forty-seven-year-old patient, anteroposterior view.

hardness. When metastases are early, the diagnosis is difficult. Aspiration biopsies, imprints, or smears, as well as sections, can be done on suspicious-appearing nodes. The metastases may occur in the retroperitoneal lymph nodes and even in the liver without inguinal node involvement. Such metastases probably take place by way of the lymphatic channels beneath the pubic arch.

According to statistics, about 75 per cent of the lymph gland enlargement occurs, usually unilaterally, on the same side as the lesion. About 50 per cent of these nodes with enlargement are found to contain metastases. The node may be enlarged but not tender to the touch. As a rule, lymph gland enlargements secondary to cancer of the body of the penis are not tender. Tenderness is elicited when there is a superimposed infection of the primary lesion.

When cancer of the penis metastasizes, it does so through a remarkably rich lymphatic chain. These vessels lead to the superficial and deep lymph nodes of the inguinal region. It has been shown over and over again that cancer of the penis may exist for years without metastasizing. Yet, when it does, it then may lodge itself in the inguinal lymph nodes on one or both sides or unilaterally on the side opposite the primary lesion. When metastasis takes place, a nest of cells breaks off from the primary lesion and enters one of the lymph vessels in the form of an embolus and travels along that vessel until it reaches a lymph vessel. The lymph gland is the first obstructing area. Sometimes the nodes contain both cancer cells and infection.

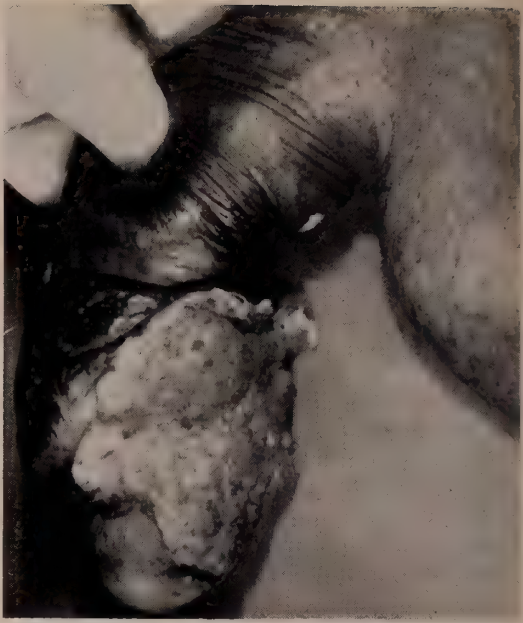

FIGURE 2. Lateral view of epithelioma of penis in forty-seven-year-old patient.

Prevention of cancer of the penis

The prophylactic treatment of cancer of the penis consists of circumcising all male infants a few days after birth. The obstetrician, pediatrician, and urologist, therefore, have a supervisory and advisory task to perform in the prevention of cancer of the penis.

Treatment of cancer of the penis

The active treatment of penile cancer must be directed toward the eradication of the primary tumor and of the metastases by surgical means, which is the most efficient method of control.

In selected cases, especially where the lesion is 2 cm. or less in diameter, radium therapy has been used with gold seeds buried in the tumor substance. Radiotherapy may be advantageous in cases where the patient is too weak for surgery and where the patient, for personal reasons, will not consent to surgery.

Where penile cancers are larger than

2 cm. in diameter, amputation of the organ is performed about 1.5 cm. proximal to any evidence of diseased area. It is unusual for a local recurrence to take place after amputation. As a rule, enough of the shaft of the penis can be saved so that the functions of urination and coitus are feasible.

If the penis is to have a substantial amputation, perhaps close to the symphysis, the operator must make a judgment as to whether or not his patient can be comfortable with a meatus in the mass of the scrotum or in the opening in the perineum between the scrotum and rectal orifice. In either case great care must be exercised to have plenty of urethral mucosa for the formation of a new meatus when the urethra is transplanted. This is to avoid contraction of the new orifice when the urethral mucosa is injured.

After completing the first stage of the operation, which is the removal of the primary growth, the second stage, if deemed necessary, should follow in a few weeks. The nodes should be removed by complete block dissections of the groin.

Prognosis

Group I. Those patients with a small, early lesion without groin metastases treated by irradiation or by amputation show 85 per cent of five-year cures.

Group II. Those with demonstrable operable inguinal metastases treated by amputation of the penis with block dissection of one or both groins show 58 per cent five-year survival.

Group III. Cure by any method of treatment cannot be expected in those cases with inguinal metastases which have broken through the glandular capsule, as shown by ulceration and fixation of underlying structures.

Case report

This is a report of a case of epidermoid carcinoma of the penis (Figs. 1 and 2) with possible metastases to the inguinal nodes in a forty-seven-year-old Negro who was treated by amputation of the penis and a perineal urethrostomy on September 11, 1959, followed by a bilateral radical lymphadenectomy on September 24, 1959.

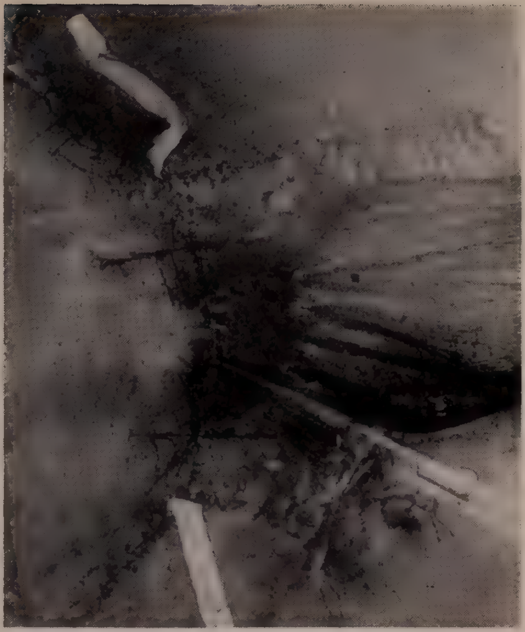

FIGURE 3. Clamp pointing to perineal urethral opening midway between scrotum and rectal opening.

The history of this patient was that one night an assailant shot him, the bullet striking the periphery of the prepuce on the right side of the penis. The patient applied home remedies to the injured tissue. Within a week or so the preputial sore became a stubborn "ulcer" which would not heal. The ulcer grew larger, but the patient did not see a doctor until two years after the gunshot wound.

The first visit disclosed a strong, well-built Negro of forty-seven years of age, who had a large, hard, ulcerated, foul-smelling tumor involving the meatus and 6 to 8 cm. of the shaft of the penis. No evidence of inguinal gland enlargement or tenderness was noted. A rectal examination produced negative findings. An x-ray film of the chest showed negative findings. A biopsy was done on August 12, 1959, showing a carcinoma of the penis.

On September 11, 1959, the penis was amputated just anterior to the bulbus urethra. The corpus, the tunica, and so forth were resected. The urethra was then freed for an inch or so and was passed through the separate raphe of the scrotum between the testicles and out through a buttonhole

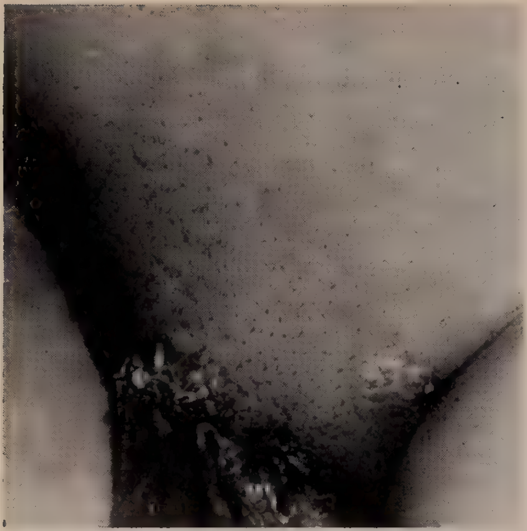

FIGURE 4. Anterior view of scrotum after amputation of penis and adenectomy.

anterior to the rectum (Fig. 3). Here it was sutured with fine interrupted silk sutures. A Foley catheter was placed into the bladder through the perineal urethrostomy.

On September 24, 1959, the patient had recovered from the resection of the penis and was prepared for radical groin resection (Fig. 4). A Pfannenstiel incision was performed joining with T incisions down the groin for about 6 inches. The proximal flap was elevated to the umbilicus, and the distal flaps were folded laterally to the buttocks and medially across the scrotum. Block resection was now accomplished from the umbilicus down across the groin, including the femoral triangle and resecting both the superficial saphenous veins until the fascia was bare from the umbilicus down across the groin to the pubic region to about 6 inches below the pubic tubercle. Incisions were made along the femoral canal along the iliac vessels, and the artery, femoral veins, and iliac veins were exposed, and the glands were resected from the femoral canal and the distal iliac region. These were hyperplastic bilaterally.

A pathology report on August 12, 1959, revealed that a biopsy of the tumor of the glans penis was positive for carcinoma of the penis.

On September 14, 1959, a pathology report stated that the specimen received in formalin was a penis amputated at the base measuring 15 cm. in length and up to 5 cm. in diameter. The glans penis was replaced almost completely by a neoplastic process which showed a yellowish, hard, nodular outer surface. The skin surface was dark, brownish, and markedly corrugated. The cut surface of the tumorous area was dark brownish-gray and homogenous with a yellowish-white, striated periphery.

The microscopic diagnosis was epidermoid carcinoma of the penis.

On September 25, 1959, a microscopic examination of the lymph nodes showed right and left inguinal and iliac nodes, right and left femoral nodes, and no tumor cells present.

Comment

We are dealing with a primary epidermoid carcinoma of the penis which arose at the site of a previous gunshot wound of the periphery of the prepuce. While a biopsy proved the tumor to be cancerous, no metastases were noted after the radical removal of lymph nodes from the inguinal, iliac, and femoral areas bilaterally. Two months after surgery the patient was able to micturate without difficulty through a new perineal urethrostomy opening. Intravenous urography showed normal kidneys, ureter, and bladder without any retention of urine. The patient was discharged from the hospital on November 2, 1959, and went back to work on December 5, 1959. As of July 10, 1961, the patient was well and working.

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Use of Steroids in Hemolytic Transfusion Reaction

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A HEMOLYTIC TRANSFUSION REACTION due to gross incompatibility in the major blood groups is an accident of rare occurrence. This is a result of the greatly improved laboratory procedures for the typing of both cells and serum and the use of at least two technics for cross matching, one of which must be the antiglobulin test. In the majority of cases where this "preventable" situation occurs the cause has usually been traced to a clerical error rather than to the laboratory test. This human weakness whereby pilot tubes become interchanged, names confused, or patients misidentified produces a hard core of irreducible minimums, unfortunately still accepted as inevitable as long as the human factor exists in transfusion therapy. Thus in 1953 the *British Medical Journal*[1] reported an average of 1 death for every 13,000 transfusions. More recent articles quote 30 incompatible transfusions with 7 deaths in a five-year period when 81,392 transfusions were given.[2] Since approximately 5 million transfusions were given in the United States during 1960,[3] the total number of deaths from this therapy is therefore not insignificant.

After the hemolytic reaction has taken place, therapy to minimize its effect becomes important. The varied treatments suggested have been particularly frustrating since the results justify the feeling that "nature proceeds while medicine supports." During the acute shock stage, therapy with vasopressors, alkali, forced or limited fluids, high dextrose concentration, compatible transfusions, antihistamines, renal diaphoresis, steroids, and fibrinogen and other clotting agents have been suggested. Subsequently, therapy directed against the anuria and azotemia has consisted of renal decapsulation, renal denervation, peritoneal dialysis, and the use of the artificial kidney.[4] These two latter formidable procedures can be obtained only at the large medical centers since skilled personnel are needed for their effective and safe use. The great variability in the response of the patient to the hemolytic crisis depends on many factors. Thus the avidity and strength of the antibody, the tolerance of the kidney, the speed of the reaction, and the underlying integrity of the cardiovascular system all play a part.

This report concerns a patient in whom a major blood group hemolytic transfusion reaction occurred. Immunologic data were obtained during her course. The eventual recovery of this patient after documentary proof of the complete, rapid hemolysis of 500 cc. of incompatible blood suggests the possibility that the therapy utilized may have contributed to the amelioration of the effects of the hemolytic episode.

Case report

The patient was a female on whom a radical mastectomy was performed for carcinoma of the breast. Toward the end of the long operation a unit of blood was transfused to compensate for the estimated blood loss during surgery. The patient's blood had been typed as group A and cross-matched to a unit of compatible group A blood preoperatively. This unit of blood was started and was completed just as the surgical drapes were being removed. As the trunk and arm were uncovered, a diffuse urticarial rash was noted. A blood speci-

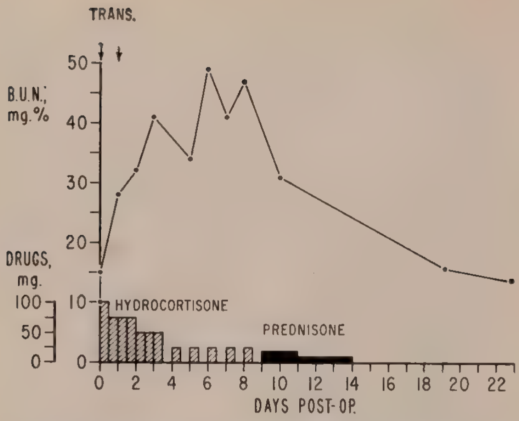

FIGURE 1. Blood urea nitrogen elevation and dosage of hydrocortisone following transfusion of "A" blood in "B" recipient.

men was immediately drawn from the other arm and sent to the blood bank laboratory with the notice of the reaction. A recheck of the specimen revealed the patient's blood to be group B and the transfused blood to be group A. Subsequently the error was traced to the mislabeling of the original blood specimen when blood from 2 patients was being drawn at the same time. The second patient had not as yet been transfused when the error was discovered, thus averting a second accident.

During the short time between the reaction and the discovery of the error the patient had been receiving intravenous hydrocortisone (100 mg. of Solu-Cortef with sodium lactate). For the first thirty-six hours she received in addition 3,000 cc. of intravenous fluids containing 5 per cent glucose in sodium lactate with 225 mg. of hydrocortisone (75 mg. in each liter) plus Benadryl hydrochloride and 500 cc. of compatible group B blood. After the second day, when the patient was no longer on intravenous therapy, the dosage of hydrocortisone was reduced to 50 mg. with oral alkali. The patient was thereafter maintained for two weeks on steroids with steadily decreasing dosages (Fig. 1). The urinary output never fell below 2,400 cc. daily, although the specific gravity of the urine did not rise above 1.006 and usually was 1.001. Hemoglobinuria and hematuria persisted for several days. The blood urea nitrogen climbed slowly during the first week to reach a maximum of 47 and subsequently fell to normal. Following the incompatible transfusion the hemoglobin fell to 9.2 Gm. but was subsequently maintained at 10.5 to 12.0 Gm. The fall of the anti-A titer with the subsequent development of a marked increase in the "immune" anti-A titer and the appearance of a very strong anti-A hemolysin is indicative of a severe reaction. The absence of any detectable A cells in the post-transfusion specimen of the patient's blood is also evidence of the total destruction of all the transfused cells (Table I).

Comment

The prognosis of any case receiving a whole unit of ABO incompatible blood depends on the degree of shock, the presence of a hemorrhagic diathesis, and the development of oliguria or anuria. Unquestionably, some patients will survive with no intensive therapy at all. The patient described here could have been in the group that would have survived without treatment, and the successful outcome following the use of steroids could have been a fortuitous coincidence. It is not possible to run a controlled study and achieve statistically significant data when dealing with a condition which occurs only in very widely spaced accidents in any institution. Unfortunately the results of animal experiments and studies in transfusion and immunologic problems are not always valid for solving problems faced in human beings.

The deleterious effects of hemoglobin on the kidney have not been clearly elucidated. Acute renal failure may be attributed to an inflammatory response by the tubular cells to the irritating effects of the mass of material suddenly deposited in the lumen. There is evidence that hemoglobin alone is not deleterious, but when it exists with any condition that may lead to some degree of renal ischemia such as shock, dehydration, or anoxia then the tubular cells become damaged by the hemoglobin.[5]

Since it is not known exactly how the products of hemolysis affect the kidney, one is on thin ground in attempting to explain how steroids may be of value. The doses used clinically do not increase the glomerular filtration rate significantly or antagonize

TABLE I. Anti-A titers, pretransfusion, post-transfusion, and four months post-transfusion

Time	Test	Agglutinin	Conglutinin	Hemolysin
Pretransfusion	Preneutralization	128	128	Negative
	Postneutralization	0	0	Negative
Post-transfusion (same day)	Preneutralization	16	16	Negative
	Postneutralization	0	0	Negative
Post-transfusion (four months)	Preneutralization	640	1,280	Positive 4 +
	Postneutralization	0	8	Positive 4 +

sufficiently the pituitary antidiuretic action. If the inflammatory reaction to the mass of precipitated material in the tubule is a vital factor in the etiology of acute renal failure, then there may be some value in the anti-inflammatory and antiallergenic effects of steroids.

Hewitt, Wheby, and Crosby[6] have shown that prednisolone is of no effect in preventing hemolysis due to incompatible ABO antibodies. Thus 1 to 3 ml. of transfused incompatible cells showed no significant difference in survival between patients receiving prednisolone and those in the control group. However, the parameter examined was solely cell survival and the major effects of a large mass hemolysis with resulting shock, renal ischemia, and oliguria were not involved. The treatment of the shock caused by the hemolytic reaction and "...the rapidity and quality of the therapy directly affects the prognosis. Direct renal injury, whether resulting from anuria or other causes, is a major determinant in the severity and duration of the uremic state which, if sufficiently prolonged, is the ultimate cause of most fatalities."[7]

Conclusion

At the present time it seems rational to treat the reaction from an incompatible blood transfusion with the usual supportive measures plus steroids as soon as the diagnosis is made. It is indeed hazardous to attempt to draw any conclusions from 1 case especially with a disease that can resolve without treatment. Nevertheless, the duration of time that steroids were used and the doses given makes it an innocuous enough modality. The authors plan to use steroids again if and when they are faced by another accident resulting from an incompatible blood transfusion. It would be of interest and of value to see what effects others may report with this safe and simple mode of therapy. In this way sufficient data could be gathered, and a more valid conclusion could be drawn as to the value of steroids in the treatment of reactions from incompatible blood transfusions.

Summary

A case is presented in which a patient with B-negative blood received a transfusion of 500 cc. of A-positive blood and was treated with intravenous hydrocortisone immediately thereafter. The possible role of steroids in the treatment of reaction from an incompatible blood transfusion is discussed. It is recommended that this mode of therapy be used until more data can be gathered.

ACKNOWLEDGMENT. The authors are grateful to Maxwell Marder, M.D., for his clinical help and Mrs. Hannah Pretschold for her technical assistance.

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Special Article

Autopsy: The Mortician's Point of View

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A QUESTION which is often asked of the funeral director is: "We're at the hospital. They want us to give permission for an autopsy. What shall we do?" What should the funeral director reply; what should he be expected to reply?

The principal function of the early undertaker was to provide a coffin and a conveyance in which to take the body to the cemetery. Later he became responsible for some care and for preparation of the dead body. Over the years embalming developed into a highly skilled technic; constant study and research added the art of restoration and cosmetic effects.

Today's funeral director provides a host of services to the living as he continues to care for the dead, and the modern funeral service has been described by psychologists, psychiatrists, sociologists, and clergy as a major contribution to the mental health of the nation.

Every state licenses funeral directors. Some require higher qualifications and more training than others, but all the licensing legislation recognizes and is predicated on the fiduciary relationship between the funeral director and his client in which a principal function of the funeral director is to guide and counsel the family in connection with the many unfamiliar problems that arise following a death.

How then, with this responsibility and the family looking to him for guidance, should the funeral director reply, when the family says the hospital wants an autopsy and asks him what they should do?

Years of study and his training in anatomy, pathology, bacteriology, and chemistry have made the funeral director a student of science, with an appreciation of its wonders. His contact with cases where the cause of death was uncertain, his familiarity with the contributions which have been made at the autopsy table toward increased longevity, and the elimination of many of the scourges of the past have convinced him that autopsies can be useful.

At his local and state association meetings he has been urged to cooperate by representatives of the hospitals, the pathologists, and organized medicine, who have all promised cooperation in return. His own association leaders have urged him to cooperate whenever he can.

And now he has this question: "What shall we do?"

In some places the funeral director need have little concern. He has had many experiences at the hospital. He knows that someone in authority will be at the hospital to receive the family when they get there. He knows that the autopsy procedure will be explained to the family. He knows that the hospital will restrict the "permit slip" to what actually needs to be done, even though the family may not realize that they have a right to limit the examination. He knows that the autopsy will be done promptly and in accordance with the proper procedures and that the body will be delivered to him promptly and in satisfactory condition.

He can tell the family that it's all right; or he can suggest that it's a matter for them to decide for themselves and that he can see no objection; or he could recommend that they discuss the matter with their family physician. The likelihood is that he loes one of these.

But what should we expect from the uneral director whose last experience with utopsies caused him to be late with "viewing hours" because the hospital deayed the autopsy so long past the promised ime that even though he and his assistant vent without dinner to prepare the body, t still wasn't ready when the first friends rrived? And what should we expect from he funeral director who recently telephoned he hospital to remind the staff that a écolleté evening dress would be used and hen had to devise a way to hide a straight-cross breast incision? And what should we xpect from the funeral director whose last ew cases took so much extra time to embalm ecause arteries were torn or cut short or eck organs were removed in such fashion as o create all kinds of special problems and oncerns?

And what should we expect from the uneral director who had to stand tongue-ied while the family on the last case kept nquiring whether or not the pathologist ad kept his promise "to limit the post to a mall incision, just like a small operation."

My purpose is not to catalog all the rongs committed, nor am I seeking to nply that every funeral director can be ounted on to cooperate, even with the most ooperative hospital, or that funeral direcors are without fault.

uneral director-hospital relations

Our State association and most of our 26 ocal associations have consistently devoted nuch time and effort to better funeral irector-hospital relations for many years. his year marks the thirtieth anniversary nce our first meeting with George Baehr, I.D., Otto Klemperer, M.D., and Ward J. IacNeal, M.D., representing the New York cademy of Medicine. Their first report nd recommendations for greater cooperaon between hospitals and funeral directors ere received with considerable doubts and ven with some hostility by some funeral irectors and by some funeral director oups, but the picture has changed conderably since that first meeting.

Better funeral director-hospital relations and methods of acquiring and promoting them have been on the agenda of every annual conference of local presidents, secretaries, and State directors of our State association for years.

The 1931 report has been revised several times. The last revision (by a joint committee representing the New York Academy of Medicine, the New York Pathological Society, the Greater New York Hospital Association, and our associations) entitled *Autopsy Manual—Required Procedures in Hospital Deaths* was published by the United Hospital Fund in a convenient sized booklet in 1958. In addition to its host of suggestions for bettering relations among all concerned, the manual outlines a satisfactory method of opening a body for purposes of autopsy which will permit the preservation of the structures essential for proper embalming.

Suggestions for better understanding

I am pleased to express my views and to offer some suggestions for fostering better understanding between hospitals, pathologists, and funeral directors. Based on my own experience as a practicing funeral director and on my observations and conversations with funeral directors and my fellow officers in our local and State associations, this is my prescription: (1) Our State Funeral Directors Association should continue to regard this subject as a matter of prime importance. (2) Every local funeral directors association should devote at least part of one meeting every year to the subject. (3) Every funeral director and his employes should have a copy of the *Autopsy Manual* and should know its contents thoroughly. (4) The Medical Society of the State of New York should assign this problem to a special committee which, among other things, should have the responsibility of keeping all county societies alerted to the need for frequent consideration of the problem. (5) Every county society should recognize its opportunity and accept the responsibility of promoting cooperation and "policing" infractions in its area. (6) Hospital administrators should make certain that every member of its visiting, attending, and house staff has a copy of the

Autopsy Manual, understands thoroughly its suggestions and limitations, and is held strictly accountable for compliance and for violations. It is particularly important that the new intern and house staff member should consider himself a committee of one to assure strict compliance with the manual, recognizing that the adverse effects and hostility that is generated from any single infraction has a way of multiplying by geometric proportions. (8) Every hospital administrator or an especially designated responsible member of his personal office staff should receive all calls or complaints; he should be charged with the responsibility and given the authority to solve any problem which might arise in connection with an autopsy.

Joint committee

I regard each of these suggestions as of great importance, but if I were limited to one single suggestion it would be that a joint committee of hospital administrators, pathologists, and funeral directors should be organized in every county to do what is being done by a similar committee in some places: promote the adoption of these eight suggestions; obtain strict compliance with the *Autopsy Manual*; be certain that every one at every hospital understands that the same attention should be paid to expediting the procedures after the consent for autopsy has been obtained as was devoted to obtaining consent for the autopsy in the first place; and serve as a permanent joint grievance committee to receive complaints, and determine and appraise the fault, if any; and do what has to be done to avoid the repetition of disrupting incidents.

Speaking for our New York State Funeral Directors Association, I am certain I can pledge our full cooperation with the Medical Society of the State of New York.

Tranquilizer and muscle relaxant in spastic disorders

Pursuant to reports of the efficacy of chlordiazepoxide (Librium) in convulsive and other neuromuscular diseases, a clinical trial of the drug was undertaken in a group of 94 institutionalized patients, mostly in the younger-age groups, with spastic and athetoid disorder Using reduction in spasticity as a criterion, ther was marked improvement in 20, moderat improvement in 71, slight improvement in and none in 1. In several patients the benefici effects were particularly marked: 2 learned t walk for the first time, and in a mongoloi patient previously considered unimprovab there was a 75 per cent reduction in bot spasticity and hyperactivity.—*C. H. Carte M.D., Archives of Pediatrics, January, 1962*

BILLSBORD

Photograph of a mirage

Although conformity is a favorite whipping boy of the modern intellectual, it was only a few years ago that some of its characteristics, that today are denounced so scathingly as symptomatic of a malignant social disorder, were praised in positive and glowing terms as desirable attitudes for social adjustment and mental health. Thus the question as to whether conformity is pathologic, physiologic, or functional remains unresolved but does not preclude our knowledge of its life history and symptomatic manifestations.

Conformity is endemic (regard the Christmas party or the dry, dry, martini); it is pandemic (consider shifters, the Hula-Hoop, or the twist); and it is epidemic. The epidemic form is occupational, and although its manifestations are identified with and peculiar to a single occupational group, it will affect others in varying degrees depending on the extent of interrelationship. So it is that the present preoccupation of public relations experts with the "image concept" influences everyone including those in medicine. It is doubtful that we could escape its influence regardless of circumstances, but in our present situation, beset on one side by political opportunists and on the other by the constant pressure of the social planner, we are a natural and compliant victim avidly grasping at the "change of image" panacea.

Our worry about rising medical costs and our awareness of the constant efforts of some people to degrade and impair our belief in the individual patient-doctor relationship have increased our feeling of insecurity. A feeling that is aggravated by the recurring intimation that we have abandoned the friendly, self-sacrificing characteristics of that kindly gentleman "the old family doctor." The public, the press, and even on occasion our fellow physicians compare us to the bygone and lamented physician of the past and always to our discredit.

No wonder we hail the alluring prospect of a change of image. The favorable image of the well-loved and respected physician of yesterday has been replaced by a new and ugly image—one of calculating greed, indifference, and preoccupation with material things such as expensive cars and luxurious homes. In short we are being depicted as profiteers in human misery.

Perhaps the judicious use of money and the adherence to popular programs recommended by the "experts" could change our present image. But is this change of image concept, so effective for aging film stars, unscrupulous dictators, or corporations in disfavor, really right or necessary for us? Doesn't this type of camouflage usually cover a festering sore? Should it be only how one looks that counts and not how one is inside?

Let this dissenting voice be heard! First, I object to the premise that today's doctor is motivated by cupidity, neglectful of his patients, and only concerned with a "fast buck."

I know, live, and work with him and can testify to his genuine interest in the welfare of his patients—not only in their health but also in their problems as individuals. I need no press release to inform me that he gives freely of his knowledge, skill, and time to those that seek his help regardless of their financial status. I know he is ethical. I also know that he welcomes new discoveries and assists in their development although they may in the end curtail his "business."

It is no accident or oversight when our critics talk in generalities and not specifics. If they were armed with actual instances of what they claim is the present-day physician's greed, refusal to treat patients who can't pay, or concealment of discoveries that might harm the medical profession economically, they would not fail to publicize such facts. They must talk in generalities because they have no specifics.

Admittedly the physician is human and liable to all errors indigenous to that state. He is fallible and makes his share of mistakes. But is it unreasonable for him to expect to get paid for his work when the recipient can afford it? He has his modicum of the vanity common to us all—so is it wrong if he succumbs to the very human urge to purchase an expensive auto or an elaborate home?

I say that today's doctor needs no apologetic representative. He hides nothing shameful in purpose or practice and does not require concealment under the mask of a "new front." A doctor has always faced a public attitude that finds him inadequate, calloused, and selfish compared with an enshrined image of the doctor of some earlier day.

If there are those who feel that the doctor of today cannot compare with the doctor of their grandfather's day, let us remember that there were those of grandfather's day who felt the same way about their family doctor.

WRC

Necrology

Arthur William Albones, M.D., of Frankfort, died on May 21 at his home at the age of eighty-three. Dr. Albones graduated in 1904 from Cornell University Medical College. Herkimer County's oldest physician, Dr. Albones was a member of the Utica Academy of Medicine, the Herkimer County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Byron Heazelton Goff, M.D., of New York City, died on June 24 at Glen Cove Community Hospital at the age of eighty. Dr. Goff graduated in 1911 from the University of Pennsylvania School of Medicine and interned at Lying-In and Woman's Hospitals. He was professor emeritus of clinical obstetrics and gynecology at Cornell University Medical College and a consultant in gynecology and obstetrics at New York and St. Luke's Hospitals. Dr. Goff was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American College of Obstetricians and Gynecologists, and a member of the American Gynecological Society, the New York Academy of Medicine, the New York Obstetrical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Francis Sloan Hyland, M.D., of Gloversville, died on May 14 at the Nathan Littauer Hospital at the age of sixty-three. Dr. Hyland graduated in 1926 from Albany Medical College. He was an attending surgeon at Nathan Littauer Hospital. Dr. Hyland was a Fellow of the International College of Surgeons and a member of the Fulton County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David Levinson, M.D., of North Miami Beach, Florida, formerly of Brooklyn, died on January 23 at the age of sixty-three. Dr. Levinson graduated in 1925 from Long Island College Hospital Medical School. He was an associate surgeon (Off Ward Service) at Beth-El Hospital. Dr. Levinson was an Associate of the International College of Surgeons and a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Leon T. Le Wald, M.D., of New York City and Carmel, died on June 16 at his home at the age of eighty-eight. Dr. Le Wald graduated in 1895 from Columbia University College of Physicians and Surgeons and interned at St. Luke's and Knickerbocker Hospitals. Retired, he was a consulting roentgenologist at Knickerbocker, Vassar Brothers (Poughkeepsie), and Hackensack (New Jersey) Hospitals. He was a former instructor in pathology and later served as head of the X-ray Laboratory at New York University-Bellevue Medical Center, and in 1939 became professor emeritus. In 1926 he was the recipient of an honorary degree in radiology from Cambridge University and at one time was a chancellor of the American College of Radiology, and a vice-president of the Radiological Society of North America, Inc. Dr. Le Wald was a Diplomate of the American Board of Radiology, an Honorary Fellow of the American College of Gastroenterology, a Fellow of the American College of Physicians, a Fellow of the American College of Radiology, and a member of the American Roentgen Ray Society, the American Association for Thoracic Surgery, the American Society of Plastic and Reconstructive Surgery, the Radiological Society of North America, Inc., the New York Academy of Medicine, the New York Gastroenterological Society, the Society of Medical Jurisprudence of New York City, the New York Roentgen Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Thomas John McBlain, M.D., of Niagara Falls, died on May 11 at his home at the age of ninety-six. Dr. McBlain graduated in 1891 from Western Ontario Faculty of Medicine, University of London. Retired, he was a former chief of the medical staff at Memorial Hospital. Dr. McBlain was a Fellow of the American College of Surgeons.

Robert Anthony McTamaney, M.D., of Newburgh, died on May 29 at St. Luke's Hospital at the age of fifty-four. Dr. McTamaney graduated in 1932 from Georgetown University School of Medicine and interned at the Mayo Clinic. He was an attending surgeon at St. Luke's Hospital. Dr. McTamaney was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the Mid-Hudson Surgical Society, the Orange County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Chaim Joel Mehlmann, M.D., of New York City, died on June 10 at The Mount Sinai Hospital at the age of seventy-eight. Dr. Mehlmann received his medical degree from the University of Vienna in 1912. He was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frederick J. Parmenter, M.D., of Buffalo, died on May 27 at his home at the age of eighty-one. Dr. Parmenter graduated in 1903 from the University of Buffalo School of Medicine. Professor emeritus of urology at the University of Buffalo School of Medicine, he was a consulting urologist at Buffalo General and Children's Hospitals and chief consulting urologist at the Edward J. Meyer Memorial Hospital. Dr. Parmenter was a Diplomate of the American Board of Urology, a Fellow of the American College of Surgeons, and a member of the American Urological Association, the Buffalo Academy of Medicine, the Northeast Section of the American Urological Association, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Carlton Frasier Potter, M.D., of Syracuse, died on June 3 at Crouse-Irving Hospital at the age of seventy-nine. Dr. Potter was graduated in 1910 from Syracuse University School of Medicine. He was a consulting radiologist and orthopedic surgeon at Crouse-Irving Hospital. With the late William L. Wallace, M.D., Herbert O. Brust, M.D., and Carl E. Muench, M.D., he helped establish Crouse-Irving Hospital and was the founder of the X-ray Department there. In 1915 he became a member of the Onondaga County Medical Society, served as chairman of the public relations committee for many years, and was its president from 1949 to 1950. From 1913 to 1945 he was secretary of the Crouse-Irving Hospital board and president from 1945 to 1954. He had been credited with establishing the first medical society grievance committee east of the Mississippi and had also served as president of the Syracuse Academy of Medicine. Dr. Potter was a Diplomate of the American Board of Radiology (Roentgenology), a Fellow of the American College of Radiology, and a member of the Radiological Society of North America, Inc., the Radiological Society of New York State, the Syracuse Academy of Medicine, the Central New York Roentgen Ray Society, the Onondaga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James Ralph Rosen, M.D., of New York City, died on January 27 in Tucson, Arizona, at the age of sixty-two. Dr. Rosen graduated in 1922 from Long Island College Hospital Medical School. Also a lawyer, Dr. Rosen was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Rosenberg, M.D., of New York City, died on January 12 at the age of seventy. Dr. Rosenberg graduated in 1914 from Long Island College Hospital Medical School. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Anthony Walter Rusin, M.D., of Brooklyn, died on January 20 at the age of eighty. Dr. Rusin graduated in 1909 from Syracuse University School of Medicine.

Albert Eugene Sellenings, M.D., of Port Jefferson, died on June 13 at St. Charles Hospital at the age of eighty-eight. Dr. Sellenings graduated in 1899 from New York University and Bellevue Hospital Medical College and interned at Bellevue Hospital. He was a consulting surgeon at New York Polyclinic Hospital and an emeritus surgeon at the John T. Mather Memorial Hospital. Retired, Dr. Sellenings was a Fellow of the American College of Surgeons and a member of the New York Surgical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

B. Edgar Spiegel, M.D., of New York City, died on June 21 at the Medical Arts Hospital at the age of seventy. Dr. Spiegel graduated in 1914 from New York Homeopathic Medical College and Flower Hospital. Retired, he was physician emeritus at Midtown Hospital.

James Steele, M.D., of Massapequa, died on June 10 at Mercy Hospital, Rockville Centre, at the age of seventy-five. Dr. Steele graduated in 1910 from Eclectic Medical Institute of New York, Rochester. He was a consulting physician at Greenpoint and St. Catherine's Hospitals.

Joseph F. Todd, M.D., of Brooklyn, died on June 12 at the age of eighty-nine. Dr. Todd graduated in 1895 from Long Island College Hospital Medical School. He was a consulting obstetrician and gynecologist at St. Peter's Hospital and former chief of obstetrics and gynecology there and at Samaritan Hospital of Brooklyn. Dr. Todd was a Fellow of the American College of Surgeons and a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

Armed Forces chapter of the ACOG formed

Formation of a new Armed Forces chapter of The American College of Obstetricians and Gynecologists has been announced by Edward C. Hughes, M.D., Syracuse, president of the College.

Chapter officers appointed temporarily by Dr. Hughes to organize the group include: Capt. Sidney L. Arje, MC, USN, chairman; Col. Edward A. Zimmerman, MC, USA, vice-chairman; and Lt. Col. Kenneth N. Morese, MC, USAF, secretary-treasurer. All are of Washington, D.C., and serve respectively as the obstetric-gynecologic consultants of the Navy, Army, and Air Force.

For further information write to: Lt. Col. Kenneth N. Morese, c/o Office of the Surgeon General of the Air Force, Washington 25, D.C.

Diabetes group elects officers

The Clinical Society, professional arm of the New York Diabetes Association, has announced the election of the following officers for the term ending in June, 1963:

Max Ellenberg, M.D., chairman; Kermit E. Pines, M.D., chairman-elect; Harold Rifkin, M.D., vice-chairman; and Rachmiel Levine, M.D., secretary-treasurer. All are from New York City.

Dr. Ellenberg has stated that "the aim of the Clinical Society this year will be to seek the extension of its programs of professional education to the medical staffs of cooperating hospitals throughout New York City." The society is also planning to establish uniform standards of patient care in the diabetes clinics of New York City.

Glorney-Raisbeck Fellowship

The Glorney-Raisbeck Fellowship in the Medical Sciences for the academic year beginning July 1, 1963, will be awarded by the Committee on Medical Education of The New York Academy of Medicine for one year of research and/or study in any field of medicine or its allied sciences. Under circumstances deemed appropriate by the Committee, the Fellowship is renewable on a year-to-year basis for two additional years.

The Fellowship, which carries a stipend of $6,000, is open only to holders of a doctor of medicine degree who have demonstrated a potential for productivity in research and teaching. In general, preference will be given to physicians from the Greater New York area.

Deadline for receipt of applications is December 1, 1962. Requests for application forms and additional information should be addressed to: Aims C. McGuinness, M.D., Executive Secretary, Committee on Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Course in electrodiagnosis and electromyography

The Department of Physical Medicine and Rehabilitation of New York Medical College—Metropolitan Medical Center will offer a one-week course on "Electrodiagnosis and Electromyography" September 24 through 28. The course is open to physicians only. It will consist of lectures, seminars, clinical demonstrations, and laboratory sessions.

For information and registration write to: Osvaldo Miglietta, M.D., Department of Physical Medicine and Rehabilitation, New York Medical College, 1 East 105th Street, New York 29, New York.

Courses on radiation at Queens Hospital Center

The Department of Radiation Medicine at the Queens Hospital Center will offer two courses on radiation this fall.

The first, "Special Radiation Procedures in the Treatment of Cancer," will be held on Monday, October 15. It will include the following: rotational and arc cobalt teletherapy; interstitial therapy with various radioisotopes; recent technics in the field of isotopes; beta-ray applicators; operative radium technics; modern technics in radium mold fabrication.

The second course, "Operative Radium Therapy Day," will be held on Wednesday, October 17. It will include the use of interstitial radiation in the oral cavity; radical insertion of radium in the neck; various applicators in carcinoma of the cervix; the Heyman applicators in carcinoma of the endometrium; radium needles in the parametria; and radon, iridium-thread, and cobalt interstitial therapy.

Both courses will be held at the Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York. For applications apply to Dr. Philip J. Kahan, Supervising Medical Superintendent.

Grant for corneal implant project

R. Townley Paton, M.D., medical director of the Eye Bank and chairman of The Lighthouse Research Committee, has announced that a grant from The Lighthouse, The New York Association for the Blind, has enabled the Eye Bank for Sight Restoration to embark on a full-scale research project relating to corneal implants.

The ten-thousand dollar Lighthouse grant will be used to obtain the equipment and personnel required for the research project, according to Dr. Miguel Martinez, project director. Consultants on the project are Dr. Karl Meyer, professor of biochemistry, Columbia University College of Physicians and Surgeons, and Arthur Linksz, M.D., clinical professor of ophthalmology, New York University School of Medicine.

The final aim of the project is the restoration of useful vision to patients with corneal scarring who are not good candidates for ordinary corneal grafts. The immediate aim is the development and testing of a synthetic corneal prosthesis for this purpose.

Central audiovisual function established

A central audiovisual function has been established for the U.S. Public Health Service at its Communicable Disease Center in Atlanta, Georgia.

Formerly the Audiovisual Section, the newly designated "National Medical Audiovisual Facility" will have the responsibility for: (1) development, production, acquisition, distribution, and utilization of medical motion pictures and other audiovisual forms; (2) maintenance of the National Medical Motion Picture Archives; (3) dissemination and exchange of scientific and other medical film information important to progress in medicine and public health; (4) encouragement of the development and production of medical films and other audiovisual aids; and (5) the stimulation of a speed-up in the circulation of medical knowledge, on a national and international basis, through audiovisual aids.

For further information contact: Director, National Medical Audiovisual Facility, Communicable Disease Center, Atlanta 22, Georgia.

New psychiatric service offered

The Department of Psychiatry, City Hospital at Elmhurst, has announced a free psychiatric consultation service available to all local nonpsychiatric physicians, general practitioners, and specialists in various fields.

The new service will make it possible for physicians to discuss with a psychiatrist the emotional problems encountered in patients in their daily practice. The program is offered as a form of graduate education related to the psychiatric training program for general practitioners and specialists conducted with the help of a grant by the National Institute of Mental Health for the past three years. It is hoped that the availability of such a consulting service will eventually lead physicians to establish contact with private psychiatrists in the community for the routine use of such consultation.

Physicians interested in the program should make an appointment with: Stanley Brodsky, M.D., Department of Psychiatry, City Hospital at Elmhurst, 79–01 Broadway, Elmhurst 73, New York. Telephone DEfender 5–3200.

Blue Shield statistics

More than 49,250,000 persons were enrolled in the 74 Blue Shield Plans located in North America as of March 31, 1962, the National Association of Blue Shield Plans has announced. Total membership in these nation-wide medical-surgical plans reached 49,252,622 at the end of March as a result of a net gain of 130,458 new members during the first three months of 1962.

Blue Shield now covers one out of every four Americans and more than 15 per cent of the total Canadian population.

Course in emotional and psychiatric problems

The New York Academy of Medicine will present the fourth in an annual series of courses on "Emotional and Psychiatric Problems in Medical Practice," starting Monday, October 22 and ending on February 8, 1963. The course, which is open to all physicians in specialty and general practice, will consist of basic and advanced sections meeting at weekly intervals for 14 one and one-half hour sessions at the Academy building, 2 East 103rd Street, New York 29, New York.

The objective of the course is to help physicians to comprehend more fully the continuous interaction of psychologic, social, and medical factors encountered in clinical practice. The course will be divided into basic sections, for the benefit of those who have not participated previously, and advanced sections for those who have already taken the basic course. The American Academy of General Practice, cosponsors of the course, will allow 21 hours of category 1 credit for its completion.

For information write to: Executive Secretary for Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Postgraduate courses

A schedule of fifteen postgraduate courses to be presented throughout the country during 1962 and 1963 has been announced by The American College of Physicians.

The concentrated courses are part of the College's postgraduate program which is aimed at providing practicing physicians with current information on internal medicine and related specialties.

Courses to be held in New York City are: "Advances in the Medical Aspects of Cancer," October 8 through 12, Memorial Sloan-Kettering Cancer Center; "Diseases of the Blood Vessels and Problems of Thromboembolism—Diagnosis and Treatment," January 21 through 25, 1963, The New York Hospital-Cornell Medical Center; "Recent Advances in Cardiovascular Disease," March 18 through 23, 1963, The Mount Sinai Hospital.

For the complete program of courses write to: The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pennsylvania.

Booklet on medical careers

A new 32-page booklet, designed to help communities interest more students in careers in medicine, has been issued by Pfizer Laboratories and J. B. Roerig and Company, ethical drug divisions of Chas. Pfizer & Co., Inc.

Titled "Your Career Opportunities in Medicine," the free booklet was prepared for high school students and college freshmen and sophomores. It provides information on a wide range of career possibilities in medicine—in family practice, specialties, research, public health, teaching, and medical administration. It was prepared in cooperation with the Council on Medical Education and Hospitals of the American Medical Association and checked for accuracy by the Division of Operational Studies of the Association of American Medical Colleges.

Free copies are available from: Education Services Department, Chas. Pfizer & Co., Inc., 235 East 42nd Street, New York 17, New York.

Directory of psychiatric services

Marvin E. Perkins, M.D., Commissioner of Mental Health Services, has announced the publication of the New York City Community Mental Health Board's Directory: "Psychiatric Services for Residents of New York City 1962." The twenty-page, pocket-sized directory gives the name, address, telephone number, and other appropriate information of over 180 governmental, voluntary, and proprietary hospitals and clinics offering psychiatric services to residents of New York City. The directory is available without charge from: The New York City Community Mental Health Board, 93 Worth Street, New York 13, New York.

Teaching material available on recordings

The California Medical Association's nonprofit subsidiary, the Audio-Digest Foundation, has just released to the medical profession a library of more than 250 one-hour tape recordings devoted to comprehensive discussions of everyday office problems.

The recordings make available to physicians, hospitals, and clinics, ideal program and teaching material in six specialty areas: anesthesiology, obstetrics and gynecology, surgery, internal medicine, pediatrics, and general practice. A number of tapes also focus on the basic sciences, cancer, psychiatry, gastroenterology, cardiology, arthritis, geriatrics, and hematology.

Copies of the new catalog and further information may be obtained from: Audio-Digest Foundation, 619 South Westlake Avenue, Los Angeles 57, California.

Booklet reports on research projects

A new 40-page booklet, "Research Projects—Volume 3," has been published by The Medical Foundation, Boston, Massachusetts. The booklet reports for the first time on all research project grants awarded by the Foundation from its inception in 1957 through 1961. It is available without charge from: The Medical Foundation, 227 Commonwealth Avenue, Boston 16, Massachusetts.

Rehabilitation center at Downstate Medical Center

The designation of a primary rehabilitation center at the Downstate Medical Center at Brooklyn, under the State-wide program for comprehensive rehabilitation centers, has been announced by Herman E. Hilleboe, M.D., Commissioner, State of New York Department of Health.

Under the terms of an agreement between the State University of New York and the State of New York Department of Health, the rehabilitation center, located in Kings County Hospital, will receive up to $40,000 a year in support of its operations.

The center is the sixth in the State-wide program calling for a network of 12 primary centers affiliated with medical schools and teaching hospitals, and 15 secondary rehabilitation centers. The plan was developed at Governor Rockefeller's request, with the assistance of the Committee on Rehabilitation of the State Interdepartmental Health and Hospital Council, which includes the Departments of Education, Health, Mental Hygiene, Insurance, and Social Welfare, and the Governor's Council on Rehabilitation.

Personalities

Speaker. Richard Drooz, M.D., Brooklyn, before the staff of the Veterans Administration Hospital, Northport, Long Island, on June 19, on the subject "Comprehensive View of Psychotherapy."

Elected. Edward B. Allen, M.D., and Edward J. Lorenze, M.D., White Plains, as secretary and treasurer respectively, of the American Geriatrics Society . . . Irving M. Pallin, M.D., Brooklyn, as president of the medical board of the Jewish Hospital of Brooklyn.

Appointed. Grace McLean Abbate, M.D., New York City, reappointed as a member of the New York City Community Mental Health Board . . . Dale E. Harro, M.D., Baltimore, Maryland, as director of the Bureau of Maternal and Child Health of the State of New York Department of Health . . . J. G. Fred Hiss, M.D., Syracuse, as director of the Bureau of Heart Disease of the State of New York Department of Health . . . Henry A. Holle, M.D., formerly of the U.S. Public Health Service, as director of health projects for The State Charities Aid Association of New York . . . Aims C. McGuinness, M.D., New York City, as a member of the New York City Community Mental Health Board . . . Kent D. Miller, M.D., Albany, as assistant director in charge of laboratories for biochemistry and immunology in the State of New York Department of Health Division of Laboratories and Research.

Heart rate during sleep studied by FM system

An FM radio system has enabled researchers to study heart rate patterns of patients during a night of undisturbed, uninterrupted sleep, according to an article by Gordon H. Ira, Jr., M.D., and Morton D. Bogdonoff, M.D., in the June 16, 1962, issue of the *Journal of the American Medical Association*. The success of the study indicates that the technic, known as radiotelemetry, will make it possible to gather information on bodily functions which were previously difficult to observe. "Though the situation of uninterrupted sleep does not present many technical difficulties, the fact that the observations were made without in any way disturbing the subject suggests that the method will have wide application."

The study revealed that the heart rate of a sleeper decreases gradually during the course of the night and eventually reaches a low point after which it may increase gradually. However, the heart rate of persons with hyperthyroidism did not decline during sleep. Pulse rates in these persons ranged from 108 to 118 beats per minute, which were not appreciably lower than their pulse rates while awake. The study revealed that there were some periods of increased heart rate during the night which were associated with body movements.

"Simultaneously recorded electroencephalograms demonstrated that the depth of sleep lightened at the time that body movement and heart rate increases occurred. The plane of sleep, therefore, is fairly consistently reflected by the contour of the heart-rate pattern: when there is variability in heart rate, the plane of sleep is light; when there is constancy in heart rate level, the plane of sleep is deep."

Prolonged and uninterrupted recordings of this type have been difficult to obtain because of limits imposed by recording equipment. Advances in electronic miniaturization have led to the development of transistorized radio instruments which make it possible to signal information without bulky recording equipment.

A transmitter the size of a package of cigarets is used in the new technic. The patient's heart beat is picked up by leads attached to his chest which are connected to the transmitter worn in a wide belt.

The transmitter, operating on a frequency allocated by the Federal Communications Commission, broadcasts an FM signal which is received on a standard FM radio. From the receiver, the signal is fed into a tape recorder and then to other machines for analyzing the data.

Abstracts

Wantz, G. E., Jr., and Moore, S. W.: Chronic occlusive arterial disease, New York State J. Med. **62:** 2471 (Aug. 1) 1962.

Chronic occlusive arterial disease includes various diseases in which chronic arterial insufficiency is a predominant manifestation. The clinical manifestations may include intermittent claudication, ischemia of the branches of the arch of the aorta, and stenosis of a renal artery. Arteriography, either percutaneous or intravenous, is the most useful method of diagnosis. Patients with occlusive arterial disease require meticulous care. They are candidates for arterial reconstruction if the occlusion is segmental, if the arterial tree distal to the occlusion is patent and adequate, and if an operation is not otherwise jeopardous because of associated or attendant conditions. The procedures include sympathectomy, endarterectomy, and grafting procedures. A successful outcome of surgery can be achieved in almost 90 per cent of the patients who meet the required surgical indication and have an adequate "run-off." The number of failures occurring months to years following an operation have been disappointingly high; however, some of the patients with late failure can be successfully operated on again.

Litchfield, H. R.: Therapy of iron-deficiency anemias, New York State J. Med. **62:** 2481 (Aug. 1) 1962.

An evaluation was made of a new iron-carbohydrate complex of low toxicity (Jefron) in 26 newborn infants, 4 severely anemic infants, 17 private pediatric patients, and 35 obstetric patients with hemoglobin values of below 10 Gm. per 100 ml. Satisfactory hemoglobin responses occurred in all groups at levels of iron lower than those which are conventionally used. There were no significant side-effects, and the complex was well tolerated.

Russell, A., and Parchment, A. R.: Field test of simple, foam-producing chemical contraceptive, New York State J. Med. **62:** 2491 (Aug. 1) 1962.

A field trial of a contraceptive foam-producing liquid used with an insertable moistened sponge (Durafoam) was carried out in Jamaica, West Indies. The study, which lasted an average period of nine months, included 640 women. There were 18 pregnancies, or 4.2 per hundred years of woman exposure, as compared with the normal rate in the population of 70 to 80 per hundred exposure years. The method is inexpensive, simple, and suited for use in women of little education and in low-income brackets.

Sands, R. X., Mayron, J., and Pinski, A. V.: A novel test for pregnancy, New York State J. Med. **62:** 2494 (Aug. 1) 1962.

A study was made of the effectiveness of the PD (Pro-Duosterone) pregnancy test which has as its physiologic basis the uterine bleeding which occurs after progesterone withdrawal. Of 122 patients on whom the PD and the AZ (Aschheim-Zondek) tests (Frank-Berman modification) were performed, 66 were found to be pregnant and 56 nonpregnant. Among the pregnant cases there were 9 false results obtained with the AZ test and 1 with the PD test, an accuracy of 98.4 per cent with the latter. In the nonpregnant group 4 incorrect results were obtained with the PD test and 1 with the AZ test. No significant side-effects occurred in this group or in an additional series of 100 cases, all known to be pregnant. In the largest number of cases a negative result becomes available within three days after the last dose of the estrogen-progesterone combination.

Mamelok, L.: Clinical evaluation of 245 ragweed-sensitive patients treated with precipitated pyridine ragweed complex, New York State J. Med. **62:** 2498 (Aug. 1) 1962.

Alum-precipitated pyridine ragweed complex was given to three groups of patients sensitive to regular aqueous ragweed extract: 87 preseasonally in 1959, 112 preseasonally in 1960, and 48 coseasonally in 1959, 1960, and 1961. In the groups treated preseasonally, from 89 to 93 per cent good or excellent results were obtained. All of the patients treated coseasonally reported good or excellent results. There were two constitutional reactions and two local reactions. Otherwise there were no systemic or local side-effects and no toxicity, and larger dosages were administered than was possible with aqueous ragweed extracts.

Fahey, D. J.: Pitfalls of mobilization surgery, New York State J. Med. **62:** 2502 (Aug. 1) 1962.

Stapes surgery has progressed from the blind, remote pressure mobilization to the total removal of the stapes, including the footplate, with a vein graft, vein plug, or a gelatin filler over the oval window and either a polyethylene or a metal wire prosthesis. The technics used today are more difficult than previous technics, and the complications are much more serious. However, the results are promising although they have not been evaluated fully as yet.

Medical Meetings

Vermont Heart Association

On Saturday, September 29, and Sunday, September 30, a seminar on "The Origin and Significance of the T Wave of the Electrocardiogram and the Ventricular Gradient" will be held in Burlington, Vermont. The seminar is sponsored by the Vermont Heart Association and the University of Vermont College of Medicine. John S. LaDue, M.D., New York City, will be among the guest speakers.

For information contact: Eugene Lepeschkin, M.D., Division of Experimental Medicine, University of Vermont College of Medicine, Burlington, Vermont.

Stamford-Darien-New Canaan Heart Association

The Stamford-Darien-New Canaan Heart Association, Inc., will hold its eighth annual medical symposium on Thursday, October 4,* in the auditorium of St. Joseph's Hospital, Stamford, Connecticut.

Among those scheduled to speak are: Marie J. Browne, M.D., New Haven, Connecticut, on "Congenital Heart Disease as Related to Medical Practice"; Mark D. Altschule, M.D., Waverly, Massachusetts, on "Cardiac Decompensation as a Metabolic Disorder"; Max G. Carter, M.D., New Haven, on "Surgery of Acquired Valvular Heart Disease"; Charles K. Friedberg, M.D., New York City, on "Coronary Artery Disease"; and Simon Rodbard, M.D., Buffalo, New York, on "Some Problems in Endocarditis."

For further information contact: Miss Antoinette Dimler, Executive Director, Stamford-Darien-New Canaan Heart Association, Inc., 318 Hope Street, Glenbrook, Connecticut.

* Postponed to March 21, 1963.

Society for the Scientific Study of Sex

The fifth annual meeting of the Society for the Scientific study of Sex will be held at 9:30 A.M. on Saturday, October 20, in the Barbizon Plaza Hotel, 106 Central Park South, New York City.

The topic for the morning session will be "New Concepts in Sex Education." Milton I. Levine, M.D., will be chairman. The afternoon session will consider the subject of "Prostitution." Robert V. Sherwin, LL.B., will be the chairman.

For information write to: Hugo G. Beigel, Ph.D., Secretary, The Society for the Scientific Study of Sex, 138 East 94th Street, New York 28, New York.

Armed Forces seminar on obstetrics and gynecology

The Armed Forces seminar on obstetrics and gynecology will be held at the Great Lakes Naval Training Station Hospital, North Chicago, Illinois, from Sunday to Wednesday, October 21 through 24.

The first meeting of a new Armed Forces chapter of the American College of Obstetricians and Gynecologists will take place at the same time. See *Medical News* for further information concerning the new chapter.

American Academy of Pediatrics

The thirty-first annual meeting of the American Academy of Pediatrics will be held in the Palmer House in Chicago, October 27 through November 1. For a complete program of the meeting write to: American Academy of Pediatrics, 1801 Hinman Avenue, Evanston, Illinois.

Abstracts in Interlingua

Wantz, G. E., Jr., e Moore, S. W.: Chronic morbo de occlusion arterial (*anglese*), NEW YORK STATE J. MED. **62:** 2471 (1 de augusto) 1962.

Chronic morbo de occlusion arterial include varie morbos in que chronic insufficientia arterial es un manifestation predominante. Le manifestationes clinic pote includer claudication intermittente, ischemia del brancas del arco del aorta, e stenosis de un arteria renal. Arteriographia—percutanee o intravenose—es le plus utile methodo diagnostic. Patientes con morbo de occlusion arterial require un meticulose sollicitude. Illes es candidatos pro reconstruction arterial si le occlusion es segmental, si le arbore arterial distal con respecto al sito del occlusion es patente e adequate, e si un operation non es alteremente riscose a causa de associate conditiones. Le procedimento include sympathectomia, endarterectomia, e graffage. Un successose resultato del intervention chirurgic pote esser obtenite in quasi 90 pro cento del patientes qui satisface le supra-listate criterios rendente un intervention chirurgic indicate. Le numero del malsuccessos que se accusa menses o mesmo annos post le operation ha essite disappunctantemente alte. Tamen, un certe procentage del patientes con malsuccesso tardive pote esser re-operate, e alora successosemente.

Litchfield, H. R.: Therapia del anemias a carentia de ferro (*anglese*), NEW YORK STATE J. MED. **62:** 2481 (1 de augusto) 1962.

Esseva evalutate un nove complexo de ferro e hydrato de carbon a basse toxicitate (Jefron) in 26 neonatos, 4 severmente anemic infantes, 17 patientes pediatric de practica private, e 35 patientes obstetric con valores pro hemoglobina de infra 10 g per 100 ml. Satisfacente responsas del hemoglobina occurreva in omne le gruppos, e isto a nivellos de ferro plus basse que illos que es usate conventionalmente. Occurreva nulle significative effectos secundari adverse. Le complexo esseva ben tolerate.

Russell, A., e Parchment, A. R.: Essayo, sub conditiones de realitate, de un simple spumigenic agente chimic de anticonception (*anglese*), NEW YORK STATE J. MED. **62:** 2491 (1 de augusto) 1962.

Un essayo con un liquido spumigenic de activitate anticonceptional, usate con un inseribile spongia (Durafoam), esseva executate sub conditiones de vita real in Jamaica, Indias Occidental. Le studio, que durava un periodo medie de novem menses, includeva 640 feminas. Occurreva 18 pregnantias, i.e. 4,2 per cento annos de femina exponite. Isto es a comparar con le cifra normal del population general de 70 a 80 pregnantias per cento annos de exposition. Le methodo es incostose, simple, e appropriate al uso per feminas de pauc education e basse strato economic.

Sands, R. X., Mayron, J., e Pinski, A. V.: Un novelle test pro le pregnantia (*anglese*), NEW YORK STATE J. MED. **62:** 2494 (1 de augusto) 1962.

Esseva studiate le efficacia del test a PD (Pro-Duosterona) pro le verification del pregnantia. Le base physiologic del test es le sanguination uterin que occurre post le retraction de progesterona. In un gruppo de 122 patientes in qui le test a PD e le test de AZ (Aschheim-Zondek; modification de Frank-Berman) esseva executate, 66 esseva pregnante e 56 non-pregnante. In le gruppo del pregnantias, 9 false resultatos esseva obtenite con le test de AZ e 1 con le test a PD. Assi le accuratia pro le test a PD esseva 98,4 pro cento. In le gruppo del non-pregnantias, 4 false resultatos esseva obtenite con le test a PD e 1 con le test de AZ. Nulle significative effectos secundari adverse occurreva in iste gruppo o in un altere gruppo de 100 feminas qui omnes esseva cognoscitemente pregnante. In le grande majoritate del casos, un resultato negative se declara intra tres dies post le ultime dose del combination de estrogeno e progesterona.

Mamelok, L.: Evalutation clinic de 245 patientes con sensibilitate pro ambrosia, tractate con precipitate complexo de ambrosia a pyridina (*anglese*), NEW YORK STATE J. MED. **62:** 2498 (1 de augusto) 1962.

Complexo de ambrosia a pyridina precipitate per alumine esseva administrate a tres gruppos de patientes sensibile pro regular extracto aquose de ambrosia. Un gruppo de 87 subjectos esseva tractate ante le saison in 1959; un secunde gruppo de 112 subjectos esseva tractate ante le saison in 1960; e un tertie gruppo de 48 subjectos esseva tractate durante le saison in 1959, 1960, e 1961. In le gruppos tractate ante le saison, inter 89 e 93 pro cento de bon o excellente resultatos esseva obtenite. Omne le patientes tractate durante le saison

reportava bon o excellente resultatos. Occurreva duo reactiones constitutional e duo reactiones local. Alteremente nulle adverse effectos secundari de character constitutional o local e nulle toxicitate esseva notate, ben que le doses administrate esseva plus grande que lo que es possibile con extractos aquose de ambrosia.

Fahey, D. J.: Aspectos problematic de chirurgia mobilisatori del stapede (*anglese*), NEW YORK STATE J. MED. **62:** 2502 (1 de augusto) 1962.

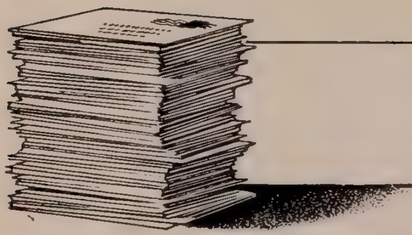
Le chirurgia del stapede ha progredite ab plus o minus occulte tentativas de effectuar su mobilisation per un pression a distantia usque ad le excision total de illo, incluse su placa basal, con un graffo o tappo venose o un inserto de gelatina super le fenestra oval e le montage de un prosthese de polyethyleno o de filo metallic. Le technicas in uso in nostre die es plus difficile que illos del passato, e le complicationes es multo plus serie. Tamen, le resultatos es promittente, ben que un evalutation complete de illos ha non ancora essite effectuate.

No liability for failure to detect fracture

Failure to detect a fracture of the neck of the femur of an elderly woman did not give rise to liability on the part of the doctors who examined her or the hospital where she was examined, according to a case reported in the May 31, 1962, issue of *The Citation*. The patient's damage suit was dismissed by a Federal district court in Louisiana for lack of any medical testimony establishing professional negligence.

The x-ray films taken in the hospital's emergency room did not show the fracture. For the lateral view, her leg was rotated less than 40 degrees, since further manipulation of the leg would have caused increased pain. Two days later, a clinical examination showed a full range of motion in the hip, and no further x-ray films were taken. The patient was discharged from the hospital without being advised to return for further checking or to call her family doctor if pain continued. After suffering for six months, the patient had additional x-ray films taken which showed the fracture and also showed that her leg had been shortened by $1^1/_4$ inches.

Although the hospital and the doctors knew that the patient was suffering from osteoporosis, which made her bones predisposed to fracture, four well-qualified orthopedic surgeons testified that the care received by the patient was in conformity with that ordinarily employed by doctors of good standing in the community. Two of these medical witnesses were called by the patient. The court dismissed the suit but took occasion to criticize the medical profession. It said that the patient's case foundered before it began on the "rock of self-interest." It also said, "Understandably, doctors are not anxious to indict fellow practitioners for malpractice. Common survival and mutual protection dictate this lack of interest. This is particularly so where, as here, the accused doctors are eminent in their profession and enjoy an outstanding reputation in the community." (*Leavell* v. *Alton Ochsner Medical Foundation*, 201 F. Supp. 805 (D.C., E.D. La., Feb. 8, 1962)



Letters to the Editor

Value of routine autopsies

To the Editor: The value of "routine autopsies" is a matter of debate at our hospital. All concede the desirability of autopsies in instances where the patients' disease was puzzling, in circumstances with medicolegal implications, and the like. There is grave question in my mind, however, as to the scientific merit of routine autopsy series.

It seems to me that an area of special interest must exist before the autopsy is performed, rather than nothing but hope that retrospective analyses of autopsy records will reveal valuable information. Usually it is just the tissues which one wishes to study that will not have been preserved or described, or else the specific details are missing. There is no such thing as an "unselected" autopsy series, and therefore most statistics based on them have limited usefulness.

At the turn of the century, large numbers of routine autopsies were performed in German hospitals, yet the number of significant new observations from them was almost nil. This is not surprising when one considers that subtle changes are not observed unless one is looking specifically for them or for related phenomena. Further, new observations are stimulated by advances in all the other clinical and basic biologic fields. Thus one expects that new pathologic entities will continue to be described and related to disease as our concepts change.

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Buffalo 3, New York

Elusive, egregious, etymologic excrescences: eponyms

To the Editor: The American medical profession has always moved with pride, and justifiably so. There are many reasons for this, too numerous to mention here. Outstanding among these is the fact that it invariably has demanded and manifested the greatest possible degree of intellectual discipline, logic, and objectivity in the pursuit of its comprehensive scope of scientific and humane endeavors. In view of the preceding and other attributes, the status of the medical vocabulary is almost incongruous. The esoteric language of medicine is replete with polyepy, contradiction, variation, polysemia, synonymy, and other philologic pitfalls. To these, one must add the seemingly infinite, labyrinthine maze of eponyms. It is this subject to which this feeble literary effort is dedicated.

The basic study of medicine and the lifelong attempt thereafter to keep abreast with current findings and concepts pose a formidable challenge to every physician. The preponderance of eponyms extant acts only as a gross deterrent. It is reasonable to expect a medical term, etymologically, to be either descriptive or distinguishing. In this respect, eponyms probably are the chief offenders, and, further, they impose a double or treble burden on the reader or would-be learner. If there were only one or two or a hundred such instances, the use of eponyms might be tolerable, if not semantically sound. However, when magnified by the thousands and thousands of such terms, it presents a hopelessly discouraging situation, and one that well bears reappraisal.

Not too long ago, the writer undertook the somewhat time-consuming task of wading through the pages of the medical dictionary for the singular purpose of determining the sectional and total numbers of eponyms. On completing such a project and surveying the results, one feels the overpowering urge to voice his reaction by the expedient of some profound, deep-meaning phrase, such as "Holy Smoke!" Indeed, the situation is far more awesome, for several reasons, than this study would indicate. First, the writer used the medical dictionary which accompanied him through medical school (ancient vintage, class of '49), and countless eponyms have been added since then; second, the host of noncapitalized terms, although obviously eponymous in origin, were omitted.

Space and time forbid presenting a complete analysis. Hence, this report will include only a general alphabetical breakdown of the findings.

Table I indicates the numbers of eponyms, presented alphabetically, and the over-all total.

TABLE I. Alphabetical frequencies of eponyms and combined total*

A—344
B—435
C—592
D—913
E—153
F—428
G—253
H—119
I—93
J—37
K—56
L—495
M—587
N—140
O—556
P—549
Q—6
R—388
S—2,089
T—1,545
U—57
V—145
W—61
X—1
Y—4
Z—23

TOTAL 10,069

* Dorland, W. A.: The American Illustrated Medical Dictionary, Philadelphia and London, W. B. Saunders Company, 20th edition.

Such is the problem, in part. It is not implied that all eponyms, per se, are equally undesirable, as some few are either descriptive or distinguishing. Unfortunately, however, these constitute an insignificant percentage of the whole, the overwhelming majority being such as to offer no clue as to their meaning or identification. Obviously, the hope of permanently committing any reasonable number of these to memory long since has transcended from the improbable to the impossible. It is conceivable that the day will come when a concerted effort is launched to discourage this trend in medical terminology. Let's hope so.

Initially, the writer, himself seeking immortality, entertained the thought of achieving such by slyly suggesting that this bit of prose hereafter be referred to as, oh, say, Gallagher's Grandiloquent Grievance, for example. But, alas! This would entail the addition of still another eponym, which might serve to topple an already staggering figure.

Ultimately, however, after prolonged and intensive deliberation, an alternate proposal emerged which would accomplish the same purpose, probably more to everyone's satisfaction (including the author's), and certainly more in keeping with the pervading theme—to inscribe it indelibly up on the glossy surface of a giant fecalith, perhaps . . .   .

NEIL D. GALLAGHER, M.D.

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EDITOR'S NOTE. Burgess L. Gordon, M.D., Associate Editor of the *Journal of the American Medical Association*, has at present in an advanced stage a complete revision of *Standard Nomenclature* which is refreshingly iconoclastic. It will be available soon.

Cystic fibrosis

Cystic fibrosis, an inherited chronic condition which produces serious disturbances in the respiratory and digestive systems of infants and young children, now ranks high as a cause of death among the diseases of childhood, it is reported by statisticians of Metropolitan Life Insurance Company.

Cystic fibrosis was identified as a disease entity less than twenty-five years ago, and its diagnosis is still difficult. Accordingly, the prevalence of the disease is not known with any degree of accuracy.

Estimates of the annual incidence of new cases in the United States range widely, from 1,500 to over 7,000 cases a year. It has also been estimated that 2,500 patients with the disease were hospitalized during 1957 and that 360, or one-seventh, died during their hospital stay.

The mortality from the disease is heavily concentrated in childhood. Nearly 95 per cent of the deaths occur among children under fifteen. Thirty per cent of the deaths occur during the first year of life, about the same proportion occurs at ages one to four, and an additional one-fourth at ages five to nine.

The case fatality rate of the disease is high, largely because of the difficulty in controlling infections. Survival has improved, however, with the greater understanding of the disease, with intensive use of antibiotics for both the prevention and treatment of infections, and with the use of pancreatic extracts to combat digestive complications.

A recent New England medical center study on the long-term outlook for children with cystic fibrosis shows encouraging results. In the study, 105 patients who had already survived at least five years were observed for a further seventeen-month period. At the end of that time, 95 were still alive, half were judged to be in better clinical condition, and only one-fifth had grown worse.

Books Reviewed

Principles of Dynamic Psychiatry. By Jules H. Masserman, M.D. Second edition. Octavo of 332 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $8.00.

This masterly volume made its debut in 1946. In a rapidly growing theoretical and clinical psychiatry rooted in dynamic psychology and other basic medical sciences, it is highly desirable to prune the original tree and make room for new growth rooted in current knowledge.

The author is professor of neurology and psychiatry, Northwestern University, and director of education, Illinois State Psychiatric Institute, Chicago. His skillful pruning hook has deleted nearly half of the 1,200 references in the original bibliography making way for pertinent recent contributions incorporated into the sections on neurophysiology, pharmacology, experimental psychology, social psychiatry, and psychoanalysis. Entirely new sections on ethology, information and systems theory, disturbances of communications, and the evolution of psychotherapy have made it expedient to eliminate discussions on combat neuroses and wartime morale which were of timely importance following World War II.

The contents are divided into two parts: Part I is concerned with the development of behavior theory in which psychiatry is designated as a science of behavior in pertinent relationship to psychologic concepts amplified by psychoanalytic theory, dynamics of adaptation, and neurotigenic and psychotic dynamisms in which minor and major mental abnormalities and their causes are delineated.

Part II elaborates on biodynamics. Herein are correlated current theories of behavior including reflexology and behaviorism, psychoanalytic theory, Meyerian psychobiology, phenomenology, and communication theory. There follows a chapter on the criteria of biodynamics and the experimental approach to biodynamic formulations. The chapter on the principle of substitution discusses the substitution of part activities in lieu of total patterns as well as the interrelationship of various adaptive patterns. The role of conflict is analyzed, and the dynamics of therapy and its evolution are discussed.

Appendixes enhance its value to the serious student of psychiatry through the inclusion of ethology and biodynamics, illustrative motion picture films, psychoanalytic formulations, and an illustrative psychoanalysis of a neurotic personality. A bibliography of 28 pages provides an excellent reference list for special reading or research. The glossary of psychiatric terms, encompassing 40 pages, are clearly defined and operationally phrased, making for rapid review in conjunction with cross reference with the index for further textual explanations. Finally, there is an index of names as well as of subjects. The volume abounds with exemplary case histories, experiments, and plates.

This book was written not only for the advanced student in psychiatry but also for the research worker as well as the practicing psychiatrist who wishes to keep abreast of an integrative approach to experimental and clinical psychology exemplified in principles of dynamic psychiatry.—FREDERICK L. PATRY, M.D.

Cirrhosis of the Liver. By Martin Seler Kleckner, Jr., M.D. Octavo of 729 pages, illustrated. Springfield, Charles C Thomas, 1960. Cloth, $24.50.

This monograph on cirrhosis of the liver is a most informative volume for the specialist and research worker. The material covered shows a wide personal experience with extensive research in this field.

The author discusses cirrhosis of the liver in children, a very important subject for the pediatrician. He also discusses cirrhosis of the liver associated with other medical entities which is often overlooked by the internist and thus may lead to serious consequences.

Of special significance are the chapters on portal hypertension and hepatic insufficiency. In the latter chapter the author discusses liver function tests together with their limitations.

The treatment of the various forms of cirrhosis is given in detail together with the dietary regimen.

This scholarly discussion of the subject is probably the best book on cirrhosis. It should be in every medical library, public and private.

As is usual with all books published by Charles C Thomas, the printing and binding are excellent. The illustrations are numerous and well done.—REUBEN FINKELSTEIN, M.D.

Injuries of the Brain and Spinal Cord and Their Coverings. Edited by Samuel Brock, M.D. Fourth edition. New York, Springer Publishing Company, Inc., 1960. Cloth, $18.50.

In the twenty years since the first edition of this comprehensive work it has grown over 100 pages. Some of the original contributors have passed on, but new distinguished workers have revised and added sections maintaining the high standards. Almost every facet of the subject is covered in detail. There are over 100 pages given to the complex psychiatric problems associated with head injuries. The pediatrician will find here an excellent chapter by Alpers on cerebral birth injuries. There is a chapter on the relationship of head injury to other organic diseases of the brain which can help the physician with some of the knotty medicolegal problems which occur.

Any doctor who sees patients who have had injuries to their central nervous system, skull, and spine will find a great deal to help him in his problems in this treasury of 25 chapters.

The editor is to be congratulated on bringing so much material together, incorporating the many modern advances with comparatively little redundancy despite the many contributing authors.—ARTHUR J. LAPOVSKY, M.D.

The Newborn Child. By David G. Vulliamy, M.D. Octavo of 163 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $6.00.

There is a laudable tendency today to write short treatises concerning medical subjects in single-book form so as to focus the physician's attention on a single subject and cover it in greater detail. The book is handy and relatively inexpensive; it may be easily slipped into a coat pocket and read at odd times.

Dr. Vulliamy's is such a book. In it the newborn infant is considered from every medical vantage point: the healthy baby, minor anomalies, routine care, the effect of maternal disease, the common types of birth injury, infections, affections of the blood and reticuloendothelial system, congenital abnormalities, genetic defects, prematurity, and postmaturity.

The care and treatments advised follow generally accepted principles and are reliable. The text is clear and concise; the illustrations are excellent. A separate section provides a list of authoritative texts for further reading with regard to the subject matter of each major heading. An excellent index is provided.

Undoubtedly the author is aiming for distribution throughout the English-speaking world. Enterprise should have dictated an American edition in which colloquial expressions and English titles of drugs might have been changed to American equivalents.

The only unacceptable advice is found under the treatment of meningitis, where 50 mg. per pound of body weight per day intramuscularly of chloramphenicol is advised for Escherichia coli meningitis. In view of the recently observed "Gray syndrome" with its high mortality in chloramphenicol-treated newborn infants, the dose seems excessive and dangerous.—KENNETH JENNINGS, M.D.

The Medical Clinics of North America. New York Number. May, 1960. Diseases of the Liver, Pancreas and Biliary Tract. Thomas P. Almy, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1960. Published bi-monthly (six numbers a year). Cloth, $18 net; paper $15 net.

This volume is a true symposium on the diseases of the liver, pancreas, and biliary tract. To review each essay is not necessary. It is enough to state that a group of distinguished contributors have discussed these subjects thoroughly. Special attention should be given to the chapters on liver function tests, clinical utilization of liver biopsy, and decision for elective cholecystectomy.—REUBEN FINKELSTEIN, M.D.

Somatic Treatments in Psychiatry. By Lothar B. Kalinowsky, M.D., and Paul H. Hoch, M.D. Octavo of 413 pages. New York, Grune & Stratton, 1961. Cloth, $9.75.

The authors are highly competent to revise and bring up to date the subjects elaborated upon in this monumental work. Dr. Kalinowsky, associate professor of neuropsychiatry, New York School of Psychiatry, is an internationally recognized pioneer in the various somatic therapies. Likewise, the coauthor, Dr. Hoch, professor of clinical psychiatry, College of Physicians and Surgeons, Columbia University, New York, and Commissioner of the State of New York Department of Mental Hygiene, is highly competent in the evaluation and recommendations found in this volume which was revised from *Shock Treatments, Psychosurgery and Other Somatic Treatments in Psychiatry* by the same publisher (first edition in 1946 and second edition in 1952). Dr. Brenda Grant is credited with yeoman assistance in the preparation of this ambitious book.

The past ten years have afforded ample opportunity for the significant appraisal of the new pharmacologic drugs which have been playing a leading role in reducing the resident population of our mental hospitals, especially during the past five years, despite an increase of admissions. There is a pertinent historical-developmental review followed by an intensive evaluation of the growing contributions of pharmacotherapy. This is followed by an evaluation of the convulsive therapies, including pharmacologic, electric, and insulin coma treatments. Psychosurgery is then reviewed with emphasis on modified operations and more limited indications for this useful method in selected, otherwise intractable, cases. Finally a section devoted to miscellaneous treatments and theoretical remarks is included for its future research value. Various pharmacologic and other therapeutic attempts, such as refrigeration, photoshock, and cerebral pneumotherapy, are noted. An extensive discriminating bibliography of 53 pages is followed by a very helpful index.

There is a real need for this volume at this time since psychiatry is fast on the march and needs expert guidance. All those working in the field of psychiatry should be grateful to the authors for making possible this volume which stands without a peer in its field.

The book is written primarily for psychiatrists and is highly recommended not only as a daily working referential tool but also for the student and research worker whose enlightened cooperation and zeal are so urgently needed in furthering the advances of psychiatry.—FREDERICK L. PATRY, M.D.

Injuries and Infections of the Hand. By Robert H. C. Robins, M.B. Octavo of 220 pages, illustrated. Baltimore, The Williams & Wilkins Company, 1961. Cloth, $13.

This book is very well done, and as a whole there can be only praise for it. The author's treatment of tendon sheath infection, however, is not good.

His comments that treatment should be aimed at preservation of the rest of the hand, especially in the elderly person, is good surgery.

Many different types of injuries are described in the book.—OTHO C. HUDSON, M.D.

Essential Hypertension. An International Symposium. Edited by K. D. Bock and P. T. Cottier. Octavo of 392 pages, illustrated. Berlin, Springer, 1960. Cloth.

This volume is a collection of papers, read and discussed by 40 specialists from 12 different countries. The articles cover a wide range of research and clinical data relative to the etiology and treatment of hypertension. The following excerpts are some of the interesting conclusions drawn by the authors.

"Arterial hypertension is a mosaic consisting of nervous, endocrine, vascular and renal elements" (I. H. Page).

"Among societies or groups consuming low-salt diets, essential hypertension is uncommon" (L. K. Dahl).

"The single gene theory (inheritance) is by no means proved, but there is ample evidence that benign hypertension is hereditary" (R. Platt).

"The treatment of hypertension by salt restriction in a certain proportion of human patients is highly suggestive " (A. Grollman).

"Essential hypertension generally develops between the ages of twenty-five and forty-five years. The course of benign hypertension is from ten to fifty years. Half of the cases of malignant hypertension develop from benign hypertension" (P. Bechgaard).

"The onset of malignant hypertension is often extremely sudden" (P. Milliez).

"Thiazide diuretics and reserpine are long-acting agents which reduce recumbent as well as standing blood pressure" (S. W. Hoobler).

"In patients with mild hypertension, chlorothiazide and hydrochlorothiazide are often capable of reducing blood pressure to satisfactory levels. Patients with a severe hypertension need a combination of saluretic drugs with other antihypertensive agents to reduce arterial hypertension to sufficiently safe values" (C. Bartorelli).

"The difference between treated and untreated patients is significant statistically. Hypotensive treatment in severe and malignant hypertension, is of great value in arresting renal deterioration" (F. C. Reubi).

"Treated patients with malignant hypertension die, not of nephrosclerosis, but of arteriosclerosis, either atherosclerosis or subintimal fibrous proliferation. Only so far as cerebral vascular disease is concerned, does arterial pressure reduction seem important for the avoidance of arteriosclerotic complications" (P. Imhof).

"Surgery elicited beneficial results in those patients presenting only functional disorders, but poor results in those with organic diseases (that is, coronary artery sclerosis, infarction, apoplexy, renal insufficiency). Contraindications to surgery are advanced cerebral arteriosclerosis, severe coronary artery sclerosis, coronary infarction, and impaired renal function" (H. Sarre).—SIMON FRUCHT, M.D.

The Medical Clinics of North America. Nationwide Number. July, 1961. Efficacy of New Drugs. Howard F. Conn, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bi-monthly (six numbers a year). Cloth, $18 net; Paper, $15 net.

Howard Conn, M.D., the editor of *Current Therapy*, has caused authorities, after three and one-half years, to reaccumulate current therapeutic knowledge. The misuse as well as the use of antimicrobics and also vaccines for viruses are presented. Metabolic and hormonal drugs are discussed. Acne, anesthetic agents, and anticoagulants are also considered and, best of all, antitussive and antiallergic agents. Muscle relaxants, radioisotopes, tranquilizers, and even depressants are evaluated. Conn is impressed with the chapters on the oral antifungal, the fibrinolytic, the hypercholesterolemic, and the antiovulatory agents. The physical format and presentations are those of master technicians. This knowledge, otherwise ferreted with great difficulty, is presented for clinicians and others interested in therapy.—BERNARD SELIGMAN, M.D.

Parkinsonism; Its Medical and Surgical Therapy. By Irving S. Cooper, M.D. Quarto of 239 pages, illustrated. Springfield, Charles C Thomas, 1961. Cloth, $16.50.

This is a report on experience with surgical treatment of parkinsonism by the surgeon who certainly has popularized, if he has not initiated, the surgical form of treatment for extrapyramidal disorders.

The author starts with a review of the clinical aspects of parkinsonism, places rather too much emphasis on the psychologic side of the condition, gives scanty attention to medical therapy, reviews the surgical methods devised for the relief of parkinsonism, and deals briefly with the anatomic and physiologic aspects of extrapyramidal disorders. He then proceeds to describe his surgical technics, mainly the occlusion of the anterior choroidal artery, chemopalidectomy, and finally chemothalamectomy. The technic receives a great deal of detailed attention, and the drawings and their correlative x-ray pictures are impressive. In the final chapter he also gives 50 selected case histories.

If the book has some weakness here and there, it represents, nevertheless, a handy compilation of the author's pioneering work in this field, and as such it deserves to be placed on a neurosurgeon's and a neurologist's shelf. The format of the book and its general finish are de luxe.—L. P. HINTERBUCHNER, M.D.

Psychopathology of Aging. Edited by Paul H. Hoch, M.D., and Joseph Zubin, Ph.D. The proceedings of the fiftieth annual meeting of The American Psychopathological Association, held in New York City, February, 1960. Octavo of 320 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $9.75.

This book records the proceedings of the fiftieth annual meeting of The American Psychopathological Association in 1960. The material has been edited by Dr. Hoch and Dr. Zubin, the former a psychiatrist and the latter a psychologist, both of whom are past-presidents of the association.

One can readily agree with the opening words of the editors when they note in the preface that "The two most crucial problems in psychopathology today are at the two ends of the life span—the increase in behavior disorders in the young and in the old". As more people live longer we will have to turn our attention more and more to the problems of old age. This book reflects the concern of psychiatrists, psychologists, sociologists, and social workers in this problem and the results of their individual experience and knowledge in the matter.

The book is divided into four parts, including: epidemiology; psychology and sociology; psychology and genetics; and management problems.

Each subject has been adequately discussed by several qualified investigators, and a résumé of the material presented is evaluated at the end of each subject. This enhances the value of the presentations.

The book should serve as a guide for all workers in the field of geriatrics and those dealing with the problems of aging.—JOSEPH L. ABRAMSON, M.D.

Bone: An Introduction to the Physiology of Skeletal Tissue. By Franklin C. McLean, M.D., and Marshall R. Urist, M.D. Second edition. Octavo of 261 pages, illustrated. Chicago, The University of Chicago Press, 1961. Cloth, $6.

As a whole this is an excellent work. The chapter on radiation, isotopes, and bone is new in this edition and particularly good.

There is a large amount of experimental laboratory work given which is essential for research but has little practical value in treatment of patients.

A few quotations should be much more widely recognized by orthopedists.

1. In "Healing of Fractures," page 201, "Stinchfield and his associates observed that anticoagulants administered to rabbits at the time of a fracture caused delayed union. Both heparin and Dicumarol have the same effect and prevent the formation of the fibrin clot between the bone ends."
2. In "Uniting of Fracture," page 206, "The healing time is directly proportional to the total volume of damaged bone and the breadth of the fracture defect. In impacted fractures a microscopic plate of fibrocartilage is formed at the line of the injury and is replaced by new bone within a few weeks. In displaced fractures the defect becomes filled with a great mass of fibrocartilaginous callus and fibrous tissue, requiring months or years to be replaced by new bone."
3. In "Healing of Fractures," page 214, "A bone graft of any kind produces a new proliferative response from the bone ends and new bone formation by induction across the fracture gap. Homogenous and autogenous bone appear to be equally effective in most cases. Inlay, onlay, and intramedullary grafts are all capable of producing union in the majority of cases. The success of the operation depends upon the proliferative response of the bone ends rather than upon the technique or the material employed. These observations suggest that the mechanical treatment of fractures can be overemphasized and that early open operations and metallic internal fixation should be used only in unusual circumstances. More reliance should be placed upon the primordial power of the human skeleton to regenerate injured and missing substance."—OTHO C. HUDSON, M.D.

A Synopsis of Contemporary Psychiatry. By George A. Ulett, M.D., and D. Wells Goodrich, M.D. Second Edition. Duodecimo of 309 pages, illustrated. St. Louis, The C. V. Mosby Company, 1960. Cloth, $6.50.

The authors are uniquely qualified to formulate this comprehensive compendium and are commended for incorporating the recent discoveries in psychopharmacology since an avalanche of psychiatric grain has been brought to the psychiatric mill for processing, evaluation, and utilization since the first edition of 1956.

The senior author, Dr. Ulett, is professor of psychiatry and neurology, Washington University School of Medicine, Saint Louis, Missouri. Dr. Goodrich is chief, Biosocial Growth Center, National Institute of Mental Health, U.S. Public Health Service, Bethesda, Maryland. Their vast experiences are clearly revealed in an eclectic approach to the broad and ever-widening scope of psychiatry in keeping with the scientific method. The authors do not pretend, in this small volume, to elaborate on alternative theories and "schools" but rather hew close to the line of clinical psychiatry as a quick reference for psychiatric residents, medical and psychologic interns, medical students, nurses, and ancillary workers.

Following a succinct review of outstanding high lights of psychiatric history and thought, the contents of the book are divided into three major parts which pertain to history-taking and diagnostic procedures, clinical syndromes, and therapeutic measures. Each part is a masterpiece in delineating the core data. Part I emphasizes the importance of the initial psychiatric interview and case study. The psychiatrist's role as a physician is sensitized by pointing up the importance of the general physical and neurologic examination to be followed, when indicated, by electroencephalographic and psychologic examination tests and inventories.

Part II defines clinical syndromes and problems of classification and appends the standard nomenclature of the American Psychiatric Association.

Part III on therapeutic measures naturally evolves out of the previous considerations and indicates the growing importance of the psychiatric treatment team, group therapy, and the importance of the doctor-patient relationship traditionally observed in individual psychotherapy. Herein are included current views concerning convulsive therapies, physical as well as pharmacologic; coma and sleep therapies; psychosurgery; chemotherapy; management of suicidal patients; psychiatric aspects of civilian disaster; problems in the military setting; forensic psychiatry; and a final chapter on preventive psychiatry in which mental illness and mental health problems and challenges are seen in perspective of the nation as well as the state and locality.

Case-finding measures for early diagnosis and treatment, as far as possible on the community level, are put in sound perspective. A plea is made for more psychiatric guidance of lay groups which often expect more than the psychiatrist at present can deliver. A multidimensional approach which involves teamwork with the neurophysiologist, biochemist, anthropologist, sociologist, educator, clergy, court, and welfare and rehabilitation worker indicates the vastness of the field of psychiatric concern. The need for comprehensive studies of human behavior with adequate controls, statistical validation, and therapeutic testing of relevant data in the light of a discriminating, capable research program should be recognized with appropriate action.

The value of this amazing publication is greatly enhanced by well-chosen references of suggested reading at the end of each chapter. The book is well illustrated by tabular information on psychotropic drugs, electroencephalographic tracings, Rorschach scoring symbols, and interpretative figures.

This gold mine of information should be within hand's reach of the psychiatrist in-the-making and the general practitioner bent on improving his psychiatric intelligence.—FREDERICK L. PATRY, M.D.

Maimonides "On Sexual Intercourse" Fi 'L-Jima. Translated from the Arabic with an introduction and commentary. Edited by Morris Gorlin. Octavo of 128 pages. Brooklyn, N.Y., Rambash Publishing Co., 1961. Cloth, $10.

This first volume of medieval Jewish medical works is introduced for its historical interest. It has been translated from the Arabic and is probably the first medical treatise written by Maimonides, the great theologian and physician of the twelfth century. It was probably the first request of the sultan from his physician. A spurious work is also included with the reasons for denying its origin from Maimonides. Listed among aphrodisiacs are brains, testes, eggs, honey water, and even wine for the broad-minded sultan who might forgo some of his Moslem scruples. Anaphrodisiacs are listed also. Gorlin stresses Maimonides' psychosomatic approach in his commentaries. This book is of medical and endocrinologic interest.—BERNARD SELIGMAN, M.D.

The Reluctant Surgeon. A Biography of John Hunter. By John Kobler. Octavo of 359 pages. Garden City, Doubleday & Company, Inc., 1960. Cloth, $4.95.

John Hunter is one of the truly great figures in medicine. He extended thoughts in medicine, surgery, and science to great horizons. The unfolding of the life of this great man is revealed in a fine biography by the author. It is a monument to the life of this eminent scientist.

The author takes us through the history of John Hunter. He paints a picture of England and Scotland of the era and weaves into the story the figures and names of the people who contribute to the growth of Hunter. This is not a book of hero worship but a story which trips along in an enchanting manner.

John Hunter united anatomy and surgery on a foundation of inquiry. In a letter to Jenner in August, 1775, he said, "I think your solution is just; but why think? Why not try the experiment." This was the life of John Hunter. This is his legacy to modern science. John Kobler, the author, emphasizes this point.—Alan A. Kane, M.D.

Evaluation of Drug Therapy. Proceedings of the Symposium on Evaluation of Drug Therapy in Neurologic and Sensory Diseases Held at the University of Wisconsin, May, 1960. Edited by Francis M. Forster. Octavo of 167 pages. Madison, Wisc., The University of Wisconsin Press, 1961. Cloth, $4.00.

Dr. F. M. Forster has edited this small volume which contains the proceedings of the symposium on evaluation of drug therapy in neurologic and sensory diseases held at the University of Wisconsin in May, 1960.

There are introductory papers dealing with the more general tasks of finding and testing new drugs and others dealing with the problem of designing a clinical study for evaluation of drug therapy in neurologic and other diseases. Of these, the paper by Shirley H. Ferebee is one of substance. The book closes with reports of panels on epilepsy, vertigo, neuralgias and neuropathies, headache, glaucoma, multiple sclerosis, diseases of muscles, parkinsonism, and other basal ganglia diseases. Little new is included in these panel reports. A clinical investigator may want to glance in this book to see if his own ideas concerning the design of a clinical trial tally with those of others. But he will not find much that he could not arrive at with his own good common sense.—L. P. Hinterbuchner, M.D.

Histopathology of the Skin. By Walter F. Lever, M.D. Third edition. Octavo of 653 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $16.50.

This book, now in its third edition has become one of the classics in its field. As indicated by the author in his preface to the first edition, its objective is the dermatologist as well as the general pathologist, whose training is usually somewhat restricted in the field of skin pathology. The fact that the book has now been twice revised is certainly an indication, to this reviewer at least, that it has fulfilled its goal.

The format of the book is essentially unchanged from previous editions. The introduction presenting the basic histologic features of normal epidermis has been brought up to date. Significant new syndromes have been incorporated. The pathology of each specific entity is preceeded by a brief clinical description where necessary. The style is clear with commendable economy of words. The recent literature has been covered very thoroughly, as evidenced by the extensive bibliography of pertinent references which follows each chapter. Where there is some controversy on interpretation of findings, the author has presented other points of view without diluting in any way his own theme. The illustrations are adequate and well spaced so that there is no difficulty in referring to them from the corresponding text.

This book has been and will continue to be of tremendous value to the dermatologist in all phases of his career from graduate student to teacher. It is also an excellent reference work for the general pathologist who will find it very useful and facile for referring to problems in this field. This book is highly recommended not only for its contents but also for the author's interest and enthusiasm in maintaining a contemporary value for his work. The changes in this field have been many, and they have been incorporated to as practical a degree as possible within the framework of a volume of this type, thereby justifying its new edition.—Irving N. Holtzman, M.D.

The Human Adrenal Gland. By Louis J. Soffer, M.D., Ralph I. Dorfman, Ph.D., and J. Lester Gabrilove, M.D. Octavo of 591 pages, illustrated. Philadelphia, Lea & Febiger, 1961. Cloth, $18.50.

The seasoned authors of this scholarly treatise have carefully gleaned the pertinent authoritative literature of adrenal physiology and biochemistry. Liberal quotations and a bibliography of the thrilling last three decades of adrenal history should satisfy any student. Dorfman has clearly and succinctly expressed biochemistry at its academic best. The clinical aspects in which the authors played roles are factually good. For a book of this caliber, Selye's conception of the role of the adaptation syndrome in disease and also the position of corticoids in disease could be more adequately covered.—Bernard Seligman, M.D.

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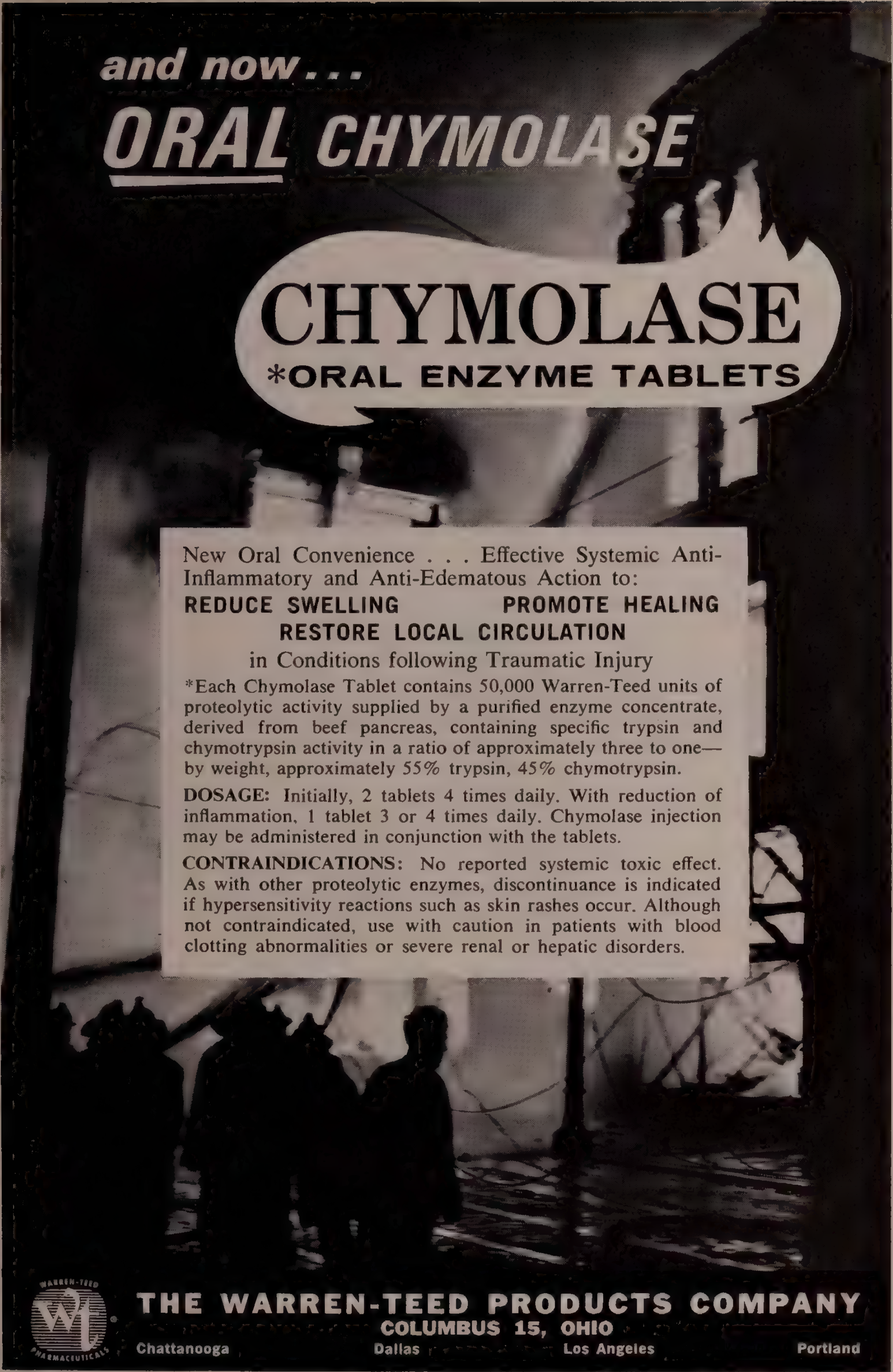

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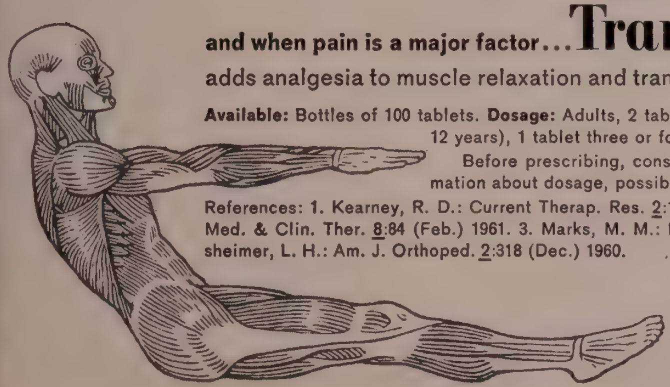

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References: 1. Kearney, R. D.: Current Therap. Res. 2:127 (April) 1960. 2. Cornbleet, T.: Antibiotic Med. & Clin. Ther. 8:84 (Feb.) 1961. 3. Marks, M. M.: Missouri Med. 58:1037 (Oct.) 1961. 4. Hergesheimer, L. H.: Am. J. Orthoped. 2:318 (Dec.) 1960.

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Phenobarbital-niacin (BARBA-NIACIN tablets) provides the full therapeutic value of phenobarbital with a much wider margin of safety.

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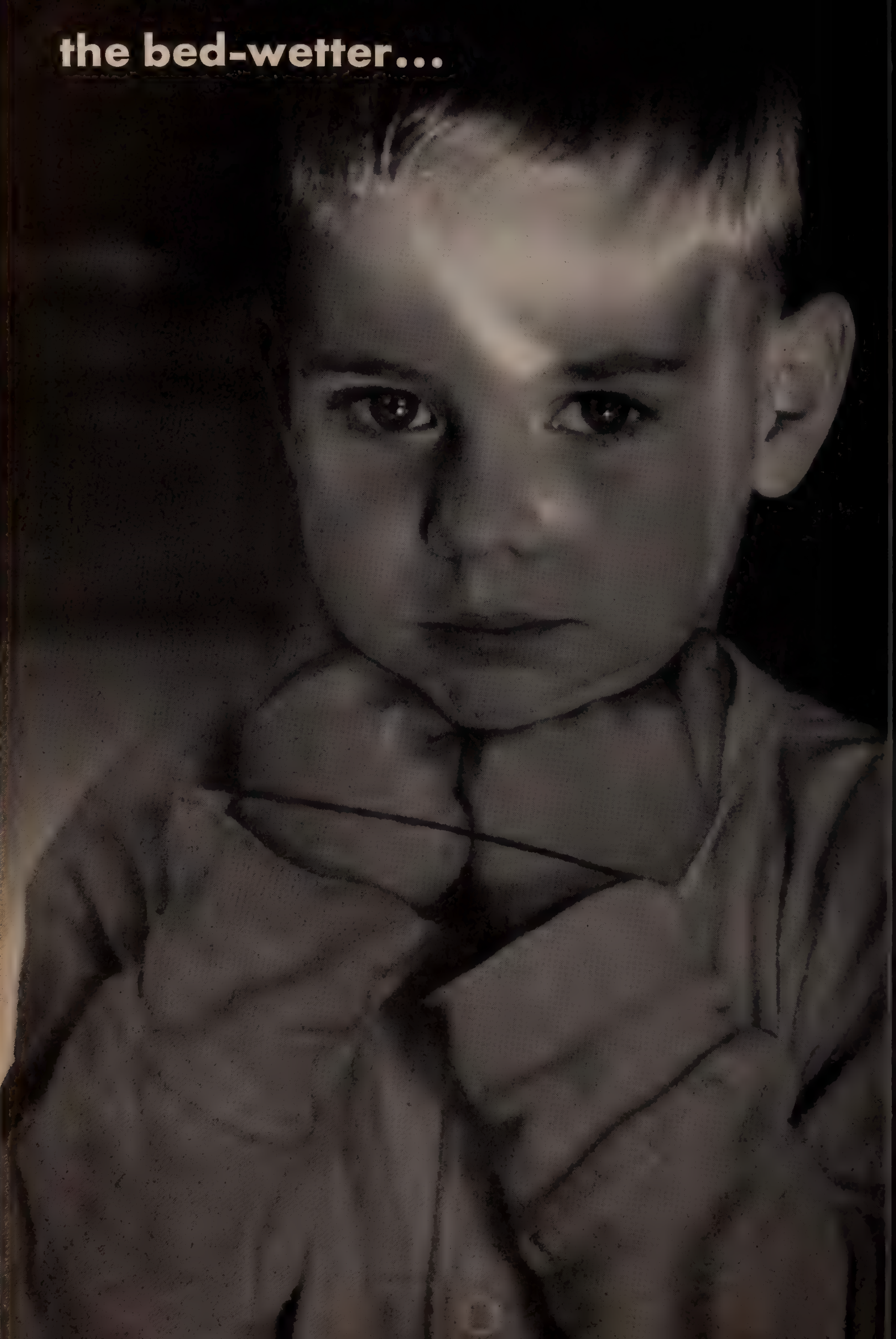
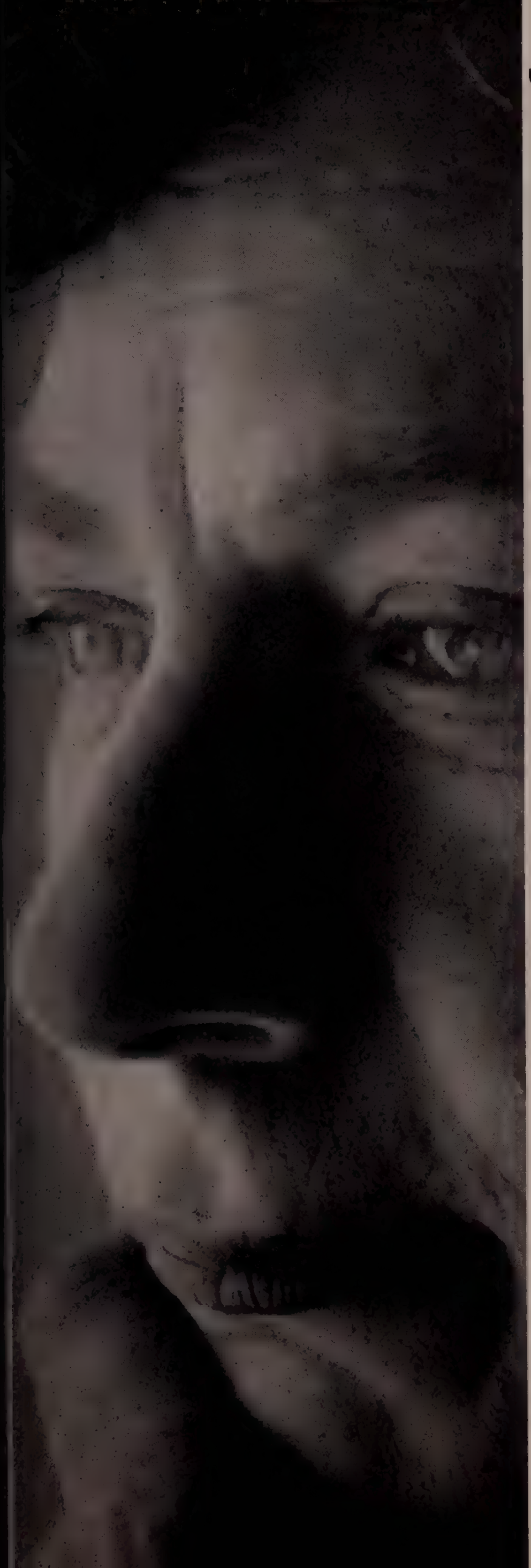
*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.



the bed-wetter...



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both victims of "communicable"* ANXIETY

both responsive to

ATARAX®

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widely favored for children

ATARAX syrup

because of its efficacy, relative freedom from side effects...*and* its excellent flavor which makes administration a pleasure instead of a project

equally effective for grownups

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and equally well tolerated by patients of any age...no dulling of mental acuity to interfere with normal activities of busy adults

FOR COMPLETE PRESCRIPTION INFORMATION, CONSULT PRODUCT BROCHURE

* Literally, of course, anxiety is not "communicable" as the word is commonly used, but you probably see many patients whose emotional disturbances are transmitted to and reflected in the people who are closest to them.

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Therapeutic capsules for vitamin-mineral supplementation

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when abortion threatens, habitually…

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Improved Progestational Therapy

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PARA 1

fetal salvage is significantly improved by Delalutin

SUPPLY: Vials of 5 cc., each cc. supplying 250 mg. hydroxyprogesterone caproate. Vials of 2 and 10 cc., each cc. supplying 125 mg. hydroxyprogesterone caproate.

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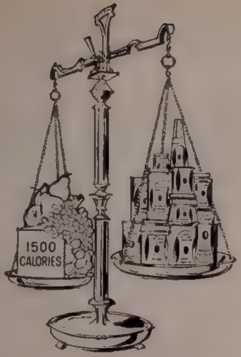

A new answer to one of America's leading health problems

60 DELICIOUS FOODS THAT MAKE WEIGHT CONTROL EASIER!

Here is a practical and down-to-earth method to help overcome obesity, the nation's No. 1 diet problem—and prime stealer of doctor's consultation time. Now a new group of 60 delicious Mott's Figure Control Food products uses the best of nutrition knowledge to create quality dishes, lower in calories by an average of 50%. Indicated calorie savings can be made pleasantly and accurately while eating normal-size portions by using these calorie-controlled foods in place of higher calorie dishes. Protein, vitamin and mineral food values are retained.

Low carbohydrate, low fat: Fats are largely extracted from meats and poultry in a way that cannot be done at home. Sauces and dressings are prepared with a high proportion of non-fat milk solids, vegetable colloids; all are delectably "natural" and tempting in flavor. Fruits, juices, desserts and sauces are prepared where indicated with non-caloric sweeteners—natural fruit values are intact, extra sugars reduced. The carbohydrate, protein and fat content appears on all labels along with the calorie count. Useful for diabetic diets, too.

Easy medical tool for doctors: Less need for drugs, no possible dangerous side effects, not even temporary dislocation of meal patterns. Figure Control Foods include: Soups, Meats, Poultry, Sauces, Salad Dressings, Preserves, Syrup, Fruits, Drinks, Desserts, Sweeteners.

New Mott's Figure Control® Foods offer Good Eating at Half the Usual Calories

	Quantity	Figure Control Calories	"Regular" Food Calories
Apple-Grape Drink	½ cup	20	52
Five-Fruit Juice Breakfast Drink	½ cup	20	52
Braised Beef and Vegetables	6½ oz.	184	380
Meat Balls in Brown Gravy	3½ oz.	84	280
Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
Cherry Pie Filling	1 oz.	20	60
Chocolate Topping	1 tbsp.	8	63
Preserves (Peach, Strawberry)	1 tbsp.	9	55
"Maplette" Syrup	1 tbsp.	9	55
Liquid or Powder Sweetener	(to equal 1 tbsp. sugar)	0	16

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PEACHES
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Orinase Case History

Orinase dosage

Mr. B. B., a 61-year-old stockbroker, was put on Orinase almost six years ago. On insulin, he had been imperfectly controlled, irritable, and "used to get overly depressed." On Orinase, 1 Gm. per day, control is smooth and Mr. B. is again his former lively self. He regularly works at home well into the night, preparing for the next day's trading.

An active man, Mr. B. occasionally exercises at the gym. He follows baseball with enthusiasm, likes a friendly game of cards, and often goes visiting the various members of his close-knit family.

Mr. B., intensely involved in his profession, describes his day as a "continual crisis." Under the stress of representing clients in the face of market fluctuations, his Orinase needs also fluctuate. Guided by his physician, Mr. B. adjusts hi dosage between 1 and 2 Gm. daily.

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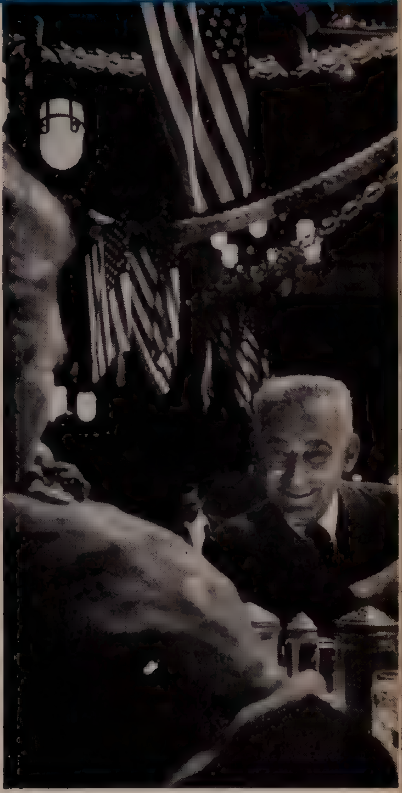
5 years of control

The patient's dosage had to be increased in 1960 at the death of his sister (also a diabetic). For two months, maintenance of control required 2.5 to 3.5 Gm. of Orinase a day; dosage then leveled off again at 1 Gm.

About a year later, when Mr. B.'s wife was incapacitated by an eye ailment, his need for Orinase increased again. During his wife's convalescence, he was taking 2.5 Gm. daily.



Mr. B. is an energetic and sociable man. His work and his philanthropic, family, and social obligations keep him extremely busy. On Orinase, he takes this life in stride.

rinase* (tolbutamide) stands in a unique position; alone, among oral antidiabetes agents, has had ve years or more of day-to-day routine clinical use the hands of thousands of physicians throughout e country. Accordingly, data on a considerable umber of truly long-term Orinase-treated patients re now available. This series of Orinase five-year ase histories has been prepared to illustrate and xemplify some aspects of actual experience in anagement. Patient data, made available to us by physicians, have been factually incorporated; however, patients' identities have been concealed. Any inquiries regarding this Orinase case history series should be addressed to: Medical Department, The Upjohn Company, Kalamazoo, Michigan.

Orinase is supplied in bottles of 50 and 200 tablets.
Each tablet contains: tolbutamide . . . 0.5 Gm.

Reminder advertisement. Please see package insert for detailed product information.

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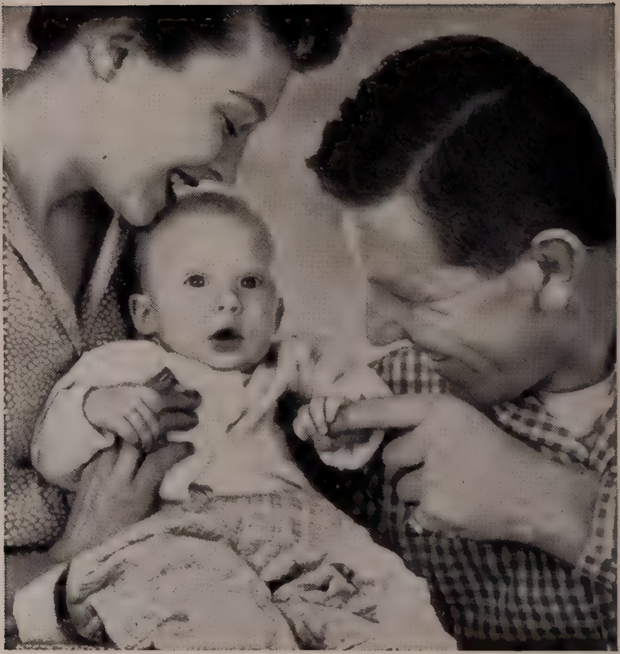
The Upjohn Company, Kalamazoo, Michigan

He needs more than money for a secure future. He needs the freedom and peace that Savings Bond dollars help to pay for.

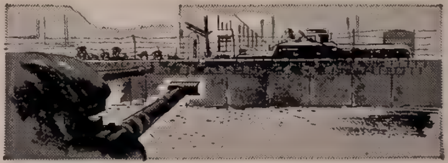


How to save more than money for your family's future

Just about any savings plan you stick to will help you build up a nice collection of money for the future. But U.S. Savings Bonds give you other rewards, too, in addition to the dollars and cents.

One of these rewards is freedom itself. The money which you invest in Savings Bonds helps provide a special source of extra strength for the nation. So you really do a lot more than just save money with Bonds. You also help your country defend your very right to enjoy it later on. With Bonds, you can save for a home—and a better world to own it in.

All it takes to start getting rewards like this is a simple visit to the Bond window at the bank. And there'll never be a better time than the present.



This wall closes roads but opens eyes. Though it runs through Berlin, this infamous wall shows the threat of tyranny to all the world. One way we can show our own determination to stay free is to invest in freedom with U.S. Savings Bonds.

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U.S. SAVINGS BONDS

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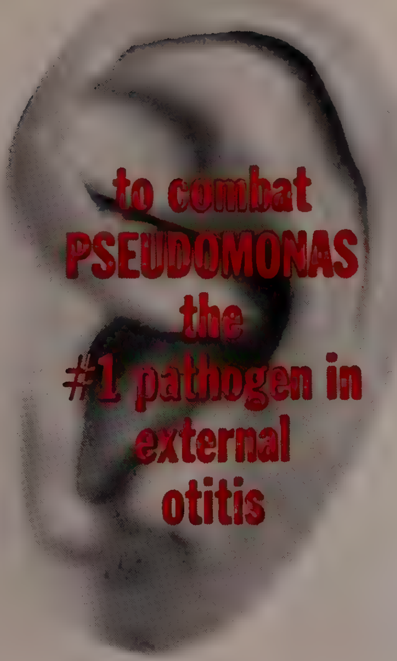

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the #1 therapy for inflamed, infected ears

Because it provides Polymyxin B for the eradication of Pseudomonas, the prime cause of external otitis, 'Cortisporin' is the logical choice of treatment for inflamed, infected ears. Polymyxin B is the antibiotic specific for *Pseudomonas aeruginosa* infections, and is, for this pathogen, the standard of effectiveness against which other antibacterials are measured.

- Anti-inflammatory
- Antipruritic
- Antibacterial

Each cc. contains:

'Aerosporin'® brand Polymyxin B sulfate	10,000 units
Neomycin Sulfate (Equivalent to 3.5 mg. Neomycin Base)	5 mg.
Hydrocortisone	10 mg. (1%)

Bottles of 5 cc. with sterile dropper.

Literature available on request.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N. Y.

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SUGAR FREE
NO-CAL
BEVERAGES

NO SUGAR,
NO SALT...
ABSOLUTELY
NON-FATTENING!

Flavorful NO-CAL adds sparkle to dull diet regimens . . . makes dieting a pleasure!

NO-CAL, America's first sugar-free soft drink, is sweetened with calcium cyclamate . . . contains no sugar, no salt, no fats, proteins or carbohydrates.

NO-CAL is completely safe for diabetics and dieters. You can prescribe it with complete confidence!

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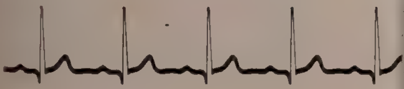
Regardless of which of these three instruments you choose, each has a valuable and unique feature: Sanborn service. It lasts long after the sale . . . from people who know your ECG and value your satisfaction.

wherever you need "on-the-spot" cardiography



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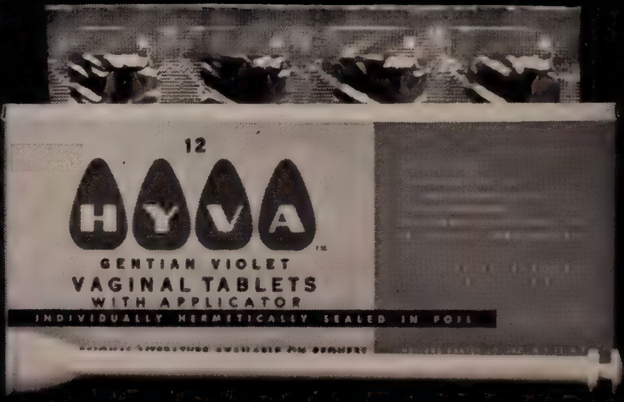
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HYVA
GENTIAN VIOLET
VAGINAL TABLETS
WITH APPLICATOR
INDIVIDUALLY HERMETICALLY SEALED IN FOIL

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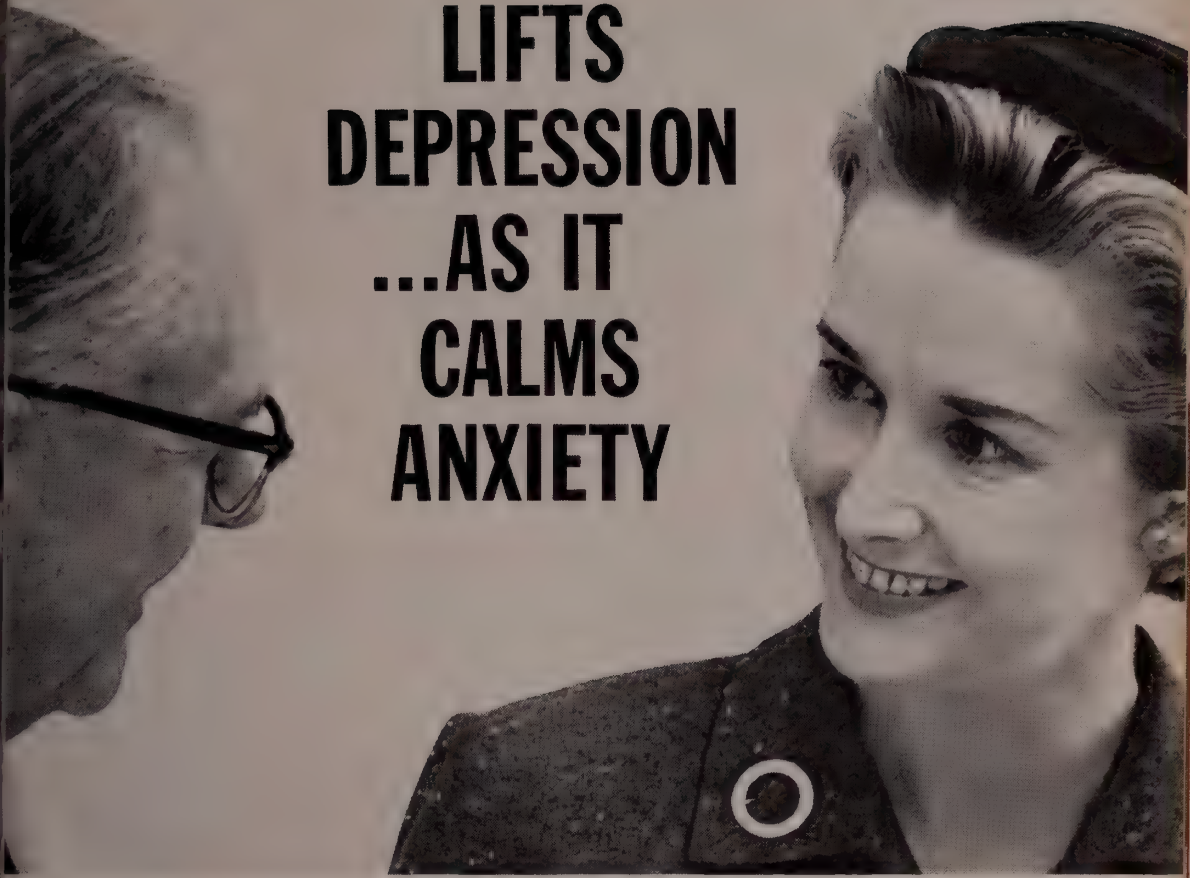
LIFTS DEPRESSION ...AS IT CALMS ANXIETY



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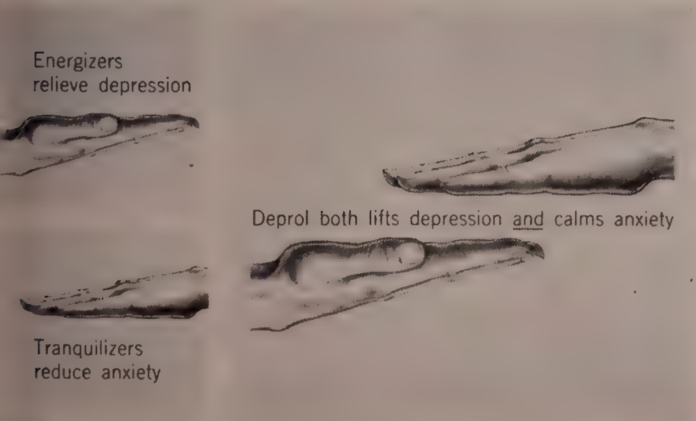
Energizers relieve depression
Deprol both lifts depression and calms anxiety
Tranquilizers reduce anxiety

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be increased gradually up to 3 tablets q.i.d. With establishment of relief, the dose may be reduced gradually to maintenance levels.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets.

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Cranbury, N. J.

CO-7287

consider
the convenience
to pregnant
women of
a tablet this size

ENGRAN

Squibb Vitamin-Mineral Prenatal Supplement

FORMULA SUPPLIES 45 MG. OF IRON – AT NO EXTRA COST

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Vitamin A 5,000 U.S.P. units; vitamin D 500 U.S.P. units; thiamine 3 mg.; riboflavin 3 mg.; pyridoxine 2 mg.; vitamin B_{12} *2 mcg.; niacinamide 20 mg.; calcium pantothenate 5 mg.; vitamin C 75 mg.; calcium 100 mg.; iron 45 mg.; iodine 0.15 mg.; copper 1 mg.; magnesium 6 mg.; zinc 1.5 mg.; manganese 1 mg.*

For full information see your Squibb Product Reference or Product Brief.

SQUIBB *Squibb Quality—the Priceless Ingredient*

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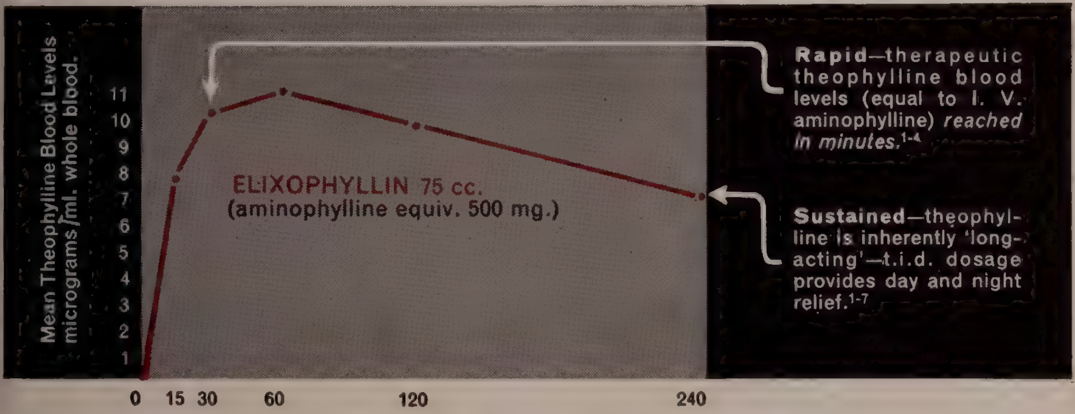
ELIXOPHYLLIN®

(theophylline in its most absorbable oral form)

...provides relief quickly, dependably, **safely.**[1-8]

...avoids the side effects and contraindications of ephedrine polypharmaceuticals or similar sympathomimetics



Rapid—therapeutic theophylline blood levels (equal to I. V. aminophylline) *reached in minutes.*[1-4]

Sustained—theophylline is inherently 'long-acting'—t.i.d. dosage provides day and night relief.[1-7]

Minutes after administration. Mean values in adult subjects following administration of the single dose commonly used in clinical practice.[8]

Each tablespoonful (15 cc.) contains theophylline 80 mg. (equivalent to 100 mg. aminophylline) in a hydroalcoholic vehicle (alcohol 20%).

Acute Attacks: single dose of 75 cc. for adults; 0.5 cc. per lb. of body weight for children.

24 Hour Control: for adults 45 cc. doses before breakfast, at 3 P.M., and before retiring; after two days, 30 cc. doses. Children, first 6 doses 0.3 cc.—then 0.2 cc. per lb. of body weight as above.
(Gastric distress rarely encountered.)

References: (1) Kessler, F.: Connecticut S.M.J. *21*:205 (March) 1957. (2) Burbank, B.; Schluger, J., and McGinn, J.: Am. J. Med. Sci. *234*:28 (July) 1957. (3) Spielman, A.D.: Ann. Allergy *15*:270 (June) 1957. (4) Greenbaum, J.: Ann. Allergy *16*:312 (May-June) 1958. (5) Kessler, F.: Medical Times *87*:1298 (Oct.) 1959. (6) Bickerman, H.A., and Barach, A. L., in Modell, W.: Drugs of Choice 1960-1961, St. Louis, The C. V. Mosby Company, 1960, p. 516. (7) Wilhelm, R. E. in Conn., H. F.: Current Therapy—1961, Philadelphia, W. B. Saunders Company, p. 417. (8) Schluger, J. McGinn, J. T., and Hennessy, D. J.: Am. J. Med. Sci. *233*:296, 1957.

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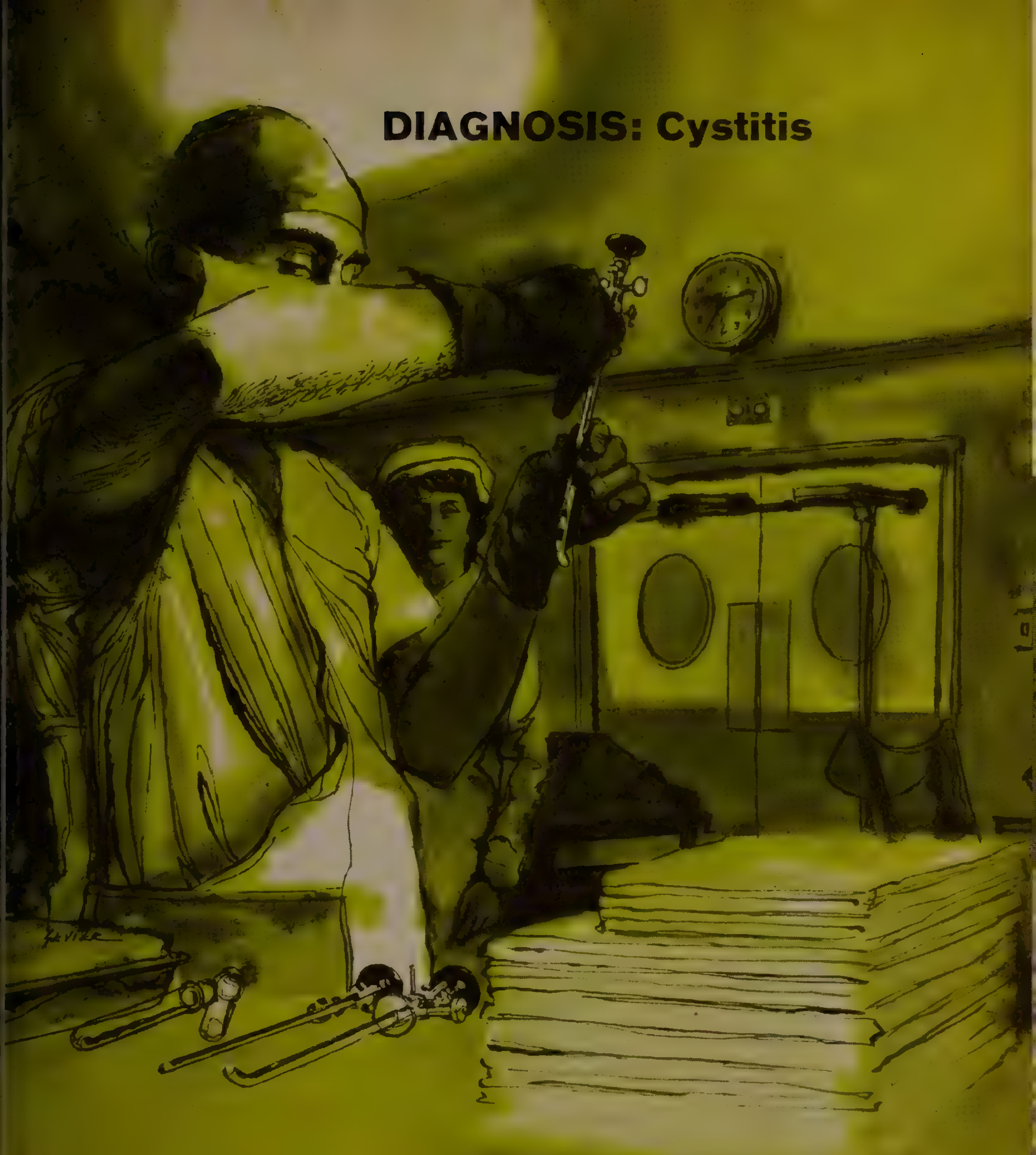

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Ratio of Linoleates* to Saturates
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S-011

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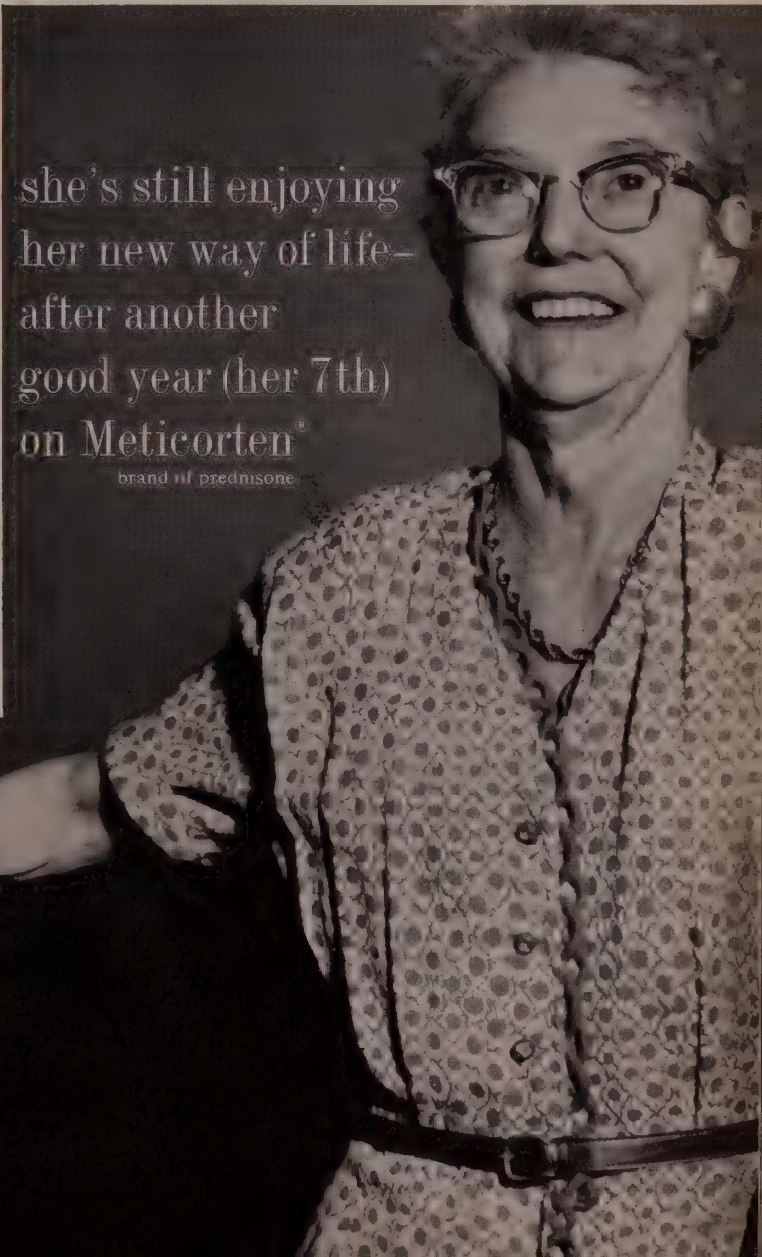
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*__COSMEDICAKE__ contains colloidal sulfur, benzalkonium chloride, salicylic acid and hexachlorophene in a smooth, greaseless base. Supplied in four skin-matching colors.

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[1] Berger, R.A., Clinical Medicine, Sept. 1961.

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To answer many inquiries; the 1961 Medical Directory is still available. The next edition will not be published until late in 1963.

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MEDICAL DIRECTORY OF NEW YORK STATE

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an effective GERIATRIC antiarthritic with distinctive Safety Factors

When arthritis afflicts the elderly, it often poses a critical problem in the choice of an effective antiarthritic that will not aggravate other common geriatric conditions . . . such as osteoporosis, hypertension, edema, hyperglycemia, peptic ulcer, renal, cardiac or hepatic damage, latent chronic infection, or emotional instability.

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[1] Ford, R. A., and Blanchard, K.: Journal-Lancet 78:185, 1958.

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Thanks to 135 tiny "doses" throughout the

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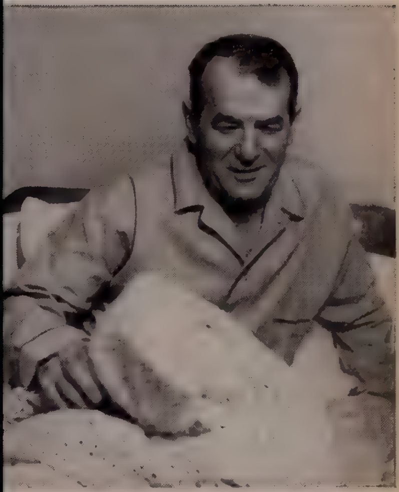

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Morning stiffness may be reduced or even eliminated as a result of therapy with the only steroid in long-acting form. And the slow, steady release of steroid makes it possible in some cases to reduce the frequency of administration and/or the total daily steroid dosage.

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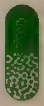

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. . . in minutes

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Nephenalin®

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One NEPHENALIN tablet provides: *air in a hurry*—through sublingual isoproterenol HCl, 10 mg. *air for hours*—through theophylline, 2 gr.; ephedrine, 3⁄8 gr.; phenobarbital, 1⁄8 gr.
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Supplied: Bottles of 50 tablets. For children: NEPHENALIN Pediatric, bottles of 50 tablets.
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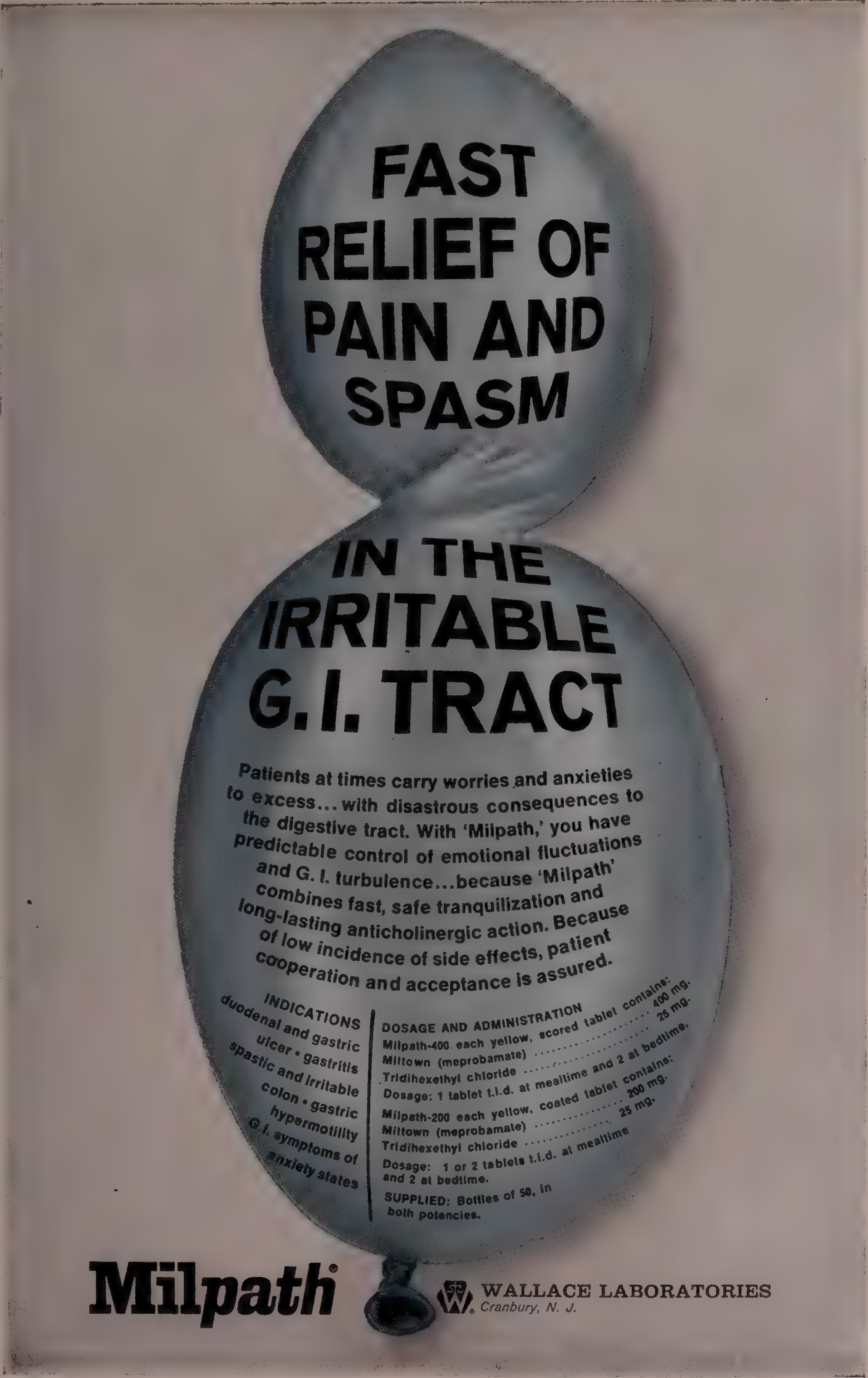

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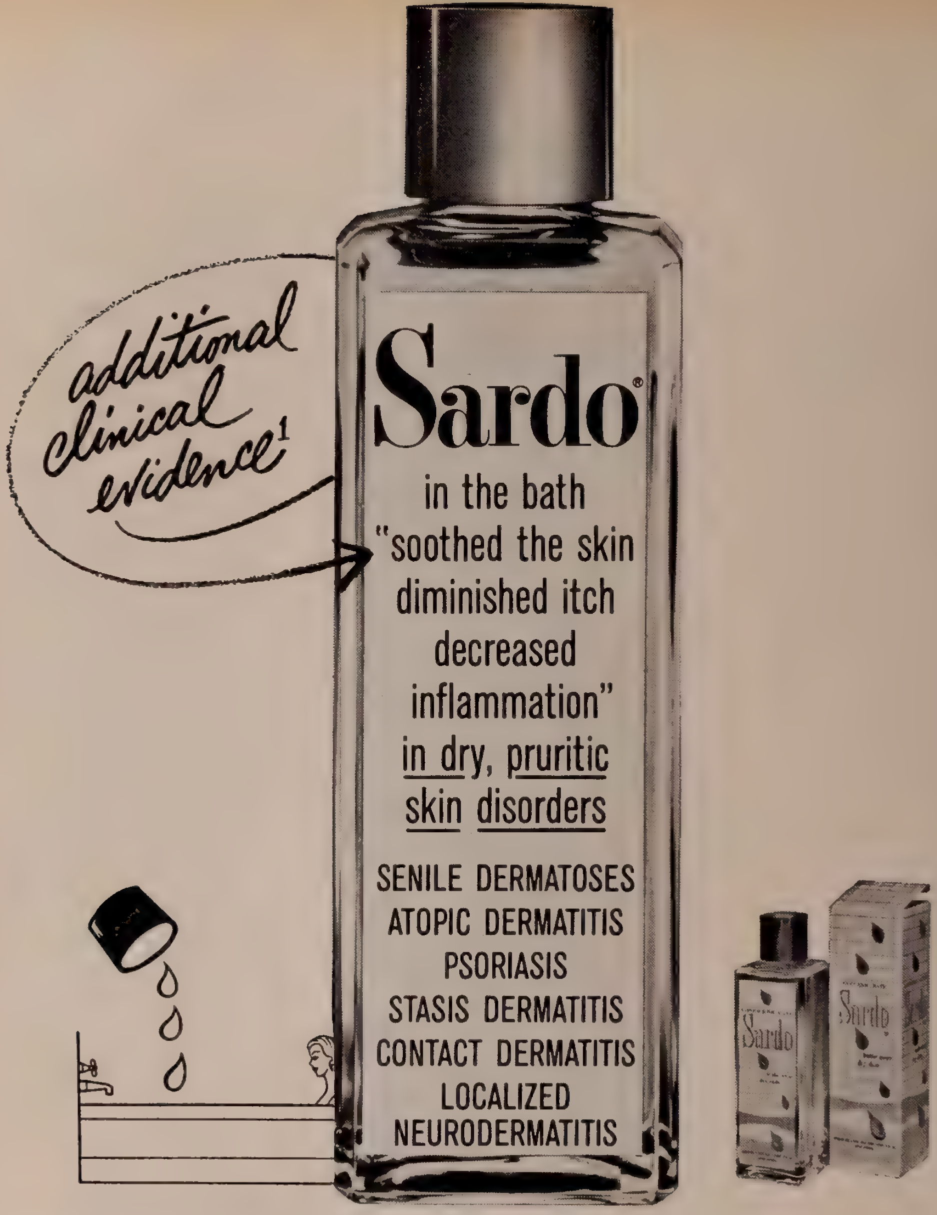
additional clinical evidence[1]
Sardo®
in the bath
"soothed the skin
diminished itch
decreased
inflammation"
in dry, pruritic
skin disorders
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BENEFICIAL RESULTS were obtained with **SARDO** in the bath in 122 of 135 patients (90%) with dry, itchy skin conditions, in most cases with beneficial effect "after the first bath." Dryness was allayed in all cases, and associated itching "either completely relieved or greatly improved." No irritation or sensitization was observed.

This new study corroborated others[2-4] showing that SARDO helps re-establish the normal physiologic lipid-aqueous skin balance.

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1. Borota, A., and Grinell, R.N.: J. Amer. Geriatrics Soc., 10:413, 1962.
2. Spoor, H. J.: N.Y. State J.M. 58:3292, 1958.
3. Lubowe, I. I.: Western Med. 1:45, 1960.
4. Weissberg, G.: Clin. Med. 7:1161, 1960.

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BENADRYL TO RELIEVE SYMPTOMS OF HAY FEVER

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“Treatment results were good, and in many cases a dramatic response was noted. Many of the cases had previously failed to respond to various types of therapy including, in some instances, other topical corticosteroid preparations.”

—Gray, H. R., Wolf, R. L., and Doneff, R. H.: Evaluation of Flurandrenolone, a New Topical Corticosteroid, Arch. Dermat., *84:*18, 1961.

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New York State Journal of Medicine

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Editorials

Fraud or deceit in the practice of medicine

In April, 1962, the Court of Appeals of the State of New York unanimously held that the State Education Department properly revoked a physician's license to practice for fraud or deceit in the practice of medicine where he had been charged with submitting false and exaggerated medical reports and bills to an attorney for use in settling personal injury cases.

The physician has been found guilty of fraud or deceit in the practice of medicine* and of unprofessional conduct† after a formal hearing before a subcommittee of the Medical Committee on Grievances. The findings of fact according to the Court were supported by substantial documentary evidence and testimony and were confirmed by the Medical Committee on Grievances and the Regent's Committee on Discipline. The Appellate Division, Third Department, unanimously confirmed the revocation of the physician's license.

The Court of Appeals was asked by the physician to determine whether or not the acts specified constituted "fraud or deceit *in the practice of medicine*."

The physician contended that the pertinent section of the Education Law authorizes the suspension or revocation of a license to practice medicine only after a finding, on due hearing, "That a physician ..., is guilty of fraud or deceit *in the practice of medicine*" and that the record in this case revealed no such fraud in "the practice of medicine," as that term is defined in subdivision 4 of section 6501 of the Education Law. This section and subdivision provides:

> . . . A person practices medicine within the meaning of this article . . . who holds himself out as being able to diagnose, treat, operate or prescribe for any human disease, pain, injury, deformity or physical condition, and who shall either offer or undertake, by any means or method, to diagnose, treat, operate or prescribe for any human disease, pain, injury, deformity or physical condition.

The physician argued that this definition, when read in the context of other provisions of the Education Law, limits discipline for fraud or deceit in the practice of medicine to practices of so-called quacks and charlatans who practice their fraud within the physician-patient relationship directly on the patient. He contended that at no time did he mistreat a patient or deliberately submit a false bill or diagnosis to a patient. His fraud, he claimed, was in the realm of the business world, was private in nature, and did not involve his practice of medicine nor cast any doubt on his behavior or ability insofar as patients were concerned.

The Court rejected these contentions in their entirety saying among other things:

> In the first place, appellant (i.e. the physician) did "hold himself out" as being able to diagnose and treat the conditions of each of the patients involved. In the case of K——, and possibly of G——, he also "offered" and "undertook" to diagnose their conditions, and this he did fraudulently, insofar as the Transit Authority and insurance company were concerned. In the cases of Mrs. T——, G—— T——, and S—— C——, appellant "offered" to the insurance company to diagnose their conditions and fraudulently submitted his diagnosis to the insurance company without having treated or examined the patients. In all cases then, appellant did "hold himself out" *and* did "offer" or "undertake" to diagnose the physical conditions of the patients. Therefore, he was engaged in the practice of medicine when he committed the fraudulent acts (sec. 6501, subd. 4, *supra*).

It went on to say:

> Nothing in the statute limits discipline for fraudulent diagnoses to cases where the fraud is perpetrated directly on the patient. Indeed, insurance companies are frequently the ultimate payers of medical bills in personal injury cases, and in this respect are just as much entitled to true medical reports and bills

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* Education Law, sec. 6514, subd. 2, par. (a).

† Education Law, sec. 6514, subd. 2, par. (g).

> as are the patients. Appellant's fraudulent scheme, of course, was dependent upon misuse of his medical license, and the submission of false reports and bills to interested persons was an integral part of his medical practice. The preparation of medical reports for various purposes has always been regarded as a necessary part of medical practice, and it makes no difference whether false reports are submitted directly to the patient, attorney, or the insurance company on behalf of the patient. The statute authorizes discipline in any event. . . . Submissions of false reports of various types to interested persons or institutions other than the patient himself have been found to constitute "fraud or deceit in the practice of medicine" in numerous cases.

The physician argued that the cases cited by the Court established that the concept of "fraud or deceit in the practice of medicine" may be extended beyond fraud in the physician-patient relationship only in cases involving the issuance of fraudulent required reports or in cases involving fraud which affects a vital public interest or interferes with government control in an area of public concern.

The Court rejected this argument saying:

> . . . assuming that appellant's argument is a sound one, the fraud on the insurance companies here involved did affect a vital public interest and did affect governmental regulation of insurance companies and their rates. The public also was, or could have been, indirectly affected by fraud against the Transit Authority. Their fraud or deceit in the practice of medicine was established, and this was sufficient to sustain the action of the board without regard to other statutes or regulations.

It went on to say that the revocation of the physician's license was also permissible under the power given to the Regents to promulgate regulations providing for discipline for "unprofessional conduct." The Court held that the Board of Regents was entitled to find that the fraudulent conspiracy involving the physician was unprofessional. It said that his

> . . . participation was malum in se and undoubtedly amounted to "unprofessional conduct" under the standards commonly accepted by physicians in this State. . . . Moreover, the acts were so obviously wrong and violative of the standards of ethics of a physician that they constituted "unprofessional conduct" even in the absence of regulations defining the term.

Fire safety in hospitals

The National Fire Protection Association states that hospitals operate under a triple threat because they incorporate all the worst fire perils of a hotel, a restaurant, and a laboratory.

Considering the large human element involved in its operation, there is no such thing as an absolutely fireproof hospital. Given a building with the best possible structural safety features, there is always a possible nidus of fire through accident or human carelessness.

An analysis of 300 hospital fires in the last sixty years discloses that three causes, electricity, careless use of cigarets and matches, and heating system defects, caused 55 per cent of the fires; other causes were oxygen explosions, spontaneous combustion, ignition of flammable fluids and combustible anesthetic agents, grease fires in kitchens, and arson.

The two absolutes of fire safety are prevention and control. Each hospital should have a fire plan and should not wait to improvise one in the presence of disaster. In addition to the operating room team and the recovery room team there should be a fire control team composed of maintenance people and nurses. They should have frequent opportunities to work together in drills. They should patrol the premises to prevent the accumulation of rubbish and see that flammable agents are stored as required by law and that electrical equipment is in good repair. They should pay particular attention to the hazardous areas: the operating rooms, rooms where oxygen is used, storage rooms for textiles and wood, workshops and paint shops, boiler rooms, machine room, kitchens and laboratories, and incinerator chutes and laundry chutes.

Smoking is a particular hazard for hospitals. It can be strictly forbidden, but this is unrealistic and leads to clandestine smoking which is more likely to initiate fires. The more sensible approach under present conditions is to recognize this widespread usage and provide for the safe handling of it.

In the event of fire, all chimney-like structures must be closed off; this means corridor firedoors, stair wells, elevator shafts, dumbwaiters, and service ducts. At the same time a preplanned system of evacuation will proceed in an orderly fashion under the direction of a preassigned firewarden, who is thoroughly familiar with each step.

Activities of the Health Research Council

To study special health problems created by the complexities of life in our largest city, the City of New York Department of Health established a unit in 1958 known as the Health Research Council. The Council chooses lines of research and awards funds for this research to scientists working in medical schools, hospitals, universities, research institutions, and city departments. To date a total of $15,756,805 has been expended for this purpose. In 1959 13 grants were awarded, in 1960 44 were given, and in 1961 125 grants were distributed. These awards ranged from $4,600 to support a one-year study of the absorption by the intestine of certain body chemicals to a grant of $812,570 for a two-year study of burns at the Bellevue Hospital research center.

Recognizing that young, productive scientists often abandon research for lack of support of themselves and their work, the Council lays heavy emphasis on this type of support. Last year it supplied 48 five-year grants to individuals, totaling just over $3 million. Applications for grants are carefully screened and approved on the merit and excellence of the proposed research. Some of the subjects under study by current grants are cancer, heart disease, genetics, blood dyscrasias, diabetes, glaucoma, neuromuscular disease, and air pollution.

Some of the projects supported during 1961 were these:

A study was undertaken of the chemistry of narcotic addiction by means of colonies of living cells in laboratory test tubes. These cells are narcotic addicts and die if their addicting drug is withdrawn.

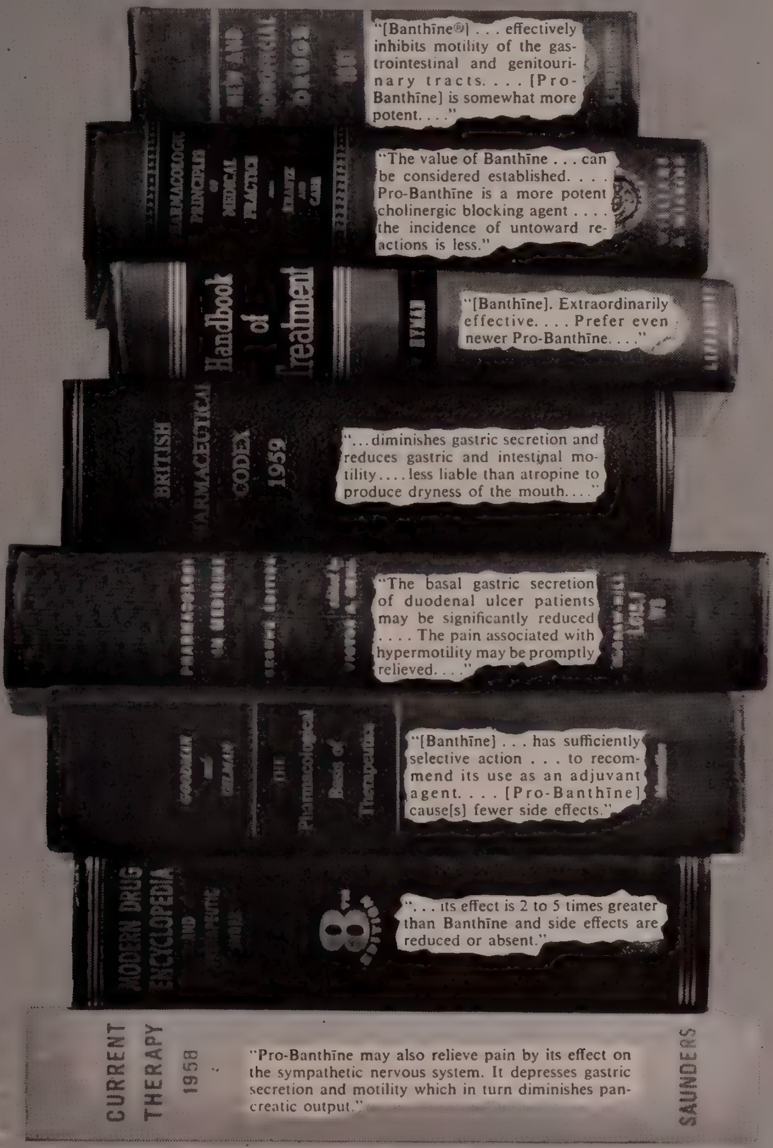
A one-year $12,500 grant went to New York University College of Engineering to design a miniature monitoring device for personal use to measure air pollution.

The City University of New York will study on a $7,500 one-year grant the relationship of hard and soft water and mortality from heart disease.

The paths of water pollution in New York waters will be studied by means of a large model of New York harbor to be constructed for this by the Army Engineer Corps.

One very astute piece of research and development with important implications has to do with people. This is a coordinated program with the U.S. Public Health Service, Selective Service, and the Department of the Army, and will refer the approximately 6,000 young men from New York City, rejected for military service annually because of medical or psychiatric reasons, to the appropriate resource for treatment and rehabilitation.

Thus it may be seen that New York City's health department does much more than test water and issue birth certificates. It employs the dynamic, forward-moving arm of education and research to seek out better ways to serve the public health.



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The Diagnostic Clinic

ZELMAN L. BERNSTEIN, M.D.
New York City
JEFFERSON J. VORZIMER, M.D.
New York City

From Beth Israel Hospital

Of all the important problems confronting teaching hospitals, two stand out as major challenges. One is providing patients with the benefits of most recent medical progress, and the other is making available to house staff physicians the widest exposure to educational opportunities.

It is accepted that the outpatient clinic is frequently regarded as a secondary service in many hospitals. Too often the clinic assignment is regarded either as the price a physician must pay for hospital privileges or as the proving ground for the younger physician.

From the undergraduate viewpoint, clinics are often attended by medical students who, in their eagerness to make contact with patients, rush to any area where they can play their role in doctor-patient activities. On the other hand, graduates reaching the status of intern or resident try their utmost to avoid outpatient clinic duty, believing that a greater yield of advanced medical knowledge can be acquired at the bedside of the inpatient.

Of all the inadequacies inherent in hospital clinics, the medical clinic suffers far more than the others. The medical clinic is usually the catchall for patients: It has the largest census, the largest number of patients with chronic illness, the most perplexing cases, and those patients with maladies for which there is no definitive therapy. In addition, the medical clinic often serves as a rapid sorting station for the other clinics. Because of this, very often the patients who attend medical clinics are hastily questioned, partially undressed, cursorily examined, quickly, and perhaps faultily, diagnosed, and consequently not adequately treated or properly referred.

It was obvious at Beth Israel Hospital that the patients who attended the outpatient department for the most part were not sharing the advanced medical care that the inpatients were enjoying. It was apparent also that the house staff was unwilling and/or physically incapable of utilizing this wealth of medical pathologic conditions advantageously. It followed also that the house staff was not exposed to the opportunity for understanding and treating the ambulatory patient who was exposed to the pressures and obligations of everyday life.

An appreciation of this problem and an analysis of its causes and effects indicated that a diagnostic clinic could correct all of the failings, and accordingly such a clinic has improved the care of outpatients, exposed hitherto untapped sources for house staff education and visiting staff interest, and instilled new life into the specialty clinics.

A description and analysis of the operation of the Beth Israel Hospital Diagnostic Clinic for its first two and one-half years is presented.

Operation of Diagnostic Clinic

Selection and eligibility of patients. Any patient who has not attended a Beth Israel Hospital clinic and has not been an inpatient within the past two years is automatically given an appointment for the Diagnostic Clinic. Patients who are obviously seeking specific services, such as prenatal care, dental care, or eye refraction, are referred directly to the appropriate specialty clinic. Patients may be referred to the Diagnostic Clinic from specialty clinics, the emergency room, or private physicians if so indicated. When there is a question as to whether or not it would be in the best interests of a particular patient to be sent to the Diagnostic Clinic, the clinic appointment clerk calls the chief medical resident for guidance.

APPOINTMENT SETTING AND PREPHYSICIAN WORK-UP. The Diagnostic Clinic meets Monday through Friday and can handle 8 new patients daily. Once registered, the patient is given an appointment on the same day if he requires immediate attention, or he is told to return in a day or two.

On that appointed day, the patient arrives at the clinic at about 11:30 A.M. A complete blood count (consisting of hemoglobin, hematocrit, white blood count, and differential count) and a urinalysis (consisting of routine and microscopic studies) are performed. A Clinic nurse then completes a four-page, questionnaire-type history. There is considerable saving of time by including social information, relevant family history, and a review of systems. By having histories taken by the nurse, who is multilingual, a great deal of information, which ordinarily might not be unearthed by physicians because of language barriers, is gathered in a minimum of time.

By 12:30 P.M. the history and laboratory reports have been completed, and the patient is in a hospital gown in a private examining room and ready for a medical examination, which usually takes from one-half to one hour, depending on the case and on the need for consultation and discussion with the attending staff.

PHYSICIAN DUTIES AND ASSIGNMENTS. *House staff*. The Clinic is attended by one of the two interns from the male medical ward and one of the two interns from the female medical ward. If a patient who is seen in the Clinic is to be hospitalized on the medical service, the patient then has the advantage of continuity of relationship with that intern. The Clinic is also attended by two assistant medical residents who are rotating through medical subspecialties, such as neurology, cardiology, gastroenterology, or pulmonary physiology. Finally, the chief medical resident attends the Clinic daily and lends valuable continuity to the Clinic management throughout the year. At noon of each day, the chief medical resident confirms with the Diagnostic Clinic clerk the number of new and follow-up patients who are present and then assigns additional house staff or excuses those regularly assigned, as indicated.

The house staff physicians arrive at 12:30 P.M., review the histories taken by the nurses, augmenting them wherever necessary, and perform complete physical examinations, including Papanicolaou smears and pelvic examinations on all female patients. Any additional history which is taken, physical findings, impressions, and the plan of medical action recommended by the physicians are then dictated by them to a recording machine. The use of the recording machine not only saves time but also adds a new dimension to clinic charts: legibility. Prescriptions are written and referral, laboratory, and x-ray request forms are completed, subject to review by the attending staff physicians when they arrive at 1:30 P.M.

Attending staff physicians. The attending staff physicians are selected from the internists on the hospital staff. The selection is based on the ability to teach at the house staff level. A senior attending physician and three younger staff members are assigned to the Diagnostic Clinic for each two-month period of the year, and the schedule is so arranged that usually no fewer than three of them are present at each day's session. Currently, the Clinic is often visited by the chief of the medical clinics and the director of the medical service of the hospital.

The attending staff physician, on arrival, reviews the already prepared history, physical impression, and proposed work-up in minute detail, constantly stressing the special handling required by patients on an ambulatory basis. In view of the fact that medical ward rounds begin daily at 2:30 P.M., every effort is made to end the Diagnostic Clinic by that time.

Laboratory and special procedures. If a laboratory test, electrocardiogram, or x-ray film is vital in deciding the diagnosis of a case or would be of great teaching value, it is possible to have these studies performed immediately. Thanks to the universal acceptance throughout the hospital of the merits of the Diagnostic Clinic, all ancillary services have made arrangements for possible additional demands being made on them between the hours of 1:30 P.M. and 2:30 P.M. daily.

Obviously, adequate studies are essential for the completion of the cases. However, as in private practice, every effort is made to use special studies selectively to control costs.

When cardiac or chest fluoroscopy is indicated, it is done immediately by the intern or resident under the guidance of the attending staff physician in the fluoroscopy room, which has been installed as an integral part of the Diagnostic Clinic. This holds true for sigmoidoscopic examinations, which likewise are done in the Clinic. When there is reason to suspect a pathologic condition in the lower colon, the house staff physician previously has instructed the nurse to give the patient a Fleet enema immediately and to bring in the sigmoidoscopic cart so that this procedure can be done if the attending staff physician concurs in its indication. All other accepted office procedures are done as indicated under supervision, such as joint aspiration and injections, infiltration of trigger points, spinal taps, laryngoscopy, Regitine test, and the like.

Consultations. When a problem arises which is traditionally considered to be out of the realm of the internist, a resident or attending staff physician in the appropriate specialty is paged and is invited to consult personally in the Diagnostic Clinic. Therefore, the nature of a pelvic mass, a bizarre dermatologic picture, or a potential psychiatric or casework problem, is most often evaluated immediately, with the house staff present, by specialists in that particular field.

Social service. A social worker is assigned to provide casework study as well as consultation with the doctors on social and community considerations. From previous experience, it is realized that the development of a diagnostic clinic requires social service participation as an aid in clarification of the diagnosis. It is anticipated that more thorough initial diagnostic evaluations result in uncovering a larger number of complex problems. These, in turn, increase the pressure on the part of the patients to make definitive decisions concerning the medical care recommendations which are presented to them. This may be, for some patients, the crucial issue in receiving good medical care. The availability of a social worker for immediate counseling and planning is often a determining factor. With a social worker on call, social problems bearing on hospital admissions and clinic follow-up, such as planning for the care of children, family confusions, and the employment situation, are taken in hand before the course of needed medical care is disrupted. The findings of the social worker and the treatment progress are entered on the medical chart progress sheet, thereby becoming part of the medical diagnostic and treatment considerations.

Planning patient care. When hospitalization is deemed necessary, arrangements are made with the patient and the admitting office before the patient leaves the clinic examining room. The dictated history and the physical and other specialty findings now will become an important part of the patient's hospital chart. The social service department also is immediately available to help the patient handle, if necessary, any personal family problems that would be raised by the patient in regard to hospitalization.

If a case presents a challenging diagnostic problem but does not require admission, the patient is given an appointment for all the additional necessary laboratory and x-ray tests and is given an additional follow-up appointment for the Diagnostic Clinic when the required studies have been completed. An attempt is made to have the patient return to the Clinic on a day when the same house staff and attending physicians will be present. However, if the case presents no diagnostic problems of particular interest, then the patient is sent for the indicated x-ray films and blood tests, he may or may not be started on therapy, and he is given an appointment, coordinated with the

TABLE I. Case load and referrals from Diagnostic and Medical Clinics of Beth Israel Hospital

Clinic	Years	Number of Patients	Total Visits	Hospital Referrals	Hospital Admissions (Per Cent)
Diagnostic	1958 to 1960	1,563	2,806	219	14
Medical	1953 to 1956	5,469	17,682	424	7.9

completion of the studies, to the appropriate specialty clinic.

In a small percentage of the cases, where special therapeutic interest or extraordinary teaching potential exists, the patient is started on therapy and given a follow-up appointment to the Diagnostic Clinic so that the house staff can gain further experience and observe the therapeutic results. When there is no need for a follow-up visit or for a referral to a specialty clinic, the patient is so informed and is told to report to the therapeutic division of the Medical Clinic if the symptoms recur at a further date.

When a significant pathologic condition is discovered in the Papanicolaou smear or biopsy, the patient is notified at home by telephone or telegram instructing him to report back to the Clinic.

Thirty-two months experience. Since the inauguration of the Diagnostic Clinic on May 5, 1958, up to December 30, 1960, many changes have been made in the procedures of the Clinic. The errors which have been experienced and the repeated re-evaluations which have been made by the staff have resulted in the procedure now being described.

Table I illustrates the case load and referrals from the Diagnostic Clinic, as contrasted with those of the Medical Clinic.

Comment

The advantages accruing to the patient attending the Diagnostic Clinic are obvious: the speed with which a patient is seen, either on the day of registration at the Clinic or, at most, three days thereafter; a complete blood count, urinalysis, history, and physical examination; specialty studies or consultations as needed; an evaluation by a highly experienced internist; and perhaps a fluoroscopic and/or sigmoidoscopic examination. All this is done for the same fee, if the patient can afford to pay, as would be paid for a single clinic visit. In addition, if a patient is referred to a specialty clinic, he arrives at that clinic with all the preceding data on his chart as well as the x-ray and laboratory studies which are needed to confirm or further elucidate his disease process. In addition, often the patient has been started on a course of therapy. This saves the patient many extra clinic visits and unnecessary delay in therapy. In 1960 there was an average of 1.6 visits per patient as compared with 4 visits per patient in the pre-Diagnostic Clinic period.

Of equal significance, the Diagnostic Clinic offers the house staff physicians a unique educational opportunity which is lacking in many teaching hospitals. For two hours a day during part of their rotation schedules, the intern and the medical resident are exposed to many of the practical problems which usually are encountered only in private practice. For the first time in his lengthy postgraduate training program, the house staff physician is given the opportunity to learn how and when hospitalization should be recommended to a patient, to evaluate and handle the neurosis and the functional illnesses, to master the simple routine office procedures, and, most important of all, to utilize selectively the amount of diagnostic and therapeutic measures necessary to care for and treat adequately the ambulatory patient. No one who is interested in medical education can help but be upset by the void which exists in the transition from the traditional house staff education program, which revolves around teaching at the bedside of the acutely ill patient, to the handling of private patients with acute or long-term illnesses outside the hospital. The Diagnostic Clinic is a step in filling this void and in giving experience in some of the more practical problems which are encountered in medicine.

Not only has patient care been improved and added scope been given to the house staff education program, but also the entire clinic organization is now being viewed in a new light by those physicians who staff the outpatient department. An assignment to the outpatient department is no longer tolerated as a necessary evil, but instead the internist knows he has been hand-picked for this on the basis of his capabilities and ability to pass his knowledge to younger physicians. This is indeed a drastic change in the concept of clinic assignments.

Another recently appreciated advantage of this Clinic to the hospital is the increased source of referrals to the ward services of the hospital. With prepayment hospital plans becoming more and more popular, many hospitals have found that the admissions to their ward services have been steadily decreasing. The Diagnostic Clinic has proved itself to be one of the best sources of patient referrals to the ward services to make up for the vanishing ward patient.

Conclusion

Whenever any innovation is introduced in medicine, it is always difficult to assess its value quickly. One of the difficulties is the initial enthusiasm of the innovators, who may tend to overlook flaws in their effort to make an idea work. Because of this, the Diagnostic Clinic was given two and one-half years to mature before its real merits were evaluated. Changes in the original program were made whenever necessary in the interests of practicality. Additional changes may be anticipated as weaknesses of the program are realized.

The success of the Diagnostic Clinic may be evaluated from the following facts: One is the ever-increasing number of new patients who present themselves to the Clinic. The other, and the most heartwarming to the administration and staff of the hospital, is the fact that the interns and residents who have finished their rotation through the Diagnostic Clinic make every effort to continue this activity because they know that there are things that can be learned only at the Diagnostic Clinic.

Summary

The Diagnostic Clinic which has been instituted at the Beth Israel Hospital has been described. The mechanical workings of the Clinic are presented in some detail. The experiences of the first two and one-half years of operation of the Clinic are described and evaluated.

Acknowledgment. We wish to acknowledge, with deep appreciation, the aid and assistance of Miss Dorothy Burrill, Director, Outpatient Department; Mrs. Freda B. Goldfeld, Director, Department of Social Service; and Mr. Raymond Alexander, Assistant Director, all of Beth Israel Hospital; and of Mr. Bernard Fuss, formerly Assistant Director, Beth Israel Hospital, now Associate Director, Mount Sinai Hospital, Detroit, Michigan.

Vitamin E

Studies shedding new light on the role of vitamin E in nutrition and metabolism were presented last week at a symposium on recent advances in vitamin E research in Zurich, Switzerland, according to an article in the June 10, 1962, issue of *The New York Times.*

Of especial significance was a study by Dr. M. K. Horwitt, associate professor of biologic chemistry at the University of Illinois College of Medicine, who presented evidence showing that adequate amounts of vitamin E are needed for the metabolism of the polyunsaturated fatty acids, believed to be a factor in reducing blood vessel and heart disease. An increased intake of these fatty acids leads to increased requirement of vitamin E.

Another finding regarded as significant was a high concentration of vitamin E in the adrenal glands, in which large amounts of the vitamin were found to persist for more than ninety-six hours. Some of the studies indicate that vitamin E imbalance may lead to pathologic changes and that once these changes are established even prolonged administration of the vitamin may reverse them only slowly or not at all.

Relative Value of Cervical and Vaginal Smears in Detection of Uterine Cancer

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THE VALUE OF the cytologic examination for cancer is well established and universally recognized. This procedure is especially useful in the early detection of uterine cancer when it is still in the unsuspected, often asymptomatic, and preclinical stage. The ease and simplicity in obtaining the smears makes them a valuable tool in the fight against cancer. As a part of the routine physical examination, the cytologic smear has proved its worth over and over again. The following illustrative cases emphasize these factors.

Case reports

CASE 1. A thirty-six-year-old woman was asymptomatic, and her physical examination indicated negative results. A routine cervical smear, however, revealed the presence of tumor cells. A ring biopsy of the cervix showed a carcinoma in situ with early invasion.

CASE 2. A twenty-nine-year-old woman had a routine physical examination. The pelvic examination revealed an erosion of the cervix but was otherwise unremarkable. A cervical smear showed the presence of tumor cells, and a ring biopsy of the cervix showed carcinoma in situ.

CASE 3. Of particular interest is a twenty-seven-year-old woman in her third month of pregnancy who had a cervical smear made as part of the routine prenatal examination. She was asymptomatic, and clinically her examination results were entirely negative. The cervical smear revealed tumor cells which were confirmed by a repeat smear. The cervical biopsy showed a focus of carcinoma in situ.

CASE 4. A similar situation was that of a four-and-one-half-month pregnant, thirty-four-year-old woman who had a routine cervical smear made as part of her prenatal examination. She was also asymptomatic and had clinically negative findings. The cervical smear revealed tumor cells, and the cervical biopsy showed carcinoma in situ.

The cervical smear is not limited in its usefulness to diagnosing cervical cancers but is also very helpful in detecting tumors of the uterine cavity. This was shown in the following cases:

CASE 5. A fifty-eight-year-old woman had had vaginal spotting on and off for about three months. A cervical smear revealed tumor cells. This was followed by curettage which showed endometrial adenocarcinoma.

CASE 6. A sixty-year-old woman had vaginal bleeding for ten days before the examination. A cervical smear showed tumor cells, and this was followed by a curettage which showed poorly differentiated adenocarcinoma with papillary areas.

CASE 7. A similar incident is that of a fifty-nine-year-old woman who had been on estrogen therapy for several years and developed postmenopausal bleeding. A cervical smear showed clusters of tumor cells, and the uterine curettings were composed of an anaplastic adenocarcinoma.

COMMENT. This type of experience has stimulated wide interest in and an acceptance of the cytologic test in the control of uterine cancer. It has been estimated

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Pathology, Clinical Pathology, and Blood Banking, May 10, 1961.

that the annual number of tests performed has risen from 50,000 in 1945 to 6 million in 1959.[1] Yet this rate, impressive as it may seem, is far from the number of cases that should be tested to achieve the goal of practical control of this type of cancer.

To accomplish this purpose the smears must be taken repeatedly from a great many women. This requires the simplest possible type of effective screening procedure. Erickson,[2] commenting on the United States Public Health Service survey in Memphis, stated that:

> Mass screening for uterine cancer detection must point efficiently, accurately, rapidly, easily, and economically at a significantly high percentage of unsuspected, asymptomatic incipient cancers.

One of the limiting factors in this test is the screening capacity of the technician and/or the cytopathologist. This, in turn, will depend on the number and quality of smears submitted in each case. While various methods of collecting specimens have been utilized, the most popular technic at present is the taking of a vaginal smear from fluid material in the posterior fornix and the taking of a cervical smear with a cotton swab or by scraping the cervix with a spatula.

The use of these two smears has given good results in our community, with the detection rate comparable to that in most reported series. In the past several years it has been our impression that, in the majority of proved cases of cancer, the cervical smear gave a much higher pick-up rate than did the vaginal smear. If one smear only could be relied on, the mass screening potentialities of our laboratories could be almost doubled, and individual costs could be reduced considerably. To test the validity of this impression, material from several sources in this community was studied, the chief purpose being to compare the relative value of the cervical and vaginal smears in detecting cancer.

Material

Studies were made of 30,135 cases from three sources: The Cancer Detection Center at the Edward J. Meyer Memorial Hospital, Buffalo, a clinic for apparently healthy persons over thirty years of age; the Central Cytologic Laboratory in Buffalo, which receives specimens from practicing physicians; and the Pathology Department of Mount St. Mary's Hospital, Niagara Falls, which includes mostly outpatient material. A total of 169 cases of cancer was recorded (Table I), each one confirmed by a tissue diagnosis. The detection rate was 0.56 per cent. Included were 93 cases of carcinoma in situ of the cervix, 50 cases of invasive cervical carcinoma, 23 cases of corpus (uterine cavity) cancer, and 3 miscellaneous cases (vaginal recurrences and metastatic lesions).

A DIFFERENTIAL EVALUATION *of vaginal and cervical smears was made in 21,944 cases. Positive or suspicious smears were discovered in 675 cases (3.1 per cent), of which 101 cases were proved cancers. Both vaginal and cervical smears were positive in 55 per cent of all uterine cancer cases and in 60 per cent of cervical cancer cases. The* cervical *smear was positive in 75 of the 101 total cases (74 per cent) and in 71 of 86 cervical cancers (83 per cent). The* vaginal *smear was positive in 61 of the 101 cases (60 per cent) and 56 of 86 cervical cancers (65 per cent). If only one of the dual smears was positive, the cervical smear was superior in the ratio of almost 5:1.*

TABLE I. Proved cancer

Type of Cancer	Number of Patients
Carcinoma in situ, cervix	93
Invasive carcinoma, cervix	50
Carcinoma in the corpus	23
Others	3
TOTAL	169

Cytologic results

A differential evaluation of vaginal and cervical smears was possible in 21,944 of these cases. In this group positive or suspicious smears (Papanicolaou class 3, 4, or 5)

TABLE II. Number of cancers found as result of smear testing

Smear Results	Cervical Carcinoma In Situ	Cervical Invasive Carcinoma	Corpus Cancer
Both negative	7	4	10
Both positive	31	21	4
Cervical positive, vaginal negative	15	4	. .
Vaginal positive, cervical negative	1	2	1
Vaginal positive, cervical unsatisfactory	1	. .	. .
TOTALS	55	31	15

TABLE III. Cytologic summary

Data	Number of Patients	Per Cent
Cases analyzed	21,944	. . .
Positive smears	675	3.1
Confirmed by biopsy	101	0.48
Both smears, false negative	21	20.8
Cervical false negative	11	12.8
Corpus false negative	10	66.7
Both smears positive	56	55.4
One smear only positive		
Cervical	19	18.8
Vaginal	4	3.9

were discovered in 675 cases, a rate of 3.1 per cent. Tissue diagnosed as cervicouterine cancer has been reported to date in 101 of these cases or in 15 per cent of the positive smears.

Comment

A study of the three main types of cancer involved (Tables II and III) reveals that the smears were reasonably accurate in picking up both types of cervical cancer but showed up relatively poorly in detecting endometrial carcinoma. While both smears were positive in over one half of the cases of cervical cancer, when only one smear was positive, the cervical smear was accurate over five times as often as the vaginal smear. Other investigators have noted the superior efficacy of the cervical scraping smear in detecting the more common cancer of the cervix. They have, however, also been reluctant to abandon the vaginal smear for fear of missing endometrial malignancy. Song, Fanger, and Murphy,[3] in a survey of 25,000 cases at Rhode Island State Cytology Laboratory, found 195 cancers of which only 19 were fundal lesions. In their 156 cervical carcinomas (both in situ and invasive) the vaginal smear was essentially negative in 51 or 32 per cent. The vaginal smear was positive alone in only 12 or 7.7 per cent of the cases. Of their 19 endometrial cancers, 4 were discovered on cervical smear alone, 5 on vaginal smear alone, and in 10 cases both smears were positive. Song, Fanger, and Murphy[3] state, "It is evident that the cervical scraping smear detected more cases of tumor than the vaginal aspiration smear," but they conclude that, "Continued examinations of both types of smears seems justified."

Miller and Von Haam[4] reported at the Inter-Society Cytology Council in October, 1960, on a four-year study of 113,000 women. They stated this study "has demonstrated the superior accuracy of the cervical scraping technic over the vaginal aspirate . . . , the latter is still a valuable method for detecting cancer." In a special study of apparent false negative results in this series (110 cases) Miller and Von Haam[4] noted that

> In 30 per cent the vaginal aspirate was unsatisfactory, negative, or atypical, whereas the cervical scraping was negative in only 3

per cent when the vaginal aspirate was suspicious. This superiority of cervical scraping technique was seen in all types of uterine cancer except for adenocarcinoma of the endometrium, where the 2 were of equal value.[4]

Day,[5] of the Strang Clinic, reported:

> Roughly speaking, the vaginal aspiration smear showed no abnormality, that it missed, approximately 20 per cent of cervical cancer cases . . . . The cervical swab smear in contrast misses very few, if any, cervical cancers.

An analysis of the results of our present study indicates the following:

1. Both vaginal and cervical smears taken simultaneously failed to detect an appreciable percentage (20 per cent) of total uterine cancer. In considering only cervical cancer, however, the rate of failures fell to 12.8 per cent.
2. Both smears were positive in 55 per cent of all uterine cancer cases and in 60 per cent of cervical cancer cases.
3. The cervical smear was positive in 75 of the 101 total cases (74 per cent) and in 71 of 86 cervical cancers (83 per cent).
4. The vaginal smear was positive in 61 of the 101 total cases (60 per cent) and 56 of 86 cervical cancers (65 per cent).
5. If only one of the dual smears was positive, the cervical smear was superior in the ratio of almost 5:1—19 positive cervical smears (18.3 per cent) versus 4 positive vaginal smears (3.8 per cent).
6. In the detection of corpus cancer the cervical smear was likely to be accurate in a high percentage of those cases in which the smears were significant (4 out of 5 in this small group).

Summary

The relative value of cervical and vaginal smears in the detection of uterine cancer was studied in a series of almost 22,000 cases which included 101 proved cancers. A comparative analysis of the cancers picked up by either or both smears revealed a superiority of the cervical scraping smear over the vaginal aspirate or swab smear. To control this disease smears must be taken on a mass scale at repeated intervals. Since there is a limiting factor of screening capacity of the technician and/or cytopathologist, restricting each case to 1 specimen only would expedite and economize greatly on this test. As a result of this study, it is felt that the cervical scraping smear alone as a screening procedure is sufficiently reliable and is adequate for the detection of cancer in the majority of instances.

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Cancer Chemotherapy in Gynecologic Malignant Conditions

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THE GYNECOLOGIST has been traditionally oriented toward surgical or radiotherapeutic approaches in pelvic malignant conditions. Unsatisfactory results in advanced pelvic malignant conditions, particularly ovarian carcinoma, have stimulated an interest in other methods of therapy. The recent advances in the attack on gynecologic cancer have been in the field of chemotherapy. This is based on our increasing knowledge of the factors that control cellular differentiation, mutation, and growth. We now recognize the cell's ability to adapt its enzyme systems to environmental changes; we recognize that there are factors in intrauterine embryonic life which regulate cell differentiation; and we are beginning to study the interplay of the local and systemic factors that control cellular growth. As fragments of information are gathered in these fields, various agents which have in vitro activity in disrupting the pathways of cellular or intracellular generation are unearthed. Many of these are available for clinical trial or usage.

From present indications, the control of gynecologic neoplastic diseases by chemical means will be a slow, increasingly complex task. Small practical advances will be associated with tremendous gains in knowledge concerning cellular physiology and pathology. The chemotherapeutic agents which have been discovered thus far are generally feeble and brief in their effects. However, conscientious and extensive clinical investigations have shown them to be of definite, although limited value. Patients and their families are superficially aware of these newer modalities and look for help from these drugs. In many cases there is little to offer, and difficult decisions must be made. The questions to be answered are: Should chemotherapy be reserved for the terminal patient only? Is prolonged hospitalization for what may be considered experimental therapy in a patient's best interest? Are the new agents indicated for all patients who are unsuitable for or represent failures of accepted therapeutic approaches? And finally, is the physician in his enthusiasm unconsciously leading a patient to accept experimental chemotherapy in preference to the more standard forms of treatment?[1]

We attempt to answer these difficult questions, sensitive to the patient's needs and problems, as objectively as possible. On the gynecology tumor service at the New York Medical College-Metropolitan Medical Center, patients with pelvic malignant conditions which are advanced beyond the limits of resectability constitute a significant proportion of our case load. At present our cancer chemotherapy program is twofold. One area may be termed experimental chemotherapy, the evaluation of new substances or new routes of therapy, and the second is practical chemotherapy, the use of established drugs in the management of certain types of cancer under specific indications. Each patient is studied intensively and presented to the tumor board for a final evaluation before a decision as to the category of chemotherapy as outlined is established.

A basic knowledge of the types of agents available today and their apparent mode of

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* By invitation.

action is a prerequisite for clinical cancer chemotherapy.

Chemotherapeutic agents fall into four classes: polyfunctional alkylating drugs or radiomimetic agents, antimetabolites, hormones, and a group denoted as miscellaneous (Table I).

Polyfunctional alkylating agents

Nitrogen mustard (methyl-bis[β-chloroethyl]amine) developed in 1946[2] is the prototype of this group. As do all the alkylating agents, it undergoes a change in chemical structure after the administration. A reaction may occur with many constituents of both normal and cancerous cells, but there is good evidence that DNA (desoxyribose nucleic acid), the presumed genetic material in the nucleus, is most vulnerable. This presumed reaction with DNA can lead to mutations, carcinogenesis, and cell death. The term polyfunctional indicates that these agents react at two or more points along the DNA filament or by cross linkage. The effect of these agents is qualitatively similar to total body radiation. The arrest of mitoses and genetic aberrations is produced. For this reason, they are termed radiomimetic drugs.

Antimetabolites

The antimetabolites are closely related to substances which are normally utilized by the cell for metabolism and growth. The various antimetabolites are unrelated to each other in chemical structure. Their value in cancer chemotherapy consists in their interference with the synthesis or structure of the nucleic acids which prevents the proliferation of many types of neoplastic cells.

As a point of reference we can consider the normal structure of the nucleoproteins. Simple carbon molecules are combined by enzymatic action dependent on folic acid in the synthesis of purines and pyrimidines. These substances are joined by 5 carbon sugars (pentoses) and phosphoric acid to form a mononucleotide. Four of these complex molecules in a linkage produce a nucleic acid. DNA and RNA (ribonucleic acid) are such compounds and differ in their pentose component and in the nature of their pyrimidine make-up.

CHEMOTHERAPEUTIC AGENTS *fall into four classes: polyfunctional alkylating drugs or radiomimetic agents, antimetabolites, hormones, and a miscellaneous group including antibiotics and colchicine. Toxic side-reactions, which affect the gastrointestinal, hematopoietic, and cutaneous systems, occur with all the chemotherapeutic agents but are especially common with the use of the antimetabolites. The most extensive use of chemotherapeutic agents in gynecology has been in the attempt to control ovarian malignant conditions. Thio-TEPA, 5-FU, and nitrogen mustard have been used in these conditions. An excellent or good response has been obtained in 6 of 16 cases treated with chlorambucil (Leukeran) in daily doses of 0.2 to 0.4 mg. per kilogram of body weight. In fundal carcinoma surgery remains the therapy of choice, but progestational drugs are being used on an experimental basis. Chemotherapeutic agents have had little trial in carcinoma of the cervix. In choriocarcinoma, combined therapy with surgery and methotrexate, in daily doses of 10 to 30 mg. parenterally for five-day courses, seems to be the regimen of choice.*

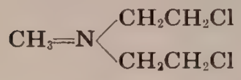
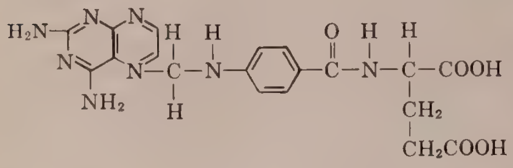
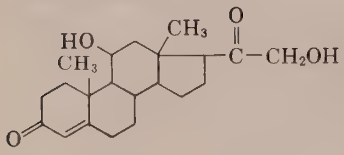
The antimetabolites have antitumor activity by interfering with nucleic acid syntheses. They may do this in three ways: by binding an enzyme and thus blocking an important function of the cell; by being incorporated into a molecule to produce an abnormal, or fraudulent substance; or by interfering competitively with a normal substrate.

Methotrexate (4-amino-N^{10}-methyl teroylglutamic acid), by interfering with the conversion of folic acid to its formyl or one-carbon derivative, blocks the availability of these simple carbon fragments for the synthesis of purines and pyrimidine.[3–5]

DON (6-diaxo-5-oxo-L-norleucine), a substance closely related to glutamine, blocks purine formation at a higher level.[6] These two agents are examples of competitive action for a substrate, folic acid and glutamine respectively.

6-Mercaptopurine acts by interfering with the conversion of fully formed purines into

TABLE I. Classes of chemotherapeutic agents

Prototype Compound	Derivatives in Clinical Use	Dosage (Mg.)	Mode of Action
I. Polyfunctional alkylating agent Methyl-bis (β-chloroethyl) amine (HN_2)  $CH_3{-}N\left\langle\begin{matrix}CH_2CH_2Cl\\CH_2CH_2Cl\end{matrix}\right.$	Nitrogen mustard	0.4 per kilogram*	Reacts at two or more sites on DNA filament with resultant changes qualitatively similar to total body radiation, that is, interference with rapidly proliferating cells leading to cell mutations and death
	Chlorambucil	0.2 to 0.4 per kilogram daily†	
	Sarcolysin	100*	
	TEM	0.12 per kilogram*	
	Thio-TEPA	0.8 to 1 per kilogram*	
	Busulfan (Myleran)	2 to 6 per day	
II. Antimetabolite Aminopterin 	Aminopterin	0.25 to 1 per day†	Blocks incorporation of simple carbon precursors into purines and pyrimidine
	Methotrexate	2.5 to 5 per day† 10 to 30 per day,* five-day courses	
	Azaserine	5 to 10 per kilogram	Blocks NH_2 transfer from glutamine in purine synthesis
	DON	0.1 to 0.3 per kilogram	
	6-Mercaptopurine	2.5 per kilogram per day†	Blocks incorporation of purines into nucleic acids
	5-Fluorouracil	15 per kilogram per day* × 5	Blocks methylation of uracil to form thymine
III. Steroid Steroid nucleus 	Testosterone Estrogen Progesterone Cortisone Aldosterone inhibitors (Aldactone)	Varies with preparation	Antagonizes opposite hormone or depresses pituitary
IV. Miscellaneous Streptomyces antibioticus	Actinomycin C	50 to 100 micrograms per day*	Not established; bone marrow depression; potentiates radiation
	Actinomycin D	75 micrograms per kilogram, total dose divided over ten days	
Colchicine	Demecolcin (Colcemid)	3 to 10 per day†	Metaphase arrest

* Intravenously.
† Per os.

nucleic acids, which is a higher level of block by enzyme binding.[7,8]

5-FU (5-fluorouracil) acts by preventing the methylation of uracil to form thymine, a pyrimidine believed to be uniquely present in DNA.[9,10] This action is an example of the formation of an abnormal or fraudulent substance to block nucleic acid syntheses.

Hormones

The third class of chemotherapeutic agents are the hormones. These may be divided into the sex hormones and the corticosteroids. The sex hormones may exert their effect by depressing the pituitary, but more probably they act by antagonizing the action of the opposite trophic hormone. When a trophic hormone such as estrogen stimulates the growth of a target organ, the net result is similar to that produced by putting the target organ's cells in tissue culture: The cells dedifferentiate, increase their rate of growth, and ultimately may undergo malignant change. There is as yet no evidence that the growth rate of a target organ's cells in tissue culture is increased by adding a trophic hormone to the medium. It is possible, therefore, that the basic effect of a trophic hormone is merely to release the cell from local restraint. It may act by coating the cell surface, like an antibody, and so prevent the entry of growth-controlling substances, or it may act by suppressing the formation of the controlling substances in neighboring cells. The opposite or antagonizing hormone apparently exerts its effect at the cellular level.

The corticosteroids have not been used widely in gynecology as chemotherapeutics, but there is some evidence that they may potentiate the action of other antitumor agents. Aldosterone inhibitors have ascites secondary to pelvic malignant conditions.

Miscellaneous

The miscellaneous group includes many unrelated agents with antitumor activity. Certain antibiotic derivatives have this property, but their mechanism of action is not fully understood. The antibiotic actinomycin D is known to potentiate the effect of radiation.[11]

Colchicine has been known for some time to block mitoses at the metaphase. Recently, demecolcin, a derivative of this drug, has become available to evaluate as an antitumor agent.[12]

Toxicity

In addition to understanding the mode of action of these chemotherapeutic agents, a thorough knowledge of the toxic side-efiects which are encountered in the use of these drugs is mandatory. These reactions may be seen to some degree with all the agents which are now used but are particularly common when administering the antimetabolites.

Three body systems are commonly affected: gastrointestinal, hematopoietic, and cutaneous.

The gastrointestinal reactions include stomatitis, proctitis, diarrhea, nausea, and emesis. One or all of these symptoms occur in 60 to 70 per cent of patients. Their appearance is usually delayed five to seven days after the onset of therapy. The gastrointestinal complications are managed in the following manner: The drug therapy is stopped with the appearance of the first ulcer at the inner lip margin or when the patient has 6 or more bowel movements daily. Vomiting and diarrhea will persist for short periods after the withdrawal of the chemotherapeutic agent. The stomatitis requires antiseptic and analgesic mouth care and the institution of a fluid diet. Nausea and emesis have been best controlled by combined barbiturate and phenothiazine administration. A typical regime for pronounced upper tract symptoms would include Amytal sodium, 250 mg. as a slow intravenous drip initially, followed by Luminal sodium, 60 to 120 mg. intramuscularly every four to six hours. Compazine is also given, 10 to 15 mg. intramuscularly every four hours. Milder symptoms have responded to oral preparations. Diarrhea can become a severe and debilitating problem associated with marked proctitis. Tincture of opium is employed as a constipating agent. Intravenous fluid and electrolyte replacement may be indicated. Burning is controlled by local analgesics, hydrocortisone rectal flushes, and parenteral sedation.

The hematologic toxic reactions appear somewhat later, usually between the ninth and fourteenth days. Complete blood counts are taken three times a week initially and daily when a depression of the cellular elements is noted. Some degree of leukopenia is universal. Its presence appears to be directly related to antitumor effect. In approximately one third of the patients counts of less than 2,500 white blood cells are encountered. In 10 per cent the counts fall below 1,000. Interestingly, the nadir of the leukopenia occurs most frequently between the ninth and fourteenth days after the onset of therapy. This indicates that the stomatitis, which is seen earlier in the course of drug therapy, is a specific toxic reaction and is not secondary to granulocytopenia. Thrombocytopenia and anemia are seen less commonly as initial side-effects.

Therapy is stopped when the white count falls below 2,500 cells or when platelets are below 100,000. The patients are placed on isolation technic. We do not use antibiotics prophylactically. However, when specific infections occur, they are treated with high doses of antibiotics, particularly penicillin and streptomycin, pending culture and sensitivity reports. Broad-spectrum antibiotics are withheld when possible to avoid fungal overgrowths in these already debilitated patients. Anemia is combated by transfusion when the hemoglobin levels fall below 8 Gm.

Cutaneous toxicity is occasionally a difficult problem. Exfoliative dermatitis is the commonest manifestation and usually responds to the withdrawal of the chemotherapeutic agent. Steroids, both oral and topical, are of value. Some degree of alopecia is seen in 10 per cent of the patients and, fortunately, is usually reversible, for no specific therapy is available. With this understanding of the mechanisms of action and toxicity as a background, we can now evaluate some of the clinical applications of these chemotherapeutic agents on specific pelvic malignant conditions.

Ovarian carcinoma

Nowhere in gynecology is the need for additional therapeutic modalities greater than in ovarian carcinoma. Most frequently the disease has progressed beyond curative resectability at the time of diagnosis. Five-year survival rates are generally reported between 10 and 30 per cent. The higher figures are seen in series with many tumors of low-grade malignancy included. We have treated 84 cystadenocarcinomas of the ovary since 1949 and have recorded but 7 five-year survivals. For this reason, the most extensive use of chemotherapeutic agents in gynecology has been in the attempt to control these ovarian malignant conditions.

Thio-TEPA, one of the polyfunctional alkylating agents, has been used by Kottmeier and others[13-17] who report definite palliative results in 25 to 30 per cent of their patients. The usual dosage is 1 mg. per kilogram per day intravenously for three- to five-day courses. These palliative results are measured by shrinkage in tumor size, decreased ascites, and lessened symptoms, particularly pain. These effects are relatively brief in duration although some two- to three-year survivals are included. These authors have stressed the value of this agent used intraperitoneally in those patients who were opened and closed because they were found to be inoperable. At a subsequent date, a "second-look" operation was performed, and in a significant percentage of cases the lesion was found to be resectable.

5-FU, which was synthesized by Heidelberger in 1957,[18] is an antimetabolite which has demonstrated antitumor activity in a wide variety of neoplasms.[19,20] Its use in ovarian carcinoma has been moderately extensive with results similar to those of the alkylating agents.[21,22]

The dosage employed is 15 mg. per kilogram per day intravenously for five days followed by half this amount every other day for an additional three doses.

One can expect 25 per cent of the patients to undergo short-term objective and subjective remissions with a decrease in ascites and tumor shrinkage. These results are not influenced by prior therapeutic regimens with other agents. This allows the physician to rotate his antitumor drugs in conjunction with external radiation so as to lessen the toxic effects of each agent. Despite this theoretical advantage, our experience with 5-FU has been disappointing. The therapeutic and toxic levels are apparently close enough so that to achieve some palliative effect we must anticipate problems in the management of drug toxicity.[9] Seven of our patients have received this drug. Four severe toxic reactions and 1 death attributable to the therapy were encountered. This particular agent has been discarded at our institution because of this hazard in therapy.

Nitrogen mustard (Mustargen) has been used parenterally with limited success in ovarian carcinoma.[23] The dosage employed is 0.1 mg. per kilogram per day for four days. It has been effective used locally for ascites or pleural effusions.[1]

At present, the agent of choice for palliative chemotherapy of ovarian carcinoma at the New York Medical College-Metropolitan Medical Center is chlorambucil (Leukeran). This is a recently developed variant of the polyfunctional alkylating group.[24] It is an oral preparation which is given in doses of 0.2 to 0.4 mg. per kilogram of body weight per day. We have used this drug in 16 cases thus far. Our initial results appear to be as good or perhaps somewhat better than those obtained in our earlier attempts with other agents. An excellent or good response, defined as the disappearance or considerable decrease in size of the tumor and an associated resolution of major symptoms, was obtained in 6 patients. Happily, we have noted a relatively small number of severe toxic reactions. Masterson, Calame, and Nelson[25] reported similar encouraging results. We are well aware that a general maxim for these chemotherapeutics may be that the toxicity is mandatory for therapeutic effect, but we agree with Wright[26] that remissions with this agent can be produced without side-effects.

The drug is used on a controlled regimen as follows: All patients who are found to have possibly malignant ovarian lesions at laparotomy are included in the trial series. Peritoneal washings are taken before and after surgical manipulation for cytologic study. All patients are started immediately on a course of chlorambucil, 0.4. mg. per kilogram of body weight initially intravenously, pending the pathology reports. Those with benign lesions are removed from the study. Those with malignant conditions are switched to oral medication as soon as the postoperative state permits and continued on an initial course for four weeks. Repeat courses are given when called for by the symptoms if hematopoietic depression is no longer present. In this way we hope to be able to evaluate the effect of chlorambucil, particularly in those cases with positive cytologic washings at the termination of surgery.

Fundal carcinoma

Chemotherapy has been used infrequently for advanced endometrial malignant conditions until recently. Several of the alkylating agents have been utilized with limited success.[27] The newer attempts have been with hormonal agents. Their use has been based on the clinical supposition of estrogen sensitivity or dependency within these tumors. Endometrial carcinoma appears to be found more frequently in association with hyperestrinemia whether it is secondary to exogenous intake or increased endogenous production as seen in granulosa cell tumors, Stein-Leventhal syndrome, or cortical stromal hyperplasia. Estrogen is a trophic hormone for the endometrium, and, although it is not necessarily directly etiologic in malignant changes of this tissue, it would seem to have detrimental growth-stimulating effects. The necessity for control of estrogenic production in this disease has been recognized for some time. Oophorectomy in the surgical therapy of endometrial carcinoma is mandatory. Recently, Kistner[28] has suggested that progestational agents would be of value in the control of advanced fundal carcinomas by estrogenic inhibition. He has used norethynodrel (Enovid) in his earlier work on adenocarcinoma in situ with favorable results.

At our institution, we have been attempting to confirm these results but have also changed to the use of pure progestational products such as progesterone (Delalutin), since norethynodrel contains small amounts of estrogen. The dosage we employ is 500 mg. of progesterone intramuscularly every other day or 60 to 80 mg. of an oral preparation daily. Insufficient time has elapsed to allow for an evaluation of these agents, but there appears to be some indication that this form of hormonal therapy may have a place in the palliative management of advanced fundal carcinoma. It may also have a place in furthering our understanding of the hormonal relationships in endometrial malignant conditions.

Carcinoma of the cervix

Carcinoma of the cervix is another area of gynecologic cancer therapy in which chemotherapeutic agents have had little trial. Klopp[29,30] has used intra-arterial nitrogen mustard in cervical and vaginal carcinomas with the production of regression in isolated cases. Palliative regimens have been reliant on the squamous lesion's proclivity for local extension and have consisted primarily of urinary and fecal diversion as indicated.

Recently workers from Memorial Hospital for Cancer and Allied Diseases, who were treating patients in Africa where suitable surgical or radiotherapeutic means were not available, issued a preliminary but exciting report on the use of methotrexate, an antimetabolite, in carcinoma of the cervix. The drug was used by direct intra-arterial continuous perfusion.[31]

We have adopted and modified their regimen in our advanced cervical carcinoma patients in an attempt to confirm their results. Our indications for what we term constant infusion with methotrexate are necessarily more limited because of the availability of conventional modes of therapy. This treatment is reserved for those patients with the following clinical picture: (1) primary inoperability and unsuitability for radiation therapy and (2) a locally recurrent tumor that fails to respond to conventional therapy. In particular, this form of chemotherapy is indicated in the control of pain, bleeding, profuse infected discharge, and bulky tumor masses.

These patients are managed in the following manner: Laparotomy is performed. The hypogastric artery on each side is ligated at its origin from the common iliac artery, and a polyethylene catheter is threaded into the artery and fixed. The catheter is brought to the skin. When the patient is stable postoperatively, infusion with methotrexate is begun. Twenty mg. per side per day are given for five days. The material is diluted in saline and delivered over twenty-four hours by a Harvard constant infusion pump. The continuous high blood concentration of methotrexate which is placed directly in the pelvic blood supply is responsible for the antitumor activity. The Memorial workers realized that considerable systemic spillover would occur and suggested the novel concept of simultaneous systemic protection by intramuscular injection of 3 to 6 mg. of Leucovorin (a folic acid-like compound) every six hours during the course of therapy. We have adopted this adjuvant and feel that some lessening of bone marrow depression and gastrointestinal toxicity has resulted.

We can discuss no results in our limited experience thus far, but Sullivan *et al.*[31] in their original African study reported objective tumor shrinkage or disappearance in 5 of 6 cases treated. Initial changes occurred from two to four weeks after the cessation of the first course of therapy.

We believe that some method of constant pelvic infusion may be a valuable addition to our chemotherapeutic attacks on gynecologic cancer if only by changing the route of administration.

Choriocarcinoma

Paradoxically, although gynecology was one of the latecomers in the field of chemotherapy, it is in our field that the first notable success occurred. Li, Hertz, and Bergenstal from the National Cancer Institute reported in 1958[32] on their initial studies in the treatment of trophoblastic tumors with methotrexate. Since that time the number of cases so treated has steadily increased. The results have been most encouraging. The drug is used in five-day courses of 10 to 30 mg. per day intramuscularly or intravenously. Severe side-effects are relatively uniform, but in view of the promising therapeutic results they must be tolerated. The initial spectacular results with this agent have been tempered by a lengthened period of observation. At present we can expect 60 to 70 per cent disappearance of primary and distant tumor masses particularly when methotrexate is used in combination with DON (0.2 mg. per kilogram) and actinomycin D (25 to 50 micrograms per day). Repeated lower dose courses are given monthly for an indefinite period.

Two of the patients who were treated successfully in the earlier trials have since carried normal pregnancies to term without evidence of a recurrence of their original growth. We realize that choriocarcinoma, which in reality is a transplant tumor from the products of conception, would be a likely area for some success in cancer chemotherapy to be found. Therefore we are not overly optimistic as to the possibilities of immediate similar results in other areas of gynecologic cancer chemotherapy.

In this growth, however, results with a chemotherapeutic agent have been impressive enough for Li and others[32] to state that its use now replaces surgery as the primary mode of therapy. The cumulative experience of any institution with this disease is limited. We must appraise our therapeutic regimens in the light of reports from those few hospitals acting as referral centers. However, our present regimen for the management of choriocarcinoma is a combined surgical and chemotherapeutic attack, particularly in those cases with clinically resectable local disease.

Conclusion

We feel that a hopeful outlook is legitimate in this area of cancer therapy. Much progress has been made since the first recorded use of Fowler's solution in leukemia by Lissauer in 1865[33] and since the description of Krumbhaar[34] of the bone marrow effects of mustard gas first employed in Flanders in 1917.

Rapidly growing anaplastic cancer cells, particularly of autologous origin, are highly susceptible to the recently developed chemotherapeutic agents. Unfortunately so are the rapidly growing embryonal cells of bone marrow and gastrointestinal mucosa. At present our difficulty is that the margin of safety between therapeutic and toxic dosages is too small. Paradoxically, the ability of cancer cells to adapt, by selection or enzymatically, is too great. Nevertheless, we are continuing both our experimental and practical chemotherapy studies in the hope that future developments in cellular physiology will bring to us in the clinical fields agents of greater and safer usage.

At the onset of this presentation we posed four questions. The answers will vary from institution to institution. Important factors include patient status, institutional facilities, experience of the staff, and, perhaps most importantly, individual preference and philosophy. Should chemotherapeutic agents be reserved for the terminal patient only? The available studies indicate the effectiveness of these agents in selected cases, and in many instances their use is indicated in early carcinoma. Is prolonged hospitalization for what may be considered experimental therapy in a patient's best interest? We differentiate experimental from practical chemotherapy. The former is best reserved for advanced or terminal cases who are undergoing prolonged hospitalization because of the nature of their disease. Are the new agents indicated for all patients who represent failures of or who are unsuitable for standard means of therapy? Recurrences should be treated with conventional modes of therapy. When these prove unsatisfactory chemotherapy is indicated. The few patients who, for varying reasons, are unsuitable for standard primary therapy present a specific group in which initial chemotherapy may prove of value. Is the physician in his enthusiasm unconsciously leading a patient to accept experimental chemotherapy in preference to the more standard forms of treatment? This possibility can be controlled by further dissemination of information on chemotherapy including indications, contraindications, and toxicity. A functioning tumor board to participate in the decision regarding therapy serves to control the personal factor.

Summary

Chemotherapeutic agents have a definite role in the management of gynecologic cancer. On the gynecology tumor service of the New York Medical College-Metropolitan Medical Center, chemotherapy is used in selected cases of ovarian, fundal, cervical, and choriocarcinoma.

In ovarian carcinoma, we recommend chlorambucil in the dose of 0.2 to 0.4 mg. per kilogram per day in four-week courses, as an adjuvant to surgery. This agent seems to be of equal or greater effectiveness than radiation therapy and has the advantage of ease of administration.

In fundal carcinoma, surgery remains the therapy of choice with the newer progestational drugs being used on an experimental basis. In carcinoma of the cervix, chemotherapy, at the moment, has no practical application. In choriocarcinoma, combined therapy with surgery and methotrexate, in the dose of 10 to 30 mg. per day parenterally for five-day courses, seems to be the regimen of choice.

The toxicity from chemotherapeutic agents involves disturbed gastrointestinal physiology and bone marrow depression.

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Fluoridation of water

When we had a chance to take a vaccine to prevent poliomyelitis, many of us jumped at the opportunity. We take advantage of the preventive measures which are available today, such as diphtheria, lockjaw, whooping cough, and smallpox vaccines, and the prevention of typhoid fever by chlorinating the water supply.

The one great field of preventive medicine which is being neglected by the vast majority of the people of this country is the prevention of dental cavities by the fluoridation of water supplies. This method is well documented and has been studied over a period of many years. It has been endorsed by the American Dental Association, the American Medical Association, the United States Public Health Service, and in fact by all who are equipped to know and to study the value of such a measure. Those who oppose fluoridation act from ignorance of the facts or from sheer unwillingness to accept the facts. They are causing untold millions to suffer the pain, the disfigurement, and the inconvenience of tooth decay.

As a practicing physician I am appalled by the mouths I see every day. Only occasionally is there one which does not have cavities, and the great number of people with dental plates, even in their early twenties, certainly indicates that something should be done. Few of our children under six are free of cavities; many of these have to suffer the pain of toothache and tooth extraction before they have hardly had a chance to use them.

It is also interesting to note that among people who have lived in areas of high fluorine content in the water, broken bones heal much faster. To date no known contraindications to fluoridation of water in adequate amounts have been found. The cost is very moderate.—*Edmond K. Yantes, M.D., for Council on Rural Health, American Medical Association*

Results of a Twenty-Five-Year Study of 1,553 Infertile Couples

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A STUDY WAS MADE *of 1,553 cases of infertility, of which 1,010 were primary sterility and 543 secondary sterility. Approximately 80 per cent were treated and followed adequately. The corrected over-all success rate was 60.4 per cent. The 16 to 20 per cent pregnancy loss in this study is comparable with that in a normal population in the United States. The over-all percentage of sterility due to the male factor was 27, to the female factor 45, to both factors 16, and with unknown cause 12. Including cases of artificial insemination with donor semen, 60 per cent of male sterility cases resulted in successful conception; however, excluding artificial insemination cases, only 30 per cent were successful. The success rate in cases in which the female factor was responsible was 50 per cent. Increasing age, particularly in the female, is associated with a decrease in the success rate. The highest success rates are associated with the shortest durations of treatment, although from 14 to 50 per cent of cases treated for from three to fifteen years may terminate in pregnancy.*

THE TREATMENT OF FERTILITY constitutes a large and important percentage of modern gynecologic and urologic practice and is also characterized by a constantly increasing percentage of success. This is due to a better understanding of physiology, advances in diagnosis, and newer methods of therapy. There are increasing numbers of statistical reviews in the literature giving the incidence and findings in cases of male and female sterility and of treatment being used with concomitant results.[1-5] Notwithstanding the emphasis on problems of increasing world population, a sizable percentage of marriages are infertile.[6]

This study was made to determine the most successful methods in the diagnosis of sterility, the incidence and factors responsible for primary and secondary sterility, the effectiveness of the medical treatment which is available, the length of time this treatment should continue before it is called a failure, and the most effective types of treatment being used.

Materials and methods

The results of a twenty-five-year study of sterility treatment of 1,553 couples are presented. Case records of these patients were selected in a random fashion from a total of 3,154 private patients requesting treatment for infertility from 1935 through 1960, in New York City. Follow-up was obtained, wherever possible, by direct contact. Information supplied by relatives or friends also was accepted. Many "failures" were converted into "successes" by later positive reports after the termination of active medical treatment. The case records were reviewed, and data were analyzed from social, medical, and surgical histories; clinical findings; laboratory and hormonal tests; semen assays; tubal patency tests; pathologic reports; special diagnostic procedures; and therapeutic measures. Marital and

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TABLE I. Results of 1,553 treated cases of sterility

Outcome	Primary Sterility Number	Primary Sterility Per Cent	Secondary Sterility Number	Secondary Sterility Per Cent	Total Number	Total Per Cent
Failures	334	32	142	26	476	30
Incomplete cases	233	23	117	22	350	23
Successes	443	44	284	52	727	47
TOTALS	1,010		543		1,553	
Successes excluding incomplete cases	443	57	284	66	727	60.4

TABLE II. Outcome of 727 successful conceptions

Type of Sterility	Live Babies Number	Live Babies Per Cent	Spontaneous Abortions Number	Spontaneous Abortions Per Cent
Primary	373	84	70	16
Secondary	228	80	56	20
TOTALS	601	83	126	17

sex habits, previous fertility, and present results also were tabulated. The types of sterility were divided into primary (those women who had never previously conceived) and secondary. The data of each of these groups were tabulated under subheadings, and the over-all figures of the total sterility cases also were presented. Cases are referred to as successes, failures, or incompletes, the latter being couples incompletely treated or lost to follow-up. The incidence of adequate and inadequate semen, impaired male potency, and pathologic conditions found in the male is presented. Because of the incidence of the permanently sterile husband, data referring to 369 cases of artificial insemination using donor semen are given, as well as 43 cases of artificial insemination treated with the husband's semen.

Data on menstrual irregularity; ovulation; hymenal, vaginal, tubal, ovarian, and uterine pathologic conditions; and treatment of female infertility are presented. Endocrine problems in both sexes, the value of x-ray stimulation of the pituitary gland and ovaries, adoption, and psychotherapy also are mentioned.

Data are tabulated to indicate the percentage of success for each of the pertinent facts, as well as corrected success rates which indicate data for the 1,203 complete cases, eliminating statistics referring to the 350 incompletely treated or followed couples.

Results

Of the 1,553 cases presented, 1,203 represent completely treated and followed cases, and 350 represent incompletely treated and/or followed. Of the 1,553 cases, 1,010 were primary sterility and 543 secondary sterility, 65 and 35 per cent respectively. There were 334 primary failures (32 per cent), 233 primary incomplete cases (23 per cent), and 443 primary successes (44 per cent). The corrected primary sterility success rate was 57 per cent. The 543 secondary sterility cases were divided into 142 failures (26 per cent), 117 incomplete cases (22 per cent), and 284 secondary successes (52 per cent). The corrected secondary sterility success rate was 66 per cent. The over-all success rate was 47 per cent with a corrected success rate of 60.4 per cent (Table I).

Of the 727 successes, 84 per cent of primary sterility conceptions resulted in live babies, as did 80 per cent of secondary sterility conceptions and 83 per cent of the total number of conceptions (Table II).

The 1,010 primary sterility cases were classified to show factors responsible for infertility, and it was noted that 28 per cent were due to the male factor, 43 per cent to the female factor, 15 per cent to both factors, and 14 per cent with an unknown cause (Table III). The secondary sterility statistics were similar with percentages of 24, 48, 17, and 11 respectively. The over-all percentage due to the male factor was 27, to the female factor 45, to both factors

TABLE III. Number and percentage of cases for each factor in infertility

Factor	Type of Sterility: Primary Number	Primary Per Cent	Secondary Number	Secondary Per Cent	Total Number	Per Cent
Male	282	28	130	24	412	27
Female	437	43	261	48	698	45
Both	150	15	95	17	245	16
Unknown	141	14	57	11	198	12

TABLE IV. Failures, incomplete cases, and successes for each factor in infertility

Type of Sterility	Factor: Male	Female	Both	Unknown
Primary				
Failure	87	156	64	27
Incomplete	33	66	23	111
Success	162	215	63	3
Uncorrected success rate (per cent)	57	49	42	2
Secondary				
Failure	19	83	28	12
Incomplete	13	45	17	42
Success	98	133	50	3
Uncorrected success rate (per cent)	75	51	53	5
Totals				
Failure	106	239	92	39
Incomplete	46	111	40	153
Success	260	348	113	6
Uncorrected success rate (per cent)	61	50	46	3

16, and with unknown cause 12. Table IV indicates that 57 per cent of the primary and 75 per cent of the secondary sterility cases due to the male factor represented successes, with an over-all corrected success rate of 61 per cent. However, these data include the results of 369 artificial insemination cases treated with donor semen. Successes in cases with the female factor responsible were 49 per cent for primary sterility and 51 per cent for secondary sterility, with a 50 per cent success rate for the over-all cases. The figures relating to cases with both factors at fault indicate a 42 per cent success rate in primary cases, 53 per cent in secondary cases, and 46 per cent for over-all cases. The over-all success rate in cases in which no responsible factor was assigned was 3 per cent.

This becomes clearer when one notes that in Table V, of the total successes 35.8 per cent occurred in cases with the male factor at fault, 47.8 per cent with the female factor at fault, 15.6 per cent with both factors responsible, and 0.8 per cent with the responsibility for infertility unknown.

TABLE V. Over-all success rate for each factor

Factor	Per Cent of Success	Per Cent of Total Successes
Male	21.6	35.8
Female	28.9	47.8
Both	9.4	15.6
Unknown	0.1	0.8
TOTALS	60.0	100.0

The average age of females was 29.5 years for primary sterility cases, 32.1 years for secondary, and 30.4 years for the over-all study. The average ages for male patients in the same groups were 33.1, 35.6, and 34 years respectively.

Table VI shows the ages of patients as related to the success rate for each age and indicates a declining success rate with advancing age in the female, beginning at approximately thirty-five years, and for the male

TABLE VI. Ages of female and male patients with success rates for each age group

Age (Years)	Number of Female Patients				Number of Male Patients			
	Primary	Secondary	Total	Success (Per Cent)	Primary	Secondary	Total	Success (Per Cent)
18 to 20	18	0	18	61	2	0	2	100
21 to 25	240	52	292	49	88	20	108	44
26 to 30	377	181	558	55	315	88	403	53
31 to 35	224	170	394	46	328	183	511	55
36 to 40	103	98	201	31	159	146	305	42
41 to 45	43	34	77	27	81	66	147	25
46 to 50	5	8	13	0	28	29	57	23
51 to 55	0	0	0	0	6	5	11	9
56 and over	0	0	0	0	3	6	9	22

TABLE VII. Number of years patients were married at the time of the first visit

Length of Time Married (Years)	Number of Patients	Per Cent
Less than 1	72	4.6
1 and 2	314	20.0
3 to 5	508	33.0
6 to 10	490	31.0
11 to 15	131	8.3
15 to 21	38	2.4
Over 21	10	0.7

TABLE VIII. Number of years that patients knew of their own infertility at the time of first visit

Length of Time Infertility Known (Years)	Number of Patients	Per Cent
Less than 1	431	27.6
1 and 2	549	35.8
3 to 5	336	21.5
6 to 10	179	11.4
Over 10	58	3.7

beginning at approximately forty years. The percentage of success in males declines at age forty to only approximately one half of what it was previously, while in females the percentage of success drops to zero, in this study, at age forty-six.

The average duration of marriage of the 1,010 primary sterility couples before they attempted to conceive was 2.14 years. For the secondary sterility pairs it was 4.62 years. The over-all average was three years.

Table VII indicates that at the time of the patients' first visit 4.6 per cent had been married less than one year, 20 per cent for one to two years, 33 per cent for three to five years, 31 per cent for six to ten years, 8.3 per cent for eleven to fifteen years, 2.4 per cent for fifteen to twenty-one years, and 0.7 per cent for more than twenty-one years.

It is also noted in Table VIII that at the time of the first visit 27.6 per cent of the patients had known of their own infertility for less than one year, 35.8 per cent for one to two years, 21.5 per cent for three to five years, 11.4 per cent for six to ten years, and 3.7 per cent for more than ten years.

TABLE IX. Results of semen analyses in patients

Count	Types of Sterility			Per Cent of Total
	Primary	Secondary	Total	
Adequate	437	261	698	45.0
Oligospermia	211	89	300	19.3
Azoospermia	221	136	357	23.0
Unknown count	141	57	198	12.7

Study of male infertility

Sperm counts in the male member of each couple were performed in 1,355 cases. Forty-five per cent of these counts were regarded as adequate, 19.3 per cent as oligospermic, and 23 per cent as azoospermic. The remaining 12.7 per cent represented those males in whom no count was done (Table IX). Table X gives an analysis of the pathologic conditions in males and the success rates for certain types. Where this rate is given, it refers to those males who themselves successfully impregnated their

TABLE X. Analysis of male factors in infertility

Pathologic Condition	Males Number	Males Per Cent	Males Successes	Artificial Insemination Donor Cases
Undescended testicle(s)	213	14	11	118
Mumps—male factor responsible	67	4	18	40
Previous inguinal surgery	104	7	10	30
Previous x-ray irradiation	27	2	3	13
Premature ejaculation or decrease in potency	95	6	8	43
Severe psychiatric disturbance	29	2	. . .	. . .
Important systemic disease	65	4	. . .	. . .
Female type of body habitus	66	4	. . .	. . .
Decreased basal metabolism rate	140	9	. . .	. . .
Venereal disease	50	3	. . .	. . .
Had testicular biopsy done	74	5	. . .	. . .

TABLE XI. Diagnostic procedures done in females

Procedure	Number of Cases
Basal metabolic rate	1,321
Rubin test	564
Salpingogram	386
Repeated tubal patency tests	192
Dilatation and curettage	217
Endometrial biopsy	153
Basal temperature chart	998
Hormonal assays	51
Culdoscopy	5
Psychiatric evaluation	14
Exploratory laparatomies	2

TABLE XII. Incidence of menstrual and ovulatory irregularities in patients studied

Type	Regular Menses	Irregular Menses	Total
Anovulatory	93	211	304
Ovulatory	1,132	117	1,249
TOTALS	1,225	328	1,553
With dysmenorrhea	257	76	333
Without menstrual pain	968	252	1,320
TOTALS	1,225	328	1,553

wives. Undescended testicles were found in 14 per cent, a previous history of mumps in 4 per cent of males at fault, a history of previous inguinal surgery in 7 per cent, a previous history of x-ray irradiation to the groin in 2 per cent, the presence of premature ejaculation or decrease in potency in 6 per cent, severe psychiatric disturbances in 2 per cent, important systemic disease in 4 per cent, a female type of bodily habitus in 4 per cent, a decreased basal metabolic rate in 9 per cent, and a history of venereal diseases in 3 per cent. A testicular biopsy was done in 5 per cent of these men.

Of the 140 oligospermic men with a decreased basal metabolic rate, 88 were treated successfully with thyroid hormone, representing approximately a 63 per cent success rate. Of the 29 males with severe psychiatric disturbances, 4 benefited from psychoanalysis. Of the 95 patients with premature ejaculation or a decrease in potency, 8 patients after counseling later successfully impregnated their wives, representing a 9 per cent success rate.

Study of female infertility

Diagnostic procedures done in female patients are listed in Table XI.

Of the 1,553 females, 1,225 had regular menses, and 7 per cent of these were noted to have anovulatory cycles. Three hundred twenty-eight patients had irregular menses, and 68 per cent of these had anovulatory cycles. Severe dysmenorrhea requiring bed rest or opiates was found in 21 per cent of the regularly menstruating women and 23 per cent of those with irregular menstrual cycles. Stated in another fashion, the 304 patients with anovulatory cycles were divided into 70 per cent with irregular menses and 30 per cent with regular menses. Of the 333 patients with dysmenorrhea, 77 per cent had regular menses (Table XII).

Table XIII indicates the effect of previ-

TABLE XIII. Effect of previous pregnancy loss on success rate

Previous Abortions	Total (Number)	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
1 spontaneous	147	72	49	66
2 spontaneous	44	25	57	70
3 spontaneous	74	43	58	68
1 or more induced	55	18	33	51

TABLE XIV. Incidence of pathologic condition in females and success rates for each

Pathologic Condition	Total Number of Cases	Success After Treatment (Number)	Success After Treatment (Per Cent)	Corrected Success Rate After Treatment (Per Cent)
Vagina				
Intact hymen	87	41	47	63
Infection	500	256	51	64
Cervix				
Stenosis	504	297	61	71
Infection	447	241	53	65
Polyps	152	71	47	55
Erosion	425	226	53	73
Uterus				
Retroversion	472	243	52	62
Fibroid tumors	444	199	45	57
Endometriosis	86	39	45	53
Previous myomectomy	14	3	22	27
Fallopian tubes				
Infection	119	52	44	52
Obstruction	191	92	48	57
1 absent tube	22	8	36	57
Ovaries				
Cyst(s)	196	90	46	56
1 absent ovary	24	10	42	62
Moderate to marked obesity	237	140	59	63
Male type of body habitus	150	78	52	60
Menopausal	27	0	0	0

ous pregnancy loss(es) on the success rate, and with the exception of patients having had an induced abortion, the corrected success rate of patients with a previous pregnancy loss ranged from 66 to 70 per cent. The success after a previous induced abortion was 51 per cent corrected.

The types of female pathologic conditions and the related success rates are found in Table XIV. Noteworthy are the markedly higher corrected success rates in patients with cervical stenosis (71 per cent), cervical erosion (73 per cent), and the marked lessening in rate in patients having had previous myomectomy (27 per cent), infection of the fallopian tubes (52 per cent), and endometriosis (53 per cent).

Eighty-seven cases (8.6 per cent) of primary sterility were due to nonconsummation of marriage. The success rates and

TABLE XV. Duration of nonconsummation of marriage in 87 patients found to have an intact hymen

Duration (Years)	Total Number of Patients	Success After Hymenectomy* (Number)	Success After Hymenectomy* (Per Cent)
Less than 1	11	6	12.7
1	7	2	8.0
2	12	5	13.8
3	7	5	8.0
4	10	5	11.5
5	8	2	9.2
6	7	3	8.0
7	4	2	4.6
8	6	5	7.0
9	4	2	4.6
10	4	1	4.6
More than 10	7	3	8.0
TOTALS	87	37	100.0

* Corrected success rate after hymenectomy—55.2 per cent.

TABLE XVI. Treatment of pathologic conditions in females with success rates after each

Type of Treatment	Total Cases (Number)	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
Hymenectomy	87	37	43	55
Local and general treatment for vaginal infection	476	200	42	53
Cervical stenosis				
Undilated	72	26	36	49
Dilated	432	211	49	58
Cervical cauterization	338	187	55	61
Cervical polypectomy	117	60	51	64
Hysterectomy	18	0	0	0
Endometriosis				
Surgical treatment	9	2	22	33
Hormonal treatment	12	4	33	44
Retroversion pessary	84	38	45	51
Repeated tubal patency tests	277	196	79	79
Ovarian surgery	26	8	31	36
X-ray stimulation of the pituitary gland and ovaries	34	19	56	63
Instruction	362	135	38	58

TABLE XVII. Estrogen, progesterone, and gonadotropin treatment

Hormone Given	Total Number of Cases	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
Estrogens	335	148	44	55
Progesterones	275	114	41	47
Gonadotropins	29	12	41	44

the duration of nonconsummation are given in Table XV. The over-all success rate after hymenectomy was 47.2 per cent with a corrected success rate of 55.2 per cent.

Table XVI indicates the types of treatment used in these infertile women and the success rates after each. Noteworthy are the relatively low rates in undilated cervical stenosis (49 per cent), surgical treatment of endometriosis (33 per cent), hormonal treatment of endometrosis (44 per cent), and ovarian surgery (36 per cent). Also to be noted are the high corrected success rates of 79 per cent after repeated tubal patency tests, and 63 per cent after x-ray stimulation of the pituitary gland and ovaries in anovulatory women.

Table XVII indicates the relatively low corrected success rate in patients treated with estrogens, progesterone, and gonadotropins. However, in Table XVIII it is noted that of 444 successes in women with a decreased basal metabolism rate approximately 95 per cent occurred in those receiving thyroid hormone. Of the 283 successes in women with a normal or slightly increased basal metabolism rate, 80 per cent occurred in those not receiving thyroid medication. Of the total successes 66 per cent occurred in women taking thyroid hormone, and 61 per cent occurred in women with a decreased basal metabolism rate. Of the over-all 1,321 cases tested with a basal metabolic rate, 68 per cent had a decreased rate, and 32 per cent had a normal or slightly elevated rate.

Table XIX shows that of the 350 successes occurring within two months of the first visit, 39 per cent occurred after the only treatment given was instruction, 11 per cent after dilatation and curettage, 11 per cent after dilation of the cervix only, 12 per cent after one tubal patency test, 11 per cent after thyroid medication, and 16 per cent after two or three of these treatments. In Table XX one notes that the corrected suc-

TABLE XVIII. Effect of thyroid hormone given to female patients

Basal Metabolism Rate	Treatment	Total Number of Cases	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
Decreased	None	87	24	28	40
Decreased	Thyroid hormone	798	420	53	62
Normal or increased slightly	None	293	224	76	89
Normal or increased slightly	Thyroid hormone	133	59	44	54

TABLE XIX. Treatment given patients conceiving within two months of first visit

Type of Treatment	Number of Patients	Per Cent Total Successes	Per Cent of 350 Successes Within Two Months
Instruction only	135	18.6	39
Dilatation and curettage	37	5.1	11
Dilation of the cervix	39	5.4	11
Tubal patency test	43	5.9	12
Thyroid medication	38	5.2	11
Tubal patency test and thyroid medication	31	4.3	9
Tubal patency test, thyroid medication, and repeated dilation of the cervix	27	3.7	7

cess rate is related to various durations of treatment. Although the highest success rates are associated with the shortest durations of treatment, from 14 to 50 per cent of the cases treated for from three to fifteen years may terminate in pregnancy. In Table XXI it is seen that 48 per cent of the successes occurred within one to two months of treatment, 25 per cent after three to six months, 23 per cent after from six months to two years, and only 4 per cent after three to fifteen years of treatment.

Artificial insemination

Forty-three patients were inseminated with their husband's semen, and 369 patients were impregnated with donor semen. Of the former there was a 32 per cent corrected success rate and for the latter an 81 per cent corrected success rate (Table XXII).

The use of donor semen in 369 cases includes 138 patients who attempted such conception for one pregnancy, 156 cases for two pregnancies, 30 cases for three pregnancies, and 45 cases for four or more pregnancies. Previous artificial insemination treatment with donor semen was reported by 26 patients and had been a failure in every case. Of these 26 patients, 80 per cent had a successful conception in this series. Noteworthy also is that of the total 476 failures in all types of cases in this series, 82 patients refused treatment by artificial insemination. Of the total number of cases, donor artificial insemination accounted for 40 per cent of the cases and donor artificial insemination successes for 42 per cent of the total successes. Although approximately one fifth of the total cases in this series were designated as incomplete, only 3.1 per cent of the artificial insemination cases were so called.

Previous treatment for infertility

One hundred fifty-four patients reported at least six months of previous infertility treatment, and 93 of these had successful conceptions in this series, representing a corrected success rate of 71.6 per cent. Seventy-six patients in this group reported later spontaneous success after successful infertility treatment. Of all the patients

TABLE XX. Duration of treatment and related success rates

Duration of Treatment	Total Number of Patients	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
1 month or less	608	248	41	77
2 months	191	102	53	63
3 months	119	64	54	60
4 to 6 months	217	117	50	57
7 to 9 months	106	54	51	52
10 and 11 months	33	17	52	52
1 year	131	61	47	49
2 years	65	37	54	54
3 years	30	10	33	35
4 years	9	4	44	50
5 years	13	4	31	31
6 years	7	1	14	14
7 to 10 years	19	6	31	31
11 to 15 years	5	2	40	40

ABLE XXI. Percentage of 727 successes occurring after different durations of treatment

Duration of Treatment	Successes (Number)	Successes (Per Cent)
to 2 months	350	48.0
3 to 6 months	181	25.0
6 months to 2 years	169	23.0
3 to 5 years	18	2.5
6 to 10 years	7	1.0
11 to 15 years	2	0.5

represented by this study, 1,118 never returned to attempt treatment for a second pregnancy, 251 returned requesting treatment for a second pregnancy, and the remainder requested treatment for third and fourth pregnancies.

Adoption

Fourteen patients adopted children after a successful conception, 34 patients after a primary sterility failure, and 22 patients after a secondary sterility failure, representing 70 infertile couples in this study who adopted children.

Psychotherapy

Six patients who were diagnosed previously as "incurably sterile" and who were in the primary sterility group conceived successfully after from one to four years of intensive psychotherapy. Two patients in the secondary sterility group conceived after two and three years of psychotherapy, respectively.

Comment

Of the 1,553 infertile cases presented, approximately two-thirds represent primary sterility problems, and one-third represent secondary sterility. As has been seen in other studies, approximately 80 per cent of the cases were treated and followed adequately.[3] The corrected total over-all success rate was 60.4 per cent. The differences in the success rates between the primary and secondary sterility cases are not statistically significant here.

The 16 to 20 per cent pregnancy loss in this study is comparable with that found in a normal population in the United States.[3] Both primary and secondary sterility cases

TABLE XXII. Success rates after artificial insemination

Type of Semen Used	Total Number of Cases	Successes (Number)	Successes (Per Cent)	Corrected Success Rate (Per Cent)
Husband's	43	10	23	32
Donor's	369	291	79	81

showed approximately the same causative factors as those represented by the over-all statistics, with the female factor responsible for approximately one half of the cases, the male factor for slightly more than one quarter, and both factors for approximately one sixth of the cases. If the unknown cases are exempted, of the remaining 1,355 cases, one-third were due to the male factor, approximately one-half to the female factor, with the remainder due to both male and female causes. Including cases of artificial insemination with donor semen, 60 per cent of male sterility cases resulted in successful conception. However, with the artificial insemination cases excluded, only 30 per cent were successful. Fifty per cent of the females at fault were eventually successful in achieving pregnancy. With both partners responsible, the success rate is lower. In this study, therefore, female sterility was treated more easily, unless artificial insemination treatment with donor semen was accepted by the couple with the male partner having permanent sterility.

It is apparent that although increasing age is associated with a decrease in the success rate, the decrease is more marked in the female and begins at least five years earlier. The decline in the success rate in males never is as great as that in females with advancing age.

Patients waited anywhere from less than one year to twenty-one years before visiting the office for the first time, the greatest number having been married for from three to five years. Many of the couples waited ten or more years after knowing of their infertility before seeking medical treatment. The duration of treatment is related to the success rates, and although 75 per cent of the successes occurred within six months after the onset of therapy, the success rate was improved by prolonged treatment, even for as long as fifteen years.

Almost one half of the males in this study had adequate sperm counts. Of the oligospermic males who had a low basal metabolic rate, more than 60 per cent were successful after being treated with thyroid hormone. Psychoanalytic therapy and the treatment of decreased potency by counseling also increased the male success rate.

Anovulatory cycles in the females were found to occur with both regular and irregular menstrual cycles, as did severe dysmenorrhea. Previous pregnancy loss did not affect the success rate in the female except for the slight decrease in successes after induced abortions. This is noted elsewhere in the literature.[7]

Cervical stenosis adequately dilated and cervical erosion adequately cauterized are seen to be associated with markedly elevated rates of success. Of the females studied, most had multiple pathologic conditions, which may or may not have interfered with fertility.[1] It appears that only previous myomectomies, endometriosis, and ovarian surgery worsened the rate of success. More than 8 per cent of the primary sterility cases were due to nonconsummation, and almost one half of these had success in conceiving after hymenectomy. Repeated tubal patency tests,[8] serving to open stubbornly closed tubes, may greatly increase the incidence of conception, as to a lesser degree may x-ray stimuation of the pituitary and ovaries in anovulatory females.[9]

Treatment with sex hormones appears to have had little effect in elevating the rate of success. However, treatment with thyroid hormone, markedly in patients with a decreased basal metabolic rate and slightly in patients with a normal or slightly elevated basal metabolic rate, does improve the chances of conception, although this finding has not been reported by others.[1,10]

It is possible that faulty sexual habits may be responsible for infertility, as is seen in many cases by the high success rate within two months of the onset of treatment after instruction was the only therapy given.

For the incurably sterile husband with a fertile wife, donor artificial insemination offers an excellent possibility for pregnancy if this is acceptable to the couple. Unfortunately, one sixth of the total failures in this series refused donor artificial insemination. Of the 369 cases of artificial insemination with donor semen, the success rate was 81 per cent. Using the husband's semen, the rate was markedly low in comparison with this, and indeed with the rate of the total study, being only 32 per cent. Many artificial insemination patients returned two, three, and four times for successful conceptions, and although one fifth of the total number of patients in the study were treated or followed incompletely, very few artificial insemination couples (3 per cent) failed to continue their treatment once they had decided to accept this mode of therapy.

Although one may have had previous unsuccessful treatment for infertility, as did 10 per cent of the patients in this study, whether it be treatment by artificial insemination or by another method, further treatment may result in conception. This suggests that if no apparent cause for failure is found after some years of therapy, it may be advisable to start a fresh investigation into the cause of the infertility.

Some patients, after being infertile and being successfully treated, return home and succeed in conceiving a spontaneous pregnancy immediately or many years later.

Medical investigation for infertility should be undertaken by a couple who have not achieved a pregnancy after six to twelve months of normal coitus, and as soon as possible in the older-age couple.

More than 60 per cent of the infertility in this study was "curable." One or two years of failure in treatment does not mean that success cannot eventually ensue, even though to achieve such success may require a long period of treatment. It is often necessary to repeat diagnostic and therapeutic procedures, such as tubal patency tests and sperm counts. Immediately on consulting the specialist in sterility all patients should be asked to keep a basal temperature chart and have a basal metabolism rate determination. For those who wish to adopt children, it should be stressed that the diagnosis and treatment of infertility should begin early, since young prospective parents are more acceptable to the adoption agency. Psychiatric help also offers advantages in the treatment of sterility.

The successful treatment of infertility may result only after many years of repeated failure and disillusionment.

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Suicide and suicidal attempts in children and adolescents

Suicide and suicidal attempts are not rare in childhood and adolescence, according to an article by James M. Toolan, M.D., in the February, 1962, issue of the *American Journal of Psychiatry*. An analysis of the vital statistics for 1958 shows that 444 children from five to nineteen years old were known to have committed suicide, but the figure is probably larger as many suicides and suicidal attempts undoubtedly go unreported. Only 3 of the 444 were in the five to nine age group; 74 were ten to fourteen; and 367 were fifteen to nineteen.

A review of statistics from Bellevue Hospital, New York City, for 1960 shows that of about 900 admissions to children and adolescent psychiatric service 102 were for suicidal attempts and suicidal threats. On the premise that many serious suicidal attempts in children may be prevented if the signs of depression can be recognized, the records of these patients were analyzed. The majority were adolescent females with character disorders reacting to stressful situations. A common background was chaotic conditions in the home, with one or both parents absent.

Some Hidden Diseases of the Larynx

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RECENTLY WE HAVE SEEN a number of laryngeal lesions, the diagnoses of which were not immediately apparent by the symptoms or by the examinations. Some diseases of the larynx remain obscure for a period of time, either through neglect at taking a proper history and doing a complete examination, or because of the failure to keep certain possibilities in mind. It occurred to us that we might discuss some of these cases and try to understand the reason for the difficulties and thus perhaps be forewarned of future embarrassment and predicaments.

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Otolaryngology, May 12, 1961.

There are abnormalities within the larynx that are unrevealed for a long while because (1) the difficulty may arise in a so-called silent area, the symptoms occurring late in the disease; (2) the patient's discomfort may be such as to call attention to other organs; (3) there are instances where the diagnosis is not immediately apparent even on direct examination; (4) a lesion within the larynx may be hidden from view at the time of indirect examination; and (5) there are congenital and functional diseases of the larynx that are not readily recognized.

Tumors of vocal cord

When a patient is seen with a history of hoarseness for several weeks and we find a malignant tumor on the cord, we recognize the fact that the lesion originated on the vocal cord. If the person has had hoarseness for many months and we see a tumor not only on the cord but creeping onto the ventricle or onto the arytenoid area, we still feel that the tumor had its origin on the vocal cord. However, we are all familiar with cases of large tumors in the larynx that we know must have de-

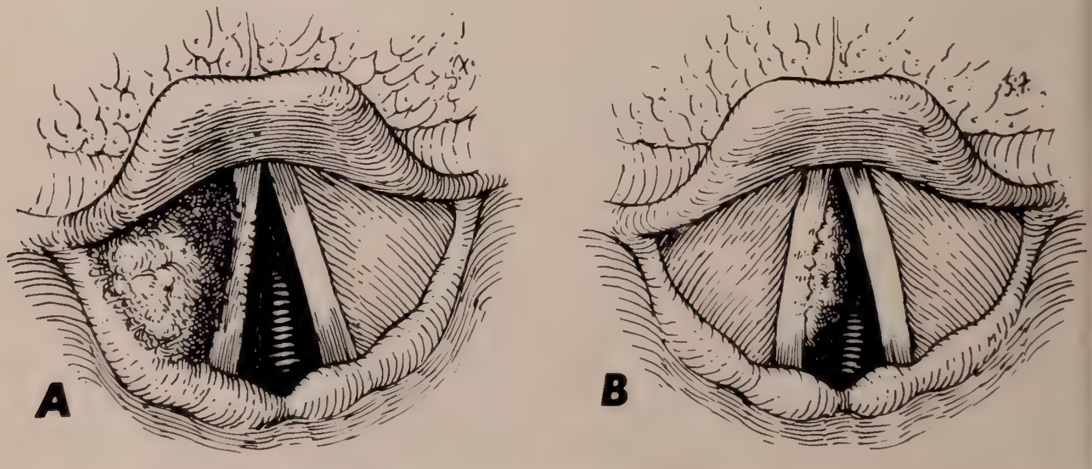

FIGURE 1. Tumor in (A) ventricle and (B) subglottic area.

veloped over many months, but the complaints are present only for a short time. A patient may complain of hoarseness for two or three weeks and a large tumor is seen in the ventricle beginning to invade the vocal cord or perhaps the arytenoid area, preventing the proper function of the cord (Fig. 1A); or there may be a subglottic tumor that eventually reaches the vocal cord, and the first symptom may be hoarseness (Fig. 1B). On the other hand, such a tumor may reach a size that partially obstructs the airway, and the patient will complain of noisy respiration or obstructive breathing.

Tumor of pyriform sinus

A patient may complain of a lump in the throat, or perhaps some pain and discomfort on swallowing, and we see a large tumor in the pyriform sinus, reaching onto the epiglottis and the aryepiglottic fold (Fig. 2A). We know that this tumor has been present for a long while, and yet the symptoms appeared late. Also, a growth on the epiglottis may not produce symptoms until it has reached large proportions, or has extended into the larynx to cause hoarseness (Fig. 2B), or into the pyriform sinus and aryepiglottic fold to cause dysphagia (Fig. 2C). All these are cases that are "hidden" for a time because they do not give symptoms until late in the course of the disease.

There are instances also where there are no laryngeal symptoms, and the patient complains of a mass in the neck (Fig. 3). There is no hoarseness, no difficulty in swallowing, but a small malignant growth is found in the pyriform sinus, or in the ventricle and aryepiglottic fold, or perhaps in the vallecula.

There are patients who complain of hoarseness as a first symptom, and a paralysis of the vocal cord is found. On further examination a small mass around the thyroid gland is palpated. If the mass is quite definite and hard, we are fairly certain that a carcinoma of the thyroid has affected the recurrent laryngeal nerve or has involved the larynx itself.

A sixty-three-year-old female complained of hoarseness and some respiratory difficulty. On examination there was a swelling of the right ventricular area with paralysis of the right vocal cord. No ulceration could be seen. Further investigation revealed a firm enlargement of the right lobe of the thyroid gland. On subsequent operation a papillary adenocarcinoma of the thyroid gland which involved the thyroid cartilage was removed by performing a radical neck dissection, a hemithyroidectomy, and a total laryngectomy. The patient has done well for three years.

THE DIAGNOSES *of certain abnormalities within the larynx may be obscured or delayed because (1) the difficulty may arise in a silent area, (2) the presenting symptoms may call attention to another organ, (3) the diagnosis cannot be attained immediately even on direct examination, and (4) some congenital and functional diseases of the larynx may not be recognized readily. Such hidden diseases include tumors of the vocal cord and pyriform sinus and carcinoma of the larynx. Congenital and functional diseases include paralysis of the vocal cord and cricoarytenoid arthritis.*

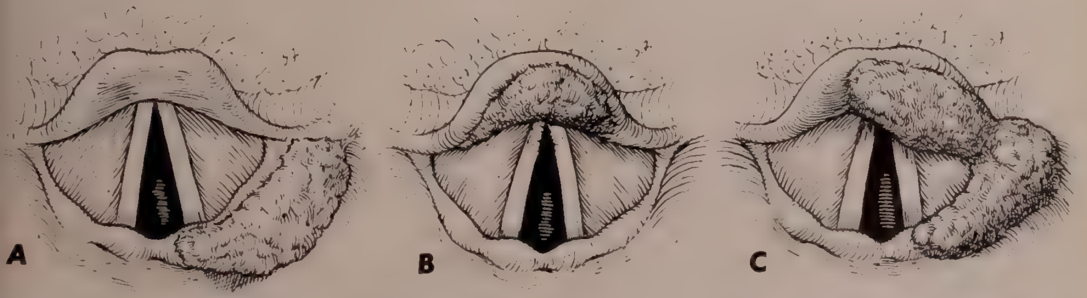

FIGURE 2. Tumor seen (A) on epiglottis and aryepiglottic fold, (B) extending into larynx, (C) extending into pyriform sinus and aryepiglottic fold.

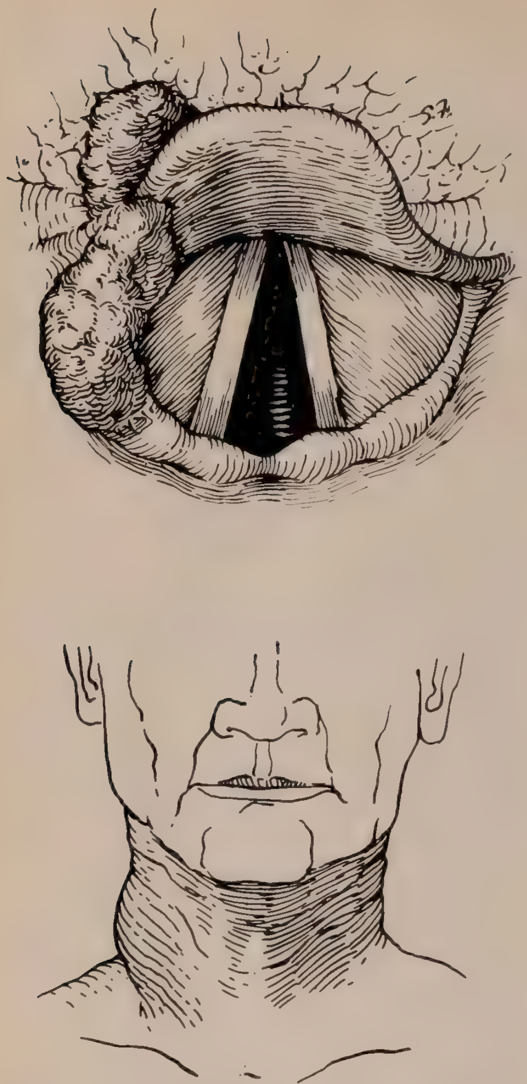

FIGURE 3. Mass in neck. Upper sketch shows artist's conception of internal mass. Lower portion shows external view.

There are times, however, when the tumor of the thyroid gland is barely palpable, and the invasion has been on its posterior surface.

A forty-three-year-old male complained of fullness of his throat, slight trouble on swallowing, and a "thickness" of speech. He had a left vocal cord paralysis. An x-ray film of his chest showed negative findings, but an examination of the esophagus showed the presence of an extrinsic mass. On palpating the thyroid gland area one could barely discern a small, hard mass, apparently emanating from the posterior aspect of the thyroid gland. At operation the tumor, an adenocarcinoma, was attached to the cricoid cartilage, the trachea, and the esophagus to such an extent that it could not be removed. This patient has had palliative treatment for four and one-half years and is still alive.

We know it is not rare for a patient to complain of pain in an ear, and in the absence of any abnormal findings in and around the ear, we examine the larynx and find a tumor in the pyriform sinus. However, many of these tumors are missed because the examiner is too rushed to think of this possibility and to examine the larynx. He is aware that a tumor of the extrinsic larynx can cause pain in the ear, but in his haste he is sometimes careless.

This is illustrated by a sixty-five-year-old male patient (Fig. 4A) who appeared with a history of pain in the ear for two months. Eustachian salpingitis was diagnosed and treated, but the symptoms of otalgia persisted. A routine examination of the larynx at the first visit produced negative findings. When the pain continued, a re-examination revealed an edema of the aryepiglottic fold, and on direct laryngoscopy a pyriform sinus carcinoma was found.

Carcinoma of larynx

On the other hand, some of us who are conscientious about a complete examination are often foiled by the patient's reluctance to follow advice.

During a routine examination for an external otitis a sixty-year-old man was found to have a right vocal cord paralysis with fixation in the midline. No lesion was visible. He failed to return, as requested, and two years later indirect inspection disclosed edema of the ventricle and aryepiglottic fold. A direct laryngoscopy and biopsy revealed an adenocystic carcinoma of the larynx emanating from the ventricle (Fig. 4B). The larynx was removed.

Dysphagia always suggests the possibility of an esophageal lesion, but one must examine the larynx carefully to rule out a growth around the epiglottis, pyriform sinus, base of the tongue, and especially postcricoid area. Not only do we find malignant tumors, but also benign tumors.

A sixty-six-year-old male gave a history of dysphagia and increasing dyspnea for one year. He was not hoarse, and two x-ray examinations of the esophagus produced negative findings. An indirect laryngoscopy revealed a subglottic mass posteriorly. On direct laryngoscopy a diagnosis

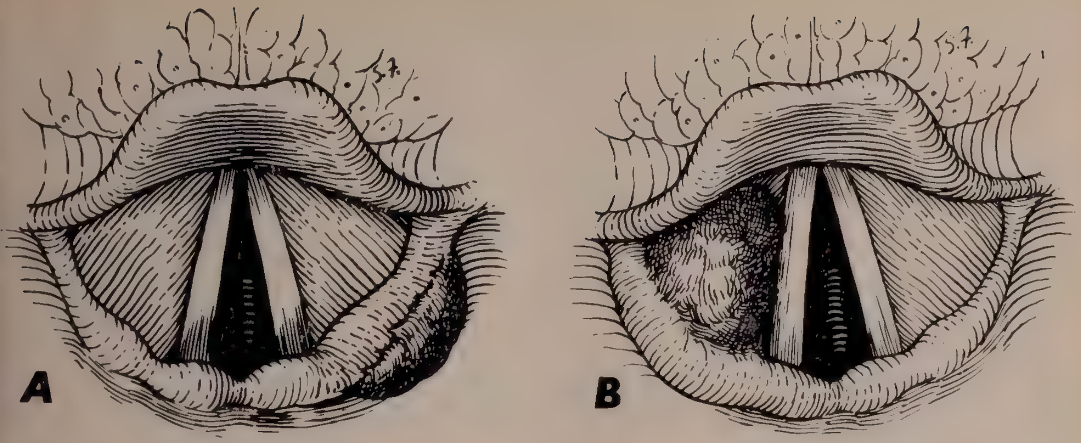

FIGURE 4. (A) Tumor of extrinsic larynx. (B) Adenocystic carcinoma of larynx emanating from ventricle.

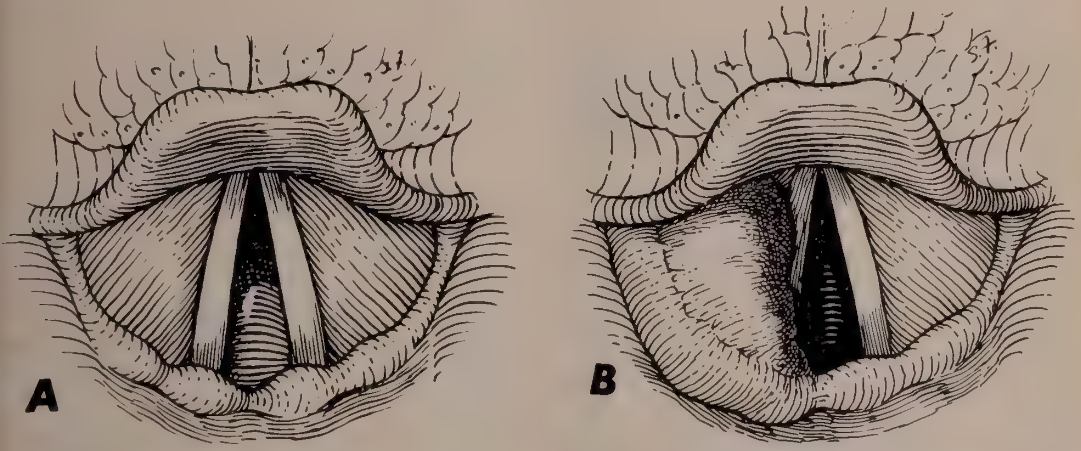

FIGURE 5. (A) Chondroma of cricoid cartilage. (B) Plexiform hemangioma with sclerosis.

of chondroma of the cricoid cartilage was made (Fig. 5A). This was removed by laryngofissure with complete relief of the dysphagia as well as of the dyspnea.

We also have seen a man who had discomfort and pain on swallowing produced by a lesion in the ventricle which turned out to be an angioma. This fifty-eight-year-old male complained of pain on the left side of his throat. A nonulcerated mass was seen in the left ventricle by indirect and direct laryngoscopy. Biopsies suggested the possibility of telangiectasia of the area. The mass was removed by the lateral transthyroid approach. On microscopic examination it was found to be a plexiform hemangioma with sclerosis (Fig. 5B).

Difficulty in diagnosis

We will now discuss a group of cases where, even on direct examination the diagnosis was not immediately apparent. Of course, in the presence of a tumor, such as a keratotic-looking lesion or a small ulceration on the vocal cord, the diagnosis depends on the proper microscopic interpretation of adequate and representative sections of the diseased tissue. There are times when areas are removed that do not reveal malignant changes which are present. This is especially true in instances of slow-growing tumors of low-grade malignancy, even in large tumors, where biopsies must be repeated to demonstrate eventually the malignant changes within the growth. A high index of suspicion combined with experience in the gross pathology of lesions will help to prevent tragic misdiagnoses.

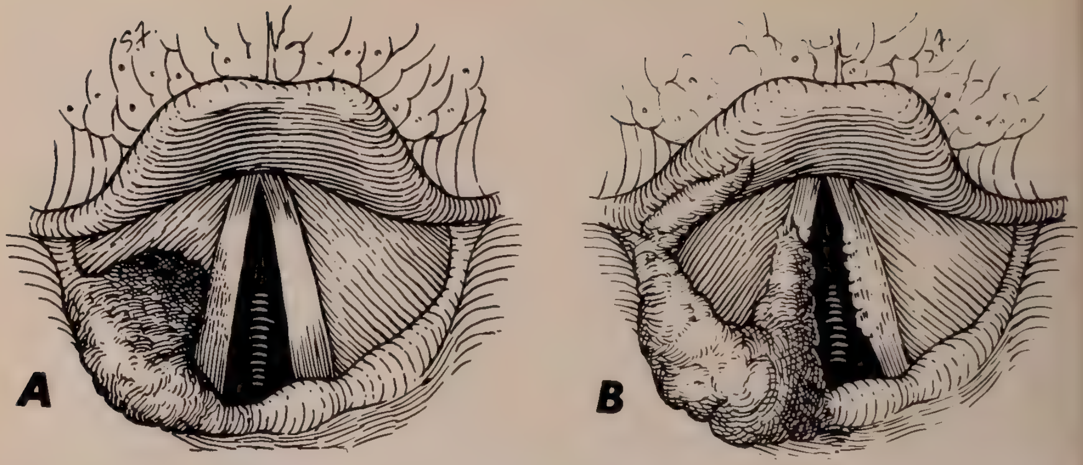

FIGURE 6. (A) Flat lesion of left ventricle. (B) Tumor involving right side of epiglottis, right aryepiglottic fold, extending down anterior portion of ventricle.

A fifty-year-old man complained of hoarseness of three months duration and had a flat lesion of the left ventricle (Fig. 6A). The surface of the ventricle was irregular and appeared inflamed rather than having the usual rough, sloughing appearance of a fungating malignant condition. The vocal cords appeared normal. A biopsy, on direct laryngoscopy, revealed chronic nonspecific inflammation of the larynx. Because this diagnosis did not appear to be consistent with the appearance of the lesion another biopsy was taken, and the tumor was then reported to be a squamous-cell carcinoma of low-grade malignancy. Another patient complained of pain on the right side of his throat and in the right ear for one year. He had a large tumor involving the right side of the epiglottis, the right aryepiglottic fold, extending down the anterior portion of the ventricle (Fig. 6B). There was also a white, thickened roughening of the left vocal cord. Multiple biopsy specimens were reported as hyperkeratosis. A second laryngoscopy and biopsy revealed carcinoma in situ developing in a hyperkeratosis. When the larynx was removed, squamous-cell carcinoma of the larynx, grade 2 to 3, and hyperkeratosis of the left vocal cord were reported.

We have seen several cases that were symptomatic of an abscess of the arytenoid area and an acute laryngeal infection with fever, pain on swallowing, hoarseness, and even laryngeal obstruction. The area of the arytenoid was markedly inflamed and swollen, and an abscess was thought to be present. Under treatment, especially with antibiotics, the condition subsided, and the larynx returned to normal. After several episodes a residual swelling of the ventricle, aryepiglottic fold, and medial wall of the pyriform sinus indicated that there was a cyst of the ventricle which became recurrently infected.

A forty-six-year-old man, in September, 1952, had an acute laryngeal infection with pain, fever, and symptoms of laryngeal obstruction. This subsided after treatment. It was thought that an abscess around the arytenoid had ruptured. In January, 1959, there was a recurrence of this left arytenoid infection which subsided under treatment. However, when the inflammation had disappeared, a cyst of the ventricle could be seen (Fig. 7A). In October, 1959, the cyst was removed by the lateral transthyroid approach.

A thirty-two-year-old man complained of hoarseness of three months duration. An examination revealed a fullness of the left ventricle as well as of the pyriform sinus, and a diagnosis of ventricular cyst was made. However, the hoarseness subsided under treatment which indicated that a secondary infection had caused the symptoms. Since this was his first attack and the cyst was very small, we thought it would be wise to wait for further trouble before recommending removal.

A thirty-year-old female recently was admitted with laryngeal obstruction. There was a subglottic mass on the left side which was partially reduced in size with local treatment and antibiotics, but the swelling persisted, and we felt we were dealing with a chondroma of the cricoid cartilage (Fig. 7B), the mucosa of which became infected. After removing this mass by laryngofissure without disturbing the mucosa of the cricoid, we discovered on microscopic examination that the growth was inflammatory and probably had been present for a long while. It is very likely that the patient had had a perichondritis in this area some time before.

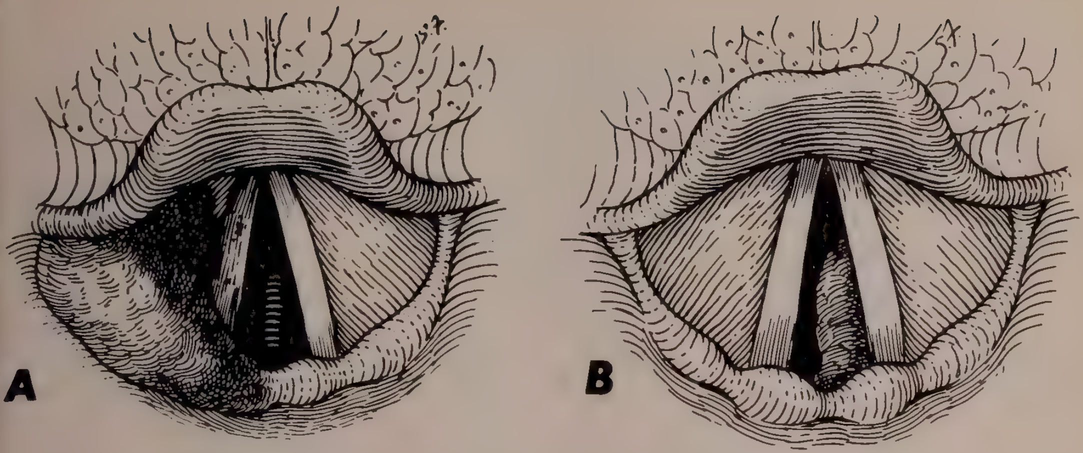

FIGURE 7. (A) Cyst of ventricle. (B) Perichondritis of cricoid cartilage.

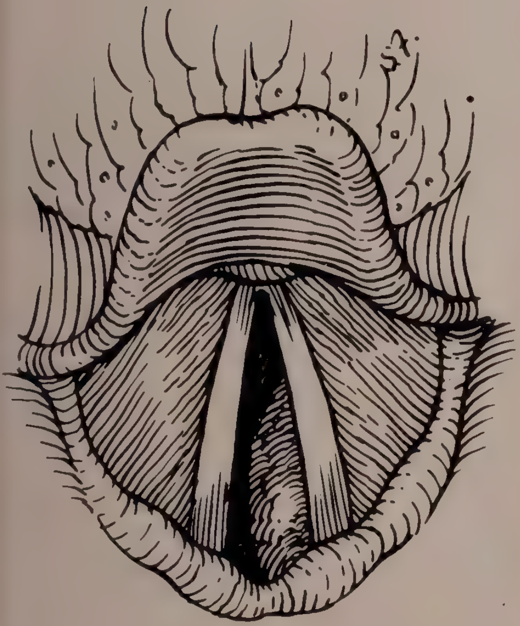

FIGURE 8. Subglottic mass.

A female infant, about nine months of age, was admitted with obstructive breathing. At three months of age she had had a tracheotomy for acute symptoms accompanying an infection of the respiratory tract. This subsided, but when she was six months old, there was a recurrence. This was controlled with steroids. Signs of laryngeal obstruction again appeared just before admission, and a subglottic mass was noted (Fig. 8). It appeared cystic and was diagnosed as a cyst of the larynx. A laryngofissure was performed with the excision of the mass which was now seen to be a little bluish and thought to be a hemangioma. The microscopic diagnosis was of a fibrous angioma. The patient made an uneventful recovery, and the tracheotomy tube was removed eventually. She has been well for over a year.

Delay in treatment

Circumstances may sway our judgment and delay proper definitive diagnosis and treatment.

This is illustrated by a thirty-three-year-old female patient who had a carcinoma of the thyroid gland treated ten years previously with total thyroidectomy and x-ray therapy. The patient had had three episodes of acute laryngeal obstruction during pregnancy. She came to our attention first during the second episode, at which time an abductor paralysis of the right vocal cord, and what appeared to be a subglottic stenotic swelling on the left side, were noted. During the last episode of laryngeal obstruction a tracheotomy was necessary. Following this, a direct laryngoscopy revealed edema of the left arytenoid, aryepiglottic fold, ventricle, and subglottic area. After the pregnancy the edema persisted, but the neck continued to show negative findings. An examination of the neck disclosed destruction of the left half of the larynx by recurrent carcinoma of the thyroid. A radical neck dissection and laryngectomy was performed. It was difficult for us to be certain that there was a recurrence after ten years, and at first we considered the possibility of late perichondritis and necrosis of the cartilage following radiation therapy.

It is not always possible to see a lesion of the larynx on indirect examination, especially if the growth is in the anterior

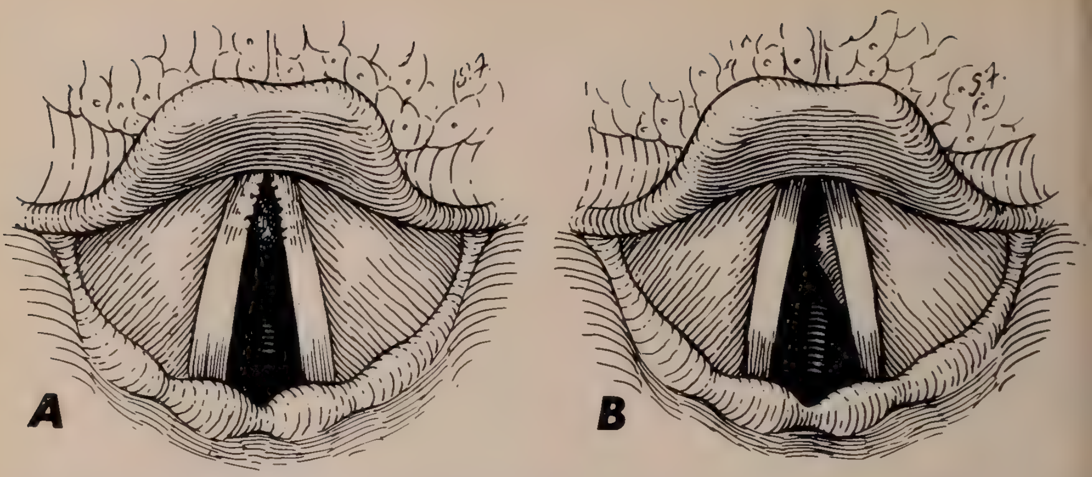

FIGURE 9. (A) Subglottic tumor seen beneath anterior commissure. (B) Subglottic elevation on right side of larynx anteriorly (chondroma).

commissure. In any complaint referable to the larynx one should always do a direct examination if the entire larynx cannot be seen with a mirror. Occasionally a benign or a malignant tumor may be discovered between the vocal cords anteriorly or on one vocal cord near the anterior commissure. Also, it is possible to miss a lesion just beneath the vocal cords or on the anterior wall of the larynx.

A male patient had hoarseness for three years. In 1956 he had had two biopsies reported as showing negative findings. An indirect examination also showed negative findings. On direct examination a subglottic tumor was seen beneath the anterior commissure (Fig. 9A). The biopsy was reported as squamous-cell carcinoma.

Another male patient was hoarse for one month. An indirect laryngoscopy showed negative findings. On direct laryngoscopy a hard, rounded subglottic elevation was seen on the right side anteriorly (Fig. 9B). A biopsy of the mucosa in this area was reported as "acute inflammatory process covering a piece of cartilage—chondroma of the larynx." The hoarseness cleared up under medical treatment. This is another example of a case where an acute process brought attention to the condition which could not be seen readily except by direct laryngoscopy.

The posterior surface of the epiglottis is sometimes difficult to see, and even on direct laryngoscopy one may miss a shallow, creeping growth in this area because the laryngoscope may cover it. This region of the larynx is occasionally hidden from view and must be examined carefully during laryngoscopy. At times, the epiglottis will cover the base of the tongue, and a malignant growth in the vallecula may be discovered when a direct laryngoscopy is done.

Congenital and functional diseases

In considering "hidden" congenital and functional diseases of the larynx one should mention paralysis of the vocal cord which may not be functional when it is due to pressure on the recurrent laryngeal nerve secondary to a growth in the thyroid gland, esophagus, or chest. Cricoarytenoid arthritis also affects the motion of a vocal cord. The immobility of this joint usually can be confirmed by direct laryngoscopy and palpation with an instrument.

It would be difficult to go into the functional disorders of the larynx caused by emotional distress, the abuse of the larynx, and the improper use of the voice. These functional disorders are in another sphere of our specialty.

A congenital lesion which was seen recently in our clinic was previously thought to be a functional ailment. This is a case of vocal cord sulcus, or double vocal cord (Fig. 10A). It is a congenital hypophasia of the vocalis muscle that produces dysplastic dysphonia. A shallow longitudinal sulcus is seen near the edge of a

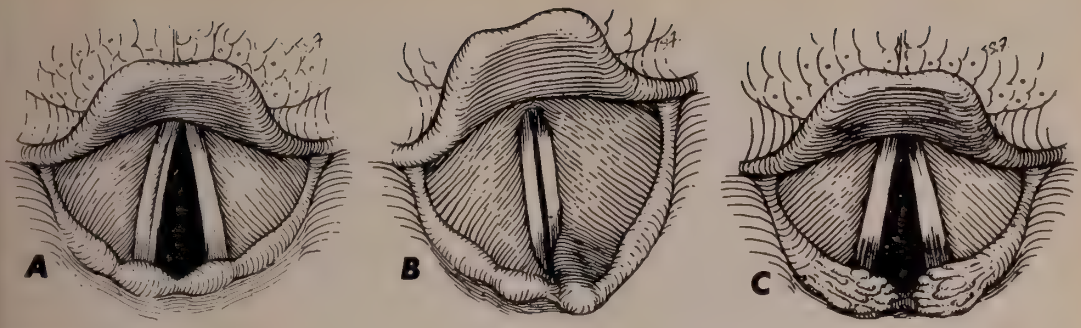

FIGURE 10. (A) Vocal cord sulcus, or double vocal cord. (B) Paralysis of cricothyroid muscle. (C) Redundant folds on superior aspects of arytenoids.

vocal cord and, if this sulcus is deep enough, the cord appears to be double. The patient had a slight whispering quality to her voice due to a bowing of the cord. Voice therapy is usually recommended for these cases since there is little else one can do. Vocal cord sulcus may be bilateral. It is an interesting finding.

The possibility of disturbed function of the cricothyroid muscle due to paralysis of the superior laryngeal nerve, or due to trauma of the muscle, either directly or indirectly by strenuous vomiting or vocal over-exertion has been mentioned. Patients with this disorder will have laryngeal anesthesia if both branches of the superior laryngeal nerve are involved (Fig. 10B). There will be a deviation of the posterior commissure to the side of the lesion, the cord will lose tension, it will appear shortened, and it will be situated on a different level from the unaffected cord. The voice will be low-pitched and husky.

Such a case came to our attention in a patient who had had a hemithyroidectomy two weeks before. About a week later the voice became husky and low-pitched. It was noted that the wound contained a hematoma which extended about 3 by 6 cm. over the extent of the thyroid incision. Apparently there was some pressure on or infiltration of the cricothyroid muscle, and the typical signs of disturbed function of the muscle were noted.

Another congenital difficulty is exemplified in the following case.

A ten-year-old female had a history of exertional dyspnea and inspiratory stridor since birth. She was said to have had congenital laryngeal stridor which was diagnosed by laryngoscopy at three months of age. On direct examination of the larynx congenital redundant folds on the superior aspects of the arytenoids were seen (Fig. 10C). These are known as "Schnarch-Falten," or snoring folds. The folds were removed by suspension laryngoscopy with the complete relief of the patient's symptoms.

Conclusion

Attention is called to certain diseases and conditions of the larynx, the diagnoses of which are sometimes obscured or delayed because (1) the difficulty may arise in a silent area, (2) the presenting symptoms may call attention to another organ, (3) the diagnosis cannot be attained immediately even on direct examination, (4) the lesion may be hidden from view at the time of the indirect examination, and (5) some congenital and functional diseases of the larynx may not be recognized readily.

103 East 78th Street, New York 21

SYMPOSIUM
AND PANEL
DISCUSSION

Treatment of Bursitis, Fibrositis, Tendinitis, and Related Conditions

Emphasis on Recent Therapeutic Modalities

Chairman
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Attending Physician, Memorial Hospital
Moderator
BERNARD M. NORCROSS, M.D., Buffalo, New York
Consulting Physician in Arthritis, University of Buffalo Chronic Disease Research Institute; Associate in Medicine, University of Buffalo School of Medicine
Panelists
SALVATORE R. LATONA, M.D., Niagara Falls, New York
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M. LAURENS ROWE, M.D., Rochester, New York
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HENRY V. MORELEWICZ, M.D., Buffalo, New York
Director, Department of Physical Medicine, Mercy Hospital; Assistant Professor of Physical Medicine and Rehabilitation, University of Buffalo School of Medicine
ROBERT DICKERSON, M.D., Rochester, New York
Chief Resident in Orthopedic Surgery, Strong Memorial Hospital

Introduction

Herbert A. Laughlin, M.D.: Our subject, "Treatment of Bursitis, Fibrositis, Tendinitis, and Related Conditions," is a bit cumbersome, but we felt that unless we described the conditions which we were planning to discuss, it would be rather ambiguous. We felt that it would be best to itemize this particular subject, because of a tremendous interest in the problems which all of us see in our offices, often many times a day. Furthermore they are conditions which often are difficult to treat, particularly to treat entirely satisfactorily.

At this time I would like to turn the meeting over to our moderator, Bernard M. Norcross, M.D., of Buffalo, who has been associated with L. Maxwell Lockie, M.D., for a number of years and is, to my mind, one of the outstanding authorities in this field. I have heard Dr. Norcross speak on many occasions including classes at the University of Buffalo, and I know that he and his panel will present the subject in a very worth-while manner.

Arthritides

Bernard M. Norcross, M.D.: As far as arthritis or connective-tissue diseases and the related soft-tissue diseases are concerned, we have had an era of considerable progress in the last ten years. I can remember vividly when the use of cortisone was first introduced in Atlantic City[1]; one of our very distinguished professors of medicine made the statement that it looked like the beginning of the end. Dr. Hench,[2] who made the discovery and the announcement of its

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use, very cleverly paraphrased that statement, saying that to him it looked like the end of the beginning. I think the last ten years have borne this out.

The adrenocorticoids have been of value, particularly in local use and also in systemic use for certain acute disorders when they are used carefully. I would make one plea to everybody, and that is: Do not start the average patient with rheumatoid arthritis on steroids just to "get him out of your hair," because sooner or later he'll come back to you and be in your hair worse than ever. This is not to say that there are not some merits in the use of systemic steroids under certain conditions, and I hope that we will be able to pinpoint their use and also some of the dangers connected with their use.

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Salvatore R. LaTona, M.D., will speak on the office diagnosis and treatment of acute rheumatic conditions.

Office treatment of acute symptoms

SALVATORE R. LATONA, M.D.: I was very pleased when I saw the title of my presentation was to be the "Office Treatment of Acute Symptoms." Therefore, I shall discuss what I do and not what happens in various series of 100 or 200 cases. I shall just tell you how I treat the arthritic patient when he walks into my office.

In the field of arthritis I think that there are illnesses without a definite diagnosis which are treated with more drugs, particularly expensive drugs, than is true of any other illness. I deplore having a patient come in and state, "I was told that I had arthritis." There is no field, no illness, in which the patient so adequately brings in all the physical findings, all the symptoms, and all the history for an adequate diagnosis.

This does not mean that we do not have problems in the diagnosis of the various forms of arthritis. It is easier to diagnose, for instance, than upper gastrointestinal pain, and yet no one would think of giving treatment for upper gastrointestinal pain without finding out whether it is the heart, the gallbladder, an ulcer, or the pancreas. Yet I see person after person who was treated for arthritis without any effort at all to make an exact diagnosis.

ACCURATE DIAGNOSIS. The patient walks into your office with an acute condition in a joint, for example, the shoulder. The patient walks in holding his arm, and he can't move the shoulder. "It came on during the night, Doctor, about three o'clock in the morning. I haven't been able to move my arm. It's been so painful. I put some heat on the shoulder, and it became worse."

The history alone points to one of the subjects that we're going to discuss: the treatment of acute bursitis, or acute calcific tendinitis, or acute periarthritis, as some people call it—the acute painful condition in the shoulder.

In this type of case you have the history which is typical. You have the physical signs: The person is holding the shoulder; you try to move the shoulder, but you can't do it. You press over the shoulder, and there you have your diagnosis. You examine the patient to make sure that there are no other lesions. You make certain that there are no other joints involved, and then you make your diagnosis. In fact, you don't even need an x-ray film, an electrocardiogram, or any laboratory measures. The diagnosis is much easier than the differentiation between an acute condition of the gallbladder and of an ulcer. In most of the conditions of arthritis in your office the diagnosis can be made by a careful history and a careful physical examination.

A young girl twenty-two years of age walks in with an acutely swollen knee, which is the only joint involved. She isn't overweight. She has no other symptoms. What can happen in a young woman which would cause an acute, red, hot, swollen knee? You think of gout, which would be so rare that you would present her at one of your hospital conferences. Could it be osteoarthritis? The patient isn't elderly or overweight. Osteoarthritis occurs in the older-age group.

Is this acute lupus erythematosus? But there is nothing else to go with lupus erythematosus. Is this one of the now rare forms of gonococcal arthritis? I'm sure a lot of the older men here have seen more than I have of gonococcal arthritis. No, the knee usually wasn't involved; it was in the wrist. Therefore you are drawn automatically to the possibility of acute rheumatoid arthritis.

Of course, you can use laboratory measures. We think that the sedimentation rate, which can be determined in any doctor's office, and does not require a high-powered laboratory, will be of help in this case.

Do you need x-ray films? We know that many times x-ray films in the diagnosis of arthritis can be very discouraging, particularly in the diagnosis of acute forms of arthritis, because severe arthritis may occur without any evidence of any changes on the x-ray film.

When the arthritic patient comes into your office, the first thing you have to do is to diagnose what type of arthritis the patient manifests before you begin to think of the treatment of acute symptoms.

To illustrate how different the treatments of the acute symptoms are for the various types of arthritis, I will discuss four of the more prominent conditions and show how you would have fallen into trouble if you had not taken the trouble to make an adequate and correct diagnosis.

ACUTE CONDITION OF THE SHOULDER. An acute condition in the shoulder may be called an acute bursitis, and may have calcium deposited in it. It also may be an acute tendinitis, with or without calcium deposited, or it may be an acute fibrositis or periarthritis around the shoulder. To you, as a practicing physician, it really doesn't make too much difference in the treatment of an acute condition of the shoulder.

Your task with the history and the physical examination is to make sure that there isn't another condition. If you have an x-ray machine available, you may take an x-ray film to see if there is any calcium deposit.

In the treatment of this acute condition of the shoulder, you have to relieve the pain. After making the diagnosis, I treat the shoulder by finding the maximum point of tenderness. If it is in the bursa, I find it right over the bursa. If it is tendinitis, I may find it in another spot. Then I infiltrate the area with procaine hydrochloride and go down slowly, probing as I go along, looking for the acute spot. At times I may encounter the calcium. I inject procaine hydrochloride as I go along. At times as I go along, the patient will give a little yelp and will say, "That's the spot." Then I infiltrate the area with procaine hydrochloride. I remove the syringe and inject 2 cc. of any of the good products of hydrocortisone or the newer derivatives into the shoulder.

Along with hydrocortisone or a derivative, I have used either phenylbutazone (Butazolidin) or oxyphenbutazone (Tandearil) orally. Lately I've been impressed with oxyphenbutazone, which is an offshoot of phenylbutazone, in the treatment of acute conditions of the shoulder. It seems to give some relief. I give patients either phenylbutazone or oxyphenbutazone, 1 tablet four times a day for two days. Along with that, I give them another analgesic agent if they still have any severe pain, either codeine or dextro propoxyphene and acetylsalicylic acid compound (Darvon compound). Many times I have been able to clear up an acute condition of the shoulder with one or sometimes two injections of procaine followed by hydrocortisone and then a treatment of phenylbutazone or oxyphenbutazone.

ACUTE GOUT. A young man of about thirty-four came to me and said, "I stubbed my toe about two days ago. My big toe hurts, and it's painful." He limped in; he couldn't wear his shoe. He had a red, hot, swollen big toe. I looked him over for any other signs of arthritis, and there were none. What else will cause an acute condition in a big toe after injury? Surely, he could have had a fracture. I took an x-ray film and ruled out fracture, but whether or not the x-ray film was absolutely necessary, I don't know. I took it because I feel that in an injury you do have to rule out the possibility of a fracture. I felt that the patient had acute gout. He came to the office at 4:00 P.M. He had taken aspirin and had eaten. Was it necessary to wait for all the tests of blood uric acid and so forth to treat this patient? He required treatment right then and there for the relief of pain.

I felt that with the examination and the history I had a good diagnosis for gout. In the treatment of acute gout, particularly in the first attack, I attempt to prove the diagnosis with specific therapy. I placed this man on colchicine. We know that phenylbutazone or, in some cases, the steroids may give faster relief a little more easily than colchicine, but, if colchicine gives relief, it will help to prove the diagnosis. In the first attack of gout or the first time that you see a patient when you want to prove a diagnosis of gout, I would use colchicine. I placed the patient on colchicine, 1 tablet every hour until either relief or diarrhea. I asked him to come in the next morning on a fasting stomach and took a blood uric acid test then.

Colchicine will not affect the uric acid levels. However, there is one thing that I want to warn you about. Some physicians say that the uric acid in their patients has been low. Many of them fail to realize that aspirin in adequate doses will bring down the level of the uric acid. If the patient has been on aspirin within forty-eight hours of the time you take the blood uric acid, the level of blood uric acid will be low.

My patient came in the next morning. He had the blood uric acid test. I saw him that afternoon, and he had complete relief of his symptoms by the use of colchicine.

OSTEOARTHRITIS. Next comes in the patient who has an acute condition of the knee. The knee is swollen, and there is fluid in it. The patient is about fifty-five years old and obese, and the knee hurts. It isn't as acute as, for instance, the acute condition of the shoulder that I spoke about earlier or the acute gout; however, it hurts, aches, and feels hot to him, although to you it doesn't feel particularly hot.

You examine the patient. You find evidence of crepitation as you move the knee joints. The patient is obese and elderly. The knee is the weight-bearing joint, so that you feel fairly sure that it is a case of osteoarthritis. The sedimentation rate will help you because it will show negative results; in other words, the blood findings and other laboratory tests show negative results in osteoarthritis as opposed to rheumatoid arthritis.

In treating the patient with osteoarthritis I give him an adequate dose of aspirin, 2 to 3 tablets every four hours. I tell him to rest. In this type of patient, I like to use mild heat, because I know that it is not an acute inflammation of the joint. In an acute condition of the shoulder or in acute gout I would use heat. If aspirin does not help the patient with osteoarthritis then I change in the next day or so to either phenylbutazone or oxyphenbutazone. I use one of these drugs for a short period of time after aspirin has failed in the treatment of osteoarthritis to get the patient over the acute symptoms.

Then if these have failed, you have the perfect indication for the use of intra-articular steroids. As Dr. Norcross indicated, this is one of the best indications for the use of steroids. In using the same method that I described for infiltrating the shoulder, I take the syringe with procaine and go down into the knee, infiltrating procaine into the knee until I get some fluid back or feel some give. I put about 2 cc. of any of the good preparations of the steroids into the knee, and in many cases relief will be obtained.

ACUTE RHEUMATOID ARTHRITIS. In acute rheumatoid arthritis you may run into a real diagnostic problem. You have to keep your mind open. You have to observe the patient, and this is where laboratory measures can be of help.

A twenty-two-year-old girl comes in with an acute condition of the joints. They are swollen; in the hand the swelling is in the proximal joints as opposed to the swelling in the distal joints which occurs in osteoarthritis. In acute and painful conditions of the joints what are we dealing with? Are we dealing with acute rheumatic fever, acute rheumatoid arthritis, or acute lupus erythematosus? Many times in this we have a difficult differential diagnosis. Of course, if there are no cardiac manifestations, this tends to rule out rheumatic fever, although not completely so because you can have rheumatic fever without cardiac manifestations. However, you look for cardiac manifestations in rheumatic fever or in lupus erythematosus. This is where a urinalysis is helpful. If you find a lot of albumin and particularly red blood cells, you wonder if you are dealing with acute lupus erythematosus. Does the patient have the blush of lupus erythematosus? I mentioned the heart. Does she have some other evidence of systemic illness? Does she have marked anemia? These are the things that you look for. If you find, after you do the complete examination, that it is a case of acute rheumatoid arthritis, what is your treatment in the office? You would treat it as you would acute pneumonia. You would put the patient to bed. You would give the patient aspirin, in adequate doses up to 90 grains a day, depending on how much is required to give relief. You would not put heat on an acutely inflamed joint.

Conclusion. I hope that I have given you a little idea of what I feel you should do when a person comes into the office. And, remember, never think of treatment until you have made the diagnosis.

Dr. Norcross: M. Laurens Rowe, M.D., will discuss rheumatic problems in the office and also the diagnosis and treatment of them in industrial work.

Orthopedic treatment

M. Laurens Rowe, M.D.: In tendon, bursal, and soft-tissue inflammatory conditions we are dealing with a great unknown. This is a medical morass at the moment. Our stakes are not firmly down, and it is an area where it is very easy to slip into medical fadism and to get off the beat as far as methods of treatment are concerned.

There are two or three general observations that I would like to make.

We have recently been interested in atypical gout as a cause of the common sorts of things that we're talking about today: bursitis of the shoulder, epicondylitis of the elbow, tendinitis of the wrist and hand, bursitis of the hip and knee, "foot strain," and even the ubiquitous "low-back strain."

So impressed have we been with the frequency of gout when we look for it, that we have used the serum uric acid determination as a routine measure in working up these patients with so-called nonspecific soft-tissue inflammatory conditions.

The second over-all observation is that I think we have been too prone to stress the importance of the mechanical or the traumatic factors in these conditions. All of us see patients with, for example, recurrent pain and swelling in an ankle who give a clear-cut history of injury six or eight months previously. They apparently recover in the accepted period of time, but then without reinjury they have recurrent episodes of ankle difficulty. We tend, I think, to emphasize in our minds this traumatic history and to overrate the mechanical side of these conditions to the detriment, actually, of our thinking in terms of the nonspecific inflammatory conditions.

The same thing applies in connection with backs. If we see a painful back of acute origin, perhaps with a minor trauma, we are inclined to regard this as a sprain or a strain, when all of our thinking should tell us that because of what we know about ankle or knee sprains this can't be a sprain. There isn't enough trauma involved, and we should look a little further for inflammatory conditions.

The other thing that is very easy to do is to see an x-ray film of a joint which shows osteoarthritic changes, perhaps rather dramatic spurring and lipping, and decide, "This is the answer!" The patient may have had these osteoarthritic spurs for many years with no trouble at all on full activity, and I think that we are leaping some hurdles that we have no right to leap if we attribute his acute symptoms to osteoarthritis. He may show such a condition but so may 70 per cent of his contemporaries who have no symptoms.

As far as the orthopedic surgical approach in these conditions is concerned, I think perhaps I can be most helpful, by listing the conditions anatomically and telling you where surgery has an application.

Shoulder. Dr. LaTona has spoken well

about acute conditions of the shoulder. I would add to what he said only that in my experience the successful treatment of acute tendinitis of the shoulder with locally injected steroids has been limited to those shoulders in which there was a point of tenderness no bigger than dime size in area and that the success of the injection depends on hitting the point of localization, no matter how long it takes to palpate and determine it accurately. If I have been unable to localize the point accurately, I will get an unsuccessful result with the injection. There are many patients with acute tendinitis of the shoulder who do not have localized tenderness at the time you see them. They just hurt all over, and everything is tender. I don't think that these shoulders are successfully treatable, at least in my hands, with a local injection. These patients should have systemic steroids, phenylbutazone, or simple analgesia and sedation, depending on your own philosophy in the matter.

We no longer operate on the acute bursitis cases. Fifteen or twenty years ago we used to open many cases of acute shoulder bursitis and wash out the calcium, either surgically or between two large trocars. This is now out of fashion.

The surgical treatment of chronic conditions of the shoulder, or frozen shoulders, similarly is on a decline. In the past we resected the acromion, feeling in our naïve thinking that we were giving more clearance for the rotator cuff tendons and that, therefore, we would increase motion. The changes are much more subtle and much more complex than just a bony ledge interfering with motion. We feel now that we cannot help most chronic frozen shoulders by surgery.

Elbow. Lateral epicondylitis, pitcher's elbow, radiohumeral bursitis, or tennis elbow is a frequent source of difficulty, and many of these cases will come from persons in industry who have sustained wrenching strains or direct blows on the lateral epicondyle of the elbow.

These patients have been difficult to cure with systemic treatment, and, since the tenderness is almost always well localized, we treat them with the local injection of steroids. The injection, to be successful, must hit the target; if you miss the area of pinpoint localization of pain, your injection has very little chance of being successful.

There is one caution in connection with the use of injections in lateral epicondylitis: These patients frequently have a great deal of postinjection pain. I think the reason is that you're injecting into the common tendon of origin of the extensor-supinator group of forearm muscles where it inserts into the lateral epicondyle. The injection is made into very tough tendon tissue. You have to push on the plunger of the syringe literally with all your might, and I think it is the high tension of the injected material which causes the postinjection pain. These patients need ice packs and adequate analgesia for the first twenty-four to forty-eight hours.

In the olecranon bursitis cases, many of which, of course, give a history of trauma, we have been tapping, draining dry with a needle, and injecting with a local steroid. Recurrences are treated similarly. If a patient has three recurrences, we resect the bursa. A study for gout in these cases seems clearly indicated.

Wrist. At the wrist, Quervain's disease, or stenosing tenovaginitis of the tendons of the thumb, which we see in industry in people who are doing a repetitive job involving abduction of the thumb, is common. If the tendinitis is truly acute with redness and increased heat and swelling, the patient frequently will respond to either local or systemic steroids. If, however, the condition is chronic, that is, of more than three or four weeks duration, we have taken the attitude that we are wasting time with conservative treatment. The patient goes directly to surgery, which consists of a simple opening of the tendon sheath. The results of this tendolysis are good.

Fingers and thumb. Tendinitis of the flexors of the fingers and thumb, if it is acute with soft-tissue swelling and increased heat, occasionally may be cleared successfully with local or systemic steroids. If, on the other hand, it has gone to the point of being a trigger finger so that it sticks down and the patient has to peel it out with the other hand, we feel that we are probably wasting the patient's time with conservative measures and that he should have an operation, which is simply an opening of the tendon sheath.

HIP. In the lower extremity, some of our most frequent diagnostic referral cases are persons with trochanteric bursitis. These individuals have an onset similar to what Dr. LaTona described for acute conditions of the shoulder: They have acute pain in the hip and find it particularly difficult to sleep because they can't lie on the painful hip and they can't lie on the other hip because the painful hip drops into adduction and stretches the tissues over the greater trochanter. These people, if there is adequate localization of tenderness, can be handled well by local injection with steroids. The diagnosis, like most diagnoses, is simple enough to make if you think of it. While these patients may describe buttock or hip pain, the key point is a marked increase of pain on adduction and internal rotation of the hip with the patient supine on the table. Other passive hip motions are not painful so that it is not too difficult to rule out an acute condition of the joint as opposed to the bursa.

KNEE. In the region of the knee, we handle prepatellar bursitis exactly as we do olecranon bursitis. We tap, evacuate the bursa with a needle, inject a local steroid, and take those steps necessary to protect the patient from more industrial aggravation in his kneeling job by using knee pads or by modifying the job. We give the condition two chances to recur. If it recurs a third time, we advise excision of the bursa.

One of the most difficult, troublesome problems around the knee has been a little bursa that occurs under the medial collateral ligament of the knee. The patient usually has been doing a job or an activity involving frequent kneeling and getting up again. With this up-and-down motion of the knee, the medial collateral ligament scrapes over the bursa, which is interposed between the ligament and the tibial plateau, and may produce an acute bursitis with severe pain. The patient elects to have his knee in a little bit of flexion for comfort, which makes you think of a torn cartilage. He has pinpoint tenderness right on the medial joint line, not too far away from the point of maximum tenderness in a torn meniscus. He has difficulty sleeping. He can't get the knee in a comfortable position, and, very characteristically, he may tell you that if he pivots on the knee, the pain is severe. This, again, is suggestive of cartilage injury.

These patients are very well handled, once the diagnosis is made, by the local injection of the bursa with one of the steroids. The most helpful points in diagnosis are, first, knowing about the condition and, second, being able to reproduce the pain by toggling the knee into valgus, that is, with the tibia relatively lateral in relation to the femur so that the tension is increased on the medial collateral ligament. This usually will not produce pain with a medial meniscus injury. It will produce severe pain in a medial collateral ligament bursitis.

ANKLE. In the region of the ankle, our problems are more likely to be mechanical, and our chief difficulty is that people will miss the full implications of what apparently is an ordinary ankle sprain. Our rule here has been that if following a sprain type of injury, the patient shows swelling both medially and laterally about the ankle, this is sufficient evidence on which to make a diagnosis of potential instability of the ankle. We feel that these people should be in plaster for from six to eight weeks, rather than treated with adhesive tape for ten days or two or three weeks as is routine.

FOOT. In the foot, we feel that arch strain has been oversold. We in orthopedics are turning increasingly away from the concept of mechanical foot pain. If a patient has gone along through a number of years without arch strain or without bad feet and then comes in complaining of symptoms in the arch or the instep of four or five weeks or two or three months duration, we are very suspicious that there is a condition that is not mechanical. We are checking these patients carefully for the inflammatory conditions and finding a significant amount of arthritis and gout in this group.

DR. NORCROSS: One remark that Dr. Rowe made that I think is particularly apropos: that trauma should be gone into very carefully, not only in single isolated instances, but also the repeated type of trauma in certain occupations or positions. However, when you are thinking in terms of aggravation, the trauma, whatever it is, must be an adequate cause of injury and not just a minor incident.

One other condition that I think is particularly important is that of interpreting spurs, particularly in the back, as the solution to the patient's complaints. Any patient who complains of severe unremitting back pain which continues at rest obviously isn't suffering from osteoarthritis even though he shows huge spurs of the spine. He has a malignant disease or other serious lesion as the basis of this type of pain.

I would like to introduce at this time Henry V. Morelewicz, M.D. He has had a great deal of experience in the use of all methods of physical medicine in the treatment of this group of diseases.

Treatment by physiatrist

Henry V. Morelewicz, M.D.: I would like to keep my remarks limited to three different areas of heat: frictional, chemical, and electrical.

Frictional heat. Frictional heat, I am sure most of us are familiar with. As you know, frictional heat is produced by manual massage. This can be done by the use of a dry hand. It is not always desirable to massage with a dry hand because one may cause excoriation of the skin if the skin is tender and not elastic. Therefore, rubbing alcohol, a rubefacient, or a neutral compound is used.

There appears to be a right way and a wrong way to use massage. One must decide when it should be used and when it should be avoided. Massage is generally given when the skin is tight because of edema, inflammation, or disease. Massage is contraindicated in acute inflammation. After massaging, the patient should obtain muscle relaxation, decrease in pain, or increase in function of the muscle or joint. The proper technic for massage is in the direction of lymph flow. Improper massaging may increase lymph to a part resulting in edema formation with an increase of pain.

The segmental massage technic has been found to be very useful. The distal part is massaged first, then the intermediate segment, and finally the proximal segment with the strokes increasing as one goes from one segment to another. If the patient has edema of the hand, massaging should be started at the elbow, then the forearm, at the wrist, and finally at the hand. If the patient has edema of the foot, massage should begin at the knee, then at the leg proper, next at the ankle, and finally at the foot.

Chemical heat. A second form of heat which is produced by exercise is the so-called chemical heat. Chemical heat is especially useful for those individuals who may complain of stiffness of the joints, tendons, or muscles; inability to move an extremity; or difficulty in ambulation especially in the morning. It is important to realize that chemical heat can be produced only by voluntary contraction of the muscle, and this cannot be reproduced either by electrical stimulation or by passive movements of the joints and muscles.

Instruction by the physician, therefore, for the patients who have difficulty in moving their extremities early in the morning is essential. The exercise program should be specific, simple in nature, and easy to perform, and it should be carried out in a bedroom, living room, or exercise room.

It may be wise that the instructions for exercise be given for short periods of time, for example, five minutes out of each hour or for four or five sessions per day. I would suggest that one be cautious in prescribing exercises. An individual who seems to have a great deal of motivation and appears to be anxious may exercise too vigorously, too strenuously, or for too long a period of time and do damage to his muscles or joints. It is wise to instruct the patient to start exercising first the larger joints and muscles of the body such as the hips and the shoulders. Then he may go down to the elbow and knees, wrists and ankles, and, finally, the fingers and toes. This is the warming-up period. Later the patient can move vigorously and do all exercises without causing damage to muscle fibers, ligaments, or joint capsules.

On the other hand, we must recognize that there is the patient who may be very apprehensive of pain and who may have a low threshold for pain tolerance. This type of individual may need, in addition to constant reassurance, some form of medication to reduce the lowered threshold for pain before starting a simple exercise program. He must be shown how the exercise is to be done and told specifically that it is to be done hourly from 9:00 A.M. to 4:00 P.M. It has been our experience that the best results are obtained if exercises are done every two hours during the day. It also has been noted that short exercise periods with frequent repetition give better results than exercises given for prolonged periods of time at less frequent intervals.

It has been noted that some people who resort to hot water bottles, electric pads, and so forth, because of pain in the shoulder, over prolonged periods of time have more stiffness and discomfort than if they leave them alone. This is owing to prolonged overheating of a joint with resultant edema. This type of patient would do better if he dispensed with artificial heating of the joint and engaged in an exercise program. Proper exercises for various areas of the body can be found in books of kinesiology.

ELECTRICAL HEAT. The third type of heat, which is used frequently in a physician's office or in the hospital situation especially in departments of physical medicine and which is not recommended, generally, to be used by the patient at home, is heat produced by electric modalities.

One of the first electric modalities to produce deep heat successfully was long-wave diathermy, which is now extinct. Heat from this modality was of especial benefit for cases of bursitis and female pelvic inflammations. Today short-wave diathermy is a popular form of deep heat. If you have such an apparatus or intend to purchase one, make sure that it is an approved machine for safety and one which will not interfere with radio and television reception both in your office and in the neighborhood. There is a word of caution: This machine is safe only in the hands of a careful physician.

Before giving a large amount of heat for a prolonged period to a patient, the following must be determined: (1) whether or not the patient suffers from an acute situation and whether or not there is a large amount of edema in the part to be treated; (2) whether or not the sensation in the part to be treated is adequate; (3) whether or not the part to be treated is in contact with metal; (4) and whether or not there is hardware fixing bones or joints in the area where one is going to treat the patient. If these conditions are present, deep heat is contraindicated.

I would suggest that, if one wishes to give a large amount of heat with short-wave diathermy, the heat be stepped up in the beginning to three quarters of full capacity for the first three minutes with a towel inserted between the patient and the machine to absorb perspiration. At the end of this time, the intensity of the heat should be lowered to the comfort of the patient and to the amount of heat the physician wishes to apply to the patient.

It has been observed that, in cases where burns with short-wave diathermy occur, the primary reaction occurs in the fatty tissue rather than in the skin. Therefore, if one suspects a burn, the skin as well as the subcutaneous fatty tissue must be examined carefully. Healing is very slow whenever adipose tissue is involved.

Another modality which is quite popular for deep-heat therapy, but which is not used quite as extensively, is microwave diathermy. This apparatus may be used with greater safety in areas of diminished cutaneous sensation. The amount of heat which seems to be most effective on patients seems to be between 40 and 100 per cent of generator capacity. The machine is to be placed no closer than 6 to 12 inches from the patient's skin.

A third electrical modality, a recent development, is ultrasound. Some medical literature condemns this modality on the one hand, and on the other there is nothing but praise for it. My own feeling is that ultrasound is another source of heat which, when used intelligently, will give good results. I do not feel that any one modality has all the qualities for proper heating or therapeutic effects.

The original ultrasound apparatus which was brought to the United States from Germany had a wattage of 0 to 15 per square centimeter. The apparatus which is being produced in the United States now is between 0 and 3 watts per square centimeter. It has been proved by experiments on animals and human beings that dosage under 3 watts per square centimeter will do very little damage to the tissue of the body, while dosage above 3 watts may cause damage to external tissues, bones, nerve, and muscle.

Modalities which destroy tissue easily are then to be handled only by those who are well trained to use this type of apparatus. Destructive doses of ultrasound can be used to destroy tissue, disintegrate renal or gallbladder stones, and break down heavy scar tissue.

I will confine my remarks now to the American-made apparatus with the dosage of 0 to 3 watts per square centimeter. The average dose which I use for cases of bursitis, tendinitis, ecchymosis, and arthritis, when indicated, is 0.5 to 1.5 watts per square centimeter. The reason that one designates dosage per square centimeter is to determine the total dosage given by a particular crystal which is found in the transducer and which may vary from 3 to 7 square centimeters in total surface area. In this way we can determine the total dosage recommended for each condition regardless as to size of crystal.

CONCLUSION. I would like to repeat that we have three forms of heat to choose from in medicine. The choice, however, depends on many factors, and this must be determined by the prescribing physician after careful evaluation of the patient's condition.

DR. NORCROSS: Robert Dickerson, M.D., will answer any specific orthopedic questions. Dr. Rowe, of course, covered his subject so well that probably no one can add anything.

This is a question for Dr. LaTona: Would you comment on the use of lidocaine hydrochloride (Xylocaine hydrochloride) instead of procaine hydrochloride (Novocain) for local anesthesia?

DR. LATONA: You can use lidocaine hydrochloride instead of procaine hydrochloride if you desire. I prefer procaine hydrochloride, but lidocaine hydrochloride is good. I'm just a little afraid of reactions.

DR. NORCROSS: Dr. Dickerson, do you have any feelings about lidocaine hydrochloride?

ROBERT DICKERSON, M.D.: Our feelings are that it doesn't make a bit of difference. There are no differences in reaction that we know of between lidocaine hydrochloride and procaine hydrochloride. Their chemical structure is essentially the same. We know of no differences in local reactions. Their effectiveness for a given concentration is practically identical.

DR. NORCROSS: The only comment that I think apropos is to exclude anyone who previously has had a reaction to any of the "caine" derivatives. It makes little difference which one you use, but I like to use the lowest concentration and the least amount required. I prefer a 0.5 per cent solution without epinephrine or any other local blocking agent. Many people prefer the use of ethyl chloride locally to avoid the possibility of a "caine" reaction.

Dr. LaTona, would you comment on the dangers of using phenylbutazone?

DR. LATONA: I will give you all the dangers of phenylbutazone. We recorded from our Buffalo group approximately 700 patients with various conditions on whom we used phenylbutazone. We found very few serious complications. Let me speak about the serious ones first. We did find depression of bone marrow in some cases so that we routinely do white blood counts and differential diagnoses on patients who are on phenylbutazone. We did not find any patients who developed permanent depression of the bone marrow. In my own practice I had 1 case of marked bone marrow depression which I felt was due to phenylbutazone.

We did find, of course, many of the minor complications. There were some gastrointestinal complaints and some rashes. If phenylbutazone is used carefully, particularly over a short period of time, we feel that it is a relatively safe drug.

DR. NORCROSS: Dr. Morelewicz, what dosage of ultrasound would you recommend for tendinitis, and is the use of ultrasound ever dangerous?

DR. MORELEWICZ: In a case of subacute or chronic tendinitis, I recommend 0.75 watt of ultrasound per square centimeter. Others feel that a dosage between 0.5 and 1.5 is indicated provided such therapy is not given for less than four minutes and does not exceed eight minutes. I would like to point out that the operator of the transducer must be present with the patient at all times to apply the proper dose in the proper time prescribed.

Unsuccessful results may be due to many reasons rather than to default of the modality itself: (1) improper diagnosis, (2) improper dosage, or (3) improper form of application. There is a word of caution: The use of this modality on a daily basis for more than two months may be dangerous with the occurrence of undesirable reactions such as decalcification and perineuritis. Also, I would like to suggest again that the average physician purchase and use an apparatus approved for therapy, 0 to 3 watts per square centimeter, rather than purchase an apparatus which may also include dosages for destructive purposes, as dissolving of calculi, scars, or tumors.

Dr. Norcross: Dr. Morelewicz, there is a third part to that question: Is ultrasound contraindicated in cases where metal parts are present in an extremity?

Dr. Morelewicz: Up to a year ago it was advocated that ultrasound not be used on extremities where there are metal parts used to repair bones or joints. However, within the last year, at the Third International Congress of Ultrasonics held in Washington, D.C., work done in Denver was presented, pointing out that if ultrasound is applied properly there are no contraindications to its use where there are metallic parts used in bone repair. One paper dealt with experiments on animals and one with experiments on human beings in which ultrasound was used in the presence of metal parts in bones or joints with no ill effects. It is recommended that ultrasound should not be used above the dosage of 0.5 watt per square centimeter for more than five or six minutes on extremities that contain metallic implants.

Dr. Norcross: I will ask this question of the entire panel: What is the latest opinion about the treatment of ganglia, particularly those at the wrist? Dr. Dickerson, would you like to comment?

Dr. Dickerson: When we see someone who has a ganglion on the wrist, we are not inclined to do anything about it unless it is quite bothersome to the patient. We are not inclined to remove the ganglion. If anything is done, it is surgical excision down to and including the origin of the ganglion from either the tendon sheath or the capsule of the interarticular bones of the wrist. Of the ganglia that we see, very few are operated on, but we do not use any other form of treatment. We don't smash them with the family Bible, and we do not recommend injecting them with hydrocortisone or other materials.

Either we advise the patient to leave the ganglion alone or, if he insists that something be done about it or it seems that something should be done about it, we advise surgical excision, usually under regional anesthesia.

Dr. Norcross: Dr. LaTona, do you have any other opinions?

Dr. LaTona: I agree with Dr. Dickerson. If the ganglia do not cause any trouble, I feel that they should be left alone. Many of them, as you know, disappear spontaneously. Maybe our forebears did have a good idea when they used to slam them with the family Bible because it did get rid of some of them. However, I feel that there is some merit to using a large boring needle to try to evacuate the ganglion and then injecting hydrocortisone. I have helped some of these patients with this. However, I only use it in the cases in which the patient is symptomatic and has trouble with the ganglion. If he doesn't have symptoms and it's just a ganglion, with nothing to it except the cosmetic look, I try to talk the patient out of doing anything. But we have had some success with trying to evacuate the ganglion and then using hydrocortisone.

Dr. Dickerson: Have you had short-term or long-term success?

Dr. LaTona: We have had long-term success. I have had some of them disappear completely. But, of course, I have had some of them disappear when they were left alone because, as you state, they may resolve with any stress in the area.

Dr. Norcross: Dr. Morelewicz, can you cure ganglia with ultrasound?

Dr. Morelewicz: We do not cure them. We do not claim to cure anything with a modality. Ganglia which are not medicated but allowed to remain quiet with an extremity splinted usually disappear spontaneously. On the other hand, when ganglia give the patient some discomfort and pain, the use of ultrasound definitely is indicated to help reduce this pain and discomfort.

As you know, ultrasound is useful because it increases the permeability of the cellular membranes and improves osmosis between the cells and the intercellular space. It also helps intercellular lymph flow. Second, as ultrasound waves strike protoplasmic molecules, a vibration is set up between the molecules. Thus, jellied material found within the cell disintegrates in the presence of ultrasound. Ultrasound may prepare the protoplasmic material and products for better osmotic transfer from cell to intercellular space and vice versa.

Dr. LaTona: I agree with Dr. Dickerson that if you excise the ganglion you should do an adequate operation to get the root, because if you don't, you're going to have trouble.

Dr. Norcross: Dr. Laughlin asks: Are any specific steroid preparations better than others for injection therapy?

I will answer that question, subject to any objections that the panel wants to make. I know many orthopedists still use hydrocortisone acetate or TBA (hydrocortisone tertiary butyl acetate). I feel that there are preparations which are superior in several respects: There is less postinjection flare, quicker improvement in the injected joint, and a longer duration of action. We all have preferences. I think that prednisolone TBA, triamcinolone acetonide (Kenalog), or Depo-Medrol are better than hydrocortisone.

Dr. LaTona, what is meant by fibrositis? Is the diagnosis made by exclusion and what is the management?

Dr. LaTona: First we have to define the term fibrositis. Some follow the school that reserves the term fibrositis for psychogenic rheumatism. True, there is a condition which we may call secondary fibrositis, or it may be called primary in some cases, in which there is more of a myositis than an actual fibrositis. However, I feel that if the term fibrositis is defined by the person using it then you will not run into trouble. I like to use the term "fibrositis" chiefly to apply to psychogenic rheumatism. However, there are cases of acute myofibrositis, such as acute torticollis, as Dr. Norcross mentioned, or the secondary fibrositis overlying, for instance, rheumatoid arthritis or rheumatoid spondylitis. There are also cases which used to be called acute lumbago or miseries in the back in which there is an acute muscle tightening of the low back area and a lot of spasm, in which you feel that you have an inflammatory condition.

As to the management of fibrositis or psychogenic rheumatism which often affects the person who is at his desk with the tension of business and who gets the feeling of tightness and soreness throughout the neck, in the low back area, or anywhere, the first thing to do is to impress on the patient that he does not have any organic disease. Many times these patients are tense, nervous, and keyed up to the point where they're worried about organic disease. When they have pain, they picture themselves as having a crippling type of arthritis. You should take the time with this type of person to tell him what he has and to explain it.

The way that I like to explain it to a person is by explaining a car. If you have a car that is traveling 60 miles an hour, it rides smoothly. If you keep the same car at a standstill and run the motor at 60 miles an hour, it begins to rattle. That's what a tense individual does. He keeps his muscles tense. Just try to keep your arm up tense for five minutes and feel the muscle ache. This, to me, is the psychogenic rheumatism, the tension fibrositis, or what have you.

Therefore, reassure the patient. I have found that in some of these cases a sedative will help. Use phenobarbital, Butisol Sodium, or any of the mild sedatives. I find that, at times, aspirin will help. In some cases, I have used either phenylbutazone or oxyphenbutazone which I mentioned earlier, although I do not advocate its use routinely or for long periods of time. But when the patient has acute symptoms, it will be of help.

As regards the acute fibrositis, the inflammatory state in which there is torticollis, you can do either one of two things. You can find a trigger area and inject this with procaine and hydrocortisone. You must find the trigger area, and sometimes you're very disappointed with the results. I do not advocate the use of this method, and yet, if you do find the trigger area and it seems to be localized in a small area, you may try it.

In these cases I like to use either phenylbutazone, oxyphenbutazone, or aspirin. I use mild heat. I like to teach these people the use of infrared at home, $2^1/_2$ feet for twenty minutes, and then tell them to use light massage. Someone should massage the area with rubbing alcohol.

Again, in the management of these two conditions I urge that you first define your terms. Is it a fibrositis or psychogenic rheumatism, or are you dealing with a true fibrositis, a true inflammatory condition of the muscle which, unless you have an underlying condition such as rheumatoid arthritis or one of the other arthritides, is not as common as is thought?

Dr. Norcross: I am sure that there will be objections to this discussion. I'll refer it to the rest of the panel.

Dr. Dickerson: I can't say much about the psychogenic rheumatism which may be a common thing, but I will say that we believe that fibrositis does exist as an organic entity. Examples of what prove to be fibrositis, histologically, are the Dupuytren's contracture in the palmar aponeurosis and a plantar fasciitis in the plantar fascia which sometimes is associated with cavus feet. Less common forms which prove to be true fibrositis pathologically are the fibroid tumors of the sternocleidomastoid, congenital torticollis, and possibly the other torticollis, although I am not aware of any noncongenital torticollis cases with histologic specimens. But when the fibrous tumor of congenital torticollis is removed, it proves to be a true fibrositis. An even less common example of fibrositis, from a pathologic standpoint, is Peyronie's disease involving the corpus cavernosum. These are actual fibrositis cases on the basis of histology. Their treatment defies generalization, but the condition does exist. They are similar to, but distinguished from, the desmoid tumor of the rectus abdominis muscles which also is a collection of fibrous tissue associated with inflammation.

Dr. LaTona: May I have a little rebuttal? We do have these cases and, as Dr. Dickerson said, they are the less common conditions, and that's what I called them—the less common conditions.

As regards histologic specimens, if you go back in the literature about twenty-five or thirty years ago, you will find series of cases in which cervical fibrositis with nodules is described, in which the histologic studies showed negative results.

I will state this: In your office you will find more cases of psychogenic rheumatism posing as fibrositis than of true fibrositis. However, as I have stated, there are true cases of fibrositis. You find them in the low back or in the torticollis, although not in the congenital type. You can find them localized in Dupuytren's contracture; that's an old, burned-out, shall we say, fibrositis. But you very seldom find a true acute fibrositis; however, it does occur and many times will follow, for instance, what is called a virus infection, leaving an acute, sore back or sore muscles somewhere.

I would like to hear what Dr. Norcross has to say. He takes the middle road.

Dr. Norcross: I think the major problem in so-called "fibrositis" is the misapplication of the term. There are the specific examples, as Dr. Dickerson mentioned, but I think the term has been used frequently by a doctor who does not want to tell a patient that his problems are psychogenic and prefers to diagnose the situation as an organic disease.

Dr. Morelewicz has two specific questions about ultrasound and peripheral vascular disease.

Dr. Morelewicz: Is there any danger in the use of ultrasound, 2 watts per square centimeter or less, in close proximity to the cervical spine? And then there is another question: Is ultrasound useful in whiplash injury?

I think that a general rule would be to use a safe dosage of ultrasound at all times, especially around the areas of the face, the spinal cord, and the brain. Anything under 2 watts per square centimeter is considered fairly safe. We do not like to go over the cervical spines themselves because of a mechanical obstruction and it is always wise to be cautious not to irritate the central nervous system per se. The reason I say this is that people sometimes come in to the department for a period of three to five weeks, practically every day or every other day, and we are not quite sure what may happen in this continuous use of ultrasound.

Before I can answer the second question, I feel that it may be necessary to define the word "whiplash" as I see it.

Patients who suffer trauma to the cervical area and whose x-ray findings are negative for fracture, dislocation, subluxation, or other pathologic conditions, but who have muscle weakness demonstrable by muscle testing and grading, complain of severe pain on motion, and have an encephalogram with negative findings, and who may or may not require medication for pain in this area, fall into the category of soft-tissue trauma to the neck which I call whiplash.

All of us see patients in the office who complain of pain in their neck area. This may be due to trauma, infection, menopause, anxiety state, or bone degeneration. These conditions would not be considered necessarily as whiplash. Here we are dealing with more specific types of situations such as myositis, fibrosis, arthritis, muscular tension, or endocrine disorder. On the other hand, if we cannot pinpoint a specific disease entity or cause for pain in the cervical area, we should call this, in my opinion, a painful neck syndrome of unknown etiology, rather than a whiplash. I am afraid that the cervical whiplash or cervical stem trauma syndrome has become a dumping ground for many conditions, confusing the diagnosis and treatment of such conditions.

When whiplash presents problems of pain, we can resort to narcotics, analgesics, sedatives, muscle relaxants, mechanical splinting devices such as cervical collars, and physiotherapeutic procedures such as heat, traction, and exercises. In some cases it may be necessary to pay a great deal of attention to correct posture. The patient may have to be provided with proper shoes and taught a proper method of walking, as well as taught the proper means of neuromuscular relaxation to correct pain in the cervical area caused by trauma.

If we desire to treat this type of patient with heat and micromassage, I would recommend ultrasound. I have reported a study of 100 cases of whiplash injuries due to trauma sustained in automobile accidents, at the International Congress of Ultrasonics in Washington in July, 1960. In a true whiplash, the pain was reduced, there was an increase in the range of motion, and a sense of well-being was noted approximately two weeks earlier when ultrasound was used, as compared with short-wave diathermy, hot packs, or infrared. In the true severe whiplash case it took approximately ten to twenty weeks of carefully guided treatment to get the desired results. In several cases where pain persisted and other factors were negative, we decided to treat these cases for a prolonged period of time. We treated this group off and on for a period of one year with no apparent improvement in the reduction of pain. In this group of patients medication in the form of analgesics or muscle relaxants was necessary to help them function in their everyday activity. I would also like to point out that many of these cases were compensable or of medicolegal nature. Since we found that most cases had relief at the end of twenty weeks of carefully planned therapy, we recommend to the patient's lawyer: "At this point settle the case, and I'm sure you're going to have a well client."

DR. NORCROSS: There are two specific questions which I will try to answer. One pertains to gout. The first part concerns probenecid (Benemid) versus the other uricosuric agents.

Probenecid has had the longest period of proved value in the treatment of gout, particularly in preventing the recurrences of gout. In a dosage of 1 to 2 Gm. a day, it works adequately in 75 per cent of the patients. We have used it for eleven years, and there has been no serious problem connected with its use. Only minor and infrequent undesirable side-effects, such as gastric irritation, itching, or frequency of urination after taking a tablet, have been observed. At this time we still consider probenecid the drug of choice for uricosuric effect.

Zoxazolamine (Flexin) and sulfinpyrazone (Anturane), which is related to phenylbutazone, are more potent uricosuric agents. However, there is a question whether or not we need the greater uricosuric effect of these drugs. If a gouty patient does well on probenecid, even though his serum urate has not been lowered below 6.5 mg. per 100 ml., if his attacks have been infrequent and he has developed no tophaceous complications or we see evidence of healing of tophi on x-ray films, we are inclined to continue the therapy with probenecid. However, if probenecid does not have satisfactory uricosuric action and the gouty attacks are not becoming less frequent and less severe, we then employ one of the newer agents (zoxazolamine or sulfinpyrazone).

You must remember also that with the increased uricosuric action, there is an increased incidence of crystalluria, and this must be watched carefully to prevent the formation of urate calculi.

Interestingly enough, both probenecid and zoxazolamine seem to have an "all-or-none" action in my experience; that is, there is a certain effective dose and exceeding that dose does not increase the uricosuric effect to any extent. With sulfinpyrazone this is not true, and the uricosuric action increases with the dosage up to 50 to 60 per cent of the available urate. Whether this is good or bad, I don't know, but I would reserve the use of the newer agents to individuals for whom probenecid is not effective. The dosage of zoxazolamine is usually 250 mg. three times a day; with sulfinpyrazone the dosage varies from 100 to 200 mg., two or three times a day.

I would encourage the patient on any of the uricosuric drugs to maintain a high fluid intake and perhaps an alkalinizing agent to keep the urates in solution.

The uricosuric drugs are used in the individual who has increasingly frequent, severe attacks of gout, who has a serum uric acid that is extremely high (over 8 mg. per 100 ml.), or who has urate deposits in bone or other tissues.

The next question concerns the dosage of gold employed in the treatment of rheumatoid arthritis. There are some individual preferences as to dosage routine. Some physicians begin with a dose of 10 mg., increasing 10 mg. weekly up to a maximum of 40 to 50 mg. a week. Some will go from 10 to 25 or 50 mg. and maintain the dose at 50 mg. weekly until the patient has received about 600 or 700 mg. of gold. If the patient is improving at that time, we then continue a maintenance dose of 40 to 50 mg. every three to four weeks. If he is not improved at this time, we would seriously question the value of continuing with gold injections.

When people are receiving gold, we do a urinalysis once a week to observe the occurrence of albuminuria and red cells. We question them carefully for itching or rash and also for the occurrence of stomatitis or glossitis. In the last ten or twelve years, on lower dosages of gold I have seen only 1 case of severe dermatitis; usually if the patient reports itching, the dosage of gold is decreased and can be continued without a severe reaction. I have encountered 2 patients in whom gold was discontinued because of severe albuminuria.

There is no standard dose for steroid therapy. Steroids are tailored to the requirement of the individual patient. We all admit that there is a small number of patients who are helpless without steroid medication. If these patients have had all other forms of conservative treatment and they can be improved remarkably on a low dose (7.5 to 10 mg. daily) of prednisone or prednisolone, we believe that adrenal steroid therapy is indicated under these circumstances.

In certain patients dexamethasone may be indicated because of its appetite-stimulating and euphoric effects. In patients in whom we want to suppress the appetite, triamcinolone could be used, but an individual side-effect of this compound is muscle weakness and atrophy.

The next question concerns the use of antimalarial drugs. I'll ask Dr. LaTona to answer this question also. In our experience, we have not been impressed with the 60 to 70 per cent improvement reported in the literature. There is no question that a third of the patients respond well, but above this figure, the response is a variable and rather inconsistent.

The major advantages are that the antimalarial drugs can be taken by mouth, at relatively low cost, and with relatively little toxicity.

Dr. LaTona: I want to reiterate what Dr. Norcross has stated, that unfortunately, in the literature there have been some glowing reports about the use of antimalarial drugs. We have now about 250 cases. We found two things: One is that we could get only some degree of improvement. In about 50 per cent of the cases, there was slight to moderate improvement. Second, this improvement was extremely variable. We feel that the antimalarial drugs should be used in conjunction with other forms of therapy. Unfortunately, outside of our report, most of the other articles in the literature report 70 per cent relief and even some excellent responses, but with three or four observers looking at our cases we could not detect this degree of relief. As I have stated, some patients did seem to improve. In some cases, we could carry them along on the other measures a little better, but we do not feel that the antimalarial drugs are a panacea.

DR. NORCROSS: Dr. Dickerson has two questions regarding the use of muscle relaxants in fibrositis.

DR. DICKERSON: The first question is: Regarding Dupuytren's contracture, would you comment as to chronic irritation as a primary cause, and in such a case would it be a compensable disease?

There are reports that there is an increased incidence of Dupuytren's contracture in those who use pneumatic hammers and in certain occupational diseases, but no one knows the answer to my knowledge, and anyone who takes a stand one way or another in reference to the causal relation of trauma is on very shaky ground. Certainly anyone who states flatly there is a causal relationship between irritation, occupation, and Dupuytren's contracture would be taking a very tenuous stand.

The other question is: In what conditions is carisoprodol (Soma) useful? I believe that there has been general disappointment in the use of muscle relaxants as a whole. The only one that has seemed helpful at all in the last few years has been intravenous methocarbamol (Robaxin) in certain cases of acute conditions of the back. These relaxants have been used extensively in the orthopedic clinic, as you can imagine, and have been used hopefully, but they have been very disappointing. I don't know of any particular place where the muscle relaxants can be said to be truly helpful other than on a suggestive basis, with the possible exception of intravenous methocarbamol in acute painful conditions of the back with associated muscle spasm.

DR. NORCROSS: Dr. Dickerson, I assume that your answer regarding the muscle relaxants includes the acute problems such as the acute low back sprains.

My only reason in asking this question is that in our hands the muscle relaxants have been disappointing in chronic rheumatic diseases, but I am informed by some doctors that in the very acute situations these compounds have definite value.

DR. DICKERSON: I don't want to say that the muscle relaxants don't have a value, but you can give the patients A.P.C. tablets or placebos and obtain some effect, so that I think one should guard against attributing the occasional improvement to muscle relaxants. The improvement which is seen occasionally with the use of methocarbamol is usually no greater than the improvement which would have been seen if nothing had been given or if a placebo or some salicylate had been given.

DR. NORCROSS: Here is a question to the panel: What is your treatment for an immediate sensitivity reaction to an injected "caine" drug in an adult?

DR. LATONA: I'll give you an example. An otolaryngologist used procaine hydrochloride, and the patient had a "caine" reaction. I walked in, and I didn't know whether to treat the doctor or the patient—I wondered which one was in most shock.

I don't know just what can be done for the immediate sensitivity-type reaction. I frankly think that if the patient is going to come out of it he is going to come out of it. If he goes into convulsions, the treatment consists of intravenous barbiturates.

DR. NORCROSS: I think that there is only one possible answer to the question as it is asked. That is the immediate use of an antihistamine agent, either intravenously or, if the reaction is very critical, by intracardiac injection together with the administration of hydrocortisone by intravenous or intracardiac route. The use of the intravenous barbiturates is helpful only when the individual has palpitation, tachycardia, convulsions, or syncope. A true anaphylactic reaction must be treated heroically.

DR. DICKERSON: There are three general types of sensitivity reactions: cutaneous manifestations, cardiovascular collapse, and convulsions. If the person simply is having a cutaneous rash or a similar reaction, intravenous Benadryl or pyribenzamine, 25 to 50 mg., is in order. If a person has a convulsion, then an intravenous barbiturate such as Seconal sodium, 25 to 50 mg., is in order. If a person has cardiovascular collapse, then intravenous Neo-Synephrine, 0.2 to 0.5 mg., is in order.

A word of caution may be indicated in reference to epinephrine, which has a tendency to produce ventricular fibrillation in the presence of anoxia. Also, caution is indicated in the use of the respiratory stimulants, such as Coramine, which have a tendency to produce convulsions.

Dr. Norcross: I have no other questions. It has been a pleasure to appear before you, and I know that I speak for all the members of this panel.

Credit policy of small hospitals

A smaller hospital's credit policy must be adapted to the economic pattern of the community it serves, according to an article by Cletus J. Turnbach, in the July 1, 1962, issue of *Hospitals*. As most rural hospitals serve agricultural populations the general credit policy must be correlated to seasonal fluctuations in income. This results in a lag in the collection of accounts receivable; for instance, a cattleman admitted as a patient in January may not sell his stock until June, at which time he will be in a position to pay his accounts.

The smaller hospital is directly connected with the geographic area, with about 90 per cent of its patients coming from the immediate vicinity. In contrast, a larger hospital will serve not only its metropolitan area but also a large peripheral region. Because of its close relationship with its community, the smaller hospital must follow the local business policies in actual billing and collection procedures.

Hospitals are among the largest grantors of credit in the country. However, in contrast to industry and commerce which use credit to increase the volume of business, hospitals use it solely to collect for services. Hospitals are faced with a paradox particular to them: Because service is the cornerstone of the hospital, it must be given, when needed, without regard to the financial situation of the patient.

The key to sound hospital credit is a coherent and functional billing and collecting policy, one that is simple and flexible and keyed to the local economic pattern. It should insure both equitable collection and facility in dealing with financial conflicts.

In most hospitals there is a close personal relationship between the various officials and staffs of the hospital and the members of the community. Under such circumstances, a more flexible billing and collecting procedure is often possible and even necessary. Personal acquaintance may result in an alteration in policy based on personal knowledge of the financial situation.

The smaller hospital is faced with a possible lag in collections, in comparison with the larger hospital. Other factors to be taken into consideration are the Blue Cross payment policies, number of patients covered by Blue Cross and other third party plans; state and county payment policies; and physician delay in completing medical records.

There are certain other factors over which the hospital has no control, but of which it must be aware. When the hospital is forewarned, it can make appropriate allowances for such factors as strikes, recessions, crop failures, chronically ill patients, epidemic sicknesses, and seasonal unemployment.

Levels of Physiologic Leukocytosis

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It is of considerable interest to review some pertinent literature concerning physiologic leukocytosis, especially in regard to the incidence of levels of total blood leukocyte counts in the range of 15,000 to 20,000.

When during routine annual periodic health examinations we first encountered such levels of total blood leukocyte counts which proved to be of nonpathologic cause, these levels of physiologic leukocytosis were supposed to be rare. Todd, Sanford, and Wells in 1953[1] stated "that physiologic neutrophilic leukocytosis is never very marked and the count seldom exceeds 12,000 or 14,000 per cubic millimeter."

For the purpose of this report we have termed those levels of total white blood cell counts between 15,000 and 20,000 as "marked physiologic leukocytosis" to delineate them from the range of the "borderline" or "slight" (10,000 to 11,999) and "moderate" (12,000 to 14,999) levels of physiologic leukocytosis.

We studied the incidence and significance of these levels of physiologic leukocytosis found among 875 employes who were in apparent good health at the time of their annual periodic health examination. The blood counts were done simultaneously.

Factors concerned in physiologic leukocytosis

Wintrobe[2] states that the leukocyte count in the circulating blood of the normal adult is between 5,000 and 10,000 per cubic millimeter and that leukocytosis refers to an increase in the total number of leukocytes above 10,000 or 11,000 per cubic millimeter. Under the term "physiologic leukocytosis" he discusses a number of factors which cause values of above 10,000 in apparently normal individuals. Garrey and Bryan[3] and Sturgis and Bethell[4] have written excellent and comprehensive reviews on the changes in the total white blood cell counts under different physiologic conditions. Garrey and Bryan[3] indicated that 11 per cent of apparently normal persons showed values above 10,000. Since daily and hourly variations are to be considered, they concluded that under basal conditions the morning leukocyte count will range in a great majority of white blood counts between 5,000 and 7,000 and that after an hour of recumbent rest in the afternoon, 90 per cent of the total leukocyte counts will fall within the limits of the morning basal counts.

Kennon, Shipp, and Hetherington[5] showed that the variations from count to count were due to changes in the granulocytes but were not rhythmic and were very slight, varying from 100 to 400 cells between the lowest and highest counts of the day. In one instance the maximum variation was 900 cells, and in another it was 1,800 cells. They could find no evidence of a "digestive leukocytosis" after breakfast or a light lunch.

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Medlar[6,7] stated that variations in the total white blood cell count of 50 per cent and in the differential count of 8 per cent may occur if repeated tests are done at five- to ten-minute intervals over a two-hour period and at unpredictable intervals. Therefore, fluctuations must be greater than these figures to be significant. He noted no significant effects of random activity if the activity is limited to mild exercise. He believed that complete relaxation, such as a night's sleep or two hours in bed, appears to bring about a more irregular distribution of the leukocytes both in the total and in the differential count than is present during a state of normal activity. Barnett[8] found that the statistically unavoidable error in differential leukocyte counts in enumerating 100 cells is about 15 per cent. Goldner and Mann[9] found that for differential leukocyte percentages ranging between 30 and 70, the maximum statistical variation is approximately ±6 per cent when 200 cells are counted. As regards routine leukocyte counting, the magnitude of the physiologic variations, however, are much larger than the technical errors.[10]

Fluctuations in the leukocyte count may occur throughout the day and from hour to hour. At first these were attributed to digestive activity or exercise, but they are known now to arise even when either of these factors is controlled or excluded. Sabin *et al.*[11] showed that the white blood cell count increased in the afternoon, independent of food intake, and attributed the entire increase to a change in the number of neutrophils. But, as already noted, Garrey and Bryan[3] were of the opinion that irregular and pronounced oscillations may occur throughout the day, but not rhythmically. Schweizer[12] found that counts taken during activity were not uniformly higher than those taken during complete rest. Bryan, Chastain, and Garrey,[13] however, showed that after severe exercise there was an average of 5,165 cells higher (the range being 3,580 to 7,244) when compared with the resting count and an average of 1,151 cells higher (the range being 331 to 2,988) between that after mild activity and the resting counts in persons whose basal counts were above the 6,000 to 7,000 level. Leukocytosis as high as 35,000 per cubic millimeter has been recorded in a racer after a quarter-mile race lasting less than one minute. Isaacs and Gordon[14] found that exercise may raise the polymorphonuclear leukocyte percentage even to 94.7 per cent. The leukocytosis after exercise is believed to be due to circulatory shifts with the liberation of sequestered leukocytes from unused capillaries throughout the body. Its degree depends on the intensity and duration of the exertion, according to Edwards and Wood[15] who found averages of 12,000, 15,000, 18,000, and 23,000 after each succeeding quarter in football players throughout an entire game. Garrey and Butler[16] showed that the emotions of fear, rage, and apprehension may raise the leukocyte count to activity levels. Excitement alone, without activity increase, may fail to affect the count.[15] In some persons the leukocytosis may be due to an increase in lymphocytes instead of polymorphonuclear leukocytes, as reported by Garrey and Bryan.[3] Sturgis and Bethell[4] state that cells of both types are returned to the circulating blood following muscular activity, but in one person the lymphocytes may be swept into the circulation from a large reservoir of lymphocytes stored in the lymphatic system,[17] while in another it may be the polymorphonuclear cells from a reservoir of these cells which are sequestered in the inactive capillaries of the spleen, liver, lungs, bone marrow, and muscles. In general, the lymphocytes more commonly respond to short severe exercise, whereas the neutrophils respond to prolonged exertion.

Bookman and Fraad[18] made weekly observations on 14 members of a football team during a period of ten weeks of almost daily and strenuous exercise. They noted that prolonged exercise and training do not have an appreciable effect on the percentage of polymorphonuclear cells in the counts. They emphasize that this is rather remarkable, since the total white blood cell counts during energetic practice and actual contest must have fluctuated violently.

Materials and methods

One thousand of our employes were originally used for this study. They were taken unselectively from the daily quota of those appearing for their annual routine periodic health examination; only those were purposely excluded who were known to be currently sick or returning from an illness of any kind within the past two weeks. They were all adults and consisted of executives, clerical workers, policemen, and laborers. Their work varied from sedentary, to moderately active, and to heavy manual duty.

They were all examined while at "random activity." In the morning session the employes reported, usually after breakfast, directly to the clinic before working. In the afternoon session they came after lunch from their usual activity, either clerical or heavy manual duty. All had been inactive for a half-hour in the clinic except for the usual sitting and walking about. None were at bed rest. The blood was drawn by finger puncture before any preventive inoculations, such as tetanus toxoid, were given and at the same session as the periodic health examination itself was held.

The technic was not different from that performed in a good routine laboratory, except that the total white blood cell counts were done in duplicate, using separate pipets on two separate drops of blood. The differential white blood cell counts were made by the usual technic of smearing and counting 100 cells.

The neutrophilic polymorphonuclear cell percentages recorded consist of the sum of the segmented and unsegmented neutrophilic forms. The physical examinations by the examining physicians were thorough. The men were completely stripped; ear, nose, throat, lymph node, chest, abdomen, skin, and rectal examinations, including digital, were done. In females pelvic and rectal examinations were omitted. In any instance in which a previous history or current symptoms showed a pelvic examination to be indicated, the case was excluded from the study. If the subject gave any history of the presence of even a slight infection of the respiratory tract, skin infection, gastroenteritis, and so forth, the subject was excluded from the study. The same exclusion was made for abnormal urinary findings, such as pus or blood. Such excluding conditions were especially sought for by the examining physician at the time of the physical examination. Fluoroscopic chest examinations were done on all who did not have a chest x-ray film taken, and electrocardiograms were done on all those over the age of forty-five. An adequate follow-up interval was allowed to elapse before the final thoroughly detailed review of the medical charts was undertaken to determine the presence of subsequent diseases which might have been deemed to be present or related to the time of the blood count. The shortest interval was two months. It was found that 125 employes had to be excluded from the study. The remaining 875 were classified as apparently healthy, and these comprise the study group.

Analysis of the data

In Table I the frequency distribution of the total leukocyte counts of our 875 employes, taken at random activity, is shown. The minimum was 4,100, and the maximum was 20,850, with a mean of 9,552. The total leukocyte counts in the 95 per cent range were 4,402 to 14,702. The findings are similar to those of Donahue[19] in his study of truck drivers on duty, in which he found the minimum to be 4,900 and the maximum 19,200, with a mean of 9,876. His 95 per cent range was 4,876 to 14,877. Chamberlain, Turner, and Williams[10] in a study of atomic energy workers, found a mean of 7,741 with a 95 per cent range of 4,500 to 12,100.

We also found that 39.08 per cent of our 875 employes had total leukocyte counts above 10,000; 16.8 per cent were above 12,000 and 3.2 per cent above 15,000.

In Figure 1 the cumulative frequency curves illustrate the incidence of "moderate physiologic leukocytosis" (12,000 to 14,000) and "marked physiologic leukocytosis" (15,000 to 20,000). They elucidate in more graphic detail not only the incidence but also the magnitude of these conditions in

TABLE I. Frequency distribution of leukocyte counts taken at random activity from 875 apparently healthy employes during an annual periodic physical examination*

Total Leukocyte Value	Frequency Distribution
4,000 to 4,999	14
5,000 to 5,999	48
6,000 to 6,999	80
7,000 to 7,999	110
8,000 to 8,999	149
9,000 to 9,999	132
10,000 to 10,999	116
11,000 to 11,999	79
12,000 to 12,999	55
13,000 to 13,999	42
14,000 to 14,999	22
15,000 to 15,999	15
16,000 to 16,999	5
17,000 to 17,999	1
18,000 to 18,999	5
19,000 to 19,999	1
20,000 to 20,999	1

* Maximum: 20,850.
Minimum: 4,100.
Standard deviation: 2,628.
Mean: 9,552.
Coefficient of variation: 27.51.

our current study and those of three others done at random activity.

In Figure 2, our current study done at random activity is compared with that of eight other studies showing the frequency distribution curves of leukocyte counts in apparently normal adults. In three studies done under basal conditions, Bryan, Chastain, and Garrey,[13] Shaw,[20] and Torday[21] found no total leukocyte counts above 10,000. The study by Schweizer,[12] however, also done at morning rest, showed total leukocyte counts as high as 11,500. The frequency curves of total leukocyte counts for those normal adults done at random activity show a higher range in leukocytosis levels. These include Osgood,[22] with an upper limit of 13,250; Galambos,[23] with an upper limit of 12,500; Donahue,[19] with an upper limit of 19,200; and Chamberlain, Turner, and Williams[10] with an upper limit of 16,000. In our current study, the upper limit is 20,850.

The differential white blood cell counts in the 119 cases of physiologic leukocytosis with total white blood cells above 12,000 were analyzed. The average neutrophilic polymorphonuclear percentages for the various levels of total leukocytes varied from 56 to 74. The range of the individual percentage of neutrophilic polymorphonuclear leukocytes in the moderate physiologic leukocytosis level (12,000 to 14,999) was from 45 to 88, but only in 4 cases (3.4 per cent of 119 cases) was there an 80 or higher percentage. In the cases of "marked physiologic leukocytosis" (15,000 to 20,999), the average percentage of neutrophilic polymorphonuclear leukocytes was somewhat higher. However, the range of individual percentages was from 48 to 82, with 4 cases (14.3 per cent) showing a percentage of 80 or higher of neutrophilic polymorphonuclear leukocytes. In the 728 cases in which the range of the total leukocyte count was between 4,000 and 11,999 we found only 3 cases (0.41 per cent) that showed 80 per cent or higher of neutrophilic polymorphonuclear leukocytes.

The incidence of low total white blood cell counts was noted in our study (Table I). No instance of a total leukocyte count below 4,100 was encountered in the 875 apparently normal adults while they were at random activity (Table I, Fig. 2). There were 14 cases of total white blood cell counts below 5,000; that is, "relative leukopenia" still within the limits of normal variation.

Comment

When during annual periodic health examinations we first encountered blood leukocyte levels of 15,000 to 20,000, which proved to be of nonpathologic cause, these levels of physiologic leukocytosis were supposed to be rare. Some of these healthy employes were subjected by their own physicians to extensive investigations, including hospitalization and diagnostic and therapeutic procedures, because there had been an impression from the general clinical knowledge of blood counts that this level of leukocytosis was most likely due to an undiscovered pathologic cause.

In reviewing the literature, several basic papers written on normal leukocyte counts seemed to confirm such an impression of rarity. Studies done under basal conditions by Bryan, Chastain, and Garrey,[13] Shaw,[20]

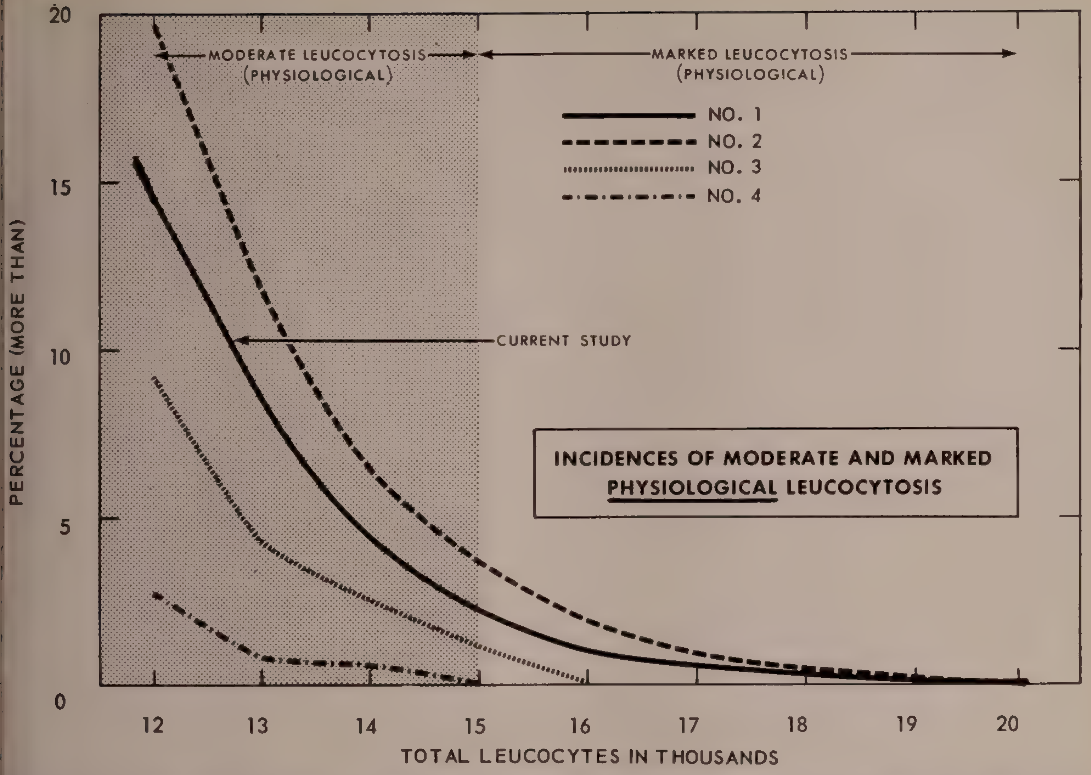

FIGURE 1. Cumulative frequency distribution of normal adults made by other authors, compared with the leukocyte counts of Port Authority employes made in this study. 1. Random counts of employes in this study. 2. Random counts of truck drivers.[19] 3. Counts of police officers coming off tunnel duty.[26] 4. Random counts of workers in the hatters' fur-cutting industry.[25]

Torday,[21] and Kuhnke[24] showed no total leukocyte counts above 11,000. Even studies by Galambos[23] and Neal *et al.*[25] of counts done at random activity did not reach the 15,000 level.

In our present study of 875 employes at random activity, we found that 39.08 per cent had leukocyte counts above 10,000, 16.8 per cent above 12,000, and 3.2 per cent above 15,000 (Table II). Thus, our studies show a greater incidence of physiologic leukocytosis at the "above 12,000 level," and what is more important, even at the "above 15,000 level." As already noted, Todd, Sanford, and Wells[1] state that this type of physiologic leukocytosis "is never very marked and the count seldom exceeds 12,000 or 14,000." Thus, our incidence of a level of leukocytosis between 15,000 to 20,000 is of considerable magnitude.

The confirmation of our findings of a higher incidence of "marked physiologic leukocytosis" and "moderate leukocytosis" (12,000 to 15,000) under similar clinical conditions can be found in the literature. In 1932 Murray and Russell,[26] in a United States Public Health Service survey of 173 of our Holland Tunnel police officers coming off tunnel duty, found that 24.85 per cent had leukocyte counts over 10,000, 9.25 per cent over 12,000, and 1.16 per cent over 15,000. Neal *et al.*, in 1937,[25] examined 293 men in the hatters' fur-cutting industry, taken randomly from the street, and found that only 9.89 per cent had a leukocyte level above 10,000, 2.73 per cent above 12,000, and none above 15,000.

In 1941, Donahue[19] reported on leukocyte counts in a study of the effects of fatigue and hours of service on interstate truck drivers. From his study we note that 45.06 per cent had total leukocyte counts over 10,000, 19.63 per cent over 12,000, and 3.67 per cent over 15,000. He emphasized that the total

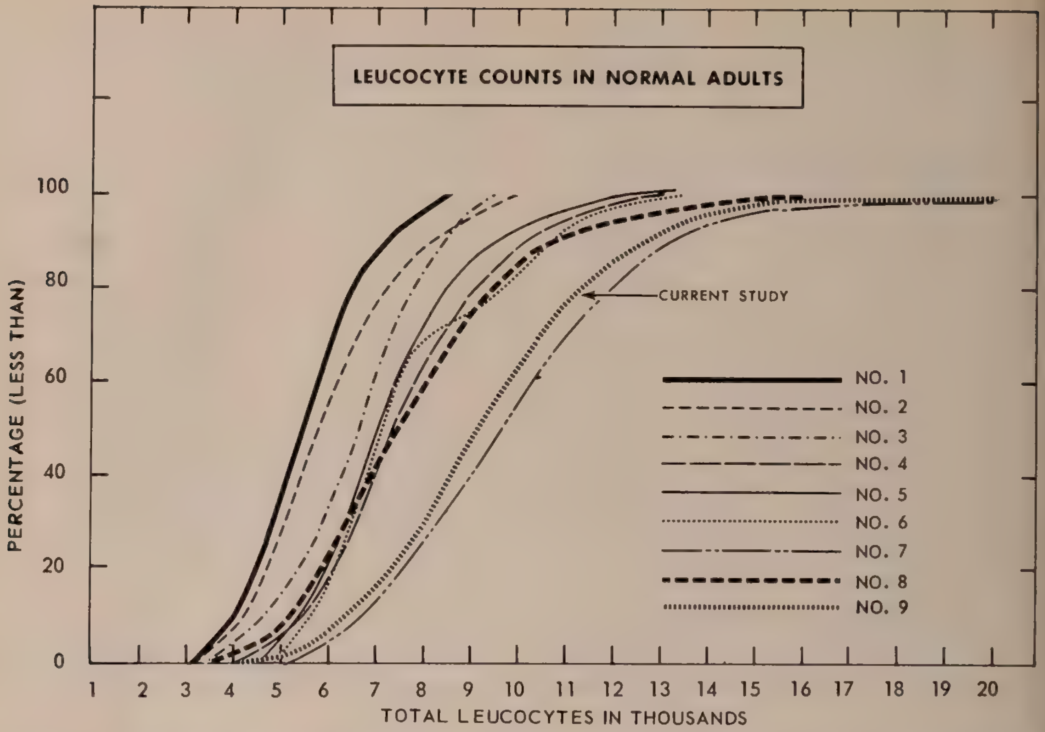

FIGURE 2. Cumulative frequency distribution curves of leukocyte counts of adults made by other authors[3,19] compared with the leukocyte counts of Port Authority employes in this study. 1. Counts after one hour's recumbent rest in the morning.[13] 2. Morning rest.[20] 3. Morning counts on fasting subjects.[21] 4. Random counts throughout the day.[23] 5. Random counts.[22] 6. Counts during morning rest.[21] 7. Random counts of truck drivers.[19] 8. Pre-employment leukocyte counts on employes in an atomic research establishment.[10] 9. Random counts of employes in current study.

leukocyte levels he found in 708 truck drivers coming off duty were higher than those usually reported for the general population. Donahue attributed these findings to the effect of work fatigue and hours of service. These are the "physiologic" factors which he stresses. In our study, other factors in addition to muscular fatigue may be operative inasmuch as our study included sedentary workers who did not have any heavy duty muscular work.

In regard to the significance of the differential portion of the leukocyte count, we have studied the average, range, and number of cases with "over 80 per cent" neutrophilic polymorphonuclear leukocytes. "Over 80 per cent" was selected to be certain that the neutrophilic polymorphonuclear leukocyte percentage would be definitely above the 54 per cent mean average of Osgood[22] and the range of 60 to 70 per cent which is given by Todd, Sanford, and Wells[1] as the normal range of polymorphonuclear neutrophils in the normal adult in the United States. The literature reveals that neutrophilic polymorphonuclear leukocytes contribute in a large way to physiologic leukocytosis under special conditions, such as vigorous exercise, strong emotions, and so forth. Our data show that at random activity physiologic neutrophilic polymorphonuclear leukocytosis is a marked factor in at least 8 of the 147 cases (5.4 per cent). Recognizing that neutrophilic leukocytosis still contributes to the raised leukocyte level in the remaining cases, it may be said, however, that to a considerable degree the total number of lymphocytes must contribute to the higher level of leukocytosis. In our current study the average mean percentage for polymorphonuclear leukocytes is 60.9 per cent, and the average mean is 35.8 per cent for the lymphocytes. Donahue[19] reported his impression that commercial truck drivers

TABLE II. Details of blood counts in the 28 cases showing physiologic leukocytosis—above 15,000

Hemoglobin* (Gm.)	White Blood Cells 1	White Blood Cells 2	Differential: Neutrophils†	Lymphocytes	Eosinophils	Monocytes
15.5	14,950	15,100	69	30	1	. . .
14.3	18,950	18,900	71	29	. . .	. . .
15.1	15,700	15,650	76	24	. . .	. . .
16.0	15,350	15,300	68	32	. . .	. . .
15.1	15,300	15,250	68	30	2	. . .
12.6	15,900	16,150	81	16	2	1
13.2	15,750	15,950	75	23	2	. . .
15.2	16,450	16,200	63	32	3	2
15.2	18,500	18,250	80	20	. . .	. . .
14.3	15,250	15,350	81	15	3	1
13.4	18,150	18,200	71	27	. . .	2
13.9	18,950	19,100	56	35	2	7
15.9	16,550	16,200	64	32	2	2
15.3	18,500	18,550	75	18	3	4
16.2	15,000	15,350	61	35	2	2
13.4	15,000	15,500	58	32	7	3
13.9	15,350	15,300	72	19	1	8
14.8	16,500	16,700	67	29	1	3
13.0	15,550	15,500	58	37	2	3
16.4	18,100	18,000	73	24	1	1
15.9	15,300	15,250	69	34	3	2
15.3	17,600	17,900	78	20	. . .	2
14.4	16,800	16,750	64	35	. . .	1
12.6	15,500	15,300	65	32	1	2
13.0	15,000	15,100	82	13	. . .	5
14.8	20,800	20,700	60	36	. . .	4
14.4	16,750	16,600	59	36	2	3
17.7	15,700	15,650	61	36	. . .	3

* Method Used: Photoelectric determination of hemoglobin as oxyhemoglobin (Van Bruggen).
† Polymorphonuclear leukocytes—sum of segmented and unsegmented.

showed a higher percentage of lymphocytes than that which he believed to be found in the general population. However, he noted no significant change in the percentage of lymphocytes when comparing the before-duty and the after-duty counts of those who did eight hours of driving. His study of the total leukocyte counts does not approach those high levels of 27,000 and 35,000 found after strenuous exercise, such as are quoted by Sturgis and Bethell.[4]

Garrey and Bryan[3] reviewed in detail their own and other authors' data showing the occurrence and the degree to which lymphocytosis as well as neutrophilic polynucleosis contribute to the total count, such as in exercise (short or prolonged, in the trained and untrained, in the fatigued and nonfatigued), and in persons with differences in circulatory reactions, especially those referable to "restlessness, tension, and overactivity,"[27] and "apprehension."[28]

Some of the factors which may have a bearing on our findings are mentioned in the section devoted to "Factors concerned in physiologic leukocytosis."

In routine leukocyte counting, Chamberlain, Turner, and Williams[10] found that the magnitudes of the "physiologic variations are very big and the coefficient of variation in an individual leukocyte count due to this cause over long periods is about 20 per cent." They then decided to suspend leukocyte counting as a method of radiation monitoring. For similar reasons, the National Committee on Radiation Protection and Blatz[29] concluded that blood counts should no longer be required as a method of radiation monitoring.

The importance of the repetition of the leukocyte count in classifying and evaluating cases with marked or moderate leukocytosis cannot be stressed too much. In our accessory data we have instances which illustrate the spontaneous drop in the total leukocyte levels, when taken at another time, in cases with "marked physiologic leukocytosis." Also, in pathologic cases we have examples of the well-known drop from the elevated total leukocyte levels on repetition of the count; these drops are related either to therapy or to spontaneous recovery. Thus, the repetition of the white blood cell counts, especially in conjunction with the clinical examination, may obviate the drawing of improper conclusions obtained from observational error, spontaneous variations, or uncertainty of isolated determinations, as pointed out by Sturgis and Bethell.[4] They also mention the unjustified denial of life-saving therapeutic agents to those patients with low total white blood cell counts, which are really not due to the agent being administered but are within normal limits.

The incidence of low total leukocyte counts was noted in our study (Table I, Fig. 2). No instance of a count below 4,100 was found in 875 apparently normal adults while at random activity. Fourteen cases or 1.6 per cent were below 5,000. This is in contrast to the higher figure of 6 per cent of low total leukocyte counts (below 5,000) recorded by Chamberlain, Turner, and Williams[10] on pre-employment examinations done at random activity. The importance of the smallness of the incidence of low total leukocyte counts found by us is noteworthy, in view of the designation of 5,000 as being the lower limit of normal given in the 1943 edition of the Recommendations of the British X-Ray and Radium Protective Committee,[10] and the observations of Turner[30] regarding total neutrophilic leukocyte counts.

Conclusion

1. In periodic health examinations of apparently healthy employes the incidence of a level of total white blood cell counts of 15,000 to 20,000 ("marked physiologic leukocytosis") is of the magnitude of 3.2 per cent when done at random activity.

2. This incidence of marked physiologic leukocytosis is much larger than its supposed rarity, especially when contrasted with previous studies done under basal conditions and some done at random activity.

3. It was found that not only the neutrophilic polymorphonuclear leukocytes, but also the lymphocytes contribute significantly to the physiologic leukocytosis in the cases observed.

4. No instances of total leukocyte counts below 4,100 were noted in our 875 apparently normal adults while at random activity. In only 1.6 per cent did the total leukocyte count fall below 5,000.

Summary

Total and differential blood leukocyte counts were done on 875 selected, apparently normal, adult employes at the time of a routine annual periodic industrial health examination while the subjects were at random activity. Marked physiologic leukocytosis, that is, total leukocytes between 15,000 to 20,000 per cubic millimeter without pathologic cause, was found in 3.2 per cent.

The present study, together with a knowledge of the related reviewed literature, describes the clinical leukocyte levels found under the nonbasal conditions of the usual daily health clinic and industrial periodic examination.

Lymphocytes, as well as neutrophilic leukocytes, contribute significantly to the physiologic leukocytosis observed in our cases.

In only 1.6 per cent did the total leukocyte count fall below 5,000 with none below 4,100.

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Silo filler's disease

Silo filler's disease is a lung condition that sometimes strikes workers whose chores require that they enter silos where feed is stored.

The first 2 cases of the disease were reported in 1954, but it was not clearly recognized until about 1956. Even today very few individuals are acquainted with the facts about silo filler's disease and its importance.

The damage is caused by nitrogen dioxide gas, which is given off from freshly stored material in a silo. Much more is produced by alfalfa than by corn silage. Gas production reaches its peak within twenty-four hours and seems to be over in two or three days. The gas is heavier than air, so that it goes to the lowest available level.

It is a yellowish gas and in high concentrations may be visible as a yellowish-orange haze. Its odor is pungent. Immediately on contact with respiratory passages it causes a burning irritation. Once in the lungs it unites with the moisture there and forms nitric acid, which damages tissue on contact. Two to five minutes exposure is fatal in a high percentage of cases.

In a matter of five minutes the exposure may be so great that the person becomes unconscious. With a lesser exposure, the person complains of coughing, trouble with breathing, and weakness. There are two forms of the disease. In the acute form the patient is very ill from the start. In a milder case the patient seems to get over initial symptoms rapidly, except for a slight cough, night sweats, and progressive weakness. In this latent type the patient becomes acutely ill in about three weeks, and the disease may prove fatal at this time or leave the person a chronic invalid. However, with good medical care he may regain his health after many months.

If people are made aware of the facts, silo filler's disease can be avoided. The way to prevent it is to stay out of a silo for at least seven to ten days after putting in fresh material. —*Charles J. H. Kraft, M.D., for Council on Rural Health, American Medical Association*

Maternal Welfare

Prepared by the Subcommittee on Maternal and Child Welfare, Committee on Public Health and Education, Medical Society of the State of New York

EDWARD C. HUGHES, M.D., Syracuse, Editor

Anesthetic and Aspiration Factors in Maternal Mortalities

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THE SUBCOMMITTEE on Maternal and Child Welfare has accumulated data on 300 maternal mortalities and deaths in pregnant women, including those women who expired within ninety days after delivery. The cases occurred in New York State, exclusive of Metropolitan New York City, during the years 1956 to 1961.

The causes of death in 18 cases are placed in four categories: (1) anesthesia: primary cause (7 cases); (2) anesthesia: probably contributory (2 cases); (3) anesthesia: possibly contributory (3 cases); and (4) aspiration (6 cases). The anesthetic agents used for vaginal deliveries and cesarean sections are listed in Table I.

An anesthetic agent was administered by a physician anesthetist in 13 cases. One anesthetic agent was given by a resident anesthetist, and one was given by an intern. The qualification of the anesthetist was not recorded in the other 3 cases. Six cases received oxytocics prior to delivery, either for induction or stimulation of labor. Pitocin (oxytocin injection) was used in 5 instances, and quinine was used in 1. No significant pattern of medication during labor or preliminary medication was apparent. Each case will be summarized briefly.

Case reports

ANESTHESIA (PRIMARY CAUSE). *Case 1.* A twenty-nine-year-old gravida 3 was admitted at term with irregular pains. She was given two doses of 5 grains of quinine. The medication during labor consisted of 50 mg. of meperidine hydrochloride (Demerol) and an unknown dose of atropine. To induce anesthesia the patient was given trichloroethylene (Trimar), which was started at 2 per cent and increased to 5 per cent. She developed tetanic contractions, rigidity, and cyanosis. The patient expired ten minutes after a spontaneous delivery. The death was signed out as an amniotic fluid embolus, but this was not confirmed by an autopsy. There was no other explanation of the mortality, the death seemed apparently due to an anesthetic reaction.

Case 2. A twenty-eight-year-old gravida 2 was diagnosed as having an intrauterine death at eighteen weeks of gestation. The patient developed a depression psychosis, and the pregnancy was interrupted by a vaginal hysterectomy under anesthesia induced with thiopental sodium (Pentothal sodium) and maintained under cyclopropane. The preliminary medication consisted of 2 mg. of Dramanine and 1/150 grains of atropine. The patient developed cyanosis during anesthesia, failed to respond, and expired one and three-quarters hours after the induction of the anesthetic. An autopsy failed to determine the exact cause of death. The clinical impression was that death was due to an anesthetic reaction.

Case 3. A twenty-five-year-old gravida 1

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* Secretary of the Subcommittee on Maternal and Child Welfare.

TABLE I. Anesthetic agents used for vaginal deliveries and cesarean sections

Agent	Vaginal Deliveries*		Cesarean Sections	
	Anesthesia	Aspiration	Anesthesia	Aspiration
Pentothal sodium and cyclopropane	1	..	..	..
Cyclopropane	..	..	1	..
Trichloroethylene	1	..	..	..
Vinyl ether	1	..	..	..
Spinal hexylcaine hydrochloride	1	..	..	..
Saddle-block hexylcaine hydrochloride	1	..	..	..
Spinal tetracaine hydrochloride	..	..	3	..
Ether	..	1	..	..
Vinbarbital sodium	..	1	..	..
Nitrous oxide	..	1	..	..
"Gas," oxygen, and ether	..	..	1	..
Chloroform and oxygen	..	1	1	..
Chloroform	..	1	..	1
Nitrous oxide and chloroform	1	..	..	..

* Includes 1 vaginal hysterectomy.

started labor at term with a complication of preeclampsia. Her progress was unsatisfactory, and the delivery was made by laparotrachelotomy after fourteen hours of labor. The medication during labor consisted of 50 mg. of secobarbital sodium (Seconal sodium), 150 mg. of meperidine hydrochloride, $^1/_{300}$ grain of scopolamine, and $^1/_6$ grain of morphine sulfate. Anesthesia was induced by cyclopropane. The patient went into shock and expired seven hours postoperatively. No autopsy was performed. The clinical impression was cerebral edema due to an anesthetic reaction.

Case 4. A thirty-three-year-old gravida 3 was transfused prior to delivery because of severe anemia. She was delivered by a secondary laparotrachelotomy at term. The preliminary medication consisted of 50 mg. of meperidine hydrochloride and $^1/_{150}$ grain of atropine. Spinal anesthesia was induced by 10 mg. of tetracaine hydrochloride (Pontocaine hydrochloride). The patient developed shock during surgery which was stopped temporarily. Following delivery, difficulty was encountered in removing a diagnosed placenta accreta. Bleeding was controlled eventually by a hysterectomy. Shock persisted and the patient expired two hours after surgery. No autopsy was performed. The clinical impression was that shock was associated primarily with an anesthetic reaction.

Case 5. A twenty-one-year-old primipara was delivered at term by manual rotation and forceps extraction. The medication during labor was not recorded. Anesthesia was induced by 500 cc. of vinyl ether (Vinethene) by the open-drop method. Ten hours after delivery the patient developed chills and fever. She went into shock and died thirty-two hours post partum. An autopsy revealed a central lobular necrosis of the liver, probably vinyl ether poisoning, associated with subacute hepatitis.

Case 6. A thirty-six-year-old primipara was hospitalized at term because of severe preeclampsia. She was delivered by an elective cesarean procedure. Her preliminary medication consisted of 0.050 Gm. of meperidine hydrochloride and 0.0004 Gm. of scopolamine. There was technical difficulty in administering the spinal anesthetic, but 15 mg. of pontocaine hydrochloride was given between the first and second lumbar vertebrae. The patient lost consciousness, and a rapid low-flap section was done. Shock persisted and the patient expired five hours later. An autopsy revealed a mild coronary arteriosclerosis, but it appeared that death was due to an anesthetic reaction.

Case 7. A thirty-four-year-old gravida 5 was delivered by a secondary cesarean section at term. A preliminary medication consisted of $^1/_{150}$ grain of atropine sulfate (the patient requested a general anesthetic, refusing a spinal block). Anesthesia was induced with chloroform and oxygen. Cyanosis developed immediately postoperatively. The patient deteriorated and expired one and one-half hours after delivery. An autopsy revealed severe pulmonary edema and failed to confirm a clinical impression of an amniotic fluid embolus. It is felt that death was due to anesthetic factors.

ANESTHESIA REACTION—PROBABLE CAUSE OF DEATH. *Case 8.* A thirty-five-year-old gravida 2 began labor at term with a premature rupture of the membranes. She was fully dilated after two hours of labor. The patient received 60 mg. of narcotic-analgesic (Nisentil) and $^1/_{150}$ grains of scopolamine. At full dilation, she was given hexylcaine hydrochloride (Cyclaine hydrochloride) at the second to third lumbar vertebrae with a 22-gauge needle). A spontaneous delivery did not occur, and the patient was given 1 ml. of an oxytocin injection (Pitocin). Eventually she was delivered by low forceps. The patient became cyanotic and expired fifty minutes after delivery. No autopsy was performed. Since there was no stated cause of death, the case was listed as a probable anesthetic reaction.

Case 9. A twenty-nine-year-old gravida 4 had normal four and one-half hours labor of the first stage at term. The patient was apprehensive and refused a spinal block. She received 50 mg. of meperidine hydrochloride and 25 mg. of Phenergan during labor. She was induced for delivery (low forceps) with nitrous oxide and oxygen and maintained with a closed chloroform nonrebreathing technic. Immediately following delivery, the patient's pulse became rapid and irregular. She failed to respond and expired one hour and forty-five minutes post partum. At autopsy the cause of death was undetermined. The clinical impression was a probable anesthetic reaction.

ANESTHESIA (POSSIBLY CONTRIBUTORY). *Case 10.* A forty-year-old gravida 4 was admitted at term with vaginal bleeding which was diagnosed as due to marginal placenta previa. The membranes were ruptured, and an oxytocin injection was administered. Approximately five hours after induction, the patient was delivered by a cesarean section because of fetal distress. The medication prior to the delivery consisted of 10 mg. of meperidine hydrochloride and $^1/_{150}$ grain of scopolamine. The anesthetic used was gas-oxygen and ether (type of "gas" not specified). During the closure of the incision, the patient became cyanotic, failed to respond to treatment, and expired fifty minutes after delivery. The autopsy diagnosis indicated shock and anoxia during the cesarean section for marginal placenta previa. Some question of anesthetic responsibility was entertained, not necessarily due to the agents used. The anesthetist centered his attention on the resuscitation of the baby following delivery instead of remaining with the mother.

Case 11. A thirty-seven-year-old gravida 7 with inactive pulmonary tuberculosis was delivered by a cesarean section because of abruptio placentae at thirty weeks gestation. Shock treatment was started prior to surgery. The patient had a temperature of 104 F. The preliminary medication consisted of $^1/_{150}$ grain of atropine. Spinal anesthesia was induced by 10 mg. of 1 per cent tetracaine hydrochloride. (Spinal block was elected because of a tuberculosis history, and a local anesthetic was not used because of a febrile condition.) Respiratory difficulty developed during surgery, and the patient expired shortly after surgery. The autopsy findings were consistent with the clinical impression that death may have been due to an anesthetic reaction.

Case 12. A twenty-year-old gravida 1 entered the hospital at term in active labor. She had a history of childhood rheumatic fever with a residual Grade II heart murmur. The patient had fifteen hours of first-stage labor. She had a short second-stage labor during which oxytocin injection was administered intravenously. The delivery was done by a forceps rotation and a midforceps extraction. The medication during labor was not recorded. Anesthesia was induced by a saddle block anesthetic, consisting of 4 mg. of tetracaine hydrochloride. There was an immediate postpartum hemorrhage during the repair of an episiotomy. The patient developed cyanosis and dyspnea, and she expired two hours after delivery. The autopsy findings were a pulmonary collapse and minimal arteriosclerosis of the aorta. Consideration was given to the possibility that the anesthetic used was a contributory factor.

DEATHS ASSOCIATED WITH ASPIRATION. *Case 13.* A twenty-nine-year-old gravida 3 had a normal term labor, and she was delivered by elective low forceps. The medication during labor was not recorded. Anesthesia was induced by ether administered by an open-drop method, and aspiration occurred at the time of the delivery of the placenta. The patient received emergency treatment for cyanosis and difficulty with respiration, but she expired two hours post partum. The clinical impression of amniotic fluid embolus was not confirmed by an autopsy which revealed grossly hyperventilated lungs with a small amount of aspirated material in the bronchi.

Case 14. A thirty-four-year-old gravida 3 had an uneventful labor at term. The medication during labor consisted of 3 grains of secobarbital sodium, $1^1/_2$ grains of Nembutal, six doses of 2 grains of quinine, 50 mg. of meperidine hydrochloride, and $1^1/_{150}$ grains of scopolamine. Anesthesia was induced by 12 cc. of vinbarbital sodium (Delvinal sodium) supplemented by drop ether. The patient vomited a large amount of undigested food during delivery and became cyanotic. Despite suction and other emergency treatment, she expired within minutes. No autopsy was performed. The clinical impression was death due to aspiration.

Case 15. A twenty-four-year-old gravida 3 started labor at term. Her progress was poor. The membranes were ruptured, and an oxytocin injection was administered. After that there was rapid progress, and the delivery was accomplished with low forceps. The medication administered during labor was not recorded. Anesthesia was induced with nitrous oxide (airway inserted). Following delivery, the patient coughed up bright blood and stopped breathing. She expired about an hour post partum. An autopsy revealed no specific cause of death, but the clinical impression was that death was due to a cardiac arrest, subsequent to aspiration.

Case 16. A thirty-two-year-old gravida 5 whose second child had been delivered by a cesarean section was admitted at twenty-five weeks of gestation because of spotting and rupture of the membranes. The fetal heart sounds were absent. Six days after admission the cervix was dilated from 3 to 4 fingers. The patient was given oxytocin injection (method was not specified). Her labor became active, and shortly after a spontaneous delivery of a small stillborn infant occurred. Anesthesia was induced with chloroform, noted as "a few whiffs." The patient became pulseless, and emergency measures included a thoracotomy and cardiac massage. About two hours after delivery a post-partum hemorrhage occurred which was handled by an abdominal hysterectomy, apparently without anesthesia. The patient expired three hours post partum. An autopsy indicated placenta accreta and possible pyelonephritis. There were 400 cc. of fresh blood in the left pleural cavity with a collapsed lung. Thick, greenish-grey material was found in the left main bronchus.

Case 17. A twenty-one-year-old gravida 4 had a five-and-one-half-hour labor at term. No medication was given during labor. Anesthesia was induced with chloroform. After the administration of 10 ml. of chloroform (there was difficulty with induction—noted as "jerky, with patient holding breath"), respirations ceased. Despite emergency treatment, the patient expired within a short time. An autopsy indicated aspiration of the stomach content into the tracheobronchial tree.

Case 18. A twenty-six-year-old gravida 1 had normal term labor, approximately eighteen hours, which was terminated by a breech extraction with Piper forceps to the aftercoming head. The medication during labor consisted of 40 mg. of narcotic-analgesic and $^1/_{150}$ grain of scopolamine. The second stage of labor was recorded at twenty minutes. Anesthesia was induced with chloroform and oxygen, with difficult induction. Respirations ceased during the delivery of the head but resumed, and an episiotomy was repaired. Emergency measures were unsuccessful, and the patient expired five and one-half hours post partum. An autopsy indicated copious amounts of mucoid material throughout the tracheobronchial tree, emphysema of the right lung, and a left hemothorax. Death was ascribed to aspiration.

Comment

It is obvious that most of the anesthetic agents used commonly in obstetrics will occasionally have untoward effects. The case summaries make it apparent that a reaction to the anesthetic agent is not always the actual cause of death. Other factors include improper dosage, faulty technic of administration, and a lack of delivery unit organization, with insufficient or improperly trained personnel available. Anesthetic agent responsibility in the aspiration cases is difficult to evaluate, and it may well be that aspiration would have occurred regardless of the type of anesthetic used.

It may be significant that chloroform, which we do not feel is used widely for obstetric anesthesia, was seemingly involved in an unusually large proportion of the cases (5 of 18 or approximately 28 per cent). It is of interest that local anesthesia was not recorded in any of the cases in the series as a possible factor in a mortality.

766 Irving Avenue, Syracuse 10

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Tonsillectomy and Resuscitation

THE INTRODUCTION of closed chest cardiac massage has provided the physician with a means of cardiac resuscitation which can be instituted immediately and which may save many lives. However closed-chest massage must be applied properly.

Case reports

CASE 1. A three-year-old white male was admitted early in the morning on a Tuesday for elective tonsillectomy and adenoidectomy. The tonsils and adenoids were said to be so large that the airway was obstructed at night and the breathing was often stertorous. There was no other significant history or physical findings.

At 8:30 A.M. atropine sulfate $^1/_{250}$ gr. was administered intramuscularly. At 9:10 A.M. open drop Vinethene induction was begun, and soon after, open drop diethyl ether was administered. There was one episode of cyanosis during the induction. A precordial stethoscope was placed, and the heart sounds were monitored continuously. Surgery began at 9:20 A.M. after a mouth gag and ether hook had been inserted. Maintenance was by ether-oxygen insufflation through an Edison vaporizer. Surgery progressed uneventfully except during the removal of the second tonsil when an episode of cyanosis was corrected by increasing the oxygen concentration insufflated. The administration of ether was continued up to the completion of surgery. Surgery was terminated at 10:10 A.M. after which the child quietly stopped breathing, and the heart sounds became no longer audible.

Immediately the surgeon began to compress the thoracic cage laterally and to press intermittently on the lower third of the sternum. The child was on a soft mattress which could be depressed a minimum of 5 cm.

The anesthetist administered positive pressure oxygen by face mask using an anesthesia machine which was in the room for just such a purpose. She then intubated the trachea. No material was aspirated from the tracheobronchial tree. The pupils were in middilatation. An electrocardiogram taken ten minutes after apnea had supervened showed deteriorating ventricular complexes at a rate of 50 per minute. There was no palpable pulse at this time in spite of the sternal compression. Within ten more minutes the electrocardiogram showed no activity. The blood loss had not been excessive.

A complete autopsy revealed no findings which could explain the death.

CASE 2. A fourteen-year-old Puerto Rican male was admitted for elective tonsillectomy and adenoidectomy. He was subject to attacks of bronchial asthma for which he received ephedrine. Because he suffered an attack of asthma on the day of admission, surgery was delayed until his third hospital day, at which time his lungs were clear to auscultation. No other significant history or physical findings were noted.

After fasting he was given premedications of 0.4 mg. of scopolamine and meperidine hydrochloride, 25 mg., at 7:10 A.M. The child

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Presented and discussed at a conference held at Bellevue Hospital, New York City, June 4, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

was apprehensive before the induction.

At 8:15 A.M. induction was begun with 2 L. each of nitrous oxide and oxygen and 0.3 per cent halothane. There was a brief excitement phase. Succinylcholine 40 mg. was administered intravenously to facilitate orotracheal intubation which was accomplished with skill atraumatically. The tonsillectomy began, and anesthesia was maintained with 2 L. each of nitrous oxide and oxygen plus from 0.5 to 1 per cent halothane. Respirations were assisted at all times. The blood pressure ranged from 110/60 to 100/50 mm. Hg. The pulse was 140 per minute on intubation and decreased to 96 per minute through the procedure. The surgery proceeded uneventfully for sixty minutes. While the surgeon was waiting for bleeding to stop after removing the second tonsil, the pulse and blood pressure suddenly became unobtainable. The surgeon immediately began to depress the sternum rhythmically and forcibly and produced a peripheral pulse with each compression. A spontaneous pulse returned in five minutes at a rate of 90 per minute with blood pressure of 90/50 mm. Hg. The pupils had been in mid-dilatation and began to constrict. Spontaneous respirations returned within forty minutes. An electrocardiogram taken twenty minutes after the arrest showed normal configuration. The boy was extubated one hour after the cardiac standstill and was crying and moving purposefully before leaving the operating room. He was discharged from the hospital without apparent sequelae on the third postoperative day.

Comment

There are numerous differences between the anesthetic management of these 2 cases. The first case was monitored by a precordial stethoscope which did not seem to serve as an adequate early warning. It may well be that the heart sounds do not correlate well with the cardiac output, and that blood pressure or pulse amplitude is more satisfactory as an index of cardiac output.

The second case had an endotracheal tube in place from the beginning of surgery while the first did not. The question as to whether children undergoing tonsillectomy should be intubated must be decided according to local hospital practice, the medical status of the patient, and the experience, skill, and preferences of the surgeon and anesthetist. But if resuscitation becomes necessary the presence of a patent endotracheal airway will save precious moments and may avoid brain damage.

In the first case diethyl ether was administered, while in the second halothane was the principal agent. We must assume in both that a momentary relative overdosage of anesthetic agent produced cardiac standstill. The patient given ether died while the one given halothane survived. The point is that there is no inherent safety in ether or in any other anesthetic agent. The administration of any anesthetic agent is associated with risk.

The principal point to be made is that the closed-chest massage in the first case was ineffective while it was effective in the second. The thorax must be on a firm unyielding surface to permit proper closed-chest cardiac massage. A peripheral pulse must be palpated with each sternal compression. If it is not, then left thoracotomy and manual systole must be performed immediately. Pressure is applied to the lower third of the sternum forcing it toward the vertebral body at a rate of 50 to 60 per minute. If the patient is lying on a firm surface, a pulse should be palpable with each compression. The floor is of course firm. A good substitute is a plywood board 3/4 inch thick about 2 feet by 3 feet in size which can be stored on the wall of the operating room, recovery room, or wherever needed. This board can be placed easily under the patient's thorax and will provide the necessary firm surface for adequate external cardiac massage.

Proper external massage might have saved the child presented as the first case.

Number one hundred twenty-six in a series of Clinical Anesthesia Conferences

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
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Carbon Monoxide Poisoning

THE NEW YORK CITY Poison Control Center was consulted concerning a patient who had been overcome by carbon monoxide poisoning in an accident in which 3 others had succumbed.

The following report relating to this case was received from Lt. A. R. Allison of the United States Naval Hospital, St. Albans:

> A twenty-five-year old white male was admitted to the sick list on November 23, 1961, transferring from Doctors Hospital in Port Jervis, New York, where he was being treated for acute carbon monoxide poisoning. The patient was involved in a hunting disaster where 3 members of a 4-man party were overcome by carbon monoxide fumes emanating from a coal fire in their hunting lodge. This occurred on November 20, 1961.
>
> He was transferred to this hospital after acute phase studies on November 23.
>
> His past history, family history, and system review were not readily obtainable but were thought to be noncontributory to the present illness.
>
> A physical examination on admission revealed a well-developed, well-nourished white male, temperature 101.2 F., normotensive. On admission the patient was comatose, showing random movements of the upper extremities, none of the lower extremities, roving eye movements, and unresponsive to spoken commands. Deep tendon reflexes were active, abdominal and cremasteric reflexes were equal and active, and Babinski reflexes were extensor bilaterally. The remainder of the general physical examination was essentially unremarkable.
>
> Laboratory work on admission revealed a white blood count of 11,300 with a normal differential; hemoglobin and hematocrit were within normal limits. A urinalysis was unremarkable except for a trace of albumin. Subsequent urinalyses were negative. Spinal tap on the day of admission showed a cerebrospinal fluid sugar of 88 mg., chloride 690 mg., and total proteins 31.4 mg. per 100 ml. The appearance was clear and colorless, no cells were noted. Serum electrolytes were within normal limits. The blood urea nitrogen was 27 mg., fasting blood sugar 75 mg. per 100 ml. Blood methemoglobin levels were done, showing 418 mg. of methemoglobin per 100 ml. of blood, the normal being from 3 to 130 mg. per 100 ml. The sputum and throat cultures were negative. Chest and skull x-ray films were within normal limits. Arterial blood studies showed an oxygen saturation of 97.8 per cent on November 25.
>
> The patient was admitted to the intensive care ward in in a comatose state. Later during the day of admission he began showing fluctuating levels of consciousness but otherwise seemed unaffected by his episode. On the day following admission he began responding to spoken commands and would answer occasional questions. His course continued to show improvement. A neurologic consultation was done on December 1, and it was the neurologist's impression that there was still evidence of impaired mental function, and he felt that there was definite organic brain syndrome manifested by both the mental changes and positive Babinski reflexes. An electroencephalogram on November 29 was interpreted as being within normal limits. Psychiatric consultation was done on November 29, and it was the impression of the psychiatrist also that the patient had an organic brain syndrome secondary to carbon monoxide intoxication, but again he felt that memory defects could

be present and that it was too early to give a final prognosis of the permanent effect. On December 15 the patient was again seen by the neurologist who felt that the patient showed further improvement, noting the mental status and affect to be seemingly within normal limits. No pathologic reflexes were evident on December 15.

Although the patient was complaining of paresthesias around the right neck and shoulder, the neurologic consultant was unable to find definite sensory loss on his examination.

It was felt there was no contraindication to moving this patient closer to his home, more specifically the U. S. Army Hospital at West Point, New York. His only therapy at this time is multivitamins and occupational therapy. Final diagnosis: poisoning, acute, secondary to carbon monoxide.

Carbon monoxide is among the leading causes of death from poisonings.

At the present time the standard therapy for carbon monoxide poisoning consists of the use of oxygen or oxygen with carbon dioxide. Recently, the use of oxygen under two atmospheres of pressure has been proposed as a superior therapeutic measure.*

The Poison Control Center has recently brought this proposed therapy to the attention of those agencies which are most intimately involved with the treatment of such poisonings locally. The advice of a recognized authority, Alvan L. Barach, M.D., was also sought and he replied as follows:

> The principle of using oxygen under pressure for carbon monoxide poisoning seems to me to be excellent.
>
> The question involves investigation of the techniques available. A chamber similar to the one at Presbyterian Hospital could be used at two atmospheres with the technique of providing abdominal increase in tidal air when necessary. The reprints reveal the types of intermittent pressure ventilation that have been used for many years in the treatment of pulmonary tuberculosis. This could operate with an auxiliary storage chamber. Mr. Emerson also builds these chambers.
>
> Although more of an engineering job, a room could be built to function at two atmospheres and in it various types of artificial ventilation could be employed. Mr. Morris Eckman in New York, Respiration Aids, (MO 5-1511) would be able and willing to discuss any or all of these methods. He worked for me for many years as research assistant and now has a manufacturing place of his own.
>
> I think that portable oxygen refillable cylinders could be used for prevention. They could be easily carried, including the one shown in Figure 1 in the paper by Beck *et al.* in the February 10 issue of the *J.A.M.A.* Instead of the venturi, a 2-oz. sodalime container might be used. Next to the importance of prevention is, of course, the earliest possible treatment. If you think that I might be of any further help to you in your consideration of this problem, please call me.

The Chief Medical Officer of the Fire Department, Gamliel Saland, M.D., writes as follows:

> Thank you so much for permitting me to read the article in the *Lancet.** The method appears pretty safe according to all the research work that has been done to date (*Bureau of Mines Information Circular* 7575, July, 1950). The time limit for man without development of symptoms under an oxygen pressure of two atmospheres is from three quarters of an hour to three hours. I am sure a patient would not require a longer period of time than three hours.
>
> The only criticism I have of the *Lancet* report is that the exposed animals, while they were unconscious, were breathing when placed in a two atmosphere environment. Under realistic conditions a victim is not only unconscious but is not breathing and therefore a resuscitator must be used. The resuscitator as constituted today can deliver 100 per cent oxygen at atmospheric pressure with the positive phase of 14 mm. Hg and a negative phase of 9 mm. Hg. We have written to Mr. Emerson of the Emerson Resuscitator Company, Cambridge, Massachusetts, to ask him about the feasibility of delivering two atmospheres of oxygen with the resuscitator and are awaiting his reply. We shall keep you advised. I am returning your copy of the *Lancet* with this letter.
>
> P. S. I just talked to Dr. Matteo of Presbyterian Hospital, who informed me that they use three atmospheres of oxygen for patients who require radiotherapy for carcinoma. To do this, they must enclose the patient in a tank and anesthetize the patient because convulsions may occur within ten minutes. They have had no experience with two atmospheres of oxygen.

Because of the implied therapeutic advantages of this method of the use of oxygen under pressure in the treatment of carbon monoxide poisoning, it would seem most worth while to call the attention of those concerned to the verification of the British experts and to the need for development of a practical economic resuscitation apparatus. The value of this measure would appear very great in the civilian, industrial, and military areas.

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* Lawson, D. D., McAllister, R. A., and Smith, G.: Treatment of acute experimental carbon-monoxide poisoning with oxygen under pressure, Lancet 1: 800 (Apr. 15) 1961.

The Department of Health through its Food and Drug Laboratory and the Poison Control Center is now offering to perform blood carbon monoxide determinations in all cases of specific carbon monoxide poisoning (5 cc. of oxalated blood is needed for such determinations).

Number ninety-six in a series of Accidental Chemical Poisonings

Health insurance coverage in the United States

More than 135 million Americans, 74 per cent of the civilian population, had some form of health insurance at the end of 1961, the Health Insurance Council reported in its sixteenth annual survey of the extent of voluntary health insurance coverage in the United States. The survey is based on reports from insurance companies, Blue Cross-Blue Shield, and other health care plans.

Both the number of persons covered and the amount of benefits paid by health insurance reached new highs last year. Coverage increased 3.1 million during 1961 to reach a total of 135,042,000.

Benefit payments by all health-insuring organizations to help cover the cost of hospital, surgical, and medical care amounted in 1961 to more than $5.4 billion, up $600 million over 1960. In addition, persons with loss-of-income policies received $855 million in benefits from insurance companies to replace income lost through disability. Thus, a grand total of $6,329,000,000 in health insurance benefits were distributed during 1961, up 11.3 per cent over 1960.

Based on early trends for 1962 it is estimated that as of June 1, 1962, some 136 million persons had hospital expense insurance, 126 million had surgical expense insurance, 94 million had regular medical expense insurance, 36 million had major medical expense insurance, and 43.5 million were insured against loss of income or had some other formal sick leave pay arrangement.

These figures also revealed the breadth of health insurance protection which Americans have. As of June 1, 93 per cent of persons with health insurance had both hospital and surgical expense insurance, and 69 per cent had hospital, surgical, and regular medical expense insurance, the last of which helps pay for doctor visits for nonsurgical care. Five years ago, the figures were, respectively, 88 and 58 per cent.

A breakdown of the number of persons with health insurance at the end of 1961, by type of coverage and type of insuring organization, is as follows:

Hospital expense insurance was provided by insurance companies to 81,369,000 persons, by Blue Cross-Blue Shield and similar groups to 58,797,000, and by other health care plans to 5,675,000. After deducting persons protected by more than one type of insuring organization, 135,042,000 persons had hospital insurance, a 2.3 per cent increase over the 131,962,000 persons so covered at the end of 1960.

Surgical expense insurance by insurance companies covered 78,861,000 persons, by Blue Cross-Blue Shield and similar groups 50,120,000, and by other plans 6,803,000. Allowing for duplication, 125,297,000 persons had surgical insurance, a 3.5 per cent boost over the 121,045,000 persons of 1960.

Regular medical expense insurance accounted for 46,190,000 persons through Blue Cross-Blue Shield and similar groups, 44,399,000 through insurance company programs, and 7,007,000 through other plans for a total, eliminating duplications, of 92,633,000 persons, a 5.8 per cent climb over the 87,541,000 persons in 1960.

Major medical expense insurance coverage through insurance company programs increased 24.4 per cent, from 27,448,000 to 34,138,000 persons. Major medical insurance is designed to help absorb the cost of serious illnesses and pays benefits up to $10,000, $15,000, or more for all areas of care prescribed by a physician.

Loss of income found 32,055,000 persons covered by insurance company policies. The number of persons who work where there are formal sick leave arrangements brought the total figure to 43,055,000 persons.

Case Report

Abdominal Lithopedion

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From the Gynecology Clinic,
the Buffalo General Hospital

THE FOLLOWING is a case report of a patient with an abdominal lithopedion which was retained for eleven years.

Case report

A thirty-two-year-old twice-married Negro female had had one known pregnancy in 1949. She was seen at the Gynecology Clinic of the Buffalo General Hospital in August, 1960, with a chief complaint of menorrhagia of three months duration. A physical examination revealed a slightly obese woman with a protuberant lower abdomen and a hard, irregular mass palpable to the umbilicus. A pelvic examination indicated no recent bleeding, and the cervix was clean and nulliparous in appearance. The abdominal mass seemed to be a part of the uterus, although it was somewhat mobile and very hard, suggesting a large fibroid. A flat x-ray plate of the abdomen was taken which revealed a large calcified fetus lying transversely in the abdominal cavity. There was an increased calcification of the skull and body, the skull bones were flattened, and the fetus appeared to have no limiting uterine shadow surrounding it. On the right side of the pelvis there was a smaller calcified mass which was thought to represent a calcified placental site (Fig. 1).

On further questioning, the patient admitted to only one pregnancy eleven years ago. In her third month of gestation she had fallen against a tree stump in the dark

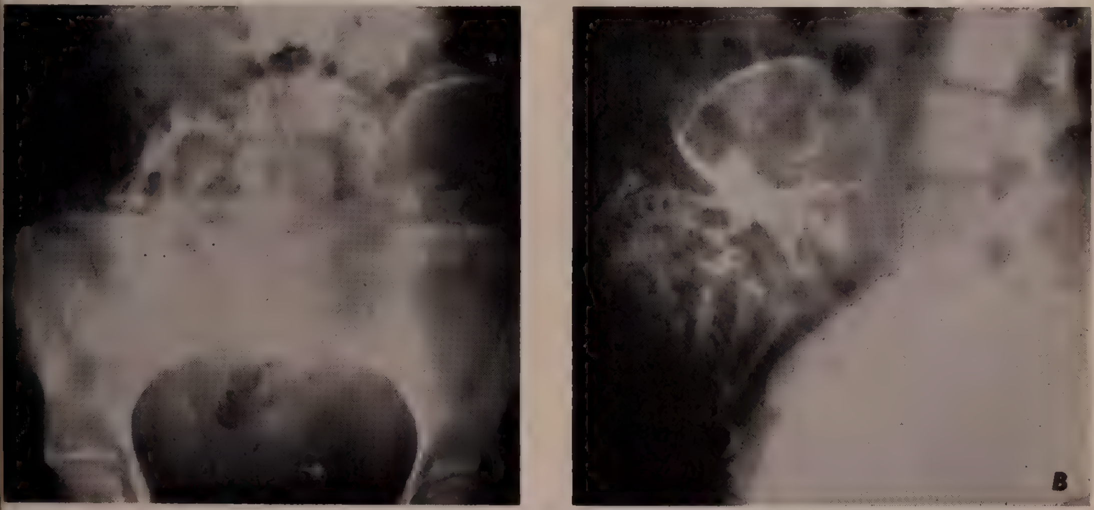

FIGURE 1. Calcified fetus. (A) Placental site is calcified mass overlying right ilium. (B) Lateral view on x-ray film.

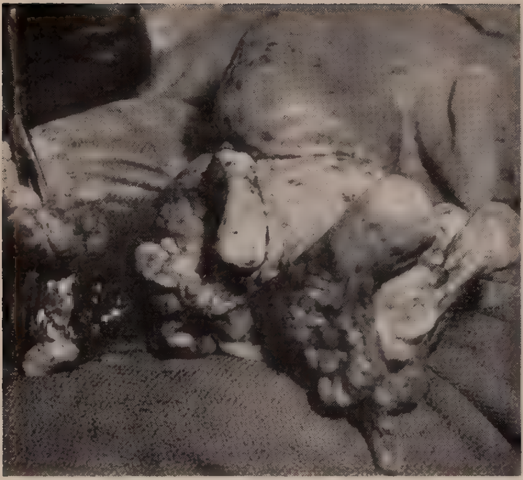

FIGURE 2. Lithopedion with omentum attached to posterior surface; hemostat on calcified end of tube with ovary posterior.

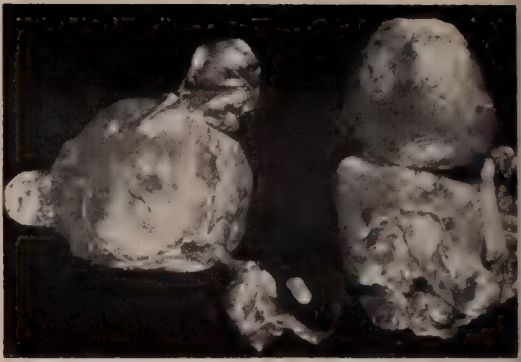

FIGURE 3. Total surgical specimen with fibroid uterus and lithopedion.

and had had severe pain in the right side. She had had moderate vaginal bleeding for four days and then had noted no further abdominal complaints. There had been no passage of tissue or clots. Her first marriage ended in divorce, and she later remarried but never became pregnant. She denied any history of pelvic infection. Her menses were always regular, lasting three days. During the past three months her periods had become progressively heavy and prolonged. Her abdomen had always remained protuberant, but this had never worried her.

A work-up consisted of Friedman's test which indicated negative findings and a hysterosalpingogram which was unsuccessful. Dye was injected into the uterine canal but flowed back into the vagina owing to an apparent obstruction at the internal os. The patient was started on a bowel preparation of Sulfathalidine for one week, and the abdomen was explored through a midline, lower abdominal incision. Attached to the greater omentum was a 20-cm. lithopedion which was remarkably free of adhesions except for the omentum. The fringed end of the right Fallopian tube contained a 4 by 3 by 2-cm. calcified mass. The right ovary was posterior to the tube and was completely free of the mass (Fig. 2). There was a hydrosalpinx of both tubes, with the left ovary replaced largely by old inflammatory cysts and densely adherent to the posterior leaf of the broad ligament. The uterus was twice the normal size and was replaced largely by fibroids. The lithopedion was delivered separately, since there was no umbilical cord or other visible attachment to the placental side of the tube. A total abdominal hysterectomy and a bilateral salpingectomy with a left oophorectomy completed the operation (Fig. 3). Postoperatively the patient did well and was discharged, enjoying her new notoriety.

Comment

When a woman has a large, irregular abdominal mass, the curiosity of the physician should be provoked enough to obtain a flat plate of the abdomen. In this case the findings were startling and were hardly in keeping with the patient's primary complaint of menorrhagia. A recent review by Woodbury and Jarrett* with a similar pathologic specimen points up the importance of this simple x-ray procedure.

An examination under anesthesia before surgery confirmed the impression of a fibroid uterus with the intra-abdominal pregnancy above, but in close proximity to, the uterus. It is presumed that this woman's fall was severe enough to cause a tubal abortion which survived for several months by the implantation of the placenta in the fimbria, only to eventually outgrow its blood supply. Unfortunately, the patient could not give accurate dates or further history of the abdominal enlargement following her fall. Her abdomen had always remained somewhat protuberant.

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* Woodbury, J. W., and Jarrett, J. C.: Abdominal lithopedion retained for 13 years. Case report with review, Am. J. Obst. & Gynec. **80**: 590 (Sept.) 1960.

Microscopically, the fimbria was a homogenous, nonspecific, calcified mass. The lithopedion had a smooth, glazed consistency and was remarkably free of adhesions except to the omentum which was attached along the back of the fetus. A crown-to-rump wedge was made in the lithopedion, and a well-preserved heart and bowel could be identified. However, it was not possible to determine the sex or distinguish facial features. The skin was of a hard, soapy consistency, and the hands and feet could not be distinguished.

It is conceivable that this lithopedion might have been carried indefinitely, had it not been for the menorrhagia, a seemingly minor complaint compared with the subsequent turn of events in this patient's life.

414 Jay Street

Physical activities in rheumatic heart patients

The restriction of physical activities in certain patients following rheumatic fever may serve no useful purpose, according to a study by Feinstein *et al.* reported in the June 23, 1962, issue of the *Journal of the American Medical Association*. This observation applies only to patients who have recovered from an acute attack of rheumatic fever without serious heart damage.

A total of 216 patients who had recovered from rheumatic fever were studied in an effort to determine whether physical and scholastic restrictions were related to the progression or development of heart disease. All of the patients were "asymptomatic," that is, they may have had abnormal heart murmurs, roentgenograms, or electrocardiograms, but strenuous exercise produced no noticeable discomfort. The patients were examined annually for an average of twenty-one years after their attack of rheumatic fever.

The results indicated that improvement or deterioration in the patients' heart condition had no direct relationship to the presence or absence of restrictions on activities. Among 141 patients whose school activities had been restricted, the heart condition of 86 per cent remained unchanged or improved while in 14 per cent it became worse. Of 75 patients with no school restrictions, the heart conditions remained the same or improved in 92 per cent while it became worse in 8 per cent.

The heart condition became worse in 15 per cent of 66 patients whose after school hours activities were restricted and in 11 per cent of 150 who observed no such restrictions. After the completion of schooling, worsened heart conditions were found in 14 per cent of 42 patients who observed restrictions and in 11 per cent of 174 patients who did not.

The psychosocial aspects of the restriction of activities also were studied. The findings indicated that in some cases restrictions had adverse effects on scholastic, occupational, and marriage plans.

Medical Memorabilia of Old Schenectady*

ELLIS KELLERT, M.D.
Schenectady, New York

ONE HUNDRED and fifty years ago the term "medical science" would have been a misnomer because so little was known of physiology, pathology, chemistry, or pharmacology. The physician had only his special senses and medical lore to guide him. No laboratory tests or specific remedies other than mercury, morphine, and quinine existed in his armamentarium. There was neither a thermometer nor a stethoscope, and the thick volume of materia medica on the physician's shelf was largely fiction. Little was known of the causes of disease, and superstition was rife. The chief usefulness of the medical practitioner was in the care of injuries, the complications of childbirth, and the setting of fractures and dislocations, the mechanics of which he understood quite well. Nevertheless, the medical graduate had the confidence of his patient, although he was well aware of the limitations of medical art.

Patients, when they were very ill, could not telephone the physician. They had to go to his office or send a messenger to call him to their homes. The doctor could not say, "Go to the hospital and I will meet you there," since hospitals did not exist. Under such circumstances, physicians became a hardy breed who rose to each emergency as it developed and by sheer native ability, fortitude, common sense, and great courage gave help to the sick although, admittedly, their knowledge of the diseases afflicting their patients was vague indeed. Since all of them were ignorant, one man's claims and ideas were as good as those of another, and since most ailments were self-limited, each practitioner seemed justified in his treatment by the outcome of the case.

Increase of scientific knowledge

The nineteenth century was a period of rapidly increasing knowledge of the natural sciences. American inventors were active and very productive, leading to the term "Yankee ingenuity." The people were avid for science information and received it in the many popular publications of the day and in the form of public lectures by prominent scientists such as Thomas Henry Huxley, John Tyndall, Agazzi, Joseph Henry, and others. Lyceums and institutes, as they were called, existed all over the country for the purpose of public instruction, and the attendance was large. Americans were eager for knowledge in all fields of human endeavor, and applied science was the favorite subject. Even physicians lectured on public health or addressed lay groups on medical discoveries.

Thus, William T. G. Morton who gave the first public demonstration of the value of ether as an anesthetic agent, lectured on this subject to a large audience in Albany in 1864 at the Albany Female Academy, a talk which netted him $3,000. He traveled throughout the country, giving lectures at which admission fees were charged, for he claimed that his efforts to introduce ether anesthesia cost him over $150,000. Morton died poor in 1868. You may recall the legal controversy that raged between him and James T. Jackson of Boston as to the priority for the discovery of ether anesthesia. As a result of the legal actions, Congress withheld a large financial award which it had planned to grant to Morton.

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* Portion of an address delivered before the Medical Society of the County of Schenectady on the Occasion of the Sesquicentennial Celebration, June 2, 1960.

Prior to 1800, Schenectady was a bustling town whose inhabitants were interested in farming, Indian trading, and furnishing supplies to the ever mounting numbers of pioneers pushing westward through the only route then available, the Mohawk Valley. Visitors came here to see the community, and some of them published their impressions. In 1768 an American lady wrote: "The first day we came to Schenectady, a little town situated in a rich and beautiful spot and partly supported by the Indian trade; though there was no polish, there was no vulgarity." Continuing her remarks, she said of the women, ". . . these unembellished females had more comprehension of mind, more variety of ideas, more original thinking than could easily be imagined."

The diet of these early residents, especially that of the farmers, consisted mainly of "sallets," probably salads, and "brawn" which was a combination of animal flesh, chopped and cooked with the edible parts of pig's head, feet, legs, and tongue. There also was pickled buttermilk to keep their phlegm from coagulating and curdling. In addition they ate "koolsloa," a sort of coleslaw, and doughnuts. Is it any wonder that after such a meal the city burghers wanted to sit quietly and smoke.

Smoking was quite common, but many men, including physicians, regarded it as an evil. It must have been a vital issue, for in 1830, at the semiannual meeting of the Medical Society of Oneida County, A. McAllister, M.D., presented "A dissertation on the medical properties and injurious effects of the habitual use of tobacco." He claimed that it caused a great variety of ills and that ". . . its antilomic or antiseptic properties depend on its sedative powers." He anticipated Freud, for he said in explaining the smoking habit: "Here is the grand secret. Man fears to be alone and when left alone to his own solitary reflections he dreads the result of self-examination. He flies for relief to his pipe, his cigar, his quid or his bottle in the vain hope of escaping from himself." The author said nothing of cigarets or of women smoking, probably unheard of in his time.

Early physicians of Schenectady

The first surgeon to visit the almost unknown Schenectady area was Harmen Meydertsz van den Bogaert, who, in 1630, traveled with two companions up the Mohawk Valley, a distance of 120 miles, on an exploring expedition. During that eventful trip van den Bogaert kept a diary which was found in 1895 in an attic in Amsterdam, Holland. This document contains the earliest written description by any American of the Mohawk Valley and the life of the Iroquois Indians. It records their adventures, the dwellings, and habits of the Indians who at that time were pleased to see the white men. Van den Bogaert noted many favorable sites for the establishment of villages. To what extent he influenced Van Curler and his associates to found a settlement here in 1661 is an interesting speculation.

Apparently the first physician of any type to practice in Schenectady was Jacobus Van Dyck who settled there in 1664. He was followed by Rynier Schaets, physician-surgeon, who came to Schenectady in 1675. This doctor and one of his two sons were killed in the massacre of 1690. Prior to their coming, Schenectady had several men who functioned as physicians and who were known as "ziekentroosters" or comforters of the sick. The small population could scarcely support a regular doctor and besides, the Dutch settlers were very healthy people. Van Dyck married a daughter of Johannes Sanders Glen in 1694 and had a son who also became a doctor.

William Adams, who settled in Schenectady in 1757, was a highly regarded physician who practiced there for more than seventy years. It is related that at the age of ninety-seven years he journeyed by stagecoach from Albany to Litchfield, Connecticut, to the home of a granddaughter. The day following this arduous trip he was seen walking about on the streets. Adams died there at the age of ninety-nine years.

Archibald Hamilton Adams, a physician, settled in Schenectady in 1806 and became the first president of this society in 1810.

Since he was a graduate of the University of Edinburgh and a talented teacher, he acquired a large number of students. One of his biographers offers the following comment on Adams:

> It is more than intimated that he had—as most men have—a failing; his was a great fondness for the weed. When his labors for the day were over, he often retired, with his long Holland pipe, the bowl resting upon the candlestick, which was placed upon a stand by his bed, and with the other end in his mouth, he regaled himself until, amid the perfumed clouds of smoke, he was lost in balmy sleep.

Adams died in 1811 at the age of forty-two years.

Beginnings of medical organization

New York was the first province to attempt the legal control of the practice of medicine. As early as 1760 candidates were examined by a commission appointed by the King. In 1806 a law was enacted requiring four years' apprenticeship which, prior to that time, was the sole means of acquiring a medical education in this country. Only three medical schools existed and they graduated only a few students. When county medical societies were formed in 1806, according to law they were authorized to decide who were qualified to practice medicine. Of course, there was a loud outcry from the numerous quacks of the day who accused the doctors of creating a monopoly.

Schenectady County was evolved from Albany County in 1809. The new laws which were passed in 1806 authorized the physicians and surgeons in each county to form a medical society for the purpose of regulating "the practice of physick and surgery" in New York State. A compliance with the law was accomplished in Schenectady County when 41 doctors met, drew up, and signed a "Constitution and By-laws." The original minute book with these signatures is still available to our members. Seven of the names of the doctors who signed are inked out for unstated reasons. The officers elected were Archibald H. Adams, M.D., President; William Anderson, M.D., Vice-President; Alexander D. Fonda, M.D., Secretary; and Cornelius Vrooman, M.D., Treasurer. It was resolved "that this society meet annually the 2nd Tuesday in June at 2 o'clock P.M. in the County Room which Time, as prescribed by the above recited Law shall forever thereafter be the anniversary meeting of the Society." How little we have strayed from that resolution.

Another meeting was held the following day at which, "Daniel McDougal was unanimously chosen as a suitable person to attend the Lectures in the City of New York on the different Branches of Medicine." This, clearly, was a postgraduate course, and the doctor selected to attend was to return and pass on the newly acquired knowledge on the latest advances in medicine to his colleagues. Individual practice was the rule at that time, but group associations were attempted, as when two doctors named Anderson and Hegeman formed a partnership in 1811.

Early diseases and remedies

There were in the early days few specific remedies, no central pharmacal agencies for information, and no government controls. Consequently, the land abounded in quacks who advertised boldly in the weekly newspapers of the day. A glance through the old issues of the *Schenectady Cabinet* around 1810 reveals numerous announcements touting the virtues of secret remedies and promising cures to patients suffering from rheumatism, gout, coughs, jaundice, biliousness, itch, scabby eruptions peculiar to unhealthy children, dizziness, dyspepsia, worms, and what was most heinous of all, offering cures for consumption. Tuberculosis was a very common disease in those days and the particular target of the quack, much as cancer has been in recent years.

Listed among other boasted remedies were such curious items as a chemical embrocation, a lotion for rubbing on; Whitwell's Original Opodeldoc, a form of soap liniment; special snuff for the fallen sickness (epilepsy?); and Dr. Chambers' Remedy for intemperance. This latter "specific" for drunkenness was available at the Medical Store of Dr. Hart at the corner of Broadway and Chambers Streets, and it was not genuine unless signed by James

H. Hart, M.D. How similar this was to the quack remedies advertised today with their fancy pseudoscientific names and unwarranted claims! In that same year a news item in the *Schenectady Cabinet* stated that, "The Selectmen of Exeter, New Hampshire, and 20 of their most confirmed drunkards have taken it, have been cured by it, and restored to their friends and to usefulness in society."

In the earliest days of the Dutch colony an occasional minister tried his hand at the treatment of the physically sick. The Dominie Rubel of King's County apparently devoted more time to the preparation of quack remedies than to the saving of souls. In 1778 he advertised as follows:

> It has pleased Almighty God to give me the wisdom to find out the Golden Mother Tincture and such a Universal Pill as will cure most diseases. I have studied European physicians in four languages. I don't take much money as I want no more than a small living whereto God will give his blessing.

At least he did not impoverish his clients, as do our cancer quacks of today.

In this connection it is of interest to find the following in the well-known materia medica written by the famous Jacob Bigelow of Boston: ". . . and there is perhaps no branch of commerce in which names are substituted for realities with more success than in the commerce of drugs." That restrained comment applies very well to the blurbs one reads in so many of our lay publications and even medical journals. However, there were remedies, used empirically, which apparently had considerable usefulness. Among these was tar water advocated by Bishop George Berkeley, an Irishman visiting the Colonies from 1729 to 1731, and Cadwallader Colden, a physician and for some years Lieutenant-Governor of the State of New York. Bishop Berkeley, although not a physician, was obliged to combine his pastoral duties with medical ministrations in a remote district in County Cork, Ireland, since there were no physicians there. In treating epidemic diarrhea, he found rosin effective. Could this possibly be the earliest application of ion exchange in therapeutic history? Colden also wrote about cold infusions of tar, as recommended by Berkeley for a variety of diseases, particularly for contagious fevers, but he had few facts to justify his views.

SMALLPOX. The story of smallpox forms one of the great chapters in medical history. In 1802 Benjamin Waterhouse of Boston became a vigorous proponent of smallpox vaccination and published articles and books on the subject. He was derided by many of his colleagues in the Boston area. For a time Schenectady also resisted vaccination and in so doing followed the lead of Albany. On May 31, 1775, the Schenectady District Committee ordered doctors and others to desist from the inoculation of smallpox. The Provincial Congress before December 1, 1775, forbade inoculation, and men were put in jail for disobeying this order. General Thomas who commanded the Northern Department of the Army refused to have his troops inoculated for smallpox. As a result, his camp became a veritable pesthole, and he fell a victim to his own injunction when he died of smallpox. However, after George Washington recommended inoculation for the Continental Army, New York removed all objections to vaccination. The Schenectady Committee of Safety referred to was similar to such committees in other areas. They were highly useful in creating public opinion and in carrying on propaganda that finally brought on the war and served as the incipient pressure toward republican government.

The value of smallpox vaccination was finally appreciated in Schenectady, and a law was passed in 1820 requiring the health officer to keep on hand active cowpox matter. In those days there were few persons who did not have the scars left by smallpox, but with the advent of Jenner's great discovery the disease became less and less frequent, and fewer and fewer children and young adults died of the dreaded pox.

CHOLERA. Asiatic cholera appeared in Canada on June 9, 1832, and spread south along the Champlain and Hudson valleys, the usual routes of travel. People left those areas by the thousands, yet the ravages of the disease among those who remained were appalling. At that time the Black Hawk War was in progress. Many soldiers passed through Schenectady to join General Scott in Buffalo, and they carried cholera along with them. One can scarcely conceive the distress that ensued in the poorly organized army. Little attention was given to the sick, many died, and many deserted and perished in the woods of cholera or starvation.

How was cholera treated at that time? No one knew anything about water and electrolyte balance. Medical ignorance was abysmal and the methods of treatment were weird. The favorite treatment for cholera consisted of administering large enemas of warm water containing small portions of brandy. Frequently, two drams of common tobacco were added. Even full doses of calomel were employed with the addition of jalap or rhubarb when the evacuations became feculent. For the collapse that so often took place the actual cautery was sometimes practiced over the spine. Somewhat naively it was suggested that for the thirst, "The patient should occasionally be indulged in his anxiety for cold water." Also, intravenous injections of solutions of opium were used.

In August, 1832, cholera broke out in Albany. James S. McNaughton, M.D., one of the founders of the Albany Medical College, wrote a letter to Thomas Spencer, M.D., President of the Medical Society of the State of New York, describing the cases of cholera he saw, their symptoms, and the treatment employed. His chief criticism was that the patients did not come to the physician soon enough. One sentence in that letter is of particular interest and states as follows: "I have tried transfusion into the veins and in one instance injected a quart of common salt and subcarbonate of soda in the proportion of one drachm of each." He tried it in only 3 other cases but could not recommend it as a safe and useful remedy. What a tragic circumstance that the wisdom did not exist to see that the cholera patient required abundant water, salt, and albumin which, in adequate amounts, prevent most deaths.

While water was denied internally, occasionally it was used externally, for it was being rumored in 1806 that dirt was dangerous to health and that more people ought to bathe. In the Mohawk Valley the consumption of beer was very high. The old building contracts in this county often stipulated the numbers of barrels of beer that must be supplied to the workers, undoubtedly because of the fear of raw water, although there may have been other reasons.

It was in 1832 that a young Union College teacher and scientist published a pamphlet advocating a method for disinfecting well water, for it was felt by some discerning persons that Asiatic cholera was somehow connected with drinking water. In those early years most of the water used in the town was derived from dug wells, some private and others public, and located at certain street intersections. Despite prohibitory laws, people frequently washed clothing at these wells and the contaminated water, of course, seeped back into the well. The laity and the medical profession were quite concerned over the appearance of cholera in Albany, and justifiably so, for soon thereafter cholera afflicted the people of Schenectady. Averill, after a study of reports from Europe on the control of putrefaction by means of chloride of lime, recommended that this chemical be added to the well water: "8 ounces of chloride of lime in a pail full of water and dispersed into the cistern."

Then, as now, it was not easy to introduce new methods, and although Averill was commended publicly for the suggestion by the famous scientist, Benjamin Silliman, of Yale College, his advice was ignored. One can only speculate on the thousands of lives that might have been saved had the well water been thus chlorinated and if McNaughton had persisted in the water and salt treatment of the disease.

Cholera was both endemic and epidemic. Frequently small children died of the disease and in the old cemeteries there still may be seen headstones which give cholera as the cause of death. Some of these grave markers have a humorous tinge. One epitaph over an infant's grave reads:

> Since I have been so quickly done for
> I wonder what I was begun for

Another one reads:

> The little hero that lies here
> Was conquered by the diarrhea

The epitaph of an older person reads:

> He lived by virtue

Hoping for immortality
And died of cholera
Caused by eating unripe fruit
Reader, go thou and do likewise

Early medical schools

In the first half of the nineteenth century medical schools were easily begun and were highly competitive. Those in the South extolled their salubrious climate, while those in the North emphasized their freedom from the heat of the South. Distances were great, travel was difficult, and as the population increased and new communities were founded, there developed a persistent demand for physicians. It was realized that no civilized community could prosper long without medical facilities. In those days a group of physicians could get together and establish a medical school. Young men in the vicinity would attend a course of lectures for from six weeks to three months. There were no clinical facilities for bedside training. Thus, in this area there were two medical schools in Vermont, one in Western Massachusetts, and one in Herkimer County, New York. None of these schools still exists.

The school established in the village of Fairfield in Herkimer County is of considerable interest to us because men from the Schenectady area were graduated from there, and several of them were teachers in the school. The school's official name was The College of Physicians and Surgeons of the Western District of New York, but it soon came to be known as the Old Pioneer Medical School. There were several reasons for establishing the school in that remote village. In the first place, the students would avoid the distractions of a large community and could concentrate on their studies. Second, room and board were very cheap. Third, it was hoped to attract young men living in the area who, after graduation, would remain on the frontier to look after the expanding population.

The Fairfield school prospered at first and received considerable financial support from the State Legislature which granted $15,000 to it during the school's existence, from 1812 to 1840. On the school's faculty were the famous brothers, Theodric Romeyn Beck and Lewis C. Beck, natives of Schenectady, and Delamater. Among the students was Frederick Crounse of Altamont. Graduates of this school practiced not only in this area, but also in far-off Oregon. The experience and influence of this school became a potent factor in the organization of Western Reserve in Ohio.

The quality of the school must have been fairly good for that time because of the eminence of the teachers who came from Albany, New York, and Boston. Among the students was Asa Gray, a native of Paris, New York, who graduated in 1831. Gray became interested in botany, one of the important courses in a medical school, taught that subject at Fairfield after graduation, and wrote a textbook, *Introduction to Structural and Systematic Botany and Vegetable Physiology*, first issued in 1875 while he was Professor of Natural History at Harvard University. The classification of plants which he devised is still in use. In addition, Gray had six other published books to his credit and was regarded as the foremost botanist in America. Gray was considered by Charles Darwin as the most capable and eloquent advocate in America of the theory of the origin of species, and in this respect he ranked with Thomas Henry Huxley of England. Gray accumulated 200,000 botanical specimens and a botanical library of 2,200 volumes which were donated to Harvard College.

Another graduate of the school was Frederick Crounse of Altamont, a fact which is stated on his tombstone. Letters written by Crounse while he was a student were brought forth by A. B. Gregg in 1933. Crounse graduated in 1830, and his letters describe life in Fairfield while he was a student. He discusses the faculty members, some of their characteristics, and his personal expense account which included such items as cord wood, candles, soap, tobacco, board, washing, entertainment, very few books, and $54 for ticket fees for lectures.

It was at this school that the students held ether parties at which they would inhale laughing gas fumes until they became semiconscious and fell to the floor. Crounse wrote, "Preparations are making to administer the protoxide of nitrogen gas to-morrow. A goodly number of students intend to take it and we expect some sport as usual." In falling, many of the students acquired bruises, but none could recall having felt any pain. Sir Humphrey Davy, who discovered nitrous oxide and was acquainted with its sleep-inducing properties, suggested that it might prove useful as an anesthetic for surgical operations.

First women physicians

Today no one is surprised to see women practicing medicine in all its branches and in so many other fields as well. The feminist movement began in the early part of the nineteenth century, and as women slowly forced their way into professional, business, and political areas, it was noted that they did quite well. In the popular *Journal of Health* for 1832 we find this significant comment:

> All that twaddle about feminine retirement and feminine ignorance has done more towards making women scolds and flirts and scandal mongers than people are well aware of—how can she do otherwise than talk scandal? What else can she talk of if she is ignorant? Why should knowledge make bad wives any more than it makes bad husbands?"

In 1873 it is said that 300 women made applications to study medicine in San Francisco. Although they were breaking into man's domain, the female practitioners usually retained their feminine characteristics. However, it is told that one early woman physician in this county tried to emulate Mary Walker, M.D., by wearing mannish dress with starched collar and tie, shaving, and speaking in as deep a voice as she could manage. It was apparent, however, that the voice belonged to one of the distaff side. Dr. Walker had a good practice and, although she was eccentric, I have been informed reliably that she gave financial assistance to a number of young people to acquire a college education.

In the early days of the nineteenth century there were no female practitioners. The first woman graduate physician in the country was Elizabeth Blackwell who graduated in 1849 from the Geneva Medical College which was derived from the Fairfield School. Her life as a physician and student has been written about extensively and even depicted in motion pictures and on the television screen. The first woman to practice medicine in Schenectady was Jane Murray, M.D., who was a personable charming lady who never tried to imitate masculinity. She was a graduate of Queens College, Canada, and came to Schenectady in 1891. Dr. Murray acquired a good practice and was highly regarded by both the public and medical profession. She joined the Society on June 13, 1893.

Contributions of early physicians

Our doctors were progressive and alert to the developing science of medicine. Through the kindness of Marcellus Clowe, M.D., I came into the possession of a letter written in 1885 by Henry V. Hull, M.D., to William T. Clute, M.D., both Schenectady practitioners, in which Hull describes a microscopic study of scrapings from an ulcer. His diagnosis was cancer, and in the report he uses terminology and drawings that correspond closely to those in use today. Thus, nearly a century ago, Schenectady had a physician who was also a microscopist and able to give practical, diagnostic information. It should be recalled that microscopes were being manufactured a half century earlier by Charles Spencer in the village of Canastota in central New York. These microscopes were fine instruments that competed favorably with those of European origin. In fact, Spencer's objectives were superior to those made abroad and won gold medals at the Paris Exposition of 1878.

During the French and Indian Wars, Richard Shuckburgh, M.D., was attached to General Abercrombie's army just south of Albany. Although his name was Germanic, Shuckburgh was descended from a long line of English ancestors and was born in the County of Warwick which, you may recall, was Shakespeare's county. While he was with that army, Shuckburgh composed the verses of "Yankee Doodle" and presented them to the Colonials as a famous marching song. Being quite simple, the Colonials adopted the verses and tune which became the most popular air during the Revolutionary War.

Shuckburgh was greatly interested in the Indians, and in 1759 he became secretary to Sir William Johnson. In 1773 while on official business in Schenectady, Shuckburgh, who was now sixty-eight years old and rather feeble, became sick with a pulmonary condition and died of pneumonia, according to one record, and of an apoplectic fit, according to another statement. No record is available to show where he was buried. A search of city and church records, conducted during the past twenty-five years, has failed to bring to light his burial site, but many records have been lost, usually in fires. At that time Schenectady and Albany Counties were one, and all legal documents were filed in Albany. Shuckburgh's original will no longer exists, but copies were printed in the documentary histories of New York State. The will made his wife the sole heir. Subsequently, Sir William wrote to her for the return of money, about 100 pounds, which he had loaned her husband. There was no interest charge.

John Cochrane, M.D., a Pennsylvanian, saw active military service with the English during the French and Indian Wars. While on a British vessel that was lying off Oswego, a shot from the French fleet entered his operating room and carried away the operating table and instruments. The record says nothing of the patient. After the war Cochrane settled in Albany for a time, but in 1776 he was recommended by General Washington for the post of Surgeon General of the Middle Department. Congress appointed him to this position, and he was attached to Washington's Staff Headquarters at $5 per day. After the war Cochrane set up his private practice in New York City, but he soon retired to Schenectady where he died on April 6, 1807, at the age of seventy-seven years.

Samuel D. Gross, M.D., of Philadelphia, was the leading surgeon in the country in 1853 when he visited Schenectady. Gross was a great teacher and a prolific writer on medical topics. He traveled by horseback down the Mohawk Valley which he recorded as beautiful and fertile. Gross stopped off in Albany to see T. Romeyn Beck, M.D., a Schenectady-born teacher and physician who was famous as the author of the first work ever published in English on medical jurisprudence. This book passed through 12 editions and was translated into several languages.

Gross, in his autobiography, comments on the Beck family of Schenectady. There were three internationally known physicians and two lawyers, all grandchildren of the Rev. Dirck Romeyn, a leader in the founding of Union College. The mother of this brood became a widow when she was quite young, yet she managed to bring up her children without serious illness or accident and give them all a college education. Following the death of her husband, this unusually capable woman managed a hotel at the corner of Union and Church streets and conducted a trade in groceries and dry goods until her decease. Apparently, in this manner she was able to support and educate her children.

One of her sons, Lewis C. Beck, M.D., studied medicine in New York City. Afterwards, at the age of nineteen years, he began to practice in Schenectady, but like his famous brother Theodric, generally known as T. Romeyn, he soon tired of the ignorance prevailing in medicine. He entered the State service and made a very comprehensive and valuable study of the mineral resources of New York State. He traveled all over the State, partly on horseback, riding in that fashion from St. Louis, Missouri, to Schenectady, noting on the way many sites for the development of cities. Among his many publications was an article entitled "Facts relating to a disease generally known by the name of sick stomach or milk sickness." This disease was responsible for the death of the mother of Abraham Lincoln and was fairly common on the Western Frontier at that time.

During the past half century many physicians from all over the world have visited Schenectady, not to see our historic sites nor to visit our excellent hospitals. They have come to see William D. Coolidge, Ph.D., and his new marvelous tungsten target x-ray tube that has advanced medical diagnosis so markedly and has made deep x-ray therapy possible. In 1913 Dr. Coolidge wrote his first report on this new tool, which was so useful in medical science. For this contribution to medical science he received honors from many nations and scientific bodies all over the world. Dr. Coolidge is an honorary member of our Society and received an honorary medical degree from the University of Zurich in 1937.

Development of County Society

Our Society minutes lapsed from 1841 to 1869. Apparently meetings were not held because of internal difficulties. We know little of the activities of the members during the Civil War period other than that four Schenectady physicians joined the Army. The minutes of January 19, 1869, contain the following:

Pursuant to a call in the *Daily Union* of the 16th inst. several physicians met in the Carley House for the purpose of organizing a county medical society, to wit: Doctors Vedder, Ellwood, James, Sammer, Cheesman, Mynders, Curmcourt, Fuller, and (name illegible). Vedder was elected president. In 1873 medical education was discussed, and a committee was appointed to devise a fee bill. Thus, nearly a century ago our members were attempting to fix minimum charges for medical services, the same as we have tried to do recently. We know that all through the years medical fees have been a subject of intense interest.

In 1873 Dr. Ellis read a report on diphtheria and Dr. Perkins read one on alcoholism. Occasionally there were charges of unethical conduct on the part of a member, but no one was ever found very guilty, and the member, if suspended, was soon restored to the good graces of the Society. The charges concerned mainly newspaper advertising. The collations are always commented on most favorably, especially those in the homes of the doctors when the attendance seldom exceeded a dozen. When Dr. Vedder died out of town in 1878, the members voted to go to the railroad depot in a body and march to the house with the remains. Usually, in those days, the members wore a black mourning arm band for a period of thirty days. The guild spirit was quite strong.

In 1879 when an applicant for membership was rejected as improperly prepared, he engaged Lawyer Palmer who demanded of the Society that his client, Mr. MacKay, be elected within thirty days or necessary legal steps would be taken to compel such action. The vote was repeated and he was declared not elected. About this time a member named Jones died, and the following resolution was adopted: "That his name be placed on the roll of honor he having died in consequence of having received the seeds of his mortal illness in the discharge of his professional duties." How often that must have happened in those days with cholera, typhoid fever, tuberculosis, and syphilis. Many doctors died quite young.

In 1883 at a special meeting it was decided to take some action in regard to those "physicians and midwifes" who had not complied with the law of the State. The irregulars ignored the notice from the Society to cease practice, and the status quo was maintained. How closely the problems of that period resemble those of today!

We now come to the modern period of our Society, the story of which would occupy many pages. Specialism has become more and more the vogue, and while we still have a large group of advanced general practitioners, we also have represented in the county all the special branches of medicine and surgery. This development has been good for the people of our county, and with the expansion of our excellent hospital facilities, it is no longer necessary for our patients to travel great distances for treatment. The management of our affairs has become more businesslike, and the records have become better preserved, thanks to the energy and interest of our officers. The Society has expanded its civic, professional, and philanthropic activities and has become one of the most energetic and highly regarded county medical societies in the State.

People's Health Program in Sweden

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The People's Health Program in Sweden is not a recent innovation in medical socialization, having been founded over a century and a half ago.

In general, medical practice is carried out by men who fall into any one of three separate categories. The first category is that of the provincial doctors and municipal doctors. These are men who have a salary from the government for a part of their support and make the remainder in fees for service rendered to any patients who may wish to go to them. The second group is made up of men who are wholly engaged in private practice. The third group is made up of men whose income comes almost entirely from salaries paid by the state (those working in university hospitals primarily) or the community and who work primarily within state or community hospitals.

When it is necessary that a patient be hospitalized in Sweden, he usually pays no fee whatsoever either for his professional care, his laboratory studies, his hospital room, or for nursing or other services. There still exist a few small private hospitals in Sweden to which patients may go if they wish to elect their own doctors for inpatient care. Table I indicates the number of hospitals and hospital beds available in this category. By and large hospitalization in these private institutions is about as expensive as it is in the United States, and not many Swedes can afford such luxury. These institutions are used primarily by elderly, wealthy patients who select this method of hospitalization as a sort of status symbol.

The provincial and municipal doctors

The provincial doctors are spread through approximately 300 provincial medical districts in the country. They care for almost all the citizens with the exception of those in the large cities in which there may be two or more municipal doctors. Both the provincial and municipal doctors have lifetime appointments from the Crown. Their homes, their offices, and their equipment are provided by the government. These men also serve as public health officers in their respective districts. The salary is in general any amount up to approximately 45,000 kronor ($9,000). The salary compensates somewhat for lesser income from fees in poorly populated areas. In total, the income of such men, including fees for professional services, is said to run from 60,000 to 65,000 kronor ($12,000 to $13,000), the total depending to some extent on the prosperity of the community in which a man practices.

The fees which provincial and municipal doctors may charge are set by the Swedish Medical Association in collaboration with representatives of the Royal Board of Health. Each patient pays his doctor directly the amount of the appropriate fee and is in turn given a receipt which he may take to his local health office for a 75 per

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Through the cordiality of Prof. Clarence Crafoord, the author spent a year's sabbatical leave (1960 through 1961) with him and his associates at the Thoracic Clinic of the Karolinska Institutet, Stockholm, Sweden, to do research on the possible role of external support in mass myocardial infarction. The work was made possible by grants from the National Heart Institute and the American Heart Association and by a fellowship from the National Heart Institute.

TABLE I. Hospitals in Sweden*

Type	Number	Beds	Average Stay (Days)	Occupancy (Per Cent)
General	106	37,696	14	78
Private	48	1,396	32	80
Independent lying-in	23	435	8	68
Tuberculosis	36	6,003	99	59
Chronic	256	13,508	260	93
TOTALS†	588	66,799	200	79

* Not listed in this table are 32,756 beds for psychiatry and 12,812 beds for feeble-minded persons.
† Included in these totals are also all other hospitals such as cottage type, epidemic, and so forth.

cent reimbursement. As an example of the scale of charges, a routine office call costs 7 kronor (about $1.40); house calls have a higher charge and are varied somewhat according to the distance which the doctor must travel.

The private practitioner

The second category of doctors is made up of general or private practitioners. These men serve in major measure as a screening mechanism to direct patients to the most appropriate special facilities for major difficulties. Although the private practitioner may charge any fee that he wishes for his services, the patient of the private practitioner may be reimbursed only 75 per cent of the legally established fees for the services rendered. Almost all these men are trained as medical specialists and practice as such. The income of these men varies but is said to run anywhere from $12,000 to $16,000 net before taxes. The Swedish income taxes are high and take about 55 per cent of the income of physicians. In contrast to the physicians, the Prime Minister is said to receive a salary of 80,000 kronor (a little less than $16,000). The medical profession, therefore, has a very favorable level of income in comparison with that of other public servants, but the government is having difficulty in maintaining salary levels high enough to match those of private industry.

The state-supported physician

The third category of doctors is made up of men who receive virtually all their income from salary paid by the state or the community. These men, by and large, are those who work inside the hospitals. Approximately two years ago the government ruled that no charges for professional services could be made if those services were rendered in a state or community hospital, regardless of the citizenship of the patient. This is not true yet, of course, in the small number of remaining private hospitals. There are facilities for private patients in the government hospitals, but the fees which patients pay to occupy such suites go only toward more luxurious accommodations and occasional special services but not at all for professional medical fees. The utilization of such private facilities appears to be a factor in the establishment of status.

The situation of surgeons in Sweden is therefore one in which virtually all income derives from the government's salary. Surgeons may take private patients to the few remaining private hospitals, and they may earn some fees for outpatient services such as follow-up visits for patients taken care of in the government hospitals. Wealthy patients of foreign citizenship, who not infrequently go to Sweden because of the eminence of some of the Swedish surgeons, are commonly taken to private hospitals for their care but may also go to the government hospitals and have care without paying fees for professional services rendered.

Basis of selection of medical directors

The doctors in charge of the government hospitals are chosen on the basis of the professional eminence which they have gained. In a government hospital other than a teaching hospital the physician-in-charge is ordinarily paid about the equivalent of $10,000 a year, regardless of the duration or the breadth of his training. These men are appointed in the name of the Crown on selection by the Provincial Medical Board from a panel of three candidates. The panel is chosen by the Royal Medical Board on the basis of a very careful scrutiny of professional qualifications. The director of the Royal Medical Board is a man of national professional eminence, and the three candidates referred to the Provincial Medical Board are very genuinely carefully chosen. These heads of the state hospitals or community hospitals, therefore, are chosen on the basis of their acceptability to the lay members of the community, as represented by the Provincial Medical Board, from among candidates selected on the basis of high professional qualifications.

The physicians-in-chief and surgeons-in-chief of the various government hospitals are permitted to charge for services rendered to outpatients. Their fees, however, are those set officially. They can commonly raise their incomes by $2,000 or $3,000 a year in this manner. Not infrequently the return visits of formerly hospitalized patients represent an assembly-line affair. At one hospital I visited in Stockholm, the surgeon-in-chief estimated that he was able to spend less than two minutes apiece with each of these appointments.

In the university clinics and teaching hospitals, the method of selection of directors, physicians-in-chief, and surgeons-in-chief is essentially the same as that already described. Here, however, the review is far more exacting. As an example, Docent Åke Senning left his position as Head of the Research Laboratory of the Thoracic Clinic of the Karolinska Institutet to accept the professorship of surgery at Zurich, Switzerland, on April 1, 1961. His successor has still not been selected, and the choice is being made in a most thorough and laborious fashion, not only by Prof. Clarence Crafoord, director of the Thoracic Clinic at the Karolinska Institutet, but also by others in high academic positions in other universities throughout Sweden. For instance, Prof. Philip Sandblom, who will come to Brooklyn as a visiting professor in the near future, and who is professor of surgery and chancellor of the University of Lund, 400 miles south of Stockholm, has also been one of those involved in reading publications and reviewing the research accomplishments of several candidates.

Some facets of the health program

Availability of accessory personnel. The availability of accessory personnel in the government hospitals in Sweden is a most attractive factor in medical care there. As Figure 1 indicates, the number of personnel available per hospital physician or per patient is larger than we have become accustomed to in the United States.

Reward for academic accomplishment. Academic accomplishment is highly regarded in Sweden, and higher education is available on the basis of academic excellence more than on the basis of financial backing. During my stay in Stockholm, one and all insisted on referring to me as Professor Dennis, never as Dr. Dennis. Those who have reached the academic rank of professor in any of the five medical schools in Sweden are more liberally paid than other physicians. It is rumored that the salaries here are the equivalent of from $16,000 to $20,000.

High tax rate. Although the tax of 55 per cent on income of physicians is breathtaking, nevertheless provisions made by the government are extremely broad. There is no need for either saving for retirement or for life insurance. An associate professor, for instance, (called Docent in Sweden) retires at the end of his career on a government income equivalent to 65 per cent of the salary he was able to earn at the peak of his career in professional life. If he should die while in active professional life, his wife is provided with an adequate income for herself and extra allotments for any children who may still be in the process of education. The expenses of practice, of course, are also much less than in the United States. All those who are municipal or provincial doctors or who work within the hospitals have no overhead at all. Another economy is that there is so little trouble with medical litigation that malpractice insurance costs

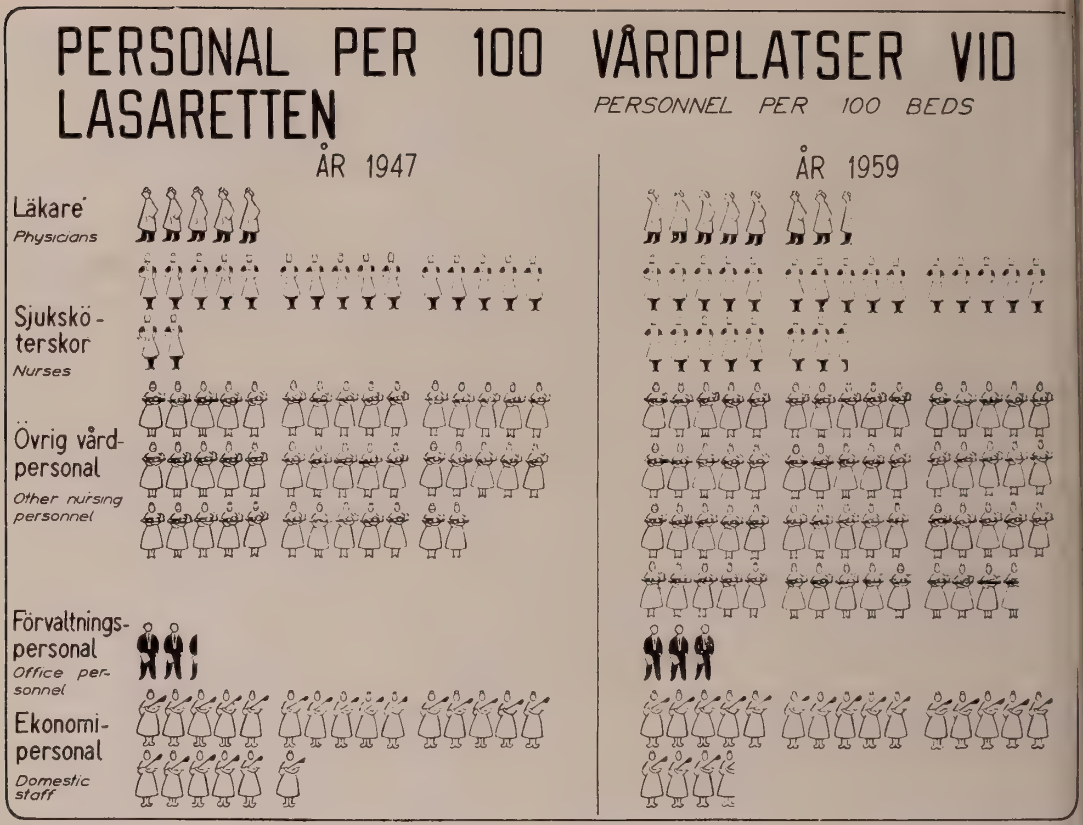

FIGURE 1. The number of personnel available per 100 beds in a Swedish government hospital. A comparison of the years 1947 and 1959.

but $9.00 per year. Education from first grade through university studies is provided without cost to all Swedish citizens who can qualify intellectually. The family or student need provide only room, board, laundry, transportation, and books. The cost of education, therefore, is even less than that in our Midwestern land-grant universities.

Physician-patient relationship. The implication of government medical care programs in Sweden, in terms of physician-patient relationships, is that a Swede may choose his own physician as long as he is an outpatient and may still have the State pay three quarters of the cost, but that, when hospitalization is required, he must go to the appropriate hospital and accept the professional personnel which has been selected by the mechanisms I have already mentioned. This, however, he may do with no cost whatever to himself. It is the feeling of most Swedes that the disadvantage of not being able to select one's own doctor for hospital care is more than offset by the free provision of that care and by the knowledge that the doctors who care for him during his hospitalization have been selected with the greatest thoroughness by a medical board headed by physicians of national eminence.

Economic aspect. Economically, a physician in Sweden is far better off than the skilled working class. A high-grade machinist earns the equivalent of $2,500 to $3,000 per year. A university-trained engineer, on the other hand, may have an income considerably above that possible for most physicians. The relatively low income gained by trained machinists in Sweden is offset by a variety of social benefits unheard of in the United States. These benefits are even broader for those of low income than for the physician. Regardless of income, the working man has a bonus given to him for any child brought into the family. If his income is less than

TABLE II. Number of Swedish physicians in the medical profession and those entering it in the years 1930 through 1959

Year	Admitted to Medical School (Number)	Active Physicians (Number)
1930	. . .	2,400
1940	194	3,240
1945	185	3,850
1950	304	4,894
1955	363	5,699
1959	408	6,897

$4,000 he receives a subsidy from the government to help him pay for his apartment rental. He also may retire on a pension, in this instance about 60 per cent of his top working salary. There is therefore no major reason for him to endeavor to lay aside a large share of his savings for emergencies and old age as we do in this country.

Of course, there still exist in Sweden some people in business and the arts who earn large incomes. Perhaps the strangest group is made up of the highly successful professional soccer players whose incomes look as astronomical in Sweden as the movie actors' do in the United States.

TABLE III. Number of inhabitants per physician in various countries as compared with Sweden.

Country	Year	Inhabitants Per Doctor (Number)
Union of Soviet Socialist Republics	1958	610
Austria	1958	610
Italy	1956	690
Switzerland	1958	700
United States of America	1958	800
England and Wales	1958	900
Sweden	1959	1,080
Poland	1957	1,260
Finland	1957	1,700

Acceptance of the program

BY THE PHYSICIAN. In general, the members of the medical profession in Sweden

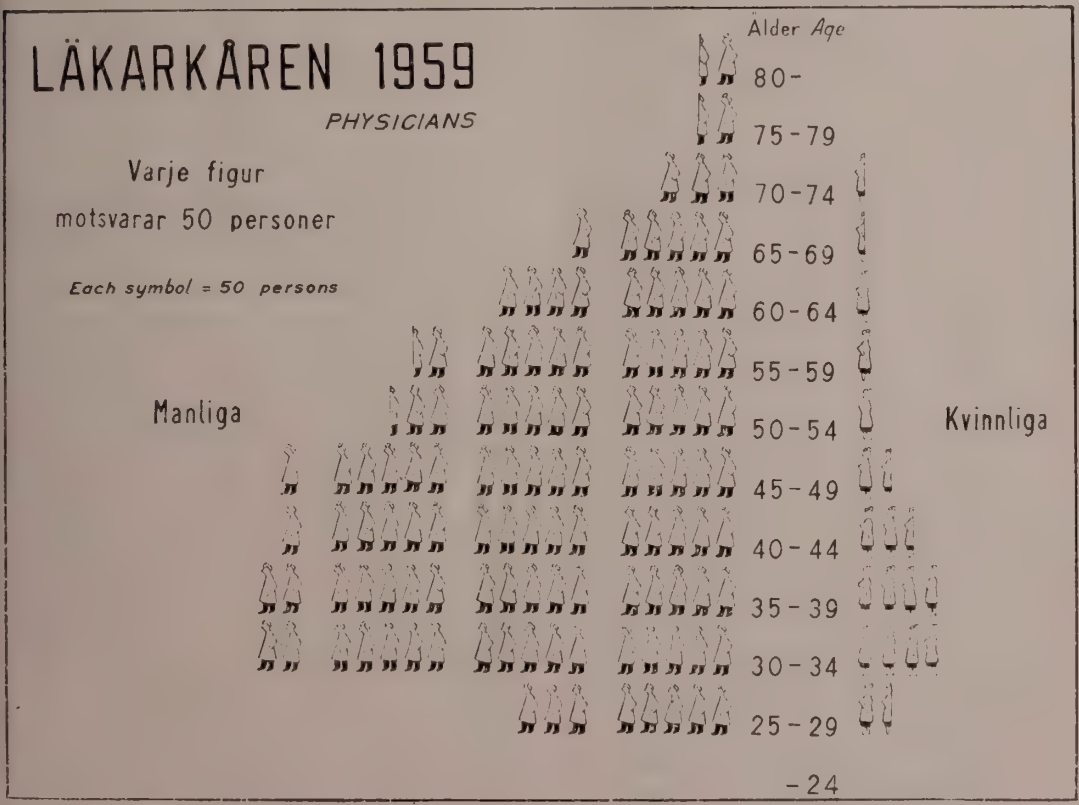

FIGURE 2. Age distribution of male and female physicians in Sweden in 1959.

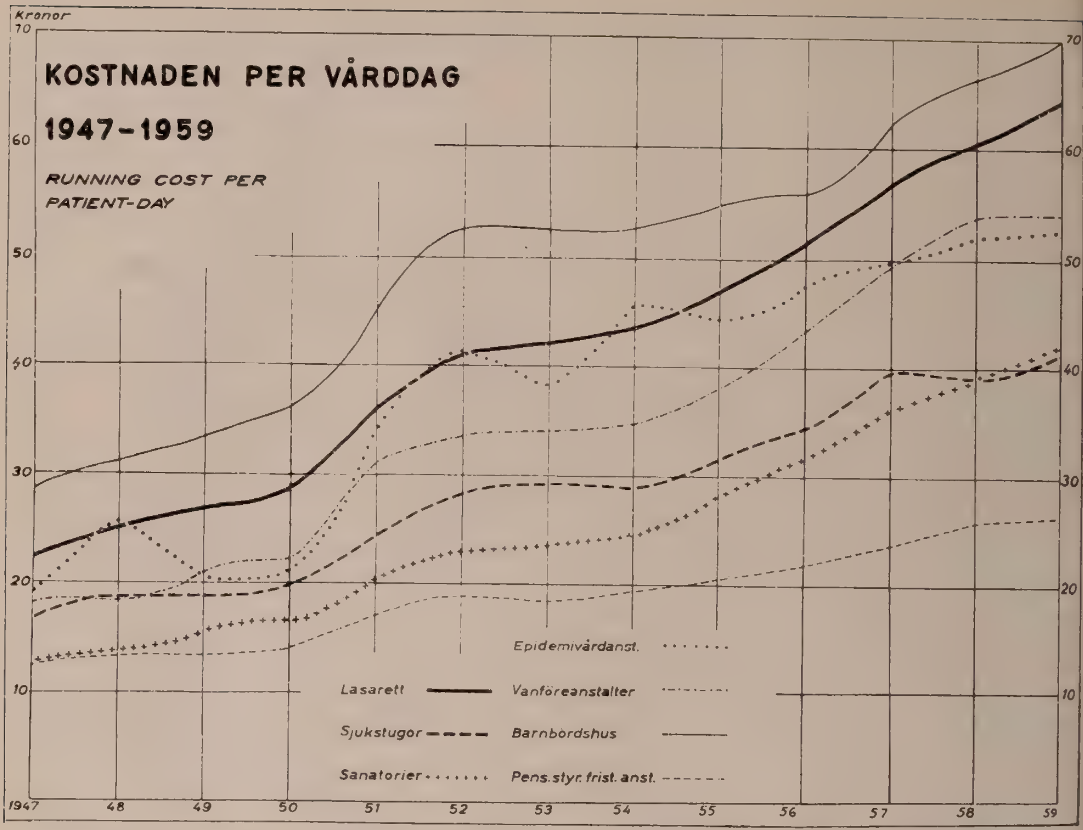

FIGURE 3. Running cost per patient day of hospital care in Sweden for the years 1947 through 1959.

appear to approve of the organization of medicine in that country. The only discontent I heard expressed came from hospital physicians and surgeons as a consequence of the decree of some two years ago denying them the privilege of charging private patient fees for inhospital service.

The number of doctors already in the medical profession plus those just entering is increasing proportionately more rapidly than the Swedish population (Table II). Entrance into the profession is sought by young people, and it is a highly esteemed profession to the laity. In spite of the increasing number of physicians, the number of Swedish inhabitants per doctor is greater than in any other countries for which I could find data except Poland, Venezuela, Finland, Yugoslavia, and Chile (Table III). The age distribution of doctors is about the same as in the United States, and there is not the tendency seen in Russia for large numbers of women to enter the profession (Fig. 2). By and large the doctors have a rather militant feeling that their profession is providing the Swedish people with the very finest possible medical care. Certainly the facilities, such as the newer government hospitals, are superb by American standards, well equipped, and beautifully maintained and staffed. The Thoracic Clinic building of the Karolinska Institutet, Stockholm, is an excellent example.

By the patient. From the patient's point of view there are some serious difficulties. There is not infrequently a long waiting period before professional care may be achieved. Emergency care is sometimes delayed by the formalities which appear to be necessary, particularly for those of foreign citizenship. Other troubles also beset patients occasionally. The American wife of a Swedish engineer, for instance, had a miserable time as an obstetric patient in one of the highly regarded hospitals in the neighborhood of Stockholm. She ran into serious troubles when complications developed six weeks after delivery, and all six of the physicians who were requested to see her for a house call refused to do so during the night. Her own obstetrician was not available, and she was required to go to the physician's office during the night with a temperature of 102 F. She was expected to return for a further call in the morning when her temperature was 104 F. Hospitalization was accomplished only by virtue of a good deal of negotiating, apparently because she wished to go in as a private patient. The troubles were such that the husband, a native Swede, swears that if his wife has another baby he will take her to the United States for delivery.

A further problem from the point of view of the physician is the relatively large amount of paper work which must be done by those in practice.

The laymen rather resent the fact that millionaires from foreign countries can come to Sweden to derive the benefits of care by internationally renowned specialists and may go into government hospitals where the charges for all services rendered are less than $15 a day and where no professional fees are concerned, a situation underwritten by the Swedish taxpayer.

The cost of the hospital services is rising as indicated in Figure 3, but it is still published as less than $15 a day.

Contrasts in the Swedish and American systems

In contrasting our situation in America with that in Sweden, I am impressed by the fact that the young man trained in surgery there utilizes that training at once without the demoralizing years of waiting to build up an appropriate practice so characteristic of surgical careers in our country. Furthermore he may start to have his family while he is young without immense concern about economic considerations. He is, in any case, a man who has entered the profession because of his interest in medicine rather than because of the hope of large financial reward. He is able to work in well-constructed, well-maintained government hospitals or to pursue his own outpatient practice, but he must qualify by sound training and evidence of intellectual superiority to assume a position of any leadership in a hospital professional area. Against these advantages, his income is somewhat less generous in actual purchasing power than that of most physicians in the United States. In addition, if he works in a hospital, he has no personal patient-physician relationship such as we cherish here. On the other hand, he is not exposed to the evils and temptations which beset members of the medical profession all about us.

Educational background. A word or two about the educational background of Swedish physicians is in order. Children in Sweden go to school at the age of seven rather than six as in this country. Those who do not wish to pursue an academic career or higher education stay in the elementary school (folkskola) for seven years of education. Those who intend to pursue an academic career and have the intellectual qualifications for this stay in the folkskola for four or five years and then go to the intermediate school (laroverk) in which they ordinarily spend eight years. The last four of these eight years are labelled "gymnasium."

When a student is approximately nineteen or twenty years of age and is at a stage of education equivalent to completion of the sophomore year of college in the United States, he is required to take the so-called "studentexamen," which is a uniform examination given by the Royal Board of Schools on a nation-wide basis. These examinations include both a written and an oral examination. The oral examinations are commonly given with a government supervisor in attendance to be sure there is no evidence of favoritism or improper examination. Those who pass this rather rigorous examination are the fortunate ones who may pursue university educations in the excellent universities in Sweden. Following the studentexamen the student ordinarily spends a year or two before going into one of the five medical schools in Sweden. Karolinska Institutet is but one. The others are Lund, Gothenburg, Uppsala, and Umeå. The student spends seven years to become a licensed physician, occasionally eight, at which time he has his internship behind him. During the last three or four years in medical school it is possible for him to get a limited license and to get a part-time job as a physician sufficient to pay his own way. In addition, students in the universities and medical schools may have loans from the government of up to $4,000 without interest and may have loans from the banks at phenomenally low rates of interest.

Early start for graduates. The undergraduate program for medical students is very similar to ours in the United States. The graduate, however, who wants to train in surgery usually has started to work as an assistant during some of the summers of his medical school career. Universal military training exists in Sweden, however, and most of the summer vacations are spent in military service. If he looks promising as he completes medical school and wishes to go into surgery, he starts with one or two years in one of the basic sciences. He then goes to the department of surgery as an assistant during which period he receives a salary with "moderate pay" of about $6,000 a year. After a year the surgical candidate is sent to one of the country or provincial hospitals for three or four years of hard surgical work, following which he returns to the university for training in surgery. The men ordinarily work for five years as assistant physicians or surgeons (underläkare), during which they usually try to write a thesis which will qualify them for the position of docent (assistant professor or associate professor). As assistant physicians they are ordinarily paid the equivalent of about $8,000. Higher positions, such as those of docent, pay $10,000 or a little more and carry a lifetime appointment from the government.

Outlook for organized medicine

The medical profession in the United States is viewed with real concern by our thinking lay public and is genuinely seriously handicapped by problems such as excessive fees, split fees, unnecessary surgery, and very poor rapport between the profession and the public. It is true that these evils would be completely eliminated by the imposition of such a system as exists in Sweden. That system, however, has been long in development, and it is highly unlikely that any such governmental organization as may be imposed on us would be as enlightened and benevolent as that which the Swedes enjoy.

Today in Saskatchewan, Canada, the organized medical profession finds itself in an almost impossible position, fomented in considerable measure by the very evils which beset us here, and which would in all probability not have developed if the profession had displayed the breadth of vision, fundamental self-cleansing, and imaginative publicity and public relations appropriate to the situation.

If, therefore, we are to enjoy that kind of medical organization which will be both most intellectually rewarding to us and professionally and economically most rewarding to the population at large, it is urgently necessary that we all join together to eliminate these shortcomings and thus reduce the pressures for governmental domination.

Acknowledgment. The author wishes to express his appreciation and thanks to Dr. Olof Norlander, Chief of Anesthesiology, Thoracic Clinic, Karolinska Institutet, Stockholm, for his careful review of the organization of medicine in Sweden on which much of the material in this paper is based.

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Necrology

Erwin Edward Benzier, M.D., of Forest Hills and Roslyn, died on July 3 at Georgetown University Hospital, Washington, D.C., at the age of forty-one. Dr. Benzier graduated in 1944 from Long Island College of Medicine and interned at Beth-El and Triboro Hospitals and City Hospital at Elmhurst. He was a staff physician in internal medicine at Booth Memorial Hospital, an associate attending physician in pulmonary diseases at City Hospital at Elmhurst, and an attending physician in the Department of Health Tuberculosis Clinic. Dr. Benzier was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, a Fellow of the American College of Chest Physicians, a Member of the American College of Gastroenterology, and belonged also to the American Trudeau Society, the American Geriatrics Society, the New York Trudeau Society, the New York Cardiological Society, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter A. Calihan, M.D., of Rochester, died on May 13 at Strong Memorial Hospital at the age of seventy-seven. Dr. Calihan graduated in 1910 from Johns Hopkins University School of Medicine. From 1927 to 1951 he was chief of surgery at Highland Hospital of Rochester and at his death was consulting surgeon at Strong Memorial and Highland Hospitals. Dr. Calihan was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the Rochester Academy of Medicine, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank P. Corrao, M.D., of Maryland, died on May 14 at the age of fifty-four. Dr. Corrao graduated in 1932 from Georgetown University School of Medicine.

Salvatore Charles Failla, M.D., of Brooklyn, died on July 3 at Wyckoff Heights Hospital at the age of fifty-four. Dr. Failla graduated in 1938 from the Stritch School of Medicine of Loyola University. He was an associate attending urologist at Wyckoff Heights Hospital. Dr. Failla was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John A. Glassbury, M.D., of New York City, died on July 7 at The Mount Sinai Hospital at the age of sixty-four. Dr. Glassbury graduated in 1916 from Long Island College Hospital School of Medicine. He was a former instructor in neuropathology at New York Post-Graduate Hospital and Medical School and a mental examiner at Bellevue Hospital. Dr. Glassbury was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Henry Knight, M.D., of Santa Barbara, California, formerly of White Plains, retired, died on July 6 at his home at the age of eighty-five. Dr. Knight graduated in 1902 from Harvard Medical School. He had been a consulting otolaryngologist at New York Hospital, Westchester Division, and White Plains Hospital Association. Dr. Knight was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the New York Academy of Medicine, the Westchester County Medical Society, and the Medical Society of the State of New York.

William Jennings MacDonald, M.D., of Mohawk, died on May 31 at University Hospital, New York City, at the age of fifty-nine. Dr. MacDonald graduated in 1930 from the University of Buffalo School of Medicine. He was an attending surgeon at Ilion Hospital. Dr. MacDonald was a member of the Utica Academy of Medicine, the Herkimer County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Campbell O'Keeffe, M.D., of Albany, was killed in an automobile accident on June 20 at the age of forty-four. Dr. O'Keeffe graduated in 1943 from Columbia University College of Physicians and Surgeons. He was an assistant attending surgeon at the Albany and A.N. Brady Hospitals, an attending surgeon at St. Peter's and Veterans Administration Hospitals, and an assistant clinical professor of surgery at Albany Medical College. Dr. O'Keeffe was a Diplomate of the American Board of Surgery and a member of the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Eggleton Clifford Soults, M.D., of Carthage, died on June 6 at his home at the age of fifty-nine. Dr. Soults graduated in 1927 from the University of Michigan Medical School. He was a member of the associate staff of the Good Samaritan Hospital, Watertown. A recipient of the Bronze Star, the Purple Heart, and five battle stars, Dr. Soults was a member of the Jefferson County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Philip Tiktinsky, M.D., of the Bronx, died on May 6 at the age of seventy-one. Dr. Tiktinsky graduated in 1917 from New York Homeopathic Medical College and Flower Hospital and interned at Cumberland Hospital. He was an associate attending physician at Morrisania Hospital. Dr. Tiktinsky was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Francis Marion Tisdale, M.D., of Canaseraga, died on June 17 at Bethesda Hospital, Hornell, at the age of fifty. Dr. Tisdale graduated in 1938 from the University of Buffalo School of Medicine. He was a staff general practitioner at Bethesda Memorial and Dansville Memorial Hospitals, Allegany County coroner, and health officer, school physician, and Selective Service medical examiner for Canaseraga. Dr. Tisdale was a member of the Allegany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Month in Washington

The American Medical Association endorsed in principle the Kennedy Administration's proposed mass immunization program but urged three important changes.

F. J. L. Blasingame, M.D., executive vice-president of the A.M.A., outlined the A.M.A.'s position in a letter to Rep. Oren Harris (D., Ark.), chairman of the House Commerce Committee which held hearings on the Administration legislation (H.R. 10541). Dr. Blasingame said:

"The American Medical Association endorses the principle of H.R. 10541 as applied to the four infectious diseases named in the bill—poliomyelitis, diphtheria, whooping cough, and tetanus—but urges that: (1) the bill be limited to the four named diseases; (2) the bill be financed as a grant-in-aid program with the states participating on a matching formula basis; and (3) the programs be administered by State Health Departments, preserving the well-established and accepted relationships between the United States Public Health Service and the States in matters pertaining to health."

The Committee accepted two of the changes proposed by the A.M.A.—that the program be limited to the four specified diseases and that it be administered by state health departments. The bill then was passed by the House and sent to the Senate where it promptly received approval of the Senate Labor and Public Welfare Committee.

The bill would authorize Federal grants to states and their political subdivisions for "intensive community vaccination" programs against the four diseases during the next three fiscal years. It would authorize $14 million for

Prepared by the Washington, D.C., office of the American Medical Association.

grants in the first year of operation and $11 million annually for the following two years. The Federal funds would be used to purchase vaccine for children under age five and for salaries and related expenses of the state and local immunization programs.

"Our House of Delegates has on many occasions adopted policy resolutions urging immunization against polio, tetanus, and other communicable diseases for which vaccine exist," Dr. Blasingame said. "Although traditionally it has been the policy of the American Medical Association to urge that the best means of administering vaccines is in the doctor's office, with the family physician vaccinating his patients, we also have recognized that intensive immunization against communicable disease is a public health matter."

* * *

The Public Health Service called on physicians to cooperate with community health officials and voluntary health agencies in launching in September a campaign to vaccinate pregnant women, persons suffering chronic debilitating diseases, and the general population over age forty-five against Asian influenza.

Surgeon General Luther L. Terry of the Public Health Service urged that as many persons in these groups as possible be protected with one shot, or two if they are prescribed, before winter.

The call for the vaccination campaign was issued after a special advisory group warned that another wave of Asian influenza is due in the United States. The committee said that while accurate predictions are difficult, recent and past patterns of influenza A2 (known as the Asian strain) indicate it probably will occur throughout the nation this winter. The committee said indications were that influenza B would be infrequent.

The committee also recommended that serious consideration be given to immunizing persons in medical and health services, public safety, public utilities, transportation, education, and communications fields. Dr. Terry said large-scale immunization should be encouraged also in other industries and large institutions where absenteeism is of particular concern.

Previous campaigns included all persons over age sixty-five, but the age limit was lowered after study of past outbreaks.

Manufacturers of influenza vaccine were asked to estimate the amount of vaccine that would be needed and to have an adequate supply ready.

* * *

The Federal Radiation Council said that indications are that radiation received by the average American from nuclear testing is "considerably less than the exposure from natural sources."

But, in a major policy statement, the Council conceded that there is little scientific data to back up this conclusion and that it is difficult to be precise in this field.

"While a considerable body of information has been accumulated on the effects of radiation on animals and man, the possible effects of low doses delivered at low-dose rates are insufficiently known to permit firm conclusions about the extremely low exposures resulting from fallout," the Council said in a report entitled "Health Implications of Fallout from Nuclear Weapons Testing Through 1961."

"We cannot say with certainty what health hazards are caused by fallout from nuclear testing. We expect there will be some genetic effect; other effects such as leukemia and cancer are more speculative and may not occur at all. We can observe that, compared to the number of these same adverse biologic effects occurring wholly apart from testing, the additional cases that might be caused by testing are a very small quantity. We conclude that nuclear testing through 1961 has increased by small amounts the normal risks of adverse health effects."

The report said radiation doses from all nuclear tests through 1961 "have generally been a small fraction" of the amount received from natural radioactive sources such as radium in the earth's crust, cosmic radiation from space, and carbon^{14} and potassium^{40} in the human body.

Basing its estimates on measurements of radioactive particles in air, rain, soil, water supplies, food, and human bodies, the Council said the dose from all atomic tests through 1961 was from one tenth to one quarter of the amount received from the natural background.

Abstracts

Bronk, T. T., and Friedland, E.: Relative value of cervical and vaginal smears in detection of uterine cancer, New York State J. Med. **62:** 2650 (Aug. 15) 1962.

A differential evaluation of vaginal and cervical smears was made in 21,944 cases. Positive or suspicious smears were discovered in 675 cases (3.1 per cent), of which 101 cases were proved cancers. Both vaginal and cervical smears were positive in 55 per cent of all uterine cancer cases and in 60 per cent of cervical cancer cases. The *cervical* smear was positive in 75 of the 101 total cases (74 per cent) and in 71 of 86 cervical cancers (83 per cent). The *vaginal* smear was positive in 61 of the 101 cases (60 per cent) and 56 of 86 cervical cancers (65 per cent). If only one of the dual smears was positive, the cervical smear was superior in the ratio of almost 5 : 1.

Weingold, A. B., and Stone, M. L.: Cancer chemotherapy in gynecologic malignant conditions, New York State J. Med. **62:** 2654 (Aug. 15) 1962.

Chemotherapeutic agents fall into four classes: polyfunctional alkylating drugs or radiomimetic agents, antimetabolites, hormones, and a miscellaneous group including antibiotics and colchicine. Toxic side-reactions, which affect the gastrointestinal, hematopoietic, and cutaneous systems, occur with all the chemotherapeutic agents but are especially common with the use of the antimetabolites. The most extensive use of chemotherapeutic agents in gynecology has been in the attempt to control ovarian malignant conditions. Thio-TEPA, 5-FU, and nitrogen mustard have been used in these conditions. An excellent or good response has been obtained in 6 of 16 cases treated with chlorambucil (Leukeran) in daily doses of 0.2 to 0.4 mg. per kilogram of body weight. In fundal carcinoma surgery remains the therapy of choice, but progestational drugs are being used on an experimental basis. Chemotherapeutic agents have had little trial in carcinoma of the cervix. In choriocarcinoma, combined therapy with surgery and methotrexate, in daily doses of 10 to 30 mg. parenterally for five-day courses, seems to be the regimen of choice.

Warner, M. P.: Results of a twenty-five-year study of 1,553 infertile couples, New York State J. Med. **62:** 2663 (Aug. 15) 1962.

A study was made of 1,553 cases of infertility, of which 1,010 were primary sterility and 543 secondary sterility. Approximately 80 per cent were treated and followed adequately. The corrected over-all success rate was 60.4 per cent. The 16 to 20 per cent pregnancy loss in this study is comparable with that in a normal population in the United States. The over-all percentage of sterility due to the male factor was 27, to the female factor 45, to both factors 16, and with unknown cause 12. Including cases of artificial insemination with donor semen, 60 per cent of male sterility cases resulted in successful conception; however, excluding artificial insemination cases, only 30 per cent were successful. The success rate in cases in which the female factor was responsible was 50 per cent. Increasing age, particularly in the female, is associated with a decrease in the success rate. The highest success rates are associated with the shortest durations of treatment, although from 14 to 50 per cent of cases treated for from three to fifteen years may terminate in pregnancy.

Cracovaner, A. J.: Some hidden diseases of the larynx, New York State J. Med. **62:** 2674 (Aug. 15) 1962.

The diagnoses of certain abnormalities within the larynx may be obscured or delayed because (1) the difficulty may arise in a silent area, (2) the presenting symptoms may call attention to another organ, (3) the diagnosis cannot be attained immediately even on direct examination, and (4) some congenital and functional diseases of the larynx may not be recognized readily. Such hidden diseases include tumors of the vocal cord and pyriform sinus and carcinoma of the larynx. Congenital and functional diseases include paralysis of the vocal cord and cricoarytenoid arthritis.

Abstracts in Interlingua

Bronk, T. T., e Friedland, E.: Le valor relative de frottis cervical e vaginal in le detection de cancere uterin (*anglese*), New York State J. Med. **62:** 2650 (15 de augusto) 1962.

Un evalutation differential de frottis vaginal e cervical esseva interprendite in 21.944 casos. Frottis positive o suspecte esseva trovate in 675 casos (3,1 pro cento). De istos, 101 esseva provate casos de cancere. Tanto le frottis vaginal como etiam le frottis cervical esseva positive in 55 pro cento de omne casos de cancere uterin e in 60 pro cento de omne casos de cancere cervical. Le frottis *cervical* esseva positive in 75 del total de 101 casos (74 pro cento) e in 71 del 86 casos de cancere cervical (83 pro cento). Le frottis *vaginal* esseva positive in 61 del total de 101 casos (60 pro cento) e in 56 del 86 casos de cancere cervical (65 pro cento). Inter le casos in que solmente un del duo frottis esseva positive, le frottis cervical esseva superior al frottis vaginal secundo un relation de quasi 5 a 1.

Weingold, A. B., e Stone, M. L.: Chimotherapia de cancere in maligne conditiones gynecologic (*anglese*), New York State J. Med. **62:** 2654 (15 de augusto) 1962.

Le agentes chimotherapeutic forma quatro classes: (1) Drogas alcoylante polyfunctional o agentes radiomimetic, (2) antimetabolitos, (3) hormones, e (4) agentes miscellanee, incluse antibioticos e colchicina. Toxic reactiones lateral, que affice le systemas gastrointestinal, hematopoietic, e cutanee, occurre con omne le agentes chimotherapeutic, sed illos es specialmente commun con le uso del antimetabolitos. Le plus extense uso de agentes chimotherapeutic in le gynecologia concerne le essayo de combatter un condition maligne del ovarios. Thio-TEPA, 5-FU, e mustarda de nitrogeno ha essite usate in tal conditiones. Un responsa excellente o bon esseva obtenite in 6 de 16 casos tractate con chlorambucil (Leukeran) in doses diurne de 0,2 a 0,4 mg per kilogramma de peso corporee. In carcinoma fundal, chirurgia remane le therapia de election, sed drogas progestational es usate in tal casos a base experimental. Agentes chimotherapeutic ha non essite essayate in alte mesura in casos de carcinoma del cervice. In choriocarcinoma, un therapia combinate de chirurgia con methotrexato (in doses diurne de 10 a 30 mg per via parenteral in cursos de cinque dies) pare esser le programma de election.

Warner, M. P.: Resultatos de un studio de vinti-cinque annos de 1.553 infertile pares conjugal (*anglese*), New York State J. Med. **62:** 2663 (15 de augusto) 1962.

Esseva studiate 1.553 casos de infertilitate conjugal, incluse 1.010 de sterilitate primari e 543 de sterilitate secundari. Circa 80 pro cento del serie total esseva tractate e tenite sub observation durante adequate intervallos de tempore. Le corrigite proportion de successos general esseva 60,4 pro cento. Le 16 a 20 pro cento de pregnantias perdite que esseva incontrate in iste studio es comparabile con illo in un population normal in le Statos Unite. Le procentage general de sterilitate causate per le factor mascule esseva 27, de illo causate per le factor feminin 45, de illo causate per ambes 16, e de illo a causa non cognoscite 12. Si casos de insemination artificial con semine ab donatores es includite, 60 pro cento del casos de sterilitate mascule resultava in conception successose. Tamen, si le casos de insemination artificial es excludite, solmente 30 pro cento del casos esseva resolvite a bon successo. Le procentage del successos inter le casos in que le factor feminin esseva responsabile, esseva 50. Avantiamento del etate, particularmente in le feminas, es associate con un declino del procentage de successos. Le plus alte procentages de successos es associate con le plus breve periodos de tractamento, sed inter 14 e 50 pro cento del casos tractate durante inter tres e dece-cinque annos pote terminar se in pregnantias.

Cracovaner, A. J.: Occulte morbos del larynge (*anglese*), New York State J. Med. **62:** 2674 (15 de augusto) 1962.

Le diagnose de certe anormalitates intra le larynge pote esser obscurate or retardate pro varie causas. (1) Il es possibile que le difficultate ha su origine in un area silente. (2) Il occurre que le symptomas de presentation concerne un altere organo. (3) Le situation es tal que le diagnose non pote esser obtenite immediatemente, mesmo con le uso de un examine directe. E (4) il existe morbos congenite e functional del larynge que non es prestemente recognoscibile. Tal occulte morbos include tumores del cordas vocal e del sinus pyriforme e etiam carcinoma del larynge. Morbos congenite e functional include paralyse del cordas vocal e arthritis cricoarytenoide.

Medical News

Section on Allergy, Medical Society of the County of Kings

The Section on Allergy of the Medical Society of the County of Kings has announced the election of the following officers for the calendar year 1962:

Solomon Slepian, M.D., president; Bernard B. Alperstein, M.D., president-elect; Harry Leibowitz, M.D., vice-president; Alexander Chester, M.D., secretary; and John E. Wolleben, M.D., treasurer.

New unit for emotionally disturbed blind children

The opening of a new 20-bed unit for the treatment of emotionally disturbed blind children has been announced by Paul H. Hoch, M.D., New York State Commissioner of Mental Hygiene.

The new facility, which will care for children up to age sixteen from the Downstate area, is located in the Children's Unit of Creedmoor State Hospital, Queens Village.

The new unit will be a pilot program. Research investigations will be carried out on the causes of the blindness and the emotional disturbance of the youngsters in the unit. Efforts also will be made to find methods of alleviating their difficulties with special training and activity programs as well as with drug therapy.

Essay contest for medical students

Abraham G. White, M.D., director of medical education at The Brooklyn Hospital, has announced that junior and senior medical students throughout the country are invited to submit entries to "The Annual Walter Reed Memorial Essay Competition of The Brooklyn Hospital."

Three cash prizes will be offered: first prize, $1,000; second prize, $750; and third prize, $500. Closing date for entries is March 1, 1963. Essays should be from 5,000 to 10,000 words in length and should be submitted in triplicate. The prize-winning essays will be the property of The Brooklyn Hospital for suitable publication. Subject material may deal with any branch of clinical medicine or surgery.

Essays should be sent to: Abraham G. White, M.D., Director, Medical Education, The Brooklyn Hospital, 121 DeKalb Avenue, Brooklyn 1, New York.

Safflower capsules ruled misbranded

A default decree entered by the United States District Court in Brooklyn has established that "Calories Don't Count" capsules are misbranded by false and misleading health and diet claims in the book *Calories Don't Count* by Herman Taller, M.D., of Brooklyn.

The Food and Drug Administration has announced that Cove Vitamin and Pharmaceutical, Inc., of Glen Cove, Long Island, withdrew its answer contesting seizure of "Calories Don't Count" capsules, stopped the distribution of the safflower oil product, and is recalling it from the market on a refund basis. According to representatives of the pharmaceutical company the decision to withdraw was made because Simon & Schuster, Inc., publishers of the book, and Dr. Taller have refused to come to the defense of the health and diet claims in the book. Nearly 2 million copies have been printed.

Some of the claims made by the book are that the capsules are effective for: weight control without regard to caloric intake, lowering the cholesterol level of the blood, the treatment of arteriosclerosis and heartburn, improvement of the complexion, increasing resistance to colds and sinus trouble, promoting health, and increasing sexual drive.

New editor for medical journal

John A. D. Cooper, M.D., professor of biochemistry and associate dean of the Northwestern University Medical School, has been named editor of *The Journal of Medical Education*, official publication of the Association of American Medical Colleges. He will succeed John Z. Bowers, M.D., who has been editor since 1957. Dr. Bowers has been awarded the Alan Gregg Travel Fellowship in Medical Education and expects to travel to Japan this summer.

March of Dimes research grants

The National Foundation-March of Dimes has announced the awarding of five research grants totaling $268,358 to medical institutions in the City of New York.

Two of the awards are to Columbia University, two to the Rockefeller Institute, and one to the New York University Medical Center. Together they cover a wide range of problems related to birth defects, arthritis, and virus diseases.

Life Insurance Medical Research Fund

The Life Insurance Medical Research Fund will give more than $1,183,000 for heart research in the coming year. This brings to $14,953,715 the fund's allocations for research since it was organized in 1945. All of its resources in the past seventeen years have been devoted to research in heart, circulatory, and allied diseases.

American College of Obstetricians and Gynecologists names fellows

The American College of Obstetricians and Gynecologists has announced the induction of the following New York physicians as Fellows of the College.

Amityville: Kenneth F. Whitaker, M.D.; *Batavia:* James S. Hursh, Jr., M.D.; *Brightwaters:* Edward R. Fogarty, M.D.; *Brooklyn:* Gemma M. Barzilai, M.D., Lindo Cione, M.D., Herbert Harris, M.D., Benjamin LoPresto, M.D., Sol H. Rogatnick, M.D., Robert J. Tufano, M.D., Cleora K. Handel, M.D., M. Grosvenor Potter, Jr., M.D., Oliver J. Steiner, M.D., and Russel J. Van Coevering, M.D.; *Douglaston:* Solly M. Scheiner, M.D.; *East Meadow:* Anthony J. Barbaccia, M.D.; *Flushing:* Gerald S. Stober, M.D.; and *Freeport:* William G. McGuinness, M.D.

Also, *Garden City:* James B. Tormey, Jr., M.D.,; *Glen Cove:* William D. McLarn, M.D.; *Hudson:* Philip A. Corfman, M.D.; *Huntington:* John Brooks, M.D.; *Jamaica:* Hyang Won Lee, M.D., and Robert G. McManus, M.D.; *Jamaica Estates:* John N. Rizzi, M.D.; *Kingston:* Kurken V. Kirk, M.D., and Herbert A. Zaccheo, M.D.; *Lancaster:* W. H. Merrilees, M.D.; *New Hyde Park:* Marvin S. Hans, M.D.; and *New Rochelle:* Selig Neubardt, M.D.

Also, *New York City:* John M. Astrachan, M.D., Theodore H. Bullard, Jr., M.D., Dolores Elyse Fiedler, M.D., Walter L. Freedman, M.D., William P. Given, M.D., Richard D. Grimaldi, M.D., Robert E. Hall, M.D., Robert Phillips Hatch, M.D., Arthur C. Lewson, M.D., Bernard N. Nathanson, M.D., Alton L. Powell, 3rd, M.D., Jerrold L. Sharoff, M.D., David H. Schonholz, M.D., Anna L. Southam, M.D., James C. Thomas, 3rd, M.D., R. Nuran Turksoy, M.D., Gray H. Twombly, M.D., Samuel W. Vernick, M.D., Alvin C. Weseley, M.D., and Joseph Wiederman, M.D.; *Niagara Falls:* Wilfred E. L. Gordon, M.D.; *Olean:* William F. Harding, M.D., and Lewis C. Reisner, M.D.; *Oswego:* Joseph E. Mather, M.D.; *Plattsburgh:* David Barber McDowell, M.D.; *Rochester:* Harold I. Nozik, M.D.; *Rome:* David S. Ellison, M.D.; *Syracuse:* Herbert Bauer, M.D., Philip L. Ferro, M.D., and Robert C. Hays, M.D.; *Valley Stream:* Wilbur J. Schefstad, M.D.; *Watertown:* James J. Finnerty, M.D.; *White Plains:* Sheldon B. Lippert, M.D.; *Woodhaven:* Edward J. Doherty, M.D.; *Yonkers:* Fathallah Chaker Maghak, M.D.; and *Yorktown Heights:* Thomas V. Kaicher, M.D.

See Medical News in the September 1, Part II, issue of the JOURNAL for a listing of New York physicians recently examined and certified in the specialty of obstetrics and gynecology by the American Board of Obstetrics and Gynecology.

Personalities

Elected. Morris B. Bender, M.D., and Melvin D. Yahr, M.D., New York City, as first vice-president and secretary-treasurer and editor of the *Transactions* of The American Neurological Association, respectively.

Honored. Howard Reid Craig, M.D., New York City, with an honorary fellowship in The Royal Society of Medicine in London, England . . .Arthur Q. Penta, M.D., Schenectady, by the alumni of the University of Vermont with a distinguished service award . . .Willard C. Rappleye, M.D., New York City, by the American Hospital Association with the title "honorary member."

Appointed. Howard C. Baron, M.D., New York City, as director of surgery at Jewish Memorial Hospital . . .Stanley I. Fishman, M.D., Brooklyn, as director of the department of medicine at Brooklyn Women's Hospital . . . Samuel Milham, Jr., M.D., Elsmere, as Associate Public Health Physician in the Development and Evaluation Group of the State of New York Department of Health . . .C. Barber Mueller, M.D., Syracuse, as a member of the Armed Forces Institute of Pathology Scientific Advisory Board of Consultants.

Speaker. Leo Wollman, M.D., Brooklyn, on August 1 before the Argentina Society of Hypnotherapy on "Psychoprophylactic (Lamaze) Technic, Grantly Dick Read's Childbirth Without Fear, and the Hypnoreflexogenous Method of Painless Childbirth"; on August 9 in Rio de Janeiro before the Brazilian Society of Medical Hypnosis on the subject "Hypnosis in Obstetrics and Gynecology"; and on August 11 at the fourth world congress on fertility and sterility of the International Fertility Association in Rio de Janeiro on the subject "Experiences in the Treatment of Infertility by Medical Hypnosis."

Medical Schools

Albert Einstein College of Medicine

Retired. Bruno Z. Kisch, M.D., medical director of Yeshiva University since 1938 and professor of philosophy and history of science, has retired. Dr. Kisch was active in organizing the American College of Cardiology in 1949 and served as its president from 1951 to 1953.

Promoted. Harold Rifkin, M.D., has been promoted to clinical professor of medicine.

Center for research in molecular biology. Within a newly-created Department of Molecular Biology, studies of the structure and function of living matter at a molecular level will be the major work of the center for research in molecular biology. Bernard L. Horecker, M.D., will be the chairman of the department and associates will be Jerard Jurwitz, M.D., and Mary Jane Osborn, M.D.

Columbia University College of Physicians and Surgeons

To retire. Aura E. Severinghaus, Ph.D., associate dean, secretary of the Faculty of Medicine, and professor of anatomy, relinquished his duties after an association with the University that began in 1915 as a student at Columbia College. He began a sabbatical leave of one year July 1 and at the end of that period will retire.

Dr. Severinghaus has been chairman of the Committee on Instruction and the Committee on Admissions since 1942.

Anesthesiology grant. A grant of $535,000 from the National Institutes of Health to support research in anesthesiology has been received by the College. Emanuel M. Papper, M.D., professor of anesthesiology and chairman of that Department, said the funds will support a number of research projects and an increase in the size of the research staff of the Department and that part of the grant will be used for equipment and other physical improvements of the Department's laboratories.

Field work. The University's Institute of Nutrition Sciences has 13 of its foreign students assigned singly or in groups doing field work in eight countries this summer. Some of the candidates for Columbia's Master of Science degree hold M.D.'s and one has a Ph.D. Three months of such work for this degree is required in some aspects of public health nutrition.

Cornell University Medical College

Appointment. William T. Lhamon, M.D., professor and chairman, Department of Psychiatry and Neurology, Baylor University College of Medicine, Houston, Texas, has been appointed professor and chairman of the Department of Psychiatry at the College and psychiatrist-in-chief, New York Hospital. Dr. Lhamon took over his post July 1.

New York Medical College

Graduating honors. Prizes and honors awarded to the members of the 1962 class are as follows: William Cullen Bryant Award—Milton Best, M.D., and Robert Bennett, M.D.; Conrad Engerud Tharaldsen Award—Joel Hendler, M.D.; Dr. Samuel Spiegel Prize—Milton Best, M.D.; Moseby Book Awards: Milton Best, M.D., Robert Bennett, M.D., Robert Greene, M.D., Joel Hendler, M.D., and Edward Umgelter, M.D.

Roche Award: Charles Ray Jones, M.D.; Merck Manual Awards—Charles Ray Jones, M.D., Robert Greene, M.D., Robert Bennett, M.D., Edward Umgelter, M.D., Howard Jewell, M.D., and Victor Grann, M.D. American Medical Women's Association Award—Aileen Kass, M.D.; and Parents Council Award—John Morgan, III, M.D.

Also: Louis Hutner Award in dermatology—Michael Schlossberg, M.D.; Stephen P. Jewett Award in psychiatry—Milton Pereira, M.D.; Leon S. Loizeaux Award in obstetrics and gynecology—Efren Olivo, M.D.; Bessie Kaplan Morais Award for research—Charles Ray Jones, M.D.; Sprague Carleton Award in urology—Edward Norcott, M.D.; New York Academy of Gastroenterology Award—Robert Bennett, M.D.; Karl Harpurder Award in physical medicine—Milton Best, M.D.; Orthopedic Surgery Award—Natale Bondi, M.D.

Members elected to the Cor et Manus honor society were: John Bucchier, M.D., Kenneth Cass, M.D., Gabriel Cuculescu, M.D., William Farlow, Jr., M.D., Victor Grann, M.D., Robert Greene, M.D., Elizabeth Grueninger, M.D., Charles Ray Jones, M.D., Robert Lieberman, M.D., John Morgan, III, M.D., and Stephen Rogers, M.D.

Appointed. Walter L. Mersheimer, M.D., formerly clinical professor of surgery, has been appointed professor and chairman, Department of Surgery.

New York University Medical Center

Grant. A new March of Dimes award of $48,534 to continue studies on a method that may help predict how well a skin graft will take has been received. The project is under the direction of Chandler A. Stetson, M.D., professor and chairman, Department of Pathology, whose group developed the new procedure.

State University of New York Downstate Medical Center

Elected. George Liberman, M.D., a graduate of the class of 1930, was elected president of the Alumni Association. Dr. Liberman is a past-president of the Brooklyn Physicians Club and a staff member at Prospect Heights and Kings County Hospitals.

State University of New York Upstate Medical Center

Grant. A grant of $33,350 from the Maurice Falk Medical Fund for the support of an eighteen-month study of medical student attrition has been received. Dr. Davis G. Johnson, assistant dean for student personnel and admissions, will conduct the study and the Association of American Medical Colleges will be actively cooperating. The purpose of the study is to analyze the extent and causes of medical school dropouts. The Maurice Falk Medical Fund was established in September, 1961, in Pittsburgh, Pennsylvania, in memory of Mr. Maurice Falk and is a nonprofit philanthropic organization created to finance research, education, and related activities in the fields of the health sciences.

Olsen Memorial Fellowships. Francis J. Citro, a junior, and Jerome C. Goldstein, a senior, are the recipients of Olsen Memorial Fellowships. Each fellowship is for $600.

Appointed. C. Barber Mueller, M.D., professor and chairman of surgery, has been appointed a member of the Armed Forces Institute of Pathology Scientific Advisory Board of Consultants. The appointment was effective July 1 and extends for a five-year term.

American Diabetes Association. Mordecai Gerstein, senior student, attended the meeting of the American Diabetes Association in Chicago in June. Mr. Gerstein is one of the authors of a paper which was presented. The paper, "An Attempt to Evaluate Pancreatic Insulin-Secreting Reserve in Normal and Diabetic Subjects," was written by David H. P. Streeten, M.D., associate professor, Department of Medicine; Donald L. Woolfol, M.D., intern, Departments of Medicine and Surgery; and Mr. Gerstein.

Elected. Four faculty members were elected officers of the Center's chapter of the American Association of University Professors. They are: president—Peter Witt, M.D., associate professor, Department of Pharmacology; vice-president—Fred Caldwell, Jr., M.D., assistant professor, Department of Surgery; secretary-treasurer—Thomas Mou, M.D., associate professor, Department of Preventive Medicine, and counsellors—Earle Lipton, M.D., assistant professor, Department of Pediatrics, and C. Barber Mueller, M.D., professor and chairman, Department of Surgery.

MEND. William Holden, M.D., professor and chairman, Department of Surgery, Western Reserve University School of Medicine, was the Medical Education for National Defense (MEND) speaker on June 22. Dr. Holden spoke on "Biology of Homotransplantation."

University of Rochester School of Medicine and Dentistry

New school aided by College. The Medical School is helping the government of Nigeria to establish the University of Lagos Medical College, the first all-African medical school in the new African nations. Leaves of absence to members of its faculty interested in helping to set up teaching and research programs at the new Nigerian medical school will be granted. Leaves have already been granted to Dr. William D. Lotspeich, professor and chairman, Department of Physiology, who will be visiting professor of physiology during the fall semester, and Dr. Franklin W. Heggenness, assistant professor of physiology, who will serve as senior lecturer in physiology for one year. A third member of the physiology staff will serve in 1963. Dr. Julius Cohen, associate professor of physiology, will be acting chairman of the Department of Physiology during Dr. Lotspeich's absence.

International commission. Philip Rubin, M.D., chief, Division of Radiation Therapy and Radioisotopes, and professor of therapeutic radiology, is in Europe to set up an international commission to study the classification of bone dysplasis—deformities in bone development, mostly in children. He also will seek to develop an exchange program for fourth-year residents in radiation therapy at the Center at some major cancer centers in England. On August 14 he presented a paper at Harrogate, England, at the International Radiation Research Society meeting on "Crysteamine Protection Against Growing Bone and Cartilage Injury." On July 6 and 7 he was a visiting professor and lecturer at the Hospital for Sick Children, University of Paris, and on July 9 and 10 took part in a symposium on "Bone Dysplasis." On August 1 he lectured on "Classification of Bone Dysplasis" at the Royal Orthopedic Hospital, London, and on

August 3 he lectured on "Radiation Cartilage Damage and Their Late Bony Sequelae" at the Royal Marsden Hospital. On August 14 following the International Radiation Research Society meeting he presented a paper on "Radiobiologic Concepts in Radiation Therapy," at the Christie Hospital and Holt Radium Institute, Manchester.

Medical Meetings

American Institute of Ultrasonics in Medicine

The seventh annual meeting of the American Institute of Ultrasonics in Medicine will be held on August 25, from 8:30 A.M. to 5:00 P.M., at the Biltmore Hotel, Madison Avenue and 43rd Street, New York City. The present and future use of clinical applications of ultrasonic energy will be considered.

The speakers are as follows: Joseph C. Curtis, Ph.D., Brown University, Providence, Rhode Island; Harry T. Zankel, M.D., Veterans Administration Hospital, Columbia, South Carolina; Justus F. Lehman, M.D., School of Medicine, University of Washington; Bernard S. Post, M.D., State University of New York Downstate Medical Center; Irvin Klein, M.D., New York State Workman's Compensation Board; Eugene Ackerman, Ph.D., Mayo Clinic; and Catherine Hinterbuchner, M.D., State University of New York Downstate Medical Center. Cortez Enloe, M.D., New York City, will be the luncheon speaker.

International College of Surgeons

The International College of Surgeons will hold its thirteenth biennial congress at the Waldorf-Astoria Hotel, New York City, September 9 through 13. A. Mario Dogliotti, M.D., Torino, Italy, president of the College, will preside. The scientific program has been arranged by Max Simon, M.D., Poughkeepsie. A high light of the meeting will be a dinner address by Edward R. Annis, M.D., Miami, Florida.

For information contact: Thirteenth Biennial Congress Program, International College of Surgeons, 1516 North Lake Shore Drive, Chicago 10, Illinois.

American College of Cardiology and National Advisory Council

The American College of Cardiology will hold a joint workshop program with the National Advisory Council on September 27, in Syracuse, at 9:00 A.M., at the Hotel Syracuse. There will be no charge for attendance.

New York State physicians who will participate are: J. G. Fred Hiss, M.D., Syracuse; Arthur M. Master, M.D., New York City; and Simon Dack, M.D., New York City.

New York State members of the National Advisory Council are: Simon Dack, M.D., Charles P. Bailey, M.D., New York City; and Israel Steinberg, M.D., New York City.

For information concerning the joint meeting contact: Goffredo G. Gensini, M.D., Director, Msgr. Toomey Cardiopulmonary Laboratory and Research Department, St. Joseph's Hospital, 301 Prospect Avenue, Syracuse 3, New York.

New England postgraduate assembly

The Council of the New England State Medical Societies in cooperation with the New England State Chapters of the American Academy of General Practice will sponsor a New England postgraduate assembly to be held at the Statler Hilton in Boston, November 6 through 8. For information write to: Mr. Getty Page, Secretary-Treasurer, Council of the New England State Medical Societies, 128 Merchants Row, Rutland, Vermont.

Books Received

*The following books were received during the month of June, 1962**

Calciphylaxis. By Hans Selye, M.D. Octavo of 552 pages, illustrated. Chicago, The University of Chicago Press, 1962. Cloth, $25.

Textbook of Pathology with Clinical Application. By Stanley L. Robbins, M.D. Second edition. Quarto of 1,190 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $19.

Textbook of Ophthalmology. By Francis Heed Adler, M.D. Seventh edition. Octavo of 560 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $9.00.

Pediatric Diagnosis. By Morris Green, M.D., and Julius B. Richmond, M.D. Second edition. Quarto of 541 pages, illustrated. Philadelphia, W. B. Saunders Company. Cloth, $13.

Pediatrics. By L. Emmett Holt, Jr., M.D., Rustin McIntosh, M.D., and Henry L. Barnett, M.D. Thirteenth edition. Quarto of 1,395 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1962. Cloth, $18.

The Immunology of Rheumatism. By Jerzy B. Kwapinski, M.D., and Marshall L. Snyder, Ph.D. Octavo of 255 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1962. Cloth, $9.00.

Essentials of Pediatric Psychiatry. By Ruben Meyer, M.D., Morton Levitt, Ph.D., Mordecai L. Falick, M.D., and Ben O. Rubenstein, Ph.D. Octavo of 208 pages, illustrated. New York, Appleton - Century - Crofts, Inc., 1962. Cloth, $6.00.

Diagnostic Tests in Infants and Children. By Hans Behrendt, M.D. Second edition. Octavo of 617 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $15.

Essentials of Gynecology. By E. Stewart Taylor, M.D. Second edition. Octavo of 566 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth $12.

Skin Surgery. By Ervin Epstein, M.D. Second edition. Octavo of 339 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $10.

An Introduction to the Study of Disease. By William Boyd, M.D. Fifth edition. Octavo of 478 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $7.50.

The Human Adrenal Cortex. Proceedings of a Conference held at the University of Glasgow, 11th to 14th July 1960. Edited by Alastair R. Currie, M.B., T. Symington, M.D., and J. K. Grant, Ph.D. Octavo of 644 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1962. Cloth, $11.

Pye's Surgical Handicraft. Volume I. Edited by Hamilton Bailey, F.R.C.S. Eighteenth edition. Duodecimo of 487 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1962. Cloth, $8.50.

Extracorporeal Hemodialysis Therapy in Blood Chemistry Disorders. By John E. Doyle, M.D. Octavo of 353 pages, illustrated. Springfield, Charles C Thomas, 1962. Cloth, $11.50.

Biochemistry. By Israel S. Kleiner, Ph.D., and James M. Orten, Ph.D. Sixth edition. Octavo of 867 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $9.75.

Practical Anesthesiology. By Joseph F. Artusio, Jr., M.D., and Valentino D. B. Mazzia, M.D. Octavo of 318 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $7.75.

Primer of Clinical Measurement of Blood Pressure. By George E. Burch, M.D., and Nicholas P. DePasquale, M.D. Octavo of 141 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $5.50.

Psychoanalysis in Groups. By Alexander Wolf and Emanuel K. Schwartz. Octavo of 326 pages. New York, Grune and Stratton, 1962. Cloth, $8.00.

Intestinal Absorption. By T. Hastings Wilson, M.D. Octavo of 263 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $11.

Psychological Development in Health and Disease. By George L. Engel, M.D. Octavo of 435 pages. Philadelphia, W. B. Saunders Company, 1962. Cloth, $7.50.

Thoracic and Cardiovascular Surgery with

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* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

Related Pathology. By Gustaf E. Lindskog, M.D., Averill A. Liebow, M.D., and William W. L. Glenn, M.D. Octavo of 1,024 pages, illustrated. New York, Appleton - Century-Crofts, Inc., 1962. Cloth, $18.

Ciba Foundation Symposium on Tumor Viruses of Murine Origin. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. Octavo of 441 pages, with 72 illustrations. Boston, Little, Brown and Company, 1962. Cloth, $10.75.

Clinical Obstetrics and Gynecology, Volume 5, Number 1, March 1962. The Newborn. Edited by Michael Newton, M.D. **Office Gynecology.** Edited by Roger B. Scott, M.D. Octavo of 320 pages, illustrated. New York, Paul B. Hoeber, Inc., 1962. Published quarterly (four numbers a year). Cloth, $18 per year.

Some Human Oddities. By Eric John Dingwall, Ph.D. Octavo of 198 pages, illustrated. New Hyde Park, N.Y., University Books, 1962. Cloth, $6.00.

Very Peculiar People. By Eric John Dingwall, Ph.D. Octavo of 223 pages, illustrated. New Hyde Park, N.Y., University Books, 1962. Cloth, $6.00.

Better Communications for Better Health. Edited by Helen Neal. Octavo of 224 pages. New York, National Health Council, 1962. Cloth, $5.00.

The Common Sense From Heraclitus to Peirce. By Arthur N. Foxe, M.D. Octavo of 284 pages. New York, Tunbridge Press, 1962. Cloth, $7.50.

Financing Medical Care. Edited by Helmut Schoeck. Octavo of 314 pages. Caldwell, Idaho, The Caxton Printers, Ltd., 1962. Cloth, $5.50.

The First Nine Months of Life. By Geraldine Lux Flanagan. Quarto of 95 pages, illustrated. New York, Simon and Schuster, 1962. Cloth, $3.95.

Tomorrow's Miracle. By Frank G. Slaughter. Octavo of 306 pages. Garden City, N.Y., Doubleday & Company, Inc., 1962. Cloth, $3.95.

Problems of Cytology and Protistology. English edition of Voprosy Tsitologii i Protistologii. Translated by Israel Program for Scientific Translations, Jerusalem, 1961. Available from The Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Cloth, $3.75.

The Biological Role of Nucleic Acids. By O. P. Chepinoga. English edition of Nukleinovye Kisloty i Ikh Biologicheskaya Rol. Translated by Israel Program for Scientific Translations, Jerusalem, 1962. Available from The Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Paper, $1.50.

Surgical Sterilization of Men and Women. A Selected Bibliography. Edited by Christopher Tietze, M.D., assisted by Lussia Neumann. Octavo of 38 pages. New York, National Committee on Maternal Health, Inc., 1962. Paper, $1.00.

Books Reviewed

Human Nutrition, Historic and Scientific. Monograph III. Edited by Iago Galdston, M.D. Octavo of 321 pages, illustrated. New York, International Universities Press, Inc., 1960. Cloth, $6.00.

Were sight somehow lost of the many other major contributions of the New York Academy of Medicine, this energetic and enterprising organization would merit distinction and gratitude for its publications alone. Its unique conception and conduction of conferences devoted to broad considerations of timely, important, and socially significant health themes have resulted in numerous valuable reports such as this—volumes which view today's problems from the added perspectives of yesterday and, especially, of tomorrow, seeking to understand and resolve them within the continuing context of history.

The present admirable amalgamation—if not integration—of the lore as well as the art and science of nutrition consists of 22 papers by acknowledged experts from several countries, in such diverse fields as anthropology, the history of medicine, experimental nutrition, clinical medicine, genetics, biochemistry, food production, and food processing. The material ranges from highly specific discussions of cholesterol metabolism and nuclear cytology, through more extensive epidemiologic observations, to aspects of the relationship of nutrition to personal survival and the public welfare. Although individual chapters reflect predominantly personal experiences, concepts, and opinions, a sense of over-all harmony, if not complete accord, characterizes the interdisciplinary exploration of this basic problem of food for life, which, for the present at least, must be concerned more with minimum needs than with optimum levels. Impressive technologic progress has been made and surely will continue, but the obstacles have become commensurately complex. The evident great promise is accompanied by an equally apparent sense of urgency. Although scientific achievement is associated with an increased recognition of social responsibility, the means of effective synthesis remain proportionately elusive. As our aspirations increase, so do our obligations, and so, seemingly, do our difficulties.

This volume provides only qualified assurances—prospects of what may be, with contingences of what, therefore, also must be. The fundamental question permeating this search for a philosophy relates not to what we are capable of doing to achieve the nutritional well-being of mankind, but to what we are willing to do to insure this indispensable ingredient of self-realization for all members of the world community. Are we as well as those for whom we also would require a sufficiency of the essentials to human dignity adequately educated—or merely informed? Can we be motivated to exercise necessary judgment and restraint, to forego the folly and vanity of conspicuous consumption and no less conspicuous propagation, to further the fulfilment of future generations? With our amply demonstrated capacity for concern for others, are we able to confront, with equal objectivity and sincerity, our own basic needs and to act in what in the long run is also our own self-interest?

The New York Academy of Medicine has had the inspiration and foresight to point up this transcendent problem of our time. Hopefully, we in the health professions will soon find the courage and wisdom to devote ourselves to its solution before others conspicuously less empathic dictate our common destiny.—ROBERT W. HILLMAN, M.D.

Direct Analysis and Schizophrenia. By O. Spurgeon English, M.D., Warren W. Hampe, Jr., M.D., Catherine L. Bacon, M.D., and Calvin F. Settlage, M.D. Octavo of 128 pages. New York, Grune & Stratton, 1961. Cloth, $4.25.

The four physicians who have formulated their clinical observations and evaluations are members of the Department of Psychiatry, Temple University Medical Center, Philadelphia, where Dr. John N. Rosen has been associate professor of psychiatry since 1956. The contents of this volume evolve from the project of direct analysis which was begun in November, 1957, when Dr. Rosen began treating 12 acute schizophrenic patients who were hospitalized in their first attack between the ages of sixteen and thirty-six but who had not previously had electroshock or other physical therapy.

The Institute of Direct Analysis was sponsored and financed by the Rockefeller Brothers' Fund for a period of three years. The treatment unit is furnished like an ordinary home and is located in the same block as the medical school. Each patient is cared for by three assistant therapists who alternate their time over the twenty-four hour period and carry out Dr. Rosen's directions which evolve from his almost daily treatment of the patient.

Of the 12 patients treated during the three-year period, all but 2 recovered sufficiently to return to the community. A young woman was not able to live at home after twenty-four months of treatment; a man committed suicide during an attempt to return to work after ten months of treatment.

Dr. Rosen's method involves treating the patient in front of a group consisting of his assistants, staff physicians, and other qualified visitors. While paying homage to psychoanalytic theory, Dr. Rosen uses a blunt direct approach to speed the therapeutic operation. He forces his interpretation of symptomatic behavior even though the patient resists. The patient must accept the doctor's on-the-spot verbal "clobbering" rather than working through material for insight. An excerpt from an illustrative case throws a bit of light on Dr. Rosen's off-the-cuff reaction to a patient's outpouring. "You don't have to lie to me. Your promises are false. You are just out to trick me. You're going to keep on making believe all kinds of nonsense. What don't you like about yourself? . . . I'm delighted to have you talk about your insanity, and maybe we'll understand it better . . . ."

The governing principle of direct analysis is that the therapist must be a loving, omnipotent protector and provider for the patient, the idealized mother who has the responsibility of bringing the patient up all over again. Dr. Rosen predicates that a patient's behavior represents escape mechanisms he adopted because relations with his real world were too anxiety-producing. Psychic threat forced the patient to regress because of unconscious malevolent mothering.

The small sampling of patients treated does not give this study much general validity as a methodology. Nevertheless, the successes reported would indicate that the method deserves further trial and study. Obviously, it is too expensive for general application to the treatment of patients with acute schizophrenia who numerically and in terms of treatment difficulty are most challenging to psychiatrists.

The book was written for psychiatrists and their ancilliary workers in this method of direct analysis. Those interested in pursuing this method of treatment would do well to digest its contents and also the publications of Dr. Scheflen and Dr. Brody who have written out of their own experiences and observations.—FREDERICK L. PATRY, M.D.

Recent Advances in Human Nutrition. By J. F. Brock, D.M. Octavo of 454 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $11.50.

Medical nutritionists, while scarcely unique in their bewilderment by conflicting scientific evidence, seem somehow particularly overwhelmed by the volume of commonly contradictory reports relating to their special field of interest. Most thorough reviews of new developments, when not actually compounding their confusion through innumerable and often irreconcilable observations on a variety of species, consider only limited aspects of human nutrition. As a timely answer to a very real need, the volume compiled by Dr. Brock is certain of an authentic welcome and sustained interest on the part of those grateful clinicians who prescribe dietary regimens for, and hopefully before, the ravages of assorted diseases, deserters, and disasters. Together with 14 eminent collaborators, the editor has both described current concepts concerning the role of malnutrition in the causation of a variety of related conditions and delineated principles for their practical control, at the community as well as individual level of management. The 18 chapters in Part I comprise the "General Review of Trends" by Dr. Brock. Part II contains 15 "Invited Contributions on Special Subjects" by the collaborating experts and concludes appropriately with a fine chapter on "Human Nutrition and the United Nations Agencies."

The material is excellent—interesting, readable, and succinctly presented. Cover-to-cover perusal should be a pleasant and rewarding experience for clinicians as well as their colleagues more directly concerned with public health programs. The book is recommended to everyone with the need to be informed of current developments in nutrition, especially to those with an added curiosity concerning the implications of these developments for the future not only of medicine but also of all mankind.—ROBERT W. HILLMAN, M.D.

Thoracic Diseases, Emphasizing Cardiopulmonary Relationships. By Eli H. Rubin, M.D., and Morris Rubin, M.D. In association with George C. Leiner, M.D., and Doris J. W. Escher, M.D. Quarto of 968 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $25.

This book attempts to orient the student in current developments in thoracic diseases. Emphasis is on cardiopulmonary relations with special emphasis on lung cancer, which is well covered including treatment.

The book has many black-and-white and colored illustrations, which enhance its teaching value, including colored pictures of pathologic specimens. The illustrations, including x-ray films, are very clear.

There are chapters on anatomy and roentgenology, maldevelopment and chest x-ray films (normal and abnormal), and angiocardiography. There are 17 pages on thromboembolism and pulmonary infarction. The section on pulmonary function tests is given in detail and is well illustrated.

Thoracic diseases in young persons are discussed so that the internist may understand the changes he finds in later life. Occupational lung diseases are discussed too. The authors stress the importance of a good history. There is a section on thoracic injuries and emergencies and uncommon and esoteric diseases of various types.

There is an extensive bibliography at the end of each chapter which the student will find useful.

A chapter is devoted to diseases of the mediastinum and diaphragm.

All chapters and subjects are illustrated by exceptionally clear roentgenograms, illustrations, and, where needed, pictures of specimens.—VINCENT ANNUNZIATA, M.D.

An Atlas of Bronchoscopy. By A. Huzly, M.D. Octavo of 94 pages, illustrated. New York, Grune & Stratton, Inc., 1960. Cloth, $12.50.

The author is in charge of both the thoracic surgery and the bronchology departments of the Sanatorium Schillerhöhe of the Lva Württemberg, Stuttgart-Gerlingen. This gives him unusual advantages with the result that his book is based on authoritative and follow-up findings. The volume contains only 94 pages but included are 30 tables in black-and-white and color, which represent the photographs taken during the bronchoscopy study. The first part of the book is devoted to the description of the pathologic status presented in the photographs; the second half shows the actual pictures, which are aptly described by short paragraphs on each opposing page. The book has been prepared with a great deal of thought, and the introduction is well worth while. Included are not only the anatomy but also the technic of bronchoscopy, as well as the instruments for endobronchial photography. Students and bronchoscopists alike may well profit by its study.—SAMUEL ZWERLING, M.D.

Officers / County Medical Societies / 1962

TOTAL MEMBERSHIP AS OF JANUARY 1, 1962—25,351

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Greene	Edmund Frede....Athens	John A. Vosburgh....Coxsackie	Mahlon A. Atkinson....Catskill
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Madison	William A. Bramley....Oneida	Felix Ottaviano....Oneida	Robert F. Schramm....Cazenovia
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Richmond	Frederic D. Regan....Staten Island	Joseph Dolgin....Staten Island	J. J. Silverman....Staten Island
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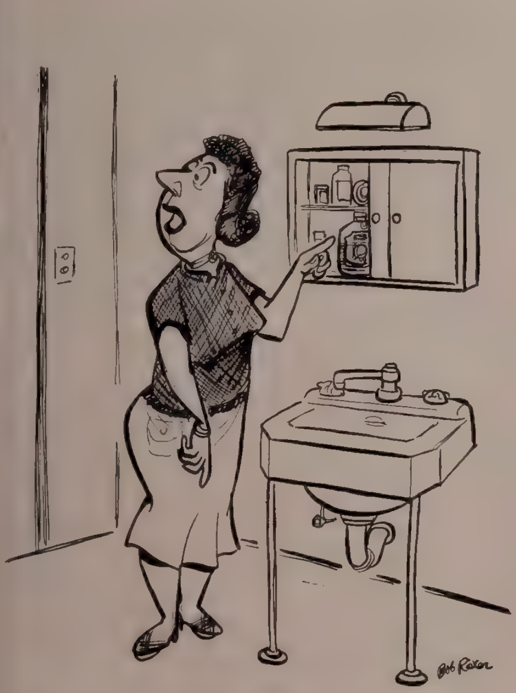

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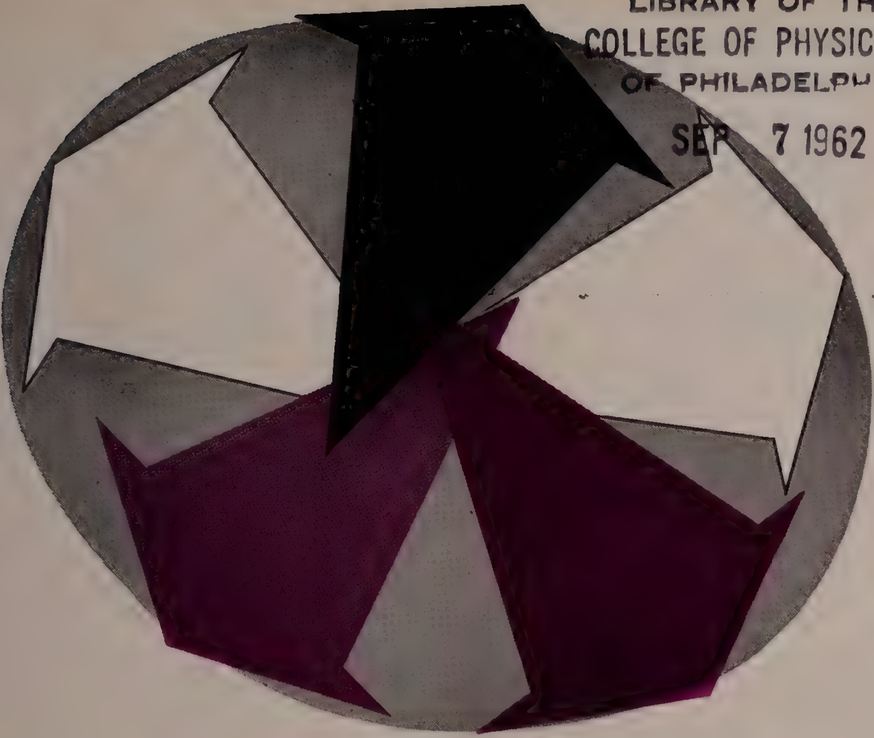

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956.
2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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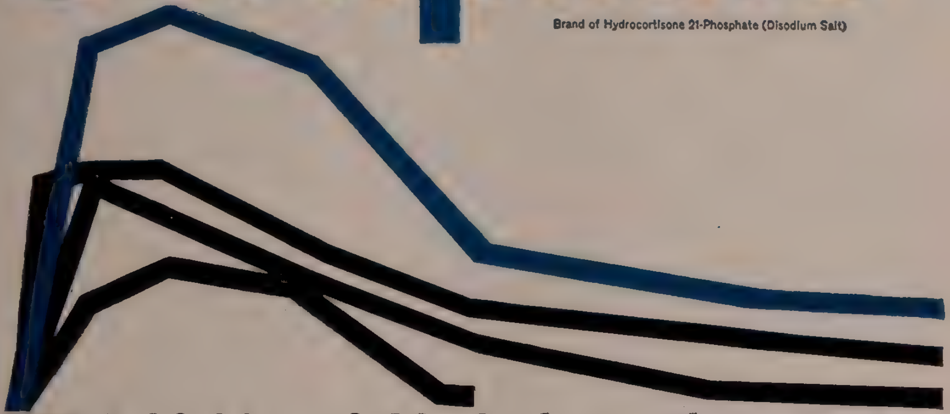

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1. Melby, J. C., and Silber, R. H.: Am. Pract. & Digest Treat. 12:156 (March) 1961. 2. Melby, J. C., and St. Cyr, M.: Metabolism 10:75, 1961

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*McCune, W. G.: M. Clin. North America 44:1479, 1960.

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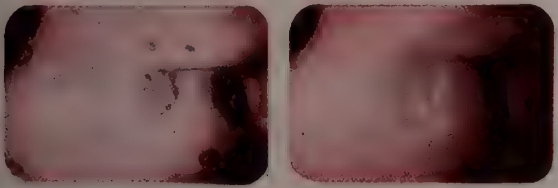

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Reference: 1. Bleiberg, J.: Clin. Med. 8:1724 (Sept.) 1961.

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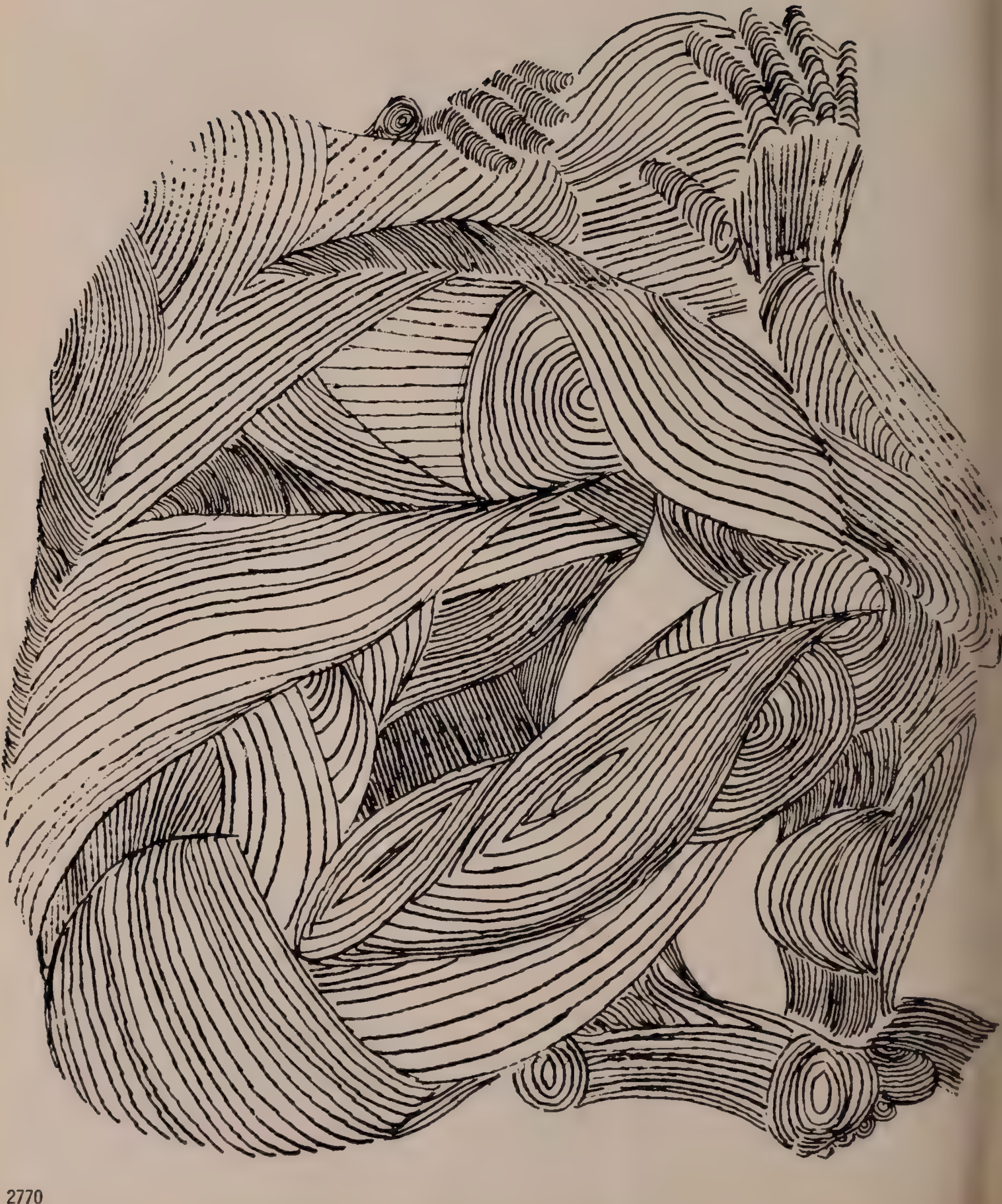

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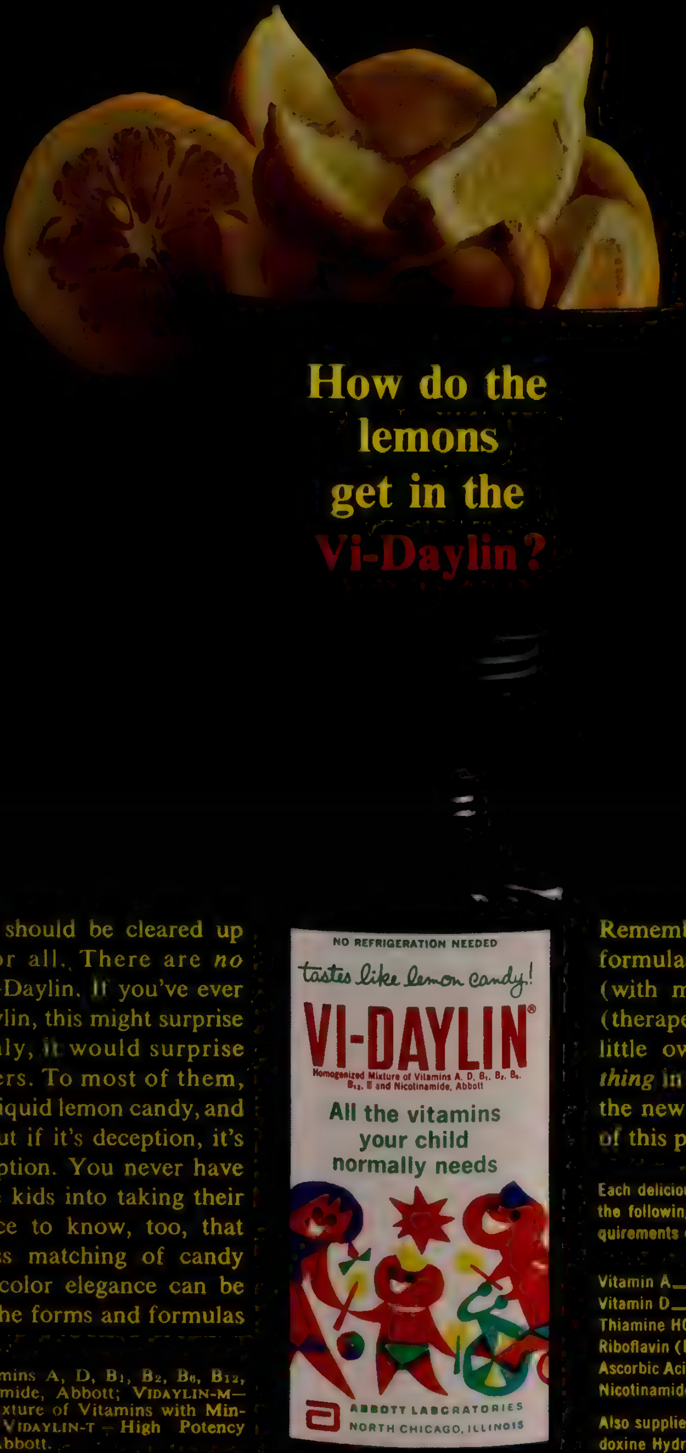
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Thiamine HCl (B_1)	1.5 mg.	2	6
Riboflavin (B_2)	1.2 mg.	1⅓	2
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Niedelman, M.L.: Am. Pract. & Digest Treat., 10:1001, 1959.

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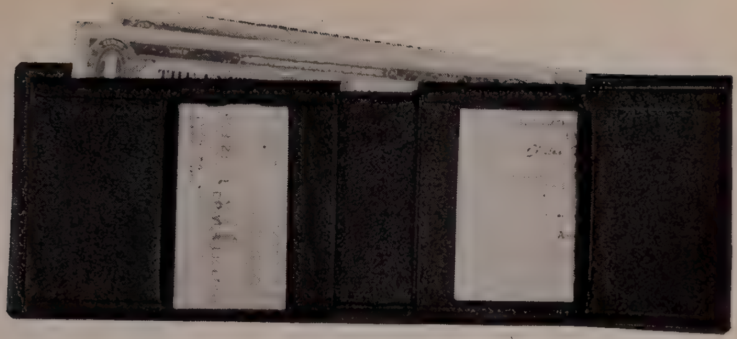

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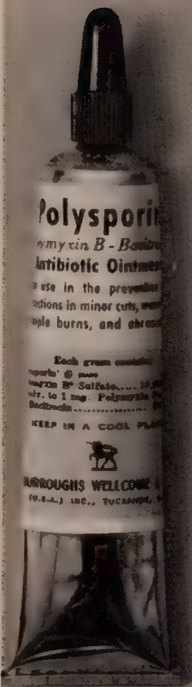
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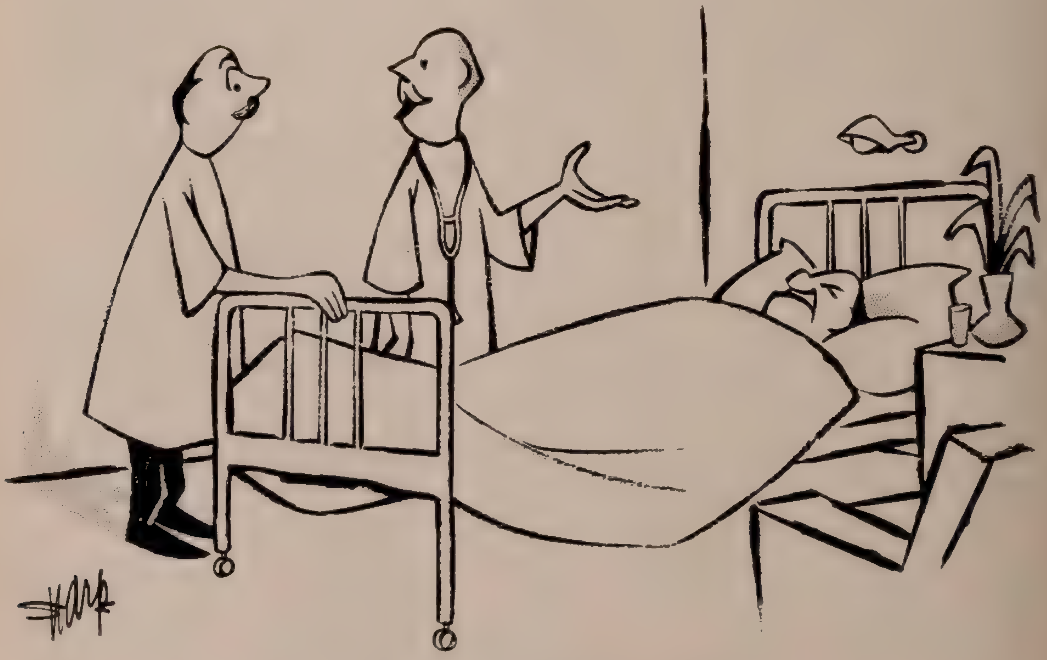

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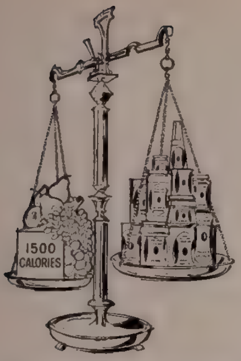

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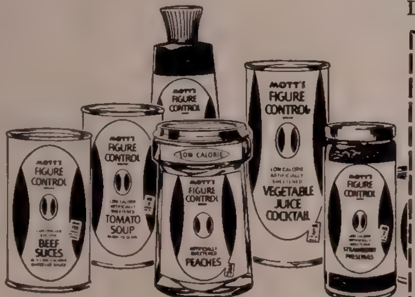

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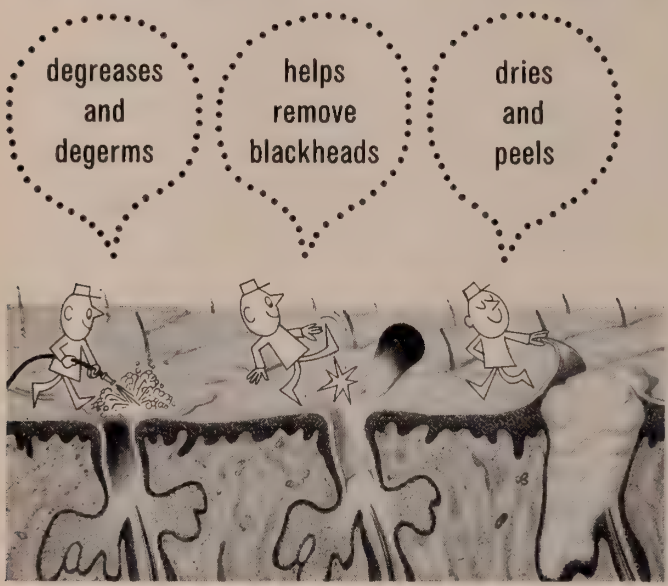

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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New York State Journal of Medicine

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An admirable constancy

The Pharmaceutical Manufacturers Association, which represents 141 corporate members who produce 95 per cent of the nation's prescribed medicines, has released some interesting and encouraging facts.

Despite the harassment of a prolonged investigation often characterized by sensationalism, the pharmaceutical industry spent 13 per cent more on research and development in 1961 than in the year previous. The pharmaceutical industry's investment in research is now three times that of average industry. In the period from 1959 to 1961 nearly 500 scientists were added to the staffs of 23 larger companies.

To offset the 13 per cent increase in research spending, the sales of prescribed drugs over the same period increased only 5 per cent world-wide. It takes financial courage as well as scientific competence to operate in this field, and doctors and patients alike respect this all the more as they learn the true facts.

It is estimated that in 1962 members of the association will spend $268 million on research as against $245.3 million in 1961, and another 600 scientists will be added to the payrolls.

Since faith is the substance of things hoped for, the companies base their faith on new and improved products as a result of increased research, which in turn leads to increased demand and sales.

The industry's faith in its competence is well founded on past performance. It will be supported by those it serves.

The A.M.A.—responsible and representative

"All that is necessary for the forces of evil to win in the world is that enough good men do nothing." This timeless truth, spoken by the eighteenth century statesman Edmund Burke, sounds a warning sharp and clear for us today.

The American Medical Association, which has just held its one hundred and eleventh annual meeting, is a unique institution of our own, founded with the high purpose of improving the quality of medical practice and with a sound record of achievement. This institution is vulnerable, as all democratic institutions are, to the neglect and nonsupport of its members. Unwarranted and misinformed criticism can be challenged with the true facts.

Uninformed criticism by our own members often parrots a "line" which goes like this: "The thing is run by a clique," "those in power," "a vast bureaucracy that does not represent me," and "They made a mistake thirty years ago."

There is one way to refute these distortions and that is to learn at first hand by attending a meeting of the House of Delegates and its reference committees. There you will hear your elected delegates in free and open debate on policy and procedure. You will hear thorough discussion, even painfully minute, before a vote is taken. The mandates of the House are the law to the trustees and to the committees.

A visit to the House of Delegates in session will acquaint one with the breadth and complexity of the fields covered by A.M.A. interest. From Federal legislation to tobacco and disease and from health insurance to seat belts, the amount of careful study and judicious deliberation displayed should call forth pride and gratitude for work well done.

There is a place for legitimate criticism. It should start at the county medical society level. If it has merit it will then work up through the State Society and eventually reach the A.M.A.

This is logical, orderly procedure. It is constructive, and it works. Shallow, ready-made criticism is destructive but cannot erode if enough good men care.

Fresh air for a dank corner

The Federal Food and Drug Administration proposes an overhaul of the regulations last written in 1941 for the control of dietary foods. Comments on the proposals have been obtained from all interested parties and are at present under study.

The new regulations will cover vitamin, mineral, and other dietary supplements, baby foods, foods for elderly persons, low-sodium foods, low-calorie and artificially sweetened foods, protein supplements, hypoallergenic foods, foods for use in the dietary management of disease, and all foods represented as having special dietary properties.

The intent of the new regulations is to assure the public that these materials are offered for what they actually are so that they may be purchased and used intelligently.

Following is a summary of the principal changes which would be made by the proposed regulations.

Food supplements: vitamins and minerals

Consumers of vitamin-mineral food supplements today encounter a great variety of tablets, capsules, powders, and so forth, containing as high as 50 to 75 ingredients, of which only a few have been shown to be of any value whatever as food supplements. It is virtually impossible for the consumer to make a rational choice based on the relative merits of these "shotgun" formulas.

The proposed regulations permit label claims of special dietary value only for those nutrients that are generally recognized as essential in human nutrition and that, in the amounts provided, are likely to be of value in supplementing the American diet.

If a nutrient is subject to deterioration, the new regulations would require an expiration date to be determined by the manufacturer.

Foods offered as vitamin and mineral sources

Under the present regulations foods represented as sources of any of six specified vitamins and four minerals known to be needed in human nutrition must be labeled to show the proportion of the "minimum daily requirement" that is present.

The term "minimum daily requirement" frequently has been misunderstood by consumers and has encouraged some manufacturers to add needlessly large amounts of some vitamins and minerals. In the proposed regulations the term "daily requirement" is used in place of "minimum daily requirement."

Foods for use in reducing or weight-control diets

Foods for use in reducing or weight-control diets would be required to state the number of calories in a one-day supply or in one unit if the foods is in wafers, tablets, capsules, and so forth. The amount in grams of protein, fat, and carbohydrates consumed in a one-day supply would be stated also.

Foods for reducing would be required to bear this prominent label declaration: "Useful only when used as a part of a calorie-controlled diet."

To be described as "nonfattening" a food could contain not more than 5 calories in a serving or 10 calories in a one-day supply.

To be described as "low-calorie" a food could contain not more than 15 calories in a serving or 30 calories in a one-day supply.

To be described as "lower in calories" the label would be required to state the name and caloric content of the food with which it is compared.

Artificially sweetened foods would be required to show the calories saved as compared with the same food with natural sweetening. If the comparison itself shows that the caloric change is insignificant, artificial sweetening should not be used.

Protein sources

Protein consumption in the United States is over 100 Gm. per person daily whereas the average adult needs only about 60 Gm. for the female and 70 Gm. for the male daily of the proteins supplied by the ordinary diet.

The proposed regulations would require foods offered as sources of protein to be labeled in terms of their protein quality and quantity. Specifications that entitle a food to be described as "excellent" or "good" dietary sources of protein are proposed. Foods which do not meet these specifications could not bear protein claims, since the quality of protein is the important factor.

Other regulations

Only minor changes are proposed in the existing regulations on the labeling of low-sodium foods, infant formulas, hypoallergenic foods, and so forth.

Medically insignificant amounts of sodium would not be required to be shown on the label of low-sodium food items.

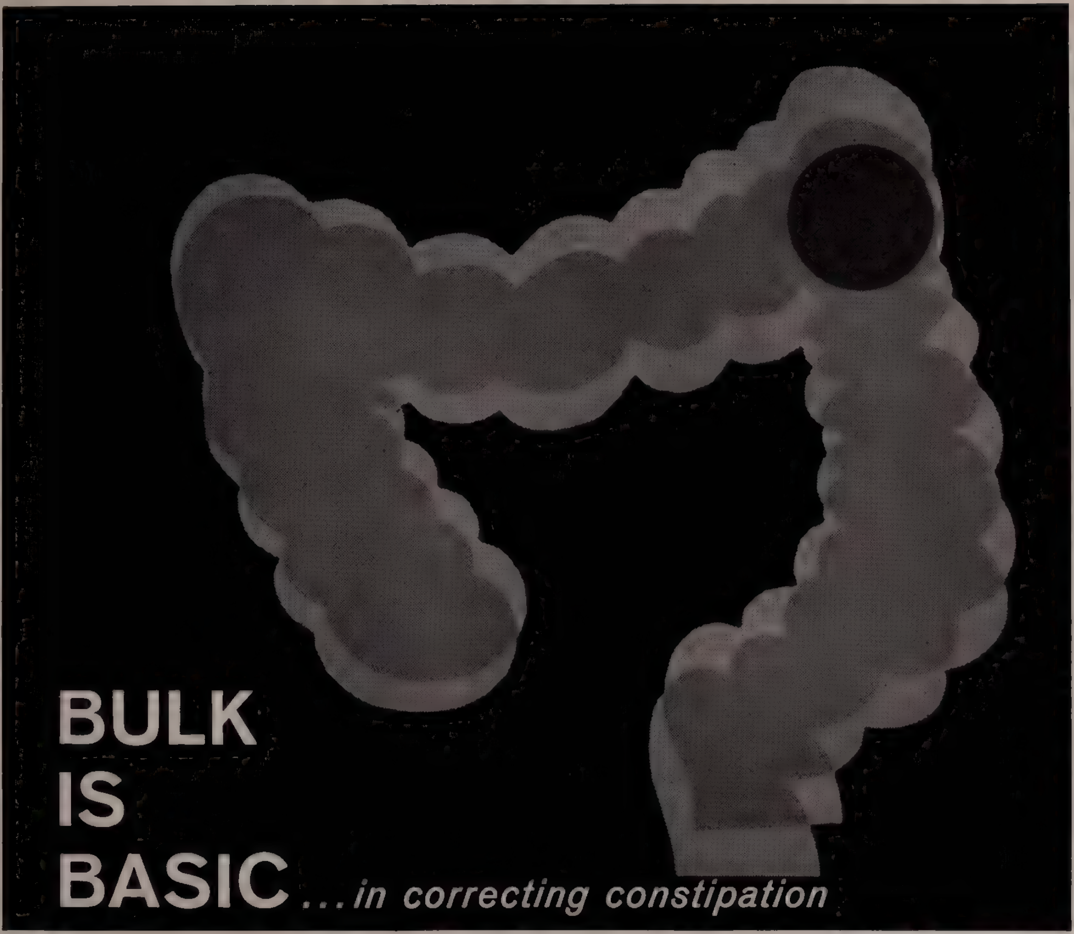
Infant foods that simulate human milk would be required to supply a specified amount of vitamin B_6 or be labeled to show that additional vitamin B_6 should be provided from other sources. The lack of vitamin B_6 has been shown to cause convulsions in babies.

No change has been proposed in labeling hypoallergenic foods.

It should be noted that the National Research Council in 1958 changed the basis of calorie requirement from activity to age level as follows:

Male		Female	
Years	Calories	Years	Calories
25	3,200	25	2,300
45	3,000	45	2,200
65	2,550	65	1,800

Many are supplementing their diet unnecessarily; for those who require such help the new regulations will furnish much needed guidance and protection.



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1. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 6, Baltimore, The Williams & Wilkins Company, 1955, p. 578.

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1. Kolodny, A.L.: Dis. Nerv. System *22*:151 (Mar.) 1961.

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Scientific Articles

Tetanus in New York City

PAUL A. SKUDDER, M.D., F.A.C.S.
New York City
ALLAN E. INGLIS, M.D.
New York City
JAMES R. McCARROLL, M.D.
New York City

From the New York Hospital

FORTY-ONE CASES *of tetanus were reported in New York City between 1957 and 1960, of which 32 were in narcotic addicts. The over-all mortality was 90 per cent: 30 of the addicts died as did 4 of the 9 patients with supposedly trivial wounds. Because of the serious disadvantages in the administration of tetanus antitoxin, physicians are urged to immunize patients with tetanus toxoid whenever feasible and to give a written record of immunization to the patient. Prophylaxis for tetanus depends on whether the wound is tetanus prone or nonprone and the immunization status of the patient. It always includes, however, good wound care and a booster dose of tetanus toxoid or active immunization, if this has not been accomplished previously.*

APPROXIMATELY 500 cases of tetanus occur yearly in the United States, and it is estimated that only about 20 per cent of all the cases are reported.[1] Mortality ranges from 90 to 100 per cent in untreated cases to as low as 27 per cent in a recent series reported by Altemeier, Culbertson, and Gonzalez.[2]

There was a total of 41 cases of tetanus reported in New York City between 1957 and 1960, with a mortality of approximately 90 per cent. Thirty-two of these cases occurred in narcotic addicts, and all but 2 of these patients died. All of the remaining nonaddicted patients had relatively minor njuries, some of which were too small to prompt the patient to seek medical attention at the time of the injury. The other wounds were similar to those seen daily in physician's offices and hospital emergency departments. Four of these 9 patients with supposedly rivial wounds died (Table I).

The following case report describes the onset and subsequent management of clinical tetanus in Case 8 of Table I. This patient was treated by us at the New York Hospital—Cornell Medical Center.

Case report

The patient was a nineteen-year-old mason's apprentice who was in good general health. He had not been immunized against tetanus as a child and had not been in the Armed Forces where immunization is mandatory. While he was at work, the patient cut his right fourth finger on a power saw which was being used to cut fresh Georgia pine. The construction site on which he was working had been a livery stable. He was taken to a hospital where x-ray films revealed a fracture of the middle phalanx in addition to the soft-tissue injury. The patient was admitted to the hospital where the wound was sutured, and he was given 1,500 units of tetanus antitoxin. He was discharged on the fourth day following the injury.

On the seventh day after injury the patient complained of some tightness in his neck and generalized irritability. These symptoms increased, and on the tenth day he returned to the emergency room of the same hospital. At this time he was complaining of generalized

TABLE I. Reported cases of tetanus among nonnarcotic addicted patients in New York City (1957 to 1960)

Case	Sex	Age (Yrs.)	Type of Injury	Incubation Period (Days)	Previous Immunization Status	Tetanus Prophylaxis	Outcome
1	M	15	Open fracture of toe	7	Unknown	Tetanus toxoid five days after injury	Recovered
2	M	53	Saw laceration of thumb	6	Unknown	None	Recovered
3	F	18	Scalp laceration	6	Unknown	None	Died
4	M	9	Open fracture of forearm	4	Unknown	0.5 ml. tetanus toxoid at time of injury	Died
5	M	36	Puncture wound of foot	11	Unknown	Tetanus antitoxin at time of injury. Amount unknown	Recovered
6	F	48	Presumed varicose ulcer infection	Not known	Unknown	None	Died
7	F	57	Cut toe while trimming toenails	4	Unknown	None	Died
8	M	20	Saw laceration of finger	12	Not immunized	1,500 units of tetanus antitoxin at time of injury	Recovered
9	F	40	Splinter in finger	Indefinite	Not immunized	None	Recovered

stiffness of all his muscles and of an inability to open his mouth. He was subsequently hospitalized with a diagnosis of systemic tetanus, and for two days he was treated with oxygen, antibiotics, and 100,000 units of equine tetanus antitoxin intramuscularly.

Convulsions increased in severity and in frequency, and during his convulsions the patient became cyanotic. On the twelfth day following injury he was transferred to The New York Hospital. At the time of admission to this hospital there was generalized rigidity of all muscle groups with classical risus sardonicus (Fig. 1A). Extensor spasms with opisthotonos occurred with the slightest stimulus. There was intermittent cyanosis, and the patient was unable to swallow.

He was given 100,000 units of equine tetanus antitoxin and 500 mg. of tetracycline intravenously. Under general endotracheal anesthesia, a tracheostomy was performed, and an endotracheal tube with an inflatable cuff was inserted through the tracheostomy. The middle phalanx of the right fourth finger was edematous. The wound edges separated when the sutures were removed, and there was considerable nonviable soft tissue but no actual pus (Fig. 1B). The Clostridium tetani could not be identified on cultures taken at the operating table. Since it was not possible to remove all nonviable tissue and salvage the finger, it was amputated at the base of the middle phalanx. The wound was left open, and hydrogen peroxide dressings were instituted.

Despite general anesthesia and large doses of succinylcholine chloride, the patient continued to convulse. Therefore, over the next four days complete skeletal muscle relaxation was maintained with D-tubocurarine chloride. During this time the patient remained in the recovery room with two nurses and an anesthesiologist in attendance at all times. Ventilatory exchange was maintained with a Bird respirator through the endotracheal tube in the tracheostomy opening. D-tubocurarine chloride, in from 6 to 9 mg. doses totalling approximately 150 mg. a day, was necessary to prevent tetany. In all, the patient received the following medications: D-tubocurarine, 150 mg. daily; pentobarbital, 100 mg. intramuscularly every three hours; equine tetanus antitoxin, 100,000 units intramuscularly daily; equine tetanus antitoxin, 100,000 units intravenously daily; Chloramphenicol, 0.5 Gm. intravenously four times daily; streptomycin, 0.5 Gm. twice daily; chlorpromazine hydrochloride, 25 mg. intramuscularly every six hours; and Chlor-Trimeton, 10 mg. intramuscularly every six hours. Nutrition and hydration were maintained with intravenous dextrose, 5 per cent in water or saline, with water-soluble vitamins added.

Fever developed on the fourth postoperative day, and a portable chest x-ray revealed atelectasis of the right upper lobe. This was due to an obstruction of the right main stem bronchus by the endotracheal tube inserted in the trachea which could be seen on the x-ray film, extending slightly beyond the carina into the left main stem bronchus.

D-tubocurarine was stopped on the fourth day, and although there was still considerable muscular rigidity with superimposed extensor spasms, a ventilatory exchange through the tracheostomy was maintained with the aid of the Bird respirator. The patient was continued on gradually-decreasing doses of barbiturates. On

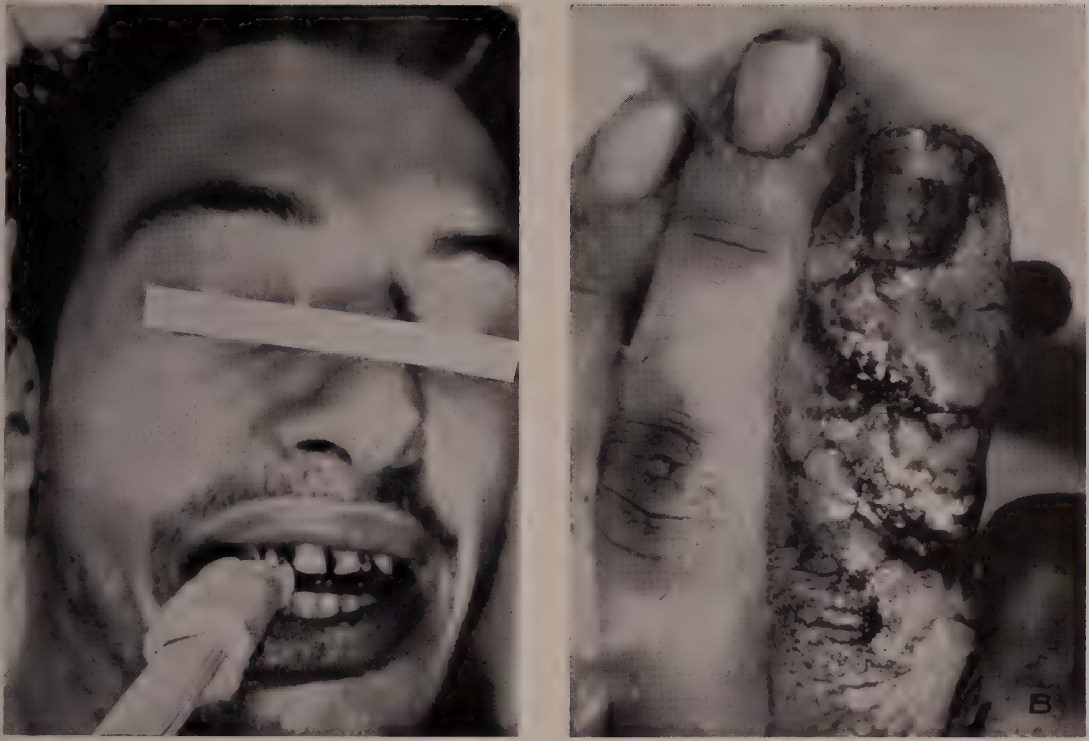

FIGURE 1. Case 8. (A) Classical risus sardonicus or lockjaw caused by spasm of the masseter muscles and muscles of facial expression. (B) Appearance of wound following removal of sutures.

the fifth postoperative day tube feedings were initiated, since the patient still had a severe spasm of the masseter muscles. Feeding by oral liquids was begun on the tenth postoperative day, and by the fifteenth postoperative day the patient was able to tolerate a regular diet.

On the seventeenth postoperative day a split-thickness graft was applied to the granulating stump on the right ring finger. The patient was discharged on the twenty-seventh postoperative day, thirty-nine days following the original injury.

Comment

The foregoing case report and case summaries emphasize that although tetanus itself is a relatively rare disease in New York City it may, nevertheless, appear after the most trivial and minor injuries. For this reason, the possibility of tetanus must be considered in any type of open or penetrating wound, and some type of protection against the disease should be offered.

THE SUPERIORITY OF ACTIVE IMMUNIZATION. No preventive measure the physician can offer his patient promises surer protection than an immunization with tetanus toxoid.[3–5] The certain protection against active disease assured by this immunization initiated at the time of injury does not produce a protective antibody level until the second stimulating dose is given approximately four weeks after the first, and the incubation period of the disease can be as short as four days (Table I). In view of this, it is a serious indictment of the effectiveness of our preventive programs that the decision to administer equine tetanus antitoxin must be made hundreds of times daily in the hospitals and physicians' offices of New York. This situation paradoxically results in far more morbidity from the prevention of a disease than would occur from the disease itself.

Over half of all persons may be expected to show sensitivity to horse serum by a skin test, and much of this undoubtedly arises from the frequent use of tetanus antitoxin at the time of injury. Even after the most rigorous skin testing and the elimination of those individuals showing immediate sensitivity to the product, at least from 5 to 10 per cent of persons who are given equine tetanus antitoxin may be expected to develop serious systemic reactions to the product.[6] This serum sickness, characterized by varying degrees of fever, generalized rash, hives, swelling, and pruritus, may appear from two to seven days after the administration of horse serum and may be severe enough to warrant hospitalization.

In addition to the possibility of producing serum sickness, the administration of equine tetanus antitoxin has several other disadvantages. One of the most likely of these is that the injection of tetanus antitoxin will sensitize the individual to horse serum, so that products of equine origin cannot be used in the future when they may be needed more urgently. A second serious disadvantage is the possibility of an immediate anaphylactic reaction which may occur even after a skin test showing negative results. Other serious delayed reactions, such as brachial plexus palsy, are also seen occasionally after the administration of foreign proteins such as horse serum. In addition to all these disadvantages is the fact that the usual prophylactic dose of 1,500 units recommended formerly has frequently failed to prevent the development of clinical tetanus. This is illustrated by our case report, as well as by others cited in the literature.[2,3,7,8]

In view of the serious disadvantages in the administration of tetanus antitoxin and the considerable amount of illness produced by its use, the Medical Society of the County of New York has recommended strongly that all its members urge their patients to be immunized actively with tetanus toxoid.[9] A resolution strongly supporting this proposal was passed by the House of Delegates of The American Medical Association at its clinical meeting in Dallas in December, 1959, and has since been incorporated in the programs of many county medical societies.

At the present time only two large groups in New York City can be presumed to have been immunized actively against tetanus. These groups are veterans of service in the Armed Forces of the United States during and following World War II and most children under the age of eighteen years. Even for those under eighteen years the presumption cannot be made with any degree of certainty, since the routine use of diphtheria-pertussis-tetanus immunization in childhood is, even today, not accomplished universally.

Accordingly, all physicians are urged to offer active immunization with tetanus toxoid to all patients whenever it is feasible. This could easily be made a routine part of a periodic health examination and check-up. Another logical opportunity occurs when a patient requests immunizations or advice before overseas or domestic travel. Since the possibility of minor injury is always present, active tetanus immunization should be included routinely for all travelers regardless of destination.

Another logical occasion for initiating active tetanus immunization is at the time of treatment for any traumatic injury. Regardless of whether or not tetanus antitoxin may be administered, active immunization should be begun with tetanus toxoid. Alum-precipitated (cloudy) toxoid is preferable for the initial immunization, particularly if antitoxin is given at the same time, and should be administered in a dose of 0.5 ml. either subcutaneously or intramuscularly, followed by a second similar dose in from four to six weeks. At from six to twelve months a third booster dose should be given which provides adequate protection for ten or more years. Once this initial protection has been accomplished there will be no need for the administration of antitoxin, and reliance may be placed on a booster dose of tetanus toxoid in the event of injury.

It should be remembered that the benefits of active immunization may be decreased greatly unless the patient is fully informed of the immunization he has been given, and receives a written record of it. Unless this is done, a subsequent physician treating an injury may feel compelled to administer tetanus antitoxin if he has no evidence of the immunity status of the patient. Immunization cards on which this data can be recorded may be obtained free of charge from The American Medical Association in Chicago.

THE PROPHYLAXIS OF TETANUS. Although there is no substitute for the active immunization of all our citizens against tetanus with tetanus toxoid, we are far from achieving this goal. Despite the continued efforts of the medical profession, the Department of Health of the City of New York, and many other cooperating agencies, many individuals in our population have not yet received active tetanus immunization. Thus, the physician treating any type of laceration or injury is constantly faced with the problem of the patient who has received no active immunization against tetanus or whose immunity status cannot be established satisfactorily. Under such circumstances the physician is forced to consider the use of various types of prophylaxis against tetanus, although some of them carry a significant potential for serious illness.

To determine which program of treatment offers the best protection for a patient and at the same time offers the least possibility of unfavorable reaction, several important facts should be kept in mind.

First, good wound care is probably the single most important factor in the prevention of tetanus. This implies thorough cleansing and removal of all foreign bodies and devitalized tissue. This is important since the tetanus bacillus is an anaerobic organism and can grow only in tissue which has a diminished or absent blood supply. Antibiotics and antiserum can never substitute for proper surgical care of injuries in the prevention of tetanus.

A second important fact is that although most strains of the tetanus bacillus are extremely sensitive to penicillin and the tetracyclines, these drugs will be distributed effectively through the blood stream only to living tissues where the oxygen supply is plentiful. Since the tetanus spores can proliferate only in tissue with a decreased blood supply, antibiotics will not reach a focus of infection in sufficient amounts to be effective and are thus no substitute for thorough cleansing and debridement.

The third significant fact is that the immunity provided by active tetanus immunization with tetanus toxoid persists for long periods of time. This immunity may be "recalled" promptly by a booster dose of toxoid for fifteen or more years after the initial immunization.[10-14]

Another advance has been the recent development of commercially available human tetanus antiserum (human tetanus immune globulin)* which avoids the dangers inherent in the administration of heterologous proteins. This preparation has the advantage of giving protective antibody levels for much longer periods than antibodies of other species which probably disappear in from seven to ten days. It also avoids the possibility of sensitizing the individual to horse serum. Bovine preparations are available, but it has been our experience that individuals who are sensitive to equine antitoxin are very likely to be sensitive to the bovine product, which seriously limits its usefulness.

It will be noted that all the following recommendations for the treatment of injuries include the initiation of active immunization against tetanus, if this has not been accomplished previously. It should be emphasized that the value of this procedure will be decreased considerably unless the full course of immunization is completed and unless the individual is given a written record of his immunization and instructed to carry it with him at all times. The administration of tetanus antitoxin at the same time as the initiation of active immunization will dampen, but not suppress completely, the antibody response to the second dose of toxoid, particularly if more than 10,000 units of antitoxin are given.

For adequate prophylaxis of tetanus, wounds may be divided arbitrarily into those considered tetanus prone and those considered unlikely to foster the development of tetanus bacilli. Any wound containing foreign material or devitalized tissue is tetanus prone, as well as crushing injuries, deep second and third degree burns, and even some avascular lesions such as varicose ulcers. Contamination, tissue injury, and a decrease in the blood supply are the principal factors to be considered in determining whether or not a wound is tetanus prone.

The severity of a wound is not a reliable guide to the likelihood of developing tetanus, since many cases arise from minor or even unnoticed puncture injuries. In wounds occurring in New York City one should remember that narcotic addicts are a particularly susceptible group, since they rarely sterilize their needles and other equipment.

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* Prepared by Cutter Laboratories, Berkeley, California.

TABLE II. Outline for prophylaxis of tetanus

In Patients Who Have Been Actively Immunized Against Tetanus Within the Past Fifteen Years

- For the tetanus nonprone wound
  1. Clean thoroughly
  2. Debride as needed
  3. Give a booster dose (0.5 ml.) clear tetanus toxoid
  4. Give no antitoxin
- For the tetanus prone wound
  1. Clean thoroughly
  2. Debride
  3. Give a booster dose (0.5 ml.) clear tetanus toxoid
  4. Give no antitoxin

In Patients Who Have Not Been Immunized Against Tetanus Or Whose Immunization Status is in Doubt

- For the tetanus nonprone wound
  1. Clean thoroughly
  2. Debride as needed
  3. Start active immunization with alum precipitated toxoid (0.5 ml.). Make arrangements for completion of the series at four weeks and six months, and give the patient an immunization record.
  4. Give no antitoxin
- For the tetanus prone wound
  1. First, question and test for sensitivity to tetanus antitoxin (horse serum)
  2. If not sensitive to tetanus antitoxin (horse serum) "negative test"
     - (*a*) Clean thoroughly
     - (*b*) Debride
     - (*c*) Start active immunization with alum precipitated tetanus toxoid (0.5 ml.).
       Make arrangements for completion of the series at four weeks and six months and give the patient an immunization record.
     - (*d*) Give equine tetanus antitoxin 3,000 units or more, depending upon degree of contamination.
  3. If sensitive by test to tetanus antitoxin (horse serum) "Positive Test"
     - (*a*) Clean thoroughly
     - (*b*) Debride
     - (*c*) Start active immunization with alum precipitated tetanus toxoid (0.5 ml.).
       Make arrangements for completion of the series in four weeks and six months and give the patient an immunization record.
     - (*d*) Give human tetanus immune globulin 1,500 units, if available, or penicillin or tetracycline for at least two weeks.
     - (*e*) Desensitization is not recommended.

Outline for prophylaxis of tetanus (Table II)

IN PATIENTS WHO DEFINITELY HAVE BEEN ACTIVELY IMMUNIZED WITH TETANUS TOXOID WITHIN FIFTEEN YEARS. *For the tetanus-nonprone wound in immunized persons.* 1. Cleanse and debride the wound thoroughly. Suture or leave open, and dress as indicated.

2. Give a booster dose of 0.5 ml. fluid (clear) tetanus toxoid.

3. Record the immunization in your own records, give the patient a written record of his immunization, and instruct him to carry it with him at all times.

4. Give no tetanus antitoxin.

For the tetanus-prone wound in immunized persons. 1. Attempt to convert the wound to a tetanus-nonprone wound by careful cleansing, removal of foreign bodies and devitalized tissue, and leaving the wound open if necessary. Puncture wounds may often be converted into nonprone wounds by the removal of the margins of the puncture, thorough irrigation, and removal of foreign bodies and devitalized tissue. A small gauze or rubber drain and moist soaks are helpful in promoting drainage.

2. Give a booster dose of 0.5 ml. fluid (clear) tetanus toxoid.

3. Record the immunization in your own records, give the patient a written record of his immunization, and instruct him to carry it with him at all times.

4. Give no tetanus antitoxin.

IN PATIENTS WHO HAVE NOT BEEN IMMUNIZED AGAINST TETANUS OR WHOSE IMMUNIZATION STATUS IS IN DOUBT. *For the tetanus-nonprone wound in unimmunized persons.* 1. Cleanse and debride the wound thoroughly. Suture or leave open, and dress as indicated.

2. Start active tetanus immunization with 0.5 ml. of alum-precipitated (cloudy) tetanus toxoid.

3. Record the immunization in your own records, give the patient a written record of his immunization, and instruct him to carry it with him at all times. Make arrangements for the completion of the series with a second dose in four weeks and the third dose in from six months to one year.

4. Give no tetanus antitoxin when the wound is tetanus nonprone.

For the tetanus-prone wound in unimmunized persons. 1. Question for a history of allergic reactions (asthma; nasal or ocular symptoms; urticaria; itching; and so forth) related to contact with horses. If there is no history of sensitivity to horses, they should be tested either 0.1 ml. of a 1:10 dilution of tetanus antitoxin intradermally or one drop of 1:10 dilution of tetanus antitoxin should be administered into the conjunctival sac. A positive test result consists of the appearance within twenty minutes of definite redness and itching of the conjunctiva or a definite area of redness and swelling at the site of the intradermal test. Epinephrine should always be available whenever tetanus antitoxin is used either for testing or for prophylaxis. The symptoms of a positive eye test may be relieved rapidly by instilling one or two drops of 1:1,000 epinephrine solution into the conjunctival sac.

2. If the sensitivity test indicates negative results and the patient gives no history of sensitivity to horses or horse serum:

(*a*) Cleanse and debride the wound thoroughly. Suture or leave open and dress as indicated.

(*b*) Start active tetanus immunization with 0.5 ml. of alum-precipitated (cloudy) tetanus toxoid.

(*c*) Record the immunization in your own records, give the patient a written record of his immunization, and instruct him to carry it with him at all times. Make arrangements for the completion of the series with a second dose in four weeks and the third dose in from six months to one year.

(*d*) In a separate site give equine tetanus antitoxin, 3,000 units or more, depending on degree of contamination.

3. If the sensitivity test indicates positive results or if the patient gives a history of sensitivity to horses or horse serum:

(*a*) Cleanse and debride the wound thoroughly. Suture or leave open and dress as indicated.

(*b*) Start active tetanus immunization with 0.5 ml. of alum-precipitated (cloudy) tetanus toxoid.

(*c*) Record the immunization in your own records, give the patient a written record of his immunization, and instruct him to carry it with him at all times. Make arrangements for the completion of the series with a second dose in four weeks and the third dose in six months.

(*d*) Give 1,500 units of human tetanus antiserum. Skin testing with this material is not necessary, and serum sickness does not occur. This material is not advocated for all tetanus-prone wounds in unimmunized individuals at present only because of its short supply and relatively high cost at the time of this writing.

(*e*) If the human tetanus antiserum is not available, substitute penicillin or a tetracycline drug in therapeutic dosage for at least two weeks.

It is generally agreed that there is little to be gained and much to be risked from attempting desensitization of those individuals giving positive skin test results. Antitoxin administered to a sensitive individual is neutralized rapidly, and it will not persist for periods long enough to cover the incubation of the disease. If the physician decides to administer equine tetanus antitoxin, at least 3,000 units should be used, and the dose may range up to 10,000 or more units, depending on the judgment of the physician. If a reaction occurs, a tourniquet above the site of injection, epinephrine (0.5 to 1 cc. intramuscularly or intravenously and repeated as needed), antihistamines, artificial respiration, and oxygen if indicated should be given. For continued shock, infusions of norepinephrine, ACTH, or hydrocortisone may be used.

Conclusions

1. All wounds should be considered potential portals for tetanus infection and some type of prophylaxis should be offered. Some wounds are more tetanus prone than others.

2. Good wound care with thorough cleansing and debridement is the single most important procedure in the prophylaxis of tetanus.

3. A booster dose of tetanus toxoid should be given to all injured patients who have been immunized more than one year previously, and active immunization should be started on all patients who have not been immunized previously.

4. Arrangements should be made for the completion of the immunization series.

5. Patients should be given a written record of all immunizations and instructed to carry it with them at all times.

6. Equine tetanus antitoxin should be used only after careful questioning and testing for sensitivity and should be reserved for those patients with tetanus-prone wounds which cannot be converted to tetanus-nonprone wounds by careful cleansing and debridement. It need not be used for patients who have been actively immunized with tetanus toxoid within fifteen years. These patients require only a booster dose of fluid tetanus toxoid.

7. Human tetanus immune globulin, if available, should be given to unimmunized patients with tetanus-prone wounds, which are found by checking the case histories or by testing to be sensitive to the equine product.

8. Penicillin or broad-spectrum antibiotics also may be used prophylactically in addition to specific prophylaxis, particularly in individuals who are found sensitive to horse or bovine antitoxin.

Summary

Nine cases of tetanus in nonaddicted patients in New York City between the years 1957 and 1960 have been summarized, and 1 case has been reported in detail. The various methods available for the prophylaxis of tetanus have been discussed. An outline for the prophylaxis of tetanus has been presented and summarized.

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Complement Titer, C-Reactive Protein, and Electrophoretic Serum Protein Patterns in Eczematous Children

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FORTY-TWO CHILDREN *in various stages of atopic eczema, ranging in age from three months to six years, were studied. The complement titers in all children were within normal limits. Seventeen patients had normal plasma protein patterns; in 6 (who showed clinical signs of infection) the gamma globulin fractions were increased and in 2 (age three and five months) decreased. The C-reactive protein result was positive in 15 (including the 6 in whom the gamma globulin was increased) and negative in 14. The latex fixation test gave negative results in the 13 children who were tested for the presence of an abnormal protein.*

THE POSSIBILITY THAT an allergic mechanism is a factor in the etiology of atopic eczema has been entertained by many investigators. It is thought that complement and its various components play an important role in some immunologic reactions. Numerous investigators have attempted to establish the immunologic nature of certain disease processes by demonstrating that the lytic activity of the serum complement is decreased.[1-9] Low serum complement titers have been reported in disseminated lupus erythematosus, acute glomerulonephritis, and the nephrotic syndrome.[5-9] In some instances, such as serum sickness, the observed fall in the serum complement in the presence of an antigen-antibody reaction has been amply confirmed.[3,4,10] In rabbits undergoing acute anaphylaxis, a definite loss of complement was noted by Schwab,[2] who felt that the fall in complement was due to antigen-antibody reactions. Elevated complement titers have been reported in measles, scarlet fever, dermatomyositis,[11] and rheumatic fever.[12]

Adequate data regarding serum complement in patients with atopic eczema have not been published. In this paper data on the complement titers, C-reactive protein, serum protein patterns, and latex fixation in a group of eczematous children are reported.

A group of 42 children in various stages of eczema were studied; their ages ranged from three months to six years; and 24 were boys and 18 were girls. Only children with findings typical of atopic eczema were included in the study. Applications of 5 per cent liquor carbonis detergens to the affected skin was the only medication used. The children were not on any type of oral medication or restricted diet.

Laboratory procedures

Venous blood was obtained from the patients and allowed to clot. Serum was

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TABLE I. Complement titers, C-reactive protein, and serum protein patterns in eczematous children

Sex	Age	Complement Titers in Units	CRP*	Serum Protein Patterns	Condition of Eczema
M	$1^{1}/_{2}$	2.2	2+	normal	chronic
F	$1^{1}/_{2}$	3.2	trace	increased gamma globulin	chronic
M	$1^{1}/_{2}$	2.4	negative	normal	chronic
M	$^{1}/_{4}$	4.0	negative	low gamma globulin	acute
F	3	2.8	1+	increased gamma globulin	chronic
M	$1^{1}/_{2}$	4.2	1+	normal	chronic
F	$^{5}/_{12}$	2.3	negative	low gamma globulin	chronic
F	4	3.0	1+	increased gamma globulin	chronic
F	1	3.5	negative	normal	chronic
M	4	1.5	negative	normal	chronic
F	2	1.8	trace	normal	chronic
M	3	2.8	trace	normal	chronic
M	2	3.7	2+	normal	chronic
M	2	3.3	negative	normal	acute
F	$^{5}/_{12}$	2.4	3+	increased gamma globulin	chronic
M	1	3.84	1+	increased gamma globulin	acute
M	$^{3}/_{4}$	2.76	negative	normal	remission
M	$^{1}/_{2}$	3.3	negative	normal	remission
M	$^{1}/_{4}$	3.3	negative	normal	acute
F	6	2.0	1+	normal	chronic
M	$2^{1}/_{2}$	1.3	negative	normal	chronic
M	$2^{1}/_{2}$	3.3	negative	normal	chronic
F	5	1.33	trace	normal	chronic
M	2	3.91	1+	increased gamma globulin	acute
F	1	3.8	trace	normal	chronic
M	$^{7}/_{12}$	3.0	negative	...	chronic
M	2	2.1	negative	...	remission
M	$1^{1}/_{2}$	3.1	negative	...	chronic
F	$^{1}/_{4}$	3.6	negative	...	acute

* CRP—C-reactive protein.

separated from the clot as quickly as possible and stored in the frozen state at minus 20 C. The complement activity of the sera was determined by titration of C_1 according to the method of Wadsworth,[13] as modified by Lange *et al.*[6] Complement activity was measured by the hemolysis of sensitized red blood cells. The degree of hemolysis, expressed in percentage values, was related to the corresponding dilution of serum and determined in units. The 50 per cent hemolysis level has been adopted as an index of complement activity. With each set of tests of unknown sera, a standard complement determination with lyophilized guinea pig complement run in duplicate was included. The dilution of the standardized guinea pig serum which produced a 50 per cent hemolysis of a specific amount of sensitized blood cells was defined as the arbitrary unit of complement. The degree of lysis was read by visual comparison with a series of lytic color standards made up of artificially standardized sheep red blood cells.

Electrophoretic analyses of the serum protein patterns were determined on a Spinco model R apparatus, using barbital buffer at pH 8.6 and ionic strength 0.075, at 6 ma., 80 volts. The strips were stained with bromophenol blue.

The latex fixation test was designed as an additional serologic technic to measure the rheumatoid factor, a gamma globulin consisting of fractions 19S and 7S. The latex fixation test, as described by Rheins and his associates,[14] was performed on the sera of 13 eczematous children.

The C-reactive protein test result is usually positive in patients with certain infectious diseases; the serum of the patient yields a precipitate in the presence of dilute solutions of the C polysaccharide of the pneumococcus. The test for C-reactive protein was determined by the capillary precipitin method as described by Anderson and McCarty[15] employing an antiserum prepared by injecting rabbits with purified crystalline C-reactive protein of human origin.

Results

The complement titers in all 42 children were found to be within normal limits (1.5 to 4 units), regardless of whether the eczema was acute, chronic, or in a state of remission. In addition to complement determinations, C-reactive protein determinations were studied in 29 of the 42 patients. In 25 children serum protein patterns were also obtained. These data are presented in Table I.

As seen in Table I, 17 patients had normal plasma protein patterns; in 6 the gamma globulin fractions were increased and in 2 decreased. The C-reactive protein result was positive in 14 and negative in 15.

The latex fixation test gave negative results in the 13 children who were tested for the presence of an abnormal protein.

Comment

In a group of 42 eczematous children in various stages of the disease, the complement titers of the serum were found to be within normal limits. This finding seems to indicate that complement or its components are not fixed or destroyed in atopic eczema. In any case, if atopic eczema is the result of an immunologic reaction, it cannot be detected by the measurement of complement. However, this does not rule out the possibility of an underlying immunologic mechanism in eczema, because it is known that certain antigen-antibody reactions do not fix complement in vitro.[16] Until the functions of the various components of complement C_1, C_2, C_3, and C_4 are studied separately in eczematous children, it is of course possible one or another of these fractions may be decreased, which our current methods of testing are too crude to detect.

Several investigators have studied the plasma protein patterns in various dermatoses.[17–20] Feldaker and his associates[17] reported a decreased albumin and increased globulin fractions in 3 of 4 patients with atopic dermatitis. Lever, Schultz, and Hurley[18] noted moderately reduced total proteins with the albumin fractions markedly lowered and the globulin fractions increased. Rezza and Castellotti[19] found the only alteration to be an increase in beta globulin; Pozzo and Gianotti[20] reported an increase in alpha globulins. These observations indicate the diversity of findings for the plasma protein pattern in the eczematous child.

In our group of eczematous children, 17 plasma protein patterns were found to be normal; 6 children had elevated gamma globulin fractions, and 2 of the children had definitely decreased gamma globulin. Lubschez[21] has demonstrated that the presence of minor infections will result in changes in all serum protein fractions except beta globulin. Such changes are most prominent in the first month after the infection but can still be detected to some degree as long as four months after the infection. Oberman *et al.*[22] have shown that a fairly abrupt rise of absolute amounts of both total serum globulins and its gamma fraction occurs in children aged from three to five years. They concluded that this rise probably reflects the increasing incidence of infection in the preschool age.

In the reports of Feldaker[17] and Lever[18] no attempts were made to explain the increase in gamma globulin in their eczematous patients. In our study, the increases noted in the gamma globulin fractions appeared to be associated with infection in every instance. In all children who had had increased gamma globulin components, the C-reactive protein determinations were elevated from a trace to 3 plus.

Low values for gamma globulin were observed in 2 children aged three and five months respectively. It is well known that the gamma globulin is often decreased during the first six months of life, remaining stable during the first week of life and falling steadily to reach low levels at three to four months of age, after which it slowly begins to rise until the period from seven to eleven months when the mean values for children do not differ significantly from adult levels. In our group of children the changes in the serum protein pattern were considered to be nonspecific—unrelated to a specific mechanism involved in eczema.

Summary

Complement titers in 42 children with eczema were within normal limits.

Gamma globulin values were normal in 17 of 25 children tested, elevated in 6, and decreased in 2 children. The 6 patients with elevated gamma globulin titer had clinical signs of infection, and the C-reactive protein reaction was positive. The 2 patients with decreased gamma globulin values were aged three and five months respectively.

The changes in the plasma protein patterns in this group of eczematous children were considered to be nonspecific.

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Average length of life in the United States

The average length of life for America's wage-earners and their families reached an all-time high of 70.8 years in 1961, according to statisticians of Metropolitan Life Insurance Company.

As shown by the experience among the company's industrial policyholders, last year was the seventh in succession in which the expectation of life at birth has been at least the Biblical three score and ten.

In recent years, however, the gains in longevity have been slight. The average lifetime of these policyholders in 1961 was 0.3 of a year greater than that in 1960 and represented a gain of only 1.0 year since 1954. In the preceding seven years the gain was 3.3 years. However, since 1909 the gain has been 24.5 years, and since 1879 to 1894 the average length of life has more than doubled.

Hirsutism in the Female

Hormonal Reclassification

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A PROPER CLASSIFICATION *of hirsutism in the female may suggest more effective methods of diagnosis and therapy. Constitutional hirsutism includes those patients with no proved endocrine abnormality, normal 17-ketosteroid excretion, and chromatogram, and no evidence of virilism or adrenal or ovarian pathologic conditions. Other classes of hirsutism may be associated with normal ovaries and adrenals, polycystic ovaries, diffuse luteinization ovaries, adrenal hyperplasia, or a tumor of the ovaries or adrenals. They are due to excessive production in the adrenal and/or ovary of the hormone involved: testosterone, adrostenedione, dehydroepiandrosterone, 11β-hydroxyandrostenedione or adrenosterone, and a combination of two or more groups. The hormonal therapy of hirsutism has been largely disappointing.*

HIRSUTISM IS A serious problem to many afflicted women and poses a difficult diagnostic and therapeutic problem for the physician. This report is not intended to be a complete review of the subject of hirsutism, but presents a simple reclassification based on recent hormonal advances. This new approach may aid in the differential diagnosis and particularly in the therapy of hirsutism.

Background

Certain endocrine disorders involving the presence of hirsutism (congenital adrenal hyperplasia, adrenogenital syndrome, Cushing's syndrome, Stein-Leventhal syndrome, ovarian hyperthecosis, arrhenoblastoma, and so forth) are recognized by the clinical picture, by the use of roentgenograms, and by the total urinary 17-ketosteroid and 17-hydroxysteroid excretion. However, the most common type of hirsutism in females, that is, idiopathic hirsutism, remains a diagnosis of exclusion. The total urinary 17-ketosteroid excretion is usually within normal limits and there is considerable variation from patient to patient in this group. Nevertheless, taken as a group, the hirsute females excrete more total 17-ketosteroids than nonhirsute women.[1-4] Improved methods of study, including 17-ketosteroid chromatogram fractionation, pregnanetriol and pregnanetriolone excretion, the application of ACTH stimulation, cortisone suppression, and gonadotropin stimulation tests have served to identify some of these patients as milder (transitional) examples of the more obvious endocrine disorders cited previously and thus remove them from the group of idiopathic hirsutism.[1-12]

In the attempt to clarify the underlying pathogenesis of the clinical picture, studies have been performed in idiopathic hirsutism,[2,13-15] congenital adrenal hyperplasia,[5,16] adult adrenogenital syndrome,[2,8,10] transitional adrenal hyperplasia,[1,4] and the Stein-Leventhal syndrome.[2,8-10,17-20] From their data on hirsute patients we can obtain information which correlates with the potential influence of various steroid patterns on the hair follicle. Since the data are obtained from studies of the chromatographed fractionation of 17-ketosteroids in the urine (which consists of conjugated end products, presumably lacking in physiologic activity), it is essential to recognize the precursors of these fractions and consider their potential

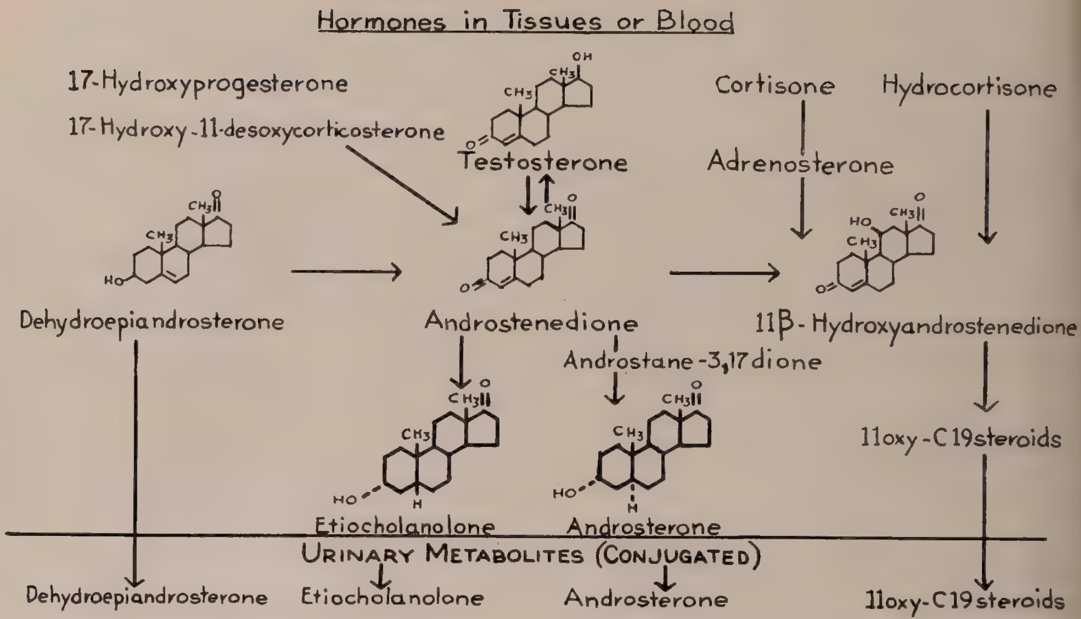
Hormones in Tissues or Blood
17-Hydroxyprogesterone
17-Hydroxy-11-desoxycorticosterone
Testosterone
Cortisone
Hydrocortisone
Adrenosterone
Dehydroepiandrosterone
Androstenedione
11β-Hydroxyandrostenedione
Androstane-3,17dione
11oxy-C19steroids
Etiocholanolone
Androsterone
Urinary Metabolites (Conjugated)
Dehydroepiandrosterone
Etiocholanolone
Androsterone
11oxy-C19steroids

FIGURE 1. Metabolism of potential hirsutism-producing hormones.

physiologic activity before inactivation by conjugation (Fig. 1).

The predominant conjugated 17-ketosteroids fractionated from the urine are androsterone (3α-hydroxyandrostane-17-one), etiocholanolone (3α-hydroxyetiocholane-17-one), and dehydroepiandrosterone (3β-hydroxy-Δ^5-androstene-17-one) which are 11-desoxy C-19 compounds. The 11-oxy C-19 compounds include 11β hydroxyandrosterone (3α, 11β dihydroxyandrostane-17-one), 11β hydroxyetiocholanolone (3α, 11β-dihydroxyetiocholane-17-one), 11-ketoetiocholanolone (3α-hydroxyetiocholane-11, 17-dione), and 11-keto-androsterone (3α-hydroxyandrostane-11, 17 dione).[12,21]

Androsterone and etiocholanolone evolve primarily, in approximately equal proportions, from metabolism of testosterone (Δ^4-androstene-3-one, 17β-ol), androstenedione (Δ^4-androstene-3, 17-dione), and dehydroepiandrosterone.[12,21] Small amounts arise from two C-21 steroids (17-hydroxyprogesterone and 17-hydroxy-11-desoxycorticosterone), with etiocholanolone produced in greater proportion than androsterone from these compounds.[12,21] Since testosterone, androstenedione, and dehydroepiandrosterone are androgenic, it is most likely that the hirsutism is related to hypersecretion of one of these compounds.[2] Clinically, this is confirmed by the finding of increased amounts of androsterone and etiocholanolone in the urine of most cases of congenital adrenal hyperplasia,[16,21] adrenogenital syndrome,[2-4,8] and the Stein-Leventhal syndrome.[2,8,17-19,22,23]

Dehydroepiandrosterone, produced by the adrenal gland[12] and the polycystic ovary,[24-26] is variable in excretion by both normal and hirsute females, so that it is unlikely to be the most common cause of hirsutism.[2] However, there are some cases in which the dehydroepiandrosterone is elevated and may be a factor in certain hirsute patients,[2,3,8,16,18,20,22,24,27-29] either directly or by conversion in vivo to androstenedione and testosterone.

Androstenedione has been isolated from normal human ovaries,[30] polycystic ovaries,[26,31] adrenal tissue,[1] and adrenal vein blood.[12] It is from 3 to 6 per cent as active an androgen as testosterone in the human being.[12] When secreted in large quantities, as might be expected in those hirsute females with high levels of total 17-ketosteroids, androsterone and etiocholanolone fractions, this hormone may be a cause of hirsutism. In addition, in vivo conversion of androstenedione to testosterone may also be a factor, since in vitro transformation has been demonstrated in ovarian slices.[32] It is also possible that under certain circumstances in vivo conversion of androstenedione to testosterone could be present in the adrenal gland.

Testosterone has been found in arrhenoblastoma tissue[33] and in ovarian slices from patients with the Stein-Leventhal syndrome.[25,34] Elevated blood levels of testosterone have been found in some hirsute women with normal total 17-ketosteroids and the Stein-Leventhal syndrome.[35] Since testosterone is markedly androgenic, small quantities could produce hirsutism without increasing the total output of 17-ketosteroids above normal or slightly elevated levels. Each individual varies as to her sensitivity of the hair follicle to androgen,[18] so that even normal amounts of circulating testosterone may be involved in the production and maintenance of hirsutism in an otherwise normal female.

Thus, previous attempts to localize the site of origin of the hirsutism-producing hormone specifically either to the ovary[4,22,23] or the adrenal gland[2,10] were complicated because three androgenic hormones, each capable of arising in either the ovary or the adrenal gland, can be involved in hirsute patients bearing some resemblance physically and in their total and chromatographed 17-ketosteroid excretion.

Classification

A proper classification of hirsutism may suggest more effective methods of diagnosis and therapy. Brooksbank,[36] in an excellent review of the subject, classified the conditions associated with hirsutism into groups according to the site of the pathologic conditions (pituitary, adrenal gland, ovary, genetic defects, central nervous system, and miscellaneous). Although this is helpful when pathologic conditions are found (tumor or hyperplasia), it does not aid in the vast majority of patients in whom no pathologic conditions are present or when the pathologic and clinical picture may be varied, as in the Stein-Leventhal syndrome.[37] Van de Wiele *et al.*[38] attempted to classify hirsutism by means of the chromatographic analysis of the urinary 17-ketosteroids. As noted previously, the end products as measured in the chromatogram may be a reflection of various metabolic pathways and do not necessarily correlate with androgenic manifestations. This is well demonstrated by the variable urinary and clinical findings in 39 patients with proved polycystic ovaries.[39]

Utilizing as a basic criterion the excessive growth of hair in a typically masculine distribution, I propose the following classification of hirsutism in the female, with emphasis on the predominant hormone or hormones involved:

CONSTITUTIONAL HIRSUTISM. Constitutional hirsutism includes those patients with no proved endocrine abnormality (normal 17-ketosteroid excretion and chromatogram and no evidence of virilism or adrenal or ovarian pathologic conditions) due to: (1) circulating ovarian or adrenal testosterone of normal amount acting on extrasensitive hair follicles, (2) a defect in hepatic inactivation of normal circulating testosterone (postulated by me), and (3) a genetic predisposition to hirsutism unrelated to any circulating androgen stimulus.

The following three groups may be associated with normal ovaries and adrenals, polycystic ovaries, diffuse luteinization ovaries, adrenal hyperplasia, or a tumor of the ovaries or adrenals. Furthermore, virilization and menstrual disorders may or may not be present. Future studies of blood levels of these hormones, when they are available in large series of cases, will determine whether or not a characteristic finding will point to a particular pathologic entity. The standard technics of determining the presence or absence of pathologic conditions in the ovaries or the adrenal glands must be pursued.

TESTOSTERONE HIRSUTISM. Testosterone hirsutism is due to circulating ovarian or adrenal testosterone of slightly increased amounts. These patients demonstrate normal or slightly elevated total urinary 17-ketosteroids and chromatogram content of androsterone and etiocholanolone and probably account for the vast majority of patients with idiopathic hirsutism. There is some evidence for the role of progesterone in the production of testosterone, particularly in the polycystic ovary.[25,31] A block of the normal pathway of progesterone metabolism, influencing more testosterone formation, could be present in some patients with polycystic ovary.

ANDROSTENEDIONE HIRSUTISM. Androstenedione hirsutism is due to excessive production of androstenedione from the ovary, the adrenal gland, or both glands simultaneously. Potential conversion in vivo of androstenedione to testosterone could add to the severity of the clinical picture. Significantly elevated total urinary 17-ketosteroids and chromatogram fractions (androsterone and etiocholanolone) would be present.

DEHYDROEPIANDROSTERONE HIRSUTISM. Dehydroepiandrosterone hirsutism is due to an excessive production of dehydroepiandrosterone from the adrenal gland or the polycystic ovary, with a potential conversion in vivo to androstenedione and testosterone. These patients have normal or elevated levels of total 17-ketosteroids, with the chromatogram demonstrating dehydroepiandrosterone in excess, as well as androsterone and etiocholanolone.

11β-HYDROXYANDROSTENEDIONE OR ADRENOSTERONE HIRSUTISM. 11β-Hydroxyandrostenedione or adrenosterone hirsutism is due to an excessive production of these mildly androgenic and interconvertible compounds, as found in Cushing's syndrome, or due to the exogenous administration of ACTH, cortisone, or hydrocortisone. Pathologically, normal-appearing adrenal glands, adrenal hyperplasia, or adrenal tumors may be present. Hydrocortisone is metabolized to 11β-hydroxyandrostenedione (Δ^4-androsten-11β-ol-3,17 dione), and cortisone is metabolized to adrenosterone (Δ^4-androsten-3,11,17-trione).[12,21] The close chemical relationship of 11β-hydroxyandrostenedione to androstenedione in the absence of the ability to convert 11β-hydroxyandrostenedione to androstenedione suggests that 11β-hydroxyandrostenedione may be able to produce some degree of hirsutism when it is present in excess. Similarly, adrenosterone may have some hirsutism-inducing activity in cortisone-treated patients. That this mechanism is not the cause in cases of hirsutism without Cushing's syndrome is demonstrated by the finding of normal or only slightly elevated levels of the urinary metabolites of 11β-hydroxyandrostenedione (11β-hydroxyetiocholanolone and 11β-hydroxyandrosterone) and adrenosterone (11-ketoandrosterone and 11-ketoetiocholanolone) in these patients.[2,10]

COMBINATION OF TWO OR MORE GROUPS. A final classification of hirsutism in the female may consist of two or more of the previously mentioned groups.

Comment

The hormonal therapy of hirsutism has been generally disappointing. Large doses of estrogen are ineffective. After the removal of a benign adrenal tumor, the hirsutism may disappear since the hirsutism-producing hormone is removed completely.[29] A wedge resection of the ovaries in the Stein-Leventhal syndrome has been unsuccessful in curing the hirsutism despite the return of menses in many of these patients,[20] probably because small amounts of the hirsutism-producing hormone are secreted by the remaining ovarian tissue and/or the intact adrenal glands. Conflicting reports[1-3,5,10,39,40] of the effectiveness of low-dosage, long-term prednisone therapy in hirsutism are probably due to the differing etiologic factors of the hirsute groups studied. Prednisone would not be expected to be effective against the group of cases in which ovarian testosterone was the cause. It might be effective in those patients in whom ACTH stimulation of adrenal androgen production was at fault, providing the hair follicles had not assumed autonomous activity. The new classification presented previously, when readily applicable in the future, would differentiate these patients properly and aid in the development of a method of suppressing or annulling the effect of endogenous testosterone, androstenedione, or dehydroepiandrosterone on the hair follicle without significantly suppressing glucocorticoid production. Clinical studies of this problem are being done by me and shall be reported in the future.

Summary

1. Hirsutism in the female has been discussed with a hormonal reclassification

into six major groups.

2. This new classification lends itself well to future intensive investigation. Studies of steroid hormone biosynthesis in normal and abnormal human ovarian and adrenal tissue in conjunction with the development of new technics for the determination of blood levels of testosterone, androstenedione, dehydroepiandrosterone, 11β-hydroxyandrostenedione, androsterone, and etiocholanolone will trace the pathogenesis of hirsutism.

3. Circulating testosterone may be the hormone affecting the hirsutism in most cases, although progesterone, androstenedione, and dedydroepiandrosterone may be involved in certain cases.

4. Ultimately by the new technics we may have a further aid in differential diagnosis and will have a more rational approach to therapy in the administration of an agent that will block the action of the hirsutism-producing hormone in the nonsurgical case.

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Changing Concepts in Psychiatric Treatment

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Most of us are aware that patients with mental illness occupy over half of the hospital beds in the country. In many states the support of this staggering patient load demands as much as one-third to one-half the operating budget.

Long ago it became apparent that the problem of treatment and prevention of mental illness had a great many facets and in one way or another involved every citizen of the community. Until 1955 there appeared to be no answer to this problem save that of building new and larger mental hospitals to keep pace with the increasing number of admissions.

Between 1903 and 1955 the population of mental hospitals in this country quadrupled. This increase occurred in spite of the use of available therapeutic tools such as insulin shock, electroshock, lobotomy, and group and individual psychotherapy. But in 1954 to 1955 a new era of psychopharmacotherapy was ushered in. The apparent ease and simplicity of drug therapy aroused the interest and enthusiasm of administrators and psychiatrists, particularly those working in large mental hospitals. This rush to use new drugs was viewed with skepticism by some who saw it as another fad that would soon pass.

For the first time in history there shortly occurred a decrease in the resident population of mental hospitals. Five or six years have passed and there is ample evidence to indicate that this trend is continuing. For instance in 1959 instead of encountering the anticipated increase of 10,000 patients in the 277 mental hospitals in the United States, there was a drop of some 2,000 patients from the high of the previous year. This made the fourth consecutive year in which such a decline had been noted.

The interpretation of this change in resident populations of our mental hospitals has led to considerable controversy. It seems that the decrease must, in large part, be attributed to the use of such drugs in treating the mentally ill, plus the addition of intensive therapy, including psychotherapy.

It is important to recognize that the use of drugs by a physician is a natural and acceptable method of treating any illness, including psychiatric illness. Accordingly, drugs have been accepted by patients, relatives, and, to a great extent, by psychiatrists. However, the acceptance of psychopharmacotherapy has been better among those physicians working in mental hospitals than among their colleagues in private practice.

It is also important to recognize that drug therapy has led to a change in the basic administrative policies of our mental hospitals. The emphasis is shifting steadily from custodial procedures to a therapeutic approach. There is now increased interest in discharging patients and following them adequately at home. This approach has created a climate of hope for mental patients both in the hospital and, more slowly, in their home communities. This climate should now be manipulated to the best advantage of the patient. Possibly the increased number of discharged patients now being maintained in communities will interest more private physicians in basic psychiatry and they will, in time, become more proficient in many aspects of outpatient care. It should eventually lead to the establishment of more psychiatric wards in general hospitals.

The State of New York was one of the first to pioneer in the use of drug treatment in its mental hospitals. In 1955 the resident population of New York State mental hospitals had reached an all-time high of nearly 94,000 patients. The annual increase was close to 2,500 patients. Over the preceding twenty-five years the population of these hospitals had doubled. In

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Keynote Address at Four-State Conference on Mental Health, Coos Bay, Oregon, April 29, 1961.

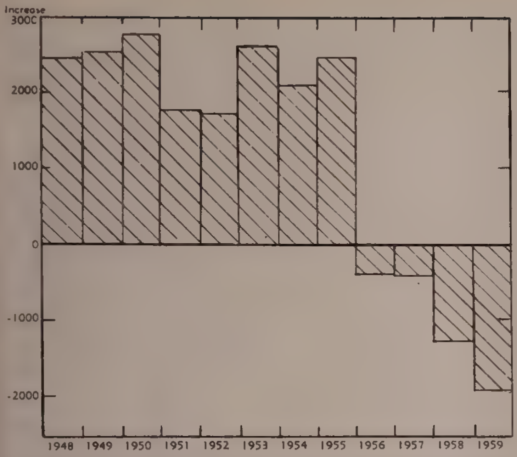

FIGURE 1. Annual increase in resident patients in mental hospitals in New York State.[1]

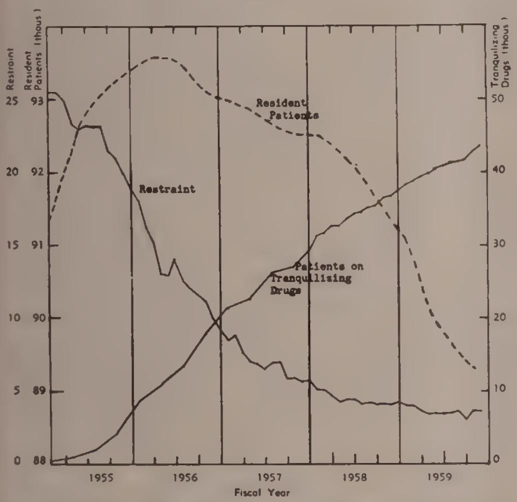

FIGURE 2. Special therapy, restraint-seclusion, and resident patients in mental hospitals in New York State.[1]

spite of the addition of new facilities, overcrowding had reached serious proportions (Fig. 1).

But this picture was reduced dramatically by our use of drugs. Although the actual decline in the hospital census (500 patients) seems small, when it is added to the expected increase for the year (2,500 patients) it represented a drop of 3,000 patients (Figs. 1 to 3). This decrease accelerated as drug use increased. In 1959 New York State hospitals reported a drop of almost 2,000 patients. This occurred in spite of a marked decrease in the use of electroshock therapy and psychosurgery.

PSYCHIATRIC TREATMENT *has been greatly influenced in recent years by the introduction of drugs. In 1955 there were 3,752 patients in the Rochester State Hospital with 523 others on convalescent care and 89 on family care. In 1960 the resident population had fallen to 3,239, whereas the number of patients on convalescent care had increased to 1,392 and the number on family care had tripled. The psychopharmacologic drugs now in use may be classified as follows: (1) the original drugs introduced into this country in 1954, consisting chiefly of chlorpromazine hydrochloride, promazine hydrochloride, and reserpine; (2) newer phenothiazine compounds based on molecular manipulation; and (3) a group of sedative and tranquilizing drugs including meprobamate and hydroxyzine hydrochloride. The monoamine oxidase-inhibitors are not recommended because of interference in liver function, but imipramine hydrochloride, another antidepressant, has proved efficacious. Drug therapy should be instituted on admission to the hospital and continued after discharge.*

Material and methods

Rochester State Hospital began using drugs early in 1954. In 1955 there were 3,752 patients in the hospital with 523 others on convalescent care and 89 on family care. Compare this with 1960. The resident population has fallen to 3,239, 1,392 patients are on convalescent care, and the number on family care has tripled. The admission rate, previously a rising curve, has now leveled off and is fairly constant (Fig. 3).

Obviously, this entire decrease is not due to the use of drugs alone. Other changes have been made, but many of them were made because the use of drugs pointed up, for the first time, the real need for them. Group and individual psychotherapy has been increased. Greater emphasis has been placed on patient freedom and open doors. Patients have been permitted rights and liberties. Programs in social, occupational, and recreational therapy have been expanded. Over half the hospital has been made an open hospital despite its proximity to main highways.

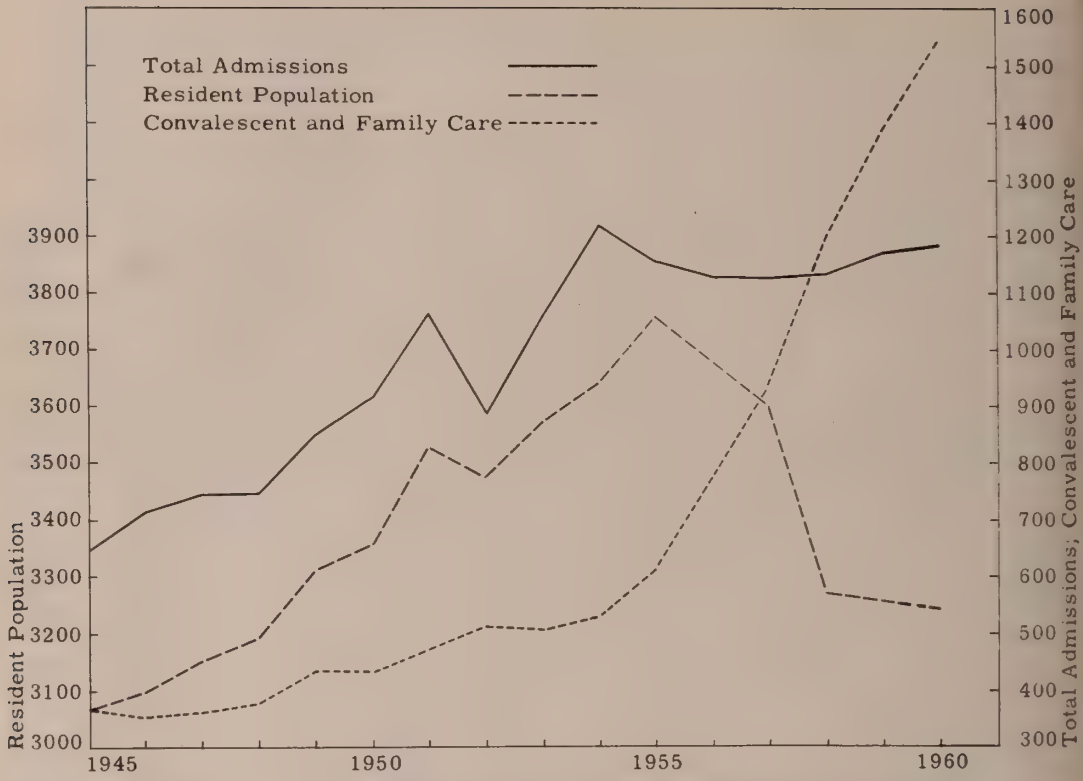

FIGURE 3. Chart of patients in Rochester State Hospital from 1945 to 1960.

These programs have meant the hiring of additional personnel. The work of the psychiatrist, rather than being decreased, has become heavier because more patients now seem amenable to combined psychotherapy and pharmacotherapy. To assist patients in readjusting to life in local communities, the social service department has been expanded tremendously and the outpatient department now functions seven days a week instead of its traditional part-time operation.

For the most part, the psychopharmacotherapeutic drugs now in use may be classified as follows: (1) The original drugs first introduced into this country in 1954, consisting chiefly of chlorpromazine hydrochloride, promazine hydrochloride, and reserpine. Today the first two, and particularly chlorpromazine hydrochloride, continue to be the most popular drugs used in the State hospital system and by experienced psychiatrists in office practice. (2) Newer phenothiazine compounds which are based on molecular manipulation. These drugs are produced by simple changes in molecular structure and, in particular, by adding piperazine rings or fluorinating compounds.[2] Most of these drugs have powerful, extrapyramidal symptoms, but they do not have the sedative effect of chlorpromazine hydrochloride. Likewise, they do not have the general application and value in the treatment of paranoid states, anxiety, and disturbed conduct. In an occasional patient they will prove more helpful alone or in combination. (3) A group of drugs (meprobamate and hydroxyzine hydrochloride) which are chiefly sedative in action but which are now being promoted as tranquilizing drugs. They are frequently claimed to be of value in severe psychotic states, but have application, if at all, in anxiety and mild neuroses.

In choosing any drug for his patients, the physician must use discrimination. It is difficult for the average psychiatrist and general practitioner to appraise realistically the validity of claims and indications for the many psychopharmacotherapeutic agents offered.

In addition to the tranquilizers that have been mentioned, a new series of so-called energizing drugs have been released following the demonstration that one, iproniazid, produced an amelioration of the depressive state in a large number of patients. However, the many complications seen with this drug and the incidence of hepatitis followed by death in a number of cases led to its virtual abandonment.

We have not been impressed by the value of the monoamine-oxidase inhibitors and use them very rarely. The writer uses them seldom if at all since it has been shown experimentally that in a third to a quarter of the patients receiving these agents a rise in the serum glucose transaminase (SGT) occurs, indicating some interference in liver function. In view of the known dangerous complications which are seen after the use of the analogue iproniazid, it would appear unwise to use these drugs unless careful controls can be instituted and laboratory follow-up maintained. For the most part this means use in the hospital.

Another antidepressant drug, chemically different from the monoamine-oxidase inhibitors, is imipramine hydrochloride (Tofranil). It has the basic formula of promazine without the sulfur radical. This drug has proved efficacious in from 60 to 70 per cent of depressions regardless of cause.[3] It can be used in true agitated depressions, manic depressions, and the psychoneurotic and organic depressions. Adequate dosage of this drug can be used without fear of dangerous complications. Side-effects may be present, but these are more annoying than dangerous. Laboratory follow-up is not required, and a physician can use this drug according to his clinical observation and judgment. Any side-effects are quickly controlled by changes in dosage.

Results

Through trial and error and six years of experience we have settled on chlorpromazine hydrochloride, with lesser amounts of promazine hydrochloride, as the tranquilizer used in Rochester State Hospital.[4-8] We use imipramine hydrochloride as an antidepressant agent. Other drugs are sometimes used if the drugs of first choice fail to provide a satisfactory response. Combinations of drugs have been, and will continue to be, employed in refractory patients.

We have also learned that patients should be started on drug therapy immediately after their admission wherever possible. There should be no delay pending an extensive examination, since there are very few contraindications to their use. There is no question that too much emphasis has been placed on possible side-effects of useful drugs.[9-12] With increasing experience and skill side-effects become uncommon, and those that do occur are more unpleasant than dangerous. The incidence of jaundice, for some unknown reason, has fallen over the past few years and now is seldom seen. Agranulocytosis is similarly a rare complication.

Today any well-administered mental hospital using drugs has little need for restraints (Fig. 2). The noisy, destructive, disturbed patients are, for the most part, hard to find.

Drug therapy must be maintained after the patient is discharged.[5,13] It is important to realize that patients who have received medication in the hospital have become accustomed to the routine of taking it. Complications, for the most part, occur during the first eight to twelve weeks while the patient is still under hospital supervision. Thus when a patient is released, drug therapy may be continued with a fair degree of confidence that no major drug toxicity will occur.

Management of discharged patient

The key to the successful management of the discharged patient is the continuation of drug therapy with an adequate maintenance dose and psychotherapy often of a superficial and supportive type.[13-15] Numerous studies have shown that long-term drug therapy helps in reducing the relapse rate from a predrug 35 per cent to something near 9 to 15 per cent. Certainly this reduced relapse rate accounts, in part, for the decrease in hospital populations. For this reason our outpatient department follows the drug therapy of patients carefully to avoid an interruption of maintenance dosage. In some cases if the patient is unable to buy medication, it is supplied to him by the hospital. This, we feel, is cheaper and more desirable than having the patient return to the hospital.

At the same time, we recognize that one of the serious problems in the management of an improving patient is convincing him that his drug must be taken in the proper dose every day. Many unexplained treatment failures are due to the fact that the patient is not taking the drug supplied to him. He often claims that he is. A survey of patients in our hospital showed that almost 10 per cent of them did not take prescribed drugs regularly. Fortunately, laboratory tests have been devised to determine the presence of drug in the body and they should be used whenever there is doubt. The Forrests[16,17] have devised simple urine colorimetric tests for this purpose and have made a valuable contribution to treatment programs. Both tests require the addition of 1 cc. of test solution to 1 cc. of the patient's urine. The intensity of the color reaction indicates whether or not the patient is following his outlined treatment program faithfully. These tests may be used both in the hospital and for outpatients, and the number of unexplained treatment failures usually drops once the patients are told that tests are being run.

Comment

All of this substantial progress in the fight against mental illness is not without its hazards. The physician is bombarded with therapeutic claims for many drugs of dubious value. Much research is still needed to assess the ultimate place of drugs, particularly newer ones, in the treatment of patients. Too often hasty conclusions are made from short-term studies of small groups of patients. On longer and more careful study these conclusions are sometimes found to be unwarranted. Some researchers in this field appear to be drawing conclusions first and then attempting to prove them. This is, of course, not research at all, but material of this sort finds its way to the attention of the physician who must then try to judge, if he can, its validity.

Research in this complicated field, which is always difficult to evaluate, should be conducted by experienced investigators. Studies conducted by immature and inexperienced workers often discredit or becloud the work done by men of considerable skill. Confusion results, and physician, psychiatrist, and general practitioner alike find themselves uncertain of the best therapeutic approach. Just as important, we sometimes forget to evaluate factors other than the use of drugs. Ancillary forms of treatment must also be examined. They may play a vital and continued role in the maintenance of good mental health.

There is still much to be learned about the use of drugs in treating mental illness. Intelligent planning and study should enable us to improve on a record that is already promising.

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PANEL DISCUSSION

PROCEEDINGS

Special Committee on Infant Mortality
Medical Society of the County of New York

Maternal Infections as Affecting the Outcome of Pregnancy

HAROLD ABRAMSON, M.D., Editor
Chairman
CARL GOLDMARK, JR., M.D., New York City
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EDWARD C. CURNEN, M.D., Director, Department of Pediatrics, College of Physicians and Surgeons, Columbia University, Babies Hospital, New York City
Panelists
JOSEPH DANCIS, M.D., Associate Professor of Pediatrics, New York University School of Medicine, New York City
HEINZ EICHENWALD, M.D., Professor of Pediatrics, New York Hospital-Cornell Medical Center, New York City
WILLIAM A. SILVERMAN, M.D., Associate Professor of Pediatrics, College of Physicians and Surgeons, Columbia University, Babies Hospital, New York City
EDWARD H. KASS, M.D., Associate Professor of Bacteriology and Immunology, Harvard Medical School, and Associate Director, Mallory Institute of Pathology, Boston City Hospital, Boston, Massachusetts

Harold Abramson, M.D.: *A consideration of the host-environment-agent balance and interaction is of more than theoretical interest. This is particularly true in the study of complex biologic-maternal-fetal relationships and of placental permeability to explain abnormal outcomes of pregnancy. The pathogenic effects and clinical manifestations resulting from the action of certain selected infectious agents on the maternal host and subsequently on the developing fetus and newborn infant are presented most provocatively in this panel discussion on maternal infections as influencing the outcome of pregnancy.*

Introduction

Carl Goldmark, M.D.: The subject about to be presented is receiving more and more attention from obstetricians and pediatricians. Although the panel is well represented by pediatricians, I hope that the obstetricians in the audience will participate in the discussion afterwards.

I would like to take this opportunity to introduce the Moderator, Edward C. Curnen, M.D.

Edward C. Curnen, M.D.: I would like to introduce our subject this evening by pointing out that this will be a discussion of the host-parasite relation. The fetus obviously is the parasite of the mother. An infectious agent may be a parasite either

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Presented at the New York Academy of Medicine before the open meeting of January 25, 1961, of the Special Committee on Infant Mortality of the Medical Society of the County of New York, Carl Goldmark, Jr., M.D., Chairman, and Harold Abramson, M.D., Secretary, Coliseum Building, 10 Columbus Circle, New York 19, New York.

of the mother, or of the child, or of both.

I think in dealing with infections during pregnancy, we could consider these in the conventional way with reference to the first, second, and third trimesters. In the first trimester, infections which involve the fetus may cause malformations. Evidence from animal experimentation shows that these influences on the fetus are usually lethal, and the fetus that survives with induced malformations is probably the exception rather than the rule. But it is very difficult to document similar observations in human experience.

In the last trimester of pregnancy, the fetus may be injured by maternal infections. The injury may be lethal or may cause premature birth. Congenital malformations are not initiated at this late stage. Less is known about events in the second trimester of pregnancy.

We do not propose, however, to conduct our program according to trimester. Rather, we have invited each of our guests to speak on a phase of the general subject that is of particular interest to him and on which he is now working, so that you can get the benefit of his experience and of most recently acquired knowledge.

Joseph Dancis, M.D., will discuss "The Placental Barrier."

The placental barrier

Joseph Dancis, M.D.: I plan to talk about the placental barrier, primarily to stress the imperfections in this barrier.

Prior to birth, the infant resides in a well-protected situation. Swimming freely in the amniotic fluid, the infant can be attacked only by infections that penetrate the fetal membranes and the amniotic fluid or by those that traverse the placenta. The former is no doubt the more common portal of entry, particularly during labor, but it is the latter that is our present concern.

It is clinical experience that infants can be infected in utero, and there is considerable evidence that some of these infections travel through the placenta. Evidently the maternal defenses must first be breached, producing a bacteremia or a viremia. If the infecting agent then invades the placenta, the route to the infant is quite apparent. However, it is not difficult to conceive of some agent passing through the placenta without producing an evident pathologic condition in the placenta.

There is reasonable evidence that the following infectious agents are among those that can pass through the placenta: the pneumococci, streptococci, salmonellae, Mycobacterium tuberculosis, Treponema pallidum, Toxoplasma, and the viruses of poliomyelitis, variola, varicella, and possibly rubella.

Now let us look at the reverse side of the problem, that is, how the permeability of the placenta may affect the ability of the fetus to resist infection.

Chemotherapeutic agents. Many chemotherapeutic agents, when they are administered to the mother, will cross the placenta readily, producing significant concentrations in the fetus. Among these are the sulfonamides, penicillin, Chloramphenicol, streptomycin, Terramycin, and erythromycin. Newer chemotherapeutic agents are developed so rapidly that knowledge concerning placental permeability frequently lags. The similarity in chemical structure of many of these medications makes similar permeability characteristics not unlikely.

The transfer of antibiotics can be very effective in eradicating a fetal infection in the course of treating the mother. This was the case with penicillin in the treatment of syphilis. But the permeability of the placenta to chemotherapeutic agents could conceivably pose a threat to the infant. Silverman *et al.*[1] have called our attention to the risk of sulfonamides in potentiating kernicterus in the newborn infant. If a slowly excreted sulfonamide, like Madribon, were administered to the mother shortly before delivery it might result in a dangerously high and prolonged level in the infant.

Antibodies. Antibodies received passively from the mother are also a source of protection to the newborn infant. It has long been known that different animal species accomplish this transfer in different ways. The calf receives most of its antibodies in the mother's colostrum after birth, the mouse gets some antibodies before and more after birth, and the guinea pig and the human fetus receive their antibodies before birth.

It was generally assumed that the transfer of antibodies before birth took place across the placenta, and a correlation was noted between the structure of the placenta and the efficiency of transfer. Grosser[2] had classified placentas according to the thickness of the membrane interposed between the maternal and fetal circulations. The antepartum transfer of antibodies occurred in animals with "thin" placentas. This suggested that the placenta acted as a physical barrier to antibody proteins and that its efficiency as a barrier varied with its thickness.

Further support for this mechanistic concept came from an investigation of antibody transfer in the course of pregnancy in the human being. During the course of pregnancy the placental membrane becomes progressively thinner. Passively transferred antibodies are in higher titer in term infants at birth than in the premature infant.

All this seemed fine until Brambell[3] reinvestigated the problem with startling results. He demonstrated that in the guinea pig and rabbit, two of the animals with "thin" placentas, the transfer of antibodies is not through the allantoic placenta at all but through a specialized membrane called the splanchnopleure. And so we find that the correlation between the thickness of placenta and transfer, while real, is not a cause-and-effect correlation.

In the human being, in whom there is no splanchnopleure, the route of transfer appears to be across the allantoic placenta.

Not all antibodies cross the human placenta with equal facility. Recently another important correlation has been made. The readily transferred antibodies are of the 7S type, while the 19S antibodies are poorly transferred. The latter have a molecular weight considerably larger than that of the former, once again suggesting a simple physical explanation for the ease with which antibodies pass through the placenta.

Evidence is already accumulating that this correlation may also be spurious, in the sense that the relation of the size of the antibody to permeability may not be the primary factor. Papain or pepsin-digested 7S antibodies are broken into considerably smaller fragments which still retain their immunologic function. However these fragments do not pass through the placenta as readily as the intact molecule.

It would appear, then, that the permeability of the placenta to antibodies cannot be explained by such simple physical mechanisms as the size of the antibody or the thickness of the placenta. The electron microscopists have suggested a vital process for the transfer, namely, "pinocytosis," the engulfing of the protein molecule by microvilli on the cell. What is needed is a biochemical explanation of why some proteins are transferred and others are not.

Summary. The infant is well protected from infection prior to birth, but the protection is not absolute. A potential route of infection, but not the most common, is through the placenta. The maternal defenses must first be overcome, permitting the infecting agent to invade the maternal blood stream. Chemotherapeutic agents and antibodies synthesized by the mother may travel the same route to the fetus and thus aid him in overcoming infections.

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Dr. Curnen: Thank you, Dr. Dancis. Our next speaker, Heinz Eichenwald, M.D., will speak on cytomegalic inclusion disease, congenital hepatitis, and toxoplasmosis.

Cytomegalic inclusion disease, Coxsackie B virus disease, congenital hepatitis, and toxoplasmosis

Heinz Eichenwald, M.D.: I thought I would review with you those congenital infections which are presently of clinical importance.

Congenital syphilis used to be a great problem, but in the past decade this disease has ceased to be of special clinical significance in this area. Many congenital infections which are seen at the present time are caused by viruses, although the rather unique protozoan, Toxoplasma, probably accounts for the majority of prenatally acquired congenital infectious illnesses.

Other organisms of importance are the salivary gland virus, the cause of the cytomegalic inclusion disease, the various agents responsible for congenital hepatitis, the Coxsackie B viruses, and herpes simplex virus. There is some disagreement whether herpes simplex infection is ever acquired congenitally or whether this agent infects the baby during or after the birth process. We need not go into this discussion.

TOXOPLASMA. Twenty years ago, Wolf, Cowen, and Paige[1] firmly established that Toxoplasma was the cause of a distinctive clinical syndrome in newborn infants and that the parasite is transmitted transplacentally from the mother, who usually shows no signs of disease. If she does have an illness, it is mild. This has now been described quite fully in the Scandinavian literature as a febrile illness resembling infectious mononucleosis.[2]

The baby, in the experience of the original investigators,[1] usually presents a classical syndrome consisting of hydrocephalus, chorioretinitis, intracerebral calcifications, and convulsions. Refinement of the various diagnostic tests has made it possible to diagnose congenital toxoplasmosis in infants with considerable ease. It is probably the easiest of all these congenital infections to identify. In fact, it is now recognized that the syndrome originally described by Wolf and his coworkers[1] represents the minority of cases of this disease. The majority of infants present a much greater variety of clinical signs and symptoms.

The clinical findings in a large series of cases of congenital toxoplasmosis at New York Hospital are presented in Figure 1. For statistical reasons Figure 1 is divided into two separate groups. In Group A are included infants who originally presented signs primarily referable to the nervous system. Group B consists of infants who presented much more generalized illnesses.

It is of interest, of course, that a great majority of infants in both Groups A and B showed chorioretinitis. Perhaps most significant is the fact that in Group B the more common signs and symptoms included jaundice, anemia, and hepatosplenomegaly. Many of the infants were originally considered as suffering from some type of blood incompatibility. In fact, babies were given exchange transfusions. Initially some infants were thought to have congenital hepatitis and some to have sepsis.

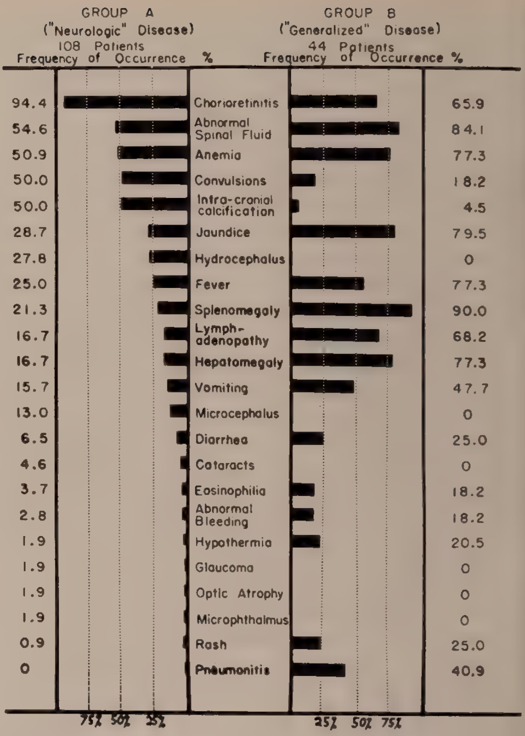

FIGURE 1. Signs and symptoms occurring prior to diagnosis or during course of acute toxoplasmosis.

Symptoms of neurologic disease may be more suggestive of the diagnosis. Anemia is also present and convulsions are commonly found. Intracranial calcifications are present in about one half of the babies and hydrocephalus in about one quarter. A very small percentage could be classified as normal.

It was soon found by investigators interested in congenital toxoplasmosis that a fair number of infants showing signs compatible with this disease do not have serologic evidence of toxoplasmic infection. Since the serologic tests had been established as being both specific and precise, it was necessary to consider other etiologies of the Toxoplasma syndrome. In recent years some data have accumulated that would shed light on this problem.

CYTOMEGALIC INCLUSION DISEASE. The first agent associated with what has been called the Toxoplasma syndrome not due to Toxoplasma gondii is the salivary gland virus, which is better known as the agent which causes cytomegalic inclusion disease in newborn infants. More rarely it also causes illness in older children and adults. Most of the signs and symptoms found in congenital toxoplasmosis can be produced by the salivary gland virus. Since methods of tissue culture have become available, it has been found with increasing frequency that this agent is the cause of congenital infection. It is responsible for a very wide spectrum of symptoms and signs which range from very severe involvement of the nervous system to a rather mild form of disease. It should be pointed out that it is possible to isolate virus in children who on repeated examination fail to have abnormal cells in the urine.

COXSACKIE B VIRUS DISEASE. Coxsackie group B virus disease in the neonatal period has also been recognized with increasing frequency in the past few years. There is some evidence to suggest that this infection is also more common than is generally realized. The disease can be transmitted postnatally as well as congenitally. In adults and in older children the etiologic role of these agents in aseptic meningitis and acute undifferentiated febrile illness is generally accepted.

In newborn infants Coxsackie B virus disease is quite different. Common early signs, in the first or second week of life, are lethargy, feeding difficulty, and vomiting. More than one half of the infants develop fever. Shortly thereafter, most will show evidence of cardiac involvement, such as tachycardia, cardiomegaly, and electrocardiographic changes, along with respiratory distress and cyanosis. Specific signs indicative of central nervous system involvement are not usually found, but pleocytosis in the spinal fluid is commonly demonstrable.

In some newborn infants the illness appears to be initiated by a sudden circulatory collapse, followed shortly by death. In other patients a similar collapse occurs a few days after the onset of the illness. The disease is generally of short duration, terminating either in death within a week or in complete recovery within two or three weeks. The mortality rate is unknown because of the bias introduced by the fact that most cases are diagnosed at autopsy.

The postmortem findings are of some interest. All infants show myocarditis, most show a focal meningoencephalitis with anterior horn cell destruction similar to that found in poliomyelitis. Many babies also show hepatic necrosis and hepatitis and pancreatitis. An occasional infant has adrenal cortical necrosis.

CONGENITAL OR NEONATAL HEPATITIS. This leads us into another fascinating group of conditions classified as congenital or neonatal hepatitis. There has been increasing attention in the past few years to this syndrome which manifests itself as a jaundice of obstructive type in infants who have neither erythroblastosis fetalis nor congenital anomalies of the biliary system.

This syndrome is characterized by the onset of jaundice during the first week of life, acholic stools, dark urine, and moderate hepatosplenomegaly. Laboratory studies show that the urine contains bile and the stools are free of both bile and urobilinogen. Flocculation test results are usually negative. The one-minute and total serum bilirubin levels are always elevated but show variable trends. Histologic examination of the liver reveals focal or widespread hepatocellular degeneration, often with the formation of multinucleated liver cells or giant cells. The follow-up on the surviving infants shows that about 60 per cent of them recover without sequelae, while some develop cirrhosis, and another group dies either as a result of cirrhosis or of the complications of attempted surgery.

It is felt that this condition may result from several different causes, none of which are fully understood. For this reason, a variety of names has been applied to the syndrome, namely, congenital, neonatal, infantile, and giant-cell hepatitis.

Various workers have postulated that this disease represents viral hepatitis transmitted to the fetus in utero. As you are all aware, there are two established causes of primary viral hepatitis in man: One is called variously infectious hepatitis, epidemic hepatitis, or hepatitis A. The other is called post-transfusion jaundice, serum hepatitis, or hepatitis B. There is no evidence whatever that the agent responsible for hepatitis A, the infectious hepatitis, is capable of crossing the placental barrier and infecting the fetus. On the other hand, there are some data to suggest that the virus responsible for hepatitis B can cross the placental barrier. Data have been presented to indicate that many adults are asymptomatic carriers of this agent and that a pregnant woman can thus infect her unborn child without having any evidence of liver disease herself.

The herpes simplex virus and the salivary gland virus have been isolated from other infants with congenital hepatitis.

Several workers have advanced theories proposing that the primary cause of some cases of neonatal hepatitis is noninfectious. Smetana and Johnson[3] have suggested on morphologic grounds that neonatal hepatitis may represent a developmental defect of liver cells resulting in aplasia of bile capillaries and malformation of liver cells. These authors believe that all changes take place in utero and that jaundice makes its appearance after birth because of the greatly augmented physiologic demands of the liver at this time. Accordingly, the pathologic process has been completed by the time the infant is born, and the basic disease process does not progress. In milder cases, the undamaged cells eventually proliferate and complete recovery may take place. In more severe cases the damage is irreversible, and cirrhosis and hepatic failure occur.

Hsia *et al.*[4] have suggested that the insult to the liver early in embryonic life, as postulated by Smetana and Johnson,[3] may be determined genetically and that at least some cases of neonatal hepatitis represent one of the ever-expanding group of inborn errors of metabolism. The evidence for this view is far from complete.

It would appear likely that multiple causes of congenital hepatitis exist. Three viruses have already been incriminated, and there may be another form, clinically indistinguishable from viral infection, which may be caused by an inherited biochemical defect.

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DR. CURNEN: Thank you, Dr. Eichenwald. Our next speaker, William Silverman, M.D., will talk about the indications for the administration of antibacterial drugs in newborn infants.

Antibacterial drugs in newborn infants

WILLIAM A. SILVERMAN, M.D.: Physicians responsible for the care of newborn infants are fully aware that their patients are exposed to the risk of acquiring bacterial infections from a contaminated environment. The exposure may occur before birth in an infected amniotic cavity, during birth while passing through the vagina, or after birth, as in a delivery room or nursery. Since the early signs of serious infection in the newborn infant are difficult to recognize and the infections themselves are notoriously severe, it has become routine practice in many hospitals to administer antibacterial drugs prophylactically to the infants who are considered high risk. Premature infants are frequently classified in the high-risk category. However, we are not certain that routine drug therapy is a satisfactory solution to the problem.

I would like to review briefly our experience in the premature nursery of the Babies Hospital for three and one-half years with 532 premature infants whose birth weights were less than 1,501 Gm. During this period we had an opportunity to observe the effect of a number of approaches to the problem of therapy in premature infants.

FIRST PERIOD. In the first period under consideration, 112 infants were admitted to the nursery. The antibacterial policy consisted of giving all infants either 10 or 20 mg. of tetracycline per kilogram of body weight per day for the first five days of life. The mortality rate was approximately 30 per cent (95 per cent confidence limits 22 to 39 per cent).

We were dissatisfied with this program of routine prophylaxis because approximately one third of the infants who succumbed had positive blood cultures and approximately one eighth had positive cerebrospinal fluid cultures. Autopsy examinations revealed several examples of major infection which had not been controlled by tetracycline.

Second period. During the second period of time we embarked on a program to determine the relative effectiveness of two contrasting policies of drug administration. Eighty infants were admitted to the premature nursery. Half the infants received drugs routinely. The control infants were given drugs when the physicians felt that a specific indication was present. The indications consisted of a history of prolonged rupture of membranes, the birth accomplished out of asepsis, and artificial ventilation at the moment of birth or other circumstances which led the physician to believe that there was exposure to an increased risk of infection. During this period the drugs which were chosen to control infection were the same for both groups, namely, penicillin, 100,000 units per day intramuscularly, and chloramphenicol, 75 mg. per kilogram per day for the first five days of life. The infants who received these drugs routinely experienced a mortality rate of 61 per cent (95 per cent confidence limits 43 to 75 per cent), as compared with the control infants whose mortality rate was 36 per cent (95 per cent confidence limits 21 to 53 per cent).

At this time we became aware of the fact that infants who had received 75 mg. per kilogram of chloramphenicol developed excessively high concentrations of this drug in the blood. Moreover, among the infants who died, many exhibited a fairly characteristic clinical syndrome consisting of peripheral vascular collapse, abdominal distention, anorexia, vomiting, and so on. No distinctive pathologic lesions were seen. Although there was only circumstantial evidence that chloramphenicol was responsible for death, the suspicion of cause and effect was strong.

Following this, infants in our nursery continued to be allotted into the same two categories. However, the dose of chloramphenicol was reduced drastically. The infants received 10 or 20 mg. of chloramphenicol per kilogram per day. Forty infants were admitted to the study. Twenty who received drugs routinely had a mortality of 10 per cent (95 per cent confidence limits 1 to 31 per cent). Twenty infants in the indication group experienced a mortality of 32 per cent (95 per cent confidence limits 11 to 54 per cent).

The concentrations of chloramphenicol in the blood of these infants were quite low. Most of the levels were below 15 micrograms per milliliter, which was considered insufficient to control infection. We saw many undisputed examples of infection with coliform organisms during this time. As a result it was decided to increase the dose of chloramphenicol to 30 mg. per kilogram per day. Coincident with the increase in dosage there was a rise in mortality. Of 140 infants admitted, 70 received penicillin, 100,000 units, and chloramphenicol, 30 mg. per kilogram per day for the first five days of life. The controls received these drugs on indication. Although the blood levels of chloramphenicol were now considered to be ideal, that is, between 20 and 40 micrograms per milliliter, we were disturbed to find that there was a rise in mortality. The death rate in the routine group was 46 per cent (95 per cent confidence limits 34 to 58 per cent), and in the indication group the rate was 35 per cent (95 per cent confidence limits 24 to 47 per cent). Moreover, undisputed examples of uncontrolled infection were encountered at the autopsy table.

Final period. The final period to be reported in this survey involved 180 premature infants. No drugs were given prophylactically during this interval. The physicians who cared for these infants restricted the use of antibacterial drugs very sharply. As compared with previous periods when almost one half of the infants admitted to the nursery were considered to have an indication for the administration of antibacterial drugs, now an attempt was made to withhold drugs unless it was considered very likely that active infection was present. Using these stricter criteria, only one sixth of the infants received antibacterial drugs in the first five days of life. Coincident with this policy, the mortality rate fell to 30 per cent (95 per cent confidence limits 23 to 37 per cent). It is interesting that this was the same rate experienced two and one-half years earlier when infants received tetracycline prophylactically.

Although our experience with antibacterial treatment during this three-and-one-half-year period has taught us principally about the hazards of administering chloramphenicol to premature infants, it has also served to emphasize that we have precious little information about the absorption, distribution, and metabolism of many of the antibacterial drugs which are used for these infants.

It is still difficult to make the early diagnosis of serious infection in premature infants. I think that we must set ourselves the task of finding a new criterion for early diagnosis in these infants. However, in the present state, I believe that we must reserve antibacterial drugs for use in infants who show the presence of active infection. Infants who have been exposed to infection must be watched very carefully, but they should not receive drugs unless the presence of infection is either quite clear or the suspicion of the presence of infection is very high.

I believe we have just passed out of a period not unlike that of the frontier days when the policy was "shoot first and ask questions afterwards."

DR. CURNEN: Thank you, Dr. Silverman. Our last speaker will be Edward Kass, M.D., who will tell us about the consequences of maternal urinary tract infection. Perhaps he will extend this to say something about the problem of hypertension in Wales!

Maternal urinary tract infection

EDWARD KASS, M.D.: Wales in Great Britain, not whales in the sea!

We are, by the nature of things, forced to view our problems in the light of what we know, even though we also realize that what we do not know occupies a vastly greater percentage of the universe. In searching for some way of attacking problems that are interesting to us, we are continually in the position of the inebriated gentleman who dropped his key in the middle of the block and looked for it on a street corner where the light was better! This means that a break into the unknown often occurs by chance because of the confining nature of working within a field in which one knows something. My talk tonight perhaps will illustrate the factor of chance in breaking into areas in which one knows nothing, and certainly no one here is less qualified to talk about perinatal mortality and prematurity than I.

The best way for me to trace our story is to tell you about it in the way that it happened. As many of you know, we have been interested in the problem of pyelonephritis as a prototype of a pattern of infectious disease of the future, namely the problem of the late consequences of relatively asymptomatic infections. Pyelonephritis seemed to us to be a model for this problem because students of the disease have known, since the work of Longcope and of Weiss and Parker, that most patients who are found to have pyelonephritis at autopsy have gone undiagnosed clinically. About 80 per cent of patients with pyelonephritis were undiagnosed clinically at the Boston City Hospital, and the frequency of missed diagnoses was as great in those who had major pyelonephritis as in those who had minor focal disease. This posed a substantial challenge and almost a threat to the clinician. It was easy to see why there should be so much untreated chronic disease due to pyelonephritis. It could also be suggested that what had been written about the diagnosis of pyelonephritis was necessarily inadequate, since it was inconceivable that clinicians were missing the classic syndrome associated with fever, flank pain, chills, and pyuria in 80 per cent of the cases, and yet only a small minority of the cases were being diagnosed.

METHOD OF DIAGNOSIS. To diagnose pyelonephritis with any degree of precision, it was necessary to develop objective methods for determining the presence of the disease when the patient had no clinical symptoms referable to this disease.

I will not try to go into all of the approaches that we explored. Suffice it to say that one of the devices that proved to be of great interest was the search for bacteria in the urine, which meant an analysis of the problem of deciding when a urine culture is positive. In the usual bacteriologic approach, a single Escherichia coli organism falling into the urine during the process of collecting the specimen cannot be distinguished from the situation in which there is infection associated with the large

TABLE I. Occurrence of bacteriuria in various population groups surveyed at Boston City Hospital

Circumstances Under Which Patients Seen	Total Number of Patients	Sex	Per Cent of Total Patients
Medical outpatient department	335	F	6
Medical outpatient department	102	M	4
Outpatient department; diabetic patients	54	F	18
Outpatient department; diabetic patients	37	M	5
Pregnant females making first prenatal visit	4,000	F	6
Patients with cystocele	52	F	23
In-lying catheters for 96 hours	100	B	98
Previously without bacteriuria; underwent single catheterization	335	F	2
Medical wards	76	F	30
Medical wards	82	M	12
Genitourinary ward	13	M	70

numbers of E. coli which are multiplying in the urine.

The solution to the separation of contamination from true infection of the urinary tract lay in the further development of the concept of quantitation of bacterial numbers in the urine. Many students of infectious disease have pointed out repeatedly that those patients who have obvious infections of the urinary tract virtually always have large numbers of bacteria in the urine. It remained simply to discover whether or not contamination would introduce smaller numbers of bacteria than those generally found in infection. It turned out to be the case that in fairly large population studies one could arrive at a statistical statement of the probability that any given number of bacteria that were discovered in freshly obtained urine represented true bacteriuria rather than contamination. I do not have time to develop this point in detail. Suffice it to say that we can now, on the basis of somewhat over 10,000 urines studied, give a reasonable statement of probability that a given level of bacterial colonies in a urine specimen does or does not indicate infection of the urinary tract. With this general approach, voided specimens can be studied with adequate precision. This development has allowed an approach to epidemiologic studies of the problem.

First, the prevalence of asymptomatic infections of the urinary tract in populations associated with the hospital were studied. Table I shows some of the data which have been collected in groups of patients at the Boston City Hospital. The prevalence of bacteriuria is remarkably high. In all of these studies, more than 100,000 bacteria per milliliter of urine were found in two successive specimens. There is a 96 per cent confidence level associated with this level of bacteriuria in two successive voided specimens.

Time does not permit a discussion of many of the implications of these data, but the one that is immediately of interest to this group is the finding of 6 per cent prevalence of bacteriuria in young pregnant women.

RELATIONSHIP BETWEEN BACTERIA AND PYELONEPHRITIS. The next question that we attacked was: What is the relationship between large numbers of bacteria in the urine and pyelonephritis as seen at autopsy? An autopsy study conducted in collaboration with R. A. MacDonald, M.D., and G. Kenneth Mallory, M.D., showed that bacteriuria was almost always found in association with active pyelonephritis. There were, of course, many instances of bacteriuria without structural changes in the tissues, as one might anticipate. The study, however, showed a highly significant association between pyelonephritis and bacteriuria.

It was then decided to determine whether bacteriuria was predictive in terms of leading to pyelonephritis, and for this phase of the study we were able to examine the urines of all women attending the prenatal clinic of the Boston City Hospital, through the kind cooperation of Benjamin F. Tenney, M.D. All patients who were less than eight months

Table II. Effect of bacteriuria during pregnancy on occurrence of pyelonephritis, prematurity, and perinatal death

Patient Group	Number of Patients	Number with Pyelonephritis	Premature Infants (Per Cent)	Perinatal Mortality (Per Cent)
Untreated bacteriuria	48	20	24	14
Treated bacteriuria	43	0	10	0
Nonbacteriuria	1,000	0	9	2

pregnant and who had bacteriuria on two successive occasions were assigned to one of two groups by a rigid scheme of alternation. One group received a placebo, and the other was treated to remove the bacteria from the urine. In most instances, a long-acting sulfonamide was used. In about 20 per cent of the patients we had to shift to another drug because of the failure of the sulfonamide to clear the bacteriuria. Nitrofurantoin usually sufficed in the 20 per cent of those patients with organisms that resisted treatment with sulfonamide.

It was felt early in the study that if treatment was discontinued while the patient was still pregnant, many of the patients might reacquire bacteriuria. The protocol was, therefore, set up in such a way that all patients with bacteriuria were treated until term. Cultures of all patients were taken at weekly or biweekly intervals. Thus, when we indicate that a patient was free of bacteriuria, we mean that the patient was under continuous observation with cultures taken regularly up to the time of delivery. The patients who received placebos were followed in the same manner. All patients were seen first by the obstetricians, in the prenatal clinic, and subsequently by ourselves in the renal clinic, on the floor below. The obstetricians did not know who was receiving placebo and who was being treated and had the option of instituting treatment in any patient who was felt to be symptomatic with respect to infection of the urinary tract. In the initial breakdown of the data (Table II) it was found that about 40 per cent of those who had received placebo developed clinical evidence of pyelonephritis before term or during the first three months post partum, whereas none of those who were freed of bacteriuria became ill. We have since approximately doubled the size of the study and have seen a small number of instances of post-partum pyelonephritis in patients who were freed of bacteriuria until term. These patients all received routine catheterization on the delivery table and perhaps for other reasons tended to reacquire bacteriuria. In any event, approximately one third of the patients were freed of bacteriuria by treatment until term, reacquired bacteriuria in follow-up post partum, and some of these became clinically ill during the post-partum period. This suggests that now the way is open virtually to eliminate pyelonephritis of pregnancy simply by looking for bacteriuria and getting rid of it before the patient becomes ill.

Perinatal mortality. We then looked to see what had happened to the babies because we had used a sulfonamide and were worried about kernicterus. There was no evidence of kernicterus, although it was hardly likely that we would have found much in a group of this size. However, we found, to our surprise, that the perinatal mortality in the untreated bacteriuric women was substantially higher than the mortality in those women who were freed of bacteriuria. When we compared these mortality patterns with those found in the thousand consecutive nonbacteriuric pregnancies, it was evident also that the bacteriuric women had a greater likelihood of having dead babies. Most of the babies who died were found at autopsy to have died of prematurity, hyalinosis, pulmonary congestion, atelectasis, and so on. They did not die with evidence of sepsis, and there was no morphologic evidence of sepsis in most of the babies.

We then looked for prematurity and found that it occurred about two and a half times as frequently in asymptomatic bacteriuric women as in women who were freed of bacteriuria. Since many of the women who had received a placebo had become ill before term, we studied this group further to see what had happened to the babies of those women who became clinically ill and, therefore, were treated. Unfortunately, we cannot come to a definitive conclusion in this latter group because it is rather small. However, it is clear that the asymptomatic bacteriuric woman has the greatest likelihood of having a dead or premature baby.

At present, the studies are being extended to the population at the Boston Lying-In Hospital, which has a somewhat different socioeconomic group. The over-all prevalence of bacteriuria is 1 to 2 per cent lower at the Boston Lying-In Hospital than it is at the Boston City Hospital, but the early indications are that the pattern of relationship of bacteriuria to prematurity will be much the same as that which was observed at the Boston City Hospital.

The findings suggest that approximately 20 to 30 per cent of perinatal death may be prevented by detecting and removing bacteriuria and that somewhere around 10 to 20 per cent of prematurity is preventable by this simple approach.

HISTORY OF BACTERIURIA. It is interesting to see when bacteriuria appears. The prevalence of bacteriuria at the time of the first prenatal visit of the mother is close to maximal by the second month of pregnancy. We do not yet know when the mothers have acquired bacteriuria but suspect that pregnancy plays a role in the acquisition of bacteriuria in the majority of these women. There is a small increase in numbers of bacteriuric conditions appearing during the last trimester of pregnancy that adds 1 to 2 per cent to the total number in the group.

The majority of untreated bacteriuric women still have their bacteriuria a year after they have delivered, but approximately one third of these women have lost their bacteriuria spontaneously. Similarly, about one third of the women who were freed of bacteriuria by term reacquired bacteriuria during the follow-up period. A small number of the bacteriuric women became clinically ill after the three-month follow-up period and were, of course, admitted to the medical service with no relationship between the bacteriuria and pregnancy suspected by the attending staff.

ACTION OF BACTERIURIA. Several questions warrant further discussion. Why should asymptomatic bacteriuria lead to perinatal death? We can rule out direct extension of sepsis because there was no evidence for this in the babies or in the mothers. An alternative possibility was that endotoxin, which is abundantly present in the common pathogens of the urinary tract, accounted for the prematurity. It has been known for from twenty to thirty years that endotoxin which is given to pregnant rabbits produces deciduoplacental congestion and hemorrhage. Therefore, L. D. Thrupp, M.D., and S. N. Hajj, M.D., in our laboratory have studied the problem further by introducing a plastic catheter into the uteri of pregnant rabbits and giving bacterial endotoxin intravenously. They have demonstrated that as pregnancy proceeds, the uterus becomes increasingly susceptible to endotoxin and within a minute or two after the infusion of endotoxin the uterus goes into violent asynchronous contractions with abortions occurring regularly.

It is possible to reproduce this increased uterine hyperirritability in some but not all of the rabbits that are given large doses of progesterone and estrogen for a couple of weeks followed by endotoxin. Curiously, also, the uterine musculature from the rabbit near term will respond to endotoxin in vitro, and this will occur before the twenty-ninth day of pregnancy when the uterus of the rabbit becomes responsive to oxytocin.

EVALUATION. In evaluating the meaning of these data, one may consider three large categories of prematurity. The first category is one in which there is a defined maternal or fetal basis for prematurity; in our figures this accounts for slightly under one third of the total, agreeing with what is generally held in the literature. The second category is a group of premature infants who are commonly seen in underprivileged populations in which the babies are physiologically normal, the length of gestation normal, and the babies happen to be small without excessive mortality. Presumably, the spread of salutary socioeconomic circumstances will dispose of this problem more effectively than will obstetricians and pediatricians. The third large category of premature infants is the one that offers the greatest challenge because these are babies who have nothing apparently wrong with them except that they are born too soon and many of them die. These are presumably salvageable since all of the evidence suggests that the premature delivery represents an acquired phenomenon that has lead to evacuation of the uterus a little soon. From this point of view, I think there is hope that we will slowly be able to piece out the various factors that lead to uterine hyperirritability and perhaps the studies with endotoxin which indicate another factor that leads to uterine hyperirritability may be relevent.

There can be no question that severe infections have always been associated with precipitous deliveries and prematurity, and it is impressive to see how seldom the infant who is born under these circumstances shows evidence of an extension of the maternal infection to the infant. The entire physiologic response, both to clinically apparent infection and to asymptomatic infection which in turn lead to uterine hyperirritability, now require detailed study.

COMMENT. There is time for just a brief word about hypertension which Dr. Curnen brought up. We have tried to extend these observations from the cradle to the grave and to look into the problem that occurs if one assumes that a great many women who have acquired their bacteriuria in earlier years will, over a period of many years, develop sufficient renal damage to lead to hypertension. We had the opportunity, in collaboration with a British Medical Research Council team, headed by William Miall, M.D., and in collaboration with K. L. Stuart, M.D., of the University College of the West Indies, to study defined populations which were carefully worked out epidemiologically. The over-all prevalence of bacteriuria in the women studied was about 4 per cent. In men it was about 0.5 per cent. The preliminary data, which we hope to have analyzed in detail soon, suggest strongly that hypertensive individuals have 2 to 3 times as great a likelihood of being bacteriuric as nonhypertensive individuals; there is suggestive evidence that in women bacteriuria will lead to hypertension. It will, of course, take many years to answer this question definitively, but at least an association between bacteriuria and hypertension in random population groups studied on a house-to-house basis seems quite clear. These data, therefore, allow us to take a new look at an old problem, using old technics and old thoughts; but perhaps fitting these into new relationships, and give us an insight into a general public health problem, of some consequence, with effects already demonstrated in terms of perinatal mortality and prematurity and with strong indications of a relationship to a portion of the problem of hypertension.

DR. CURNEN: Thank you Dr. Kass. I think all of you will agree that we are very lucky to have Dr. Kass here with us when he could be studying hypertension if not in Wales then in Jamaica! I now ask all of our panelists to be willing targets for your questions.

Question and answer period

JONATHAN T. LANMAN, M.D.: Dr. Dancis has told us about the transfer of inorganic and organic materials across the placenta. I would be curious to know what he could tell us about the transfer of cells, either living or otherwise, across the placenta? We know that occasionally a baby will bleed into a mother, and I guess all the components of the blood go into the mother at that time. I do not know how regular an occurrence this is or whether it is even possible, with the present technics, to look for it very actively unless it is in rather massive amounts.

Then, in addition, even if there is no break in the placental membranes, cells such as white cells are ameboid and might be able to go some places that red cells could not go. I wonder if there is any evidence on that, Dr. Dancis?

DR. DANCIS: There is a good evidence that red blood cells will find their way across the placenta in small amounts quite commonly. It has been assumed that this takes place through minute ruptures in the fetal blood vessels. It is also possible that red cells may cross the barrier without breaks in the epithelium. In experiments on guinea pig placenta, increased resistance in the umbilical vein made the placenta extremely permeable even to red blood cells. This phenomenon was readily reversible. Ruptures in the fetal vessels could not be detected.

There is nothing known about the transfer of white blood cells across the placenta. It is evident that with either of the mechanisms described we would expect white cells to find their way across the placenta with the red cells. I know of no data concerning the ability of white cells to migrate across the placenta through ameboid motility.

William A. Blanc, M.D.: Dr. Kass quoted the high incidence of bacteriuria in the female and relatively low incidence in the male. I would like to know what the actual incidence of hypertension of females is in relation to hypertension in males? Is it actually about six times as high as it is in the male?

Dr. Kass: No, it is not quite that bad. In general, women have somewhat more hypertension than men if one studies individuals beyond the age of forty. Below forty, blood pressures in males tend to be somewhat higher than in females pretty much throughout the world. Without doubt, the removal of bacteriuric patients from the female population will lower somewhat the number with elevated blood pressures in groups of females over those in groups of males. However, it is well to keep in mind that we are discussing only a small fraction of the entire hypertension problem and that, therefore, those patterns that are characteristic of bacteriuria in relation to hypertension would not necessarily influence the over-all group of hypertensive persons.

It is, however, clear that further studies on essential hypertension should be accompanied by studies for bacteriuria and the separate treatment of bacteriuric patients. The present evidence suggests, in agreement with Pickering's hypothesis, that hypertension is a multifactorial disease; that the level of blood pressure of a given individual, as Miall and Oldham* have shown, tends to be reflected in the blood pressure patterns of close relatives; and that the factor of environment seems to play a much larger role in the determination of level of blood pressure than has previously been accepted. On the other hand, we have no clear evidence that bacteriuria is associated with most of the findings that are characteristic of hypertensive patients. Instead, one could suggest that bacteriuria has simply provided a way of defining one of the factors in the multifactorial disease pattern.

Dr. Blanc: Another question is that I as a pathologist know how difficult it is to diagnose discrepancies between various persons. Now, in the group of patients who had just bacteriuria or who had actual evidence of vascular pyelonephritis, do you know whether in the study this was evaluated by examination of the kidneys showing the actual stages?

Dr. Kass: Yes. There are two things I should like to say about this. The first is that we have suggested, and hoped others will take the suggestion seriously, that we no longer talk about pyelonephritis per se and that we no longer talk about chronic pyelonephritis per se. Our data relate to active pyelonephritis, whether acute or chronic. By "active" we mean the presence of foci of acute inflammation in the interstitial areas of the kidney. Our correlations are limited to this group. Once polymorphonuclear leukocytes have disappeared from the interstitium, one has the morphologic picture of healed pyelonephritis, or inactive chronic pyelonephritis, with no correlations with bacteriuria. The more one examines the problem of healed, or chronic, inactive pyelonephritis the less certain one is that much is known about it. We are not at all sure that all chronic inactive pyelonephritis is a consequence of active infection; there is every reason to suppose that there are many etiologic factors that are as important as active bacterial infection.

Therefore, our present data relate only to active pyelonephritis, and, so far as I am concerned, we know so little about healed chronic pyelonephritis that at present we cannot discuss the problem adequately.

With respect to the second point, we have not done biopsies of the kidney, although others have. The obvious reason for not using biopsy data too definitively is that pyelonephritis is often a focal disease, and there are now several demonstrations that a random needle inserted into the kidneys at autopsy may miss critical lesions in the kidney. What is interesting is to see how frequently needle biopsies have shown lesions, suggesting that the disease is often more diffuse than we have recognized. There is no doubt, however, that the failure rate with needle biopsy will be high and therefore, cannot be relied on for negative information.

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* Miall, W. E., and Oldham, P. D.: Factors influencing arterial blood pressure in the general population, Clin. Sc. 17: 409 (Aug.) 1958.

Martin L. Stone, M.D.: I want to make a few comments and to compliment the speakers on their excellent papers. I have no questions to ask of the first speakers. Dr. Kass' work I find most provocative and will just come in briefly and ask the Chair if Joseph Wiederman, M.D., of our staff at New York Medical College, who is doing similar work, may comment on his observations. We sit at meetings of the Special Committee on Infant Mortality and Harold Jacobziner, M.D., reports from the Department of Health that unless we reduce prematurity, we cannot get anywhere in reducing perinatal mortality. Dr. Kass did speak on one aspect of the problem.

We are more or less agreed that the pediatricians cannot do much to reduce the number of premature infants that we obstetricians give them. But perhaps Dr. Silverman will soon be able to tell us what antibiotic to use.

Dr. Curnen: Or not to use.

Dr. Stone: Or not to use. Unfortunately, the figures just inherited on prematurity are still new. Dr. Kass comes up with something that is very stimulating and perhaps very simple in making a real contribution in the reduction of prematurity. He does not claim complete success as yet, but I think this is something that opens up many channels for further research in public health studies as well as in clinical obstetrics.

Joseph Wiederman, M.D.: Dr. Stone, the director of our Department of Obstetrics and Gynecology at New York Medical College, in his attempt to find ways to decrease perinatal mortality planned a full study of bacteriuria in pregnancy. First, we wanted to know whether or not the bacteriurias in pregnancy are indeed asymptomatic. We agree with Dr. Kass. They are asymptomatic even though symptoms of dysuria and frequently nocturia are present in about 80 per cent of all pregnant patients in early pregnancy. We did find cases of bacteriuria without these symptoms.

Second, why is the incidence greater in pregnant women than in other women? We have gotten full histories from several hundred patients about their ways of hygiene. We did observe that most of these women actually handled themselves in such a way that they clean from the perineal area up to the vagina. Our incidence of infection was 11.2 per cent. We have had the patients from the first up to the third month. We did go into other facets of the problem, namely, to see what the uterine response to endotoxins was because we observed that our patients reported uterine activity. These patients came into the emergency room and frequently were admitted as cases in early labor. The women had bacteriuria. We are now working with the effects of endotoxins, using guinea pig muscle and perfusion technics.

Dr. Kass: Perfusion of the uterine vessels?

Dr. Wiederman: Of the uterine muscle. We plan to do work in vivo. With electronic equipment we intend to take interamniotic pressures in patients with bacteriuria to evaluate their contractions. If they develop clinical pyelonephritis or pyelitis, we can record these contractions and compare with the previous contraction tracings, then treat them and study these contractions.

Edwin M. Gold, M.D.: I enjoyed the program immensely, particularly the talk by Dr. Kass. He has put his finger on a situation that clinically we have observed for many years in pyelitis. We always were aware that it is necessary to treat changes quickly and reduce their febrility and relieve their urinary block. We even went to the extent of catheterizing the urine in attempting to treat these patients because we feared the increased contractility of the uterus and the development or the onset of premature labor. We never lost these babies in utero. We always lost them because of the onset of premature labor. We figured in those days that the premature labor or the increased contractility of the uterus was secondary to the febrility of the disease. But now you throw a much more refreshing light to explain the increased uterine contractility. I found it fascinating. Thank you.

Jean Pakter, M.D.: I would like to ask Dr. Kass whether, in analyzing the data, there were other variables that were considered? First of all, what was the ethnic composition of the group in relation to the number of premature infants born, whether treated or untreated? Also, what were the weight groups of those premature infants who were born and also any other conditions that were present during the woman's pregnancy other than the bacteriuria that you mentioned? I wondered, for example, if you might have had some complications, placenta previa or anything else, that might have affected the outcome?

Dr. Kass: These are entirely valid questions. Our groups are now large enough so that the ethnic compositions are the same. About one third of our pregnant women are Negroes. It does not look as though this mattered in relation to bacteriuria, although it obviously matters in terms of the over-all figures. The City Hospital had a slightly higher prematurity rate than the Lying-In Hospital, for this general reason, but I think in the two groups, treated versus untreated, this has come out fairly well.

There were, as I mentioned, something in the neighborhood of 27 per cent of the women who had some sort of abnormality, placenta previa, huge myoma, and so on.

It is interesting that of all the women with a definable basis for prematurity, only one so far was bacteriuric. So they seem to be quite independent factors. If you like it the other way, the effect of bacteriuria was limited to the so-called salvageable group.

I think the changes are self-evident. There are some curious things. We get an occasional death in the 7-pounder with hyaline disease whose mother is bacteriuric. The occurrence of toxemia in these patients is so low that we are not prepared to make any statement about how bacteriuria and toxemia are related.

A small point that is of interest: We have explored a reasonable number of these women to see whether there was any obvious reason why some of them had bacteriuria and others not. A few things are not relevant to the problem. First, the glucose tolerances in the bacteriuric women are not different from those in the nonbacteriuric women. Second, residual urines in the bladder were measured by a method that R. S. Cotran, M.D., had to devise because catheterization was not permitted. We worked out a phenolsulfonphthalein method, which turned out to be quite simple; there was no difference between bacteriuric and nonbacteriuric women in terms of bladder residuals.

Third, and this may be relevant to the comment Dr. Wiederman made, we can find no difference in the bacterial flora of the vagina. As you know, it is relatively uncommon in a young woman of this age group to find coliforms in the vaginal flora.

In a group of consecutive bacteriuric women, only 1 out of 10 had E. coli in any numbers in the vaginal exudate, although all these women were voiding huge numbers of E. coli in the urines regularly.

Dr. Pakter: I wonder whether, in considerations of this sort, there are events that might have an influence on the outcome. First of all, the incidence of prematurity, premature births, and then the survival rates of premature infants: Has this been given consideration?

Walter Levy, M.D.: I would like to ask Dr. Eichenwald whether or not he has any explanation as to why toxoplasmosis is seen in only one offspring and not in subsequent deliveries?

Dr. Eichenwald: There is a ready explanation for this. It has been shown, both in animal experimentation and by some human evidence, that the mother can transmit the infection only if she has the organism in her blood stream during pregnancy.

Now we also know that in human beings parasitemia occurs only during the first two weeks of the illness, and after that time the antibodies suppress it. The mother can, therefore, infect her fetus only if she acquires the disease during the pregnancy. In the succeeding pregnancies, she has a high antibody level. There will be no parasitemia and, therefore, no infection of the fetus.

Harold Jacobziner, M.D.: I, too, would

like to commend the panel for this very informative presentation. I would like to endorse, however, what Dr. Silverman has said relating to the exercise of caution in administering drugs to premature infants. I would like, moreover, to extend Dr. Silverman's statements not only to premature infants of low weight, but also to all individuals. We must weigh the therapeutic advantage against possible hazards. Perhaps 90 per cent of the drugs which are now administered would perhaps remain in the pharmaceutical manufacturer's domain.

DR. GOLD: I just hope maybe I can draw Dr. Kass out on this relationship between his findings and the development of toxemia of pregnancy. In the late thirties Peters of Yale kept reiterating the close association between childhood pyelonephritis in females and the subsequent development of toxemia of pregnancy during their pregnancies. Dexter and Weiss also elaborated on this later on. Does your finding now, even prematurely, show any trend of development of a similar cause and relationship?

DR. KASS: I am not trying to avoid your question. I do believe that this is a much more complicated question than the earlier studies suggested, for several reasons. First, when one tries to find in the paper just what was meant by toxemia, it was a general clinical view. But clinicians differ in their diagnoses. Some regard any hypertensive disease as a toxemia, others will regard any renal disease, and still others limit themselves to a fairly defined syndrome. In the last year or two Victor Pollack, M.D., has tried to define this situation more precisely, using renal biopsies, and has found a glomerular lesions that seems to be quite characteristic of a fair number of women who have edema and proteinuria.

I recently spent some time with Robert Kark, M.D., and Dr. Pollack, and urged them to look for bacteriuria and see whether the fibrinoid that is sometimes seen in the glomeruli and bacteriuria were in some way related. They are at it now, and we ought to know in a fairly short time.

As far as our hospital is concerned, the prevalence of toxemia is too low for a good answer. In toxemia clinics the prevalence of bacteriuria in women is usually greater than in other women. But a great many of these women have had difficulties before. A remarkable number of them have undergone a retrograde study of the urinary tract. In other words, there may be many reasons for them to have bacteriuria that are different in nature from those for the usual pregnant woman. So that I think on epidemiologic grounds we would be very insecure in making any statement. I suspect that there is something here, but I also suspect that the ordinary toxemia of pregnancy, if you were to define it in the most rigid sense, is quite separable from bacteriuria and pyelonephritis. Most pyelonephritic patients are salt losers, and it would be difficult to be an edematous salt loser under most circumstances. My suspicion is that we are dealing with two diseases that often coincide in the same individuals. But we will have to look into this further.

DR. CURNEN: I shall now thank our panelists for their contributions and thank all of you for coming tonight.

DR. GOLDMARK: Thank you very much, Dr. Curnen and panelists.

A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Diuretics in Ophthalmology

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ALTHOUGH DIURETICS have been used in ophthalmology for more than half a century, their effects on intraocular pressure have been induced by physiologic reactions which are unrelated to diuresis.[1,2] Early work centered about the use of hypertonic solutions whose method of action was apparently related to the osmotic differential created between the extracellular space and the globe.[3] In recent years considerable attention has been focused on the use of urea as such an agent.

The carbonic anhydrase inhibitors constitute the other broad family of drugs that influence intraocular pressure and that are secondarily diuretics. Presumably these agents reduce the aqueous flow reversibly and only minimally alter osmotic gradients.[4-6] The most familiar drug of this group is acetazolamide.

Osmotic agents

Studies of isosmotic agents revealed that these might induce an increase in intraocular pressure[7]; however, this action was later attributed to changes primarily in vascular volume.[8] Cantonnet[1,9] showed clearly that both intraocular pressure and ocular volume might be reduced with hypertonic saline. Similarly, it was suggested that the osmotic differential of diabetic coma might account for the hypotony associated with this condition.[10,11] Conversely, injections of hypotonic materials resulted in a rise of intraocular pressure.[12,13]

Hertel[2,14] further reported the successful treatment of glaucomatous patients with the intravenous administration of from 150 to 200 cc. of a 10 per cent solution of saline. Reports of the use of 3-molar intravenous glucose as a preoperative ocular hypotensive agent soon appeared.[15] It was clearly shown that a variety of osmotic agents would influence intraocular pressure, the most active being the smallest molecule.[8,16,17] However, hypertonic saline in doses too small to influence osmotic gradients were also claimed to be beneficial.[18,19]

The influence of osmotic agents on vascular pressure and volume was studied in detail by Duke-Elder.[8,20,21] He also noted that hypertonic saline decreased intraocular pressure, as did hypertonic glucose. A 30 per cent solution of glucose was required to obtain the osmotic effects of a 4.5 per cent solution of saline.[8,20] He used 30 per cent saline intravenously to treat glaucoma.[21]

Further data of a similar nature were obtained by Fremont-Smith,[22] who studied 30 per cent saline intraperitoneally and intravenously, 50 per cent urea intraperitoneally, and 50 per cent glucose intravenously in animals. All of these agents lowered the intraocular and intracranial pressures.

Because of the limitations of hypertonic

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TABLE I. Comparison of osmotic potentials of equal weight of various agents*

Substance	Formula	Molecular Weight	Milliosmols per 70 Gm. of Substance	Milliosmols per Liter of Body Water
Urea	NH_2CONH_2	60.06	1,165.5	27.75
Sucrose	$C_{12}H_{22}O_{11}$	342.30	204.52	4.87
D-sorbitol	$C_6H_{14}O_6\,{}^{1}/_{2}H_2O$	191.18	366.15	8.72
D-glucose, anhydrous	$C_6H_{12}O_6$	180.16	388.54	9.25
D-glucose	$C_6H_{12}O_6H_2O$	198.17	...	...
Mannitol	$C_6H_{14}O_6$	182.17	384.25	9.15

* The last column represents the theoretically obtainable milliosmol change per liter of body water (assuming total body water diffusion) from the administration of 70 Gm. of each substance.

saline in patients with cardiac and renal disease, as well as the secondary rise in intraocular pressure noted with this agent and with glucose, reports of other agents soon appeared.[23] Intravenous sucrose lowered intraocular pressure[24] but caused renal damage.[25] Detailed studies of sorbitol as such an agent were reported.[23,26] A tonographic analysis of this material led to the conclusion that primarily it altered flow without influencing the outflow facility.[27] However, the lack of steady-state conditions, as well as of data of vascular volumes and pressures, militate against such conclusions.

There has been considerable recent interest in the use of hypertonic urea as an ocular hypotensive agent.[28,29] This drug has also been used extensively in neurosurgery, where it profoundly reduces cerebrospinal fluid pressure.[30,31] This agent has been clearly shown to act by means of the osmotic gradients established, although earlier reports indicated other mechanisms.[32] A comparison of the osmotic potentials established by urea and sucrose demonstrate clearly the relationship of intraocular pressure decrease to the gradient of blood hyperosmolality.[33] This has also been demonstrated for mannitol.[34] A comparison of the molecular weights of various osmotic agents appears in Table I, which demonstrates clearly the osmotic differentials obtainable with urea, sucrose, D-sorbitol, D-glucose, D-glucose anhydrous, and mannitol.

The osmotic mechanism of this agent was clarified further in a study of the ratio of blood urea nitrogen to aqueous urea nitrogen following intravenous administration.[35] This ratio is greatest at the time of minimum intraocular pressure, and intraocular pressure returns to control levels soon after the blood-to-aqueous ratio approaches control levels. The normal ratio of aqueous urea nitrogen to blood urea nitrogen is 0.8, so that an osmotic gradient for this agent exists in the normal eye.[36]

The extensive use of urea has prompted several claims requiring substantiation.[37,38] It was originally stated that there was no pressure rebound with urea[31]; however, evidence clearly shows that this is not so for the cerebrospinal fluid pressure.[39] This rebound is not as significant with respect to the eye.[40] Claims of a reduction of orbital volume facilitating orbital surgery also remain clinically unsubstantiated. However, in those conditions in which an osmotic agent is desirable, urea has proved to be of great efficacy.

The clearest indication for its use is in acute angle-closure glaucoma, where miotics will often be ineffective owing to the presence of iridoplegia.[41-43] Furthermore, since aqueous flow is spontaneously decreased as intraocular pressure rises, carbonic anhydrase inhibitors may often be without effect.[44] Urea permits ocular dehydration without opening the angle. At the low levels of intraocular pressure induced by this drug, miotics often take hold and terminate the cycle.[43] A clearing of the cornea at this time usually facilitates gonioscopy as well.[43]

Another very useful application of this agent is in surgery for retinal detachment. Drainage of the subretinal fluid may often be avoided if the ocular hypotony present is sufficient to permit the plumbage technic. This is also of advantage in the more classical forms of scleral buckling.[45]

Presently, urea is most frequently used as a 30 per cent solution of lyophilized ammonia-free urea in 10 per cent invert sugar at a dosage of 1 Gm. per kilogram of body weight.[33,38,44,46] It is claimed that hemoglobinuria is reduced when invert sugar is used as a solvent; however, clinical verification of this complication requires further investigation.[47] The rate of administration is significant and it is suggested that from 3 to 5 cc. be given per minute.[44]

Various untoward effects have been noted with the use of urea. During the infusion, headache is common.[48] Occasionally patients exhibit skin pallor and may complain of nausea.[37] Phlebitis may occur even without extravasation of the agent,[48] although its leakage extravascularly may cause severe tissue necrosis.[49,50]

Urea is an agent of low toxicity, and its use is not contraindicated by moderate increases in blood urea nitrogen levels. However, at blood levels of greater than 370 mg. per 100 ml. it is toxic,[51] and such high initial levels militate against its use. The increased vascular volume induced may provoke congestive failure in patients with severe cardiac disease.[52]

Urea has also been used orally, but it is extremely unpalatable. Furthermore, it is a gastric irritant, so that even if its horrible taste is well disguised, nausea and vomiting are frequent. However, under certain circumstances, this may be the only technic available for the prolonged reduction of intraocular pressure.[53]

Not all of the studies of osmotic agents have been concerned with reducing intraocular pressure. Indeed, water has been used to provoke glaucoma. It has been clearly demonstrated that the ingestion by the patient of 1 L. of water while he is in the fasting state produces an average reduction in blood osmolality in the range of 8 milliosmols in both normal subjects and glaucomatous patients.[54,55] Intraocular pressure rises, usually less than 6 mm. Hg in the normal and greater than 6 mm. Hg in glaucomatous eyes.[54,55] Furthermore, this change is clearly proportional to the change in blood osmolality.[56]

The data accumulated indicate that fluid enters the eye on the basis of the induced osmotic gradient.

Tonographic studies indicate no significant change in outflow facility, but the absence of steady-state conditions introduces theoretical errors in utilizing quantitative tonography following water ingestion.[57]

Carbonic anhydrase inhibitors

Carbonic anhydrase is present in various concentrations in the different ocular tissues, including the iris and ciliary processes.[58,59] The intravenous administration of S^{35}-labeled acetazolamide is followed by high concentrations of this drug in the ciliary process.[60] Acetazolamide could inhibit up to 93 per cent of the carbonic anhydrase activity in the ciliary body, with 40 per cent of this activity still being inhibited as long as seventeen hours after the administration of acetazolamide.[61]

Intravenous acetazolamide decreases aqueous flow approximately 50 to 60 per cent in rabbits.[5,62–64] Despite massive doses of the drug, the remaining 40 to 50 per cent is unaffected.[5] Flow suppression in man is of a similar magnitude.[63] These data have been obtained by measuring alterations in steady-state chemistry, turnover of test substances, fluorescein appearance time, the prolonged restoration time following anterior chamber puncture, and ascorbic acid concentration.[5,6,62,65–69] It has further been demonstrated that there is no change in outflow facility in patients treated with acetazolamide.[65] Extensive literature reports changes in electrolyte concentration, particularly the bicarbonate ion, in the aqueous humor induced by these agents.[4,70–73] Suffice it to say that the significance of these changes is not known, but it has been suggested that a decrease in bicarbonate buffering within the secretory cells would lead to intracellular acidosis and a change in the equilibriums of many enzymes.[74]

The lack of intraocular pressure reduction on topical or local use of carbonic anhydrase inhibitors has led some workers to conclude that the effect of acetazolamide on intraocular pressure is secondary to its systemic effects.[75–78] It has been suggested that the fall in intraocular pressure results from altered osmotic balance between the blood and aqueous, and further that a fall in the sodium, chloride, and potassium ions in the plasma may induce ocular hypotony.[37,79] However, this argument is readily refuted by the fact that the chlorothiazide and mercurial diuretics also lower the concentration of these ions with virtually no fall in intraocular pressure.[80–83]

Other explanations for the effect of the carbonic anhydrase inhibitors have been alterations in the venous pressure[84,85] as well as changes in the iris arteries.[86] It has also been suggested that there may be some influence on the hypothalamic-pituitary-adrenal axis.[87]

Acetazolamide may be administered intravenously or by mouth. When it is given intravenously, the intraocular pressure begins to fall within the first two minutes.[88] Given by mouth, the fall in intraocular pressure begins in from twenty minutes to one hour.[89–92] Typically, when 500 mg. are given by mouth, the intraocular pressure begins to fall in half an hour, reaches its maximum depression in three hours, remains low for two more, and then returns to pretreatment levels over the next five hours.[90]

There is a decreasing diuresis to maximum therapeutic amounts of 5 mg. per kilogram four times a day with successive doses, a point of no effect being reached in three or four days. With the cessation of treatment for a few days, effectiveness is regained.[90] However, there is no falloff in the ability to maintain decreased intraocular pressure in glaucomatous patients.[91,93–95]

Acetazolamide is used in the treatment of all types of glaucoma. Frequently it is employed along with miotics and epinephrine in the treatment of open-angle glaucoma.[92,94–100] It may be used in acute glaucoma preoperatively and can be used to maintain a soft eye after intravenous urea has decreased the intraocular pressure.[43,44,94,100–103] Preoperatively, it is useful in most cases in which intraocular pressure is elevated. Postoperatively, it may prevent the rise in pressure which often follows cyclodiathermy.[90] Other uses for acetazolamide require further substantiation.[90,92,94,100,103–108]

Since the prolonged use of acetazolamide in angle-closure glaucoma, with excessive delay in surgical therapy, may result in progressive synechias, its long-term use in this condition is condemned.[94,100]

Less than maximum levels of therapy are often indicated and may be related specifically to variations in diurnal levels of intraocular pressure.[94]

Among the frequent complications of acetazolamide therapy are paresthesias, anorexia, weight loss, excessive weakness, and shortness of breath.[91,94,95] More rarely there are severe acidosis, dysuria or ureteral colic, skin rashes, transient myopia, thrombocytopenia, agranulocytosis, and drug fever.[94,95,109,110] These may be transient and not force a discontinuance of therapy.

Other agents have been introduced in an effort to eliminate undesirable reactions. These include ethoxzolamide[105,111,112] and methazolamide,[41,113–117] but they offer little significant advantage over acetazolamide.

Recently, a delayed form of acetazolamide has been introduced, and although some benefit has been claimed, a detailed study of patients receiving this form of medication fails to reveal any significant benefit as compared with regular acetazolamide.[118]

Summary

Although diuretics have been employed in ophthalmology, their primary effects have been unrelated to diuresis. Hypotonic solutions have been used to elevate intraocular pressure in provocative testing for glaucoma, while hypertonic agents have been employed to lower intraocular pressure. The most significant application of the latter appears to be in the treatment of acute angle-closure glaucoma. In this regard, urea appears to be the drug of choice.

Carbonic anhydrase inhibitors still remain the sole medical agents for reducing aqueous flow. Few advances have been made in explaining their mode of activity or, for that matter, in improving on acetazolamide which was the first of these agents to be used extensively in ophthalmology.

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Number one hundred sixteen in a series of Recent Advances in Medicine and Surgery.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
March 28, 1962

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by MARCEL TUCHMAN, M.D.

Acute Chest Pain and Hematemesis

Case history

Jim Harris, M.D.: A forty-six-year-old Negro male was admitted to Knickerbocker Hospital on March 5, 1962, complaining of the acute onset of pain in the chest, shortness of breath, and vomiting blood. He had been in good health until the day of admission when he noticed occasional fleeting epigastric pains which he ignored. Later that day he developed nausea and retched several times. With considerable effort he vomited, and the vomitus consisted of dark red blood. Within a few minutes he experienced a severe crushing pain in the left side of the chest and rapidly developed intense shortness of breath.

He had no past history of abdominal pain, nausea or vomiting, hematemesis or melena, diarrhea or constipation, food intolerance, anorexia, jaundice, heartburn, or weight loss. He denied significant alcoholic intake. He had had a left-sided pneumonia about three years previously.

On admission to the emergency room he was in acute respiratory distress, but afebrile. The pulse was 120, and the blood pressure was 90/70. His respiration was splinted, and breathing caused severe pain and was accomplished at great effort. He was well developed and well nourished. An examination of the head, eyes, ears, nose, and throat was unrevealing. The heart was not enlarged; the rhythm was regular and rapid, and there were no murmurs. There was dullness to percussion and absence of breath sounds over the base of the left lung. There was no abdominal tenderness or rigidity, and no organs or masses were felt. A rectal examination revealed grossly bloody stool. The extremities were not remarkable, and a neurologic examination produced findings within normal limits.

The urine had a specific gravity of 1.020, was acid, and contained 3 plus albumin but no sugar or acetone. The hemoglobin was 10.3 Gm. per 100 ml., and the white blood cell count was 5,200 with 75 per cent neutrophils, 20 per cent lymphocytes, and 5 per cent monocytes. A sickle-cell preparation gave negative results. The blood sugar was 151 mg. per 100 ml., and the nonprotein nitrogen was 60 mg. per 100 ml. An electrocardiogram showed only sinus tachycardia. A chest roentgenogram (Fig. 1) showed a pleural effusion at the base of the left lung with an air-fluid level. Roentgenograms of the abdomen with the patient in the flat and upright positions showed normal findings.

Within an hour after admission a water-sealed drain was inserted into the left side of the chest. Nasogastric suction was instituted, and large quantities of blood were aspirated. Large doses of antibiotics were administered. During the next twenty hours he received 6 units of whole blood. However, he continued to complain of chest pain, and dyspnea persisted. His temperature rose abruptly to 104 F. and then fell to 101 F. He continued to border

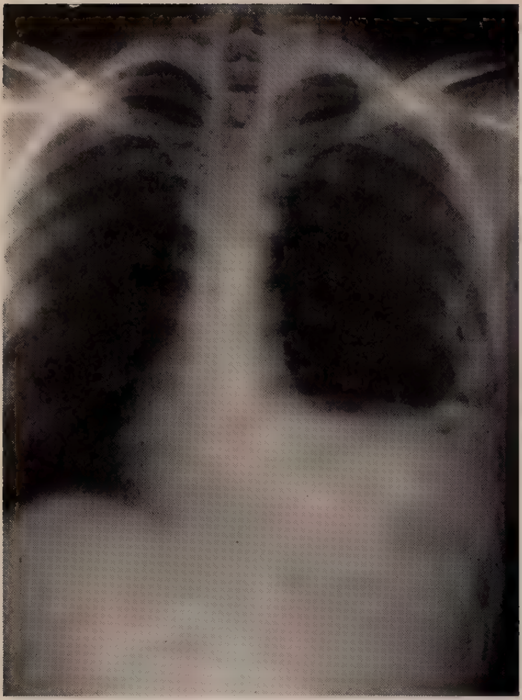

FIGURE 1. Chest roentgenogram shortly after admission showing fluid in the left pleural space with an air-fluid level. There is hazy infiltration in the lower field of the right lung. There is no air under the diaphragms.

on peripheral vascular collapse. Surgical intervention was decided on, but the patient expired on the table less than twenty-four hours after admission.

Discussion

MARCEL TUCHMAN, M.D.*: I would like to draw your attention to the following paragraph in the protocol: "Later that day he developed nausea and retched several times. With considerable effort he vomited . . . .Within a few minutes he experienced a severe crushing pain in the left side of the chest and rapidly developed intense shortness of breath." This chronologic account of the onset of this patient's illness brings to mind a strikingly similar catastrophic event about which I read while preparing this discussion.

In 1724, the eminent Baron van Wassenaer, Grand Admiral of the Dutch Fleet, then fifty years old, having overindulged in food and drink, wanted to relieve his full stomach. Therefore, he thrust his finger down his throat. He retched repeatedly, then cried out with a terrific pain and the feeling of imminent death. He died eighteen and one-half hours later in collapse. This, I believe, is the first recorded instance of so-called spontaneous rupture of the esophagus, described in the literature by Boerhaave.[1] Since then, over 200 people have fallen victim to this catastrophic event, and I believe that this patient was another.

The major features of the case are repeated retching and vomiting followed by the sudden onset of severe chest pain and the development of acute dyspnea. The most significant observation made in the hospital was the x-ray film showing a hydropneumothorax. If one were to separate these major signs and symptoms, one could invoke several diagnostic possibilities. Spontaneous pneumothorax alone can produce chest pain and dyspnea. The presence of fluid in the chest, although usually a later development, does not really exclude spontaneous pneumothorax. However, hematemesis and subsequent death despite effective decompression do not suggest a simple pneumothorax. The protocol does not describe the material obtained by draining the chest. If it resembled gastric contents rather than being clear fluid, spontaneous pneumothorax is clearly ruled out.

A pulmonary embolism can produce chest pain, dyspnea, collapse, and death. However, cyanosis is not mentioned as a feature. Nor does a simple pulmonary embolus produce fluid in the chest or hematemesis. Other forms of vascular accident occur to one. Could this be a dissecting aneurysm of the aorta with rupture into the upper portion of the gastrointestinal tract? This is not very likely in a normotensive man of forty-six years, nor does the chest x-ray film confirm it by demonstrating either an overt aneurysmal dilatation of the aorta or some mediastinal widening. Nor does a dissecting aneurysm produce air in the chest. Also, although fusiform or saccular aneurysms of the abdominal aorta may rupture into the duodenum and produce exsanguination due to massive gastrointestinal hemorrhage, dissecting aneurysms of the thoracic aorta do not rupture into the gastrointestinal tract; rather, they rupture into the mediastinum and give diffuse hemorrhage into the soft tissue and then into the pleural spaces.

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Now, let us turn to the hematemesis. Of 101 patients who died of gastrointestinal hemorrhage, Chalmers *et al.*[2] assigned 50 cases to benign peptic ulcers of the stomach, duodenum, or esophagus; 32 cases to ruptured esophageal varices; and 19 cases, including 3 cases of the Mallory-Weiss syndrome, to miscellaneous causes. I doubt that this patient had esophageal varices. First, there was no evidence of liver disease or portal hypertension. Second, varices rupture into the lumen; they do not perforate. I also will exclude a bleeding ulcer of the stomach or duodenum. To be sure, peptic ulcers can remain quite silent until a hemorrhagic episode occurs, but an ulcer would not explain the chest pain, the dyspnea, or the hydropneumothorax. The same reasoning applies to a hemorrhage from acute alcoholic gastritis.

It is evident that an analysis of individual symptoms leads nowhere. We must take the entire constellation of symptoms in their proper order. It is possible that an alcoholic bout initiated the nausea, retching, and vomiting, but this also could have developed from some other cause as well. In any event, the patient vomited with some force, and with considerable straining he vomited dark red blood. At this point he must have sustained a laceration at the cardioesophageal junction. If we assume that he continued retching and straining, a few minutes later he extended the laceration through the muscularis and ruptured the esophagus into the posterior mediastinum. Speculating further, the rupture was so forceful that it perforated the adjacent parietal pleura, which was signified by the crushing chest pain and dyspnea. The hydropneumothorax soon followed as the gastric contents were emptied into the mediastinum and pleural cavity. The loculations of the hydropneumothorax suggest pre-existing pleural adhesions, possibly a sequel of the left-sided pneumonia of three years previously. In fact, the absence of mediastinal emphysema possibly suggests mediastinal adhesions, although cases have been described in which mediastinal emphysema developed only after hydropneumothorax, or even did not develop at all.

The importance of recognizing spontaneous rupture of the esophagus promptly cannot be overstated. If not treated, only about one third of the patients survive the first twenty-four hours and only about 10 per cent the first forty-eight hours. Effective surgical treatment consists of open thoracotomy, drainage of the chest, repair of the rupture, and meticulous postoperative decompression of both the chest and the stomach. Even with prompt surgical intervention the mortality rate is about 35 per cent.

The present case presents one unusual aspect which merits comment. Mallory and Weiss[3,4] described a series of alcoholic patients who developed massive gastrointestinal hemorrhage from longitudinal lacerations at the gastroesophageal junction. They attributed the lesion to violent vomiting against a contracted cardiac sphincter. None of their original 15 patients[3] had an actual esophageal rupture, but 1 of the 2 cases in their second publication did.[4] Hematemesis is not a very prominent feature of spontaneous esophageal rupture, occurring in only about 55 per cent of the cases. Also, when it occurs, it is seldom massive. Therefore, I would postulate that this case represents a combination of syndromes which may overlap on occasion, that is, the Mallory-Weiss syndrome of esophageal laceration and the Boerhaave syndrome of esophageal rupture. Admittedly, this can be a fairly narrow distinction, but I think it is important. Massive hematemesis from longitudinal laceration without rupture can be treated with transfusions and other supportive measures. Rupture of the esophagus requires immediate surgical intervention regardless of the patient's general condition. Cummins and Wedgwood[5] have described such a situation, and a case reported by Trubek[6] presents further complexities.

In this latter case, x-ray studies revealed both subcutaneous emphysema and free air under the diaphragmatic leaflets as well as signs of peritoneal irritation such as one might find in a perforated gastric or duodenal ulcer. Because of this set of observations the patient was explored through an abdominal incision, and the rupture in the esophagus was missed. In the present case there was no abdominal pain, no rigidity, and no free air under the diaphragm, hence no reason to suspect a perforated peptic ulcer. Not infrequently, however, the pain from a ruptured esophagus is epigastric rather than thoracic, and this may lead to confusion.

One more complication must be considered. Peptic ulceration of the gastric mucosa in diaphragmatic hernias has been reported. Johnston and Twente[7] reported an example of an incarcerated diaphragmatic hernia with such an ulcer which did perforate, producing a situation indistinguishable from esophageal rupture. The same would be true for perforated peptic esophagitis. However, almost uniformly, the rupture is through a previously normal esophagus. Most ruptures occur supradiaphragmatically in the posterolateral aspect where the esophagus is not supported by surrounding muscle fibers. In such cases one should look for subcutaneous emphysema. Sometimes a crunching sound due to retrocardiac air is heard on auscultation of the heart. Some patients even report a sensation that "something tore inside," giving the diagnosis to the alert clinician.

Maxwell L. Gelfand, M.D.: If one is fortunate enough to see patients with a rupture of the esophagus early enough, the x-ray picture of the fluid in the chest may give the characteristic V sign. However, when there is a larger amount of fluid, the V-shaped contour disappears.

Michael S. Bruno, M.D.: Among the antecedent causes for the Mallory-Weiss syndrome are not only forceful vomiting but also severe persistent coughing in patients with chronic respiratory disease.

Mackenzie VerDrehen, M.D.: Among the physical signs of a rupture of the esophagus is the so-called "crunch" sign described by Hamman. It is heard as a crunching sound over the anterior wall of the chest. Also in your analysis of the case by symptoms, you might have mentioned acute myocardial infarction in the differential. Any patient with crushing chest pain, acute dyspnea, and death in twenty-four hours conceivably could have had one.

Dr. Tuchman: Quite so. In fact, Fishberg[8] has reported just such a case. However, in this patient the association of hematemesis and hydropneumothorax makes such a contingency remote, even as it does for aortic aneurysm.

René Silva, M.D.: Have any cases of rupture of the esophagus been described in which the rupture was through a traction diverticulum?

Dr. Tuchman: Not to my knowledge. The usual site of rupture is at the terminal esophagus. Traction diverticula are usually higher up. However, I did run across a reference in which both conditions were present but unrelated.

Abraham Sunshine, M.D.: I would like to emphasize that when such patients are operated on through a thoracotomy incision, the surgeon must explore the esophagus very thoroughly. The actual site of rupture in the esophageal adventitia may be very inconspicuous. Often there is so much edema and early exudate in the vicinity that the site of rupture is obscured.

Thomas Silverberg, M.D.: How rapidly was the syndrome recognized in this patient?

Dr. Harris: Actually, the diagnosis was made within an hour of the patient's admission to the hospital.

Dr. Gelfand: Then why wasn't the patient operated on sooner?

Dr. Harris: The patient was in profound vascular collapse soon after admission. Apparently, the service hoped to improve his chances of surviving an open thoracotomy by restoring his circulatory equilibrium and reducing the severe respiratory embarrassment by decompressing the chest.

Clinical diagnoses

1. *Spontaneous rupture of esophagus*
2. *Hydropneumothorax, left*

Dr. Tuchman's diagnoses

1. *Spontaneous rupture of esophagus*
2. *Loculated hydropneumothorax, left, with ?empyema*
3. *Pneumonia, lower lobe of right lung*

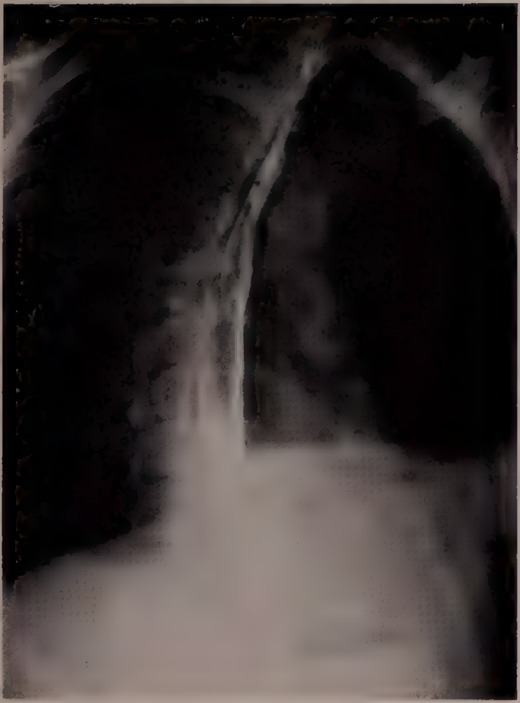

FIGURE 2. Chest roentgenogram following a swallow of radiopaque medium showing extravasation of contrast material from the terminal esophagus toward the left pleural space.

Pathologic report

Salvatore Baldino, M.D.: Actually, we withheld one roentgenogram. Following the demonstration of the hydropneumothorax, we had the patient swallow a small amount of Hypaque and were able to demonstrate its passage through the esophagus toward the left pleural space (Fig. 2).

William B. Ober, M.D.: At autopsy there was a linear, longitudinal laceration of the terminal esophagus about 2.5 cm. long, located just above the esophagogastric junction along the anterior wall (Fig. 3). It had perforated anteriorly and had leaked into both pleural cavities. The left pleural cavity contained air under pressure and about 1,500 cc. of turbid, dirty fluid resembling gastric contents. The right pleural cavity contained about 400 cc. of similar fluid, somewhat less turbid. The pleural surfaces of the lower lobes of both lungs were covered with a shaggy fibrinopurulent exudate, pronounced on the left, less so on the right. Sections of the underlying lung did not disclose pneumonia. There was, however, an intense, acute exudative mediastinitis, which was probably the immediate cause of death. Minimal mediastinal emphysema was present, chiefly near the site of rupture, but it did not extend upward to any great degree. The liver showed no evidence of fatty change or cirrhosis.

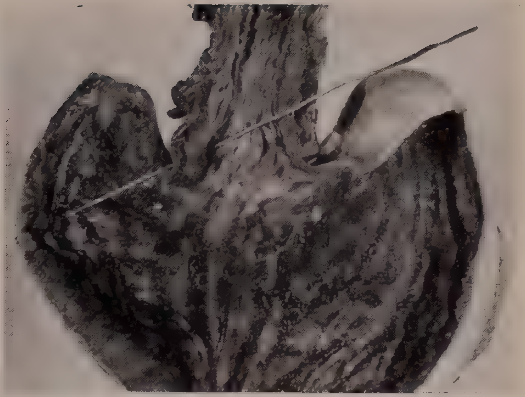

FIGURE 3. Gross view of the terminal esophagus and cardiac portion of the stomach. The linear defect is seen in the anterior wall of the esophagus, and the probe passes through the site of perforation.

Anatomic diagnoses

1. *Spontaneous rupture of the esophagus, anterior wall*
2. *Acute fibrino-purulent pleuritis, bilateral*
3. *Acute exudative mediastinitis with slight emphysema*

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Nutrition Excerpts

Prepared with the cooperation of the faculty
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DAPHNE A. ROE, M.D., Editor

Biochemical Advances in Vitamin Research

Partial Replacement and Interference of Vitaminic Functions by Pseudovitamins

DONALD B. McCORMICK, PH.D.
Ithaca, New York

NOT VERY MANY years ago, if one were to ask about the mechanism of action of a particular vitamin, the reply would undoubtedly have been that it cures or prevents the onset of a specific set of symptoms characteristic of a deficiency in that vitamin. For example, thiamine cures beriberi. Today the same question can be answered more completely from an understanding of the underlying biochemical functions of the physiologically active form of the vitamin, the coenzyme. An interesting analogy between the tools of a carpenter and coenzymes has been made by Theorell[1] who discusses the mechanism of action of water-soluble vitamins. The carpenter uses the same tools for producing many sorts of things, just as protein enzymes make use of the same coenzymes in a wide variety of purposes. A relatively small number of coenzymes serve a large number of enzymatic functions.

Following the classic studies of the nutritional aspects in the intact organism, much of our current information on the particular functions of vitamins has been gained from biochemical investigations of the systems involved, ultimately including both enzymes which catalyze the conversions of vitamins to coenzymes and the roles played by these coenzymes as functional moieties of other enzymes.

Pseudovitamins

The elucidation of the structures of each vitamin and coenzyme has led to the syntheses of many analogues or pseudovitamins in attempts to correlate chemical and physical properties with biologic activities. Studies which have been made with pseudovitamin forms of riboflavin and of its two known coenzyme forms, FMN (flavin mononucleotide) and FAD (flavin adenine dinucleotide), will serve to illustrate the means by which vitaminic properties can be characterized and the medicinal uses which can result from such research. Now there are several cases where the primary site of action of the pseudovitamin is known. Two basic types of systems are involved, those wherein the flavins are converted to coenzymes and those in which flavins are coenzymes.[2]

Conversion of vitamins to coenzymes

The occurrence and function of flavokinase, which catalyzes the formation of FMN from riboflavin and ATP (adenosine triphosphate), remained uncertain in the mammal until recently. It now has been demonstrated that extracts from several rat tissues contain flavokinase activity which is largely masked by phosphatases.[3] A comparative study of tissues from several animals showed that acid phosphatases which hydrolyze FMN are widespread but apparently do not catalyze transphosphorylation with usual phosphate esters and riboflavin.[4] With the partial purification and separation of flavokinase from phosphatase in rat liver,[5] sufficiently active kinase preparations were available to make a general characterization possible.[6] Despite the intrinsic importance of the kinase, only the enzyme from yeast had been studied in reasonable detail,[7] especially with regard to flavin specificity.[8] Insofar as comparisons were made, the specificity of the liver enzyme appears similar to that of the yeast kinase.[6] In addition to those structural analogues of riboflavin which were used to ascertain incompletely the specificity of the yeast kinase,[8] several others have now been examined for the mammalian enzyme.[9,10]

Studies of flavin specificity revealed that some analogues, such as 6,7-diethylriboflavin and 6,7-dichlororiboflavin, are phosphorylated thereby being converted into pseudo-FMN forms. Other flavins, such as lumiflavin and 6,7-dimethyl-9-(2′-hydroxyethyl)-isoalloxazine, are competitive inhibitors of the phosphorylation of riboflavin but are not themselves phosphorylated. A large number of other flavins, such as isoriboflavin and D-galactoflavin, are apparently inert in the flavokinase system.

The other coenzyme form of riboflavin, FAD, is formed by phosphorylation of FMN with ATP as catalyzed by FAD synthetase.[11] This system also may be effected by pseudovitamin or pseudocoenzyme analogues, but information is not yet available.

Functions of coenzymes

Those flavins which are converted to pseudocoenzymes, for example phosphorylated analogues of FMN formed in the flavokinase system from diethyl- or dichlororiboflavin, may act either as substitute coenzymes or as competitive inhibitors of coenzyme function.[2] FMN can be replaced partially by 6,7-diethylriboflavin-5′-monophosphate as a coenzyme, whereas 6,7-dichlororiboflavin-5′-monophosphate is inhibitory. Some flavins, such as isoriboflavin and D-galactoflavin, which are inert with flavokinase, nevertheless inhibit flavoprotein enzymes which require FMN or FAD as a coenzyme. Quinine and atabrine inhibit by similar means.

Correlations with biologic activities

The biologic properties of many of the flavin analogues have been well reviewed,[2,12,13] but some of the more salient points may now be correlated with the known sites of reactivity of certain of those compounds as described previously. The diethyl analogue can replace the natural riboflavin partially, as the former is converted to a functional pseudocoenzyme. Although the dichloro analogue is likewise converted to a pseudocoenzyme, this latter cannot functionally replace the natural coenzyme forms of riboflavin, and the analogue is a growth inhibitor. Since 6,7-dimethyl-9-(2′-hydroxyethyl)isoalloxazine prevents the utilization of riboflavin by inhibiting its conversion to FMN, this flavin is used as an antiprotozoan drug. The apparent riboflavin deficiency produced in an animal on the administration of isoriboflavin or D-galactoflavin is caused by their interference with coenzyme function and not in the conversions of riboflavin to coenzymes. Quinine, atabrine, and similar antimalarial drugs also appear to interfere with flavin coenzyme function in the pathogenic plasmodia.

Comment

Although nature often works with great economy, it is certain that the very best item is not yet used in every instance. Through evolutionary development improvements are continually forthcoming. The extension of this process may include vitamins and coenzymes. Some pyridine nucleotide-linked enzymes work faster and better with artificial coenzyme analogues than with their natural coenzymes.[14]

Certain of those analogues which act as antagonists to vitamins, either by preventing their conversions to coenzymes or by disallowing normal reactivity of the latter, have already found use in chemotherapy. It is highly probable that more such drugs will become available in the near future.

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Number thirty in a new series of Nutrition Excerpts

Microsensors implanted in human body

Tiny microminiaturized radio stations implanted in the human body could be a major aid to medical science in its fight to conquer the ills of the human race, according to an address by John R. Moore, president of North American Aviation's Autonetics Division, at the 1962 Joint Automatic Control Conference at New York University.

Microsensors implanted in the body could broadcast their findings to a nearby control center or to a microminiature receiver-memory carried on the body. By this means quantitative, dynamic measurements could be introduced into medical science. These technics could be used both to determine the range of normal readings more accurately and to correlate these readings with causal phenomena to diagnose the existence or severity of an ailment.

"Microsensors could be used to detect the effect of drugs well in advance of any gross symptoms detectable by the patient or by more conventional medical means. This more precise 'error' detection might be used as a part of a feedback loop to determine the quantity of medication optimum for the particular patient under the particular circumstances of the moment." Measurements of this sort, used in combination with a medical "automatic oracle," would be invaluable assistance in diagnosis. The "oracles" will be the results of the marriage of microminiaturization technics with bionics, the concept of reproducing electronically many of the capabilities of thinking, learning, and reacting which characterize living beings. Such "oracles" involve the use of learning machines to become expert in certain classes of questions or in the analysis of particular problems. "This concept can be applied to almost any field of human mental activity, limited only by the 'oracle's' internal capability and logic and by the time available to teach it to become an expert in a particular specialty."

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Oxygen and the Anesthesia Machine

THE PREVENTION OF HYPOXIA is one of the major tasks confronting the anesthetist. Usually hypoxia is caused by respiratory factors such as hypoventilation or obstruction or by circulatory factors such as cardiovascular failure or severe anemia. Occasionally, however, factors of a mechanical nature may be responsible for hypoxia.

Case report

A twenty-nine-year-old male with a diagnosis of prolapsed intervertebral disk was scheduled for lumbar laminectomy. His hematocrit on admission was 49. His history, physical examination, and laboratory studies were otherwise unremarkable.

On the day of surgery, meperidine hydrochloride 100 mg. and scopolamine 0.4 mg. were administered one hour prior to the induction of anesthesia. The preanesthetic vital signs were a blood pressure of 120/80 mm. Hg, pulse 80 per minute, and respiratory rate 24 per minute. The patient was calm.

The induction of anesthesia was accomplished smoothly with 250 mg. of 2.5 per cent thiopental sodium intravenously. Nitrous oxide at 4 L. per minute plus oxygen at 4 L. per minute from a Foregger Texas machine* plus 1.5 per cent halothane vaporized through a Fluotec† were then administered by face mask. Six minutes later 40 mg. of succinylcholine were administered, and orotracheal intubation was accomplished with ease, atraumatically, and under direct vision using a number 38 anode (wire-embedded) tube.

The patient was then placed prone, with long bolsters along each side of the body to suspend the thoracic cage and abdomen in such a fashion as to permit adequate chest excursion and not to interfere with venous return.

The maintenance of anesthesia during the excision of the herniated intervertebral disk was with nitrous oxide 4 L. per minute and oxygen 4 L. per minute plus 1 per cent halothane.

Two hours after the induction, during the closure, the anesthetist noted that the pulse rate rose suddenly from 90 to 110 per minute and the respiratory rate from 16 to 32 per minute. The blood pressure which had been 120/80 was 110/70 mm. Hg. About fifteen minutes later the anesthetist observed that the patient had become deeply cyanotic. The anesthetist attempted to fill the rebreathing bag by using the oxygen flush valve and discovered that the oxygen tank which had been in use was empty, although the rotameter was showing a 4 L. per minute flow ot oxygen. He opened the reserve tank of oxygen immediately, discontinued nitrous oxide and halothane, and administered only oxygen for the last thirty minutes of the closure. The vital signs returned to the patient's normal levels rapidly.

Presented and discussed at a conference held at Bellevue Hospital, New York City, June 4, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

* Distributed by the Foregger Company of Roslyn Heights, Long Island.

† Distributed by Fraser Sweatman, Inc., Buffalo, New York.

The patient recovered from his bout with anoxia without apparent sequelae.

Comment

The rotameter in the oxygen flow meter became stuck after the oxygen tank had emptied. Oxygen and nitrous oxide rotameters do not readily become stuck because the openings of the tapered tubes are relatively large. A small opening in the cyclopropane tapered tube becomes clogged easily and explains the frequent development of stuck rotameters for this gas.

Recently devices have been developed which prevent the delivery of oxygen-deficient mixtures from anesthesia machines. Epstein *et al.** base their device on a single control pressure supplied by oxygen which is called a slave-proportioning regulator system. To quote them: "Since the percentage of oxygen in the anesthetic mixture is of paramount importance, oxygen pressure is used as the control pressure. In this way should the oxygen pressure change, the flow rates of all component gases automatically change proportionally. Should the oxygen input pressure fall to zero, the diaphragms of all slave regulators close and gas flow ceases."

A new anesthetic machine called the Quantiflex† incorporates an "oxygen fail safe system" such that should oxygen supply fail all other gases automatically shut off.

The Foregger Company and the Ohio Chemical and Surgical Equipment Company† can incorporate a similar oxygen protective system in new anesthesia machines and in certain instances may be able to incorporate this system in existing equipment.

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* Epstein, R. M., Rackow, A., Lee, A. S. J., and Papper, E. M.: Prevention of accidental breathing of anoxic gas mixtures during anesthesia, Anesthesiology 23: 1 (Jan.-Feb.) 1962.

† Both of New York City.

Number one hundred twenty-eight in a series of Clinical Anesthesia Conferences

Birth characteristics of children dying of malignant neoplasms

In a study of birth and death records of children dying of malignant neoplasms over a ten-year period, reported by Brian MacMahon, M.D., and Vaun A. Newill, M.D., in the January, 1962, issue of the *Journal of the National Cancer Institute*, the mortality from leukemia was associated with birth order and with the age of the mother. For first children, the death risk was about 50 per cent higher than for fifth and later births. Also, the death risk from leukemia was about 40 per cent higher for children born to women over forty and to those under twenty. These associations were independent. Except for leukemia, no form of neoplasm showed any significant association with either birth order or maternal age. There appeared to be no association of the death rate from leukemia or any other neoplasms with birth weight, number of prior stillbirths, or twins. There was one set of twins in the series, both of whom died of leukemia, but they were not unduly represented in the records.

Accidental Chemical Poisonings

From the Poison Control Center,
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Triflupromazine Hydrochloride, Aspirin, and Phosphorus Poisonings

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Agent	*Age*	*Sex*
Tranquilizer suppository	$8^1/_2$ years	Female

This incident was reported by the service of Henry Barnett, M.D., director and chairman of the Department of Pediatrics of Albert Einstein College of Medicine of Yeshiva University and Abraham Jacobi Hospital of the Bronx Municipal Hospital Center.

According to the report the patient was apparently in good health until five days prior to her admission when she developed fever, sore throat, vomiting, and cough. She was treated symptomatically by her parent and her illness showed a variable up and down course. Because of persistent symptoms her local medical doctor was called three days prior to her admission. He made a tentative diagnosis of measles because of the patient's exposure to this disease. Achromycin was started at this time without effect. One day prior to admission the patient was still vomiting and running intermittent fevers. Her local physician then prescribed triflupromazine hydrochloride tranquilizer suppositories, 35 mg. each, and cough syrup. The patient was given the first rectal tranquilizer suppository twenty-four hours prior to hospital admission and fell into a deep sleep during which time the typical measles rash began to appear on her face.

Twelve hours prior to admission the patient was given another suppository with some relief of vomiting. Four hours prior to admission the patient experienced the first of several "seizures." These were characterized by contortion of the face, a stiffening of the body, inturning of the hands and feet, and arching of the back. Her eyes stared straight ahead, but there was no loss of sphincter tone, frothing at the mouth, tonic clonic movements, or loss of consciousness. The local physician was called and found the patient to be well essentially except that she was aphasic. However, she was able to open her mouth and to obey commands. The patient was taken to Misericordia Hospital and given 60 mg. of sodium luminal intramuscularly. She was then sent to Abraham Jacobi Hospital for admission. On transit and in the emergency room of the hospital three other similar seizures occurred. She was given 5 cc. of paraldehyde and 60 mg. of phenobarbital intramuscularly and admitted to the hospital. The patient's past history is remarkable only in that she is allergic to penicillin. The family history is noncontributory except that a maternal grandmother has diabetes.

PHYSICAL EXAMINATION. The patient was a slim, white female lying in bed with obvious measles rash and rousable only by painful stimuli. Other than the maculopapular measle rash, the skin was not remarkable. An examination of the hair, eyes, ears, nose, and throat revealed a slightly erythematous pharynx with vesicles on both anterior fornices. The remainder of the examination, except for the neurologic aspects, was within normal limits. A neurologic examination revealed the patient to be semicomatose and responsive only to painful stimuli. All the extremities moved well but were markedly hypotonic. The patient's reflexes were bilaterally depressed but symmetrical and revealed no pathologic changes. The cranial nerves and sensation were intact. There were no meningeal signs. The patient's temperature was 100 F., the pulse rate 108 and regular, the blood pressure 100/70, and respirations 36.

LABORATORY DATA. On admission the patient's hematocrit was 38, the white blood cell count was 6,050, with 10 lymphocytes, 3 monocytes, 1 eosinophil, 75 mature polymorphonuclear leukocytes, and 13 bands. The urinalysis on admission was within normal limits except for a trace of albumin and 8 to 10 white blood cells. A repeat urinalysis forty-eight hours after admission showed results within normal limits. On admission the blood sugar was 95, the carbon dioxide 26, chloride 100, sodium 141, and nitrogen 418 mg. per 100 ml. The admission lumbar puncture was atraumatic. There were no cells. The closing pressure was 65 and the protein 16, sugar 53, and blood sugar 95 mg. per 100 ml. The purified protein derivative test for tuberculosis intradermally was negative after forty-eight hours. The results of an electroencephalogram taken twenty-four hours after admission were read as being normal for the patient's age.

COURSE. On admission the patient exhibited signs of deep sedation. The assistant medical director of the pharmaceutical company that produced the tranquilizer suppository was contacted and the seizures and the patient's history were described to him. It was his feeling that the clinical course was more suggestive of an idiosyncratic reaction to the tranquilizer than indicative of measles encephalitis. On his recommendation the anticonvulsive therapy in the form of Dilantin and phenobarbital was stopped and the patient was observed closely. She slept through the first twelve to sixteen hours after admission, during which time she was given an intravenous infusion of one-third normal saline. The following morning she was much more alert and was able to carry out commands. However, she was still not able to talk. Later that morning the patient had the last of her seizures which was quickly terminated by 10 mg. of intravenously administered diphenhydramine hydrochloride (Benadryl). The physician administering the diphenhydramine hydrochloride was not certain whether the seizure stopped before the diphenhydramine hydrochloride could take effect or whether the diphenhydramine hydrochloride actually stopped the seizure immediately. By the following afternoon and two days after admission she was walking around the ward completely asymptomatic. On the fourth hospital day the patient was discharged completely afebrile and asymptomatic in the care of her family physician.

FINAL DIAGNOSIS. Rubeola; herpangina; and idiosyncratic reaction to a triflupromazine hydrochloride tranquilizer in suppository form. The prognosis was considered to be excellent.

While the extrapyramidal symptoms from the phenothiazines have been reported with great frequency, reports concerning triflupromazine hydrochloride, have not been numerous. We have noted that the use of suppositories to administer drugs frequently causes more severe reactions than administration by the oral route. This has been particularly noticeable in cases following the use of aminophylline suppositories.

Our experience also indicates a special need for caution with regard to dosages. Doses intended for adult use should not be used in treating children.

INCIDENT 2

Agent	*Age*	*Sex*
Aspirin	22 months	Male

The patient was admitted to the hospital because of an overdose of aspirin. The mother of the patient found the bottle of 5-grain aspirin tablets half empty on the floor. One of three siblings involved in the incident volunteered the information that all of them swallowed some of the aspirins, but that the infant (patient) swallowed most of it. The child was taken to Queens General Hospital. The most prominent symptom on admission was hyperpnea. In spite of the usual therapeutic measures employed the infant died two hours following admission. According to the mother the aspirin bottle was discarded in the garbage can, but it was retrieved by the visiting Public Health nurse and brought to the Poison Control Center.

Although aspirin continues to be the drug most frequently involved in childhood poisonings, severe incidents and fatalities are fortunately uncommon. In spite of the fact that this case involves a fatality, the clinical data reported to this Center was shockingly meager.

We believe strongly that in severe cases, and particularly in fatalities, there is an obligation on the part of the hospital administration staff to report in detail the symptomatology, pathology, diagnosis, treatment, and outcome of each such case.

INCIDENT 3

Agent	*Age*	*Sex*
J-O Rat Poison	18 years	Female

This eighteen-year-old patient supposedly went into the bathroom to take a shower but came out dizzy and lay down on the bed. According to her girl friend the rat poison paste was in the kitchen closet but was taken by the patient with her to the bathroom. Her girl friend relays that she found the patient in a comatose condition and took her to a hospital emergency room.

On admission to the hospital the patient's stomach was lavaged and vomiting was induced. In spite of the therapy the patient expired five hours following ingestion of the paste and two hours following admission to the hospital. A postmortem examination was done by Medical Examiner, Dominick J. Di Maio, M.D., and the report was sent to the Poison Control Center through the courtesy of the Chief Medical Examiner, Milton Helpern, M.D.

The autopsy report is as follows:

> The body is that of a well-developed and well-nourished eighteen-year-old female, 5 feet 4 inches tall and weighing 96 pounds. There is an unusual pallor to the skin and mucous membranes. The teeth are in good condition. The neck, chest, abdomen, and genitalia are normal. There are no external evidences of injury.
>
> The scalp is incised and retracted in the usual manner, revealing no evidence of trauma. There is no skull fracture. The brain weighs 1,150 Gm. The leptomeninges are smooth and glistening. The arteries at the base of the brain are soft and collapsible. On serial section, there are no signs of trauma, tumefaction, infection, or areas of softening.
>
> SECTION. The pleural, pericardial and peritoneal cavities are normal. The lungs weigh 650 Gm., are reddish-gray mottled with black, and ooze a small quantity of edema fluid. The heart weighs 320 Gm. The epicardium, mural endocardium, and myocardium are normal. The valves and coronary arteries are normal. The liver weighs 1,500 Gm. Externally, and on cut section, it shows no significant pathologic changes. The biliary system is normal. The spleen is normal in size. On section it reveals no unusual pathologic condition. The pancreas is firm, lobulated, and tan in color. The adrenals are grossly negative. The kidneys weigh 280 Gm. together. On section, corticomedullary markings are distinct. The calyces, pelves, ureters, and bladder are normal.
>
> There is a marked hyperemia of the gastric mucosa, with contents that emit a phosphorous odor. The stomach and its contents have been removed for chemical analysis. The uterus appears normal. There is a corpus luteum of the right ovary, and the endometrium is in the secretory phase. The remainder of the internal genitalia are normal. The brain, liver, and the stomach and its contents have been removed for chemical analysis and determination of alcohol, and phosphorus content.
>
> ANATOMIC DIAGNOSIS. Acute corrosive gastritis.
>
> CAUSE OF DEATH. Acute phosphorus poisoning caused by ingestion of rat poison. An apparent suicide.

Among the poisons for which no specific antidote is available, phosphorus is outstanding. It is widely used in suicidal attempts, and the fatality rate remains unusually high.

Number ninety-seven in a series of Accidental Chemical Poisonings

Case Reports

Fatal Hemoptysis From Tracheal Vascular Node

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From Matteawan State Hospital

THE SITE AND etiologic conditions of fatal hemoptysis are usually diagnosed by the clinician. An unusual case of fatal hemoptysis is reported because it was clinically asymptomatic and originated from a rare site and structure, namely, a vascular node in the trachea. I was unable to find a similar case in the literature.

Case report

A seventy-one-year-old white male had been admitted twenty-four years prior to this admission for a paranoid condition. His present hospital stay was uneventful and he did not have any physical complaints. Routine chest x-ray films were taken and failed to reveal any pathologic conditions. Routine urine and blood examinations revealed negative findings. On one occasion, at the time of a routine physical examination, the blood pressure was 110/170. Subsequent blood pressure readings were 95/110. On the day of his death, suddenly and without apparent reason, the patient was coughing up blood so profusely that some of it came out through his nose. Before any treatment could be instituted, his pulse became weaker and faded away.

On autopsy the findings were concentrated on the lungs. There was considerable blood aspiration into the lungs, and there were no infiltrations or masses in the lungs. The bronchi and trachea contained fresh blood. A careful study of the lungs and bronchi failed to reveal any pathologic conditions responsible for this massive hemorrhage. However, the trachea showed a vascular nodule, filled with fresh blood. This nodule, 1.5 cm in diameter, was freely movable just below the larynx (Fig. 1A). Microscopically the node consisted of blood-filled dilated vessels without any malignant or inflammatory changes (Fig. 1B).

Comment

Laryngeal nodes (singer's nodes) are located in the larynx and constitute the pathologic conditions of the true cord mucosas.[1] Hemoptysis may be one of their clinical symptoms. Benign papillomas or cancer of the larynx also may produce hemoptysis. Similarly, benign or malignant tumors of the trachea, bronchi, or lungs can also produce hemorrhage. Systemic diseases involving blood vessels, such as the Rendu-Osler-Weber disease[2] or juvenile nasopharyngeal angiofibroma,[3] may produce hemoptysis, since they can involve the respiratory tract also. However, in our case with gross and histologic examinations we found no involvement of any other organs. The site of the source of the fatal hemoptysis was a vascular node in the trachea, a singular node in an elderly patient.

It is possible that bronchoscopy would have enabled an earlier diagnosis and treatment in a more cooperative, less paranoid patient.

Summary

We have reported a fatal hemoptysis originating from a vascular node in the trachea in a seventy-one-year-old male.

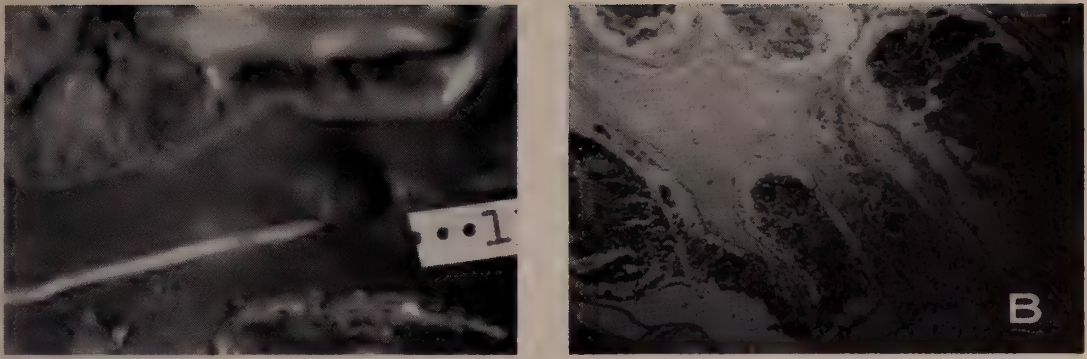

FIGURE 1. (A) Trachea with node. (B) Microscopic view of vessels with blood.

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Population increase in the West

The American people are still taking Horace Greeley's advice to heart. They are going west.

Families in the United States have grown in number by more than 6.5 million since 1950, and, generally, the most rapid gains were in the mountain and the Pacific states, according to statisticians of Metropolitan Life Insurance Company.

At the 1960 census, the number of families totaled 45.1 million, and indications are that the number will pass the 50 million mark before the end of the 1960's.

A substantial increase occurred also in families with dependent children. In 1960, 57 per cent of families had dependents under eighteen years of age living with them, compared with 53 per cent in 1950.

Alaska nearly doubled its number of families during the decade, while Florida experienced a gain of 80 per cent and Nevada 75 per cent. Arizona recorded a 71 per cent gain.

Rapid growth in family units also developed in California (42 per cent), New Mexico (39 per cent), and Delaware (38 per cent).

Only moderate increases occurred in the New England and Middle Atlantic states, averaging about 13 per cent during the 1950's. However, the two exceptions, New Jersey and Connecticut, which have had large suburban growth, showed increases of about 25 per cent.

Only three states showed losses in the number of families. In Arkansas and West Virginia, the number dropped by more than 4 per cent and in Mississippi by almost 2 per cent. The District of Columbia showed an even sharper drop: 11.5 per cent.

A number of southern states, however, had appreciable increases. Aside from those already mentioned, Maryland, Virginia, and Texas reported increases in family units ranging from more than 20 per cent to almost 30 per cent.

Extrapyramidal Reactions to Prochlorperazine and Perphenazine in Same Patient

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The development of extrapyramidal symptoms following the oral or parenteral administration of "thiazine" preparations is a well-documented entity. There may be reactions ranging from motor dyskinesias[1] to tetanus-like syndromes[2,3] and epileptiform seizures.[4,5] These disturbances have no relation to dosage or duration of therapy, rather they apparently represent a psychomotor response to an effect of the drug on the central motor system.

It has been stated that since recurrent attacks may occur with the reintroduction of the medication, it would be preferable to use another drug of the thiazine group should further therapy be necessary.[6,7] The purpose of this report is to describe a case of similar reactions to prochlorperazine dimaleate and perphenazine on separate occasions, each drug having been given in small therapeutic doses by different routes of administration.

Case report

A twenty-year-old white female received an injection of 4 mg. of perphenazine from her physician for the treatment of a pruritic rash. The medication was administered at about 3:00 o'clock in the afternoon. That evening she became drowsy and went to sleep early. On arising the following morning she had a stiffness of the neck which became more severe during the next two hours. She then developed involuntary contractions of her neck and back muscles which forced her into an opisthotonoid position. Her speech became thick, her eyes were forced involuntarily to the left, and her limbs were rigid. She was brought to the emergency room of Meadowbrook Hospital and displayed rigidity of all four extremities, oculogyric crisis to the left, and opisthotonus. She was given 50 mg. of diphenhydramine hydrochloride intravenously, and within five minutes there was evident muscle relaxation. One hour later she was completely asymptomatic and had no abnormal physical findings, except for a pityriasis versicolor on the chest, abdomen, and back.

Eighteen months previously, this patient had been given tablets of prochlorperazine dimaleate for nausea and vomiting of pregnancy. She had taken the medication for one day, following which she had experienced a similar reaction, consisting of rigidity, tremors, and opisthotonus. She was taken to another hospital, treated, kept overnight, and discharged. She had no history of any other known allergies or similar experiences in the past.

Comment

This patient has, on two occasions, demonstrated a full syndrome of extrapyramidal reactions following the administration of a thiazine preparation. It is of interest that the maximum reaction did not occur until approximately fourteen to sixteen hours following an intramuscular injection, whereas the therapeutic effect of the medication is reported to last from four to six hours.

It is apparent that certain individuals are susceptible to the phenothiazine derivatives and will manifest this sensitivity by developing any one or a combination of neurologic disorders. These reactions are controlled by cessation of the drug and by the administration of sedatives and antiparkinsonian preparations. It may further be said that once a patient demonstrates such sensitivity, that patient should not be given any phenothiazine preparation by any route of administration in the future, since the probability of a similar or more severe reaction is greatly enhanced.

Conclusion

A patient demonstrating a tetanus-like syndrome following the oral administration of prochlorperazine dimaleate and eighteen months later the same syndrome following parenteral perphenazine is reported. It is recommended that any patient exhibiting sensitivity to any phenothiazine derivative not be treated by any other phenothiazine derivative in the future.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

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William L. Watson, M.D.
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Effect of Histamine Treatment on Cold Allergy

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In 1924 to 1925 DUKE[1] introduced the concept of physical factors as the cause of changes in mucous membranes and skin and the similarity to inhalant food and drug sensitivities. Since then, the manifestations in the sensitive individual resulting from exposure to such agents as cold, light, heat, mechanical irritation, or physical effort have become well recognized in the spectrum of allergic disorders. Nevertheless it is desirable to emphasize and disseminate the knowledge in the general medical literature of the protean manifestations of organ involvement that these physical modalities can effect in the sensitive host.

In a short span of time we have found 2 cases of cold sensitivity. One patient was referred to us following a shock-like syndrome which ensued while he was swimming during the summer of 1960. The other patient was being observed and treated for bronchial asthma.

Case reports

CASE 1. A twelve-year-old white male was referred for observation in October, 1960, because of urticarial lesions following an exposure to cold wind and water. The lesions were limited to the exposed parts, but symptoms of abdominal pain, wheezing, and nasal obstruction frequently accompanied more severe skin manifestations. There was a history of "shock" while he was swimming in the summer of 1960.

The patient's past history revealed a vague cough and sneezing episodes in the month of August for the past three years, frequent episodes of upper respiratory infections in the winter season, and diarrhea following the ingestion of cold products (milk, ice cream, soda) for the past several months. The family history revealed a background of atopy.

A physical examination was essentially normal. Nasal smears revealed no eosinophils, and the blood count and urinalysis indicated negative results. Sinus and chest x-ray studies were normal. Tests for serum cryoglobulins revealed negative results.

A contact with a test tube containing cold water produced a marked local urticarial wheal within ten minutes, the outline of which corresponded to the shape of the test tube. No systemic effect was noted. When the hands were submerged in ice water, marked swelling and erythema of the parts occurred within three minutes, with pain and pruritus. There was also a systemic effect of tachycardia and lightheadedness. All symptoms subsided promptly after the application of warm water to the extremities. Intracutaneous testing with the common atopens revealed slight-to-moderate reactions to extracts of wool, orris root, dust, dog epithelium, ragweed, timothy, silkworm, and green pea.

The patient was placed on a treatment of daily histamine injections (technic to be described later), reaching a top dose of 0.5 cc. of histamine base (1 mg. per cubic centimeter). The mother of the patient was then instructed in the technic of administering a subcutaneous injection, so that this top dose was continued daily for a period of three months. The patient, who initially had to wear a Navy-type Arctic mask when going outdoors, eventually was able to go out in 5 F. weather without this cover, showing only minimal erythema without edema.

At this point repeated provocative testing with cold water revealed only local erythema without edema. Attempts to transfer passively this cold sensitivity according to the technic of Sherman and Seebohm[2] both before and after histamine therapy were not successful.

CASE 2. A thirty-year-old white female gave a history of asthmatic episodes from infancy to ten years of age and then a disappearance of symptoms until twenty years of age when wheezing recurred. From twenty-three through twenty-nine years of age the patient had perennial asthma, questionably worse in the winter months. An environmental survey revealed numerous sources of possible difficulty (for example, dust, wool, feather sources, dog exposure, smoke, and odors). These sources were eliminated successfully.

A physical examination revealed negative results except for an occasional expiratory wheeze and boggy nasal mucous membranes. A nasal smear revealed no eosinophils and a blood smear revealed an eosinophilia of 27 per cent. Intracutaneous skin testing with the common atopens was made difficult by a marked hyperresponsiveness of the skin. The suggested reactors were dust, feathers, ragweed, alternaria, trees, and pineapple.

The patient was placed on perennial therapy with ragweed, trees, alternaria, and dust extracts, and her symptoms were generally diminished but never alleviated completely. A food diary was maintained, and certain foods were excluded by trial with no revealing effect.

About one year after treatment was instituted, the patient developed urticarial lesions on the exposed parts of the body and also had increased wheezing when she was standing in a cold wind. An ice cube applied to the skin produced marked erythema and edema after from three to five minutes of contact. Avoidance of exposure to cold produced a mitigation of both the urticaria and the asthma. However, the patient was then unable to carry out the simplest of household chores which involved any contact with water and the refrigerator.

She then was placed on daily injections of histamine solution reaching a top dose of 0.3 cc. of histamine base (0.1 mg. per cubic centimeter). This procedure was continued by the patient for a period of two months. The results were most gratifying, and the patient was able to go out into the cold wind with a minimum of adverse reaction. She was also able to do her usual household chores, including the handling of frozen food, with minimal erythema and pruritus and no edema. The attempt at avoidance of cold appeared to reduce the respiratory symptoms markedly. A repetition of the test with an ice cube in contact with the skin now revealed only moderate erythema without edema, pruritus, or pain even after ten minutes of exposure. The passive transfer of the ice-cube test was not achieved.

Comment

Nonspecific factors, such as temperature variation, humidity, odors, and others are often important elements in clinical allergy and contribute to the specific effects of food, pollen, dust, and mold sensitivity. However, the concept of the specificity of physical agents to cause common atopic symptoms of asthma, urticaria, and rhinitis was introduced by Duke in 1924.[1,3] In the decades since this important contribution, many case reports have been published, and its secondary importance in unselected allergic cases of all varieties as reported by Swineford[4] has been recognized. Of the specific physical factors, an allergic reaction to cold is not uncommon.

In the original discussion by Duke, symptoms produced by physical agents were placed into the categories of local "contact reactions" and "reflex-like reactions" involving distant shock organs. Thus, the symptoms can be legion in that many organ systems can be involved theoretically, and indeed such symptoms as urticaria, angio-edema, asthma, rhinitis, migraine, cardiac arrhythmias, syncope, purpura, hemoglobinuria, abdominal pain, and diarrhea are reported in the literature.[5] Many cases of sudden death following swimming have been cited,[6] and indeed our first case presented a vascular collapse without the slightest antecedent history.

The diagnosis of cold allergy is often made by the history of an intolerance to cold. The use of ice cubes, iced wet towels, hand immersion in cold water (48 F.), ice water in a test tube, all representing the application of cold to the skin with readings at from one-to ten-minute intervals, have been proposed. Symptoms in those patients who have bronchial mucous membrane involvement can be provoked by breathing air passed over ice or through a refrigerated apparatus.

In 1937 Walzer,[7] in a critical review of the literature on physical allergy, analyzed the case reports of passive transfer studies made in a number of instances of cold allergy. In the majority of cases attempts to transfer the cold sensitizing "antibody" were unsuccessful. In those reports in which antibodies had been claimed to be demonstrated, Walzer felt that the results were dubious. Only in the studies of Harris, Lewis, and Vaughan[8] did Walzer feel that some variety of antibody was involved.

Harris, Lewis, and Vaughan demonstrated the presence of a very labile cold antibody by testing the serum site within a period of five hours after the injection of the serum. In another case only the precipitable portion of the serum in a case of essential cryoglobulinemia produced positive skin reactions to ice when it was transferred after six hours.[9] It was demonstrated in 1 case of cold urticaria that several electrophoretically separated protein fractions of the patient's serum (albumin and alpha globulin, beta and gamma globulin, and gamma globulin) were necessary in achieving a successful positive transfer.[2] However, the vast majority of cases of cold sensitivity are not transferred passively.

The mechanism of cold allergy has been difficult to determine owing to the unpredictability of antibody demonstration. The scattered positive transfers of specific reagin give substantial substance to the premise that in these instances a true allergic phenomenon is involved. Many patients specifically reactive to physical agents give positive family and personal histories of atopy and associated symptomatology, as demonstrated by our patients. Associated eosinophilia is not demonstrated regularly in such patients, and the degree of eosinophilia is usually governed by associated atopy. Tissue eosinophilia has not been observed regularly in the cold-induced wheal.[7]

To explain the majority of instances of unsuccessful transfer, many theories have been proposed. Karady[10] reported the production of anaphylaxis in experimental animals by the injection of a homologous serum exposed to cold and subsequently exposing the animals to cold or by the reinjection of the cold-treated sera. Karady suggested the concept that proteins of the blood or tissues were modified by low temperatures to act as complete antigens. Shortly afterward Richardson[11] repeated these experiments in detail, and in no instance were Karady's results duplicated. On the other hand, evidence has been presented to show that physical allergy may be mediated by a nonallergic mechanism involving chemical mediators, such as histamine or the generation of a toxic substance from the tissue on exposure.[12] Horton and Brown[13] demonstrated that the secretion of hydrochloric acid rose in association with an attack of cold urticaria, implying the role of a histamine-like agent. Indeed, Horton, Brown, and Roth in 1936[14] presented evidence of an increased amount of histamine in plasma obtained from patients with cold urticaria. This was confirmed by Henderson, Code, and Roth.[15] However, in the urinary excretion studies in 2 patients with cold urticaria with labeled histamine and its metabolites, Lindell, Nilsson, and Rorsman[16] revealed no difference as compared to healthy subjects. They could not give an explanation for the absence of histaminuria in spite of a reported demonstration of increased plasma histamine levels in such cold-sensitive patients. No theory yet presented is fully adequate in explaining all the observed phenomena.

Preferably the treatment of cold sensitivity is its prevention by the avoidance of exposure. However, this is often unfeasible. The use of antihistamines is usually found to be valueless,[9] and epinephrine is effective only transiently and is used only for symptomatic relief. Horton, Brown, and Roth[14] suggested the method of exposure of the hands in water to lower temperatures progressively in an attempt to "desensitize." This method had also been used by Duke.[17]

In 1932 Bray[18] reported the use of histamine injections in cold allergy. Later Roth and Horton[19] used similar means in the treatment of cold-sensitive patients. In our cases we have attempted to achieve the highest possible dosage of histamine short of systemic effects. In Case 1, 0.5 cc. of histamine base (1 mg. per cubic centimeter) was achieved with only an occasional abdominal cramp, and this was continued for three months. Initially, injections were given at daily or twice-daily intervals, starting with 0.1 cc. of histamine base (0.0001 mg. per cubic centimeter), with subsequent tripling or quadrupling of the dose, being guided by the local as well as by the presence of a systemic undesirable effect. The second case tolerated a dose of 0.3 cc. of histamine (0.1 mg. base per cubic centimeter), and a higher dose caused the patient to experience generalized pruritus and headache. In both cases successful results were not observed before histamine had been administered for from two to three months. Fortunately both patients achieved maximum benefit in the coldest phase of the winter and tolerated exposure well.

Summary

Two case reports of cold allergy have been presented with a short review of the literature. Histamine desensitization proved very beneficial, although its etiologic role in the pathogenesis of this sensitivity is yet vague. In neither case was the passive transfer of the cold sensitivity achieved.

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Medical Care Insurance

A series of articles on health insurance prepared by the Associated Blue Shield Plans of New York State

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Prognosis for Private Practice*

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OVER THE PAST several months newspapers, magazines, radio, and television have devoted much space and time to the King-Anderson Bill. The more I read, heard, and thought about this bill, the more I became impressed with the idea that the demand for this type of legislation constitutes but a symptom of more fundamental changes which are occurring in our medical order. This is not an isolated phenomenon. It is an offshoot of the increasing search for social security in its broadest sense—a means of providing protection against the uncertainties of a world kept in perpetual turmoil by economic upheaval, international power politics, and the prospect of a personal disaster brought on by a prolonged disabling illness.

This latter concept, superimposed on the philosophy that it is a proper function of government to provide the basic necessities (and proper medical care has come to be regarded as one) beyond the ability of the individual to secure for himself, has engendered the demand for what, oversimplified, is called "socialized medicine." Farm supports, Federal housing, Federal aid to education, the Hill-Burton Act, Federal road-building, and Federally-backed mortgages are but a few other manifestations of the same deep stirring, which is not local or national but world-wide in its scope.

We doctors have tended to rationalize our situation and to defend the position that this all-pervading philosophy, having arisen outside the profession, is not of our doing and is beyond our power to overcome or modify. This is but partially true. There are many sins of omission and commission for which we are responsible, which have had considerable adverse influence. The correction of these, conversely, may help to reverse the trend in our own particular field of interest. If the public had been receiving all the medical care it required at a price it could afford to pay, the demand for socialization of medicine most probably would not have arisen or at least would have been delayed and taken different forms.

Within the memory of a good many of us, the practice of medicine was a comparatively simple system. It was recognized that certain segments of the population were unable to pay for their own medical care, and it was accepted that their care was properly the responsibility of local government—city, county, or state. The patient who could afford to pay entered into a contract, verbal or tacit, to pay the doctor of his choice a given fee, adjusted according to ability to pay, for certain medical services which the doctor rendered. The doctor-patient relationship was direct, personal, and uncomplicated by any third party interest or involvement.

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True, workmen's compensation medicine imposed the responsibility for the costs of medical care for injuries sustained while at work on the employer, who in turn insured himself against these costs. This created a third party, the insurance company, with a valid interest in treatment and outcome, and modified, to some extent, the initial simple relationship. But even here, many states, by allowing for a free choice of doctor in compensation cases, caused only a minimal variation from the traditional practice.

Changes brought by depression

Soon, however, many factors came into being to produce profound pressures which were to initiate fundamental changes in this relatively simple system.

During the depression of the thirties, a significant segment of the population, previously solvent, became unable to pay for their medical care and called on government to supply it. Local relief plans were expanded or created, and, for the first time, the Federal government subsidized civilian medical care through such programs as Old Age Assistance. There was a crescendo of voices calling for an all-out takeover of medical care by the Federal government.

The medical profession at large, fearful of the deficiencies and drawbacks it felt were inherent in government medical control, sought a means of providing good medical care for the people at a reasonable price.

The Blue Cross program was launched, demonstrating that hospitalization costs could be paid for through the insurance principle. The Blue Shield idea followed, again utilizing insurance to spread costs and give broad population coverage. There arose, in connection with it, a relatively new concept, that of "medical indigency." The medically indigent person was defined as an individual who could keep his head above water economically under ordinary circumstances—pay his rent and his food bill, clothe his family and so forth—but who did not have the wherewithal to cope with the costs of a major illness. And so the idea of Service Benefits came into being. Medicine's spokesmen proclaimed that voluntary health insurance was the instrument that was to be used to provide, qualitatively and quantitatively, adequate medical care. The truly indigent person would still be the responsibility of government, the medically indigent individual would receive paid-in-full care through medical expense insurance, and the citizen whose economic level exceeded that of these two groups would still pay his own way in the traditional manner, possibly aided by indemnity payments from insurance coverage.

This system was predicated on several major basic assumptions. Among these, first, was that the best medical care is provided on a free-choice, competitive fee-for-service system. (It is noteworthy that the A.M.A. continues to adhere to this tenet.) Second, it was assumed that the profession would provide care under the conditions outlined.

Problems of financing medical care insurance

Unfortunately, although this entire thesis is fundamentally sound, certain practical considerations imposed themselves. Surgical care, relatively predictable on an actuarial basis, adapted itself well to insurance. Nonsurgical therapy, on the other hand, required considerable experience before it could be integrated into the picture. As an example, let us suppose that the actuaries have determined that the average family requires 5 house calls yearly. The insurance company then offers a policy which covers house calls as one of the benefits and bases its premium structure on the average of 5 calls per family.

Human nature being what it is, an insured family, feeling entitled to coverage for house calls, calls in the doctor more frequently than previously and the actual utilization may then be double or triple the predicted demand, with a consequent major dislocation of the insurance company's finances. With experience, it is possible to calculate the effect of this added factor and provide for it. But experience takes time, and impatient, apathetic, and outright hostile persons maintained that the system was unworkable, that it was only a surgeon's plan, or that government control was the only solution.

Other inadequacies soon became apparent. Besides inadequate nonsurgical coverage, there were too many exclusions: tuberculosis, mental illness, and congenital defects, conditions which constitute catastrophic illness to the average family. Beyond these were abuses by both the patient and the doctor: demands for unnecessary hospitalization, collusive defrauding of the insurance company, bill-padding, and increasing fees above normal because there was insurance coverage. Admittedly these abuses were relatively few in number, but they were enough to give added ammunition to the opponents of the voluntary system. An additional weakness was the refusal of a significant portion of the profession to agree to render Service Benefits. This reduced the appeal of the program to the medically indigent group and those who bargained for them.

Other pressures produced by prosperity

We were able, by adjustment and compromise, to ride out difficulties of this sort, to expand Blue Cross and Blue Shield to their present extent, and to remove many of the "bugs" which hampered the program. As the nation moved into an era of prosperity, it might have been thought that most of the problems apparently engendered by the depression would have been eliminated. But prosperity, in its turn, produced other pressures on the system of medical care. As wages increased and finally reached a level beyond which management was unwilling to go, unions began to bargain for what we now refer to as fringe benefits, prominent among which are the costs of medical care. Union spokesmen, complaining that the limited coverage offered those of their members who were ineligible for Service Benefits was inadequate, pushed more and more for complete, paid-up care.

To meet this demand, major medical insurance coverage was conceived. Again inherent weaknesses, such as potential abuse and overutilization, were brought to light during increasing experience with this type of insurance. So, deductibles and coinsurance were introduced as countermeasures. Since these entailed out-of-pocket expense by the subscriber, the union leaders continued to demand an extension of eligibility for service coverage. In other words, their aim became full coverage of the costs of medical care for a fixed annual fee. This would constitute Service Benefits eligibility based, not on medical indigency, but on the social concept that total medical costs should be absolutely predictable for the individual.

The only agency which has indicated a willingness to provide care on this basis is the closed-panel group. We have witnessed the growth of many such groups. The acceptance of the closed panel would mean the abandonment of the free-choice principle, of fee-for-service, and of traditional solo practice, all of which, organized medicine contends, would be detrimental to the quality of medical care received by the consumer public.

More private patients

A collateral phenomenon affecting medical practice and directly traceable to the rise of voluntary health insurance is the diminution of the number of ward patients available for teaching purposes in the training of medical students, interns, and residents. This has come about as a result of the conversion of the medically indigent group from ward patients to private patients of doctors of their own choosing. It has led many university and university-affiliated hospitals to form closed-panel groups of their own, which have gone into medical practice in competition with the neighborhood doctor, to provide "clinical teaching material." In a recent instance, a medical school in New York City announced that such a group had contracted with a large union to supply full medical care to the union membership on a paid-up basis.

Faced with this type of competition, the neighborhood physician is threatened with the loss of a significant number of his patients.

This has become a point of bitter contention between the educators and the practicing physicians, but it is not the only one. The general practitioners resent the fact that they are more and more excluded from a hospital by the program of accreditation which, again, is controlled by the educators. The drying up of the supply of American-trained medical graduates to fill internships and residencies in nonuniversity-affiliated hospitals and the loss of foreign medical graduates imposed by the Educational Council for Foreign Medical Graduates program are other sore points which sharply divide the educator from the independent practitioner, since they affect practice in the community hospital where the latter treats his patients.

A further force, tending to alter the traditional methods of practice and to widen the gap between the educator and the practitioner, arises from the numerous rapid advances on all fronts of the science of medicine. The increasing complexity of certain diagnostic and therapeutic methods requires highly specialized apparatus and institutions for their application. Medically useful isotopes, open-heart surgery, high voltage irradiation, prosthetic vascular replacement, and kidney transplant are typical of the varied and only recently available advances in this category. The existence of these and like modalities has been used as the basis of the theorem that the teaching institution should be the hub, indeed the fountainhead, of all medical knowledge and that the researcher and the teacher should set the standards for and man the controls of medical practice. This concept is used as another justification for the practice of medicine by hospitals affiliated with medical schools.

It has been estimated that about 80 per cent of medical needs can be met by the individual solo general practitioner and about 10 per cent additionally by a single consultant. Does it not seem uneconomic then to gear the entire system to the needs of a small minority? But beyond the economics of the situation is the simple human and time-tried idea that medicine must constitute a personal service and that it is not utilized to its full extent unless it combines art with science. The imposing laboratory, the betatron, and the heart-lung machine play but a small part in the totality of medical care. I do not depreciate modern scientific medicine, but I maintain that it must be kept in proper perspective. The scintillation counter cannot make a night call, and the ivory tower is quite remote from the family problems and home factors which in large measure determine the course and outcome of many an individual ailment.

Government's larger role in health care

We glibly talk about having fought off socialized medicine thus far. But such legislation as the King-Anderson Bill not only would socialize medical care for social security recipients, but also would be, it is maintained, a foot in the door. It would set the pattern for more and more coverage by the Federal government of increasingly larger segments of the population.

What is not generally recognized, however, is that, in large measure, we already have socialized medicine. Starting with veterans with service-connected disabilities, medical service by the government has extended to encompass nonservice-connected disabilities, service men and their families and dependents, government civil service employes, Federal compensation cases, and many others on a national level; comparable groups on state and municipal levels; and Old Age Assistance recipients, persons eligible under disability legislation, and others. While I have no accurate figures, I would guess roughly that the total of all of these approaches affects about one quarter of the entire population.

Lest the objection be raised that some of this coverage is on an insurance basis with nominal free choice of physician, let me cite but one example of how government can subvert these mechanisms and assume de facto control. We all know of the rather recently ballyhooed "Hometown Veterans' Medical Care Plan" under which it was stated that veterans eligible for care by the Veterans' Administration could elect to be treated by physicians of their own choice. This glowing promise was accepted by the medical profession, which agreed to cooperate. Once the system was installed, all of the evils of government control became evident. The multitudinous reports, the need for authorizations for various types of treatment, the irritating encounters with petty officialdom, the arbitrary interpretations of fee schedules, and many others. But the crowning touch was the issuance of a directive, after a short time, that the treatment of an eligible veteran by his own doctor would not be authorized where veterans' facilities were "feasibly available." In other words, all veterans within arbitrarily fixed radii of veterans' hospitals or clinics were excluded, by fiat, from participation under the originally agreed-on terms. Such instances—and they can be multiplied manifold—indicate the degree of control which may be exerted in instances where government pays the bill for medical care.

Malpractice and private practice

Also of importance is the malpractice problem as an increasingly important instrumentality influencing private practice. When I started practice, my annual malpractice insurance premium was $65. Malpractice suits were relatively rare and did not affect day-to-day practice, my most recent premium was over $500, approaching 10 times what I originally paid thirty years ago. The responsibility for this change comes from many quarters. Medicine is more complex, and there are more chances for error. Patients are better informed as to what results to expect and demand redress for anything short of their expectations, regardless of whether or not the doctor is at fault. Plaintiffs' lawyers have found a lucrative field for exploitation and are unquestionably responsible for the incidence of a sizable number of suits. Courts are social-minded and are evolving new philosophies and broadening interpretations of old ones. Inflation has affected verdicts, too, and damages awarded by the courts have skyrocketed.

"Liability without fault" is a new idea: that a bad result should be compensated for despite the lack of culpability on the doctor's part. Res ipsa loquitur is being extended to include more and more cases in which the physician is obliged to prove that he did not do wrong, rather than the plaintiff proving that he did, a direct reversal of the fundamental legal principle that a man is presumed innocent until proved guilty.

A prime example of the dilemma in which we find ourselves is illustrated by the so-called "cancerophobia decision" on the one hand, in which liability ensued because the doctor explained a possible sequel of injury to a patient, and, on the other hand, the need for "informed consent" in which liability results from not detailing every possible eventuality of a given treatment. Between the Scylla of cancerophobia and the Charybdis of informed consent, we are liable to lose more than just a few tail feathers, which was the sole damage to the pigeon of the Argonauts.

Such facts as these cannot but color one's practice. We may refrain willfully from certain indicated treatments because they entail legal hazards or undertake unnecessary measures which add to the patient's costs without benefiting him to protect ourselves from malpractice claims.

It would be comforting to assume smugly that the malpractice problem is purely a social phenomenon which cannot be laid at our own door. But a study of the instances in which suits are predicated on carelessness, indifference, patient-exploitation, or unjustified criticism by doctors of their colleagues does not allow the profession to escape shouldering its share of the blame.

Need for broader and better health insurance

Space limitations do not permit an exploration of the full details of all of the foregoing nor a discussion of innumerable other potential sources of alteration of private practice, but I believe that some conclusions may be drawn from the thoughts herein expressed. With respect to medical expense insurance, it seems obvious that we must broaden its coverage, fill in its inadequacies, root out its abuses, and make it work truly to provide medical care for the entire population. The plan that selects only large groups, which are better insurance risks, does not accomplish this, since it leaves uncovered the small groups and the individual, who are poorer risks. We must devise a system of community rating if voluntary insurance is to serve the function for which it was created. If voluntary prepaid medical care insurance fails, private practice must inevitably fail with it. Diagnostic coverage keeping pace with modern scientific advance is another feature that must be incorporated, and this may entail a sacrifice of the fee-for-service principle, since under the present system diagnostic costs are uninsurable except in a very insufficient degree.

The malpractice problem must be met head-on. We must fearlessly expose and punish wrongdoers within our ranks. We must convince the public that there is no "conspiracy of silence" and that we will testify willingly to improper practice in the courts. But by the same token, the unscrupulous lawyer and the unjustified lawsuit must be eliminated also. Relief from unduly extended statutes of limitations, from unfair philosophies such as those represented by distortion of the doctrine of res ipsa loquitur, and from liability without fault must be obtained through legislation.

We must resolve our intraprofessional differences. The educator and the practitioner, both ostensibly striving for the same goal, must delineate their proper fields of activity to their mutual satisfaction to the end that they shall complement rather than oppose each other.

Adequate guardianship of the health of the public must be the true aim of the entire profession. We must assume in earnest the role of noble and selfless public servants in which we have been traditionally cast. The common thread which binds all of these thoughts is that the individual doctor's treatment of the individual patient is the key to the survival of private practice. Medicine must remain a personal service, rendered wisely, informedly, and warmly by an interested doctor to a patient whom he recognizes as human and sensitive. When this has come about, the future of private practice will be assured.

Number eighteen in a series of special articles on Medical Care Insurance

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Abstraction in Art and Psychiatry

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PEOPLE DIFFER IN their needs and capacities to contemplate the world in which we live. Accordingly they may constrict or broaden their attitudes toward it. For example, a medical scientist may be especially interested in studying, by means of laboratory experiments, the chemical characteristics of ascorbic acid. Another scientist may be interested in the relationship of ascorbic acid to disease of the gums or, more broadly, to other parts of the body. Still others may be preoccupied with social and economic factors which influence ascorbic acid deficiency in the diet. The gamut thus is run from basic science to varying degrees of a broader outlook, or applied science.

To focus attention on a limited field obviously may be constructive. In fact, it is essential for the solution of many problems. In this fashion, a mathematical theoretician, working with formulas on paper, may solve problems with far-reaching effects on our lives. However, a preoccupation with basic principles may be accompanied by neglect of how such fundamentals relate to the broader aspects of living. Many pioneers in atomic science have been surprised and disturbed by what their theoretical ruminations have wrought.

Similarly in many abstract forms of art, withdrawal of intellectual activity into a more confined area and away from the world we usually call reality, may be observed. The abstractionists in painting, and particularly the nonfigurative abstractionists who may depict only basic structures and geometric forms, are divorcing their intellectual interests from part of the world they are attempting to interpret. As do the theoretical scientists, they are concentrating on a study of fundamental structures or forms or colors, with diminished attention to the world of overt reality which overlies these basic factors. We therefore see the rectangles of a more recent Mondrian canvas or the color patterns of Kandinsky.

The abstractionist artist, like the theoretician, is free to choose his field of endeavor and to limit his interest and his specialization. His choice, however, should be recognized for what it is—a way of narrowing the focus, of separating intellectual activity from contemplation of the more immediate world around us. It is like concentrating on the structural girders of a building and excluding consideration of the roof, the walls, the paint, and the furnishings which constitute the more immediate world with which we come in contact. It is like ignoring the beauty of the heavens, the emotional reactions to the stars and planets, or the immensity of the universe and man's place in it and concentrating only on the mathematical formulas and physical principles by which the heavenly bodies move.

In art, it should not become a matter of which is preferable, realism or abstraction. One should realize that both types of expression are needed to depict and interpret the world in which we live. From one point of view, the more comprehensive production encompasses both forms and excludes neither.

Similar variations in approach may be seen in the specialty of psychiatry. Within the subspecialty of psychoanalysis, a group exists which believes psychiatry is unrelated to the practice of medicine. It deplores the concept of illness in psychologic functioning as well as the "medical model" which most psychiatrists still follow.

The abstractionist in psychiatry

Psychoanalytic theorists are interested in the workings of the mind. They postulate various concepts of mental mechanisms dealing with basic patterns of behavior learned in the impressionable early years. These patterns are the building blocks on which our later reactions depend. Aberrations, however, occur in these patterns which result in what is commonly called mental illness. Many varying factors can trigger these aberrations. They may be hereditary, toxic, biochemical, traumatic, neoplastic, infectious, or environmental.

The theoretician, however, has narrowed his field of interest and continues to focus on the building blocks, the basic and admittedly fundamental, mental mechanisms. In varying degrees he turns away from the innumerable other possible factors in the real (medical) world which may influence them. He is the abstractionist in psychiatry, comparable to the abstractionist in art. He becomes preoccupied with a limited group of patterns and their neurotic variations. In his extreme form, like the nonfigurative abstractionist artist, he will ignore all but the early parental influences on the developing child.

As is his privilege, he withdraws from the care of the sick and enjoys the intellectual exercise of pondering the mental dynamisms of those who are seeking an "educational experience." He therefore must withdraw from the diagnosis of mental illness, for his narrower focus and consequent inexperience prevent recognition of medical causes. He must also abstain from the treatment of most patients with schizophrenia, manic-depressive psychosis, and the organic mental illnesses. This will include those patients with cerebral effects and mental aberrations associated with diabetes, or pernicious anemia, or multiple sclerosis, or pellagra, or porphyria, or numerous other medical conditions, often amenable to treatment without any attention to the details of the psychologic status.

This psychiatric theoretician then, as does the artistic abstractionist, withdraws his intellectual interest from the real world of mental illness around him. Unlike the artist, however, who perceives the relationship of his nonfigurative forms to other more realistic productions, he protests that there is no relationship between (his definition of) psychiatry and that real world (of illness).

Comment

The performance of the abstractionist, both in art and in psychiatry, may be associated with varying degrees of emotional expression. Purist geometric figures appear devoid of overt emotion, but the chaotic spatterings of a Jackson Pollack reveal a great intensity of abstract expression. The orthodox analyst, in analogous fashion, at times will present a blank wall to his patient, sitting out of his view, being vocally unresponsive and making every effort to eliminate overt emotional response. Other, less conforming analysts, however, permit themselves varying degrees of overt emotional reaction to their patients' difficulties.

There are many accomplished artists who have narrowed their field of endeavor to the fundamentals of art expression in abstraction, although they are well endowed and have displayed their ability to express themselves more comprehensively. This is undoubtedly also true in psychiatry. The theoretician in psychology, preoccupied as he might choose to be in the fundamentals of psychologic functioning, has a more comprehensive grasp of his subject when he does not isolate his abstract formulations from the realities of mental disturbance around him.

On the other hand, there are those abstractionist artists who take refuge in this form because of technical or other inability to effect more realistic productions. Similarly some psychiatrists take refuge in their psychologic preoccupations because of their lack of knowledge of the medical world of reality. Specialization of any kind is often an escape from areas in which we are not proficient into areas where we feel more comfortable. Specialization in mental mechanisms may fit the same pattern.

Abstraction in its extreme, therefore, as expressed in art or psychiatry, is a withdrawal of focus from the outside world of reality. It is a form of basic science divorced from applied science, divorced from its applications in the real world. Complete withdrawal into abstract, although basic, principles exclusively rejects the largest part of the world with which we are in contact. Somewhere in psychiatry there is a happy, comprehensive medium.

Summary

The relationship of abstraction to more comprehensive forms of expression in painting is compared with the relationship of psychoanalytic purism to more comprehensive attitudes in psychiatry.

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The doctors of the U.S.A. are being asked to send their medical journals—after they have read them—to colleagues overseas (Asia, Latin America, and Africa) who wish to have access to current medical literature but, either because of currency regulations or actual cost involved, cannot themselves subscribe to medical periodicals. We can supply you with the name, address, and medical specialty of doctors in these areas who would be happy to receive these much wanted journals, particularly specialty journals.

This is a direct "Doctor-to-Doctor" program which is being promoted by the United States Committee of The World Medical Association to help alleviate the lack of current medical publications and to further international good will. Your cooperation in this program will be greatly appreciated and your contact with these colleagues in other countries, we can assure you, will prove very gratifying. If you wish to participate in this program, send your name, address, and titles of journals you will contribute to United States Committee, The World Medical Association, 10 Columbus Circle, New York 19, New York.

BILLSBORD

Secondary professional characteristics

The popularization and ready acceptance of the status symbol focuses attention on individual groups and their idiosyncrasies. One is exposed to dissertations of group behavior and its relationship to the "pecking order" in such diverse circumstances as a service club meeting, an academic forum, or a corner bar. Apparently anyone, after acquisition of a smattering of jargon, becomes expert and so embarks, without fear or hesitation, on an analytical interpretation of the home, dress, hobby, behavior, family, or work habits of some ethnic, occupational, religious, or environment-centered group with all the enthusiasm and judgment one finds in a teenage scavenger hunt.

All this would be inconsequential nonsense if there were not indigenous to some groups a common innate pattern of group development basically different from the acquired behavior patterns of status significance. Recognition of criteria providing accurate identification of the stages of this developmental process enables an observer to gauge the progress or lack of progress of an individual in group maturation. Herein lies the value of a workable classification of the steps of such development in any group entity. One for medicine that has been found logical, definitive, and clinically adaptable is herewith presented, based on a symbolization factor—one that is universal, utilitarian, and identifiable. This is the stethoscope a familiar and constant companion of every physician from the early days of his medical training, and it lends itself to psychologic identification as a part and extension of the body itself because it actually enters a body cavity when in use.

Classification

STAGE I. Overt exhibitionism (group infancy).

STAGE II. Pseudorepression (group adolescence).

STAGE III. Adult exhibitionism (group adulthood).

STAGE IV. Adult repression (group maturity).

Stage I. Stage I is found in the early period of medical school at about the time one is introduced to the art of physical diagnosis and acquires a stethoscope. It represents overt, awkward, and blatant expression of one's exhibitionistic impulse. The stethoscope is carried in the jacket side pocket, carefully arranged to hang half out and be readily visible to the fellow passenger on bus or subway or to any casual passerby. The only exception to this common pattern is in northern areas during the winter months when the stethoscope is similarly carried in an overcoat pocket.

Stage II. Stage II also occurs during student days although of variable onset. There is revulsion to the ostentation of the earlier period. As in most conflicts of adolescence, however, one does not really want to abandon the satisfactions attached to childish behavior but since it is no longer possible to seek them in a childish manner they must be concealed from the world and even from oneself by a veneer of adult camouflage. The adopted adult approach is superficial and imitative, however. At this stage the stethoscope is moved from an exposed, always contrived visibility to a clandestine recess commonly described as a hip pocket. Curious it is that wherever one observes this, it is folded and inserted in the pocket in a precise uniform manner as though a common manual of instruction had been issued. Now one makes no open, attention-calling display but is never without the instrument and will, on the slightest provocation, explain with a slight deprecatory laugh that one has a feeling of nakedness without it. So there it sits, and if perchance one is invited to join in the search for buried treasure, off comes the coat revealing the stethoscope coyly peeking out with both ears cocked ready to catch any passing murmur or errant rale. Occasionally one may also catch a fleeting glimpse of it on a dance floor as the owner gyrates gracefully around with coattails flying thus providing the orchestra leader with a graphic reminder of his chronic emphysema.

Stage III. Stage III comes with hospital training. Now the weak adult-imitative attempt at denial of the underlying desire is abandoned and the feeling of exhibitionism is allowed full expression but in a more sophisticated and mature manner than in Stage I. The stethoscope is draped casually about the neck with the bell (medicine), or diaphragm (surgery), or both (gynecology and obstetrics) hanging down the shirt front. It is worn with a touch of negligence and considerable nonchalance. When the time comes to use it, it must be rediscovered with an obvious air of surprise that in turn must be quickly suppressed. In the unlikely event one is caught without it in pendant position, one must reach to the neck and evince chagrin at not finding it thereby maintaining the illusion of its careless, intimate position of visibility by calling attention to its absence.

Stage IV. Stage IV, a period of maturity, sees the exhibitionistic tendency repressed in an adult manner. This stage usually takes place about the time of entry into one's chosen medical field. The stethoscope is removed from any direct bodily contact unless in use. It is relegated to a bag to become one of many accessories so carried and is available for use when the need arises.

FIXATION IN STAGES. This system of classification provides an accurate method of determining the level of development of any individual as well as of establishing the delay or fixation at any one point of this professional maturation process. As one might expect we found no fixation of professionals at Stage I, although it was observed in some ancillary groups. At Stage II there is a small but consistent percentage identified. The adult imitative character of this phase permits a superficial adjustment that appears satisfactory despite the fact their necks have been graced by nothing more glamorous than soap, and they never toted a bag. There is no evidence of an emotional upheaval, but one can't help but shudder at the thought that some fashion designer or tailor might eliminate the trouser hip pocket as they did the vest. Fixation at Stage III is frequent and alarming since it is associated with apprehension at the prospect of leaving the hospital's protective environment.

As to Stage IV one must admit some disquieting observations of late that suggest it might not be as stable and permanent as was first thought.

The first of these observations concerns the "film badge" of the radiologist. Why should this useful but prosaic and unattractive gadget be so conspicuously displayed? Function would not suffer if carried in concealment. Why on the shirt or belt front? Certainly not for convenience of removal for it is seldom removed. One sees these badges at medical meetings both local and remote, at dinner, and even on the golf links. Does this mean regression? Certainly it falls into the sphere of overt exhibitionism of the sophomore period. But it also could be an adult deviation precipitated by the double frustration of deprivation of the use of the "adult symbol" in his own practice and at the same time the fact that his fellow physicians use his services to provide information formerly provided by the use of the adult symbol. If this is so it is not regression but a graphic display of a protest symbol to emphasize that it no longer is universal.

The second instance carries no implication of regression but would appear a definite adult deviation based on a subgroup desire for exclusive identification. This observation pertains to internists who reached the stage of maturity seemingly without difficulty. Soon, however, one noted the trend of this group to the use of smaller and smaller bags. When the trend started bags were large and unwieldy and all groups turned gratefully to the smaller bag. This only resulted in the use by the internist of an even smaller bag. Thus, over a period of time, a competitive pattern of smaller and smaller bags has developed until today when the bag carried is so small as to approach the absurd. For the life of me I can't conceive what could be contained in this size bag that would be useful in an examination of a patient unless of course the carrier was a one-armed gynecologist!

WRC

Oral manifestations of leukemia

Of 17 patients with various types of leukemia, 9 showed oral manifestations of the disease, according to a report by James F. Smith, D.D.S., Ph.D., in the February, 1962, issue of the *Journal of the Tennessee State Medical Association.* Seven of these 9 were children with acute forms, and 2 were adults, 1 chronic and 1 acute. The manifestations included bleeding and bogginess of the gingivae, ulceration, loosening of the teeth, and hyperplasia. When they occur, oral changes in all types of leukemia begin early in the course of the disease and may be the first indication. In the chronic forms, oral changes are likely to be nonspecific in character, whereas in the acute types local gingival hemorrhage may cause the patient to seek dental consultation. In such patients, unnecessary dental procedures may exacerbate the acute symptoms. Early diagnosis, therefore, is important.

Necrology

Amedeo Aristides de Poto, M.D., of Malverne, died on June 23 at Jamaica Hospital at the age of sixty-five. Dr. de Poto graduated in 1921 from New York University and Bellevue Hospital Medical School. He was former chief of staff at Jamaica Hospital and unofficial team physician for John Adams High School, Ozone Park, Hofstra College, and the Greenwald Jewelers team in the Queens Football Alliance. Dr. de Poto was a Fellow of the American College of Surgeons.

Lilian K. P. Farrar, M.D., of Lake Placid Club, retired, died on June 22 at the age of ninety. Dr. Farrar graduated in 1900 from Cornell University Medical College. From 1918 to 1935 she served as assistant professor of gynecology and from 1916 to 1920 as chief of clinics at Cornell. The first woman governor of the American College of Surgeons, she successfully campaigned for women's internships at Bellevue Hospital and at New York Women's Hospital where she had also served as a junior attending surgeon. Dr. Farrar was a Diplomate of the American College of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, and a member of the American Gynecological Society, the New York Academy of Medicine, the New York Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Nathan Hirsch, M.D., of Forest Hills, retired, died on July 17 at the Menorah Home and Hospital, Brooklyn, at the age of seventy-two. Dr. Hirsch graduated in 1914 from Long Island College Hospital Medical School.

William Hadden Irish, M.D., of Bethel, Connecticut, formerly of New York City, died on May 9 at the age of seventy-one. Dr. Irish graduated in 1916 from New York University and Bellevue Hospital Medical School. He was an attending orthopedic surgeon at University Hospital, a consulting orthopedic surgeon at Northern Westchester and Dobbs Ferry Hospitals, and an honorary orthopedic surgeon at Phelps Memorial Hospital Association, North Tarrytown-on-the-Hudson. Dr. Irish was a Fellow of the American College of Surgeons and a member of the American Academy of Orthopedic Surgery, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York and the American Medical Association.

Vera H. Koshkin, M.D., of New York City, died on July 19 while vacationing in Hurleyville, at the age of seventy-eight. Dr. Koshkin received her medical degree from the University of Geneva in 1907. For twenty-three years she had been a staff physician at the House of Detention for Women and was to have retired on August 1. Dr. Koshkin was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Homer Hollett Oaksford, M.D., of Gloversville, died on June 28 at the Nathan Littauer Hospital at the age of seventy-three. Dr. Oaksford graduated in 1912 from Albany Medical College. He was an attending cardiologist at the Nathan Littauer Hospital. For a number of years he had served as Fulton County coroner, retiring in 1950, and had served also as a physician in the Gloversville School System and as an examining surgeon for the board of pensions of Fulton County. Dr. Oaksford was a member of the Fulton County Medical Society (and a past-president), the Medical Society of the State of New York, and the American Medical Association.

Max Salzberg, M.D., of the Bronx, died on July 17 at his home at the age of sixty-four. Dr. Salzberg received his medical degree from the University of Prague in 1929. He was a senior clinical assistant attending physician in gastroenterology at the Bronx Hospital Outpatient Department. Dr. Salzberg was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Woodard Shaw, M.D., of Gloversville, died on June 5 at the Nathan Littauer Hospital at the age of seventy-one. Dr. Shaw graduated in 1913 from Albany Medical College. He was an honorary staff physician at the Nathan Littauer Hospital and former superintendent of the Fulton County Laboratory and Summit View Sanitorium. Dr. Shaw was a member of the Fulton County Medical Society and the Medical Society of the State of New York.

Harry A. Steckel, M.D., of Syracuse, died on July 14 at his home at the age of seventy-five. Dr. Steckel graduated in 1910 from the University of Pennsylvania School of Medicine. He was a consulting psychiatrist at Syracuse Memorial, Marcy State, Syracuse Psychiatric (where he had also served as the first director), and Willard State Hospitals and senior consulting psychiatrist at University Hospital. A professor at the Syracuse University College of Medicine, he headed a National Research Council committee on psychiatry from 1941 to 1943, in 1922 conducted a survey of prison populations in New York State for the National Committee for Mental Hygiene, was director of clinical psychiatry at Binghamton State Hospital until 1929 when he became superintendent of the State School for Mental Defectives in Newark, New York. Dr. Steckel was a Diplomate of the American Board of Psychiatry and Neurology (Psychiatry), a Fellow of the American College of Physicians, a Life Fellow of the American Psychiatric Association, and a member of the Academy-International of Medicine, the Syracuse Academy of Medicine, the Onondaga County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Winfield E. Stumpf, M.D., of Forest Hills and Brooklyn, died on March 2 at Brooklyn Hospital at the age of fifty-seven. Dr. Stumpf graduated in 1931 from Columbia University College of Physicians and Surgeons. He was an associate attending obstetrician and gynecologist at Brooklyn Hospital. Dr. Stumpf was a Fellow of the American College of Obstetrics and Gynecology, and a member of the New York Academy of Medicine, the Brooklyn Gynecological Society, the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

G. Edwin Thibault, M.D., of Chittenango, died on June 20 at his home at the age of forty-nine. Dr. Thibault graduated in 1937 from Syracuse University School of Medicine. He was an attending physician in general practice at Crouse-Irving Hospital and Town of Sullivan health officer, school physician, and former president of the Chittenango Board of Education. Dr. Thibault was a member of the American Academy of General Practice, the Madison County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harvey Judson Vary, M.D., of Rochester, died on June 29 at his home at the age of eighty-four. Dr. Vary graduated in 1903 from Columbia University College of Physicians and Surgeons. For many years he had served as a physician of the Presbyterian Home, on the board of managers of Iola Sanatorium, and as a member of its medical staff for five years. Dr. Vary was a member of the Rochester Academy of Medicine, the Monroe County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Windwer, M.D., of Brooklyn, died on May 10 in Brooklyn at the age of seventy. Dr. Windwer graduated in 1920 from Fordham University School of Medicine. He was director of medicine at Brooklyn Women's Hospital, an associate attending gastroenterologist at Jewish Hospital of Brooklyn, and a consulting gastroenterologist at Jewish Chronic Disease Hospital. Dr. Windwer was a Fellow of the American College of Gastroenterology, a Fellow of the American College of Physicians, and a member of the Brooklyn Society of Internal Medicine, the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Wolins, M.D., of Riverhead, died on July 15 at his home at the age of fifty-two. Dr. Wolins graduated in 1931 from Long Island College Medical School. He was chief of the radio-isotope service at Brooklyn Veterans Administration Hospital, a former attending physician at the Medical Research Center, Brookhaven National Laboratories, Upton, and at Central Suffolk Hospital Association, and a consulting physician at the John T. Mather Memorial Hospital in Port Jefferson. Dr. Wolins was a Diplomate of the American Board of Internal Medicine and a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Abstracts

Skudder, P. A., Inglis, A. E., and McCarroll, J. R.: Tetanus in New York City, NEW YORK STATE J. MED. **62:** 2793 (Sept. 1) 1962.

Forty-one cases of tetanus were reported in New York City between 1957 and 1960, of which 32 were in narcotic addicts. The overall mortality was 90 per cent: 30 of the addicts died as did 4 of the 9 patients with supposedly trivial wounds. Because of the serious disadvantages in the administration of tetanus antitoxin, physicians are urged to immunize patients with tetanus toxoid whenever feasible and to give a written record of immunization to the patient. Prophylaxis for tetanus depends on whether the wound is tetanus prone or nonprone and the immunization status of the patient. It always includes, however, good wound care and a booster dose of tetanus toxoid or active immunization, if this has not been accomplished previously.

Fontana, V. J., Sedlis, E., Prose, P. H., Messina, V. P., and Holt, L. E., Jr.: Complement titer, C-reactive protein, and electrophoretic serum protein patterns in eczematous children, NEW YORK STATE J. MED. **62:** 2801 (Sept. 1) 1962.

Forty-two children in various stages of atopic eczema, ranging in age from three months to six years, were studied. The complement titers in all children were within normal limits. Seventeen patients had normal plasma protein patterns; in 6 (who showed clinical signs of infection) the gamma globulin fractions were increased and in 2 (age three and five months) decreased. The C-reactive protein result was positive in 15 (including the 6 in whom the gamma globulin was increased) and negative in 14. The latex fixation test gave negative results in the 13 children who were tested for the presence of an abnormal protein.

Griboff, S. I.: Hirsutism in the female; hormonal reclassification, NEW YORK STATE J. MED. **62:** 2805 (Sept. 1) 1962.

A proper classification of hirsutism in the female may suggest more effective methods of diagnosis and therapy. Constitutional hirsutism includes those patients with no proved endocrine abnormality, normal 17-ketosteroid excretion, and chromatogram, and no evidence of virilism or adrenal or ovarian pathologic conditions. Other classes of hirsutism may be associated with normal ovaries and adrenals, polycystic ovaries, diffuse luteinization ovaries, adrenal hyperplasia, or a tumor of the ovaries or adrenals. They are due to excessive production in the adrenal and/or ovary of the hormone involved: testosterone, adrostenedione, dehydroepiandrosterone, 11β-hydroxyandrostenedione or adrenosterone, and a combination of two or more groups. The hormonal therapy of hirsutism has been largely disappointing.

Pollack, B.: Changing concepts in psychiatric treatment, NEW YORK STATE J. MED. **62:** 2810 (Sept. 1) 1962.

Psychiatric treatment has been greatly influenced in recent years by the introduction of drugs. In 1955 there were 3,752 patients in the Rochester State Hospital with 523 others on convalescent care and 89 on family care. In 1960 the resident population had fallen to 3,239, whereas the number of patients on convalescent care had increased to 1,392 and the number on family care had tripled. The psychopharmacologic drugs now in use may be classified as follows: (1) the original drugs introduced into this country in 1954, consisting chiefly of chlorpromazine hydrochloride, promazine hydrochloride, and reserpine; (2) newer phenothiazine compounds based on molecular manipulation; and (3) a group of sedative and tranquilizing drugs including meprobamate and hydroxyzine hydrochloride. The monoamine oxidase-inhibitors are not recommended because of interference in liver function, but imipramine hydrochloride, another antidepressant, has proved efficacious. Drug therapy should be instituted on admission to the hospital and continued after discharge.

Medical News

Caleb Fiske Prize Essay

The Trustees of the Caleb Fiske Prize of the Rhode Island Medical Society have announced two subjects for this year's essay contest—"Etiologic Factors in the Development of Congenital Anomalies" and "Progress in the Relief of Hearing Defects."

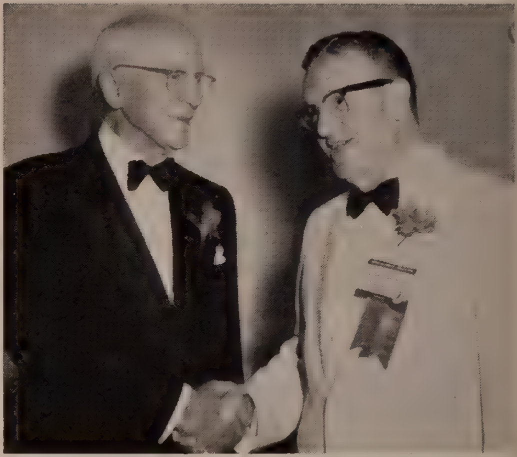
The contest is open to any doctor of medicine in the United States. Entries must be typewritten, double-spaced, and should not exceed 10,000 words. Closing date for the contest is December 11. Entries should be sent to: Secretary, Fiske Fund, Rhode Island Medical Society, 106 Francis Street, Providence 3, Rhode Island.

New York physician receives A.M.A. award

Russell L. Cecil, M.D., New York City, was recently awarded the American Medical Association's Distinguished Service Award for 1962.

Widely known among physicians as senior editor of the *Textbook of Medicine*, Dr. Cecil has, in recent years, turned his interest to research in the field of chronic disabling arthritis.

The eighty-year-old physician has served as president of the American College of Physicians and the New York College of Physicians and holds membership in more than a dozen medical organizations. Currently, he is president of the New York-Metropolitan Chapter of the American Medical Writers Association.



Russell L. Cecil, M.D., New York City, (left) is congratulated by Joseph A. Lane, M.D., Rochester, president of the Medical Society of the State of New York, on receiving the American Medical Association's Distinguished Service Award for 1962.

Grants for respiratory disease research

The American Thoracic Society, the medical section of the National Tuberculosis Association, offers grants for research in respiratory diseases, including tuberculosis. Grants are awarded for medical and social research in these fields.

Deadline for applications for the grant year beginning July 1, 1963 is December 15, 1962. Full information and forms can be obtained from: Division of Research and Statistics, American Thoracic Society, 1790 Broadway, New York 19, New York.

Pollen sampling network

The State of New York Department of Health has announced the participation this year of 29 communities in the Department's daily pollen sampling network. Daily reports will be issued by the network until the beginning of October.

This is the fifth year that the network has been in operation during the pollen season. The public interest shown has resulted in yearly expansion of the program. In 1958, at the start of the network, only 6 stations were set up. Last year 24 stations participated.

The sampling stations are being operated by volunteers with supplies furnished by the State Health Department. Stations have been set up in Albany, Barker, Batavia, Binghamton, Buffalo, Canton, Corning, Cortland, Fleischmanns, Geneva, Glens Falls, Gloversville, Hornell, Hudson, Islip, Massena, Mineola, Newburgh, Niagara Falls, Olean, Rotterdam, Schenectady, Shrub Oak, Troy, Tupper Lake, Utica, Warsaw, Waterloo, and White Plains.

Association for the Advancement of Psychoanalysis elects officers

The Association for the Advancement of Psychoanalysis, Inc., has announced the election of the following officers for 1962–1963:

Jack L. Rubins, M.D., New York City, president; Joseph Zimmerman, M.D., Brooklyn, vice-president; Melvin Boigon, M.D., New York City, secretary; Albert L. Deutsch, M.D., Brooklyn, treasurer; and Frederick A. Weiss, M.D., New York City, councillor.

Study of chronic myelogenous leukemia

The cooperation of physicians is requested in a study of chronic myelogenous leukemia being conducted by the Chemotherapy Service of the National Cancer Institute at the Clinical Center, National Institutes of Health, Bethesda, Maryland.

Referrals of patients with chronic myelogenous leukemia are needed. Particularly needed are those in the twenty- to forty-year age group with high white blood cell counts and platelet counts for studies of newer chemotherapeutic agents and as a source of white cells and platelets for in vitro and in vivo study.

Physicians wishing to refer a patient should write or telephone to: Paul P. Carbone, M.D., Chemotherapy Service, Medicine Branch, National Cancer Institute, Bethesda 14, Maryland, Telephone 496–4251.

Fellowship in radiation medicine

The Department of Radiation Medicine of Queens Hospital Center, Jamaica, Long Island, is offering one-year fellowships in radiation medicine and cobalt teletherapy to begin January 1, 1963, or July 1, 1963.

Training in the diagnostic and therapeutic uses of a wide variety of isotopes, cobalt teletherapy, and chemotherapy will be given. Two full-time physicists and a full-time radiation biologist will provide instruction in physics, radiation biology, and nuclear instrumentation. Research will be encouraged; ample facilities are provided.

The Fellow will also be given the opportunity to participate in the courses given annually by the Department of Radiation Medicine.

For information and application forms write to: Philip J. Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York.

Course on psychiatric problems in medical practice

A 10-session course on psychiatric problems in medical practice will be given by the American Institute for Psychoanalysis at the Karen Horney Clinic Building, 329 East 62nd Street, New York 21, New York. Sessions will be held on Wednesdays at 8:30 P.M. and will begin on October 3.

The course is designed to present the general practitioner with those fundamentals of theory and practice which he requires for the diagnosis, treatment, and referral of the psychiatric problems he meets in his practice. There is no fee for the course.

Applications should be sent to: Harold Kelman, M.D., Dean, American Institute for Psychoanalysis, 329 East 62nd Street, New York 21, New York.

Examinations for American Board of Obstetrics and Gynecology

The next scheduled part 1 (written) examination of the American Board of Obstetrics and Gynecology will be held in various examining centers of the United States, Canada, and on military bases outside the continental United States on Friday, December 14, at 2:00 P.M.

Candidates eligible to take the examination will be notified where to appear for examination on or about November 1. The current bulletin of the Board may be obtained from: Robert L. Faulkner, M.D., Executive Secretary and Treasurer, American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Course in gastroenterology

The annual course in postgraduate gastroenterology of the American College of Gastroenterology will be given at the Morrison Hotel in Chicago, November 1 through 3. The moderators will be Owen H. Wangensteen, M.D., chairman and head of the Department of Surgery of the University of Minnesota School of Medicine, and I. Snapper, M.D., director of medical education, Beth-El Hospital, Brooklyn.

For further information write to: American College of Gastroenterology, 33 West 60th Street, New York 23, New York.

Rehabilitation center at Albert Einstein

The designation of a primary rehabilitation center at the Albert Einstein College of Medicine, Bronx, under the State-wide program for comprehensive rehabilitation centers has been announced by the State of New York Department of Health.

Under terms of an agreement between Yeshiva University and the State Department of Health, the rehabilitation center, located in Jacobi Hospital and adjacent to the University's Albert Einstein College of Medicine, will receive up to $40,000 a year in support of its operations.

The center is the eighth in a State-wide program of centers designed for the evaluation and treatment of disabled persons presenting unusually complicated rehabilitation problems.

Course on surgery of the nasal septum

An introductory course in expanded surgery of the nasal septum and closely related structures will be presented at the Loma Linda University School of Medicine, Los Angeles, October 29 through November 1. The program will be under the cosponsorship of the University's Department of Otolaryngology and the

American Rhinologic Society.

Maurice H. Cottle, M.D., Chicago, will be the guest director. Richard B. Hadley, M.D., Rye, will be among the guest lecturers.

For further information write to: Leland R. House, M.D., Head, Department of Otolaryngology, Loma Linda University School of Medicine, Los Angeles 33, California.

Course in emotional and psychiatric problems

The New York Academy of Medicine will present the fourth in an annual series of courses on "Emotional and Psychiatric Problems in Medical Practice," starting Monday, October 22, and ending on February 8, 1963. The course, which is open to all physicians in specialty and general practice, will consist of basic and advanced sections meeting at weekly intervals for 14 one-and-one-half-hour sessions at the Academy building, 2 East 103rd Street, New York 29, New York.

The objective of the course is to help physicians to comprehend more fully the continuous interaction of psychologic, social, and medical factors encountered in clinical practice. It will be divided into basic sections for the benefit of those who have not participated previously and advanced sections for those who have already taken the basic course. The American Academy of General Practice, cosponsors of the course, will allow twenty-one hours of category 1 credit for its completion.

For information write to: Executive Secretary for Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Glorney-Raisbeck Fellowship

The Glorney-Raisbeck Fellowship in the Medical Sciences for the academic year beginning July 1, 1963, will be awarded by the Committee on Medical Education of The New York Academy of Medicine for one year of research and/or study in any field of medicine or its allied sciences. Under circumstances deemed appropriate by the Committee, the Fellowship is renewable on a year-to-year basis for two additional years.

The Fellowship, which carries a stipend of $6,000, is open only to holders of a doctor of medicine degree who have demonstrated a potential for productivity in research and teaching. In general, preference will be given to physicians from the Greater New York area.

Deadline for receipt of applications is December 1, 1962. Requests for application forms and additional information should be addressed to: Aims C. McGuinness, M.D., Executive Secretary, Committee on Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Pathologists get diplomate certification

The American Board of Pathology has announced that a total of 314 pathologists passed the semi-annual examinations held this spring for certification as diplomates in pathology.

This brings to approximately 4,000 the number of physicians certified in one or more of the seven classifications of pathology since the founding of the Board in 1936. Although certifications are increasing steadily many more pathologists are needed to keep pace with the demands of laboratory medicine in health care. It is estimated that by 1970 the number must be increased to 10,000 to fill the requirement of one pathologist for every 3,500 hospital admissions per year. This figure does not take into account the 1,000 or more pathologists needed solely for teaching and research.

Physicians to advise City on malpractice claims

An advisory panel of four physicians has been formed to aid the City of New York in the settlement of malpractice claims in municipal hospitals. The four physicians will serve without pay. They are: William L. Wheeler, Jr., M.D., president-elect of the Medical Society of the State of New York; Milton Helpern, M.D., president of the County of New York Medical Society; Horace Ayers, M.D., president of the New York Medical Jurisprudence Society; and Philip D. Wilson, Jr., M.D., associate professor of clinical surgery, Cornell University Medical College.

Courses at N.Y.U. Post-Graduate Medical School

The New York University Post-Graduate Medical School offers the following courses for the fall session:

Surgery of the Cornea—a full-time, five-day course, September 10 through 14, under the direction of Ramon Castroviejo, M.D.

Gynecologic Endocrinology—a full-time, five-day course, October 1 through 5, under the direction of Herbert S. Kupperman, M.D.

For application and further information write to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

Orientation course in psychoanalysis

The American Institute for Psychoanalysis announces a 5-session orientation course in the theory and practice of psychoanalysis. Psychiatric interns and residents of hospitals approved by the American Medical Association are eligible to apply for the course which is open to them without fee.

The course will be given by members of the faculty of the Institute at the Karen Horney Clinic Building, 329 East 62nd Street, New York 21, New York. Two series of five lectures will be given on Tuesdays at 8:30 P.M. beginning on October 2, 1962, and March 2, 1963.

For information contact: Harold Kelman, M.D., Dean, American Institute for Psychoanalysis, 329 East 62nd Street, New York 21, New York.

Postgraduate course in rehabilitation medicine

The State University of New York Downstate Medical Center will hold a fall course in rehabilitation medicine. The course has been designed for the general practitioner and specialists of related disciplines and will consist of a series of informal discussions with demonstrations of patients of the Medical Center's Department of Rehabilitation Medicine. The practical aspects will be stressed, confining the theoretical discussion to a minimum.

Members of the Academy of General Practice will receive credit for attendance. The sessions will be held on Wednesdays at 3:30 P.M., October 3, 10, 17, 24, and 31, and November 7, 14, and 21. Registration closes on September 28.

For application and information write to: Office of Continuing Medical Education, State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

Specialists named in obstetrics and gynecology

The following physicians were recently examined and certified in the specialty of obstetrics and gynecology by the American Board of Obstetrics and Gynecology:

Albany: Alexander G. Gabriels, Jr., M.D.; *Bronx:* Robert C. Dyson, M.D., and Saul Zelnick, M.D.; *Brooklyn:* Daniel H. Clark, M.D., Anthony F. Giffone, Jr., M.D., Dolores F. Paganelli, M.D., Abraham Prostkoff, M.D., Sol H. Rogatnick, M.D., and Robert J. Tufano, M.D.; *Buffalo:* Marvin J. Pleskow, M.D., Milton G. Potter, Jr., M.D., Robert J. Powalski, M.D., and Oliver J. Steiner, M.D.; *Douglas Manor:* Alfred Lapin, M.D.; *Elmira:* Donald L. Brooks, Jr., M.D.; *Flushing:* Mabelle A. Cremer, M.D., Alfred C. Levin, M.D., and Joseph A. Pennisi, M.D.; *Glen Cove:* James N. Nicklas, M.D.; *Glendale:* Stephen S. Sapega, M.D.; *Holliswood:* James H. Nelson, Jr., M.D.; *Jamaica:* John N. Rizzi, M.D.; and *Kingston:* William C. Feldman, M.D.

Also—*Lackawanna:* Francis A. Fote, M.D.; *Lancaster:* William H. Merrilees, M.D.; *Larchmont:* Robert N. Melnick, M.D.; *Lockport:* Joseph J. Daly, M.D.; *Mount Kisco:* Frank P. Berg, M.D.; *New Hyde Park:* Marvin S. Hans, M.D.; *New Rochelle:* Emil E. Maffucci, M.D., and Selig Neubardt, M.D.

Also—*New York City:* Moise M. Abitbol, M.D., Frederick R. Abrams, M.D., Philip M. Boehrer, M.D., Alan Davidson, M.D., Keith F. Deubler, M.D., Walter L. Freedman, M.D., Richard D. Grimaldi, M.D., Robert P. Hatch, M.D., Clinton R. Hathaway, Jr., M.D., John R. Langstadt, M.D., Warner Nash, M.D., Thomas M. O'Hearn, M.D., John T. Parente, M.D., David H. Schonholz, M.D., Samuel Soichet, M.D., Michael Truppin, M.D., and Marvin B. Zuckerman, M.D.

Also—*Plainview:* Sol Feigman, M.D.; *Plattsburgh:* David B. McDowell, M.D., and Charles A. Stevens, Jr., M.D.; *Rochester:* Allan R. Law, M.D., Edward T. McDonough, M.D., and Marion C. Potter, M.D.; *Saratoga Springs:* Stanley Friedman, M.D.; *Sayville:* Oliver J. Blaber, M.D.; *Stapleton:* Robert A. Marks, Jr., M.D.; *Syracuse:* Donald J. Adams, M.D., Philip L. Ferro, M.D., and Robert H. Zimmer, M.D.; *Tonawanda:* John H. McArdle, M.D.; *Utica:* John G. Chanatry, M.D.; *Watertown:* George G. Couch, M.D.; *Westbury:* Henry G. Reinhardt, M.D.; *West Point:* John Lukasik, Jr., M.D.; *Whitestone:* Arthur Leber, M.D.; and *Yorktown Heights:* Thomas V. Kaicher, M.D.

Postgraduate courses in chest diseases

The American College of Chest Physicians will present its fifteenth annual postgraduate course on recent advances in the diagnosis and treatment of diseases of the heart and lungs from September 17 through 21 at the Warwick Hotel, Philadelphia. For information contact: American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Postgraduate courses in Georgia

The Department of Continuing Education of the Medical College of Georgia has planned a series of five postgraduate courses for the fall and winter 1962–1963.

The courses are as follows: "Clinical Pathology in Medical Practice," October 23 through 25; "Diagnosis and Practical Management of Arthritis," November 13 through 15; "Orthopedics in General Practice," December 4 through 6; "Growth and Development—Management of Common Behavior Disturbances," February 12 through 14; and "Gynecologic Problems in Private Practice," March 12 through 14.

Each course is acceptable for 18 hours of credit by the American Academy of General Practice. For information write to: Claude-Starr Wright, M.D., Director, Department of Continuing Education, Medical College of Georgia, Augusta, Georgia.

Personalities

Elected. Leonard L. Heimoff, M.D., Bronx, as surgeon of the New York State Department of the Veterans of Foreign Wars.

Speakers. Richard I. Brasfield, M.D., and Ulrich K. Henschke, M.D., New York City, on the subject of breast cancer at the eighth International Cancer Congress in Moscow, Union of the Soviet Socialist Republics on July 24. . .William Paul Brown, M.D., Pomona, on the subject "The Parish Lay Apostolate" at the National Council for the Spanish Speaking, held in Milwaukee, May 8.

Appointed. Brig. Gen. Sheldon Seymour Brownton, New York City, as Special World's Fair Health Officer of the City of New York Department of Health. . .Ralph M. Gofstein, M.D., Natick, Massachusetts, as assistant director of the Bureau of Nutrition of the State of New York Department of Health. . .Edwin P. Maynard, Jr., M.D., Brooklyn, to the newly-created post of director of development at The Brooklyn Hospital. . .Samuel Milham, Jr., M.D., Elsmere, as associate public health physician in the State of New York Department of Health Public Health Research, Development, and Evaluation Group. . .George H. Wiedeman, M.D., to the Marion E. Kenworthy Chair of Psychiatry at the New York School of Social Work, Columbia University.

Medical Meetings

World forum on syphilis and other treponematoses

A world forum on syphilis and other treponematoses, sponsored by the American Social Health Association, the American Venereal Disease Association, and the U.S. Public Health Service with the World Health Organization and the International Union Against Venereal Disease and the Treponematoses as participating agencies, will be held September 4 through 8 at the Sheraton-Park Hotel in Washington, D.C.

Venereal disease (especially syphilis) incidence rates have increased alarmingly throughout the world in the last several years. In 1961 in New York State, exclusive of New York City, physicians reported 830 cases of early (infectious) syphilis and a total of 2,500 cases of syphilis to health departments. Infectious syphilis has increased 500 per cent from the State's 1957 low level, and more cases were reported in 1961 than in any year since 1948. Based on the data of the first six months of 1962 the incidence rate this year may be even greater than that of last year.

To combat this health menace an increased number of trained Venereal Disease Program representatives now is available through local health departments and State District Health Offices to aid practicing physicians by providing effective epidemiologic assistance. Adequate and thorough case finding, interview, and follow-up of cases and their contacts is the basic element of an effective program for venereal disease control. Such a program is possible only through cooperative effort of physicians, health officers, and experienced Venereal Disease Program representatives. The individual clinician may wish to learn more about the clinical and other aspects of these problems and their solutions.

For further information concerning the Forum contact the State of New York Department of Health Bureau of Adult Health and Geriatrics or your local health officer.

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis will present a panel discussion on "New Developments in Psychoanalysis" on September 26, at the New York Academy of Medicine, Fifth Avenue and East 103rd Street, New York City.

The panel will consist of: Marianne H. Eckardt, M.D., Bethesda, Maryland, and Harold Kelman, M.D., Leon Salzman, M.D., Frederick A. Weiss, M.D., and Antonia Wenkart, M.D., New York City.

The participants will report on the proceedings of the International Psychoanalytic Forum that was held in Amsterdam in July.

National Foundation and Vanderbilt University School of Medicine

The National Foundation and Vanderbilt University School of Medicine will cosponsor a symposium on birth defects to be held in the Vanderbilt Law School Auditorium, Nashville, Tennessee, September 27 and 28.

Experts on congenital defects will report on the latest developments in basic and clinical research and care of patients. James L. German, 3rd, M.D., of New York City will be among the guest speakers. The conference is being held in connection with the dedication of a circular-wing addition to the University's Hospital which will house a birth defects clinical study center supported by The National Foundation.

Association of Medical Illustrators

The Association of Medical Illustrators will hold its seventeenth annual meeting October 1 through 3 at Detroit and Ann Arbor Michigan. The theme of the meeting will be the uses of television in medical education.

For information write to: Mr. Emil W. Hospodar, Association of Medical Illustrators, 1853 West Polk Street, Chicago 12, Illinois.

Districts I and II, The American College of Obstetricians and Gynecologists

The annual meetings of districts I and II of The American College of Obstetricians and Gynecologists will be held jointly this year at the Queen Elizabeth Hotel, Montreal, Canada, October 11 through 13.

For further information contact district secretary: Martin L. Stone, M.D., Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York 29, New York.

American Medical Writers' Association

"The Information Explosion—Its Challenge and Problems" will be the theme of the nineteenth annual meeting of the American Medical Writers' Association at the Sheraton-Park Hotel in Washington, D.C., October 12 and 13.

The first day will be devoted to what medical journal editors, authors, educators, pharmaceutical companies, and medical writers can do to meet the challenge of the flood of new medical information. On the second day, the meeting will consider the promise of recent advances in information storage and retrieval, in utilization of the "newer" communication media, and in professionalism among medical communication personnel.

For details and registration forms write to: Mr. John Sargeant, Chairman of the Local Arrangements Committee, Medical and Chirurgical Faculty of Maryland, 1211 Cathedral Street, Baltimore 1, Maryland.

New York Diabetes Association

Metabolic and structural alterations in the prediabetic phase of diabetes will be the theme of the all-day symposium of the Clinical Society of the New York Diabetes Association on Saturday, October 13, from 9:00 A.M. to 4:30 P.M. at the Barbizon Plaza Hotel, 58th Street and Avenue of the Americas, New York City.

Medical students, interns, and residents and members of the Clinical Society will not be charged a registration fee.

American Society of Anesthesiologists

The American Society of Anesthesiologists will hold its annual meeting October 20 through 26 at the Statler-Hilton Hotel in New York City.

American Rhinologic Society

The American Rhinologic Society will hold its eighth annual meeting in Los Angeles, November 1 and 2, at the Statler-Hilton Hotel. C. Andrew L. Bassett, M.D., New York City, will be among the guest speakers.

For further information write to: Robert M. Hansen, M.D., Secretary, American Rhinologic Society, 2210 Lloyd Center, Portland 12, Oregon.

American Society of Cytology

The American Society of Cytology (formerly the Inter-Society Cytology Council), will hold its tenth annual scientific meeting at the Chase-Park Plaza Hotel, St. Louis, Missouri, November 8 through 10. For further information write to: Paul A. Younge, M.D., Secretary-Treasurer, American Society of Cytology, 1101 Beacon Street, Brookline 46, Massachusetts.

Hahnemann Medical College and Hospital

The Hahnemann Medical College and Hospital of Philadelphia will present a symposium on medical considerations in the surgical patient at the Sheraton Hotel, 1725 Pennsylvania Boulevard, Philadelphia 3, Pennsylvania, December 12 through 14.

The major medical problems which the physician encounters in the surgical patient will be considered. The program will be divided into the following sections: (1) Evaluation and preparation of patients with difficult cardiovascular problems; (2) therapy of cardiovascular-pulmonary problems in the postoperative period, with special emphasis on fluid and electrolyte problems, cardiac surgery problems, and the diagnosis and management of shock; (3) evaluation of endocrine problems in the pre- and postoperative periods; and (4) evaluation and management of gastrointestinal disorders in the pre- and postoperative periods.

For further information write to: Wilbur W. Oaks, M.D., Director, Hahnemann Medical College and Hospital, 230 North Broad Street, Philadelphia 2, Pennsylvania.

Abstracts in Interlingua

Skudder, P. A., Inglis, A. E., e McCarroll, J. R.: Tetanus in Citate New York (*anglese*), New York State J. Med. **62:** 2793 (1 de septembre) 1962.

Quaranta-un casos de tetanus esseva reportate in Citate New York inter 1957 e 1960, incluse 32 in narcomanos. Le mortalitate total esseva 90 pro cento: 30 del narcomanos moriva e etiam 4 del 9 patientes con vulneres presumitemente trivial. A causa del serie disavantages que inhere in le administration de antitoxina anti tetanus, il es recommendate urgentemente que le medicos immunisa lor patientes con toxoide de tetanus quandocunque isto es practicabile e que illes transmitte al patientes in forma scribite un certificato del immunisation. Le prophylaxia pro tetanus depende de si le vulnere es tetano-susceptibile o nonsusceptibile e del stato immunisational del patiente. Tamen, in omne casos illo require bon attendimento al vulnere e un dose de reinfortio de toxoide de tetano o immunisation active, si isto ha non essite effectuate previemente.

Fontana, V. J., Sedlis, E., Prose, P. H., Messina, V. P., e Holt, L. E., Jr.: Titro de complemento, proteina C-reactive, e configuration electrophoretic del proteinas seral in juveniles eczematose (*anglese*), New York State J. Med. **62:** 2801 (1 de septembre) 1962.

Esseva studiate 42 juveniles in varie stadios de eczema atopic e de etates de inter tres menses e sex annos. Le titros de complemento in omne le subjectos esseva intra limites normal. Dece-septe habeva normal configurationes del proteinas del plasma; in 6 (con signos clinic de infection) le fractiones de globulina gamma esseva augmentate; in 2 (de etates de tres e cinque menses) iste mesme fractiones esseva reducite. Le test pro proteina C-reactive esseva positive in 15 (incluse le 6 in qui le globulina gamma esseva augmentate) e negative in 14. Le test a fixation de latex produceva resultatos negative in le 13 juveniles testate pro le presentia de un proteina anormal.

Griboff, S. I.: Hirsutismo feminin; reclassification hormonal (*anglese*), New York State J. Med. **62:** 2805 (1 de septembre) 1962.

Un plus correcte classification de hirsutismo in femininas es possibilemente capace a suggerer plus efficace methodos de diagnose e de therapia. Hirsutismo constitutional include le patientes con nulle provate anormalitate endocrin, con excretion normal de 17-cetosteroide, con chromatogramma normal, e con nulle evidentia de virilismo, o de conditiones pathologic adrenal o ovarian. Altere classes de hirsutismo pote esser associate con ovarios normal e adrenales normal o con ovarios polycystic, ovarios a luteinisation diffuse, hyperplasia adrenal, o un tumor del ovarios o adrenales. In iste classes le hirsutismo es causate per un excessive production—in le adrenales o ovarios o ambes—de hormones pertinente, i.e. testosterona, androstendiona, dishydroepiandrosterona, 11β-hydroxyandrostendiona, adrenosterona, o un combination de istos. Le therapia hormonal de hirsutismo ha essite—a generalmente parlar—disappunctante.

Pollack, B.: Evolvente conceptiones in le tractamento psychiatric (*anglese*), New York State J. Med. **62:** 2810 (1 de septembre) 1962.

In recente annos, le therapia psychiatric ha essite influentiate in alte mesura per le introduction de drogas. In 1955, le numero del patientes residente al Hospital Statal Rochester esseva 3.752; in plus, 523 patientes recipeva attendimento pro convalescentes e 89 attendimento in familia. In 1960, le population residente habeva declinate a 3.239, durante que le numero del patientes recipiente attendimento pro convalescentes habeva crescite a 1.392, e le beneficiarios de attendimento in familia se habeva triplicate. Le drogas psychopharmacologic currentemente in uso pote esser classificate sequentemente: (1) Le drogas original introducite ad in iste pais in 1954, consistente principalmente de hydrochloruro de chlorpromazina, hydrochloruro de promazina, e reserpina; (2) plus recente compositos de phenothiazina, resultante del manipulation del molecula; e (3) un gruppo de sedativos e de agentes de tranquillisation, incluse meprobamato e hydrochloruro de hydroxyzina. Le inhibitores de oxydase monoaminic non es recommendate a causa de lor interferentia in le function hepatic, sed hydrochloruro de impipramina (etiam un agente antidepressive) se ha provate efficace. Therapia a droga deberea esser instituite al tempore del admission al hospital e continuate post le dimission.

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Vitamin D (Adult's and Child's Need)	62%

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FIFTY-SIXTH ANNUAL

District Branch Meetings

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Fifth and Sixth District Branches / First Combined Annual Meeting

Friday, Saturday, and Sunday, September 7, 8, and 9, 1962

Whiteface Inn, Lake Placid, Whiteface, New York

Friday, September 7

Evening

4:00 P.M. Registration (Main Lobby)
7:00 P.M. Cocktail Party (Colony Room)
8:00 P.M. Informal Dinner Dance (Main Dining Room)
Greetings: George F. Nevin, M.D., President, Sixth District Branch

Saturday, September 8

Morning

Panel Discussion: **Recent Advances in the Care of the Cancer Patient** (Convention Hall); all speakers are from Roswell Park Memorial Institute, Buffalo, New York

10:00 A.M. **Therapy of Breast Cancer**
Arnold Mittelman, M.D., Associate Cancer Research Breast Surgeon
Role of the Pathologist in the Care of the Malignant Diseases
Edith Sproul (Mittelman), M.D., Associate Chief Cancer Research Pathologist

11:05 A.M. Business Meeting; Election of Officers
Fifth District (Convention Hall)
Sixth District (Pool Lounge)

11:20 A.M. **Gynecologic Cancer Detection**
John Graham, M.D., Chief of Gynecologic Surgery
Ruth Graham, M.D., Associate Cancer Research Scientist
Advances in X-Ray Therapy
Walter Murphy, M.D., Chief of Therapeutic Radiology
Chemotherapy as an Adjuvant to Surgery
George E. Moore, M.D., Director

Afternoon

2:30 P.M. Recreation
Golf Tournament
Ninety-Minute Scenic Cruise ($1.25 per person)

Evening

6:45 P.M. Reception for State Officers (Colony Room)
8:00 P.M. Banquet (Main Dining Room)
Toastmaster: William R. Carson, M.D., President, Fifth District Branch
Introduction of Officers
Remarks: Joseph A. Lane, M.D., President, Medical Society of the State of New York
Remarks: Mrs. Herbert J. Ulrich, President, Woman's Auxiliary to the Medical Society of the State of New York

Sunday, September 9

Morning

10:00 A.M. Film: **Diagnosis and Treatment of Cancer** (Convention Hall)

Afternoon

12:30 P.M. Lunch
2:00 P.M. Ninety-Minute Scenic Cruise ($1.25 per person)

Officers—Fifth District Branch

President	William R. Carson, M.D., Potsdam
First Vice-Pres.	William L. Dorr, M.D., Auburn
Second Vice-Pres.	Felix Ottaviano, M.D., Oneida
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Delegate	Arthur F. Gaffney, M.D., Clinton

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Tioga	Philip Nichols, M.D., Owego
Tompkins	Herbert K. Ensworth, M.D., Ithaca

Nominating Commtttee Appointed

The following Nominating Committee for 1962–1963 has been appointed by Joseph A. Lane, M.D., President, Medical Society of the State of New York, and approved by the Council on June 22:

District Branch	*Committee Member*
Second	John M. Galbraith, M.D., Nassau, *Chairman*
First	Thurman B. Givan, M.D., Kings
Third	Homer L. Nelms, M.D., Albany
Fourth	Edward Siegel, M.D., Clinton
Fifth	Irving L. Ershler, M.D., Onondaga
Sixth	James Greenough, M.D., Otsego
Seventh	Charles M. Smith, M.D., Seneca
Eighth	Harold F. Brown, M.D., Erie
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At large	Solomon Schussheim, M.D., Kings

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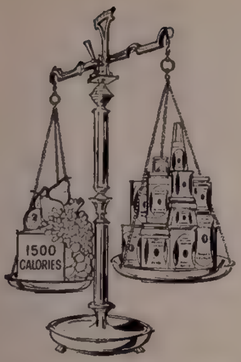

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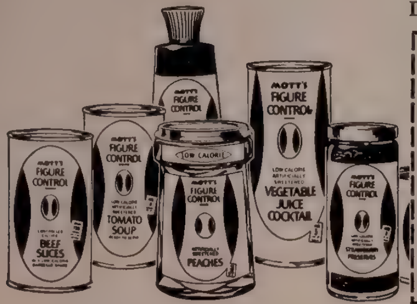
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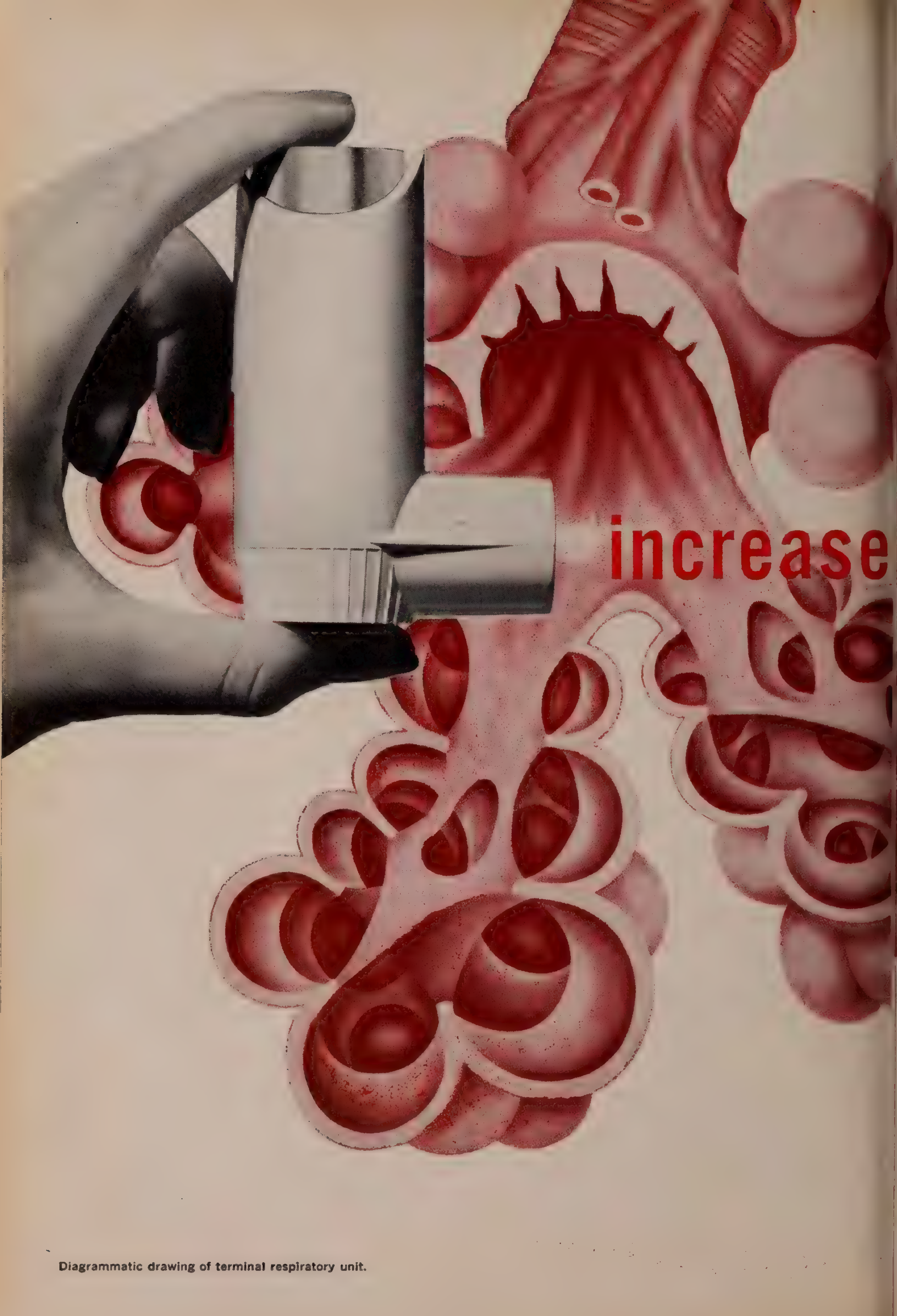

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*Schwartz, I. R.:
Current Therap. Res. 3:29, Feb., 1961.

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1. Ford, R. V.: Clin. Res. Notes 2:1 (Dec.) 1959. 2. Ford, R. V.: Cur. Therap. Res. 2:92 (Mar.) 1960. 3. Elliott, J. P., Jr., and Goldman, A. M.: South. M.J. 54:794 (July) 1961.

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Unlike chlorothiazide or hydrochlorothiazide, Naturetin has virtually no carbonic anhydrase activity. Thus, Naturetin causes less bicarbonate loss and less alteration in urinary pH than these other agents. This helps maintain a more favorable acid-base balance, and the less alkaline urine reduces the risk of existing urinary infection becoming resistant to therapy. Further, since Naturetin has less influence than the other thiazides on normal uric acid excretion, it is considered the thiazide of choice in patients with a tendency to hyperuricemia or gout.[1,2]

AVAILABLE: Naturetin 5 mg. and 2.5 mg. tablets. **ALSO AVAILABLE:** Naturetin c̄ K (Squibb Bendroflumethiazide 5 mg. and 2.5 mg. capsule-shaped tablets, each with 500 mg. Potassium Chloride), for use when disease or concomitant therapy increases the risk of hypokalemia. For full information, see your Squibb Product Reference or Product Brief.

1. Cohen, B. M.: M. Times 88:855 (July) 1960. 2. Cohen, B. M.: Méd. et Hyg. (Genève) #494, p. 210 (Mar. 15) 1961.

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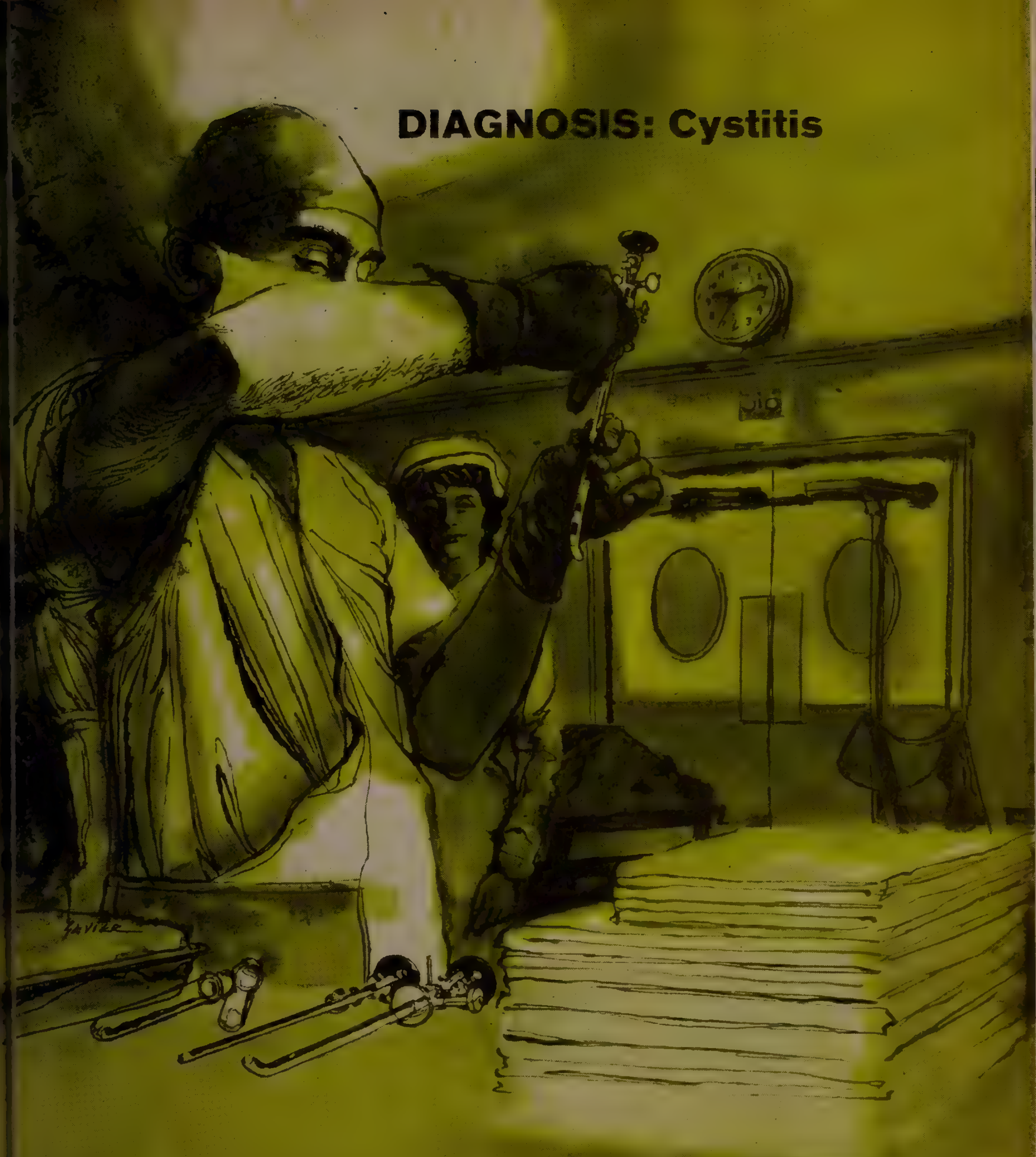

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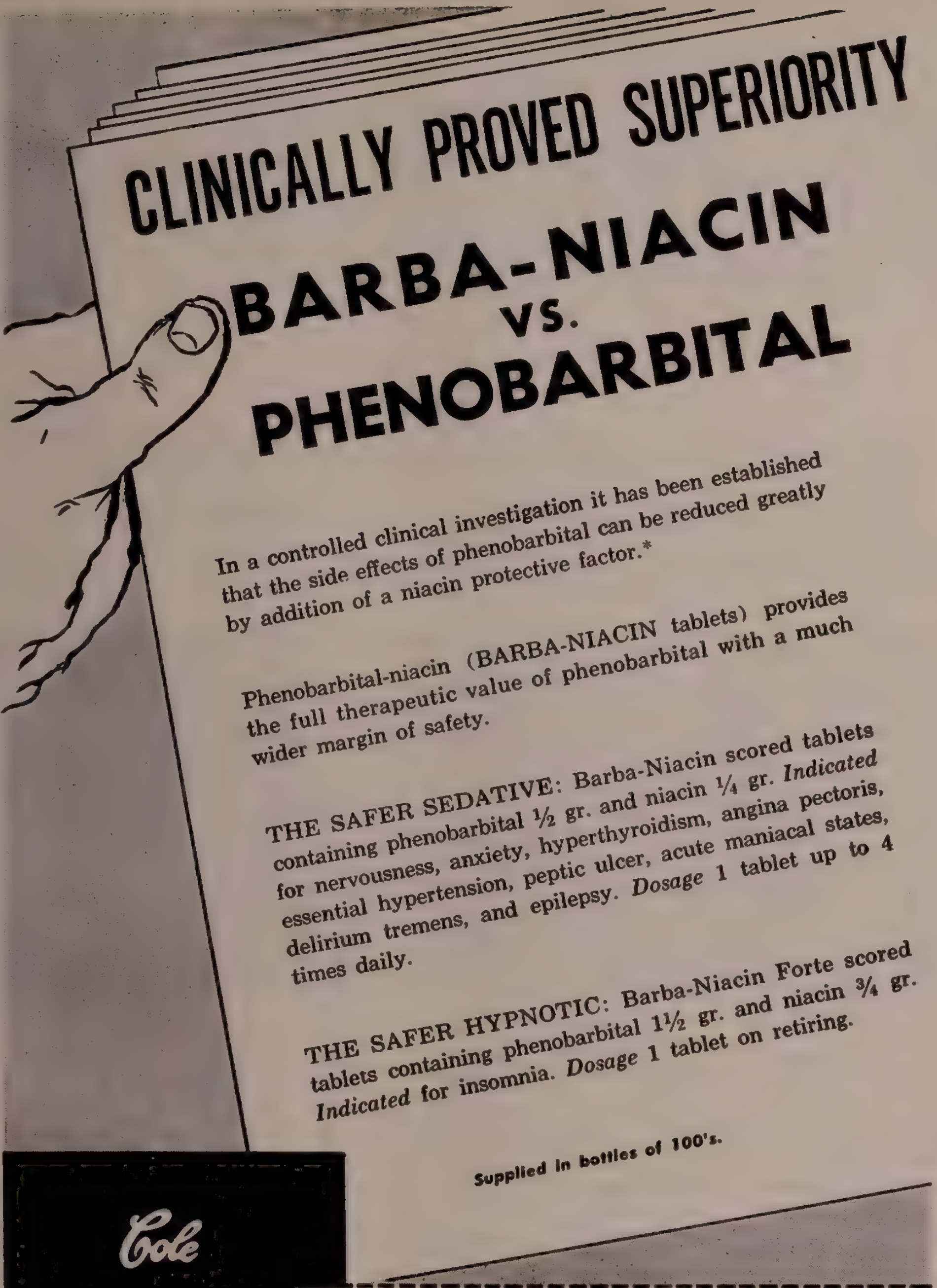

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Phenobarbital-niacin (BARBA-NIACIN tablets) provides the full therapeutic value of phenobarbital with a much wider margin of safety.

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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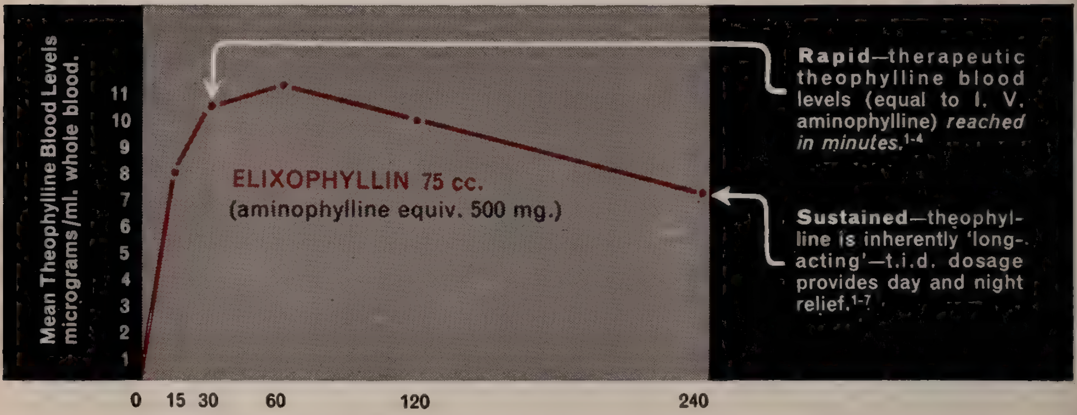
(theophylline in its most absorbable oral form)

...provides relief quickly, dependably, **safely.**[1-8]

...avoids the side effects and contraindications of ephedrine polypharmaceuticals or similar sympathomimetics



Rapid—therapeutic theophylline blood levels (equal to I. V. aminophylline) *reached in minutes.*[1-4]

Sustained—theophylline is inherently 'long-acting'—t.i.d. dosage provides day and night relief.[1-7]

Minutes after administration. Mean values in adult subjects following administration of the single dose commonly used in clinical practice.[8]

Each tablespoonful (15 cc.) contains theophylline 80 mg. (equivalent to 100 mg. aminophylline) in a hydroalcoholic vehicle (alcohol 20%).

Acute Attacks: single dose of 75 cc. for adults; 0.5 cc. per lb. of body weight for children.

24 Hour Control: for adults 45 cc. doses before breakfast, at 3 P.M., and before retiring; after two days, 30 cc. doses. Children, first 6 doses 0.3 cc.—then 0.2 cc. per lb. of body weight as above.
(Gastric distress rarely encountered.)

References: (1) Kessler, F.: Connecticut S.M.J. *21*:205 (March) 1957. (2) Burbank, B.; Schluger, J., and McGinn, J.: Am. J. Med. Sci. *234*:28 (July) 1957. (3) Spielman, A.D.: Ann. Allergy *15*:270 (June) 1957. (4) Greenbaum, J.: Ann. Allergy *16*:312 (May-June) 1958. (5) Kessler, F.: Medical Times *87*:1298 (Oct.) 1959. (6) Bickerman, H.A., and Barach, A. L., in Modell, W.: Drugs of Choice 1960-1961, St. Louis, The C. V. Mosby Company, 1960, p. 516. (7) Wilhelm, R. E. in Conn., H. F.: Current Therapy—1961, Philadelphia, W. B. Saunders Company, p. 417. (8) Schluger, J. McGinn, J. T., and Hennessy, D. J.: Am. J. Med. Sci. *233*:296, 1957.

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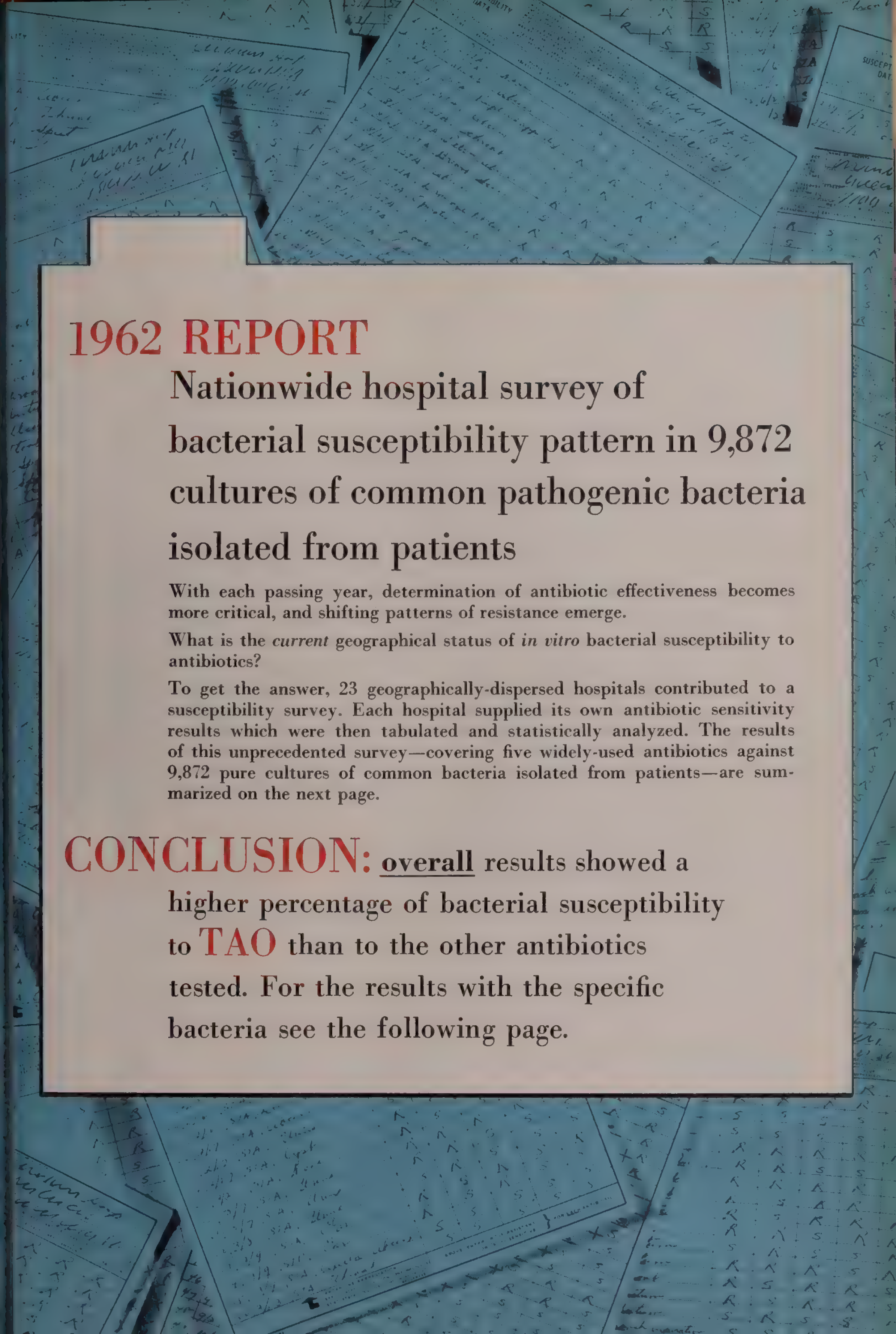


1962 REPORT

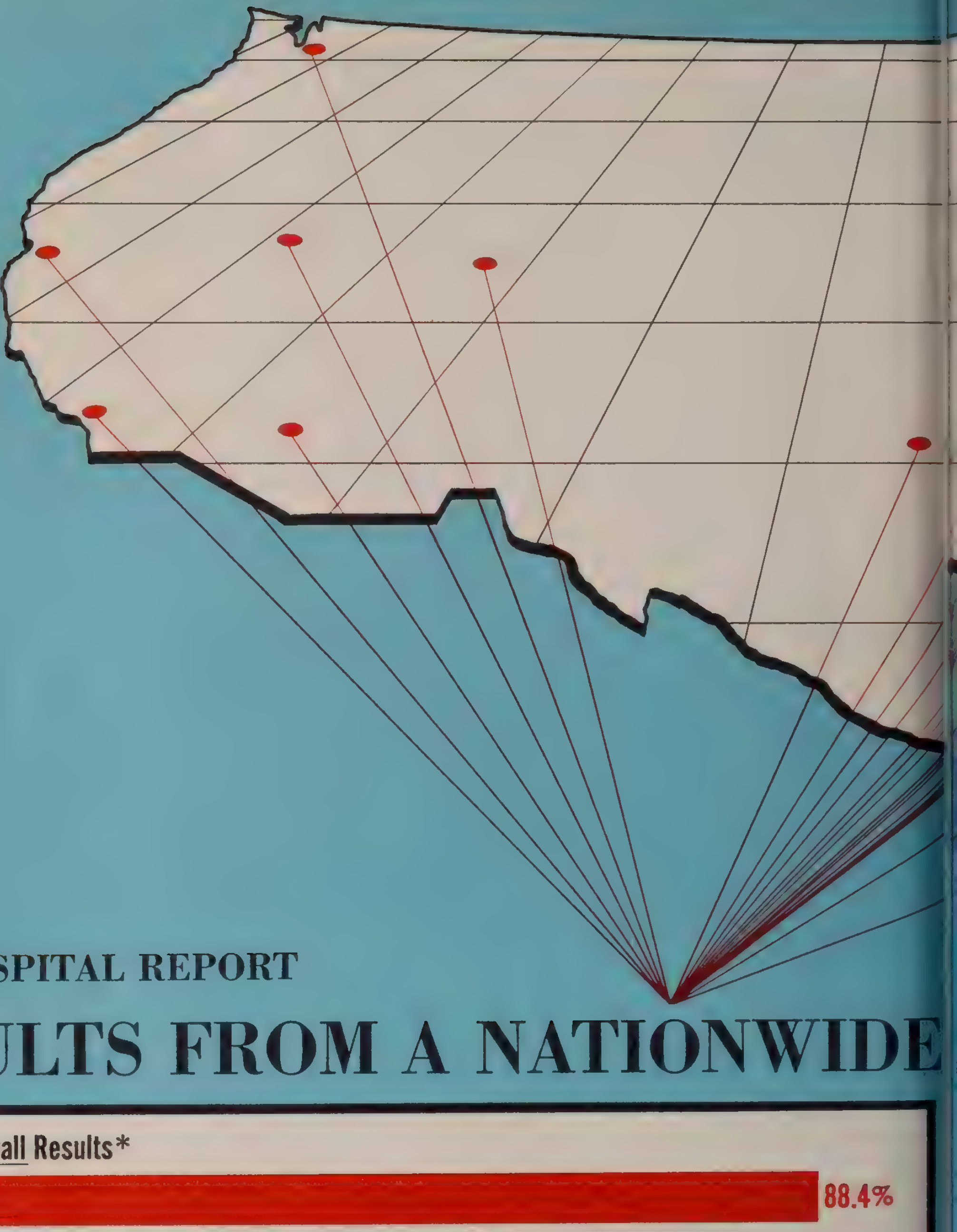
Nationwide hospital survey of bacterial susceptibility pattern in 9,872 cultures of common pathogenic bacteria isolated from patients

With each passing year, determination of antibiotic effectiveness becomes more critical, and shifting patterns of resistance emerge.

What is the *current* geographical status of *in vitro* bacterial susceptibility to antibiotics?

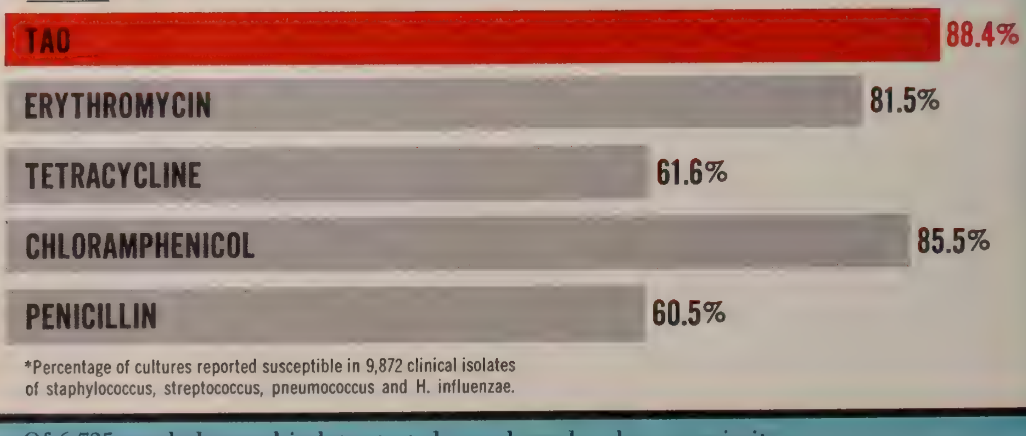
To get the answer, 23 geographically-dispersed hospitals contributed to a susceptibility survey. Each hospital supplied its own antibiotic sensitivity results which were then tabulated and statistically analyzed. The results of this unprecedented survey—covering five widely-used antibiotics against 9,872 pure cultures of common bacteria isolated from patients—are summarized on the next page.

CONCLUSION: overall results showed a higher percentage of bacterial susceptibility to TAO than to the other antibiotics tested. For the results with the specific bacteria see the following page.



1962 HOSPITAL REPORT

RESULTS FROM A NATIONWIDE



*Percentage of cultures reported susceptible in 9,872 clinical isolates of staphylococcus, streptococcus, pneumococcus and H. influenzae.

Of 6,725 staphylococcal isolates tested TAO showed a clear superiority; of 2,488 streptococcal and 463 pneumococcal isolates tested results were about equal. Of 196 H. influenzae isolates tested TAO was less effective.

SURVEY OF ANTIBIOTICS

Staphylococcus, streptococcus, pneumococcus and H. influenzae isolated from patients were the organisms challenged by five widely used antibiotics. All the antibiotics have been in clinical use at least five years: penicillin, erythromycin, triacetyloleandomycin, tetracycline and chloramphenicol. Only results of susceptibility studies on pure cultures were considered valid; the disc testing technique was utilized.[1]

TAO®
(triacetyloleandomycin)
an antibiotic
that time
hasn't changed

Active against common pathogenic bacteria. Even after five years of general use, triacetyloleandomycin (TAO) is highly active against common pathogens. For specific information on the many TAO dosage forms, its uses in acute pediatric, skin and soft tissue, and respiratory infections, turn the page.

1. "Bacterial Susceptibility Patterns: A Geographic Survey." Fowler, J. Ralph, M.D., and Watters, John L., M.D. Scientific Exhibit presented at the Annual Meeting of the American Society of Clinical Pathologists, Chicago, Ill., August 31 to September 8, 1962.

TAO® an antibiotic that time hasn't changed

(triacetyloleandomycin)

You can expect TAO to produce a rapid, decisive response in acute common infections caused by most Gram-positive and some Gram-negative bacteria, including those resistant to many other antibiotics:

Acute respiratory infections: otitis media, sinusitis, tonsillitis, pharyngitis, bronchitis, lobar and bronchopneumonia, lung abcess, bronchiectasis.

Acute skin and soft tissue infections: furuncles, carbuncles, impetigo contagiosa, ecthyma, eczema, infected cysts, abscesses, infected contact dermatitis, cellulitis, infected traumatic or surgical ulcers and wounds.

Acute pediatric infections: particularly streptococcal.

Other acute genitourinary, gastrointestinal and miscellaneous infections: pyelonephritis, pyelitis, ureteritis, cystitis, urethritis (including gonococcal urethritis), acute salpingitis, endometritis, bartholinitis, staphylococcal enterocolitis, osteomyelitis, septic arthritis.

a TAO form for use . . . in patients of all ages . . . in home, office or hospital
TAO capsules (250 mg.; 125 mg.)
TAO Ready-Mixed Oral Suspension (raspberry-flavored) (125 mg./5 cc.)
TAO Pediatric Drops (100 mg./cc.)
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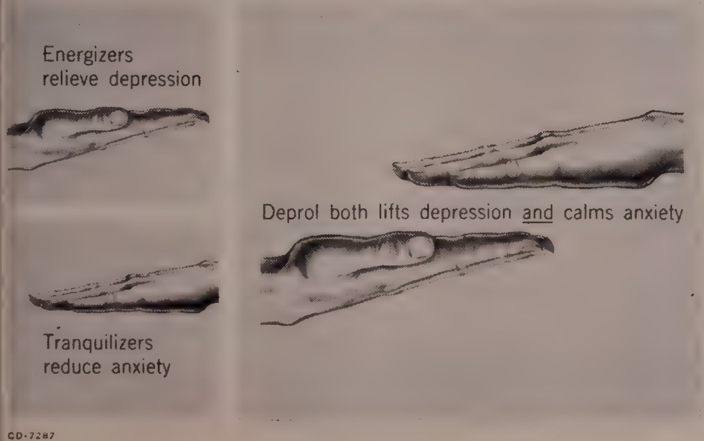
"I feel like my old self again!" Balanced Deprol therapy has helped relieve her insomnia and fatigue – her normal energy, drive and interest have returned.

Brightens up the mood, brings down tension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relieve depression
Deprol both lifts depression and calms anxiety
Tranquilizers
reduce anxiety

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be increased gradually up to 3 tablets q.i.d. With establishment of relief, the dose may be reduced gradually to maintenance levels.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets.

Write for literature and samples.

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Orinase Case History

Mr. B. B., a 61-year-old stockbroker, was put on Orinase almost six years ago. On insulin, he had been imperfectly controlled, irritable, and "used to get overly depressed." On Orinase, 1 Gm. per day, control is smooth and Mr. B. is again his former lively self. He regularly works at home well into the night, preparing for the next day's trading.

An active man, Mr. B. occasionally exercises at the gym. He follows baseball with enthusiasm, likes a friendly game of cards, and often goes visiting the various members of his close-knit family.

Mr. B., intensely involved in his profession, describes his day as a "continual crisis." Under the stress of representing clients in the face of market fluctuations, his Orinase needs also fluctuate. Guided by his physician, Mr. B. adjusts his dosage between 1 and 2 Gm. daily.

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5 years of control

The patient's dosage had to be increased in 1960 at the death of his sister (also a diabetic). For two months, maintenance of control required 2.5 to 3.5 Gm. of Orinase a day; dosage then leveled off again at 1 Gm.

About a year later, when Mr. B.'s wife was incapacitated by an eye ailment, his need for Orinase increased again. During his wife's convalescence, he was taking 2.5 Gm. daily.

Mr. B. is an energetic and sociable man. His work and his philanthropic, family, and social obligations keep him extremely busy. On Orinase, he takes this life in stride.

Orinase* (tolbutamide) stands in a unique position; it alone, among oral antidiabetes agents, has had five years or more of day-to-day routine clinical use in the hands of thousands of physicians throughout the country. Accordingly, data on a considerable number of truly long-term Orinase-treated patients are now available. This series of Orinase five-year case histories has been prepared to illustrate and exemplify some aspects of actual experience in management. Patient data, made available to us by physicians, have been factually incorporated; however, patients' identities have been concealed. Any inquiries regarding this Orinase case history series should be addressed to: Medical Department, The Upjohn Company, Kalamazoo, Michigan.

Orinase is supplied in bottles of 50 and 200 tablets.
Each tablet contains: tolbutamide ... 0.5 Gm.

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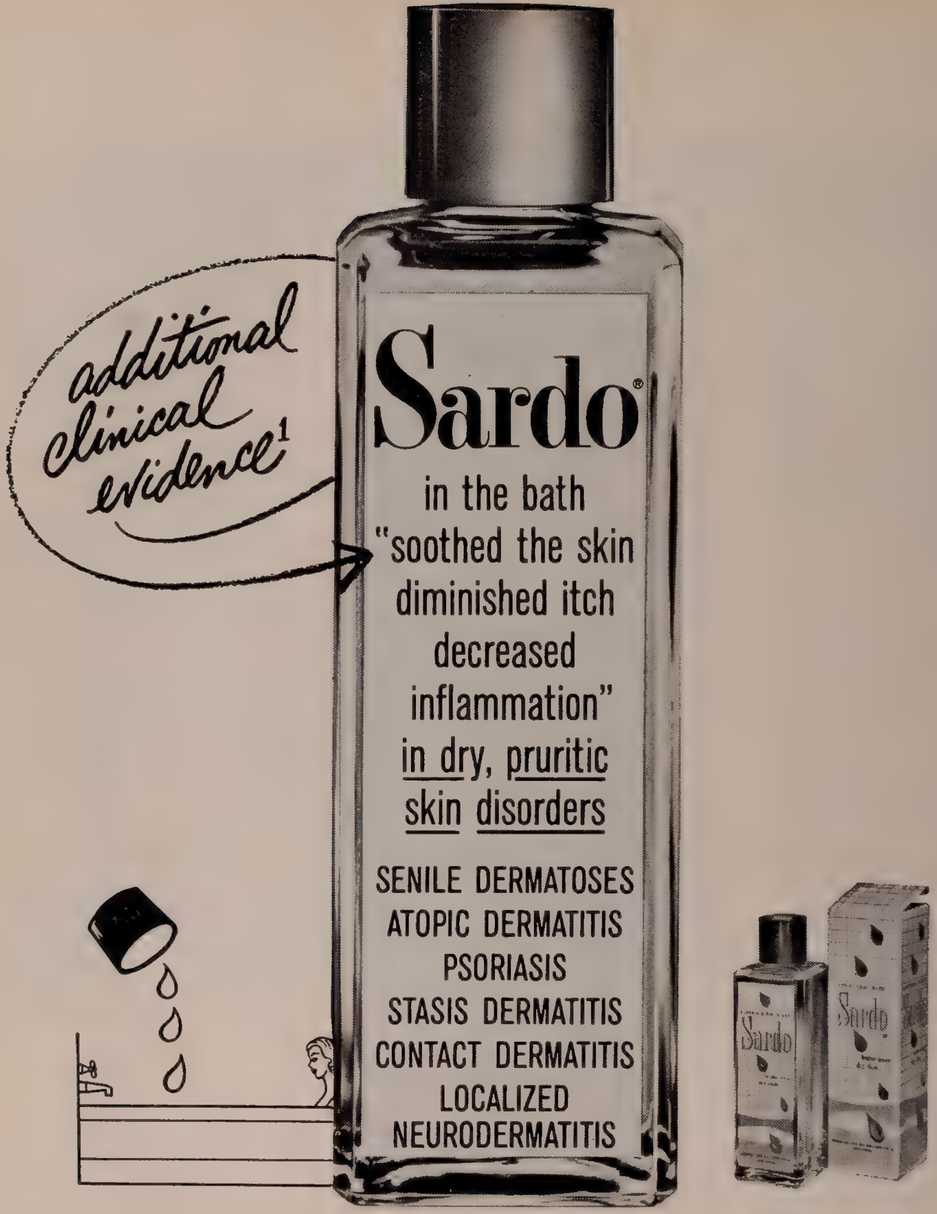
additional clinical evidence[1]
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"soothed the skin
diminished itch
decreased
inflammation"
in dry, pruritic
skin disorders
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BENEFICIAL RESULTS were obtained with **SARDO** in the bath in 122 of 135 patients (90%) with dry, itchy skin conditions, in most cases with beneficial effect "after the first bath." Dryness was allayed in all cases, and associated itching "either completely relieved or greatly improved." No irritation or sensitization was observed.

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1. Borota, A., and Grinell, R.N.: J. Amer. Geriatrics Soc., 10:413, 1962.
2. Spoor, H. J.: N.Y. State J.M. 58:3292, 1958.
3. Lubowe, I. I.: Western Med. 1:45, 1960.
4. Weissberg, G.: Clin. Med. 7:1161, 1960.

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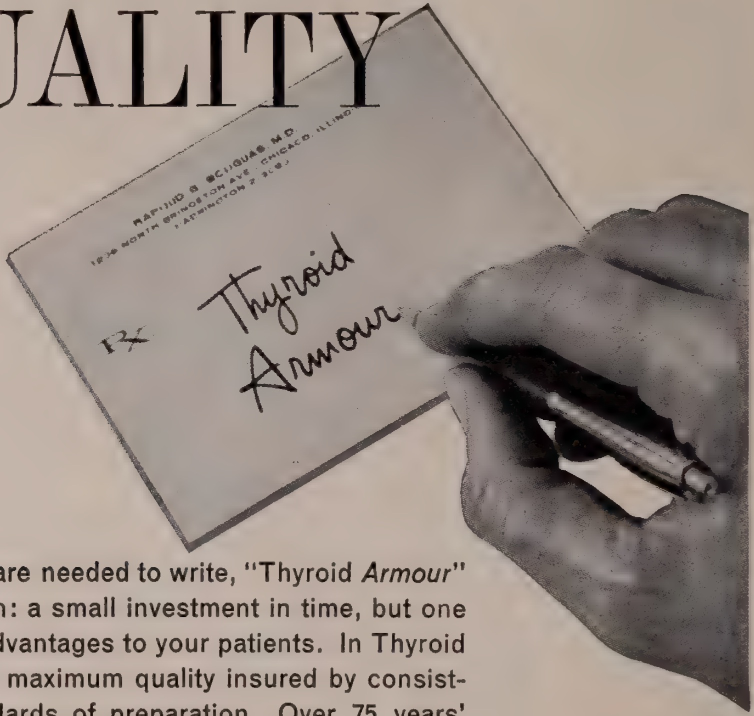

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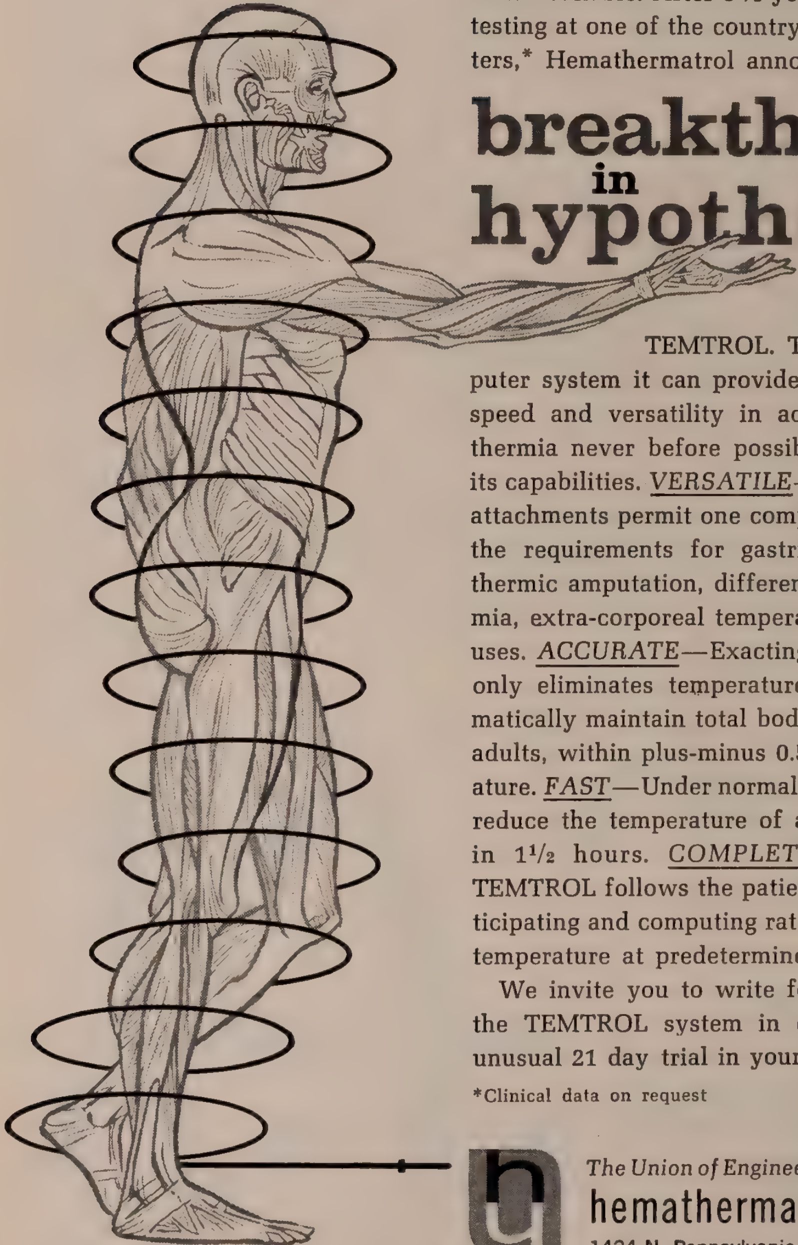

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What animal work has been done with this new anticholinergic?[2,4,5]

What effect does Robinul have on antral motility?[8]

results with Robinul and Robinul-PH in 795 ulcer patients, from 69 clinical investigators*

DIAGNOSIS	ROBINUL					ROBINUL-PH				
	*No. Patients	Excellent	Good	Fair	Poor	*No. Patients	Excellent	Good	Fair	Poor
Marginal Ulcer	11	3	3	3	2	1	0	1	0	0
Pyloric Channel Ulcer	6	3	1	0	2	2	1	1	0	0
Pyloric Ulcer	4	2	1	1	0	1	1	0	0	0
Gastric Ulcer, bleeding	3	1	2	0	0					
Gastric Ulcer	48	31	11	1	5	12	5	7	0	0
Gastric Ulcer, penetrated	1	0	1	0	0	1	1	0	0	0
Gastric Ulcers, multiple	1	1	0	0	0					
Duodenal Ulcer	494	220	195	48	31	99	41	38	13	7
Duodenal Ulcer, bleeding	38	19	15	3	1	2	1	0	1	0
Duodenal Ulcer, obstruction	13	4	3	1	5					
Duodenal Ulcer, perforated	5	2	1	0	2	6	0	3	1	2
Gastric and Duodenal Ulcer	4	2	2	0	0					
Peptic Ulcer, unspecified	25	19	4	0	2	18	8	7	2	1
TOTALS	653	307	239	57	50	142	58	57	17	10
		83.6%					81.0%			

*Clinical reports on file, A. H. Robins Company, Inc.

How does Robinul compare in the matter of side effects?[3,7]

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Bibliography of recent articles on Robinul: 1. Abbott, William E., et al.: "Effect of Glycopyrrolate (Robinul) on Basal and Histamine- or Insulin-induced Gastric Secretion," Annals of the New York Academy of Sciences, 99:163, Feb. 28, 1962. 2. Alphin, R. S., et al.: "Action of Glycopyrrolate (AHR-504) on Gastric Secretion in Dogs," Federation Proceedings, 20:251, March, 1961. 3. Epstein, Jerome H.: "Clinical Observations with a New Anticholinergic, Glycopyrrolate," The American Journal of Gastroenterology, 37:295, March, 1962. 4. Franko, Bernard V., et al.: "Pharmacodynamic Evaluation of Glycopyrrolate in Animals," Annals of the New York Academy of Sciences, 99:131, Feb. 28, 1962. 5. Franko, Bernard V., and Lunsford, C. D.: "Derivatives of 3-pyrrolidinols-III. The Chemistry, Pharmacology and Toxicology of some N-substituted-3-pyrrolidyl α-substituted Phenylacetates," Journal of Medicinal and Pharmaceutical Chemistry, 2:523, May, 1960. 6. Moeller, Hugo C.: "Physiological Effects and Clinical Evaluation of Glycopyrrolate in Peptic Ulcer," Annals of the New York Academy of Sciences, 99:158, Feb. 28, 1962. 7. Sun, David C. H.: "Comparative Study of the Effect of Glycopyrrolate and Propantheline on Basal Gastric Secretion," Annals of the New York Academy of Sciences, 99:153, Feb. 28, 1962. 8. Young, Robert, and Sun, David C. H.: "Effect of Glycopyrrolate on Antral Motility, Gastric Emptying, and Intestinal Transit," Annals of the New York Academy of Sciences, 99:174, Feb. 28, 1962.

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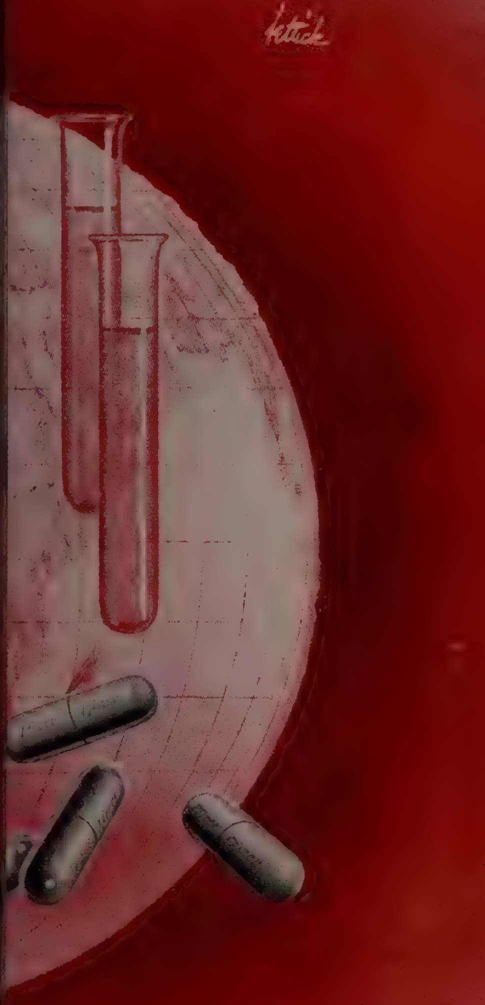

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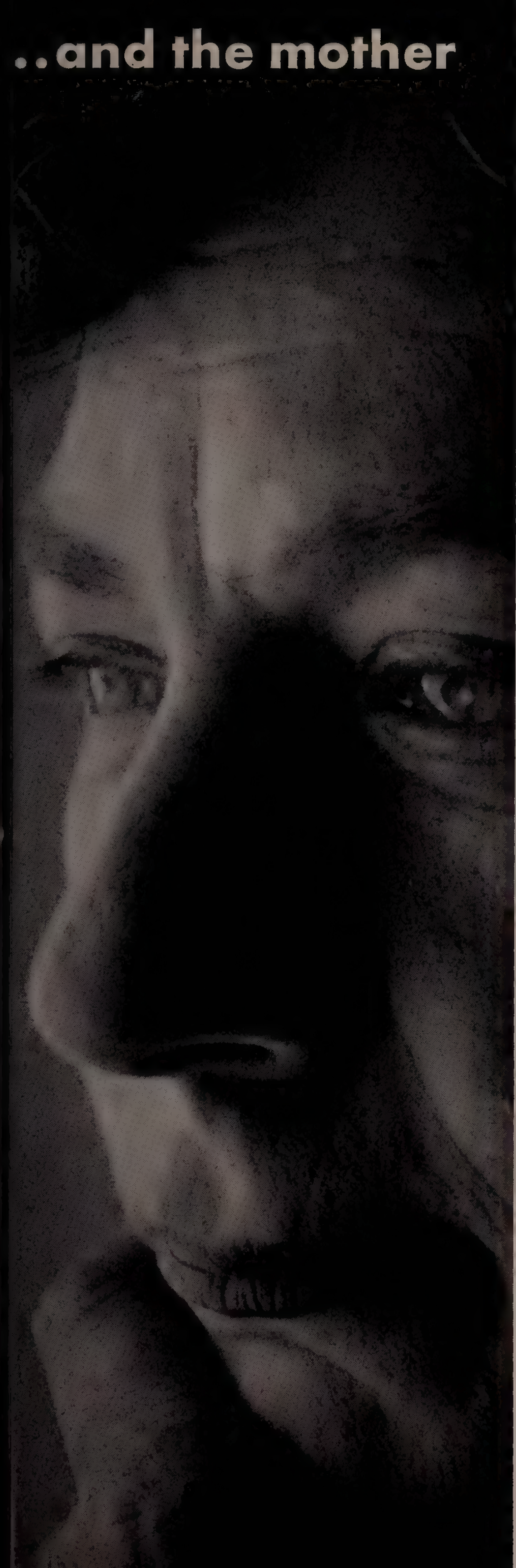

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Editorials

Deductibility of medical expense

The United States Supreme Court on April 30, 1962, in a decision of far-reaching significance held that housing expenses incurred by an ill taxpayer for himself and his family during a Florida trip prescribed for medical reasons are not deductible medical expenses, under the provisions of Section 213 of the Internal Revenue Code of 1954.

The taxpayer, now deceased, was an attorney practicing law in Newark, New Jersey. In December, 1953, when he was forty-three years of age and had suffered four heart attacks during the previous eight years, he was advised by a heart specialist to spend the winter season in a warm climate. He, his wife, and his three-year-old daughter proceeded immediately to Fort Lauderdale, Florida, where they resided for the ensuing three months in an apartment rented for $1,500. Two months of the succeeding winter were also spent in Fort Lauderdale in an apartment rented for $829.

The taxpayer claimed the two rental payments as deductible medical expenses in his 1954 and 1955 income tax returns. These deductions were disallowed in their entirety by the Commissioner of Internal Revenue. The Commissioner conceded that the taxpayer's sojourn in Florida was not for vacation purposes but was "a medical necessity and . . . a primary part of necessary medical treatment of a disease" from which the taxpayer was suffering, that is, atherosclerosis.

The Tax Court reversed the Commissioner's determination to the extent of one third of the deductions, finding that proportion of the total claimed attributable to the taxpayer's own living accommodations. The remaining two thirds it attributed to the accommodations of his wife and child, whose presence, the Tax Court concluded, had not been shown to be necessary to the medical treatment of the taxpayer's illness.

The U.S. Court of Appeals for the Third Circuit, sitting in New Jersey, held, by a divided vote, that the full rental payments were deductible as expenses for "medical care" within the meaning of the Internal Revenue Code.

The U.S. Circuit of Appeals for the Second Circuit, sitting in New York, reached a completely contrary conclusion in a subsequent similar case. The Supreme Court therefore agreed to review the whole matter to resolve the conflict.

As construed by the Tax Court, the 1939 Code permitted the deduction of living expenses incidental to the cure of disease. This construction was based on that Court's study of the legislative history of that law.

The Supreme Court, in turn, felt that its decision had to be based on an examination of the legislative history. It made a detailed examination of the House and Senate Committee Reports concerning the 1954 Code and concluded that the Tax Commissioner's ruling was the correct one. The Court pointed out that in enacting the medical expense deduction of the 1954 Code, Congress used virtually the same language as in the 1939 Code but harbored a contrary intent. It called attention to the fact that the House and Senate Committee Reports state that Section 213 "specifically excludes deduction of any meals and lodging while away from home receiving medical treatment." The Reports assert that in the case of a patient advised to go to Florida for his health "the cost of the patient's transportation to Florida would be deductible there." They go on to state: "However, if a doctor prescribes an appendectomy and the taxpayer chose to go to Florida for the operation not even his transportation cost would be deductible." (*Commissioner* v. *Bilder*, U.S. Sup. Ct., Harlan, J., April 30, 1962)

Emergency resuscitation

The cessation of breathing and beating of the heart is an emergency of the greatest magnitude and must be treated promptly and properly to obtain the survival of the patient without permanent brain damage. In general, anoxia of the brain which lasts more than four minutes usually produces irreversible changes in the central nervous system which in turn may lead to the occurrence of a "vegetable state" if the patient should survive.

The treatment of this emergency has been greatly improved during the past few years by the development of two therapeutic procedures, both of which are usually necessary in this situation. These are mouth-to-mouth breathing and closed-chest cardiac massage. These procedures have proved to be of great value, and from fragmentary reports it would seem that several hundred lives already have been saved in New York State alone. Many of these individuals who have been saved are entirely normal, as their cardiac arrest was caused by some temporary factor such as electrocution, anesthesia, shock, and so forth. The others, of course, still have the disability that produced the arrest, but in some instances this is a mild condition so that the person can engage in many normal activities including useful employment.

However, like nearly every medical or surgical procedure, if emergency resuscitation is done improperly or when it is not indicated, much harm or even a fatality may result. Fractured ribs and ruptured blood vessels and organs already have been noted in several cases, nearly always in instances in which the technics were used incorrectly. Even an appendectomy can be dangerous or fatal if it is performed improperly. The same can be said for the administration of many medications. Because of the two dominating features, it is imperative (1) that a large number of people be familiar with the methods and (2) that the procedures be done promptly, correctly, and with an awareness of the dangers.

All physicians should become familiar with this potentially lifesaving procedure at once. To aid physicians in obtaining authentic instruction, the Medical Society of the State of New York, the State of New York Department of Health, the New York State Heart Assembly, the New York State Hospital Council, and the medical schools of the State are cooperating to set up a large series of courses in the hospitals of the State (outside of New York City) to be held between now and December 31, 1962. Instruction will be given by especially trained members of the medical school faculties using lectures, films, and life-size mannequins for actual individual practice. In this way it is hoped that every physician in the State can be reached and instructed.

Much has been written in the lay press about this lifesaving measure, and quite properly the laity expects every doctor of medicine to be familiar with it and every hospital to be equipped and organized to treat this type of emergency properly, including the use of a defibrillator when indicated.

Has your hospital arranged for an "emergency" course? If not, contact at once the Subcommittee on Heart Disease of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

J. G. FRED HISS, M.D.

President's Page

JOSEPH A. LANE, M.D.

In my first communication to you through the pages of our JOURNAL, I feel it necessary to call attention to one or two problems that disturb me considerably.

The first concerns a complaint that was sent to the State Society office about the failure of physicians to respond to a call at a theater in New York where a man had a serious heart attack and later died in the hospital. Three doctors were contacted by telephone, and each one refused to respond, the reasons for this not being available to me at the present time. This incident caused widespread discussion in New York, and a television broadcast concerning it was extremely critical of the medical profession. Under similar circumstances, my opinion is that every effort should be made by a physician to provide whatever care is possible at the moment even if only to prevent criticism of doctors. The State Society has been offered time on the CBS network to controvert this incident, but it seems best not to do anything further about it at the present time. Even though the Governor failed to sign the "Good Samaritan Bill," it would seem highly unlikely that one could get into serious legal problems by answering a call such as the one that caused the current problem.

The other point that I wish to discuss at the present time is in regard to legislation, particularly to that referring to medical care to needy aged persons. The action of Congress recently has given us more time to continue our educational programs so that the public can be better informed of the limitations of a government-sponsored bill similar to King-Anderson or the modification of Senator Javits. It is disappointing to me that our two New York State Senators supported the compromise bill. I feel that we should all be extremely active in the next few months to try either to get better implementation of the Kerr-Mills Bill or to provide some method of adequate medical care for those who need it and who are unable to provide it financially by themselves. Continued close contact with our legislators is probably the best method we have to insure our outlook for better legislation, and extra effort should be expended continuously to obtain our objectives.

JOSEPH A. LANE, M.D., *President*

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6

Scientific Articles

SYMPOSIUM
AND PANEL
DISCUSSION

Massive Upper Gastrointestinal Hemorrhage

Moderator
VERNON A. WEINSTEIN, M.D., New York City
Associate Surgeon, The Mount Sinai Hospital; Attending Surgeon, City Hospital at Elmhurst
Panelists
JOHN L. MADDEN, M.D., New York City
Attending and Director, Department of Surgery, St. Clare's Hospital; Associate Clinical Professor of Surgery, New York Medical College, Flower and Fifth Avenue Hospitals
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Protocol for Management of Massive Upper Gastrointestinal Hemorrhage

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New York City
B. I. KORELITZ, M.D.
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CARLOS DIAZ, M.D.
New York City

Massive upper gastrointestinal hemorrhage is a problem that always taxes the clinician's therapeutic ingenuity. Despite numerous improvements in the technics of diagnosis and therapy there is still a high mortality rate associated with this condition. My purpose is to introduce this subject by giving a brief summary of the present methods of treatment as practiced in two large general hospitals in New York City: The Mount Sinai Hospital and City Hospital at Elmhurst.

In general, the methods of management to date have fallen into one of three categories: (1) the exclusively medical approach, in which surgery is never performed or at most only as a last resort. The adherents of this method claim that most of these bleeding episodes will stop and that the patient should be supported until that occurs; (2) the exclusively surgical approach, in which the viewpoint is taken that we do not know which cases will stop bleeding and that therefore surgery should be performed for all; and (3) the selective management which is

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Surgery, May 12, 1961.

TABLE I. Massive upper gastrointestinal hemorrhage: comparative results from the literature

Author and Type of Therapy	Number	Total Mortality (Per Cent)
Nonoperative approach or surgery as last resort		
Crohn[1]	2,875	10.3
Lesnick and Colp[2]	328	6
Gott, Smith, and Dornan[3]	195	5.6
Karlson *et al.*[4]	58	14
Operative approach or prompt surgery for all		
Stewart, Cosgriff, and Gray[5]	193	12.9
Karlson *et al.*[4]	37	14
Crohn[1]	805	10
Combined management or selective surgery		
Welch[6]	269	17
Karlson *et al.*[4]	35	14
Korelitz, Baronofsky, and Weinstein[7]	51	11.8

based on the premise that surgery during a bleeding episode carries greater risk than interval surgery but which tries to avoid delay in operating on those cases which probably will not stop bleeding spontaneously. This involves the use of diagnostic methods to aid in the recognition of such situations.

The medical literature abounds with reports of various types of therapy for massive upper gastrointestinal hemorrhage. Unfortunately, comparative statistics are often unreliable because of variations in the type of patient, the definitions of "massive," and the type of pathologic lesions which are encountered. The results obtained in city hospitals handling a large per cent of poorly nourished, elderly, and often medically neglected patients just cannot be equated with those obtained in institutions treating a younger or better cared for patient population. Also a high incidence of bleeding esophageal varices and gastric ulcers in a series always makes for poor statistical results. Obviously if the series is concerned with mild or moderately severe bleeding cases, the figures are better. In short, reports often reflect these variations rather than the efficacy of the therapeutic methods which are employed. Reports from the literature on the three approaches to therapy are briefly compared in Table I. The conclusions which are drawn from such total mortality figures are prone to be faulty. For example, even the report of Karlson *et al.*[4] in which a well-controlled series of cases was handled in three ways by the same investigators has been criticized for variations in case selection and the small number of cases. Nevertheless, certain valuable information can be culled from the literature. All studies show that the mortality rate increases with age and that some lesions are more dangerous than others. For example, it is evident from Table II that the bleeding gastric ulcer is much more dangerous than the bleeding duodenal ulcer. We have been impressed by the studies of Lesnick and Colp[2] on a series of massive upper gastrointestinal hemorrhage cases treated at The Mount Sinai Hospital at a time when these cases were never operated on during an acute bleeding episode and when blood transfusions were not given as readily as at present. They found that although the gastric ulcer mortality rate was 35 per cent, the duodenal ulcer mortality rate was only 4 per cent. Gott, Smith, and Dornan's[3] figures for duodenal ulcer are similar and equally impressive. Certainly the selective or surgery-for-all methods do not equal these results for duodenal ulcer.

We are of the opinion that the selective management offers the best results in therapy and therefore practice and teach this method. Since, however, this selective method depends on past personal experience and knowledge of the literature, it offers more difficult problems in the training of residents than the all-or-none approach of the first two modes of therapy. It is desirable to allow the trainee considerable freedom of action, and yet he must be supplied with a background of experience to guide him. With this in mind, the following protocol was outlined for the guidance of the residents at The Mount Sinai Hospital. These instructions are based on our convictions concerning massive upper gastrointestinal bleeding as outlined.

1. Bleeding in elderly patients is less likely to stop spontaneously than in young patients.

2. Certain lesions are more likely to cause fatal bleeding than others as follows:

TABLE II. Percentage results in duodenal versus gastric ulcers

Author	Duodenal Ulcer Operated On (Per Cent)	Duodenal Ulcer Mortality (Per Cent)	Gastric Ulcer Operated On (Per Cent)	Gastric Ulcer Mortality (Per Cent)
Lesnick and Colp[2]	0	4.0	0	35
Gott, Smith, and Dornan[3]	0	2.6	0	31.6
Atik and Simeone[8]	18.4	14.5	31	31
Smythe *et al.*[9]	35.5	8.8	75	25
Korelitz, Baronofsky, and Weinstein[7]	41.3	10.3	53	11.7
Stewart, Cosgriff, and Gray[5]	100	8.1	100	18

TABLE III. Results in massive upper gastrointestinal hemorrhage at City Hospital at Elmhurst, 1959 to 1960

Therapy	Number	Fatalities	Per Cent
Medical	17	6	35
Emergency surgery	15	6	40
Elective surgery	9	0	0
TOTALS	41	12	29

bleeding gastric ulcers more than duodenal ulcers, gastric neoplasms, or hiatus hernias. Bleeding from esophageal varices must be controlled promptly to avoid exsanguination or hepatic coma.

3. Surgery for diffuse gastric lesions is hazardous and should be avoided.

4. Early diagnosis is, therefore, vital and should be confirmed promptly by roentgenography or endoscopy.

5. A decrease in mortality may be expected if surgery is performed promptly in the elderly patient with dangerous lesions.

6. Emergency surgery carries a higher mortality than elective surgery. The experience of one of us (C.D.), noted in Table III, documents this fact.

Protocol

The following protocol is to be used as a general guide for the medical and surgical staffs.

The patient should be seen immediately and followed by both medical and surgical residents regardless of which service is primarily responsible. Call for urgent consultation* for all complicated problems on dangerously ill patients involving massive upper gastrointestinal bleeding.

DIAGNOSIS KNOWN. *Duodenal ulcer.* In cases of duodenal ulcer, operate for unusually massive continuous hemorrhage or recurrent severe hemorrhage while the patient is in the hospital.

If it is the first bleeding episode and the patient is under fifty years old, treat intensively with a medical regimen and blood replacement with no specific time limit for surgical intervention; if the patient is over fifty, operate if bleeding persists in the hospital up to twenty-four hours.†

If this is a second or subsequent bleeding episode and the patient is under fifty, treat intensively with a medical regimen and blood replacement, but operate if the bleeding persists up to twenty-four hours; if the patient is over fifty and prompt response to an intensive medical program is not evident, operate urgently.

Gastric ulcer. In gastric ulcer immediate surgical intervention is called for unless a cessation of bleeding is evident soon after blood replacement.

Combined gastric and duodenal ulcers. Combined gastric and duodenal ulcers are to be managed like gastric ulcers.

Esophageal varices. In esophageal varices local gastroesophageal cooling should be used. If the bleeding is not controlled, a decision can be made as to (1) further diagnostic procedures, (2) the use of a Sengstaken balloon, or (3) operation.

Gastric tumors. Gastric tumors should have emergency operative treatment after preliminary transfusions, with the exception of known inoperable or metastatic tumors.

DIAGNOSIS UNKNOWN. *Surgery.* If the circulation cannot be stabilized with blood transfusion, urgent surgery will probably be needed. Call consultants.

---

* Consultants are specifically named by the medical and surgical services.

† The use of specific age and time limits (for example, twenty-four hours) may seem unnecessarily arbitrary, but since the protocol is a guide, there must be some specifics, or it becomes worthless.

TABLE IV. Results of 63 emergency barium meal examinations*

Diagnosis	Positive	Negative
Proved correct	32	0
Proved false	4	6
Unconfirmed	15	6
TOTALS	51	12

* The Mount Sinai Hospital, 37; City Hospital, 26.

X-ray examination. If the patient is not in shock after blood transfusion is started, perform an upper gastrointestinal x-ray series immediately after lavaging the stomach with cold water, using an Ewald tube and strong suction, to remove the liquid and clots. The blood transfusion is to be continued in the x-ray department. A resident or assistant will accompany the patient during the x-ray examination.

If a diagnosis is made by x-ray, follow the program outlined previously for a known diagnosis.

If no diagnosis can be made by x-ray, flexible esophagoscopy should be performed. If bleeding varices are seen, treat as outlined previously for varices. If after esophagoscopy there is still no diagnosis, treat as for duodenal ulcer according to the age group. Gastric cooling may be utilized at this point.

Results with use of protocol

We have found the use of a barium meal x-ray examination most rewarding even during acute bleeding as noted in the protocol. The preliminary stomach lavage with cold water through a large tube to remove clots, plus continuing transfusions and careful supervision by the surgical or medical resident staff, in attendance at the time of the x-ray examination, are essential to this method. Table IV gives the results of such examinations at two hospitals. We have had no instances in which bleeding seemed to be increased as a result of the x-ray examination, although in 1 case at City Hospital an unsuspected perforated lesion was aggravated by the administration of barium.

The results of our experiences with the use of this selective method at The Mount Sinai Hospital over a three-year period are summarized in Table V. It is evident that an aggressive surgical approach was employed since a high percentage of patients were operated on: 41 per cent of duodenal ulcers and 53 per cent of gastric ulcers. A two-thirds to three-quarters gastrectomy was performed for all duodenal ulcers and most of the gastric ulcers brought to surgery. In 5 of the duodenal ulcer cases vagotomy was added. Suture ligation and local excision only were used in 2 gastric ulcer patients.

Summary

It is our conviction that the therapy for massive upper gastrointestinal bleeding should be selective. Prompt surgery, therefore, is advised for lesions and in patients known to be least likely to stop bleeding spontaneously. Emergency surgery is discouraged for lesions that are likely to stop or that experience has shown are not amenable

TABLE V. Results of combined management of massive upper gastrointestinal bleeding at The Mount Sinai Hospital, 1956 to 1959

Final Diagnosis	Number	Number Operated On	Number Survived	Mortality (Per Cent)
Duodenal ulcer	29	12 (41 per cent)	26	10.3
Gastric ulcer	17	9 (53 per cent)	15	11.7
Gastritis, erosions	3	3	2	. .
Gastrojejunal ulcer	5	5	4	. .
Gastric neoplasms	4	4	2	. .
Metastatic neoplasms	4	2	2	. .
Hiatus hernia only	2	0	2	. .
Not made	6	0	5	. .
TOTALS	70*			17.2†

* Esophageal varices excluded.
† Mortality in peptic ulcer only, 11.8 per cent.

to surgery. This regimen involves the use of definitive diagnostic measures, for example, x-ray and endoscopy, and broad clinical experience to permit the proper selection of therapy.

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Vagus Resection in Treatment of Bleeding Duodenal Ulcer

JOHN L. MADDEN, M.D.
New York City

MY TOPIC is vagotomy and pyloroplasty for acute massive hemorrhage. We instituted this method of treatment in May, 1960, and during the past year 12 patients have been treated in this manner (Table I).

It is most important to classify cases of acute massive upper gastrointestinal hemorrhage into those in whom the bleeding is controlled and those in whom it is uncontrolled since both the morbidity and the mortality vary accordingly.

In 5 of the 12 patients the operation was done for the control of active bleeding. In the remaining 7 patients the operation was elective and was performed at varying periods following the cessation of bleeding.

This series of cases is interesting in relation to the age of the patients. Those patients with uncontrolled bleeding were on the average five years younger than those in whom the bleeding was controlled. The average age was forty-five and fifty years respectively. It is believed most arbitrary to base the type of treatment to be employed on a given age of the patient. A twenty-year-old patient may bleed to death as well as a patient sixty years of age. Each patient should be rigidly individualized and treated according to the clinical manifestations presented and the response to treatment rather than according to age per se.

Procedure

In 2 of the 5 patients with uncontrolled bleeding the ulcer bed was plicated, and vagotomy and pyloroplasty were performed. In another an anterior wall ulcer was first excised. In the fourth patient the site of bleeding was undetermined. In the last patient the source of bleeding was a marginal ulcer as a complication of vagotomy and gastroenterostomy which were performed eighteen months previously.

In the 7 patients in whom the hemorrhage was controlled there were no deaths following elective operations. The age range and hemoglobin values for this group of patients are as indicated in Table I.

In 1949 Westland, Movius, and Weinberg[1] suggested gastroduodenotomy, plication of the ulcer, pyloroplasty, and vagotomy in the treatment of acute massive uncontrolled hemorrhage. In the first 6 patients treated, a vagotomy was not done concomitantly but

TABLE I. Vagotomy and pyloroplasty for acute massive upper gastrointestinal hemorrhage

Condition	Number of Patients	Average Age* (Years)	Sex M	Sex F	Deaths Number	Deaths Per Cent
Hemorrhage uncontrolled	5	45.8	3	2	1	20
Plication of ulcer	2				1	
Excision of ulcer	1				0	
Site undetermined	1				0	
"Marginal" ulcer	1				0	
Hemorrhage controlled	7	50.6	7	0	0	0
TOTALS	12	49	10	2	1	8.3

* Range: 26 to 68 years; hemoglobin values: 6 to 9 Gm.

TABLE II. Vagotomy and pyloroplasty for acute massive upper gastrointestinal hemorrhage

Author	Number of Patients	Failures Number	Failures Per Cent	Deaths Number	Deaths Per Cent
Westland, Movius, and Weinberg, 1949 to 1958[1]	24	1	4.1	0	0
Farris and Smith, 1955 to 1960[2]	48 (18)*	3	6.2	2	4.1
Madden, 1960 to 1961	12 (7)*	0	0	1	8.3
Combined totals	84	4	4.7	3	3.5

* Patients in whom bleeding controlled prior to operation.

was deferred for from a week to ten days. One of these 6 patients died of recurrent hemorrhage two weeks after the operation before a vagus resection had been done. In 24 subsequent patients vagus resection was done concomitantly. Accordingly, the first 6 patients have not been included in this discussion. In this group of 24 patients there was 1 failure and no deaths. Farris and Smith,[2] using the same procedure, reported a series of 48 patients in 18 of whom the bleeding was controlled before operation. There were 3 failures and 2 deaths. These series combined total 84 patients with 4 failures (4.7 per cent) and 3 deaths (3.5 per cent) (Table II).

I recently reviewed our own experience over the past five years and analyzed the various procedures that were done in the treatment of acute massive upper gastrointestinal hemorrhage (Table III). The disparity in the mortality rates between the emergency and elective operation is strikingly shown. As Dr. Weinstein previously stated, his mortality rate was 40 per cent when gastrectomy was done to control acute active gastric bleeding.

In 20 patients vagotomy and hemigastrectomy were performed, and 1 (5 per cent) died. Scott and his associates[3] recently reported their experience with this operation in 765 patients. In 317 of the patients a gastroduodenostomy (Billroth I) was done, and in 340 a gastrojejunostomy (Billroth II) was performed. In 200 of the 765 patients hemorrhage was the indication for operation, but it was not stated how many operations were done to control acute and active bleeding. In a discussion of the efficacy of any operation performed in the treatment of upper gastrointestinal hemorrhage, I should like to emphasize the importance of separation of the patients treated into 2 groups: (1) those in whom the operation was done as an acute emergency measure for the control of bleeding and (2) those in whom the operation was an elective procedure after bleeding had ceased. The disparity in the mortality rates in each group was mentioned previously (Table III).

In 49 patients vagotomy and gastroenterostomy were done, all of which were elective operations. There was 1 (2 per cent) death. The remaining 12 of the total series of 112 patients comprised those in whom vagotomy and pyloroplasty were

TABLE III. Procedures used in treatment of acute massive upper gastrointestinal hemorrhage

Procedure	Number of Patients	Average Age	Deaths Number	Deaths Per Cent
Partial gastrectomy	31	54.8	4	12.9
Emergency	17	54.8	4	23.5
Elective	14	54.8	0	0
Vagotomy and hemigastrectomy	20	49.1	1	5
(Scott *et al.*, 765 patients)	(200)		(9)	(4.5)
Vagotomy and gastroenterostomy	49	52.3	1	2
Vagotomy and pyloroplasty	12	49.0	1	8.3
Emergency	5	45.8	1	20
Elective	7	50.6	0	0
TOTALS	112		7	6.2

done. Of the 112 patients operated on for hemorrhage, either emergency or elective, 7 died, a mortality rate of 6.2 per cent.

In a review of our own experience, which numbers 650 patients, in whom resection of the vagus nerves was either the sole procedure or a concomitant of a combined operation, the relatively high incidence of the postoperative malabsorption syndrome gave us considerable concern. Accordingly, during the past nine months, selective vagotomy and pyloroplasty have been practiced. In this operation, too early to comment on, the branches of the vagus nerves to the stomach are severed, leaving intact the hepatic, celiac (pancreatic), and intestinal innervation. A final comparison will indicate the efficacy of this particular operation.

Conclusion

In conclusion I would like to say that in the treatment of acute massive upper gastrointestinal hemorrhage, particularly in the patient with uncontrolled bleeding, gastroduodenotomy, plication of the bleeding vessel when indicated, pyloroplasty, and vagotomy, in that order, comprise a simplified anatomic and physiologic approach to a serious surgical challenge.

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Experiences with Local Gastric Hypothermia

ARTHUR B. VOORHEES, JR., M.D.
New York City

DURING THE COURSE of a year we see a reasonably large number of acute gastrointestinal bleeders at the Presbyterian Hospital. Knowing that it is dangerous to lump figures together since there are vast differences in the circumstances involved in each instance, it seems fair, nevertheless, to state that approximately two thirds to three quarters of the patients bleeding from the upper gastrointestinal tract, predominantly from peptic ulceration, stop spontaneously while on conservative supporting therapy.

The patients who do not stop on simple supporting measures require some sort of surgical intervention in most instances, and in this group there is roughly a 10 per cent hospital mortality rate associated with our efforts to control the bleeding.

On a recent review of our experiences over the past five years in controlling bleeding from esophageal varices, we were particularly disappointed to learn that we had effected satisfactory control in approximately 50 per cent of such patients who came to our hospital.

In 1958 O. H. Wangensteen, M.D.,* at the University of Minnesota, adopted a technic which had been designed originally to diminish hyperpyrexia in children as a method of controlling bleeding from the upper gastrointestinal tract. Because of the obvious potential advantages of controlling bleeding by this technic, Stephen L. Wangensteen, M.D., initiated a program at the Presbyterian Hospital which has been in effect for the past fourteen months. It is certainly too early to advance any significant data, but I would like to share with you some of the earlier figures that we have accumulated.

Material and method

The initial subjects for the technic were selected from a group of patients who were not suitable for operative intervention, who were bleeding rapidly from the upper gastrointestinal tract, and who did not respond to the usual conservative measures.

The (O. H.) Wangensteen cooling device is composed of a coaxial nasogastric tube connected to a balloon which is inserted in the stomach. A cold fluid is circulated at a known rate through this circuit which in turn cools the stomach wall and the adjacent tissue to a predetermined amount.

Dr. Stephen Wangensteen with the cooperation of the manufacturers has devised a commercially produced device which is simple to operate and exerts precise control over the circulation and temperature of the refrigerant.

The gastric balloon, which contains between 500 and 1,000 cc. of an alcohol-water mixture, is in contact with the major surface area of the stomach and the lower portion of the esophagus. In most instances that will be reported today, the temperature of the cool solution is maintained at approximately 4 C.

A compact device has been developed, regulated by a simple control panel on the front of the unit. The unit can be wheeled to the bedside of the patient and occupies no greater space than that which is taken up normally by an oxygen tent. The actual control of the machine can be mastered after a few minutes of instruction. Although the technic is simple, we feel at this stage of our development that close monitoring of the patient is essential to avoid a possible accident.

The gastric balloon is of simple construction: It utilizes a toy balloon which, when it is inflated, assumes a gourd shape. After insertion into the stomach, the neck of the gourd-shaped balloon lies in the lower portion of the esophagus, and the body of the balloon lies in the cardia and fundus of the stomach.

Results

Utilizing this particular method of the esophagogastric cooling in a highly selected group of upper gastrointestinal tract bleeders over the past fourteen months, we have attempted to control hemorrhage in 31 patients. In this group there have been 11 bleeding from esophageal varices. All have been controlled, which represents a substantial change from the results which we experienced prior to this time with other methods of treatment for the control of bleeding from this source. Of the group of 11 patients whom we have treated for bleeding esophageal varices, 10 were caused by cirrhosis of the liver and 1 by an extrahepatic portal block which was due to a portal vein thrombosis.

In addition to these 11 patients bleeding from varices, we have treated an additional 6 patients bleeding from gastric ulcers, which were confirmed by subsequent operation or by a gastrointestinal series. In the gastric ulcer group, the bleeding was controlled in 50 per cent of the patients, or 3 of the 6.

Four bleeding duodenal ulcers were treated, and the bleeding was controlled in all 4.

The remaining 10 patients had stress ulcers and steroid-produced ulcers in the stomach and duodenum. In this group of

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* Wangensteen, O. H., *et al.*: Depression of gastric secretion and digestion by gastric hypothermia: its clinical use in massive hematemesis, Surgery **44**: 265 (Aug.) 1958.

10, the bleeding has been controlled in 50 per cent of the cases.

Summary

We believe that gastric hypothermia is an excellent device for controlling bleeding but does not represent a method of correction of the basic cause of the bleeding.

We feel that the value of this technic clinically is as a method of holding the patient in a state in which the blood loss is held at the minimum and that this holding period gives the surgeon an opportunity to prepare the patient for a definitive procedure.

The recurrence rate of bleeding after the cessation of cooling is high; therefore plans for definitive surgical measures should be made during the period of time in which the bleeding has been held in abeyance.

Management of Massive Bleeding from Esophageal Varices and Indeterminant Gastric Lesions

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In spite of the fact that for several years surgeons have become actively engaged in the salvage of patients who are bleeding from esophageal varices associated with cirrhosis of the liver, no spectacular progress can be reported presently in the over-all picture. The mortality rate still remains high for this complication of liver disease. We are still in the experimental phase of the development of a sound policy for handling this problem in which one's opinion changes with experience. Much of the new experience, I might say, has been disheartening.

Emergency surgical intervention using portacaval shunts, ligation of varices, or transection of the stomach carries a high mortality in my experience, particularly in those patients whose situation is desperate. Reports on the use of surgery have shown promise in some instances, but there are no convincing statistics involving a large number of patients showing a reduction of the death rate from hemorrhage by operating. Tamponade by using the Blakemore-Sengstaken tube has been a disappointment, not because this tube does not stop hemorrhage, for it usually does, but because hemorrhage usually recurs after the release of the tamponade, and the deterioration of the patient's liver proceeds rapidly. I have always felt that surgery is the only really effective means for stopping hemorrhage. These patients are extremely fragile, however, and a selection of patients who have a better chance by operation must be made to avoid making bad matters worse, which latter will surely follow indiscriminate operative intervention.

The mortality rate for hemorrhage in patients with cirrhosis depends on the cases included in any series. We are interested in the group for which something might conceivably be done. This would exclude patients dying of liver disease in whom a final hemorrhage occurred. These patients cannot be helped and should be excluded from a practical estimation of the clinical problem. Perhaps a mortality rate of 40 to 50 per cent is a fair estimate of the situation in patients who are not terminal and for whom something might be done.

Over the past ten years I have tried almost all approaches to the control of hemorrhage from varices. On the nonoperative side I have used the Blakemore-Sengstaken tube tamponade technic and, more recently, gastric hypothermia. Both of these methods usually will stop the hemorrhage, but unfortunately not permanently, nor for long enough time for the patient to recover sufficiently so that an elective portacaval shunt can be carried out with a low mortality rate. Repeat bleeding within a few days after tamponade is the rule in the majority of patients, and general deterioration with impaired liver function results. Operations to be undertaken at this time (the second bleeding) seem indicated in a desperate situation, but they are often fatal, and the over-all results do not recommend them highly. Nevertheless, there is little else to do.

I have had a shorter experience using gastric cooling, but I am inclined to favor it over tamponade, although I believe that rebleeding will be found to occur as commonly. Cooling, therefore, is a temporary expedient to stop hemorrhage also.

The problem is to stop bleeding permanently, which means that surgery must be done as soon as possible before the patients rebleed. But to justify the intervention which entails a portacaval shunt or ligation of the varices is hard to do for the majority of bleeding cirrhotic patients. I have employed emergency portacaval shunt, ligation of esophageal varices, both by the transthoracic and the transabdominal route, gastrectomy, and gastric transection (Tanner's procedure), all with poor results, that is to say, with a high mortality rate. Most of my patients had been treated several days by tamponade and were operated upon on rebleeding. The proponents of early emergency surgery would say that such operations were done too late. That is to say, temporizing with tamponade, expectant treatment, and waiting until a second bleed forces one's hand is a losing game. If emergency surgery is to be done it must be carried out preferably within eight hours. Liver deterioration follows hemorrhage rapidly, and indeed these patients do die of liver failure after surgery. There may be considerable merit to the idea of true emergency surgery since almost all of the patients I see have bled several days before and either have stopped or have a tamponade treatment for variable periods. However, my experience still makes me doubt the advisability of rushing these patients to the operating room.

The fortunate patient who has bled from varices is he who stops spontaneously. He should be subjected to portacaval shunt as soon as possible if he is a reasonable risk from the standpoint of liver function. Roughly speaking, such a patient is one without jaundice and ascites and with reasonably good liver function. Whenever bleeding has to be stopped by tamponade, the patient is in for trouble.

Selection of patients

We classify our patients in Groups, A, B, and C, to decide whether or not we shall do an early operation after having stopped bleeding by tamponade or cooling. The operation we prefer is a direct end-to-side portacaval shunt rather than preliminary ligation of the varices. These groups could be called "Yes," "Maybe," and "No." Group A patients (Yes) should have shunts as soon as they are stabilized. These patients, as I said, have no jaundice or ascites, and their appearance is good. They would be acceptable for an elective shunt. Group C (No) includes all terminal failure patients who bleed and those who have poor liver function, as exhibited by clinical jaundice, ascites, prolonged prothrombin times, and so forth. Group B (Maybe) represents a class from which one may select certain patients for surgery based on the clinical circumstances of the hemorrhage and their liver function. Patients with borderline liver function whose appearance is good and who have bled only recently fall into this group for early operation. Portacaval shunts which are done after preliminary treatment by tamponade or cooling cannot be classified as emergency surgery. More correctly, this approach may be called urgent surgery. That is to say, its object is to perform a portacaval shunt before the patient bleeds again. This means that a shunt is performed from forty-eight hours to one week after the initial bleed.

Patients with cirrhosis who do not stop bleeding with the tamponade technic probably should be explored if they fall into an acceptable risk group (A and B). In these individuals hemorrhage from a gastric or duodenal ulcer is to be suspected. Possibly gastric varices or gastritis may be the cause of hemorrhage in some such instances.

Management

I have been asked to describe the management of patients bleeding from the upper gastrointestinal tract in whom the cause of bleeding cannot be determined. This brings us to a discussion of diagnosis. The first thing to be done in all clinical problems of bleeding from the upper gastrointestinal tract is to rule out liver disease. This can be done almost always with the combination of history, physical examination, and liver function tests for making the decision.

Once liver disease is excluded, the patient is presumed to be bleeding from an ulcer, gastritis, or indeterminate cause. Whether or not such patients need be subjected to emergency surgery depends on their course. If one is dealing with an exsanguinating hemorrhage requiring much blood replacement to maintain blood pressure, the patient must be operated on at once without an extensive diagnostic work-up. Patients of this sort are bleeding from the erosion of a major branch of the gastroduodenal artery, from a gastric ulcer, or from gastritis. For the slower bleeder, offering less difficulty in maintaining blood pressure but requiring 2 to 4 pints of blood per day, it may be profitable to perform a barium study of the stomach. Continued bleeding, however, is an indication for exploration, whether or not a positive diagnosis can be made.

In general, I recommend partial gastrectomy for patients bleeding from a gastric ulcer, gastritis, or indeterminate lesions. For patients with a hiatus hernia, who may be bleeding from esophagitis and gastritis, I employ repair of the hernia, vagus nerve resection, and pyloroplasty. For patients with duodenal ulcer, partial gastroduodenectomy is still the operation of choice for the good-risk patient. For the poor-risk patient, the combination of vagus nerve resection, transfixion of the bleeding vessel in the ulcer, and pyloroplasty is probably the best choice. The latter operation is the safest and should be used by surgeons of limited experience of gastric surgery. It is a good choice if the anatomic situation looks technically difficult. One should remember that the mortality of gastric surgery is due to the operation principally; that is to say, dehiscence of the duodenal closure in the Billroth II procedure is the bête noire of gastrectomy. The combination of vagotomy, suture of the bleeding vessel in the ulcer, and pyloroplasty avoids this hazard, and this procedure seems to be very effective in controlling duodenal ulcer hemorrhage.

Question and Answer Period

Dr. Voorhees: Dr. Madden, do you reserve your particular approach for duodenal ulcers only?

Dr. Madden: We have used it in gastric ulcers. Oddly enough, the most common lesion in the female has been the gastric ulcer rather than the duodenal ulcer. In the group of 12 patients in whom pyloroplasty was done, we had 1 who had a gastric ulcer. This was a woman who was massively bleeding and had gone into shock on two occasions before she was operated on. At operation she had a hugely distended stomach, and, when we evacuated the clots, we saw a spurting vessel in the base of an ulcer on the lesser curvature. We plicated the bleeding vessel and closed the stomach, and then we did a vagus resection. We also repaired a diaphragmatic hernia and performed a pyloroplasty. That was the only patient with a gastric ulcer in this series.

Dr. Voorhees: But you would say, wouldn't you, that gastrectomy is preferred for gastric ulcer?

Dr. Madden: Yes, gastrectomy is preferred for gastric ulcer, but I have yet to see a high-lying, lesser-curvature, massively bleeding ulcer which was malignant. The resection of these ulcers extends greatly the magnitude of the gastric resection. I should say parenthetically that I was brought up as a resectionist. However, when one follows the patients who have had high gastric resections one finds that persistent anemia and nutrition difficulties are disturbing complications. I do not believe that resection is the best operation. That is why in 1949 we switched to vagus resection plus a drainage procedure. It is a much more physiologic procedure than gastrectomy. I think that the advisability of removing two thirds to three quarters of the stomach in the treatment of benign gastric and duodenal disease certainly should be questioned.

Dr. Madden: How many times have you seen massive gastric hemorrhage proved to be due to carcinoma?

Dr. Weinstein: In our series of massive hemorrhage cases, in three years we had 17 patients with benign gastric ulcers, 2 with benign multiple ulcerations, and 3 with gastric carcinomas. We also had 3 benign tumors of the stomach, not carcinomatous, that bled massively. In short, carcinomas do bleed, not nearly as often as benign ulcers, but they do bleed massively at times.

Question: Dr. Welch, what do you do when, following a partial gastrectomy, bleeding occurs from the remaining unresected stomach?

Dr. Welch: Usually, of course, such a patient has multiple superficial ulcerations. I have seen these patients bleed ferociously from the remaining gastric remnant. I have washed the stomach out with cold water and have been able to stop them by this simple gastric cooling technic. However, they often bleed the moment we stop cooling. I feel that this is merely a temporizing measure. The best thing to use is the Blakemore tube, exerting upward pressure to control the bleeding from the remaining gastric pouch.

Dr. Weinstein: I have a question which I would like to introduce by saying that Palmer,[a] a noted gastroenterologist, but not a surgeon, advised an urgent total gastrectomy for massive bleeding from diffuse gastritis and/or superficial ulcerations. Dr. Welch, do you find it necessary to do total gastrectomy for hemorrhagic gastritis?

Dr. Welch: Dr. Voorhees mentioned that he has done it on a few occasions. I have not. When I say that I have not had a patient who died of such bleeding, that is in my own personal practice. We certainly have had them in our hospital, but I have never done a total gastrectomy for that condition.

Question: Dr. Voorhees, how much hemostatic action results from the tamponade effect on esophageal varices, and how much is due to refrigeration?

Dr. Voorhees: The question has often been asked as to how much tamponade effect we get from the water-filled, gourd-shaped balloon. There is no doubt that there is pressure being exerted on the posterior wall of the esophagus and on the stomach in contact with this balloon.

We do not know how to assess the actual effect of this. We do know, however, that bleeding control seems to be independent of the size of the balloon and often the position of the balloon; and by size, I mean the exact volume content. We have stopped esophageal bleeding when the balloon, through error or through deliberate intent, has been left in the stomach and not in the esophagus; in such cases there has been no tamponading effect in the esophagus itself.

The amount of pressure exerted in those instances in which the balloon was in the esophagus probably is very small and limited to the posterior wall. I think it is asking a little too much of pure chance to claim that all the patients in whom bleeding was controlled were bleeding from a varix situated directly posterior.

Perhaps the most significant factor is the reduction in the circulation of the stomach and the esophagus. At operation these are practically white organs which scarcely bleed when you cut them.

Dr. Welch: Dr. Voorhees, I would like to ask you to comment on the emergency ligation of esophageal varices. I have never really heard your experience with this method.

Dr. Voorhees: I think our experience has been precisely the same as yours.

Prior to the use of gastric hypothermia, we ran into a 50 per cent over-all failure rate in the control of acute hemorrhage from varices. We divided them into two major groups: those with ascites and those without.

During a two-year period, out of a group of 60 consecutive cases treated by the same team, 25 were admitted to the hospital bleeding actively. Of the group that did not have associated ascites with their disease (a hallmark of an advanced state of their disease), the balloon tamponade technic, using the Blakemore-Sengstaken balloon without refrigeration, stopped bleeding in 6. The balloon failed to stop the bleeding in 3, and 3 stopped spontaneously before the balloon was put down. So, roughly, our batting average on that was 9 cases out of 12, or 75 per cent.

In the group that had ascites at the onset of bleeding, the Blakemore balloon stopped only 3 and failed to stop 10.

In the past when we resorted to ligation of esophageal or gastric varices, our mortality rate was nearly 100 per cent. Of course, this was a particularly selective group, selected by virtue of the fact that more conservative measures had not stopped the bleeding. The mortalities were due either directly to the surgical procedure itself and the attendant shock or to the subsequent disruption of our suture lines with massive sepsis.

QUESTION: Dr. Voorhees, do you think that there is any value to general or systemic hypothermia in the treatment of bleeding varices?

DR. VOORHEES: Yes, I do. As Dr. Welch has mentioned earlier, we are dealing primarily with an individual with liver disease who has coincident hemorrhage. When such an individual comes into the hospital, assuming that he has Laennec's cirrhosis, a very substantial part of the functioning liver tissue is virtually on the brink of anoxia. Most are in a hypovolemic state, and many of them are in true shock. It is reasonable to assume that damage has been done to the hepatic cell which may not become apparent to the clinician for some time following the episode.

It has been postulated that if we could reduce the metabolic demand on these people during the time of their acute hemorrhage we would diminish in some way the demand on a liver that has been damaged by the hemorrhage and the attendant anoxia. Based on this, we have tried in certain instances in what would be Dr. Welch's Group B and perhaps even Group C to carry these people not only on local gastric hypothermia but also on general systemic hypothermia. Technically this is very simple because if we don't warm these people and keep their body temperatures up, they become hypothermic from gastric refrigeration alone. We have carried several people successfully for periods of upwards of a week in an artificially induced hibernation from which they wake up from time to time; subsequently they are operated on at the end of five, six, or seven days following the initial control of their hemorrhage. Although it is dangerous to draw any conclusions from these early experiences, it has been perfectly astonishing how well they have done over this period; whether or not the hypothermia itself has contributed to the protection of the hepatic cells I do not know.

DR. WEINSTEIN: In summary, then perhaps we may say that local hypothermia stops the bleeding, and the general hypothermia helps the body withstand the hypovolemic state.

DR. MADDEN: Dr. Voorhees, have you any plans for the use of this technic in converting the emergency and urgent cases of massive gastric hemorrhage into elective ones?

DR. VOORHEES: At the moment, I think that the technics that we are using have to be limited by the facts that we really don't know the parameters and that we have had a very substantial number of complications. For instance, we have had 2 instances of gastric rupture.

In addition to this, with a patient under gastric hypothermia, you convert the individual into something physiologically quite different. For example, the hypothermia will induce an ileus, and this in a cirrhotic patient who has a gut filled with blood may result in profound episodic stupor which in itself becomes a great problem.

Added to these problems, drug dosages have to be altered. A man with gastric hypothermia and systemic hypothermia will sleep for three or four days on perhaps a total of 200 mg. of barbiturates.

At the moment we know relatively little about this treatment, and it has to be carried out under strict control. At this time, it is not practical to use it as a means to defer urgent surgery. On the other hand, from what we have seen, its ultimate value will be as a method of converting urgent to elective surgery.

QUESTION: Can the technic of gastric cooling be applied to a stomach full of clots?

DR. VOORHEES: The answer here is no. We have to introduce into the stomach a very large monitoring nasogastric tube (22 to 24 French) through which we can evacuate the clots.

We have gotten into troubles in the past with stomach rupture as a result of an undetected retained clot. The volume of the clot plus 1,000 cc. of refrigerant in the balloon may exceed the gastric capacity and lead to rupture. In addition, a retained clot does not transmit heat exchange effectively.

Dr. Weinstein: Are you really successful in getting the clots out by using the nasogastric tube coincidentally with the balloon?

Dr. Voorhees: Yes. We put down the nasogastric tube first. In addition to removing the clots, it tells you whether or not the person is still bleeding and whether or not gastric hypothermia is indicated.

Dr. Madden: Although this question is not strictly apropos, I had better answer it so that I will not be misinterpreted. The question is: "What is the rationale of vagus resection for gastric ulcers?"

Others have reported that vagotomy has no place in the treatment of gastric ulcers, and I agree with that. From 1949 to 1952 in the early part of our experience, we performed vagotomy alone on 13 patients with gastric ulcers, and I subsequently performed partial gastrectomies and gastroduodenostomies on 7 of these.

However, I want to impress on the group that we are now talking about massive upper gastrointestinal hemorrhage and the operation to be done as a lifesaving measure. I would like to mention 1 patient in the group who had hemorrhage from a gastric ulcer. We did a transfixion plication and a biopsy of the ulcer. The biopsy specimen was benign. Of course, one can say, "Well, that's not a good idea, either, because you may not get the malignant tissue in your biopsy specimen." That is true; but in the face of acute massive hemorrhage it was believed to be the proper procedure. In short, then, vagus resection has no place as far as the definitive treatment of gastric ulcers is concerned. The ideal treatment of gastric ulcers is partial gastrectomy. There is only one exception, and that is the massive gastric hemorrhage from multiple superficial, mucosal ulcerations. I do believe that here vagus resection has a definite place.

Dr. Weinstein: Dr. Madden, you said in your earlier presentation that a bleeding duodenal ulcer even in very young patients may not stop spontaneously. I was just wondering if you had ever seen a young man, or indeed any one under thirty years, who bled to death from a duodenal ulcer.

Dr. Madden: Yes; one, a twenty-five-year-old man who bled to death from a duodenal ulcer.

Dr. Voorhees: I had one, too. He didn't bleed to death, but he had two cardiac arrests before we stopped the bleeding, so I think that is close enough. Some of these cases don't even reach the hospital.

Dr. Welch: I mentioned the fact that in these terribly ferocious bleeders the ulcer usually has eroded a large vessel, and this may occur in a young person, although the incidence is small. Actually, the incidence of death in the over-all statistics of those under forty or fifty years old was about 2 per cent, and those could be accounted for in young people by an erosion into major vessels. Those have to be operated on immediately.

Dr. Weinstein: In our series we had 8 massively bleeding duodenal ulcers in patients under fifty years of age. We operated on 3 of these because we felt that they wouldn't stop bleeding; but these 3 were all in their forties. Crohn,[b] in a review of a large series of massive bleeding peptic ulcer cases, states that it is extremely rare for a patient under thirty years of age to die from a bleeding duodenal ulcer.

If there are no further questions, I would like to thank the panelists and the other members of the program for a very interesting morning.

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[a] Palmer, E. D.: Hemorrhage from erosive gastritis and its surgical implications, Gastroenterology **36:** 856 (1959).

[b] Crohn, B. B.: Need for aggressive therapy in massive upper gastrointestinal hemorrhage, J.A.M.A. **151:** 625 (Feb. 21) 1953.

Research in Demyelinating Disorders

Current Trends

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THE DEMYELINATING DISORDERS *may be divided into those which appear in adult life and are characterized by a long remitting course and eventual severe morbidity and those of childhood or infancy which are characterized by a relatively short course, progressive and steady development of signs and symptoms, and early death. The first group consists of multiple sclerosis and the second of the leukodystrophies, in which dysmyelination, rather than true demyelination, occurs. An exacerbation of a demyelinating process is often preceded by an infection of the respiratory, gastrointestinal, or urinary tract. Encephalomyelitis has been produced experimentally in animals, but not without inflammation, and the chronic remitting course of human multiple sclerosis has never been reproduced. Environmental and genetic factors are probably involved in the demyelinating diseases, but adequate studies have yet to be done.*

I HAVE SOME INTEREST in research and shall review some significant recent developments in the field of multiple sclerosis and demyelinating disorders in general, but I must confine my remarks to the most promising lines of inquiry in this field.

It might be interesting to review some recent discoveries[1-5] regarding the biology and formation of myelin. Many new advances have taken place in the last decade, stimulated by the newer technics of electron microscopy, x-ray defraction microscopy, and neurochemical methods. For example, electron microscopy has given us information which indicates that all fibers are myelinated, although the smallest so-called unmyelinated fibers may simply be covered by a monomolecular or a bimolecular layer of myelin. Functionally, the physiologists still consider these fibers nonmyelinated, but from the morphologic and chemical standpoint all nerve fibers must be considered as covered by a myelin sheath.

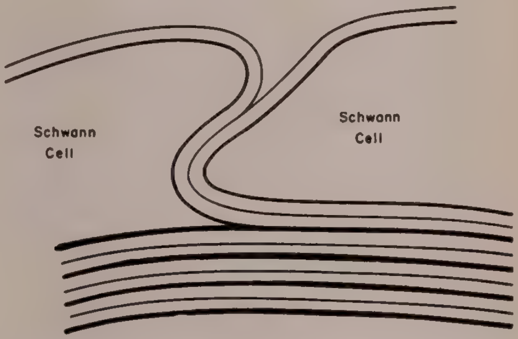

FIGURE 1. Cytoplasm of Schwann Cell showing myelin.[1]

Neurochemistry has shown us that the structure of myelin is formed by proteolipids as well as by cerebrosides and sphingomyelin. The myelin sheath is composed of several concentric layers which are made up of parallel strands of proteolipid with radiating radial spokes of lipid material interspersed. One of the most interesting developments in recent years has been the discovery that myelin is actually a part of the cytoplasm of the Schwann cell (Fig. 1).

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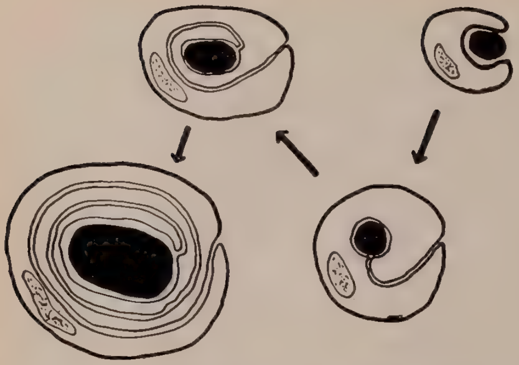

FIGURE 2. Formation in peripheral nerves of myelin in spiral fashion with Schwann cell migrating along axon and rotating around it.[3]

The myelin layers are continuous with the outermost layers of the Schwann cell. Myelin is laid down (in the peripheral nerves) in a spiral fashion with the Schwann cell presumably migrating along the axon and rotating around it (Fig. 2). There is considerable evidence to show that myelin is a product of this cell but that it is elaborated only in the presence of an intact axon. At the site of a disrupted myelin sheath numerous mitochondria congregate in the axoplasm prior to the formation of a myelin layer. This suggests active participation by the axon in myelin formation.

Currently, there is controversy about the presence or absence of small canals or breaks in the myelin sheath, and the structure of the nodes of Ranvier is little understood. All this has bearing on the electrophysiologic changes which take place during the excitation of the axon and the passage of various ions across the cellular membranes during activation. It is increasingly clear that in the central nervous system there is only a small extracellular fluid compartment in contrast to those in other areas in the body. The glial cells probably perform the function of an extracellular space and interpose between the capillaries and the nerve cells, performing a function of transfer rather than passive diffusion of ions. Katzman[6] has performed some original research on this point.

In the central nervous system the more or less traditional role of oligodendroglia in the production and maintenance of the myelin sheath is being questioned at the present time. It is possible that astrocytes are as important as the oligodendroglia in the formation and maintenance of the myelin sheath. The role of the myelin sheath itself is not fully elaborated. Myelin must have insulating as well as nutritive functions and may have some function in supporting the long axon of the nerve cell. It is possible to think of myelin as analogous to collagen in other tissues, performing a function of support without which the central nervous system could not function.

Classification of demyelinating conditions

Passing on to the classification of demyelinating conditions, I will introduce a new concept which has been proposed by Poser.[7] In a simplified fashion demyelinating disease can be separated into those which appear in adult life and are characterized by a long remitting course and eventual severe morbidity and those of childhood or infancy which are characterized by a relatively short course, progressive and steady development of signs and symptoms, and early death. The first group would then be labeled multiple sclerosis, of the type familiar to all of us. This would probably include some of the demyelinating conditions of infancy such as Schilder's disease, but it would exclude those conditions which have been described as leukodystrophy. It is the second group for which Poser has proposed the term dysmyelination.

In the first group the pathophysiology involves a progressive breakdown of myelin through a prelipid stage to neutral fats. The neutral fats are then engulfed by histiocytes which are carried away in the blood stream. There is, secondarily, progressive scarring in the form of gliosis in the area of plaque formation. The axis cylinders are well preserved. In the second group, that is, leukodystrophy or dysmyelination, myelin elements do not break down into neutral fats, but remain in a prelipid state. This results in the peculiar staining properties of the accumulations of myelin catabolism.

This second group is being studied intensively by histochemical technics. It is currently thought that prelipids accumulate in abnormal amounts in the central nervous system, and, indeed, in some conditions, such as metachromatic leukodystrophy, they have appeared in other organs and can even be identified in urinary sediment. Occasionally, particular lipid complexes may be elaborated which act as foreign body stimulants resulting in the production of giant macrophages known as globoid cells. It is this group in which Brain and Greenfield[8] have described the degeneration of the interfascicular oligodendroglia as an integral part of the pathologic picture. These facts suggest a primary metabolic abnormality of myelin formation, linking the leukodystrophies to the well-known lipid storage diseases such as Tay-Sachs and Niemann-Pick. It is for this group that Poser[7] has proposed the term dysmyelination, clearly identifying it as inborn error of myelin synthesis rather than a breakdown of normal myelin: (1) Pelizaeus-Merzbacher disease; (2) leukodystrophies of the simple storage type (formerly known as the "glial insufficiency" type, including both the prelipoid and metachromatic types; (3) the globoid-cell type; (4) the type characterized by spongy degeneration of the neuraxis (spongy sclerosis); (5) the "neutral fat" type; and (6) special and combined types.[7]

Infection preceding demyelinating process

Proceeding to the classical form of the demyelinating process with which we are all familiar, it has been our frequent clinical experience to note an exacerbation of a demyelinating process after an illness of the respiratory, gastrointestinal, or urinary tract. Indeed, any local infection is apt to precede an exacerbation of multiple sclerosis. This experience is not unique[9] and has been commented on recently by Ferraro.[10] The exact role which a preceding infection plays in an acute attack in a patient with multiple sclerosis is not clear.

A similar clinical situation is presented by another demyelinating process, the so-called Guillain-Barré syndrome, which is often preceded by an acute bacterial or viral illness of a minor nature. We think that the Guillain-Barré syndrome is a demyelination of motor roots and peripheral nerves.

Postexanthematous encephalomyelitis is primarily a perivenous demyelinization which occurs days to weeks after the primary infection has subsided. It often results in permanent neurologic defects and thus provides a bridge to typical adult chronic multiple sclerosis.[11] Ferraro and Jervis[12] considered postexanthematous encephalomyelitis an allergic or hypersensitivity reaction to a systemic infectious agent. Brain tissue is broken down and liberated, resulting in the production of substances which are antigenic to the body tissues. Autoantibodies to brain antigens are then elaborated which result in a further breakdown of brain tissue.

Japanese workers[13] in 1957 reported studies of the central nervous system effects of antirabies vaccine. The clinical and pathologic picture of rabies encephalomyelitis is often similar to the changes found in adult multiple sclerosis. The inflammatory response in the nervous tissue was often more intense than that seen in adult multiple sclerosis and in some cases involved the overlying meninges. However, chronic adult multiple sclerosis is rare in Japan, and all of the cases which these authors were able to collect had been treated at one time or another with antirabies vaccine. The Japanese workers considered most cases of demyelinization in Japan to be due to postrabies encephalomyelitis of the hypersensitivity type.

Sporadic cases of acute disseminated encephalomyelitis or so-called acute multiple sclerosis are occasionally documented in this country. These cases are often preceded by a minor illness. The patient has an acute attack with a relatively sudden onset of neurologic signs and symptoms and a mild cellular response in the subarachnoid space. This inflammatory response is more intense than is seen in the chronic case of multiple sclerosis, and the inflammation is not confined entirely to the white matter. These cases present difficulties in classification since they are neither typical of chronic adult multiple sclerosis, nor are they clear examples of the postexanthematous type of encephalomyelitis. In children a favorite location would seem to be the cerebellum.

As a result of these clinical observations, considerable attention is being directed to hypersensitivities or autoallergic mechanisms in multiple sclerosis.

Experimental encephalomyelitis

In the past two decades it has been possible to produce an encephalomyelitis in various experimental animals. Numerous species have been studied, and considerable information is available on this subject. Some of the original work was done by Ferraro and Jervis[12] in the monkey. An intense hemorrhagic encephalomyelitis is produced in this target animal. In other species the response may be slightly different. In no experimental animal is the condition confined to the white matter, and the pathology has not been similar to that of multiple sclerosis. For example, in the rabbit histologic changes are often found in the spinal cord, spinal ganglia, and overlying meninges. There is an intense inflammatory response which is primarily perivascular and consists of lymphocytes and mononuclear cells.

To my knowledge no one has produced in an experimental animal a straight demyelinating process without inflammation. Furthermore, the chronic remitting course of human multiple sclerosis has never been reproduced. In the animal the clinical and histologic changes are thought to be due to the development of antibrain antibodies which then may continue to act on the central nervous system for days or weeks perpetuating the disease process. In theory experimental encephalomyelitis, postexanthematous encephalomyelitis, acute disseminated encephalomyelitis, and possibly chronic adult multiple sclerosis can be likened, but there are still many dissimilarities.

The general method of producing experimental encephalomyelitis is to inject homogenized homologous brain tissue combined with Freund's adjuvant (a strain of killed tubercle bacilli) to enhance the immune response. We have used rabbits as the target animal. In this animal the lesions produced are located primarily in the spinal cord, the spinal ganglia, and the peripheral nerve roots. These lesions are characterized by perivascular infiltration of inflammatory cells and perivascular demyelination.

There are many problems presented by the study of experimental encephalomyelitis in animals.[14] One of the chief objections to the use of this method in studying demyelinating diseases is the inability to demonstrate the circulating antibodies on which the theory depends. A further objection has been the failure to isolate a specific substance which contains the active fraction capable of producing experimental encephalomyelitis in the target animal. It has been found that whole brain extracts, crudely prepared, are as effective, if not more effective, than more purified forms of brain tissues. Bornstein and Appel[2] have shown a specific solution of myelin in tissue cultures when they are exposed to serum from animals with experimental encephalomyelitis. They were able to tag antibrain antibodies with fluorescein and show specific staining of the myelin sheath in tissue cultures. Our researches have attempted to tag circulating antibodies with fluorescein which then can be used as a specific stain or tracer to locate the site of action of the antigen-antibody reaction in the living animal. We have not shown such specific staining to date.

Environmental and genetic factors

Several good recent surveys of the geographic incidence of multiple sclerosis have been published.[13–16] There is excellent evidence that the demyelinating diseases occur two or three times more frequently in patients who reside in northern latitudes. Geographic differences have been well documented in continental North America as well as within the individual states extending over 4 degrees of latitude. These differences can possibly be linked to the greater incidence of respiratory infections in colder climates, but the evidence for this is not available at this time.

Also it has long been known that there is a higher incidence of multiple sclerosis in England as compared with the United States. This may indicate a genetic factor in the Anglo-Saxon population and must be taken into account in any geographic study of the incidence of multiple sclerosis. A truly international study of the problem comparing race, economic backgound, and environmental and other factors has not been carried out. The difficulties of obtaining accurate information regarding the true incidence of multiple sclerosis are very great. Such factors as the relative medical sophistication of the patient population, the ready availability of medical centers or individual practitioners trained to render accurate diagnosis, and the lack of adequate postmortem facilities may seriously hamper the collection of epidemiologic data reregarding multiple sclerosis. Kurland[16] studied multiple sclerosis in Winnepeg, Boston, and New Orleans. He observed that of 25 patients who died with a clinical diagnosis of multiple sclerosis, this diagnosis was confirmed by autopsy in 20 cases in Boston. In New Orleans, in a similar number of clinical cases, no autopsies were available for confirmation of the diagnosis.

Finally, we must consider that occasional families have been studied in which several generations have been affected by demyelinating processes. Unfortunately, insufficient information prevents an accurate assessment of the genetic factors involved. The criteria for establishing the diagnosis in previous generations are vague and often uncertain. Postmortem observations confirming the diagnosis have been difficult to obtain.

Viruses, bacteria, and spirochetes have not been isolated from cases of human multiple sclerosis in spite of heroic attempts.[17] I will dismiss as meaningless the occasional report of the isolation of spirochetes from such patients. I think that it is generally agreed that these are probably technical artifacts due to myelin breakdown.

Summary

To summarize our current thinking, then, concerning multiple sclerosis, one may begin with a patient who resides in northern latitudes where he may be exposed to more frequent respiratory and bacterial infections. These infections in a genetically susceptive individual may result in a breakdown of brain substances liberating antigenic materials (haptenes). These brain antigens stimulate the production of antibodies which cause a further breakdown in brain tissue. The process then becomes self-perpetuating. In the leukodystrophies there may be an inborn error of metabolism resulting in a failure of normal myelin synthesis or the development of an abnormal pathway for myelin synthesis rather than true demyelination.

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Discussion

Wilbur K. Smith, M.D., *Rochester, New York*. Dr. Sinton and Dr. Ortelee have discussed a number of the problems relating to demyelination in the central nervous system. There are just a few points which I should like to emphasize regarding this very devastating and very puzzling process.

It is well known that in the nervous system the loss of myelin may be associated with a number of pathologic processes such as postinfectious encephalomyelitis and various degenerative diseases, infarction, tumor, and hypoxia. The characteristic pattern of the pathology in these conditions, namely demyelination associated with marked changes in other neural elements, sets these apart from those demyelinating diseases, such as multiple sclerosis, in which the loss of myelin appears to be the primary pathologic condition and other changes play a less conspicuous or secondary role. Although the relationship of the loss of myelin to other alterations in the tissue varies in these disease processes, the difference in pathology between these two groups of disorders is such as to lead some investigators to limit the term demyelinating diseases to the latter group, of which multiple sclerosis is the outstanding example.

In spite of the great amount of work which has been done on the primary demyelinating disorders, the basic etiology of the demyelinating process remains a mystery. The so-called "causes" that have been discovered, including viral and bacterial infections, vascular pathologic conditions resulting from thrombosis or hypoxia, toxic effects of lead and cyanide, and the late spirochetal origin of the pathologic condition appear to have succumbed because of a lack of evidence to support them. The enzymatic theory postulating the local release of a lipolytic enzyme which attacks the myelin is attractive but difficult to uphold at present. The experimental production of allergic encephalomyelitis in animals has yielded important information regarding the demyelinating process. Attempts to isolate the responsible factor indicate that the protein fraction may be the important antigen. In man the greatest accidental experiment in this field is the one reported from Japan in which a demyelinating disorder resembling multiple sclerosis appeared among patients who had received the Pasteur antirabies treatment.

In assessing the present status of our knowledge of this subject, it seems evident that although the allergic theory of demyelination has the most evidence to support it at the present time, it is far from being proved to be the modus operandi. Any theory designed to explain the process will have to account for the geographic and climatic distributon of the disorder, the apparent racial differences in incidence, the age incidence of the disease, and the occurrence of remissions and exacerbations, including apparent cure in many instances.

In conclusion, it can be stated that after more than a half century of theories and experiments no really significant advance appears to have been made in elucidating the cause of the primary demyelinating disorders in man, of which multiple sclerosis is the outstanding prototype.

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Scientific Program

Any State Society member who wishes to present a paper before a scientific section or a general session is requested to write to **Bernard J. Pisani**, M.D., Chairman, Convention Committee, 170 West 12th Street, New York 11, New York, before October 15, 1962. A short abstract of the proposed presentation should accompany the letter.

Survey of 419 Cases of Acute Poisoning

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IN A GROUP *of 419 cases of acute poisoning, acetylsalicylic acid, household substances, and solvents were responsible for a high percentage of the pediatric cases, whereas barbiturates were responsible for 45 per cent of the poisonings in adults. Coma occurred in 43.7 per cent of the adult patients; of these 21.8 per cent required intubation of the trachea, and 11.2 per cent required mechanical respiratory assistance. Aspiration secondary to gastric lavage occurred in 20.8 per cent of the comatose patients and was commonly due to failure to isolate the airway during lavage, as tracheal intubation must be performed when the protective reflexes are obtunded or absent. Twelve patients (2.8 per cent of the total) died.*

A NOTEWORTHY AMOUNT of literature has accumulated in recent years describing the incidence and treatment of poisoning with a variety of individual substances. There is, nevertheless, a dearth of recent information relating to the frequency of occurrence of accidental or intentional ingestion of toxic agents. Cumming[1] recently surveyed 516 cases of acute poisoning admitted to the General Hospital, Birmingham, England. Additional information can be culled from the reports of several poison control centers, particularly from the five-year report of the New York City Poison Control Center[2] and the semiannual summary of the Florida Poison Control Center.[3] To gain further insight into the frequency with which toxic substances were being ingested in the area serviced by our institution, as well as the efficiency of our treatment of these patients, the records of the Bronx Municipal Hospital Center were reviewed for a period extending from January, 1955, to December, 1960. A survey of this type is, by its very nature, difficult. Although the *Standard Nomenclature of Diseases and Operations* is employed by the medical records library, a review of cases by reference to code number was impossible. Hospitalization for prolonged medical or psychiatric therapy frequently results in the coding of the chart by discharge rather than by admitting diagnosis. However, all hospitals and physicians in the City of New York are required to report all poisonings to the Board of Health of the City of New York. A record of these reports for the six-year period surveyed provided a complete list of all patients who had ingested a toxic substance and were admitted for treatment in the emergency room of their own volition, via the ambulance service, or on a referral from their physician.

The Bronx Municipal Hospital Center, a 1,400-bed institution, serves the northeastern division of New York City. This is primarily a middle- and low-income residential area, with a small industrial complex on its periphery. An active ambulance service has been in operation since November, 1955. During the period surveyed, 280,861 patients were seen in the emergency room or outpatient departments. Of these patients, 67,169 required admission. Of these, 455 were hospitalized as the result of accidental or intentional ingestion of some toxic substance. This represents an overall incidence of 0.68 per cent. Of these cases, 419 were sufficiently documented for a review in detail. The results of this survey are summarized in this article.

Total incidence

There has been a decline in the number of patients hospitalized as a result of poisoning in the past four years (Fig. 1). This relative decrease in ingestion is apparently a

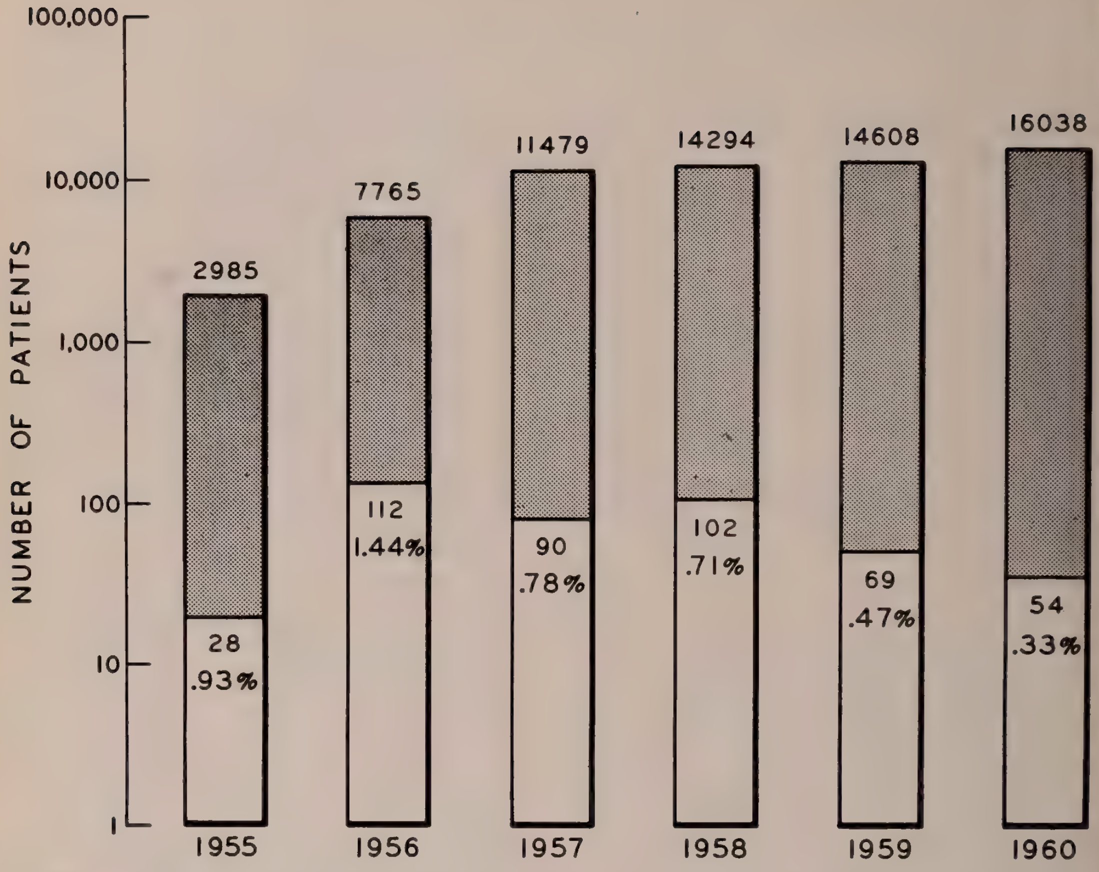

FIGURE 1. Ratio of admissions following ingestion of toxic substances to total number of patients admitted.

local situation, since the over-all incidence in New York City has not varied significantly during the same period.[4] No seasonal variation in incidence was demonstrable when the ratio of poisonings to total admissions was tabulated on a monthly basis for the period studied.

Age and sex

A distribution by age and sex is shown in Figure 2. In the group under five years of age the incidence is higher in males, as is perhaps to be expected. This in all probability reflects a greater curiosity in boys of this age. The low incidence between the ages of six and fifteen years could have been predicted on the basis of other reports.[1-3] In patients past the age of fifteen years the occurrence of poisoning by ingestion, both intentional and accidental, is higher in females (67.7 per cent). This is a reflection of the higher incidence of attempted self-destruction by the ingestion of toxic agents in women.[5,6] Seventy-seven per cent of the cases of intentional ingestion of toxic substance were in females. The high incidence of ingestion in the sixteen- to fifty-year age group and the decline in patients past the fifth decade of life have been observed previously.[1]

Agents

The toxic substances encountered have been divided into the following nine groups: barbiturates; acetylsalicylic acid; phenothiazine derivatives; meprobamates (Equanil, Miltown); nonbarbiturate hypnotic drugs, for example, glutethimide (Doriden), ethinamate (Valmid), and ethchlorvynol (Placidyl); internal medications; external medications; solvents; and household substances, for example, detergents, bleach, and

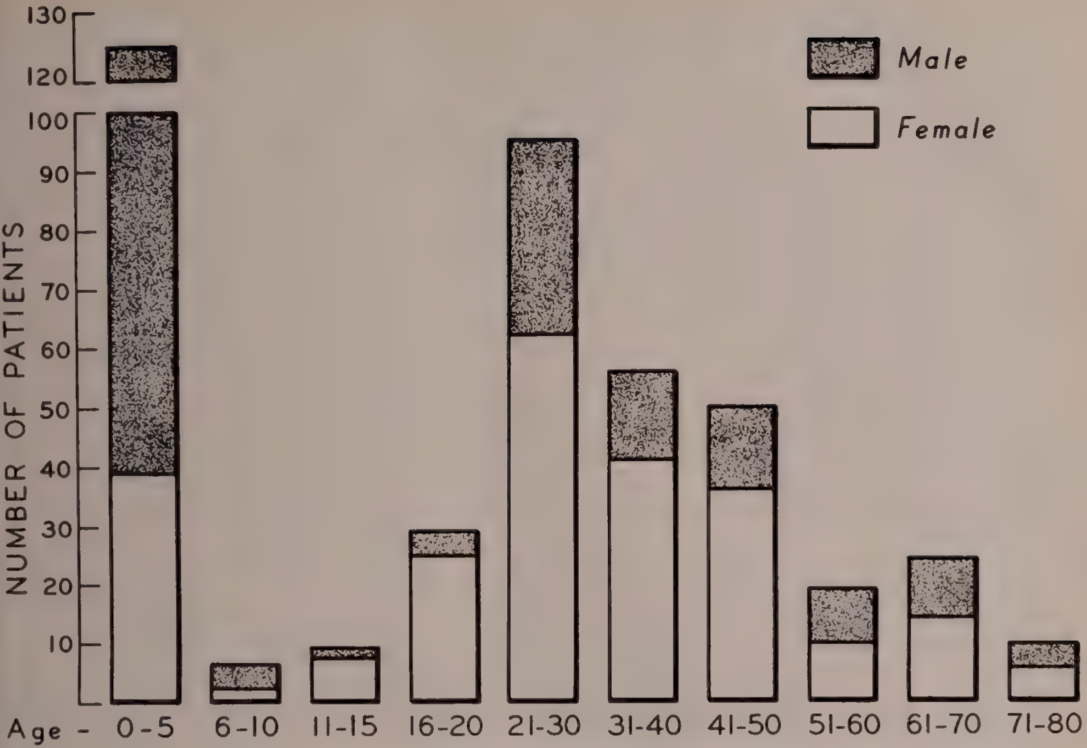

FIGURE 2. Incidence of ingestion of toxic agents by age and sex.

lye. The distribution of the substances ingested by each age group is shown in Figure 3. The high incidence of poisoning in children by acetylsalicylic acid, household substances, and solvents reflects their availability and accessibility. It is noteworthy that the phenothiazine derivatives accounted for 11.4 per cent of the poisonings in children up to fifteen years of age, whereas the barbiturates were incriminated in only 3.5 per cent of the poisonings in the pediatric age group. This represents a difference in the parental attitude toward the relative dangers from these two groups of drugs, influenced by misleading advertising and casual prescription by physicians.

Barbiturates were the etiologic agents in 31 per cent of the cases. If only the 279 adults are considered, derivatives of barbituric acid were responsible for 45 per cent of the poisonings. The vast majority of these patients represent attempts at self-destruction. Seventy-nine patients (19 per cent) ingested drugs introduced into therapeutics in the last decade, for example, phenothiazine derivatives, meprobamate, or nonbarbiturate hypnotic drugs. The number of persons who ingest toxic amounts of these drugs has increased in a striking manner during the latter years of the survey.

Fourteen patients (3.3 per cent) ingested two or more agents. For purposes of classification, these patients were included in a group according to the predominant effect, as determined by the relative amounts ingested as well as by the relative potency of the drugs involved. There were no children in this group, nor were any accidental poisonings the result of more than one drug. Thirteen of these patients ingested a barbiturate in combination with a phenothiazine, meprobamate, glutethimide, or meperidine hydrochloride. One patient ingested chlorpromazine (Thorazine) and a sedative (Sominex). Two of these 14 patients expired.

Coma and complications

One hundred and twenty-five patients were comatose on admission. This represents 29.8 per cent of those patients admitted

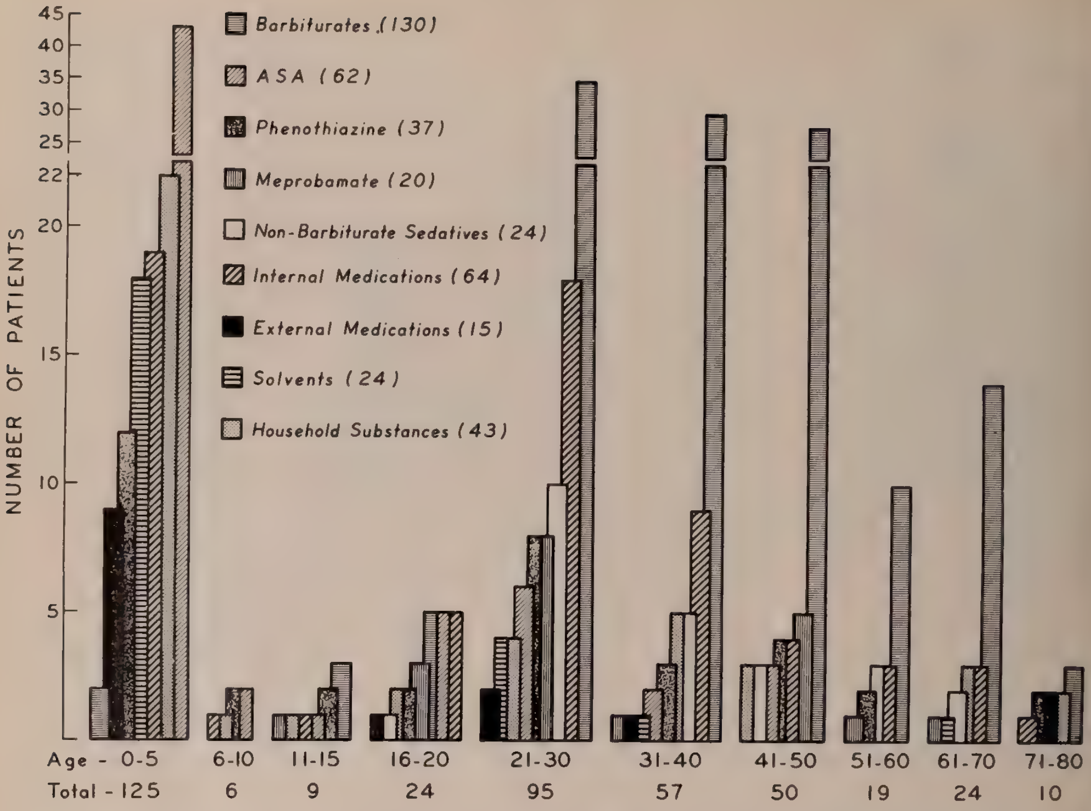

FIGURE 3. Distribution of toxic substances ingested by various age groups (419 cases).

because of the ingestion of toxic substances. If the 140 pediatric poisonings, where the incidence of coma was 2.1 per cent, are excluded, 43.7 per cent of the remaining 279 patients were admitted in a comatose state. Forty-three comatose patients were seen in consultation by an anesthesiologist. This represents 10.2 per cent of the series or 34.4 per cent of the patients admitted in coma. Twenty-six patients, 20.8 per cent of those who were comatose on admission, required intubation of the trachea either to maintain a patent airway or to isolate the lungs during a gastric lavage. Fourteen patients (11.2 per cent of those who were in coma, 32.5 per cent of those seen by an anesthesiologist, or 53.8 per cent of those who were intubated) required ventilatory assistance with some type of an intermittent positive pressure device. Twenty-six patients, 20.8 per cent of those who were comatose when first seen in the emergency room, showed signs of having aspirated gastric contents. Only 1 of these patients was seen by an anesthesiologist before gastric lavage was instituted. In this instance lavage was performed following the passage of an endotracheal tube. Aspiration probably occurred before the airway was isolated.

Twelve patients expired. This represents 2.8 per cent of the patients admitted because of an ingestion of toxic substances. Only 1 of these patients was not comatose on admission; the death rate in the comatose patients, therefore, was 8.8 per cent. Three per cent of those patients who had ingested a barbiturate died, as did 5.4 per cent of those who had ingested a phenothiazine derivative. The barbiturates accounted for 5 deaths; chlorpromazine, prochlorperazine (Compazine), methadone (Dolophine hydrochloride), iproniazid (Marsilid), and bromides accounted for 1 death each; and methyl salicylate accounted for 2 deaths. There was no significance to the age distribution in this group. In 2 cases death was due to aspiration. The incidence of coma and complications by agent is shown in Figure 4.

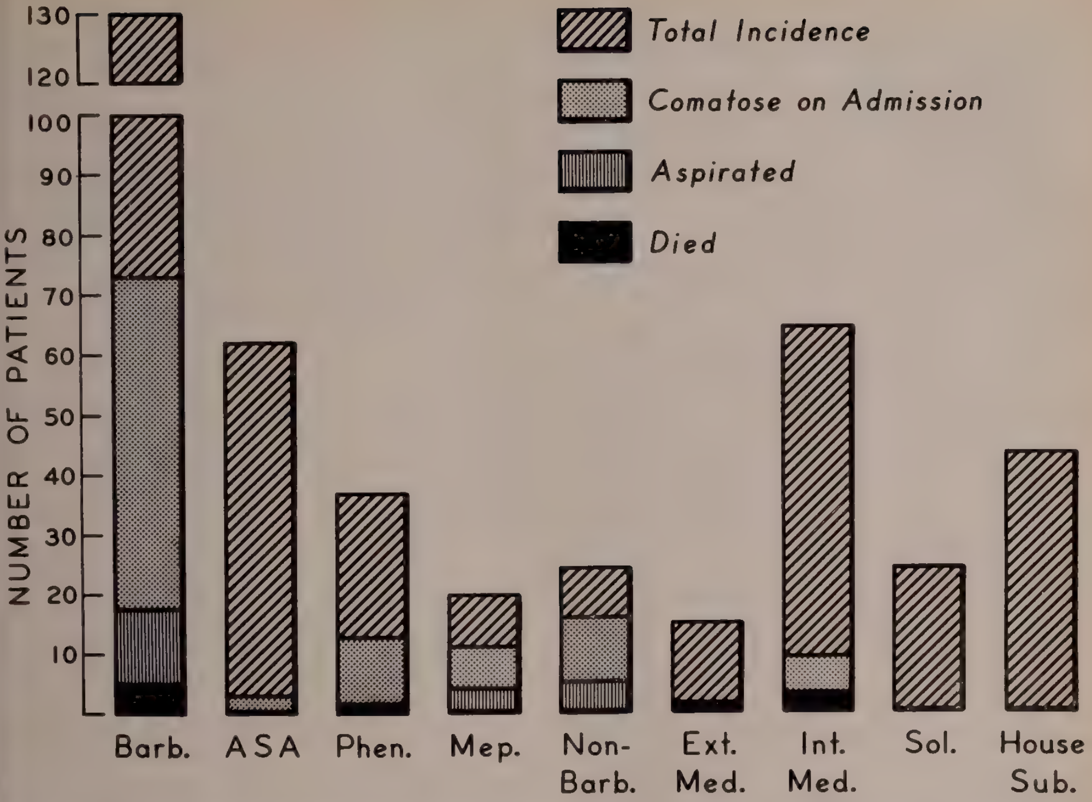

FIGURE 4. Distribution of complications following ingestion of specific agents. Barb. = barbiturates, ASA = acetylsalicylic acid, Phen. = phenothiazine derivatives, Mep. = meprobamate, Non-barb. = nonbarbiturate hypnotic drugs, Ext. Med. = external medications, Int. Med. = internal medications, Sol. = solvents, and House Sub. = household substances.

Comment

It is difficult to make any comparisons with other studies, since the incidence by agent is dependent on several variables. Climate, social and economic status, as well as age distribution of the population surveyed, influence the frequency of the ingestion of a particular agent. Similarly, there is great variation in the agents ingested in urban, suburban, and rural communities. In spite of these variations, some trends do emerge from this and other studies. The ratio of the number of patients who were comatose on admission as a result of the ingestion of a toxic agent to the total number of hospital admissions in this series is almost identical with that reported by Rovenstine in 1945.[7] The ingestion of toxic substances by children in the one- to five-year age group is extremely high and accounted for 48 per cent of the cases reported to the New York City Poison Control Center in the years from 1955 to 1959.[2] Thirty per cent of our patients were also in this age group. Acetylsalicylic acid remains the most commonly ingested agent in the pediatric age group. In adults, on the other hand, barbiturates are still the most common offending agents. It was inevitable that the newer therapeutic agents should become responsible for an increasing number of poisonings. The morbidity and mortality following the ingestion of these agents is alarming.[8] In many instances it reflects an inadequate knowledge of toxicity and side-effects on the part of the prescribing physician as well as on the part of those who are called on to treat these patients following an overdose. The literature, both professional and pharmaceutical, fails to emphasize the toxic potential of these drugs in an unbiased manner.

In this series the high incidence of morbidity as a result of aspiration was avoidable. Admittedly some patients aspirate prior to admission; however, in the vast majority of patients, aspiration occurs when gastric lavage is performed in the absence of pharyngeal and laryngeal reflexes or when these reflexes are obtunded. If the airway is isolated before lavage, aspiration does not occur. It is our opinion that when the patient with obtunded reflexes will not tolerate an endotracheal tube, intubation should be performed with the aid of a muscle relaxant, and the airway should be isolated before gastric lavage is instituted. In such a patient, following lavage and after complete muscle power has returned, the endotracheal tube may be removed. The present problem, however, is no longer one of the insertion of the endotracheal catheter but of the recognition by emergency room personnel of the danger of aspiration. When this problem was recognized, lavage was carried out without an incident; when it was not, aspiration occurred in over 70 per cent of the patients who were lavaged. Two patients in this series died as a result of aspiration.

A more efficacious management of these 2 patients would have reduced the overall death rate by 0.5 per cent; deaths due to barbiturate intoxication would have been decreased to 2.3 per cent. The 2.3 per cent figure approaches the mortality reported by Clemmesen and Nilsson[9] and is probably approaching the lowest figure one can expect to obtain when treating poisonings of this severity.

The fact that 20 per cent of the patients in coma required intubation and that respiratory assistance was necessary for varying periods of time in over 50 per cent of these people illustrates dramatically the necessity for an early consultation with an anesthesiologist.

Summary

Four hundred and nineteen cases of poisoning by ingestion were received. Acetylsalicylic acid is the most common offending agent in children, while the barbiturates are incriminated most frequently in adults. Nineteen per cent of the drug intoxications seen in the five-year period surveyed were the result of the ingestion of drugs which were introduced in the last decade.

Coma is the most common complication occurring in 43.7 per cent of the adult patients. Aspiration secondary to gastric lavage was responsible for prolonging the period of hospitalization in 20.8 per cent of the comatose patients. Since aspiration was commonly due to a failure to isolate the airway during lavage, tracheal intubation must be performed when the protective reflexes are obtunded or absent. Respiratory assistance with a mechanical ventilator was necessary in 11.2 per cent of the comatose patients, and endotracheal intubation established an airway in 20.8 per cent of these individuals. The incidence of pulmonary complications and respiratory depression makes an early consultation with an anesthesiologist mandatory.

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Nature and Treatment of Blepharitis

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BLEPHARITIS *is a chronic inflammation of the lid border. The specific etiologic agents have not been established; thus many medications have been advocated. Adequate lid hygiene is essential. Thirty patients with either seborrheic or ulcerative blepharitis were treated twice daily with a medication combining antiseptic and keratolytic agents with sodium versenate (Blef-Dome), in which the chelating agent aids in cellular penetration and reduces the concentration requirement of the antiseptic and keratolytic agents. Patients with uncomplicated seborrheic blepharitis benefited generally, and the majority were sufficiently improved so that the frequency of medication could be reduced to once weekly or biweekly. Patients with ulcerative blepharitis were slow to respond although signs and symptoms were diminished progressively with diligent care and therapy.*

BLEPHARITIS HAS been defined as a chronic inflammation of the lid border.[1] The presently accepted classification of this entity is divided into two major orders. The first, and probably the most common, is the seborrheic type in which the lid border is reddened and in which dry or greasy scales are present at the base of the lashes. The lid margin's contour is usually normal in this type, with little or no evidence of scarring. The second major category is that of the ulcerative type in which lashes are frequently missing; the lid border is reddened, more in certain areas than others; and often small pustules are present. In both types of blepharitis chronic conjunctivitis and mild keratitis may be present.[2]

Although blepharitis may be associated with other systemic and local diseases, the seborrheic and ulcerative types encompass virtually all cases which are seen in an average practice. With respect to the ulcerative type, the staphylococcus organism has been incriminated in a majority of instances in which this subject has been studied in detail. There is clinical evidence to indicate a relationship between this offending organism and the disease process. Frequently, this form of blepharitis is unilateral and involves small segments of the lid. There are often associated hordeola and chalazia, and often the desquamated tissue is difficult to remove so that a mild oozing of blood will ensue on the mechanical removal of the scale. Permanent scarring of the lid margin with residual puckering of follicles and the loss of lashes as well as the high incidence of keratoconjunctivitis strengthen the staphylococcic relationship.

In seborrheic blepharitis the etiologic significance of bacterial or fungus infection on the one hand and some disturbance in the sebaceous gland metabolism on the other hand has been a recurring source of controversy among dermatologic investigators for over fifty years. Pityrosporum ovale, Corynebacterium acnes, staphylococcus epidermitis, Staphylococcus albus, the morococcus of Unna, and the various streptococci have all been incriminated separately or in combination for the explanation of seborrhea in various parts of the body.[3-7] However, it has been shown clearly that there is no significant difference between the surface flora of seborrheic dermatitis of the scalp and normal scalps.[8,9]

These same findings have been noted by various investigators evaluating the flora of the lid. There does seem to be a preponderance, though, of budding yeast forms which have never been clearly shown to be the causative agents in this entity.[10]

The therapy for blepharitis varies owing to the presumed different etiologic factors. In seborrheic blepharitis keratolytic agents, cleansing of the skin, massage of the meibomian glands, and the elimination of seborrhea elsewhere have been recommended. In ulcerative blepharitis similar cleansing and expression of the meibomian glands are necessary. However, there is an additional need for antibiotics as well as for occasional staphylococcal desensitization.[11]

It is the purpose of this communication to report on the treatment of seborrheic and ulcerative blepharitis, utilizing solely a keratolytic-antiseptic-chelating combination without antibiotics or steroids. This medication combines the classical antiseptic and keratolytic agents with sodium versenate.* Theoretically, the chelating agent alters the metallic element concentration in cell membranes, making tissues more permeable both to antiseptic and to keratolytic agents. Furthermore, it has been shown that certain organisms resistant to antiseptic or enzymatic destruction are made susceptible to such agents by the addition of sodium versenate.[12,13] Consequently, since antisepsis, exfoliation, and debridement are aided or induced, the requirements for therapy in both types of blepharitis are met.

Materials and methods

Patients were chosen from the private practices of several ophthalmologists, as well as from the general ophthalmology clinic of The New York Hospital-Cornell Medical Center. This report deals with 30 cases in which cultures and scrapings of the lid margins were taken prior to and following therapy (Table I). Following the initial studies, the patients were instructed to place the ointment on a cotton-wound toothpick and to massage the lid margins and roots of the lashes in the mornings and evenings. Massage was to continue until all scales were removed. Therapy was continued twice daily until the lid margins were clean, then once daily, then once every other day, and then as required. No antibiotics, steroids, or other medications were utilized in any patient.

TABLE I. Cultures of lid margins in 30 consecutive cases of blepharitis prior to and following keratolytic therapy

Cultures	Before Therapy	After Therapy
Staphylococcus aureus (coagulase)	16	3
Alpha streptococcus	4	0
Beta streptococcus	1	0
Pneumococcus	1	0
Proteus	1	0
Pseudomonas	1	0
Budding yeast	10	3
Mixed Staphylococcus aureus (coagulase) and budding yeast	14	4
Normal flora	8	24

Results

The results of cultures of the lid scrapings prior to and following therapy are listed in Table I. The pattern of organisms is relatively consistent with previously published data.[1] It should be noted that a significant change in the lid flora is induced by the medication, although no antibiotics are utilized. In general, the clinical impression was substantiated by laboratory studies, although one could not make a specific diagnosis based solely on a bacteriologic examination.

Essentially, patients with uncomplicated seborrheic blepharitis benefited universally from this preparation. The majority of patients were sufficiently improved so that the frequency of medication could be reduced to once weekly or biweekly, provided lid care and hygiene were maintained. It should be noted that although this entity is quite cyclical, in that patients may remain clear for months without any therapy, obvious benefit accrued from the use of medication. On the other hand patients with ulcerative blepharitis frequently were slow to respond, although signs and symptoms were diminished progressively with diligent care and therapy. The duration of therapy for ulcerative blepharitis has been essentially continuous in that patients must pay daily attention to their lids. The incidence of recurrent hordeola in this group has been reduced. In patients suffering from recurrent chalazia the results have not been as impressive, but a small measure of success was noted.

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* Supplied as Blef-Dome by Dome Chemical Co., New York City.

Comment

Seborrheic dermatitis is one of the most common dermatologic entities. Classified roughly in the group of eczematous eruptions, it is distinguished by morphology, distribution, course, and the absence of known specific etiologic factors. On the scalp, ear canals, chest, upper back, axilla, and umbilicus the lesions are usually demarcated sharply, ranging in size from pinhead, follicular macules to plaques covering the entire central chest. On the glabella, supraorbital ridges, eyelid margins, nasolabial folds, postauricular areas, groins, and perianal regions lesions are generally marginated less sharply. Although quite variable, the color of seborrheic dermatitis is usually erythematous with tints of yellow or tan. The degree of grimy or greasy scaling, crusting, oozing, or weeping is also subject to a great variation with intertriginous areas, especially the postauricular fold, tending to show acute involvement more frequently. Dry, chronic lesions often have a greasy texture. The clinical range of the disease is enormous, from the almost universal, noninflammatory dandruff to the very rare, desquamated erythroderma of infants, regarded by some authorities as a generalized infantile form of seborrheic dermatitis. A certain haziness of definition is unavoidable in a condition lacking both distinctive histopathology and no known etiologic factors, yet for the most part the clinical diagnosis of this disease is made easily. The term "seborrheic diathysis" is evoked commonly to denote individuals showing a predisposition to recurrent attacks of seborrheic dermatitis or showing a low-grade, unremitting involvement which undergoes repeated exacerbations and partial remissions. Apart from a tendency to oiliness of the skin, there is no recognizable difference between these individuals and the rest of mankind except for their susceptibility to the disease.

The belief that seborrheic dermatitis is in some way related to quantitative or qualitative abnormalities in skin lipid metabolism is inherent in the very name of the disorder and has a basis in certain clinical facts. Seborrheic dermatitis of the scalp seems to be more prevalent on oily heads. Seborrheic dermatitis is not uncommonly seen to develop at puberty when sebaceous glands are undergoing great enlargement. The areas of predilection of seborrheic dermatitis are precisely those areas which are richest in oil glands. The microorganisms that are claimed to be associated with the disease are by and large lipophilic yeasts and bacteria, although their presence may represent nothing more than the preference of certain saprophytes for a fatty environment. In Parkinson's disease where there is marked sebaceous gland hyperplasia, severe seborrheic dermatitis is a common complication. A study in which the lipid film from the upper back in subjects with seborrheic dermatitis was compared with that of normal patients revealed no significant quantitative difference, but the results from the seborrheic patients indicated an increase in the cholesterol content, a decrease in squalene, and a lower iodine number.[14]

Our ignorance regarding the etiologic factors of seborrheic dermatitis and blepharitis is summarized well in the work of Pillsbury, Shelley, and Kligman[15] in which the following causative factors are listed: sebaceous dysfunction, acute and chronic bacterial infection, mycotic infection (sometimes secondary to antibiotic therapy), mechanical trauma, contact irritation and sensitization, internal disease, sweat retention, and specific ingestants.

With respect to seborrhea of the lids, there is essentially no gross difference between this entity and seborrhea elsewhere except that some authors have indicated that seborrheic blepharitis, to be held in check, must include treatment of any accompanying seborrhea of the scalp.[16,17] However, it is difficult to subject this precept to a rigidly controlled clinical study.

A knowledge of a systemic disorder relating to ulcerative blepharitis is also not clear-cut. In certain patients the presence of acne both on the face and back, cyclic variations in furuncles, and the recurrent formation of pustules on the body and lid margins tend to indicate a staphylococcic origin associated with some additional fundamental physiologic abnormality. However, although a considerable amount of material has been published on the subject, the specific etiology remains obscure.

A vast array of medications have been used in the treatment of both forms of this disease. From the therapeutics of earlier days sulfur, salicylic acid, and ammoniated mercury emerged as effective medicaments. More recently, hydrocortisone and its synthetic derivatives and diiodohydroxyquin and related quinolines have come into favor in the treatment of glabrous skin lesions. Hexachlorophene, biphenamine, sulfanilylacetamide, and coal-tar extracts are popular additives to shampoos for the management of seborrhea of the scalp. Selenium sulfide has achieved a good measure of success in the treatment of both scalp and lid seborrhea.[18-20] Systemic corticosteroids are dramatically effective in the suppression of widespread acute incapacitating seborrheic dermatitis. However, in its local manifestation in the lids, there seems to be little need for steroids. In addition to the foregoing, a variety of antibiotics and germicidal agents have been employed to eliminate staphylococci when such therapy has appeared warranted.[21]

The agent described in this study has been as effective as those reported previously in the literature with several extensions of benefit, both in the seborrheic and in the ulcerative forms of blepharitis. Since certain aspects of ulcerative blepharitis may be considered a close-spaced infection, topical antibiotics are often ineffective. Germicidal agents, as well, may not penetrate the keratin layers of the skin. Furthermore, keratolytic agents often add to the detritus in which bacteria flourish. The chelating agent contained in this medication may aid in the penetration of both germicidal and keratolytic agents. Consequently, concentrations of both may be reduced and yet still be effective. Keratolysis and the detachment of detritus is enhanced as well. Finally, sodium versenate has been shown to enhance the destruction of bacteria in the presence of certain enzymatic or germicidal agents.

It is also well recognized that a secondary infection of seborrheic blepharitis with staphylococci or other organisms increases the severity of the disease and compounds the difficulty of therapy. It is worth while, therefore, to have an agent that exerts an effect in both conditions.

The tolerance of patients to this medication has been excellent. Safety has been well demonstrated in the past, since sodium versenate has been used directly on the cornea in considerably higher concentration than that employed in this study. In the past two and one-half years, more than 250 patients with blepharitis have been treated, and 2 cases of lid sensitivity have been encountered. These sensitivities subsided when use of the drug was terminated.

It is not the intention of this study to deter investigators from seeking etiologic agents in this disease, but the results of this study and others indicate that specific etiologic agents will rarely be found. Diligent lid care plus the use of a keratolytic and antiseptic agent with the addition of a chelating agent appear to be effective therapy in both forms of blepharitis.

Summary

An agent for the treatment of ulcerative and seborrheic blepharitis is described. It combines the usual keratolytic and antiseptic agents with a chelating agent. The chelating agent aids in cellular penetration and reduces the concentration requirement of the antiseptic and keratolytic agents. In more than 250 cases it has proved an effective agent when it is combined with adequate lid hygiene.

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ANNUAL CONVENTION: Medical Society of the State of New York

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The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

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Committee on Prize Essays

Contact Lenses

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Contact lenses are hardly new to the field of ophthalmology. The first known lens was made in 1889 by Mueller for a patient with lagophthalmos.[1] This lens had no optical properties but was worn for many years filled with ointment for the protection of the cornea. Zeiss started making blown glass lenses with ground optical sections as early as 1911. Since that time there has been a steady increase in the demand for contact lenses by the public. This demand has gone through tremendous upsurges from time to time as some new developments have occurred. Obrig,[2] of New York, in the 1940's, did much to popularize contact lenses. He spent many years trying to find a fluid that could be worn with the old fluid, or conventional, contact lenses which would not produce corneal edema and blurring of vision. In the late 1940's the revolutionary ideas of Tuohy produced another overwhelming demand that has brought us to our present-day state of confusion.[3] It is interesting that these developments always have been commercially guided, which largely accounts for the publicity, advertising, and hence the public demand. While contact lenses have been improved greatly in the past few years, it is hardly conceivable that they will ever replace spectacles.

There are some indications, but more contraindications, for the fitting of contact lenses. These, plus the complications, will be discussed.[4-11]

Indications for contact lenses

Improvement of vision. Improvement of vision is the first and by far the most important indication for contact lenses. There are situations in which spectacles cannot adequately correct the vision, but marked improvement may be achieved with contact lenses. In cases of advanced keratoconus, irregular astigmatism, corneal scars, and some cases of albinism and nystagmus, there is no comparison.[4-11] It is not uncommon to correct spectacle vision of 20/200 or less to 20/20 in these cases with contact lenses. In many of these cases it is the only way that the patients can obtain useful vision. These cases produce by far the most gratifying results.

Anisometropia. The use of contact lenses in unilateral aphakia and anisometropia where it is impossible to produce binocular vision with spectacles is ever increasing in popularity.[12-17] Stereopsis is not always obtained, but the chances are greatly enhanced. Frequently it is possible for individuals with unilateral aphakia to continue to work in positions that they would not be able to maintain if it was not for the vision that they can obtain with the use of a contact lens. Examples of such occupations are railroad engineers, bus drivers, firemen, and so forth.

Extremes of refractive error. Many patients with high myopia, hyperopia, astigmatism, and aphakia may obtain far better vision with contact lenses than with spectacles. The annoying symptoms of spherical aberrations, distortion, and so forth usually are eliminated with the use of contact lenses. These individuals also obtain a somewhat larger field of vision.

Trichiasis, districhiasis, lagophthalmos, ectropion, entropion, and neuroparalytic keratitis. Contact lenses can be fitted to many individuals with

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certain eyelid disorders to improve their vision and protect the cornea from a loss of vision due to scarring.[18–23] They also may do much to relieve the irritation and pain that accompany some of these conditions. In neuroparalytic keratitis the corneal lens is not recommended. While a number of cases have been reported, the author is somewhat reluctant to fit these patients.

Occupations hazardous to the spectacle wearer. Contact lenses are particularly valuable to individuals with refractive errors who participate in violent occupations, particularly professional athletes where body contact is extreme, as in football, basketball, wrestling, and so forth. Many of these individuals would be unable to pursue these occupations if they did not have access to contact lenses.

Occupations where spectacles are impractical. People with appreciable refractive errors who work in extremes of humidity and temperature, particularly cold, have great difficulty with the lenses in spectacles clouding and frosting. Also, individuals who must work in all types of weather have difficulties with spectacles in rain and snow. These problems usually do not exist when contact lenses are worn. Frogmen, skin divers, and those in similar occupations cannot wear spectacles but may do very well with contact lenses.

Occupations where spectacles are a cosmetic detriment. Actors, actresses models, dancers, television personalities, and so forth, many times will not or cannot wear spectacles in their work and are greatly benefited by contact lenses.

Cosmetic fitting. By far the greatest demand for the fitting of contact lenses is in the purely cosmetic field. It is here that the highest percentage of failure is encountered. If the fitting of contact lenses could be limited to the other categories, the success would be greatly enhanced. However, if the incentive for cosmetic fitting is great enough in individual cases, many persons will overcome the problems encountered in adapting to this foreign body in the eye. If more ophthalmologists would accept this responsibility, a greater service to patients would be done. All ophthalmologists see patients whom they try to discourage from obtaining contact lenses. All too frequently this is impossible, and if they will not fit them, someone else will. Would it not be far better to have these people under the supervision of an ophthalmologist than someone less capable or commercially minded? For some of these people it is a very effective form of psychotherapy.

IN FITTING CONTACT LENSES, *the indications, contraindications, and possible complications should be considered. Indications for the fitting of contact lenses include: improvement of vision in such cases as advanced keratoconus, irregular astigmatism, corneal scars, and some cases of albinism and nystagmus; anisometropia and unilateral aphakia; extremes of refractive error; trichiasis, districhiasis, lagophthalmos, ectropion, entropion, and neuroparalytic keratitis; occupations which are hazardous to the spectacle wearer, where spectacles are impractical, or where spectacles are a cosmetic detriment; and cosmetic fitting. Contraindications include: infection; degenerative diseases of the cornea; mental incompetence or irresponsibility; occupational contraindications; glaucoma; and corneal staining. Complications from the wearing of contact lenses which have been reported include: epithelial staining; corneal scarring; infection; corneal vascularization; filamentary keratitis; contact lens ruptured into the orbit; and corneal infiltrates.*

The cosmetic fitting of badly scarred and unsightly eyes with contact lenses is another field that will not be discussed in this paper.

Contraindications to the fitting of contact lenses

Infection. Acute or chronic recurrent infectious disease of the lids, conjunctivas, or corneas is a definite contraindication to the fitting of contact lenses. These eyes do poorly, since the lenses irritate and exacerbate the condition and predispose to a more serious spread of the disease. One possible exception that has been reported is that chronic nonspecific corneal ulcers seem to heal when patients wear contact lenses.[24] It is one of the scleral lenses and certainly not the corneal lens that is recommended here. The author has had no experience with such conditions.

Should infection develop while contact lenses are being worn, they should be discontinued until recovery is complete.

Degenerative disease of the cornea. One arbitrary point has been argued by some of the ophthalmologists. Some feel that degenerative disease processes, such as epithelial and endothelial dystrophies, are accelerated by the wearing of contact lenses. The author lacks experience here, but would be hesitant to do such fittings, particularly in the presence of epithelial dystrophy.

Mental incompetence or irresponsibility. Precautions must be taken when individuals incapable of following instructions or too irresponsible to care are to be fitted. Children must be included in this category unless the parents are willing and able to maintain close supervision and accept the responsibility. Even intelligent adults frequently will fail to follow instructions and attempt to adapt to the lenses too quickly or wear them for excessive periods of time. The results may be extremely painful, if not disastrous.

Occupational contraindications. Occupations that expose individuals to dust, smoke, and irritating gases contraindicate the wearing of contact lenses, particularly those of the corneal type. The lenses greatly increase the irritation produced.

Glaucoma. Huggert[25-27] demonstrated a slight rise in the intraocular pressure following the wearing of scleral contact lenses. Ascher[28] also reported interference in the drainage of the aqueous veins with the wearing of these lenses. This would seem to contraindicate the wearing of scleral contact lenses in individuals with glaucoma. The author knows of no incidence of glaucoma that has been incited or exacerbated by the use of contact lenses, and there would seem to be no contraindication to the use of corneal lenses.

Corneal staining. Despite apparent satisfactorily fitted contact lenses, persistent staining of the corneal epithelium will be seen in some eyes. This is usually not associated with discomfort or blurring of vision, and it may not be seen until the lenses have been worn for many hours. It is for this reason that these patients must be checked periodically and particularly after the lenses have been worn for a long period of time. It is the author's contention that persistent or repeated staining is a contraindication for the continued use of contact lenses. Anything that disrupts the corneal epithelium predisposes the eye to infection of the cornea and loss of sight.

Complications from the wearing of contact lenses

With the thousands of fitters of contact lenses at large in the world today, it is hard to believe that many more complications have not been seen. As time goes on and more and more lenses are injudiciously prescribed, the incidence of severe complications must increase. Undoubtedly, the greatest redeeming feature is that if the lenses are not properly fitted, they cannot be tolerated, and the eyes thus are protected.

Epithelial staining. The most common problem encountered with the fitting of contact lenses is corneal staining. Abrasions frequently result from the improper insertion of the lenses, especially in the early stages when patients are first learning the technic of insertion and removal. Lenses that are improperly fitted, especially if the curvature is too flat, will cause staining of the apex of the cornea. This is seen frequently in cases of keratoconus. If the lenses are too loose, they may slip off the cornea into the conjunctival folds, and an attempt to replace them on the cornea may result in abrasion. Foreign bodies and even bubbles under the lens will produce abrasion of the cornea. Lenses worn too long, especially in the adaptation stages, will result in epithelial staining. It is possible to denude the entire cornea of epithelium if the lenses are worn too long.

Epithelial staining per se is not necessarily a serious complication, but the potential after-effects could be disastrous.

Corneal scarring. Surprisingly few cases of permanent scarring of the cornea have been reported. This is usually the result of infection and ulceration following a break in the corneal epithelium.

Infection. Conjunctivitis is not uncommonly seen in contact lens wearers.

Carelessness probably accounts for most cases.

Unbelievable as it may seem, some contact lens fitters recommend the use of saliva as a wetting agent for contact lenses before insertion. Granted saliva is an excellent wetting agent, it is also the harbinger of countless infectious agents.

CORNEAL VASCULARIZATION. One case of total vascularization of the cornea has been reported following the extended use of contact lenses. This is undoubtedly the result of corneal infection. Cases also have been seen where, after extended wearing of the fluid lens without apparent infection, the corneas have shown a growth of vessels into the stroma from the periphery.

FILAMENTARY KERATITIS. One case of filamentary keratitis following the use of contact lenses has been reported.

CONTACT LENS IN THE ORBIT. A case has been noted[29] in which a contact lens was displaced into the upper fornix and after a prolonged period of time penetrated the conjunctiva and entered the orbit. An attempted surgical removal resulted disastrously with a complete ptosis.

CORNEAL INFILTRATES. The author saw 1 case where the corneal lenses were left in place on the cornea continuously for one and one-half years without removal. The patient had many fine white infiltrates in the corneal epithelium which disappeared several months after the lenses were removed.

Undoubtedly, many other complications to the wearing of contact lenses have been seen. Unfortunately, very few of these have been reported in the literature. Most of the complications listed have been from personal communication from ophthalmologists who fit contact lenses rather extensively. If these complications, as seen, would be reported, it might be possible statistically to show them to be the potential source of danger that they are.

There are many facets to this increasing problem in the field of ophthalmology that need clarification. Time does not permit a more extensive discussion and, therefore, it has been limited to indications, contraindications, and complications of contact lens fitting.

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Discussion

H. GORDON ANDERSON, M.D., *Troy, New York.* Dr. McGraw has indicated that there are many facets to the problem of contact lenses, and the time does not permit a discussion of all of these. However, he is to be congratulated in bringing together in such a concise and compact manner the most important facets of this problem.

Ophthalmologists are involved and are going to be involved to a greater extent, whether we like it or not, just because there are indications, contraindications, and complications. Many of these problems, in fact most of them, demand good medical judgment for their solution, and it is unfortunate that to a great extent we have allowed other, less qualified groups to take the lead in the promotion and application of contact lenses.

This interest of other groups, whose interest is, for the most part, commercial, raises another facet of this problem—the legal aspect. The New York State Ophthalmological Society has expended many, many hours of hard work in an attempt to have this aspect clarified and to have legislation modified so that the medical profession assumes its rightful niche. At the time of this writing, one of the opticians in our area has been judged to have violated the present law in that he fitted contact lenses without the personal supervision of a physician. His case has been appealed, and it is my understanding that the State of New York has agreed not to press the case any further until the Legislature meets again. While each contact lens patient should be under the supervision of an ophthalmologist because of the indications, contraindications, and complications, it is obviously unnecessary that the doctor be physically present at all times during the fitting and adaptation period. We should recognize, however, that we do have a very real responsibility and should be in a position really to supervise and check the cases.

Indications

Dr. McGraw has listed very adequately the indications for contact lenses. It almost would be possible to write a paper on each one of the indications and to cite cases where these indications have been fulfilled. In our practice we have had experience with the different types of cases that Dr. McGraw has listed, except those in the group which includes trichiasis, districhiasis, and so forth. There are two indications that Dr. McGraw mentioned which I would like to emphasize. The first of these is anisometropia. The monocular aphakic patient with a successfully fitted contact lens is a satisfied and satisfying patient. It is possible also to obtain useful binocular vision in children with marked anisometropia using contact lenses. We have at least 2 children with high astigmatic or high myopic errors in one eye who have been wearing a contact lens in one eye successfully for approximately two years. These children were approximately six years of age when the lenses were fitted. In these cases the children can obtain binocularity and do not suffer the complications which may occur if they are not binocular.

The other indication that I would like to emphasize is what I would call psychologic. Many young patients with high myopia definitely are benefited by contact lenses. The changes that occur in their personalities are amazing. A shy, retiring, self-conscious individual wearing very thick glasses often is changed to one with a confident, extroverted attitude. I feel that this is an important indication, and when it is accomplished successfully, we have performed a real service.

Contraindications

Again, Dr. McGraw has listed the important points, and it is in this area that the ophthalmologist performs what I believe is his greatest service. Some people just should not wear contact lenses. This may be due to pathologic conditions, as indicated by Dr. McGraw, or because of their whole psychologic and nervous makeup. One very simple and effective way to weed out obvious failures is to take their tension. If, after anesthesia of the cornea, the patient will not allow you to take his tension, he probably will never successfully achieve the wearing of contact lenses.

If we are able to select our cases correctly (and for every patient in our practice for whom we recommend contact lenses, 2 are discouraged from trying them) then one has a chance for a greater percentage of successes and fewer complications.

Complications

It is amazing that we do not see any more serious complications with contact lenses.

In approximately 150 cases in our practice, we have not seen any complications more serious than a severe corneal abrasion or a lens lost in the upper fornix. As Dr. McGraw has indicated, it must be that if the lenses are not fitted correctly, the eye will not tolerate them. The amazing, and at times recuperative, power of the corneal epithelium prevents and limits complications.

I have read recently of an ophthalmologist who within a week saw 2 cases of pyocyaneous ulcers of the cornea as a result of wearing contact lenses. I am sure that one would need only 1 such case to realize that these lenses are not to be prescribed without due consideration of all the possible complications.

The whole problem of contact lenses is and will be a much more serious problem than most doctors realize. We are going to be involved more and more as time goes on in deciding the indications and contraindications and then treating the complications.

One of the most important aspects is selecting the cases carefully. If we do this, the complications will be minimized.

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A series of review articles dealing with medical progress

Recent Advances in Medicine and Surgery

ROBERT TURELL, M.D., Editor

Clinical Tests of Gastric Acidity

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In parallel with advances in understanding the normal and pathologic physiology of the stomach, there has been the development of new tests of function for clinical use and a re-evaluation and modification of older ones. By the use of tests based on physiologic principles, better diagnostic and prognostic accuracy can be achieved. This essay will review the current status and physiologic background of those tests that relate to gastric acid.

Indications for studying gastric acid

At one time a large proportion of medical patients were subjected to some gastric test, but it now appears that there are only a few clinical situations in which studies of gastric acid can give information of value. They are:

1. To establish whether or not the patient's stomach can produce any acid at all; that is, to establish or exclude achlorhydria in the presence of anemia, especially macrocytic, or a neurologic disorder.
2. To measure how much acid a patient's stomach does or can produce, to help in the diagnosis of duodenal ulcer, assess patients with ulcer for surgery, evaluate their condition after surgery, and diagnose hypersecretory states, for example, the Zollinger-Ellison syndrome.

Tests involving intubation

Collection of specimens

The importance of adequate collection seems so obvious that one hesitates to discuss it, except for the fact that in practice adequate care often is not taken. The patient should have fasted a sufficient length of time, preferably twelve hours overnight, so that the stomach is empty of residual food at the start of the test. A tube with a lumen of sufficient caliber should be selected to minimize plugging. We use a Levin tube, 14 or 16 French. The tube, or at least the tip, should be radiopaque so that after passage, the position of the tube may be adjusted fluoroscopically. The tube itself should lie along the greater curvature, and the tip should be in the most dependent position of the stomach, about the midline. The need for fluoroscopic verification of the tube position is to be stressed. We have found that without this precaution, the tube would have been placed inadequately in at least half the tests.

After the tube is positioned, the patient should lie obliquely with his left side down and his head raised about 45 degrees. In this position secretions can be aspirated most adequately from the pool in the lower left portion of the body of the stomach,

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and loss through the pylorus is minimized. The patient is instructed to spit out and not swallow his saliva.

Although the complete recovery of secretions is impossible, in a comparative evaluation of different methods of aspiration, one group found constant hand aspiration to be the most efficient method,[1] while another found continuous mechanical suction to be best.[2] The method we have found to be most practical, yet efficient, is interrupted mechanical suction as provided by a Gumco suction apparatus, supplemented by periodic flushing of the tube with from 10 to 20 ml. of air from a syringe to dislodge mucus or mucosa blocking the tube.

Analysis of specimens

Acidity is measured by titration with 0.1-normal sodium hydroxide, either electrometrically or colorimetrically. "Free acid," measured by Töpfer's reagent or bromphenol blue, reflects hydrogen ion concentration and is inversely affected by the buffering capacity of the gastric aspirate. "Total acid" measures the total amount of acid, free and combined, in a specimen. Physiologically, the titration of "total acid" to neutrality is a more meaningful measurement than "free acid" because even slight amounts of acid, free and buffered, are detected. Phenol red (pH 7 to 7.4) is a more suitable indicator than phenolphthalein whose end point of pH 8 to 9 is in the alkaline range.

As important as the concentration of acid is the measurement of acid output (concentration multiplied by volume). Current theoretic consideration suggests that the parietal cell secretes acid at a concentration of about 160 mEq. per liter. Clinically, concentrations are always below this level because of the mixing of the acid parietal component with the alkaline nonparietal component, saliva, and duodenal reflux, and possibly because of an exchange of sodium for hydrogen after secretion. However, patients producing about the same concentration of acid may produce very different volumes of secretion. Under these circumstances the acid output would be quite different, some patients having a normal output, and others being either hyper- or hyposecretors.

In accordance with modern chemical terminology, results should be expressed in milliequivalents of acid, either per liter or per unit time, as are concentrations of other electrolytes. Although numerically equal, the older terms, such as "clinical units" and "cubic centimeters of sodium hydroxide per 100 cc." are obsolete.

When very small amounts of acid are produced, it may be difficult to establish the presence of this acid by titration. Under these circumstances, the measurement of the pH is of value. The complete absence of acid secretion is indicated by a pH of 7 or above, which cannot be lowered by parietal cell stimulation. Any reduction of the pH below this level indicates some, even if minute, secretion of acid. In the absence of a pH meter, indicator paper of the appropriate range can be used. The measurement of pH is less suitable for specimens of high acidity, since large changes in hydrogen ion concentration may be associated with a minimal shift in pH.

Augmented histamine test

PHYSIOLOGIC BASIS. The augmented histamine test devised by Kay in 1953[2] measures the capacity of the stomach to secrete acid. It is based on the observation that in man, with increasing doses of histamine, the output of acid increases until at a dose level of 0.04 mg. histamine acid phosphate per kilogram maximum output is achieved, and a further increase in histamine dosage produces no further increase in acid output. It is possible to use these large doses of histamine in man only with the prior administration of antihistamines, since these counteract all the effects of histamine except its stimulation of acid secretion.

When the maximum output of acid is achieved, it is assumed that all functioning parietal cells are secreting. Hence, this test is a measure of the number of functioning parietal cells, the parietal cell mass. This theory is supported by correlations, both in man and dog, between maximum acid output and parietal cell counts.[3,4] Since the number of parietal cells in any individual is more or less constant over short periods of time, the results of the augmented histamine tests should be fairly reproducible. This has proved to be true within 10 per cent. This reproducibility, not previously obtainable, is one of the major advantages of this test.

TECHNIC. After the proper insertion and positioning of a Levin tube, the basal secretion is collected for one hour. A suitable antihistamine is administered intramuscularly. Kay used mepyramine maleate (Anthisan). We have found chlorpheniramine maleate (Chlor-trimeton maleate) 10 to 20 mg. suitable, but other antihistamines may be used.

Thirty minutes after the antihistamine, histamine acid phosphate 0.04 mg. per kilogram is injected subcutaneously. Collections are made for the next four fifteen-minute periods, during which hour the output rises to a maximum level and then decreases. Although Kay expresses results as the output of acid during the middle half hour, there are many patients in whom the attainment of the maximum rate is delayed. For this reason others express results as the output for the entire hour. One of us (J.H.B.) has found that the output during the peak half hour, whether this be the middle half or last half, is the most reproducible and satisfactory collection period.

SIDE-EFFECTS AND CONTRAINDICATIONS. Some side-effects are produced in the course of the test because of the large dosage of histamine, but they are usually not severe and are easily tolerated. Flushing and lachrymation are frequent, and occasionally headache ensues. These symptoms usually subside by the time the test is completed. After the histamine has been administered there may be a mild transient hypotension which has not been a problem. Because of the lethargy sometimes produced by the antihistamine, outpatients should rest until they are recovered and should be instructed not to drive for several hours.

Because of possible reactions we have not performed the test in asthmatic patients or in patients with severe cardiac, pulmonary, or renal disease. Also, we have not performed the test in a patient with recent gastrointestinal bleeding. During the test the aspirate may become a dark brown coffee-ground color, suggesting acid hematin. However, this material produces a negative guaiac reaction and is not blood. Its exact nature is unknown. Occasionally it interferes with titration. Bile, due to reflux, may be present in some specimens, but this usually occurs during the basal period and does not interfere significantly during the period of maximum output, although some duodenal reflux is unavoidable.

INTERPRETATION. *The diagnosis of achlorhydria.* With the introduction of the augmented histamine test, it was rapidly established that many of the patients formerly thought to be achlorhydric were either normal or hyposecreters. The only group of patients who invariably have true achlorhydria are adults with pernicious anemia, although it can occur occasionally in other diseases, such as hypochromic anemia, rheumatoid arthritis, diabetes mellitus, aplastic anemia, steatorrhea, gastric carcinoma, and in relatives of patients with pernicious anemia.[5,6]

The diagnosis of duodenal ulcer. Although previous tests have shown that patients with duodenal ulcer on the average secrete twice as much acid as normal patients, the overlap was considerable. After the introduction of the augmented histamine test, it was hoped that it would be possible to improve the diagnostic discrimination. However, the overlap seen with previous tests also occurs with this test, although less. There exists a threshold level of maximum acid secretion below which a duodenal ucler is highly unlikely. At the upper end of the spectrum of maximum acid output there is a level above which a duodenal ulcer is very probable. In general, the diagnosis of duodenal ulcer is made by x-ray examination, but this test can be of value in patients with upper gastrointestinal complaints whose x-ray films are not definitely diagnostic. The exact levels of acid output at which these separations can be made will vary from one laboratory to another, depending on variations in technic and population. The acid output also tends to be higher in men than in women and decreases with age.

Our own means and ranges of maximum acid output for all ages are shown in Table I.

One of us (J.H.B.) concluded that a patient over thirty years probably has duodenal ulcer disease if the maximum acid output is more than 35 mEq. per hour in a man and 15 mEq. per hour in a woman. A patient over thirty years probably does

TABLE I. Means and ranges of maximum acid output for all ages

Sex	Normal (mEq. per hour)	Duodenal Ulcer (mEq. per hour)
Male	17 (0.1 to 42)	34 (11 to 58)
Female	10 (0.3 to 28)	26 (12 to 70)

not have an active duodenal ulcer if the maximum acid output is less than 11 mEq. per hour. A duodenal ulcer is also suggested by a high basal acid output, more than 5 mEq. per hour in a man over thirty years and more than 3 mEq. per hour in a woman. However, this diagnosis cannot be excluded by a low basal output.

On the whole, patients with gastric ulcer have maximum acid outputs within the normal range. Moreover, benign gastric ulcer cannot be separated from gastric carcinoma on the basis of any secretory study, unless achlorhydria can be demonstrated by an augmented histamine test, since such achlorhydria excludes active benign peptic ulceration. This point is to be stressed since in the past attempts at differentiation by secretory tests often have been misleading.

Evaluation of patients for surgery. Patients with duodenal ulcer have parietal cell masses and maximum acid outputs extending over a wide range. Since all operations for duodenal ulcer are designed to reduce gastric acid output, if surgery is indicated, it is reasonable to assume that patients with a very high maximum acid output will require more extensive resection of their parietal cell mass if a recurrent ulcer is to be avoided. Patients whose preoperative study indicates a small maximum acid output then could be treated either by a more limited gastric resection or by decreasing stimuli to their parietal cell mass by vagotomy and/or antrectomy. Moreover, there is some evidence that one can predict preoperatively the results of a vagotomy. The effect of atropine and hexamethonium ("medical vagotomy") on the maximum acid output is correlated with the reduction effected by surgical vagotomy.[7] Knowing the size of the parietal cell mass and the probable effect of the vagotomy, the surgeon is better able to select an operation suited to each individual patient. It is hoped that by such means mortality and morbidity will be reduced.

Stomal ulcers. After surgery dyspepsia may be due to stomal ulceration, which may be difficult to demonstrate either radiographically or gastroscopically. This diagnosis may be excluded reasonably if the postoperative augmented histamine test demonstrates little or no acid, since stomal ulcers usually are found with high maximum acid outputs.[8] In patients with stomal ulcer, the presence of a gastroenterostomy does not significantly affect the collection of secretion or the validity of the test.

Zollinger-Ellison syndrome. A gastrin-secreting islet cell tumor of the pancreas, producing gastric hypersecretion, peptic ulceration, and/or diarrhea, may be suspected on the basis of gastric secretory tests. In this condition the measurement of basal secretion is of particular value, since these patients secrete large volumes of juice with high concentrations of acid. A basal output of more than 200 ml. or 20 mEq. per hour from the unoperated stomach is suggestive of this syndrome. Although the maximum acid output is higher than normal, usually in the upper range of duodenal ulcer, the parietal cell mass in this syndrome is being stimulated pathologically by the gastrin of the tumor so that the ratio of basal to maximum secretion is always abnormally high, usually over 50 per cent and occasionally 100 per cent.[9]

Other tests occasionally indicated

TWELVE-HOUR NIGHT SECRETION. In the twelve-hour night secretion test the basal, interdigestive secretion is measured over a longer period than the one-hour morning basal collection.

The patient has nothing to eat after a small semisolid meal about 4:00 P.M. Later, a tube is passed, and the position is adjusted fluoroscopically. At about 7:00 P.M. the patient is given a hypnotic dose orally or by injection. If possible, the patient should be alone in a side room, screened from the sight or smell of food. At 8:00 P.M. the stomach is emptied, and suction as described previously is maintained for twelve hours. The tube then may be removed, or some other procedure,

TABLE II. Normal values in rounded figures[10,11]

Values	Range	Mean	Significant Difference	Mean + 2 Significant Differences
Volume (ml. per 12 hours)				
Men	170 to 1,200	640	220	1,080
Women	150 to 900	460	220	900
Acid output (mEq. per 12 hours)				
Men	0.4 to 94	20	19	60
Women	0.6 to 68	14	14	40

such as the augmented histamine test, may be performed.

Normal values as derived from the data of Levin *et al.*[10,11] and rounded off are indicated in Table II.

A twelve-hour output of more than 1,000 ml. is found in only 1 in 20 normal subjects, but in nearly half the patients with duodenal ulcers, and rarely in patients with gastric ulcer and carcinoma. A twelve-hour output above 1,200 ml. or 60 mEq. of acid suggests that the patient probably has a duodenal ulcer, and values below 300 ml. or 10 mEq. of acid every twelve hours suggest that a patient probably has not a duodenal ulcer. Outputs above 2 L. suggest the possibility of the Zollinger-Ellison syndrome.

We do not use this test, since it has no advantages over the morning basal secretion and has the additional disadvantages that it can be done only in a hospital, that patients dislike keeping a tube in so long, and that nurses find it difficult to check frequently to see that the pump is working and that the tube is not blocked.

Single intubation. The diagnosis of pernicious anemia is in general excluded by any test which demonstrates the presence of acid in the stomach. The simplest screening test is to sample the gastric contents one hour after an appetizing meal, which is in itself a potent stimulant of acid secretion. If no acid is obtained, an augmented histamine test must be performed before achlorhydria can be established.

The presence of pyloric stenosis is established by the demonstration of an abnormally large gastric residue. The normal stomach is almost empty three hours after a meal. In a patient suspected of having pyloric stenosis, a large-bore stomach tube should be passed four hours after a meal, the stomach emptied, and the tube removed. A gastric residue of more than 250 ml. is an almost certain indication of pyloric stenosis.[12]

Insulin test. The completeness of a previous surgical vagotomy can be tested by the failure of the stomach to secrete acid in response to hypoglycemia, a central vagal stimulus.[13]

The fasting contents (FC) of the stomach are collected completely (specimen FC 1), and two further specimens of fasting juice (FC 2, FC 3) are collected at fifteen-minute intervals. Blood is taken for sugar analysis, and from 10 to 20 units of regular insulin are injected intravenously. The stomach is emptied completely every fifteen minutes for two hours, and blood specimens are taken every thirty minutes during this period. Each specimen is tested after its withdrawal with Congo red paper, and if no free acid is present, a histamine test should be done before the tube is withdrawn. Fifty per cent dextrose must be available for an immediate intravenous injection should symptoms or signs of severe hypoglycemia develop.

Interpretation. Vagal innervation is present if there is a rise in the concentration of acid of 10 mEq. per liter above the base line, if the resting contents were anacid. If free acid is present in the basal specimens, the acidity of two consecutive specimens after insulin must be at least of a concentration of 20 mEq. per liter above the mean acidity of FC 2 and 3.

Vagal innervation is absent if there is no change or a decrease in acidity in response to adequate hypoglycemia and if the stomach is known to be capable of secreting free acid.

Equivocal results are obtained if there is a slight or indefinite rise in acidity. The test should be repeated.

Inadequate results are obtained if the test produces negative findings but the blood sugar does not fall below 50 mg. per 100 ml. The test should be repeated, and if necessary a larger dose of insulin should be given.

No conclusion can be drawn about vagal innervation if no acid is secreted (achlorhydria) either during the insulin test or after histamine.

Prolonged sampling of gastric contents in patients with upper gastrointestinal hemorrhage

With a syringe small samples (5 to 10 ml.) of gastric contents are aspirated hourly, and the pH of each sample is measured. It may not be possible to check the position of the tube fluoroscopically if the patient is too ill to move.

By the inspection of each specimen at the bedside the presence of bloodstaining sometimes indicates further hemorrhage before clinical or fecal evidence of further hemorrhage suggests it. There are three diagnostic patterns of acidity in the hourly samples: high night acidity, suggestive of duodenal ulcer; nocturnal neutralization, suggestive of chronic gastric ulcer; and achlorhydria, suggestive of acute ulceration or erosion. It has been reported that in half to two thirds of patients with upper gastrointestinal hemorrhage, such secretion patterns accurately predict the final diagnosis.[14] We have had no personal experience with this procedure.

Tubeless tests of gastric acid

Intubation may be avoided in the exclusion of achlorhydria by the use of cation exchange resins which dissociate in the presence of acid in the stomach, the cation then being absorbed and excreted in the urine where it can be measured easily.[15] These resins are available commercially, and the makers' instructions should be followed for the details of the test. If the test is performed correctly, a positive result signifies the ability of the patient's stomach to secrete acid, excluding the diagnosis of pernicious anemia. A negative test result may mean that the patient has achlorhydria, but this result must be checked with an augmented histamine test. Misleading results, both false negative and false positive, may be obtained where abnormalities of absorption or excretion exist, for example, after partial gastrectomy, in pyloric stenosis, malabsorption states, diarrhea, and renal disease.

Other tests in current use but not recommended

FASTING ASPIRATE. A tube is passed in the morning on a fasting patient, part or whole of the gastric contents are removed, and the concentration of acid is measured.

FRACTIONAL TEST MEAL. After the gastric residue has been removed, the patient is given some form of meal, whether gruel, soup, biscuits, toast, alcohol, or water. Samples are removed every fifteen minutes for two or three hours and the concentration of acid is measured and shown graphically.

HISTAMINE TEST. Instead of a meal, 0.5 to 1 mg. (or 0.01 mg. per kilogram) of histamine acid phosphatase is given subcutaneously, and samples are taken as before for the measurement of acid concentration.

These tests have been used clinically for nearly half a century on hundreds of thousands if not millions of people all over the world. Such tests, although the best available at the time, can no longer be justified today. Apart from the finding of acid excluding a diagnosis of pernicious anemia, these tests are of little or no diagnostic value. They fail because they are not reproducible, because the stimuli are arbitrary and inadequate, and because the results represent the concentration of acid in the samples of mixed meal and the gastric juice and depend on the rate of emptying as well as on the rate of secretion of the stomach. Therefore, such tests can provide no information on the output of acid gastric juice as are provided by the quantitative measurements of basal and maximum secretion described previously.

Summary

Clinical tests of gastric acid are indicated to establish or exclude achlorhydria, to assist in the diagnosis of duodenal ulcer, to evaluate ulcer patients before and after surgery, and to aid in the diagnosis of the Zollinger-Ellison syndrome.

The methods for the collection and analysis of gastric secretion are described in detail.

The physiologic basis, technic, and interpretation of the various tests are discussed.

The clinical value of the augmented histamine test has been stressed, and it is suggested that many of the previous procedures should be abandoned in its favor.

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Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Lebanon Hospital
The Bronx, New York
January 18, 1962

Conducted by JOSEPH C. EHRLICH, M.D.,* and
SAMUEL J. SCHNEIERSON, M.D.†

Discussed by BERNARD S. KAHN, M.D.,** and
RUDOLF PLATT, M.D.††

Congestive Heart Failure with Acute Abdominal Catastrophe

Case history and discussion

Bernard S. Kahn, M.D.: The patient, a fifty-year-old white male, was a gasoline station attendant. In the late morning of May 1, 1961, while he was at work, he was alarmed suddenly by the sight of a car backing toward and almost striking a child. Immediately thereafter he had severe epigastric pain, causing him to stop work and go home. He had no desire for food, but was not nauseated and did not vomit. The abdominal pain remained constant during the rest of that day. He could not lie on his abdomen; the pain was unaffected by positional changes. His physician prescribed tablets which I believe contained belladonna, atropine, or some other anticholinergic drug. These gave slight relief. His pain continued through May 2 and 3. After an oral dose of Demerol hydrochloride on May 3, he vomited a small amount of yellowish fluid. His physician arranged for a radiographic study of the gallbladder on May 4 and administered the appropriate tablets the night before. At his physician's office on the morning of May 4, after a single film had been taken, his pain became so intense that he was admitted to the hospital seventy-two hours after the onset. He had had no bowel movement from the onset of his symptoms until the night before his admission, when he passed two loose stools. Whether or not this resulted from the ingestion of the dye cannot be stated with certainty.

His previous history revealed an episode of similar abdominal pain of lesser severity about four years ago, lasting two days, and subsiding spontaneously. Fifteen years ago he was rejected as a Navy yard laborer because of "heart trouble." He first came under the care of his present physician three years ago, at which time diagnoses of rheumatic heart disease and atrial fibrillation were made. At that time there was evidence of mild congestive failure for which a digitalis preparation and an injection of mercaptomerin sodium (Thiomerin sodium) were given. Since then, he visited his physician at irregular intervals of two or three months, usually complaining of dyspnea on exertion and ankle edema. These were relieved by digitalis and mercaptomerin sodium. Systolic and diastolic apical murmurs were heard at each visit.

At the time of admission the patient was quite comfortable and free of pain. This, I felt, was due to a recently administered dose of opium alkaloids (Pantopon). He was not nauseated. His face was flushed; the skin was warm. The neck veins were not distended in the recumbent position, and he was not in respiratory distress. The tongue was furred and dry. The chest was of the emphysematous type. The heart was enlarged to the left with the point of maximal impulse in the fifth intercostal space in the anterior axillary line. The rhythm appeared grossly regular with a rate of 84 per minute. However, an electrocardiogram tracing showed atrial fibrillation with a bigeminal rhythm typical of digitalis toxicity. There was no graphic evidence of myocardial infarction. No murmurs were heard. The blood pressure on admission was 180 mm. systolic; one-half hour later it was 150/100. At the bases of both lungs there were scattered rales which disappeared after coughing. The abdomen was soft and moderately distended. It was tender on the right side and in the epigastrium, but no rigidity was found. No organs, masses, or hernias were palpated. A rectal examination did not reveal prostatic enlargement or masses. The color of the stool on the examining finger was raspberry red with a blackish cast and was strongly positive for blood.

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Because of the relative comfort of the patient and the minimal abdominal findings seventy-two hours after the onset of the symptoms, operative intervention was postponed until more data could be obtained and the course of the illness observed without the effects of the opium alkaloids. The digitalis toxicity was treated by an infusion of 5 per cent glucose with 20 mEq. of potassium chloride. Triplex, a potassium preparation, was given by mouth. Laboratory studies before the institution of therapy showed the following: blood sugar 180 mg. per 100 ml., amylase 308 Victor Meyer units, and the urine negative for sugar and albumin. Microscopically, 3 to 5 white blood cells were found. The hemoglobin was 16.6 Gm. per 100 ml., and the white blood cell count 21,700 with 62 per cent polymorphonuclear leukocytes, 12 per cent bands, 22 per cent lymphocytes, and 4 per cent monocytes.

At this point, it would be appropriate for Dr. Friedenberg to demonstrate the radiographic findings.

Richard M. Friedenberg: A routine abdominal series, including films with the patient in the decubitus, erect, and supine (Fig. 1) positions, was carried out at the time of his admission. An opacity in the right upper quadrant of the abdomen represents a small, contracted gallbladder filled with contrast material. A small amount of similar material remained in the stomach. The stomach was enormously dilated, extending down to the iliac crest and across to the right side of the abdomen. There was marked fluid retention indicative of the patient's inability to empty the stomach by vomiting. There was marked dilatation of numerous loops of small bowel, primarily in the proximal and midjejunum, with gas present in the colon. The colonic gas which you see in the pelvic region indicates that the patient did not have a low colonic obstruction producing small-bowel dilatation. The dilatation of the stomach (Fig. 2) confirms the likelihood of an ileus rather than an intestinal obstruction. We assume that this represents some form of paralytic ileus due either to an acute inflammatory condition, such as pancreatitis, or secondary to mesenteric thrombosis.

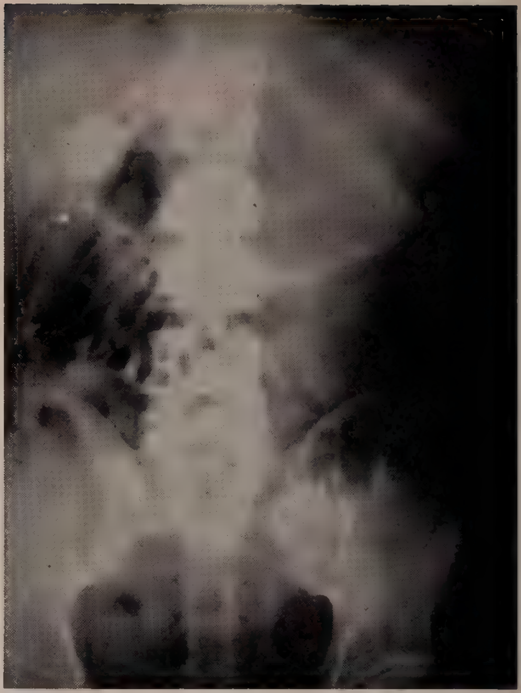

FIGURE 1. Plain supine radiograph of abdomen showing contrast medium in gallbladder and retained contrast medium in a dilated stomach; dilated loops of small intestine.

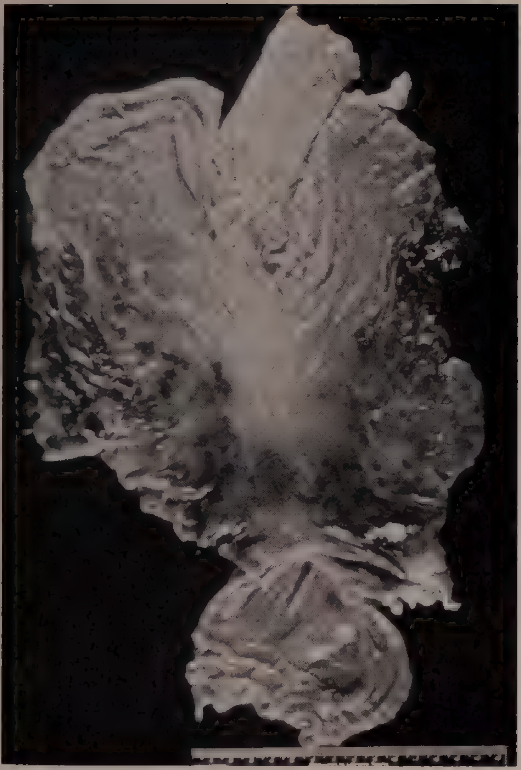

FIGURE 2. Dilated stomach and duodenum (esophagus above, pylorus and first portion of duodenum below). Acute hemorrhagic infarction of body and antrum of stomach.

Either of these diagnoses would be acceptable, except that in pancreatitis we would expect to see dilatation of the transverse colon with this degree of small-bowel dilatation. The functioning gallbladder also argues against the diagnosis of pancreatitis, in most cases of which gallbladder visualization is not obtained. Occasionally, a long-standing obstruction of the jejunum may induce secondary ileus with dilatation of the stomach. This can be excluded in the present case because of the acute onset and short duration.

It is my feeling that in cases such as this, where it is necessary to differentiate among obstruction, perforation, and ileus, gastrointestinal studies utilizing oral Hypaque or Renografin should be performed. There is no danger to the patient except for the delay of an hour of two because of the study itself. The procedure is performed without fluoroscopy. The site of the obstruction or perforation, if present, often will be demonstrated.

In this case, our conclusion is that there is a paralytic ileus affecting the stomach and the proximal jejunum, perhaps secondary to a local inflammatory condition, but more likely secondary to mesenteric arterial or venous thrombosis.

DR. KAHN: Three hours after the patient was examined, he developed excruciating pain in the abdomen. Tenderness was present at this time in the left lower quadrant on both sides of the abdomen at the level of the umbilicus. A laparotomy was performed at once. The preoperative diagnoses considered were mesenteric thrombosis, acute pancreatitis, and penetrating or perforated peptic ulcer.

The surgeon reported that on opening the abdomen there was a cadaveric smell, the bowel was discolored throughout, having a faint bluish tinge, and through the coats of the large intestine a darker blue was present that was thought to represent intraluminal blood. He also noted that the bowel "didn't feel right," that it did not feel like "live" bowel. At the midzone of the jejunum there was a serosal deposit of plastic exudate. The small bowel and the stomach were markedly dilated, and the duodenum appeared to be four to five times the normal diameter. There was very little fluid in the abdomen, but some seropurulent material was found in the pelvis. Stasis was noted in all the veins of the small bowel. The superior mesenteric artery pulsated strongly throughout its palpable length. On exploration, no perforation was found; there was no obstructing band, hernia, or evidence of a recently released obstruction. Fat necrosis was not observed. The abdomen was closed; intravenous fluid with added potassium chloride was administered. The blood pressure and pulse shortly became unobtainable. Levophed was given by slow drip without any effect in elevating the blood pressure. The patient became comatose and died fourteen hours after the operation.

In discussing the differential diagnosis, I am fortunate to have at my disposal the findings at operation of an experienced and careful surgeon. Prior to surgery, the following conditions might have been considered: biliary colic, acute cholecystitis, perforating or penetrating peptic ulcer, acute pancreatitis, acute intestinal obstruction, dissecting aneurysm of the aorta, acute porphyria, benign paroxysmal peritonitis, and mesenteric thrombosis of diverse etiologic origin, including embolic occlusion from bacterial endocarditis. When the abdomen was opened, all but two of these diagnoses were eliminated. One is acute pancreatitis; the other is gangrene of the bowel on a vascular basis. Despite the fact that no evidence of fat necrosis was present, there were clinical findings that make a diagnosis of acute pancreatitis a most important consideration. I shall discuss these findings and certain considerations which might have prevented abdominal exploration in this case.

In a patient who has no history of diabetes, who has abdominal pain suggestive of an acute condition of the abdomen, and who has an elevated blood sugar or glycosuria, acute pancreatitis is a strong possibility. This patient, who did not have diabetes during a three-year period of observation, had a blood sugar of 180 mg. per 100 ml.

Arkin[1] states "the elevation of serum amylase above 400 Somogyi units, or over 200 units when performed seventy-two hours or more after the onset of symptoms, confirms the diagnosis of acute pancreatitis." This patient had a serum amylase of 308 units seventy-two hours after the onset of his symptoms. However, there are pitfalls in taking the dictum of Arkin literally.

The elevation of serum amylase can occur for reasons other than acute pancreatitis. Technical error may result from adulteration of the incubation mixture by pipettes contaminated by saliva. Peritonitis may produce an elevation of amylase; opiates, especially morphine, may elevate the amylase, and patients with advanced renal disease may retain amylase because of poor kidney function. Mumps, viral hepatitis, and high intestinal obstruction may be associated with high amylase. An additional factor in our laboratory is that we use the Victor Meyer method, not the Somogyi method; the former gives a higher normal figure, because of what are believed to be optimal conditions for the activity of this enzyme. Still, in looking over our figures, I believe that 200 units might well be set as the upper limit of normal. Our chemist, Max M. Friedman, M.D., thinks 300 units is the upper limit of normal for the Victor Meyer method. In any case, I believe that 308 units here represents an elevated amylase.

Other findings conform to the diagnosis of acute pancreatitis. A relatively soft abdomen is not unusual in pancreatitis, but it is uncommon with a perforated ulcer. The so-called sentinel loop of the distended jejunum in acute pancreatitis also may occur in other conditions. Electrocardiographic changes may occur in acute pancreatitis but are usually nonspecific. Blood in the stool is the most difficult symptom to squeeze into the diagnosis, but O'Brien and Thayer[2] report the passage of red blood per rectum in 4 patients with acute pancreatitis; they attribute this phenomenon to mucosal changes in the bowel overlying the inflamed pancreas.

Thus, by gathering a series of possible improbabilities, a good case might have been made out for acute pancreatitis, and an operation might have been avoided. You might say that in this case the outcome could not have been worse. But the lesson to be drawn is that when you stay out of an abdomen because you have decided that the patient has acute pancreatitis, you had better be certain of your diagnosis. A very high titer of serum amylase early in the illness, a history of chronic gallbladder disease, and a clinical picture that has few "ifs" or "buts" should be present; even then, one is apt to suspect that he may be missing a condition curable only by surgery.

While the diagnosis of acute pancreatitis, for the reasons stated, is attractive, I cannot overlook the surgeon's description of the intestines. It suggests gangrene even though the classical picture of a black gut was not present. The cadaveric smell, the bowel that "didn't feel alive," the bluish tinge, the venous stasis, all speak for early intestinal gangrene and immediately suggest the possibility of mesenteric arterial or venous thrombosis. In addition, massive gangrene of the bowel may occur without vascular occlusion. Careful necropsy dissection in such cases has disproved the contention of the operating surgeon that the thrombus was missed by the prosector. Ende[3] states that it is quite possible for intestinal infarction to develop without arterial occlusion, especially in the presence of severe cardiac disease. He believes that severe cardiac failure can create a situation similar to symmetrical peripheral gangrene complicating myocardial infarction.

The presence of a fully pulsating mesenteric artery therefore makes one of two diagnoses probable: intestinal infarction with gangrene without vascular occlusion, or mesenteric venous thrombosis as the cause of the gangrene. However, the bowel necrosis is too extensive for venous thrombosis.

Harris Blinder, M.D.: The electrocardiograms showed bigeminy, and the question of digitalis toxicity as the cause of this bigeminy was raised. However, in some of the leads, where there were no extrasystoles, the rate of the fibrillation was fairly rapid. This would incline me to believe that the bigeminy and extrasystoles were due to myocardial insufficiency rather than to digitalis toxicity.

Leon Sasson, M.D.: I believe that the clinical picture, course, and findings at laparotomy clearly point to the diagnosis of mesenteric vascular occlusion. However, I would like to state my reasons for thinking that the occlusion was on the venous side. At laparotomy, it was found that the veins were dilated; in my opinion this suggests probable thrombosis of the superior mesenteric veins. When the pathologic process is less rapid, the symptoms are less acute; congestion and ischemia develop gradually. Finally, ischemic necrosis of the wall of the small intestine occurs with clinical evidences of shock and paralytic ileus. I think the essential problem in this case is concerned with the cause of the mesenteric venous thrombosis. First, we have to consider appendiceal inflammation. I think we can rule this out because there was a thorough exploration. Other causes also can be eliminated because of negative findings at the laparotomy. These include pelvic inflammatory disease, trauma, and compression by a tumor. Cases due to thromboangiitis obliterans have been reported. Occasionally, venous mesenteric thrombosis occurs in association with carcinoma of the pancreas. Carcinoma of the pancreas may have been present in this case; it may have been small in size and concealed in the body of the pancreas. This also might explain the elevated blood glucose. As far as the patch of plastic exudate on the wall of the jejunum is concerned, I think this is secondary to early ischemic necrosis of the bowel. This also would account for the fetid odor when the abdomen was opened. Of course, any inflammatory disease of the viscera drained by the portal or superior mesenteric veins may cause thrombosis of these veins. For example, this patient may have had a jejunal ulcer.

Should this be the case, I would guess that it was a secondary and not a primary jejunal ulcer, because the latter is a rare condition, and we have no evidence to support such a diagnosis. The slightly elevated amylase also could be secondary to ischemic necrosis of the bowel wall.

Samuel J. Schneierson, M.D.: In view of the patient's atrial fibrillation, I think that on a statistical basis it is much more likely that his infarction of the bowel was due to arterial obstruction by an embolus, despite the operative findings.

Samuel Weiskopf, M.D.: I would like to ask if bowel sounds were noted early in the course of the abdominal pain. If such sounds were present and disappeared subsequently, this would favor the diagnosis of mesenteric thrombosis, since it would suggest the development of paralytic ileus on a nonmechanical basis.

Dr. Schneierson: The following observation is a little facetious. Dr. Kahn read a long list of entities that he was willing to exclude from consideration because of the operative findings. Among them was benign peritonitis. I dare say that he could have excluded that diagnosis even without the information available from surgery.

Herman L. Frosch, M.D.: While the presence of auricular fibrillation favors arterial embolization, I would prefer to think of multiple seeding of small arteries, in view of the fact that the surgeon reported normal pulsation of the major arteries.

Dr. Schneierson: Dr. Frosch then, like Dr. Walter Alvarez, is on the side of "small strokes."

Lester L. Ostrove, M.D.: I find

myself in complete agreement with Dr. Sasson's diagnosis of thrombosis of the superior mesenteric vein. I would like to suggest as one possible cause the extreme fright experienced by the patient on the day he began to have pain. It could be postulated that with the fright he had a marked adrenal response with engorgement of the visceral blood vessels, followed by the development of the venous thrombosis.

Joseph C. Ehrlich, M.D.: Dr. Kahn offered two interpretations of the bowel infarction: one without and one with vascular occlusion. I wonder if he would care to state his preference.

Dr. Kahn: Well, if you want me to make a diagnosis, not with a shotgun, but with a rifle, I think that you did not find a thrombosed vessel at autopsy. I believe that we are dealing with an infarction in the absence of a vascular occlusion. It is quite similar to finding myocardial infarction without coronary thrombosis. I don't think that you found venous thrombosis either, because this condition has an entirely different set of causes, any one of which could have been recognized easily at laparotomy. Furthermore, venous thrombosis has to be quite extensive before interference with circulation sufficient to cause infarction occurs.

Benjamin Sherwin, M.D.: My findings at laparotomy with exploration already have been described in detail and need not be repeated by me.

In a recent paper, Berger and Byrne[4] reported an analysis of 110 cases of gangrene of the bowel at the Boston City Hospital. Twenty-three of these were unassociated with occlusive disease of either mesenteric arteries or veins. I have had one previous experience, in an elderly cardiac patient, of encountering a gangrenous bowel at laparotomy without being able to find a thrombus in either the mesenteric artery or the vein.

I agree with Dr. Kahn's interpretation of this case as an infarction of the bowel without mesenteric vascular occlusion.

Clinical diagnosis

1. Paralytic ileus of unknown etiologic cause, possibly due to mesenteric venous thrombosis

2. Arteriosclerotic heart disease; atrial fibrillation; digitalis toxicity

Dr. Kahn's diagnoses

1. Intestinal infarction without vascular occlusion

2. Arteriosclerotic heart disease with atrial fibrillation and congestive heart failure

Pathologic report

Rudolf Platt, M.D.: The necropsy was performed two hours after the patient's death. The patient, who was a well-developed, middle-aged male, had a barrel-shaped chest, and there was a slight cyanosis of the lips. There was no peripheral edema. The pericardial and pleural cavities did not contain excessive fluid. The abdomen was extremely distended. The heart was moderately enlarged and weighed 530 Gm. There was a tight stenosis of the mitral valve, whose narrowed orifice was reduced to a curved "button-hole" opening measuring 1.5 cm. transversely by 0.5 cm. anteroposteriorly. At one of the fused commissures there was a pocket filled with an adherent fibrin clot. I don't believe that this fibrin clot had further compromised the already narrowed opening of the mitral valve. Both atria and the right ventricle were dilated. The pattern of mitralization included hypertrophy of the right ventricle and dilated pulmonary artery branches with yellow atheromatous plaques. There was severe chronic passive congestion of the lungs with hemosiderin; in addition, they were markedly emphysematous. The right auricular appendage contained an organized thrombus; this had not embolized to the lungs. There was severe chronic passive congestion of the liver, and sections showed evidences of coagulation necrosis in the centrolobular areas. The kidneys were moderately enlarged; their surfaces were pale yellow and presented several small, healed infarcts. In addition, the right kidney contained two fresh ischemic infarcts, one measuring 3 cm. and the other measuring 1 cm. in diameter. On section, the cortices of the kidneys were edematous and pale yellow. Microscopically, there was marked hydropic degeneration of the tubular system. The parenchymal changes in the liver and the kidneys are ascribable to postoperative shock and anoxia due to circulatory insufficiency. The fresh infarcts in the right kidney probably resulted from emboli arising from the thrombus on the mitral valve. The coronary arteries were slightly sclerotic but not narrowed or occluded, and the myocardium was free of scars.

The abdomen was extremely distended. The peritoneal cavity contained about 100 cc. of dark red bloody fluid. The entire gastrointestinal tract was distended and had a dusky, purplish-red color. The serosa of the small intestine and the parietal peritoneum were covered by thin layers of fibrinopurulent exudate. The stomach, although dilated, was not as enormous as it appeared to be in the radiographs. The small and large intestines also were markedly dilated and were filled with fresh blood. There was extensive hemorrhagic infarction of the stomach, involving chiefly the body and antrum (Fig. 2). The lesser curvature and the pyloric ring escaped infarction. The duodenum; the entire small intestine; and the ascending, transverse, and descending portions of the colon also showed extensive hemorrhagic infarction. Microscopically, the necrosis seemed to become more severe as one proceeded distally. In the stomach, duodenum, and upper jejunum, the infarctive hemorrhage and necrosis were limited chiefly to the mucosa and submucosa. In the lower jejunum, ileum, and the transverse and descending portions of the colon, the infarction involved all the layers of the bowel.

A cautious dissection of the mesenteric vessels failed to disclose evidence of either an old or a recent occlusion in the arteries or veins. The mouths of the celiac, superior mesenteric, and inferior mesenteric arteries were widely patent. There was moderate arteriosclerosis of the aorta but no ulcerated plaques.

This is an instance of non-occlusive infarction of the intestinal tract. This condition should not be confused with so-called abdominal angina or the mesenteric insufficiency syndrome,* which is associated with an old occlusion or marked narrowing of at least one main artery to the gut without intestinal infarction. In the latter group, weak or absent pulsation of the affected vessel usually will be found at the time of an exploratory laparotomy.

The recent literature indicates an increasing awareness of nonocclusive infarction of the bowel. Glotzer and Shaw,[5] who studied 31 cases of fatal intestinal infarction, were unable to demonstrate vascular occlusion in 9 cases. Berger and Byrne's[4] statistics already have been referred to by Dr. Sherwin. Decompensated cardiac failure is a prominent feature of most of the reported cases. In the 11 cases of nonocclusive gangrene of the gut reported by Gazes *et al.*[6] all of the patients had had extensive digitalis therapy, and some showed evidence of digitalis intoxication. Only 6 of their cases were in congestive heart failure.

Dr. Frosch: Were the small arteries of the bowel studied microscopically for thrombi?

Dr. Platt: Yes. None were found. About three years ago we performed a necropsy on a patient fifty-nine years of age with heart disease, arteriosclerotic in nature, but the patient was not in congestive failure. That patient had entered the hospital with an acute condition of the abdomen and died on the day of admission. In that case, too, we found massive necrosis of the gut without vascular occlusion.

Dr. Ehrlich: Our department had been alerted to the issues in this case prior to the necropsy. The abdominal portion of the aorta was opened in situ, and the mouths of the superior mesenteric and celiac arteries were inspected for thrombotic, embolic, or other obstructions. The contents of the aorta were sifted for thrombi which might have been dislodged during the preliminary dissection. None were found. Special care was exercised to carry out the evisceration with a minimum of disturbance so that the intestinal vasculature could be studied in as near to a natural state at the time of death as possible.

The participation by the stomach in the infarctive process is most unusual. Reiner *et al.*[7] stated that the stomach seems to be immune to ischemic damage from arterial occlusions. Cohen[8] found that experimental gastric infarction requires both arterial and venous impediment. He reported 4 patients with an infarction of the stomach. There was an arterial, venous, or combined arterial and venous impediment in each. In the case discussed by Grier and Reiner,[9] the stomach was infarcted along with the small intestine and the cecum. At laparotomy the superior mesenteric artery was pulseless; when the artery was opened, there was no flow of blood. A catheter was inserted into the artery proximally, and the vessel was irrigated with heparin solution, after which the blood flowed freely and pulsation returned. This was interpreted as relief of the spasm. It is equally possible that an occluding thrombus was dislodged by this procedure and forced back into the aortic lumen.

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* Dyspraxia arteriosclerotica intestinalis (Ortner's syndrome).

The occurrence of an infarction of the bowel without regional mechanical vascular obstruction can no longer be questioned. Pathogenetic mechanisms which have been considered include arterial spasm, anaphylaxis, impaired capillary permeability, and dissolution of thrombi by fibrinolysin.[10] An alternative possibility is that despite patent vascular lumina, impaired biochemical transport due to circulatory insufficiency in relation to local tissue demands may lead to a net deficit below the critical level for cell survival. Such mechanisms have been invoked to explain not only myocardial infarction and peripheral gangrene without mechanical vascular occlusion, but also cerebral infarction.[11]

Anatomic diagnoses

1. *Nonocclusive hemorrhagic infarction of stomach, small intestine, and large intestine*

2. *Chronic rheumatic heart disease with severe mitral stenosis and insufficiency; organizing mural thrombus in right auricular appendage; congestive heart failure*

3. *Diffuse centrolobular necrosis of liver*

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Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

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Carbon Tetrachloride Poisoning

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Cleaning Fluid	16 years	Male

This patient, who is employed in a local department store, reported to their medical department because for the past few days he had been bleeding from the lips, gums, and nose and also had some hemorrhagic spots on the skin. The history obtained by the medical director indicated that the patient was cleaning his clothes in a closed room with a spot cleaner containing carbon tetrachloride two days prior to the onset of symptoms. The medical director referred him to a hospital where he was a member of the staff. The patient, however, went to a hospital in The Bronx where he was not treated but was referred to still another Bronx hospital.

At this hospital, the mother was told that they would need the services of a private physician. The family then decided to have the patient admitted at a hospital in Manhattan. On admission to this hospital the presenting symptoms were nausea and hemorrhagic purpuric spots on the skin. The examining physician felt that the patient had inhaled fumes of carbon tetrachloride while he was cleaning his clothing, that some of it had spilled on his bed clothes, and that presumably the patient had inhaled some of the product during the night while he was asleep.

The laboratory findings included hemoglobin 14.10 Gm. per 100 ml., hematocrit 45; white blood count 10,800 with stabs 4, segments 43, lymphocytes 46, and monocytes 7. The platelet count was 120,000 and the red blood count 4,960,000.

The urine showed a trace of albumin. A tentative diagnosis of carbon tetrachloride poisoning with hemorrhagic purpura was made. The patient was given whole blood and was transfused with packed cells. Prednisone also was administered 5 mg. four times daily, and vitamin C 250 mg. was given four times daily. Four hundred mg. of Miltown were given, and 2 tablets of Gelusil also were given four times daily.

From conversations with the mother there was a strong suspicion that this boy might be addicted to sniffing because of some questionable associates. This hypothesis appeared to be tenable. The exposure to carbon tetrachloride fumes hardly would account for the severity of the presenting symptoms. After unsuccessful attempts to obtain an accurate history, this hypothesis was finally discarded because it was ascertained that the youth had been in the habit of ingesting an enormous amount of aspirin at the slightest onset of a headache. Unfortunately, a salicylate determination level was not done during his hospital stay of twenty-three days. It is thus postulated that the bleeding was due to chronic aspirin ingestion, and as is often the case, the diagnosis was confused by a supposedly incriminating incident.

This case illustrates the need for a thorough examination. No possibility for the determination of the true etiologic factor should be overlooked. Of course, it is possible that the bleeding in this case was caused by multiple etiologic factors.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Carbon Tetrachloride	23 years	Male

The Poison Control Center was called by a physician from Summit, New Jersey, relating to a case of carbon tetrachloride poisoning. At the time the Poison Control Center was called, the patient was actually moribund. The history was as follows: Three days before admission the patient cleaned his shoes in a closed closet with carbon tetrachloride (Carbona). It was also ascertained that the patient ingested some alcohol prior to the cleaning. These facts were not revealed until the day of his death.

The presenting symptoms on admission to the hospital were nausea, vomiting, and diarrhea. The patient died seven days following the onset. The cause of death was attributed to carbon tetrachloride poisoning, and the findings on autopsy were hepatic necrosis, uremia, nephritis, pulmonary edema, and cardiomegaly.

Comment

The continuing involvement of carbon tetrachloride in serious, nonfatal as well as fatal accidents is an indication that there is no justification for the use of this chemical in the home, especially since there are available much safer and equally effective products. There already has been an encouraging trend on the part of some of the distributors of these products to affect this substitution.

Since the use of carbon tetrachloride has been disappearing from the dry cleaning industry itself, there is an urgent need to accelerate this disappearance also from home use.

Treatment

There is no known antidote for carbon tetrachloride poisoning. This product depresses and acts as a cell irritant to the central nervous system, liver, kidneys, and blood vessels.

It has been found that alcohol ingestion increases the damage of carbon tetrachloride on the tissues. Poisoning can occur from all routes, such as inhalation, absorption, and ingestion. The best treatment is, of course, total prevention.

In the treatment of carbon tetrachloride poisoning, artificial respiration should be begun and kept up until consciousness returns if the product was inhaled. Contaminated clothing should be removed. If the product was ingested, induced vomiting and gastric lavage are indicated. Otherwise, treatment must be supportive and symptomatic. The blood pressure should be maintained with the aid of 5 per cent glucose intravenously.

One must be cautioned not to give any stimulants, and particularly epinephrine and ephedrine should be withheld to prevent ventricular fibrillation. A high carbohydrate and high calcium diet is recommended to prevent liver damage. If kidney damage occurs and if renal shutdown is imminent, dialysis may be lifesaving. Since kidney damage is common, frequent urinalysis and blood chemistries should be done as guides for indicated therapy.

In chronic poisoning the immediate removal from an injurious environment is essential, otherwise treatment is symptomatic and supportive and essentially the same as for acute poisoning.

Number ninety-eight in a series of Accidental Chemical Poisonings

Case Reports

Sarcoid and Malignant Teratoma of the Lung

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Sarcoidosis continues to be a riddle with our failure to discover a specific etiology. The diagnosis, in the absence of a specific etiologic agent, is based almost entirely on a histologic analysis of tissue, supported by laboratory tests.

In 1948 the National Research Council gave the following definition of sarcoidosis:

> Sarcoidosis is a disease of unknown etiology. Pathologically it is characterized by the presence in any organ or tissue of epithelioid cell tubercles with inconspicuous or no necrosis and by the frequent presence of refractile or apparently calcified bodies in the giant cells of the tubercles. The characteristic lesion may be replaced by fibrosis, hyalinization, or both.
>
> Clinically, the lesions may be widely disseminated. The tissues most frequently involved are the lymph nodes, lungs, skin, eyes, and bones, particularly of the extremities.
>
> The clinical course usually is chronic, with minimal or no constitutional symptoms; however, there may be acute phases characterized by a general reaction with malaise and fever. There may be signs and symptoms referable to the tissues and organs involved.
>
> The intracutaneous tuberculin test result is frequently negative; the plasma globulins are often increased.
>
> The outcome may be clinical recovery with radiographic evidence of residue, or impairment of function of organs involved, or a continued chronic course of the disease.[1]

None of these features is pathognomonic for sarcoidosis, and a wide variety of agents occasionally can cause the production of a similar tissue reaction.[2] Thus the epithelioid tubercle, which may present itself in response to many unrelated stimuli, is the key to the diagnosis of a disease which may not be a true disease entity. Ten Seldam[3] emphasizes that sarcoid-like tubercles can and do form in a variety of diseases.

The finding of sarcoid-like lesions in the midst of tumor tissue was first noted by Nickerson.[4] Ellman and Hanson[5] have summarized the literature and record only 10 cases of carcinoma with coexistent sarcoid either in the malignant lesion itself or in lymph nodes draining the area of the malignant lesion.

The coexistence of carcinoma with so-called sarcoidosis in the same organ raises the question of whether these two "diseases" of unknown etiology are together by coincidence or as the result of a mutual interrelationship.

Case report

A fifty-three-year-old white man was admitted to the hospital on June 5, 1958, because of severe abdominal cramps and vomiting of six hours duration. The pain was in the lower abdomen, persistent, with varying intensity; it was relieved somewhat by vomiting and was not related to bowel movement. The patient had not eaten since the onset of the episode. Vomitus consisted of white foamy mucus and was not bloody.

Previously, the patient had always been well. There had been no previous operations. He smoked two packs of cigarets and a few cigars daily and drank alcoholic beverages moderately.

At the time of his admission, the patient

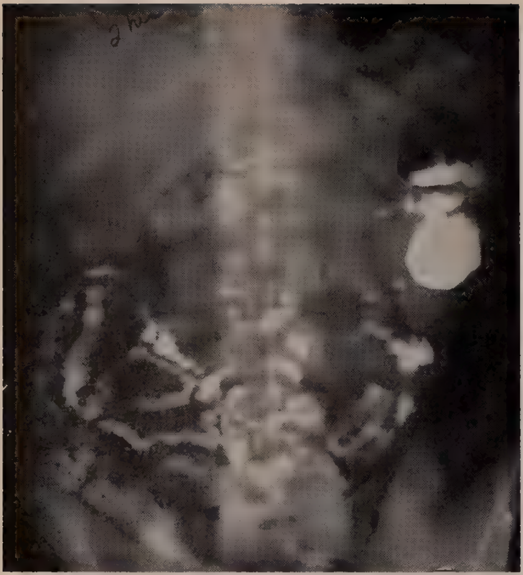

FIGURE 1. Small-bowel study showing group of jejunal diverticula. These probably accounted for patient's gastrointestinal complaints. There were no other gastrointestinal abnormalities.

was noted to be an obese middle-aged man in apparent distress due to pain. He was clear mentally and cooperative. His temperature was 98 F., pulse 92 per minute, blood pressure 150/100 mm. Hg, and respirations 20 per minute. He was not dyspneic. The neck was flexible; the abdomen was tender in the left upper quadrant, but there was no rigidity or rebound tenderness. There was no percussion tenderness in the loins, nor was there jaundice. A rectal examination revealed a prostate of normal size; the feces were of normal brown color without blood or mucus. The remainder of the physical examination was noncontributory. Laboratory studies on admission revealed a hemoglobin of 15 Gm. per 100 ml. and a hematocrit of 48. The white cell count was 13,000 with a normal differential blood count. The fasting blood glucose, urea nitrogen, and amylase were within normal limits. The blood Kahn test result was negative. The serum calcium was 11 mg. per 100 ml., the albumin-globulin ratio was 4.4:2.9 (1.5:1), and the sputum examination gave negative results and was repeated for acid-fast bacilli. A Papanicolaou smear test of sputum was negative for malignant cells; the Vollmer patch and Mantoux intradermal tuberculin tests, 1:10,000 and 1:100, gave negative results.

Parenteral fluids and atropine, administered hypodermically, were given promptly on admission. Within one hour the pain

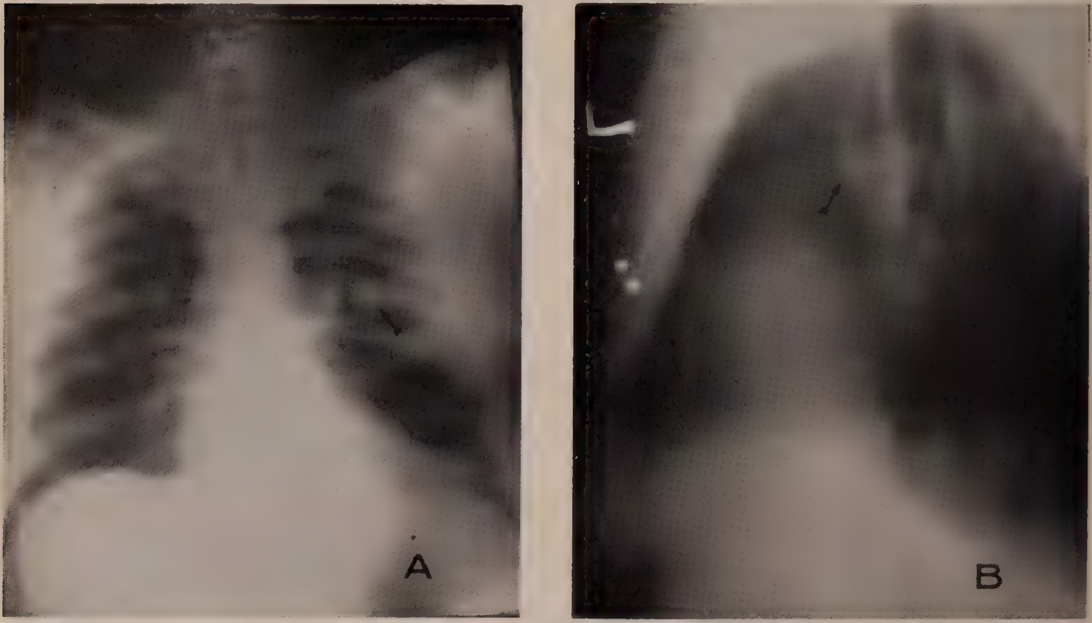

FIGURE 2. Roentgen-ray films. (A) "Coin" lesion in midfield of left lung discovered on routine chest film. There are enlarged left hilar lymph nodes. (B) Preoperative lateral tomogram at left hilar level showing enlarged left hilar lymph nodes.

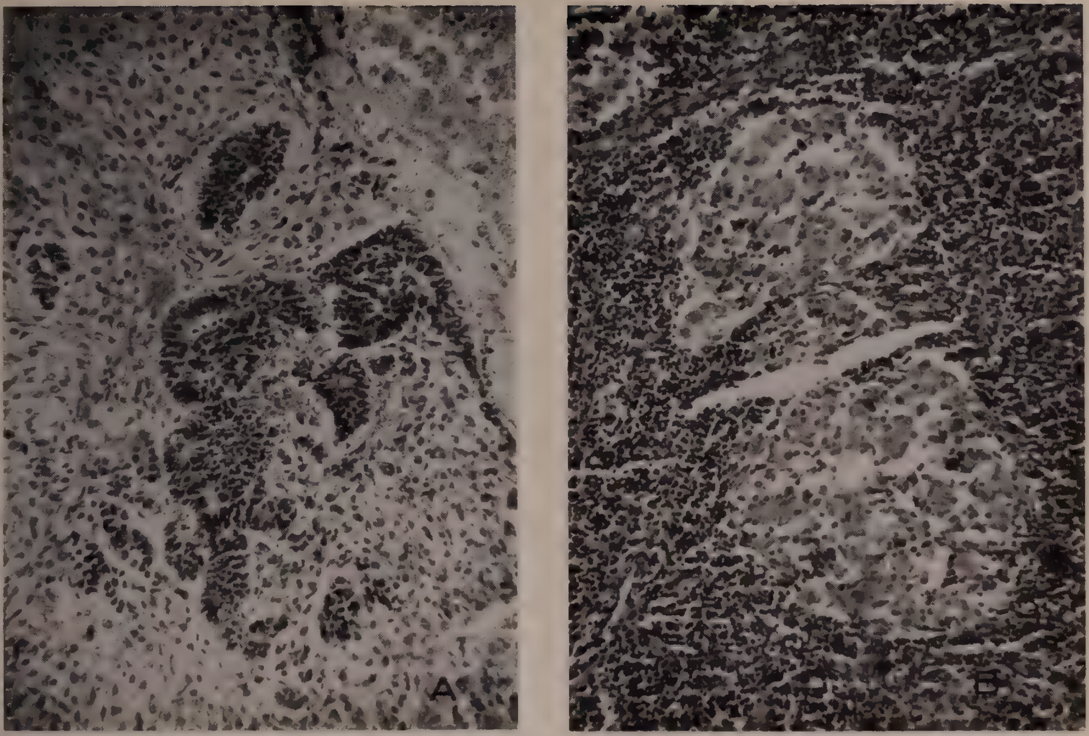

FIGURE 3. Photomicrographs. (A) Malignant teratoma of lung. Note arrangement of tumor cells into organoid structures resembling early stages of embryo formation. (B) Granulomas in hilar lymph node. Granulomas demonstrate numerous giant cells and no necrosis noted. (Paraffin, Hematoxylin and Eosin Stain, × 200)

lessened considerably and proceeded to disappear gradually. The vomiting ceased. A few days later, a barium enema and a gastrointestinal series, including a small-bowel study, were done (Fig. 1). These x-ray studies revealed a large diverticulum of the jejunum in the left upper quadrant and numerous small diverticula in the sigmoid.

More significant information was obtained from a routine chest x-ray film. A "coin" lesion of approximately 1 $^1/_2$ cm. in diameter was seen in the midfield of the left lung (Fig. 2A). Tomography verified the existence of the lesion (Fig. 2B).

Bronchoscopy on June 16, 1958, revealed that the lower lobe of the left bronchus was elevated and displaced anteriorly. Papanicolaou and cell-block studies of bronchial washings and direct expectoration were negative for abnormal cells.

A thoracotomy of the left side of the chest was performed on July 10, 1958. On exposing the lung, the visceral pleura was seen to be studded with pinhead-sized lesions. A careful search of the lung failed to yield a tumor, other than a large clump of lymph nodes in a position corresponding to the "coin" lesion of the x-ray film. This clump and other nodes at the bronchus were excised. A "pinhead" pleural lesion was also taken for biopsy study.

> REPORT ON BRONCHIAL NODES AND PLEURAL BIOPSY. *Microscopic* (1) A flattened, semicircular 1.2-cm. fragment of bluish-gray and dark brown tissue containing a 5-mm. nodule appears, as well as (2) a bean-shaped structure measuring 1.2 cm. in greatest dimension, its outer surfaces invested by a fibrous capsule (Fig. 3A). The cut surface is mottled and gray and black in color. (3) A section of the bronchial lymph nodes shows a deposition of tubercles surrounded by numerous lymphocytes and anthracotic material. These tubercles consist of numerous epithelioid cells with an occasional Langhans' giant cell. There is no evidence of caseation or necrosis (Fig. 3B). (4) A section of the lung shows several small areas of tubercle deposition without caseation or necrosis. These tubercles consist of epithelioid cells and some

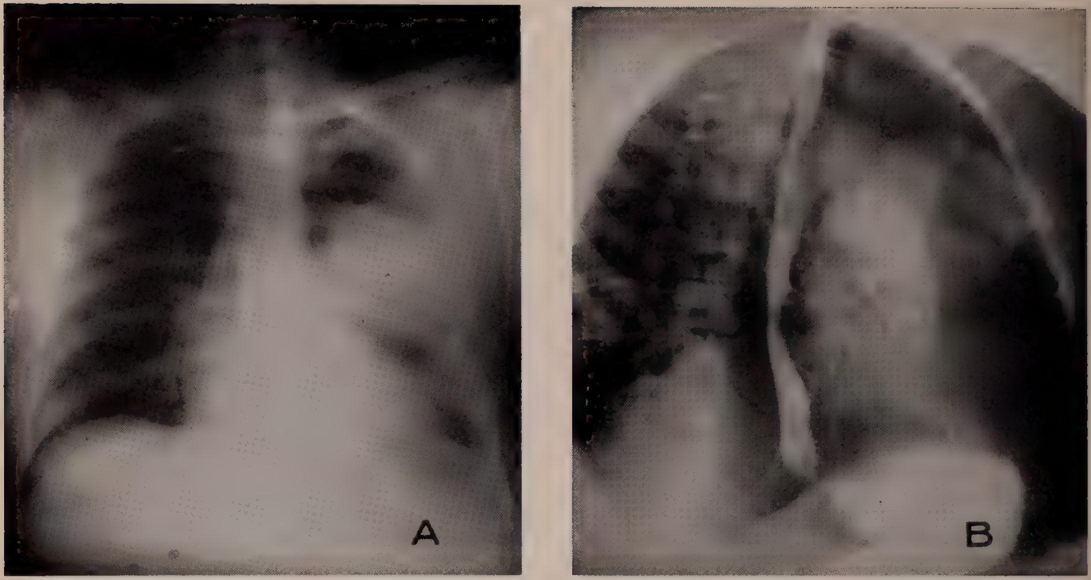

FIGURE 4. Fourteen months after exploratory thoracotomy. Patient asymptomatic up to this time and did not return for follow-up until sudden hemoptysis occurred immediately preceding these films. (A) Large well-circumscribed homogeneous mass at site of original tumor in midfield of left lung. (B) Right anterior oblique view shows tumor to be anteriorly located.

lymphocytes with an occasional Langhans' giant cell.

Diagnosis. The diagnosis was: Boeck's sarcoid of the lung and bronchial lymph node.

The patient made an uneventful recovery from this thoracotomy. He left the hospital on July 22, 1958, with no abdominal complaints.

He was not heard from again until August 24, 1959, at which time he stated that he had spat up a mouthful of blood. He was hospitalized immediately. An x-ray film of the chest showed a round mass about 8 cm. in diameter occupying almost the entire lower field of the left lung (Fig. 4).

Another thoracotomy was performed. The upper lobe of the left lung was seen to be almost completely replaced by tumor tissue. The tumor had become adherent to the pericardium. The mediastinum seemed relatively clear. A left pneumonectomy was performed, with removal of the adherent portion of the pericardium. The patient did fairly well after the first few stormy postoperative days. He left the hospital on the ninth postoperative day, ambulatory and quite comfortable.

PATHOLOGIC REPORT ON SURGICAL SPECIMEN. A biopsy of the left lung and regional lymph node shows non-necrotizing miliary granulomas consistent with sarcoid.

A biopsy of the mass in the upper lobe of the left lung shows a malignant neoplasm, the type and origin undetermined. It is probably a malignant teratoma of the lung.

After having been home about three weeks, he complained of rapidly progressive dyspnea. He was readmitted to another hospital on October 14, 1959, in severe dyspnea, went into coma and shock, and died shortly thereafter.

POSTMORTEM EXAMINATION REPORT. *Cavities.* Thoracic: The right lung is free of adhesions, but about 500 cc. of clear liquid occupies the pleural space. On the left side there are many adhesions between the wall and the pleura. This also involves the pericardium.

Pericardial: There are adhesions between the pericardial surface and the left pleura. Opening the pericardium shows the normal amount of fluid and no adhesions.

Peritoneal: The organs of the peritoneum are in normal situ. No liquid or adhesions are present.

Cardiovascular system. The heart weight is 475 Gm. From the outer surface a bulging mass in the left ventricle is noted and felt.

The epicardial surface is not significant. The coronaries arise from their normal positions and are patent in their course. The sclerosis is minimal; opening of the heart chambers discloses in the left auricle a huge thrombus-like tumor mass measuring 7.5 by 5 cm. attached to the left pulmonary vein, which has been closed by sutures. This mass is oval-shaped like an eggplant, of soft consistency and grayish-white color. A cut section shows a uniform appearance. There is no necrosis or liquefaction, with whorl-like zones throughout the mass. The right side of the heart is somewhat hypertrophied, its wall measuring 0.6 cm.; the left side measures 1.7 cm. and is also hypertrophied.

The following ring measurements were recorded. The tVr is 13, pVr 8.5, mVr 10.5, and aVr 8.5 cm. The endocardium and values are not remarkable. The aorta shows minimal sclerosis.

Respiratory system. The right lung weighs 900 Gm.; the left is not present. There is a great amount of pulmonary edema and emphysema.

Gastrointestinal system. The esophagus is in the midline and is not remarkable on examination. The stomach shows some postcongestive changes. The duodenum is normal. The small and large intestines have scattered diverticula. These are best seen in the sigmoid, transverse colon, and ascending colon. The appendix is present and nonsignificant.

Glandular system. Each of the testicles weighs 15 Gm. A cut section shows normally preserved architecture.

The thyroid weighs 30 Gm. It is homogeneous and of tan color.

The tracheobronchial lymph nodes are small and firm; a cut section shows a white-gray color. They appear to be the same as the mass in the heart.

Final Diagnosis

1. Postoperative status, recent (September, 1959) left pneumonectomy: *Undifferentiated malignant tumor of the lung; Boeck's sarcoid in lymph node*
2. *Metastatic tumor to the left auricle and mediastinal lymph nodes*
3. *Pulmonary emphysema and edema*
4. *Right hydrothorax*
5. *Diverticula coli*
6. *Cardiac hypertrophy*

Comment I

At the time of the first thoracotomy in the case presented, a thorough search was made for a parenchymal lesion that would correspond to the "coin" lesion previously seen on x-ray film, and none was found. It is a fair assumption that the clump of nodes found in the surface of the lung, corresponding reasonably to the site of the "coin" lesion, was the "coin" lesion. However, the recognition of a large carcinomatous mass one year later raises doubt as to just what had taken place. One thought is that a malignant focus may have been present but was far too small to be recognized on the gross examination.

Another thought can be divided into two parts: (1) Some product of the carcinoma, which may have been present, stimulated the production of sarcoid-like granulomas in the regional draining lymph nodes. (2) The scar tissue of a pre-existent sarcoid lesion, normally containing rapidly growing cells, was the site of origin of a malignant condition.

Ten Seldam[3] contends that an intrathoracic malignant disease may provide the stimulus to a sarcoid-like reaction.

Gherardi[6] observed a case of carcinoma of the bile ducts in which the neighboring lymph nodes were the only foci in the body with a sarcoid-like reaction.

Actual sarcoid-like structures were found inside tumors by Schiller.[7] Refvem[8] believes that sensitization may play a part in the cause of the lesion of sarcoidosis.

Even though the experimental evidence to date is rather disappointing, a relationship between sarcoid-like lesions in certain lymph nodes and a carcinoma in the region which they drain cannot be discarded lightly.[3]

Nadel and Ackerman[9] described 5 cases of malignant disease in which sarcoid-like structures were found in the draining lymph nodes. Symmers[10] described another 5 such cases.

The finding of sarcoid-like lesions in biopsies of scalene or other lymph nodes should arouse suspicion of a malignant lesion in the area drained by that lymph node.

Comment II

Raeburn and Spencer[11] are of the opinion that malignant changes can occur in peripheral lung scars of postinflammatory origin. The granulomatous nature and mode of healing of sarcoid nodules produce scars similar to postinflammatory lesions in many respects, and it seems logical, therefore, that malignant changes may occasionally arise in association with healing or healed sarcoid nodules.[5]

Apart from this association with malignant disease, sarcoid-like granulomatous lesions have been noted in many other conditions: leprosy, tuberculosis, brucellosis, leishmaniasis, Hodgkin's disease, regional ileitis, Whipple's disease, and following exposure to chemical agents, especially beryllium, medicated oils, and other drugs.[12]

Middleton[13] states: "The trend of recent years has been towards broadening of the diagnostic base" (in sarcoidosis).

Cummings, in 1958,[14] at the fiftieth annual meeting of the American Society for Clinical Investigation, reported data suggesting that the pollen of pine trees may be capable of inducing sarcoid-like granuloma.

Robinson and Pound[15] are of the opinion, "It is only possible to state that a particular lesion shows a sarcoid structure. The diagnosis of sarcoidosis is to be made only by taking into account the biological behavior of the condition." Sarcoidosis cannot be diagnosed in the absence of generalization; an isolated lesion with a typical histologic structure may be some other condition. As no criterion is specific, the diagnosis must depend on the assessment of all the features present.[15]

Summary

A case of coexistent sarcoidosis and teratoma of the lung is presented and discussed.

The lack of specificity in the diagnosis of sarcoidosis is suggested.

A possible biologic relation between the sarcoid and the adjacent malignant condition is presented, with a review of the literature.

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Carcinoma Developing in Queyrat's Erythroplasia

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Erythroplasia of Queyrat is best interpreted as Bowen's disease (an epidermoid carcinoma in situ) occurring on the glans penis or prepuce. In a recent (1955) critical review of the world literature Blau and Hyman[1] analyzed and tabulated all published American cases, adding 14 previously unreported cases, and found the patient of Friedman[2] to be the youngest (thirty-nine years of age) with carcinoma developing in erythroplasia of Queyrat. We have been unable to find a report of a patient younger than thirty-nine published since 1955.[3-8] Because of the rarity of the condition, the youth of our patient, and our departure from conventional therapy, we believe it is of interest to add another report to the literature.

Case report

A thirty-four-year-old married Caucasian clerk was admitted to the Bronx Municipal Hospital Center on November 18, 1959, because of a lesion on his penis. He had undergone circumcision at another hospital seventeen months previously for phimosis and a "pimple" on his penis which had been present for an unknown period of time. The removed tissue had not been submitted for pathologic examination. The "pimple" remained after circumcision and occasionally discharged a watery fluid.

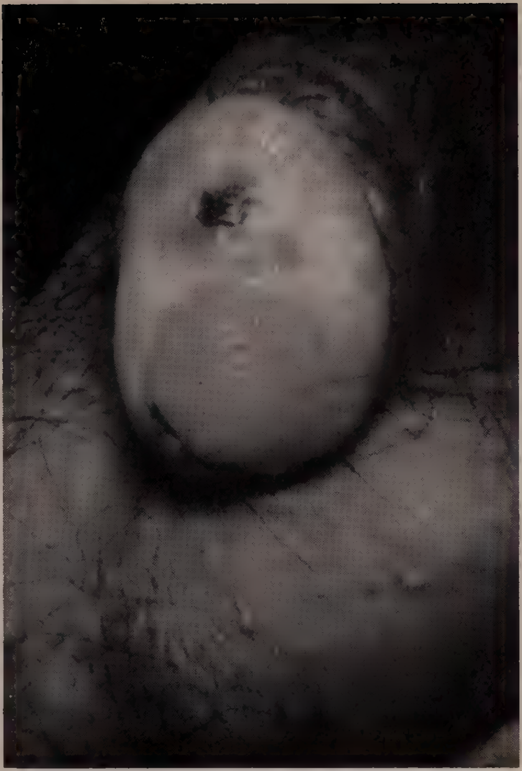

FIGURE 1. Clinical appearance, preoperatively.

Aside from gonorrhea fourteen years previously, there was no other history of venereal disease or of trauma. He had suffered from pain in the left flank, chills, fever, and dysuria three months earlier. The patient's past history and systems review were otherwise noncontributory.

The abnormal findings on physical examination were limited to the glans penis. Chiefly on the left side, extending from the corona to the meatus, a sharply demarcated, dry, irregularly shaped, salmon-colored, slightly thickened plaque was seen. Dorsally and proximally within this plaque was a crusted-ulcer 1 by 1.5 cm. in size. The penile shaft was normal. There was no palpable inguinal lymphadenopathy or urethral discharge (Fig. 1).

Laboratory data, including a routine urinalysis, hemoglobin determination, white blood count and differential study, serologic test for syphilis, total serum protein, and albumin-globulin ratio were all normal. An

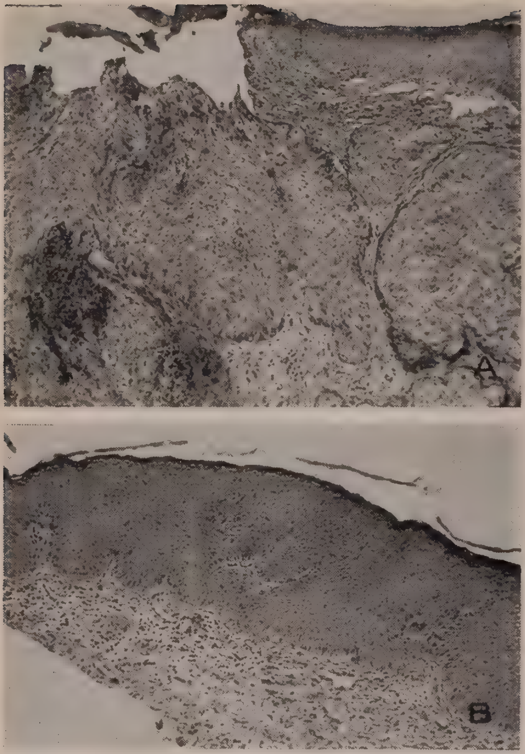

FIGURE 2. Histopathologic findings. (A) Crusted tumor. (B) Plaque.

electrocardiogram, chest film, plain film of the abdomen, and intravenous urograms were interpreted as being within normal limits. A Frei test result was interpreted as positive.

On November 24, 1959, under local anesthesia, an excision biopsy of the ulcer was carried out. The wound was closed primarily without difficulty.

The histopathologic findings were as follows: A microscopic examination of the ulcerated area revealed a disruption of the epithelium. Extending from the surface into the upper stroma was an epithelial tumor, fairly well differentiated, forming irregular nests. There were many mitotic figures and moderate variation in nuclear size and shape (Fig. 2A). The nonulcerated adjacent epithelium showed marked cellular atypia and scattered mitoses throughout its full thickness. The inflammatory reaction was slight (Fig. 2B). Evidence of vascular invasion was lacking. All surgical margins were free of tumor. The diagnosis was: erythroplasia of Queyrat of glans penis with infiltrating squamous cell carcinoma of the glans penis.

The decision was made to withhold partial amputation of the penis and to treat the lesion with x-radiation because of the superficiality of the malignant condition, the lack of any evidence of local metastases, and the active sexual life of such a youthful patient. Should the course of x-ray therapy fail to cure or should it give an unsatisfactory result for other reasons, it was reasoned that surgery then could still be employed.

A course of x-ray treatments was carried out under the direction of John Evans, M.D., as follows: A total of 4,950 r, skin dose, half value layer 1.5 mm. of copper, was given to the entire dorsum of the glans penis, fractionated into 40 daily treatments beginning December 7, 1959. As a result of this treatment, as expected, an acute transient radiodermatitis developed.

A follow-up visit on February 26, 1962, showed the patient to be well. The glans penis appeared atrophic and whitish at the site of the former ulcer. The surface of the glans appeared slightly scaly, shrunken, and indurated (Fig. 3A). The urethral meatus was somewhat narrower than normal, but adequate; the patient voided with a good stream (Fig. 3B). There was no residual evidence of erythroplasia. No inguinal nodes were palpable. The patient stated that sexual intercourse was becoming less frequent because of an impaired sensation in the glans and failure to achieve successful erection. There was no pain or abnormal sensitivity.

Comment

Several features of this case are interesting: (1) This patient is, to the best of our knowledge, younger than any previously reported with carcinoma developing in erythroplasia of Queyrat. (2) The failure to show the typical clinical picture, namely a plaque which is moist, bright red, and velvety, is explained by the therapeutic circumcision and the consequent absence of a moisture-retaining prepuce overlying the lesion. This in no way invalidates the general rule that carcinoma or true erythroplasia of Queyrat is rarely, if ever,

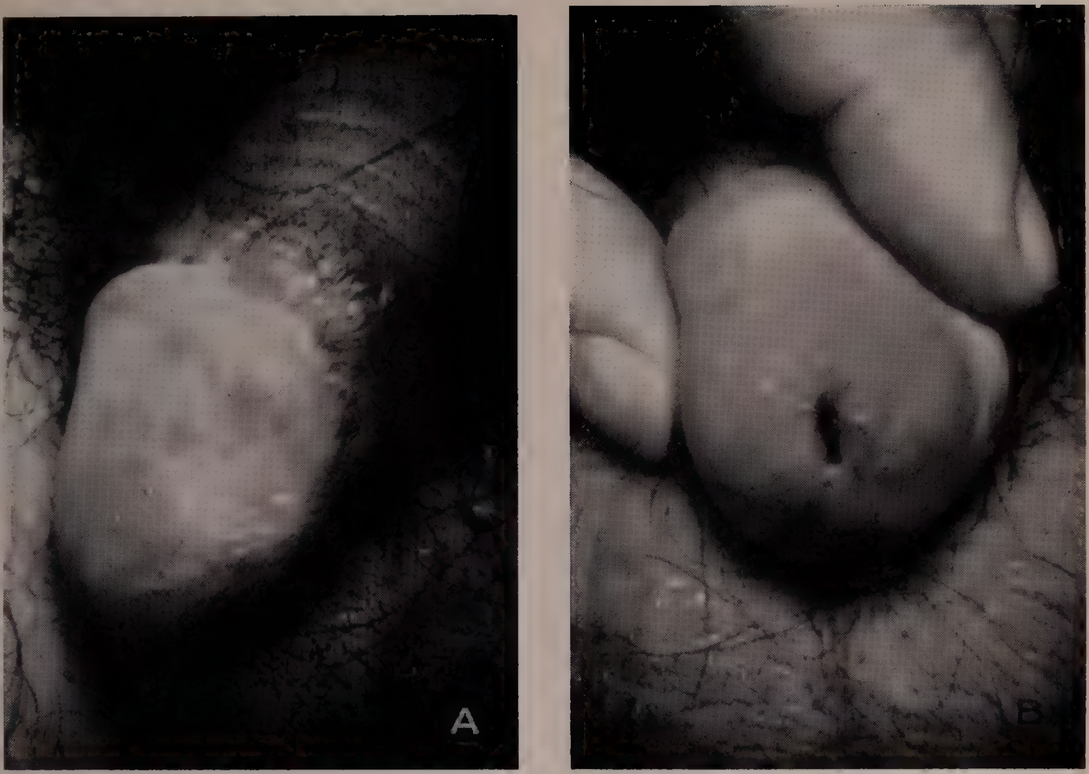

FIGURE 3. Clinical appearance. (A) Twenty-eight weeks after treatment concluded. (B) Twenty-eight weeks after treatment concluded, to show meatus.

found in individuals circumcised in infancy. (3) To date radiotherapy, although more conservative than partial phallectomy, has resulted in hypesthesia and some interference with sexual function. The slightly stenotic urethral meatus has not interfered with urinary function.

Summary

A thirty-four-year-old man with clinical and histologic erythroplasia of Queyrat of the glans penis and epidermoid carcinoma arising therein was treated with radio-therapy. A follow-up of twenty-seven months shows him to be clinically free of disease and to have a hypesthetic glans penis with a slightly narrowed urethral meatus. This patient is, to our knowledge, the youngest patient who has been reported to show the development of a malignant condition in a disease which is now understood to be carcinoma in situ, probably preventable by circumcision in early life.

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Special Articles

Orthopedics and Anthropology

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THE STARTING POINT in any perceptive consideration of man's physical well-being is the recognition of the significance of mutating forces in his biologic and social evolution.

Man's gradual emergence from the status of a stooped but upright cave dweller has been a matter of constant adaptation to environment, imperative in the beginning because of his needs in an instinctive struggle for survival. In his search for the necessities of life he moved about, and his continuing adjustment to surroundings has been mirrored in the Neanderthal Man, the Bushmen of Africa, the Tasmanians, the Philippine Moros, and the American Indians, until at today's milestone in the long journey we see modern man who, through his ultimate achievement, the true erect posture, not only has adapted to his environment but also is capable to a very great extent of shaping it to conform to his own needs

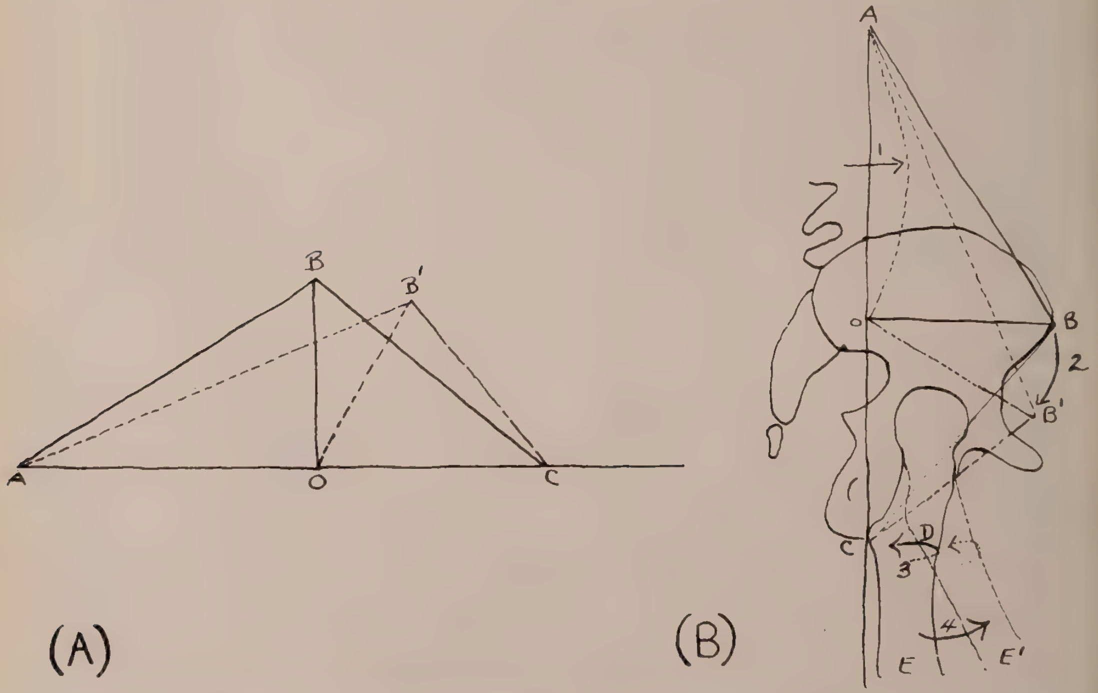

FIGURE 1. (A) Tenseness of wire ABC may be released AB'C by deflecting BO to B'O. (B) Methods of releasing tension of the iliopsoas in man by (1) adjustive lumbar lordosis, (2) anterior tilt, (3) flexion of hip, and (4) external rotation of lower limb. (Michele, A. A.: Iliopsoas; Development of Anomalies in Man, Springfield, Illinois, Charles C Thomas, 1962.)

and desires.

Environment is ever-changing, and even though man has reached the goal of erect posture, he must now be equipped constantly to maintain it, since failure to do so constitutes the potential of an abnormal force capable of destroying all the benefits of his achievement. We cannot change gravitational force, but simply because man has established his own line of gravity in attainment of erect posture, that force can break him when he has not adjusted his body structures to the purpose. Here one calls to mind the aphorism that man would not suffer backache if he were content to revert to "all fours, or stooped posture."

True erect posture and its maintenance

It is useless to attempt a true evaluation of physical fitness, or the lack of it, without a complete comprehension of the formation of true erect posture and what is involved in its maintenance.

In considering the approach to ideal posture, one in which all systems are in balance, we commence with that of the cave dweller or Neanderthal Man. He is stooped, which implies an anteriorly flexed pelvis, flexed hips and knees, and externally rotated lower members. This does not mean that he could not fully extend his hip or his knee, but to do so the incomplete axial rotation of the lower limb first necessitated the rotation of the member to 90 degrees to acquire a powerful extensor (gluteus maximus) which, with a shift in joint position, was converted from an abductor and mild extensor of the hip to a powerful extensor. As soon as he acquired the 90-degree axial rotation of the limb, of necessity there must have occurred an adaptive elongation of the iliopsoas, since the rotation adds the function of an external rotator to that of the flexory action of the muscle. Furthermore, his back would have gone into exaggerated lordosis at the level of the lumbar spine (Figs. 1 and 2).

The concomitant extension of the hip was met with extension and "screw-home" position of the knee, and the vastus medialis accepted the challenge of this accomplishment.

To assume the erect posture, several variables at the hip are manifested. The antetorsion present in the externally rotated limb finds a release from the back-vector potential of the iliopsoas when adaptive elongation occurs, or an increase when it fails to adjust. Subsequently there is a change in the angle of the neck of the femur, which in Neanderthal Man approaches that of coxa vara. This too, to approach the average inclination in man's anthropologic progression to the erect posture, must be accompanied by an ade-

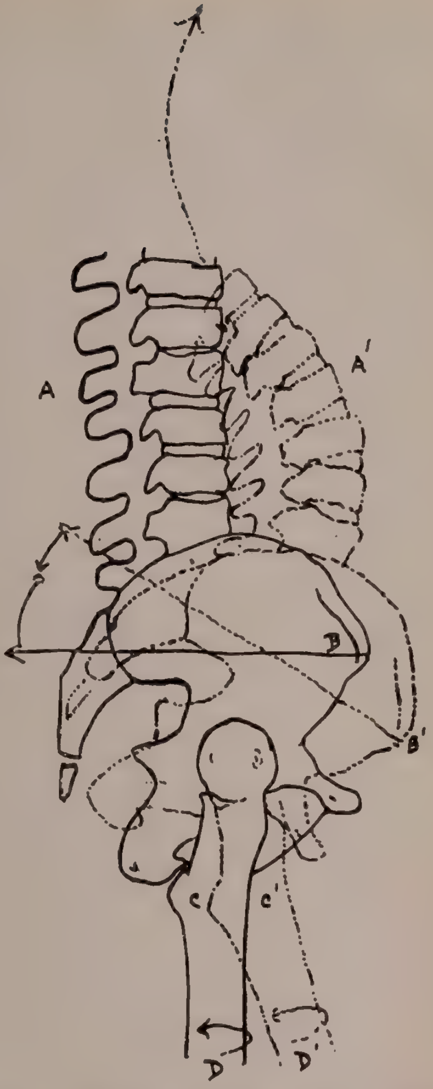

FIGURE 2. Direction of force potential of stooped but upright posture which must be overcome by adjustive lengthening of iliopsoas to achieve erect posture. (Michele, A. A.: Iliopsoas; Development of Anomalies in Man, Springfield, Illinois, Charles C Thomas, 1962.)

quate elongation of the iliopsoas; otherwise the factors of weight-bearing and a non-elongated iliopsoas will cause the hip joint to revert toward coxa vara.

Coxa valga formation in modern man is a method of compensation, enabling an individual to adapt to the erect posture in the presence of an insufficiently elongated iliopsoas. It appears to decompress the force potential of that muscle by shifting the axis of the femoral neck parallel to the line of muscle tendon and thus permitting the limb to fall readily into the 90-degree axial rotation necessary for the erect posture.

The lordosing action of the lumbar spine and pelvic tilt is determined by the nature and extent of axial rotation of the limb and adjustive lengthening of the iliopsoas. The remaining curvatures of the spine must seek an equilibrating position which is initially determined by the lordosing attitude of the lumbar spine influencing a primary dorsal curvature and a secondarily acquired cervical curvature.

It follows that many aberrations of the erect posture will be manifested when man fails to adapt by an adequate elongation of the iliopsoas muscle. These aberrations may (1) develop during intra-uterine life with the beginning of axial rotation of the lower limbs; (2) occur during the weight-bearing vertical skeletal growth of infancy and the juvenile and adolescent periods as a result of the failure of adjustive lengthening of the iliopsoas muscle; or (3) take place during the adolescent, adult, and senile phases of life triggered by wear-and-tear situations and acute insults caused by a malfunctioning or maladjusted iliopsoas muscle to the spine and hip joint.

Steindler* taught that "There is in medicine a natural law that any single manifestation, subjective or objective, has behind it a multiplicity of organic causes, just as any single pathological event is bound to project itself into a number of different clinical manifestations." We must, therefore, search for the single pathologic event that occurs when modern man fails to adapt himself to the erect posture and to which he constituted himself heir when he started toward that goal.

Conclusion

A study of modern man and his environment is a study of action and reaction, adaptation and maladaptation in relation to the gravitational force as they are brought about by the exigencies of that environment, chiefly the erect posture.

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Role of the Private Practitioner in the Control of Syphilis

I. JACKSON TARTAKOW, M.D., M.P.H.
Mineola, New York

From the Nassau County Department of Health

THE UNITED STATES has declared war on Treponema pallidum. Everywhere health departments are mobilizing and preparing for a struggle which is expected to last ten years. Additional personnel is being enlisted and trained, and arsenals containing therapeutic and prophylactic ammunition are being replenished. Nothing short of the complete destruction of the enemy will be acceptable.

Last spring, at the request of the House Appropriations Committee and the recommendation of the Public Health Service Advisory Committee on Venereal Disease Control, Surgeon General Luther L. Terry appointed a Task Force under the chairmanship of Leona Baumgartner, M.D., Commissioner of Health, City of New York, the purpose of which was "to evaluate present efforts to control syphilis and to recommend principles and methods that will make it possible to establish a timetable leading to the eradication of syphilis as a public health problem."[1] The Task Force submitted its report to the Surgeon General on December 29, 1961. It recommended an intensive and aggressive program in two general areas of activity, namely, epidemiology and education.

The war against syphilis, however, cannot be won alone by public health authorities. The technical skills of private physicians must be allied with the organized and coordinated efforts of the official health agencies. Such a united front can serve not only as a bulwark against the advancing assaults of this enemy of mankind, but also as an entrenched position from which aggressive onslaughts may be launched, for in this type of biologic warfare attack is the best defense.

Epidemiology

What part does each of the two aggressors play? The physician fires the first barrage: He diagnoses the disease, he treats the infection, and he reports the case to the health department. The public health official follows up with a cannonade fired over the head of the patient so as to destroy, so to speak, his supply depot—the infective agent harbored in the sex partner or partners responsible for his infection—and to cut his lines of communication—the infection in the persons with whom he has since had sexual relations. This is accomplished by interviewing the infected patient and obtaining from him information which will lead to the discovery of these contacts. The health officer then arranges for the examination of these individuals and for the treatment of those found to be infected.

Victory will depend on the thoroughness with which each ally carries out his own objective and on the mutual support one gives the other. The health officer may assist the private physician in various ways, and conversely the practitioner, as he does when treating other communicable diseases, can make a valuable contribution to the public health.

Education

There are, however, a number of physicians, particularly those who received their training during the postpenicillin period, whose experience in the diagnosis and treatment of syphilis is somewhat limited. Many have lost the high degree of suspicion of the "great imitator" once held by their predecessors. Some may have difficulty in

Presented at the 58th Annual Health Conference, Syracuse, New York, June 13, 1962.

determining the significance of a reactive serologic test. Others may not have kept up with the changes in diagnostic technics and treatment methods.

The health officer is ready to assist these physicians. He makes available to them a consultation service whereby patients with suspicious lesions may be seen, laboratory reports discussed, and modern methods of treatment recommended. He offers the services of a public health laboratory where dark-field examinations and serologic tests, as well as definitive specific tests to rule out false biologic reactions, are performed. He arranges for seminars and talks at medical society meetings, hospital staff conferences, and medical schools.

Movies, slides, film strips, exhibits, manuals, and other visual aids are used to aid the physician in updating his knowledge and maintaining a high level of technical information of syphilis. Medication, in the form of benzathine penicillin G, which maintains a prolonged adequate penicillinemia, is supplied without charge to physicians, and its dosage is discussed. In the absence of clinics, payment is made to the private physician for the treatment of indigent infected patients. Personal visits by health department personnel to the offices of physicians to discuss with them the part played by the health officer as well as their own responsibility in the venereal disease control program have proved productive. At such times, it is possible to urge physicians to strengthen what may be considered the weakest area in their line of attack, namely, the reporting of cases of syphilis to the local health authorities.

In a recent joint study made by the Association of State and Territorial Health Officers, the American Venereal Disease Association, and the American Social Health Association,[2] estimates were obtained from the state health officers as to what per cent of the total number of cases of primary and secondary syphilis treated by private physicians are reported to the health departments. Eight states claim that less than 25 per cent of such cases are reported, 9 states estimate that 26 to 50 per cent are reported, 10 states claim 51 to 75 per cent reporting, and 13 states believe that health departments are informed of over 76 per cent of the cases. Only one state boasts that private physicians report 100 per cent of the syphilis cases they diagnose and treat.

The report of the Task Force indicates that only slightly more than one half of such cases seen by physicians throughout the nation are reported by them to the local health authorities. It is, therefore, evident that the actual incidence of infectious syphilis is considerably underreported.

In the past, when treatment for early syphilis was a prolonged and expensive procedure, infected patients visited department of health clinics. With the advent of penicillin therapy, a higher proportion of such patients are being treated by private physicians. It is regrettable that in spite of the fact that the reporting of venereal disease is mandatory in all states, physicians remain delinquent in this duty.

Methods

Why is it important for physicians to report such cases to the health authorities? The answer is that the spread of syphilis cannot be controlled unless all infected persons, in addition to being treated, are interviewed so that their infected sexual contacts may be brought to treatment. The busy physician does not have the time to conduct such an epidemiologic investigation properly. For that reason, college graduates who are selected carefully for their intelligence, personality, integrity, and tact, are especially trained by the U. S. Public Health Service in interviewing technics and are assigned to state and local health departments. They assist the physician in taking over the task of case finding.

It is estimated that at least 4,600 persons who are treated for infectious syphilis are not interviewed for sex contacts each year because their physicians do not report them. Unless physicians report all these cases, infected sexual contacts remain undiscovered and untreated, and consequently continue to spread the disease, building up a considerable untapped reservoir of infection.

Various reasons are given by physicians when they are asked why they failed to report a case of early syphilis. Some claim that is is too much bother to fill out the report card. Others feel that they would violate the physician-patient relationship and would not be protecting their patient's confidence if a third person is brought into the situation. Some are requested not to notify the health department by patients who have a strong feeling of guilt or who fear marital reverberations and the social stigma associated with the disease. If the patient became infected through homosexual practices, this fear is intensified.

There is really no justification for these objections. The report card issued to the busy physician requires only the time to write the patient's name and address and to check several boxes. These records are strictly confidential. As far as the physician-patient relationship is concerned, if anything, it is strengthened by the interviewer. At no time is a private patient interviewed unless permission has been given by his physician. Great emphasis is placed on the extremely confidential nature of the procedure. The interviewers are taught never to reveal to anyone the names of patients or their contacts. Under no circumstances are sexual contacts told who has named them. Marital problems are handled with tact and are usually referred back to the physician for his personal consideration. The investigator will cooperate in every possible way with the physician and will abide closely by his instructions. Patients who are deliquent in taking their treatment, or who require follow-up, are located by the investigator at the request of the physician and returned to his office.

The interviewer, by virtue of his training, very frequently succeeds in obtaining valuable epidemiologic information which leads to the discovery of persons whose infection had been unknown. These are referred by him to their physicians for treatment. The occasional physician who refuses to permit his patient to be interviewed does the community a disservice, fails to do his share in preserving the public health, and gives comfort and aid to the spirochete.

Conclusion

It may be stated that if one were to indulge in fantasy, one could say that if all cases of infectious syphilis were treated adequately and reported to the health authorities, if all such patients were interviewed skillfully, if the names and locations of all their sexual contacts were obtained, if all these contacts were examined and all those who are found to be infected were brought to treatment and in turn interviewed for all their contacts, a time would soon come when syphilis would be eradicated. Unfortunately, these utopian conditions are as yet nonexistent, although it is hoped that with the inauguration of a vigorous attack, such as that recommended by the Task Force, this vision may be realized within the next decade.

References

1. The Eradication of Syphilis, Task Force Report to the Surgeon General, Public Health Service, on Syphilis Control in the United States, Bethesda, Maryland, U. S. Department of Health, Education, and Welfare, Public Health Service, 1961.

2. Today's VD Control Problem, joint statement by Association of State and Territorial Health Officers, American Venereal Disease Association, and American Social Health Association, New York City, American Social Health Association, 1962.

Abstracts

Sinton, D. W., and Ortelee, M. F.: Research in demyelinating disorders; current trends, New York State J. Med. **62:** 2953 (Sept. 15) 1962.

The demyelinating disorders may be divided into those which appear in adult life and are characterized by a long remitting course and eventual severe morbidity and those of childhood or infancy which are characterized by a relatively short course, progressive and steady development of signs and symptoms, and early death. The first group consists of multiple sclerosis and the second of the leukodystrophies, in which dysmyelination, rather than true demyelination, occurs. An exacerbation of a demyelinating process is often preceded by an infection of the respiratory, gastrointestinal, or urinary tract. Encephalomyelitis has been produced experimentally in animals, but not without inflammation, and the chronic remitting course of human multiple sclerosis has never been reproduced. Environmental and genetic factors are probably involved in the demyelinating diseases, but adequate studies have yet to be done.

Zauder, H. L., West, K., and Orkin, L. R.: Survey of 419 cases of acute poisoning, New York State J. Med. **62:** 2959 (Sept. 15) 1962.

In a group of 419 cases of acute poisoning, acetylsalicylic acid, household substances, and solvents were responsible for a high percentage of the pediatric cases, whereas barbiturates were responsible for 45 per cent of the poisonings in adults. Coma occurred in 43.7 per cent of the adult patients; of these 20.8 per cent required intubation of the trachea, and 11.2 per cent required mechanical respiratory assistance. Aspiration secondary to gastric lavage occurred in 20.8 per cent of the comatose patients and was commonly due to failure to isolate the airway during lavage, as tracheal intubation must be performed when the protective reflexes are obtunded or absent. Twelve patients (2.8 per cent of the total) died.

Galin, M. A., and Berger, R.: Nature and treatment of blepharitis, New York State J. Med. **62:** 2965 (Sept. 15) 1962.

Blepharitis is a chronic inflammation of the lid border. The specific etiologic agents have not been established; thus many medications have been advocated. Adequate lid hygiene is essential. Thirty patients with either seborrheic or ulcerative blepharitis were treated twice daily with a medication combining antiseptic and keratolytic agents with sodium versenate (Blef-Dome), in which the chelating agent aids in cellular penetration and reduces the concentration requirement of the antiseptic and keratolytic agents. Patients with uncomplicated seborrheic blepharitis benefited generally, and the majority were sufficiently improved so that the frequency of medication could be reduced to once weekly or biweekly. Patients with ulcerative blepharitis were slow to respond although signs and symptoms were diminished progressively with diligent care and therapy.

McGraw, J. L.: Contact lenses, New York State J. Med. **62:** 2970 (Sept. 15) 1962.

In fitting contact lenses, the indications, contraindications, and possible complications should be considered. Indications for the fitting of contact lenses include: improvement of vision in such cases as advanced keratoconus, irregular astigmatism, corneal scars, and some cases of albinism and nystagmus; anisometropia and unilateral aphakia; extremes of refractive error; trichiasis, districhiasis, lagophthalmos, ectropion, entropion, and neuroparalytic keratitis; occupations which are hazardous to the spectacle wearer, where spectacles are impractical, or where spectacles are a cosmetic detriment; and cosmetic fitting. Contraindications include: infection; degenerative diseases of the cornea; mental incompetence or irresponsibility; occupational contraindications; glaucoma; and corneal staining. Complications from the wearing of contact lenses which have been reported include: epithelial staining; corneal scarring; infection; corneal vascularization; filamentary keratitis; contact lens ruptured into the orbit; and corneal infiltrates.

Abstracts in Interlingua

Sinton, D. W., e Ortelee, M. F.: Recercas in disordines dismyelinisatori; tendentias currente (*anglese*), New York State J. Med. **62:** 2953 (15 de septembre) 1962.

Le disordines dismyelinisatori pote esser di vidite in (1) illos que appare in le vita adulte e es characterisate per un prolongate curso con remissiones e, ultimemente, sever morbiditate e (2) illos que appare in le pueritia o infantia e es characterisate per un relativemente breve curso, con un progressive e constante disveloppamento del signos e symptomas, e un morte precoce. Le prime gruppo consiste de multiple sclerosis, le secunde del leucodystrophias. In istos il occurre *dys*myelinisation plus tosto que *dis*myelinisation. Un exacerbation del processo dismyelinisatori es frequentemente precedite per un infection del vias respiratori, gastrointestinal, o urinari. Encephalomyelitis ha essite producite experimentalmente in animales, sed non sin inflammation. E le curso chronic con remissiones que es characteristic de multiple sclerosis human ha nunquam essite reproducite. Factores de milieu e factores genetic es probabilemente interessate in le morbos dismyelinisatori, sed adequate studios es non ancora disponibile.

Zauder, H. L., West, K., e Orkin, L. R.: Revista de 419 casos de invenenamento acute (*anglese*), New York State J. Med. **62:** 2959 (15 de septembre) 1962.

In un gruppo de 419 casos de acute invenenamento, acido acetylsalicylic, substantias de uso domiciliari, e solventes esseva responsabile pro un alte procentage del casos pediatric, durante que barbituratos esseva responsabile pro 45 pro cento del invenenamentos in adultos. Coma occurreva in 43, 7 pro cento del patientes adulte; de istes, 20,8 pro cento requireva intubation del trachea, e 11,2 pro cento requireva mechanic assistentia respiratori. Aspiration secundari a lavage gastric occurreva in 20,8 pro cento del patientes comatose e esseva communmente le consequentia de que le vias aeree non habeva essite isolate durante le lavage. Intubation del trachea debe esser effectuate quando le reflexos protective es obtundite o absente. Dece-duo patientes (2,8 pro cento del total) moriva.

Galin, M. A., e Berger, R.: Le natura e le tractamento de blepharitis (*anglese*), New York State J. Med. **62:** 2965 (15 de septembre) 1962.

Blepharitis es un chronic inflammation del margine del palpebra. Le specific agentes etiologic ha non essite establite. Per consequente, multe differente medicationes ha essite recommendate. Un adequate hygiene palpebral es essential. Trenta patientes con blepharitis seborrheic o ulcerative esseva tractate duo vices per die con un medication que combinava agentes antiseptic e ceratolytic con versenato de natrium (Blef-Dome) in que le agente de chelation promove le penetration cellular e reduce le requirimentos de concentration del agentes antiseptic e ceratolytic. Patientes con non-complicate blepharitis seborrheic beneficiava in omne casos, e le majoritate de illes experientiava un sufficientemente marcate melioration pro render possibile le reduction del medication a un vice per septimana o per duo septimanas. Patientes con blepharitis ulcerative respondeva lentemente, ben que le signos e symptomas declinava progressivemente sub le effecto de un meticulose sollicitude e therapia.

McGraw, J. L.: Lentes de contacto (*anglese*), New York State J. Med. **62:** 2970 (15 de septembre) 1962.

In equipar un patiente con lentes de contacto, on debe considerar le indicationes, le contraindicationes, e le possibile complicationes. Le indicationes pro lentes de contacto es (1) melioration del vision in casos como ceratocono avantiate, astigmatismo irregular, cicatrices in le cornea, e (selectivemente) albinismo e nystagmo, (2) anisometropia e aphakia unilateral, (3) extremos del error refractive, (4) trichiasis, districhiasis, lagophthalmia, ectropion, entropion, e ceratitis neuroparalytic, (5) occupationes que rende le portar de berillos hasardose o casos in que illos es impractic, e (6) considerationes cosmetic. Le contraindicationes es (1) infection, (2) morbos degenerative del cornea, (3) incompetentia o irresponsibilitate mental, (4) contraindicationes occupational, (5) glaucoma, e (6) dyscoloration del cornea. Le complicationes que pote resultar ab le uso de lentes de contacto e que se trova reportate es (1) dyscoloration epithelial, (2) cicatrisation del cornea, (3) infection, (4) vascularisation del cornea, (5) ceratitis filamentari, (6) ruptura del lente ad in le orbita ocular, e (7) infiltratos in le cornea.

FIFTY-SIXTH
ANNUAL

District Branch Meetings

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Fourth District Branch

Saturday, September 22, 1962

Queensbury Hotel, Glens Falls, New York

Morning

9:00 A.M. Registration
10:00 A.M. *Panel Discussion:* **Auto Crash Injuries: Treatment of Multiple Crash Injuries**
Lester C. Huested, M.D., Glens Falls, *Moderator;* Department of Surgery, Glens Falls Hospital
Preston A. Wade, M.D., New York City, Director of Fracture Service, New York Hospital and Hospital for Special Surgery; Clinical Professor of Surgery, Cornell University Medical College
William E. Gazeley, M.D., Schenectady, Chief of Orthopedic Surgery, Ellis Hospital; Professor of Surgery, Albany Medical College of Union University
Carleton M. Cornell, M.D., Cambridge, Department of Surgery, Mary McClellan Hospital

Afternoon

12:00 NOON Luncheon
1:45 P.M. *Panel Discussion:* **Recent Advances in Diagnosis and Investigations of Certain Gastrointestinal Diseases**
William P. Simmonds, M.D., Glens Falls, *Moderator;* Department of Medicine, Glens Falls Hospital
Panel members are from McGill University Clinic, Montreal General Hospital, Montreal, Quebec, Canada
Douglas G. Kinnear, M.D., Department of Gastroenterology
J. Lawrence Hutchison, M.D., Department of Hematology
Fleming McConnell, M.D., Department of Radiology
4:30 P.M. Business Meeting; Election of Officers

Evening

6:00 P.M. Social Hour (courtesy of the Medical Society of the County of Washington)
7:00 P.M. Dinner Dance
Introduction of Officers
Address: Henry I. Fineberg, M.D., Executive Vice-President, Medical Society of the State of New York
Remarks: Mrs. Herbert J. Ulrich, President, Woman's Auxiliary to the Medical Society of the State of New York

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Seventh District Branch

Thursday, Friday, Saturday, and Sunday, September 20, 21, 22, and 23, 1962

Grossinger's, Grossinger, New York

Thursday, September 20

Afternoon

2:00 P.M. Registration (Lounge)

February, September 21

Morning

9:30 A.M. **Cancer Teaching Day** (Night Watch Room); all speakers are from Memorial Hospital for Cancer and Allied Diseases, New York City

Cancer of the Breast
Arthur I. Holleb, M.D., Associate Medical Director

Cancer of the Ovary
Hugh R. K. Barber, M.D., Gynecology Service, Department of Surgery

Cancer of the Thyroid
Hollon W. Farr, M.D., Head and Neck Service, Department of Surgery

Cancer Detection Examination
Emerson Day, M.D., Director, Strang Cancer Prevention Clinic; Chairman, Department of Preventive Medicine

Saturday, September 22

Morning

9:30 A.M. Professional Conduct in and out of the Courtroom (Night Watch Room)

Practice
Milton Helpern, M.D., Chief Medical Examiner, City of New York

Ethics
William J. McAuliffe, Jr., Chicago, Illinois, Director, Medical Ethics Department, American Medical Association

Malpractice
William F. Martin, Esq., New York City, Counsel, Legal Department, Medical Society of the State of New York

11:30 A.M. Business Meeting

Evening

6:00 P.M. Social Hour (Host, Grossinger's)
7:00 P.M. Dinner (informal, for members, auxiliary, and guests)
Introduction of Officers
Address: Joseph A. Lane, M.D., President, Medical Society of the State of New York
Remarks: Mrs. Herbert J. Ulrich, President, Woman's Auxiliary to the Medical Society of the State of New York

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Medical News

New York physician does study in Poland

Stephen Nordlicht, M.D., New York City, assistant professor of psychiatry at the New York Medical College, worked in Poland during the month of August for the World Medical Association. Dr. Nordlicht's study concerned an investigation of juvenile delinquency.

Nursing problems in radiation

A course covering nursing problems in radiation, designed primarily for directors, supervisors, and instructors of nursing personnel, will be offered at the Queens Hospital Center.

Sessions will begin on Tuesday, November 13, and will be held for six consecutive weeks from 1:30 to 4:00 P.M. For information write to: Philip J. Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York.

Rehabilitation center slated for Strong Memorial Hospital

The designation of a primary rehabilitation center at Strong Memorial Hospital in Rochester, in conjunction with the School of Medicine and Dentistry of the University of Rochester, has been announced by the State of New York Department of Health in Albany.

Under terms of an agreement between the University of Rochester and the State Department of Health, the rehabilitation center will receive up to $50,000 a year in support of any deficit resulting from its operation.

The center is the seventh in the State-wide program calling for a network of 12 primary centers affiliated with medical schools and teaching hospitals, and 15 other rehabilitation centers.

Work evaluation unit for cardiac patients

A work evaluation unit for the rehabilitation of cardiac patients will be established at the Institute of Physical Medicine and Rehabilitation, New York University Medical Center, by the New York Heart Association.

The unit is scheduled to open this month under the direction of Menard M. Gertler, M.D., associate attending physician in medicine at University Hospital and director of research at the Institute.

The new facility will provide a means of assessing the cardiac patient's ability to carry on work activities patterned to his individual economic and social needs. Demonstrations in cardiac rehabilitation will be provided for professional groups, and reports on the unit will serve as teaching models for industry and for physicians. Basic research in new methods of work evaluation of cardiac patients and in the frequency of cardiac failure in relation to the working cardiac patient will be conducted.

Physicians are being invited to refer patients for evaluation to the new unit.

Surveillance system to detect incidence of malformed infants

The State of New York Department of Health has instituted a system of continuing surveillance that will permit early investigation to detect the cause of any unusual incidence of malformed infants. The system is based on a continuing analysis of the certificates of births and stillbirths filed by attending physicians.

The need for some means of detecting unusual factors associated with congenital malformations was graphically illustrated on the European Continent and in England by the birth of several thousand deformed infants following the use of an hypnotic drug during the early months of pregnancy. A surveillance system would have detected the abnormal situation when the number of cases was still small.

Rehabilitation awards offered

Reader's Digest International Rehabilitation Awards totaling $6,500 will be presented at the ninth world congress of the International Society for Rehabilitation of the Disabled in Copenhagen, June 23 through 29, 1963. Applicants (societies, associations, or professional groups in any country of the world concerned with rehabilitation of the handicapped) must submit their reports to the International Society by January 31, 1963, for consideration by the selection board.

Two general awards of $2,500 and $1,500 and five regional awards of $500 each will be presented to those organizations showing the most progress in developing and enlarging services to the handicapped in a community for the two-year period, January 1, 1961, to December 31, 1962. For further information write to: International Society for Rehabilitation of the Disabled, 701 First Avenue, New York 17, New York.

Medical motion picture catalog

The 1962 Public Health Service Film Catalog of medical and health related motion pictures and filmstrips has recently been published by the National Medical Audiovisual Facility, a part of the Public Health Service's Communicable Disease Center in Atlanta, Georgia. Single copies of the 78-page catalog are available to persons and institutions with teaching functions in the health sciences. The majority of the films are technical in nature and would not be of interest to the general public.

Course on atherosclerosis and hypertension

A three-day full-time course on atherosclerosis and hypertension will be offered by the New York University Medical Center, November 8 through 10, under the chairmanship of Roy H. Clauss, M.D., associate professor of surgery, and Jere W. Lord, Jr., M.D., professor of clinical surgery.

The course is designed for physicians and surgeons interested in diseases of the vascular system and will emphasize a current analysis of atherosclerosis and hypertension. Aspects of causes, prevention, and the spectrum of therapy will be debated, and surgical and medical consideration of patients with diseases of extracranial cerebral arteries, renal and peripheral arteries, portal hypertension, and neurovascular syndromes will be evaluated.

For further information write to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

Course in emotional and psychiatric problems

The New York Academy of Medicine will present the fourth in an annual series of courses on "Emotional and Psychiatric Problems in Medical Practice," starting Monday, October 22 and ending February 8, 1963. The course, which is open to all physicians in specialty and general practice, will consist of basic and advanced sections meeting at weekly intervals for 14 one-and-one-half-hour sessions at the Academy Building, 2 East 103rd Street, New York 29, New York.

The objective of the course is to help physicians to comprehend more fully the continuous interaction of psychologic, social, and medical factors encountered in clinical practice. The course will be divided into basic sections for the benefit of those who have not participated previously and advanced sections for those who have already taken the basic course. The American Academy of General Practice, cosponsors of the course, will allow 21 hours of category 1 credit for its completion.

For information write to: Executive Secretary for Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Papers invited on chest diseases

The medical sessions committee of the American Thoracic Society invites submission of papers on all scientific aspects of tuberculosis and nontuberculous respiratory and cardiopulmonary disease for presentation at the 1963 annual meeting of the society in Denver, Colorado, May 13 through 15. Abstracts of papers should be submitted as soon as possible before January 4, 1963. Authors will be notified by February 8, 1963, whether or not their papers have been accepted for presentation.

For full details on specifications for abstracts write to: Charles LeMaistre, M.D., Chairman, Medical Sessions Committee, American Thoracic Society, 1790 Broadway, New York 19, New York.

The Doctors' Gun Club

The Doctors' Gun Club, a rifle and pistol club composed of physicians and dentists in the Metropolitan-New York area, has recently been organized.

The club is chartered by the National Rifle Association and is an affiliate of the New York State Rifle and Pistol Association. Excellent range facilities and locker space are available. Rifle and pistol instruction is given for beginners. All interested doctors are invited to join.

For information contact: William Greenfield, D.D.S., 110 East 36th Street, New York 16, New York, Telephone MUrray Hill 3–0367.

Nassau Heart Association formed

Announcement has been made of the formation of the Nassau Heart Association, Inc. The Association's headquarters are at 114 Seventh Street in Garden City. Asher S. Chapman, M.D., Glen Cove, has been named president of the organization.

Course in corneal surgery

A three-day course in corneal surgery will be offered at the Brooklyn Eye and Ear Hospital on Thursday, Friday, and Saturday, December 13 through 15, under the direction of A. Benedict Rizzuti, M.D.

Present concepts of various phases of corneal surgery will be stressed. Allied subjects such as instrumentation, beta radiation, contact lenses, and operating room photography will be discussed. Surgical procedures in the operating room will be demonstrated according to availability of donor material. Participants will be offered an opportunity to apply surgical technics on animal eyes.

For further information write to: Mr. Frederick Upton, Administrator, Brooklyn Eye and Ear Hospital, 29 Greene Avenue, Brooklyn 38, New York.

Kings County pediatricians elect officers

The Pediatric Section of the Medical Society of the County of Kings and the Academy of Medicine of Brooklyn recently elected the following officers to serve from October 1, 1962, to September 30, 1963: Ernest T. Heffer, M.D., president; Hyman Lieberman, M.D., vice-president; Richard D. Turin, M.D., secretary; and Felix Feldman, M.D., treasurer.

Patients sought for study of Reiter's syndrome

The cooperation of physicians is asked in the referral of patients for a study of Reiter's syndrome conducted by the National Institute of Arthritis and Metabolic Diseases in the Clinical Center of the National Institutes of Health, Bethesda, Maryland. Renewed efforts are being made to recover and identify the causative agent of Reiter's syndrome.

Reiter's syndrome is characterized by a triad of arthritis, urethritis, and conjunctivitis. Cases lacking conjunctivitis would still qualify for this study. The presence of gonococcus and urethral discharge would not preclude a case from this study, provided this organism is not present in the synovial fluid. The appearance of cutaneous manifestations (balanitis, keratodermia blennorrhagica, maculopapular eruption on penis, and hard papules on soles) help establish the diagnosis. Most desirable for study are cases within the first two weeks of onset.

Physicians who wish to have patients considered for this study should write to: Joseph J. Bunim, M.D., Clinical Director, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Maryland.

Mount Sinai training grants

The receipt of five training grants from the National Institute of Mental Health has been announced by Mount Sinai Hospital, New York City. They will be used for training programs to be carried out by the hospital's Department of Psychiatry.

These programs will get underway with the opening of the Institute of Psychiatry, part of the hospital's new clinical center on Madison Avenue at 100th Street, scheduled for completion this fall. The Institute will be the largest psychiatric unit of any general hospital in the country.

Cerebral palsy symposium

A two-day symposium on the "Recognition and Management of Cerebral Palsy," sponsored by the New York Academy of Medicine, the Department of Health of the City of New York, and the Professional Advisory Council of United Cerebral Palsy of New York City, Inc., will be held November 29 and 30 at the New York Academy of Medicine, 2 East 103rd Street, New York City.

Inquiries should be directed to Dr. Martin E. McCavitt, Executive Director, United Cerebral Palsy of New York City, Inc., 70 Fifth Avenue, New York 11, New York.

Prize essay competition

The New York State Academy of Preventive Medicine has announced a prize essay competition for second, third, and fourth year medical students attending medical colleges in New York State. Topics should be concerned with preventive medicine or some aspect of public health.

A cash prize of $350 and a certificate will be awarded at the time of the commencement in 1963 to the successful competitor.

The chairman of the department of preventive medicine in each of the medical schools in New York State has been asked to make the announcement to the medical students and to assist in the selection of suitable topics and the collection of the essays for submission to the judges.

Program in individual psychology

A three-year psychotherapy program in individual psychology is being offered at the Alfred Adler Institute, New York City. Classes will begin October 9, 1962, and will be held on Tuesday and Thursday evenings from 8 to 10 P.M. at 333 Central Park West (93rd Street), New York City. Registration begins September 25, 7 to 9 P.M.

It is hoped that physicians may deepen their knowledge about the psychologic forces which may be blocking the physical as well as the mental recovery of some of their patients.

Further information about the program may be obtained from the Institute, 333 Central Park West, New York 25, New York.

Cancer Society grants

Grants of $1,013,955 for 43 research projects and $2,991,224 in renewals of grants for 128 continuing projects have been announced by the American Cancer Society.

This raised to $11,557,943 the research expenditures made by the society for the fiscal year 1961–1962.

John P. Blass, Ph.D., of Columbia University's College of Physicians and Surgeons, was awarded a three-year research scholarship of $26,750 leading to an M.D. degree.

William K. Hass, M.D., assistant professor of neurology at New York University School of Medicine, was granted $17,703 to study brain tumor tissue.

Renewal grants went to: Cornell University Medical College, $123,550; New York University, $105,333; Sloan-Kettering Institute for Cancer Research, $86,702; Columbia University College of Physicians and Surgeons, $65,023; Flower and Fifth Avenue Hospitals, $25,000; New York City Public Health Research Institute, $13,748; Veterans Administration Hospital, The Bronx, $10,800; Rockefeller Institute, $9,102; and Yeshiva University, $6,437.

Laboratory methods course

The laboratory consultation and development section of the Communicable Disease Center, Public Health Service, will offer a course on "Laboratory Methods in the Diagnosis of Tuberculosis and Related Mycobacterial Infections" in Atlanta, Georgia, January 14 through 25 and January 28 through February 8, 1963.

This course is open to all grades of employed laboratory personnel who are approved by their health officers. Practical laboratory training in all phases of tuberculosis bacteriology, including preparation of culture media, microscopy, cultural procedures, diagnostic use of animals, biochemical technics, and testing of drug susceptibility will be included. Demonstration and training in technics for the isolation and identification of unclassified acid-fast bacilli also will be presented.

Laboratory directors and senior laboratory staff members also may make application for this course.

No tuition or laboratory fees are charged. Reservations for this course should be made well in advance.

Application forms may be obtained from the Laboratory Branch, Communicable Disease Center, Public Health Service, Atlanta, Georgia.

Doctors' Orchestral Society

The Doctors' Orchestral Society of New York will begin its silver anniversary season with a rehearsal at 8:00 P.M., September 20, at Stuyvesant High School Auditorium, 345 East 15th Street, New York City. For further information call Harvey Salomon, M.D., at AXtell 1-6611.

Heart Association fellowship

The establishment of a Homer W. Smith Research Fellowship in renal physiology has been announced by the New York Heart Association. The fellowship, tenable at any institution in the United States, will provide a total of $60,000 for an established investigator over a period of five years, beginning July 1, 1963. The stipend will be $10,000 the first year, with annual increments of $1,000.

Nomination for the fellowship should be in the form of a letter from the chairman or director of the sponsoring department or institution, accompanied by biographical data on the proposed fellow, a bibliography of his research, and a brief discussion of his scientific interests and achievements that would qualify him for the award.

Nominations must be received before November 1. They will be reviewed by the Advisory Council on Research of the New York Heart Association in December, and its decision will be announced shortly thereafter.

Referral of patients asked

The continued cooperation of physicians is requested in the referral of patients with glycogen storage disease for a study currently in progress at the Clinical Center, National Institutes of Health, Bethesda, Maryland.

Patients known or suspected of having one of the forms of glycogen storage disease are needed for further study of metabolic errors leading to this group of disorders and for the elaboration of methods for the prevention and treatment of these conditions.

New types of glycogen storage disease due to other enzymatic defects will undoubtedly be found if a careful search is made for them. Striking hepatomegaly, cardiomegaly, or muscular weakness in varying combinations should raise the question as to glycogenosis.

Physicians interested in having their patients considered for admission to this study should write to: Paul A. di Sant'Agnese, M.D., National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda 14, Maryland.

Medical student research

The Salmon Foundation has announced the expansion of its program to include grants for medical students. For the coming academic year the Foundation has made available from one to four medical student research fellowships in the basic sciences or clinical fields to the following schools:

Albany Medical College, Albany; Columbia University College of Physicians and Surgeons, New York City; Cornell University Medical College, New York City; State University of New York, Downstate Medical College of Medicine, Brooklyn; State University of New York, Upstate Medical Center, Syracuse; New York University College of Medicine, New York City; University of Rochester School of Medicine and Dentistry, Rochester; Albert Einstein College of Medicine, New York City; and McGill University School of Medicine, Montreal, Canada.

Personalities

Speakers. Arthur J. Bedell, M.D., Albany, on the subject "Serial Fundus Photographs of Choroiditis, Optic Neuritis, and Papilleodema" at the Oxford Ophthalmological Congress in England . . . Hans J. Behrend, M.D., New York City, on the subject "Rehabilitation of the Chronically Ill" at the International Congress of Internal Medicine in Munich, on September 6 . . . Brittain F. Payne, M.D., New York City, in Mexico City, at the invitation of the Mexican Ophthalmological Society in September.

Appointed. I. Murray Rossman, M.D., Helmuth, as director of the new Bronx State Hospital . . . Samuel Standard, M.D., New York City, as chief of the division of surgery of Morrisania Hospital and attending surgeon at Montefiore Hospital.

Relocated. Arnold N. Benson, M.D., fellow in internal medicine at the Mayo Foundation in Rochester, Minnesota, has left that City and will be located in New York City.

Medical Meetings

The Society for Surgery of the Alimentary Tract

The third annual meeting of The Society for Surgery of the Alimentary Tract was held in Chicago on June 24. New York physicians who attended the meeting were: Warner F. Bowers, M.D., New York City; Theodore Drapanas, M.D., Buffalo; Irving F. Enquist, M.D., Brooklyn; Robert S. Grinnell, M.D., New York City; S. Arthur Localio, M.D., New York City; John F. Prudden, M.D., New York City; David State, M.D., Bronx; Robert Turell, M.D., New York City; Herbert Volk, M.D., Bronx; and C. Stuart Welch, M.D., Albany.

Dr. Welch delivered an address entitled "Ulceration in the Cirrhotic." Dr. Turell demonstrated three newly-created fiberoptic endoscopes, the choledoscope, the coloscope, and the sigmoidoscope.

The newly-elected officers of the society are: Walter G. Maddock, M.D., Chicago, president; Robert M. Zollinger, M.D., Columbus, Ohio, president-elect; and Dr. Turell, secretary-treasurer.

The next annual meeting of the society will be in Atlantic City, New Jersey, June 16, 1963.

American Medical Writers' Association

The section on advertising and public relations of the Metropolitan New York Chapter, American Medical Writers' Association, will present a panel discussion on "Control of Medical Information to the Public? Why? Who? How?" on September 19 at 8:00 P.M. The meeting will be held at the Helena Rubinstein Auditorium, 655 Fifth Avenue, New York City. Among the panelists will be Mr. William B. Arthur, *Look* magazine; Barbara Hertz, *Parents Magazine;* Prof. Hillyer Kreigbaum, New York University; Granville W. Larimore, M.D., State Health Department, Albany; and Louis C. Lasagna, M.D., Johns Hopkins School of Medicine, Baltimore, Maryland.

All interested are invited to attend as guests of the chapter. Cochairmen for the meeting are L. W. Frohlich, New York City, and Martin Sampson, M.D., Bloomfield, New Jersey.

International symposium on comparative medicine

The first international symposium on comparative medicine will be held at the Waldorf-Astoria Hotel, New York City, October 10 through 12. The symposium is sponsored by New York City's Animal Medical Center and is supported by a grant from Eaton Laboratories Division of The Norwich Pharmacal Company. Physicians and veterinarians are invited to attend the symposium which will bring together investigators in human and veterinary medicine in the following areas: Behavior, infectious disease, cardiovascular disease, neoplastic disease, and the liver and disorders of metabolism.

Women's Medical Society

The 56th fall meeting of the Women's Medical Society of New York State, Inc., will be held on October 13 at the Corinthian Club, 930 James Street, Syracuse. A scientific paper on "Studies of Catecholamine Metabolism in Neuroblastoma" will be presented by Mary L. Voorhess, M.D., from the Upstate Medical Center in Syracuse.

New England postgraduate assembly

The nineteenth annual New England Postgraduate Assembly will be held November 6 through 8 at the Statler Hilton, Boston, Massachusetts.

The Assembly is sponsored by the Council of New England State Medical Societies in cooperation with the New England State Chapters of the American Academy of General Practice.

The Assembly is open to all physicians. For further information write to: Mr. Getty Page, Secretary, 128 Merchants Row, Rutland, Vermont.

American College of Chest Physicians

The American College of Chest Physicians will hold its annual interim session at the Ambassador Hotel in Los Angeles November 24 and 25. Full day scientific sessions will be held, followed by administrative sessions on November 26.

Subjects will include clinical virology, atypical pneumonias, prevention and management of influenza and the common cold, pulmonary tuberculosis, diagnosis and treatment of coronary heart disease, impending myocardial infarction, and surgical treatment of congenital cardiac anomalies.

A program may be obtained by writing to Mr. Murray Kornfeld, Executive Director of the College, at 112 East Chestnut Street, Chicago 11, Illinois.

American Psychosomatic Society

The American Psychosomatic Society will hold its twentieth annual meeting at the Chalfonte-Haddon Hall in Atlantic City, New Jersey, on Saturday and Sunday, April 27 and 28, 1963.

The program committee invites interested persons both to attend the meeting and to submit abstracts of original work for consideration for presentation. Accepted abstracts will be printed and circulated to the membership prior to the meeting and will be available at a minimal price at the meeting itself.

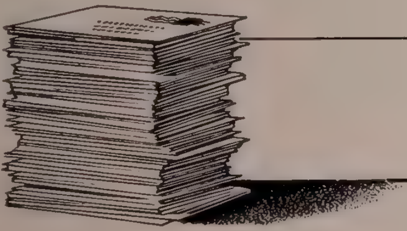
Abstracts should be submitted in ten copies by December 1 to: Julius B. Richmond, M.D., Chairman, Program Committee, American Psychosomatic Society, 265 Nassau Road, Roosevelt, New York.

Congress of Gerontology

The Sixth International Congress of Gerontology, hosted by Denmark, Finland, Norway, and Sweden, will be held August 11 through 16, 1963, in Copenhagen, Denmark, with one-day sessions being held in Sweden.

Symposia and sessions for papers are being organized within four divisions: Biological research, medical and clinical research, social science and psychological research, and social welfare research.

Information on the submission of papers may be obtained from Ralph Goldman, M.D., School of Medicine, Department of Medicine, University of California Medical Center, Los Angeles 24, California.



Letters to the Editor

Suggestion for control of epilepsy

To the Editor: In an attempt to control a very difficult epileptic patient whose seizures were much aggravated by her time for menstruation I used norethynodrel (Enovid) to suppress the period. With this treatment the seizures ceased.

I offer this as a suggestion in the control of epilepsy and for women in whom aggravation at the time of their period is noted.

Donald N. Groff, M.D.

622 Pennsylvania Avenue
Elmira, New York

Woman's Auxiliary

Redefining our objectives

Now that twenty-six years of Auxiliary history have been written, it seems to me that this might be a good time to look back and see how well we have carried out the hopes of our founders and to plan how to carry them out in the future.

With this in mind, I have selected as the theme for 1962–1963 "Redefining Our Objectives."

Our objectives, as defined by our constitution, are:

> First: To assist the Medical Society of the State of New York in its program for the advancement of medicine and public health;
>
> Second: To coordinate and advise concerning the activities of constituent auxiliaries;
>
> Third: To encourage friendly relations and promote mutual understanding among physicians' families.

The first objective calls for assisting in the program for the advancement of medicine and public health. We assist not by sitting by but by doing something. When legislation is proposed that will hinder and not advance medicine, we, as physicians' wives, must speak up in lay groups and make our voices heard. If legislation harmful for the American people is enacted, it will be too late to say, "They should have done something about it. That's what we pay dues to an organization for. We're too busy." We cannot shift the responsibility. We are "they." It is a privilege and an honor to be a doctor's wife, and there are responsibilities that go with the position. Our programs on legislation, American Medical Association Education and Research Foundation, and public relations afford the opportunity to fulfil these responsibilities, and if we truly define our objectives, this is what we will attend to first.

Naturally, we know that as a State organization we exist to carry out our second objective of coordinating and advising the county auxiliaries. This we accomplish through conventions, fall conferences, and correspondence, as well as personal contacts wherever possible. But we can't do this unless the officers of the county auxiliaries seek our advice. Set Fall Conference dates aside now—September 23 to 25. Bring future presidential material from your county with you. Hear our problems discussed, and help us with their solution. Let's have an exchange of ideas and then put them to work, remembering that ideas won't work unless we do.

And that brings us to our third objective of encouraging friendly relations and promoting mutual understanding among physicians' families. Sir William Osler said of physicians, "Amid an eternal heritage of sorrow and suffering, our work is laid." It is a unique and exacting profession, and we, as partners in it, can find friendship and understanding in this organization.

And so, let's redefine our objectives in the coming year. You know which project your particular auxiliary is interested in and enthusiastic about—do it! Don't try to do them all. Be sure that the ones you select conform to our objectives and are not ones that could be done just as well by a lay group.

We need recruits and reinforcements. We must keep working to narrow the gap between the number of men who belong to medical societies and the number of women who are members of auxiliaries. And after new members have joined, we must encourage them to take an active part.

A successful man once said, "I believe that every right implies a responsibility, every opportunity an obligation, every possession a duty." We, as wives of physicians, are privileged to have many rights, opportunities, and possessions. Let us not forget the responsibilities, the obligations, and the duties that go with them.

In this coming year, let us redefine our objectives and strive to carry them out.

MRS. HERBERT J. ULRICH, *President*
33 Parkside Avenue
Buffalo, New York

Excerpted from the State Auxiliary president's inaugural address, presented at the annual Auxiliary convention, New York City, May 16, 1962.

Necrology

Irving C. Fischer, M.D., of New York City, died on July 28 at his home at the age of fifty. Dr. Fischer received his medical degree from the University of Vienna in 1936 and interned at Morrisania Hospital. He was a senior clinical assistant attending physician in gynecology and obstetrics at The Mount Sinai Hospital, an adjunct obstetrician and gynecologist at Jewish Memorial Hospital, and an associate attending obstetrician and gynecologist at Metropolitan Hospital, Bird S. Coler Memorial Hospital and Home, and Flower and Fifth Avenue Hospitals, and an assistant attending gynecologist at New York Polyclinic Hospital, as well as an assistant professor of obstetrics and gynecology at New York Medical College. Dr. Fischer was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American College of Obstetricians and Gynecologists, and a member of the American Association for Research in Psychosomatic Problems, the Academy of Psychosomatic Medicine, the Association of Military Surgeons of the United States, The American Society for the Study of Sterility, the New York Academy of Medicine, the Bronx Gynecological and Obstetrical Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Gianquinto, M.D., of Brooklyn, died on April 10 at the age of sixty-one. Dr. Gianquinto graduated in 1923 from Long Island College Hospital Medical School. He was an associate attending physician in orthopedics at Long Island College Hospital. Dr. Gianquinto was a Fellow of the American College of Surgeons, a Fellow of the American Academy of Compensation Medicine, Inc., and a member of the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Louis M. Hickernell, M.D., of Westbrook, Connecticut, formerly of Syracuse, retired, died on July 13 at the age of seventy-five. Dr. Hickernell graduated in 1926 from Syracuse University College of Medicine. He was formerly director of student health at Syracuse University. Dr. Hickernell was a Fellow of the American College of Physicians and a member of the Onondaga County Medical Society and the Medical Society of the State of New York.

Harold Kushel, M.D., of the Bronx, died on August 9 at Fordham Hospital at the age of sixty. Dr. Kushel graduated in 1926 from New York University and Bellevue Hospital Medical College and interned at Fordham Hospital. He was an attending surgeon at Fordham Hospital. Dr. Kushel was a member of the Bronx Surgical Society, the Bronx County Medical Society, and the Medical Society of the State of New York.

Rudolph Duryea Moffett, M.D., of New York City, retired, died on August 5 at Lenox Hill Hospital at the age of seventy-five. Dr. Moffett graduated in 1908 from Long Island College Hospital Medical School. He was a consulting pediatrician at Lenox Hill Hospital Outpatient Department. Dr. Moffett was a Diplomate of the American Board of Pediatrics, a Fellow of the American College of Physicians, and a member of the Pan-American Medical Association, the American Academy of Pediatrics, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Morris Robinson, M.D., of Brooklyn, died on July 28 at Brooklyn Jewish Hospital at the age of seventy-seven. Dr. Robinson graduated in 1912 from Long Island College Hospital Medical School.

Alexander Sarafianos, M.D., of Brooklyn, died on July 26 at the Swedish Hospital in Brooklyn at the age of sixty-three. Dr. Sarafianos received his medical degree from the University of Athens in 1922. He was an attending surgeon at the Swedish Hospital in Brooklyn. Dr. Sarafianos was a member of the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Nathaniel Sipilesko, M.D., of the Bronx, died on March 31 at the age of sixty-one. Dr. Sipilesko graduated in 1928 from New York University and Bellevue Hospital Medical College and interned at Bronx Hospital. He was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Alfred L. C. Ulrich, M.D., of Buffalo, died on July 9 at Edward J. Meyer Memorial Hospital at the age of sixty. Dr. Ulrich graduated in 1927 from the University of Buffalo School of Medicine. He was an attending psychiatrist at Edward J. Meyer Memorial Hospital and professor of psychiatry at the University of Buffalo School of Medicine. With Emerick Friedman, M.D., in 1936 he helped perfect the first shock technic for treating mental illness by the administration of a drug. Dr. Ulrich was a Fellow of the American Psychiatric Association and a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Month in Washington

Reports of possible serious side-effects of three drugs led to studies and investigations by the drug industry, the American Medical Association, and the Federal government.

Most attention was given to thalidomide, a nonbarbiturate which produces sleep without a "hangover." Births of malformed babies, mostly in foreign countries, by mothers who took the drug during pregnancy were widely reported.

The Pharmaceutical Manufacturers Association established a special drug safety group to broaden scientific knowledge regarding predictability of the effect of potent drugs on humans.

The A.M.A. started a special study of thalidomide. A Senate subcommittee opened an investigation. One of the first official acts of the new secretary of Health, Education, and Welfare, Anthony J. Celebrezze, was to order a tightening of F.D.A. controls over drug testing.

Thalidomide was first marketed in West Germany about five years ago. It was consumed widely in West Germany, Great Britain, Australia, Portugal, and Canada. One of its uses was as an antidote for the morning sickness of early pregnancy. No significant side-effects, either proved or suspected, were reported until 1961.

The parent company of The Wm. S. Merrell Co. of Cincinnati, Ohio, obtained in 1959 the North American marketing rights for the drug. Merrell conducted laboratory and mass clinical tests, put the drug on the market in Canada, and in September, 1961, applied for F.D.A. approval for U.S. sales.

Frances O. Kelsey, M.D., a newly employed medical officer at F. D. A., moved cautiously on the application and withheld approval. In February, 1961, she read a letter in the *British Medical Journal* suggesting that thalidomide might be causing peripheral neuritis.

For withholding F.D.A. approval of the drug, Dr. Kelsey was awarded the Distinguished Federal Civilian Service Medal by President Kennedy. The President at the same time renewed his request to Congress that it approve the Administration's drug legislation.

First reports linking thalidomide with birth malformations reached Merrell from the German drug manufacturer in November, 1961, after a German scientist reported such indications at a medical meeting. Merrell promptly sent a warning to Canadian doctors and the approximately 1,200 American doctors conducting clinical tests with it. It was requested that the drug not be given to women of child-bearing age. Merrell so advised the F.D.A. at the time also. In early March, 1962, Merrell withdrew the drug from the Canadian market and experimental use

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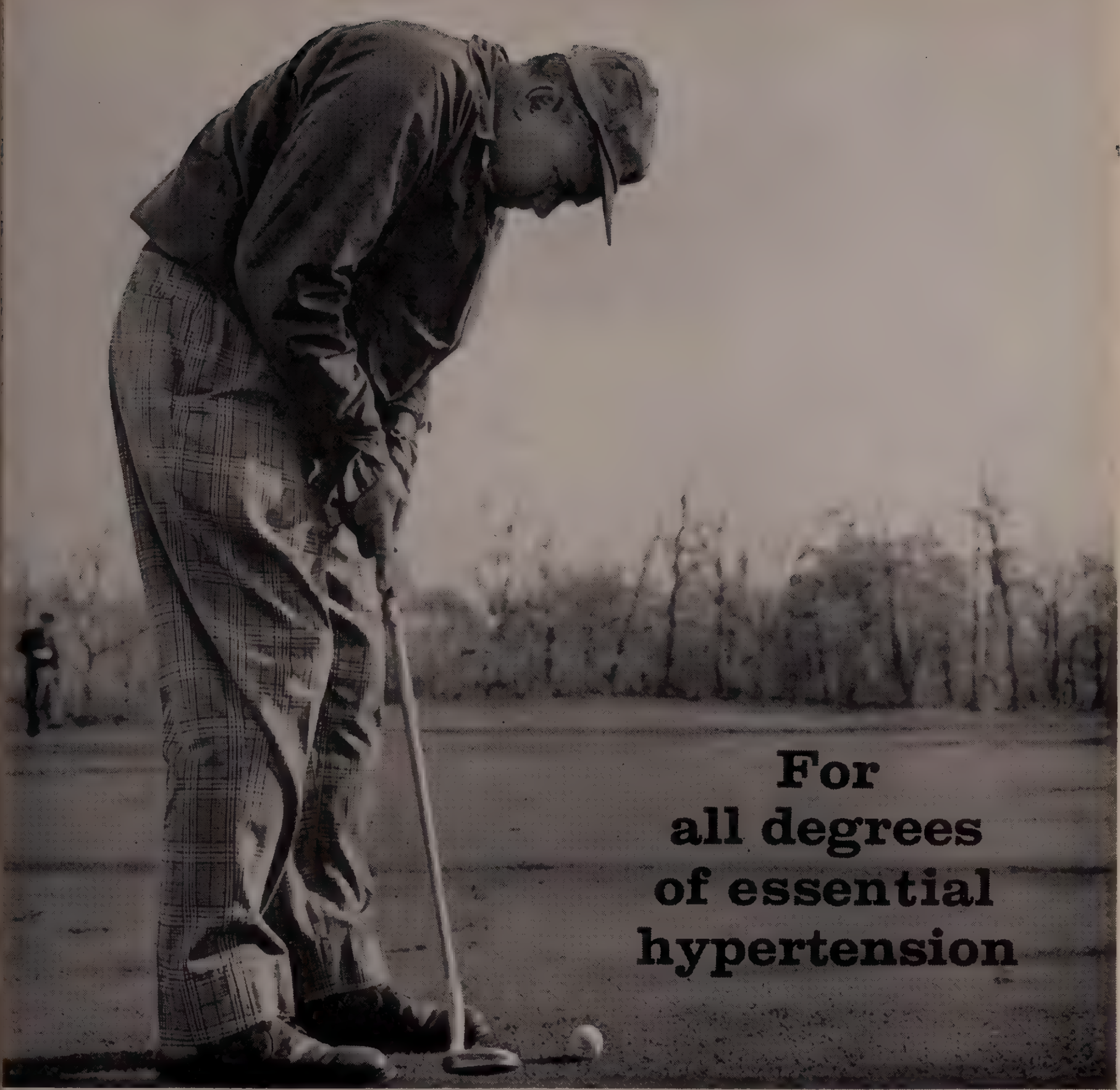
Prepared by the Washington, D.C., office of the American Medical Association.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†Hutchison J. C.: Current Therap. Res. 2:487 (Oct.) 1960.

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continued from page 3020

in this country, and dropped its F.D.A. application.

The P.M.A. announced establishment and financing of a Commission on Drug Safety to, among other activities, "investigate an unpredictable problem which is assumed to be connected with use of the European drug (thalidomide)." Lowell T. Coggeshall, M.D., a leading U.S. scientist and vice-president of the University of Chicago, was named chairman of the commission. He formerly was president of the American Association of Medical Colleges and of the American Cancer Society.

"The basic purpose of our commission is to study the broad and complex problems of making available to the public, with adequate safeguards for both the doctor and the patient, the therapeutic advances which will result from the enormous programs and rapid pace of medical research," Coggeshall said.

"However promising new agents may be in the laboratory, no amount of laboratory experimentation and testing can provide complete assurance of effectiveness or safety when a new drug is administered to a human being. We must attempt to reduce danger to the lowest possible degree without discouraging the imaginative research from which flows mankind's increasing release from disease."

The A.M.A. Council on Drugs began a comprehensive analysis of the effect of thalidomide on unborn infants.

In a statement, the council said:

"The A.M.A. has been concerned about the reports of distinctive congenital malformations occurring in the offspring of patients receiving thalidomide in early pregnancy . . .

"It has been under clinical evaluation here since 1956. There have been no published reports in scientific journals of such malformations developing in connection with these trials in the United States.

"On the evidence which has been presented, it would appear that the increased incidence of extromelia in Germany, Great Britain, and Australia may be related to the use of thalidomide during the early weeks of pregnancy.

"A careful analysis of the whole problem is needed. This has not yet been done, and the Council on Drugs proposes to undertake a comprehensive analysis. Through such studies, it is hoped that further knowledge will be gained on the problem of congenital malformations and appropriate measures will be determined to safeguard our population."

F.D.A. Commissioner George P. Larrick and Dr. Kelsey both agreed in testifying before the Senate Subcommittee that Merrell had acted with reasonable diligence in withdrawing thalidomide from the market. Dr. Kelsey said that if the entire matter had been up to her alone she would not have withdrawn it much sooner than the company.

Larrick also said that the F.D.A. had not found any infants born deformed in this country as a result of thalidomide administered in the mass clinical testing program. But he said the birth of deformed infants in this country had been reported where mothers had taken the drug after it had been procured in other nations where it had been marketed.

A Federal grand jury was investigating Merrell in connection with another of its drugs, MER-29, which was designed to inhibit formation of cholesterol in the blood.

The F.D.A. in April, 1960, approved an application for marketing the drug. It was an instant success. But it was withdrawn in April of this year after reports that some patients taking it had developed eye cataracts and had suffered hair loss, skin changes, and leukemia.

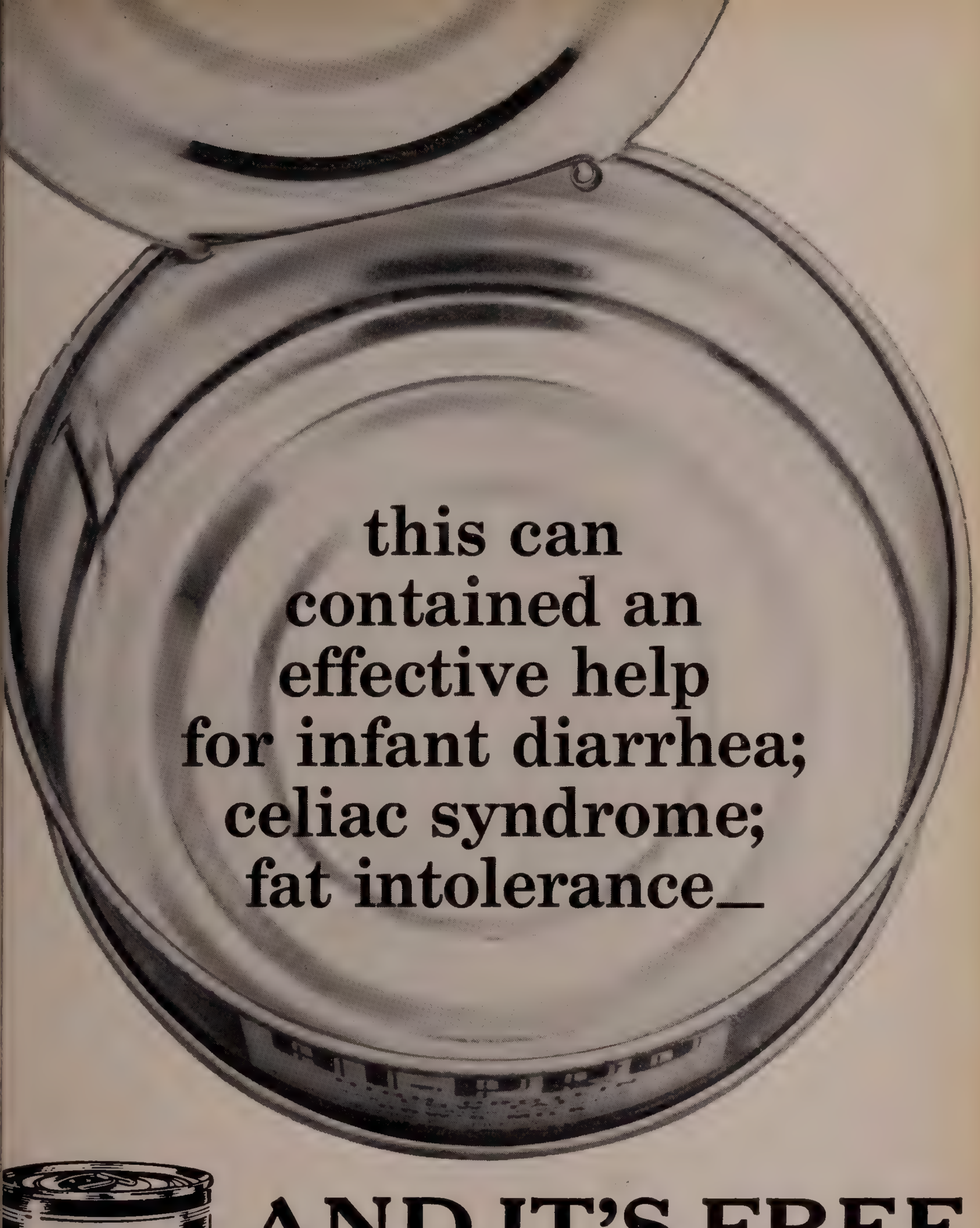
The A.M.A. Council on Drugs recently reported that "much longer and more careful studies" were needed to prove the safety of the drug in general or long-term use.

The F.D.A. also investigated Enovid, a birth control pill. The F.D.A. said there had been 28 cases reported since September in which women given the contraceptive pill developed a blood clot called thrombophlebitis. Six of them died. But the agency cautioned that fatal blood clots can be caused by many things unrelated to any drug.

The pill's manufacturer, G. D. Searle & Co. of Chicago, said a "super-charged atmosphere over thalidomide" was responsible for the F.D.A.'s investigation of Enovid.

The company said a woman taking oral contraceptives runs no more risk of blood clots than a woman in normal pregnancy.

It was the second investigation ordered into the contraceptive pill since it was approved for commercial sale in May, 1960, on the basis of what the F.D.A. called "extensive research data."



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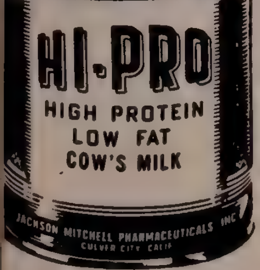
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Books Received

*The following books were received during the month of July, 1962**

Clinical Nutrition. Edited by Norman Jolliffe, M.D. Second edition. Octavo of 1,012 pages, illustrated. New York, Harper & Bros., 1962. Cloth, $23.50.

Gynecology and Obstetrics. By John William Huffman, M.D. Quarto of 1,190 pages, illustrated. Philadelphia, W. B. Saunders Co., 1962. Cloth, $28.

Gynecology. By Langdon Parsons, M.D., and Sheldon C. Sommers, M.D. Quarto of 1,250 pages, illustrated. Philadelphia, W. B. Saunders Co., 1962. Cloth, $20.

The Gynecologic Patient. A Psycho-Endocrine Study. By Somers H. Sturgis with Doris Menzer-Benaron in collaboration with Thomas A. Morris, Joseph Sabbath, Phillip Gates, Alfred O. Ludwig, Richard Wilson, Robert Eisendrath, Benjamin Murawski, and Harriet Robey. Octavo of 243 pages, illustrated. New York, Grune & Stratton, Inc., 1962. Cloth, $7.75.

Synopsis of Obstetrics. By Charles E. McLennan, M.D. Sixth edition. Duodecimo of 464 pages, illustrated. St. Louis, The C. V. Mosby Co., 1962. Cloth, $6.75.

Fundamental Skills in Surgery. By Thomas F. Nealon, Jr., M.D. Octavo of 289 pages, illustrated. Philadelphia, W. B. Saunders Co., 1962. Cloth, $8.50.

Clinical Biochemistry. By Abraham Cantarow, M.D., and Max Trumper, Ph.D. Sixth edition. Octavo of 776 pages, illustrated. Philadelphia, W. B. Saunders Co., 1962. Cloth, $13.

Diagnosis and Management of Pain Syndromes. By Bernard E. Finneson, M.D. Octavo of 261 pages, illustrated. Philadelphia, W. B. Saunders Co., 1962. Cloth, $8.50.

Tobacco and Health. Edited by George James, M.D., and Theodore Rosenthal, M.D. Octavo of 408 pages, illustrated. Springfield, Charles C Thomas, 1962. Cloth, $13.75.

Ciba Foundation Symposium Jointly with Co-ordinating Committee for Symposia on Drug Action on Enzymes and Drug Action. Editor for the Co-ordinating Committee J. L. Mongar, Ph.D. Editor for the Ciba Foundation A. V. S. de Reuck, M.Sc. With 90 illustrations. Octavo of 556 pages. Boston, Little, Brown & Co., 1962. Cloth, $12.50.

Strabismus. Symposium of the New Orleans Academy of Ophthalmology. Edited by George M. Haik, M.D. Octavo of 369 pages, illustrated. St. Louis, The C. V. Mosby Co., 1962. Cloth, $18.

Urology in Medical Practice. By Frank C. Hamm, M.D., and Sidney R. Weinberg, M.D. Second edition. Quarto of 323 pages, illustrated. Philadelphia, J. B. Lippincott Co., 1962. Cloth, $9.75.

Current Psychiatric Therapies. Vol. II, 1962. Edited by Jules H. Masserman, M.D. Octavo of 289 pages, illustrated. New York, Grune & Stratton, Inc., 1962. Cloth, $8.75.

Illustrated Manual of Neurologic Diagnosis. By R. Douglas Collins, M.D. Octavo of 177 pages, illustrated. Philadelphia, J. B. Lippincott Co., 1962. Cloth, $12.

College Students in a Mental Hospital. By Carter C. Umbarger, James S. Dalsimer, Andrew P. Morrison, and Peter R. Breggin. Duodecimo of 168 pages. New York, Grune & Stratton, Inc., 1962. Paper, $5.75.

The Rights and Rewards of the Medical Witness and Medical and Dental Appraiser. By Nils Nordstrom, Jr., M.D. Octavo of 104 pages. Springfield, Charles C Thomas, 1962. Cloth, $5.00.

Body Fluid Disturbances. Edited by W. D. Snively, Jr., M.D. Octavo of 122 pages, illustrated. New York, Grune & Stratton, Inc., 1962. Cloth, $4.75.

Sex in Marriage: New Understandings. By Dorothy Walter Baruch, Ph.D., and Hyman Miller, M.D. Octavo of 277 pages. New York, Harper & Bros., 1962. Cloth, $4.95.

Properties of Membranes and Diseases of the Nervous System. By Donald B. Tower, Sarah A. Luse, and Harry Grundfest. Octavo of 102 pages, illustrated. New York, Springer Publishing Co., Inc., 1962. Paper, $4.50.

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* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

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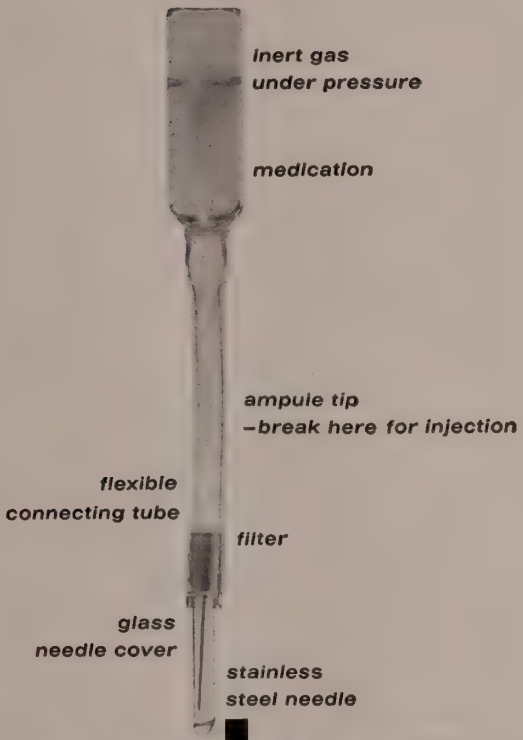

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continued from page 3024

Recent Data on the Pharmacology and Clinical Aspects of Phenothiazine Derivatives. Transactions Vol. I. Edited by V. V. Zakusov. English edition of Novye dannye po farmakologii i klinike proizvodnykh fenotiazinovogo ryada. Translated by Israel Program for Scientific Translations, Jerusalem, 1962. Available from The Office of Technical Services, U.S. Department of Commerce, Washington 25, D.C. Paper, $2.00.

Between Us Women. A Woman Doctor's Handbook on Pregnancy and Birth. By Laura E. Weber, M.D. Octavo of 153 pages, illustrated. Garden City, N.Y., Doubleday & Co., Inc., 1962. Paper, $1.95.

New Opportunities for Negroes in Medicine. Octavo of 34 pages, illustrated. Chicago, National Medical Fellowships, Inc., 1962. Paper.

The Consumers Union Report of Family Planning. By Alan F. Guttmacher, M.D. and the Editors of Consumer Reports. Octavo of 146 pages, illustrated. Mount Vernon, N.Y., Consumers Union of U. S., Inc., 1962. Paper, $1.75.

Logic of Operating Room Nursing. By Jacqueline Willingham, R. N. Octavo of 93 pages. New York, Springer Publishing Company, Inc., 1962. Paper, $1.75.

The Reluctant Surgeon. A Biography of John Hunter. By John Kobler. Duodecimo of 439 pages. Garden City, N.Y., Doubleday & Co., Inc., 1962. Paper, $1.45.

Mechanisms of Regulation of Growth. Report of the Fortieth Ross Conference on Pediatric Research. Octavo of 72 pages, illustrated. Columbus, Ross Laboratories, 1962. Paper, n.p.

Farm chemicals

A warning to farmers and farm workers concerning the possible role of chemical poisoning as a factor in farm accidents comes from the University of Rochester Department of Pharmacology, nationally known center for research on the toxicity of common household and farm products. According to the July, 1962, issue of the Department's *Bulletin,* "the farm provides an especially hazardous working environment since exposure to a multitude of potent chemicals is combined with the use of dangerous machinery, both under marginal supervision."

Symptoms of chemical poisonings may include acute excitation of the central nervous system followed by depression and can occur following exposure to chemicals, such as xylene, used in manufacturing insecticides and other pesticides, solvents, cleaners, paint removers, and so forth.

Among such symptoms are anxiety, jitters, tremors, disturbed behavior, exhaustion, lethargy, weakness, and sleepiness. Any of these symptoms "can increase a person's accident-liability. The exposure to toxic chemicals does not necessarily have to be severe, nor the symptoms disabling. On the contrary, a symptom produced by an exposure so mild it is unrecognized may often prove all the more insidious and harmful because the victim is unaware of the danger.

"For example, a farmer, in preparing his tractor for field work, may inhale enough gasoline fumes to produce what is commonly known as a 'naphtha jag,' the symptoms of which closely resemble those of alcoholic intoxication. He may not feel inebriated when he takes his tractor out into the field. A boulder lies in his path. Ordinarily, he would automatically stop his tractor in time to avoid hitting the boulder or successfully maneuver the machine around it. With his coordination and reflexes below their normal capacity, he hits the boulder, his tractor turns over, and another farm casualty is reported: 'His tractor overturned, crushing the driver.' Rarely is there a mention of a contributing cause: 'He was slightly intoxicated by the inhalation of gasoline fumes.' "

Any farm worker engaged in a hazardous activity is urged to watch for symptoms, no matter how slight, and "ask himself if there has been an exposure to a poisonous chemical through inhalation or an ingestion of food that has come in contact with a toxic substance. If there has been such an exposure, hazardous activities should be curtailed until the symptoms are gone. Otherwise another farm casualty may be added to the statistics that make up the appallingly high morbidity and fatality rates due to farm accidents."

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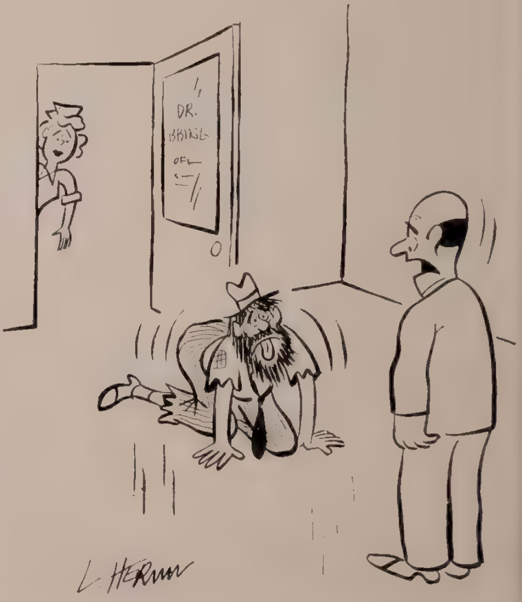

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Proceedings of the House of Delegates

MEDICAL SOCIETY OF THE STATE OF NEW YORK

156th Annual Meeting
May 14 to 17, 1962
New York City

MINUTES *of the Annual Meeting*

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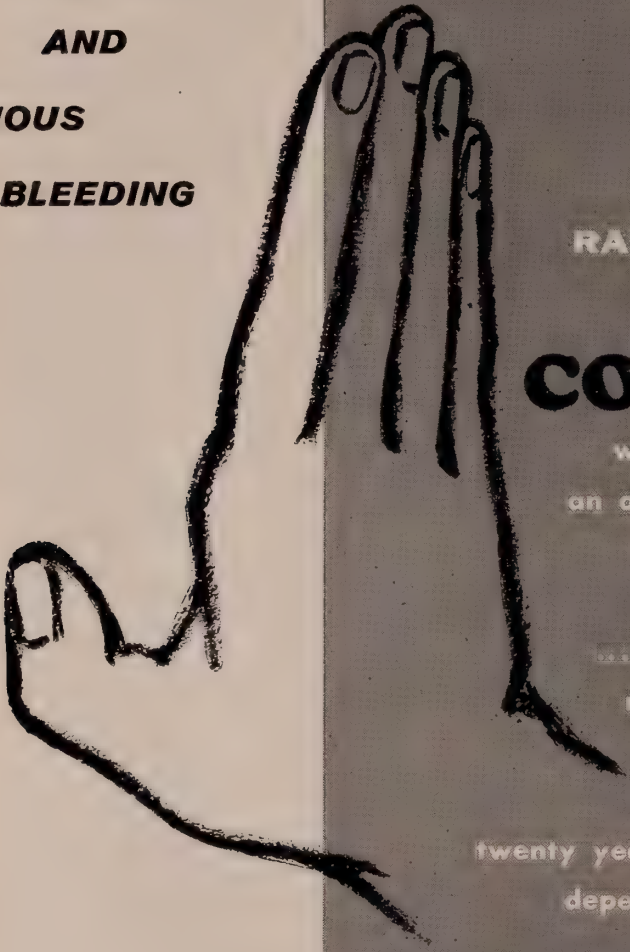

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The Annual Meeting, 1962

Herewith is presented the complete minutes of the House of Delegates at the 156th Annual Meeting held at the Statler-Hilton Hotel in New York City, May 14 to 18, 1962. The Speaker of the House, Frederick A. Wurzbach, Jr., M.D., called up 57 resolutions to the floor of the House. Because the time allotted to the House of Delegates was extended this year to four days, with a full day for reference committee deliberations, the work on the floor of the House was less time-consuming. All the resolutions were discussed thoroughly in the reference committee meetings. This required less debate on the floor and is reflected this year in fewer pages in these minutes.

Several important decisions were taken. Beginning in 1964, the annual convention will be held in New York City in February, instead of in May. This has been done in order to avoid conflicting with so many other medical groups which seem to meet during the month of May. Recommendations of the Planning Committee to streamline the committee work of the Society were accepted. The number of committees will be reduced. The membership will be reduced to no more than five regular members on most committees and the tenure of office of committee members will be reduced. A Commission on Public Services will consolidate the work of the Public Relations and Legislation Committees and their various subcommittees. This year two new awards were made, the Laurance D. Redway Award for Medical Writing and the Albion O. Bernstein, M.D., Award.

John M. Galbraith, M.D., in his retiring address as president, spoke of the necessity of keeping alert politically to avoid unwise legislation directed toward the practice of medicine. Dr. Galbraith spoke also of a closer rapport with osteopathic physicians and continuing discussions with a committee from this group. During the year an Association of the Professions was incorporated for the purpose of taking action on questions of mutual concern. This new association is composed of the Medical Society of the State of New York and the official state societies of the dentists, architects, engineers, pharmacists, and veterinarians.

Joseph A. Lane, M.D., in his president-elect's address, emphasized the many problems before the Society and asked for support of his recommendations for action. These included revision of committee structure, change in name, support of Physicians' Home, increase in dues and a realistic budget, and support of the Kerr-Mills Act the Metcalf-McCloskey Act.

It is interesting to compare the presidential addresses of today with those of fifty years ago. In the past the principal effort seemed to be on improving the competence of the members. This now is not so much necessary, since doctors are better educated and better trained before assuming practice. The emphasis now is on the responsibility of the medical profession in economic and sociologic affairs. It is evident, from reading presidential addresses from year to year, that while the medical profession has to some extent been pushed into some of these things, it has not gone in blindfolded and has shown considerable understanding and skill in dealing with the manifold problems of modern life.

The scientific sessions at this convention were centered around the work of the ten medical centers in the State. Each medical school presented a program which gave a view of the work going on in the institution. This was a most valuable contribution and it is hoped that it will be continued and expanded. The many scientific exhibits were up to a high standard. The first prize in the category of scientific research went to Drs. Feldman, Rubenfeld, and Collica for their exhibit on "The Radioactive (I^{131} Tagged) Rose Bengal Hepatoscan." The second prize went to Drs. Mahajan, Cliffton, and Watson, for their exhibit on "Visualization and Perfusion of Bronchial Arteries: Application in the Treatment of Lung Carcinoma." Honorable mention was given to Drs. Goldberg, Kara, and Tabowitz for their exhibit on "The Use of Radioactive Phosphorus (P^{32}) in the Diagnosis of Ocular Tumors." In the clinical research category the first prize was given to Drs. Rabin and Teirstein for their exhibit on "Physical Diagnosis of Chest Disease: 15 New or Neglected Signs." The second prize went to Drs. Grace and Mitty for their exhibit on "Bleeding Peptic Ulcer and Heart Disease." Honorable mention was given to Dr. Sherman for his exhibit on "Mammography, An Examination of Technics."

These proceedings, which appear in print as Part II of the September 1 issue of the JOURNAL each year, may seem prosaic and hard-going. They would not seem so to one who attended the reference committee meetings or spent a short time as a spectator on the floor of the House of Delegates. Here these things come alive and have much more meaning. This is an educational experience that every member of the Society should have.

We trust that you will make provision to attend in future years.

MEDICAL SOCIETY OF THE
STATE OF NEW YORK

House of Delegates

Minutes of the Annual Meeting

May 14 through 17, 1962

The 156th Annual Meeting of the House of Delegates of the Medical Society of the State of New York convened at the Hotel Statler Hilton, 7th Avenue and 33rd Street, New York City, on Monday, May 14, 1962, at 10:00 A.M.*, Frederick A. Wurzbach, Jr., M.D., Speaker; E. Dean Babbage, M.D., Vice-Speaker; William L. Wheeler, Jr., M.D., Secretary; Ezra A. Wolff, M.D., Assistant Secretary.*

SPEAKER WURZBACH: Will the delegates please be seated?

Ladies and gentlemen of the House, the invocation will be given by the Reverend Christopher G. Kane, assistant director, Division of Health and Hospitals, The Catholic Charities of the Archdiocese of New York. Will you please stand?

Section 1

Invocation and National Anthem

REV. CHRISTOPHER G. KANE: At the outset of their deliberations, the delegates of the Medical Society of the State of New York convened here this morning establish themselves in the power of God to guide them, the might of God to uphold them, the wisdom of God to teach them, the eye of God to watch over them, and the ear of God to hear them, the word of God to speak for them, the hand of God to protect them, the way of God to lie before them, the shield of God to shelter them, and the host of God to defend them.

Our Father Who art in heaven, hallowed be Thy name, Thy kingdom come, Thy will be done on earth as it is in heaven. Give us this day our daily bread and forgive us our trespasses as we forgive those who trespass against us, and lead us not into temptation but deliver us from evil.

Present, O Lord, our actions, and carry them on by Thine assistance, that every prayer and work of ours may begin always with Thee and through Thee likewise be ended.

And so the delegates of the Medical Society of the State of New York acknowledge the need for Divine Guidance and approval before we can presume success in the many serious tasks before us. Amen!

SPEAKER WURZBACH: Will you please remain standing for the rendition of "The Star-Spangled Banner."

. . . National Anthem . . .

SPEAKER WURZBACH: Report from the Reference Committee on Credentials.

Section 2

Report of the Reference Committee on Credentials

GARRA L. LESTER, M.D., *Chautauqua:* Mr. Speaker, there are 198 registered delegates present; no contested delegates.

SPEAKER WURZBACH: Thank you, sir. Mr. Secretary, do we have a quorum?

SECRETARY WHEELER: We do, Mr. Speaker.

SPEAKER WURZBACH: Then I declare the 156th Session of the House of Delegates open for the transaction of business.

Section 3

Memorial Tribute

SPEAKER WURZBACH: Ladies and gentlemen, since our last meeting of the House of Delegates there have been several members who are deceased. I ask you to rise while I read the list of the deceased members: Aaron Kottler, Kings County, county delegate 1947–1961; Samuel Frant, New York County, county delegate 1956–1961; Isaac Levine, Kings County, county delegate 1953–1961; Elton R. Dickson, Broome County, county delegate 1945–1960; Reuben M. Dicker, Queens County, section delegate, 1961. May we have a moment of quiet in their memory?

. . . The delegates arose and stood for one minute in silence in memory of their departed confreres . . .

Section 4

Approval of Minutes of 1961 Meeting

Speaker Wurzbach: The first order of business is the approval of the minutes of the 1961 session, which appeared in Part II of the September 1, 1961, issue of the New York State Journal of Medicine. Are there any corrections?

Leo T. Flood, M.D., *Nassau:* I move they be accepted as so printed and distributed.

Thomas F. McCarthy, M.D., *Bronx:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 5

Reference Committees

Speaker Wurzbach: The appointments to reference committees were published in the April 1 issue of the Journal.

. . . The list of reference committees referred to is as follows:

Credentials

Garra L. Lester, Chautauqua, *Chairman*
Michael C. Armao, New York
Henry J. Barrow, Bronx
John L. Clowe, Schenectady
John H. Jakes, Tioga
Charles F. McCarty, Kings, *Adviser*

Reports of Officers

President
President-Elect
Secretary
Treasurer
Board of Trustees
Executive Vice-President
War Memorial
Budget

Arthur H. Diedrick, Westchester, *Chairman*
William R. Carson, St. Lawrence
Kenneth H. Eckhert, Erie
Edward H. Robitzek, Richmond
Solomon Schussheim, Kings

Commission on Medical Services—A

Economics
Liaison with U.S. Veterans Administration
Public Medical Care
Medical Care Insurance
Medicare

Jason K. Moyer, Broome, *Chairman*
Walter Einhorn, Bronx
Irving Ershler, Onondaga
Louis J. Morse, Queens
Bernard J. Pisani, New York

Commission on Medical Services—B

Workmen's Compensation
Industrial Health
Hospital and Professional Relations
Questions of Ethics
Medical Service (Rural)

C. Joseph Delaney, New York, *Chairman*
Philip D. Allen, New York
David Kershner, Kings
Joseph J. Thompson, Fulton
Victor J. Tofany, Monroe, Section on Anesthesiology

Public Health and Education

Public Health and Education
Accident Prevention
Addiction to Alcohol and Narcotics
Aging and Nursing Homes
Cancer
Child Accidents
Diabetes
General Practice
Glaucoma and Other Diseases of the Eye
Hard of Hearing and the Deaf
Health Aspects of Ionizing Radiation
Heart Disease
Maternal and Child Welfare
Medical Film Review
Mental Hygiene
Operating Room Deaths
Physical Medicine and Rehabilitation
School Health

Thomas S. Bumbalo, Erie, *Chairman*
Abraham W. Freireich, Nassau
Samuel Leo, Bronx
Edward F. Shea, Ulster
James L. Harrington, Jefferson

Legislation and Legal Matters

Malpractice Insurance and Defense Board
Legal Counsel
Legislation
Licensure of Clinical Laboratories
Federal Legislation
Autopsy and the Dead Human Body
Cults
Judicial Council

Milton Helpern, New York, *Chairman*
Joseph A. D'Errico, Niagara
Harold T. Golden, Herkimer
George Himler, New York
Milton B. Spiegel, Kings

Medical Communication

Publication
Public Relations
Cooperation with Media of Information
American Medical Association Education and Research Foundation
Convention

Merle D. Evans, Monroe, *Chairman*
William Benenson, Queens
Earl W. Douglas, Suffolk
John F. Kelley, Oneida
David Lyall, New York

Organization and Policies

Planning
Osteopathic Society, Ad Hoc Joint Committee with
District Branches
Office Administration and Policies
Constitution and Bylaws
Conference of County Medical Society Officers
Membership

Charles C. Mangi, Queens, *Chairman*
Charles M. Brane, Westchester
Thomas M. Flanagan, Chenango
Frank LaGattuta, Bronx
Angelo F. Leone, Orleans

Medical Care

Disability Determinations, Advisory to Bureau
Disaster Medical Care
Columbia University Study, Advisory

Irving M. Pallin, Kings, *Chairman*
James M. Jones, Westchester
William B. Rawls, New York
Philip M. Standish, Ontario
Sirkka Elisabeth Vuornos, Sullivan

Ancillary Groups

Woman's Auxiliary
Nursing Education
Bar Association
Empire State Medical, Educational and Scientific Foundation
New York State Association of Professions

Samuel Lieberman, Bronx, *Chairman*
William Hall Lewis, Jr., New York, Section on Space Medicine
Morris Maslon, Warren
Robert McMahon, Onondaga
H. John Mellen, Albany

Miscellaneous Business

American Medical Association

Walter S. Bennett, Washington, *Chairman*
Maxwell Gosse, Dutchess, Ninth District Branch
John A. Hatch, Yates
Michael Lefkowitz, Rockland
John Edward Lowry, Queens

Sergeant-at-Arms

Carl Goldmark, Jr., New York, *Chairman*
Raymond J. Byron, Schenectady
Herbert G. Cohen, Bronx
Alfred L. George, Genesee
Joseph Shanaphy, First District Branch

Speaker Wurzbach: Any resolutions that may be brought in should be presented to Miss Lewis, who will see that they follow the routine course.

Section 6

Reference of Reports and Supplementary Reports

Secretary Wheeler: The secretary moves that reports and supplementary reports of officers, Council, trustees, legal counsel, special committees, and district branches that have been published and distributed to the members of the House be referred to the appropriate reference committees without reading.

Jerome Flynn, M.D., *Bronx:* I second that.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Speaker Wurzbach: These are referred to the respective reference committees.

Section 7 (see 125) Report 62–A

Annual Report of the Planning Committee for Medical Policies

To the House of Delegates, Gentlemen:

The Planning Committee for Medical Policies consists of the following:

James Greenough, M.D., *Chairman*	Otsego
Renato J. Azzari, M.D.	Bronx
George A. Burgin, M.D.	Herkimer
Henry I. Fineberg, M.D.	Queens
Leo E. Gibson, M.D.	Onondaga
Thurman B. Givan, M.D.	Kings
Norman S. Moore, M.D.	Tompkins
John M. Galbraith, M.D., President, *ex officio*	Nassau
Joseph A. Lane, M.D., President-Elect, *ex officio*	Monroe
William L. Wheeler, Jr., M.D., Secretary, *ex officio*	New York
Maurice J. Dattelbaum, M.D., Treasurer, *ex officio*	Kings
Frederick A. Wurzbach, Jr., M.D., Speaker, *ex officio*	Bronx

After organization the committee decided to review four subjects and to recommend to the House of Delegates their suggestions for action.

Committees and Tenures of Office

The committee took up Dr. Moore's report to the 1961 House of Delegates, which recommended improvement in the committee setup with definite rules of tenure of office. As Dr. Moore pointed out, much waste of the Society's funds results from lack of organization and of adequate preparation for committee meetings. Dr. Moore felt that lack of interest on the part of committee members was the reason for these defects. He believed that a system could be established by which interested persons could be appointed to committees and their work judged so that those who prove to be capable could be retained and advanced, while those who have shown lack of interest could be replaced.

Dr. Wurzbach suggested that a file be set up similar to the one kept on reference committees of the House. Each chairman of a reference committee reports on attendance and performance of the members of his committee, and his report is filed by the speaker. It was suggested that a system of commissions should be considered and that commission chairmen could function in this capacity.

Size of committees was reviewed, and reduction of membership of each committee was suggested, so that its efficiency could be increased and its cost reduced.

By limiting the time a man may be in office, members of committees would be replaced after a certain period, and no one would be offended. A man who had shown genuine capacity for committee work could be appointed to another committee or reappointed to the same committee after one year, thus allowing the Society to avail itself of efficient committee members.

Another suggestion was made that each county society might be requested to inform the State Society of any members who did outstanding work on county society committees.

A summary of the State Society committees, which had been presented to the Management Survey Committee in January, 1961, was reviewed and submitted for further study.

A subcommittee was appointed, consisting of Drs. Azzari, Burgin, Fineberg, Galbraith, and Moore, chairman, to study the entire subject of commissions and committees.

Following is the recommendation of the subcommittee, as amended and approved by the Planning Committee. It is recommended to the House of Delegates for approval if the House so decides.

COMMISSION AND COMMITTEE ORGANIZATION. Following are the recommended numbers for Society committees.

1. *Council Committees.* Budget: 5 members, the treasurer and the chairman of the Board of Trustees and 3 other members. Membership on committee shall be limited to three years, except the treasurer and the chairman of the Board of Trustees who shall be members during their terms of office.

Constitution and Bylaws: 3 members plus the speaker and the vice-speaker.

Dinner Subcommittee: Annual ad hoc committee.

Guest Reception Subcommittee: Annual ad hoc committee.

Industrial Exhibits Subcommittee: Annual ad hoc committee.

Motion Picture Subcommittee: Annual ad hoc committee.

Scientific Awards Subcommittee: 5 members. Membership on committee shall be limited to five years.

Scientific Exhibits Subcommittee: 5 members. Indefinite term of office.

Scientific Program Subcommittee: 3 members and the chairmen of scientific sections and sessions. Indefinite term of office.

Joint Committee with the Bar Association: 3 members from Medical Society. Membership on committee shall be limited to three years. Counsel shall be ex officio member.

Legislation: 5 members. Membership on committee shall be limited to five years. There shall be 1 adviser from the State Health Department.

Subcommittee on Licensure of Clinical Laboratories: Discontinue and put activity under Legislation Committee.

Subcommittee on Cults: Discontinue and put activity under Legislation Committee.

Federal Legislation Subcommittee: 3 members and the chairman of the Legislation Committee. Membership on subcommittee shall be limited to three years, except chairman of Legislation Committee.

Membership Committee: Discontinue and the duties of the committee be referred to the office of the executive vice-president.

Nursing Education: 3 members. Membership on committee limited to three years.

Public Relations: 5 members. Membership on committee limited to five years.

Subcommittee on Cooperation with Media of Information: Discontinue and duties be absorbed by the Public Relations Committee.

Publication: 5 members. Membership on committee limited to five years.

Advisory to Woman's Auxiliary: Eliminate committee and delegate duties to office of executive vice-president.

Public Health and Education: 5 members and the Commissioners of Health of the State of New York and the City of New York and the Commissioner of Hospitals of the City of New York as advisers.

Subcommittee on Accident Prevention: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health and 1 adviser from insurance carrier.

Subcommittee on Child Accident Prevention: Discontinue and incorporate in the Accident Prevention Subcommittee.

Subcommittee on Addiction to Alcohol and Narcotics: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health and 1 adviser from State Department of Mental Hygiene.

Subcommittee on Aging and Nursing Homes: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Subcommittee on Cancer: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health, 1 adviser from City Department of Health, and 1 adviser from American Cancer Society.

Subcommittee on Chronic Pulmonary Disease: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Subcommittee on Continuing Postgraduate Education: 4 members. Membership on subcommittee limited to four years.

Subcommittee on Diabetes: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health.

Subcommittee on Film Review: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health.

Subcommittee on General Practice: 5 members. Membership on subcommittee limited to five years.

Subcommittee on Glaucoma and Other Diseases of the Eye: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health and 1 adviser from New York State Commission for the Blind.

Subcommittee on Hard of Hearing and the Deaf: 3 members. Membership on subcommittee limited to three years. Two advisers from organizations concerned with hearing and 1 adviser from State Department of Health.

Subcommittee on Health Aspects of Ionizing Radiation: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health, 1 adviser from New York City Department of Health, and 1 adviser from Atomic Energy Commission.

Subcommittee on Heart Disease: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Subcommittee on Maternal and Child Welfare: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Subcommittee on Mental Hygiene: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Mental Hygiene.

Subcommittee on Operating Room Deaths: 3 members. Membership on subcommittee limited to three years. One adviser from State Department of Health.

Subcommittee on Physical Medicine and Rehabilitation: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Subcommittee on School Health: Change to Subcommittee on Youth Health and Physical Fitness. 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Health.

Commission on Medical Services: Chairman and chairmen of Committees on Economics, Ethics, Hospital and Professional Relations, Industrial Health, Medical Care Insurance, Rural Medical Care, and Workmen's Compensation.

Economics: 5 members. Membership on committee limited to five years.

Subcommittee on Public Medical Care: 5 members. Membership on subcommittee limited to five years. One adviser from State Department of Social Welfare and 1 adviser from New York City Department of Health.

Subcommittee on Liaison with U.S. Veterans Administration: 3 members.

Questions of Ethics: 3 members. Membership on committee limited to three years.

Hospital and Professional Relations: 6 members. Membership on committee limited to three years. (See action of the House of Delegates, NEW YORK STATE JOURNAL OF MEDICINE, September 1, 1960, Part II, pages 142–143.)

Industrial Health: 5 members. Membership on committee limited to five years.

Medical Care Insurance: 7 members, one representing each Blue Shield Plan. Membership on committee limited to five years.

Medical Service: Change to Rural Medical Care. 5 members. Membership on committee limited to five years. One adviser from Department of Rural Sociology of New York State College of Agriculture and 1 adviser from State Department of Health.

Workmen's Compensation: 9 members, one from each district branch. Membership on committee limited to three years.

2. *Ad Hoc Committees.* Committee to Arrange Conference of County Medical Society Officers: Ad hoc committee at pleasure of president.

Study of Organization and Functions of Scientific Sections and Sessions: Ad hoc committee at pleasure of president.

3. *Special Committees.* American Medical Education and Research Foundation: Discontinue and assign duties to office of executive vice-president.

Autopsy and the Dead Human Body: Change to ad hoc committee at pleasure of president.

Disaster Medical Care: 3 members. Membership on committee limited to three years. One adviser from State Department of Health.

Constitution and Bylaws (House Committee): 5 members. Appointed by the speaker annually.

Advisory to Bureau of Disability Determinations: Discontinue and delegate duties to Committee on Workmen's Compensation.

Executive Committee: See Bylaws, Chapter IV, Section 1 (b), page 17. Amend this section to read: "The Council shall establish an executive committee to be composed of the president, the president-elect, the *past-president*, the secretary, the treasurer, and *two* additional members of the Council."

Joint State Committee with Hospital Association: 2 members. Membership on committee limited to four years.

Judicial Council: No change. See Constitution, Article VII, page 3; Bylaws, Chapter VI, Section 1, page 22.

Malpractice Insurance and Defense Board: See Bylaws, Chapter XI, Section 2, page 34. Amend this section to limit term of office to two consecutive terms of five years each.

Nominating Committee (House Committee): See Bylaws, Chapter XI, Section 4, page 35. Amend this section to read: ". . . and two additional members at large to be *appointed* to this committee by the president."

Office Administration and Policies: Eliminate committee and delegate duties to executive vice-president.

Planning Committee for Medical Policies (House Committee): 5 most recent past-presidents and 2 members at large elected one each year for a term of two years. (See action of the House of Delegates, NEW YORK STATE JOURNAL OF MEDICINE, September 1, 1961, Part II, pages 101–102 and resolution 61-8.) President, president-elect, secretary, treasurer, and speaker ex officio. Senior past-president is chairman.

Prize Essays: 3 members. Membership on committee limited to three years.

We recommend amending the Bylaws so that a chairman of a commission need not be a member of the Council. (See Bylaws, Chapter

IV, Section 10, page 20.)

Tenures of Office. The subcommittee further recommended, and the Planning Committee concurred, that (1) the secretary, treasurer, assistant secretary, and assistant treasurer may not be elected to more than five successive one-year terms but could be re-elected one year thereafter; (2) councillors may not have more than three consecutive three-year terms but could be re-elected one year thereafter; (3) trustees may not have more than one five-year term and may not be eligible for re-election thereafter.

Annual Meeting

The second matter to be studied by the Planning Committee had to do with the annual meeting.

The House of Delegates recommended "that there be established a permanent Convention Committee of the House." The previous section of this report, recounting the recommendations of this committee regarding standing committees, concurs with the recommendation of the House that the Convention Committee be changed to a permanent committee. Therefore, no further action is required here.

The committee requested Dr. Wurzbach, speaker of the House, to investigate the possibility of changing the date of the annual meeting and any other matters associated with holding of the meeting.

Dr. Wurzbach, after reviewing the matter with Mr. Charles L. Baldwin, rendered the following report:

There is a contract with the Statler Hilton Hotel in New York City for May, 1962, and for May, 1963. The 1962 meeting of the House opens May 14, 1962, which will be too late to alter the 1963 contract. The Americana Hotel will be completed by 1963, and its management is able and willing to enter into contracts with the Society for the convention, the meeting of the House of Delegates, and for other arrangements through the year.

The Constitution, Article VIII, states: "There shall be an annual meeting of the Society and of the House of Delegates to be held at a time and place designated by the House of Delegates." The Bylaws, Chapter II, Section 3, state: "The annual meeting of the House of Delegates shall be at the call of the Speaker, at least two, and not more than four days before the annual meeting of the Society." In Chapter IV, Section 9, "The duties of the Council shall also include the study and supervision of the following activities . . . (f) Arrangements for the annual meeting."

Mr. Baldwin has submitted a two-page report concerning the advantages of changing the meeting date to February:

"At the end of August, you asked me to give you a report on the annual meeting as it concerned the moving of this meeting from its present dates in May to another time of the year. There are several reasons why it would be expedient for the Society to consider such a change at this time. All of these involve competition.

"The first competition we have to face, and one of the most important, has to do with participation in the scientific program. The annual scientific sessions of the Medical Society of the State of New York have always been well attended because good people have been on the programs. However, with more meetings being held throughout the country, the services of these people are harder to secure.

"If the meeting were changed to a late February date, I believe there would be more participants to choose from. These participants, regardless of when the meeting is held, must be chosen for the interest that their fellow physicians have in them and in what they have to say.

"As I go around the country to meetings of convention management groups and pharmaceutical groups, I hear more about the falling off in interest at state conventions. This need not be so at all if the quality of the program is maintained on a high level and if the meeting dates do not conflict with those of many other group sessions. We must always bear in mind that we are competing for attendance as well as for program participation.

"Furthermore, during the crowded month of May we are also competing for exhibitors. The exhibitors pay most of the cost of our conventions, and I believe that if the meeting were to be held in New York City during the latter part of February, we could more than pay the cost by attracting more exhibitors.

"It is my conviction that the annual meeting of the Medical Society of the State of New York can continue to be one of the nation's topnotch medical gatherings provided we are willing to make innovations of the type already mentioned.

"For purposes of comparison, there are 40 medical meetings in May and eight in February. There are 22 state meetings in May and two in February. These are Colorado and Oklahoma. They have shifted only recently from spring dates. October is another month when many medical meetings are held, and thus we should not consider that time of year.

"Another advantage that would accrue for the February meeting would be a lower hotel rental for the space we use. At the Americana Hotel this would be the difference from $19,000 to $13,000.

"It must be remembered that the meeting of the Medical Society of the State of New York in the coming years will have to compete in the spring with some of the country's largest meetings, namely, the American College of Physicians, the American Academy of General Practice, the American College of Surgeons, and, of course, the A.M.A. These will not all come to New York City in the same year, but will provide strong competition over a period of years.

"If our meeting could be held, as it was during the Sesquicentennial, in February, ours would be the first large meeting of the year. This is important when dealing with three factors: scientific program participation, attendance, and exhibitors.

"The House of Delegates could meet either with the scientific sessions in February or could hold the May dates and meet all around the State. The latter might be a good public relations aspect to consider. As far as the cost goes for such meetings, it could be made up by increased income from the scientific meeting in February.

"It should be pointed out that the old objection to holding a meeting in the winter because of bad weather is no longer valid with modern transportation. Some of the most successful meetings in other fields are held in New York City during January and February."

Dr. Wurzbach also reported that holding the meeting on Monday, Tuesday, and Wednesday was becoming more and more difficult with the large number of resolutions and reports which must be considered. Evening sessions, as have been customary on Tuesdays, have been unsatisfactory and lead to hurried and careless action on matters before the House. Dr. Wurzbach recommended that the House sessions be held Monday through Thursday, with the election on Thursday morning. The annual meeting could still be held on Wednesday evening. No change in the Bylaws would be involved.

The Planning Committee approved Dr. Wurzbach's report and recommends to the House of Delegates:

1. The annual meeting of the Society and of the House of Delegates shall be held in the second half of February, 1964, and thereafter at this time.
2. Contracts be sought from the Americana Hotel or other hotel for February, 1964, and annually thereafter.
3. The annual meeting of the Medical Society of the State of New York be continued to be held on Wednesday evening of the week in which the House of Delegates meets.
4. The House of Delegates meet four days; the final meeting, election, to be Thursday morning.

This action would mean that the terms of councillors, trustees, and officers would be reduced by about three months in the year the change is made.

Policy Toward Labor

The committee planned to review and to make recommendations regarding the policy of the Society toward labor. Consideration of this matter was postponed awaiting receipt of a report from the subcommittee of the New York City Central Labor Council AFL-CIO Professional Advisory Committee and the Hospital and Medical Care Committee, which was considering community policy, hospital performance, and physicians services. The report was received March 9, 1962, which was too late for careful study and decision. We feel that it should be recommended to the Council and the House of Delegates that the Medical Society of the State of New York should be represented by carefully selected individuals on the New York City Central Labor Council AFL-CIO Professional Advisory Committee. It is the understanding of the subcommittee that the representatives of the Medical Society will have an equal status with those of management and labor and that this is an extra step forward in the relationship between the involved groups. However, we feel that this is a very small segment of the problems involved with management and labor and that the Planning Committee should go into more detailed discussions with management and labor on a much broader field, that closed panel practice should receive careful consideration, as well as the full-time men in teaching hospitals, concerning their usefulness to the State Society. The Planning Committee therefore recommends continued study of this matter during the next year.

Review of Management Survey Report

The Planning Committee, through a subcommittee consisting of Drs. Azzari and Fineberg, reviewed the Management Survey Report to determine any suggestions in that report on which further action was advisable at this time. It was concluded that no action was called for at present.

The chairman wishes to express his appreciation to the members of this committee for their active interest and cooperation through the year and also to thank Miss Doris K. Dougherty and Miss Roslyn Feinberg for their invaluable assistance.

He wishes to recommend that this committee be continued by the House of Delegates and that consideration be given by the House of Delegates to making it a permanent committee of the House.

Respectfully submitted,
JAMES GREENOUGH, M.D., *Chairman*

Section 8 (see 180) Report 62-B

Annual Report of the Speaker of the House of Delegates

To the House of Delegates, Gentlemen:

A special meeting of the House of Delegates of the Medical Society of the State of New York was requested by the Council on January 25, 1962. The speaker called this special meeting for Saturday, February 10, in the Grand Ballroom of the Summit Hotel, Lexington Avenue and 51st Street, New York City, at 10:00 A.M., to consider the following agenda: (1) the best medical care for the people of New York State, (2) chiropractic licensure, (3) amendment to Metcalf-McCloskey Law, (4) health care of the aged, and (5) summary action program for 1962.

All delegates and all county medical societies were notified of this special meeting. Copies of four resolutions to be introduced were mailed to each delegate.

The special meeting was called to order on February 10, 1962, at 10:00 A.M. by the speaker, Frederick A. Wurzbach, Jr., M.D. Registration was from 9:00 to 10:00 A.M. The invocation was given by Dr. Jesse Lyons of the Riverside Church, Riverside Drive at 122nd Street, New York City. The chairman of the Credentials Committee, Frank A. Gagan, M.D., reported there were present 151 qualified delegates (final total 208 delegates) and no disputed delegations, and all on the rolls were entitled to vote. The secretary stated that a quorum was present. A quorum is 100 delegates.

PRESIDENT'S ADDRESS

President John M. Galbraith, M.D., Glen Cove, New York, gave the following address:

As president of the Medical Society of the State of New York, I would like to comment briefly on the task we have before us today at this special session. Basically, the time for dramatic and forceful action by the medical profession in New York State is at hand on both the State and national legislative fronts.

On the State level, we are confronted by two vital issues. These concern the licensing of chiropractors and amendments to the Metcalf-McCloskey Law concerning medical assistance to the needy aged. Since the Legislature is now in session, it is most urgent that medicine's views on these problems be voiced immediately.

Although the question of chiropractic licensure has been a perennial problem for a great many years, there is no doubt that this is the year of decision. We must face this fact head on and at this special session take action whereby we make it clear to the public and our State Legislature medicine's stand on this crucial health problem.

On April 1, 1961, the Metcalf-McCloskey Law went into effect. This law implemented the Federal Kerr-Mills Law providing medical assistance for the needy aged. As a profession we have backed this State law but are dissatisfied with the manner in which it has been implemented. There have been many complaints from areas throughout the State that the spirit of the law is not being carried out.

It is a purpose of this special session to discuss the weaknesses in this law and to agree upon specific amendments to be proposed to the Legislature at its present session.

On Capitol Hill in Washington, one of the top priority goals of the administration is the enactment of the King-Anderson Bill providing medical care for the aged under the Social Security system. Immediate action is necessary. Thus, a purpose of this special session is to alert our members to the need for immediate participation in the campaign to prevent enactment of HR 4222 and to discuss specific plans of action in the days ahead. The action on this issue taken by this House today will greatly strengthen the hands of the representatives of our State Medical Society who will make personal visits to our Congressmen and confer with our two United States senators in Washington at the end of this month.

In connection with the proposed administration program, there has been a dramatic development on the national scene. This is the recently announced Blue Shield plan for the aged which has received the blessing of the A.M.A. It is a plan which can help our senior citizens under the voluntary system. Discussion of this plan in connection with the national crisis in the field of the health of the aged is another reason why this session of the House of Delegates was called.

We hope that this special session of the House will result in an expression of unity on the part of the physicians of our State on the issues to be discussed. In true democratic fashion we have assembled from all sections of the State to consider these urgent matters affecting the health care of the people we serve. We know that the physicians of New York State, whom we represent, are always deeply concerned with proposed legislation concerning their patients and at this particular time in regard to the items before this House.

When such is the case, it is the duty of the House of Delegates to raise its voice in protest against harmful legislation. It is the duty of the House to protect the people of New York from harmful legislation. It is the duty of the House to offer constructive criticism.

By constructive action we can answer those who would distort public opinion by saying that spokesmen for the Medical Society of the State of New York are not representatives of practicing physicians.

The actions of this House today will be most important and most necessary. The action of this House, however, is not enough. We must have the support of every member of the Medical Society of the State of New York in whatever decisions are made by this body.

The two worst enemies of a fighting man are (1) overconfidence and (2) a numbness to ever-present danger.

Frankly, gentlemen, I have seen too many signs of both these attitudes. When combined with apathy or indifference, they threaten defeat by default of all that we are fighting for: our principles, our way of life, and our personal convictions.

I will not pull my punches today because the time for caution and hesitation is long past. Those who would license chiropractors to give medical care and socialize our patients and our profession are breathing heavily on our necks, and we can no longer pretend that they are not there.

Although many physicians have been fighting courageously and tirelessly for many years, too many of our colleagues have let them do all the fighting. Relentless warfare can be discouraging, especially when the warriors are not supported by those for whom they are fighting.

Allow me to address the remainder of my remarks to one of the greatest threats to our American system of free enterprise: the administration's proposal for medical care for the aged.

This is medicine's most critical hour. If we do not fight together, and fight hard, we will lose. And we can lose only once! May I repeat that: And we can lose only once! This is not my idea; the great statesman, Senator Kerr, from Oklahoma, has made this remark on several occasions. If you lose the battle once, you have lost it forever, because once we lose, we will be forced into a series of retreats until the entire practice of medicine is taken over by the Federal government.

I don't want to be accused of crying "wolf" or of arousing my colleagues to a danger that really isn't there.

No, I feel I am being somewhat conservative when I say that American medicine is faced with a crucial challenge at this very moment.

There is no longer time for arguments, debates, and academic haggling. The free, unrestricted practice of medicine is in mortal peril, and only immediate action can save it.

If any one of us fails to fight with all his energy for the principles of American medicine, you can be sure that one morning soon we will awaken to find a bureaucrat practically sitting alongside us in the consulting room, a politician almost at our elbow in surgery, and government clerks approving or rejecting our prescriptions.

Perhaps you think that this is exaggerating and overdramatizing the problem. You all know, however, that passage of the King-Anderson Bill at this session of Congress would place the Federal government in the position of providing care for one part of our population.

If this bill passes, the Federal forces will then be able to expand their area of influence until all our population is under a system of government medicine.

Every one of us knows that our superb system of medical care has flourished only because it has been free. Research, medical education, and medical practice thrive in the soil of freedom, but they will be choked and stunted by the weeds of bureaucracy and political control unless we keep our earth well hoed.

The best system of medical care in history will not continue to grow on its own. It needs constant attention and jealous guarding to preserve it.

I do not intend to give you detailed arguments against the King-Anderson Bill. You know them well. Let me point out, however, that our opponents have been diligently making hay while too many physicians of America have been silent. The leaders of the medical profession have been speaking out for years, but now is the time for every doctor to be heard.

Our profession and our organizations have been the targets of verbal abuse from the opposition. We have been vilified; we have been called names. Gross distortions of our position and principles have been repeated again and again by the politicians who see the aged as a powerful voting block.

Remember, ours may be an ideologic fight, but those on the other side are looking at the practical aspects of swapping a limited amount of medical care in exchange for votes. This kind of strategy ultimately will bring about a government-controlled system of medical care similar to that now existing in England. It will result in the greatest raid on the tax dollar that the American people have ever experienced. The social security or welfare state payments of the people of England have never come close to paying the full load. The politicians have dipped deeply into the general tax fund.

Some politicians and bureaucrats have attempted to "snow" the American people with untruths. If you gentlemen read the *Saturday Evening Post* editorial a couple of weeks ago, you know what I mean. I was appalled. I happen to have peddled the *Country Gentleman* and the *Saturday Evening Post* about forty-five years ago, and I have always held it in great respect, but that editorial hit an all-time low. Through such devious means they are distorting the position of American medicine and attempting to convince the people that we are heartless, greedy men.

Do you like to be called heartless and selfish? Do you agree when the politicians tell the American people that the physicians are against helping our old people in need of medical care, against voluntary health insurance, against anything that would change the status quo? I don't! Yet every one of these charges has been repeated again and again, often by men in responsible positions.

Contrary to our opponents' accusation, our only interest in this issue is preserving the high quality of medical care and keeping it free from the mediocrity that is inherent in government medicine. Let us reiterate again and again that our primary concern is the health of our patients.

Gentlemen, medicine has taken such a verbal lambasting from our opponents that some doctors are now starting to talk of compromise. They believe that just because they are called names in print, the battle is lost. No one ever entered a battle without getting a few scars.

Our position on compromise is this: There is no room for compromise on matters of principle. So long as the politicians insist on using the Social Security mechanism to finance health care benefits for the aged, so long as Federal regulation and control of the program are demanded, so long as eligibility is based on age rather than on need, and so long as the whole scheme is compulsory rather than voluntary, then we cannot and shall not compromise.

Gentlemen, I have tried to impress you with the importance of immediate, spontaneous action by every physician, so that we may be victorious in this crisis.

The four resolutions before you today are vital to the interests of the people and vital to the medical profession of the State of New York. They deserve your most thoughtful consideration.

By your actions today you can give your elected officials sound ammunition to present to our lawmakers on both a State and a national level. By your actions today you also can reassure the people of the State of New York that our main objective is to protect the science and art of medicine from unscientific methods in New York State and to prevent the encroachment of government on the practice of medicine which would be to their own personal detriment. By your actions today, you can gain the support of the people in the State of New York in these two crucial areas which vitally concern their health and the health of their children and generations to come.

RESOLUTION TO SUSPEND BYLAWS

A resolution to suspend certain portions of the Bylaws was adopted as follows:

> WHEREAS, The Council of the Medical Society of the State of New York on January 25, 1962, pursuant to Section 6 of Chapter VIII of the Bylaws of this Society, requested the speaker to call a special meeting of this House to consider the following resolutions, to wit: (*a*) S62–1, entitled "Principles of Medical Care"; (*b*) S62–2, entitled "To Uphold the Standards for Licensure to Practice the Healing Arts in the State of New York"; (*c*) S62–3, entitled "Improving the New York State Medical Aid for the Aged Program"; and (*d*) S62–4, entitled "HR 4222 (Medical Care for the Aged under Social Security)"; and
>
> WHEREAS, The business of this special meeting of the House is limited, pursuant to *Robert's Rules of Order, Revised*, to the foregoing resolutions, and it is desirous that the business of this House proceed with expedition; now therefore be it hereby
>
> *Resolved*, That Section 7 of Chapter II (Order of Business) and Sections 1 and 2 of Chapter X (Reference Committees) of the Bylaws be suspended pursuant to Section 6 of Chapter XV of the Bylaws of this Society; and be it further
>
> *Resolved*, That the Speaker may in his discretion fix the order of business of this special session.

ACTIONS OF HOUSE

Resolutions S62–1, S62–2, and S62–3 were discussed and passed in final form at the morning session. The morning session concluded at 12:00 NOON, and a recess for lunch was taken until 2:00 P.M. when the House was again called to order, and resolution S62–4 was discussed and passed in final form.

After this had been concluded, a statement on the part of Henry I. Fineberg, M.D., executive vice-president, concerning summary action program of 1962, was presented whereby delegates were requested to do all in their power to carry out and implement the presentation of these four resolutions.

The four resolutions in their final form are as follows:

Resolution S62–1

Principles of Medical Care

Introduced by Joseph A. Lane, M.D., President-Elect

> WHEREAS, The medical profession traditionally has cared for the sick by rendering the best medical care possible; and
>
> WHEREAS, The Medical Society of the State of New York is charged by its Constitution "to enlighten and direct public opinion in regard to the problems of medicine and health for the best interests of the people of the State"; and
>
> WHEREAS, The Medical Society of the State of New York is deeply concerned by prospects of legislative action that would result in lowering the standards of medical care; now therefore be it hereby
>
> *Resolved*, By this House of Delegates that the people be assured of the dedication of the medical profession in the State of New York by reiteration of the following principles:
>
> Physicians are trained to take care of sick people. As stated in Chapter 1, Section 1, Principles of Professional Conduct, Medical Society of the State of New York, "The prime object of the medical profession is to render service to humanity; reward or financial gain is a subordinate consideration";
>
> We physicians rededicate our adherence to this ideal and pledge to provide the very best care to all people in the State—regardless of age, regardless of income, regardless of race or creed;
>
> We further pledge ourselves to continue to work for improvements in our medical system so as to elevate the standards of care and the quality of service provided to individual patients. We will not work for or cooperate with any action—legislative or otherwise—that would lower the standards of care or the quality of service; and be it further
>
> *Resolved*, That the Medical Society of the State of New York take immediate steps to

disseminate this statement of dedication to elected officials and the people of the State.

Resolution S62–2

To Uphold the Standards for Licensure to Practice the Healing Arts in the State of New York

Introduced by James M. Blake, M.D., Councillor

WHEREAS, The Medical Society of the State of New York, since its organization in 1807, has maintained as one of its primary purposes the continued improvement in medical practice and in medical education; and

WHEREAS, The ethical physician of this State has fought consistently to improve the high standards of medical practice and medical education for which the State of New York is recognized throughout the world; and

WHEREAS, We, as members of the Medical Society of the State of New York, cannot at this time condone the recognition as a part of the healing arts of any group of poorly trained, inexperienced practitioners of a completely unscientific and unproved method of the treatment of disease; and

WHEREAS, We do not believe that because groups of this type cannot meet the high standards of medical education as practiced in the State of New York is reason to lower these standards; and

WHEREAS, We do not believe that the Legislature of the State of New York wishes to endorse an unscientific practice in the treatment of disease by establishing a second, or a double standard in medical care and medical education; and

WHEREAS, The Medical Practice Act of the State of New York is clearly defined and we believe further that the legal agencies so charged should be adequately provided so that they can rigidly enforce this act, thus preventing the illegal practice of medicine by illegal practitioners; and

WHEREAS, The Medical Society of the State of New York is pledged to the highest quality of medical care for the people of our State, we must therefore reject any legislative action that will lower the standards of the quality of medical care and medical education in the State of New York; and

WHEREAS, The recognition as a part of the healing arts of an improperly trained and unqualified group of cultists, such as chiropractors, would thereby endanger the health of the people of this State; and

WHEREAS, The approval of an unqualified practitioner by his colleagues and the granting of licensure to an unqualified practitioner of the healing arts does not alter the basic fact that he is still unqualified; and

WHEREAS, The attention of the people of our nation has been called to, and they have been warned against, substandard medical practices at the National Congress on Quackery held in Washington, D.C., in October, 1961; now therefore be it hereby

Resolved, That this House of Delegates of the Medical Society of the State of New York, meeting in special session in New York City, on February 10, 1962, maintains and upholds this policy of high standards of medical practice and medical education, maintaining that the laws of the State of New York governing the practice of the healing arts continue to eliminate from our State unqualified practitioners; and be it further

Resolved, That we make it known that we have no objection to anyone practicing the healing arts in the State of New York providing that his training is adequate in this field and that he takes and passes the same license examination as do doctors of medicine and osteopathy; and be it further

Resolved, That the Legislature of the State of New York be urged not to set up a double standard of medical practice with the establishment of special licensure for chiropractors or other cultists; and be it further

Resolved, That the legal authorities so charged continue and increase their efforts to eliminate illegal practitioners of medicine in the State of New York; and be it further

Resolved, That the Medical Society of the State of New York once again re-emphasize its opposition to the recognition of, and licensure of, chiropractors and other cultists as a part of the healing arts and thus the establishment of the double standard of medical practice; and be it further

Resolved, That a copy of this resolution be sent to the Governor of the State of New York and to each member of the Legislature of the State of New York in order that the attitude of the Medical Society of the State of New York toward the standard of medical practice in our State be clearly established.

Resolution S62–3

Improving the New York State Medical Aid for the Aged Program

Introduced by Waring Willis, M.D., Councillor

WHEREAS, The Medical Society of the State of New York believes that a strong medical aid for the aged program, administered by the State of New York, is a sound method of providing care for those aged who need help; and

WHEREAS, It is realized that the Metcalf-McCloskey Act to implement the Federal Kerr-Mills Law was passed under pressure of time and thus is not so effective an instrument as its proponents had hoped it would be; and

WHEREAS, Many elderly people who can provide adequately for the ordinary necessities of life, such as food, clothing, and shelter, but who cannot meet medical care expenses are forced to become welfare clients, thereby unnecessarily increasing the rolls of the Department of Social Welfare; and

WHEREAS, Experience with the MAA program in New York has given physicians and others an opportunity to evaluate administrative problems; now therefore be it hereby

Resolved, That this House of Delegates recommend that the Metcalf-McCloskey Act be strengthened and made to coincide more closely with conditions set forth in the Kerr-Mills Law by amending the Act to provide for

1. Changing of provision for potential financial support to include only husband and wife;
2. Taking jurisdiction for administration of the program out of the hands of the Department of Social Welfare. Services that involve direct medical care should be brought under an agency directed by physicians;
3. Broadening of services to include "total health care" elements as recommended by the Kerr-Mills Law. This would encompass such items as eyeglasses, dentures, prostheses, rehabilitation, and ambulance services; and be it further

Resolved, That the above provisions be incorporated in a proposed law amending the Metcalf-McCloskey Act to be introduced as soon as possible at the 1962 session of the State Legislature through the mechanism of the Society's Council Committee on Legislation; and be it further

Resolved, That the Medical Society of the State of New York and its component societies undertake to supervise actively all services rendered under the Metcalf-McCloskey Act with a view toward sponsoring further improvements in it as the needs for these become apparent.

Resolution S62–3A

Amendment to the Metcalf-McCloskey Law

Introduced by Carl R. Ackerman, M.D., Bronx

WHEREAS, The passage of the Federal Kerr-Mills Law provided matching funds to the states to aid in the financing of medical care for those over sixty-five who need assistance; and

WHEREAS, While the Kerr-Mills Law includes the indigents who are recipients of old-age assistance, it also includes another group of citizens over sixty-five who, while otherwise self-supporting, have such modest incomes that assistance in the financing of medical care is needed; and

WHEREAS, The Metcalf-McCloskey Law was passed as an amendment to the New York State Welfare Law to make eligible these medically indigent people for the Federal financial assistance accruing to New York State through the passage of the Kerr-Mills Law; and

WHEREAS, These self-supporting people should retain the right to select their own physicians and their own arrangements for obtaining medical care; and

WHEREAS, It is against their interest and against the public interest to force these people into the category of wards of the Welfare Department of New York State; now therefore be it hereby

Resolved, That the Medical Society of the State of New York recommends to the Legislature that the Metcalf-McCloskey Law be so amended that these self-supporting but medically indigent citizens over sixty-five be afforded the opportunity to obtain, for themselves and their dependents, voluntary health insurance coverage with freedom of choice as to selection, and that the cost of such health insurance protection be paid for in all, or in part, by the State of New York; and be it further

Resolved, That the Medical Society of the State of New York supports legislation directed toward achieving the objective set forth in the preceding "resolved," and that interested parties in the State government, in the Legislature, and others be informed of this resolution.

Resolution S62–4

HR 4222 (Medical Care for the Aged Under Social Security)

Introduced by George J. Lawrence, Jr., M.D., Councillor

WHEREAS, The Medical Society of the State of New York believes that the elderly people of the State deserve the same high quality medical care provided to everyone; and

WHEREAS, This proposed plan is national in scope, is reasonably priced, provides uniform benefits, and offers nationwide service benefits to those over sixty-five who have low or modest incomes; and

WHEREAS, The voluntary approach of this proposed plan and its implementation through Blue Shield are consistent with the often reiterated principles of the medical profession regarding voluntary health insurance; and

WHEREAS, Physicians responsible for patient care would be hampered by a Federal program that would stifle freedom of medical practice; and

WHEREAS, Such a Federal program would regiment the care of the individual; now therefore be it hereby

Resolved, That this House of Delegates recommends to the county medical societies continuous action for the proper implementation of the Federal Kerr-Mills Law providing medical assistance for the needy aged and vigorous sponsorship of the Metcalf-

McCloskey Act changes approved by the Medical Society of the State of New York to provide an improved version of the Kerr-Mills Law in New York State; and be it further

Resolved, That this House of Delegates endorses the recently proposed A.M.A.-sponsored Blue Shield uniform program for the elderly; and be it further

Resolved, That this House of Delegates recommends this plan to the county medical societies for prompt endorsement and implementation in their areas; and be it further

Resolved, That this House of Delegates registers strong opposition to HR 4222 (Medical Care for the Aged Under Social Security) and any similar proposals and recommends that Congress take no action on HR 4222 or any similar proposals; and be it further

Resolved, That physicians and other responsible citizens of the State of New York be urged to take immediate action, individually and through organized efforts, to prevent passage of this legislation.

In addition a resolution from the floor was adopted. It follows:

WHEREAS, There has been a constant menace in the use of ionizing radiation by those not qualified to practice medicine in any form; and

WHEREAS, The New York State Radiological Society has been active in giving aid and support to one of our members who by his office as Commissioner of Health of the State of New York was sued for his efforts to protect the public in enforcing the law in order that the people of the State of New York be properly protected and spared from the indiscriminate use and danger of uncontrolled and unnecessary radiation; and

WHEREAS, It has been decreed by a recent decision of Judge Albert Conway that the use of ionizing radiation be limited only to those qualified and licensed in the State of New York as follows: "Chiropractors are not licensed in the State of New York to practice any of the healing arts or indeed to do anything in our State"; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York in special session convened on February 10, 1962, take cognizance of the fact that one of our members, Herman E. Hilleboe, M.D., singlehandedly and courageously led the fight against great odds in the suit by the Chiropractic Association of New York, Inc., on behalf of itself and individual members, versus Herman E. Hilleboe, M.D., as Commissioner of Health of the State of New York, November 15, 1961; and be it further

Resolved, That the delegates of the Medical Society of the State of New York hereby request the president of the Society to write to Commissioner Hilleboe to express our appreciation of his untiring and successful efforts in this regard in our efforts to further protect the health and welfare of the people of the State of New York.

The speaker wishes to thank the entire House for its magnificent cooperation, for the very fine and thoughtful presentations, discussion, and amendments presented on the floor. The speaker thinks that this meeting was of great value to the Society and that it certainly was a great credit to the House of Delegates.

Respectfully submitted,

FREDERICK A. WURZBACH, JR., M.D., *Speaker*

Section 9 (see 146) Report 62–C

Supplementary Report of the Public Relations Committee

To the House of Delegates, Gentlemen:

The following report of the Public Relations Committee's subcommittee on the New York State Medical Assistants Association, prepared by Irving M. Pallin, M.D., Kings, chairman, John Latcher, M.D., Otsego, and Marcelle Bernard, M.D., Bronx, members of the subcommittee, is presented for your approval.

NEW YORK STATE MEDICAL ASSISTANTS ASSOCIATION

Background and History. The American Association of Medical Assistants credits its origin in 1955 to the Kansas City Medical Assistants Society. In October, 1956, a constitution was written and approved in Milwaukee, at which time 13 states and many local units were represented. Physicians representing the American Medical Association served as advisers. At that same year's end, the House of Delegates of the A.M.A. passed a resolution commending the objectives of the American Association of Medical Assistants. The national association has grown to almost 10,000 members, and the component state societies to 30.

The New York State Medical Assistants Association was founded on September 11, 1959. The following county chapters participated: Albany, Broome, Columbia, Dutchess, Erie, Nassau, Orange, and Onondaga. Medical assistants from the following counties were present as observers: Bronx, Chemung, New York, Oneida, Queens, Rockland, Suffolk, and Westchester. Since then chapters have been formed in the Bronx and New York.

The first annual convention was held in New York City in May, 1960, the second convention in Albany in May, 1961. Approximately 40 delegates attended the 1960 meeting, and twice that number attended the Albany meeting. The third annual convention was held in Syracuse, April 27 through 29, 1962. The total attendance was 98, of which 73 were active members. There were six speakers on the program of the 1962 convention, two of whom were Mr. Jack Pardee, director of the Communications Department, and John McClintock, M.D., councillor and chairman of the Public Relations Committee. The chairman of this subcommittee served as adviser throughout the convention.

On recommendation of our Public Relations Committee on October 24, 1958, the Council on November 13, 1958, approved that "the Bureau be empowered to assist in bringing about a State-wide organization in New York State." The Council suggested to each county medical society that it assume an advisory position with regard to the formation and organization of medical assistants groups in their districts. This action authorized our communications staff to lend assistance in organizing the association.

Purpose of the N.Y.S.M.A.A. The purpose of the New York State association is to federate into one organization all the county chapters. The general objectives of the organization parallel those of the medical profession—"to inspire members to render honest, loyal, and more efficient service to the profession and to the public which it serves, to strive in improving public relations, to render educational services for the self-improvement of its members, and to stimulate among them a feeling of fellowship and cooperation." Its constitution specifically states, "It is not nor shall it ever become a trade union or collective bargaining agency."

Progress of the N.Y.S.M.A.A. This organization has now created a publication called *The Reflex;* it is newsworthy, attractive, and has considerable promise. Active efforts are being made to institute courses under university and college auspices for possible credit toward certification. It is in the process of setting up standards for certification. It is organizing medical assistants societies at county levels; the general impression prevails that this program is progressing satisfactorily.

It intends to hold annual meetings and to support county meetings. The 1961 meeting in Albany indicated a definite progression in interest and recruitment of members. The chairman of the subcommittee has been informed that the annual meeting of the A.A.M.A. held in Reno, Nevada, October 13, 14, and 15, was very successful. The membership was reported as about 10,000. With our blessing and consent, the N.Y.S.M.A.A. invited the A.A.M.A. to hold its fall, 1965, annual meeting in New York City.

At the executive board meeting of the N.Y.S.M.A.A., the chairman of this subcommittee, recognizing the need, directed that a payment of $250 be made to the society because the treasury was completely depleted. The chairman of our subcommittee requested that our Communications Department print the journal, *The Reflex*, for the N.Y.S.M.A.A.

Recommendations. The subcommittee on the New York State Medical Assistants Association makes the following recommendations:

1. The State Medical Society should continue its approbation of the New York State Medical Assistants Association indefinitely.
2. The State Medical Society should approve support of the N.Y.S.M.A.A. through its Public Relations Committee and continue to provide professional, administrative, and clerical assistance, particularly in preparation of documents such as constitution and bylaws, publication of *The Reflex*, management of its annual meetings, and all-out assistance when the A.A.M.A. meets in New York City. The committee should allocate $1,000 in its budget for this aid.
3. The State Medical Society should encourage the formation of medical assistants associations throughout this State at county levels and urge component county medical societies to lend their approval and support. However, it is recommended to our component societies that such approval and support be given those county medical assistants programs which join the State and national groups.
4. A specific member of the Communications Department should be assigned to the chairman of this subcommittee to assist him in his liaison duties with the N.Y.S.M.A.A.

Respectfully submitted,
JOHN C. MCCLINTOCK, M.D., *Chairman*

Section 10 (see 98, 99, 100, 101, 103, 105, 109, 110, 113) Report 62–D

Supplementary Report of the Public Health and Education Committee

To the House of Delegates, Gentlemen:

There have been no further meetings of the Council Committee on Public Health and Education since the original annual report was rendered. There are two matters to be reported, however, which do not fall within the jurisdiction of any of the subcommittees.

1. Your chairman attended a meeting of the Advisory Committee on Poliomyelitis with the State Department of Health in Albany on April 17. At that time the policy in regard to immunization by killed or live attenuated viruses was discussed. Recommendations were drawn up, and following the meeting Commissioner Herman E. Hilleboe and President John M. Galbraith jointly transmitted these in a letter to the physicians of the State.
2. On February 28 a letter was sent by the chairman to all county medical society presidents relative to the various subcommittees of this Council committee and the possibility of each county establishing similar committees. A questionnaire was enclosed which included a section on the county society's views on postgraduate education for the membership. We have had 18 replies thus far. Many

interesting suggestions and data are being accumulated.

Rather than submit separate supplementary reports for the subcommittees we shall incorporate them herein.

Aging and Nursing Homes. On March 28 at the Nassau Academy of Medicine in Garden City the New York State Joint Council to Improve the Health Care of the Aged held its second regional conference, where a representative of each of the four member organizations presented a survey of the current care of the aging patient in relation to the hospital, the nursing home, the physician, and the dentist. The spokesman for the Medical Society of the State of New York was Lawrence S. Kryle, M.D., a member of the Subcommittee on Aging and Nursing Homes. The chairman of that committee, Joseph J. Witt, M.D., again was moderator, as at the first such conference held in Buffalo last September. There were about 85 persons present. As one result of the conference, the Suffolk County Medical Society will seek to set up a meeting with the officers or a committee from the county nursing home association to discuss problems of mutual concern.

Governor Rockefeller's Office for the Aging sponsored a Conference on Aging in New York City on May 1 attended by approximately 600 persons. Your chairman and Dr. Witt were present. At the morning sessions there was emphasis on adequate medical facilities in connection with housing for and home care of the aging. This policy would undoubtedly increase the number of aged who could be treated outside the hospitals and would provide better medical facilities at decreased cost. The afternoon meeting was addressed by Commissioner Herman E. Hilleboe of the Health Department, Superintendent Thomas Thacher of the State Insurance Fund, Mr. J. Douglas Colman, president of the Associated Hospital Service of New York, and Commissioner Raymond E. Trussell of the New York City Department of Hospitals. They stressed the need for improving the supervision of new hospital construction to help bring about better utilization of hospital beds.

Accident Prevention. The chairman of the parent committee attended a meeting of the National Health Council in Cleveland, March 19 to 22. About 350 organizations were represented. Those present were divided into five groups: emergency call, home and school safety, occupational safety, auto and pedestrian safety, and recreational safety. Your chairman was assigned to the group considering the vehicle and the roads from two points of view, how to prevent accidents and, when accidents occur, how to reduce the severity of the injuries to those involved. There will be a short report published in approximately two months and the complete report will be available in one year. Both of these should be of much value to the subcommittee.

Cancer. Under the auspices of the Subcommittee on Cancer and the American Cancer Society there will be an exhibit on "Lung Cancer Prevention and the Physician" at the 58th Annual Health Conference of the Department of Health in June at Syracuse.

Diabetes. At its meeting on March 23 the Subcommittee on Diabetes reviewed the motion picture, "Diabetes and Its Long-Range Control," filmed under the direction of the New Jersey Department of Health. The viewing was arranged at the request of the New York State Department of Health to determine whether or not the film conveyed the proper information to the profession and was technically satisfactory. The consensus was that the picture was too technical for lay audiences and contained too much lay material for physician audiences. It was thought it might be of assistance to the general practitioners of a hospital staff or to interns who had not had any experience with diabetes. The hospitals which have shown the print owned by the State Health Department's Film Library will be requested to report their opinions of it.

There was discussion of the likelihood of various agencies becoming involved in any diabetes detection project, such as tuberculosis and health associations, men's service clubs, Lions' Clubs, sororities, and others. There is no common approach for these organizations to follow and their services are not utilized to the best advantage. It was decided to try to arrange a conference with representatives of such organizations and perhaps prepare an outline of their respective roles.

Health Aspects of Ionizing Radiation. This subcommittee held a meeting in Albany on May 2 with the State Health Department. They are planning an educational project to disseminate information to the physicians of the State about hazards due to ionizing radiation and the reduction of this danger.

Heart Disease. Plans are going forward for providing courses in "emergency resuscitation." It is hoped that seminars for physicians, to be conducted in hospitals, will be scheduled throughout the State in the late summer or early fall.

Mental Hygiene. The ad hoc group attempting to determine a procedure for instituting and carrying out in the State programs in psychiatry for the nonpsychiatric physician met for the third time on April 12. It was reported that the Nassau County course of seminars had enrolled 70 physicians and would continue for six weeks. The Bronx County course was also most successful, with 60 registrants. Specific steps have been taken to initiate a pilot course in Onondaga County, with the coordinator of the graduate training program at the Upstate Medical Center as chairman.

Respectfully submitted,
James Greenough, M.D., *Chairman*

Section 11 (*see 111*) Report 62–E

Annual Report of the Subcommittee on Maternal and Child Welfare

To the House of Delegates, Gentlemen:

The Subcommittee on Maternal and Child Welfare has the following membership:

Edward C. Hughes, M.D., *Chairman*	Onondaga
Samuel Karelitz, M.D.	Nassau
Frank A. Disney, M.D.	Monroe
Anne M. Drislane, M.D.	Albany
Eugene R. Duggan, M.D.	Monroe
Edwin M. Gold, M.D.	Kings
Edward S. Goodwin, M.D.	Albany
A. Wilmont Jacobsen, M.D.	Erie
Harold Jacobziner, M.D.	New York
Schuyler Kohl, M.D.	Kings
Jean Pakter, M.D.	New York
Clyde L. Randall, M.D.	Erie
Ferdinand J. Schoeneck, M.D.	Onondaga
Frederick H. Wilke, M.D.	New York
Tyree Wyatt, M.D.	Onondaga

There have been no formal meetings of the subcommittee but the members have been active during the past year. Maternal deaths have been surveyed and catalogued on special punch cards. This analysis has been limited to upstate New York and does not include the hospitals of New York City. It is hoped that in the near future maternal deaths from this portion of the State can also be included in our punch card system. The records have been completed on a county basis and statistical surveys of any important topic related to this field can be obtained rather quickly for research purposes.

This year the following articles have been published in the NEW YORK STATE JOURNAL OF MEDICINE, written by Ferdinand J. Schoeneck, M.D., under the aegis of the subcommittee. These articles have tended to point up the important phases of obstetric practice which seem to need comment after surveying the mortalities of the State. Titles included were: "Reduction of Perinatal Mortality by Better Prenatal Care," "Organization of Delivery Units," "Controllable Factors in Mortalities Associated with Pregnancy," "Acute Viral Hepatitis in Pregnant Women," "Roentgen Radiation and the Female Reproductive System," "Problems Involved with Modern Hospital Obstetric Records," "Routine Oxytocic Induction of Labor," and "A Study of the State of Pregnancy at Which Patients Start Prenatal Care."

This subcommittee also has started to work on perinatal mortality and at present there is a study being carried out involving the counties of Cayuga, Cortland, Hamilton, Herkimer, Madison, Oneida, and Onondaga. The purpose of this study is to attempt to introduce a standardization of prenatal, natal, and postnatal records in the hospitals of these areas. Also perinatal mortality committees have been appointed in most of the major hospitals to study this important phase of the specialty. It is hoped that eventually uniform records in all the hospitals of this area and in the entire State will be so designed that they will meet the requirements of the hospitals and physicians. This would tend to make statistical analysis accurate and uniform.

Section 12 (*see 124*) Report 62–F

Supplementary Report of the Advisory Committee to Columbia University Study of Nonprofit Prepaid Medical Care Insurance Plans

To the House of Delegates, Gentlemen:

The members of the Advisory Committee to the Columbia University Study of Nonprofit Prepaid Medical Care Insurance Plans in New York State received copies of a 94-page document entitled, "Chapter One, Discussion and Recommendations" on April 23 or April 25, 1962. The covering letter signed by Ray E. Trussell, M.D., M.P.H., director, and Frank Van Dyke, associate study director, admitted an additional section was still to be written, but they requested our comment and suggestions by April 25.

Preliminary study by three of the committee who received copies April 23 revealed many inaccuracies. The committee was unanimous in its decision that competent review of the material was impossible in the time allotted. Accordingly, the following telegram was sent to Mr. Frank Van Dyke on April 25:

> "Receipt is acknowledged of the chapter, 'Summary Discussion and Recommendations,' of your study on prepaid medical care plans. The material is so challenging it must be studied in depth by a qualified committee of our Society. Two days is not adequate to review the efforts of several years work by your study staff. We would appreciate receiving the section dealing with payment by plans to physicians in certain hospitals.
>
> (Signed) John C. McClintock, M.D.,
> Chairman"

The Advisory Committee is continuing its review of the material. As of May 1, 1962, the section concerning payment by plans to physicians in certain hospitals has not been received. No final report can be made at this time but will be submitted to the Council at the earliest possible date.

Respectfully submitted,
JOHN C. MCCLINTOCK, M.D., *Chairman*

Section 13 (*see 126*) Report 62–G

Annual Report of the Joint Committee with the New York State Osteopathic Society

To the House of Delegates, Gentlemen:

In 1961, the House of Delegates of the Medical Society of the State of New York approved a resolution from Erie County, as follows:

> *Resolved*, that the House of Delegates of the Medical Society of the State of New York approve the principle that the relationship of doctors of medicine to doctors of osteopathy be a matter for determination by the various state medical societies and not by the American Medical Association; and be it further
>
> *Resolved*, that the delegates of the Medical Society of the State of New York to the American Medical Association be instructed to introduce this resolution at the next meeting of the delegates of the American Medical Association.

Your delegates to the American Medical Association did introduce this resolution into the House of Delegates of the American Medical Association, which was in harmony with the report of the Judicial Council to the A.M.A. House of Delegates on osteopathy. The reference committee therefore adopted a statement incorporating much of the Judicial Council's report as a substitute for the many resolutions of the various state delegations, including New York, on the subject of osteopathy. This report is reprinted as follows:

> "Your reference committee considered at the same time the report of the Judicial Council, Resolution 33 from the New York Delegation, Resolution 60 from the Missouri Delegation, and Resolution 88 from the New Jersey Delegation, since they all deal with the subject of osteopathy. Your reference committee concurs in the intent of the report and these resolutions. It would, however, recommend that the House of Delegates adopt the following statement of A.M.A. policy:
>
> "1. There can never be an ethical relationship between a doctor of medicine and a cultist, that is, one who does not practice a system of healing founded on a scientific basis.
>
> "2. There can never be a majority party and a minority party in any science. There cannot be two distinct sciences of medicine or two different yet equally valid systems of medical practice.
>
> "3. Recognition should be given to the transition presently occurring in osteopathy, which is evidence of an attempt by a significant number of those practicing osteopathic medicine to give their patients scientific medical care. This transition should be encouraged so that the evolutionary process can be expedited.
>
> "4. It is appropriate for the American Medical Association to *reappraise its application of policy* regarding relationships with doctors of osteopathy, in view of the transition of osteopathy into osteopathic medicine, in view of the fact that the colleges of osteopathy have modeled their curricula after medical schools, in view of the almost complete lack of osteopathic literature and the reliance of osteopaths on and use of medical literature, and in view of the fact that many doctors of osteopathy are no longer practicing osteopathy.
>
> "5. Policy should now be applied individually at state level according to the facts as they exist. Heretofore, this policy has been applied collectively at national level. The test now should be: Does the individual doctor of osteopathy practice osteopathy, or does he in fact practice a method of healing founded on a scientific basis? If he practices osteopathy, he practices a cult system of healing and all voluntary professional associations with him are unethical. If he bases his practice on the same scientific principles as those adhered to by members of the American Medical Association, voluntary professional relationships with him should not be deemed unethical."

At the September, 1961, meeting of the Council, I reported as follows:

> "In order to implement the mandate of the State Society's House of Delegates to this Council that the relationship between osteopathy and medicine be further explored, I would propose that this Council accept as basic tenet the A.M.A. Judicial Council's report." (*Approval was voted*.)
>
> "To implement further the House of Delegates mandate to the Council, I recommend that the president appoint an ad hoc committee to explore further some of the problems connected with osteopathy and medicine in this State, including the compensation schedule and various other problems that are keeping the profession from harmonizing this Judicial Council report". (*Approval was voted*.)
>
> (It was understood that an equal group would be appointed by the Osteopathic Society and that they would finance their half of the study.)

Following the September meeting of the Council, the president, John M. Galbraith, M.D., appointed an ad hoc liaison committee whose function and duties were to meet and discuss mutual problems of the two professions. The medical members of the committee are John M. Galbraith, M.D., E. Dean Babbage, M.D., Henry I. Fineberg, M.D., James M. Blake, M.D., and Norman S. Moore, M.D., chairman pro tem. The members appointed by the Osteopathic Society are W. Kenneth Riland, D.O., William O. Kingsbury, D.O., Francis J. Beall, Jr., D.O., William E. Kaufmann, D.O., and C. Fred Peckham, D.O.

Four meetings of the joint committee have been held. Dr. Moore presided at two of these and Dr. Riland chaired two of the meetings. Progress has been made in several problem areas, for example, ethical association, educational programs, hospital appointments, and legislation affecting both professions. It is definitely understood by both groups making up the membership of the ad hoc committee that each profession represented wishes to maintain its individual identity, and amalgamation was neither suggested nor contemplated.

At the last meeting of the liaison committee, the question of hospital appointments was raised in connection with accreditation of hospitals by the Joint Commission on Accreditation of Hospitals, and a letter from Kenneth Babcock, M.D., executive director of the Joint Commission, was read. Dr. Babcock stated the following, which was approved by the Council of the Medical Society of the State of New York at its April meeting:

> "Over a year ago the Joint Commission stated that if a hospital credentials and executive committee, in its judgment, believed that an osteopath was deserving of staff appointment to a hospital, the hospital could do so. No mention was made as to whether he could do surgery, interpret electrocardiograms, deliver babies, or anything else.
>
> "It is up to a hospital medical staff to utilize its responsibilities and integrity and judge whether this man is capable of doing surgery or anything else. If they do not know from his qualifications, then they should put him on probation and observe him for three to six months. . . . A man should not be judged by his label; he should be judged by his individual capabilities, and these must be reviewed with integrity, as stated, by the hospital medical staff before they give him privileges."

Thus the question of osteopaths being given hospital appointments has no relation to accreditation per se. This action eases the obstacle of Medical Society membership mentioned in the formal statement of the chairman pro tem, which was approved by the Council of the Medical Society of the State of New York at its March meeting, reprinted as follows:

> "At the annual meeting of the American Medical Association in New York City last June, the relationship between doctors of osteopathy and doctors of medicine was discussed.
>
> "Among other things, it was agreed that (1) it was appropriate for the A.M.A. to reappraise its application of policy regarding relationships with doctors of osteopathy and (2) the policy should now be applied individually at the state level according to the facts as they exist. If the osteopath bases his practice on the same scientific principles as those adhered to by members of the A.M.A., voluntary professional relationships with him should not be deemed unethical. In other words, the state medical association is fully competent to ascertain the facts and evaluate them.
>
> "With this in mind, and with the approval of the Council, our president appointed an ad hoc committee—to be part of a joint committee with representatives of the Osteopathic Society—to explore further some of the problems connected with osteopathic medicine in this State.
>
> "Thus far this joint committee has convened three times. The meetings have been harmonious and amiable.
>
> "The results of the conferences, approved by the Council, are summarized as follows:
>
> "1. Osteopathy in this State is no longer considered to be cultism—since osteopaths hold the license to practice medicine and surgery, granted by the State Board of Medical Examiners, and if they adhere to the same scientific principles embraced by doctors of medicine.
>
> "2. Doctors of medicine may associate professionally, on a voluntary basis, with doctors of osteopathy who hold full licenses to practice medicine and surgery granted by the New York State Board of Medical Examiners.
>
> "3. It was agreed that *What Goes On* should be distributed to doctors of osteopathy to apprise them of what is taking place in the postgraduate education field. At the next meeting of the Council, it will be recommended that county medical societies invite doctors of osteopathy to their scientific meetings and seminars. In return, the osteopaths will send invitations to the doctors of medicine for them to attend osteopathic conferences.
>
> "Consideration has been given to the problem of hospital appointments. Of course, one obstacle to the hospital appointments of osteopaths is the requirement of county medical society membership. The idea has been presented that this requirement might be altered to read—'membership in a recognized local or state professional society of osteopathic physicians or doctors of medicine.' This matter will be discussed again at subsequent meetings.
>
> "Also, legislation problems affecting both groups have been studied. The proposals for chiropractic licensure are of great concern to both. There are other areas of legislation which should be approached jointly. It was suggested that the two legislation chairmen get together and confer about mutual legislation plans and procedures so that each group will understand what the other is doing.
>
> "Negotiations will continue."

It is recommended that the ad hoc liaison committee be continued for at least another year and that it continue to work toward a mutual, meaningful, ethical professional relationship. This is a progress report to the House of Delegates directed by the Council of the Medical Society of the State of New York at its March meeting.

Respectfully submitted,
NORMAN S. MOORE, M.D., *Chairman*
Medical Component

Section 14 (see 177) Report 62–H

Supplementary Report of the Board of Trustees

To the House of Delegates, Gentlemen:

Since our preliminary report was published in the April 1 issue of the JOURNAL, our auditors have completed their work, and the Auditor's Certificate is on pages 25 through 29 in the House of Delegates Handbook. Their report includes a statement of our general and other funds on page 29. Our auditors tell us we should have a surplus equal to three years' dues.

In our preliminary report we stated that our deficit for 1959, 1960, and 1961 was $271,722. The treasurer in his report, page 32 of the Handbook, estimates a deficit for 1962 of $185,000.

In table I of the treasurer's report is a detailed account of our receipts and expenditures from 1956 to 1961. In table II of this report is the JOURNAL financial status from 1956 to 1961.

The following figures taken from tables I and II will account to some extent the reasons for our deficit for the last three years.

	1956	1961	Increase over 1956
Membership dues	$567,476	$833,199	$+265,726
Number of employes	63	74	+11
Administration	134,845	270,337	+135,492
Public relations	69,521	155,834	+86,313
Travel	30,233	65,532	+35,299
Annual meeting	5,487	36,826	+30,826
JOURNAL—net gain	42,645	993	−41,562
Dues allocated to the JOURNAL	60,610	125,800	+64,190

Our rent has increased from $30,500 in 1956 to $74,300 in 1961.

Journal. Notwithstanding the new format of the JOURNAL and the marked improvement of the scientific articles as the result of the hard work of William Hammond, M.D., our editor, the decrease in our advertising between 1959 and 1961 was $117,714.

This in no way is due to any lack of energy or efficiency on the part of Mr. Charles L. Baldwin, our business and advertising manager, and his staff. Other state journals and medical publications also have had a decline in their advertising during this period. Mr. Baldwin is very hopeful that our advertising will increase over the balance of this year as a result of improved conditions in the pharmaceutical industry. Our advertising has declined approximately $22,000 during the first four months of 1962 as compared with 1961. We maintain records of advertising contracts for the year as they are received. As of the middle of April, we had received contracts and insertion orders for 1962 amounting to approximately $235,000. As of the same date in 1961, we had received contracts and insertion orders amounting to approximately $250,000. At this time we therefore have about $15,000 less advertising for the coming year. Mr. Baldwin stated that this in part might be due to the fact that advertisers are issuing insertion orders on a month-to-month basis rather than having signed contracts for a full year.

In our preliminary report we stated that only three state societies had lower dues than ours and that 33 states had dues from $50 to $100. Our treasurer in his report stated that he would need an increase in dues of about $11 a year to meet our expenses. Last year the House of Delegates passed a resolution for required membership in the A.M.A. at a cost of $35 and took no action about the large deficit the State Society had in 1959 and 1960 and the deficit facing us in 1961. Next year A.M.A. dues will be $45, and it does not appear to be consistent that dues we pay the A.M.A. should be greater than in our own Society. For information, a comparison of 1961 and 1962 dues for all the states and the District of Columbia is shown in Table I.

Last year, commencing in September, we borrowed a quarter of a million dollars to pay for our Society's operation. Interest costs were $3,400. This year we will probably start borrowing in July or August. Much depends on the amount of dues received from members and the amounts spent for general operation. We have heard it said, "Why worry about our deficit—take it from our surplus." The way we have been conducting our financial affairs during the past few years, if continued, will result in our having little or no surplus in the not too distant future unless we reverse our actions. We have been able to borrow money each fall since 1959 because we have had unrestricted collateral to secure our loans. We feel sure that we would have difficulty in borrowing without collateral. So long as our banker knows that his client is responsible, not letting his affairs get out of hand, not doing foolish things with his money, and is efficient in running his business, his credit will be good. But when these virtues do not seem to be apparent, the client is in for real trouble.

At the last meeting of the Board of Trustees, our executive vice-president, Henry I. Fineberg, M.D., assured us that (1) he would continue to do everything possible to eliminate any unnecessary spending, (2) he is preparing a manual for office procedure, and (3) it is his intention to have our budget prepared in a more detailed and realistic manner.

Recommendations. 1. That the House of Delegates make a serious and unhurried study of the reports of officers, bureaus, departments and all other reports.

2. That in the future, neither the Council nor Board of Trustees approve any budget where

TABLE I. Comparison of 1961 and 1962 dues for all states

State	1961 Dues	1962 Dues	Remarks
Alabama	$ 50	$ 50	.....
Alaska	75	75	.....
Arizona	70	85	$15 AMEF allocation
Arkansas	35	35	$5 for medical education
California	65	75	.....
Colorado	60	60	.....
Connecticut	33	33	.....
Delaware	50	50	Plus $5 for scholarships
District of Columbia	70	70	.....
Florida	40	40	.....
Georgia	40	40	.....
Hawaii	40	60	$6 for journal
Idaho	83	83	.....
Illinois	80	80	$20 for AMEF
Indiana	50	50	$19.25 for various funds
Iowa	80	90	.....
Kansas	50	50	.....
Kentucky	50	50	.....
Louisiana	50	50	.....
Maine	55	55	.....
Maryland	50	50	.....
Massachusetts	35	35	.....
Michigan	75	80	.....
Minnesota	55	55	$4 goes to indigent physicians and scholarships
Mississippi	50	50	.....
Missouri	35	35	$15 increase recommended
Montana	65	65	.....
Nebraska	35	35	.....
Nevada	100	100	$20 to AMEF and 1962 additional $100 building assessments
New Jersey	35	35	.....
New Mexico	90	90	.....
New York	35	35	.....
North Carolina	50	50	.....
North Dakota	100	100	.....
Ohio	30	30	Proposed $5 increase for 1963
Oklahoma	42	47	$5 to scholarship fund
Oregon	50	50	.....
Pennsylvania	60	60	.....
Puerto Rico	52	52	Plus $27 for life insurance plan
Rhode Island	50	50	.....
South Carolina	35	35	Plus $10 voluntary for AMEF
South Dakota	75	100	.....
Tennessee	40	40	.....
Texas	45	45	.....
Utah	75	85	.....
Vermont	55	65	.....
Virginia	25	25	Licensed more than 5 years
Washington	45	45	Increase proposed $15
West Virginia	35	38	$6 for scholarship fund
Wisconsin	75	90	.....
Wyoming	50	50	.....

the amount of budget exceeds our anticipated income and that the budget be submitted to the Council and Board of Trustees for adoption prior to the beginning of the next fiscal year.

3. That any resolution of the House of Delegates requiring expenditure of money not provided in the budget shall be referred to the Council and Board of Trustees to ascertain if the money is available from any other source.

4. That our dues for 1963 be increased a minimum of $10.

Conclusion. Unless basically sound economic truths are observed and practiced in the conduct of our affairs, we shall pay bitterly for our neglect. An observance of these principles will save a lot of time of the members of the House of Delegates and reference committees and relieve your officers and our executive vice-president of many of their worries.

We would like to conclude this report with the following quotation: "If something goes wrong, it is more important to talk about who is going to fix it, than who is to blame."—Frances J. Gable.

We feel sure you can fix it if our recommendations meet with your approval.

Respectfully submitted,
JOHN J. MASTERSON, M.D., *Chairman*

Section 15 (see 121) Report 62–I

Annual Report of the Empire State Medical, Scientific and Educational Foundation, Inc.

To the House of Delegates, Gentlemen:

For the information of the House of Delegates, a balance sheet (Exhibit A) and a summary of income and expenditures (Exhibit B) of the Empire State Medical, Scientific and Educational Foundation are appended.

The prime activity of the Foundation during 1961 was the study of maternal and perinatal mortality. The Department of Health of the State of New York is providing funds for the study. During 1961 we received $21,754.34 from the Department of Health and spent $19,199.56, leaving a net income of $2,254.78 from the project (Exhibit B).

In addition, the Medical Society of the State of New York contributed $8,000 to provide working capital. Of this, $1,291.22 has been used for office and sundry expenditures. There

EXHIBIT A. Balance Sheet as at December 31, 1961

Assets		
Current assets		
Cash	$5,023.93	
Due from New York State	8,574.16	
Total current assets		$13,598.09
Prepaid insurance		6.00
Total assets		13,604.09
Liabilities and Surplus		
Current liabilities		
Accounts payable	146.68	
Accrued taxes	1,029.05	
Total current liabilities		1,175.73
Surplus		
Surplus, December 31, 1960	3,164.80	
Excess of income over expenditures, period ended December 31, 1961	9,263.56	
Surplus, December 31, 1961		12,428.36
Total liabilities and surplus		13,604.09

EXHIBIT B. Summary of Income and Expenditures for Twelve Months Ended December 31, 1961

Income		
Contribution from Medical Society of the State of New York	$ 8,000.00	
Reimbursement from New York State	21,754.34	
Total income		$29,754.34
Expenditures		
Maternal and Perinatal Mortality Study		
Salaries	14,749.94	
Travel	299.20	
Payroll taxes	665.48	
Repairs and services	48.93	
Stationery and supplies	1,013.30	
Dues, subscriptions, books	67.66	
New equipment	2,248.41	
Postage and express	31.64	
Photos, artwork, reprints	75.00	
Total Maternal and Perinatal Mortality Study expenditures		19,199.56
Administrative		
Travel	29.51	
Rent	471.95	
Electricity	22.75	
Telephone and telegraph	207.42	
Postage and express	82.15	
Stationery and supplies	128.83	
Insurance	50.08	
Repairs and services	13.38	
Sundry	285.15	
Total administrative expenditures		1,291.22
Total expenditures		20,490.78
Excess of income over expenditures		9,263.56

is a balance of $6,708.78 remaining from the original $8,000 contribution (Exhibit B).

As to the over-all picture, the Foundation had an excess of net income over net expenditures of $9,263.56 for the year.

As at December 31, 1961, a surplus of $12,428.36 existed. Working capital amounted to the same figure.

The Medical Society of the State of New York has appropriated the amount of $8,000 should additional working capital be required during 1962.

Respectfully submitted,

MAURICE J. DATTELBAUM, M.D., *Treasurer*

Section 16 (*see 178*) Report 62–J

Supplementary Report of the Executive Vice-President

To the House of Delegates, Gentlemen:

This communication is an addendum to the preliminary report which was published in the April 1 issue of the NEW YORK STATE JOURNAL OF MEDICINE.

Your executive vice-president is happy to report that there has been much progress in the preparation of the staff handbook. A considerable amount of data has been collected, and a rough preliminary draft has been compiled and distributed to the directors of bureaus and departments and to the officers of our Society for study and comments. It is our hope that the final form will be available in the not-too-distant future.

We are curtailing our expenses as much as possible. During the early part of March we transmitted a memorandum to the heads of departments and bureaus pointing out the dismal financial situation of our Society. We stressed the fact that, since this year's budget is out of balance and we are in the "red," the funds allotted to each division must be used only for essential services and items. "Luxuries" must be eliminated. Instructions were issued that we must be kept informed of the progress in this direction. Requests for expenditures are being screened very carefully.

As we have explained previously, in the very near future we expect to develop new procedures in submitting budget estimates. The Budget Committee has agreed that many of our present methods are not in keeping with modern business systems and require study and total revampment. By early fall we expect that our entire budgetary routine will be changed in accordance with the trends of the times.

Since our preliminary report was submitted, your executive vice-president has attended the following conferences (again, routine meetings excluded):

1. A meeting with the executive secretaries of county medical societies at headquarters in New York City on February 9. It lasted most of the day. Local county medical society problems were discussed and the relationships between the local organizations and the State Society were explored. We found that the local county medical societies have problems of their own which require the advice and assistance of the State Society. Special attention was given to A.M.A. membership, collection of dues, and finances in general.

2. A meeting of the reference committee of the United Medical Service in New York City on February 17. Your executive vice-president represented the president.

3. A meeting with the Hon. Raymond E. Houston, Commissioner of the Department of Social Welfare of the State of New York, and his staff in New York City on February 16. Also present were our president, the chairman of the Committee on Public Health and Education, the chairman of the Committee on Economics, the chairman of the Committee on Public Medical Care, the chairman of the Committee on Legislation, the director of the Bureau of Medical Care Insurance, the director of the Department of Communications, and the assistant to the executive vice-president.

This was a harmonious conference. Matters concerned with MAA were discussed and the conclusion was reached unanimously that there must be improvements in the implementation of the program.

Since then it has been announced that Commissioner Houston has resigned.

4. The 1962 National Aircade for Citizenship Action, conducted by the Chamber of Commerce of the United States in New York City on February 26. The National Aircade for Citizenship Action consists of a series of one-a-day issue-discussion meetings in key cities of the United States. This year the meetings were held in 15 cities within a limited span of nineteen days. The key words "Citizenship Action" reflect the basic purposes and intent of the meetings—to stimulate greater citizenship action on major national issues before Congress and the nation. These are not ordinary meetings in that they do not consist of formal lectures—rather they are built around maximum audience participation.

5. A meeting of the Empire State Health Council in Albany on March 7. The problem of cigaret smoking in teenagers was the main topic on the agenda.

6. The annual meeting of the board of directors of the United Medical Service. Mr. John McCormack announced his retirement as president. Leonard J. Raider, M.D., has been appointed to take his place.

7. A seminar for science medical writers, sponsored by the American Cancer Society, in Phoenix, Arizona, March 9 through 13. This was one of the finest meetings that we have attended in some time. A panel of close to 60 experts from all parts of the United States and elsewhere presented papers before about 50 science writers. The State of New York was well represented. The agenda included the role of the endocrines, nucleic acids and proteins, chemotherapy, radiation, carcinogenesis, viruses and immunity, and prevention and cure.

We came away from this conference with the feeling that there has been much progress in the fields of research and clinical management of cancer, but there is still a great deal of work to be done. We must eliminate the shackles of conventional thinking and proceed fearlessly into new areas. Cynical attitudes must be eliminated. Better communication must exist between the researchers and the clinicians. Gaps in communication must be reduced to an irreducible minimum, "so that new concepts are given early hearings and that all areas of promise are rapidly explored" (Thomas Carlile, M.D., president of the American Cancer Society).

8. The annual meeting of the Governor's Committee on "Employ the Physically Handicapped," in New York City on March 16. The main discussion concerned the mentally retarded and the blind.

9. The annual legislative correspondents dinner in Albany on March 17.

10. Session of the Legislature in Albany (several days during the last week). Many will remember that it was during this period that the chiropractors, for the second time, "marched on" Albany in order to urge, in a very vivid manner, the passage of the chiropractor licensure law. Undoubtedly, what we were able to accomplish will be described more fully by the chairman of the Committee on Legislation. However, it should be reported that Herman E. Hilleboe, M.D., and Mr. George Foy, who is our legislative counsel in Albany, played an

important role in defeating the chiropractors' attempt to gain recognition. Dr. Hilleboe, Mr. Foy, and your executive vice-president were privileged to meet with the Governor of our State and the problem of the chiropractor was discussed in detail.

11. A meeting and dinner of the Queens chapter of the American Academy of General Practice in Forest Hills on April 4.

12. A meeting of the medical section of the New York Board of Trade in New York City on April 9. Nursing homes, the shortage of nursing personnel, and other matters pertaining to public health and welfare were discussed and analyzed.

13. The opening of a library on legal medicine, in honor of Milton Helpern, M.D., chief medical examiner of the City of New York. The ceremonies were held at the new building of the Medical Examiner in New York City on April 17. Speakers representing the medical profession, the bar, and the courts addressed the assembly. The Medical Society of the State of New York was well represented by the president-elect, the secretary, the immediate past-president, and the executive vice-president.

14. A meeting of representatives of the Fifth and Sixth District Branches in Utica on April 19.

15. The Medallion Ball and dinner of the Nassau County Medical Society in Lido Beach on April 28. Your executive vice-president was afforded the great honor of acting as master of ceremonies. Several of the past-presidents, including John M. Galbraith, M.D., and the outgoing president were awarded gold medallions. This was a very fine affair.

16. The fiftieth anniversary meeting of the United States Chamber of Commerce in Washington, D. C., on April 30 and May 1. Your executive vice-president was present when President Kennedy discussed management and labor. What he had to say has been fully reported in the newspapers of our country.

17. The annual meeting of the Connecticut State Medical Society in Hartford. Your executive vice-president attended the meeting of the House of Delegates on April 22. He presented the greetings of the officers and members of the Medical Society of the State of New York.

As we travel around and visit other state societies, we find that their problems do not differ materially from those which face us here in the Empire State.

18. The annual meeting of the Bronx chapter of the American Academy of General Practice in the Bronx on May 9.

On May 10, the chairman of the Council Committee on Legislation and your executive vice-president appeared on a radio program (WTRY-Troy) to discuss quacks and quackery. Previously, a number of chiropractors were given the privilege of appearing on the program.

Again, your executive vice-president wishes to express his sincere gratitude to all the folks who have assisted him during the past twelve months.

We look forward to the years that lie ahead with great confidence and with the knowledge that all of you will continue to give the staunch support that we have received in the past.

Respectfully submitted,
Henry I. Fineberg, M.D.
Executive Vice-President

Section 17 (see 197, 215) Report 62–K

Supplementary Report of the Committee on Legislation

To the House of Delegates, Gentlemen:

From the point of view of legislation affecting medicine, the 1962 session of the New York State Legislature was perhaps the busiest that we have seen for a number of years. An unusually large number of bills pertaining to medicine and medical practice were introduced into the Legislature. Unfortunately many of these were poorly drawn and truly bad legislation, and these were given little consideration by the various committees and members of the Legislature.

There is attached a summation of the legislation action, as well as the Governor's action on the various bills in which we were particularly active during the session.

In addition to those listed, one other item of legislation in which we were particularly concerned was that presented by the Medical Society of the County of Erie and referred to the Reference Committee on Public Health and Education, namely, oral prescription for class B narcotic compounds.

In cooperation, we attempted to initiate legislation in this respect through the State Department of Health as an administration bill. Unfortunately, Governor Rockefeller did not view this favorably and would not accept such as part of the administration program. In view of this attitude, it did not seem logical to introduce it as an independent bill since the Governor had expressed himself as being opposed to such and would undoubtedly have vetoed the legislation.

Summary of Legislative Action—1962 Session of the New York State Legislature. The following bills were sponsored by the Medical Society:

1. S. Intro. 1015, Pr. 4143 (Barrett) Education Committee; A. Intro. 2040, Pr. 2907 (Dudo) Education Committee. AN ACT to amend the education law, in relation to authorizing the counties of the State outside the City of New York to award scholarships for professional education in medicine conditioned upon the promise of scholarship holders to practice medicine in such counties for limited periods of time following their licensing as physicians.

This bill passed the Assembly but was killed in the Senate Education Committee because of the active opposition of Senator Ernest I. Hatfield of Poughkeepsie. Senator Hatfield was acting as chairman of the Education Committee in the absence of Senator Earl Brydges who suffered a heart attack during the session. Senator Brydges would have been in favor of the bill, and we believe that the bill will pass the 1963 session of the Legislature.

2. S. Intro. 1280, Pr. 1290 (Bush) Taxation Committee; A. Intro. 2570, Pr. 2594 (Plumadore) Ways and Means Committee. AN ACT to amend the tax law, in relation to deduction of the cost of tuition, textbooks, and laboratory fees incurred in connection with attendance at a medical college.

This bill was killed in committee in both houses because of opposition from the Director of the Budget.

3. S. Intro. 1375, Pr. 1395 (Brydges) Education Committee; A. Intro. 2037, Pr. 2042 (Bartlett) Education Committee. AN ACT to amend the education law, in relation to authorizing members of any profession to organize an association to engage in the practice of their profession in corporate form, providing for the regulation of such association and of its members and employes and prescribing their powers and duties.

The above bills were prepared and introduced in the Legislature. After introduction, the New York State Association of Professions requested that these bills not be pressed for passage until further study was made. It was agreed that the New York State Association of Professions would prepare, for introduction at the 1963 session, a bill satisfactory to all professions in New York State.

4. Senate Resolution 19 (Cornell) Finance Committee; Assembly Resolution 145 (Ashbery) Ways and Means Committee. AN ACT creating a joint legislative committee on licensure in the healing arts and making appropriation for expenses, etc.

These resolutions were introduced in both houses of the Legislature. They were killed in committee due to opposition from the Division of the Budget.

5. S. Intro. 1602, Pr. 3384 (Speno) Education Committee; A. Intro. 2090, Pr. 5240 (Bartlett) Judiciary Committee. AN ACT to amend the education law, in relation to exemption from liability of physicians and surgeons rendering gratuitous emergency treatment.

This bill was prepared, introduced, and passed both houses but was vetoed by the Governor. Copy of veto memorandum is attached hereto.

6. S. Intro. 3363, Pr. 3653 (Condon) Labor and Industry Committee; A. Intro. 4671, Pr. 4963 (Dudo) Labor and Industry Committee. AN ACT to amend §13-a (4) of the Workmen's Compensation Law, in relation to reports of physicians.

This bill was introduced at the request of the Council Committee on Workmen's Compensation of the Medical Society of the State of New York. The bill was reported out of committee in the Assembly and defeated after debate on the floor.

7. S. Intro. 3430, Pr. 4399 (Condon) Labor and Industry Committee; A. Intro. 4670, Pr. 5891 (Dudo) Labor and Industry Committee. AN ACT to amend §13-g of the Workmen's Compensation Law, in relation to the payment of bills for medical care.

This bill was introduced at the request of the Council Committee on Workmen's Compensation of the Medical Society of the State of New York. This bill passed both houses. The bill was approved by the Governor and became Chapter 490 of the Laws of 1962.

Over 200 bills were introduced in the Legislature which directly affected the Medical Society of the State of New York. These bills were screened by your Legislation Committee and counsel. The most important of these bills are as follows:

1. S. Intro. 2769, Pr. 3336 (Peterson) Finance Committee; A. Intro. 4137, Pr. 5265 (Goddard) Ways and Means Committee. AN ACT to amend the education law, in relation to the practice of chiropractic and making an appropriation therefor.

The Senate bill was reported out of committee in the Senate but was never brought to a vote due to opposition of the State Health Department and the Medical Society. The Assembly bill was killed in committee.

2. S. Intro. 3093, Pr. 4702 (Speno) Finance Committee; A. Intro. 1588, Pr. 5985 (Mrs. Lawrence) Ways and Means Committee. AN ACT to amend the public health law, in relation to the practice of radiation technology and the creation of a radiation technician advisory board.

This bill was sponsored by the Health Department. The bill was reported out of Assembly committee but was recommitted the last week of the legislative session at the suggestion of the State Health Department.

3. A. Intro. 2217, Pr. 2226 (Fehrenbach) Judiciary Committee. AN ACT to amend the lien law, in relation to liens of physicians.

This bill was not sponsored by the Medical Society, but we cooperated with the sponsor in attempting to pass it. The bill was killed in committee, primarily because of objections of the insurance companies and various bar associations.

4. S. Intro. 1063, Pr. 1066(Thaler) Taxation Committee; A. Intro. 2183, Pr. 2189 (Savarese) Taxation Committee. AN ACT to amend the real property law, in relation to exemption from taxation of real property owned by medical societies, and repealing §470 of such law relating thereto.

This bill passed both houses of the Legislature. It was sponsored by the Queens County Medical Society, and the Medical Society of the State of New York representatives actively supported this bill. The bill was vetoed by the Governor at the request of the City of New York. Copy of Governor's veto memorandum is attached.

5. S. Intro. 2743, Pr. 2916 (Bush) Health

Committee; A. Intro. 4069, Pr. 5370 (Mintz) Codes Committee. AN ACT to amend the public health law, in relation to licensing and regulating the practice of bioanalysis.

This bill had the approval of the State Health Department, passed the Assembly, but was defeated after a vote in the Senate on the last day of the session.

6. S. Intro. 1660, Pr. 1711 (Bernstein) Judiciary Committee; A. Intro. 4366, Pr. 5730 (Kapelman) Judiciary Committee. AN ACT to amend the personal property law, in relation to the ownership of prints of x-ray plates taken by physicians and hospitals.

This bill passed both houses of the Legislature. It was opposed by the New York State Health Department, the Association of Hospitals, and others. The bill was vetoed by the Governor. Copy of veto memorandum is attached.

7. S. Intro. 1689, Pr. 4323 (Laverne) Education Committee; A. Intro. 2740, Pr. 5745 (Waters) Education Committee. AN ACT to amend the education law, to provide that an ophthalmic dispenser holding a certificate may fit contact lenses upon written prescription of physician, etc.

This bill was sponsored by the New York State Ophthalmological Society, Inc. Your legislative representatives cooperated with them in attempting to pass this bill. It was reported out of committee in the Assembly but was defeated after extended debate in the Assembly.

8. S. Intro. 4979, Pr. 5415 (Committee on Rules) Public Health Committee. AN ACT to amend the public health law, in relation to prohibiting discrimination in hospital staff appointments and privileges.

The Medical Society strongly supported this bill. The State Health Department also supported the bill. This bill passed the Assembly but was killed in the Senate Health Committee because of the opposition of the chairman of the Senate Health Committee and a Catholic hospital group.

9. S. Intro. 1780, Pr. 1839 (Hughes) Codes Committee; A. Intro. 1939, Pr. 1943 (Volker) Codes Committee. AN ACT to amend the civil practice act, in relation to time for commencement of action to recover damages for malpractice.

This legislation was introduced on the recommendation of the Law Revision Commission. We vigorously opposed passage of this bill, and the bill was killed in the Assembly Rules Committee.

In addition to the foregoing legislation, we have appeared as *amicus curiae* in a proceeding brought pursuant to Article 78 of the Civil Practice Act in the Appellate Division. This proceeding will be argued at the next term of court of the Appellate Division. The following are the facts in this case:

§7126, Subd. 1, of the Education Law prohibits ophthalmic dispensers from practicing medicine but allows them to "fit contact lenses under the personal supervision of a physician."

The Commissioner of Education brought Fred Leon Yerdon and two others up on charges for violating this section. He decided that this section requires the personal attendance of the physician at all phases of the fitting, and consequently the dispensers had violated the law.

The medical profession feels that this interpretation is too strict. Many of the acts to be performed are of a routine nature and do not require the physical presence of a physician. The public receives adequate protection, and the statute is complied with if the physician sees the patient from time to time and directs what shall be done. DEGRAFF, FOY, CONWAY AND HOLT-HARRIS

Respectfully submitted,
JAMES A. BLAKE, M.D., *Chairman*

Following are the Governor's veto memorandums.

State of New York
Executive Chamber
Albany

April 30, 1962

MEMORANDUM filed with Senate Bill, Introductory Number 1602, Print Number 3384, entitled: "AN ACT to amend the education law, in relation to exemption from liability of physicians and surgeons rendering gratuitous emergency treatment"

#247

NOT APPROVED

This bill would exempt a physician or a surgeon from liability for injuries sustained by a person by reason of the negligence of the physician or surgeon in rendering emergency medical treatment. He would only be liable for wilful neglect or gross negligence.

The sponsors argue that the bill is necessary to counteract an "unprecedented increase" in malpractice actions growing out of situations where a doctor, in an emergency, away from proper medical equipment, voluntarily lends assistance.

The following objections have been raised to the bill:

—It represents an undesirable lowering of the standard of accepted conduct which has prevailed for many years. To require a reasonable degree of care in all instances is a proper standard since what is reasonable depends in any situation on all the surrounding circumstances.

—The exemption is related to situations where no proper medical equipment is available. Present law already holds a physician or surgeon in such cases to a lesser standard of performance. This bill, however, would introduce the tests of "wilful neglect or gross negligence" which appear to be unnecessarily low.

—The exemption would only apply to the rendering of "gratuitous" first aid or emergency treatment. Presumably a physician or surgeon could preserve his exemption from liability by omitting to send a bill or refusing to accept a tendered fee for services negligently rendered.

—If the principle laid down in this bill is sound, there is no reason to restrict the exemption to physicians and surgeons. Very often first aid is given in emergencies by lay persons who should similarly be granted exemption from liability and to whom the protection of liability insurance would not ordinarily be available.

In view of the fundamental questions raised by this bill, I have sought the opinions of authorities in the field of tort law. Professors Fowler V. Harper and Fleming James, authorities in the field, have commented: "As a matter of tort liability of physicians for malpractice, it is our view as teachers and scholars in the field of Torts that the liability should be the same whether medical service is rendered gratuitously or for compensation and regardless of whether the situation involves an emergency or not."

The Dean of New York Law School, the Association of the Bar of the City of New York, and the Bronx County Bar Association are among those urging disapproval.

The bill is disapproved.

Nelson A. Rockefeller

State of New York
Executive Chamber
Albany

April 24, 1962

Memorandum filed with Assembly Bill, Introductory Number 2183, Print Number 2189, entitled: "AN ACT to amend the real property tax law, in relation to exemption from taxation of real property owned by medical societies, and repealing section four hundred seventy of such law relating thereto."

#86

NOT APPROVED

This bill proposes to grant exemption from real property taxes (without limitation as to amount) to medical societies for real property owned anywhere in the State.

Under present law, medical societies are granted such exemption up to $150,000 in the Counties of Kings, Queens, and New York and up to $50,000 in the other counties of the State. I am informed that the Queens County Medical Society has sponsored this measure. The Mayor of the City of New York has expressly requested that the bill be disapproved.

The Board of Equalization and Assessment urges disapproval in the absence of a compelling demonstration of the need for expanding state-wide the present exemption from taxation.

The bill is disapproved.

Nelson A. Rockefeller

State of New York
Executive Chamber
Albany

April 24, 1962

Memorandum filed with Assembly Bill, Introductory Number 4366, Print Number 5730, entitled: "AN ACT to amend the personal property law, in relation to the ownership of prints of x-ray plates taken by physicians and hospitals."

#69

NOT APPROVED

This bill would add a new Section to the Personal Property Law to provide that title to prints of x-ray plates taken by a physician or hospital shall pass to the patient upon his payment of the charges therefor and shall be delivered to him or his authorized agent upon demand.

Until recently it was not practical to make prints of x-ray plates, and few hospitals today have facilities for the production of such prints. The Association of the Bar of the City of New York, in urging disapproval, points out that this bill, by assuming the existence of prints, would not deal with the great majority of cases where a demand for prints would require their production as well as their delivery.

In addition, the Department of Health has stated: "(W)e would recommend disapproval of the Bill on the grounds that it would represent an added expense to the patient without filling a real need and without sufficient evidence to indicate that the resulting 'print' called for by the Bill would be of diagnostic quality so that it would not represent a real medical hazard when used for comparison purposes."

The bill is disapproved.

Nelson A. Rockefeller

Section 18 (see 198, 216) Report 62–L

Supplementary Report of the Subcommittee to Combat Cults

To the House of Delegates, Gentlemen:

You are all familiar with the activity which took place during the last session of the Legislature pertaining to the licensure of chiropractic. This was reported to you in detail through "Capitol News," also by personal communication to the various counties.

This question continues to be a perennial one with increasing intensity from year to year. What the eventual answer will be is yet to be determined.

There is attached a copy of the sustaining action of the New York Supreme Court, Appellate Division, in the case of Chiropractic Association of New York, Inc., against Herman E. Hilleboe, M.D., Commissioner of Health of the State of New York.

Respectfully submitted,
James M. Blake, M.D., *Chairman*

SUPREME COURT
Appellate Division
Third Judicial Department
Decision handed down May 4, 1962
2916

Chiropractic Association of New York, Inc., on behalf of itself and its individual members, and Ernest E. Quatro, Appellants
v.
Herman E. Hilleboe, as Commissioner of Health of the State of New York, Respondent.

Judgment affirmed, with costs to respondent.
Opinion by Gibson, J.
Coon, Herlihy, Reynolds and Taylor, concur.

STATE OF NEW YORK SUPREME COURT
APPELLATE DIVISION THIRD DEPARTMENT

CHIROPRACTIC ASSOCIATION OF NEW YORK, INC., on behalf of itself and its individual members, and ERNEST E. QUATRO,
Appellants,
—against—
HERMAN E. HILLEBOE, as Commissioner of Health of the State of New York,
Respondent.

Argued March 12, 1962.
Decided May 4, 1962.

Before:
HON. William H. COON,
Justice Presiding,
HON. James Gibson
HON. J. Clarence Herlihy,
HON. Walter B. Reynolds,
HON. Donald S. Taylor,
Associate Justices.

—. . . . . .—

APPEAL from a judgment of the Supreme Court, entered November 15, 1961, in Albany County, upon the decision of an Official Referee (Albert Conway, Off. Ref.) which dismissed the complaint in an action for a judgment which would, among other things, declare unconstitutional Regulation 19, Chapter XVI, of the New York State Sanitary Code and enjoin the defendant Commissioner of Health from enforcing it. (Opinion 31 Misc 2d 554.)

—. . . . . .—

BLISS AND BOUCK (F. WALTER BLISS of counsel), Attorneys for appellants, 107 Columbia Street, Albany, New York.

LOUIS J. LEFKOWITZ, Attorney General (PAXTON BLAIR and EDWARD R. MURPHY of counsel), Attorney for respondent, The Capitol, Albany, New York.

—. . . . . .—

OPINION FOR AFFIRMANCE

GIBSON, J.

The plaintiff membership corporation, claiming to represent about half of the State's chiropractors, and the individual plaintiff, a chiropractor, appeal from a judgment which dismissed their complaint in an action brought to have declared unconstitutional Regulation 19 of Chapter XVI of the New York State Sanitary Code and to restrain its enforcement. Concededly, such enforcement would seriously impede the practice of chiropractic.

Chapter XVI is entitled "Ionizing Radiation" and the questioned Regulation 19 thereof provides as follows:

> *Regulation 19. Limitations on application of radiation to humans.* No person shall apply radiation to a human being unless such person is licensed or otherwise authorized to practice medicine, dentistry, podiatry or osteopathy under the provisions of the Education Law of the State of New York. Radiation shall be applied by a licensed or otherwise authorized person to only those parts of the human body specified in the law under which such person is licensed or authorized to diagnose and treat.
>
> This regulation shall not prohibit the use of radiation by a technician, nurse or other person, if such use is directed or ordered by a person licensed or authorized to practice medicine, dentistry, podiatry or osteopathy under the provisions of the Education Law of the State of New York.
>
> The sale, lease, transfer or loan of x-ray or fluorocopic equipment or the supplies appertaining thereto, except to persons engaged in an occupation where such use is permitted, and except to hospitals, infirmaries and medical and dental schools, institutions and clinics, is prohibited. However, this restriction shall not apply to persons intending to use such equipment and supplies solely for the application of radiation to other than human beings, nor to the acquisition of such equipment or supplies by wholesalers, distributors or retailers in the regular course of their trade or business.

The regulation was promulgated by the Public Health Council of the State of New York pursuant to section 225 of the Public Health Law, which, by subdivision 3 thereof, authorizes the council, with the approval of the Commissioner of Health, "to establish, and from time to time, amend and repeal sanitary regulations, to be known as the sanitary code of the state of New York," which may, according to paragraph (a) of subdivision 4 of the same section, "deal with any matters affecting the security of life or health or the preservation and improvement of public health in the state of New York."

It was found upon adequate evidence that when x-rays of the full spine are taken, the gonads or reproductive organs of the male or female patient are in the direct primary beam and susceptible to damage affecting the reproductive cells by producing deleterious changes in the genes and chromosomes of those cells, leading to mutations and resulting in serious abnormalities in the offspring in future generations; that leukemia may also be a consequence of x-ray exposure; and that the effects of a patient's exposures are additive and cumulative.

As alleged and proven, "the practice of chiropractic is a method of detecting and correcting, by manual or mechanical means, structural imbalance, distortion or subluxations in the human body for the purpose of removing nerve interferences where such interference is the result of or related to distortion, misalignment or subluxations of or in the vertebral column." Plaintiffs further aver that it is necessary for chiropractors "to use, take and interpret x-rays of the spinal column in order to detect structural imbalance, distortion, misalignment or subluxations of and in the vertebral column." The practice of chiropractic is not forbidden in New York; nor has the State acted to regulate or control it, whether by requirement for licensure or otherwise; and practice within the limitations implicit in the definition which has been quoted has never been held to constitute the unlawful practice of medicine. Acts and practice exceeding, or alleged to have exceeded those limitations, have been dealt with on an individual basis. (See, e.g., *People* v. *Maybrook*, 276 App. Div. 192, affd. 301 N.Y. 637, holding sufficient an indictment which charged that the defendant chiropractor's practice entailed diagnosis and treatment of such nature as to invade the field of medicine.)

Asserting, then, that chiropractors pursue a lawful calling, plaintiffs urge that the regulation, particularly in the light of the provision thereof which excepts from the initial prohibition "the use of radiation by a technician, nurse *or other person*," if directed or ordered by a physician, dentist, podiatrist or osteopath, contravenes the Constitution of the State of New York and, in certain respects, that of the United States as well; as constituting an invalid delegation of legislative power (cf. N.Y. Const., art. III, 1); as discriminatory against chiropractors, and so denying equal protection of the laws (U.S. Const., 14th Amdt.; N.Y. Const., art. I, 11); and as deprivative of property without due process of law (U.S. Const., 14th Amdt.; N.Y. Const., art. I, 6). Thus, appellants contend, the regulation delegates to members of the medical and other professions named the power to determine who may take x-rays, but fails, when so doing, to set standards for such determination or for the qualifications of the taker or the conditions of the taking. It is further urged that because, in appellants' view, a physician would not direct the use of radiation by a chiropractor, however skilled and competent, in violation of the rules of professional ethics inhibiting cooperation with cultists—the profession regarding chiropractors as such; and since, indeed, defendant Commissioner's testimony indicated his view that, under Regulation

19, chiropractors would not be permitted to take x-rays; the regulation is unconstitutionally discriminatory and constitutes a denial of equal protection; and serves, in addition, to deprive chiropractors of their right to pursue their calling and of the use of their lawfully acquired x-ray equipment, without due process of law.

Turning again to the proof, it seems evident to us, but in any event the promulgators of the regulation were clearly entitled to find, that medical knowledge and diagnostic skill are essential to evaluate the necessity of x-ray procedures in any particular case and to weigh the attendant risk as against the possible benefit to be derived. From the record itself, as from the common usage among chiropractors of obtaining spinal x-rays in a very large percentage of their cases (e.g., 75 per cent to 90 per cent in the cases of two of plaintiffs' witnesses as against less than 3 per cent of the cases under medical supervision in Johns Hopkins Hospital), arises the inescapable inference that the technical education, training and skill of chiropractors are, in general, substantially deficient in these vital areas of knowledge and judgment. Further, it is doubtful indeed whether technical knowledge in the requisite degree, if possessed by a particular chiropractor, could be applied to the problem posed by spinal x-ray without thereby constituting an unlawful invasion of the field of medical practice. In the testimony of a medical expert, which the Referee quite properly accepted, appears the succinct statement, "The thesis on which we operate is (that) radiation is undesirable and hence the clinical indications for the taking of a film or series of films must be established beforehand." Among chiropractors utilizing it, however, x-ray is usually the first or preliminary procedure. We find, therefore, that such relevant issues as arose with respect to the knowledge, competence and skill of chiropractors, as such, in the particular areas of judgment and decision thus far discussed, were properly resolved against appellants. We do not, however, regard the findings upon those issues as completely determinative of the case. They do serve to negate any suggestion—whether or not advanced by these particular litigants—that chiropractors, as such, are possessed of such knowledge and skill as to render arbitrary their exclusion from the class of practitioners of named professions authorized to apply radiation to human beings or to direct or order its application; and serve further to relegate chiropractors to the classes dealt with in the subsequent proviso regarding the use of radiation by other persons, including lay persons, upon the specific order or direction there provided for.

We turn, then, to appellants' argument, the main thrust of which is directed to the supposed exclusion of chiropractors from this latter class as well. It may be noted, parenthetically, that if exclusion exists it is not by reason of the proviso alone but as an effect of the extraneous factor of the ethical code to which we have alluded. We need not pass upon this factual issue, which appellants deem established, nor do we explore its legal effect, as we prefer to rest our decision upon the broader issues which the case presents and, accordingly, proceed to a consideration of them.

While disputing the validity of this specific regulation, and asserting its ineffectiveness to deal with the particular problem, appellants narrow the issues, both legal and factual, by their statement that, "Plaintiffs do not contend that a proper regulation may not be promulgated dealing with the taking of x-rays of human beings, nor that, if improperly taken, such an operation is not attended by a certain amount of danger to the subject of the operation." In seeking to combat that danger, the council could and did recognize the initial necessity of technical knowledge and skill to determine, in each case, the advisability of x-ray procedure, in the light of the clinical evidence at hand, the attendant risk and possible effects, and thereupon, in the event x-ray should be indicated, to direct the method, nature and number of exposures, and thus, in effect, prescribe the quantity of radiation to be applied. Consequently, the promulgators of the regulation committed an effective degree of responsibility and control to those most competent to exercise it. This was accomplished by providing that only those licensed under our law to practice medicine or one of the other professions named, and whose highly technical education, knowledge and skill had thus been determined and certified, should apply radiation, or direct its application, to a human being. Certainly the standards and requirements of qualification thus imposed could scarcely be more definite and certain or their fulfillment more readily demonstrable. Implicit in the two pertinent paragraphs of the regulation, when read together and viewed in the light of the record before us, is the intent to confer upon the authorized practitioner a measurable degree of authority and control. In context, the language as to radiation "directed" or "ordered" by a physician or other practitioner within the designated class, implies a form of direction and at least indirect supervision by professional authority, one of the more important factors of which is that thereby the amount of radiation to be applied to a particular area is prescribed and controlled by that authority. Additionally, the power of selection of the particular technician or operator implies a professional responsibility which, in practical effect, is not without weight and, indeed, its improper exercise could well give rise, in some conceivable situations, to legal liability as well.

Appellants would, however, and by what seems to us a forced construction, read into this otherwise simple provision a more complicated purpose and effect. They contend that thereby the practitioners of the professions named are empowered "to determine who may take x-rays," this pursuant to delegation of legislative power which is unlawful as fixing no standards of qualification or any guide for administrative action. (*Packer Collegiate Inst.* v. *University of State of N.Y.*, 298, N.Y. 184, 189.) The effect of the exceptive proviso permitting "other persons" to use radiation, when ordered or directed by a physician or other practitioner of a profession named, is not to confer a continuing privilege or a status akin to licensure on the part of the person directed to undertake a specific x-ray procedure upon a particular patient or to create a class of operators or technicians to which equally qualified persons are entitled to be admitted. If, however, the regulation could be deemed to set up a classification, such being conjoined with the provision for professional direction and control, a resultant exclusion of otherwise qualified persons would not necessarily—in a case involving public health and safety—invalidate the regulation (see *Matter of Stracquadanio* v. *Department of Health*, 285 N.Y. 93) but we do not reach that question. The standards which appellants find lacking do exist and are those required of the professional person at whose order or under whose direction the prescribed procedure is to be performed and the prescribed quantity of radiation applied.

That the Public Health Council chose to approach the problem from the angle of professional analysis, direction and supervision and not from that of the mechanical operation itself, or that the council failed to utilize both approaches, does not invalidate the resulting regulation. (Cf. *Radice* v. *New York*, 264 U.S. 292; *Central Lbr. Co.* v. *South Dakota*, 226 U.S. 157)

Since our construction of the exceptive proviso denies the creation of any classification, the case of *Matter of Sausser* v. *Department of Health* (242 N.Y. 66), upon which appellants strongly rely, is inapplicable. It is clearly distinguishable, in any event, as concerning not the validity of the regulation involved but the arbitrary action of the respondent under it.

The judgment should be affirmed.

Section 19 (*see 199*) Report 62–M

Supplementary Report of the Subcommittee on Federal Legislation

To the House of Delegates, Gentlemen:

The following is a resume of the activities of the Subcommittee on Federal Legislation since the report published in the April 15 issue of the NEW YORK STATE JOURNAL OF MEDICINE.

1. Arrangements were made to have Congressman Thomas B. Curtis, noted member of the House Ways and Means Committee, an aggressive foe of the Administration's plan for health care of the aged, HR 4222, speak at the annual meeting of our Society on May 16. Mr. Curtis was invited in an attempt to counteract the appearance of President Kennedy at Madison Square Garden on May 20 before a stacked audience of elderly citizens. Every attempt is being made to obtain as much coverage by radio, TV, press, and other media of information.
2. The April issue of the *Newsletter* was devoted to a special report on health care for the aged. It featured a rundown of developments up to the time of publication, sample advertisements for use by county medical societies, and an order blank for materials to be distributed by physicians in their offices. Other issues of the *Newsletter* gave considerable space to the campaign against HR 4222.
3. In early April an urgent plea was made to all county medical societies to set in motion immediately a crash program to offset the rapidly changing developments in regard to the King-Anderson Bill. This six-point program urged the societies to: (*a*) contact their congressmen during the Easter recess when they would be at home; (*b*) conduct an advertising campaign in all newspapers stating why the King-Anderson Bill should be defeated; (*c*) enlist the support of allied health groups; (*d*) reactivate the speakers bureaus; (*e*) urge their own members to write letters to their local congressmen and members of the House Ways and Means Committee; and (*f*) call on the Woman's Auxiliary for support in all phases of the outlined campaign.
4. A sample advertisement based on the one published by the Nassau County Medical Society was sent to every county medical society in the State. The purpose of this mailing was to stimulate as many societies as possible to conduct similar advertising campaigns.
5. An appeal was made by John M. Galbraith, M.D., our president, through a letter to key outside organizations, such as chambers of commerce, farm bureaus, dental associations, hospital associations, pharmaceutical associations, and others to join our fight by expressing opposition to HR 4222 to their own congressmen and to the House Ways and Means Committee.
6. Editors of county medical society bulletins were asked to use their publications to implement our efforts.
7. County medical societies were requested to follow up Dr. Galbraith's letter to outside organizations at the local level by personal contact in their own communities.
8. A special personal letter to all members of our Society and the Woman's Auxiliary was prepared for Dr. Henry I. Fineberg's signature on personal stationery. The purpose of this letter was to have as many doctors and their wives as possible write to their congressmen immediately after President Kennedy's address at Madison Square Garden on May 20. Plans called for the personal letter in an attempt to have as many doctors as possible read the message. These plans had to be abandoned because of lack of funds in the Federal Legislation Subcommittee's budget. The letter, however, was covered in the May issue of the *Newsletter*.
9. Many requests for speakers to address lay audiences were filled.

The end result of all these projects has been encouraging. As this report is being written more than 50,000 pamphlets have been distributed. The use of the order blank in the *Newsletter* and a special order blank mailed out to county medical societies brought numerous requests for these pamphlets. Several county medical societies have run ads in their local papers, notably Nassau and Monroe. Other county medical societies are planning radio, television, and press coverage. In one instance in order to defray these expenses a county medical society, Oneida, voted a special assessment of $25 per member. The county medical societies have been very active in supplying speakers for local groups. Numerous articles have appeared in county medical society bulletins.

Although sufficient time has not yet elapsed to receive many replies to Dr. Galbraith's letters to outside groups, those received have been in favor of our position.

We will continue our efforts to prevent the enactment of the King-Anderson Bill or any similar type of legislation. Your chairman, however, strongly urges every member of the House to supplement our efforts by cooperating in all our projects. At this particular time, we ask you to write your congressmen opposing HR 4222 immediately after President Kennedy makes a personal appearance in Madison Square Garden on May 20. Request your wives, relatives, friends, and patients to do likewise.

We wish to thank all who have assisted the subcommittee in our activities, particularly the Department of Communications.

Respectfully submitted,

GEORGE J. LAWRENCE, JR., M.D., *Chairman*

Section 20 (see 120) Report 62–P

Annual Report of the New York State Bar Association, Joint Committee with

To the House of Delegates, Gentlemen:

The joint committee of the Medical Society of the State of New York and the New York State Bar Association consists of the following members:

Medical Society of the State of New York

Milton Helpern, M.D., *Chairman*	New York
George A. Burgin, M.D.	Herkimer
Samuel Sanes, M.D.	Erie

New York State Bar Association

William F. Martin, Esq., *Chairman*	New York
R. Newell Lusby, Esq.	New York
Franklin R. Brown, Esq.	Erie

The joint committee did not hold any meetings during the year 1961–1962. A number of matters, especially the proposed lien law for physicians, were discussed by the cochairmen. The matter of the lien law proposal will be considered by the full committee at its next meeting, which is planned for the fall of 1962.

Dr. Helpern, one of the cochairmen, also spoke at a meeting of the Queens County Medical Society in September, 1961, on the activities of the office of the Chief Medical Examiner in New York City. During the year he has spoken on this and related subjects at a number of meetings of medical groups in the State.

In November, 1961, he appeared by invitation at a hearing held in Albany before the Law Revision Committee of the Legislature designated by the Governor to recommend new legislation which will provide for the establishment of a medical examiner's system in those counties desirous of abolishing the office of coroner and the appointment of qualified doctors of medicine to assist the coroner in those counties in which the office of coroner was continued and the coroner was a layman. This legislation accomplishing these aims was passed by both houses and signed by the Governor and is now Chapter 897 of the county laws.

In April, 1962, at Lyons, one of the cochairmen, Dr. Helpern, addressed a combined meeting of the Medical Society, the Dental Society, and the Bar Association in Wayne County on the inadequacies of existing statutes covering the operation of coroners offices in those New York State counties which use the coroner system.

Respectfully submitted,

MILTON HELPERN, M.D., *Cochairman*

SPEAKER WURZBACH: In your black book you have the place of meeting of each of the reference committees, all on the first floor of the hotel.

All reports will be mimeographed and distributed to the House. Those members interested will, of course, appear before the reference committees.

Section 21

Presentation to Speaker; Remarks of Speaker

GEORGE A. HOWLEY, M.D., *Bronx:* On behalf of the delegates of the Bronx County Medical Society, I should like to make a presentation to one who has been an associate of long standing, who has progressed to an esteemed honor, and who is a great friend. This is a compendium of parliamentary law, a simple explanation of the methods of organizing and conducting the business of societies, *Robert's Rules of Order.* May he not vary from these rules! To our esteemed friend, Frederick A. Wurzbach, Speaker of the House of Delegates, Medical Society of the State of New York, May, 1962, from the Delegates of the Bronx County Medical Society.

. . The delegates arose and applauded . . .

SPEAKER WURZBACH: This is a very, very pleasant gesture on the part of the Bronx County Medical Society, and I appreciate it, as well as the nice things that Dr. Howley had to say. I certainly will try not to deviate from the rules of order as laid down by the good Mr. Roberts.

There are a few things I would like to speak about. This in some ways is a new departure in this House of Delegates. We have instituted the idea that only delegates be in the enclosed areas, and this is the first time that the House of Delegates will be meeting for four days. It is certainly not an attempt to waste your time. We have felt for some time, especially Dr. Lane and myself in the last three years, that the rapid progress from meeting to meeting has in some cases brought before this House business that was not properly considered and was not in the proper form. We hope that this can be avoided in our present activity of four days, where this afternoon and all day tomorrow are set aside for the deliberations of the reference committees. We are very hopeful that this will prevent a great deal of discussion on the floor of the House, and that compromise, or adjustment of views is a different way of putting it, can take place at the level of the reference committee.

This morning when our reference committee chairmen met with Dr. Babbage and myself we outlined a course which I hope will make it easy for all you people attending the reference committees. These will meet individually in their rooms and will have the hearings. If there is any area of controversy, I have asked the chairman to notify the doctors appearing before the reference committee when he will have his rough draft of his report ready. He will then reconvene the reference committee, and again those interested could appear, and they could go over the rough draft, and perhaps at that time iron out the smaller difficulties. We hope that this will expedite the business of the House.

There is one other thing that I think is very important, and that is finances. Occasionally reports and resolutions come through with a very broad idea this could be financed by action of the Council and the Board of Trustees. We would hope that anyone presenting a resolution requiring expenditures would state the amount considered necessary to carry out this expenditure. In the reference committee we would ask that under these circumstances the treasurer, Dr. Dattelbaum, the chairman of the Budget Committee, Dr. Holcomb, and the comptroller, Mr. Alexander, be requested to appear at the reference committee to help in the decision on the expenditure.

There is plenty of time, as you know, to express your views before the reference committees, and we hope that everyone will do so. Even if you have not any special thing to present to the reference committee, we hope that you will go there even if it is just to understand better the democratic actions of this House of Delegates.

Dr. Babbage and I hope to expedite the acceptance of the reference committee reports by these procedures, but we promise you that in no manner will we attempt to stifle debate in the House or refuse the floor to any delegate.

Section 22

Introduction of New Delegates

SPEAKER WURZBACH: Now, gentlemen, we have a group of new delegates of the House. These neophytes are going to require a lot of guidance, and we hope that the wiser and certainly the older members will help them. I will ask each one as I call his name to stand and we will give them a little acclaim at the end of the list:

County Delegates

H. John Mellen, Albany
George C. Hamilton, Broome
Robert Barbieri, Dutchess
Irving Cohen, Dutchess
Raymond Koloski, Dutchess
Eugene J. Hanavan, Erie
Louis S. Hornstein, Kings
Harry S. Lichtman, Kings
Earle E. Barnes, Lewis
Hobart L. Boyd, Monroe
Allen H. Keniston, Orange
William S. Montgomery, Orange
Garrett W. Vink, Putnam
John J. Pohl, Rensselaer
James Alva Dingman, Rockland
William R. Carson, St. Lawrence
Jesse W. Mahoney, Suffolk

Section Delegates

Richard D. Wiseman, Allergy
Victor J. Tofany, Anesthesiology
Richard L. Saunders, Dermatology and Syphilology
Michael R. Deddish, Gastroenterology and Proctology
Henry Siegel, Medical-Legal and Workmen's Compensation Matters
Arthur Gordon, Medicine
Frederick H. Hesser, Neurology and Psychiatry
George M. Trainor, Otolaryngology
Vernon Weinstein, Surgery

District Delegates

Albert M. Biglan, Second
Lee R. Tompkins, Third
Milton Tully, Seventh

These are the new members. Suppose we greet them! (*Applause*)

Section 23 (see 174) Report 62–O

Supplementary Report of the President

SPEAKER WURZBACH: I will now ask Dr. Flood and Dr. Sullivan to escort President Galbraith to the rostrum.

. . .Leo T. Flood, M.D., and Paul M. Sullivan, M.D., escorted President Galbraith to the rostrum amid applause . . .

. . . President Galbraith then delivered his supplementary report as follows:

To the House of Delegates, Gentlemen:

This is a supplement to my annual report, which was published in the Delegates Handbook and in the NEW YORK STATE JOURNAL OF MEDICINE.

Many important events have taken place since I assumed the office of president last year, but the most important has been the unceasing drive by the Kennedy Administration to enact the King-Anderson Bill providing for medical care for the aged under Social Security.

Indeed, as we meet here at our annual convention, this campaign is in process of reaching its peak, with President Kennedy scheduled to appear at Madison Square Garden on May 20. The purpose of this rally is to arouse popular support for the Social Security approach to the financing of medical care for the aged, and I have a feeling that organized medicine will be the butt of many an attack.

We do not mind criticism; in fact, we welcome fair and open discussion of all issues affecting the American people. However, I suspect that what will be said at the rally will make the doctors of America look like selfish individuals who are more concerned with making money than ministering to the sick.

I feel fairly certain, moreover, that reference will be made to the action of those New Jersey physicians who, in their desire to express their abhorrence of the King-Anderson Bill, signed a resolution in which they threatened to "boycott" the program if Congress was ever unwise enough to adopt it.

Now, I am not sure that our colleagues across the Hudson did the best possible thing in taking the action they did, but I certainly sympathize with their feelings. After all, the King-Anderson Bill would harm the doctor-patient relationship. It would result in a lower quality of medical care. It would threaten the fiscal soundness of the Social Security system, thus placing intolerable burdens on the working people and future generations. And it would lead inexorably to further government intrusion into medical and hospital care, until the entire practice of medicine was, indeed, socialized.

Our critics will undoubtedly say that we have taken a negative approach to the problem, but my reply is that, if they were truly honest about the matter, they would acknowledge that medicine has in fact assumed a positive, constructive position in its support of the Kerr-Mills Law. Peculiarly, not many people seem to know about this statute, but even those who do appear in many instances to have little understanding of its provisions. As a result, physicians are accused of opposing medical care for the aged per se. As a matter of fact, it is because we are concerned about the aged that we are opposed to the King-Anderson or Social Security method of financing their medical care.

I would like to ask one question: "What group of individuals except the medical profession has cared for the health needs of the aged all through the years before politicians found it politically expedient to corrupt these needs for their own selfish interests?" If the Kennedy Administration could accomplish one one-hundredth of the significant aid and help to the aged that the doctors of this country have accomplished, and are accomplishing, every day, I would be the first person to applaud its efforts. As it is, the Administration's sole interest lies in the political advantages that it is attempting to foster. Recent statements by the Secretary of Health, Education, and Welfare, Abraham A. Ribicoff, clearly indicate a philosophy that local and state governments are either incompetent or too feeble to do anything constructive about the health care of the aged. Evidently, only big government in Washington "knows best" in spite of its known inefficiency and appalling costs in carrying out any projects.

Only last week, the executive vice-president of the A.M.A., F. J. L. Blasingame, M.D., called for an investigation of Secretary Ribicoff to determine if he had committed a criminal act. A telegram was sent by Dr. Blasingame to Attorney General Robert F. Kennedy, charging that the Secretary had published a booklet on health care for the aged and in doing so was lobbying for legislation in violation of Federal law. He pointed out that the Department of Health, Education, and Welfare has used tax funds collected from everyone to propagandize for a bill which many people and many groups have vigorously opposed. He said that, under the law, the publishing of this kind of booklet without congressional authority is a criminal act, punishable by a fine or imprisonment, or both, and removal from office.

Dr. Blasingame contended that a foreword in the booklet by Mr. Ribicoff certainly constitutes printed or written matter intended to influence members of Congress to enact the King-Anderson Bill, now pending in the House Ways and Means Committee.

Members of the House, I have discussed the issue of medical care for the aged at some length because in my view it overshadows all else at this time. However, I shall now consider a number of questions affecting our Society as a Society, so that we can emerge from this annual meeting stronger and better equipped to meet the many problems confronting us.

Osteopathy. As the delegates know, the American Medical Association last year declared that relations between medicine and osteopathy were matters for the respective states. Your Society implemented this policy statement when, with the approval of the Council, I appointed an ad hoc committee to confer with representatives of the Osteopathic Society and discuss mutual problems with them.

The two committees or, rather, the joint committee consisting of representatives of the two professions has held three meetings. Norman S. Moore, M.D., chairman of our delegation, and I can report that the conferences have been harmonious and friendly, and that an understanding was reached on the following points:

1. Osteopathy in this State is no longer considered a cult, since osteopaths are licensed to practice medicine and surgery by the State Board of Medical Examiners and adhere to the same scientific principles as are embraced by doctors of medicine.

2. Doctors of medicine may associate professionally, on a voluntary basis, with doctors of osteopathy who hold full licenses to practice medicine and surgery from the State Board of Medical Examiners.

3. It was agreed that our Society's publication, *What Goes On*, will be distributed to doctors of osteopathy to apprise them of what is taking place in the field of postgraduate medical education. We also agreed to recommend to our county medical societies that they invite doctors of osteopathy to their scientific meetings and seminars. For their part, the osteopaths agreed to invite doctors of medicine to attend their conference.

The joint committee will hold additional meetings in the future, so that the two professions can come to an even better understanding of each other. Among the matters that have yet to be thrashed out are hospital appointments for osteopaths and possible cooperation on certain legislative questions. In connection with hospital appointments, the idea has been proposed that the requirement regarding county medical society membership might be altered to include the following clause: "Membership in a recognized local or state professional society of osteopathic physicians or doctors of medicine."

As to legislative matters, there have already been useful discussions of the chiropractic question and other issues of mutual concern. Osteopaths hold to the same point of view as we do in terms of Kerr-Mills and King-Anderson legislation.

I foresee good results from these efforts.

Visit to Washington. Repeating the successful journey made in 1961, a delegation of 20 physicians from our Society visited Washington at the end of February, to confer with members of Congress from New York State. As was the case last year, the congressmen we talked to showed great interest in our views even when occasionally they did not agree with us. As for Senator Javits and Senator Keating, we had a special conference with these two gentlemen, at which we expressed our opinions concerning the King-Anderson Bill.

I believe these trips to the nation's capital are very useful. We may not see immediate, tangible results from them, but I believe they create a favorable climate that will, in the long run, pay off. I recommend that they be continued in the future.

I again wish to commend the A.M.A. staff in Washington, D.C. They represent American medicine in a forceful, dignified way.

Change of Name of Our Society. I have mentioned this matter before, but I should like to recommend that we change the name of the Society from the Medical Society of the State of New York to the New York State Medical Society. I make this recommendation for several reasons: (1) Our present name gives the impression to some people that we are an official or semiofficial governmental agency; (2) It is so long that, frankly, I rarely hear anyone using it in its entirety; (3) The news media never use it, preferring the New York State Medical Society or the State Medical Society.

I urge the House to give this matter appropriate consideration and not defer action for another year.

New York State Association of the Professions. I have already referred to the New York State Association of the Professions in my earlier report, but I consider the creation of this organization so important that I should like to make a few additional comments. As I view the matter, the time is ripe for all professions to join forces and take action on questions of mutual concern. As physicians, we have special problems, but we have many that also affect dentists, architects, engineers, pharmacists, veterinarians, and others. There is much common ground, therefore, and if this new organization had not already been formed, something like it would surely have had to be formed sooner or later. All professions are concerned with becoming socialized by the Federal Government.

Periodic Review of Policy. Like virtually all organizations, our Society has taken positions over the years on various issues. Most of our policies are probably still pertinent but the likelihood is that many no longer meet the needs of the times and should be changed.

Accordingly, I recommend that we deal with this matter in the same way as such other groups as the U.S. Chamber of Commerce have done, and that is to establish a special policy review committee or to assign this task to a committee already in being—in our case probably the Planning Committee.

The job of such a body would be to review a certain percentage of all State Society policies each year, say one third, so that in three years time, consideration of all our policies would have been made, and recommended necessary changes or modifications would be presented to the House of Delegates. In this manner, the Society's officers and staff will know at any particular time just what our current position is on a given issue, and not wonder whether the resolution or statement that had been approved many years before was really the present position of the organization.

Commission on Public Affairs. Our State Society has now had a Commission on Medical Services for a period of time and, by all accounts, it has been a successful instrument. In view of the overlapping that now exists in the areas of public relations and legislation, I recommend that the Society consider the establishment of a Commission on Public Affairs.

In my opinion, such a commission would bring about greater coordination and integration of our activities in public relations and legislation, thus strengthening the implementation of our program. At the same time it would provide us with the opportunity of, perhaps, making a full committee out of the present Subcommittee on Federal Legislation, so that the Commission would consist, at least at the beginning, of three committees: Public Relations, State Legislation, and Federal Legislation, and could include the Special Committee on American Medical Education and Research Foundation, Prize Essays, and New York Association of the Professions.

I think that such a commission would have further value in being able to cope with problems impinging on public affairs that are now in a sort of "never-never land." I mean problems that are not clearly within the area of any one committee and yet call for consideration or action on our part.

I cannot conclude this report without expressing my thanks to all those who made my burdens somewhat lighter during the past year; in fact I enjoyed this a great deal. I am especially grateful to my fellow officers, the members of the Council, the trustees, and many of the committee chairmen, who gave me invaluable assistance in carrying out my duties.

As for the administrative functions of the State Society, I would like to compliment Dr. Fineberg on the excellent way he has carried out the administrative functions of the Society during his first year of service as executive vice-president. It has not been easy.

There is one point which I would like to bring to your attention. It is important in the future that all members recognize that in contacting the Society, even though they are communicating directly with the staff under the function of the executive vice-president, they at all times should work through his office. This office must not be bypassed but must be kept informed so that final administrative decisions can be carried out under the direction of Dr. Fineberg.

The same is true of the staff. When they are working with officers and committee members, they are, in essence, the official representatives of the executive vice-president.

It would be remiss of me not to make special mention of the scientific program starting today. A special vote of thanks must go to Alfred P. Ingegno, M.D., chairman of the scientific portion of our program, as well as to Bernard J. Pisani, M.D., convention chairman, and Samuel Wagreich, M.D., dinner chairman.

The theme of the program, "Medical Centers on Parade," is unique, and I know that it will prove most beneficial to all physicians who participate in it. It pleases me very much that the medical centers are playing a key role in our program because I believe that there should be greater cooperation and understanding between our full-time doctors and practicing physicians.

Allow me to thank the Society for electing me its president, for this has been an eventful and rewarding year, a year I shall never forget.

I leave office, however, with the knowledge that the Society during the next year will be in capable hands. The man who will serve as your president, Joseph A. Lane, M.D., has the character, intelligence, and fortitude to steer our particular ship to safe harbor. Storms there will be aplenty, and even some hurricanes, but we have a good ship, a gallant crew, and a topnotch corps of officers, and we know where we are going, which is a lot more than most people do.

There is no doubt that we will have a successful voyage.

Respectfully submitted,
John M. Galbraith, M.D., *President*

. . .The House arose and applauded . . .

Speaker Wurzbach: The matters presented by the president in this supplementary report will be referred to the proper reference committees as portions of it are found to be relevant to that reference committee's work.

Section 24 (see 175) Report 62–N

Report of the President-Elect

Speaker Wurzbach: Now I would like to have Dr. Mathews and Dr. Tully come forward and present Joseph A. Lane, M.D., our president-elect, at the platform.

. . . Charles R. Mathews, M.D., and Milton Tully, M.D., escorted President-Elect Lane to the rostrum amid applause . . .

. . . President-Elect Lane then delivered his report as follows:

To the House of Delegates, Gentlemen:

It scarcely seems possible that a year has elapsed since you were kind enough to elect me to this high office in the State Society. It has been a very busy year spent in congenial working arrangements with my predecessor, John M. Galbraith, M.D., and I hope that my successor will find his year as pleasant and as productive as I have found the past twelve months.

I come before you to discuss several items that I think are of major importance to all members of the State Society. I am fairly sure that you are all cognizant of the fact that the Planning Committee has been completely revised and has been very active in the past year. You will find a detailed report by its chairman, James Greenough, M.D., elsewhere, and I refer you to it.

However, some of the recommendations of the Planning Committee have a definite bearing on operations of the Society in the future, and especially this coming year.

A subcommittee of the Planning Committee, headed by Norman S. Moore, M.D., made a rather extensive study of committee structure and has recommended extensive changes. These changes were recommended for facility of action as well as to help reduce operating costs for the Society. With few exceptions, committees will not be composed of more than five members; many committees will be composed of only three members. Advisers and staff members will be indicated only in those instances where it is felt important that they should be so indicated. The latter will be assigned, in most instances, by the executive vice-president of the Society. Often committees have been eliminated completely, one or two have been absorbed into other committees of which they seem to be an integral part, and one or two new committees have been formed, particularly as subcommittees of the Public Health and Education Committee. It is hoped that these changes will be very effective in many ways as we learn by experience with them.

Dr. Galbraith has already alluded to the recommendation to change the name of the Society. I heartily endorse his recommendation and hope the reference committee will take proper action on this recommendation.

At a meeting of our county society recently, I was greatly disturbed to learn that the Physicians' Home received very poor financial support. Out of an active membership of 850, there was a shockingly low total of only $660 donated to this organization by my own county society. This included the $2.00 voluntary contribution which is listed on the county society bill. I wonder how many of you realize that there must be recipients of this fund in your own neighborhood or in your own county society. These people are never indicated by name, and many of them are existing almost exclusively on the funds supplied by the Physicians' Home. You receive a request annually for donations other than the $2.00 voluntary contribution, and I cannot urge you too strongly to support this worthy cause. May I suggest that each one of the delegates here likewise strongly urge his own county society members to contribute a minimum of $10 annually to this cause.

Over the years one of the difficulties of operating the State Society has been to project a budget for the future. Regularly recommendations have been made in the Council as well as in the House of Delegates for activities which involve the expenditure of funds. The policy has been that these requests for funds be referred to the Board of Trustees for their consideration and approval or disapproval. Until recently there has been great hesitation on the part of the Board of Trustees, of which John J. Masterson, M.D., is currently the chairman, to turn down these recommendations. This liberal policy has resulted in approval of funds, sometimes far in excess of anything that was anticipated at the beginning of the fiscal year. During the past year a great effort has been made to tighten the purse strings and to live within the budget. This coming year, under the direction of our executive vice-president, it is anticipated that each department will be required to submit a line budget which will have to be approved by the Board of Trustees, after study by the Budget Committee, and the departments involved will have to live within this budget. Until now we have been existing in an era of deficit financing. This new method of budgeting, it is hoped, will be one means by which deficits can be eliminated in the future.

We must face facts at this session and be realistic; therefore, you will be asked to approve an increase in dues which will allow your Society to eliminate the current deficit and to operate in the black in the future. I can assure you that a great deal of time, thought, and consideration has been given to this very serious problem during the past few months.

In your black book you have a page to which I would refer you, which lists the dues of all of the state societies throughout the country (*see Table I in Supplementary Report of Trustees, Section 14*). If you peruse that carefully you will note that there are only three state societies in the country whose dues are less than ours, and at best 33 above ours, going up to $200 for one state and $100 for another.

I cannot compliment adequately the members of the Budget Committee headed by Frederic W. Holcomb, M.D., the Board of Trustees, and the staff members involved, for their efforts in trying to bring about a resolution of our financial problems. They deserve your wholehearted support in spite of the fact that your pocketbook may be pinched a little bit.

Another problem in the home office has been to set up a job analysis, which has been completed, and within which structure the office now operates. A handbook is now being prepared for all the staff so that they will know their responsibilities, their privileges, and their assignments. Henry I. Fineberg, M.D., deserves commendation for his special work in this area.

In legislation, our main problem still continues to be vigorous opposition to the King-Anderson Bill and strong support of the Kerr-Mills Law as implemented in our State by the Metcalf-McCloskey Act. I believe it is evident to everyone that the Administration is going all-out in its efforts to gain support for the King-Anderson Bill. We must do all we can to support Kerr-Mills and Metcalf-McCloskey.

We have reached medicine's most crucial hour in American history. It is the duty of each one of us, as citizens and as physicians, to voice our vigorous opposition to HR 4222 by writing or wiring our congressmen on May 21. I strongly urge you to enlist also the support of your wives, relatives, friends, and patients in expressing their disapproval to their congressmen.

I am sure that you have all read that the appeal of the chiropractors regarding the use of x-rays has been denied and will now be taken to the highest court in the State. It is very satisfactory to note that the appeal was denied by a unanimous vote of the court. It is planned to have a meeting in the near future between representatives of the Governor of your State and of representatives of the Osteopathic Society in order to discuss plans for next year's legislative program concerning chiropractors.

In the past many of the reports of officers have received laudatory commendation by the reference committee to which they have been assigned, but other than that no action has been taken concerning the recommendations made in the particular report. May I ask the reference committee to give serious consideration to the recommendations I have made in this report as well as any important recommendations that have been made in the reports of other officers. This cooperation will be greatly appreciated.

May I suggest that appropriate resolutions be formulated by the appropriate reference committee to be presented to the House to implement these recommendations.

Allow me to thank you for your indulgence today, and may I ask for your support during the coming year. I anticipate that the next twelve months will be a most active period, filled with numerous problems. These, I am certain, can and will be solved through the excellent cooperation you have demonstrated in the past.

Thank you very much.

Respectfully submitted,
JOSEPH A. LANE, M.D., *President-Elect*

. . .The House arose and applauded . . .

SPEAKER WURZBACH: These remarks by President-Elect Lane will be referred to the Reference Committee on Reports of Officers.

Awards and Guests

Section 25

Greeting from State Health Department

Speaker Wurzbach: Will Dr. Moore please present Dr. Larimore at the platform?

. . . Norman S. Moore, M.D., presented Granville W. Larimore, M.D., at the platform amid applause. . .

Speaker Wurzbach: Ladies and gentlemen of the House, Dr. Herman Hilleboe is very busy today teaching. Not only is he the Commissioner of Health of the State of New York, but he is a very active teacher. He has designated that the assistant commissioner, Dr. Larimore, represent him at this time, so I will call on Dr. Larimore for a few words.

Granville W. Larimore, M.D.: Thank you very much. Dr. Hilleboe expressed his regrets in not being able to be here this morning to express to you the very great appreciation which we in the State Department of Health have toward the State Medical Society, and for the very cordial working relationships which we enjoy in the State. We are most pleased to work with you as coworkers for the health of the State and to join with organized medicine in its many battles which it faces.

Thank you very much! (*Applause*)

Speaker Wurzbach: Thank you, Commissioner Larimore.

Section 26

Presentation of Award to Outstanding General Practitioner

Speaker Wurzbach: I now wish that the committee consisting of Drs. Howley, McCarthy, Bernard, and Lieberman present at the podium Dr. Wagreich to receive his citation as the Outstanding General Practitioner of the Year.

. . . George A. Howley, M.D., Thomas F. McCarthy, M.D., Marcelle T. Bernard, M.D., and Samuel Lieberman, M.D., escorted Samuel Wagreich, M.D., to the podium amid applause. . .

President Galbraith: Members of the House, it is indeed a great pleasure for me to give the annual award of the Medical Society of the State of New York for the Outstanding General Practitioner of the Year to Dr. Samuel Wagreich in recognition of his selection as such by the Council for the year 1962. (*Applause*)

Samuel Wagreich, M.D.: Dr. Galbraith, Mr. Speaker, ladies and gentlemen of the House, I accept this award with mingled emotions of humility and pride, and a great expression of appreciation and the feeling that this award that I have just received in truth does not belong to me but belongs to the very many people who have contributed to this annual award. So it is proper at this time that I express my appreciation, first, to the members of the House of Delegates who have accepted me amongst them for the past ten years to have by virtue of their friendship and brotherhood exhibited the kind of indoctrination which has made it possible for me to continue to work in behalf of medicine and the public we serve.

I wish to express my appreciation to the speaker who, as a personal friend of mine for many years, has encouraged me and helped me to work on behalf of the causes that we espouse.

I would like to express my appreciation to the presidents of the State Society, more recently Dr. Henry Fineberg, Dr. Norman Moore, and Dr. John Galbraith, and the many others who have preceded them, the officers of the State Society, and the Council who have given me an opportunity to serve on behalf of the Medical Society of the State of New York.

I would like to express my appreciation to the officers and members of the Coordinating Council of the First District Branch of the Medical Society of the State of New York, who have supported me and given me an opportunity for leadership, and have represented a very strong body in New York City medicine.

I particularly want to express my appreciation to the membership of the comitia minora of my Bronx County Medical Society, and standing here with me I wish especially to express my appreciation to our present president, the leader of our delegation, Dr. George Howley, as well as Tom McCarthy, and to tell you how much they have meant to me in the work which I have had an opportunity to perform. Also the sponsor of my campaign, I understand now belatedly, and one who perhaps singlehandedly has done more than anybody else to win this award for me, the chairman of our awards committee, Marcelle Bernard, on my left, who has certainly done a yeoman job, and also with us, Dr. Samuel Lieberman, the chairman of the board of directors of the State Academy of General Practice and the president of the Bronx Chapter of General Practice, who have espoused my cause and have helped me to accomplish this honor; to the very many organizations who have contributed and who have sent in letters on my behalf, I am truly grateful. In the final analysis they by giving me an opportunity to work for their organizations have helped me and directed me in the course of the activities which I have performed.

And, of course, as is usual in this type of situation, it is always proper to express one's appreciation to my wife and family who have stood by, encouraged, and have put up with all my many "shenanigans" over these many years. All these factors have served to contribute, to help, to give me direction, have enriched my life, have given it meaning and purpose.

To all of these I am truly grateful, and now in conclusion over the last few weeks you may perhaps have read a good deal about the Hippocratic Oath. I think it is proper and fitting that I, in the presence of this House of Delegates and in the presence of my peers, renew and swear again my allegiance to the Oath of Hippocrates, and swear that I will continue to serve the people of our community, and that I will serve to reflect credit and honor on medicine, which truly is the noblest profession of all. I swear it, so help me God.

Thank you! (*Applause*)

Section 27

Presentation of Redway Award

Speaker Wurzbach: Our next order of business is the presentation of the Redway Medal and Award for outstanding medical writing. I would ask Jerome A. Urban, M.D., to come forward to accept this, and I would ask Dr. Masterson please to present Mrs. Redway at the platform.

President Galbraith: Members of the House, it is a distinct pleasure to announce at this time the winner of the first Redway Award. This annual award, in honor of our late editor, Laurance David Redway, M.D., of a gold medal and a cash prize of $500 will be awarded each year to the writer of the article judged best of those published in the New York State Journal of Medicine during the preceding year. The award this year goes to Dr. Jerome Andrew Urban for a three-part article on "Current Trends in Breast Cancer Treatment," which appeared in the Journal September 15, October 1, and October 15, 1961. This comprehensive review of a difficult and complex subject was written with great clarity and distinction and made a definite contribution to the literature on the subject.

Dr. Urban graduated from Columbia University College of Physicians and Surgeons, is a Fellow of the American College of Surgeons, associate attending surgeon at Memorial Hospital, and clinical assistant professor of surgery at Cornell University Medical College.

We are most fortunate in having with us today Mrs. Virginia Larkin Redway, who will present the medal in honor of her late husband to the winner, Dr. Jerome A. Urban.

Mrs. Virginia Larkin Redway: Mr. Speaker, Dr. Galbraith, president of the Medical Society of the State of New York; Dr. Ingegno, chairman of the Publication Committee, members of the House of Delegates, and Dr. Hammond, editor of the Journal: I have many things to thank you for—your kindness in establishing the Laurance D. Redway Award for Medical Writing; the splendid plaque of my husband, which is so skillfully sculptured by Carl Schmitz, which Dr. Hammond brought to me last week. It really seems like a speaking likeness. I am so grateful to you all for the special copy you gave me last spring of the memorial issue of the Journal, January 1, 1961.

Today I want to thank you for choosing me to make the presentation of the first Laurance D. Redway Award for Medical Writing. I am happy in being a part of this program.

The memorial issue of the Journal voiced many beautiful tributes to my husband. Among them was the very understanding one written by your president, Dr. Galbraith. He spoke of what he considered outstanding characteristics of Larry, namely, his humor and humility.

I agree with him, and with your permission would like to cite two short examples: In the category of humor, the riotous and fabulous book he wrote called *The Springtime of Physick*, being a diverting outline of the history of medicine and surgery. He dedicated it to me, "To my wife who has let me alone."

And in the category of humility I want to present a short excerpt from his beautiful editorial for the 1956 Christmas issue. You, no doubt, have all read it, but I would like to read it again to you:

> The Journal is a collective enterprise . . . It is the product of men's minds and hearts, of their toil and ingenuity throughout these years. To what end? That knowledge and scientific truth shall flow continuously from its sources to our readers. In a small way the Journal seeks to aid the great advance of learning, to present the picture, in vignettes, of the procession of medical history of the State, to further the peaceful arts of healing to the comfort of mankind.
>
> Surely there is here in our privilege to write and publish freely much to be thankful for, much to gladden the heart and uplift the spirit. To have a part, however small, in the great purpose of the Creator is a joyful thing. So to you all wherever you may be, season's greetings.

Now it is my privilege to present this to Dr. Jerome Urban.

Jerome A. Urban, M.D.: It is with a great deal of humility and a sense of great respect for your husband, in whose honor this award is given, that I accept it with thanks.

Section 28

Address of President of Woman's Auxiliary

Speaker Wurzbach: Now, ladies and gentlemen of the House, I am going to break into the routine for just a moment. I am going to ask Dr. Moore to present at the platform the president of the Woman's Auxiliary to the Medical Society of the State of New York, Mrs. Eugene Wolff.

Mrs. Eugene F. Wolff: Thank you very much. Dr. Galbraith, Dr. Wurzbach, Dr. Moore, Dr. Fineberg, and all distinguished delegates and members, as the twenty-sixth president of the Woman's Auxiliary to the Medical Society of the State of New York, I note a difference of one hundred thirty organizational years between us. We are proud of our twenty-six years and our relatively brief history.

For your information I submit some Auxiliary highlights and statistics for 1961–1962: We have 52 organized counties; one new county organized this year, Putnam County in the Ninth District; one county reactivated, Fulton County in the Fourth District.

The president sent out 325 notes of welcome to new members.

Auxiliary members in New York State number 4,971; your Medical Society figure is 25,273.

We have 116 nursing scholarships given this year and 3 medical scholarships. Over $22,264 were given in scholarships in this 1961–1962 year, and since the inception of the program 823 scholarships and over $209,000.

Legislation was and is our number one priority. Almost every county participated. Letters and telegrams were sent to senators and congressmen favoring the Kerr-Mills Bill and opposing King-Anderson legislation and chiropractic licensing.

A total of 37 counties played the A.M.A. record, "Operation Coffee Cup." Schenectady County did this neighborhood by neighborhood. Dutchess County organized a legislation study group, with the approval of its county medical society which helped finance the course. Westchester County Medical Society coordinated with a panel moderated by Dr. Charles Brane and Dr. Sudbay, legislation chairman, and this program supplemented the Auxiliary legislation program.

For the A.M.E.R.F. we have raised over $9,229 to support the medical schools. The County of Albany was the highest contributor with $2,756.

By June I will have completed 16,000 Auxiliary miles.

I would like to quote to you from Goethe, because this expresses my feelings quite well: "To walk with you, Doctor, is honorable and beneficial."

I thank you. (*Applause*)

SPEAKER WURZBACH: Thank you very much, Mrs. Wolff.

Section 29 (see 186)

Presentation of Bernstein Award

SPEAKER WURZBACH: Next is the presentation of the Albion O. Bernstein, M.D., Award, which has been made possible by the father of this young physician, Mr. Morris Bernstein. I will ask Mr. Morris Bernstein to come to the platform with Dr. James O. Elam for the presentation of this award, please.

PRESIDENT GALBRAITH: We are deeply honored today to be able to inaugurate an award that will become an annual event here at our annual meeting. I am sure that you have all read in our *Newsletter* or in the publicity that has been circulated about the Albion O. Bernstein, M.D., Award.

This award has been started in memory of a brilliant young doctor whose untimely death occurred while he was making an emergency medical call. This award of $1,500 and a scroll are to be given annually to the physician, surgeon, or scientist who makes the greatest contribution to medicine during the preceding year.

The Special Committee on Prize Essays of the Medical Society of the State of New York has chosen as this year's recipient of the Albion O. Bernstein, M.D., Award James O. Elam, M.D. Dr. Elam earned the plaudits of his colleagues who recommended him so highly for this honor for his research in the field of resuscitation.

JAMES O. ELAM, M.D.: Mr. Speaker and delegates of the Society, as a physician I am deeply grateful to you because in this award I interpret the recognition of the value of a method of mouth-to-mouth breathing.

You know there is often a paradox between something that is obvious and works and the popular acceptance of it, and in the field of resuscitation it has often been the tendency for physicians to leave the selection of methods to others, who find it difficult to make the wise decision.

As an anesthesiologist, I am very grateful for this award because to me this implies a recognition of the fallacy of the manual method, which is simply that of airway structure. Had it not been for studies in anesthetized patients, our leading method of resuscitation might still be unrecognized, knowing the chest will move air into and out of the lungs despite complete obstruction by the tongue.

Finally, I would like to mention the rewarding trend that one sees today in resuscitation, namely, that physicians all over this country and all over the world are assuming the leadership, the supervision, and the consultation in this extremely important field and not leaving it to the first aider who very much needs our counsel and our help.

Thank you very much. (*Applause*)

Section 30

Citation for Meritorious Service

SPEAKER WURZBACH: Our next Citation for Meritorious Service for New York State from the President's Committee on Employment of the Physically Handicapped goes to James H. Sterner, M.D., medical director, Eastman Kodak Company.

PRESIDENT GALBRAITH: It is a pleasure to present the Presidential Citation for Meritorious Service to James H. Sterner, M.D., medical director of the Eastman Kodak Company. The State Medical Society recommended Dr. Sterner for this award in recognition of his outstanding service in the field of rehabilitation employment of the handicapped. Dr. Sterner is the nominee for the national award by the President's Committee on Employment of the Physically Handicapped.

JAMES H. STERNER, M.D.: Mr. Speaker, delegates and friends, I am, of course, highly honored to have this recognition, but I have a deep understanding that in accepting this we are really honoring the legion of handicapped workers whom enlightened management and whom the general public have helped restore to useful life, and this honor really goes to the people that we have helped who have proved that our efforts have been worth while.

Thank you! (*Applause*)

Section 31

Presentation of Industrial Health Award

Speaker Wurzbach: Next is the presentation of the Industrial Health Award to William P. Shepard, M.D., of New York County, past chairman of the Council on Occupational Health of the American Medical Association. This presentation will be made by Dr. DiNatale.

Peter J. DiNatale, M.D.: Mr. Speaker and members of the House, on behalf of the Medical Society of the State of New York through its Committee on Industrial Health, I have the distinct honor to present to William P. Shepard, M.D., this plaque in recognition of his many years of service in the field of occupational health. Dr. Shepard, congratulations!

William P. Shepard, M.D.: Mr. President, Mr. Speaker, and friends, I have sometimes had the feeling that it has fallen to my lot to be a prophet without honor in his own land. I have no reason for feeling that way now. I had to allocate my voluntary services to such agencies as seemed to be most interesting, and thus could take on only one or two things at a time.

Most of my time was spent with the A.M.A., as you know as chairman of the Council on Occupational Health, a job which I am so glad Jim Sterner has taken over and which I am sure he will cover with much greater distinction than I.

It has been a matter of pride to me, likewise I am sure I speak for the Council—I am sure Dr. Sterner would endorse this—that the Medical Society of the State of New York was to my knowledge the first to appoint a full-time executive in the field of occupational medicine and workmen's compensation. This is an accomplishment indeed and one which we think will be followed by other societies.

It has been a pleasure to work with Dr. Katz, the director. It has been also a pleasure to work with Pete DiNatale, who like the postman comes sleet, or rain, or snow, and gets down here for meetings from the upper part of the State on each occasion.

I thank you very deeply and I am greatly honored. (*Applause*)

Section 32

Presentation of New York Service Scroll

Speaker Wurzbach: In regard to the next presentation, were the speaker to request any individual person in this room to present the recipient at least one hundred others would feel greatly slighted. This man is so outstanding in the work he has done and is so close to us, so many of us personally, that I am going to ask him to rise and come forward entirely on his own, Dr. David J. Kaliski, please.

. . . The House arose and applauded. . . .

President Galbraith: Developing the workmen's compensation program in New York State is really a mammoth job, and we are proud to present this scroll to David J. Kaliski, M.D., for the dedicated endeavors he has put forth in this cause. He has pioneered this work in our State, and on behalf of the physicians of New York it is my pleasure to recognize the many years of his devoted efforts today.

David J. Kaliski, M.D.: Mr. Speaker and gentlemen, I am very happy that the work which we began actually in 1931 is being so well carried out, and that the law which was amended as a result of the Governor's Commission at that time has remained in effect without any material changes.

I want to thank you very much for this presentation. (*Applause*)

Section 33

President's Citation for Distinguished Community Services

Speaker Wurzbach: Next are the President's Citations for Distinguished Community Services.

President Galbraith: Mr. Speaker and members, my predecessor, Dr. Norman Moore, on leaving office last year initiated the President's Citation in recognition of physicians who have done outstanding work in their communities during the year.

I have the honor of following in the footsteps of Dr. Moore by again this year presenting this citation to physicians who have been designated by their peers and lay leaders in their communities as worthy of recognition for distinguished public service in community affairs.

It is always a great pleasure to extend these awards as tokens of the State Society's appreciation of public service performed by its individual members; but this year, coming at a time when the profession of medicine is being maligned by the various pressure groups proposing socialized medicine, it was particularly gratifying to read the letters of commendation about the recipients and to learn how much unheralded civic work is done by our individual physicians.

So at this time we take the opportunity to present the following President's Citations. I ask each of the recipients to step forward as his name is announced. Please withhold your applause until the citations have been presented:

Henry J. Barrow, Bronx
Charles M. Brane, Yonkers
Jeff J. Coletti, Old Westbury
Abraham W. Freireich, Malverne
I. Melbourne Greenberg, Freeport
John W. Hirshfeld, Mohawk
Harvey P. Hoffman, Buffalo
Gordon D. Hoople, Syracuse
Richard C. A. Jaenike, Rochester
David Kershner, Brooklyn
William L. LaDue, Plattsburgh
John E. Lowry, Flushing
John D. Naples, Buffalo

John L. Norris, Rochester
Clarence R. Pearson, Scottsville (deceased)
Charles Prudhon, Watertown
Fred C. Sabin, Little Falls
Cassius D. Silver, Plattsburgh
John Shell, Freeport
Reginald R. Steen, Hempstead
Rudolf H. Steinharter, Hempstead
Charles L. Steyaart, Lyons
W. Walter Street, Syracuse
Walter Scott Walls, Buffalo
Earl C. Waterbury, Newburgh
John E. Wattenberg, Cortland
Karl N. Wechtel, Woodmere
Myron E. Williams, Jr., Batavia
John R. Williams, Sr., Rochester

"This citation is hereby presented in recognition and grateful appreciation for distinguished community services." (*Applause*)

Section 34

Presentation of Checks from A.M.A. Education and Research Foundation

Speaker Wurzbach: The next order of business is the presentation of checks from the A.M.A. Education and Research Foundation to the deans of the medical schools in the State of New York.

President Galbraith: To Albany Medical College, we are presenting a check for $7,215.07; to Cornell University Medical College $14,832.57; to University of Buffalo School of Medicine $7,980.57; to Albert Einstein College of Medicine $5,264.15; to New York Medical College $7,675.57; to State University of New York Downstate Medical Center $5,758.07; to Upstate Medical Center $5,983.57; to New York University School of Medicine $8,827.13; to Columbia University College of Physicians and Surgeons $10,743.22; to University of Rochester School of Medicine $6,860.07. (*Applause*)

Section 35 (see 96, 135, 182)

Introduction of Guests

Speaker Wurzbach: Now, ladies and gentlemen, it is a very pleasant part of the speaker's duties to welcome to the platform the representatives of jurisdictions other than our own. I first take great pleasure in asking Dr. Fineberg to present the president of the Connecticut State Medical Society, Clyde L. Deming, M.D.

Clyde L. Deming, M.D.: Mr. Speaker, President Galbraith, officers and members of the House of Delegates, and guests, it is a great pleasure and a real privilege to bring to you the best wishes and greetings from the Connecticut State Medical Society.

We are having some problems which I find that you are having in the State of New York. One especially is public relations, and you have already made reference to that. However, I want to tell you that we are still making headway and trying to do everything we can to meet the problems which now face us.

We extend to you wishes for a great success in your meeting. May you solve your problems so that you may practice medicine in peace with freedom and with pleasure.

Thank you! (*Applause*)

Speaker Wurzbach: There is somebody walking up the aisle who is not going to get away with a thing, Dr. Herman Hilleboe.

Herman E. Hilleboe, M.D.: Mr. Chairman, ladies and gentlemen, I am sorry I was delayed this morning. I had a little teaching stint I had promised to do way last fall. I am delighted to be here, and if I can be of any help, please call on me. (*Applause*)

Speaker Wurzbach: Thank you, sir.

The representative from the Medical Society of New Jersey, Dr. Levi M. Walker.

Levi M. Walker, M.D.: Dr. James Moore back there happens to be my cousin, so we are neighbors in more ways than one. I am very happy to be here as the representative of the New Jersey Medical Society. I want to convey our best wishes always to you, our neighbor. We hope and expect to get a lot of help for our Society from the things you do over here, because we know that you do them very well.

Thank you very much for letting me visit with you. (*Applause*)

Special Committee on Constitution and Bylaws

Section 36

Report of Special Committee on Constitution and Bylaws

Speaker Wurzbach: Ladies and gentlemen, we will now continue with our next order of business which will be the report of the Special Committee on Constitution and Bylaws, of which George A. Burgin, M.D., is chairman, and I will ask the vice-speaker to take over at this point.

George A. Burgin, M.D., *Councillor:* Mr. Speaker and members of the House, I think my report this morning will arouse a little controversy.

The following amendments to the Constitution and Bylaws of the Medical Society of the State of New York, submitted as resolutions at the annual meeting of the House of Delegates in 1961, were studied carefully at a meeting of the committee on December 15, 1961. A representative of legal counsel was also present.

The proposed amendments and the committee's recommendations follow:

Resolution 61–75—Amendment to the Bylaws Regarding Membership of Planning Committee; Introduced by Louis H. Bauer, M.D., Past-President.

This amendment provides that the Planning Committee, which now consists of the five most recent past-presidents of the Medical Society of the State of New York and two others appointed by the president, be changed so that the two members-at-large shall be nominated by the Nominating Committee and elected by the House of Delegates at its annual meeting.

The resolution reads as follows:

> WHEREAS, The Planning Committee at present is composed of the five most recent past-presidents and two members-at-large appointed by the president for a term of one year with the advice and consent of the Council; and
>
> WHEREAS, The Planning Committee is a committee of the House and it has by its past actions elected the past-presidents to their office and it is desirable that the House should have the ultimate responsibility for determining the composition of the entire committee, including the members-at-large; now therefore be it hereby
>
> *Resolved*, That Chapter III, Section 1, of the Bylaws be amended to add the words "and one member-at-large of the Planning Committee" following the words "Board of Trustees" in the first sentence of said section; and be it further
>
> *Resolved*, That Chapter III, Section 2, of the Bylaws be amended to add the following new paragraph after the paragraph beginning "Four members of the Council . . ."
>
> "In the year 1962 the Nominating Committee shall nominate two members-at-large for terms of two years and one year, respectively. Thereafter, one member-at-large shall be nominated and elected annually for a term of two years."

The committee unanimously approves the resolution, and I move its adoption.

ALFRED A. HARTMANN, M.D., *Franklin:* I second the motion.

VICE-SPEAKER BABBAGE: You have all heard Dr. Burgin's motion that his committee approves this recommendation. This must be passed by a two-thirds vote of this House of Delegates. All those in favor say "aye," contrary "no." It is adopted.

This will mandate that the Nominating Committee have a special meeting and nominate two men, one to serve for a two-year period and one to serve for a one-year period.

THOMAS M. D'ANGELO, M.D., *Queens:* I am heartily in accord with this resolution. I just bring up a point of order. This resolution was introduced last year, I understand, but was it sent to a reference committee at that time?

DR. BURGIN: It was referred to the House Committee on Constitution and Bylaws.

DR. D'ANGELO: Don't you think it would be proper for these resolutions coming before us at this time that have never been given for open discussion by members of a reference committee that they also be referred to a reference committee so they may be discussed before we get them on the floor?

SPEAKER WURZBACH: According to the Constitution, these, when presented, are turned over to the Special Committee on Constitution and Bylaws, who thereupon reports them in full in the proceedings, and then they are brought on the floor. They are never presented to a reference committee per se.

DR. D'ANGELO: Mr. Chairman, don't you think it is the prerogative of the speaker, if he so desires, to refer these matters to a reference committee before coming to a vote? There may be controversial changes in the amendment which would require a lot of time. I don't like to see it spent on the floor by the delegates here if that could be done in a reference committee.

SPEAKER WURZBACH: I don't think that a reference committee has any rights in this matter. This is presented only for action of the Special Committee to be presented to the House, not a reference committee.

ASSISTANT SECRETARY WOLFF: Mr. Speaker and members of the House, Dr. d'Angelo is correct when he says that this should be presented before reference committees because our Bylaws specifically state that any proposition that is brought up on the floor of this House must be presented to a reference committee except where the Bylaws concern reference committees they may be suspended by a majority vote of the House. That has been done in the past. A number of years ago these changes were always referred to reference committees and were talked over in open discussion there and recommendations made to the House by the reference committee. It was after that happened for a number of years that the special committee was created. The last few years it has become the policy of the House to bypass the requirement for reference to a committee; however, under certain circumstances I can see that it might be wise to do that, but that is entirely at the discretion of the House.

SPEAKER WURZBACH: If my memory serves me right, when this Special Committee on Constitution and Bylaws was set up the procedure outlined in that action at that time has been followed by the House since that time.*

VICE-SPEAKER BABBAGE: Is there any other discussion on this? You have already passed it.

DR. BURGIN: The second resolution:

Resolution 61-64—Amendment to Constitution and Bylaws to Change Title of Executive Director to Executive Vice-President; Introduced by George A. Burgin, M.D., Councillor.

The resolution follows:

> WHEREAS, The American Medical Association and many state medical societies designate their chief administrator as "executive

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* In May, 1952, the Speaker was empowered by the House to create a special committee of three on amendments to the Constitution and Bylaws so that such proposed amendments might be studied during the year, since it was felt that they deserved more study than a reference committee could give them during the course of the House of Delegates meeting. See Section 184 of the House of Delegates Minutes for 1952, pages 119 and 120 of the NEW YORK STATE JOURNAL OF MEDICINE, September 1, 1952, Part II. *Secretary*

vice-president" rather than "executive director"; and

Whereas, It is desirable for purposes of clarity and uniformity that the chief administrator of the Medical Society of the State of New York bear a similar title; now therefore be it hereby

Resolved, That the title of the chief administrator be changed from "executive director" to "executive vice-president"; and be it further

Resolved, That the Constitution and Bylaws of the Medical Society of the State of New York be amended as follows:

Amend the Constitution, Article IV (Council), first sentence of the second paragraph, to substitute the words "vice-president" for the word "director"; and amend the Bylaws, Chapter IV (Council), Section 1 (a), last sentence, to substitute the words "vice-president" for the word "director."

Your committee unanimously approves this resolution, and I would like to move its adoption.

Assistant Secretary Wolff: I second it.

. . .There being no discussion, the motion was put to a vote and was unanimously carried. . .

Dr. Burgin: The third and last resolution:

Resolution 61–46—New Sections of the Society; Introduced by Ezra A. Wolff, M.D., Assistant Secretary.

The resolution follows:

Whereas, Sections of the Medical Society of the State of New York should be of sufficient interest to attract a sizable number of members in order to justify their costs and usefulness to the Society; and

Whereas, The creation of sections without first demonstrating a demand for them by having had their subject matter presented in the form of one or more annual sessions is inadvisable; now therefore be it hereby

Resolved, That the Bylaws of the Medical Society of the State of New York be amended by adding to Chapter XII a new section (Section 6) to read as follows:

> Section 6. No new section shall be created unless a session devoted to its subject matter or specialty shall have been held at at least two successive previous annual meetings.

Mr. Speaker, your committee unanimously approved this resolution, and I move its adoption.

Philip D. Allen, M.D., *New York:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried. . .

Dr. Burgin: Mr. Speaker, I would like to move the acceptance of this report as a whole.

Assistant Secretary Wolff: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried. . .

Dr. Burgin: Before I leave the rostrum, I would like to thank the members of my committee, Philip D. Allen, Alfred A. Hartmann, Robert F. Warren, and Ezra A. Wolff, and also Miss Doris K. Dougherty for the great help she has given me.

Resolutions

Section 37 (see 155) Resolution 62–1

Combining Services of State Welfare and Health Departments

Introduced by Monroe County Medical Society

Whereas, In New York State, welfare costs are mounting constantly until they have become a major source of public expenditure; and

Whereas, Medical costs represent an ever-increasing percentage of this expenditure, and an increasing share of the medical costs is borne for maintenance of persons who could care for themselves wholly or in part if proper rehabilitation services were available; and

Whereas, Historically, medical care in welfare departments has largely been provided for treatment rather than for prevention and rehabilitation; and

Whereas, The services administered by the health departments of the State through physicians, nurses, and allied health professions have been preventive and rehabilitative; now therefore be it hereby

Resolved, That the Medical Society of the State of New York urge the appropriate measures be undertaken by the State Government to combine the services of the Department of Social Welfare with those of the State Health Department under the State Health Department as rapidly as possible so that human resources and public funds may be most advantageously used.

Referred to Reference Committee on Commission on Medical Services—A.

Section 38 Resolution 62–2

Proportional Representation for A.M.A. Delegates

Introduced by Monroe County Medical Society

Whereas, Many of our members are antagonistic toward compulsory membership in the American Medical Association; and

Whereas, Many members feel that the A.M.A. House of Delegates does not represent adequately the opinion of members of the profession at the "grass roots" level; and

Whereas, The Monroe County Medical Society can point to instances in which that Society's opinions, supported by the State Society House of Delegates, have been buried in the A.M.A. House of Delegates; now therefore be it hereby

Resolved, That the Bylaws of the Medical

Society of the State of New York be amended to provide that delegates to the American Medical Association be elected one half from the State Society House of Delegates and one half from the various district branches, or combination of such, as proportional representation would allow, as follows:

Amend Chapter III, Section 6, of the Bylaws, by inserting in the second sentence, following the word "Nominations," the words "one half from members of the House of Delegates and one half from the district branches, in proportion to the membership thereof," so that the sentence will then read: "Nominations, one half from members of the House of Delegates and one half from the district branches, in proportion to the membership thereof, shall be made for not less than double the full number of delegates to be elected";

and in the next portion of the sentence, by inserting the words, "one half to be elected from those nominated from the House of Delegates and one half to be elected from those nominated from the district branches" so that that portion of the sentence will then read, "and the delegates shall be declared elected in the order of the highest number of votes cast until the allotted number shall have been chosen, one half to be elected from those nominated from the House of Delegates and one half to be elected from those nominated from the district branches";

and in the next portion of the sentence by inserting the same words so that that portion will then read, "a corresponding number in the next highest order of votes cast shall be declared alternate delegates, one half to be elected from those nominated from the House of Delegates and one half to be elected from those nominated from the district branches."

Referred to Special Committee on Constitution and Bylaws.

Section 39 (*see 201*) Resolution 62–3

Change in Welfare Laws and Regulations

Introduced by Genesee County Medical Society

WHEREAS, The State Department of Social Welfare requires that a physician file form M-1 within five days of the inception of care of a welfare patient in order to authorize payment of the physician's fee; and

WHEREAS, The patient seldom informs the physician of his welfare status, especially if no previous visit to the particular physician involved has been made; and

WHEREAS, The patient may mistakenly state that he has some other medical and/or surgical insurance; and

WHEREAS, The Department of Social Welfare often knows a patient is a welfare case and does not so inform the physician; and

WHEREAS, In cases under investigation a patient may be accepted for welfare assistance weeks before the attending physician becomes aware of this fact; and

WHEREAS, The Welfare Department does not notify physicians when it does determine that a patient is on welfare status following such investigation; and

WHEREAS, Telephone notification of the Welfare Department by the physician has been held invalid; and

WHEREAS, The doctor is always more concerned with caring for patients than with determining the source or method of payment for his services and may neglect to ask the patient this fact; and

WHEREAS, It is patently self-evident that any welfare patient who is hospitalized must of necessity be under a physician's care and that another physician or specialist may be called for such patient and said physician or specialist may be unaware of the patient's welfare status and liable, therefore, to refusal of payment of his fee by the Welfare Department; and

WHEREAS, It is the obligation of the Welfare Department to pay the legitimate medical expenses of welfare cases rather than utilize legal technicalities to avoid such payment; now therefore be it hereby

Resolved, That the Medical Society of the State of New York sponsor legislation to amend the Welfare Laws and Regulations of the State of New York to affirm that when the responsibility for payment of hospital and/or medical care has been accepted by the Department of Social Welfare, either at the request of the patient, the hospital, the attending physician, or a consultant, then all fees accruing from the care of said physicians, medical specialists, medical consultants, anesthetists, and/or assistants be paid by the Welfare Department in accordance with its established schedule on application by said physician on form M-1, this payment to the physician to be made without regard to whether or not any or each physician has notified the Department and only with regard to the fact that the patient is in truth a welfare case.

Referred to Reference Committee on Legislation and Legal Matters.

Section 40 Resolution 62–4

Amendment to Bylaws to Provide for Partial Remission of Dues

Introduced by Nassau County Medical Society

WHEREAS, The Bylaws of the Medical Society of the State of New York provide that when a component county medical society remits the dues of a member on account of illness or financial hardship, the Medical Society of the State of New York will also remit the member's dues; and

WHEREAS, The situation occasionally arises where a member is partially disabled to a degree which restricts the member to part-time practice enabling the member to pay, without hardship, only a portion of his dues; and

WHEREAS, There is no provision at the present time in the Bylaws of the Medical Society of the State of New York for partial or fractional remission of dues; now therefore be it hereby

Resolved, That the Bylaws of the Medical Society of the State of New York be amended to provide for partial remission of dues on the recommendation of the component county medical society, as follows: Chapter XIV, Section 2, final paragraph, insert the words "in whole or in part" following the word "year" in the third line of the paragraph, so that the paragraph will read: "The dues of any active or junior member of the Medical Society of the State of New York may be remitted for the current year in whole or in part on account of illness, financial hardship, or temporary service in the armed forces or in the United States Public Health Service, when the request is made by the member's component county medical society."

Referred to Special Committee on Constitution and Bylaws.

Section 41 (*see 168*) Resolution 62–5

Differential in Fees for Osteopaths in Workmen's Compensation Schedule

Introduced by Charles C. Mangi, M.D., Medical Society of the County of Queens

WHEREAS, The Council of the Medical Society of the State of New York has issued a statement on osteopathy in which the Council states that osteopathy in this State is no longer considered to be a cult if they adhere to the same scientific principles embraced by doctors of medicine and that doctors of medicine may associate professionally, on a voluntary basis, with doctors of osteopathy who hold full licenses to practice medicine and surgery granted by the New York State Board of Medical Examiners; and

WHEREAS, The House of Delegates of the Medical Society of the State of New York, in May, 1959, passed a resolution protesting the fact that the schedule of fees for doctors of medicine in general practice is lower than the schedule of fees for osteopaths and requested the Chairman of the Workmen's Compensation Board to adjust the fees paid to physicians and osteopaths to remove this basic inequity; and

WHEREAS, The latest Workmen's Compensation Fee Schedule, dated July 1, 1960, still maintains this inequity with each fee for osteopathy including osteopathic manipulation; and

WHEREAS, "Osteopathic manipulation" is not supported by the scientific principles embraced by doctors of medicine; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York request that all inequities in fee schedules between osteopaths and doctors of medicine in general practice based on osteopathic manipulation be abolished immediately before doctors of medicine are allowed to associate professionally with doctors of osteopathy.

Referred to Reference Committee on Commission on Medical Services—B.

Section 42 (*see 142*) Resolution 62–6

Endorsement of Empire Medical Political Action Committee

Introduced by Medical Society of the County of Erie

WHEREAS, Organized medicine from a sense of duty has frequently expressed its views to public office holders on legislation and matters affecting the public health and the practice of medicine; and

WHEREAS, Such expressed views have often been ignored because public office holders believe that the health professions are not a significant force in the political sphere; and

WHEREAS, There recently was formed in New York State a political action organization known as "The Empire Medical Political Action Committee"; and

WHEREAS, The Empire Medical Political Action Committee, a nonprofit, nonpartisan, and nonsectarian organization, has as its purpose the stimulation of physicians to a greater interest and a more active role in the election of persons to public office who favor free enterprise and who will stand with medicine on matters affecting the health and general welfare of the public; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York endorse the formation and the purposes of the Empire Medical Political Action Committee; and be it further

Resolved, That the House of Delegates of the Medical Society of the State of New York recommend and urge that individual physicians become interested and active in the Empire Medical Political Action Committee so as to make it a potent force in protecting the legitimate interests of medicine and the health and welfare of the public.

Referred to Reference Committee on Miscellaneous Business.

Section 43 Resolution 62–7

Amend Bylaws to Provide for Selection of Branch Members of Nominating Committee

Introduced by Medical Society of the County of Erie

WHEREAS, It is and should be the intent of the Bylaws of the Medical Society of the State of New York that the members of the Nominating Committee chosen from each district branch be individuals who are representative of their respective district branches; now therefore be it hereby

Resolved, That Chapter XI, Section 4, of the Bylaws be amended to provide that the choice of the member of the Nominating Committee from each district branch shall be from a list of at least two candidates furnished the president of the Society by the president of the district branch, as follows:

Amend Chapter XI, Section 4, of the Bylaws by the addition after the words "each district branch" of the following language: "from a list of at least two candidates designated by the president of each district branch, such list to be furnished within thirty days after request is made by the president of the Society. In the event such list of candidates is not furnished within the specified time, the choice of the member from the district branch failing to name candidates shall be made by the president of the Society," so that Chapter XI, Section 4, will then read: "The Nominating Committee shall comprise eleven members, one member to be chosen from each district branch from a list of at least two candidates designated by the president of each district branch, such list to be furnished within thirty days after request is made by the president of the Society. In the event such list of candidates is not furnished within the specified time, the choice of the member from the district branch failing to name candidates shall be made by the president of the Society, and two additional members at large to be nominated to this committee by the president, in conformity with Chapter VII, Section 1, of these Bylaws. It will be the duty of this committee to propose and nominate members of the Society for all vacancies to be filled at the annual meeting of the House of Delegates succeeding their appointment. These recommendations shall be made to the House of Delegates in the same manner as prescribed in Chapter X, Section 2, of the Bylaws."

Referred to Special Committee on Constitution and Bylaws.

Section 44 (*see 132*) Resolution 62–8

Changing Name of Section on Physical Medicine to Section on Physical Medicine and Rehabilitation

Introduced by Milton B. Spiegel, M.D., Medical Society of the County of Kings

WHEREAS, The designation "Physical Medicine and Rehabilitation" is usually and universally applied to this discipline; and

WHEREAS, The recognized specialty certification is from an American Board of Physical Medicine and Rehabilitation; and

WHEREAS, The appropriate subcommittee of the Council Committee on Public Health and Education is referred to as the Subcommittee on Physical Medicine and Rehabilitation, and the minutes and records of the Medical Society of the State of New York are replete with references to such a section; now therefore be it hereby

Resolved, That, in the interests of consistency and conformity with usual usage, the name of the Section on Physical Medicine be changed to the Section on Physical Medicine and Rehabilitation.

Referred to Reference Committee on Organization and Policies.

Section 45 Resolution 62–9

Amendment to Bylaws to Rescind Action on Mandatory A.M.A. Membership

Introduced by Medical Society of the County of New York

WHEREAS, The Medical Society of the State of New York, at its 1961 annual meeting, amended its Bylaws making membership in the American Medical Association mandatory for all its own members; and

WHEREAS, Unequivocal opposition to that amendment has been indicated by the membership of The Medical Society of the County of New York; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York amend Chapter I, Section 1, of the Bylaws by deleting from the first sentence thereof the words "and the American Medical Association" appearing at the end of such sentence; and further, amend Chapter I, Section 3, of the Bylaws by deleting from the first sentence thereof the words "or the American Medical Association" and by changing the word "their" appearing in such sentence to "its."

Referred to Special Committee on Constitution and Bylaws.

Section 46 (*see 133*) Resolution 62–10

County Society Liaison with Physicians' Home

Introduced by George Himler, M.D., Medical Society of the County of New York

WHEREAS, Physicians' Home is a corporation organized in 1919 under the laws of the State of New York and administered by practicing physicians to help needy and destitute physicians of this State, their wives, widows, and dependent children in their own communities; and

WHEREAS, The main support of Physicians' Home has come from voluntary contributions of $2.00 from members of the county medical societies throughout the State, from the annual membership drive, and from bequests and inheritances which bring in sufficient funds to meet requests for aid; and

Whereas, The efficient administration of Physicians' Home requires the cooperation of the State and county societies and of the membership of the State Society not only for financial support but also for liaison with the State-wide membership of the societies; and

Whereas, The economical and efficient administration of the affairs of Physicians' Home necessitates frequent interviews with applicants living in all parts of the State, correspondence with their friends and with officials of the county medical societies to investigate and validate claims from physicians, their wives, widows, and children, and especially to bring to our attention the needs of physicians eligible for aid but unfamiliar with Physicians' Home and its purposes; now therefore be it hereby

Resolved, That the Medical Society of the State of New York, in convention assembled, in order to facilitate and improve the administration of Physicians' Home in an economic manner, and to assure the cooperation of the State and county societies and their membership, direct the president of each county society each year to designate the secretary, the executive secretary, or some other official or committee to maintain liaison with the officials of Physicians' Home to the end that claims for aid may be more efficiently and economically investigated and aid more promptly given when needed.

Referred to Reference Committee on Organization and Policies.

Section 47 (see 201) Resolution 62–11

Plan to Bring About Changes in Welfare Medical Programs

Introduced by Broome County Medical Society

Whereas, It is becoming increasingly apparent that the intent of the Metcalf-McCloskey Law is not being carried out under implementation by welfare departments at the local and State level; and

Whereas, State Senator George R. Metcalf, coauthor of this legislation, has publicly voiced his displeasure at implementation under strict Department of Social Welfare control; and

Whereas, Organized medicine in New York State officially endorsed and strongly supported the original intent of the Metcalf-McCloskey Law; and

Whereas, All our attempts to suggest changes in implementation have apparently failed; and

Whereas, The New York State Department of Social Welfare and its local departments have apparently decided to ignore the intent of this Law as well as medicine's recommendations and suggestions; now therefore be it hereby

Resolved, That the Medical Society of the State of New York formulate and implement a plan which will establish the rights of organized medicine to meet, negotiate, and bring about needed changes in all welfare medical programs in this State.

Referred to Reference Committee on Legislation and Legal Matters.

Section 48 (see 202) Resolution 62–12

Court Decisions Affecting Workmen's Compensation Law

Introduced by Broome County Medical Society

Whereas, Two decisions rendered recently in the New York State Supreme Court, Appellate Division, alter the basic concept of the Workmen's Compensation Law, State of New York; and

Whereas, These decisions require wage loss by a claimant with an occupational dermatitis or occupational hernia before medical service can be rendered at the expense of a compensation insurance carrier; and

Whereas, It is known that at least one compensation insurance carrier, the State Insurance Fund, is using one of these decisions to controvert a case of occupational dermatitis; and

Whereas, These two decisions may lead to further broadening of the base of occupational diseases and injuries affected by future court decisions with these as a precedent; and

Whereas, These decisions complicate the practice of medicine as related to the Workmen's Compensation Law, State of New York, by making it difficult to render proper medical care to a claimant with certain occupational diseases; now therefore be it hereby

Resolved, That the membership of the Medical Society of the State of New York be informed of this change in the Workmen's Compensation Law and the State Society be instructed to exert every and all legitimate, legal, and legislative means to reverse or circumvent these decisions.

Referred to Reference Committee on Legislation and Legal Matters.

Section 49 (see 156) Resolution 62–13

Review and Revision of Fee Schedules for Welfare Patients

Introduced by Broome County Medical Society

Whereas, It has become apparent that a review of welfare attitudes, practices, and programs is necessary; and

Whereas, The medically indigent are no longer medically indigent after they are accepted for welfare care; and

Whereas, The truly medically indigent are those people who cannot meet health care expenses with their source of income but are not on welfare, and physicians realize their responsibilities in caring for this group; and

Whereas, The welfare patient has no financial problem in obtaining physicians' services, hospital services, and prescription medication; and

Whereas, The financial obligations for the medical care of welfare patients have been assured by governmental agencies, which certainly cannot be classified as indigent; and

Whereas, There is no reason why governmental agencies cannot pay physicians a fair fee, and this should be at least the same as customarily paid by private patients; now therefore be it hereby

Resolved, That the State Department of Social Welfare be notified of the content of this resolution, and that necessary revision of the fee schedules be accomplished promptly through the Medical Society of the State of New York; and be it further

Resolved, That these fee schedules should be reviewed yearly by the State Medical Society for necessary changes, and if changes are necessary, that they should be made promptly.

Referred to Reference Committee on Commission on Medical Services—A.

Section 50 (see 142) Resolution 62–14

Endorsement of Empire Medical Political Action Committee

Introduced by Broome County Medical Society

Whereas, Organized medicine's views have not been adequately and consistently expressed to members of legislative bodies; and

Whereas, Candidates for public office and office holders have frequently ignored organized medicine's views because they are convinced that the health professions are not an important force in public affairs; and

Whereas, Organized medicine has a well-recognized duty to lead the people of the State of New York and the nation in matters pertaining to the health of the individual and the public; and

Whereas, The future of the American way of free enterprise depends in great measure on the preservation of the private practice system of medicine; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York commend and support the efforts and leadership of the Empire Medical Political Action Committee.

Referred to Reference Committee on Miscellaneous Business.

Section 51 Resolution 62–15

Amendment to Bylaws to Change Method of Selection of Nominating Committee

Introduced by Medical Societies of the Counties of Oneida, Herkimer, and Madison

Whereas, The present method of selection of the Nominating Committee for elective offices of the Medical Society of the State of New York was proposed as an improvement over previous methods of selection; and

Whereas, The general complexion of the Nominating Committee has not changed materially, in spite of the new method of selection; and

Whereas, This has caused a good deal of criticism of the present method of selection; now therefore be it hereby

Resolved, That Chapter XI, Section 4, of the Bylaws of the Medical Society of the State of New York be changed as follows:

The words "to be chosen from" be changed to "to be elected by" each district branch, so that the sentence will then read: "The Nominating Committee shall comprise eleven members, one member to be elected by each district branch and two additional members at large to be nominated to this committee by the president, in conformity with Chapter VII, Section 1, of these Bylaws."

Referred to Special Committee on Constitution and Bylaws.

Section 52 (see 203) Resolution 62–16

Amendment to Civil Practice Act to Prevent Use of Minutes of Hospital Tissue Committee Meetings

Introduced by Medical Society of the County of Oneida

Whereas, Section 296 of the Civil Practice Act of the State of New York provides for the production of all books, papers, records, etc., by a party to a litigation, or another, on order of the Court pursuant to a subpoena duces tecum; and

Whereas, The Joint Commission on Accreditation of Hospitals requires that hospital staffs appoint tissue committees for the purpose of studying and evaluating the nature and quality of the medical work being performed in a hospital; and

Whereas, The meetings of the tissue committee must be reported to the staff and recorded in the minutes of the meetings of the staff in order to inform the staff of the cases that were studied by the tissue committee and pertinent data as to correctness of diagnoses and indication for surgical procedures; and

Whereas, Such information is very important for the proper supervision by the staff of the work of its members in order to assure that the patients receive the best possible medical care, correct diagnoses, and that only indicated surgical procedures are performed; and

Whereas, Such information is sought after and is subject to review under a subpoena duces tecum by a patient and his attorney who "like to fish in troubled waters" in order to come up with a reason for malpractice litigation; and

Whereas, The only defense to such a subpoena duces tecum is that no minutes of tissue committee meetings are kept, or that no tissue committee is functioning in the hospital, which impairs the quality of medical services rendered to the public and forces the hospital to run the danger of loss of accreditation; and

WHEREAS, Many states have approved legislation making the minutes of tissue committees immune from the demands on a subpoena duces tecum; now therefore be it hereby

Resolved, That the Medical Society of the State of New York, through its Committee on Legislation, encourage and foster the preparation of legislation purporting to amend Section 296 of the Civil Practice Act of the State of New York so as to prohibit the courts from approving a subpoena duces tecum or other judicial process that would call for the production of the minutes of the tissue committees in hospitals for any purpose whatsoever.

Referred to Reference Committee on Legislation and Legal Matters.

Section 53 (see 140) Resolution 62–17

Admonishment for Comments on General Practitioners

Introduced by Section on General Practice

WHEREAS, One of our councillors, turned columnist, has been using his lofty perch in a column of a most successful commercial business magazine to issue his learned opinions on many facets of medicine and life from the boudoir to the "Twilight of General Practice"; and

WHEREAS, These pronouncements have a wide audience, including all the many lay advertisers in this business magazine; and

WHEREAS, The most recent column is derogatory and derisive of the general practitioner whom he calls a "Jack-of-all-trades who is no longer possible or needed," despite his own quoted definition of the general practitioner, as approved by the A.M.A. in 1959, as the doctor who "assumes comprehensive and continuing responsibility for the patient and his family"; and

WHEREAS, He offers no substitute for the general practitioner except for internists and pediatricians who would need "a few embellishments"; and

WHEREAS, This councillor is an elected representative of a Society with a membership of about 50 per cent general practitioners; now therefore be it hereby

Resolved, That this House of Delegates admonish this councillor for such an intemperate column and advise him not to downgrade a group of doctors who are still the backbone of medicine today.

Referred to Reference Committee on Miscellaneous Business.

Section 54 (see 169) Resolution 62–18

Workmen's Compensation Fee Schedule on Time-Rate Basis

Introduced by Medical Society of the County of Ulster

WHEREAS, The existing New York State Workmen's Compensation Fee Schedule provides a fixed fee for physicians' assistants in surgical procedures; and

WHEREAS, Many surgical procedures involve up to several hours of such physicians' time; and

WHEREAS, The services of other physicians, such as anesthetists, are compensated on a time-rate basis; now therefore be it hereby

Resolved, That the New York State Workmen's Compensation Board be requested to establish a fee schedule on a time-rate basis for payment for the services of a practicing physician as assistant at a surgical procedure when the absence of resident physicians make it necessary to employ the services of such practicing physicians.

Referred to Reference Committee on Commission on Medical Services—B.

Section 55 (see 142) Resolution 62–19

Endorsement of Empire Medical Political Action Committee

Introduced by Medical Society of the County of Ulster

WHEREAS, Organized medicine's views have not been adequately and consistently expressed to members of legislative bodies; and

WHEREAS, Candidates for public office and office holders have frequently ignored organized medicine's views because they are convinced that the health professions are not an important force in public affairs; and

WHEREAS, Organized medicine has a well-recognized duty to lead the people of the State of New York and the nation in matters pertaining to the health of the individual and the public; and

WHEREAS, The future of the American way of free enterprise depends in great measure on the preservation of the private practice system of medicine; now therefore be it hereby

Resolved, That the House of Delegates of the Medical Society of the State of New York commend and support the efforts and leadership of the Empire Medical Political Action Committee.

Referred to Reference Committee on Miscellaneous Business.

Section 56 (see 204) Resolution 62–20

Endorsement of A.M.A. Resolution on Supervision of Clinical Laboratories

Introduced by John J. Clemmer, M.D., Section on Pathology, Clinical Pathology, and Blood Banking

WHEREAS, During the June, 1961, American Medical Association meeting in New York City, resolution 17 was endorsed unanimously by the Reference Committee on Miscellaneous Business, R. J. Azzari, M.D., New York; R. H. Kiene, M.D., Missouri; A. A. Morrison, M.D., California; L. R. Pyle, M.D., Kansas; and Kenneth C. Sawyer, M.D., Colorado, chairman, and passed without dissent by the House of Delegates, the resolution being as follows:

"Subject: Laboratories Should Be Supervised by Qualified, Licensed Physicians

"WHEREAS, The practice of pathology, both clinical and anatomical, has been declared repeatedly to be the practice of medicine by the A.M.A., by the Illinois State Medical Society, by other state and county medical societies, by the College of American Pathologists, and other special professional societies, by the courts of record having certain legal jurisdictions, and by opinions of record of attorneys general of certain states; and

"WHEREAS, There are medical laboratory technicians and other non-professional persons operating independent medical laboratories on a commercial basis without medical licensure, without adequate education or training, and without proper professional supervision; and

"WHEREAS, Persons operating such commercial laboratories are not constrained by law or by their education and training to adhere to professional ethical principles guarding the public interest; and

"WHEREAS, Such commercial laboratories frequently charge fees to physicians under conditions fostering the division of fees between the laboratory and the referring physician; and

"WHEREAS, It is desirable to encourage scientists of professional status, such as chemists and bacteriologists with doctoral degrees, to work cooperatively with physicians for the welfare of patients and in the interest of public health; and

"WHEREAS, The independent practice of laboratory medicine, generally known as pathology, by persons without medical licensure degrades the practice of medicine and of pathology in particular, is against the public interest and seriously lowers the medical and scientific standards of medical practice; and

"WHEREAS, The continued operation of commercial medical laboratories operated by unqualified persons is not possible without the patronage of the medical profession; and

"WHEREAS, The medical profession generally has always placed the common good above self interest and has adhered to ethical and moral principles; therefore be it

"*Resolved*, That the American Medical Association hereby declares that the proper conduct of laboratory analyses is a medical professional responsibility and all specimens for such analyses should be referred to laboratories supervised by fully qualified and licensed physicians."; and

WHEREAS, The points made in the preamble of resolution 17 are very pertinent to New York State; and

WHEREAS, There are many excellent ethical medical laboratories under the direction of fully qualified and licensed physicians, including those approved under the provisions of the New York State Sanitary Code (listed in NEW YORK STATE JOURNAL OF MEDICINE, April 15, 1962, pp. 1293–1296); and

WHEREAS, The proper recognition of such medically directed and supervised laboratories by the licensed medical clinicians in New York State would encourage their growth and multiplication; now therefore be it hereby

Resolved, That the Medical Society of the State of New York hereby declares that it endorses resolution 17, as adopted by the House of Delegates of the A.M.A. at its session in New York City in June, 1961.

Referred to Reference Committee on Legislation and Legal Matters.

Section 57 (see 157) Resolution 62–21

Health Insurance Coverage for the Over-Sixty-Five Age Group

Introduced by Bronx County Medical Society

WHEREAS, Voluntary health insurance has had a continued rapid expansion in serving the needs of the American people; and

WHEREAS, Blue Shield has developed and proposed a national program for coverage of those over sixty-five; and

WHEREAS, The voluntary prepayment insurance approach aids and supports our present highly valued system of medical care; and

WHEREAS, A government plan poses a threat to the quality of medical care in the United States and could impede future progress of voluntary health insurance coverage; now therefore be it hereby

Resolved, That the Medical Society of the State of New York endorse and support the proposed National Blue Shield Program for those over sixty-five and recommend to all physicians that they support and participate in both the national effort and the efforts of their local Blue Shield Plans to provide coverage for those over sixty-five; and be it further

Resolved, That the Medical Society of the State of New York urge all Blue Cross and Blue Shield Plans of New York State to extend their full cooperation in the development of a nation-wide program of coverage for the aged embodying the principle of service benefits for those of modest income; and be it further

Resolved, That the Medical Society of the

State of New York ask the elected representatives of the State of New York in Congress to support health care legislation which is based on the actual financial need of the individual and which secures for the aged their traditional rights and freedoms in the selection of doctor and hospital.

Referred to Reference Committee on Commission on Medical Services—A.

Section 58 (*see 205*) Resolution 62–22

Opposition to Chiropractic Licensure

Introduced by Bronx County Medical Society

WHEREAS, Many groups and organizations, such as universities, foundations, special study commissions, health and welfare groups responsible for the expenditure of health and welfare funds, public health organizations, social service organizations, ancillary medical service groups, and government departments involved in health and welfare matters, are actively interested in the quality of medical care received by the people of New York State; and

WHEREAS, Many of these influential groups have initiated and financed organized studies concerning the quality of medical care; and

WHEREAS, The licensing of chiropractic as a form of medical treatment has been proposed for many years in the New York State Legislature; and

WHEREAS, The medical profession, in the public interest, has regularly opposed such licensure and has been in the forefront in expressing its opposition to the licensing of chiropractic; now therefore be it hereby

Resolved, That the Medical Society of the State of New York through its Council request all organizations interested in the quality of medical care to make known to the members of the State Legislature their considerations and opinions as to the value of chiropractic so that the Legislature may be further guided in protecting the health and care of the citizens of our State; and be it further

Resolved, That this effort to arouse interest and concern in the issue of chiropractic be continued throughout the year and not be limited to the period of the legislative session.

Referred to Reference Committee on Legislation and Legal Matters.

Section 59 (*See 138*) Resolution 62–23

Six-Year Combined Course for Medical Schools

Introduced by Bronx County Medical Society

WHEREAS, The American Medical Association and the medical schools are deeply concerned by the lack of Grade A college students applying for entrance into medical schools; and

WHEREAS, Grade A students realize that the extra years of preparation shorten the productive years of their lives; now therefore be it hereby

Resolved, That the Medical Society of the State of New York request the American Medical Association to urge medical schools to have a six-year combined course, such as exists in a number of schools, so that Grade A college students may be encouraged once more to apply for entrance to medical schools.

Referred to Reference Committee on Miscellaneous Business.

Section 60 (*see 170*) Resolution 62–24

Two-Year Internships for American Medical School Graduates

Introduced by Bronx County Medical Society

WHEREAS, The American Medical Association and the accredited hospitals of the United States of America are rightfully concerned with the shortage of American graduates as interns and residents in our hospitals; and

WHEREAS, Seven thousand graduates cannot conceivably fill 14,000 positions on a one-year internship, and

WHEREAS, No excellence of teaching program or any other device—monetary or psychologic—can fill 14,000 approved positions with 7,000 American graduates; and

WHEREAS, A two-year internship is the only mathematic possibility of solving this problem; and

WHEREAS, The enlarging of existing medical schools and the building of new ones may take many years, while the need for practicing physicians is great right now; now therefore be it hereby

Resolved, That the Medical Society of the State of New York request the American Medical Association to encourage medical schools to advise their graduates to take two-year internships; and be it further

Resolved, That the Medical Society of the State of New York request the American Medical Association to use its influence on the surgical boards to join the medical boards in granting one year of residency credit to interns for a "straight" second year of internship following a first-year rotating internship.

Referred to Reference Committee on Commission on Medical Services—B.

Section 61 (*see 139*) Resolution 62–25

Production of More Practicing Physicians

Introduced by Bronx County Medical Society

WHEREAS, There is the prediction of an increasing shortage of physicians necessary to treat the people of the United States of America; and

WHEREAS, There is no prospect of a marked increase of medical school graduates in the immediate future; and

WHEREAS, Medical school programs, intentionally or unintentionally, slant students toward investigative rather than clinical medicine; now therefore be it hereby

Resolved, That the Medical Society of the State of New York request the American Medical Association to encourage the medical schools to consider the advisability of having their courses so arranged that those students desiring a future of investigative medicine be separated, at the proper stage, from those desiring a future of clinical medicine; and be it further

Resolved, That the Medical Society of the State of New York consider all possible efforts to provide more practicing physicians.

Referred to Reference Committee on Miscellaneous Business.

Section 62 (see 206) Resolution 62–26

"Good Samaritan" Legislation

Introduced by Bronx County Medical Society

WHEREAS, It has occurred repeatedly that physicians giving first aid in accident cases without regard to compensation are subsequently forced to defend themselves against malpractice claims arising out of such intervention; and

WHEREAS, Such occurrences tend to make physicians unwilling to offer their help in accidents and emergencies; and

WHEREAS, This state of affairs is contrary to the public interest; and

WHEREAS, This condition may lead to otherwise avoidable losses of life and health; and

WHEREAS, Several states of the Union have already enacted such legislation; now therefore be it hereby

Resolved, That the Medical Society of the State of New York petition the Legislature of the State of New York to enact legislation to provide that a duly licensed physician or surgeon rendering first aid or emergency treatment to unconscious, ill, or injured persons shall not be liable for damages for injuries sustained unless caused by willful neglect or gross negligence.

Referred to Reference Committee on Legislation and Legal Matters.

Section 63 (see 142) Resolution 62–27

Endorsement of Empire Medical Political Action Committee

Introduced by Medical Society of the County of Queens

WHEREAS, The views of the medical profession of this country have not been adequately and consistently expressed; and

WHEREAS, The physicians of this country have a duty to take an active and effective role in civic and political affairs; and

WHEREAS, The medical profession has a well-recognized duty to lead the people of the nation and the State of New York in matters pertaining to the health of the individual and the public; and

WHEREAS, The Empire Medical Political Action Committee is an organization which will help achieve these objectives; now therefore be it hereby

Resolved, That the Medical Society of the State of New York approve the aims and efforts of the Empire Medical Political Action Committee.

Referred to Reference Committee on Miscellaneous Business.

Section 64 (see 204) Resolution 62–28

Supervision of Laboratories by Qualified Licensed Physicians

Introduced by Medical Society of the County of Queens

WHEREAS, The practice of pathology, both clinical and anatomical, has been declared repeatedly to be the practice of medicine by the American Medical Association, by other state and county medical societies, by the College of American Pathologists and other special professional societies, by courts of record having certain legal jurisdictions, and by opinions of record of attorneys general of certain states; and

WHEREAS, There are medical laboratory technicians and other nonprofessional persons operating independent medical laboratories on a commercial basis without medical licensure, without adequate education or training, and without proper professional supervision; and

WHEREAS, Persons operating such commercial laboratories are not constrained by law or by their education and training to adhere to professional ethical principles guarding the public interest; and

WHEREAS, It is desirable to encourage scientists of professional status, such as chemists and bacteriologists with doctoral degrees, to work cooperatively with physicians for the welfare of patients and in the interest of public health; and

WHEREAS, The independent practice of laboratory medicine, generally known as pathology, by persons without medical licensure degrades the practice of medicine and of pathology in particular, is against the public interest, and seriously lowers the medical and scientific standards of medical practice; and

WHEREAS, The continued operation of commercial medical laboratories operated by unqualified persons is not possible without the patronage of the medical profession; and

WHEREAS, The medical profession generally has always placed the common good above self-interest and has adhered to ethical and moral principles; now therefore be it hereby

Resolved, That the Medical Society of the State of New York hereby declares that the proper conduct of laboratory analyses is a medical professional responsibility and all specimens for such analysis should be referred to laboratories supervised by fully qualified and licensed physicians.

Referred to Reference Committee on Legislation and Legal Matters.

Section 65 (see 137) Resolution 62–29

Request to American Medical Association to Rescind Dues Increase Scheduled for January 1, 1963

Introduced by Medical Society of the County of Queens

WHEREAS, In 1961 the board of trustees of the American Medical Association voted to increase American Medical Association dues by ten dollars on January 1, 1962, and January 1, 1963; and

WHEREAS, This action was taken before mandatory membership in the American Medical Association was required of members of the Medical Society of the State of New York; and

WHEREAS, The increase in cash receipts accruing to the American Medical Association as a result of the increase in membership from New York State may make an increase in American Medical Association dues beginning January 1, 1963, unnecessary; now therefore be it hereby

Resolved, That the Medical Society of the State of New York through its delegates to the House of Delegates of the American Medical Association request the board of trustees of the American Medical Association to rescind the increase of dues scheduled for January 1, 1963.

Referred to Reference Committee on Miscellaneous Business.

Section 66 (see 148) Resolution 62–30

Listing of Previous Hospital and Research Affiliations in Medical Directory

Introduced by Medical Society of the County of Queens

WHEREAS, The *Medical Directory of New York State*, an official publication of the Medical Society of the State of New York, lists the names of physicians who are licensed by and either reside in or practice medicine in the State of New York; and

WHEREAS, Among other professional data this *Directory* lists with official titles present medical staff and research appointments in accredited hospitals; and

WHEREAS, The *Directory* omits the listing of past affiliations in these institutions; and

WHEREAS, The *Directory* is often referred to for the determination of a physician's qualifications and for biographic data; and

WHEREAS, The omission of past affiliations penalizes those physicians who voluntarily no longer hold such appointments; and

WHEREAS, These omissions may at times lead to an entirely inadequate conclusion as to a physician's qualifications; now therefore be it hereby

Resolved, That the Medical Society of the State of New York hereafter list in its *Directory* and designate as such all past medical staff and research appointments with the last rank held, provided this affiliation had lasted for a period of three years or more.

Referred to Reference Committee on Medical Communication.

Section 67 (see 207) Resolution 62–31

Review of Medical Practice Act

Introduced by Broome County Medical Society

WHEREAS, The Medical Society of the State of New York was mandated by the 1961 House of Delegates to seek enactment of the review of the Medical Practice Act (Senate Resolution 19, Cornell; Assembly Resolution 145, Ashbery); and

WHEREAS, This legislation is long overdue and desperately needed in order to protect and preserve the health of the citizens of this State; and

WHEREAS, This legislation failed even to be reported out of committee during the last State Legislature session; now therefore be it hereby

Resolved, That this House of Delegates again instruct the Council of the Medical Society of the State of New York to direct its energies toward introduction and enactment of similar legislation in 1963; and be it further

Resolved, That every member of the Medical Society of the State of New York be apprised of the contents of this resolution; and be it further

Resolved, That every member of the State Medical Society do his utmost as an individual citizen and physician to convince his local New York State Assemblymen and Senators of the need for this legislation.

Referred to Reference Committee on Legislation and Legal Matters.

Section 68 (see 158) Resolution 62–32

Approval of New York Over Age Sixty-Five Insurance Plans

Introduced by Gerald D. Dorman, M.D., Councillor

WHEREAS, The Governor of the State of New York on April 2, 1962, signed Assembly Bill 4871-S-3448 into law which encourages private insurers to underwrite jointly on a nonprofit basis hospital, surgical, medical, and major medical expense insurance on residents of this State aged sixty-five and over; and

Whereas, These amendments to the New York Insurance Law became effective immediately after signature by the Governor; and

Whereas, The Medical Society of the State of New York supported this legislation; and

Whereas, The American Medical Association has approved in principle the payment of reduced expenses for persons over sixty-five when indicated, whether paid by the Blue Cross-Blue Shield or by private insurance carriers; and

Whereas, Private insurance, recognizing the need, is presently formulating plans and programs for implementing the above-named statute; now therefore be it hereby

Resolved, That the Medical Society of the State of New York hereby go on record as approving in principle this service to those individuals sixty-five and over; and be it further

Resolved, That the Council of this Society be instructed to cooperate in the implementation of this law.

Referred to Reference Committee on Commission on Medical Services—A.

Section 69 (see 159) Resolution 62–33

Social Security for Physicians

Introduced by Philip D. Allen, M.D., Medical Society of the County of New York

Whereas, Results of polls by state medical societies and independent organizations clearly demonstrate that a substantial majority of the nation's self-employed physicians desire to be included under the Social Security program; and

Whereas, Members of the House of Delegates of the American Medical Association have continued to oppose Social Security coverage at American Medical Association annual and clinical meetings despite the overwhelming evidence that a majority of the medical profession want it; and

Whereas, Congress has been reluctant to enact a law to include physicians under Social Security in view of the House of Delegates opposition to such legislation; and

Whereas, Unless the A.M.A. House of Delegates changes its attitude and begins to reflect the real wishes of the majority of physicians on this issue, physicians and their families will continue to be the only professional group in the nation that is deprived of the protection and benefits of the Social Security program; now therefore be it hereby

Resolved, That the delegates of the Medical Society of the State of New York to the House of Delegates of the American Medical Association be instructed to introduce a resolution to provide for Social Security coverage for physicians.

Referred to Reference Committee on Commission on Medical Services—A.

Section 70 (see 141) Resolution 62–34

Recognition of Service of Mr. Thomas E. Walsh

Introduced by George Gordon Knight, M.D., and Michael P. Lefkowitz, M.D., Medical Society of the County of Rockland

Whereas, It has come to the attention of certain members of the Medical Society of the County of Rockland, and especially to past presidents, that Mr. Thomas E. Walsh, while a member of the staff of the Medical Society of the State of New York, gave more than fifteen years of service to the members of the Society; and

Whereas, In addition, the service Mr. Walsh has rendered to the members of the Medical Society of the County of Rockland has always been outstanding; and

Whereas, Mr. Walsh has been available to provide this service at any hour and on any day; now therefore be it hereby

Resolved, That the members of the Medical Society of the State of New York extend a vote of thanks to Mr. Walsh for his long, efficient, and faithful service.

Referred to Reference Committee on Miscellaneous Business.

Section 71 (see 171) Resolution 62–35

Rights of Patient and Physician

Introduced by Medical Society of the County of Richmond

Resolved, That the Medical Society of the State of New York:

(1) Publicly reaffirm the right of the patient to seek the physician of his choice as well as the right of the physician to select his patients;

(2) Suggest that those in public life who refer to the Hippocratic Oath be urged to show some evidence of at least having read it;

(3) Reaffirm the right of the individual, including the physician, under Constitutional guarantee, publicly or privately to state his opinion of any law or proposed law with freedom from fear of blackmail of expressed or implied governmental reprisals.

Referred to Reference Committee on Commission on Medical Services—A.

Section 72 (see 208) Resolution 62–36

Condemnation of King-Anderson Bill

Introduced by Louis H. Bauer, M.D., Past-President

Speaker Wurzbach: There is one resolution that is presented by a man who is not here, and I am going to ask Dr. Fineberg to read this resolution stating who the presenter is.

Executive Vice-President Fineberg: Mr.

Speaker and members of the House, first before I talk about the gentleman referred to by our speaker, I hope that you will bear with me if I assume a little privilege and perhaps be a little more provincial than I should be, but I would like personally to welcome the president of the Connecticut State Medical Society because Dr. Deming is professor of urology at Yale, and I am very proud to state that he was my professor at the time I was in school. It is grand to see you again.

Ladies and gentlemen, last Friday afternoon I had the very distinct pleasure of visiting one of the dear friends of this State Society, and one of the dear friends of medicine everywhere. I refer, of course, to the great medical statesman not only of this country but of the world, Louis H. Bauer, M.D.

Unfortunately, he cannot be with us this morning. Most of you know he has been quite ill, but I would like to say that despite the fact that he has a physical weakness his mind is as acute and as keen as it has ever been.

While I was with him he discussed in quite some detail the affairs of the Society and what is going on in the world today as it concerns our profession. He was worried about what the impact might be of the action that took place in New Jersey, and with that in mind he has given me the privilege of speaking for him this morning.

He would like to present for your consideration a resolution. Much of what is contained in this resolution, my friends, is well known to you, but it is stated in such succinct language and is so clarified that I know you will listen to it and understand why we are presenting it to you this morning.

I will read you all of the "whereases" with your permission because they are not too long and will not take up too much of your time.

> WHEREAS, The Medical Society of the State of New York has always been desirous that all persons of every age shall receive the best possible medical care; and
>
> WHEREAS, There has been a great deal of misleading propaganda and distortions of fact broadcast both as to the nature of the King-Anderson bill on Medical Care for the Aged now before the Congress and as to the attitude of the medical profession towards it; and
>
> WHEREAS, This misleading propaganda and distortions of fact have been of the following nature:
>
> 1. An attempt to gloss over the fact that the King-Anderson bill fails to cover over 3,000,000 people sixty-five years or over;
> 2. An attempt to gloss over the fact that there are many thousands of people sixty-five who are already protected by voluntary insurance and well able to do so;
> 3. A failure to stress to the people that any person accepting hospital care under this bill must pay ten dollars a day with a maximum of ninety dollars and a minimum of twenty dollars;
> 4. An attempt to belittle the effects of the Kerr-Mills Law now operating in the states, with particular false statements in reference to its operation in West Virginia;
> 5. A statement by the Secretary of Health, Education, and Welfare that doctors seem to be willing to work in hospitals partially built by Federal funds but unwilling to accept fees from the Federal government, but carefully refraining from pointing out that in hospitals built under the Hill-Burton Act there are matching funds from the communities and the Federal government retains absolutely no control over the administration of these hospitals, whereas under the provisions of the King-Anderson bill the Federal government retains complete control of its operation;
> 6. The sponsors of the bill have tried to create the impression that it is an insurance plan, whereas it has no relation to insurance but is primarily a tax-supported, political, vote-getting scheme;
> 7. The sponsors of the bill have scoffed at the idea that they will later attempt to expand its provisions to cover all people, whereas many of them have been working for years to enact compulsory health insurance in this country;
> 8. The sponsors of the bill have ignored and covered up the fact that wherever else in the world the government has stepped into the field of medical care, the costs have tremendously increased and the character of the medical care steadily deteriorated; and
>
> WHEREAS, The members of the medical profession are the only ones who can deliver medical care and are the best judges of what is good medical care; and
>
> WHEREAS, The sponsors of the bill are in no sense competent to judge what is good medical care, nor how it can best be delivered; and
>
> WHEREAS, The medical profession will do its utmost to see that every person receives the best medical care available regardless of his age or ability to pay; now therefore be it hereby
>
> *Resolved*, That the Medical Society of the State of New York condemns the King-Anderson bill because it misleads the public, and the propaganda issued in favor of the bill has resulted in many of the public being lulled into a false sense of security; and be it further
>
> *Resolved*, That copies of this resolution be sent to the President of the United States, the Secretary of Health, Education, and Welfare, the members of the Senate Committee on

Finance, the House Ways and Means Committee, and to the United States Senators and Representatives from the State of New York.

Referred to Reference Committee on Legislation and Legal Matters.

Section 73 (*see 209*) Resolution 62–37

Activity Against Chiropractic

Introduced by Medical Society of the County of Schuyler

WHEREAS, The danger of passing a chiropractic licensure bill was again avoided this year in both houses of the New York State Legislature; and

WHEREAS, All evidence shows this same or a similar bill will again be introduced and stands good chance of passing in the next session; and

WHEREAS, Licensing of chiropractors not only would establish a double standard of medical care but also would influence our entire philosophical thinking pursuing the truth, and thereby would be detrimental to our national cultural development in general; and

WHEREAS, The Medical Society of the State of New York's attitude always has been more or less *defensive;* and

WHEREAS, We have not yet set up a collection of facts which happen daily, in order to strengthen our ability for actively attacking chiropractic; now therefore be it hereby

Resolved, That each component county society set up a committee to collect and investigate each case of practicing medicine by a chiropractor, especially each case with tragic consequences; and be it further

Resolved, That the county society should report its committee's findings to the executive vice-president of the Medical Society of the State of New York in order to furnish the Medical Society of the State of New York with authentic material as a help for counter-attacking chiropractic.

Referred to Reference Committee on Legislation and Legal Matters.

Section 74 (*see 206*) Resolution 62–38

Promotion of "Good Samaritan" Law

Introduced by Medical Society of the County of Westchester

WHEREAS, A "Good Samaritan" law was passed at the session of the Legislature but vetoed by the Governor; and

WHEREAS, It is evident that there is recognition on the part of our legislators of the need for such a law; now therefore be it hereby

Resolved, That the Committee on Legislation of the State Medical Society again promote the introduction and passage of an appropriate "Good Samaritan" law at the next session of the Legislature of the State of New York.

Referred to Reference Committee on Legislation and Legal Matters.

Section 75 (*see 172*) Resolution 62–39

Hospital Utilization Committees

Introduced by Medical Society of the County of Westchester

WHEREAS, The most effective hospital bed utilization is essential in order to provide adequate hospital care for the community; and

WHEREAS, Hospital building and operating costs continue to mount, thus causing inevitable increases in health costs and health insurance premiums; and

WHEREAS, Public opinion is extremely conscious of the increasing costs of health care, particularly of hospitalization; and

WHEREAS, The effective use of hospital utilization committees will tend to make members of the attending staff more conscious of the necessity for economy in bed utilization; and

WHEREAS, The operation of utilization committees also helps to convince the public that every effort is being made to achieve the most effective and most economic use of hospital facilities; now therefore be it hereby

Resolved, That the Medical Society of the State of New York, through the county medical societies, encourage and urge the establishment of utilization committees in every hospital throughout the State.

Referred to Reference Committee on Commission on Medical Services—B.

Section 76 (*see 210*) Resolution 62–40

Principles Regarding Medical Care for the Aged

Introduced by Medical Society of the County of Monroe

WHEREAS, There are now multiple proposals before the Congress of the United States to provide health care for the aged from public monies; and

WHEREAS, Support for some form of new Federal legislation for medical care of the aged has been expressed by members of both parties in Congress; and

WHEREAS, A major defect in HR 4222 is its placement of the Federal government as a direct provider of health care on the basis of age alone; now therefore be it hereby

Resolved, That the Medical Society of the State of New York adopt the following principles relating to such legislative proposals; (1) Voluntary prepayment plans should be interposed between government and recipient; and (2) Participation of the government in any such plan should be based on the recipient's income.

Referred to Reference Committee on Legislation and Legal Matters.

Section 77 (see 160) Resolution 62-41

Social Security Poll

Introduced by Monroe M. Broad, M.D., Queens, as an individual

WHEREAS, Considerable doubt exists that the American Medical Association as represented by its House of Delegates reflects the majority expression of practicing physicians with regard to their inclusion on the Social Security rolls; and

WHEREAS, The American Medical Association has repeatedly failed to take a popular referendum to ascertain the actual feelings of the majority; now therefore be it hereby

Resolved, That the Medical Society of the State of New York, committed to obtaining Social Security benefits for its 25,000 members, join with other state societies similarly minded in financing and administering a popular referendum of all practicing physicians to determine the wishes of the majority with regard to this inclusion on the Social Security rolls.

Referred to Reference Committee on Commission on Medical Services—A.

Section 78 (see 211) Resolution 62-42

Lien Law

Introduced by Bronx County Medical Society

WHEREAS, This Society is on record for the passage of a Lien Law for doctors; and

WHEREAS, A Lien Law has been introduced in the State Legislature for the past three years and has never come out of committee; and

WHEREAS, The main objection to this bill has come from the insurance companies and legal profession; now therefore be it hereby

Resolved, That the Legislation Committee of this Society form a special committee to meet with the insurance companies and legal profession and all other opponents of this bill so that this bill will be favorably received in the new Legislature.

Referred to Reference Committee on Legislation and Legal Matters.

Section 79 Resolution 62-43

Amendment to Constitution and Bylaws to Shorten Terms of Office

Introduced by Medical Society of the County of Monroe

WHEREAS, Many of the elected officers of the Medical Society of the State of New York have served innumerable terms; and

WHEREAS, Many of the elected officers have served in dual capacities, having two elected offices; and

WHEREAS, This has caused a great burden to such officers serving in a dual capacity; and

WHEREAS, The above facts have lessened the desire of younger individuals to seek an elective office in the Society, thus depriving the Society of new blood, ideas, and interests; and

WHEREAS, The younger individuals are being deprived of training and indoctrination in the complex work of the Society, thus becoming unable and unwilling to serve; now therefore be it hereby

Resolved, To amend Section 1 of Chapter III of the Bylaws to add the following new final sentences to said section:

> "No person shall serve more than three consecutive terms as president, vice-president, secretary, assistant secretary, treasurer, assistant treasurer, speaker, vice-speaker, councillor, trustee, or delegate to the American Medical Association. No person shall be eligible for election to any of the foregoing positions until at least one year has elapsed following completion of the third consecutive term of office as aforesaid. No person shall be eligible for election to any of the foregoing positions having attained the age of 69 years. No person shall be eligible for election to or hold more than one elective position at the same time."

Referred to Special Committee on Constitution and Bylaws.

Section 80 Resolution 62-44

Amendments Introduced at Request of Special Committee on Constitution and Bylaws

Introduced by James Greenough, M.D., Past-President

WHEREAS, The Planning Committee in its report, 62-A, makes recommendations that would require amendments to the Constitution and Bylaws; now therefore be it hereby

Resolved, That the Bylaws be amended as follows:

1. Amend Section 2(c) of Chapter I to add the following new final sentence: "The secretary shall forthwith notify the American Medical Association of said termination of membership."
2. Amend Section 1(b) of Chapter II to change the date, "May 31," to "April 1." (This for conformity with Section 5 of Chapter XIV of the Bylaws, p. 39)
3. Amend Sections 9 and 10 of Chapter VII to substitute the words, "Board of Trustees" for the word "Council." (This for conformity with Section 3 of Chapter V of the Bylaws, p.21)
4. Amend Section 3 of Chapter XI to eliminate the words, "within thirty days after appointment" in the last sentence of said section.

Referred to Special Committee on Constitution and Bylaws.

Section 81 Resolution 62–45

Amendments to Constitution and Bylaws to Limit Terms of Officers

Introduced by Medical Society of the County of Erie

WHEREAS, The Bylaws of the Medical Society of the State of New York do not now limit the number of consecutive terms certain officers, certain members of the Council, and the members of the Board of Trustees may serve; and

WHEREAS, It is highly desirable that a reasonable limitation be imposed on the number of consecutive terms certain elected officers, certain members of the Council, and the members of the Board of Trustees may serve; and

WHEREAS, Such reasonable limitation on consecutive terms of service in elective office is widely resorted to in order to enable organizations to function at maximum effectiveness and in a more democratic manner and to provide the opportunity for, and to encourage, nonincumbents to stand for elective office; now therefore be it hereby

Resolved, That Chapter III, Section 1 of the Bylaws be amended by the addition of the following language: "No member of the Society, who has served six consecutive terms as vice-president, assistant secretary, treasurer, assistant treasurer, speaker, or vice-speaker, or who has served two consecutive three-year terms on the Council, or who has served two consecutive terms on the Board of Trustees, shall be eligible to serve a further consecutive term for the same office.

"A member elected to serve an unexpired term on the Council shall not be regarded as having served a term unless he has served for at least two years.

"A member elected to serve an unexpired term on the Board of Trustees shall not be regarded as having served a term unless he has served for three or more years."

Referred to Special Committee on Constitution and Bylaws.

Section 82 Resolution 62–46

Amendments to Constitution and Bylaws to Implement Planning Committee Report

Introduced by James Greenough, M.D., Past-President

WHEREAS, The Planning Committee in its report, 62-A, makes recommendations that would require amendments to the Constitution and Bylaws; now therefore be it hereby

Resolved, That the Bylaws be amended as follows:

1. (Reference recommendation that a chairman of a commission need not be a member of the Council)

Amend Section 10 of Chapter IV to delete last sentence (i.e., "the chairman of each commission shall be a member of the Council").

2. (Reference recommendation that the secretary, treasurer, assistant secretary, and assistant treasurer shall be limited to five consecutive terms of office)

Amend Section 2 of Chapter III to add the following new sentence to the first paragraph of said section:

"No person may serve more than five consecutive terms as secretary, treasurer, assistant secretary, and assistant treasurer, respectively."

3. (Reference recommendation that councillors shall be limited to three consecutive terms as councillors)

Amend Section 2 of Chapter III to add the following new sentence to the *second* paragraph of said section:

"No person shall serve more than three consecutive terms as a councillor."

4. (Reference recommendation that trustees shall be limited to two terms and be ineligible for re-election thereafter)

Amend Section 3 of Chapter III to add the following new *final* sentence to said section:

"No person shall serve more than one term as a trustee."

Referred to Special Committee on Constitution and Bylaws.

Section 83

Announcements

SPEAKER WURZBACH: The speaker wishes to state that any resolutions brought in this afternoon or tomorrow will be sent to the reference committees handling that business; however, the subjects of the resolutions and the names of the reference committee to which they were referred will be one of the first orders of business Wednesday to have them properly presented, but by this manner your reference committees can consider and work on these resolutions.

THOMAS F. MCCARTHY, M.D., *Bronx:* The resolutions that are introduced tomorrow—how are we going to get them to the members if we don't have a meeting of the House of Delegates?

SPEAKER WURZBACH: They will be distributed on Wednesday morning here or they may be obtained in the Dartmouth Room in the interval.

DR. MCCARTHY: They already will have been referred and have been acted on by the reference committees before we get them?

SPEAKER WURZBACH: Yes, they will be referred to the reference committees so action may be considered on them; otherwise the reference committees will all have to go back into session on Wednesday, which will prevent any reference committee from reporting.

If there is no further business to come before the House at this time, we stand recessed until 9:00 A.M. on Wednesday morning.

. . . Whereupon at 12:15 P.M. the meeting recessed . . .

MAY 16, 1962 | WEDNESDAY MORNING SESSION

The session convened at 9:15 A.M.

SPEAKER WURZBACH: Ladies and gentlemen of the House, will you come to order?

Mr. Secretary, is there a quorum present?

SECRETARY WHEELER: Mr. Speaker, the secretary sees a quorum.

Additional Resolutions

Section 84 Resolution 62–47

Amendment to Constitution and Bylaws to Limit Terms of Office

Introduced by Monroe M. Broad, M.D., Queens County, as an individual

> WHEREAS, The Medical Society of the State of New York reflects the thinking and aspirations of all its members; and
>
> WHEREAS, It is desirable that as wide a representation as possible should exist among the elected officers of the Society; and
>
> WHEREAS, The obligations, duties, and labors of these elected officers should not be foisted on a small group, regardless of their willingness to serve; now therefore be it hereby
>
> *Resolved*, That the first paragraph of Section 2 of Chapter III of the Bylaws be amended by the addition of the following sentence: "No officer above-mentioned with the exception of president and president-elect shall serve for more than *three* consecutive terms of office"; and be it further
>
> *Resolved*, That the second paragraph of Section 2, Chapter III of the Bylaws be amended by the addition of the following sentence: "No member shall serve as a councillor for more than *two* consecutive terms of office."

Referred to Special Committee on Constitution and Bylaws.

Section 85 Resolution 62–48

Date for Payment of State Society Dues

Introduced by Medical Society of the County of Westchester

> WHEREAS, Medical Society membership in the State of New York is now tripartite covering county, State, and A.M.A. membership dues; and
>
> WHEREAS, Because the date when a member is considered in arrears and no longer "a member in good standing" in the A.M.A. is the first of June but the date of delinquency for payment of State dues is the first of March, a great deal of confusion inevitably results in regard to a member's standing in his various medical organizations; now therefore be it hereby
>
> *Resolved*, That the Bylaws be amended as follows:
>
> 1. Amend Section 2(b) of Chapter I of the Bylaws to change the date, "March 1," to "June 1."
>
> 2. Amend Section 2 of Chapter XIV of the Bylaws to change the date, "March 1,"

to "June 1" in the third paragraph of said section.

3. Amend Section 5 of Chapter XIV of the Bylaws to change the words, "the first day of April," to "the first day of June."

Referred to Special Committee on Constitution and Bylaws.

Section 86 Resolution 62–49

Recommending a Change in the Bylaws of the Medical Society of the State of New York, Chapter VII, Section I, re the Appointment of the Nominating Committee

Introduced by Fourth District Branch

WHEREAS, The present status of giving the president of the Medical Society of the State of New York "carte blanche" in the appointment of a Nominating Committee usually results in a "rubber stamp" committee, in which many of the appointees are selected on the basis of personal friendship, and not always because of their interest or activity in the affairs of the Medical Society; and

WHEREAS, In the interest of greater harmony with the State Society, each district branch should have the right to select its own representative to be a member of this important committee; now therefore be it hereby

Resolved, That the Bylaws be amended as follows:

Add the following new sentence following the present fourth sentence of Chapter VII, Section 1: "Members of the Nominating Committee chosen from the several district branches shall be appointed by the president after consultation with and from a list of one or more persons submitted by the executive committee of the district branch concerned to the president."

Referred to Special Committee on Constitution and Bylaws.

Section 87 (see 212) Resolution 62–50

Revision of the Autopsy Consent Law

Introduced by Medical Society of the County of Queens

WHEREAS, The present statute dealing with consent for autopsy in New York State still requires written consent by *all* of next of kin of equal rank; and

WHEREAS, This requirement introduces unnecessary difficulties and has been observed more in the breach than in adherence to the statute; now therefore be it hereby

Resolved, That the Medical Society of the State of New York petition His Excellency, the Governor, to refer to the existing Commission on the Medical Examiner's Law and the Autopsy, the evaluation of the present Wisconsin law, which requires consent of only any *one* of equal rank of kin, provided others of like kinship do not object, to give legal consent for autopsy; and be it further

Resolved, That, after due consideration and evaluation of the comparative advantages of such a revision of the existing Section for Consent for Autopsy, the Commission be requested to formulate legislation to be submitted to the Legislature of the State of New York at its next session, and recommend its adoption and support by the Governor, to correct the existing problem of properly fulfilling the legal requirement for autopsy consent.

Referred to Reference Committee on Legislation and Legal Matters.

Section 88 (see 213) Resolution 62–51

Compilation and Revision of Existing Body of Law Dealing with the Dead Human Body

Introduced by Medical Society of the County of Queens

WHEREAS, There exist many ambiguities, conflicts, and inadequacies in the numerous scattered statutes dealing with the dead human body, as they have been adopted at many different times to meet specific problems; and

WHEREAS, The existing Governor's Commission on Estates is dealing with many tangential problems in this realm; now therefore be it hereby

Resolved, That the Medical Society of the State of New York petition His Excellency, the Governor, to include in the charge to the existing Commission on Estates the survey of the existing body of law dealing with the dead human body, and the clarification of the laws pertaining to the dead human body, and to assure conformity with such legal requirements, by necessary compilation and review, and recommend a revised group of statutes, with such additional statutes as such a survey may indicate; and be it further

Resolved, That the Commission on Estates be charged to submit necessary legislation to accomplish these objectives to the Legislature of the State of New York, and recommend its adoption by the Legislature and the support of the Governor in this effort.

Referred to Reference Committee on Legislation and Legal Matters.

Section 89 (see 161) Resolution 62–52

Protection of Individual Physician Employed by Purveyor of Health Care

Introduced by Samuel Z. Freedman, M.D., Assistant Treasurer

WHEREAS, In the rapidly changing pattern of medical economics, more and more physicians are becoming employes on salary; and

WHEREAS, They may be employes without

tenure and often at the mercy of unilateral decisions made by their employers; and

WHEREAS, A similar situation existed prior to the founding of the trade union movement, which now provides satisfactory protection for the individual union worker; and

WHEREAS, The only organization that can protect the employed doctor in this situation is his county and/or State medical society; now therefore be it hereby

Resolved, That the Medical Society of the State of New York encourage local county medical societies to create a mechanism, which might have the name "Physicians Grievance Commission," to provide the instrument that an individual doctor can call on to protect his interests in cases where he feels he is unjustly treated; and be it further

Resolved, That such grievance commissions offer their services to the employers of medical services so that, by investigation, advice, and counsel, they can implement equity and justice for physicians in the economics aspects of medicine.

Referred to Reference Committee on Commission on Medical Services—A.

Section 90 (*see 214*) Resolution 62–53

Private Hospital Insurance for the Aged

Introduced by Nassau County Medical Society

WHEREAS, The physicians of the Medical Society of the State of New York will always respond to the medical needs of all the people of the State of New York; and

WHEREAS, The King-Anderson Bill would regiment the care of the individual and deny the senior citizen his right to choose his own doctor and hospital; and

WHEREAS, More efficient processing of hospital care insurance can be accomplished at the same cost by utilizing the vast experience of the insurance industry; and

WHEREAS, Utilizing a government assistance of $33^1/_3$ per cent for the needy aged and a tax credit of 50 per cent for the purchase of the nationally proposed Blue Cross coverage or other comparable insurance at an estimated total cost of $11 per month would enable senior citizens or their relatives to purchase this insurance at a net cost of only $3.75 per month; and

WHEREAS, A tax credit alone of 50 per cent for the purchase of the nationally proposed Blue Cross plan or similar coverage at an estimated $11 per month would enable the remainder of our senior citizens or their relatives to purchase this coverage at a reduced net cost of only $5.50 per month; and

WHEREAS, This principle of assistance and tax credit for the senior citizens would enable them to be protected by insurance without being subjected to government restrictions, red tape, delay, and confusion, or administrative expense to the government; now therefore be it hereby

Resolved, That the Medical Society of the State of New York strongly endorse the principle of financing hospital insurance for the needy aged utilizing the principle of government assistance as provided by the Kerr-Mills Law and tax credit for the purchasers of this insurance; and be it further

Resolved, That the Medical Society of the State of New York urge the Congress of the United States not to enact legislation which would drastically affect the future course of health care and which would further centralize government control by financing hospital care through the mechanism of Social Security taxation; and be it further

Resolved, That the delegates of this Society be instructed to introduce and actively support a similar resolution at the June, 1962, meeting of the House of Delegates of the American Medical Association; and be it further

Resolved, That copies of this resolution be sent to the President of the United States, the Secretary of Health, Education, and Welfare, the members of the Senate Committee on Finance, the House Ways and Means Committee, and to the United States Senators and Representatives from the State of New York.

Referred to Reference Committee on Legislation and Legal Matters.

Section 91 Resolution 62–54

Change in Name of the Medical Society of the State of New York

Introduced by Nassau County Medical Society

WHEREAS, John M. Galbraith, M.D., in his supplementary report to the House of Delegates, has requested that the House consider and pass his recommendation that the official name of the Medical Society of the State of New York, as cited in Article I of the Constitution, be changed to the New York State Medical Society; and

WHEREAS, The present name gives the impression to some people that the Society is an official or semiofficial governmental agency; and

WHEREAS, It is so long it hardly ever is used in its entirety; and

WHEREAS, The news media *never* use it and prefer the name "New York State Medical Society"; and

WHEREAS, Changing the present name to the New York State Medical Society would effect an economy of effort in correspondence and facilitate general reference; now therefore be it hereby

Resolved, That the Constitution and Bylaws be amended as follows: Constitution, Article I, first sentence, delete the words

"Medical Society of the State of New York" and substitute the words "New York State Medical Society," so that the sentence will then read, "The name and title of the Society shall be the New York State Medical Society."

Referred to Special Committee on Constitution and Bylaws.

Section 92 (*see 173*) Resolution 62–55

Creation of Commission to Study Problems of Patient Care, Medical Practice, Hospital Service, and Medical Education

Introduced by Medical Society of the County of Queens

WHEREAS, It is desirable that many mutually interrelated problems confronting medicine in patient care, medical practice, hospital service, and medical education be evaluated in proper perspective to obtain a wholly unbiased viewpoint of the many facets of the problems and their suggested solutions, as offered by individual groups in no relation to the whole and the over-all problem of patient welfare and public health; and

WHEREAS, It is imperative to establish proper balance and priorities between the existing groups, agencies, and organizations now working independently, and often unwittingly at cross purposes, based on their own sole and isolated viewpoint; and

WHEREAS, The study of the individual problems by the separate councils and committees of the American Medical Association has yielded recommendations and solutions of particular problems corresponding to the particular charge given to each council and committee separately, but has so often led to new and occasionally more difficult situations in one or all of the other fields involved in medical practice, medical care, hospital service, and medical education; and

WHEREAS, There is every assurance that the problem of expense for such a commission can be underwritten by support from one or more of the foundations interested in medical care and public health; now therefore be it hereby

Resolved, That delegates of the Medical Society of the State of New York introduce at the next meeting of the House of Delegates of the American Medical Association a resolution calling for the creation of a commission, with representation from all groups involved, to study the many problems noted above from the over-all viewpoint, to set forth fundamental goals and objectives, and to recommend priorities and a program of action; and be it further

Resolved, That such a commission, after deliberation and study, suggest specific immediate steps and formulate an ultimate program for the betterment of patient care. medical practice, hospital service, and medical education.

Referred to Reference Committee on Commission on Medical Services—B.

Section 93 Resolution 62–56

Amendment to Bylaws for Early Presentation of Resolutions

Introduced by Medical Society of the County of Schenectady

WHEREAS, It has been increasingly apparent that the majority of resolutions voted on by the Medical Society of the State of New York are presented to the State Society during the annual meeting of the House of Delegates; and

WHEREAS, Many resolutions are presented by individual delegates without regard to the county medical societies they represent; and

WHEREAS, The local county medical societies have no cognizance or understanding of these resolutions until after they have been voted on by the House of Delegates of the Medical Society of the State of New York; now therefore be it hereby

Resolved, That the Constitution and Bylaws be amended as follows:

Amend Section 4 of Chapter VII of the Bylaws to add the following new third sentence in place of the present third sentence: "All resolutions submitted for presentation to the House of Delegates must be forwarded to the speaker at least forty-five days in advance of the annual meeting of the House and referred by him to the president of each component county society, the president of each district branch, the chairman of each section, and the appropriate reference committees; and no resolution presented subsequent to forty-five days may be received or referred to a reference committee except by a two-thirds vote of the delegates."

Referred to Special Committee on Constitution and Bylaws.

Section 94 (*see 134*) Resolution 62–57

Appointment of Members of the Society to Committees

Introduced by James I. Farrell, M.D., Section on Ophthalmology

WHEREAS, In the past, members of the Medical Society of the State of New York have been appointed to committees and subcommittees dealing with certain specialties, and these appointments have been made without consultation with the chairmen of various specialty sections involved; now therefore be it hereby

Resolved, That this House of Delegates hereby request the president and the Council that whenever committees and subcommittees dealing with certain specialties are appointed, the section chairman of each specialty involved be consulted concerning such committee and subcommittee appointments.

Referred to Reference Committee on Organization and Policies.

Physicians' Home

Section 95

Physicians' Home

Speaker Wurzbach: The first order of business we will have this morning is to have one of our past-presidents, a very great friend of the Society, a man who has worked tremendously on the Physicians' Home, give us his report. Dr. Gordon Heyd. (*Applause*)

Chas. Gordon Heyd, M.D., *Past-President:* Mr. Speaker and members of the House of Delegates, for a number of years it has been the pleasure of the Physicians' Home to make a report to you. It is my purpose to do that this morning, very briefly.

First, there is no physicians' home. That was tried many years ago and practically bankrupted the Physicians' Home. It was the creation of doctors and has been maintained and run by doctors. Out of 27 directors, only one is a layman, and that is the legal counsel. All of the others are physicians who carry on the manifest duties of their position.

Last year, the Physicians' Home expended in beneficial aid to physicians $96,000 and received in contributions $90,000, so there was a deficit of $6,000 that is made up from investment income.

The problem of indigency is greater in the big cities, and without any sense of discrimination we will select four of the big cities. New York County on the voluntary assessment of $2.00 contributed approximately $4,000 and $19,000 from the $10 membership. Well, now, how much did we spend for the aid of New York County? We received $23,000 and expended $31,000. As for Bronx County, we received $5,500, and we spent $10,000. In Kings County we received $14,000 and expended $9,000. Kings County is on the high road this time. Queens contributed $4,000, and we expended $9,000.

We took care of 82 individuals: 27 doctors, 9 wives, 34 widows, and 12 dependents. You will see the percentage of widows is nearly a 100 per cent increase over the males.

We have been able to extend our usefulness to create reserves. Some of our patients need dental work, some of them need chairs, some of them need crutches, and we have that reserve for that particular purpose. And we have to bury some of our guests; in fact, we had three deaths last year and two burials that we looked after in detail.

Now, how much does this organization cost? It is running its business on 12 cents per $1.00; 88 cents out of every $1.00 goes to the benefit of our guests.

What is necessary to become a guest? Very simply you must be an American citizen, and you must have paid dues for ten consecutive years. You can live anywhere you want. A budget is arrived at legally. It is given the beneficiary guest, and the road is made easy. It is a pleasure to do this work, and I must doff my hat to the men who are on the board of directors who have been so faithful. The pleasure of this thing is that it is not a charity. The medical profession, you, are taking care of our less fortunate members.

Two little quotes, and then I will be on my way:

> My father's recent death has made more vivid to me the realization of how much your aid over the last few years had meant to him. Your generous assistance made it possible for father to live out the last years of his life in relative comfort and dignity. The family shall always be grateful that these last years were made possible by your kindness.
>
> I have just received your wonderful letter with the enclosed check, for which I am most grateful. I say wonderful letter for the wording has instilled such a different feeling as if I am not accepting charity. Of course I am, but somehow it seems different. It is very difficult for me to find words to express my sincere gratitude to Physicians' Home for your favorable decision in brightening the days to follow which had appeared so black.
>
> I want to thank you and the executive committee for their wonderful help to us. You made the doctor very happy, and he said you gave him back his self-respect.

Thank you very much!

Speaker Wurzbach: Thank you, Dr. Heyd. To me it is always one of the highlights of the convention to hear of this wonderful assistance; I refuse to call it charity.

Additional Guests

Section 96 (see 35, 135, 182)

Introduction of Guests

Speaker Wurzbach: Gentlemen, we have some of our distinguished guests here, and I would like to ask Dr. Freedman to present at the platform James A. MacDougall, M.D., president of the Maine Medical Association.

Samuel Z. Freedman, M.D., *Assistant Treasurer:* It is with a great deal of pleasure that I present to you the president of the Maine Medical Association. Having been up there on two occasions as your representative, if we can reciprocate even half the way they have been treating me up there, I think we will not have done justice to them. They are a wonderful organization, liberal but at the same time very realistic. We can learn a lot from them.

It is with a great deal of pleasure that I therefore introduce to you Dr. MacDougall, the president of the Maine Medical Association.

JAMES A. MACDOUGALL, M.D.: Mr. President, ladies and gentlemen, it has been a great privilege for me that I should be appointed to represent the State of Maine at this great convention of yours.

I am not accustomed to speaking to such gatherings as this, but I feel that a visit with you today very amply pays for any extra effort on my part in attempting to get here. I must apologize for being a day or two late, but I am just back from Montreal where I attended a joint meeting of the Vermont, New Hampshire, and Quebec Medical Associations, and the exigencies of general practice delayed me a day in getting here so I did not arrive until yesterday afternoon.

I have great pleasure in tendering the best wishes of the Maine Medical Association, and if I may introduce something of a personal attribute to what I have to say, I would like very much to meet all of you but particularly anyone who has such a claim to antiquity as to have graduated in 1920 or thereabouts from McGill University. I would like very much to meet them.

Thank you very much! (*Applause*)

SPEAKER WURZBACH: Thank you, Dr. MacDougall.

I will now ask Dr. Moore to present at the platform two distinguished representatives from the State of Pennsylvania, the president, Daniel H. Bee, M.D., and one of their past-presidents, Thomas W. McCreary, M.D.

NORMAN S. MOORE, M.D., *Trustee:* Mr. Speaker and gentlemen of the House, it is a great privilege for me to introduce these two fine gentlemen. We may not know what hospitality is, but they do, I assure you, and I hope that we can reciprocate in some measure. Dr. Daniel Bee and Dr. Tom McCreary.

DANIEL H. BEE, M.D.: Thank you, Dr. Moore.

Mr. Speaker, distinguished members of the Medical Society of the State of New York, the presidents of the Pennsylvania Medical Society appreciate the opportunity of appearing before you. Last year in Rochester it was my great privilege to do this job for the then president, Dr. Thomas McCreary. With the permission of the speaker and with the will of the House, I would like today to yield my prerogative of addressing this House to Dr. Thomas McCreary for the purpose of bringing greetings and best wishes from Pennsylvania.

THOMAS W. MCCREARY, M.D.: Mr. Speaker and members of the House of Delegates, I don't know whether I should thank Dr. Bee for this privilege, but I am certainly going to exercise it because I did miss your meeting in Rochester last year on account of a conflict in dates. At this time of the year there are many state medical societies meeting and meetings within our own society which demand the attention of our president, and Dr. Bee is on such a ten-day tour right now.

Allow me to express my appreciation and thanks and the appreciation of the Pennsylvania Medical Society for the opportunity of appearing before you today. Along with Dr. Bee, I bring you our most sincere greetings.

What I have thought of today to say in a few moments, I know you have heard many times. I am thinking of our problems nationally. I believe that our attendance here attests to the cooperation and the cohesiveness of the various constituent state medical societies with the American Medical Association, and this in defiance of those who claim that the A.M.A. does not truthfully represent the doctors of medicine. It indicates that we are prepared to fight, and to fight together, with the officers of the A.M.A. to preserve freedom in the United States.

I would like to impress on everybody that we are not fighting for freedom only for medicine, but we are fighting for freedom—freedom in all of its aspects—freedom which our children and our children's children have the right to inherit. They have the right to inherit it in this country as it was handed down to us by our forefathers unhampered and unmortgaged. Your president, Dr. Galbraith, very well sounded the battle cry of freedom in his presidential address, and I congratulate him for his substance and his clarity.

I was astounded when I arrived in New York two days ago to turn to my television set in the hotel room and to find the members of the railroad brotherhood standing in a station in New York City and asking people to sign petitions in favor of the King-Anderson Bill. Does history not repeat itself? What has happened to the railroads in this country? Do we desire the same thing to happen to medicine?

It has been said recently by a very, very high officer of our national government that this is politics. Gentlemen, I submit to you that this is politics, a pure political issue conceived to reap the harvest of votes. Thank God, gentlemen, that we have many true Americans in the Congress of our United States who refuse to trade our freedom for security and who are resisting the many pressures being put on them by the Administration, pressures to impress on them to vote favorably to surrender those freedoms which we have inherited. But, gentlemen, they need help and plenty of help. Everything that you have done in the past may be insignificant with what you face in the future. Are we doing all that we can? Are we asking our patients to do all that they can?

Recently the Ambassador from England said, "It may be well to be undisturbed and sporting in losing a game providing that that game is not your freedom."

Again, I thank you for the privilege of the House. (*Applause*)

SPEAKER WURZBACH: Thank you, Dr. McCreary, for this very statesman-like expression of greeting.

Now from the North—what about Walter H. Rath, M.D., from the Vermont State Medical Society?

Dr. Azzari, will you come forward with Dr. Rath?

RENATO J. AZZARI, M.D., *Trustee:* Mr. Speaker and members of the House, it was my privilege just last week to extend the greetings of the Medical Society of the State of New York to the convention in Montreal, which was held there by the Vermont State Medical Society, the New Hampshire State Medical Society, and the Quebec Division of the Canadian Medical Association.

It is now my great pleasure to present to you Dr. Rath from the very wonderful, conservative State of Vermont.

WALTER H. RATH, M.D.: Thank you very much for the honor and privilege of addressing this distinguished assembly. It is true that I, too, am not a speaker and that I come from a state with a total membership less than this House of Delegates. However, we have found a great deal of benefit from something that has been mentioned twice this morning and somehow takes a bit of the wind out of my sails, namely, that we have found in the State of Vermont that a joint meeting with two other states, the State of New Hampshire and now the Province of Quebec, is of great benefit, particularly in these days of repeated crises with which we are constantly faced.

It is, therefore, with great pleasure that I have been authorized to suggest to this august body that in the near future we hold further joint meetings, particularly between the Houses of Delegates, and, if this is too large an assembly, perhaps between the councils of the various state bodies.

It is again a great privilege to be here. Thank you for your hospitality, and I hope each and every one of you will visit us some time in the near future. Thank you! (*Applause*)

SPEAKER WURZBACH: Thank you, Dr. Rath.

Dr. Moore: will you present Dr. Clark of the New York State Veterinary Medical Society?

DR. MOORE; Mr. Speaker and gentlemen of the House, it is my privilege again to come to the platform to introduce to you Robert E. Clark, D.V.M., the representative of the New York State Veterinary Medical Society.

ROBERT E. CLARK, D.V.M.: This is indeed a pleasure to attend this meeting. I really did not expect to have to give a talk, which I will not. I want to extend from the New York State Veterinary Medical Society our very best wishes to the Medical Society of the State of New York on the occasion of this convention. I know it will be a success, and I appreciate the opportunity to attend and see how other groups do things through your House of Delegates. Thank you very much! (*Applause*)

Section 97

Reference of Resolutions Distributed Since Monday

SPEAKER WURZBACH: Now, the speaker wishes to present to the House the resolutions which were brought for action during the recess.

. . . Speaker Wurzbach then read by title and introduced resolutions 62–47 through 62–57 and announced the reference committees to which each had been referred . . .

These are now presented to the House. They have been sent unofficially to the reference committees, and they may now report on them officially.

Reference Committee on Public Health and Education

Section 98 (*see 10*)

Report of Reference Committee on Public Health and Education: Public Health and Education

THOMAS S. BUMBALO, M.D., *Erie:* Mr. Vice-Speaker, your Reference Committee on Public Health and Education reviewed and discussed the reports of the parent Council committee and its seventeen subcommittees. Its meeting was attended by a group of interested physicians who were not members of the reference committee but who participated in its deliberations.

The annual reports of the above committees are presented on pages 61 to 72 of the Handbook and in Supplementary Reports 62–D and 62–E.

Your reference committee has reviewed the report of Chairman James Greenough and notes with approval the following changes in the structure of the Committee on Public Health and Education:

1. As of October, 1961, the chairman undertook to work full time for the committee.
2. Two new subcommittees have been approved by the Council and were appointed as of March 1, 1962. These are the Subcommittee on Chronic Pulmonary Diseases, including tuberculosis, and the Subcommittee on Continuing Postgraduate Education.
3. With the start of the new Medical Society year, it is planned that each subcommittee have a vice-chairman as well as a chairman.

Your reference committee discussed the

functions of the new Subcommittee on Chronic Pulmonary Diseases and deliberated on whether or not they should include lung cancer. It was agreed that for the present, at least, they should not, inasmuch as the administrative setup of the State Health Department demands that cases of pulmonary tuberculosis and those involving carcinoma of the lung be treated in separate units.

Mr. Speaker, I move approval of this portion of the report.

SAMUEL LEO, M.D., *Bronx:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 99 (see 10)

Report of Reference Committee on Public Health and Education: Postgraduate Education

DR. BUMBALO: It was indicated by Dr. Greenough that the new Subcommittee on Continuing Postgraduate Education would endeavor to evaluate the present program of the State Society in relation to the needs of the physicians and their desire for certain types of presentation, such as the seminar type. Its study will be correlated with the survey which is being planned by a committee appointed by the Governor.

Your reference committee suggests that one specific function of the subcommittee might be to approach the Joint Commission on Accreditation of Hospitals to permit hospitals to claim attendance credit by their staff members when attending meetings with the staffs of other hospitals. This would achieve broader dissemination of education among the members of the profession, who often are on the staff of several hospitals and cannot give the time required to attend the staff meetings of all of them, as well as meetings of their respective specialty groups.

Mr. Speaker, I move approval of this portion of the report.

EDWARD F. SHEA, M.D., *Ulster:* I second it.

VICE-SPEAKER BABBAGE: It has been moved and seconded. Is there any discussion of this portion of the report?

GERALD D. DORMAN, M.D., *Councillor:* I would like not to speak against this at all, but on the Joint Commission on Accreditation it is up to the individual hospitals to decide how many staff meetings they have to have. It might be that they would also agree where there are hospitals in an area that they would allow cross meetings. I know that it has been discussed in the past, and the Joint Commission on Accreditation feels it is up to each individual hospital to control that and not to throw it on a group of hospitals because each hospital is responsible for its own board. I see no objection to submitting this to them however. I am speaking not against this, but it is something that has been considered. I see no objection to considering it again.

VICE-SPEAKER BABBAGE: Thank you.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 100 (see 10)

Report of Reference Committee on Public Health and Education: Accident Prevention

DR. BUMBALO: It was pointed out that the form of the Subcommittee on Accident Prevention will be changed with the new Medical Society year. This committee will work toward specific recommendations or measures to be followed in assisting to reduce automotive accidents and injuries. A body of advisers to the subcommittee will, as before, make recommendations to the State Health Department and the Motor Vehicle Bureau in questionable cases of issuing or reissuing of operator's licenses.

Your reference committee urges the establishment in schools of a street crossing drill comparable to the fire drill as an additional educational measure in the prevention of accidents. Parent participation, through the P.T.A., would be desirable to complete the project.

Mr. Speaker, I move approval of this portion of the report.

JAMES L. HARRINGTON, M.D., *Jefferson:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 101 (see 10)

Report of Reference Committee on Public Health and Education: Aging and Nursing Homes

DR. BUMBALO: Your reference committee is especially impressed by the fact that this Subcommittee on Aging and Nursing Homes devoted two of its meetings entirely to matters of legislation pertaining to medical assistance to the aged.

In its deliberation the reference committee commented on the desirability of urging the total approach to the care of the aged, including housing, recreation, nutrition, employment, and so on. However, it is not the intent of this recommendation to advocate isolation of the aged in a community of their own.

The reference committee has noted with interest and recommends the use of day centers for the older person as they exist in some metropolitan areas.

Mr. Speaker, I move approval of this portion of the report.

ABRAHAM W. FREIREICH, M.D., *Nassau:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 102

Report of Reference Committee on Public Health and Education: Addiction to Alcohol and Narcotics

DR. BUMBALO: The Subcommittee on Addiction to Alcohol and Narcotics has had several interesting meetings, and your reference committee commends the subcommittee for its dynamic approach to the problems in this field. We would emphasize the recommendation for promotion of education in the schools on alcoholism and narcotic addiction.

Mr. Speaker, I move approval of this portion of the report.

DR. SHEA: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 103 (see 10)

Report of Reference Committee on Public Health and Education: Cancer

DR. BUMBALO: Your reference committee is in accord with the views of the Subcommittee on Cancer in endeavoring to promote the wider use of cytology in the detection of cancer but would urge that all possible avenues for the early detection, diagnosis, and treatment be employed, including cytologic examination in the private physician's office, in clinics, and in hospitals, even though at times this might mean duplication of examination.

It was the consensus that intensive physician education in cytology should be encouraged.

Mr. Speaker, I move approval of this portion of the report.

DR. LEO: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 104

Report of Reference Committee on Public Health and Education: Child Accidents

DR. BUMBALO: The Subcommittee on Child Accidents has made numerous recommendations to help reduce the incidence of child accidents. The reference committee is in accord and commends the subcommittee for its detailed study.

It was announced by the chairman of the parent committee that this subcommittee will be eliminated as such and its functions be incorporated in the revised Subcommittee on Accident Prevention, thus making the latter a more inclusive one. It is the feeling of the reference committee that the subcommittee will function more expeditiously and economically as a result of this change.

Mr. Speaker, I move approval of this portion of the report.

DR. SHEA: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 105 (see 10)

Report of Reference Committee on Public Health and Education: Diabetes

DR. BUMBALO: Your reference committee approves the activities of the Subcommittee on Diabetes to develop ways of improving education and means of detecting diabetics in as many communities as possible. We also note and approve the efforts to enlist the assistance of other organizations and agencies, both lay and professional, which are interested in this problem.

Mr. Speaker, I move approval of this portion of the report.

DR. HARRINGTON: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 106

Report of Reference Committee on Public Health and Education: General Practice

DR. BUMBALO: At a meeting of the Subcommittee on General Practice on May 15, attended by the chairman of your reference committee, there was discussion of methods of stimulating interest in a general practice section in our medical schools. The subcommittee is preparing a list of recommendations stemming from a survey by the Academy of General Practice of the plans used at the Universities of Kansas and Tennessee, which are functioning successfully. Your reference committee is in accord with these plans and urges continued intensified study in this area.

As a constructive step toward better liaison, this reference committee recommends that the county medical society, where possible, elect to its comitia minora a full-time teacher from the medical school and, where this is not possible, appoint some other full-time government-employed doctor to the comitia minora.

I move the approval of this portion of the report.

DR. LEO: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 107

Report of Reference Committee on Public Health and Education: Glaucoma and Other Diseases of the Eye

DR. BUMBALO: Your reference committee notes with approval the activities of the Subcommittee on Glaucoma and Other Diseases of the Eye and is in accord with the change in the name of the committee to Subcommittee on Glaucoma and Other Diseases of the Eye.

Mr. Speaker, I move the approval of this portion of the report.

DR. FREIREICH: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 108

Report of Reference Committee on Public Health and Education: Hard of Hearing and the Deaf

Dr. Bumbalo: The reference committee would like to call attention to the fact that hearing defects in children in the smaller rural areas probably are not detected as early or as universally as they should be, and it recommends that physicians in these localities refer suspected hearing defects to private otologists wherever possible or to hearing centers if necessary.

Mr. Speaker, I move approval of this portion of the report.

Dr. Leo: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 109 (see 10)

Report of Reference Committee on Public Health and Education: Health Aspects of Ionizing Radiation

Dr. Bumbalo: Your reference committee is in accord with the activities of the Subcommittee on Health Aspects of Ionizing Radiation and approves the educational project to disseminate much-needed information to the physicians of the State about the hazards of ionizing radiation and the reduction of this danger. This will be accomplished through the New York State Journal of Medicine and brochures which will be distributed to the profession. These articles will be prepared in conjunction with the Health Departments of the State and the City of New York and with the Atomic Energy Commission.

Mr. Speaker, I move approval of this portion of the report.

Dr. Shea: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 110 (see 10)

Report of Reference Committee on Public Health and Education: Heart Disease

Dr. Bumbalo: Your reference committee commends the Subcommittee on Heart Disease for its well-organized plan to educate the physicians of the State in the newer technics for emergency resuscitation.

Mr. Speaker, I move the approval of this portion of the report.

Dr. Leo: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 111 (see 11)

Report of Reference Committee on Public Health and Education: Maternal and Child Welfare

Dr. Bumbalo: Your reference committee notes with approval the activities of the Subcommittee on Maternal and Child Welfare and particularly the articles which have appeared in the Journal directed toward the reduction of maternal morbidity and mortality.

Mr. Speaker, I move the approval of this portion of the report.

Dr. Harrington: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 112

Report of Reference Committee on Public Health and Education: Medical Film Review

Dr. Bumbalo: The reference committee calls attention to the list of 16 films on a variety of medical subjects which have been reviewed by the Subcommittee on Medical Film Review and added to the State Department of Health's film library.

It is urged that the list of available films be publicized regularly in the New York State Journal of Medicine and by the Health Department to encourage its use by the physicians of the State.

Mr. Speaker, I move the approval of this portion of the report.

Dr. Freireich: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 113 (see 10)

Report of Reference Committee on Public Health and Education: Mental Hygiene

Dr. Bumbalo: Your reference committee, after studying the report of the Subcommittee on Mental Hygiene, recommends the addition of the following sentence to the last paragraph of item 4 of the annual report (bottom of page 70 of the Handbook): "The judiciary should, of course, retain its function of protecting the civil rights of patients."

Mr. Speaker, I move the approval of this portion of the report.

Dr. Shea: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 114

Report of Reference Committee on Public Health and Education: Operating Room Mortality

Dr. Bumbalo: Your reference committee recognizes the need for the epidemiologic approach to the study of immediate anesthetic-surgical mortality that has been commenced in New York City and recommends its expansion to the entire State.

Mr. Speaker, I move the approval of this portion of the report.

Dr. Harrington: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 115

Report of Reference Committee on Public Health and Education: Physical Medicine and Rehabilitation

Dr. Bumbalo: Your reference committee approves the projected plan to compile a directory of rehabilitation facilities and agencies in the State. It is the feeling of the reference committee that there is a real need for such a directory.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Leo: I second it.

Vice-Speaker Babbage: It has been moved and seconded. Is there any discussion on this portion of the report?

Maurice J. Dattelbaum, M.D., *Treasurer:* Mr. Speaker and members of the House, I have been listening to these recommendations. I hope you have also. But I call your attention to the fact that if there is any money to be spent for any extra work, printing, or anything, we would like to know how much it would cost and see whether it is available to put it into the budget or not. You must see to it that the expenses are kept down. Thank you.

Vice-Speaker Babbage: Thank you, Dr. Dattelbaum.

Is there any further discussion?

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 116

Report of Reference Committee on Public Health and Education: School Health

Dr. Bumbalo: Your reference committee was informed that the meeting planned with Dr. E. R. Van Kleeck, of the State Education Department, mentioned in the annual report, has not yet taken place. However, Dr. Greenough is arranging a conference to include members of the Subcommittees on School Health and General Practice.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Leo: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Bumbalo: I move the adoption of the report as a whole.

Dr. Leo: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Bumbalo: The chairman of your reference committee wishes to thank the members of his group for their interest and real contribution to the deliberations in connection with each of the reports reviewed. Stimulating discussion was engendered which benefited not only the members of the committee but the observers as well. His thanks go also to the secretary, Miss Susan V. Baker.

Reference Committee on Ancillary Groups

Section 117

Report of Reference Committee on Ancillary Groups: Report of New York State Association of the Professions, Inc.

Samuel Lieberman, M.D., *Bronx:* Ancillary groups includes the Advisory Committee to the Woman's Auxiliary, the Council Committee on Nursing Education, the Empire State Medical, Scientific and Educational Foundation, Inc., the New York State Association of the Professions, Inc., and the Joint Committee with the New York Bar Association.

The New York State Association of the Professions, Inc., is an association comprising the Medical Society of the State of New York, the New York State Association of Architects, the Dental Society of the State of New York, the New York State Society of Professional Engineers, the Pharmaceutical Society of the State of New York, and the New York State Veterinary Medical Society, with an invitation for membership extended to the New York State Society of Certified Public Accountants. The purposes of the organization are 11 in number, aimed to encourage the participation of learned professions in programs having for their purpose the advancement of professional ideals and professional welfare, the promotion of a better understanding between the professions, an interchange of opinions, and a closer liaison. This organization is in its infancy; several meetings have been held. At a meeting in January, 1962, it was decided that the New York State Association of the Professions, Inc., would consider and take action on legislation matters in the public interest which affect two or more State organization members and should oppose legislation which tends to socialize or lower the standards of any of the professions. Effort is being made by this organization to amend the Education Law to authorize the members of any profession to organize an association to engage in the practice of their profession in corporate form and thereby enjoy certain tax advantages accorded to corporations.

The reference committee considers this report as one exhibiting a great deal of work on the part of the members of the association and offers its commendation to the committee and to its chairman pro tem, Henry I. Fineberg, M.D.

Mr. Speaker, I move the adoption of this portion of this report.

Robert F. McMahon, M.D., *Onondaga:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 118

Report of Reference Committee on Ancillary Groups: Advisory to Woman's Auxiliary

Dr. Lieberman: The report of the Advisory Committee to the Woman's Auxiliary was considered. A fine piece of work has been done by the ladies on assistance in explaining the implementation of the Kerr-Mills Act and their opposition to the King-Anderson Bill. They have been most helpful in their efforts to reach senators and congressmen. Membership has increased during the year, and a new auxiliary started in Putnam County, with a reactivation of the auxiliary in Fulton County. Several county auxiliaries have planned and carried out to successful conclusions health career days and programs to encourage students to enter the fields of medicine, nursing, and other ancillary medical professions.

The Woman's Auxiliary magazine, *Distaff*, Mrs. Milton Spiegel, editor, which is published three times yearly, has a new cover and format, and the circulation procedure has been completely revised.

The committee has recommended that the A.A.P.S. Essay Contest, resolution 61–27, endorsed by this Society in May, 1961, be discontinued due to the lack of support and scarcity of participants in this contest. In keeping with their previous efforts, the Auxiliary expects to make continued efforts to increase contributions for the Physicians' Home.

The reference committee accepts the report of the advisory committee, James J. McCartney, M.D., Albert Vander Veer, II, M.D., and Norman S. Moore, M.D., chairman, in its expression of thanks to Mrs. Eugene F. Wolff, president of the Woman's Auxiliary, its officers, and members, for their cooperation.

Mr. Speaker, I move adoption of this portion of the report.

H. John Mellen, M.D., *Albany:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 119

Report of Reference Committee on Ancillary Groups: Nursing Education

Dr. Lieberman: The reference committee calls attention to the fact that this year no meetings of the Committee on Nursing Education have been held because of the illness of the chairman. Since the question of nursing education and the present shortage of nurses is a serious situation, the reference committee recommends that in the future, when a chairman of a committee unfortunately becomes ill and/or is unable to fulfill his duties as a chairman, notice should be given immediately to the State Society officers that the work of the committee is not being carried out. It will then be possible for the Society to appoint another chairman so the necessary program may be carried out. The reference committee further recommends that serious consideration be given to the appointment of the next Committee on Nursing Education for the all-important part that such education plays in the provision of necessary ancillary personnel for good medical care.

Mr. Speaker, I move adoption of this portion of this report.

Morris Maslon, M.D., *Warren:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 120 (see 20)

Report of Reference Committee on Ancillary Groups: Joint Committee with the New York State Bar Association

Dr. Lieberman: No formal meetings of the Joint Committee of the Medical Society of the State of New York and the New York State Bar Association were held in 1961–1962. The cochairmen of the committee did discuss the proposed lien law for physicians which will be considered in the fall of 1962. Milton Helpern, M.D., one of the cochairmen, has spoken of the activities of the chief medical examiner of New York City at many medical meetings and has appeared before the law revision committee of the Legislature to discuss legislation which will provide for the establishment of a medical examiner's system in those counties desirous of abolishing the office of the coroner and/or the appointment of qualified doctors of medicine to assist the coroner in those counties in which the office of coroner is continued and the coroner is a layman.

This legislation was passed by both houses and signed by the Governor.

Dr. Helpern has also addressed a combined meeting of the Medical Society, the Dental Society, and the Bar Association in Wayne County.

The reference committee is of the opinion that this Joint Committee with the New York State Bar Association has done an excellent job and should be commended for its activities and reports.

Mr. Speaker, I move adoption of this portion of this report.

Dr. Mellen: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 121 (see 15)

Report of Reference Committee on Ancillary Groups: Empire State Medical, Scientific and Educational Foundation, Inc.

Dr. Lieberman: The Foundation has had as its planned activities during 1961 the study of maternal and perinatal mortality. Funds for this study were provided by the Department of Health of the State of New York, amounting to $21,754.34, of which sum $19,199.50 was spent on this activity, leaving a net income from this project of $2,554.78. The Medical Society of the State of New York contributed $8,000 to provide working capital. The balance sheet, as of December 31, 1961 (Report 62–I) reveals a surplus of $12,428.36. An appropriation has again been made in the budget for 1962 for $8,000, should additional working capital be required during the year 1962. The project on maternal and perinatal mortality, we are informed, has been of great value. The Foundation looks forward to other worth-while projects in which it hopes to engage in the future. The delegates are advised that the original $8,000 contributed by the Medical Society of the State of New York is for working capital. In a like manner, the provision is made for a similar sum of money in the budget for 1962. These sums of money represent evidence of participation in the activity of this fund by the Medical Society of the State of New York. Such outlay is essential for three reasons:

1. It is the policy of the State agencies not to pay grants until the monies have been spent. Therefore, the money is needed for working capital until such time as State reimbursement is made.
2. Participation of the Medical Society of the State of New York in this fund, through its contribution, will make it possible for the fund to operate on a tax-free basis and, in so doing, will attract the contributions of other monies from other sources interested in furthering the efforts of the Foundation.
3. The reference committee has been informed that many of the programs of the Society, as, for example, postgraduate education, could eventually be financed through this Foundation.

The reference committee is of the opinion that the Empire State Medical, Scientific and Educational Foundation, Inc., is a worth-while project and that the Medical Society of the State of New York should continue its sponsoring and contribution of funds to the organization.

The officers, directors, and members of the Foundation, John M. Galbraith, M.D., Norman S. Moore, M.D., James Greenough, M.D., Edward C. Hughes, M.D., Maurice Dattelbaum, M.D., Joseph A. Lane, M.D., Herman E. Hilleboe, M.D., Granville W. Larimore, M.D., William L. Wheeler, Jr., M.D., Henry I. Fineberg, M.D., Renato J. Azzari, M.D., Frederic W. Holcomb, M.D., William F. Martin, Esq., Richard Burns, Esq., and Thomas E. Alexander, are to be commended for the time and effort they have devoted to this worthy project.

I move the adoption of this portion of the report.

Dr. Maslon: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Lieberman: Mr. Speaker, I move the adoption of the report as a whole.

Dr. Mellen: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Lieberman: Mr. Speaker and members of the House of Delegates, the chairman of your reference committee wishes to thank the members of his committee for their cooperation and contribution in the deliberations relative to the subject matter discussed. We are in addition indebted to our secretary, Mrs. Cathleen Thayer, for her help and cooperation.

Reference Committee on Medical Care

Section 122

Report of Reference Committee on Medical Care: Medical Advisory Committee to the Bureau of Disability Determinations

Irving M. Pallin, M.D., *Kings:* Our first item has to do with the Medical Advisory Committee to the Bureau of Disability Determinations.

The reference committee has considered the report of the Medical Advisory Committee to the Bureau of Disability Determinations which appears in your Handbook. The report states that no meeting was held during the current year and that one item brought to its attention was referred to the Economics Committee. In the absence of subject material or recommendations, this material is for information only.

Mr. Speaker, I move the adoption of this part of the report.

William B. Rawls, M.D., *New York:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 123

Report of Reference Committee on Medical Care: Disaster Medical Care

Dr. Pallin: Your reference committee wishes to commend Edward Burkhardt, M.D., and his Committee on Disaster Medical Care for the progress they have made in liaison between the governmental agencies and voluntary groups and the physicians who have participated in these disaster training programs. Your reference committee recommends that the report be approved in principle and that the county medical societies be urged to establish advisory committees to stimulate all medical and administrative staffs of hospitals within their geographic area in the formation of disaster units and to aid in the organization and implementation of disaster training programs.

Mr. Speaker, I move the adoption of this part of the report.

PHILIP M. STANDISH, M.D., *Ontario:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 124 (see 12)

Report of Reference Committee on Medical Care: Columbia University Study of Nonprofit Medical Insurance Plans

DR. PALLIN: Concerning the Columbia University Study of Nonprofit Medical Insurance Plans, the limited material which appears in your Handbook and Supplementary Report 62–F was reviewed. The chairman of the advisory committee of the Medical Society of the State of New York to the above committee, John C. McClintock, M.D., was kind enough to appear and to provide background material on the work of his committee. It should be noted that this advisory committee has been hampered in its deliberations by the tardiness and incompleteness of the report submitted to them. This 94-page document was received about April 23 but without the final chapter containing the recommendations. Dr. McClintock intimated that inaccuracies were found. The chairman further explained that the report was contracted for by the Commissioner of Insurance and that his release of this report is necessary for its availability. To date it has not been released and was not available to your reference committee.

After prolonged discussion your reference committee decided that in the absence of subject matter for consideration, it should not come to any conclusions on this report. Dr. McClintock and his committee should be commended for undertaking such a massive study so intensively. This reference committee recommends that the advisory committee as constituted be continued until completion of this study.

Mr. Speaker, I move adoption of this portion of the report.

JAMES M. JONES, M.D., *Westchester:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. PALLIN: Your reference committee also noted the statement in the Handbook that this advisory committee "especially objected to reducing the number of doctors of medicine on the boards of directors of Blue Shield Plans." Therefore, your reference committee recommends that the House of Delegates go on record as being opposed to any change in the present ratio of doctors of medicine on the boards of directors of Blue Shield plans.

Mr. Speaker, I move adoption of this part of the report.

SIRKKA E. VUORNOS, M.D., *Sullivan:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. PALLIN: Mr. Speaker, I move the adoption of the report of the Reference Committee on Medical Care as a whole.

DR. RAWLS: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. PALLIN: I wish to take this opportunity to express my gratitude to the members of the Reference Committee on Medical Care for their help in the preparation of this report.

I wish to thank our secretary, Mrs. Beatrice E. Doherty, for her assistance and all those members of the Society who were kind enough to participate in the discussion.

Reference Committee on Organization and Policies

Section 125 (see 7)

Report of Reference Committee on Organization and Policies: Planning Committee for Medical Policies

CHARLES C. MANGI, M.D., *Queens:* Mr. Speaker and members of the House of Delegates, your reference committee wishes to report first on the Planning Committee for Medical Policies as outlined in the annual Report 62–A.

1. Committees' tenure of office: Your reference committee discussed the report of the Planning Committee for Medical Policies and reviewed the subject of tenure of office for committee members to improve the committee setup with definite rules for tenure of office. The size of committees was reviewed, and a reduction of membership in each committee was suggested, so that the efficiency could be increased and the cost to the Society reduced. By limiting the time a man may be in office, members of committees could be replaced after a certain period, and no one would be offended.

Your reference committee approves these recommendations of the Planning Committee.

Mr. Speaker, I move adoption of this portion of the report.

CHARLES M. BRANE, M.D., *Westchester:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: Your reference committee suggests that the State Society request each county society to submit the names of the men who have done outstanding work on their county society committees and who are willing to serve on State Society committees.

Mr. Speaker, I move adoption of this portion of the report.

ANGELO F. LEONE, M.D., *Orleans:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: The commission and committee structure were reviewed. The Council committees were also reviewed, and it was noted that eight committees have been eliminated and their duties delegated to other committees or to the office of the executive vice-president. These include Subcommittee on Cults, Membership Committee, Subcommittee on Licensure of Clinical Laboratories, Subcommittee on Cooperation with Media of Information, Advisory Committee to the Woman's Auxiliary, Committee on Child Accident Prevention, Advisory Committee to the Bureau of Disability Determinations, and the Committee on Office Administration and Policies.

Your reference committee approves these recommendations of the Planning Committee.

Mr. Speaker, I move adoption of this portion of the report.

THOMAS M. FLANAGAN, M.D., *Chenango:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: Your reference committee also considered the proposal made in the supplementary report of the president. Dr. Galbraith suggested the formation of a Commission on Public Affairs to prevent the overlapping that exists in the areas of public relations and legislation. Such a commission would bring about greater coordination and integration of all activities in these fields and would provide us with the opportunity of making a full committee out of the present Subcommittee on Federal Legislation. The commission would consist, at least in the beginning, of three committees—Public Relations, State Legislation, and Federal Legislation—and could include any other appropriate committees. It is felt that such a commission would have further value in being able to cope with the problems impinging on public affairs that are not clearly within the area of any one committee and yet call for consideration or action on our part. Your reference committee feels that the formation of this commission will expedite the activities of the various committees and represent a financial saving to the Society.

Your reference committee recommends approval of these recommendations of the president. Please note that it is not the recommendations of the Planning Committee but of the president.

Mr. Speaker, I move adoption of this portion of the report.

DR. BRANE: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: Tenure of officers: Your reference committee has reviewed the recommendations on tenure of officers. The Planning Committee has recommended:

1. Secretary, treasurer, assistant secretary, and assistant treasurer may not be elected to more than five successive one-year terms but could be re-elected one year thereafter.

2. Councillors may not have more than three consecutive three-year terms but could be re-elected one year thereafter.

3. Trustees may not have more than one five-year term and may not be eligible for re-election thereafter.

Your reference committee agrees with the recommendations except that it suggests that councillors may not have more than two consecutive three-year terms, instead of three consecutive three-year terms as recommended by the Planning Committee.

Mr. Speaker, I move adoption of this portion of the report.

FRANK LAGATTUTA, M.D., *Bronx:* I second it.

SPEAKER WURZBACH: Is there any discussion?

SAMUEL Z. FREEDMAN, M.D., *Assistant Treasurer:* I would just like to raise the question whether this does not involve a change in our Constitution and Bylaws and, if it does so involve a change of Constitution and Bylaws, does this not have to lay over for a year?

SPEAKER WURZBACH: I think it does.

JAMES GREENOUGH, M.D., *Past-President:* To implement this will require a change in the Bylaws and/or the Constitution, and those motions are in and referred to the House Committee on Constitution and Bylaws. However, I see no reason why this House of Delegates should not approve the report of the committee which will not make it active until the resolutions I mentioned have been acted upon.

WILLIAM F. MARTIN, ESQ., *Legal Counsel:* But it does have to stay over one year.

DR. GREENOUGH: Yes.

SPEAKER WURZBACH: In other words, this House is being asked to approve the principles herein involved, although no implementation can be taken until the Constitution and Bylaws Committee reports next year.

ARTHUR J. BEDELL, M.D., *Past-President:* I most heartily disagree with this proposition. It is not based on historical fact. We do not go on record as approving something until we vote and so decide. I sincerely hope the motion will not prevail.

SPEAKER WURZBACH: We are only voting on the principle. We are not voting on any action because no action can be taken, which is certainly understood.

DR. BEDELL: It should be so worded in the resolution.

Thomas F. McCarthy, M.D., *Bronx:* Inasmuch as this has promoted some controversy, would the chairman think it advisable to present these things separately? In other words, there are three distinct recommendations, one involving officers, one involving councillors, and one involving trustees. Possibly we might differ on one. In other words, we are being offered a proposition, and either you approve all or none. I think if you recommend one at a time, we could maybe arrive somewhere.

Speaker Wurzbach: I believe that this could be handled a great deal differently if we consider this as information only because no action, definitive action, can be taken.

Chorus: Yes.

Speaker Wurzbach: All in favor of considering this as information say "aye," opposed "no." It is so ordered. Continue, Dr. Mangi.

Dr. Mangi: The second item on this report was the annual meeting.

Dr. Wurzbach, the speaker of the House, was asked by the Planning Committee to investigate the possibility of changing the date of the annual meeting. He has submitted an excellent report. The Planning Committee approved of Dr. Wurzbach's report and recommended the following to the House of Delegates:

1. The annual meeting of the Society and of the House of Delegates shall be held in the second half or in the month of February, 1964, and thereafter at this time.
2. Contracts be sought from the Americana Hotel or other hotel for February, 1964, and annually thereafter.
3. The annual meeting of the Medical Society of the State of New York be continued to be held on Wednesday evening of the week in which the House of Delegates meets.
4. The House of Delegates meet four days. The final meeting, election, to be Thursday morning.

Dr. Wurzbach has obtained the following dates from the Americana:

1964—February 9 to 14
1965—February 7 to 12
1966—February 13 to 18
1967—February 12 to 17

It is felt that changing the time of the meeting to February would entail less expenditure on the part of the State Society. It is estimated that about $4,500 in rental would be saved. An increase of about 20 per cent in exhibit space can be anticipated. It is also felt that February would be a time when there would not be any competition with other major medical meetings and that there would be a greater availability of speakers for the scientific sessions. It is also expected that there will be a better attendance on the part of members. Further, it was brought out that a February meeting would give the State Society ample time to prepare any resolutions that would be introduced at the A.M.A. House of Delegates meeting in June.

Your reference committee recommends approval of these recommendations of the Planning Committee.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Flanagan: I second it.

Speaker Wurzbach: Is there any discussion?

Gerald D. Dorman, M.D., *Councillor:* I do not oppose this resolution, except I want it very clear that the Americana does not have a monopoly at this time. It does say "or other hotel."

Speaker Wurzbach: Definitely.

Dr. Dorman: But with the A.M.A. we have to be sure that the people who implement the resolutions of the A.M.A. House have enough freedom so that the hotel does not say you were mandated to have it here, because very often if there are competitive bids, we can get a better deal. It does so state in this resolution "Americana Hotel or other hotel," but I just want to point out that this is understood by the House.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Mangi: The third item was on policy toward labor.

The Planning Committee planned to review the policy of the State Society toward labor. It felt that it should be recommended to the Council and the House of Delegates that the Medical Society of the State of New York should be represented by carefully selected individuals on the New York City Central Labor Council, AFL-CIO Professional Advisory Committee, representatives having equal status with those of management and labor, so as to improve the relationship between medicine and these groups. The Planning Committee believes that it should go into more detailed discussions with management and labor on a much broader basis and that closed panel practice should receive considerable attention. The Planning Committee recommends continued study of these matters during the next year.

Your reference committee heartily agrees with the sentiments of the Planning Committee and recommends approval of the report.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Brane: I second it.

Speaker Wurzbach: Is there any discussion?

Dr. Freedman: I would submit for your consideration the addition of several words. I will start from the beginning of the sentence where it says, "It felt that it should be recommended to the Council and the House of Delegates that the Medical Society of the State of New York should be represented by carefully selected individuals," and so on. I would say, "carefully selected individuals by the State Society and/or local medical societies that may be interested in the area in which this is being done."

SPEAKER WURZBACH: In other words, you mean put in there State and locally?

DR. FREEDMAN: No, but chosen by.

SPEAKER WURZBACH: State and locally?

DR. FREEDMAN: Medical Society of the State of New York and/or local county societies. I submit to you that in the City of New York we have had some very unpleasant experiences where the members chosen from the medical profession on these committees have not necessarily been those recommended by the local county societies, and if this is to be of any value at all, I think this is essential that it be recommended. I therefore move that this be added.

. . . The amendment was seconded . . .

SPEAKER WURZBACH: This addition to the report has been recommended. Is there any discussion on this addition, as presented by Dr. Freedman?

SAMUEL LIEBERMAN, M.D., *Bronx:* Mr. Speaker and members of the House of Delegates, I feel reasonably certain that local societies in selecting a man to represent them on a council or committee like this would naturally pick men of ability in whom they think they can place their trust, so you would have that kind of appointment.

SPEAKER WURZBACH: I certainly don't think Dr. Freedman meant any disparagement of any local society. I think, therefore, we will just move forward in the consideration of the addition of Dr. Freedman. Is there any objection to it?

CHORUS: Reread your amendment.

CARL R. ACKERMAN, M.D., *Bronx:* This was considered at the Coordinating Council meeting or rather the meeting of the First District Branch. The arrangement is that both the State Society has been approached to make suggestions as to membership, and through the Coordinating Council the local societies have been approached. I believe that in the consideration of the committee they were only dealing with that portion that deals with State Society policy. I don't think there is any need to add the other words because this is the way it is structured now.

SPEAKER WURZBACH: Is there any further discussion?

DR. FREEDMAN: May I explain what I had in mind? I believe it is being misunderstood. I am concerned about what has already taken place. I can only speak for the City of New York, and I can speak for many, many years that have gone by in which it has happened that the different committees have been chosen on which physicians have been represented. No one in the City of New York who has been interested in what is going on in this area would deny that we have found fault with the medical men who have been chosen for these committees because they were not appointed on the recommendation of the local county societies. It is my hope that it will be so stated that those who are setting up committees on which physicians are to be appointed will appoint such physicians on the recommendations of the local county societies and/or the State Society where it involves the State. This is all that is involved, that they should not be choosing individuals that please them rather than choosing individuals who are recommended to them by organized medicine.

SPEAKER WURZBACH: Dr. Freedman's statement is, therefore, that they should be carefully selected individuals following the presentation of their names by the State Society or by the local county medical societies, that being the consideration before the House. Is there any further discussion? All those in favor of the adoption of this portion as presented by Dr. Freedman say "aye," those opposed "no." It is carried unanimously.

Now, on the full recommendation as amended. Is there any further discussion on the full recommendation as amended? All those in favor of the adoption of this portion of the report say "aye," opposed "no." It is so ordered.

DR. MANGI: The Management Survey Report was read for information, and no further action was deemed advisable at this time.

Mr. Speaker, I move adoption of this portion of the report.

DR. BRANE: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: Mr. Speaker, I feel that the entire Planning Committee for Medical Policies, with James Greenough, M.D., as chairman, are to be commended for a job very well done.

Section 126 (see 13)

Report of Reference Committee on Organization and Policies: Joint Committee with the New York State Osteopathic Society

DR. MANGI: The next item is the report of the Joint Committee with the New York State Osteopathic Society, which is Report 62–G that has been issued to us.

In order to implement the mandate of the State Society's House of Delegates of 1961 to the Council that the relationship between osteopathy and medicine be further explored, the Council accepted as a basic tenet the A.M.A. Judicial Council's report. The president of the Society appointed an ad hoc committee to explore further some of the problems with osteopathic medicine in this State, including the compensation schedule and various other problems which are keeping the profession from harmonizing with the Judicial Council report. Four meetings of the joint committee have been held. It is definitely understood by both groups of the ad hoc committee that each profession represented wishes to maintain its individual identity, and amalgamation was neither suggested nor contemplated.

The question of hospital appointments in connection with accreditation of hospitals was discussed. The Joint Commission on Accreditation of Hospitals has stated that if a hospital credentials and executive committee believed that an osteopath was deserving of staff appointment to a hospital, he could be appointed to that hospital staff. He could be judged by his individual capabilities as to the extent of his privileges. The Council of the State Society approved this statement.

The results of these conferences have been approved by the Council and are enumerated in the committee report. They are summarized as follows:

1. Osteopathy in this State is no longer considered to be cultism, since osteopaths hold the license to practice medicine and surgery granted by the State Board of Medical Examiners, and if they adhere to the same scientific principles embraced by doctors of medicine.
2. Doctors of medicine may associate professionally, on a voluntary basis, with doctors of osteopathy who hold full licenses to practice medicine and surgery granted by the New York State Board of Medical Examiners.
3. It was agreed that *What Goes On* should be distributed to doctors of osteopathy to apprise them of what is taking place in the postgraduate education field. At the next meeting of the Council, it will be recommended that county societies invite doctors of osteopathy to their scientific meetings and seminars. In return, the osteopaths will send invitations to the doctors of medicine for them to attend osteopathic conferences.

These results of the committee's deliberations have been published in the April 19, 1962, *Newsletter* as an "Important Statement on Osteopathy." It was stated that the Council, at its last meeting on March 22, approved this statement on osteopathy and medicine. The statement is made that negotiations will continue. Your reference committee feels that it was inappropriate to have published this statement on osteopathy in the *Newsletter* before this matter had been discussed by the House of Delegates.

The ad hoc committee recommends that the liaison committee be continued for at least another year and that it continue to work toward a mutual, meaningful, ethical professional relationship.

Your reference committee feels that the inequity in the Workmen's Compensation Fee Schedule should be resolved as speedily as possible.

Your reference committee strongly commends the excellent work that was done by the ad hoc committee consisting of Norman Moore, M.D., chairman, E. Dean Babbage, M.D., James M. Blake, M.D., Henry I. Fineberg, M.D., and John M. Galbraith, M.D.

Mr. Speaker, I move adoption of this portion of the report.

SPEAKER WURZBACH: Is there a second?

DR. BRANE: I will second it.

. . . After discussion by Drs. Bedell, Moore, Wolff, and Einhorn, it was voted to change the wording in the reports of the Joint Committee and of the reference committee in order to delete all use of the word "allopathy" in any of its forms.*

. . . A discussion followed carried on by Dr. Alper of Oneida, Dr. Moore, Dr. Wolff, Dr. Mathews of Monroe, Dr. Borrelli of the Section on Radiology, Dr. Hilleboe, Dr. Davis of the Section on General Practice, and Dr. Rawls of New York. The discussion covered the following points:

1. the extent to which osteopaths now practice osteopathic manipulation; that is, the fact that there are 600 osteopaths in the State and that only about 75 of them depend exclusively on this type of treatment;
2. the recommendation of the A.M.A.'s Judicial Council that the decision as to the relationship between doctors of medicine and osteopaths be made at a state level;
3. the purpose of the New York State Osteopathic Society as expressed in the 1962 edition of their constitution;
4. the statement of policy adopted by the A.M.A. House of Delegates in June, 1961, particularly the sentence, "The test now should be: Does the individual doctor of osteopathy practice osteopathy, or does he in fact practice a method of healing founded on a scientific basis?";
5. the fact that osteopaths in one section of the State frequently give six osteopathic manipulations a month to patients suffering from such ailments as arteriosclerosis, heart disease, and pernicious anemia;
6. the role of the State Board of Medical Examiners in preventing unqualified osteopaths from other states from practicing in New York State;
7. the fact that the report of the Joint Committee is a progress report, that no conclusions have been reached, that the continuation of negotiations is requested;
8. the fact that osteopathic physicians have recently taken postgraduate courses provided by the Department of Health which are identical with the courses provided for doctors of medicine;
9. the fact that osteopathic physicians do use manipulative therapy but do not use it exclusively;
10. the practice of giving inappropriate manipulative treatments in workmen's compensation cases;
11. the question of whether or not osteopaths have ever disclaimed the original ideas that all diseases are due to "subluxation" and dislocations and disturbances of the spine.

Dr. McCarthy of the Bronx asked what the question before the House was. Dr. Mangi replied by reading the recommendation of the Joint Committee:

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* Accordingly, all uses of the term have been edited from these minutes. *Secretary*

"The ad hoc committee recommends that the liaison committee be continued for at least another year and that it continue to work toward a mutual, meaningful, ethical professional relationship." . . .

Dr. McCarthy: Everybody seems to think it is a final decision. They did not read that.

Chorus: Question.

Speaker Wurzbach: The question is called for, which is nondebatable, and which must be passed by a two-thirds vote. All those in favor of calling the question say "aye," those opposed "no." The question will be called.

All those in favor of the adoption of this portion of the report say "aye," those opposed "no." It is adopted.

Section 127

Report of Reference Committee on Organization and Policies: District Branches

Dr. Mangi: Regarding district branches, your reference committee notes the reports of the district branches and feels that the methods used by the branches to promote attendance at their meetings should be commended. District branches are serving a very useful purpose.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Flanagan: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 128

Report of Reference Committee on Organization and Policies: Membership Committee

Dr. Mangi: Regarding Membership Committee, your reference committee has reviewed the report of the Membership Committee, including an appreciation of the work that has been done by its chairman, George McCormick, M.D. As part of the Planning Committee for Medical Policies report, it has been noted that the Membership Committee be discontinued and the duties of the committee be referred to the office of the executive vice-president. This is for information.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Brane: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 129

Report of Reference Committee on Organization and Policies: Office Administration and Policies

Dr. Mangi: The Office Administration and Policies Committee, led by John J. Masterson, M.D., is to be commended for its work with the personnel of the State Medical Society staff, specifically as to its job evaluation program and the actions taken to improve morale. One important item discussed was the high rental for the office space. The recommendations on this appear under the report of the Board of Trustees.

I move adoption of this portion of the report.

Dr. Freedman: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 130

Report of Reference Committee on Organization and Policies: Conference of Medical Society Officers

Dr. Mangi: The report of the conference was reviewed, and the committee responsible for this conference is to be praised for a job well done. There have been opinions expressed that the value of this conference did not justify the amount of expenditure for it.

Your reference committee is in accord with this opinion and recommends that the conference be discontinued.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Brane: I second it.

Speaker Wurzbach: Is there any discussion?

Dr. Freedman: I think there is a misapprehension that should be corrected. It says, "There have been opinions expressed that the value of this conference did not justify the amount of expenditure for it." With that I would have to disagree. I think that the meetings that have been held have been of some value. What has been recommended, based on the fact that there is no further necessity at this time for these conferences, is that they be discontinued at this time, but to malign the value of those that have been held—I don't think that anybody who is acquainted with what has taken place would agree with that opinion, so I would suggest that be changed and put in its proper context.

Speaker Wurzbach: Would it be all right if we incorporate your remarks as part of the report?

Dr. Freedman: I certainly would be agreeable to that.

Speaker Wurzbach: Is there any objection to incorporating these remarks as part of the report? Hearing none, we will therefore call the question on the adoption of the report. All in favor say "aye," opposed "no." It is carried.

Section 131

Report of Reference Committee on Organization and Policies: Constitution and Bylaws

Dr. Mangi: The committee has reviewed the request of the Council for all proposed changes in the constitutions and bylaws of the county medical societies and the district branches which have been submitted since the last meeting of the House of Delegates. The committee and its chairman, Ezra A. Wolff, M.D., are to be commended for their usual good work.

Mr. Speaker, I move adoption of this portion of the report.

DR. BRANE: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 132 (see 44)

Report of Reference Committee on Organization and Policies: Changing Name of Section on Physical Medicine to Section on Physical Medicine and Rehabilitation

DR. MANGI: Your reference committee took action on the following three resolutions:

Resolution 62–8, "Changing Name of Section on Physical Medicine to Section on Physical Medicine and Rehabilitation":

> *Resolved*, That in the interests of consistency and conformity with usual usage, the name of the Section on Physical Medicine be changed to the Section on Physical Medicine and Rehabilitation.

Your reference committee sees no objection to this resolution and recommends its approval.

Mr. Speaker, I move adoption of this portion of the report.

DR. LAGATTUTA: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 133 (see 46)

Report of Reference Committee on Organization and Policies: County Society Liaison with Physicians' Home

DR. MANGI: Resolution 62–10, "County Society Liaison with Physicians' Home," we felt that it is important to read the "resolved," which states:

> *Resolved*, That the Medical Society of the State of New York, in convention assembled, in order to facilitate and improve the administration of Physicians' Home in an economic manner, and to assure the cooperation of the State and county societies and their membership, direct the president of each county society each year to designate the secretary, the executive secretary, or some other official or committee to maintain liaison with the officials of Physicians' Home to the end that claims for aid may be more efficiently and economically investigated and aid more promptly given when needed.

Your reference committee feels that any steps taken to improve the administration of the Physicians' Home are worth-while and recommends approval of this resolution.

Mr. Speaker, I move adoption of this portion of the report.

DR. LEONE: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 134 (see 94)

Report of Reference Committee on Organization and Policies: Appointment of Members of the Society to Committees

DR. MANGI: Resolution 62–57, "Appointment of Members of the Society to Committees":

> *Resolved*, That this House of Delegates hereby request the president and the Council that whenever committees and subcommittees dealing with certain specialties are appointed, the section chairman of each specialty involved be consulted concerning such committee and subcommittee appointments.

Your reference committee recommends approval of this resolution.

Mr. Speaker, I move adoption of this portion of the report.

DR. BEDELL: I second it.

SPEAKER WURZBACH: Is there any discussion?

MATTHEW BRODY, M.D., *Kings:* Would you object to including "or specialty organization?"

DR. BEDELL: Yes, I would.

DR. BRODY: Because, as far as psychiatry is concerned, there is a very large psychiatry organization which has worked in close cooperation with the State Medical Society, and I think there should be liaison with the American Psychiatric Association, area 2, which covers New York State.

DR. BEDELL: This was introduced by the Section on Ophthalmology, and it is introduced as a section resolution. I cannot accept anything else besides what the section itself wants.

DR. BRODY: Can I move an amendment?

SPEAKER WURZBACH: You can move to amend, yes.

DR. BRODY: To include those words "or specialty organization."

SOLOMON SCHUSSHEIM, M.D., *Kings:* I will second it.

DR. WURZBACH: This opens it up to a tremendous group of specialty organizations which would have to be consulted in the appointment of any committee and, to a large extent, would take it out of the hands of the State Society.

DR. BEDELL: Gentlemen of the House, the proposition was brought to you by the ophthalmologists because there has been a so-called State committee recently appointed. I have to be very careful in my wording. Some are not very acceptable to us. I move we disapprove the amendment.

SPEAKER WURZBACH: Is there further discussion on the amendment? If not, all those in favor of the adoption of this amendment say "aye," opposed "no." The amendment is lost.

Now, we will go on to a discussion on the resolution as presented by the reference committee. Is there any further discussion? All those in favor of the adoption of the resolution as presented say "aye," opposed "no." It is adopted.

DR. MANGI: I now move adoption of the report of the Reference Committee on Organization and Policies as a whole, as amended.

DR. BRANE: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MANGI: Your reference committee is deeply appreciative of the attendance of those delegates who appeared before its meeting and gives special thanks to Thomas M. d'Angelo, M.D., Gerard V. Farinola, M.D., Arthur F. Gaffney, M.D., Thurman B. Givan, M.D., James Greenough, M.D., John J. Masterson, M.D., Norman S. Moore, M.D., Ezra A. Wolff, M.D., and Frederick A. Wurzbach, Jr., M.D. The chairman gives his cordial thanks to each committee member who has contributed to the preparation of this report and to Miss Sheila Treacy, our very efficient secretary.

Section 135 (see 35, 96, 182)

Introduction of Guests

SPEAKER WURZBACH: Ladies and gentlemen, I am going to ask J. Stanley Kenney, M.D., to present to you the president of the Medical Society of the State of Rhode Island, Arthur E. Hardy, M.D.

J. STANLEY KENNEY, M.D., *Trustee:* Mr. Speaker, ladies and gentlemen of the House, it is my privilege to introduce to you the president of the Rhode Island Medical Society. He is at present the alternate but will be a delegate to the A.M.A. at the next session, Arthur E. Hardy, M.D.

ARTHUR E. HARDY, M.D.: Mr. Speaker and members of the House of Delegates, I am not going to take up your time because it is getting late in the morning. I just want to say I am happy to be here. I have attended several of your sessions and have always enjoyed them very much. Thank you!

SPEAKER WURZBACH: Thank you, Dr. Hardy.

Reference Committee on Miscellaneous Business

Section 136

Report of Reference Committee on Miscellaneous Business: Reports of A.M.A. Meetings

WALTER S. BENNETT, M.D., *Washington:* Mr. Speaker and members of the House of Delegates, this is the report of the Reference Committee on Miscellaneous Business.

The report of the meeting of the A.M.A. held in New York City in June, 1961, and the clinical meeting held in Denver in November, 1961, as reported by our delegates, was read and examined with considerable interest.

Your committee desires to compliment the Society and those who maintained and operated our hospitality suite which, according to the report of the delegates, was well received by visitors.

The report of the action of the A.M.A. House was incorporated in the report of our delegation as presented by F. J. L. Blasingame, M.D., executive vice-president of the A.M.A., which gave a full and complete report of the action of the House and was examined with great interest. We would especially direct your attention to the following resolutions:

Resolution 61–32, "Use of General Practitioners as Assistants at Operations": This committee asks that this resolution be reintroduced at the next meeting of the House of Delegates of the A.M.A. for definitive action in June, 1962. This committee feels that a general practitioner, when available, should be permitted to assist in place of nonmedical personnel.

Resolution 61–23, "Social Security for Self-Employed Doctors of Medicine": We recommend that the resolution be reintroduced favoring Social Security for the self-employed doctors of medicine.

Mr. Speaker, I move adoption of this portion of this report.

MAXWELL GOSSE, M.D., *Dutchess:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. BENNETT: While we had several candidates for different offices in the A.M.A., none was elected.

It was noted that at the clinical meeting held in Denver in November, we had a full delegation present as well as numerous others in attendance.

Peter Murray, M.D., spoke concerning the admission of Negro physicians to the A.M.A. and stated that with the exception of one state, Negro physicians have some kind of medical society membership.

This reference committee recommends to the House of Delegates of the Medical Society of the State of New York that they instruct our delegates to the A.M.A. to further their efforts for full membership of the Negro physicians in medical societies throughout the United States and that eligible physicians be admitted to their county societies, regardless of race, creed, color, or national origin.

Mr. Speaker, I move adoption of this portion of this report.

Michael P. Lefkowitz, M.D., *Rockland:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Bennett: The actions of the A.M.A. board of trustees were reviewed by this committee. In regard to the problem of the A.M.A. disability insurance plan, our delegates should continue to oppose the national plan in favor of local plans which are now in existence and working.

Mr. Speaker, I move adoption of this portion of this report.

John Edward Lowry, M.D., *Queens:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Bennett: In regard to medical discipline, this committee believes that medical discipline should be administered at the local level and our delegates to the A.M.A. should be instructed to vote for that principle.

Mr. Speaker, I move adoption of this portion of this report.

John A. Hatch, M.D., *Yates:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 137 (see 65)

Report of Reference Committee on Miscellaneous Business: Request to American Medical Association to Rescind Dues Increase Scheduled for January 1, 1963

Dr. Bennett: Resolution 62–29, "Request to American Medical Association to Rescind Dues Increase Scheduled for January 1, 1963": With regard to resolution 62–29 we approve this resolution and recommend that our delegates work toward this result.

Mr. Speaker, I move adoption of this portion of this report.

Dr. Lowry: I second the motion.

Speaker Wurzbach: Is there discussion?

Felix Ottaviano, M.D., *Madison:* Some of us are instructed from time to time on how to vote on some of these issues, and we have pointed out that maybe we make a mistake when we mandate our delegates to the A.M.A. to make certain moves. It is perhaps far better to instruct them to do the best they can. On this particular problem some of us have been instructed to disapprove the intent of this resolution. Rescinding the dues which already have been passed, as a matter of fact, may be a rather difficult thing. It would only put our delegation on the spot. I suggest we consider this for a minute or two before we give approval to this.

Jerome Leon, M.D., *Queens:* Mr. Speaker, I am not so naive, and we in Queens are not so naive, as to believe that this request to rescind the increase—not the dues but the increase—scheduled for January 1, 1963, will be well supported at the House of Delegates of the A.M.A. However, I think for home consumption and for practical county society politics and functioning we should endeavor this year, the year after the mandate to membership in the A.M.A. first came into being, to hold the dues at a plateau for at least two years before we go ahead with an increase. I know that the initial $10 will not throw any doctor from financial stability onto the welfare rolls. This is an emotional thing rather than a financial one, but those doctors on the periphery who are reluctant to become incorporated into the Medical Society affairs, or who are reluctant to stay as Medical Society members, this $10 has been used as an excuse rather than as a reason. I believe it would be good, practical, down-to-earth manipulation if we could introduce this, not with the hope that it will be accepted but with the knowledge that this would be a practical thing to do to keep the dues stabilized for a couple of years before we go ahead with the increase.

Speaker Wurzbach: Is there any further discussion?

Norman S. Moore, M.D., *Trustee:* Mr. Speaker and gentlemen of the House, there is a point here which I think this is as good a time as any to decide. Which course shall we take with the A.M.A.? It is quite true that this will not be received by the delegations to the A.M.A. in good light, and it will throw the New York delegation into a bad light.

There is a certain principle that we have preached to the county societies: that if they want to get things done in the A.M.A., they had better support it, and get their delegates in, and get officers elected and trustees elected, and that sort of thing.

Now, if we preach to the county societies to belong to the A.M.A., so that you can have a voice in it, we cannot cut that advantage off by continually mandating unpopular legislation in the House of Delegates. Rather we should give the delegation the authority to utter its judgment, and if the judgment of the delegation is such, it will create no difficulty in getting some of our people elected to the board of trustees or onto the various councils where we can have influence. But how are we going to correct these things if we cannot have any officers or members in the councils of the A.M.A. where the power is?

I feel that we must think in these terms every time the House mandates this delegation. I have been in the House of Delegates of the A.M.A. for perhaps ten or twelve years, and I have watched. I have watched the star rising in the states whose delegations can use their judgment, and I have watched our star setting further and further down because we cannot use judgment about certain things that seem obviously rather extraordinarily ill-advised to the delegations around us.

I think that we have to think of what Dr.

Leon said, that we have to speak for public consumption. How many people, for the sake of public consumption, would sacrifice a career? That is what we are doing. We have to decide whether we are going to have a career and try to influence American medicine or whether we are going to sit continually on the sidelines. I am not speaking definitely for this resolution one way or the other, but I feel the House should consider this in every resolution that it mandates the New York State delegation to the A.M.A. House of Delegates.

Gerald D. Dorman, M.D., *Councillor:* I would like to say that we have just passed two instructions to our delegates to the A.M.A. The first is in regard to full membership of Negro physicians in medical societies throughout the United States.

When Peter Murray first came to the House of Delegates, there was a resolution to compel all county medical societies to accept Negro members. Peter Murray spoke against this because the A.M.A. cannot direct how membership shall be in county medical societies, and Peter Murray said, "I feel very strongly that no man should be kept out of a county medical society because of color," but he said, "I do not feel that this is the way to do it."

It has been pointed out that there is one society that is not accepting Negroes into some sort of membership. Your delegation has been asked to work for full membership. They can work for full membership, but if they bring it out as a resolution to compel counties, this would be extremely unfortunate, and I think it would not work to the best interests of our colored confreres.

The second resolution is a direction in regard to the problem of A.M.A. disability insurance plans. This has already been passed, gentlemen. It has been opposed by your people. It was opposed by me in the A.M.A. board of trustees, but it is now a fact. You are instructing your people again to go up and work against an accomplished fact.

On the question of the A.M.A. increase of dues, I don't vote for an increase of dues freely and often, because a lot of people can use their money other ways. You are going to have to be voting for an increase of dues here in this House for the State Society. This is going to be on top of whatever A.M.A. dues there are. The reason that the board of trustees finally decided to go to the House for an increase of dues is that the income from the A.M.A. to a large extent is based on income from advertising, and only a small portion of it is based on the dues from physicians. We, the physicians, are only supplying a portion of the income to the A.M.A. When we get a recession, we are going to have to cut back some of the activities that the A.M.A. carries on for you people. Don't think that this means necessarily just in political affairs, because what money we use in political affairs, if you want to call it that, even though it is not direct lobbying, is less than 6 per cent of the A.M.A. budget. It means that we cannot give you the support that you need on such problems as drugs, on such problems as support for education, and on such problems as scholarship loans for our young medical students and younger people coming up.

I do not like to see funds expended. I can assure you that I look through the budget, and we take five days on the budget after Dr. Blasingame has made sure it is balanced, and I have opposed even a small balance because the House always mandated more things. We have to have a cushion when we start our budget year. Our budget at the A.M.A. is looked over every quarter, and it is readjusted every quarter to make sure that your funds are properly expended, and when any large expenditures come up before the trustees at our meetings—and we have had to hold them every four to eight weeks—we again look at the budget very carefully. Your money will not be spent and squandered. That I can assure you, but to mandate your people to go into the House without knowing what the circumstances are when they arise, I think, can decrease the stature of your delegates. You people are going to choose your delegates. If there are delegates that you cannot trust to decide wisely and in your interests, don't elect them. Get somebody else, but don't tie their hands too tightly.

J. Stanley Kenney, M.D., *Trustee:* Mr. Speaker, as one who has spent as many years in the House as anybody in this room, with the possible exception of Dr. Masterson, I would like to endorse strongly everything that Dr. Moore said and what Dr. Dorman has just supported.

Maurice M. Maltinsky, M.D., *Monroe:* I agree that no one should be mandated when they go to the A.M.A. meeting, but I think there is a basic principle involved which we should all bear in mind, and that is, I don't think we should prostitute ourselves for the sake of expediency and gaining certain offices at a national level. I would hate to think that our members went there without due regard to the fact that we are part of the entire 50 states that go to the A.M.A. I think that we have a right to assert ourselves and assert our opinion, whether or not it agrees with the national policy. That is why I have the privilege right now of standing in front of this House as a little voice in the wilderness exclaiming for individuality. That is what we men are here for if we have an opinion. This is a democratic state. We have a right to express it whether it agrees with the entire organization or not. I think that we should not mandate our men, but we should nevertheless not sacrifice our individuality as New York State members.

Arthur J. Bedell, M.D., *Past-President:* Mr. Speaker and members of the House, it is time you relaxed. After thirty years of constant re-election every two years, according to my record in the House of Delegates of the A.M.A., we were never approached during that time. New York State was the leader. As Dr. Dorman has told you, we never went to the A.M.A. told what we must do. We were allowed to use our judgment as to the best interests of all, not a simple political thing. New York State had its share of presidents, but today one of the prize requisites to become a president of the American Medical Association—and listen closely—is to become a G.U. man. (*Laughter*) It is quite evident from the number of them, and the frequency with which they are elected, that they have contacts that most of us do not have.

More seriously, gentlemen of the House—and this is serious—I urge you not to tell your men what they must do. As Dr. Dorman has told you, we trust our men. We make it clear to the men that represent us in the House what we think is best, but we must allow them to use their discretion.

Thank you, gentlemen of the House, I just wanted you to relax a little. (*Applause*)

SAMUEL Z. FREEDMAN, M.D., *Assistant Treasurer:* Members of the House, I can assure you as a G.U. man that I will never be the president of the A.M.A. (*laughter*), and there is not a blessed thing to do about it whether I am a good urologist or a poor one. There are other factors involved in becoming president of the A.M.A., as there are in becoming president in other organizations. Certainly, even if I could, I would never rate for that kind of office on the basis of always trying to be popular, in other words, agreeing with individuals whether you believe what they stand for or not.

Let me state at the outset that I am also against mandating a delegation on every issue, but there are instances in which I think you will all agree that you cannot do otherwise. You come here with mandates from your own county societies, and they have a right to mandate you, but as I say, on principle, I go along with our representative form of government in this country, and we rely on our representatives in any organization to represent the thinking of their constituents.

I am primarily talking on this subject because you will have to meet the issue of an increase in dues later on in the session, and therefore, I would hope that our delegates to the A.M.A., when they voted for this increase in dues, were firmly convinced that that was essential, and if some of them thought it was not essential, they had the courage—I am using this word rather carefully—to stand up and object, whether or not they would be popular. Therefore, I assume that they felt that that increase in dues not only for one year but for the second year was essential. About this, I am not so certain, but I only mention it now because when the matter of dues comes up, I intend to have something to say. I don't think that in our behavior toward other types of legislation, we are looking for popularity. Certainly, we are in a minority on many issues in this country, and the very individuals from the A.M.A. down who are encouraged to stand up and if necessary go down fighting are leading us. Why use one type of philosophy in one area and then use another type in another area just to make a point for yourself? I say it is up to you to talk for the good of the future, and let the chips fall where they may, and I think on that basis this should be considered. As I say, in talking just to the motion—and I have gone off it through the indulgence of the Chair, as others have been allowed to go off the subject—I am opposed to mandating but am not willing to accept the principle that a body which sends you to an organization has no right to mandate you.

EXECUTIVE VICE-PRESIDENT FINEBERG: Mr. Speaker and members of the House, I would like to tell you that your delegation to the A.M.A. does have courage, and you need not worry about it. You mandated your delegation last year to vote for Social Security for physicians. It was one of the most unpopular issues in the House of Delegates at the A.M.A., and we stood up as a unit and voted in favor of it, and we were only 18 of 30. Only 30 men in the House of Delegates voted in favor of Social Security, and the New York delegation arose as a unit and voted for it. Don't worry about the courage of your delegation.

SPEAKER WURZBACH: Now, we are about to vote on the following "resolved," so there will be no question:

> *Resolved*, That the Medical Society of the State of New York through its delegates to the House of Delegates of the American Medical Association request the board of trustees of the American Medical Association to rescind the increase of dues scheduled for January 1, 1963.

Your committee moves the adoption of this, so if you vote yes, you vote that they ask for the rescinding of this dues increase; if you vote no, you vote it down. All those in favor say "aye," opposed "no." The motion is lost.

DR. DORMAN: Mr. Speaker, in the wording of this, it said the board of trustees. The board of trustees does not fix the dues. It has to be the House of Delegates of the A.M.A. I just point that out. I want to thank the House for their confidence in their delegation and their officers.

Section 138 (*See 59*)

Report of Reference Committee on Miscellaneous Business: Six-Year Combined Course for Medical Schools

DR. BENNETT: Resolution 62-23, "Six-Year Combined Course for Medical Schools," was approved in principle, and we recommend that further study be made.

Mr. Speaker, I move adoption of this portion of this report.

DR. LEFKOWITZ: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried. . .

Section 139 (*see 61*)

Report of Reference Committee on Miscellaneous Business: Production of More Practicing Physicians

Dr. Bennett: Resolution 62–25, "Production of More Practicing Physicians," was approved in principle, and this committee recommends that further study be made.

Mr. Speaker, I move the adoption of this portion of this report.

Dr. Gosse: I second it.

. . . There being no discussion, the motion was put to a vote, and was unanimously carried. . .

Section 140 (*see 53*)

Report of Reference Committee on Miscellaneous Business: Admonishment for Comments on General Practice

Dr. Bennett: Resolution 62–17 was discussed at length, and since it involves matters of policy, which are not in the province of this reference committee to decide, we recommend that this resolution be referred to the Council for further study, appropriate action, and establishment of policy for the future.

Mr. Speaker, I move adoption of this portion of this report.

Dr. Hatch: I second it.

Speaker Wurzbach: Is there any discussion?

Dr. Dorman: I would like to point out that usually we do not move something to the Council for establishment of policy. I think that they might formulate something to bring back to the House, but in this there is a statement that the Council is authorized to establish policy, and I want the House to be sure that they agree to that before they delegate such authority. Policy rests with the House.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried. . . .

Section 141 (*see 70*)

Report of Reference Committee on Miscellaneous Business: Recognition of Service of Mr. Thomas E. Walsh

Dr. Bennett: Resolution 62–34, "Recognition of Service of Mr. Thomas E. Walsh," is approved by the reference committee, and we recommend its adoption.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Lefkowitz: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried. . . .

Section 142 (*see 42, 50, 55, 63*)

Report of Reference Committee on Miscellaneous Business: EMPAC

Dr. Bennett: Resolutions 62–6, 62–14, 62–19, 62–27. All four resolutions were introduced on the subject of EMPAC. While we are in sympathy with the aims and objects of all four resolutions, resolution 62–27 seems to embody the thoughts of all four resolutions most succinctly with the additional "whereas":

> Whereas, EMPAC is an organization which is completely separate and in no way an integral part of the Medical Society of the State of New York.

The "resolved" is:

> *Resolved*, That the Medical Society of the State of New York approve the aims and efforts of the Empire Medical Political Action Committee.

Mr. Speaker, I move the adoption of this portion of this report.

Speaker Wurzbach: Is there a second?

. . . The motion was seconded by several. . .

Speaker Wurzbach: Is there discussion?

. . . After discussion by Dr. Broad of Queens, Dr. Fineberg, Dr. Bedell, and Dr. Freedman, the question was moved. This motion (to vote on the reference committee recommendation immediately, without further discussion) was lost. After further discussion by Dr. Ershler of Onondaga, Dr. Kenney, Dr. Lawrence, Dr. d'Angelo of Queens, Dr. Emerson of Nassau, Dr. Dorman, and Dr. Freedman, there were calls for the question. . .

Speaker Wurzbach: There is a call for the question, which is nondebatable. The question requires a two-thirds vote. All in favor of the immediate call of the question say "aye," opposed "no." Definitely this time it is carried, and the question is now before the House, which is the recommendation of the reference committee for the adoption of the "resolved," that the Medical Society of the State of New York approve the aims and efforts of the Empire Medical Political Action Committee. All those in favor of the recommendation of the committee will say "aye," opposed "no." It is carried.

Dr. Bennett: Now, finally, Mr. Speaker, I move the adoption of the report as a whole as amended.

Dr. Hatch: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried. . .

Dr. Bennett: I would like to thank my committee whose assistance, counsel, and advice were invaluable in the preparation of this report; also our secretary, Mrs. Patricia Salter, and those members of the House who came before us and assisted us with their advice and counsel.

Speaker Wurzbach: Thank you, Dr. Bennett.

We are recessed until two o'clock.

. . . Whereupon at 12:20 p.m., the meeting recessed. . .

The session convened at 2:10 P.M.

SPEAKER WURZBACH: The House will come to order. The first order of business this afternoon will be to take up the report of the Reference Committee on Medical Communication, Merle D. Evans, M.D., chairman. Dr. Babbage will chair the House.

Reference Committee on Medical Communication

Section 143

Report of Reference Committee on Medical Communication: Cooperation with Media of Information

MERLE D. EVANS, M.D., *Monroe:* Your Reference Committee on Medical Communication, after hearing extensive and searching discussions of its assigned committee reports, presents the following report:

The Subcommittee on Cooperation with Media of Information is to be commended on having formulated so all-inclusive a "Guide for Cooperation for Doctors, Hospitals and Reporters" that it needs no changes for 1962. However, the existence of this guide should be emphasized, and ways of acquainting the Society membership with its existence should be formulated. This subcommittee will undoubtedly be absorbed by the Public Relations Committee, as you heard this morning.

Mr. Speaker, I move adoption of this portion of the report.

JOHN F. KELLEY, M.D., *Oneida:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 144

Report of Reference Committee on Medical Communication: American Medical Association Education and Research Foundation

DR. EVANS: The consolidation of the two foundations, the American Medical Research Foundation and the American Medical Education Foundation, into one, the American Medical Association Education and Research Foundation, is laudable.

Although the number of contributions during 1961 increased about 33 per cent and the amounts contributed increased by 24 per cent, according to the report only about 19 per cent of the Society membership contributes. The fund would greatly improve if some way could be found to encourage the other 81 per cent of the membership to contribute.

The above figures regarding the percentage of member contributions are inaccurate because many of our members who contribute, particularly to their own schools, fail to report such to the Foundation.

Your reference committee suggests that all contributions to the education or research Foundation or to student loan funds be reported to the State Society so that credit to the individual and to the medical profession can be recorded.

We strongly recommend that contributions to these funds be directed more to a student loan fund in the interest of increasing the number of future doctors.

Mr. Speaker, I move the adoption of this portion of the report.

WILLIAM BENENSON, M.D., *Queens:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 145

Report of Reference Committee on Medical Communication: Convention

DR. EVANS: The Convention Committee report consists of the final report of the 1961 committee and the preliminary report of the 1962 Convention Committee.

Definite action has been taken on the suggestions of the 1961 committee regarding future annual meetings. The results of such study are fully discussed in the report of the Planning Committee, as already reported on by the Reference Committee on Organization and Policies.

Your reference committee recommends acceptance of the Convention Committee report.

Mr. Speaker, I move adoption of this portion of the report.

EARL W. DOUGLAS, M.D., *Suffolk:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 146 (see 9)

Report of Reference Committee on Medical Communication: Public Relations

DR. EVANS: A detailed, comprehensive report was given of the activities of the Public Relations Committee and the Communications Department in promoting the fundamental purposes of the Medical Society of the State of New York through the areas of (1) communication within the profession, (2) communication with the medical community, and (3) public education.

After extensive and exhaustive discussion of the duties, activities, and responsibilities of the Public Relations Committee, we find that there is a vast field of overlapping activities, including many associated and allied fields of medical communication.

The main problem of the Public Relations Committee can be identified under the following categories: (1) insufficient personnel, (2) budget limitations, and (3) overlapping of departmental activities and expenditures, particularly concerning legislation matters.

It has been determined that approximately 50 per cent of the personnel time and 25 per cent of the budget allocated to the Public Relations Committee is used for the activities of various departments with parallel aims and functions.

The hearings showed repeatedly that the intangible and far-reaching results of our Public Relations Committee cannot properly be evaluated in dollars and cents in a report.

As a result of the hearings and investigations, your reference committee feels that a more efficient Communications Department can be effected by endorsing Dr. Galbraith's suggestion for the creation of a Commission on Public Affairs, as outlined in his supplementary report of the president.

This commission should include the following: public relations, State legislation, Federal legislation, New York Association of the Professions, A.M.A.E.R.F., and all presently handled associated activities involving public relations and medical communications.

The creation of such a commission would work for a stricter correlation of activities with closer liaison in all these fields and a more efficient administrative organization, all under a more realistic and understandable budget, properly allocated.

Therefore, your reference committee strongly recommends the establishment of a Commission on Public Affairs. This is a little bit behind time. That is the trouble with two reference committees handling the same problems. This that we have just suggested was done this morning by the Committee on Organization and Policies.

SPEAKER WURZBACH: That is right.

DR. EVANS: So we lost part of our thunder. However, Mr. Speaker, I move adoption of this portion of the report.

DAVID LYALL, M.D., *New York:* I second it.

SPEAKER WURZBACH: Is there any discussion?

THOMAS M. D'ANGELO, M.D., *Queens:* May I ask for a point of information? I note here two sentences which seem to be contradictory. We say one problem is insufficient budget limitations for the committee, but in the next paragraph we say that 25 per cent of the allotted budget is used for other than public relations purposes, for other committees. Now, where would the budget limitation exist in the original committee if they can afford 25 per cent for other committees?

DR. EVANS: That is exactly a limitation on them. They have a certain budget within which they are supposed to live and do their work, but they find that they cannot carry out all of their work and answer some of the questions from some of the doctors, "Why don't we get some better results from the Public Relations Committee?" They have not got the money because they have already had to spend part of their budget to cover part of the other bills.

VICE-SPEAKER BABBAGE: Is there any other discussion?

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 147

Report of Reference Committee on Medical Communication: Publication

DR. EVANS: The report of the Publication Committee is complete, enlightening, and interesting in its description of the committee's aims and management of its responsibilities, the NEW YORK STATE JOURNAL OF MEDICINE, the *Medical Directory of New York State,* and the Medical Society Library.

We endorse the committee's goal as to its functions, namely, "since the JOURNAL represents the State Society on library shelves throughout this country and the world, it should continue to have the status not of a mere house organ but of a respected and authorized scientific publication."

As a result of the hearings, the following recommendations are made:

1. That the NEW YORK STATE JOURNAL OF MEDICINE be continued in its present form.
2. That the State Society continue to publish the JOURNAL according to the present program.
3. That the recent improvements in the quality of the JOURNAL be continued and developed.
4. That a contingency reserve fund for the JOURNAL be created.

We recommend that the Council committee continue its study of the entire problem of the NEW YORK STATE JOURNAL OF MEDICINE.

We endorse the present idea of improvements in the form of listings in the 1963 *Directory,* now under development, and hope that this "streamlining" will be continued in future volumes.

We recommend the possibility of changing the *Directory* from a bound volume to a loose-leaf form. This would facilitate more frequent updating and undoubtedly bring about a reduction in cost of production as well as increased income through advertising.

The Medical Society's Library has been well maintained and well serviced by the Kings County Medical Society Library, and a special commendation is due Mr. Wesley Draper, librarian.

Mr. Speaker, I move adoption of this portion of the report.

DR. KELLEY: I second the motion.

VICE-SPEAKER BABBAGE: Is there any discussion of this portion of the report?

MAURICE J. DATTELBAUM, M.D., *Treasurer:* I want to know what is meant by "a contingency reserve fund for the JOURNAL." I want to know how much, and what they are going to do and what they mean by it. They have no fund because if we did not allocate membership dues to the JOURNAL, there would be a deficit. The membership dues allocated to the JOURNAL the year before were $75,000. This is $3.00 a head. This year, which so far they have gone into the red, we allocated $5.00 a head, giving them $50,000 more than before, and they only came out with a surplus of nine hundred and some odd dollars.

What do they mean by a contingency fund? If they will ever be in the black, will it reduce the allocation from the membership dues? That should be the first step. If they are making money, we should reduce the allocation back to $3.00 and not continue giving them $5.00 and they should have a contingency fund. I don't see the logic of it. So I would be opposed to that part of the report in which they would set up a contingency reserve fund. The Society is the contingency fund.

VICE-SPEAKER BABBAGE: Would you like to discuss that, Dr. Evans—how much your committee felt it should be?

DR. EVANS: We had no definite amount, but I can discuss it with Dr. Moore.

NORMAN S. MOORE, M.D., *Trustee:* Mr. Speaker and gentlemen of the House, I represent Alfred P. Ingegno, M.D., who had to preside at a scientific session this afternoon. He asked me to help clarify anything that was confusing.

The confusing issue here is that over the years the JOURNAL did make a great deal of profit, which was put into the general fund. It was brought out in the hearings that the *New England Journal of Medicine* had a million dollar surplus, and they could weather some bad storms of low advertising years and so forth because of this contingency fund without encroaching on the Massachusetts Medical Society. I believe this is a fact, that they have this reserve fund. Our JOURNAL has never had a reserve fund, even in its good days, because anything more than it was necessary to take care of the current year was put in the general fund of the Society.

I am sure that this is the explanation that Dr. Ingegno believes this intends. In other words, if the JOURNAL makes money, first, as Dr. Dattelbaum says it should go to reduce the allocation of dues, and if and when it makes money in addition to the allocation of dues, it should have a reserve fund of its own, but there is no likelihood of this occurring except in the far distant future.

DR. EVANS: May I say something on this? Our idea in suggesting this contingency reserve fund is not to ask any extra funds from Dr. Dattelbaum. As Dr. Moore told you, in the past the JOURNAL has made money from its advertising. This last year, it lost, because of factors beyond our control. We do have a dues allocation, and that is what we call it, each year, and our idea was this: If, when the smoke clears away, there is even one dollar profit, it would go into a contingency fund earmarked for use by the JOURNAL only, instead of as at the present being put back into the general treasury. Then in the future, if we have lean spots like this year, we will have a fund that is waiting there, and you don't have to go to the treasurer and to the Board of Trustees and say, "Look, we need help." This is in effect a bookkeeping problem, and it merely earmarks those extra funds that you have in good years that must be used to clear the poor years of that same group.

ASSISTANT SECRETARY WOLFF: Mr. Speaker and members of the House, I may be in error, but to my knowledge the JOURNAL has not, certainly in the last ten or fifteen years, made a profit before dues allocation. The dues allocation originates because of a postal regulation. Second class mailing privileges are granted only to publications that have a bona fide subscription list, and these dues allocations are the way that the subscription lists are supplied. Every member then is assumed to be paying the amount of the dues allocation as the price of his subscription, and he gets the JOURNAL, and that allows the JOURNAL this saving on postal rates.

Originally, the dues allocation I believe was 50 cents, and this was simply a token to take care of the postal regulation. However, when the JOURNAL began to get more and more into the red, the way it was financed was by increasing the dues allocation so that the books always showed a profit, but that was after dues allocation, as Dr. Dattelbaum has explained to you. It has now come up to $5.00. Now, the proposition is where does paying up the deficit come from? It comes from the general funds, but when there is a surplus, it stays with the JOURNAL, so that they can spend. That removes the need for going through the budget.

Gentlemen, I submit that where there is money, it will be spent. I do not think that it is too much trouble for the Publication Committee to come to the general membership, to its representatives in the Council and here in the House, and say, "We are now running short. We need money." I am sure that money will be forthcoming, but I do not like to circumvent the Budget Committee by creating such a fund. I don't know where this fund is coming from, but even in this nebulous state, I would still like to have the purse strings in the hands of people who are constitutionally charged to guard our money, and I would move that this portion of the report be amended by deletion of this recommendation.

Dr. Dattelbaum: I second it.

Vice-Speaker Babbage: Is there any discussion on this amendment?

John J. Masterson, M.D., *Trustee:* For the information of the House the last time the Journal made a profit before dues allocation was in 1951.

Vice-Speaker Babbage: Is there any other discussion on this amendment to delete this portion of the report? If you vote yes, you are voting to delete this portion of the report about the contingency reserve fund for the Journal. All those in favor say "aye," opposed "no." The chair is a little in doubt. I think it is probably in favor of the "ayes," but would you try it again? Those in favor say "aye," opposed "no." I am quite sure the "ayes" have it. This portion of the report will be deleted.

Is there any other discussion on this portion of the report that we are discussing now? This has to do with the Journal. If not, those in favor of accepting that portion of the report please say "aye," any opposition "no." It is carried. Will you proceed, Dr. Evans.

Section 148 (see 66)

Report of Reference Committee on Medical Communication: Listing of Previous Hospital and Research Affiliations in Medical Directory

Dr. Evans: Resolution 62–30, "Listing of Previous Hospital and Research Affiliations in *Medical Directory*," introduced by Medical Society of the County of Queens:

> *Resolved*, That the Medical Society of the State of New York hereafter list in its *Directory* and designate as such all past medical staff and research appointments with the last rank held, provided this affiliation had lasted for a period of three years or more.

Mr. Speaker, your reference committee recommends disapproval of this resolution because it would work directly against the present attempt to make a more efficient and economic *Directory*, and it is not clear that any great service would be performed.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Douglas, *Suffolk:* I second it.

Vice-Speaker Babbage: Is there any discussion?

Albert Douglas, M.D., *Queens:* I think it is evident that a long list of past appointments would add to the size and expense of the *Directory*, but I do not believe that the addition of a single title would be prohibitive. Even this would help establish a physician's qualifications more accurately.

I move, therefore, that resolution 62–30, introduced by the County of Queens, be approved with the "resolved" to be amended as follows: In place of "all past medical and staff research appointments," substitute the following, "the last rank held in a single past medical staff or research appointment designated by the physician listed as his most important."

Dr. d'Angelo: I second that.

Dr. Douglas, *Suffolk:* The present status of the *Directory* should be for present information only, in line with saving money. We are going against ourselves if we add a single line where we are trying, at the present time, to delete and cut down much of the material which has been overdue in being removed from our *Directory*. The present status of the person is really what we need our *Directory* for.

Vice-Speaker Babbage: Is there any other discussion?

Dr. d'Angelo: If the only objection to including this one line be the question of funds or costs, I think we could work more equity if this were discussed on the question of whether or not it is appropriate. Regardless of the very small amount that may be involved, if in our opinion the good that will be done will greatly overcome the small amount of money that would be necessary to bring that about, I think the fact that it costs a little more should not enter into our consideration at this time. I think the question should be primarily whether or not it is proper and whether or not it would give more information to those individuals who are looking up information in the *Directory*. Personally, I think that one line such as this would give a great deal more information. For instance, there are a number of individuals who have had very high appointments in their respective hospitals and communities. Suddenly because of age that is terminated. Therefore, in the *Directory* there would be only one small line left without anybody knowing what his qualifications were at the time they are looking at the *Directory*.

Dr. Moore: I arise again out of duty to a friend, Dr. Ingegno, who said if this came up, that he wished the House to know that he was for the recommendation of the reference committee.

Executive Vice-President Fineberg: Mr. Speaker and members of the House, to me has been assigned the task of streamlining your *Directory*. I have studied it for the last eight months, and I can tell you that it is medieval and obsolete. It contains information which in no way determines the qualifications of a doctor of medicine or tells us what his specialty is or what he is permitted and what he can do. We must streamline it. Now don't hamstring this streamlining. If we are wrong, take us to task two years from now. The idea is this: When I look at the *Directory*, what I want to know is naturally the name; I want to know where he lives; I want to know his telephone number; I want to know whether he is a member of his county society; I want to know whether he is a member of the State Society and of the A.M.A.; I want to know whether he is a member of a college, a board, or an academy, which are the recognized standards for medical practice in this country; and I want to know what hospital appointments he holds right now, not what he held ten, twelve, or twenty years ago. Some men lose their appointments for legitimate reasons. My dear people, let us stick to the facts. This is my Bible. I look at it three, four, five, or ten times a day. Let us find out what the true qualifications of a man are, and give us a little leeway. Don't hamstring us and say we must include the last appointment he had. The last appointment may have been in 1906.

Vice-Speaker Babbage: Thank you, Dr. Fineberg.

Is there any other discussion? We are working on the substitute motion now, and that is to add in place of "all past medical and staff research appointments," "the last rank held in a single past medical staff or research appointment designated by the physician listed as his most important."

All in favor of this substitute motion or adding this to the original resolution, please say "aye," opposed "no." It is lost.

Now, we have to vote on the original recommendation. Will you reread it, Dr. Evans?

Dr. Evans: Your reference committee recommends disapproval of this resolution because it would work directly against the present attempt to make a more efficient and economical *Directory*, and it is not clear that any great service would be performed.

. . . The question was called, and the motion was put to a vote and was carried . . .

Dr. Evans: I move adoption of this report as a whole as amended.

Dr. Kelley: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Evans: Your reference committee wishes to thank all those who appeared before it; to congratulate the chairmen and their committee members for their very exhaustive and complete committee reports and the personnel of the Communications Department and the Journal and *Directory* staffs. We express our thanks to Miss Vera Battersby for her very efficient secretarial services. May I add my own personal thanks to my committee, which was very excellent and very efficient.

Reference Committee on Commission on Medical Services—A

Section 149

Report of Reference Committee on Commission on Medical Services—A: Economics Committee

Jason K. Moyer, M.D., *Broome:* Your reference committee reviewed the report of the Economics Committee, headed by Waring Willis, M.D., and compliments his committee on the clarity and concise presentation of the numerous matters considered at its four meetings this year.

It is noted that the relative value study has been pursued for more than a year and that the various county societies have not responded as promptly as hoped. Your reference committee suggests that the counties that have not returned their work sheets do so promptly in order that this important program can be completed and a report and recommendation made to the Council.

Mr. Speaker, I move adoption of this portion of this report.

Walter Einhorn, M.D., *Bronx:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Moyer: It is noted that the Economics Committee has acted as liaison between New York State Retired Teachers Association and the Associated Blue Shield Plans of New York State in an attempt to aid this group to improve their insurance program.

The matter of hospital utilization studies was considered at length by your reference committee, and there was considerable discussion concerning the best methods of establishing utilization studies within the State. Your reference committee felt strongly that this type of professional survey should be conducted by local physicians in their own hospitals rather than by an outside agency.

Mr. Speaker, I move adoption of this portion of this report.

Irving Ershler, M.D., *Onondaga:* I second the motion.

Vice-Speaker Babbage: Is there any discussion?

Waring Willis, M.D., *Councillor:* Mr. Speaker, am I to assume from this report that the reference committee feels that the Economics Committee should not go along with a study on the setting up of the basis for doing utilization and audit studies in hospitals?

Dr. Moyer: The reference committee felt that an outside agency as was mentioned should not. It was felt the University of Michigan, the group at the Business Administration School, should not be employed to conduct such a program. I believe this was the reference committee's opinion.

Dr. Willis: I would like to explain to the House that a year ago the State Society Committee on Economics set up a program to coordinate the activities of Nassau County, Monroe County, and Wyoming County, so that we could have a basis for understanding exactly what utilization committees should do, how they should go about their duties, and what kind of statistics they should amass.

We picked Nassau County because they were far ahead of any other county in this State in this type of study, and they represented a suburban county. We picked Monroe County for the same reason and because they represented an industrial county. And we picked Wyoming County because it is a typical rural county, and by this study we could see whether or not this type of control could be easily carried out under these three different circumstances.

Correlating the work in these three counties, we find that we are without any experience. We are without any guide lines. We do not know what we are particularly looking for. Accordingly, we were in this dilemma of trying to get baselines, and Nassau County up to this time carried on some negotiations with the Department of Medical and Business Administration of the University of Michigan to see if they would help in setting up these standards.

We worked with Nassau County, and we felt that we could very nicely enlist the aid of departments with experience of this kind to get us started on the road to make these studies. I feel that without it we are going to take a long time to get down to business and come up with any real effect of utilization committees.

The money that would be spent doing this would not come from the State. We would hope to enlist the aid of foundations, and there would be no money spent by the State Society.

All we are doing is exploring this affair. We cannot commit ourselves without permission from the Council. This is merely exploratory, and it seems to me we are taking a step backward if we prohibit the Economics Committee and the Council from exploring this.

Dr. Moyer: Do you recommend deleting this last sentence, Dr. Willis?

Dr. Willis: I would recommend that we delete that this body is against further exploration of this field, which is essentially what this recommendation says.

Dr. Moyer: If you leave out the last sentence, it says that.

Ralph S. Emerson, M.D., *Nassau:* I would like to reaffirm what Dr. Willis has just said. I don't know whether or not you are all aware of the importance of these utilization committees. Granted we don't have the exact guide lines we need or the criteria for drawing this up, but it is a very pertinent part of any national program. We may have a government program dropped in our lap in a very short time, and within this bill is a specific requirement for the utilization committee. You all have or should have your medical audits and efficiency committees, but you also must have utilization committees.

At the National Utilization Study conference that Carlton Wertz and I attended back about a month ago, I think it was the general feeling that this is a tremendous task. A great deal of information must be gathered from the standpoint of statistical study, but it is essential that we do it.

It was also felt that if you were going to do this on a comprehensive basis, as we may be forced to do, we will have to consider very seriously a computer type of statistical study within the hospitals. Many of the hospitals are going into this, particularly out in the Midwest. There is a study group out there or a service called PAS that is rendering service to a number of hospitals in the Midwest, and there are a few in the East that have this under study. I think you should give this consideration and speak to your hospital administration and learn more about it when it does come up because it is going to be before us in a very short time, and certainly any action which would deter the Economics Committee from further exploration in this field I think would be unwarranted at this time.

Vice-Speaker Babbage: Thank you, Dr. Emerson. Is there any other discussion?

Dr. Willis: Mr. Speaker, I would further like to say there was no intention of the committee to take over the work of the individual physicians in the individual hospitals. They are the ones that are going to do utilization studies. They are going to control them, and they must control them. However, if we don't make a move to get some mechanism and give them some aid in doing it, other authorities will step in and take it over from us. This is merely to give all of the hospitals and all of the utilization committees guidance. I would just like to see deleted, and I would like to move, that this last sentence "survey should be conducted by local physicians in their own hospitals rather than by an outside agency," be deleted. There was no intention for an agency to take over the survey.

Dr. Emerson: I second it.

Dr. Einhorn: I had the honor to be a member of the reference committee that made this recommendation. We have given this a great deal of thought and discussion. It was not arrived at lightly. On the other hand, I personally have the feeling that the agencies that we are apt to call in from outside not only have just as little experience in these matters as we have but also lack the medical knowledge that we do have. The results, therefore, from the calling in of such an outside agency that brings in its own arbitrarily arrived at standards have usually been very poor and, from the point of view of organized medicine, in many instances bitterly disappointing.

That was the reason for the reference committee's feeling so strongly against the calling in of foundations, outside agencies, and the like. These generally distinguish themselves from the activities of physicians only by the superarrogance they exhibit and not by their increased knowledge. I do believe, therefore, that we should support the maintenance of this last sentence; if we want our statistics, we will have to make them ourselves. If they are going to be made for us by other people, we are going to pay the piper. We cannot rely on any kind of university agency to create our own standards. We have to make them ourselves and be responsible for them ourselves. If that means some more work for us, we will have to take it on. It will have to be our own, or it will not be worth anything.

VICE-SPEAKER BABBAGE: Is there any other discussion?

DR. WILLIS: Mr. Speaker, again I would like to emphasize that these studies are going to be done in hospitals as we visualize it at present in Nassau County, Monroe County, and Wyoming County, and it is going to be those county medical societies that are going to control this study.

The other point is that we do not have in medicine the know-how or statistical experience to go about a problem of this kind. We have to have outside aid. I am not making any point for the University of Michigan; as a matter of fact, we can throw this out and other departments of other universities may come in on the study. We can see which one presents the best protocols, but the fact is that we are not prepared in medicine to set up the standards for statistical analysis.

DR. MOYER: I believe the intent of the committee was that this study be controlled by the hospital group and not by an outside group. It may be worded poorly, but I believe that was the intent of the committee.

VICE-SPEAKER BABBAGE: If there is no other discussion on this, we are voting on whether we will delete the last sentence in the middle of the page there, which reads, "Your reference committee felt strongly that this type of professional survey should be conducted by local physicians in their own hospitals rather than by an outside agency." It has been moved and seconded that this be deleted. We are now voting on that proposition. Those in favor say "aye," opposed "no." The chair is a little bit in doubt. Would you try it again? Those in favor say "aye," opposed "no." The "ayes" have it, and it will be deleted.

DR. MOYER: I move the adoption of this portion of the report as amended.

VICE-SPEAKER BABBAGE: Is there any discussion on the rest of the report? Hearing none, those in favor say "aye," opposed "no." It is carried.

DR. MOYER: Your reference committee supports the Economics Committee's recommendation in voicing opposition to lifetime sickness benefit programs as recommended by the board of trustees of the American Medical Association. The plan appears to be actuarially unsound and would imperil the stability of those group disability plans now in existence in New York State.

Mr. Speaker, I move adoption of this portion of this report.

BERNARD J. PISANI, M.D., *New York:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MOYER: The actions on the two resolutions referred to the Economics Committee by the 1961 House of Delegates were considered by your reference committee.

Resolution 61–21, requesting that the State Society endorse the initiation of a deductible or coinsurance provision in all hospital insurance plans, was forwarded to the State Commissioner of Insurance, and his attention was called to the fact that this was a practical way of reducing hospitalization insurance premiums.

Resolution 61–16, requesting that the State Society take steps to obtain an agreement from all insurance carriers concerned with medical and surgical coverage by joining the physician's and patient's names as payees on any check paid for medical and surgical services, was referred to the Committee on Liaison with the Bar Association. The Economics Committee felt it was necessary to have the backing of the Bar Association for implementation of this matter. Your reference committee notes there has been no further action on this matter and urges the Liaison Committee with the Bar Association to implement this 1961 resolution promptly.

Mr. Speaker, I move adoption of this portion of this report.

LOUIS J. MORSE, M.D., *Queens:* I second the motion.

VICE-SPEAKER BABBAGE: It has been moved and seconded that this portion of the report be accepted.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. MOYER: The matter of loss of coverage under group disability insurance programs arising from the transfer of a physician from one county to another was discussed. Testimony before your reference committee suggested that the best solution to this problem was for each county society to re-examine its individual policy and renegotiate contracts where it is indicated. The director of the Bureau of Medical Care Insurance assured his cooperation in handling this matter.

Mr. Speaker, I move adoption of this portion of the report.

DR. ERSHLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 150

Report of Reference Committee on Commission on Medical Services—A: Liaison Committee with Veterans Administration

DR. MOYER: Your reference committee approves the report of the Liaison Committee with Veterans Administration.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Einhorn: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 151

Report of Reference Committee on Commission on Medical Services—A: Bureau of Medical Care Insurance

Dr. Moyer: Your reference committee has reviewed the report of the Bureau of Medical Care Insurance and commends the industrious efforts of this bureau during the past year.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 152

Report of Reference Committee on Commission on Medical Services—A: Subcommittee on Public Medical Care

Dr. Moyer: The report of this Subcommittee on Public Medical Care was reviewed. Your reference committee notes the necessity of separating the MAA program from the indigent welfare program under the Department of Social Welfare and also calls attention to the action of the House of Delegates at its 1961 session, recommending that all health services dispensed by the State of New York be placed under the aegis of the New York State Department of Health.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Morse: I second it.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. Is there any discussion?

Gerald D. Dorman, M.D., *Councillor:* I want to point out on this last situation that although I am in favor of this under the present setup, much of it would cause a change in the State constitution, and a change in the State constitution is a long and slow process. If you take most of this out from under the welfare and put it under health, you are going to get into some long difficulties. I sympathize with it, but I don't think they realize all of its implications on this particular matter.

The question of MAA, the Federal law, states that old-age assistance will not be placed under MAA, the medical care of the health of the aged; yet that is what has been done in this State. The Welfare Department has not been willing to face up to it or has not had any court action to make them conform to the Kerr-Mills Law. I sympathize with this statement, but it is going to be hard to get any actual changes in it, I believe.

Vice-Speaker Babbage: Thank you, Dr. Dorman.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 153

Report of Reference Committee on Commission on Medical Services—A: Medicare

Dr. Moyer: The administration of the Medicare program was discussed, and testimony presented revealed that there has been a reduction in the fee paid for processing claims. Your reference committee unanimously agreed that the advantages to the physicians of the State warrant continuation of this program for another year.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 154

Report of Reference Committee on Commission on Medical Services—A: Medical Care Insurance Committee

Dr. Moyer: The report of this committee recommended approval of the seven Blue Shield Plans in the State of New York, and this recommendation is supported by your reference committee.

Your reference committee recommends approval of this portion of the report.

Dr. Pisani: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 155 (see 37)

Report of Reference Committee on Commission on Medical Services—A: Combining Services of State Welfare and Health Departments

Dr. Moyer: Seven resolutions were referred to the reference committee. No action was taken on resolution 62–1 concerning the combining of services of the State Welfare and Health Departments, inasmuch as it is felt that the intent of this resolution is better expressed in resolution 62–11, which has been referred to the Reference Committee on Legislation and Legal Matters.

Your committee recommends approval of this portion of the report. I so move.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 156 (see 49)

Report of Reference Committee on Commission on Medical Services—A: Review and Revision of Fee Schedules for Welfare Patients

Dr. Moyer: Resolution 62–13, concerning

the review and revision of fee schedules for welfare patients, was disapproved by your reference committee for the following reasons:

1. It is felt that the "resolved's" do not logically follow the "whereases."

2. The provision for local option in establishing fees by the permissive program under the State Welfare Law makes this a local matter.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 157 (see 57)

Report of Reference Committee on Commission on Medical Services—A: Health Insurance Coverage for the Over Sixty-Five Age Group

Dr. Moyer: Resolution 62–21, concerning health insurance coverage for the over sixty-five age group, re-emphasizes a stand previously taken by the Medical Society of the State of New York and therefore is recommended for approval.

Mr. Speaker, I move adoption of this portion of the report.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 158 (see 68)

Report of Reference Committee on Commission on Medical Services—A: Approval of New York Over the Age of Sixty-Five Insurance Plans

Dr. Moyer: Resolution 62–32, concerning the approval of New York over the age of sixty-five insurance plans, stimulated considerable discussion in the reference committee. The following facts were pointed out:

1. Permissive legislation was passed by the New York State Legislature this year allowing private insurance carriers to underwrite jointly, on a nonprofit basis, hospital, surgical, medical, and major medical expense insurance.

2. This allows a new group of insurers to compete with already established groups.

3. To offset the threat of Federal legislation, increased coverage for this age group is desirable.

4. The intent of this resolution recognizes the desirability of physicians participating in establishing fees in such programs.

Therefore, your reference committee recommends approval of this resolution with one change: In the fourth "whereas," the word "expense" should be changed to "health costs."

I move approval of this portion of the report.

Dr. Ershler: I second it.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be approved. Is there any discussion?

Thomas F. McCarthy, M.D., *Bronx:* I can recognize one danger in approving this. First, I would take it that this is a nonprofit insurance arrangement established under similar conditions as those for nonprofit insurance companies. We have established over a period of years in the State Society certain standards for the approval of nonprofit insurance plans, in that we have refused to endorse other nonprofit insurance plans because they have not met the standards set by the State Medical Society.

The danger to me would be that this might be misinterpreted, and I would suggest to the committee that they make a change in the language, namely, in the first "resolved," that the Medical Society of the State of New York commends this effort to serve those individuals sixty-five and over and that it be further resolved that the Council of this Society be instructed to cooperate in the implementation of this program. But I would also add, in addition to that, this does not constitute endorsement of the program by the Medical Society of the State of New York. Would you accept that?

Dr. Moyer: You will notice the first "resolved" says approving in principle. It is not endorsing the program; it is approving it in principle.

Dr. McCarthy: I want it on the record that in your opinion that does not constitute endorsement of this program by the Medical Society of the State of New York.

Dr. Moyer: I think the reference committee approved this in principle.

Dr. McCarthy: I beg your pardon. I want to know was that considered, and did they feel that this did not constitute endorsement of the program, or did they consider that?

Dr. Moyer: Yes, I think they considered endorsement.

Dr. McCarthy: They considered this to be endorsement of the program?

Dr. Moyer: They considered this to be approving it in principle. The law is on the books. This permissive legislation has been passed by the State of New York.

Dr. McCarthy: There are two other companies operating in the City of New York who are operating under this law that we have refused to give approval to. Do you realize that? Did the committee realize that?

Dr. Moyer: We did not realize two had been refused.

Dr. McCarthy: I think the committee is remiss in not investigating it further before you approved anything in principle.

Dr. Dorman: I introduced this resolution, and I would like to say to Dr. McCarthy through our speaker that this approval in principle was very carefully put in there because this program has not been spelled out, and I would refuse to permit this House, if I could avoid it, to approve anything which has not been spelled out. I was anxious to get this approval in principle so that the House could implement the assistance of the private insurance carriers in setting up the lines of this thing. The plan is still being drawn up. The legislation has been passed. The private carriers are allowed to set up a separate foundation, or company, or association, which will not be subject to the fair trade laws which prevent a group of private competing companies working together. This is going to be a nonprofit organization. The details have not been spelled out, and therefore we cannot approve it in detail. Approval in principle is all that is needed in this case. This follows very much the over sixty-five plan that they have set up already and that is functioning in Connecticut, and I can assure you that if this is handed over to the Council as the suggestion has been for implementation, we will keep a sharp eye on this thing as it is developed. In fact, I might tell you that I understand that at a meeting among the insurance companies yesterday the fact that this resolution was before the House made them consider that they would want to call on the doctors for their advice.

Vice-Speaker Babbage: Thank you, Dr. Dorman.

Is there any other discussion of this? If not, then we will vote on it. Those in favor of accepting the recommendations of the reference committee will say "aye," any opposition "no." The ayes have it. It is carried.

Section 159 (see 69)

Report of Reference Committee on Commission on Medical Services—A: Social Security for Physicians

Dr. Moyer: Resolution 62–33, concerning Social Security for physicians, was considered, and your reference committee recommends the following resolution be substituted:

> Whereas, The Medical Society of the State of New York has annually for the past several years indicated its desire to have Social Security for physicians; now therefore be it hereby
>
> *Resolved*, That the delegates of the Medical Society of the State of New York to the House of Delegates of the American Medical Association be instructed to introduce a resolution to provide for Social Security coverage for physicians.

I move adoption of this portion of the report.

Vice-Speaker Babbage: Is it seconded?

. . . It was seconded by several . . .

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. It is now open for discussion.

Robert F. McMahon, M.D., *Onondaga:* I would like to amend the last sentence to say where it is politically feasible.

Vice-Speaker Babbage: Does anybody second that?

. . . There was no response . . .

Vice-Speaker Babbage: It has not been seconded.

Royal S. Davis, M.D., *Section Delegate:* I thought we had a discussion this morning about instructing or not instructing delegates. I thought we were not going to instruct them. Are we going to instruct them when we feel like it?

Vice-Speaker Babbage: Is there any other discussion?

Dr. McMahon: My point being it is ridiculous to introduce a resolution when you know you can't win. I think you should introduce it when you have a chance of winning so that you can make friends, not enemies.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 160 (see 77)

Report of Reference Committee on Commission on Medical Services—A: Social Security Poll

Dr. Moyer: Resolution 62–41 recommends that the Medical Society of the State of New York participate in a nationwide referendum on the matter of Social Security for physicians. Your reference committee doubts the authority of our State Society to enter the jurisdiction of other state societies for this referendum and, in addition, feels that the expense incurred would further jeopardize our already precarious financial position. Your reference committee disapproves this resolution.

I move adoption of this portion of the report.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 161 (see 89)

Report of Reference Committee on Commission on Medical Services—A: Protection of Individual Physician Employed by Purveyor of Health Care

Dr. Moyer: Resolution 62–52 deals with the protection of individual physicians employed by a purveyor of health care. Your reference committee feels that all county medical societies have grievance and mediation committees which could provide the instrument for this service.

Your reference committee feels that if there is an economic factor which cannot be resolved by grievance or mediation committees at the county level, the Economics Committee of the Medical Society of the State of New York should study the matter further and make appropriate recommendations.

I move the adoption of this portion of the report.

Dr. Pisani: I second it.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. Is there any discussion?

JAMES GREENOUGH, M.D., *Past-President:* Does this involve disapproval of the resolution?

DR. MOYER: It recommends disapproval of the resolution.

SAMUEL Z. FREEDMAN, M.D., *Assistant Treasurer:* As the introducer of the resolution, I think it is incumbent on me to tell you why I drew that up.

The "whereases"—I don't know how many read the "whereases"—give the background of why I think at this time it is essential that organized medicine become the instrument by which the individual physician be protected in the economic turmoil of today. There are so many individuals, particularly in New York City—and I emphasize in New York City—where a lot of these things have started and perhaps have been strange to people in other parts of the State, where individuals are now working for an employer. I recall very many years ago that one of the things that made me think of going into medicine was the advice that it is better to have a thousand employers rather than to have one, but of course this idea of having a thousand employers is being reduced because we are having more and more centralization of the selling of medical care. More and more doctors are finding themselves now employes, whether it be a union plan or some sort of individual setup, whereby they have one employer, and if they are discharged, their entire source of income for the time being is removed. Therefore, it occurred to me that we should not be remiss in providing for the individual physicians of this State Society a service which is now being provided by law, though it took many, many years to get it on the books, for the workers in all other areas.

I think it would be folly for us to disapprove a thing like that and not be able to tell the individual physicians that your county society particularly, and perhaps your State Society, should be in a position, if nothing else, to be a shoulder on which an individual can cry if he thinks he has been discharged or fired from a position.

I can't see that that would be bad public relations for us. I can't see why it would be detrimental to us. If anything, I can see where it would provide a means to start making contact with the employers of individual physicians so that we could provide for these physicians the service which everybody else in the country seems to have but the physician.

VICE-SPEAKER BABBAGE: Is there any other discussion?

DR. FREEDMAN: I would like to amend the resolution to take no action on the report.

IRWIN ALPER, M.D., *Oneida:* I second it.

DR. ERSHLER: As a member of this reference committee, I think it was the intent of the committee not to do anything about this because adequate facilities are now available for grievances of doctor against doctor, doctor against the public, or anybody else against doctor. These exist in almost all component medical societies, and if there is any situation, particularly of an economic nature, which cannot be handled by the county societies, we do still have the Economics Committee of the State Society to appeal to. Therefore, we felt, in the reference committee, that the formation of another committee was not necessary, adequate facilities being available. We thought we did not need to do anything about it except to approve the report.

DR. DORMAN: On the amendment, I would like to point out that if you approve the report you are practically disapproving the resolution, and then you turn around and say you will take no action on the resolution. I think there has to be a little clear thinking on this. You are either going to take no action on the report and on the resolution, or you are going to have to take action pro or con on the resolution.

VICE-SPEAKER BABBAGE: You are talking about the report. Do you mean this portion of the report or the report as a whole?

DR. DORMAN: I am speaking on this question of the amendment, which was to accept the report, this portion of the report, and take no action on the resolution. It is a conflicting thing to do unless you want to take no action on the report and no action on the resolution.

VICE-SPEAKER BABBAGE: This portion of the report which we are now discussing only has to do with this resolution, is that right?

DR. DORMAN: That is right, but the report backs a negative action on the resolution. Then your amendment is to take no action on the resolution. If you accept the report, you are practically rejecting the resolution, and when it is amended to take no action on the resolution, I don't think it clarifies it for the House.

DR. ERSHLER: I think perhaps I can clarify this. The report indicates the desirability of having some instrument whereby a physician, who has been summarily discharged or some other terrible thing happens to him, has some method of airing his grievance to proper people. The report indicates that this portion of the resolution indicates that the instrument for handling this situation already exists. That portion of the resolution which says you must have another committee we disagree with. Therefore, we felt that no action was necessary on the resolution, but we approved that portion of the report that the doctors should have some mechanism by which they can air their grievances, which they have.

DR. FREEDMAN: Will the last speaker or the chairman of the reference committee tell me where. I am not aware that there is any place to which a physician can go in the circumstances that I have described, which is the purpose of this resolution. I will give you an example which made me think about this: A doctor working for one of the union health centers—not the Union Health Center, but one of the union health centers—was summarily discharged by the medical director of this setup because they got into a little dispute. Will anybody tell me where this doctor could go at this time to have somebody take up the cudgels for him? I am not aware of it.

Dr. Moyer: The committee felt there is no reason why mediation committees existing in the county societies cannot be used for this purpose.

Dr. Freedman: That is something else. There is no setup right now.

Dr. Moyer: Mediation and grievance committees.

Vice-Speaker Babbage: The chair will now rule that we will vote on this recommendation of the reference committee. First of all, we do have this amendment, which was to take no action on it, and I believe that was seconded. We have discussed it, and we will now vote on whether we take no action, and I think this vote means we will take no action. All those in favor indicate by saying "aye," opposed "no." The "ayes" have it, and there is no action on this resolution.

Dr. Moyer: We now come to a relatively noncontroversial part of this report. Your chairman would like to thank the members of his reference committee for their excellent cooperation and Mrs. Alice Arana for her excellent secretarial help.

I move the adoption of this report as a whole as amended.

Dr. Ershler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 162

Telegram of Greetings

Speaker Wurzbach: I have here a telegram received by Executive Vice-President Fineberg:

> Hearty best wishes for a most successful meeting. Regret I cannot extend greetings in person but will have you know that the Dental Society of the State of New York pledges support in this area of responsibility to the medical profession of New York in its dedicated efforts for the longer, healthier life of the people we are privileged to serve.
>
> Walter E. Taylor, *President*
> Dental Society of the State of New York

Reference Committee on Commission on Medical Services—B

Section 163

Report of Reference Committee on Commission on Medical Services—B: Workmen's Compensation

C. Joseph Delaney, M.D., *New York:* Your reference committee has reviewed the extensive work done by the Council Committee on Workmen's Compensation under the chairmanship of Carl F. Freese, M.D.

Recommendations were made to the Workmen's Compensation Board's Advisory Committee for the Medical Fee Schedule and Allied Problems relating to changes in the fee schedule. Those accepted by the advisory committee involved the application of the Unna boot, fluoroscopy, and osteopathic fees. Other changes still under consideration are matters dealing with fees for preoperative medical examinations by operating surgeons and fees for the care of injuries where specialists services are not required.

Changes in code letters are now under way, some being deleted while others will be assigned only as a part of a multiple rating.

Recommendations of the Council committee to the advisory committee, which are still pending, relate to the increase of fees for witnesses and fees for assistants to surgeons and anesthesia fees.

Two bills were introduced in the Legislature during the past session. One related to the extension of time allowed to a physician for reporting a compensation case from its present limitation of forty-eight hours. This was defeated in the Assembly. The second bill related to the payment of bills for medical care. It now becomes mandatory on an insurance carrier to pay the physician within fifteen days after all controverted issues have been decided in favor of the claimant. This bill passed both houses and was signed by the Governor.

The introduction of these bills was the result of a mandate from the House of Delegates in 1961 for the Council Committee on Workmen's Compensation to review the Workmen's Compensation Law, especially in matters dealing with medical care. This review is continuing.

Your reference committee wishes to praise the educative, consultative, and liaison work carried out during the past year among county medical societies and various groups involved in the proper functioning of the Workmen's Compensation Law. Work along these lines is most beneficial to the medical profession.

The work of the arbitration committee throughout the State and especially in the New York City area has been very successful, as the following indicates: 1,959 cases scheduled for hearing, 1,210 decided by arbitration, 362 settled without hearing, 51 settled by direct negotiations, and 387 postponed.

Your reference committee wishes to commend to you the fine work done by this Council committee and the bureau under the leadership of Carl F. Freese, M.D., chairman, and Robert Katz, M.D., director of the bureau.

Mr. Speaker, I move the adoption of this portion of the report.

Philip D. Allen, M.D., *New York:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 164

Report of Reference Committee on Commission on Medical Services—B: Industrial Health

Dr. Delaney: The Council Committee on Industrial Health under the chairmanship of Peter J. DiNatale, M.D., continued throughout the year to project its efforts to improve and expand health services throughout the State. This they have done by advising county medical society committees on industrial health, setting up programs, establishing exhibits, as at the Coliseum in 1961, participating in study groups, and working with other organizations interested in the same field.

The committee reviewed the Guides for Management of Union Health Centers put out by the American Medical Association. These Guides are just that—guides, not rules, or even policy. However, your Council committee finds them comprehensive, clear, and conclusive enough to be of great assistance to local county medical societies who are the ones who still set policy regarding this type of medical practice.

The bureau studied nine union health centers in the Greater New York area. The comments regarding these centers are interesting, but conclusions regarding these matters have been deferred until the formal evaluation of the study is brought out by the bureau, which it plans to do in the near future.

Your reference committee commends highly Dr. DiNatale, the committee chairman, and Dr. Katz, the director of the bureau, for the fine work done by their groups.

Mr. Speaker, I move the adoption of this part of the report.

Victor J. Tofany, M.D., *Section Delegate:* I second that motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 165

Report of Reference Committee on Commission on Medical Services—B: Hospital and Professional Relations Committee

Dr. Delaney: Your reference committee has noted with great interest the joint activities of the Hospital and Professional Relations Committee and the medical affairs committee of the Hospital Association of New York State in assisting and making recommendations to Commissioner Herman E. Hilleboe with reference to the study that has been undertaken relative to the appointments to medical staffs. Your reference committee concurs in the following policy statement given Dr. Hilleboe on this matter:

> The governing body of a hospital has the legal right to appoint the medical staff and the moral obligation to appoint only those physicians who are judged by their fellows to be worthy, of good character, qualified, and competent in their respective fields.
>
> Individual character, competence, experience, and judgment should be the criteria for selection.
>
> 1. Under no circumstances should the accordance of staff membership or professional privileges in the hospital be dependent solely upon certification, fellowship, or membership in specialty board or society.
> 2. The applicant's race, creed, and national origin should not influence his appointment.
> 3. His hospital or medical insurance affiliation should not be a consideration in his appointment.
> 4. The continuation of any physician's appointment should depend upon his fulfilling the obligations of membership on the medical staff of the hospital.

Your reference commitee recommends amending number three by adding the words, "the sole," so it would read:

> 3. His hospital or medical insurance affiliation should not be the sole consideration in his appointment.

Mr. Speaker, I move the adoption of this portion of the report.

David Kershner, M.D., *Kings:* I second the motion.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. Is there any discussion?

Julia V. Lichtenstein, M.D., *New York:* This is the second time sex has been left out of it. While we have never had any difficulty in getting a woman appointed, I think it might be desirable to include that with race, color, and creed.

Vice-Speaker Babbage: Dr. Delaney, will you accept that?

Dr. Delaney: I am sure the committee would be very happy to accept that addition.

Michael J. Crino, M.D., *Monroe:* Under number 4, "The continuation of any physician's appointment should depend upon his fulfilling the obligations of membership on the medical staff of the hospital"; that means that the appointment can be perpetuated throughout his life. Is that what you mean?

Dr. Delaney: My understanding of number 4 is that when a man is appointed to a staff, he should fulfill his obligations to the hospital as required by the rules and regulations, he should attend meetings, he should abide by the rules, he should keep his charts up to date, and that sort of thing. That is the way I understand that.

Dr. Crino: But his tenure of office has nothing to do with this item 4.

Dr. Delaney: I don't see anything about it in that respect.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Vice-Speaker Babbage: That was adopted as amended.

Dr. Delaney: The New York State Department of Social Welfare proposed a draft of rules and recommendations for hospitals in New York State. After extensive critical review by a joint advisory committee, composed of members of the Council committee as well as members selected from the New York State Hospital Association, it was concluded that the rules drafted were not practical, although the draft did contain some good recommendations. When it was brought to the attention of the Department of Social Welfare that the Joint Commission on Accreditation of Hospitals had a set of rules which were applicable to the running of hospitals and, in fact, were in use throughout the State as a means of classifying hospitals, the Department of Social Welfare agreed to study the rules of the Joint Commission. Up to the present time, no word has been received from the Department of Social Welfare relative to any future action along these lines.

We wish to extend our sincere thanks to Raymond S. McKeeby, M.D., chairman, and his committee for the outstanding work done throughout the year.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Allen: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 166

Report of Reference Committee on Commission on Medical Services—B: Medical Service

Dr. Delaney: The work of this committee under the chairmanship of Edward C. Hughes, M.D., was confined mostly to the problems of medicine outside the larger cities of the State. The committee instituted numerous informational health forums for the public throughout the State. This proved to be a very successful venture and was well received. Over 2,000 people attended these forums.

The committee gave much time and study to the critical problem of obtaining physicians for rural areas. Questionnaires were prepared, and methods for obtaining physicians for these areas were studied.

Your reference committee critically reviewed the recommendations of the Medical Service Committee relative to the use of the Empire State Medical, Scientific and Educational Foundation. The Medical Service Committee had recommended that the Foundation be given the responsibility for planning the program, assisting in the fund raising, and obtaining physicians who would actively participate in the plan. Your reference committee feels that the Medical Service Committee should continue to participate, even loosely, with the Foundation in this endeavor and not turn it over entirely to the foundation.

Your reference committee also feels that the various medical centers throughout the State should be advised of the critical shortage of physicians in some areas and should be asked to place more emphasis on the problems of practice in rural areas.

Your reference committee wishes to thank Dr. Hughes, the committee chairman, and his committee for the fine work they have done.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Tofany: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 167

Report of Reference Committee on Commission on Medical Services—B: Questions of Ethics

Dr. Delaney: This committee, presided over by Harold F. Brown, M.D., held one meeting during the year.

The business of the committee otherwise was conducted by telephone consultation or by personal action of the chairman. Most of the work consisted of answering inquiries relating to the interpretation of the code of ethics. None of the problems given to the committee during the year appeared to be earth-shaking, and all were well handled.

In closing his report, Dr. Brown wishes to call to the attention of the House that the Committee on Questions of Ethics is not mentioned in the Constitution and Bylaws and that nowhere is there delineated the scope of activity of such a committee.

Your reference committee wishes to call this observation to the attention of the Planning Committee now functioning.

Your reference committee wishes to thank Dr. Brown and his committee for the work they have done this year.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Allen: I second the motion.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. Is there any discussion?

Gerald D. Dorman, M.D., *Councillor:* The Committee on Ethics comes under the Commission on Medical Services, of which I am chairman. There has been some discussion, as implied here, about the fact that since it is not in the Constitution and Bylaws, it is redundant as compared to the Judicial Council, which is in our Constitution and Bylaws, and does not therefore serve a necessary purpose.

I notice that the reference committee does not make a recommendation that this be eliminated. It is acting now as a sort of answerer of questions, and this function might be turned over to the executive vice-president with questions which he could not answer being sent to the Judicial Council. The question has come up at times whether this Committee on Ethics is serving a useful purpose. At this point there is no recommendation that it either be eliminated or be continued. It is merely pointed out to the House that it is not in the Constitution and Bylaws.

Does the reference committee have a recommendation on this point?

DR. DELANEY: The reference committee has no recommendation but refers it to the Planning Committee. I think they mention it in their new setup.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 168 (see 41)

Report of Reference Committee on Commission on Medical Services—B: Differential in Fees for Osteopaths in Workmen's Compensation Fee Schedule

DR. DELANEY: Your reference committee took action on the following resolutions:

Resolution 62–5, "Differential in Fees for Osteopaths in Workmen's Compensation Fee Schedule," introduced by Charles C. Mangi, M.D., of Queens.

Your reference committee recommends that the fourth "whereas" of this resolution be deleted and the "resolved" be amended to read as follows:

> *Resolved*, That the House of Delegates of the Medical Society of the State of New York request that all inequities in fee schedules between osteopaths and doctors of medicine in general practice based on osteopathic manipulation be abolished.

Mr. Speaker, I move the adoption of this portion of the report.

DR. KERSHNER: I second it.

VICE-SPEAKER BABBAGE: The motion for the adoption of the report has been made and seconded. Is there any discussion?

CHARLES C. MANGI, M.D., *Queens:* I wish to make a substitute motion to the report of the reference committee to reinsert in the original resolution the "whereas" that has been deleted and also to put in the last phrase that had been present in the "resolved." After it is seconded, I would like to speak on this motion.

THOMAS M. D'ANGELO, M.D., *Queens:* I second it.

DR. MANGI: The reason for this resolution, gentlemen, is this: There has been an inequity in fees between the osteopaths and the fees in general practice, and the fees for general practice do not apply merely to general practitioners. They apply to all doctors under workmen's compensation who are treating any patients not within their particular specialty, so that the general practice fees will apply to all doctors. There has been a basic inequity with the osteopaths always having a differential in fees. This differential has been protested and actions taken in this House of Delegates in 1959, 1960, and 1961.

The chairman of the Workmen's Compensation Board in 1959 was advised by William L. Wheeler, Jr., M.D., our secretary, to correct this inequity in fees. In 1960, William F. Pelow, M.D., had also pointed out this inequity in fees. This morning, I appeared as chairman of your Reference Committee on Organization and Policies, and we approved of association with osteopaths provided that they adhered to the same scientific principles that are recognized by doctors of medicine. This had been included in my first "whereas," that if they adhered to these scientific principles, we could associate with them.

The last "whereas" that has been deleted by the reference committee states:

> WHEREAS, osteopathic manipulation is not supported by the scientific principles embraced by doctors of medicine; now therefore be it hereby resolved

I fail to see, gentlemen, how we can possibly agree that osteopathic manipulation is supported by scientific principles. I understand that the reason it was deleted by the reference committee was so as not to offend or hurt the osteopaths. I think this is nonsense. We have been negotiating. Dr. Moore has done an excellent job with these osteopaths for the past year, but the osteopaths have had the opportunity for the past three years to renounce at least voluntarily this particular inequity.

One further thing, gentlemen, the fee schedule for 1960 that had been promulgated on July 1, 1960, which is the latest one, has osteopathic manipulation as part of each and every based fee of the osteopath, so that you will assume, gentlemen, that every osteopathic physician who sees a patient, whether it be in his office, or in a hospital, or at home, will give an osteopathic manipulation. If this is according to the scientific principles of doctors of medicine, I fail to see it.

One further thing too: These fees in the latest fee schedule are listed, believe it or not, under specialists' fees. Now, I maintain that if a doctor of osteopathy is collecting a fee for osteopathic manipulation under workmen's compensation, then he is not abiding by our scientific principles, and we should not be allowed to associate with him professionally. Therefore, the last part of the "resolved" that has been abolished by the reference committee should be inserted before doctors of medicine are allowed to associate professionally with doctors of osteopathy.

This is not in conflict with the action we took today. The osteopaths could very well renounce osteopathic manipulation under workmen's compensation, and we would all be very happy.

DR. D'ANGELO: I would like to ask a question. They left out the fourth "whereas," which you heard Dr. Mangi read. Am I to understand that the reference committee considers osteopathic manipulation as a scientific principle because they deleted it?

Dr. Delaney: No, Dr. d'Angelo. We thought the intent of this motion was to recommend removing the inequities between the medical doctors and osteopaths. The questions that are brought up in this "whereas" and in the final sentence of the "resolved," we felt, were now being studied by this special committee of the House. They are trying to discuss all these problems about manipulation and the relationship of osteopaths to the practicing physicians, and rather than bring this out as a *de facto* thing in a resolution, we thought we would allow this to be developed by this special committee and use this resolution purely to request a removal of the inequities of the fees.

Dr. d'Angelo: Am I to understand that this particular "whereas" was redundant?

Dr. Delaney: We did not think it was redundant, and we did not agree with it necessarily, but we thought putting it into the resolution and having it passed at this time would be taking something out of the hands of the special committee that is going to find either for or against these things later on in their relationship with the osteopaths.

Dr. d'Angelo: That is exactly the answer I thought you were giving me because that in itself negates for us as physicians our basic principles based on scientific medicine, if this osteopathic manipulation in our opinion is not based on scientific medicine. Therefore, I see no reason why that "whereas" should not remain where it is. We should not in any way sell our ethics for expediency.

Vice-Speaker Babbage: Is there any other discussion on this substitute motion? Don't forget we are talking about the substitute motion.

. . . There were calls for the question . . .

Vice-Speaker Babbage: All in favor of accepting the substitute motion in favor of the original report—the substitute motion as given by Dr. Mangi in place of the original report of the reference committee—all those in favor say "aye," opposed "no." The "ayes" have it; therefore, the substitute motion of Dr. Mangi now goes into the report of the reference committee.

Section 169 (*see 54*)

Report of Reference Committee on Commission on Medical Services—B: Workmen's Compensation Fee Schedule on Time-Rate Basis

Dr. Delaney: Resolution 62–18, "Workmen's Compensation Fee Schedule on Time-Rate Basis": Your reference committee recommends that the second and third "whereases" be omitted and the following be substituted:

> Whereas, the shortage of interns and residents makes it necessary to call in adequately trained physicians which is in the best interest of good medical care;

and the "resolved" portion of this resolution be amended to read as follows:

> *Resolved*, That the New York State Workmen's Compensation Board be requested to establish a fee schedule for payment for the services of a practicing physician as assistant at a surgical procedure when the absence of resident physicians makes it necessary to employ the services of such practicing physicians and that the assistant be paid $25 minimum or 25 per cent of the operating surgeon's fee, whichever is greater.

Mr. Speaker, I move the adoption of the resolution as amended.

Dr. Allen: I second it.

Vice-Speaker Babbage: It has been moved and seconded that this portion of the report be accepted. Is there any discussion?

Dr. Dorman: I just want a clarification. Is that 25 per cent of the operating surgeon's fee to be out of the surgeon's fee or in addition to it?

Dr. Delaney: As I understand it, it is to be paid by the insurance carrier as a separate fee.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 170 (*see 60*)

Report of Reference Committee on Commission on Medical Services—B: Two-Year Internships for American Medical School Graduates

Dr. Delaney: Resolution 62–24, "Two-Year Internships for American Medical School Graduates," introduced by the Bronx County Medical Society: No action was taken on this resolution. The reference committee felt that the presentation of this resolution has become perennial, with the result that no action has ever resulted from its passage. Your reference committee feels, however, that there is a need for general practitioners throughout the State of New York, and teaching hospitals should be encouraged to provide comprehensive internships which would prepare men to enter general practice, as opposed to confining their work to a specialty.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Kershner: I second the motion.

Vice-Speaker Babbage: Is there discussion?

. . . Dr. Rawls of New York made a substitute motion, changing the phrase, "the presentation of this resolution has become perennial with the result that no action has ever resulted from its passage," to "the presentation of this resolution was unnecessary as the family practice internship has been established and the entire problem of intern and resident training is now under study by a special committee of the A.M.A." This was seconded by Dr. Wagreich of the Bronx.

Dr. Angrist of Queens expressed the opinion that adoption of the report as presented by the reference committee would tend further to diminish the number of general practitioners. He supported the substitute motion but proposed an amendment calling for introduction of resolution 62–24 or an equivalent resolution in the A.M.A. House of Delegates. He urged that every recourse be used to achieve the objectives of the two-year rotating internship and the training of men for general practice. The amendment was seconded by Dr. Wagreich. The motion to amend was discussed by Dr. Lieberman of the Bronx, Dr. Rawls of New York, Dr. Delaney of New York, and Dr. Maltinsky of Monroe.

The amendment and the substitute motion as amended were carried . . .

Dr. Delaney: I move approval of this portion of the report as amended.

Dr. Allen: I second it.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 171 (see 71)

Report of Reference Committee on Commission on Medical Services—B: Rights of Patient and Physician

Dr. Delaney: Resolution 62–35, "Rights of Patient and Physician," introduced by Richmond County: Your reference committee took no action on this resolution. It was felt that the issue is redundant because it will be brought up and resolved by a resolution from another reference committee.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Allen: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 172 (see 75)

Report of Reference Committee on Commission on Medical Services—B: Hospital Utilization Committees

Dr. Delaney: Resolution 62–39, "Hospital Utilization Committees," introduced by the Medical Society of the County of Westchester: Your reference committee recommends approval of this resolution. I so move.

Dr. Kershner: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 173 (see 92)

Report of Reference Committee on Commission on Medical Services—B: Creation of Commission to Study Problems of Patient Care, Medical Practice, Hospital Service, and Medical Education

Dr. Delaney: Resolution 62–55, "Creation of Commission to Study Problems of Patient Care, Medical Practice, Hospital Service, and Medical Education," introduced by the Queens County Medical Society: Your reference committee recommends approval of this resolution.

Mr. Speaker, I move the adoption of this portion of the report.

Dr. Tofany: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Dr. Delaney: Your chairman would like to thank the members of his reference committee for their excellent cooperation and Miss Alice E. Wheeler for her secretarial help.

I move the adoption of this report as a whole.

Dr. Allen: I second it.

Vice-Speaker Babbage: It has been moved and seconded that the report as a whole as amended be accepted. Is there any discussion? Those in favor of approving the report as a whole as amended will say "aye," opposed "no." It is carried.

Thank you very much, Dr. Delaney.

I will now turn the chair back to Dr. Wurzbach.

Reference Committee on Reports of Officers

Section 174 (see 23)

Report of Reference Committee on Reports of Offices: Report of the President

Arthur N. Diedrick, M.D., *Westchester:* Mr. Speaker, ladies and gentlemen, this is the report of the Reference Committee on Reports of Officers.

The first report is that of the president. Our president has given a clear, concise account of his administration. He has solved satisfactorily many of the problems which existed when he took office but is faced with new problems that will remain to be solved by the president-elect. We recognize the fruits of his efforts to awaken everybody in our fight to preserve "medicine's freedom."

It appears to us that the change to alternate bimonthly meetings of the Council and the Board of Trustees has proved to be a success, both in saving the time of our members and expense to our State Society.

We believe that the necessary amendment to the Constitution and Bylaws should be passed relative to the Planning Committee for Medical Policies.

The suggestion that the terms on committees be limited to three years with ineligibility for reappointment seems sound. It would give greater rotation among the great wealth of knowledge of many members of the State Society.

The next paragraph is deleted from the report inasmuch as it was approved this morning in the report of the Ancillary Committee.

(The paragraph referred to, which appeared in the distributed report, is as follows: "We approve of the Empire State, Medical, Scientific and Educational Foundation and feel that its potential is excellent, but expansion has been obstructed by delay in obtaining tax exemption. The $8,000 budgetary item for this year is noted, but this committee sees no immediate reason for it being in the future budget.")

We are of the opinion that our joining the New York State Association of the Professions is a step in the right direction.

The reorganization of the staff of our Society has been a great help in improving the efficiency and morale of the staff.

Your reference committee feels that the Communications Department should be re-evaluated. We believe that the public relations portion of the work should be expanded. The current ancillary functions, which absorb the bulk of the allocated funds, require no such expansion. We recommend that a substantial increase in the budget is in order for public relations and that line-by-line budgeting in the Communications Department be presented to the Medical Society each year.

Our Woman's Auxiliary has again completed a supreme task in supporting us. We urge their continued assistance in the future.

The "Capitol News" serves us all well and should be continued.

The section on medical education is reviewed with interest.

The reference committee recommends continued exploration of the mutual problems between the Medical Society and the Osteopathic Society and approves the president's report on osteopathy.

We congratulate the delegation who visited Washington in February and think this important liaison with our lawmakers should be continued.

The periodic review of policy should prove to be most helpful, and we recommend that this be an ongoing service.

The Commission on Medical Services has worked out well, and we approve the establishment of the suggested Commission on Public Affairs, as outlined in the president's supplementary report.

We hail the report of the president.

Mr. Speaker, I move approval of this portion of the report.

William R. Carson, M.D., *St. Lawrence:* I second the motion.

Speaker Wurzbach: Is there discussion?

Jerome Flynn, M.D., *Bronx:* Back here where your reference committee feels that the Communications Department should be reevaluated, I would like to substitute a recommendation that this be deleted, and this be put in its place—

Speaker Wurzbach: It is a substitution?

Dr. Flynn: A substitution that an appropriate committee be appointed by the Council to review the structure and functions of the communications and public relations services of this Society and that this committee shall make recommendations regarding changes if needed.

The reason I give this is because I believe there is a great need to maintain efficient services of communication and public relations. We are allotting for this purpose about 18 per cent of our budget, which is $150,000 out of $833,000, as compared to the A.M.A.—I believe these figures are correct; Mr. Pardee stated them—which allows 3 per cent of their income or $500,000 out of $16,000,000. Therefore, I would like to move that this recommendation be accepted.

Speaker Wurzbach: You wish a new committee to be formed. Of the House, the Council, or what?

Dr. Flynn: An appropriate committee be appointed by the Council to review the structure and functions of the Communications Department of this Society, and this committee to make recommendations regarding changes, if needed.

Speaker Wurzbach: Is there a second?

George A. Howley, M.D., *Bronx:* I second it.

Speaker Wurzbach: Is there any further discussion? All those in favor of the substitution of the paragraph as presented say "aye," those opposed "no." It is adopted.

Now, we are on the report of the president as a whole as amended. If there is no further discussion, all those in favor of the adoption of this report as amended will say "aye," opposed "no." It is adopted as amended.

Section 175 (see 24)

Report of Reference Committee on Reports of Officers: Report of the President-Elect

Dr. Diedrick: The president-elect presented his report before the House of Delegates on Monday of this week. It was received with enthusiasm, and we look with favor and anticipation to a most successful year. We were impressed by his enthusiasm to continue and implement the policies started by Dr. Galbraith and feel that his strong support of the Planning Committee's change in the committee structure will save the Society money and will bring younger men into State Society affairs.

His remarks concerning the Physicians' Home are strongly endorsed by your reference committee, especially his recommendation that a minimum of $10 be contributed annually by each member. It is our feeling that if the Journal could carry a published report of the Physicians' Home, the membership will have a better idea as to its functions and activities and will be more likely to make a contribution as recommended.

His remarks concerning the finances of the Society will be dealt with under the Trustees' report.

Mr. Speaker, I move approval of this portion of the report.

Kenneth H. Eckhert, M.D., *Erie:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 176

Report of Reference Committee on Reports of Officers: Report of the Secretary

Dr. Diedrick: The secretary has worked diligently during the course of the year. His report has been extended to meet the request from the floor of last year's meeting of the House of Delegates to show that our membership is 25,351.

He has explained the activities of the Physicians Placement Bureau.

Of the important occurrences during the year, he reports the special meeting of the House of Delegates, the first since 1932.

Mr. Speaker, I move approval of this portion of the report.

Solomon Schussheim, M.D., *Kings:* I second it.

Speaker Wurzbach: Is there any discussion?

Thomas F. McCarthy, M.D., *Bronx:* I am going to request of our efficient secretary the usual question I put every year. Will he kindly report the number of active members who pay dues into the Society?

Secretary Wheeler: Mr. Speaker, the active dues-paying members for the past year were 23,339, and in addition, there were 321 junior members who paid reduced dues.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 177 (see 14)

Report of Reference Committee on Reports of Officers: Report of the Board of Trustees

Dr. Diedrick: The Board of Trustees have reported on their meetings and the outcome of recommendations made by them. Of outstanding interest is the transfer of $500,000 of securities from the Investment Fund to the Building Fund.

They delineate our good fortune in having Henry I. Fineberg, M.D., as our executive vice-president. Your reference committee unequivocally agrees with this.

This committee feels that it would be derelict in its duty if it did not point out that Chapter V, Section 2 of the Bylaws, specifically states: "The budget prepared by the Council shall be submitted to the Board for its approval, and all resolutions or recommendations of the House of Delegates or Council pertaining to expenditures of money must be approved by the Board of Trustees before the same shall become effective."

Without doubt, this puts the control of the fiscal stability of the Society strictly in the hands of the Board of Trustees. Good judgment would compel them to keep the Society solvent at all times and to live within our current income.

We recommend that the Board of Trustees require the budget for the ensuing year be in their hands not later than July 1 of the preceding year.

Their comments on dues will be included in our remarks on the treasurer's report.

Mr. Speaker, I move approval of this portion of the report.

Edward H. Robitzek, M.D., *Richmond:* I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 178 (see 16)

Report of Reference Committee on Reports of Officers: Report of the Executive Vice-President

Dr. Diedrick: This is the first time that our Society has received a report from an executive vice-president. Your committee feels that after reviewing the report and activities carried out, the Medical Society of the State of New York is fortunate in having a man of Henry Fineberg's caliber in the administrator's chair. His heartfelt interest in our welfare is demonstrated from day to day.

The Willers Report and recommendations have been implemented with satisfaction and success.

Mr. Speaker, I move approval of this portion of the report.

Dr. Eckhert: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 179

Report of Reference Committee on Reports of Officers: Report of the War Memorial

Dr. Diedrick: The War Memorial Fund has been well administered. This undoubtedly has proved a great benefit to the children of our colleagues who died in the service of their country.

Mr. Speaker, I move approval of this portion of the report.

Dr. Schussheim: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 180 (see 8)

Report of Reference Committee on Reports of Officers: Report of the Speaker

Dr. Diedrick: The speaker's report of the February 10 special meeting of the House of Delegates at the Summit Hotel has been reviewed by the committee. We completely concur with the importance of the report and the resolutions adopted. We recognize that the special meeting was called in a sincere belief that it would be of value and in the hope of achieving a certain impact in our legislation campaign. Unfortunately, the benefits derived are not commensurate with the time and expense involved in such a meeting.

We strongly recommend that extreme caution be exercised before such meetings are called in the future.

We compliment the speaker on the fine and democratic manner in which he has chaired the House of Delegates.

Mr. Speaker, I move approval of this portion of the report.

Dr. Carson: I second it.

Speaker Wurzbach: Discussion?

Joseph A. Lane, M.D., *President-Elect:* Mr. Speaker and members of the House of Delegates, in reference to our special meeting of the House of Delegates in February, if you remember in passing resolution S62–1, we included in there the paragraph as follows: "We further pledge ourselves to continue to work for improvements in our medical system so as to elevate the standards of care and the quality of services provided to individual patients. We will not work for or cooperate with any action, legislative or otherwise, that would lower the standards of medical care or the quality of service."

This paragraph has been a source of considerable criticism of the action of the House at that time, to which I might call your attention as a committee of the whole, and has been interpreted frequently as indicating that we are willing to participate in action something similar to some of our neighbors across the river.

I would like to ask the indulgence of the House to consider changing this paragraph to read as follows: "We further pledge ourselves to continue to work for improvements in our medical system so as to elevate the standards of care and the quality of service provided to individual patients. We will not work for or support any action which would lower the standards of care or quality of service."

Speaker Wurzbach: Do you enter this as a motion, sir?

Dr. Lane: Yes, sir.

Speaker Wurzbach: Is there a second?

Dr. Lane: This is from resolution S62–1 from the special session of the House of Delegates of February 10. I am not sure it is out of order, in view of the fact that the House at that time acted as a committee of the whole. I believe that the House can suspend the rules or by a two-thirds vote accept this recommendation.

Speaker Wurzbach: May I suggest, Dr. Lane, that an action of the Council referred this report of the speaker as an annual report of an officer to this House of Delegates. Therefore, it is open for action in this House of Delegates.

Henry J. Barrow, M.D., *Bronx:* I second it.

Speaker Wurzbach: Is there any discussion?

Dr. Flynn: I would like a definition of the semantics. The resolution as it was passed by the February meeting said we would not comply with or work with what I understood at that time was a brand of socialized medicine. I would just like the proposer, Dr. Lane, to please explain that little phrase he put in. Will it change the intent of the resolution?

I had a discussion with others on this, and I was of the opinion that we may not have been so definite, but I thought that we had already said in this House almost the same words that they said in New Jersey. Now that there has been a bonfire that has been lighted, it looks like we are stepping away after throwing a ball some place.

I would like Dr. Lane, who was the proposer of the first motion, to spell this out please.

Speaker Wurzbach: May I make a statement on this? If this action in New Jersey was delivered as a statement concerning the King-Anderson Bill, this action that we have here is a reiteration of the care of the patient being the primary consideration of the physician in the State of New York. The difficulty has come in the interpretation on the part of some people as to making this an absolute statement about the King-Anderson Bill. It was never intended as such. Right?

Dr. Lane: Yes.

Assistant Secretary Wolff: Mr. Speaker and members of the House, I am a little at a loss to know how we can amend a resolution that was passed at the special session. However, assuming that the speaker is correct that it can come up for action at this time, I suspect that if this is something we are not proud of, we should not have passed it in the first place. It has been buried in the files some place. Stirring it up now will simply add fuel to the fire. I think that it were better left unsaid if you don't want it. On the other hand, if we are men, and we meant what we said, we should reiterate what we said. If we are mice, we might turn around and water it down so that it does not mean a thing. This is definitely watered down. This doesn't mean anything. It is a very benign, pious wish, a statement of no policy, rather than a positive statement of policy, and I would suggest that we leave it as it was.

Speaker Wurzbach: Is there further discussion?

Dr. Lane: The original motion, as introduced in the House in February, did not contain this particular phrase. This was an amendment to the original motion. Rather than being buried, this thing has been a thorn in our side since that time. It has brought up the question repeatedly by press, radio, and television as to what we meant by this. What I am trying to do here today is to correct the impression that exists that this State Society is also in favor of an action similar to that which is now current in New Jersey. We want to emphasize the fact that we will, and can, and intend to continue to take care of patients, even though legislation might be passed by the Federal government that we would be very unhappy about. The intent is to eliminate those words referring to legislation and to a statement of fact that we would not work under legislation of that type, which was in the February 10 resolution; therefore, this substitute is recommended.

SPEAKER WURZBACH: Is there any further discussion?

CHARLES B. MATHEWS, M.D., *Monroe:* Will you reread the present wording?

DR. LANE: The present wording would be this: "We further pledge ourselves to continue to work for improvements in our medical care system so as to elevate the standards of care and the quality of service provided to individual patients. We will not work for or support any action which would lower the standards or quality of medical care."

SPEAKER WURZBACH: We are actually changing the words "cooperate with" to "support" and, as I have it before me here, eliminating the words "legislative or otherwise."

Is there any further discussion?

ROYAL S. DAVIS, M.D., *Section Delegate:* Are we saying, in other words, when they ask us, what do you doctors mean when you said you would not practice under these conditions, legislative or otherwise, that we don't mean anything? Is that what it is proposed we say?

SPEAKER WURZBACH: If there is no further discussion, all in favor of the substituting of the word "support" for "cooperate with" and the elimination of three words, "legislative or otherwise," as presented by Dr. Lane will say "aye," opposed "no." We will have a standing vote on this. Those in favor of Dr. Lane's motion will stand. There is no question about the passage of it, and the "ayes" have it.

DR. DIEDRICK: I move the acceptance of the speaker's report as amended.

DR. LANE: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 181

Report of Reference Committee on Reports of Officers: Reports of the Budget Committee and the Treasurer

DR. DIEDRICK: Again the reports of the treasurer and the Budget Committee are of great concern. The Budget Committee reports that we are facing a deficit of $185,000 for 1962. The treasurer estimates accumulated deficits from prior years will swell our total deficit December 31, 1962, to $260,000.

Your reference committee urges that the State Medical Society be placed on a sound financial basis with a balanced budget. This can be accomplished by reducing the expenditures to meet the income and/or increasing the dues. An increase in dues seems most logical. Currently, our State Society dues remain within the lowest ten states in dollar costs.

The treasurer calculates that an $11 increase in dues will only balance the present budget. To allow for an increase in services, your committee recommends an increase of $15 per year in dues. We feel that the increase in dues is not only necessary but imperative. However, we also are of the opinion that with such increase, there must be firm assurances of installation of a line budget and administrative adherence to it. We believe we have received such assurance, couched in unmistakable language by the executive vice-president and as contained in the concluding recommendations in the supplementary report of the Board of Trustees.

Mr. Speaker, I move approval of this portion of the report.

SPEAKER WURZBACH: Is there a second?

. . . The motion was seconded by several . . .

SPEAKER WURZBACH: Is there any discussion?

. . . Dr. McCarthy of the Bronx asked why the budget contained a figure of $676,102 as estimated income for the year 1962 since the secretary reported 23,339 active dues-paying members, whose dues at $35 each would amount to $816,865. The treasurer replied that when the budget was prepared it was not known what the actual number of dues-paying members would be. He also stated that a loan of $250,000 taken out in 1961 had been paid from 1962 dues.

Dr. Freedman, assistant treasurer, pointed out that the 1962 deficit projected by the treasurer was $185,000 although that anticipated in the report of the Budget Committee was only $138,932. He felt that any figure presented as the probable deficit would be simply a conjecture and that the Budget Committee estimate was as dependable as the figure appearing in the treasurer's report. Consequently he moved that the reference committee recommendation be amended to call for an increase of $10 rather than $15 in the annual dues. The amendment was seconded by several members of the House.

Dr. Dattelbaum stated that there would be an increase in rent during the year and many expenses due to providing additional space for some departments and to setting up and maintaining some of the offices in another building. He added, however, that he would be satisfied with a $10 increase in dues.

John L. Clowe, M.D., of Schenectady, asked why the accumulated deficit of $250,000 could not be paid from the reserve fund. He stated he had been informed that the reserve fund should be enough to cover expenses for two years. He pointed out, however, that the present reserve fund of $833,000 represented expenses for only one year and wished to know what inconvenience could be caused by paying the bank from the reserve fund.

The speaker stated that the bank had already been paid.

Dr. McCarthy pointed out that the present assets of the Society were more than $1,700,000 and that they increased every year.

Dr. Holcomb, trustee, spoke in support of the motion to increase the dues by $10 stating that this was needed to put the Society on a sound basis. He stated we do not actually have $1,700,000 because most of that money is in special funds for specific purposes and cannot be spent. He also stated that the remaining $500,000 reserve might have depreciated due to stock market conditions and might be needed to buy a new headquarters building.

Dr. Bedell, past-president, suggested that money could be saved by using the JOURNAL as a medium for publicizing the Society's activities and by reducing the number of mailings to the membership. He moved that there be a dues increase of $5 rather than $10 or $15. Dr. Freedman seconded the motion.

Dr. Leon of Queens stated it would be unwise to raise both the State dues and the A.M.A. dues in one year. He said that county medical societies attempt to budget within their incomes and that the State Society and the A.M.A. should do so, too.

Dr. Carson expressed the opinion that it would not be possible to decrease the expenses of the State Society and that the dues increase recommended by the reference committee was necessary.

Assistant Secretary Wolff stated he was in favor of cutting down expenditures and turning down any dues increase.

Dr. Clowe stated that either the increase should be at least the $10 requested by the Board of Trustees or there should be no increase and that yearly requests for raising the dues should be avoided in the future.

Dr. Freedman expressed sympathy with Dr. Leon's desire to spare the members dual or multiple dues increases in one year. He stated it is very difficult for a young member to start the private practice of medicine "in the way we are so happy to be able to practice and hope to preserve" and that it is also difficult to explain to such a doctor what advantage there is in State or county society membership.

Dr. Eckhert stated that the reference committee had proposed the $15 increase in order to make it possible to eliminate the accumulated deficit, that the treasurer had reported that, with an increase of $11, it would be possible to avoid increasing the deficit, and that the reference committee felt the officers and trustees should have seen to it that a budget was prepared early each year which could be adhered to.

Dr. Masterson, chairman of the Board of Trustees, stated that the usable reserve amounted to $536,000, that this might be an overvaluation due to changes in stock market prices, and that, if it were used to eliminate the deficit, we would have no collateral and would be unable to borrow. He stated no one had presented a resolution telling the officers and trustees where it would be possible to cut expenditures. He asked that the House of Delegates provide sufficient money to continue running the Society as at present and promised that Dr. Fineberg would see that expenditures did not exceed income.

Dr. d'Angelo of Queens expressed the opinion that expenditures would increase if the work of the Society is to continue and that in some departments an increase in the budget is absolutely necessary. He favored a $10 increase in dues.

Dr. Bauckus, past-president, spoke in favor of increasing the dues by $10.

There were calls for the question . . .

SPEAKER WURZBACH: The question is called for. We are now on the amendment to the amendment that the dues be raised $5.00. All those in favor of this say "aye," opposed "no." The noes have it.

DR. BEDELL: It did not sound that way.

SPEAKER WURZBACH: There is a question on the vote. All in favor of raising the dues $5.00 will stand. The vote is lost.

We are now on the amendment to the report of the reference committee which is that the dues be raised $10. That is the amendment to the committee's report. All those in favor of raising the dues $10 per year say "aye," those opposed "no." The ayes have it.

DR. DIEDRICK: I move approval of this portion of the report as amended.

DR. ROBITZEK: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. DIEDRICK: Now, I move approval of the entire report as a whole as amended.

DR. ECKHERT: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

DR. DIEDRICK: Mr. Speaker, I would like very much at this time to thank all of the members of my committee and also especially I would like to extend my warmest thanks to Miss Roslyn Feinberg for her able assistance to us.

SPEAKER WURZBACH: I wish to thank this House for having handled nine reference committee reports today. Tomorrow we will have one, Reference Committee Report on Legislation and Legal Matters.

We will recess until nine o'clock tomorrow.

. . . A recess was taken at 5:30 P.M. . . .

MAY 17, 1962 | Thursday Morning (Closing) Session

The session convened at 9:10 A.M.

Speaker Wurzbach: Will the House please come to order?

Mr. Secretary, is there a quorum present?

Secretary Wheeler: The secretary sees a quorum.

Speaker Wurzbach: The House will then come to order officially.

Section 182 (see 35, 96, 135)

Introduction of Guests

Speaker Wurzbach: It is now my pleasure to present to you the president-elect of the Massachusetts Medical Society, and I want to ask Dr. Greenough, to bring to the rostrum Urban H. Eversole, M.D.

. . . The House arose and applauded as James Greenough, M.D., conducted Urban H. Eversole, M.D., to the rostrum . . .

Urban H. Eversole, M.D.: Mr. Speaker and members of the House of Delegates of the Medical Society of the State of New York, as the official representative of Massachusetts I am most happy to be here. I believe we are moving toward more regional consideration of problems and with less fragmentation than has been the custom in the past.

As I have looked over your resolutions, it seems that the problems of New York are not very much different from the problems of Massachusetts. The resolutions look much the same as they do in Massachusetts. I am happy to see closer cooperation with the interchange of representatives between the medical societies. We are moving toward it in New England with our New England Council. Instead of having Connecticut, Massachusetts, Rhode Island, and all of the states sometimes pulling separately, we are trying to get a council. We are no longer feared as the colossus by some, and we are happy to cooperate too.

It is indeed a pleasure to be here today.

Speaker Wurzbach: Thank you, Dr. Eversole.

The speaker now has one of the most pleasant tasks that any speaker of this House of Delegates could possibly have. I wish to ask Louis H. Bauer, M.D., to rise. He is with us today.

. . . The House arose and applauded . . .

Speaker Wurzbach: I know, Dr. Bauer, the applause will tell you how dear you are to our hearts, and how happy we are that you are with us today. Thank you, Dr. Bauer, for being here.

Section 183

Appointment of Tellers

Speaker Wurzbach: Now, gentlemen, the first order of business at this session, according to our Bylaws, is the election of officers. We will now proceed with the election of officers. Is there a quorum present, Mr. Secretary?

Secretary Wheeler: There is, Mr. Speaker.

Speaker Wurzbach: Then I will ask the chairman of the Credentials Committee to come forward and read his list of tellers.

Garra L. Lester, M.D., *Chautauqua:* Mr. Speaker, the following people have been appointed as tellers:

Joseph F. Shanaphy, District Branch
Herbert G. Cohen, Bronx
Samuel Leo, Bronx
David Farber, Kings
Arthur E. Lamb, Kings
Louis Pellman, Kings
Leslie H. Tisdall, Kings
Michael J. Crino, Monroe
Leo T. Flood, Nassau
William A. Cooper, New York
Julia V. Lichtenstein, New York
Albert H. Douglas, Queens
John Lowry, Queens
Harold J. Dunlap, Westchester
James M. Jones, Westchester
Joseph J. Russo, Albany
Swen L. Larson, Chemung
Harold T. Golden, Herkimer
Richard D. Eberle, Onondaga
Walter D. Heldmann, Richmond
Philip Parillo, Schenectady
John A. Hatch, Yates
Richard L. Saunders, Section Delegate
Arthur F. Gaffney, District Delegate
Irwin Felsen, Allegany
George Hamilton, Broome
Philip Hust, Delaware
Keith O. Guthrie, New York
Allen H. Keniston, Orange

This completes the list of the tellers, Mr. Speaker.

Speaker Wurzbach: Thank you, Mr. Chairman.

These tellers will, at the conclusion of the voting, go into the Cornell Room, and they will count their ballots and report their returns to this House.

Section 184

Report of Nominating Committee

Speaker Wurzbach: Now, gentlemen, I am going to call on the chairman of the Nominating Committee, Norman S. Moore, M.D., to present the report of the Nominating Committee.

NORMAN S. MOORE, M.D., *Trustee:* Mr. Speaker and gentlemen of the House, the candidates of the Nominating Committee are as follows:

President	Joseph A. Lane, Monroe
President-Elect	William L. Wheeler, Jr., New York
Vice-President	John F. Kelley, Oneida
Secretary	Waring Willis, Westchester
Assistant Secretary	Ezra A. Wolff, Queens
Treasurer	Maurice J. Dattelbaum, Kings
Assistant Treasurer	Samuel Z. Freedman, New York
Speaker	Frederick A. Wurzbach, Jr., Bronx
Vice-Speaker	E. Dean Babbage, Erie
Councillors (three years)	James M. Blake, Schenectady Charles M. Brane, Westchester Peter J. DiNatale, Genesee George J. Lawrence, Jr., Queens
Trustee (five years)	John J. Masterson, Kings
Trustee (to fill unexpired term, two years)	John M. Galbraith, Nassau

There are twice as many delegates to the American Medical Association nominated as can be elected. In alphabetic order they are as follows:

Phillip D. Allen, New York
William T. Boland, Chemung
Harold F. Brown, Erie
Peter J. DiNatale, Genesee
Ralph S. Emerson, Nassau
Irving L. Ershler, Onondaga
Merle D. Evans, Monroe
Henry I. Fineberg, Queens
John M. Galbraith, Nassau
Thurman B. Givan, Kings
Carl Goldmark, Jr., New York
Alfred P. Ingegno, Kings
John F. Kelley, Oneida
Joseph A. Lane, Monroe
Warren A. Lapp, Kings
Charles R. Mathews, Monroe
John C. McClintock, Albany
Irving M. Pallin, Kings
Robert F. Warren, Kings
Carlton E. Wertz, Erie
William L. Wheeler, Jr., New York
Waring Willis, Westchester
Ezra A. Wolff, Queens
Frederick A. Wurzbach, Jr., Bronx

I had a message from Robert F. Warren, of Kings, that he wished to withdraw. The Nominating Committee met Monday briefly after the Bylaws had been passed changing the Planning Committee and allowing for two members-at-large. The Nominating Committee nominated for the one-year post Renato J. Azzari, of the Bronx, and for the two-year post George A. Burgin, of Herkimer.

SPEAKER WURZBACH: This, gentlemen, is the report of the Nominating Committee. I will now open the nominations from the floor.

Section 185

Balloting

. . . The president-elect, vice-president, secretary, assistant secretary, treasurer, assistant treasurer, speaker, vice-speaker, one trustee for five years, one trustee for two years to complete an unexpired term, a member-at-large of the Planning Committee for one year, and a member-at-large of the Planning Committee for two years were unopposed and were elected by a single ballot cast by the secretary.

After nominations from the floor, the nominees for election of four councillors for three years were as follows:

James M. Blake, Schenectady
William T. Boland, Chemung
Charles M. Brane, Westchester
Peter J. DiNatale, Genesee
George J. Lawrence, Jr., Queens
Samuel Wagreich, Bronx

. . . After nominations from the floor and after the withdrawal of two candidates, the nominees for election of 12 delegates and 12 alternate delegates to the A.M.A. were as follows:

Philip D. Allen, New York
William T. Boland, Chemung
Harold F. Brown, Erie
John L. Clowe, Schenectady
Peter J. DiNatale, Genesee
Ralph S. Emerson, Nassau
Irving L. Ershler, Onondaga
Merle D. Evans, Monroe
Henry I. Fineberg, Queens
John M. Galbraith, Nassau
Thurman B. Givan, Kings
Carl Goldmark, Jr., New York
Alfred P. Ingegno, Kings
John F. Kelley, Oneida
Joseph A. Lane, Monroe
Charles R. Mathews, Monroe
John C. McClintock, Albany
Irving M. Pallin, Kings
Carlton E. Wertz, Erie
William L. Wheeler, Jr., New York
Waring Willis, Westchester
Ezra A. Wolff, Queens
Frederick A. Wurzbach, Jr., Bronx

. . . The following members of the House of Delegates were called on to cast their ballots:

OFFICERS, COUNCILLORS, TRUSTEES

John M. Galbraith
Joseph A. Lane
Reid R. Heffner
William L. Wheeler, Jr.
Ezra A. Wolff
Maurice J. Dattelbaum
Samuel Z. Freedman
Frederick A. Wurzbach, Jr.
E. Dean Babbage
John J. Masterson
James M. Blake
Peter J. DiNatale
George J. Lawrence, Jr.
Waring Willis
Gerald D. Dorman
Edward C. Hughes
Alfred P. Ingegno

Raymond S. McKeeby
Harold F. Brown
John C. McClintock
George A. Burgin
Joseph G. Zimring
Frederic W. Holcomb
J. Stanley Kenney
Leo E. Gibson
Thurman B. Givan
Norman S. Moore
Renato J. Azzari

PAST-PRESIDENTS

Orrin Sage Wightman
Chas. Gordon Heyd
Arthur J. Bedell
Herbert H. Bauckus
Louis H. Bauer
Carlton E. Wertz
Edward T. Wentworth
Andrew A. Eggston
James Greenough
Henry I. Fineberg

COMMISSIONER, NEW YORK STATE DEPARTMENT OF HEALTH

Herman E. Hilleboe

DISTRICT DELEGATES

Wilfrid M. Anna
Albert M. Biglan
Arthur F. Gaffney
Maxwell Gosse
Milton J. Greenberg
Norman C. Lyster
Joseph F. Shanaphy
Lee R. Tompkins
Milton Tully

SECTION DELEGATES

Frank J. Borrelli
John J. Clemmer
E. Craig Coats
Royal S. Davis
Michael R. Deddish
Richard A. Downey
James I. Farrell
Henry Fleck
Arthur Gordon
Frederick H. Hesser
Michael J. Jordan
William Hall Lewis, Jr.
Frederick Lee Liebolt
William E. Mosher
Arthur Q. Penta
Norman Plummer
Richard L. Saunders
Henry Siegel
Victor J. Tofany
George M. Trainor
Vernon Weinstein
Richard D. Wiseman

DELEGATES FROM COMPONENT COUNTY SOCIETIES

Albany (4)
H. John Mellen
James A. Moore
Joseph Russo
Francis A. Stephens

Allegany (1)
Irwin Felsen

Bronx (12)
Carl R. Ackerman
Henry J. Barrow
Herbert G. Cohen
Walter Einhorn
Jerome Flynn
Leonard L. Heimoff
George A. Howley
Frank LaGattuta
Samuel Leo
Samuel Lieberman
Thomas F. McCarthy
Samuel Wagreich

Broome (3)
George C. Hamilton
John A. Kalb
Jason K. Moyer

Cattaraugus (1)
Maurice G. Sheldon

Cayuga (1)
Bernard J. Hartnett

Chautauqua (2)
Herbert A. Laughlin
Garra L. Lester

Chemung (2)
William T. Boland
Swen L. Larson

Chenango (1)
Thomas M. Flanagan

Clinton (1)
Edward Siegel

Columbia (1)
Carl G. Whitbeck

Cortland (1)
George Nevin

Delaware (1)
Philip Hust

Dutchess (3)
Robert Barbieri
Irving Cohen
Raymond Koloski

Erie (8)
Antonio F. Bellanca
John C. Brady
Thomas S. Bumbalo
Max Cheplove
Kenneth H. Eckhert
Martin L. Gerstner
Eugene J. Hanavan
John D. Naples

Essex (1)
James E. Glavin

Franklin (1)
Alfred A. Hartmann

Fulton (1)
Arthur Howard

Genesee (1)
Sydney L. McLouth

Greene (1)
Edwin Mulbury

Herkimer (1)
Harold T. Golden

Jefferson (1)
James L. Harrington

Kings (21)
George E. Anderson
Louis Berger
Matthew Brody
Leo S. Drexler
David Farber
John J. Flynn
S. Louis Hornstein
David Kershner
Arthur E. Lamb
Warren A. Lapp
Harry S. Lichtman
Charles H. Loughran
John G. Masterson
Charles F. McCarty
Irving M. Pallin
Louis Pellman
Solomon Schussheim
Abraham D. Segal
Milton B. Spiegel
Vincent J. Tesoriero
Leslie H. Tisdall

Lewis (1)
Earle E. Barnes, Jr.

Livingston (1)
Melville A. Hare

Madison (1)
Felix Ottaviano

Monroe (6)
Hobart L. Boyd
Michael J. Crino
Merle D. Evans
Donovan M. Jenkins
Maurice M. Maltinsky
Charles R. Mathews

Montgomery (1)
Roman R. Violyn

Nassau (8)
Jeff J. Coletti
Ralph S. Emerson
Gerard V. Farinola
Leo T. Flood
Abraham W. Freireich
E. Kenneth Horton
Reginald R. Steen
Paul H. Sullivan

New York (25)
Philip D. Allen
Michael C. Armao
Samuel B. Burk
William A. Cooper
C. Joseph Delaney
James H. Ewing
William W. Field
Carl Goldmark, Jr.
August H. Groeschel
Keith O. Guthrie, Jr.
Milton Helpern
George Himler
W. Graham Knox
Ely Elliott Lazarus
Julia V. Lichtenstein
David Lyall
Ira A. McCown
George W. Melcher, Jr.
Bernard J. Pisani
William B. Rawls
Guy F. Robbins
Adelaide Romaine
Theodore Rosenthal
Mary Spalding
Maus W. Stearns, Jr.

Niagara (3)
Joseph A. D'Errico
Harvey Braden FitzGerald
John T. Donovan, Jr.

Oneida (3)
Irwin Alper
Anthony G. Jarosewicz
John F. Kelley

Onondaga (5)
Richard E. Eberle
Irving Ershler
Robert F. McMahon
William E. Pelow
W. Walter Street

Ontario (2)
Robert Price
Philip M. Standish

Orange (3)
Allen H. Keniston
William S. Montgomery
John D. VanZandt

Orleans (1)
Angelo F. Leone

Oswego (1)
Kent W. Jarvis

Ostego (1)
John Latcher

Putnam (1)
Garrett W. Vink

Queens (13)
Alfred A. Angrist
Sol Axelrad
William Benenson
Monroe M. Broad
Thomas M. d'Angelo
Albert Douglas
Frank W. Farrell
John L. Finnegan

Angelo Bologna
John Edward Lowry
Charles C. Mangi
Louis J. Morse
Kurt Rosenberg

Rensselaer (2)

Allen G. Gifford
John J. Pohl

Richmond (3)

Herbert Berger
Walter T. Heldmann
Edward H. Robitzek

Rockland (3)

James Alva Dingman
George Gordon Knight
Michael P. Lefkowitz

St. Lawrence (1)

William R. Carson

Saratoga (1)

Webster M. Moriarta

Schenectady (3)

Raymond J. Byron
John L. Clowe
Philip Parillo

Schoharie (1)

John H. Wadsworth

Schuyler (1)

Fritz Landsberg

Seneca (1)

Stanley Folts

Steuben (2)

Thomas S. Cotton
Maynard W. Gurnsey

Suffolk (5)

Earl W. Douglas
Charles W. Shlimbaum
Sol Shlimbaum
John L. Sengstack
Jesse W. Mahoney

Sullivan (1)

S. Elisabeth Vuornos

Tioga (1)

John H. Jakes

Tompkins (1)

C. Stewart Wallace

Ulster (2)

Eugene F. Galvin
Edward F. Shea

Warren (1)

Morris Maslon

Washington (1)

Walter S. Bennett

Wayne (1)

Joseph J. Kaufman

Westchester (8)

Charles M. Brane
Arthur H. Diedrick
John N. Dill
Harold J. Dunlap
Robert E. Healy
Thomas C. Jaleski
James M. Jones
Wallace M. Sheridan

Wyoming (1)

Willard J. Chapin

Yates (1)

John A. Hatch

Assistant Secretary Wolff: Is there anybody whose name I have not called who is entitled to vote?

Speaker Wurzbach: Has everyone voted who is entitled to vote?

. . . One so indicated . . .

Speaker Wurzbach: Ladies and gentlemen of the House, Dr. Lester, chairman of the Credentials Committee, states that as of the call of the assistant secretary, 220 ballots have been cast. This makes 221.

Has everybody voted who is entitled to vote?

. . . There was no response . . .

Speaker Wurzbach: 257 are on the list; 221 have balloted on the call of the Assistant Secretary, who has called off 257, which is the membership of the House.

If everyone has voted who is entitled to vote, I therefore declare the ballotting closed and ask the tellers to take the ballots cast to the Cornell Room, where the ballots will be counted, and to return as quickly as possible to the House of Delegates.

The ballot box has been removed, and the tellers have left the room. I will now call on Alfred A. Angrist, M.D., to present his report for the Special Committee on Prize Essays.

Section 186 (see 29)

Report of Special Committee on Prize Essays

Alfred A. Angrist, M.D., *Queens:* Mr. Speaker and members of the House of Delegates, the Special Committee on Prize Essays had a total of four essays submitted for the two prizes. The unanimous opinion of the committee is as follows for the essays submitted:

For the Merit H. Cash Prize: "The Use and Value of Extension in Volkmann's Ischemic Contracture" by Joseph K. Surls, M.D., 218 East 72nd Street, New York City.

For the Lucien Howe Prize: "Radiation Cataractogenesis" by Sidney Lerman, M.D., of the University of Rochester, Strong Memorial Hospital.

The committee was also requested to select the winner of the newly established Albion O. Bernstein, M.D., Award and to obtain the necessary information for making such a decision. From the names of candidates submitted the committee chose James O. Elam, M.D., of Roswell Park Memorial Institute, 666 Elm Street, Buffalo, New York, for his work in promoting the mouth-to-mouth method of resuscitation and his experimental demonstration of the proper head-tilt airway maintenance for effective respiration exchange by means of cinefluorography.

It was the unanimous opinion of the committee that this first Albion O. Bernstein, M.D., Award should go initially to an individual who has made such a definite dramatic clinical contribution of this kind. This award was presented at the opening session of the House of Delegates, Monday morning, May 14.

I do want to thank David Kimball Miller, M.D., of Erie, and Benjamin G. Dinen, M.D., of Westchester, for their assistance and cooperation in what must have been a time-consuming task on many occasions.

Speaker Wurzbach: Thank you, Dr. Angrist.

Section 187

Election of Life Members

Speaker Wurzbach: Gentlemen, there is the election of life members. There is a considerable list printed in your Handbook. However, there is an additional list which I will ask the secretary to read at this time.

Secretary Wheeler: The secretary would like to move the election to life membership of those whose names are printed in the Handbook, with the exception of Philip B. Becker, M.D., of New Rochelle, New York, who unfortunately died after his name was printed in the life membership list.

In addition, there is the supplementary list for election to life membership. Mr. Speaker, I move the election of those on the printed and on the added list to life membership.

. . . The motion was seconded, and as there was no discussion, it was put to a vote and was unanimously carried, the complete list referred to being as follows:

Charles W. Aitcheson, Yonkers
M. Leon Andrzejewski, Colden
Milton Aronowitz, Albany
Marion William Astarita, New York City
Charles Auer, New York City
James Woods Babcock, New York City
John Harry Bailey, Brooklyn
Percival Dee Bailey, Norwich*
Artashes B. Balayan, Forest Hills
Morgan Otto Barrett, Albany
William Price Bartels, Hempstead
Alfred Kelley Bates, Delray Beach, Florida*
Louis Hopewell Bauer, Rockville Centre
Samuel Dennis Bell, New York City
Arthur Jerome Bendick, New York City
Archibald K. Benedict, Sherburne
C. Albertson Bennett, Yonkers
William Berkowitz, New York City
Joseph Berte, Brooklyn
Joseph Zachary Biegeleisen, Jamaica
Samuel Ernest Bilik, New Rochelle
Henri H. Birnbaum, New York City
Joseph Blinder, Brooklyn
Flora Boenheim, New York City
Maxwell M. Booxbaum, Bronxville
Charles Frederick Bove, Patchogue
Leopold Brahdy, New York City
Walter James Bolt Brown, Lewiston
Ernst Ludwig Brunell, Jackson Heights
Harry Dominic Bucalo, Sayville
L. Agnes Buck, Syracuse
William Fowler Burke, Buffalo
Aaron Burman, Syracuse*
Frank G. Calder, Johnstown
Salvatore Caliva, Syracuse
Eugene Calvelli, Port Washington
Benjamin E. Carmel, Brooklyn
Frederick Carpenter, Corona
John Casagrande, Brooklyn
Isaac Chassin, Maspeth
Hugh S. Chidester, Saugerties
Louis Cohen, Newburgh
Samuel Colliss, Brooklyn*
Smith A. Combes, Hempstead
Carl Rodney Comstock, Saratoga Springs
John Edward Conboy, Bronx
Lawrence Henry Cotter, New York City
Max Philip Cowett, New York City
Francis R. Coyle, Buffalo
Clifford Alexander Crispell, Poughkeepsie
Frank Ephraim Cross, New York City
Isaac Dall, Long Island City
LeGrand Augustus Damon, Conesus
John Horton Daniels, New York City
Cornelius A. Dennehy, White Plains
Rudolph Dery, Rockville Centre
George Deylen, Brooklyn
William Brown Doherty, Saratoga Springs
Gertrude Davies Doyle, Newfane
Stanley B. Doyle, Brooklyn*
Dwight Guilford Dudley, Endicott*
Ernest T. Duschak, New York City
Lowell Brown Eckerson, Brooklyn
Ammi Ballinger Edgar, Glendale
Ellis H. Edwards, White Plains
Andrew A. Eggston, Mount Vernon
Lawrence W. Ehegartner, Syracuse
Carl William Ehrenstein, Rochester
Frederick Estabrook Elliott, Brooklyn*
Henry Edward Elwood, Jr., Corning
Irving Epstein, Valley Stream
Mihran H. Exerjian, Astoria
Charles L. Farabaugh, Newburgh
Waldo Beattie Farnum, New York City
Raymond Durston Fear, Poughkeepsie
Botho F. Felden, New York City
Raymond E. Fenner, Syracuse
William Samuel Fink, Brooklyn*
Charles Frank Fisher, Brooklyn
Louis Fisher, Brooklyn
Tracy Lyman Fisk, Bronx
Paul Charles Fleri, Brooklyn
Adolph Foti, New York City
Kate Frankenthal, New York City
Frank Meyer Frankfeldt, Bronx
Frederick C. Freed, New York City
Mary Friedman, New York City
William Friedman, New York City
Alfred Fritsch, New York City
Nicholas Furedi, Yonkers
Raymond J. Gaffney, New York City
Jacob Geiger, New York City
Joseph Francis Gennaro, Brooklyn*
Arthur Glaser, New York City
Joseph S. Glickman, New York City
Arthur Clair Glover, Horseheads
Herman D. Godwin, New York City
Jacob Gold, Belle Harbor
Martin M. Goldbach, New York City
Harry Goldberg, Brooklyn
Charles Goldman, Brooklyn
Frederick Warren Goodrich, Catskill
Julius Gottesman, New York City
Don Ulinn Gould, Sherburne
Eric S. Green, Rush
Leon Willis Green, Brooklyn
Louis Greenberg, Brooklyn*
Marius B. Greene, Flushing
Bruno L. Griesman, New York City
Meyer Grollman, Brooklyn
Samuel Gross, New York City
Vincenzo Grossi, New York City
Chauncey W. Grove, Geneva
Maurycy Grynbaum, New York City
Philip Conrad Hacker, Albany*
Lee A. Hadley, Syracuse
John Edward Hanawalt, Seaford
Ken G. Hancher, Pelham
Hanford Kendall Hardy, Rushford
Helen Harrington, New York City
Bruce Alexander Harris, Pipersville, Pennsylvania
John Joseph Hauff, Brooklyn
Ewald Anthony Hawel, Millbrook
Erich B. Hecht, Jackson Heights
Siegfried Hein, Binghamton
Robert W. Helm, Ossining
Joseph P. Henry, Rochester
Victor G. Hentz, New York City
Fred Henry Herlitz, Syosset
George Hirschfeld, Baldwin
Axel M. Hjort, Fort Lauderdale, Florida*
Arthur Edmund Hoag, New York City
Morris Hoffman, Bayside Hills
Willy Hofmann, New York City
Joseph C. Horan, New York City
George Ralph Horton, Brooklyn
Yolande H. Huber, New York City
Carl Francis Hugger, New York City
Allen Hull, Brooklyn
S. Ingram Hyrkin, Brooklyn
William Hadden Irish, New York City
Claude Smith Johnson, Clinton

* Retroactive to May 10, 1961.

Samuel Chester Johnson, King Ferry
Daniel Jung, Snyder
Julius Theodore Kane, Lake Placid
Carl Kaplan, Huntington*
Murray E. Keisman, New York City
John Joseph Kilcourse, Long Island City
Morris Kimberg, Bronx
Joseph C. Klauber, Staten Island
Ludwig S. Kleeberg, New York City
George Kornfeld, Brooklyn
Abraham Kosseff, Beacon
Benjamin Kramer, Brooklyn
Arthur Krida, New York City
Max Krieger, Elmhurst
Harry A. Kurland, Mamaroneck
Ernst Lang, Jamaica
Franz J. Langendorff, Forest Hills
Herbert Leonard Langer, Arverne
Edwin George Langrock, New York City
August Lascola, Buffalo
William Leavitt, Brooklyn
Rudolph George Lederer, Lake George
Martin B. Lehnen, Rochester
Maurice Lenz, New York City
Robert Lenz, New York City
John Jacob Levbarg, Flushing
Manoh Levieff, New York City
Bella Naumovna S. Levin, Brooklyn
Solomon Levine, Brooklyn
Bertram S. Levinson, Syracuse
Morris L. Levy, Brooklyn
Glendon Richard Lewis, DeWitt
David H. Lothringer, Fresh Meadows
Hugo Lott, Binghamton
Nils Oscar Lundell, Far Rockaway
Charles T. Lunsford, Rochester
G. Creighton Lusk, Newark Valley
Michael Joseph Lynch, Bronx
Marcus M. Maier, Hempstead
Jacques W. Maliniac, Yorktown Heights
William M. Mallia, Kennebunkport, Maine
Louis Mamelok, Brooklyn
Andor Mandel, New York City
Victor Mandler, Bellmore
Thomas F. Manley, Norwich*
Joseph Anthony Manzella, Brooklyn*
Isidore Margaretten, New York City
Searle Bisset Marlow, Syracuse
Samuel Mausner, New York City
Walter Ambrose McCoy, Bronx
Frederick Francis McGauley, Schenectady
Monroe A. McIver, Cooperstown*
William Francis McKenna, Ogdensburg
Harold William McNitt, Binghamton*
Gaetano Joseph Mecca, New York City
Jacob Meisel, Brooklyn
Maurice Meltzer, New York City
Max Mensch, Brooklyn*
Albert Nathan Meyerstein, Farmingdale
Arthur H. Milbert, Yonkers
Samuel W. Mills, Sr., Middletown
Svetozar Moacanin, New York City
Jakob Mohr, New York City
Emil Mosbacher, Kew Gardens
Lester Moskowitz, New York City
Eric Peter Mosse, New York City
Hanna Mulier, New York City
Peter Marshall Murray, New York City
Arthur I. Neuberg, Spring Valley
Babette Neuberg, Spring Valley
Siegfried Neuberger, Brooklyn
Lewis Alfred Newfield, Queens Village
Morris Head Newton, Little Falls
Carroll Leja Nichols, Brooklyn
Walter John Norris, Corona
Arthur J. O'Connor, Scarborough
Richard Offenbacher, Brooklyn
George Guttman Ornstein, New York City
Hyman A. Osserman, New York City
William Ostrow, Brooklyn
Ethelbert Gutherie Padgham, Geneva
Samuel Parnass, Brooklyn
Harry D. Pasachoff, Bronx
Harold P. Peckham, Waterford
Charles Anthony Perilli, New York City
Ralph E. Perry, Lynbrook
Frederick H. Petters, Buffalo
Ralph Baker Post, Ballston Spa
Paul Georg Prausnitz, Forest Hills
Douglas A. Quick, New York City
Moses B. Radding, Elizabeth, New Jersey
Boris M. Raskin, Brooklyn
Waldemar Reichmann, New York City
Henry Barber Richardson, New York City
Charles Rieger, Staten Island
Ernest M. G. Rieger, Niagara Falls
Joseph G. Rivkin, Miami Beach, Florida
Meyer Seymour Robinson, Brooklyn
Arthur Grant Rodgers, Jr., Syracuse
Leopold Rosanes, New York City
Philip Rosenberg, Syracuse
Gustave Rosenburg, Forest Hills
Bruno Rosenhain, Forest Hills
Gertrude H. Rosenhain, Jackson Heights
Leopold Rothschild, New York City
Max Ira Roven, New York City
Leo James Rozan, Niagara Falls
Herman Harold Rubin, New York City
Foster Coleman Rulison, Syracuse
Paul William Sack, Jamaica
Warren Edward Saile, Syracuse
Lajos L. Samets, Massena
Theodore Michael Sanders, New York City
Bertram Julian Sanger, New York City
Aaron I. Saper, Brooklyn*
Edward Schall, Richmond Hill
Richard David Schindler, New York City
Walter Arthur Schmitz, Middletown
Hermand Bernard Schoenberg, New York City
James I. Schoonmaker, Woodhaven
Joseph C. Schreiner, Flushing
Karl Schutz, Woodstock
Peter J. Sciarrino, Niagara Falls
Winfield W. Scott, Rochester
Marcus Fowler Searle, Brooklyn
Leopold Seidenberg, Forest Hills
Royal F. Sengstack, Suffern
Cypra Shulman, Bronx
Byron G. Shults, Herkimer
Clare Nelson Shumway, Painted Post
John Smith, Jr., New York City*
Windsor Robert Smith, Binghamton*
Ramsay Spillman, Scarsdale
Leo Spira, Elmhurst
Frederick Duane Squire, Stony Brook*
Charles Daniel Squires, Binghamton
Roland Leighton Stacy, Ogdensburg
Henry Edward Stadlinger, Buffalo
Edward Stebbins, Lewiston
George Stein, Larchmont
Reuben Steinholz, New York City
Harry Eldredge Stevens, Southold
Ursula G. Stewart, Massapequa
Raymond P. Sullivan, New York City
Daniel Joseph Swan, Flushing
Frank Tannenbaum, Bronx
Robert Willis Tate, Brooklyn
Clifford E. Terry, Brooklyn

Philip Tiktinsky, Bronx
Robert M. Toll, New York City
Bruno Tyson, New York City
Jacob Urdang, Brooklyn*
Hobart Sanford Van Nostrand, Little Neck
Samuel Varco, Buffalo
Joseph L. Watnick, New York City
Frederick B. Weil, Jackson Heights
Aaron Weinberg, New York City
Tobias Bernard Weinberg, New York City
Max Weisenbeck, Onondaga Hill
Samuel Frederick Weitzner, Bronx
May Georgiana Wilson, New York City
Joseph Wrana, Amityville
Isadore Zadek, New Rochelle*

Section 188

Resolutions of Thanks

Speaker Wurzbach: There are some business details which we would ask to continue.

The chair recognizes J. Stanley Kenney, M.D.

J. Stanley Kenney, M.D., *Trustee:* Mr. Speaker, ladies and gentlemen of the House, we are about to conclude what has been one of the most successful conventions that we have held, and it would have been impossible except for the efforts of a great many people. I would like to take this opportunity to thank the general convention chairman, Bernard Pisani, M.D., and all of the members of his committee for the very fine job they have done.

Speaker Wurzbach: I don't think we need to go through the formality of voting on these motions unless you wish.

James Greenough, M.D., *Past-President:* Members of the House, I move thanks to the chairman and the members of the Scientific Program Subcommittee for the splendid work that they have done, the chairman being Alfred P. Ingegno, M.D.

Peter J. DiNatale, M.D., *Councillor:* Mr. Speaker and members of the House, on behalf of the Medical Society of the State of New York, we wish to thank Miss Doris K. Dougherty, Miss Alvina Rich Lewis, Miss Mollie Pesikoff, Mr. George P. Farrell, Mr. George Forrest, Robert Katz, M.D., Miss Mary Singer, Miss Camille Marra, Miss Alice Wheeler, Miss Susan V. Baker, Mr. William Bonzer, Mr. Charles Struzinski, Mr. Eugene Dombrowski, and all others of the staff who have worked to make this convention the success that it is.

Gerald D. Dorman, M.D., *Councillor:* I would like to mention specifically the members of the staff who worked so hard under our executive vice-president, an indefatigable morale booster, Henry I. Fineberg, M.D.

I would like also to commend our convention manager, Mr. Charles L. Baldwin; our comptroller, Mr. Thomas E. Alexander, who keeps us on the budget as much as he can under a good deal of pressure; and the Department of Communications, under Mr. John Pardee, and his assistants in the department.

To all of these I move a vote of thanks and appreciation.

James I. Farrell, M.D., *Section Delegate:* Mr. Speaker, may I on behalf of this House of Delegates extend our very sincere thanks to the management and staff of this hotel for the excellent arrangements and cooperation extended, and a special vote of thanks to Mr. Joseph Sesata.

Frederic W. Holcomb, M.D., *Trustee:* Mr. Speaker, I would like this House of Delegates to extend a vote of thanks and appreciation to the members of the Scientific Motion Picture Subcommittee, William J. Sullivan, M.D., and members of his committee for their very excellent work.

Carlton E. Wertz, M.D., *Past-President:* Mr. Speaker and members of the House, I would like to have a vote of thanks of this House extended to the Subcommittee on Guest Reception and its chairman, Sol Axelrad, M.D.

Dr. Kenney: In all of these encomiums of praise, two of the most important people in the House have not been mentioned, and I would like to have a very strong vote of thanks for the fine way the speaker of the House and his assistant, Dr. Babbage, have conducted this meeting.

Speaker Wurzbach: On behalf of Dr. Babbage and myself, it has been a lot of fun. We have had a good time. You have been most cooperative, and we thank you for this expression of your interest.

Vice-Speaker Babbage: I want to thank all of you too. I know all of you realize this was my first try at it, and you have been most cooperative. It did get a little bit rugged a couple of times yesterday afternoon, but on the whole I think we did all right.

Leo E. Gibson, M.D., *Trustee:* Mr. Speaker and members of the House, I would like to move a vote of thanks to the Subcommittee on Technical Exhibits, and especially William A. Rawls, M.D., its chairman.

Arthur J. Bedell, M.D., *Past-President:* I move a vote of thanks to all those who have been forgotten and not specifically mentioned.

Speaker Wurzbach: Dr. Bedell, your consideration is as it always was.

Dr. DiNatale: Mr. Speaker, I would like to move a vote of thanks to the Dinner chairman, Samuel Wagreich, M.D., and his committee.

Speaker Wurzbach: We are waiting for the statement on the scientific exhibits awards. At that time Thurman B. Givan, M.D., will make the report. We are not yet ready with it because the committee has not given its final statement as to the winners of the scientific exhibits awards.

With over 40 members of the House out as tellers it would not be proper to go ahead with the business of the House. There remains one reference committee report, that on legislation and legal matters, to be presented by Milton Helpern, M.D. However, we cannot do that at this time until the tellers report.

Secretary Wheeler: Mr. Speaker and members of the House, I would like a vote of thanks to be given to our excellent and long suffering stenotypist, Mrs. Augusta Grimm.

John F. Kelley, M.D., *Oneida:* Mr. Speaker and members of the House of Delegates, I asked for the floor for one reason. This year I thought we had the best reference committee chairmen I have ever seen in all of the years I have been in the House of Delegates. They did a wonderful job. Everybody had the privilege of going to the reference committee meetings and stating their views and were given every consideration. After the reference committee makes its report, it is taken apart completely, and put together again, and then when it comes to the floor of the House, it is discussed all over again. I talked to a young delegate last night, who has been here five times, and who said he is not going to come back because there is a lot of unnecessary talk that is a waste of time.

There is a rule on the books that says we have the privilege of speaking once on any subject for a period, I think, of five minutes. I believe that rule should be adhered to. Thank you very much!

Speaker Wurzbach: As speaker, I will take that under very serious advisement.

Section 189

The General Practitioner

Charles C. Mangi, M.D., *Queens:* Mr. Speaker and gentlemen, with your kind permission I would like to insert into the record the president's page of one of our county medical society bulletins.

Speaker Wurzbach: Name it.

Dr. Mangi: The *Bulletin of the Medical Society of the County of Kings*, April, 1962, issue. So that nothing will be quoted out of context the entire page will be read:

> There seems to be little doubt that the prestige of the medical profession, in recent years, has become lessened considerably in the eyes of the general public. This is due in part to the ascendancy of the "space age scientist" who has caught the interest and aroused the imagination of our gifted youth. Medical school statistics reveal that the top students are not applying for admission at the same high rate as in past years. This challenge is a healthy one and can be met only by a resurgence of the high ideals and ethics of the private practitioner of medicine.
>
> However, there also seems to be little doubt that the major reason for our damaged prestige is the fault of the medical profession itself. The popular concept of "the doctor" today is the cigar-smoking specialist riding in his limousine en route to the golf course, a member of the so-called "wealthy and privileged class," totally indifferent to the responsibilities of his profession and the welfare of his patients. Perhaps the prototype of this image exists. Thank God, I have never met him. It has been my experience that the average doctor is devoted to the interests of his patient and ready to meet his responsibilities to him. Nevertheless there are many ways in which we have permitted the dignity of our profession to suffer. First and foremost, we have allowed the status of the general practitioner to be sullied. This is the fault of medical schools, hospitals, and specialty groups alike, who have consistently and constantly downgraded the doctor in the general practice of medicine. The fact is that the general practitioner is the backbone of medicine and that it was he, with his intimate knowledge of his patients' ills and background, as well as his unstinting devotion to their needs, who raised the profession of medicine to the shining heights it once enjoyed. Let the medical schools encourage their students to become general practitoners, let the hospitals welcome and permit this group to participate in the care of their patients to the extent of their capabilities; and let the specialty groups recognize the fact that the general practitioner forms the shock troops of medicine and that their sharing in patient care is for the benefit of all concerned.
>
> When we have restored the general practitioner—the family doctor—to his rightful place of honor, then we will have gone a long way to regain the lustre of our noble profession which is now dimmed.

I am very proud of the fact that the man who wrote this, Leslie H. Tisdall, M.D., of Kings County, is a classmate of mine.

Speaker Wurzbach: You made a motion, sir, that this be included in the proceedings of this House?

Dr. Mangi: I so move that this be included in the proceedings of the House.

Royal S. Davis, M.D., *Section Delegate:* I second it.

Speaker Wurzbach: Is there any discussion?

Arthur J. Bedell, M.D., *Past-President:* Mr. Speaker, this is an innovation. I think it very unwise to publish such a thing as part of our transactions, and I do so because the laity do not read carefully. They will translate many portions of this, take excerpts from it, and instead of adding to the prestige of the profession, it will pull it down.

While we have not anything better to do, just listen: In 1844 the Medical Society of the State of New York met in Albany and at that time they proposed that there should be a national medical association. The president at that time started off with the statement that the profession of medicine has dropped from its high pedestal of regard. Of course it is a little more than one hundred years ago, and we get the same reverberations that don't mean a thing.

I sincerely trust you do not put this in nor allow any outside extraneous thing of this type to appear in our transactions. This is a deliberative body, not to receive outside things. Had it been presented as a resolution to have been referred for thought, that would be one thing, but certainly not this. I trust you will not. It will add to the increased cost of our publications.

Speaker Wurzbach: Is there any further discussion? The motion before the House is that this be included in the proceedings of this

House. All in favor say "aye," opposed "no." It is so ordered.

Dr. Givan, are you ready with your report?

Section 190

Report of Scientific Exhibits Awards Subcommittee

THURMAN B. GIVAN, M.D., *Trustee:* Mr. Speaker and members of the House, your Scientific Exhibits Awards Subcommittee went over in detail all of the scientific exhibits. There are a great many that were very, very good this year. We divided the awards into two categories, those of clinical research and those of scientific research:

CLINICAL RESEARCH

First Award. "Physical Signs of Chest Disease: 15 New or Neglected Signs," Coleman B. Rabin, M.D., and Alvin S. Teirstein, M.D., The Mount Sinai Hospital, New York City.

Second Award. "Bleeding Peptic Ulcer and Heart Disease," William J. Grace, M.D., and William F. Mitty, Jr., M.D., New York University School of Medicine, New York City.

Honorable Mention. "Mammography, An Examination of Technics," Robert S. Sherman, M.D., Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases, and Cornell University Medical College, New York City.

SCIENTIFIC RESEARCH

First Award. "The Radioactive (I^{131}-Tagged) Rose Bengal Hepatoscan," Frieda Feldman, M.D., Sidney Rubenfeld, M.D., and Carl Collica, B.S., New York University School of Medicine, New York City.

Second Award. "Visualization and Perfusion of Bronchial Arteries: Application in the Treatment of Lung Carcinoma," D. Raj Mahajan, M.D., Eugene E. Cliffton, M.D., and William L. Watson, M.D., Sloan-Kettering Institute, Memorial Hospital for Cancer and Allied Diseases, New York City.

Honorable Mention. "The Use of Radioactive Phosphorus (P^{32}) in the Diagnosis of Ocular Tumors," Bernard Goldberg, M.D., Gerald B. Kara, M.D., and David Tabowitz, A.B., New York Eye and Ear Infirmary, New York City.

I wish to thank the Scientific Exhibits Subcommittee headed by William Watson, M.D. They did a wonderful job. Thank you!

SPEAKER WURZBACH: It would be manifestly unfair to continue with the reference committee report with 40 members of the House absent. The speaker will declare a recess until the tellers are ready to report. Please do not go too far so that the House can convene promptly.

. . . Recess . . .

SPEAKER WURZBACH: Will the House come to order? Now, we will have the report of the tellers.

Section 191

Report of Tellers

GARRA L. LESTER, M.D., *Chautauqua:* Mr. Speaker, I would like to announce the election results:

For Councillor

George J. Lawrence, Jr.	201
James M. Blake	195
Charles M. Brane	160
William T. Boland	155
Samuel Wagreich	76
Peter J. DiNatale	65

For Delegates to the A.M.A.

Henry I. Fineberg	210
Joseph A. Lane	200
Frederick A. Wurzbach, Jr.	192
John M. Galbraith	187
William L. Wheeler, Jr.	185
Carlton E. Wertz	176
Waring Willis	174
Thurman B. Givan	173
John F. Kelley	160
Philip D. Allen	155
John C. McClintock	127
Carl Goldmark, Jr.	118
Ezra A. Wolff	62
Peter J. DiNatale	52
Ralph S. Emerson	52
Irving M. Pallin	41
Harold F. Brown	39
William T. Boland	38
Alfred P. Ingegno	34
Charles R. Mathews	32
Merle D. Evans	28
Irving L. Ershler	17
John L. Clowe	16

SPEAKER WURZBACH: Will you read out the top 12 names?

DR. LESTER: The first 12 are Drs. Fineberg, Lane, Wurzbach, Galbraith, Wheeler, Wertz, Willis, Givan, Kelley, Allen, McClintock, and Goldmark.

SPEAKER WURZBACH: These are the top 12 and will be the delegates to the A.M.A.; the balance of the list, which is at the present time 11, will be the alternate delegates.

Will you read the top four on the councillors?

DR. LESTER: The top four on the Council are Drs. Lawrence, Blake, Brane, and Boland.

SPEAKER WURZBACH: These four have been elected for councillors for the next three years.

All other officers, of course, were elected previously.

I therefore announce at this time that these gentlemen have been elected respectively as councillors and as delegates and as alternate delegates to the A.M.A.

All of the uncontested places on the list I now declare elected as officers of this Society.

May I ask John J. Masterson, M.D., to bring forward our new president, Joseph A. Lane, M.D.

. . . The audience arose and applauded . . .

Section 192

Address of Incoming President

INCOMING PRESIDENT LANE: Mr. Speaker

and members of the House of Delegates, again I wish to thank you for letting me be your representative in the State Society. I have only one or two short comments to make, one that I was going to make yesterday when there was a little discussion about the finances of the Society.

You have been generous enough to vote an increase in dues, which is extremely necessary. I assure you that with the help of the Budget Committee, the Board of Trustees, and Dr. Fineberg everything will be done to conserve your monies and that nothing will be spent foolishly.

I am looking forward to a busy, interesting year, and with your cooperation I am sure we will be able to accomplish many of our purposes. I thank you very much. (*Applause*)

Speaker Wurzbach: We now consider it a great pleasure to take by the arm our newly elected president-elect and go with him over to the "mike."

Section 193

Address of Incoming President-Elect

Incoming President-Elect Wheeler: Mr. Speaker, ladies and gentlemen of the House, I cannot tell you how honored and humble I am at this wonderful appointment which you have so generously given to me. I just hope that I will be able in some measure to follow in the footsteps of my illustrious predecessors. Thank you very much! (*Applause*)

Speaker Wurzbach: Now, gentlemen, there remains one order of business before the House, which is the report of the Reference Committee on Legislation and Legal Matters, Milton Helpern, M.D., chairman.

Reference Committee on Legislation and Legal Matters

Section 194

Report of Reference Committee on Legislation and Legal Matters: Malpractice Insurance and Defense Board

Milton Helpern, M.D., *New York:* Mr. Speaker, ladies and gentlemen of the House, your reference committee wishes to report on the following:

The first report considered by your reference committee was that of the Malpractice Insurance and Defense Board. This report states that there have been no developments in connection with malpractice that were especially noteworthy or alarming. The upward trend in new malpractice cases which had continued during 1960 almost leveled off in 1961 on a curve which for fifteen years had risen persistently, although irregularly. It was pointed out that although there was an increase of nearly 8 per cent in the number of new cases reported in 1961 as compared to 1960, this to a large extent was associated with an increase of about 6 per cent in the number of insured members.

Although the report of the actuarial consultant would justify a modest rate increase on the basis of loss experience, the insurance company has agreed to postpone any change in the present rate schedule pending the results of efforts being made to improve the loss experience.

A claim prevention program is being initiated as a result of conferences between company representatives and the indemnity representative. The program will include the dissemination to specialists of recommended measures particularly applicable to them.

The report includes a detailed discussion of expanded coverage, and there was wise discussion on limits of coverage. Recommended minimum limits for the nonsurgical and surgical and anesthetic practices were given, and it was pointed out that double the minimum limits in each category at the present time are not to be considered excessive. The larger amounts indicated in the report are also available.

It is the opinion of your reference committee that the Malpractice Insurance and Defense Board, working together with legal counsel of the State Society, are doing everything they can to keep loss experience down and recommend and make available adequate coverage to the members. The Malpractice Insurance and Defense Board, in the opinion of your committee, is performing an excellent service to this Society and in a most efficient and understanding manner.

I move adoption of this portion of the report.

George Himler, M.D., *New York:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 195

Report of Reference Committee on Legislation and Legal Matters: Autopsy and the Dead Human Body

Dr. Helpern: The second item to be considered is the report of the Subcommittee on Autopsy and the Dead Human Body. This report was reviewed by your committee and includes information about the developments in the *Brown* v. *Broome County* case and the reversal of the Binghamton decision by the Court of Appeals. This reversal again pointed out the inadequacy of the then existent statute pertaining to the authority of the coroner which prevented him from performing an autopsy in a coroner's case in which he did not have reason to believe that death had resulted by homicidal or suicidal violence, without permission of the next of kin. This suit against the coroner for the performance of an autopsy in a case within his jurisdiction was one of the reasons for the Law Revision

Commission's undertaking a study, out of which came recommendations for new legislation to provide for the establishment of medical examiner's systems in those counties desirous of abolishing the office of coroner and the appointment of qualified doctors of medicine to assist the coroner in those counties in which the coroner was a layman. Legislation accomplishing these aims was passed by both Houses and signed by the Governor and is now Chapter 897 of the county laws.

The legal shortcomings which have to do with this subject are evident in the resolutions introduced by the able and diligent chairman, Alfred A. Angrist, M.D.

I move the adoption of this portion of the report.

MILTON B. SPIEGEL, M.D., *Kings:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 196

Report of Reference Committee on Legislation and Legal Matters: Judicial Council

DR. HELPERN: Your reference committee notes from the report of the Judicial Council that an organization meeting was held on May 10, 1961, and that the Council reports that no appeals were presented during the year.

I move the adoption of this portion of the report.

HAROLD T. GOLDEN, M.D., *Herkimer:* I second it.

Section 197 (see 17, 215)

Report of Reference Committee on Legislation and Legal Matters: Legislation

DR. HELPERN: Your reference committee has reviewed the excellent report of the 1961 fall meeting of the Committee on Legislation covering many resolutions submitted to it by the 1961 House of Delegates, and action taken on these and other resolutions is supported. In its supplementary report there is a summary of legislative action taken by the 1962 session of the New York State Legislature.

It was the intention of the Legislation Committee that it would continue the alerting of various county societies of legislative activities through the medium of "Capitol News." It was anticipated that with greater regularity in the publication and distribution of the newsletter, this program of keeping county societies informed would be more effective. Meanwhile, much of the communication to the county societies was through personal contact and communication.

The chairman of the Legislation Committee, James M. Blake, M.D., pointed out that the legislators have commented that the medical profession, if it is to be effective in regard to medical legislation, must assume the responsibility of meeting their representatives on a local level.

In the supplementary report of the Committee on Legislation, it is pointed out that an unusually large number of bills pertaining to medical practice were introduced, but that many were poorly drawn and considered bad legislation and given little consideration by committees and members of the Legislature. A summary of all legislative action and that of the Governor on various bills in which the Legislation Committee was active during the session was reviewed by your reference committee.

The reference committee agreed with the recommendation of the Legislation Committee that designated defeated bills should be introduced again or reintroduced at future sessions of the Legislature.

A bill to amend the Education Law, in relation to exemption from liability of physicians and surgeons rendering gratuitous emergency treatment, was passed by both Houses but vetoed by the Governor, who filed a memorandum with his veto. Your reference committee, in seeking information for the need for such a law, was unable to learn of any case in which a physician or surgeon acting in good faith had been found liable for rendering such treatment. Since there does not appear to be any problem in this connection in this State, your committee recommends that no further action be taken on this bill at this time.

Your reference committee again notes that resolutions directed at securing a lien law for physicians have been introduced regularly in the House of Delegates for the past few years. In last year's report to the House of Delegates by the Reference Committee on Legislation and Legal Matters, it was pointed out that at least one factor in the opposition to a lien law was the lack of an acceptable fee structure and that there are other problems involved in the passage of such a law. Last year's reference committee and this one are of the opinion that carefully documented information on objections to this law is necessary if such a law is to be passed. In this connection, a meeting of the Joint Committee of the Medical Society of the State of New York and the State Bar Association will be held in September, 1962.

An act to amend the real property law, in relation to exemption from taxation of real property owned by medical societies, and repealing Section 470 of such law relating thereto passed both houses of the Legislature. The bill was vetoed by the Governor at the request of the City of New York. His veto was accompanied by a memorandum, and in view of its content, your reference committee does not recommend reintroduction of this bill at this time.

An act to amend the personal property law, in relation to the ownership of prints of x-ray plates taken by physicians and hospitals, passed both houses of the Legislature. It was opposed by the New York State Health Department, the

Association of Hospitals, and others and vetoed by the Governor with a veto memorandum. Your reference committee recommends that if this bill is reintroduced, it again be opposed by the Society.

An act to amend the public health law, in relation to prohibiting discrimination in hospital staff appointments and privileges, was strongly supported by the Medical Society and the State Health Department and passed the Assembly but was killed in the Senate committee.

An act to amend the civil practice act, in relation to time for commencement of action to recover damages for malpractice, was introduced on the recommendation of the Law Revision Commission, and your Committee on Legislation vigorously opposed its passage. The bill was killed in the Assembly rules committee.

Last year the reference committee made a recommendation in which was pointed out the importance of accurately defining and enforcing the scope of permissible activity of paramedical groups. It also called attention to the fact that the problem of limits of therapy presently permitted to these groups was a matter of interpretation by the State Department of Education based on an outmoded Medical Practice Act. It was considered important that this act be brought up to date. The resolution was introduced at this past session of the Legislature without success. It was considered encouraging that more interest was being shown in this problem and that it might be possible next year to seek a more definitive and stronger resolution. Your reference committee this year reaffirms this opinion.

Your reference committee acknowledges with appreciation the enormous task which the Legislation Committee has carried out under the able and dedicated leadership of James M. Blake, M.D.

I move the adoption of this portion of the report.

JOSEPH A. D'ERRICO, M.D., *Niagara:* I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 198 (*see 18, 216*)

Report of Reference Committee on Legislation and Legal Matters: Committee to Combat Cults

DR. HELPERN: The interesting initial and supplementary reports of the Council Committee to Combat Cults and the account of the activities of the chiropractors in their repeated, unsuccessful attempts to have legislation passed for licensure and the copy of the opinion of the Appellate Division of the New York State Supreme Court in the case of the Chiropractic Association of New York, Inc., against Herman E. Hilleboe, M.D., State Commissioner of Health, affirming the original verdict in his favor, provide instructive information on the continuing hazard which the cult of chiropractic poses to the public.

Your reference committee deplores the increasing activity and pressure for licensure on the part of the chiropractors which this year was expressed in a most intensive campaign with considerable misinformation given out by legislators to the effect that licensure of chiropractors was acceptable to the medical profession, a statement promptly and actively refuted by the Medical Society.

I move adoption of this portion of the report.

DR. HIMLER: I second the motion.

SPEAKER WURZBACH: Is there any discussion?

JOSEPH G. ZIMRING, M.D., *Councillor:* I thought that the committee would take an opportunity now to give the House of Delegates a recommendation of more definitive action on the chiropractic law and its organization.

SPEAKER WURZBACH: Is there any further discussion?

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 199 (*see 19*)

Report of Reference Committee on Legislation and Legal Matters: Federal Legislation

DR. HELPERN: The report of the Subcommittee on Federal Legislation was reviewed by your reference committee. In its detailed account it reflects the active work which this subcommittee carried out during the year in its "Operation Counterattack" program. A very intensive campaign was conducted among the officers and chairmen of county society legislation committees, utilizing the Communications Department of the State Society. A large majority of the 43 congressmen in the State of New York were contacted by local county medical societies. The purpose of the over-all program was to oppose HR 4222 (King-Anderson Bill).

On recommendation of the Subcommittee on Federal Legislation to the Council, a special session of the House of Delegates was called, which reiterated the Society's opposition to HR 4222. This session was held February 10 in New York City and was well attended. Four major resolutions of crucial concern to the public of this State were adopted.

There is a detailed description of the visit to Washington by the delegation of the State Society. The subcommittee felt that a great deal was accomplished in these visits and conferences with congressmen and senators from this State.

A summary of the actions of the House of Delegates taken at its annual session was presented to the congressmen and senators and is reported to have made a great impression. A total of 32 out of 43 congressmen and both senators were contacted, and the reception by these legislators was most cordial. The report indicates that the visit gained prestige for the Society.

Action was also taken by the subcommittee in connection with HR 10 (Keogh Bill), which would authorize self-employed individuals to contribute up to 10 per cent of their earned income or $2,500, whichever is less, toward a retirement plan. The status of its progress is included in the subcommittee's report.

In the conclusions of the report, the subcommittee recommends that its activities be continued and intensified and that appropriate funds be set aside for this purpose. It specifically recommends continuation of the annual visits to Washington.

Further activities of the Subcommittee on Federal Legislation are contained in a supplementary report and include a six-point program in opposition to the King-Anderson Bill.

Your reference committee notes that the report of the Subcommittee on Federal Legislation does not contain any mention of the financial expenditures involved in the aforementioned projects, and although it is aware that such activities require necessary expenditures, it recommends that the Council consider the financial cost to the Society in relation to the over-all results obtained from these projects.

Your reference committee further recommends that each project of this type be considered anew and that no policy of automatic continuation be established.

I move the adoption of this portion of the report.

DR. SPIEGEL: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 200

Report of Reference Committee on Legislation and Legal Matters: Legal Counsel

DR. HELPERN: Your reference committee has reviewed with considerable pleasure and satisfaction the scholarly and instructive report of its legal counsel. The material contained in this report, in essence, comprises a monograph on the subject of medical malpractice, based on the experience of counsel and his associates in the defense of malpractice actions against members of the Society. The magnitude of the problem, not only in this State, but throughout the country and also in England is emphasized. The report, documented with many cases, also points out that much more than one half of all professional liability claims and suits are without the slightest meritorious foundation, but nevertheless, such suits against a physician, even though unjustified, are harmful to that physician as well as to the entire profession.

Your reference committee not only commends our legal counsel, Mr. William F. Martin, and the entire firm of Martin, Clearwater and Bell, for the work they have been doing on behalf of the Society's membership, but also recommends to the House that the report of legal counsel be reprinted and distributed to all fourth-year medical students in the State as a treatise on the very important subject with which it deals.

I move adoption of this portion of the report.

DR. HIMLER: I second the motion.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 201 (see 39, 47)

Report of Reference Committee on Legislation and Legal Matters: Change in Welfare Laws and Regulations

DR. HELPERN: Your reference committee considered resolution 62-3, "Change in Welfare Laws and Regulations," introduced by Genesee County, and resolution 62-11, "Plan to Bring About Changes in Welfare Medical Programs," introduced by Broome County.

These two resolutions were considered together and, with the consent of the proposers, are being referred to the Council Committee on Legislation for study and action. Neither resolution involves action by the legislators, and both are concerned with existing regulations within the State Department of Social Welfare.

I move the adoption of this portion of the report.

DR. GOLDEN: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 202 (see 48)

Report of Reference Committee on Legislation and Legal Matters: Court Decisions Affecting Workmen's Compensation Law

DR. HELPERN: Resolution 62-12, "Court Decisions Affecting Workmen's Compensation Law," introduced by Broome County:

> *Resolved,* That the membership of the Medical Society of the State of New York be informed of this change in the Workmen's Compensation Law and the State Society be instructed to exert every and all legitimate, legal, and legislative means to reverse or circumvent these decisions.

This resolution was promulgated because of two decisions rendered recently in the New York State Supreme Court, Appellate Division, that altered the basic concept of the Workmen's Compensation Law, State of New York. Based on these court decisions, wage loss is now required by a claimant with an occupational dermatitis or occupational hernia before medical services can be rendered at the expense of the compensation carrier.

Your reference committee approves this resolution.

I move adoption of this portion of the report.

DR. D'ERRICO: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 203 (see 52)

Report of Reference Committee on Legislation and Legal Affairs: Amendment to Civil Practice Act to Prevent Use of Minutes of Hospital Tissue Committee Meetings

DR. HELPERN: Resolution 62-16, "Amendment to Civil Practice Act to Prevent Use of Minutes of Hospital Tissue Committee Meetings," introduced by Oneida County:

> *Resolved,* That the Medical Society of the State of New York, through its Committee on Legislation, encourage and foster the preparation of legislation purporting to amend Section 296 of the Civil Practice Act of the State of New York so as to prohibit the courts from approving a subpoena *duces tecum* or other judicial process that would call for the production of the minutes of the tissue committees in hospitals for any purpose whatsoever.

This resolution was considered by your reference committee and discussed extensively with its proponents and with counsel. After deliberation and on advice of counsel, it was the consensus of your reference committee that no action should be taken.

I move adoption of this portion of the report.

DR. GOLDEN: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 204 (see 56, 64)

Report of Reference Committee on Legislation and Legal Matters: Supervision of Laboratories by Qualified Licensed Physicians

DR. HELPERN: Resolution 62-20, "Endorsement of A.M.A. Resolution on Supervision of Clinical Laboratories," introduced by John J. Clemmer, M.D., Section on Pathology, Clinical Pathology, and Blood Banking, and resolution 62-28, "Supervision of Laboratories by Qualified Licensed Physicians," introduced by Queens County: Because of their similarity, both of these resolutions were considered together and approved in principle. Resolution 62-28 was amended, in part, to read as follows and then was approved by your reference committee:

> *Resolved,* That the Medical Society of the State of New York hereby declare that the proper conduct of laboratory analyses is a medical, professional responsibility and all specimens for such analyses should be referred to laboratories operated under direct supervision of fully qualified and licensed physicians, preferably clinical pathologists.

I move the adoption of this portion of the report.

DR. HIMLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 205 (see 58)

Report of Reference Committee on Legislation and Legal Matters: Opposition to Chiropractic Licensure

DR. HELPERN: Resolution 62-22, "Opposition to Chiropractic Licensure," introduced by Bronx County: This resolution was amended, by changing and incorporating the third and fourth "whereases" and the "resolved's" and then was approved. The amended resolution reads as follows:

> WHEREAS, Many groups and organizations, such as universities, foundations, special study commissions, health and welfare groups responsible for the expenditure of health and welfare funds, public health organizations, social service organizations, ancillary medical service groups, and government departments involved in health and welfare matters, are actively interested in the quality of medical care received by the people of New York State; and
>
> WHEREAS, Many of these influential groups have initiated and financed organized studies concerning the quality of medical care; and
>
> WHEREAS, The licensing of chiropractic has been proposed for many years in the New York State Legislature, and the medical profession, in the public interest, has regularly opposed such licensure; now therefore be it hereby
>
> *Resolved,* That the Medical Society of the State of New York through its Council request all organizations interested in the quality of medical care to make known to the members of the State Legislature their considerations and opinions as to the lack of any scientific basis for the practice of the cult of chiropractic so that the Legislature may be further guided in protecting the health and care of the citizens of our State; and be it further
>
> *Resolved,* that this interest and concern with the problem of chiropractic be continuous and not limited to the period of the legislative session.

I move the adoption of this portion of the report.

DR. HIMLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 206 (see 62, 74)

Report of Reference Committee on Legislation and Legal Matters: "Good Samaritan" Legislation

DR. HELPERN: Resolution 62-26, on "Good Samaritan" legislation, introduced by Bronx County, and resolution 62-38, "Promotion of 'Good Samaritan' Law," introduced by Westchester County: Your reference committee considered both of these resolutions together because of their similarity. After a review of the Governor's reasons for vetoing the legislation introduced in the past session of the Legislature and the fact that there have been no reported instances in which physicians were sued for malpractice as the result of having given first aid in accident cases and on the advice of counsel, your reference committee recommends that no action be taken on these resolutions at this time.

I move the adoption of this portion of the report.

Dr. Spiegel: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 207 (*see 67*)

Report of Reference Committee on Legislation and Legal Matters: Review of the Medical Practice Act

Dr. Helpern: Resolution 62–31, "Review of the Medical Practice Act," introduced by Broome County, was approved by your reference committee. Your committee commented on this problem in its review of the report of the Committee on Legislation, under the subheading "Review of the Medical Practice Act and the Healing Arts."

I move the adoption of this portion of the report.

Dr. Golden: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 208 (*see 72*)

Report of Reference Committee on Legislation and Legal Matters: Condemnation of King-Anderson Bill

Dr. Helpern: This resolution, 62–36, introduced by Louis H. Bauer, M.D., past-president, was approved in its entirety by your reference committee.

I move the adoption of this portion of the report.

Dr. Himler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 209 (*see 73*)

Report of Reference Committee on Legislation and Legal Matters: Activity Against Chiropractic

Dr. Helpern: Resolution 62–37, "Activity Against Chiropractic," introduced by Schuyler County: Your reference committee approved this resolution in principle, but its implementation was not considered feasible, and it is therefore recommended that no action be taken on its specific proposals at this time.

I move the adoption of this portion of the report.

Dr. D'Errico: I second it.

Speaker Wurzbach: Is there any discussion?

Alfred A. Angrist, M.D., *Queens:* I move an amendment to this aspect of the report to read as follows: "Your reference committee approved this resolution in principle." I would urge that we not take any further action, but by including the statement that we are not taking any further action, I think we are discouraging county societies from initiating this kind of a proposition, which I think is of importance in gathering the information which we should try to collate for increasing our effectiveness in opposition to the chiropractic law. It is the malfeasance and the disturbed type of practice which we can document by such data and can use, I think, very effectively, but we must have some means of collating and collecting the data. This resolution offers such a means and, by amending it in the paragraph I have suggested, leaves it as a voluntary proposition without compulsion or any type of overhead machinery necessary.

Irving Cohen, M.D., *Bronx:* I second the amendment.

. . . There being no discussion, the motion on the amendment was put to a vote and was carried . . .

Speaker Wurzbach: We now vote on the amended report of the reference committee.

. . . There being no further discussion, the motion was put to a vote and was carried . . .

Section 210 (*see 76*)

Report of Reference Committee on Legislation and Legal Matters: Principles Regarding Medical Care for the Aged

Dr. Helpern: Resolution 62–40, "Principles Regarding Medical Care for the Aged," introduced by Monroe County, was approved in principle by your reference committee, but because most of its provisions are contained in resolution 62–53, it was recommended that no action be taken on resolution 62–40.

I move the adoption of this portion of the report.

Dr. Himler: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 211 (*see 78*)

Report of Reference Committee on Legislation and Legal Matters: Lien Law

Dr. Helpern: Resolution 62–42 "Lien Law," introduced by Bronx County: Your reference committee approves this resolution and also wishes to call attention to the fact that this subject will be on the agenda of a meeting of the Joint Committee of the State Society and the Bar Association in September, 1962.

I move the adoption of this portion of the report.

Dr. Spiegel: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 212 (see 87)

Report of Reference Committee on Legislation and Legal Matters: Revision of the Autopsy Consent Law

DR. HELPERN: Resolution 62–50, "Revision of the Autopsy Consent Law," introduced by Queens County, was amended in part to read as follows and was then approved:

> *Resolved*, That the Medical Society of the State of New York petition the Governor to refer to the Law Revision Commission for evaluation the present Wisconsin Law, which only requires consent for autopsy of one of equal rank of next of kin provided none of the others has objected; and be it further
>
> *Resolved*, That after consideration of the advantages of such a revision of the existing section for consent for autopsy, the Law Revision Commission be requested to recommend appropriate legislation to the Legislature of the State of New York at its next session.

I move the adoption of this portion of the report.

DR. HIMLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 213 (see 88)

Report of Reference Committee on Legislation and Legal Matters: Compilation and Revision of Existing Laws Dealing with the Human Body After Death

DR. HELPERN: Resolution 62–51, "Compilation and Revision of Existing Laws Dealing with the Human Body After Death," introduced by Queens County, was amended to read as follows and was then approved:

> WHEREAS, There exist many ambiguities, conflicts, and inadequacies in the numerous overlapping statutes dealing with the human body after death, as they have been adopted at many different times to meet specific problems; and
>
> WHEREAS, The existing Governor's Commission on Estates is dealing with many related problems; now therefore be it hereby
>
> *Resolved*, That the Medical Society of the State of New York petition the Governor of the State of New York to include, in the charge to the existing Commission on Estates, a survey and clarification of all the existing laws dealing with the human body after death, and recommend a revised group of statutes, with additions as may be indicated.

I move the adoption of this portion of the report.

DR. HIMLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

Section 214 (see 90)

Report of Reference Committee on Legislation and Legal Matters: Private Hospital Insurance for the Aged

DR. HELPERN: Resolution 62–53, "Private Hospital Insurance for the Aged," introduced by Nassau County, reads:

> WHEREAS, The physicians of the Medical Society of the State of New York will always respond to the medical needs of all the people of the State of New York; and
>
> WHEREAS, The King-Anderson Bill would regiment the care of the individual and deny the senior citizen his right to choose his own doctor and hospital; and
>
> WHEREAS, More efficient processing of hospital care insurance can be accomplished at the same cost by utilizing the vast experience of the insurance industry; and
>
> WHEREAS, Utilizing a government assistance of $33^1/_3$ per cent for the needy aged and a tax credit of 50 per cent for the purchase of the nationally proposed Blue Cross coverage or other comparable insurance at an estimated total cost of $11 per month would enable senior citizens or their relatives to purchase this insurance at a net cost of only $3.75 per month; and
>
> WHEREAS, A tax credit alone of 50 per cent for the purchase of the nationally proposed Blue Cross plan or similar coverage at an estimated $11 per month would enable the remainder of our senior citizens or their relatives to purchase this coverage at a reduced net cost of only $5.50 per month; and
>
> WHEREAS, This principle of assistance and tax credit for the senior citizens would enable them to be protected by insurance without being subjected to government restrictions, red tape, delay, and confusion, or administrative expense to the government; now therefore be it hereby
>
> *Resolved*, That the Medical Society of the State of New York strongly endorse the principle of financing hospital insurance for the needy aged utilizing the principle of government assistance as provided by the Kerr-Mills Law and tax credit for the purchasers of this insurance; and be it further
>
> *Resolved*, That the Medical Society of the State of New York urge the Congress of the United States not to enact legislation which would drastically affect the future course of health care and which would further centralize government control by financing hospital care through the mechanism of Social Security taxation; and be it further
>
> *Resolved*, That the delegates of this Society be instructed to introduce and actively support a similar resolution at the June, 1962, meeting of the House of Delegates of the American Medical Association; and be it further
>
> *Resolved*, That copies of this resolution be sent to the President of the United States,

the Secretary of Health, Education, and Welfare, the members of the Senate Committee on Finance, the House Ways and Means Committee, and to the United States Senators and Representatives from the State of New York.

Your reference committee discussed the provisions of this resolution and approved it. Your committee considers this resolution to be a constructive proposal for the health care of the aged which would preserve the essential elements of adequate assistance within the framework of free choice.

I move the adoption of this portion of the report.

Dr. D'Errico: I second it.

Speaker Wurzbach: Is there any discussion?

Thomas M. d'Angelo, M.D., *Queens:* I think this is a very important resolution. We should be very careful of the facts involved, and I would like to call your attention to the second "whereas":

> Whereas, The King-Anderson Bill would regiment the care of the individual and deny the senior citizen his right to choose his own doctor and hospital.

It is my understanding that the King-Anderson Bill has nothing to do with the private physician. It only has to do with hospital care and involves only those doctors who are employed in the hospital. Therefore, Mr. Speaker, I would amend that second "whereas" to read:

> Whereas, The King-Anderson Bill would regiment the care of the individual and deny the senior citizen his free choice of hospital.

Sol Axelrad, M.D., *Queens:* I second that amendment.

Speaker Wurzbach: We are now discussing the amended "whereas" presented by Dr. d'Angelo.

Dr. Himler: We recognized in the reference committee there was no direct denial of the patient's free choice of physician, but it must be pointed out we do not have universal hospital privileges. The limitation of free choice of hospital necessarily implies the limitation of the free choice of physician. It was on that basis this language was adopted.

Ralph S. Emerson, M.D., *Nassau:* This was put in because of the reasons that were brought out last night by Congressman Tom Curtis and also because of the provisions within HR 4222, which do restrict the physicians or the patients to choose those physicians unless they have to go to a hospital that makes a contract with the government. Although it is a technical point, it can very definitely apply if it is carried out to the letter of the law.

Speaker Wurzbach: Is there any further discussion of the amended "whereas" by Dr. d'Angelo?

Dr. d'Angelo: I would like to answer Dr. Himler first. That restriction is already in effect in the hospitals as they exist today. If a private physician has not got the privileges of the hospital, he thereby suffers under a restriction that is already in effect, and I don't think it has anything to do with the law itself.

My understanding of Mr. Curtis last night was the fact that unquestionably—and I agree with him wholeheartedly—this is only a beginning.

Speaker Wurzbach: Is there any further discussion?

Dr. Himler: I think Dr. d'Angelo has commented on a nonspecific circumstance, although I hate to take issue with so gifted a speaker. There are limitations which apply to physicians practicing in hospitals, but their payment to the hospital services cover such services as are rendered, so in that way this resolution is accurate, and I would urge its adoption.

. . . There being no further discussion, the amendment was put to a vote and was lost . . .

Speaker Wurzbach: The amendment is lost.

Dr. Emerson: In view of the fact that this resolution was due to come up yesterday afternoon, and the resolution was placed on the desks, the releases were given out. There has been information before the press prior to the coming of this report to the House of Delegates. Unfortunately, through the democratic process, our meeting yesterday was longer than anticipated, and we did not get a chance to take it up beforehand. But I think to clarify a few points, so as to make sure there is no misunderstanding about this, particularly the delegation from Nassau County would like to emphasize the following statement:

1. There is no deviation or compromise with the A.M.A. position. We have always believed not only the aged but all of our citizens should have the best care, and we strongly believe that
2. The vast experience of our great insurance industry, extending over many decades, was more qualified and more efficient in accomplishing this objective than the government could possibly be, as eventually another large bureaucracy would emerge.

What we have done in essence is to tie together the ideas of:

1. Government assistance for the needy to purchase private health insurance, which would supplement the Kerr-Mills Law.
2. Recommending tax credit of 50 per cent to relatives who purchase (health) hospital insurance on behalf of the aged by amending Section 213 and Section 152 of the Internal Revenue Code to include liberalization of tax concessions on a broader base.
3. To demonstrate that the above principles, even if applied to all of the aged sixty-five years or older, are not only financially sound and feasible and can be delivered at the same cost or less than financing through Social Security taxes.

It can be delivered utilizing the proposed comprehensive nationwide Blue Cross hospital plan, or comparable private insurance plans, more efficiently and on a personalized basis to the purchaser utilizing (*a*) government subsidy for the needy aged at $33^1/_3$ per cent, plus tax concession and (*b*) tax credit of 50 per cent alone at a net cost of approximately $66 a year. For example, if the premium is $11 per month, the individual, whether it is a relative and regardless of whether he is the main support of the aged member, would get as a net tax credit after he works out his final tax: Say his final tax is $100, and he pays $100 for his insurance, he would get 50 per cent of that $100 as a tax credit, which would reduce his tax from $100 to $50. This is not a tax deduction; it is a tax credit.

A government subsidy for the $33^1/_3$ per cent for the needy aged plus using a tax credit of 50 per cent alone at a net cost of approximately $66 a year.

Both of these proposals are considerably below the deductible of $10 a day for the first nine days of every hospital admission which the aged citizen would be required to pay for an average length of hospital stay, and you know that the average length of hospital stay of those sixty-five and over is over ten days. It is nearer eleven and a half days.

The government assistance feature would complement the Kerr-Mills principle in this way: The Kerr-Mills principle is broad in concept and is being implemented by each state to obtain its maximum goal, but in the interim the government assistance plus tax credit would offer inducement to obtain coverage for those aged citizens who cannot qualify under Kerr-Mills provisions in some states at the present time. This would give them protection against hospital and nursing home expenses at an earlier date.

If these same principles of government assistance and tax credit were applied to the purchase of Blue Shield or other carriers for physician services, the net cost of the entire package would be less than the deductible expenses our senior citizens would be required to pay under the financing through Social Security.

SPEAKER WURZBACH: You are speaking in approval of the action of the committee?

DR. EMERSON: I am speaking in very strong support of this resolution.

SPEAKER WURZBACH: All those in favor say "aye," contrary "no." It is carried.

Section 215 (*see 197*)

Reconsideration of Report of Reference Committee on Legislation and Legal Matters: Legislation

ASSISTANT SECRETARY WOLFF: I move your indulgence on a matter that I did not think of at the time it was presented. I would like to move for a reconsideration of that portion of the report which concerns an amendment to the real property law which was passed by the Legislature and vetoed by the Governor. This affects peculiarly only Queens County in the entire State.

We have reason to believe that we can have an acceptable law passed, and I would like to move to change the recommendation of the committee. I would, therefore, move that we reconsider this matter.

SPEAKER WURZBACH: All you need to move is to recommend reintroduction of this bill and not opposition to it.

DR. WOLFF: That will be the substance of my motion, but does it not have to be moved for reconsideration before I can talk about it?

SPEAKER WURZBACH: That is right.

SAMUEL Z. FREEDMAN, M.D., *Assistant Treasurer:* I second the motion for reconsideration.

SPEAKER WURZBACH: All in favor of the reconsideration say "aye," those opposed "no." We are now on the reconsideration of the paragraph.

ASSISTANT SECRETARY WOLFF: Now, Mr. Speaker, may I move an amendment, in place of the recommendation that the bill not be reintroduced, to the effect that we recommend restudy of this bill by the Legislation Committee to the end it may be altered in such a way as to become acceptable. This will give us a chance to change it so we can get some tax relief in Queens.

SPEAKER WURZBACH: What is your reaction to it, Dr. Blake?

JAMES M. BLAKE, M.D., *Councillor:* I approve.

. . . There being no further discussion, the motion was put to a vote and was unanimously carried . . .

Section 216 (*See 198*)

Reconsideration of Report of Reference Committee on Legislation and Legal Matters: Committee to Combat Cults

GERALD D. DORMAN, M.D., *Councillor:* I would like to ask, may I move a reconsideration for an addendum?

SPEAKER WURZBACH: Is it seconded?

. . . The motion was seconded by several . . .

DR. DORMAN: I move that there be the following addition to that report in answer to a question posed by Dr. Zimring. I move that the matter of long-range ways and means of combating the cult, chiropractic, in its attempt to be licensed, be referred to the Planning Committee and the Committee on Legislation and these committees be directed to develop specific suggestions by next fall.

SPEAKER WURZBACH: You are making this as a new motion?

DR. DORMAN: It is an addendum.

DR. ZIMRING: I second it.

SPEAKER WURZBACH: Is there any discussion?

INCOMING-PRESIDENT LANE: I would like to call to the attention of the House that it has been recommended, and will be implemented, that a special meeting will be arranged early with the representatives of the State Legislature, the Governor's office, the Medical Society of the State of New York, and the Osteopathic Society, to try to implement such recommendation as has just been made here. I wonder if this motion is necessary. We are going to take care of that as promptly as we can.

SPEAKER WURZBACH: This is therefore an explanation by Dr. Lane. Is there any further discussion?

HERBERT A. LAUGHLIN, M.D., *Chautauqua:* I think it is only appropriate, before this committee's report as a whole be passed, that some recognition and some thanks be given to Herman E. Hilleboe, M.D., for his untiring efforts on our behalf on this chiropractic x-ray situation. I think this House should go on record as thanking him very kindly and very sincerely for his efforts on our behalf. (*Applause*)

SPEAKER WURZBACH: I am certain Dr. Hilleboe understands the feeling of this House. We are now, however, on the addendum. Is there any discussion? All those in favor of the addition of this addendum to the report will say "aye," opposed "no." It is carried.

DR. HELPERN: The chairman wishes to acknowledge with gratitude the active cooperation and the judgment and understanding of all of the members of the reference committee, and on their behalf, I extend our thanks to individual members of the House of Delegates, the officers and members of the staff of the State Society, and the legal counsel, who assisted us with information and advice. A special mention should be made of the continuous assistance of Miss Anne Brugnone, who worked without respite during all the busy sessions of the committee and late into the night in taking dictation and transcribing this long report.

Mr. Speaker, I move the adoption of this report as amended and addended in its entirety. (*Applause*)

SPEAKER WURZBACH: Mr. Chairman, the applause of this House shows you it is accepted.

Section 217

Closing Remarks of the Speaker

SPEAKER WURZBACH: Is there any further business to come before the House? If not, the speaker wishes to make a few remarks.

First, I wish to thank the entire membership of this House for its wonderful attention and its careful consideration of all of the business that has been brought before it. I think that the chairmen and all of the members of the reference committees have certainly done a magnificent piece of work. I think there has been a minimum of dissension through their reports. There is very little the speaker can add except to say how much he thanks the secretary and the assistant secretary personally, and how much he thanks Dr. Babbage and all members of the staff, and certainly above all the three members of the staff without whom this House certainly would not function in the manner in which it functions now, and that is Dr. Fineberg, Miss Dougherty, and Miss Lewis. (*Applause*)

I now will accept a motion for the closing of the House.

SECRETARY WHEELER: I so move.

DR. HIMLER: I second it.

. . . There being no discussion, the motion was put to a vote and was unanimously carried . . .

SPEAKER WURZBACH: The House is now adjourned sine die.

. . . The House of Delegates adjourned at 12:30 P.M., sine die . . .

Announcement

1962 District Branch Meetings

Branch	*Date*	*Place*
FIRST	May (at time of State Society meeting)	New York City
SECOND	Sunday, Monday, Tuesday November 11, 12 13	Grossinger's Grossinger, New York
THIRD	(*to be announced*)	
FOURTH	Saturday, September 22	Queensbury Hotel, Glens Falls, New York
FIFTH	Friday, Saturday, Sunday September 7, 8, 9	Whiteface Inn, Lake Placid, New York
SIXTH	Joint meeting with Fifth District Branch	
SEVENTH	Thursday, Friday, Saturday September 20, 21, 22	Grossinger's Grossinger, New York
EIGHTH	Thursday, October 4	Bartlett Country Club Olean, New York
NINTH	May (at time of State Society meeting)	New York City

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the margin of success

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[1] Spielman, A. D.: Evaluation of a Combination Tablet of Theophylline, Ephedrine Sulphate, Phenobarbital, Thenyldiamine and Glyceryl Guaiacolate in the Treatment of Chronic Asthma, Ann. Allergy 18:281 (Mar.) 1960.

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1. Teitel, L.H., *et al.*: Indust. Med. 29:150, 1960. 2. Billow, B.W., *et al.*: Southwestern Med, 41:286, 1960. 3. Beck, C., *et al.*: Clin. Med. 7:519, 1960. 4. Clinical Reports to the Medical Department, Armour Pharmaceutical Company, 1960.

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*Brown, G. W.; Tuholski, J. M.; Sauer, L. W.; Minsk, L. D., and Rosenstern, I., J. Pediat. 56:391 (Mar.) 1960.

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1. Clinical and Physicians' Reports to the Medical Department, Armour Pharmaceutical Company, 1960-1961. 2. Billow, B. W., *et al.:* Southwestern Med. *41*:286, 1960. 3. Taub, S. J.; Clin. Med. 7:2575, 1960. 4. Teitel, L. H., *et al.:* Indust. Med. *29*:150, 1960.

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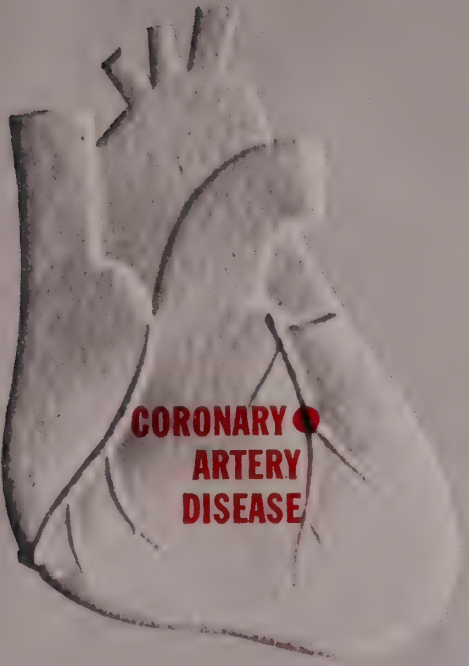

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Diseases of the cardiovascular-renal system account for about three-fourths of deaths among diabetic patients, with heart disease responsible for approximately one-half the total,[2,3] and coronary atherosclerosis the major cause of cardiac lesions.[1] While some feel that diabetics are predisposed, perhaps by heredity, to early onset of vascular disease, considered opinion is that vascular degeneration can be delayed or modified with "...careful and consistent control of diabetes from the time of diagnosis...."[4]

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References: (1) Root, H. F., and Bradley, R. F., in Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: The Treatment of Diabetes Mellitus, ed. 10, Philadelphia, Lea & Febiger, 1959, pp. 411, 437. (2) Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: *ibid.*, pp. 188-189. (3) Marks, H. H., *et al.:* Diabetes 9:500, 1960. (4) Marble, A., in Summary of Conference on Diabetic Retinopathy, Survey Ophth. (Part 2) 6:611-612, 1961.

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References: (1) Shaw, J. H., in Wohl, M. G., and Goodhart, R. S.: Modern Nutrition in Health and Disease, ed. 2, Philadelphia, Lea & Febiger, 1960, pp. 574-580. (2) Statement on Fluoridation of Public Water Supplies, by the House of Delegates of the American Medical Association, Philadelphia, December 3-6, 1957. (3) Accepted Dental Remedies, ed. 27, Chicago, American Dental Association, 1962, pp. 137-139. (4) Council on Dental Therapeutics, J. Am. Dent. A. 56:589-591 (April) 1958.

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the margin of success

in asthma therapy, it's the expectorant in Bronkotabs

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[1] Spielman, A. D.: Evaluation of a Combination Tablet of Theophylline, Ephedrine Sulphate, Phenobarbital, Thenyldiamine and Glyceryl Guaiacolate in the Treatment of Chronic Asthma, Ann. Allergy 18:281 (Mar.) 1960.

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[1] Ford, R. A., and Blanchard, K.: Journal-Lancet 78:185, 1958.

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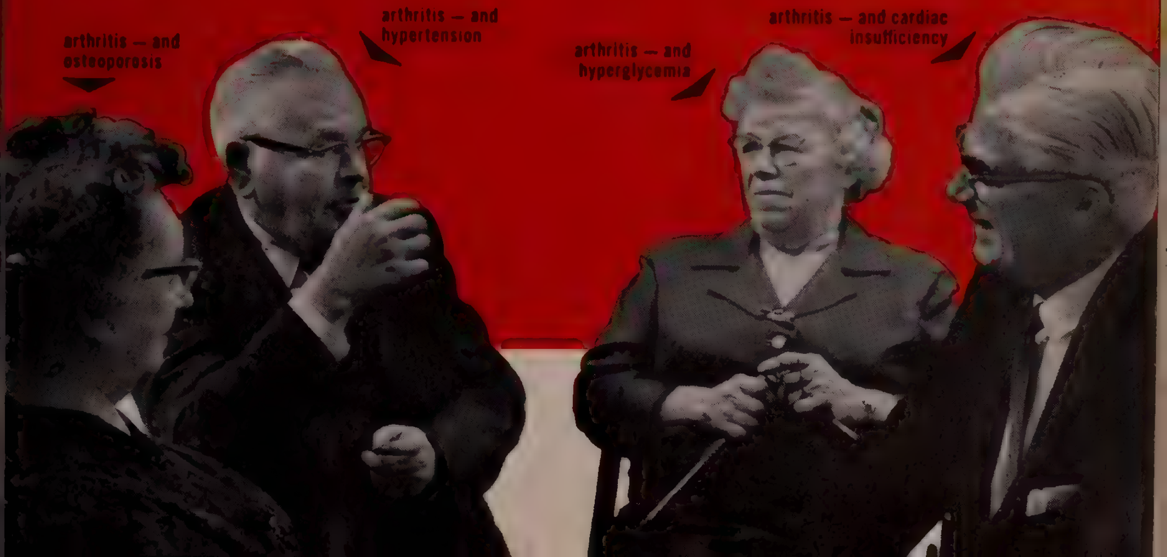
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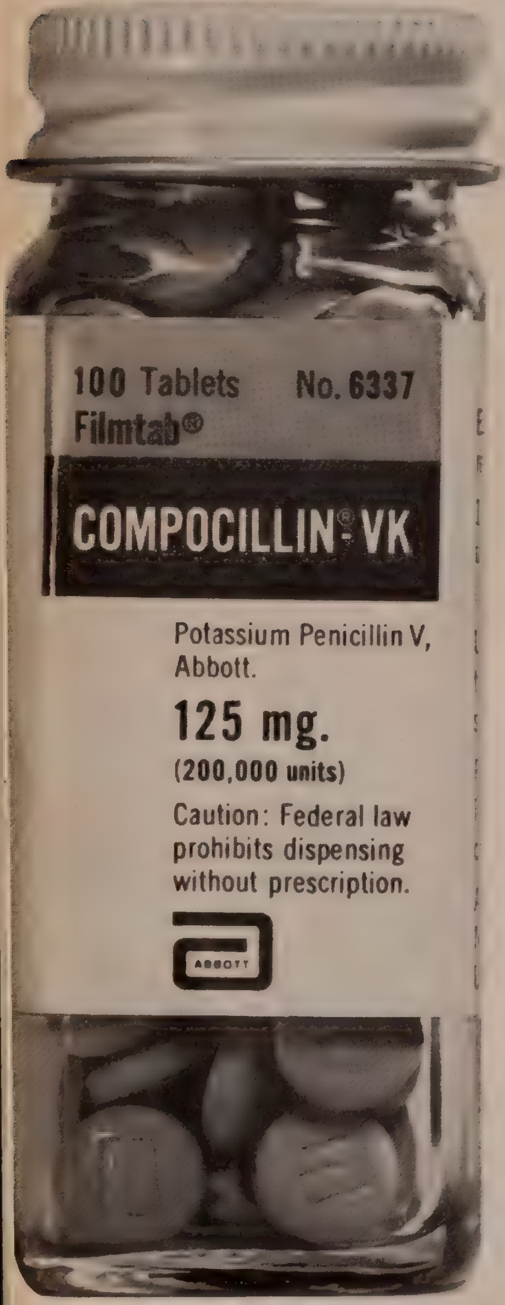
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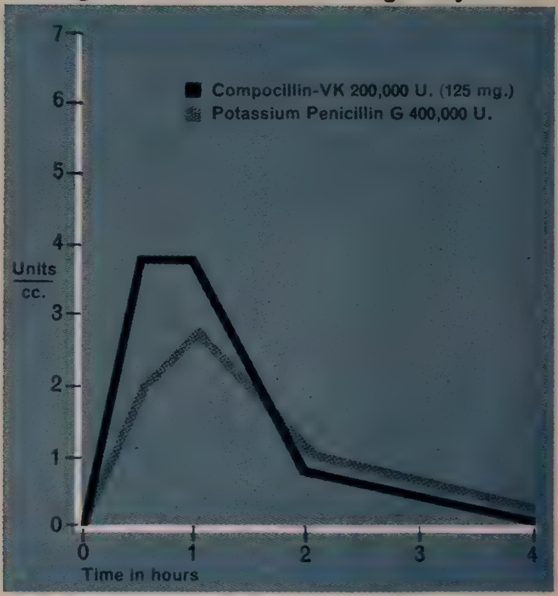

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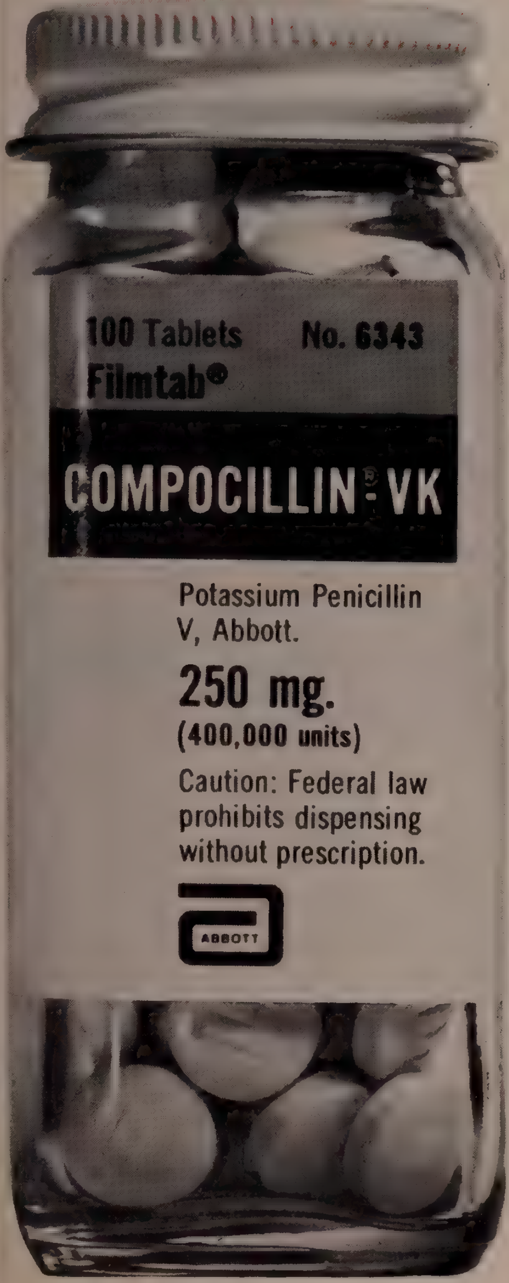
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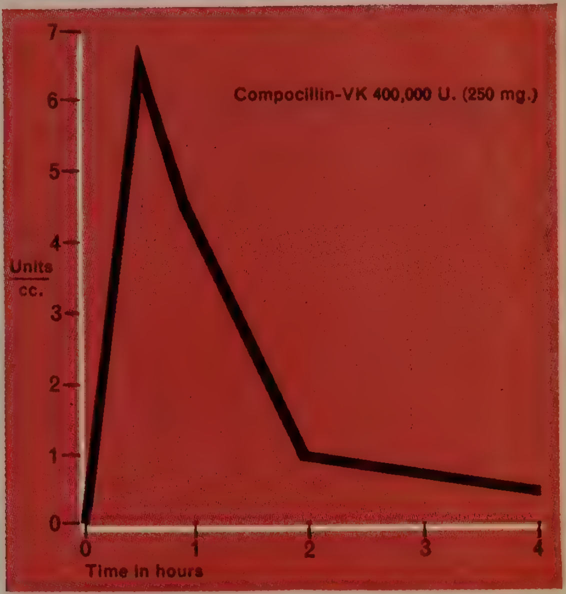

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*Chart data from two separate studies completed by the Microbiologic and Medical Departments of Abbott Laboratories.

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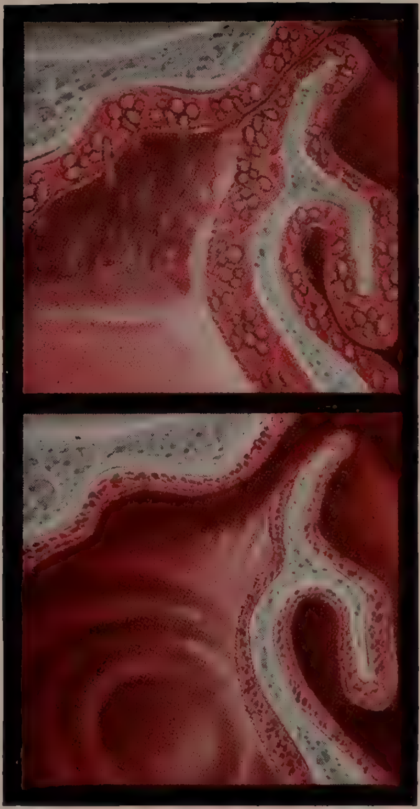

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1. Grant, L. E.: Coryza and nasal sinus infections, **Clin. Med. & Surg.** 42:121, March, 1935. 2. Putney, F. J.: Sinus infection, in Conn, H. F. (Ed.): Current Therapy 1952, Philadelphia, W. B. Saunders Company, 1952, p. 110. 3. Simonton, K. M.: Current treatment of sinusitis, **Journal-Lancet** 79:535, Dec., 1959.

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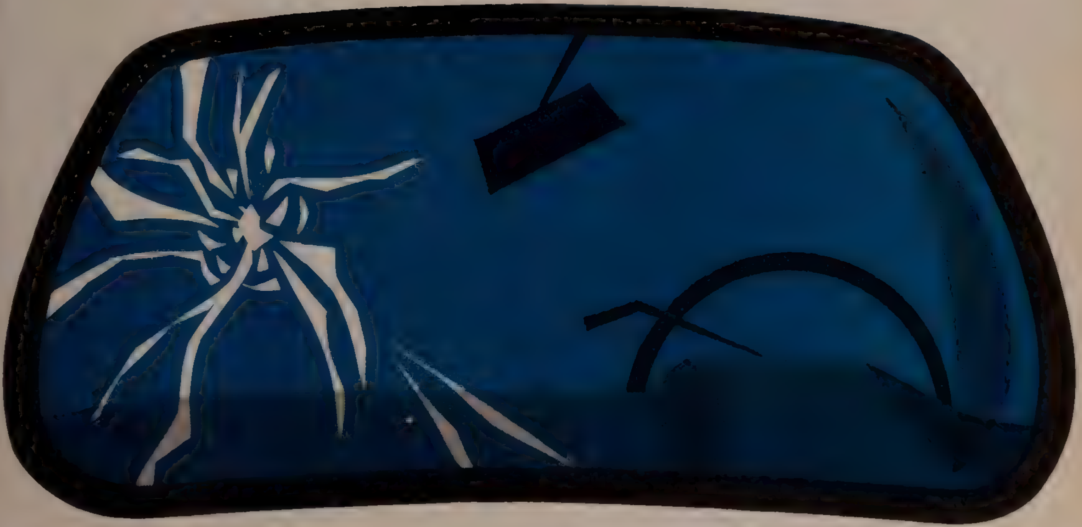

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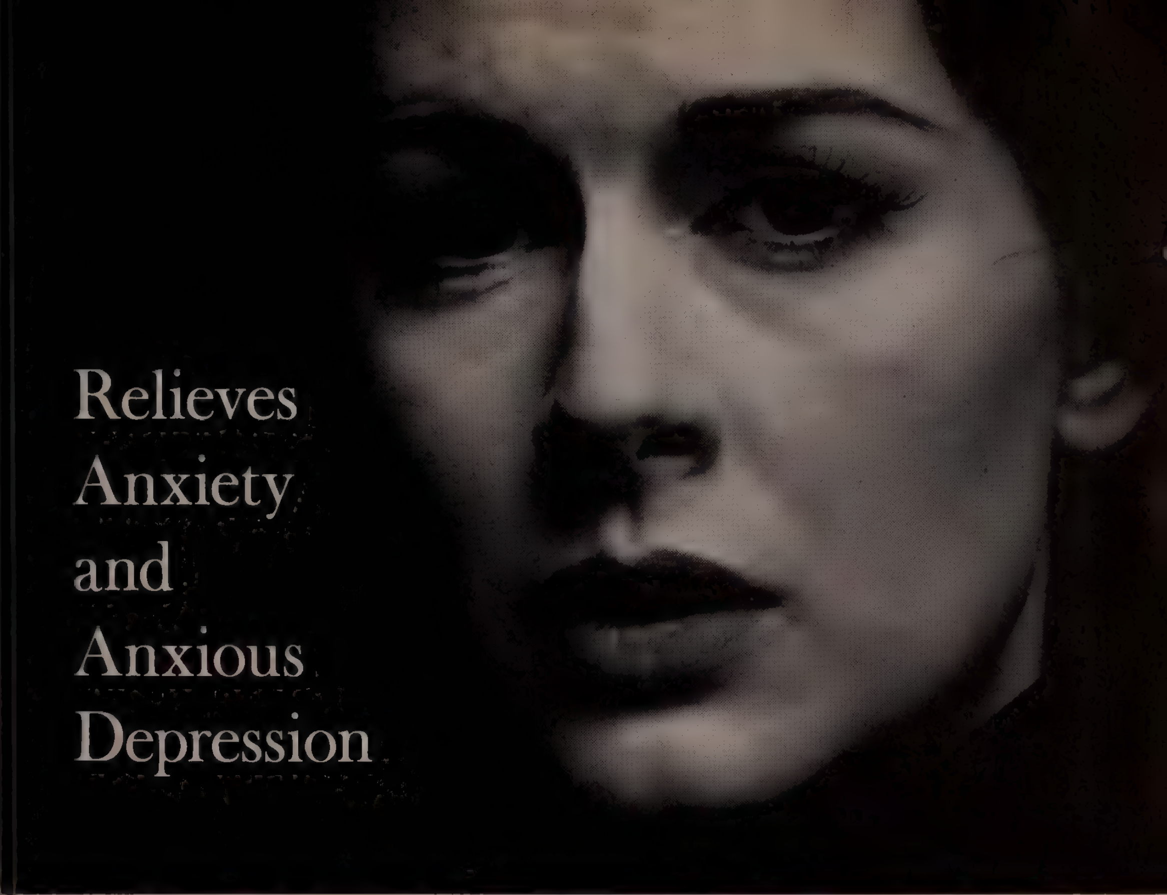

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*Scal, J. C.: Eye Ear Nose & Throat Month. **38**:738 (Sept.) 1959.

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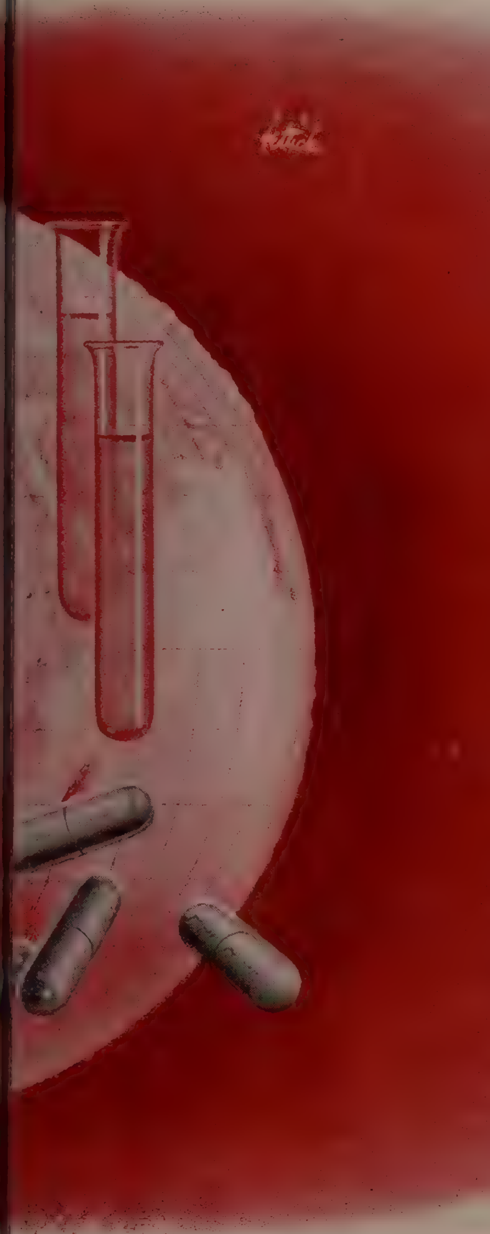

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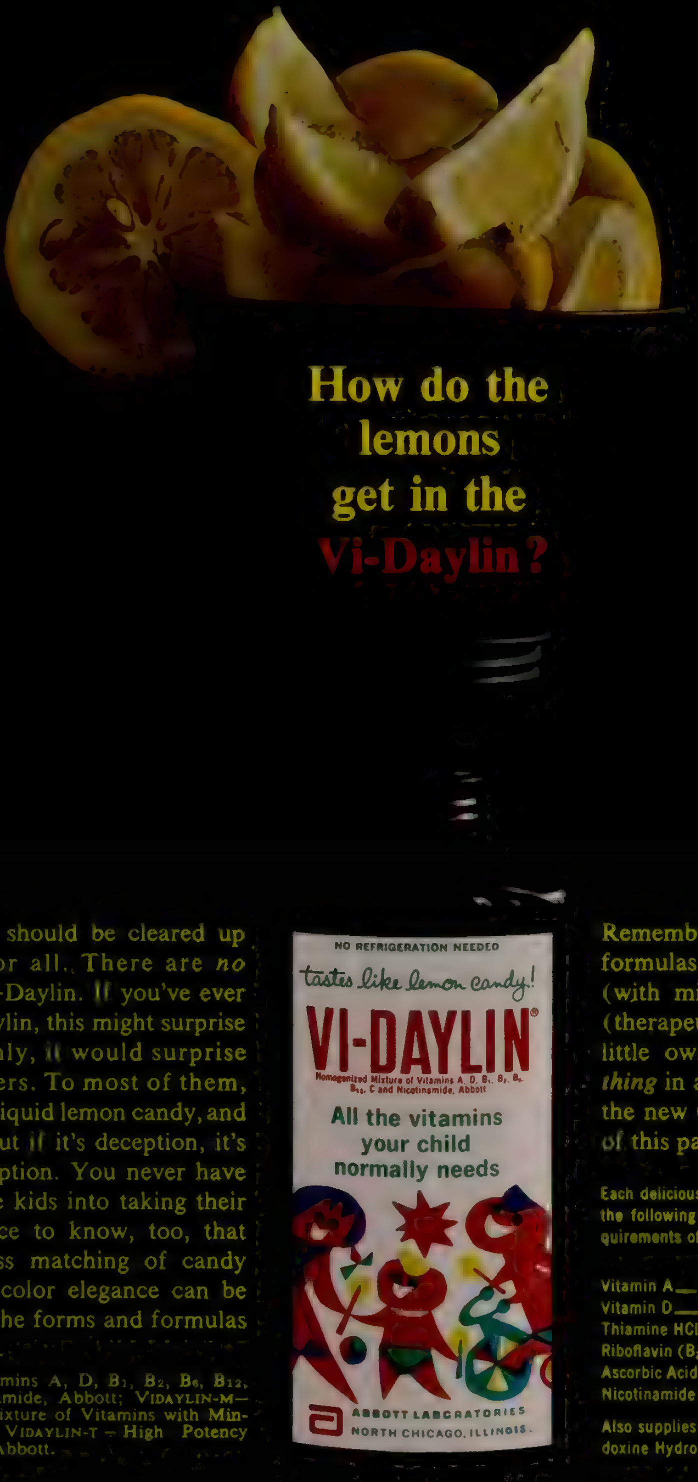
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*Alexander, F.: Psychosomatic Medicine, New York, W. W. Norton, 1950, p. 101.

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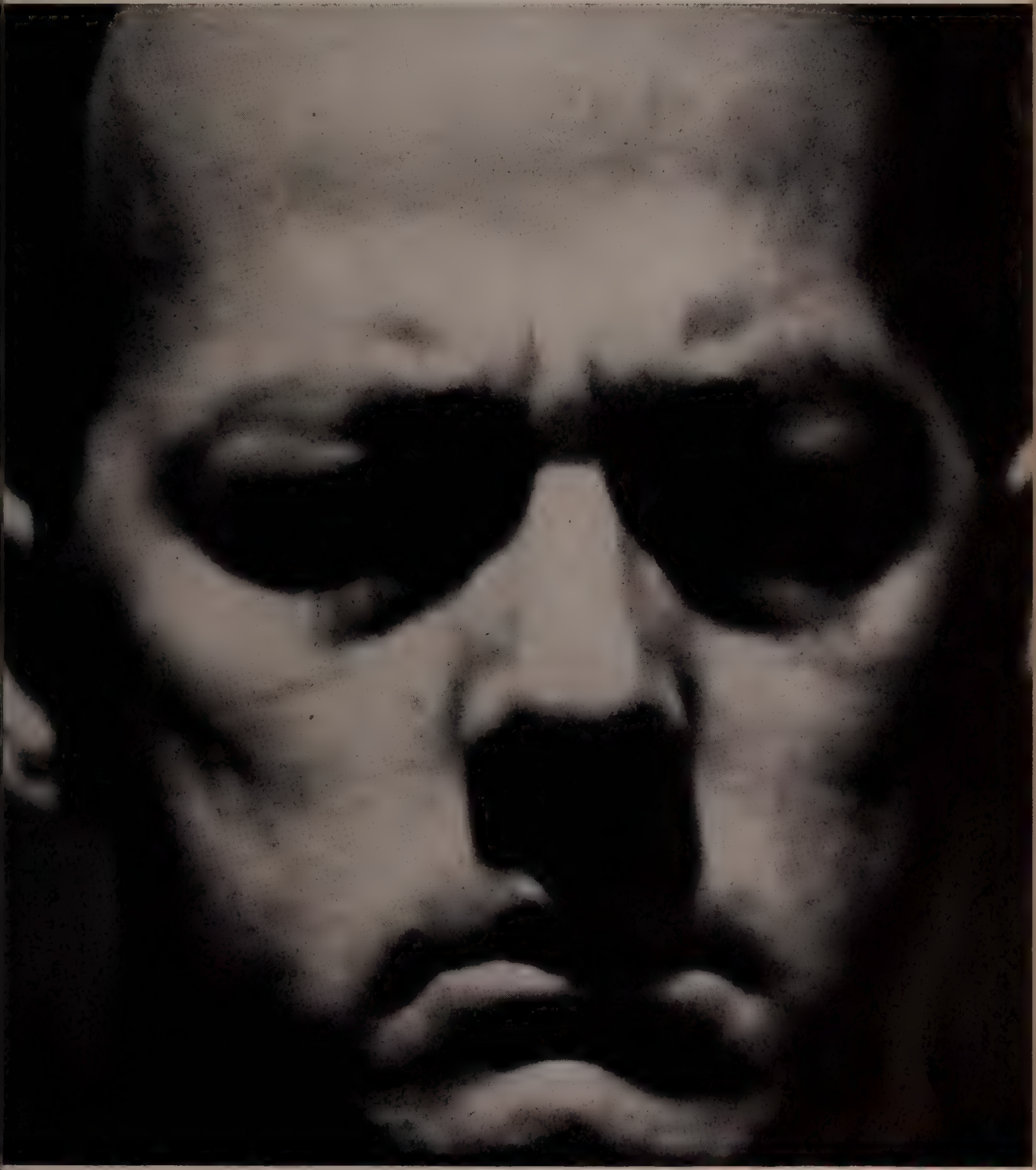

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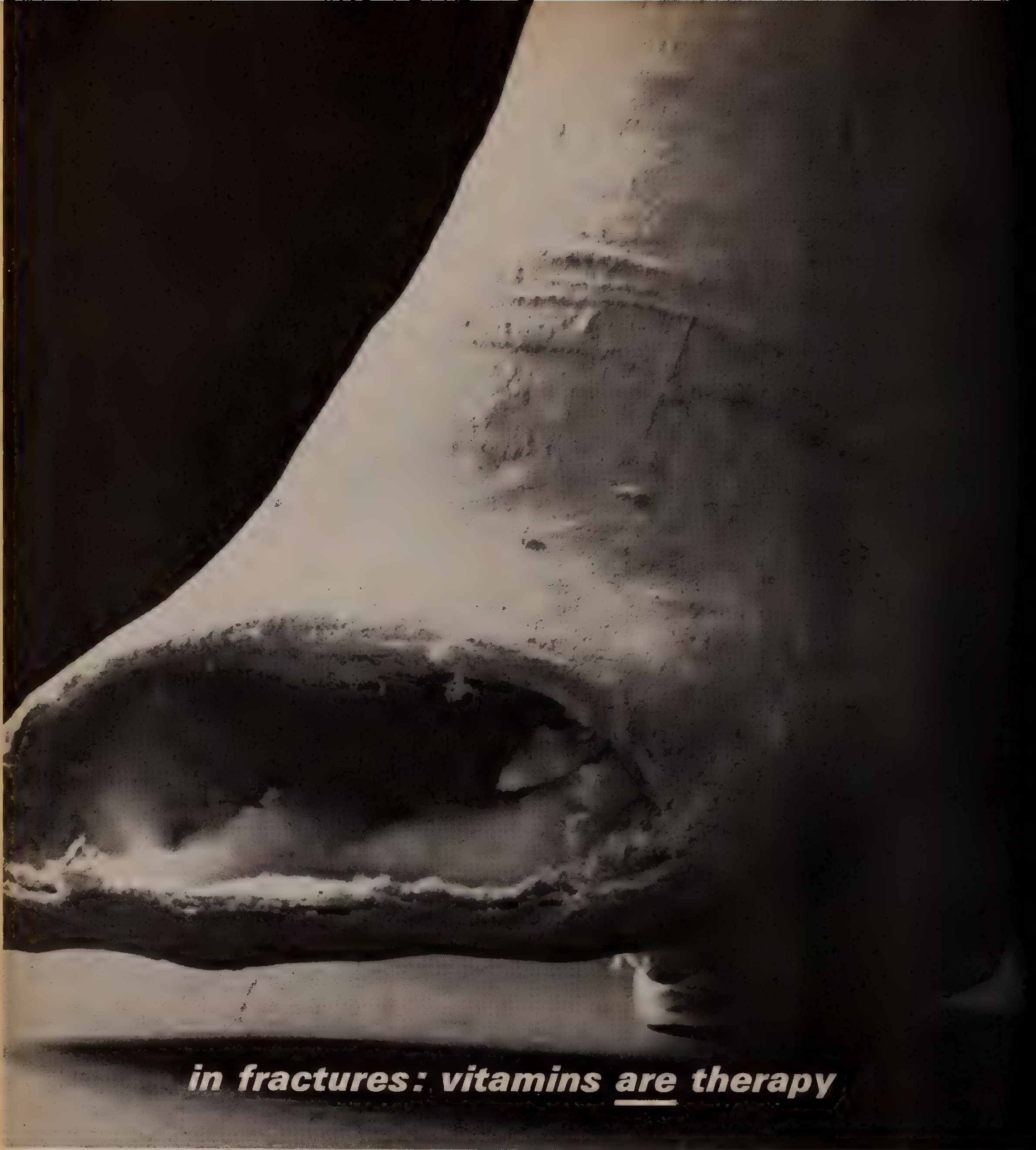

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*McCune, W. G.: M. Clin. North America 44:1479, 1960.

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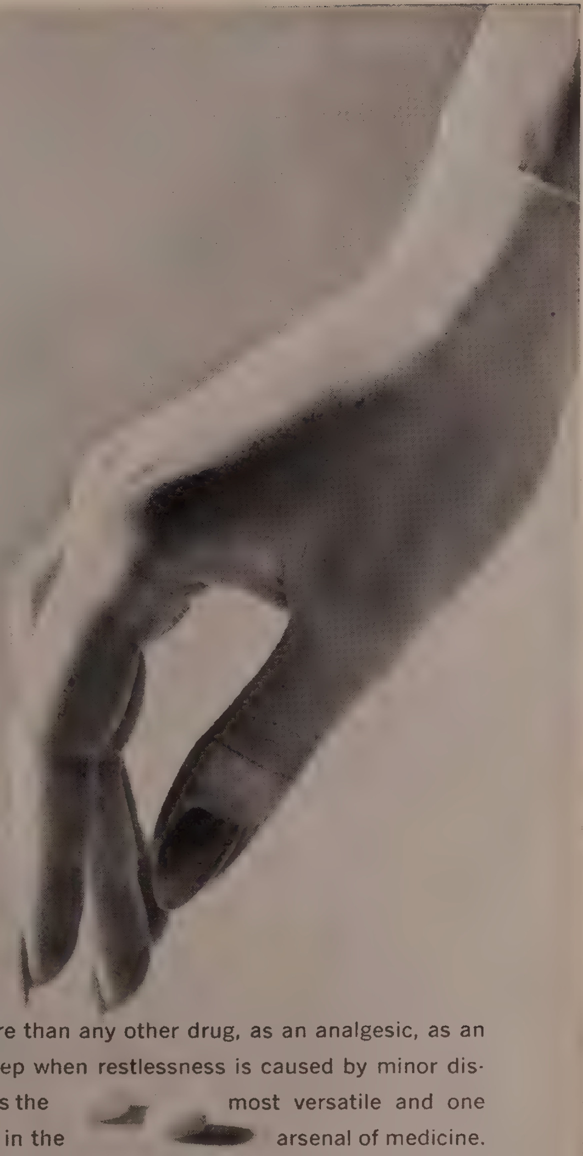
what your patients need to know about Aspirin



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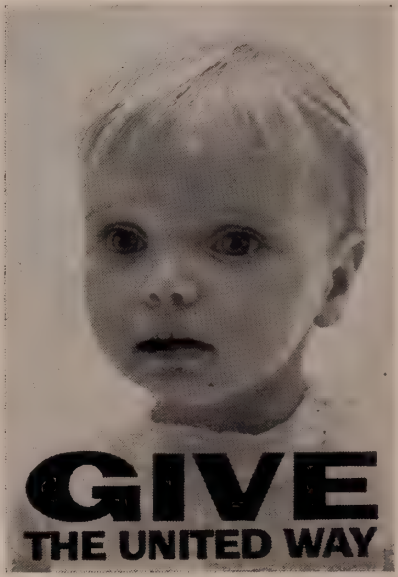

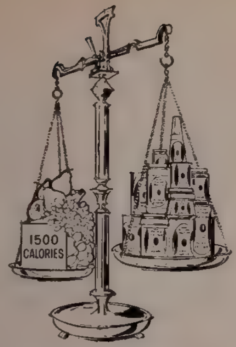

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Chopped Chicken Livers	1 oz.	31	100
Chicken à la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
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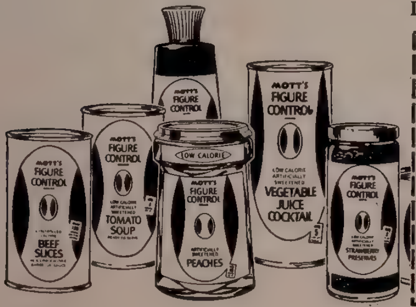

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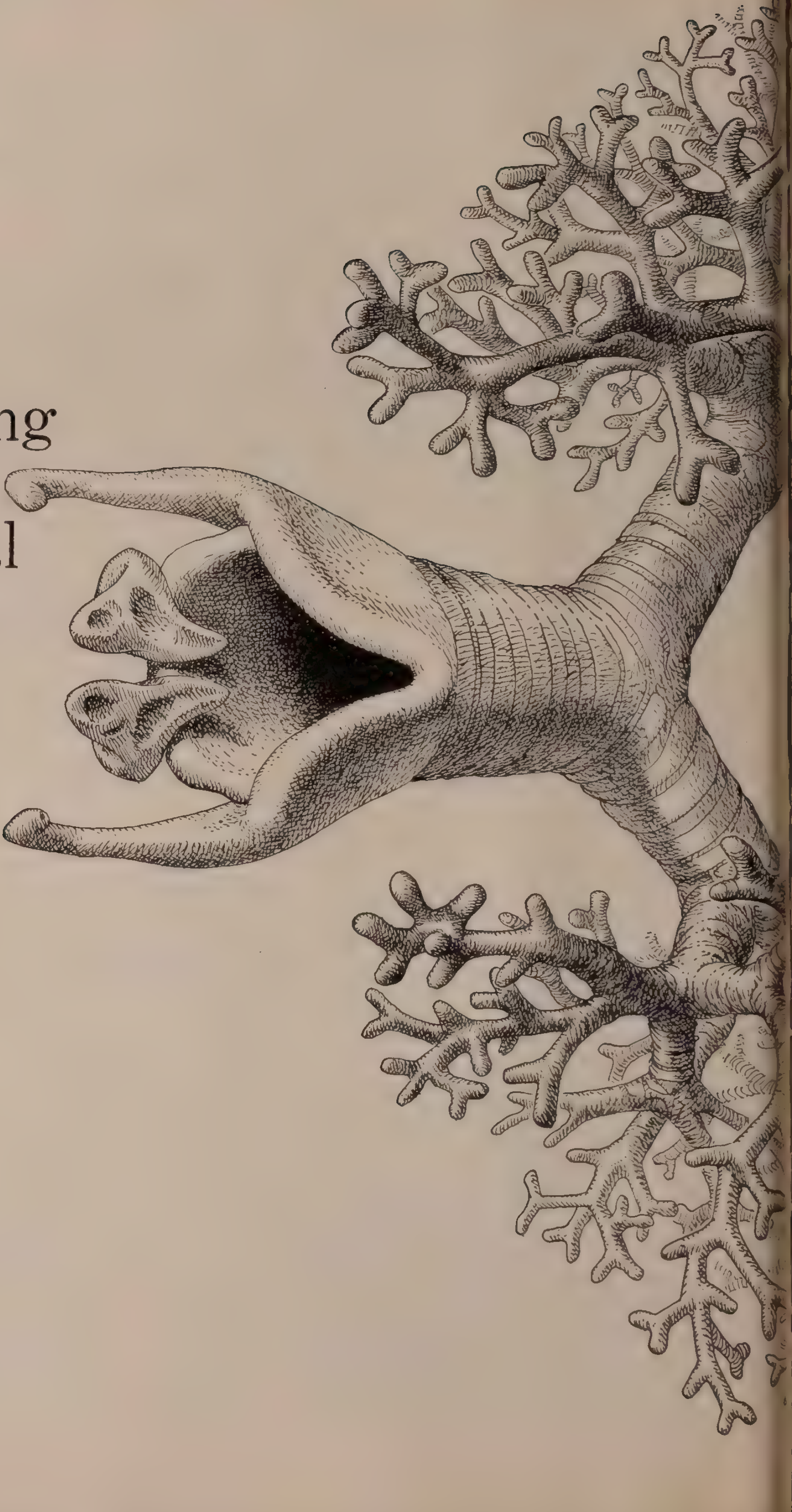

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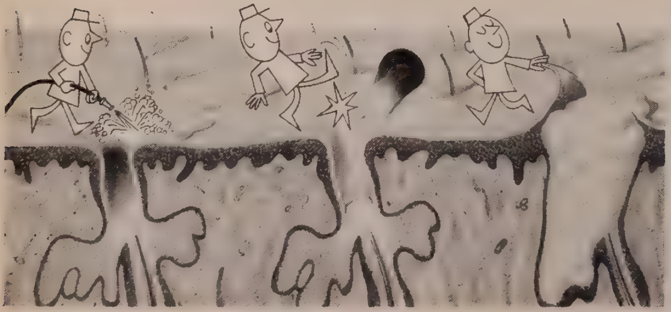

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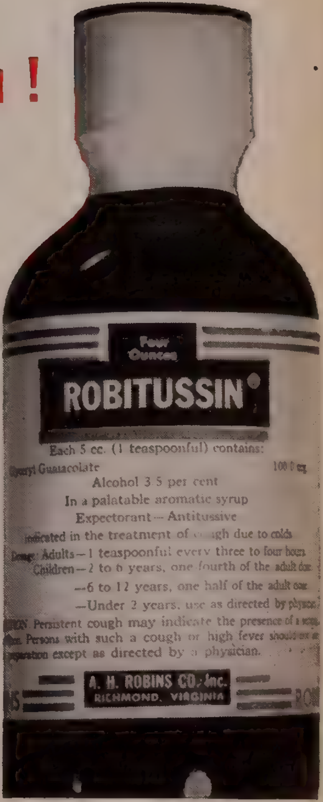
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*Cass, L. J., and Frederik, W. S., Am. Pract. Dig. Treat., 2:844, 1951.

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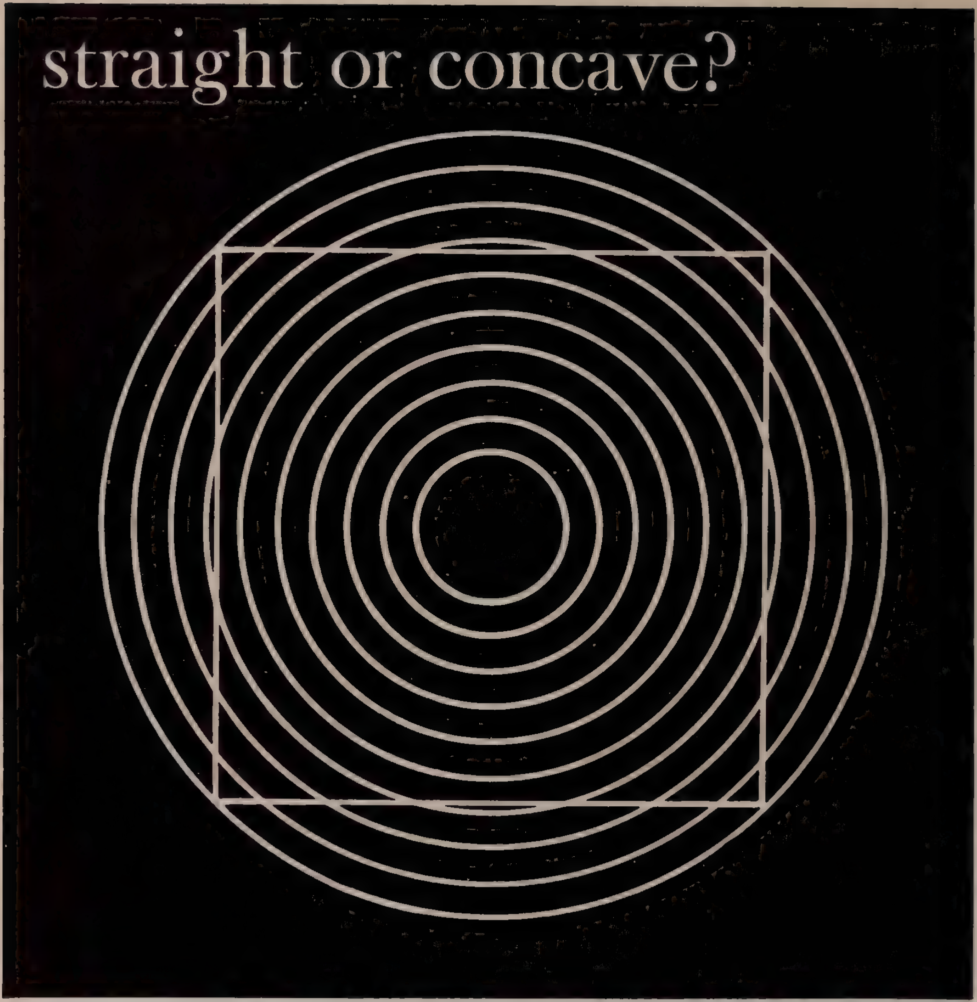
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[1] Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.

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Editorials

Mushroom poisoning

About 100 fatalities from mushroom poisoning occur annually in this country. It is a constantly recurring problem. The differences between the edible mushroom (Agaricus campestris) and the poisonous mushroom (Agaricus fastibilis) are matters for the expert fungologist, and amateurs who are not close to the soil should not attempt decision.

There were two nonfatal outbreaks of mushroom poisoning reported in this State last year in September and October: they involved 5 individuals who picked and ate wild mushrooms; these were described as orange in color and long-stemmed. Three hours following ingestion the victims were seized with violent abdominal cramps, nausea, vomiting, and diarrhea.

The poisonous varieties of mushroom are generally of the Amanita group, the muscaria (fly agaric), the phalloides (death cup), pantherinia (the panther), and the Gyromitra esculeta, the false morel.

Muscaria contains the alkaloid muscarin which acts on the end organs of the parasympathetic system and also stimulates smooth muscle.

Phalloides contains a toxin which also is injurious to all parenchymal cells and brain tissue and, in addition to gastrointestinal symptoms, produces jaundice, oliguria, hematuria, pulmonary edema, mental confusion, convulsions, and coma. Poisoning from phalloides causes a 50 per cent fatality rate.

Immature mushrooms known as buttons are particularly dangerous because at this stage it is extremely difficult to differentiate between the poisonous and the edible varieties.

A considerable folklore about mushrooms has been built up, much of it fallacious. The assertions that a silver coin will tarnish if it is placed in a container with poisonous mushrooms or that those which peel easily are edible are both erroneous. The presence of insects on fungi is no guide since insects infest both edible and poisonous mushrooms. Likewise the notion that soaking or boiling poisonous mushrooms in salt water will render them harmless has no foundation in fact.

Gone are the days of innocent childhood when mushrooms were gathered from the parade ground, rigidly inspected by grandmother who was an expert, and the caps dotted with butter and sautéed on the lid of the cookstove. The taste lingers on and grows more piquant with the years.

Like the parade ground and the horses that fertilized it, the mushrooms are gone and so are the venturesome children; they have grown and now buy their mushrooms at the supermarket. It is better so.

Comment on timely commencement of malpractice case

In two recent cases the Appellate Division of the Supreme Court of the State of New York, Second Judicial Department, has been asked to decide whether or not the time in which to sue a physician for malpractice can be extended by continuation of the treatment after the date of alleged malpractice.

In the first case the plaintiff alleged that the physician had committed malpractice in July, 1954. Since the action was not commenced until July, 1957, it would normally be barred by the two-year Statute of Limitations applicable to malpractice actions.* However, it was argued that since the doctor continued to treat the patient for the same condition, the Statute would not commence to run until the entire treatment was terminated. Since it was admitted that there was no claim of malpractice in the treatment subsequent to July, 1954, the issue was clearly before the Court:

Does the mere continuation of treatment by a physician in the absence of continuing negligence on his part extend the time in which a patient may sue his doctor? The Court held that since the continuing treatment was not negligent, it did not extend the Statute, and the action was accordingly barred because it was not commenced within two years of July, 1954. (227 N.Y.S. 2d 523)

The second case was an action against the City of New York arising out of the treatment of an infant plaintiff at the Kings County Hospital. It was conceded that the last act of alleged malpractice occurred on November 25, 1957, even though the infant was not discharged from the hospital until February 14, 1958.

A notice of claim pursuant to Section 50E of the General Municipal Law was served on April 18, 1958. Since the notice of claim must be served within ninety days of the date on which the claim arises, the Court had to decide whether the time period started to run from November 25, 1957, or February 14, 1958.

The Court held that the claim arose at the time of the alleged malpractice and not when the infant was discharged from the hospital; since notice was not given within ninety days, the complaint was therefore dismissed.

Both of the decisions appear to be well justified. Any other result would seriously impair the effectiveness of the statutes in question.

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* The Statute of Limitations in malpractice actions has been increased to three years, effective September 1, 1963.

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Announcement

1962 District Branch Meetings

Branch	*Date*	*Place*
FIRST	May (at time of State Society meeting)	New York City
SECOND	Sunday, Monday, Tuesday November 11, 12 13	Grossinger's Grossinger, New York
THIRD	*(to be announced)*	
FOURTH	Saturday, September 22	Queensbury Hotel, Glens Falls, New York
FIFTH	Friday, Saturday, Sunday September 7, 8, 9	Whiteface Inn, Lake Placid, New York
SIXTH	Joint meeting with Fifth District Branch	
SEVENTH	Thursday, Friday, Saturday September 20, 21, 22	Grossinger's Grossinger, New York
EIGHTH	Thursday, October 4	Bartlett Country Club Olean, New York
NINTH	May (at time of State Society meeting)	New York City

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Lucien Howe Prize Essay

Radiation Cataractogenesis

SIDNEY LERMAN, M.D.
Rochester, New York

From the Department of Surgery, Division of Ophthalmology,
University of Rochester School of Medicine and Dentistry

THE EYE IS *unusually sensitive to many forms of the two major types of radiation: the electromagnetic spectrum and corpuscular radiation. Radio waves, long-wave diathermy, and visible rays usually do not produce cataracts, but short-wave diathermy and infrared and ultraviolet radiation have a definite cataractogenic potential. While grenz rays, beta radiation, and cosmic rays may produce cataracts, they are of little significance in comparison with other forms of radiation cataractogenesis. Neutrons, roentgen rays, and gamma rays possess the most serious cataractogenic potential. The cataracts produced by these three forms of radiation are similar in appearance and structure, consisting initially of posterior subcapsular and cortical opacities, requiring latent periods before becoming visible, and occurring with doses that do not necessarily produce any other clinically evident lesions. One of the earliest chemical changes observed in the lens following exposure to x-radiation is a rapid fall in the level of SH (sulfhydryl) groups. Experiments on rats have suggested that the initial direct effects of x-radiation of the lens may be due to its action on RNA (ribonucleic acid) and DNA (desoxyribose nucleic acid) within the lens.*

THERE ARE two major types of radiant energy: the electromagnetic spectrum and corpuscular radiation. The former consists of energy which varies in wave length from millimicrons (cosmic rays) located on the short end of the spectrum to many meters (radio waves) on the long end. Included in this category are the following bands, starting from the long end: radio, diathermy, infrared, visible, ultraviolet, grenz rays, roentgen rays, gamma rays, and cosmic rays. The corpuscular radiations are actually the subatomic particles, such as the electrons and the neutron. Almost all of these bands of radiant energy have now been shown to exhibit a cataractogenic action to a varying degree.

As Cogan[1] has pointed out, the eye is unusually sensitive to many forms of radiation. Certain portions of the eye are more susceptible to particular wave lengths. This susceptibility is due to the specific absorption by the anterior segment of the globe of particular bands of radiant energy and the transmission of other wave lengths by these structures to the interior of the eye. Thus the long radio and diathermy waves are readily transmitted through the globe (there is little if any absorption) and therefore do not give rise to any deleterious effects on the lens. However, the shorter diathermy waves, of the order of several centimeters, can be harmful to the anterior half of the eye because of the serious heating effects they produce.

The penetration of the infrared rays is inversely proportional to their wave length; the longer rays are absorbed mostly by the cornea and aqueous humor while the shorter wave lengths can easily reach the retina. The visible spectrum or white light is a mixture of wave lengths located between 770 and 390 millicrons, and their degree of ocular penetration is directly proportional to their length. That is, there is much greater penetration of the red end of the spectrum than of the violet end. Most of the ultraviolet rays up to 320 millimicrons are absorbed by the cornea, while the lens absorbs those between 320 and 390 millimicrons. The vast majority of the grenz rays are absorbed by the cornea, but as one approaches the shorter end of the radiation spectrum, the penetrating powers of the rays are greater. Thus the ordinary x-ray with the potential of from 100 to 250 kilovolts, which is employed most frequently in radiotherapy, is capable of penetrating the globe quite effectively. Gamma and cosmic rays and neutrons can penetrate the eye with ease, even more efficiently than x-rays. Beta and alpha particles, because of their low penetrating power, can be harmful only to the cornea and rarely to the lens.

The lens is probably one of the more susceptible organs in the body with respect to radiation damage. This statement is particularly applicable to the young and rapidly developing lens. Since many of the biologic effects of radiation have not as yet been fully defined, the mechanisms responsible for the enhanced susceptibility by this organ must await further investigation. However, many clues are now available, particularly with respect to x-ray cataractogenesis, which may enable one to arrive at a reasonable hypothesis.

Aside from the detailed histopathologic, histochemical, and biochemical studies which have been pursued over the last few decades, and which will be presented later, there are several more generally obvious factors which might serve to enhance the susceptibility of the lens to the deleterious effects of radiation. As Cogan[1] has noted, this organ is not only avascular, but is also located at least 2 mm. or more from any blood supply, thus making it much less effective in dissipating heat as compared with most other tissues and organs. Since many forms of radiant energy are particularly associated with the production of intense heating, for example, the shorter diathermy waves and infrared waves, this factor may be an important consideration in the enhanced susceptibility of the lens to certain forms of radiation cataract. Another important consideration is the rather unique method of differentiation and growth which is present in the lens. The major metabolic activity, particularly oxidative respiration, occurs within the layer of epithelial cells located only in the anterior subcapsular region extending toward the equator. Thus damage to this area may require a relatively lengthy latent period prior to the clinical manifestation of lenticular opacities. This might apply particularly to the effects of radiant energy on RNA (ribonucleic acid) and DNA (desoxyribose nucleic acid).

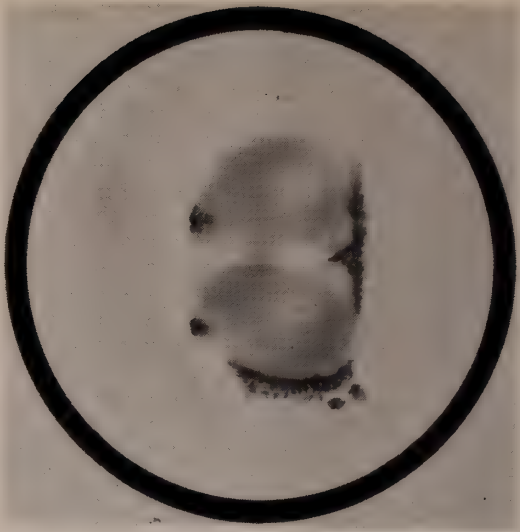

FIGURE 1. Drawing as seen through ophthalmoscope of posterior cortical cataract five weeks after exposure of rabbit eye to microwaves. (Permission Am. J. Ophth. 34: 1001.[5])

Radio waves and diathermy

Radio waves and long-wave diathermy do not produce cataracts at the intensities which are usually employed. However, short-wave diathermy, or microwaves, has been shown to produce cataracts in a variety of experimental animals,[2–8] and there are also well-documented cases of microwave cataractogenesis in man.[9,10] In the experimental animal, the exposure to micro-

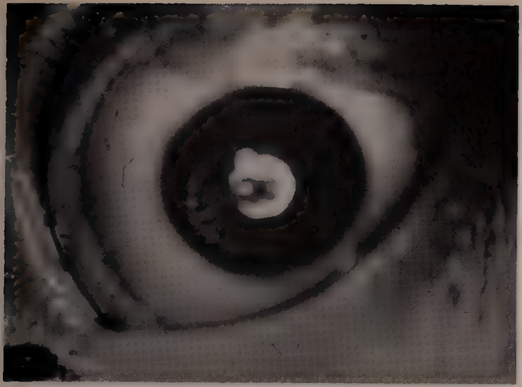

FIGURE 2. Photograph of circumscribed posterior cortical cataract several months after exposure of rabbit eye to microwaves. (Permission Am. J. Ophth. **34**: 1001.[5])

wave diathermy results in the development of two types of lesions.[4,5,7] The first occurs immediately after exposure and consists of grossly visible damage to other ocular structures such as the cornea, iris, and anterior chamber, as well as to the lens. The lenticular lesion consists of a subcapsular opacity which progresses rapidly and coalesces until complete opacification occurs. The second type of lesion is concerned almost entirely with the lens and requires a latent period of several days to several weeks before any changes become visible. Here the lenticular damage is fairly well limited to the posterior cortical zone (Figs. 1 and 2). The mechanism responsible for microwave cataractogenesis is believed to be mainly a thermal one in which the maximum heating effect is produced adjacent to or within the epithelial layer of the lens.[1,2,6]

Infrared and visible radiation

The cataractogenic potential of infrared radiation has long been recognized and was first observed in glassblowers, hence the name glassblower's cataract.[11] Similar lesions have been reported in other industries in which workers were exposed to excessive amounts of heat.[12] This type of cataract occurs only after an individual has been exposed to intense heat for many years. The resulting lesion usually consists of posterior cortical opacification combined with a characteristic lamellar splitting of the anterior lens capsule (Fig. 3) and usually is referred to as exfoliation of the lens capsule. This condition may result in secondary glaucoma if the exfoliated pieces of the lens capsule succeed in plugging completely the trabecular pores, the inlet of the aqueous humor drainage mechanism.[13]

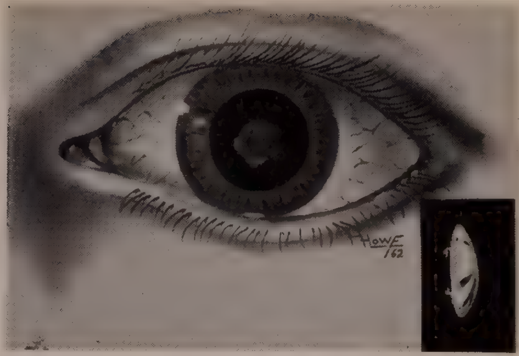

FIGURE 3. Drawing of glassblower's cataract.

The experimental production of infrared cataracts, which requires heat much greater than the intensities to which human beings are ordinarily exposed, indicates that the lesion results from a local thermal effect rather than from the absorption of specific rays by the lens fibers, as advocated by Vogt.[14,15] Recent experiments by Langley, Mortimer, and McCulloch[16] indicate that the lenticular lesions following the exposure of an animal to an infrared cataractogenic dose of radiation are located adjacent to burned areas of the iris. These studies tend to confirm Goldmann's[17] observations that the lenticular changes occur secondarily to heating. That is, the infrared rays are absorbed by the iris pigment epithelium and then converted to heat, thus damaging the adjacent lens epithelium.

Although there is a greater incidence of cataracts in the tropical countries and their age of onset is earlier than in the temperate climates, it is unlikely that visible radiation by itself is responsible for this phenomenon. In these tropical zones the population not only is exposed to more intense sunlight and hence more infrared radiation, but also many inhabitants are subject to dietary conditions which are different from our standards of nutrition. It is quite likely that this latter consideration together with possible genetic factors are of greater importance in the apparently higher incidence of cataracts in tropical zones.

Ultraviolet radiation

Since the cornea absorbs almost all of the ultraviolet rays up to 320 millimicrons, this form of radiation, when it is employed as a cataractogenic source, will be accompanied by severe corneal damage. Furthermore, several investigations on the transmittance and absorbance of ultraviolet radiation including the longer rays (over 320 millimicrons) indicate that the amount of this form of radiation required for a minimum or threshold response in the lens would be two or three times the amount necessary for a similar reaction in the cornea.[18–20] It would seem thus that under ordinary circumstances the deleterious effects of ultraviolet radiation with respect to its cataractogenic action is of little significance. Severe corneal burns would have to ensue prior to the development of lenticular damage.

Of interest is a recent report by Cloud, Hakim, and Griffin[21,22] concerning the photosensitization of the guinea pig and mouse eye with methoxsalen. These workers have demonstrated that laboratory animals can be sensitized to a previously harmless form of radiant energy, the long ultraviolet rays (320 to 400 millimicrons), resulting in a high incidence of cataracts as well as some damage to the cornea and iris. Since this compound has been employed recently in this country as a suntanning agent and has also been used for many years in treating vitiligo, methoxsalen could be a potential source of serious intraocular lesions. The authors mention several other photosensitizing drugs in common usage here such as chlorothiazide (Diuril), tolbutamide (Orinase), and phenothiazine, but they believe that only methoxsalen and phenothiazine should be considered the most potentially harmful drugs with respect to intraocular damage since they are activated at wave lengths above 320 millimicrons and thus are transmitted beyond the cornea.

Aside from the dangers inherent in the use of methoxsalen, it is important to note that phenothiazine has been widely employed as one of the popular tranquilizer agents, and thus the potential for intraocular damage with this drug may be much greater. Several reports have already appeared in the literature regarding ocular complications resulting from the use of phenothiazine tranquilizers.[23,24] These lesions include pigmentary and toxic retinopathy and toxic amblyopia. However, the mechanisms responsible for these lesions apparently are not related to photosensitization. This form of ocular toxicity is due to a specific enzyme inhibition in the retina as well as to a high concentration of this drug in the uvea.[25]

Grenz rays

Although grenz rays are capable of inducing cataracts, their relatively low degree of penetration renders them of little practical significance with respect to other forms of radiation cataractogenesis. Severe corneal damage would always ensue if these rays were employed as cataractogenic agents. The same is true of beta radiation, although this form of corpuscular energy has been employed too frequently in the treatment of anterior ocular lesions, for example, pterygium and corneal vascularization, without proper precautions, which results in cataract formation.[26–31] Experimental beta radiation cataracts have also been produced by several investigators.[29,32,33] Since the cataractogenic threshold dose is lower when the beta applicator is applied over the limbus at which point it is closest to the lens, one should be particularly careful when employing this form of therapy for limbal or perilimbal lesions.

Neutrons, roentgen rays, and gamma rays

Of the remaining forms of radiant energy to be considered in this discussion, cosmic rays do not constitute at present a hazard to the lens. The neutron and roentgen ray, however, possess the most serious cataractogenic potential, and this problem is one of ever-increasing gravity because of the prevalence of x-ray therapy and the increasing development and application of neutron

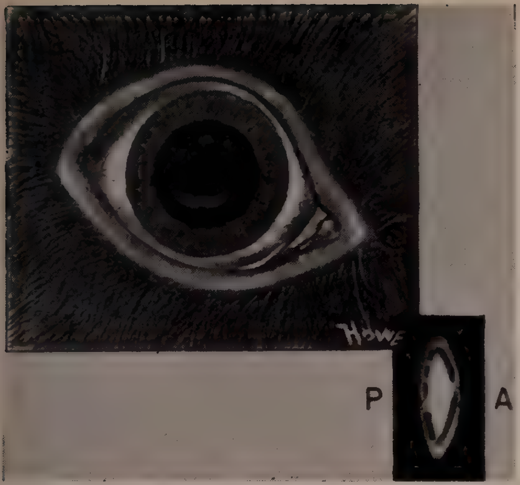

FIGURE 4. Drawing of posterior cortical opacity in dog two and one-half years following exposure to 1,000 r x-radiation. (Reproduced by permission of Dr. S. Michaelson, Atomic Energy Commission, University of Rochester.)

emitters. Aside from the lenticular changes induced by the two nuclear explosions in Japan, scattered reports have appeared in the literature regarding the occurrence of cataracts in individuals exposed to neutron beams emitted from cyclotrons.[31–47] The experimental production of neutron cataracts also has received considerable attention.[48–60] It is now evident that the cataracts which result from exposure to neutrons, x-rays, and gamma rays, both clinically and experimentally, are all similar in appearance and in structure (Fig. 4), consisting initially of posterior subcapsular and cortical opacities. They all require latent periods before becoming visible, and they can occur with doses that do not necessarily produce any other clinically evident lesions. Furthermore, the greater the dose of these forms of radiation is, the shorter the latent period is, the more intense the damage to the lens, and the more rapid the progression of the opacities.

In studying the relative biologic effectiveness of neutron, x-rays, and gamma rays for the production of lenticular opacities in the experimental animal, Upton and his coworkers[61] concluded that cyclotron neutrons of 1 to 2 million electron volts mean effective energy, given at high intensity, had from two to four times as effective a cataractogenic action as 250 kilovolts peak x-rays and were from three to four times as effective as 1.2 million electron volts gamma rays. They found also that there was a species variation with respect to the radiosensitivity of the lens. In the species they studied, the mouse lens exhibited the greatest sensitivity followed by the lens of the rat, guinea pig, and rabbit in a decreasing order of sensitivity. Very little is known regarding the biochemical mechanisms involved in the pathogenesis of the neutron cataract; however, many investigators believe that the biologic effects of neutron and roentgen radiation are similar. The similarity in the appearance and structure and the requirement of a latent period for both of these forms of radiant energy has already been cited.

CLINICAL AND EXPERIMENTAL INVESTIGATIONS. Of all the forms of radiation cataract that have been observed, x-ray cataracts have been subjected to the most intensive clinical and experimental investigations. In 1897, two years after x-rays were first described, Chalupecky[62] noted that rabbit eyes which were subjected to x-radiation showed pathologic changes. This was probably the first report of the deleterious effects of x-rays on ocular tissues, and since then numerous clinical,[1,63–85] pathologic, and histochemical studies in the human being as well as in the experimental x-ray cataract[86–120] have appeared in the literature. The minimal dose level of x-radiation cataract has also received considerable attention,[61,121–129] and it is now generally accepted that the threshold dose for the human being is of the order of 500 to 600 r with the type of x-rays usually employed (100 to 250 kilovolts peak). In the experimental animal, the dose exhibits a species variation.[61] These cataractogenic doses refer to a localized portal rather than whole body radiation. Although the single cataractogenic dose is similar to an epilation or erythema dose, small repetitive exposures will result in cataract formation at a total dose level which is considerably less than the amount required for any other clinical abnormality, including erythema and epilation.[130]

The duration of the latent period for the

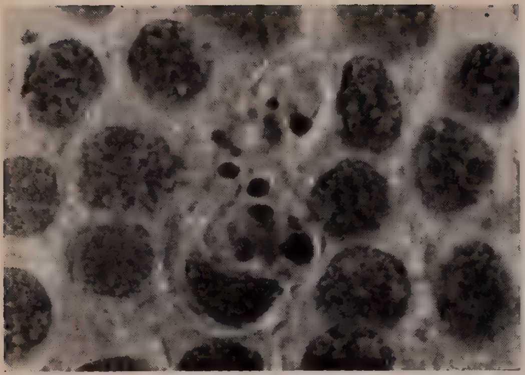

FIGURE 5. Nuclear fragmentation and extrusion of Feulgen-positive material into cytoplasm and extracellular phase. Lens epithelium three days after irradiation of rabbit eye with 2,000 r. (Permission A.M.A. Arch. Ophth. **48:** 276.[172])

lenticular opacities to become clinically manifest (which is usually six to twenty months) in general is related inversely to the dose. There is a similar relationship between the susceptibility of the lens and the age of the animal, the fetal lens being the most vulnerable to x-ray damage. Experiments in which specific portions of the lens were shielded indicate that the actively growing equatorial portion is most sensitive to injury by roentgen radiation while the pupillary zone is least sensitive.[131-134]

MORPHOLOGIC AND HISTOCHEMICAL INVESTIGATIONS. The extensive morphologic and histochemical investigations on x-ray cataractogenesis previously cited[86-120] have shown that the initial changes in such lenses occur mainly in the epithelial layer and lenticular opacities develop because of pathologic alterations in these cells. The most striking changes develop within the cell nuclei particularly in those cells located at the equatorial zone. Von Sallmann and others[92-94,97,98,102,103,108,109,114,115] have demonstrated that microscopically apparent early radiation damage precedes the development of clinically visible changes by many days or weeks. He noted the rapid and marked inhibition of cellular mitosis which occurs soon after exposure to roentgen rays and the nuclear fragmentation, degeneration, and extrusion of chromatin material from these cells which become manifest shortly thereafter (Fig. 5). The initial and marked depression of cell division was followed by a relatively short-lived but marked increase in mitoses after varying periods of time. In the rat this "overshoot" occurred from two to four days after exposure, and in the other species studied (mice, dogs, cats, and monkeys) this phenomenon did not become apparent until from seven to ten days postirradiation.

Von Sallmann and Locke[135] suggested that the pathogenesis of x-ray cataract might be explained by postulating two sets of lesions. The primary lesion would be located in the nuclei of the germinative cells, which are found at or near the equator of the lens, while the secondary state, which leads to the destruction of the lens fibers and eventual dense opacification, could be due to chemical changes. They proposed that the latter might be due to an alteration in the permeability of certain phase boundaries within the lens.

BIOCHEMICAL STUDIES. A considerable number of reports have appeared in the last decade dealing with biochemical studies on x-ray cataractogenesis.[42,136-154] On the basis of extensive biochemical investigations, Pirie[154] has also concluded that the development of radiation cataracts may proceed in two stages; the first is due to the direct effects on the lens epithelium while the second stage involves damage to the lens fibers. She suggested that many of the biochemical alterations observed during the formation of x-ray cataracts may belong to this second stage.

One of the earliest chemical changes observed in the lens following exposure to x-radiation is a rapid fall in the level of SH (sulfhydryl) groups.[137,138,142,143,145] The most marked decline occurs in the concentration of glutathione and becomes evident twenty-four hours after exposure. Similarly the activity of those enzymes which require SH groups is affected prior to the enzymes which are not SH-dependent. However, this change in enzyme activity occurs a good deal later than the decline in glutathione concentration.

Studies in this laboratory on the effect of x-radiation on protein, carbohydrate, and RNA metabolism in the rat lens indicate that a marked alteration in RNA metabolism develops within six hours of exposure.[155] The lens contains at least three forms of RNA: soluble, microsomal, and albuminoid, and it is the latter which initially is most affected by x-radiation.[155,156] Although an RNA fraction analagous to albuminoid RNA has been found in certain bacteria, no similar fractions have as yet been reported in other animal tissues.[157-159] In the five-week-old rat lens, albuminoid RNA represents about 12 per cent of the total RNA while soluble RNA (SRNA) represents approximately 15 to 20 per cent.[155,156] As the rat ages there is a decrease in total RNA; the most marked fall occurs in the microsomal fraction which is most striking in senile rats and can be correlated with an almost complete cessation of soluble protein synthesis.[156] However, the synthesis of albuminoid protein continues throughout life, albeit at a progressively slower rate, and albuminoid and soluble RNA may be required for this process, hence the relatively smaller change in these two fractions as compared with microsomal RNA.

The earliest effect of roentgen rays on the lens of a five- to six-week-old rat that has been demonstrated so far is a marked increase in the turnover of albuminoid RNA (50 to 100 per cent increase) as measured by radioactive phosphorus (P^{32}) incorporation experiments. This phenomenon occurs within six hours after exposure and continues for at least one week while microsomal and soluble RNA remain unchanged.[155,160] The turnover of albuminoid RNA then returns to relatively normal limits by the second or third week, at which time the initial changes in carbohydrate metabolism first become manifest. The concentration of lactic acid begins to decrease at the third to fourth week postirradiation, and a decline in the activity of glucose-6-phosphate dehydrogenase as well as some of the glycolytic enzymes becomes manifest shortly thereafter.[154,160] A measurable loss in adenosine triphosphate (ATP) can be seen one week after irradiation although the activity of the oxidative enzymes of the Krebs cycle remains unimpaired for a relatively long time.[154] There is a slow and progressive decline in the level of soluble protein in x-irradiated lenses as compared with control lenses[151,154,160]; however, a slight increase in the concentration of albuminoid protein becomes evident at three to four weeks postirradiation.

The results of these biochemical experiments indicate that there is an initial direct effect of x-irradiation on at least one fraction of lenticular RNA. It is quite likely that this effect might be similar to the one observed on the nucleic acid from tobacco mosaic virus (TMV).[161-165] The RNA isolated from irradiated tobacco mosaic virus was found to be less viscous than that isolated from the control virus, and there was an inactivation in the infectivity of such irradiated viruses. These effects were shown to be due to radiation-induced breakage of the RNA strand somewhere in the main chain. Albuminoid RNA is tightly bound to the insoluble protein fraction of the lens and as such may be similar in some of its physicochemical states to tobacco mosaic virus RNA which is rigidly embedded in the viral protein.[166] Thus x-radiation may have a similar action on albuminoid RNA.

Since the lens contains so little DNA as compared with RNA (less than one twentieth) it is difficult to do any specific analyses on this moiety. However, it is not unlikely that roentgen rays also exert an initial direct effect on lenticular DNA. The morphologic and cytochemical studies by von Sallmann referred to previously do in fact indicate that such is the case. Working with tissues containing much larger quantities of DNA than the lens, for example, the thymus, regenerating liver, and so forth, several investigators have shown that x-radiation does have a definitive inhibitory action on DNA synthesis which may be temporary or permanent.[167-171] This effect may be due to a blockage of one or more enzymes necessary for DNA synthesis or to damage of the DNA in such a manner that it cannot be replicated, perhaps by inhibiting its priming action.

Thus the initial direct effects of x-radiation on the lens may be due to its action on RNA and DNA. The second stage in radiation cataractogenesis, which involves damage to the lens fibers and opacification, is probably due to the biochemical alterations previously cited, which develop during the many weeks of the latent period present in this form of cataractogenesis.

The interesting phenomenon reported by several workers regarding the protective action of SH compounds, especially cysteine, against radiation damage to the lens is not too well understood but quite likely is related to the fall in SH groups (glutathione) following exposure to x-rays.[172–174] Recently Pirie and Lajtha[174] have proposed a hypothesis based on their experimental observations. They noted that cysteine arrests cell division in the epithelial cells of the rabbit lens. If this compound was injected prior to exposing the rabbit to x-irradiation the number of fragmented nuclei that usually develop afterward is reduced. They postulated, therefore, that cysteine protection may be related to its ability to arrest mitosis, acting on the cell early in the interphase prior to the locus at which x-radiation exerts its effects (late interphase and/or prophase). Thus such protection would be incomplete since not all cells are in the same phase of reproduction at the same time; in fact cysteine protection against x-ray damage has never been found to be complete. However, there is insufficient experimental evidence regarding this hypothesis, and it is also possible that cysteine-treated cells are capable of an enhanced recovery.

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Prepared Saccharin Solution for Study of Circulation Time

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TABLE I. Normal patients

Patients	Age (Years)	Time (Seconds)* Initial	Repeat
1	18	12	12
2	23	14	13
3	25	13	14
4	25	15	12
5	26	18	. . .
6	27	10	10
7	28	13	15
8	29	11	13
9	30	12	. . .
10	30	11	12
11	30	13	15
12	34	13	15
13	36	10	. . .
14	39	12	12
15	43	12	. . .
16	46	12	. . .
17	47	12	13
18	50	15	. . .
19	52	14	. . .
20	60	15	13
21	61	12	. . .
22	66	15	12
23	70	11	. . .
24	76	11	. . .
25	76	16	18
26	76	15	. . .
27	86	18	. . .

* Mean = 14.2 ± 2.4

THE CLINICAL VALUE of determining the circulation time is well established.[1] Unfortunately, nearly all of the substances used in performing this test are either associated with a degree of systemic toxicity or involve the use of equipment which is not readily available at the bedside.

Sodium dehydrocholate (Decholin), the material most commonly used in studying the circulation time, is highly satisfactory as to its end point and reproducibility. However, reports of dangerous allergic reactions to this drug have appeared in the literature[2,3] and have spread by word of mouth. Anxiety regarding the use of sodium dehydrocholate has reached such proportions that many students and physicians avoid its use and, therefore, fail to gain the valuable information available from a determination of the circulation time.

The sharp end point and minimal toxicity of saccharin led Morris and Blumgart[1] to state that this substance "is one of the most desirable" for the measurement of the circulation time. In the past, the material for injection had to be prepared by dissolving soluble saccharin in distilled water and then heating this until the substance went into solution. This time-consuming procedure has apparently prevented the widespread use of saccharin.

The development of soluble saccharin compounds for sweetening beverages led us to seek a saccharin solution preparation for intravenous use. This material was made available especially for our clinical investigative purposes* and has been studied. It is the purpose of this report to describe the reliability and apparent safety of this new intravenous saccharin solution.

Materials and methods

Saccharin, 2.5 Gm., was dissolved in a glycerin and water base such that the total volume was 4 cc. The material was prepared in individual, sterile ampules. At room temperature, the fluid is clear and transparent. It is suggested that the ampule be warmed in the hand before it is used to ensure a crystal-free solution.

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* Prepared through the courtesy of E. R. Squibb & Sons, New York City.

Normal volunteers or patients without evidence of cardiac disease, fever, anemia, or metabolic disorders associated with a high cardiac output were selected as subjects. The majority of the individuals were studied under basal conditions; all were in the recumbent position. Four cc. of the saccharin preparation were injected rapidly into an antecubital vein through a number 17 needle. The injection time was two seconds or less. The circulation time was measured from the start of the injection to the reported perception of a sweet taste in the tongue.

A STUDY WAS MADE *of a new intravenous saccharin solution, suitable for storage in ampule form, to determine the arm-to-tongue circulation time in 27 normal subjects and 13 patients with congestive heart failure. The technic was safe, and the results were accurate with a reproducible end point; no systemic reactions occurred. The data are comparable to those obtained using sodium dehydrocholate but with none of the allergic reactions frequently reported with the latter.*

Results

The circulation times determined in the 27 normal subjects are presented in Table I. The range of circulation time in these individuals (42 determinations) was from ten to eighteen seconds (mean = 14.2 ± 2.4 seconds). Of the total, 33 (78 per cent) were between twelve and sixteen seconds. These data are entirely comparable to those obtained using sodium dehydrocholate.[1,4] The end point was sharp and definite in all 42 determinations. To determine reproducibility, the test was performed on two occasions in 15 normal subjects. The results did not differ, if at all, by more than two seconds in 13 individuals; 2 subjects demonstrated a variation of three seconds.

Thirteen patients (Table II) with congestive heart failure were studied. In all the end point was definite, but its sharpness appeared inversely related to the circulation time. In 3 patients with prolonged circulation times, the results were found to be reproducible. In 8 patients with heart failure, determinations were repeated after therapy and showed a return to the normal range.

Saccharin has been a widely and well-studied substance. Its toxicity in animals has been investigated by Fitzhugh, Nelson, and Frawley[5] who did not find any serious side-effects when saccharin was administered orally or parenterally. In earlier studies of the use of saccharin for the determination of circulation time, no allergic or systemic reactions have been reported.[6,7]

Our subjects were selected without regard to a prior history of allergy. In 18 patients, the circulation time was repeated at least twice at intervals varying from five minutes to two weeks. No systemic reactions were observed.

Table II. Patients with congestive heart failure

Patient	Etiology	Age (Years)	Time (Seconds) Initial	Time (Seconds) Repeat
1	Myocarditis	34	35	34
2	Rheumatic heart disease	37	25	23
3	Arteriosclerotic heart disease	51	19	19
4	Arteriosclerotic heart disease	54	30	. . .
5	Arteriosclerotic heart disease	54	27	. . .
6	Rheumatic heart disease	57	42	. . .
7	Arteriosclerotic heart disease	57	23	. . .
8	Hypertensive cardiovascular disease	62	38	. . .
9	Rheumatic heart disease	66	23	. . .
10	Arteriosclerotic heart disease	69	36	. . .
11	Arteriosclerotic heart disease	71	32	. . .
12	Hypertensive cardiovascular disease	76	20	. . .
13	Arteriosclerotic heart disease	79	40	. . .

In all 200 injections of the saccharin preparation have been given, including those which followed the primary investigation of this material. In three instances, a large portion of the saccharin was inadvertently administered subcutaneously, resulting in immediate, moderately severe local pain, followed by a low-grade, inflammatory reaction in the area of injection. The prompt application of an ice pack readily ameliorated the pain, and the local reaction subsided without other treatment in from four to seven days. No evidence of suppuration developed.[8] Transient arm pain following an uncomplicated injection was reported by 4 subjects, 1 of whom developed a painful local thrombophlebitis on the following day. Two individuals developed an overt, superficial thrombophlebitis, extending two thirds of the way up the arm, two days after a painless injection; these subsided rapidly without therapy. A palpable, venous cord, not associated with any known infiltration, was noted by 2 subjects several days after their injections.

Three patients noted mild nausea at the time of the end point. This response seemed related to the intensity of the sweet taste and was abolished by halving the dose. (It is noteworthy that the sharpness of the end point was reduced at a lower dosage.) Some subjects commented on an associated facial warmth at the time they preceived the sweet taste.

When it is administered intraperitoneally in animals, saccharin has been reported to cause a slight lowering of the blood sugar.[9] Jorgensen[10] reported an inconstant decrease in blood sugar following the ingestion of large oral doses of saccharin. No hypoglycemic symptoms were noted in our subjects, who were usually in the fasting state. The blood glucose levels were not measured.

Comment

A suitable agent for the determination of the circulation time should be nontoxic, convenient, relatively inexpensive, with a reproducible end point. Sodium dehydrocholate has achieved widespread popularity, but the possibility of severe adverse reactions has impaired its usefulness. Magnesium sulphate and calcium gluconate have also been associated with significant reactions.[1]

Sodium succinate has been associated with at least one instance of sudden death following its use.[11] In addition, Schoenfeld and Messeloff[4] have demonstrated its lack of reliability. A determination of the circulation time by means of fluorescein or radioactive isotopes is somewhat impractical for routine clinical purposes.

Saccharin has been demonstrated to be safe and accurate with a reproducible end point.[6,7] Using the ampules prepared for this study, these features have been confirmed, and the criterion of convenience is now fulfilled. Extravasation of the material into subcutaneous tissues and local thrombophlebitis represent the only potential hazards to date. The end point is pleasant and easily described to the patient. Repeated injections do not impair a perception of the sweet taste.[6]

Summary

A new saccharin solution, suitable for storage in ampule form, has been found to be without systemic toxicity and satisfactory for measuring the arm-to-tongue circulation time. Local thrombophlebitis occurred in only 3 of 200 injections.

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Symptomatic Abdominal Aortic Aneurysm

Need for Accurate Diagnosis and Prompt Surgery in Improving Surgical Salvage Rate

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AN ANALYSIS WAS MADE *of 14 patients with ruptured or rapidly expanding abdominal aortic aneurysms. The cause of death in the 14 cases, all subjected to emergency surgery, was hemorrhage with renal shutdown and continued shock in 11, coronary occlusion in 2, and cerebral vascular accident in 1. Unnecessary delay occurred in almost every instance, and early, accurate recognition of the lesion and prompt surgical intervention might have improved the salvage rate. Over a period of five years the mortality rate for elective resection of these lesions, when intact, was 9 per cent, whereas with those lesions treated after rupture or rapid enlargement, the mortality rate was 80 per cent.*

THE PURPOSE of this report is to emphasize the significant role early and accurate diagnosis and prompt surgical intervention can play in improving surgical results in the treatment of ruptured or rapidly expanding abdominal aortic aneurysms. An analysis of an experience with 14 patients with these lesions, treated surgically at St. Luke's Hospital in the period 1954 to 1961, will be presented.

The wide disparity between the mortality rate obtained from the surgical removal of the intact, often asymptomatic, abdominal aneurysm and that resulting when the aneurysm has undergone rapid expansion or rupture is common knowledge.[1-3] In our total experience of the past five years, the mortality rate for elective resection of these lesions, when intact, was 9 per cent; whereas with those lesions treated after rupture or rapid enlargement, the mortality rate was 80 per cent (Table I). The majority of patients in the latter category were in a critical condition preoperatively, and all but 2 were in shock at the time of surgery. The cause of death in the 12 cases, all subjected to emergency surgery, was hemorrhage with renal shutdown and continued shock in 9, coronary occlusion in 2, and cerebral vascular accident in 1.

In surveying this series of 14 patients, it was readily apparent that, in most instances, irreversible shock and its related complications negated much chance of salvaging many of the cases before the surgical procedure was undertaken. It was obvious that any improvement that could be expected depended principally on early, accurate recognition of the lesion and prompt surgical intervention. A careful review of the charts of the patients operated on for aneurysmal rupture indicted unnecessary delay as a constant common denominator in almost every instance. Factors for this delay fell mainly into four categories:

1. Delay in hospital admission following the onset of symptoms related to the aneurysm.
2. Undue delay in the hospital in establishing the diagnosis and in evaluating the patient's cardiac, renal, vascular, and cerebral status.

TABLE I. Aneurysm of abdominal aorta: St. Luke's Hospital, 1954 to 1961

Resection Procedure	Number of Patients 1955 to 1959	Number of Patients 1957 to 1961	Deaths 1954 to 1957 Number	Deaths 1954 to 1957 Per Cent	Deaths 1957 to 1961 Number	Deaths 1957 to 1961 Per Cent
Elective	14	31	5	36	3	9
Emergency	3	11	3	100	9	80

3. Hesitancy on the part of the internist in declaring the case a true surgical emergency with any patient presenting a symptomatic abdominal aortic aneurysm.
4. Inaccurate diagnosis with time spent in summoning consultants to rule out orthopedic, urologic, or intestinal etiology for the patient's complaints.

Case reports

CASE 1. A seventy-five-year-old male was admitted on June 27, 1959, with a known aneurysm of the abdominal aorta, existing for three years. For two weeks prior to admission he had had recurring attacks of back pain, and twenty-six hours prior to admission the pain became excruciating in character. The patient was seen by his physician in the morning and again in the afternoon of the day of his admission to the hospital, but he was not admitted to the hospital until 6:00 P.M. The aneurysm was easily palpable on abdominal examination. The hemoglobin was 16.7 Gm. per 100 ml. on admission. En route to the operating room two hours following admission, the patient went into shock and died on the operating table as the abdominal incision was being performed. A large ruptured abdominal aortic aneurysm was found.

COMMENT. In our experience and that of others it is a documented fact that, in the majority of patients, overt rupture of an aneurysm is very often preceded by limited hemorrhage into the retroperitoneal space, with temporary tamponade and clot occluding the initial rent in the aneurysmal wall.[1,2,4] This interval of temporary delay may precede exsanguination from the aneurysm by many hours or, in some instances, even several days. In the case described it is obvious, in retrospect, that the patient should have been offered elective surgical excision three years prior to his admission. Short of that, therapy instituted at the onset of mild symptoms two weeks prior to admission or prompt intervention at the time of the marked increase in severity of the pain—utilizing the latent period of twenty-six hours prior to admission—might very well have allowed an uncomplicated surgical removal of the aneurysm and salvage of the patient.

TABLE II. Ruptured abdominal aortic aneurysms: time interval from onset of severe symptoms to hospital admission

Time Interval (Hours)	Number of Patients
Under 4	0
4 to 8	2
8 to 12	2
12 to 24	7
24 to 48	2
Over 48	1
TOTAL	14

As outlined in Table II, it is interesting to note that no patient of the 14 in our series was admitted to the hospital less than four hours following the onset of symptoms related to aneurysmal enlargement or rupture. In actual fact, the average time per patient between the onset of localizing symptoms and hospital admission approximated thirty-six hours. This delay in instituting prompt hospital admission has also been emphasized by Szilagyi and his colleagues.[2] Such data are prime evidence of a facet of the problem, where much improvement can be accomplished.

CASE 2. A sixty-five-year-old male was admitted in July, 1959, with a history of chronic constipation and mild lower abdominal discomfort for one day prior to admission, associated with low back pain for two or three days. The patient had had his lower back strapped by his family physician two days before his admission. His entrance physical examination was reported as showing a moderately distended abdomen with an easily reducible incisional hernia and slight tenderness to palpation in both lower quadrants. No mass was described by the examiner. The initial impression was diver-

TABLE III. Ruptured abdominal aortic aneurysms: mistaken admission diagnosis

Diagnosis	Number of Patients
Low back syndrome	4
Ureteral stone	2
Intestinal obstruction	1
Appendicitis	1
Diverticulitis	1
TOTAL	9

ticulitis and partial small-bowel obstruction. The admission hemoglobin was 12.7 Gm. per 100 ml. An abdominal flat plate film done on hospital admission revealed a calcific outline suggesting an abdominal aortic aneurysm and was so reported by the roentgenologist. A Miller-Abbott tube was passed because of an increase in the abdominal distention. The resident's notes made no mention of aneurysm being considered in the differential diagnosis. At 5:00 A.M., twenty-one hours following the admission, the patient complained of excruciating back pain. The blood pressure was recorded as 60/20 mm. Hg, and the diagnosis of ruptured aneurysm was first considered. At 8:15 A.M., an aneurysmectomy was performed with the insertion of a knitted Dacron prosthesis. The patient recovered from the operative procedure but died of renal shutdown on the fifth postoperative day, undoubtedly related to the protracted period of hypotension both before and during the emergency operation.

COMMENT. Again undue delay, this time after hospital admission, may be indicted for the demise of a patient. Although the abdominal roentgenogram revealed the lesion shortly after the hospital admission, a period of twenty-two hours delay occurred, necessitated by the treatment of the patient for the mistaken diagnosis of intestinal obstruction. In actual fact, the intestinal obstruction was secondary to the retroperitoneal hemorrhage. Here a combination of error in diagnosis and delay in prompt surgical intervention prevented operative excision prior to the fateful exsanguination episode. As can be noted from Table III, diverticulitis and/or intestinal obstruction are not uncommon misdiagnoses in cases of aneurysms with impending rupture.

In this series, 9 of the 14 cases were misdiagnosed on hospital admission (Table III). Back pain, so prominent a feature in the symptomatology of expanding or leaking aneurysm, led to consultation with an orthopedist in the case of 4 patients. This entailed time, effort, and delay in the prompt surgical handling of the patient. The pain pattern in the remaining 5 patients was believed to be caused by ureteral stone in 2, intestinal obstruction in 1, and appendicitis and diverticulitis respectively in the remaining 2 cases. In each case, appropriate therapy was erroneously undertaken for the treatment of these conditions prior to the recognition of the true cause of the patients' symptoms.

It has been alleged by many competent authorities that, except in the markedly obese, the aneurysm can be palpated in 80 per cent of patients.[4,5] Janower[6] and others have stated that a lateral roentgenogram of the abdomen, combined with abdominal palpation, can establish the diagnosis in almost 90 per cent of individuals. In reviewing the hospital records in the present series of patients, it was noted that in 5 instances frequent reference to palpable femoral pulses was made by many clinicians, as if to suggest that the diagnosis of a ruptured aortic aneurysm could thus be excluded. It is to be emphasized that the presence or absence of femoral pulses plays little, if any, role in establishing the diagnosis of a rapidly enlarging or leaking aneurysm. The symptoms of back pain, associated with hypotension and a palpable abdominal mass, should indicate the diagnosis clearly in the great majority of patients.

Having been so sensitized by the gloomy results in this experience, we have stressed in our institution that any patient with an abdominal aortic aneurysm and associated back pain or abdominal pain should be operated on as an emergency, with the minimum of diagnostic procedures performed preoperatively.

This attitude may, in rare instances, result in a laparotomy being performed for lesions simulating leaking aortic aneurysms, as occurred one time in our recent experience.

CASE 3. A sixty-one-year-old female was admitted to the medical service on June 19, 1961, with the complaint of weight loss, weakness, and fatigue. Her admission physical examination revealed a slight abdominal distention and a questionable mass deep in the epigastrium. The hemoglobin on admission was 9.4 Gm. per 100 ml. After an extensive work-up the patient was transferred to the surgical service, unimproved.

On July 10 it was noted that the patient's pulse was elevated consistently to 120 per minute. Her hemoglobin had fallen to 7.4 Gm. per 100 ml. and a lateral roentgenogram of the abdomen was suggestive of an aortic abdominal aneurysm. Her blood pressure fell to 80/50 mm. Hg, and the patient was operated upon on the same day with the presumptive diagnosis of a slowly leaking abdominal aortic aneurysm. A laparotomy revealed an extensive retroperitoneal sarcoma. The patient died subsequently of her malignant condition.

COMMENT. The error in this patient can be justified when one considers the prohibitive mortality rate associated with surgery initiated on patients after aneurysmal rupture has occurred.

Conclusion

By reviewing our present experience with symptomatic aneurysms, one cannot help but comprehend that the avenue for greatest improvement for the successful surgical removal of leaking aneurysms lies in the realm of prompt, accurate diagnosis and early surgery. The vascular surgeon confronted with the potentially awesome pathologic condition of a symptomatic aneurysm needs little prodding. The diagnostician, who may not be quite so cognizant of the prohibitive mortality rate accompanying these lesions, must expedite hospital admission and early surgery for his patients with such a diagnosis if improvement in the salvage rate is to be expected.

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ANNUAL CONVENTION: Medical Society of the State of New York

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Pyloric Stenosis Due to Lye Ingestion

WHEREAS INGESTION *of corrosive acid causes damage primarily to the stomach, ingestion of caustic alkali (lye) causes severe damage to the esophagus and may produce pyloric obstruction. The factors responsible for the gastric insult are: the amount reaching the stomach, the degree of pylorospasm produced, and the extent of neutralization in the stomach. Pain is a constant feature of pyloric stenosis. Radiologic evidence of virtually complete obstruction is usually obtainable. The treatment is surgical with gastroenterostomy and tube gastrostomy the preferred procedures.*

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GASTRIC SEQUELAE after the ingestion of corrosive substances were first noted in France by Robert[1] in 1828. His patient developed pyloric stenosis after drinking sulfuric acid. Later reports appeared in the European literature so that by 1902 Quenu and Petit[2] were able to collect 84 case histories. In 1917 Halstead[3] published the first report from the United States in which sulfuric acid was also the causative agent. Since then there have been other descriptions of pyloric stenosis due to substances other than acids.[4-7]

The following case summary illustrates some of the features of gastric injury due to caustic alkali (lye) which are well established and yet not widely known.

Case report

A twenty-nine-year-old Japanese girl swallowed Drāno, a lye product, on January 24, 1960, with suicidal intent. She was taken immediately to a hospital where a gastric lavage was performed. A liquid diet was allowed, although swallowing caused pain. She was transferred to The Mount Sinai Hospital seven days later.

COURSE. On admission, the complaints were severe burning in the mouth and throat and pain on swallowing. Her temperature was 101 F. There were marked redness and ulceration, covered by exudate, of the palate and pharynx.

Penicillin and streptomycin were administered. Prednisone by mouth was started. A liquid diet was permitted, but supplementary infusions were also needed.

The first esophagoscopy was performed five days after admission, on February 5, 1960, under intravenous thiopental sodium (Pentothal sodium) anesthesia with tracheal intubation. The esophageal luminal surface was necrotic, covered with exudate, and bled easily along its entire extent to the junction of the middle and distal third of the esophagus, beyond which the endoscope could not be passed. Silk-woven bougies up to number 26 French were passed through the narrowed portion into the stomach. During the subsequent five weeks the esophagoscope with bougienage was used eight times to examine the patient. Intravenous thiopental sodium anesthesia with tracheal intubation preceded by succinylcholine chloride was used in all but one examination.

Between the third and fourth week after the original injury, pyloric obstruction developed as indicated by epigastric and substernal pain (to the right of the midline), epigastric distention, and increasing gastric retention which was relieved by the Levin tube. The clinical findings were confirmed by a roentgen examination which showed pyloric obstruction (Fig. 1).

OPERATION. Operative relief of the obstruction was deemed necessary. On February 21, 1960, the peritoneum was opened through an upper midline abdominal incision. The stomach was the site of a marked inflammatory process, chiefly occupying the antrum. Along a distance of about three inches, extending from the pylorus cephalad, the stomach was considerably reddened, indurated, and narrowed into a tube with a width of about one inch. The remainder of the stomach above the constricted antrum was normal in size, but the inflammatory process extended further upward beyond the antrum along the lesser curvature to the esophagogastric

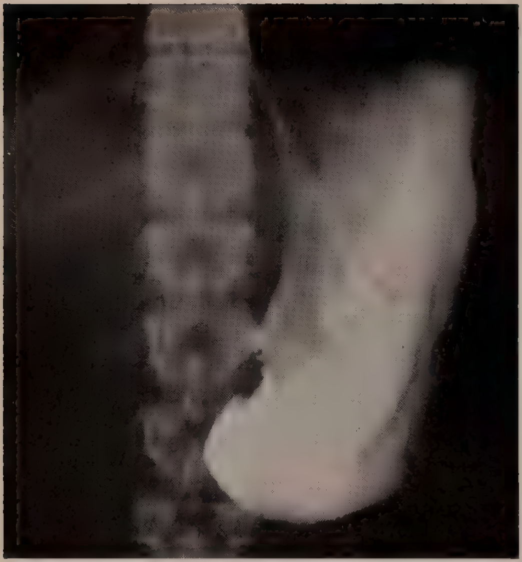

FIGURE 1. Roentgenogram showing pyloric and antral obstruction.

junction and into the esophagus. The greater curvature above the antrum was essentially free of this process, but the entire stomach wall was edematous.

A retrocolic gastroenterostomy was performed. The blood vessels were more numerous and larger than would be expected ordinarily. A gastrostomy with a 28 French tube was made proximal to the gastroenterostomy. Before the tube was inserted, a strong linen thread was tied to the tip of the Levin tube, which was brought up through the nose by the anesthetist. The lower end of the string was threaded through the gastrostomy tube before its insertion. The gastrostomy tube was brought out through a stab wound. The abdominal wound was closed with buried, figure-of-eight, number 30 steel wire sutures. Silk was used to approximate the skin edges.

Postoperative course. The subsequent course was uncomplicated. The gastrostomy tube after the first week was used to supplement the fluid and caloric intake by mouth. The linen thread was bitten and swallowed inadvertently by the patient two weeks after the operation. At the time of discharge, on March 24, 1960, the patient was feeling well, eating a liquid diet, and gaining weight. The gastrostomy was used for occasional supplementary feedings. The esophagoscopic bougienages were performed approximately twice weekly. She left for Japan where treatment was to be continued.

Roentgen studies. A barium meal examination of the stomach preoperatively on February 19, 1960, by the instillation of barium through the Levin tube, was carried on for a period of three hours. Only a very small amount of barium seemed to pass from the stomach into the small bowel (Fig. 1). The mucosa on the lesser curvature side appeared effaced. The mucosa on the greater curvature was prominent, especially near the fundus. Neither the duodenal bulb nor the pyloric antrum could be visualized.

A barium meal examination on the eleventh day after the gastroenterostomy showed the upper part of the esophagus to be slightly narrowed with an irregular caliber. The lower two-thirds was considerably narrowed, and the mucosa was not clearly visualized. The gastroenterostomy opening was functioning.

Laboratory examinations. A laboratory examination revealed that the hemoglobin values varied from a low point of 9 to a high value of 12.2 Gm. The white blood cell count also varied from 12,350 to 4,050. The differential counts remained approximately normal. The blood electrolytes were maintained within normal limits. One transfusion was administered during the operation.

Administration of antibiotics and corticoids. In addition to the penicillin and streptomycin which was first used on admission, Chloromycetin and tetracycline were later administered. Prednisone 30 mg. daily was started by mouth immediately after admission. During the periods when the patient was unable to take fluids by mouth, hydrocortisone administered parenterally was substituted, especially immediately after the operation when a total of 150 mg. of hydrocortisone was given on the day of operation. Corticoids were maintained until the fifth week. They were reduced and finally discontinued before the patient left for Japan.

Comment

Gastric involvement after ingestion of caustic substance. According to Marchand,[8] the stomach is always involved to some extent after the ingestion of a caustic substance, but the clinical evidence of injury is often absent. Of 133 patients with esophageal alkali burns, 7 developed pyloric obstruction, 2 diffuse fibrosis, and 1 an hourglass-shaped stomach (a total incidence of about 7 per cent). Heindl[9] reported an even higher incidence (20 per cent) of pyloric stenosis in 160 cases of esophageal stricture due to lye.

Contrarily, corrosive acids cause damage primarily to the stomach, involving the esophagus less often.[10] Thus, whereas virtually all patients with caustic injury to the stomach also have severe esophageal damage, only 20 per cent of patients with gastric damage due to acids have esophageal stricture.[6,11-13]

CAUSATION OF GASTRIC INJURY. The type of noxious substance (acid or caustic alkali) influences the extent and distribution of the injury.[5] Apparently the factors responsible for the gastric insult are: the amount reaching the stomach, the degree of pylorospasm produced, and the extent of neutralization in the stomach.

Since alkalis cause severe necrosis in the esophagus and are fixed in the tissues,[5,8,10] only small amounts usually reach the stomach. The larger the amount ingested, the greater is the likelihood of gastric injury. Usually the stomach is involved only when esophageal damage is great. Acids, however, apparently pass rapidly through the esophagus and have their greatest influence on the stomach.[5,14]

Once the offending substance has reached the stomach, passing along the lesser curvature to the pylorus, spasm of the pyloric outlet holds the agent in contact with the mucosa. Testa[15] showed that severe pylorospasm was produced merely by incorporating a small amount of caustic in a barium meal.

The degree of neutralization of the agent may also be a factor in determining the gastric injury.[8] Thus, alkalis are less injurious because of the counteracting effects of the gastric acid secretions, whereas swallowed acids are less likely to be neutralized. With both types of harmful substances, food in the stomach acts as a protector and a buffer and moderates the effects on the stomach wall.[5,16]

EXTENT OF INJURY. Early necrosis of part or all of the stomach by caustic alkali (lye) apparently may lead to virtual dissolution of the stomach wall. Lesser degrees of injury cause intense inflammation followed by fibrosis.[4] In the present case, there was thickening and fibrosis of the entire antrum, which extended along the lesser curvature to the esophagus, the route usually followed by ingested fluids.[5] There was much less inflammation of the greater curvature proximal to the narrowed antrum, but edema and congestion were present.

Peritoneal adhesions to the stomach are universally reported to be almost absent,[8] as was the finding in the patient in our case report.

DIAGNOSTIC FEATURES. When damage to the stomach is severe, the symptoms of peritonitis may be present. Most of the time, as in the present instance, the gastric symptoms after lye ingestion are absent or overshadowed by the effects of esophageal injury. A free interval supervenes until the symptoms of pyloric obstruction occur. The usual interval between the time of injury and the occurrence of gastric sequelae is between three and four weeks[17] (in our patient, obstruction occurred in the third week). However, the appearance of symptoms may be delayed for several months[16] and occasionally for years.[18] In some, the gastric complication becomes manifest only after the esophageal stricture has been treated effectively. Copious vomiting may occur if the esophageal lumen is not constricted, but often the narrowing of the esophagus prevents emptying of the stomach.

Pain is a constant and characteristic symptom of the pyloric stenosis, often occurring just to the right of the midline in the epigastrium.[8] This was the complaint which directed attention to the stomach in our patient.

Confirmation of the pyloric obstruction in our case was obtained both by the passage of a Levin tube and by a barium meal examination. When esophageal stricture is too narrow to permit intubation, roentgen proof alone is then necessary.[8,10] The gastric findings on roentgen examination can be mistaken for carcinoma or for ulcer if one has not been supplied with the history of lye ingestion and esophageal injury.[5,6,18]

MANAGEMENT. *Esophageal injury.* The treatment of injury to the esophagus by caustic alkali is a separate entity in itself, about which there is no uniformity of opinion. The question of whether or not to pass any tube for gastric lavage immediately after the ingestion is not settled. The advantages of extracting the noxious agent must be weighed against the hazard of increasing the damage to the esophageal wall.[19-23]

The optimum time for performing an esophagoscopy also is not clear. Marchand[24] suggests early endoscopy for diagnosis but cautions against bougienage sooner than the second week. Hardin[25] postpones esophagoscopy until the second or third week and then advises, as have others,[26] the performance of a gastrostomy with string insertion for retrograde bougienage if an esophageal stricture is present.

An esophagoscopy was performed on our patient on the twelfth day. Bougienage was begun and repeated at intervals of approximately four days. Retrograde bougienage was prepared for at the time of the operation for pyloric stenosis, but the subsequent swallowing of the string prevented its use.

Corticoids were used in our patient as soon as she was admitted to the hospital, but this was one week after the ingestion occurred. The corticoids were continued during the entire hospital course except for the gradual discontinuance prior to discharge. The role played by these agents in this patient's course cannot be determined. The reported general results with corticoids in the treatment of esophageal burns must await further experience for adequate evaluation.

GASTRIC INJURY. During the days immediately after lye ingestion, if advanced damage to the stomach has occurred, the symptoms of peritonitis may appear.[4,8,10,25] Actual perforation, however, is uncommon. Patients subjected to a laparotomy at this stage usually have shown a generally necrotic stomach without perforation. In these instances, a jejunostomy for feeding purposes has been performed, leaving the stomach undisturbed, as it is apparently difficult to find undamaged tissue in either the stomach or the esophagus through which transection or anastamosis can be accomplished.

On the other hand, the experience of many has demonstrated clearly that conservative management of the pyloric stenosis which develops later is doomed to failure. The stenosis results from a fibrosing process with progressive narrowing. The obstruction occurs after several weeks and is not the result of pylorospasm but of organic occlusion.

The choice of the surgical procedure to be employed depends on the findings at operation.[6,10,13] Pyloroplasty and gastric resection have sometimes obtained satisfactory results, but usually the distribution and extent of the damage have prevented their use.[18] In our patient, the advanced narrowing and induration of the antrum and the severe involvement of the entire lesser curvature precluded either resection or pyloroplasty. A gastroenterostomy, as in other reported experience, relieved the obstruction promptly. A tube gastrostomy was an added protection as well as a means of feeding if the esophageal stricture later had become progressive.

Summary

The ingestion of caustic alkali (lye) causes severe damage to the esophagus and may produce pyloric obstruction, usually after an interval of greater than two weeks. Acid injury, on the other hand, affects the stomach primarily and the esophagus less frequently. The extent of gastric injury depends on the amount of the offending agent reaching the stomach, the length of time it remains, the contents of the stomach at the time of injury, and the degree of neutralization by the gastric secretions. Pain is a constant feature of the pyloric stenosis produced. Radiologic evidence of virtually complete obstruction is usually obtainable. The treatment is surgical. Gastroenterostomy and tube gastrostomy are the preferred procedures.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

ALFRED A. ANGRIST, M.D., *Chairman*
Committee on Prize Essays

Chronic Alcoholism Treated via Half-way House and Citrated Calcium Carbimide

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At least 4 million Americans have chronic alcoholism.[1] The loss of manpower and the cost of hospital and prison facilities devoted to these patients is staggering. The lack of success in treating alcoholism is well borne out by the enormous variety of therapeutic approaches and the number of different organizations which deal specifically with the problem.[2-7] There have been relatively few reports in the literature of the results of therapy by groups such as Alcoholics Anonymous which deal with large numbers of alcoholic persons seen over extended periods. The purpose of this report is to present the results of therapy in a group of 125 chronic alcoholic patients who were seen in an eighteen-month period. We define an alcoholic person as a compulsive drinker in whom alcohol has interfered with a major life adjustment area such as family, job, health, or community relations.

Materials and methods

The patients to be reported on constitute two separate groups. There were 79 homeless alcoholic males treated at a "half-way" house known as the "Brick House." This was a semiprotected environment where the men lived and received room and board at a nominal fee or none at all. There was a psychiatric social worker in charge, and the men received some individual counseling and group therapy. Any specific medical problems were treated, but the emphasis was on rehabilitation through the Brick House and not on any drug therapy. The patients were encouraged but not required to join Alcoholics Anonymous and find employment. Continued sobriety was required to remain at the Brick House.

The other 46 patients, including 10 women, were seen in private practice. A complete history was taken of each patient and a physical examination prior to the initiation of drug therapy. The standard procedure was then to provide 50-mg. tablets of citrated calcium carbimide* and instruct the patient to take one pill each morning prior to breakfast. Each patient was given a thorough explanation of the effects of citrated calcium carbimide before its use. Various amounts of chlorpromazine hydrochloride were used as required to treat excessive anxiety and agitation, but this was discontinued as promptly as possible after the first few initial visits. The patients were given an ample opportunity to discuss their personal problems. Patients were usually followed at monthly intervals except initially. They were encouraged but not required to join Alcoholics Anonymous and seek employment. Patients who were incapable of caring for themselves were hospitalized briefly. In some instances follow-up information was obtained from other professional people who were dealing with alcoholism in the community. All the patients treated in both groups had longstanding chronic alcoholism. Many of the patients in both groups were referred by the local committee on alcoholism, local police, the county penitentiary, and various hospitals and social agencies.

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* Supplied as Temposil by Russel Cahoon, M.D., of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

A STUDY WAS MADE *of 79 homeless severely addicted alcoholic males treated at a "half-way" house by conventional methods and 46 severely addicted alcoholic patients, including 10 women, who were seen in private practice and treated with a daily 50-mg. tablet of citrated calcium carbimide (Temposil). The results in the 46 patients in the citrated calcium carbimide groups were: excellent, 7; good, 12; fair, 16; and poor, 11. The results in the 79 patients in the half-way house group were: excellent, 18; good, 6; fair, 6; and poor, 49. The drug-treated group had significantly higher worth-while results, and there was a lack of serious toxicity.*

Criteria for improvement

In any study of this type there are those authors who claim symptomatic improvement but who do not report details of objective evidence.[8] Relatively rigid criteria of sobriety are necessary for the analysis of results. Patients who continued to drink were considered to have had a poor result. In addition any patient who was not followed for two months was considered a poor result.* This includes patients who were lost to follow-up because of death, moving to another city, or transfer to a State hospital. A minimum of two months sobriety were necessary for the designation "fair" result. Good results were obtained in patients with at least four to six months of sobriety. Patients who were sober for over six months and who were steadily employed were considered excellent. Many of these patients had not had over two weeks sobriety in the several years prior to their inclusion in this study.

Results

The follow-up periods and the results obtained in each group are listed in Table I. The duration of follow-up was longer in the Brick House group. The majority of the patients were followed for over four months and many for over six months. This compares very favorably with the follow-up reported in similar studies in chronic alcoholic patients. The Brick House group contained more excellent and many more poor results. If patients with excellent or good results are considered to have worth-while improvement, then the citrated calcium carbimide group had significantly higher worth-while results. The Brick House group had 62 per cent poor results as compared with 24 per cent for the citrated calcium carbimide group. It is apparent from Table I that among the 56 men seen at the Brick House and followed for over six months most of the results are excellent or poor with few in the intermediate categories, which implies that only a minority of the men benefited. Of the 20 followed on citrated calcium carbimide, only 2 or 10 per cent were classified as poor, and 75 per cent had good or excellent results.

Comment

The results of this study require cautious interpretation. It is not possible to have adequate controls on alcoholic persons who are treated as outpatients. Previous investigations usually have had relatively brief

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* This was done to avoid any bias in favor of therapy, although some of those lost to follow-up may have improved.

TABLE I. Follow-up and results

	Citrated Calcium Carbimide Group					Brick House Group				
Months of Follow-Up	Number of Patients	Excellent	Good	Fair	Poor	Number of Patients	Excellent	Good	Fair	Poor
0 to 2	6	. . .	. . .	. . .	6	11	. . .	. . .	. . .	11
2 to 4	15	. . .	. . .	12	3	4	. . .	. . .	. . .	4
4 to 6	5	. . .	4	1	. . .	8	. . .	. . .	3	5
Over 6	20	7	8	3	2	56	18	6	3	29
TOTALS	46	7	12	16	11	79	18	6	6	49

follow-up, and in dealing with chronic alcoholism temporary results have little meaning.[6,8] In studies with adequate long-term follow-up disulfiram (Antabuse) has been used with limited success.[2,3] Rudfeld[2] reported good results in 50 per cent of 333 alcoholic patients treated for over eighteen months with disulfiram. Jacobsen[3] reported 22 per cent excellent and 31 per cent good results in treating 266 patients. Unfortunately the use of disulfiram is not without risk and there have been occasional deaths attributed to it.[3] The toxic effects of disulfiram include fatigue, sleepiness, headache, dizziness, impotence, toxic psychosis, metallic taste in the mouth, unpleasant body odor, nausea, dyspnea, and skin rashes. Recently citrated calcium carbimide has been shown to cause an acetaldehyde reaction similar to disulfiram after alcohol is ingested and has been reported to be much less toxic.[4-7] An acetaldehyde reaction usually follows the ingestion of either disulfiram or citrated calcium carbimide shortly and includes yawning, choking, flushing, headache, nausea, palpitations, and tachycardia. The reaction is generally intense enough to discourage further drinking. In an occasional patient who drinks and is treated with citrated calcium carbimide, the reaction will not occur. This is usually owing to the more rapid turnover of citrated calcium carbimide as compared with disulfiram, which remains in the body for as long as a week.

The present study permits some comparisons between the group treated through the Brick House and the group receiving the drug. The men at the Brick House were relatively more "captive" since to remain there they had to stay sober. The men generally accepted the restrictions prior to entering the Brick House so that there were fewer one-day turnovers than there were in the citrated calcium carbimide study.

The Brick House group was initiated approximately one year prior to the drug study. A much longer follow-up was available in this group. This in part explains the larger number and greater degree of excellent responses. The patients also had a secondary gain at the Brick House in terms of their receiving room and board at a minimal cost, or none at all in some instances. This undoubtedly provided some motivation to stay sober in some of the men. On the other hand most of the group seen privately had the advantage of having a home and whatever support their families were able to give them. Thus the groups are not entirely comparable. However, in every case the patients of both groups were known to be severe chronic alcoholic persons, and no real difference in the severity of the disease in either group was apparent. It is important to note that the present study included patients seen only once or for less than a one-week follow-up. These patients were obviously poorly motivated and fell entirely within the poor result category. The elimination of this group would improve the statistics of both groups, particularly the drug-treated group, but would introduce a definite bias of case selection.

There is an expectation of some regression of a temporary or permanent nature in some of the patients with worth-while results. It is impossible to predict with certainty the future course of the patients reported. Some of those who are presently doing poorly may improve markedly. This uncertainty makes it mandatory to continue the follow-up therapy of patients with chronic alcoholism for several years. If the attitude of the physician treating the patient is unrealistically short-term, then the patient is provided with only temporary help and one additional source of blame for his own inevitable regression.

The relative safety of citrated calcium carbimide is shown by the lack of serious toxicity; only 2 patients had any rashes which necessitated the cessation of therapy. The fact that there was an improvement in over-all worth-while results and a diminution of poor results in the drug-treated group suggests that the agent is a valuable aid in the treatment of severe chronic alcoholism under medical supervision.

Summary

The results of treating 125 chronic alcoholic patients are reported. Seventy-nine were homeless men treated in a halfway house with environmental support and

some group and individual counseling by a psychiatric social worker. The remaining 46 were seen in private practice and received 50 mg. of citrated calcium carbimide daily. The follow-up exceeded six months in the majority of cases. The results were most satisfactory and there were more worthwhile results and fewer poor results in the citrated calcium carbimide-treated group. The toxicity of the drug is relatively small, and there were no serious side-effects. The drug is of value in the treatment of chronic alcoholic patients.

Addendum

A statistical analysis of the data presented in Table I was undertaken. The coefficient correlation as relates to the distribution of results in both the citrated calcium carbimide and Brick House groups was determined. The coefficient of correlation was derived from the formula:

$$R = \frac{N.\Sigma XY - (\Sigma X)(\Sigma Y)}{\sqrt{N.\Sigma X^2 - (\Sigma X)^2}\sqrt{N.\Sigma Y^2 - (\Sigma Y)^2}}$$

where R = coefficient of correlation
X and Y are variables
N = number of observations
Σ = sum of

Using the level of significance at 0.05 with the following criteria we reject the null hypothesis of no correlation if $R < \frac{-1.96}{\sqrt{N-1}}$ or $R > \frac{1.96}{\sqrt{N-1}}$ and accept as significant $\frac{-1.96}{\sqrt{N-1}} \leq R \leq \frac{1.96}{\sqrt{N-1}}$. With these formulas we determined that the results at the Brick House do not exceed chance distribution. The results obtained for the citrated calcium carbimide-treated group demonstrate definite statistical significance beyond the element of chance.

A further test employing the chi-square test demonstrated that the distribution of the proportions associated with the "R alternatives," that is excellent, good, fair, or poor results for the citrated calcium carbimide group, was statistically significant and not due to chance. The results of the Brick House group did not meet the chi-square test requirements.

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Ophthalmic Survey of 162 Mentally Retarded Children

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PUBLISHED STUDIES regarding ophthalmic defects in mentally retarded children are scarce. Breakey[1] showed that 56 per cent of individuals with cerebral palsy manifest ocular abnormalities. Guibor[2] had previously reported a high incidence of eye abnormalities in children with cerebral palsy. In the study of retardates recorded by Fletcher and Thompson,[3] the most frequent ocular disturbances were strabismus and unusually severe refractive errors.

This survey was undertaken to learn whether or not the following questions could be reasonably answered:

1. Does the child see with each eye?
2. What ocular defects exist which interfere with educational rehabilitation?
3. What therapeutic measures may be employed to correct any existing ocular defects?
4. What effect do these therapeutic measures have in improving the over-all functioning of the individual child?

When the ophthalmologist is confronted with the task of evaluating the retardate, the presence or absence of the following categories of disease should be investigated: (1) blindness; (2) ocular motility disturbances and/or abnormal head posture; (3) monocular amblyopia due either to uncorrected refractive errors or to disease processes such as strabismus or neoplasms; and (4) any associated congenital or developmental defects.

Method of examination

Let us first discuss the manner in which the retardate is examined at The Shield of David Institute for Retarded Children. The importance of a pleasant, nonmedical environment cannot be overemphasized. Most retardates exhibit unusually fine cooperation if they are not intimidated or frightened. No one in the room should be clothed in a white uniform. Whenever possible, a member of the child's family or the child's own teacher should be present to offer moral support. A few minutes invested in developing rapport with the child will be amply rewarded during the ensuing examination. Among the group of 162 children included in this survey, only 6 were uncooperative and unmanageable enough to prevent an adequate examination.

During the initial investment period, many pertinent observations can be made about the ocular status. The examiner must utilize all possible impressions of the child's alertness such as the ability to grasp for different-sized toys in various fields of gaze. The fixation movements of both eyes offer insight into the orthoptic status of the patient and into the potential visual acuity of each eye. All possible objective means must be incorporated into the examination routine: scrutinization of the pupillary reflexes to light and convergence, testing the blink reflex, and, whenever possible, using the optokinetic drum to elicit the nystagmus reflex.

In the retardate who is able to learn the "E" game, a subjective measurement of visual acuity can actually be determined. An intensive effort should be exerted by the teacher to instruct the child daily until he mimics the direction of the arms of the "E." Retardates with perceptual difficulties will not learn this test readily.

The children are studied during at least two sessions. During the first session, an examination of the visual acuity by means of the "E" test whenever possible, of the anterior segments, and of the orthoptic status is performed. Prior to the second

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TABLE I. Ocular abnormalities in 162 mentally retarded children

Condition	Number of Cases		
Refractive abnormalities			28
High myopia		5	
Moderately severe myopia		11	
High hypermetropia		2	
High astigmatism (both myopic and hypermetropic		6	
Anisometropia		4	
Strabismus including ptosis			21
Esotropia		12	
Alternating	5		
Monocular with suppression amblyopia	5		
Intermittent	2		
Exotropia		7	
Alternating	2		
Monocular with suppression amblyopia	2		
Intermittent exophoria-exotropia	3		
Monocular ptosis		2	
Miscellaneous			21
Conjunctivitis		7	
Nystagmus		4	
Subalbinism		3	
Optic atrophy		2	
Coloboma		2	
Papilledema (etiology not determined)		1	
Congenital glaucoma		1	
Congenital cataracts		1	

session, the child's pupils have been dilated with a cycloplegic agent so that during this session a cycloplegic refraction and thorough funduscopic examination are performed. If any further tests are required or if the child has been uncooperative, a third visit is scheduled.

When any unusual findings are detected which warrant further investigation, the child is scheduled for an examination under anesthesia at the Flower and Fifth Avenue Hospitals. Such an indication might be in the case of a child who manifests signs of possible congenital glaucoma, congenital cataracts, or intraocular tumor. Only by lightly anesthetizing the child, after approval by the pediatric department has been granted, can adequate studies be made of potentially curable diseases.

By the end of the examination, the ophthalmologist can answer unhesitatingly the questions listed previously in a large percentage of children.

AN OPHTHALMIC SURVEY, *including external and orthoptic evaluations, cycloplegic refractions, and adequate funduscopy through dilated pupils, was undertaken of 162 mentally retarded children. High refractive errors and strabismus were the most frequent abnormalities detected. Others included: conjunctivitis, subalbinism, optic atrophy, ptosis, nystagmus, colobomas, congenital glaucoma, congenital cataracts, and papilledema. The incidence of ophthalmic defects was higher than in the population at large. The long-term therapeutic effects have not yet been determined, but an ophthalmic examination is recommended as an integral part of the multiphasic diagnostic approach to the retardate.*

Question results

1. DOES THE CHILD SEE WITH EACH EYE? Very few of the 162 children included in this survey were taught the "E" game. Therefore, no quantitation of their visual acuity was possible. By means of the technics discussed before, it was found that in 6 children one eye was not being used at all. Fifteen children were found to have significantly limited visual function. The causes for the decreased visual function in these cases will be discussed in answering the second major question.

2. WHAT OCULAR DEFECTS EXIST WHICH INTERFERE WITH EDUCATIONAL REHABILITATION? The ocular abnormalities detected in this survey were distributed as shown in Table I.

Of the 15 children mentioned previously who were found to have significantly limited visual function, all fell into one of the categories of refractive errors.

Of the 6 children who were found to be using only one eye, 4 fell into the group of monocular strabismus with suppression amblyopia. The other 2 children manifested optic atrophy to account for their rejection of the affected eye.

3. WHAT THERAPEUTIC MEASURES MAY BE EMPLOYED TO CORRECT ANY EXISTING OCULAR DEFECTS? For those children who simply manifest refractive errors, the prescription of spectacles should amply correct the defect adequately in a large majority of

cases. In the case of children with strabismus, the therapeutic approach is somewhat more difficult. Depending on the type of strabismus, the treatment is either surgical or conservative. The latter approach consists of various orthoptic exercises designed to overcome the basic muscular abnormality. Heretofore, this approach has never been tried in retardates. However, a few enthusiastic teachers at The Shield of David Institute for Retarded Children are attempting to prove that this mode of therapy is possible and practical. The only comments which I will make about the conditions in the miscellaneous group are that the treatment of conjunctivitis is by the use of antibiotics and the treatment of congenital glaucoma and cataracts is by surgery.

4. WHAT EFFECT DO THESE THERAPEUTIC MEASURES HAVE IN IMPROVING THE OVER-ALL FUNCTIONING OF THE INDIVIDUAL CHILD? This is the most difficult question of the four to answer validly. In my experience, the following observations are pertinent: When the proper lenses in accurately fitted frames were given to the children with significant refractive errors, no resistance to the use of the spectacles was encountered. As a matter of fact, many of the children seemed to enjoy wearing the glasses.

Some of the children seemed to benefit from the use of the glasses in their over-all functional capabilities. An outstanding exception to this generalization was among the mongoloid children. These children persisted in closely approximating their object of regard despite the use of lenses when indicated. This is possibly attributed to their muscular laxity and other related problems.

The 4 children who were operated on for correction of their strabismus did not improve appreciably in their performance level immediately postoperatively. The cosmetic improvement was greatly appreciated by the parents. Furthermore, the long-term effects have not been determined in these cases.

Pertaining to this question, I would like to quote from an excellent article by Fletcher and Thompson.[3] In their conclusions, they state:

> As yet, there is no way of knowing what part a visual handicap plays in determining the level at which the retardate will function or how much it may contribute to behavior or emotional disturbances. . . .
>
> Little immediate effect of visual correction was noted in this study but it is possible that the future development of the children may be altered. Improved vision at an early age may help prevent confusion and poor contact with their environment even though mental or other defects exist, and pave the way for the individual to become a more productive and well-adjusted member of the group in which he must live.

Summary

This survey was undertaken to learn whether or not four basic questions could be answered about visual problems in retardates. The ocular examination was usually conducted in two sessions: The first was devoted to external and orthoptic evaluations, and the second concentrated on cycloplegic refractions and adequate funduscopy through dilated pupils.

High refractive errors and strabismus were the two most frequent abnormalities detected. Conjunctivitis, subalbinism, optic atrophy, ptosis, nystagmus, colobomas, congenital glaucoma, congenital cataracts, and papilledema comprised the other diseases which were diagnosed during the survey. That the incidence of ophthalmic defects among mentally retarded children is higher than in the population at large is demonstrated by this survey.

Although the immediate effect of the therapy employed for these ocular defects was difficult to evaluate, it is recommended unequivocally that an ophthalmic examination should be an integral part of the multiphasic diagnostic approach to the retardate. Any indicated therapy should be offered as a possible means of enhancing the long-term functional capabilities of each child.

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Scientific session held at the
Hotel Beekman Tower,
New York City,
March 14, 1962
SHEPPARD SIEGAL, M.D.,
President, Chairman

PROCEEDINGS

New York Allergy Society

MURRAY DWORETZKY, M.D.
Editor

Differentiation Between Allergic and Nonallergic Headache

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Sheppard Siegal, M.D.: Our meeting tonight is devoted to two somewhat unusual aspects of clinical allergy. Our first presentation will be a consideration of the problem of allergic and nonallergic headaches and the second one will be about the problem of hearing impairment, especially in children, and the possible role of allergy of the respiratory tract in this problem.

You may have noticed that on the back page of your program there is a reminder to give tetanus toxoid. This immunization is too often neglected. Allergists are particularly aware of the dangers associated with the administration of tetanus antitoxin and the difficulties which confront the doctor who must use it in a serum-sensitive patient. Therefore, we remind you to give tetanus toxoid to all your allergic patients and to encourage all physicians to immunize their patients and to give boosters every four years. Such active immunization actually confers dual protection, not only in preventing tetanus, but also in preventing an exposure to serious allergic reactions.

Someone has said that there is nothing so difficult as knowing what is going on inside another man's head. Arnold P. Friedman, M.D., has become justly famous for his many studies and publications in the problem of headache. He is going to speak to us on the differentiation between allergic and nonallergic vascular headache.

Arnold P. Friedman, M.D.: Possibly the most common affliction of modern man is headache. As a symptom alone, headache may be an indication of an underlying disturbance within the cranium, in other systems of the body, personality, environment, or a combination of these factors. About 90 per cent of all headaches in office practice are more or less benign, involving psychophysic factors rather than a permanent structural change or serious illness. Our purpose is, first, to present some observations on the vascular type of migraine headache and, second, to consider the clinical aspects of certain types of vascular headaches, namely, vascular headaches of the migraine type and allergic headache. Last, we shall discuss some recent studies in the pharmacologic treatment of vascular headache.

Features of migraine headache

Features of the migraine attack can be divided conveniently into the preheadache or nonpainful phase and the headache or painful phase. Both stages are intimately related to changes in the structure and function of cranial vessels.

In the preheadache phase there is a vasoconstriction of the arteries supplying the cerebrum and occasionally the retina which in some instances produces transient sensory and motor disturbances.[1] Apparently this occurs in an artery or in a set of arteries, suggesting a local neurogenic reaction rather than a generalized involvement. About 10 per cent of migraine headache attacks are preceded by visual disturbances which take various forms including scintillating scotomata, fortification phenomena, and various visual field defects. In some instances the scotomata can be eliminated by vasodilators and induced and intensified by vasoconstricting agents.

In the headache phase pain is associated with the vasodilatation of the extracranial arteries and the altered sensitivity of the blood vessels. The sensitivity of the blood vessels is due in part to local vascular changes, particularly arterial and capillary, and the accumulation of a polypeptide neurokinin and a neurokinin-forming enzyme in the subsurface tissue.[2] It has been stated that the concentration of these local headache substances which are present in the subsurface fluids parallels closely the intensity of pain. A continued dilatation of the vessels leaves them hard, tender, and rigid. A study of the bulbar conjunctiva at this point reveals vasodilatation and edema. Finally, in the late headache and postheadache phase there is excessive muscle contraction of the scalp and the nuchal region. This is associated with soreness and tenderness of the scalp area, local edema, and a lowering of the deep pain threshold.

The pain of vascular headache is transmitted by the fifth, ninth, and tenth cranial nerves and the upper cervical nerves. The end-organ mediator in the arterial wall is presumed to be acetylcholine. However, the sensory innervation of the vessels surrounding the tissues is usually supplied by the fifth nerve and possibly by the sympathetic fibers which descend in the cervical and sympathetic trunk.

The evidence so far available indicates that the pain of vascular headache of the migraine type can be seen as the outcome of the combined effects of cranial artery dilatation plus the action of pain threshold-lowering substances which accumulate in the blood vessel walls and arterial vascular tissues. This apparently results in the neurogenically induced sterile inflammatory reaction.

However, an alteration in the tone, lumen, and pain threshold cannot alone explain the complex symptomatology of the migraine attack. Recent studies suggest that both the general and local changes observed during the migraine attack may be related to certain circulating neurohumoral substances which have a function in the neurocirculatory system. One of these agents which was thought to be implicated in vascular headache is serotonin because it may function as a vasodilator and also as a neurohumor. According to some observers, serotonin induced headache when it was injected intravenously or locally around the superficial temporal artery of patients who were immersed in warm water.[3]

The results of our experience are at variance with these observations.[4] We found that intravenous serotonin did not produce headache; indeed, in some instances, the intravenous injection of serotonin interrupted a spontaneous migraine headache or relieved headache produced by reserpine.

Our studies showed that norepinephrine, injected intravenously, relieves headache, and that adrenergic blocking agents, such as Dibenzyline, fail to induce headache. These observations also may indicate that the painful vasodilatation which occurs with headache is not a sequel of or a reaction to the vasoconstriction present in the preheadache phase.

At the present stage of our study of migraine evidence has accumulated that none of the known neurohumors thus far studied can by virtue of their peripheral action initiate migraine headache. Their effect on the central nervous system must still be considered. We were unable to initiate a vascular headache of the migraine type in 16 migrainous patients by the administration of serotonin, acetylcholine, norepinephrine, or histamine.

At this point I should like to present some of our interesting observations on reserpine-induced headache. When reserpine, 2.5 mg., was given subcutaneously to 6 patients, typical unilateral headaches with marked flush were induced some six hours after the injection. This effect could be due to (1)

TABLE I. Factors distinguishing between allergic and migraine headache

Factors	Headache Allergic	 Migraine
Family history	Uncommon	Common
Character of pain	Variable	Pulsatile
Prodromata	Uncommon	Common
Gastrointestinal symptoms	Occasional	Common
Response to allergens, inhalants, and ingestants	Common	Uncommon
Relief with allergic management	Yes	Not usually

the release and action of serotonin, (2) a parasympathomimetic effect with an increase in acetylcholine activity, (3) a secondary release of histamine due to the release and depletion of serotonin, or (4) an early depletion of norepinephrine or other catechol amines. It is of interest that smaller doses of reserpine, 1.2 mg., which may be sufficient to deplete the central nervous system of norepinephrine but not of serotonin, produce a vascular effect but no headache.

In addition to the alteration in the structure and function of the cranial vessels during migraine headache, there may be a disturbance involving other body systems. It is not uncommon for patients with vascular headache to experience weight gain preceding their headache, followed by a diuresis with weight loss, as the headache diminishes in intensity. Ten of our migraine patients were studied to determine whether or not there is any relationship between fluid retention and the development of headaches.[5] The patients were hydrated by rapid intravenous infusions of 5 per cent glucose in water and then were given an endogenous and exogenous antidiuretic hormone (endogenous, aqueous Pitressin; exogenous, nicotine). No abnormal findings were obtained in any of these patients, and no patients developed headache during or subsequent to the tests.

The excretion of water, sodium, potassium, and creatinine are decreased significantly prior to and during the early stages of the migraine attack. In these cases the rates of excretion of these substances usually increase as the headache attack subsides. In the migraine patient it would appear that these fluids and electrolyte and renal changes are not related causally to the onset, intensity, or duration of the attack but are effects of the physiologic alterations which occur during the migraine syndrome.

Among a group of our migrainous patients no consistent change in 17-ketosteroids, 11-hydroxysteroids, or catechol amines has been found to accompany headache.

Vascular type of migraine headache

The vascular type of migraine headache usually presents few diagnostic difficulties and can be classified as follows:[6]

"CLASSIC" MIGRAINE. Classic migraine is a vascular headache with sharply defined, transient visual, and other sensory or motor prodromes, or both.

"COMMON" MIGRAINE. Common migraine is a vascular headache without striking prodromes and is less often unilateral than the classic migraine and the "cluster" headache. Synonyms are "atypical migraine" or "sick headache." Calling attention to certain relationships of this type of headache to environmental, occupational, menstrual, or other variables are such terms as: "summer," "Monday," "weekend," "relaxation," "premenstrual," and "menstrual" headache.

CLUSTER HEADACHE. Cluster headache is vascular headache, predominantly unilateral on the same side, usually associated, with flushing, sweating, rhinorrhea, and increased lacrimation. It is brief in duration and usually occurs in closely-packed groups separated by long remissions. Identical or closely allied conditions are erythroprosopalgia (Bing), ciliary or migrainous neuralgia (Harris), erythromelalgia of the head or histaminic cephalagia (Horton), and petrosal neuralgia (Gardner *et al.*).

"HEMIPLEGIC" AND "OPHTHALMOPLEGIC" MIGRAINE. Hemiplegic and ophthalmoplegic migraine constitute the form of vascular headache featured by sensory and motor phenomena which persist during and after the headache.

TABLE II. Factors distinguishing between migraine headache and localized allergic response

Factors	Migraine Headache	Localized Allergic Response
Periorbital discomfort	Severe	Moderate
Eye-bulbar conjunctival vasodilatation	Unilateral	Bilateral
Nose		
Edema Hyperemia Increased secretion	Unilateral	Bilateral
Sneezing	Rare	Common
Associated symptoms (gastrointestinal, and so forth)	Prominent	Infrequent
Pharmacology		
Antihistamines	No relief	Frequent relief
Steroids	No relief	Frequent relief
Vasoconstrictors	Relief	Relief
Pathologic conditions—cellular infiltration	Not present	Present

"LOWER-HALF" HEADACHE. Lower-half headache is headache of possible vascular mechanism, centered primarily in the lower face. In this group there may be some instances of "atypical facial" neuralgia, sphenopalatine ganglion neuralgia (Sluder), and vidian neuralgia (Vail).

Comment

However, when dealing with headache, the clinician must be alert to other conditions which mask themselves in a migraine profile including aneurysms, angiomatous malformations, and, late in life, temporal arteritis, insufficiency syndrome of the basilar or carotid artery, and glaucoma. The criteria in Table I help to distinguish between the allergic and migraine headache.

Many features of the migraine attack resemble localized allergic responses including vascular headache, bulbar conjunctival vasodilatation, and edema. However, certain differences are apparent (Table II). It should be noted that in those patients who are subject to migraine an attack may be precipitated by the administration of an allergen to which the patient is sensitive.

Pharmacologic treatment of vascular headache

Previous studies have demonstrated the capacity of ergotamine tartrate and related agents to interrupt vascular headaches of the migraine type. This is presumably due to their ability to induce constriction of painfully dilated cranial arteries. However, efforts to prevent chronic vascular headache by the use of drugs have been uniformly unsuccessful.

In the past two years striking benefits in some patients with migraine have been achieved by the prophylactic use of methysergide maleate (Sansert) UML 491 (1-methyl-d-ly-sergic acid butanolamide), a potent serotonin antagonist.[7] However, this drug lacks the capacity to eliminate an existing headache. That methysergide maleate may relate its prophylactic effects in migraine to its antiserotonin action is illustrated by Table III. However, recent evidence indicates that methysergide maleate, in addition to its inhibition of central vasoconstrictor reflex effects and anti-inflammatory properties of a nonspecific nature, may secondarily induce peripheral vasoconstriction.[8] It has been suggested that the vasoconstrictor effect is dependent on the capacity of methysergide maleate to increase the sensitivity of the individual to his own vasoconstrictor substance. Such vasoconstriction, indirectly induced, is presumed to be the basis of therapeutic action which this agent possesses in the prevention of vascular headaches. Methylation of lysergic acid derivatives in position 1 not only increases serotonin antagonism but it decreases all the other generally known pharmacodynamic properties of these compounds, including vasoconstriction. Whatever its specific action, in twenty-six months of use methysergide maleate has

TABLE III. Antiserotonin activity in vivo in relation to clinical efficacy as migraine prophylaxis

	Inhibition of Serotonin-Induced Edema in Rat's Paw		
Compound	Effective Dose (50 Mg. per Kilogram)	Relative Value*	Relative Clinical Effect†
Hydergine	833	7	+
BOL 148**	196	29	+
Cyproheptadine hydrochloride	26	150	++
Methysergide maleate	13	440	++++

* LSD-25 = 100
** Brom-lysergic acid diethylamide tartrate.
† Range: 0 to ++++

reduced the frequency and severity of headaches in 65 per cent of a group of 400 patients. This is significantly different from placebo response. Average doses for patients with migraine in this series were 6 mg. daily, administered in 2-mg. doses spread out over the day. The desirability of titrating doses in each individual to obtain optimum effect cannot be overemphasized. Side-effects have generally been mild and include nausea, anorexia, lightheadedness, and feelings of unreality. Reactions suggesting vascular spasm have occurred in a few patients. As yet there is no way of predicting which patient with vascular headache will or will not benefit from methysergide maleate. However, in the patient whose headache is sufficiently severe and frequent to warrant preventive measures, this drug should be given a trial period of at least three weeks.

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Discussion

Dr. Siegal: Lucie Adelsberger, M.D., will open the discussion. She has been associated, as an allergist, with Dr. Friedman in his work at the Headache Unit at Montefiore Hospital.

Lucie Adelsberger, M.D., *New York City.* Headache and allergy are very fascinating problems which definitely deserve the interest of the physician concerned with the variety of allergic manifestations. In this respect, observations of patients at the Headache Unit of Montefiore Hospital have been highly interesting; they have shown again that there are some patients whose headaches are due solely to allergy. These patients are sent to us either because they have a history of allergy or seasonal symptoms or because they react well to antihistamines. Some patients are referred because of concomitant nasal symptoms, such as a persistent rhinitis or a clogged nose with postnasal drip. All of these patients have undergone a thorough physical examination, have had a variety of clinical and laboratory tests, and most of them have had a neurologic examination including an electroencephalogram before they come to the allergist. This is, of course, a great advantage to us in the Headache Unit, since one of the prerequisites for the diagnosis of true primary allergy is fulfilled, namely, to exclude, as far as possible, the presence of an organic disease as a cause of the symptoms.

Some of these patients state immediately that they are allergic to many things which give them headaches. These headaches are rarely found to be due to allergy. Other patients have no inkling at all that they have allergic headaches, but they have a history of hay fever or other allergies. These are often the very patients with allergic headaches. It is important to stress this point. A previous history of allergy, especially of hay fever and asthma which may have more or less subsided, should be an indication for an allergic work-up of a patient with a headache without organic cause. The same holds true for patients with a strong family history of allergy even if evidence of the patient's allergy has not been established previously.

Dr. Siegal: Thank you, Dr. Adelsberger. We now welcome questions from the floor.

Question and answer period

Joseph Fries, M.D.: Is there any evidence of a mechanism in the histamine type of headache? From a practical viewpoint, a general practitioner can only use aspirin or Empirin for headaches. Can you suggest any other practical drug?

Dr. Friedman: Paroxysmal attacks of cluster headaches have been well documented in the literature during the past ninety years under a variety of clinical entities and eponyms. Many authors have described close variations of the syndrome at different times and under different names. Mollendorff in 1867 described it as a red migraine headache with hemicrania, homolateral redness of the face, injection of the eye, lacrimation, and dilation of the temporal arteries. Bing in 1910 called the condition erythromelalgia of the head. Sluder in 1908 and 1913 characterized it as sphenopalatine neuralgia or lower-half headache. Pasteur Vallery-Radot with Blamoutier and others, in 1925 and in subsequent years, published reports of such cases under the title "Syndrome of hemicephalic vasodilatation of sympathetic origin." Harris in 1926 and 1936 called it ciliary (migrainous) neuralgia. Brickner and Riley in 1935 preferred to call it autonomic faciocephalalgia. Horton, McLean, and Craig in 1939 spoke about a new syndrome which they originally named erythromelalgia of the head but changed to histamine cephalalgia in 1941. Gardner and co-workers in 1947 described it as petrosal neuralgia. Symonds in 1956, in agreement with other authors, thought of it as a migraine variant. Almost as many theories exist as authors who described the syndrome. Most of the theories seem to agree that we are dealing with periodic attacks of local dilatation of extracranial vessels in areas supplied mainly by the branches of the external carotid arteries. The always appealing theory of some kind of allergy due to foods or inhaled allergens as the cause of the syndrome has been advocated by different authors. Nevertheless, the percentage of patients who show other evidence of allergy by history or tests is small in all series; skin tests alone do not provide satisfactory evidence of food allergy in headaches, and both allergy and headache may coexist independently in the same person. The incidence of allergy is not greater in this group than in the general population. On the other hand, treatment with antihistamine drugs and dietary or other antiallergic precautions have always given poor results and, when successful, are of transitory nature.

As for treatment, the simplest and best remedy for occasional headache is still acetylsalicylic acid. However, there are three areas in which the effect of the drug must be considered: first, the original pain sensation and its mechanism; second, the anxiety associated with pain; and third, the secondary increase in dysfunction, including the additional pain sensation which accompanies the anxiety. As ordinarily used, the nonaddicting analgesics alone are seldom efficient in relieving an acute attack of tension headache. Likewise, tranquillizers and sedatives rarely control the discomfort. But an analgesic combined with a tranquillizer or sedative is extremely effective, for in combination these drugs affect not only the pain threshold but also the reaction to pain. An analgesic combined with a sedative or a tranquillizer or both gives effective relief in over 70 per cent of treated cases, whereas nonnarcotic analgesics or sedatives, when used alone, are less effective (55 per cent). It should be noted that placebos are effective in approximately 45 per cent of these patients. The ideal analgesic for the treatment of tension headache should be effective at levels not impairing sensorium or vital functions, and it should be free of addicting properties, have negligible side-effects or toxicity, and be simple to administer.

M. William Amster, M.D.: Do you think there is any such thing as a caffeine-withdrawal headache, and if so, where does it fit into your classification?

Dr. Friedman: There can be a caffeine-withdrawal headache. Its mechanism is probably vascular.

Samuel J. Prigal, M.D.: What is the actual incidence of allergic headache? I would like to know how you know that a given headache is allergic. My own experience has been that there are very few headaches so proved. Most of the headaches that I have treated seem to come from muscle spasm or muscle tension.

Dr. Adelsberger: It is true that allergic headaches are relatively rare. Actual figures cannot be given. Considering the very large census of the Headache Unit, the number of patients seen by the allergist is small; but if there are only 1 or 2 per cent whose headaches are due to allergy and who can be relieved from incapacitating headaches, it is worth while to test and treat those patients.

The second question concerns the diagnosis of allergic headache. Skin tests in headache patients are helpful only in the few instances where an injection of specific allergens is followed regularly and repeatedly by headaches. With ragweed pollen this was quite often the case, especially shortly before or during the season. A patient whose headache is caused by sensitivity to ragweed pollen very often reacts to the intracutaneous test or to the eye test with headache. This makes the treatment of these patients somewhat difficult because they react frequently with headaches following an injection of ragweed pollen extract. Ophthalmic tests with increasing concentration of allergens have been very helpful in differentiating allergic from nonallergic headaches. The patients reacted to specific allergens with conjunctival reactions and concomitant headache but did not react in the same manner to other allergens and to placebos.

Question: Dr. Adelsberger, were those ophthalmic tests done with inhalant substances?

Dr. Adelsberger: Ophthalmic tests were done with both inhalants and with food allergens. Reactions to inhalants, such as ragweed pollen, were characterized, as mentioned before, by a local inflammation in the eye combined with headaches developing either during the tests or within the next hour. By contrast, ophthalmic tests with dust showed a different pattern. These tests rarely caused a headache, and the patients developed mostly respiratory symptoms such as a clogged nose, wheezing, or asthma. Apparently a completely different mechanism was involved. Ophthalmic tests with food allergens proved of greater diagnostic value in headache patients than the skin tests.

Question: Dr. Adelsberger, what strength foods would you use for the ophthalmic tests?

Dr. Adelsberger: The tests were done according to the method used by Mary Hewitt Loveless, M.D., with increasing allergen concentrations, starting with 10 units per milliliter and continuing with twofold stronger concentrations up to concentrations of 5,120 or 10,240 units. A local reaction in the eye and headache usually developed at concentrations of from 1,280 to 5,120 units. Interestingly enough, the titer in the same patient was approximately the same at repeated tests, even if there was an interval of several weeks between these tests. In some instances saline drops were given prior to the allergen instillation, so that the patients could not rely on the number of drops given. In these instances it was also seen that the titer was quite persistent.

Joseph Harkavy, M.D.: In the first place, I think many of the cases sent to us are those patients who have reacted favorably to antihistamines, so that allergy is suspected. Second, some patients give a clinical history of allergy in the family or in themselves. When they come to us, the story of a seasonal variation in the headache is very helpful. A very important role is played by inhalants, mainly dust, molds, and pollens. I have patients who are being immunized to dust and molds just as if they had respiratory allergy. Finally, there is a group of patients in whom allergy is suspected but who do not give distinct reactions. I find that by putting these patients on special types of elimination diets, we finally discover that they are sensitive to certain foods. The eye tests, like the skin tests, are not always reliable. Dr. Adels berger believes that an eye test showing positive results is more likely to cause a headache by causing a reaction which is nearer the head.

Dr. Siegal: The second subject this evening is one to which we allergists have not given enough attention—the problem of hearing impairment and the possible role of allergy in the upper respiratory tract in its etiology. We have with us a husband and wife team from New Haven who are going to discuss this problem.

Allergic Paracusis: New Allergic Syndrome

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From St. Raphael's Hospital

Our subject may best be introduced by the following case report.

Case report

The patient was a seven-year-old child. He was quiet, prone to daydream, and considered a "lamb" by his teachers. His scholastic achievement in reading, spelling, and language usage was startlingly poor in contrast to capable, grade-level performance in primary arithmetic. The paradox was duly noted on the school record, the patient was classified as immature, and then the matter was left to time.

On March 23 a routine school hearing survey showed that the patient had a moderate degree of hearing loss. With a note that he had a cold at the time the test was made, the school nurse discounted the results and scheduled him for retesting. Because school pupil loads are what they are, he was retested in a year, the following March. The results of the test and the health picture were just about the same, as was his school performance, but no correlation of these findings was suggested. The otologist who saw the patient on referral two months later found scarcely any disturbance of hearing, and he advised the patient's mother to "wait and see."

In the last week of September of the same year, the patient's hearing was retested and was found demonstrably superior. This should have proved once more, as it is claimed so often, that hearing tests on young children are notoriously unreliable, and the case should have been closed. However, another test was performed just ten days later. Suddenly a degree of loss similar to that demonstrated in the previous March was found again. Now we had a problem. By which test should the confused family and school be guided?

It is one of our purposes to demonstrate that all of these seemingly contradictory results are, in fact, accurate and reliable measurements of function reflecting the interaction of environmental and physiologic variations.

Cutaneous testing confirmed the clinical history of hypersensitivity to house dust. On October 3, between the test that showed excellent hearing and that which again showed a hearing loss the hot-air heat had been turned on in the patient's home. Typically, the patient's mother had never considered her son an allergic child. In her opinion, he simply had a cold all winter long, every winter; and it was just a runny nose, never anything serious. Each person who was consulted or involved in this case had been satisfied with knowing a fragment of the truth. None realized that these fragments, when integrated, might form a whole pattern that would be basic in helping a whole child.

Hyposensitization therapy on the patient was begun in October, 1960, and concurrently he received antihistamines for symptomatic relief. A correlation with the patient's school progress was made possible by the cooperation of his principal and school nurse. Prior to therapy and despite objective evidence of at least normal intelligence, the patient's achievements all indicated that he had needed four years of schooling to make two and one-half years of scholastic progress. After therapy was initiated and remedial reading help received during the summer, the patient made a year's progress during a year of schooling, with one notable exception. In language usage, which depends on alertness to the total speech environment rather than on cumulative formal schooling, he advanced two years to a performance at his own grade level.

When hyposensitization therapy succeeded in making the patient symptom-free, antihistamines were discontinued. Audiometric examinations in March and November, 1961, revealed a normal hearing acuity. While it cannot be proved that this was due to therapy rather than to simple physical maturation, the chronic upper-respiratory congestion present at these seasons in previous years was no longer in evidence.

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Results of study

Otologic literature is replete with reports on the incidence of conductive hearing loss, and allergists have frequently shown allergy to be a causative factor in such a loss. However, such patients have generally presented symptoms of known hearing loss. The study which we initiated was concerned with a group of allergic patients without a known hearing loss as a presenting problem and includes 120 such patients, all having either allergic rhinitis (perennial or seasonal), asthma, eczema, or combinations of all of these symptoms.

All of the patients were without infectious complications, were old enough to give valid responses to standard pure-tone audiometry, and cooperated by completing all the diagnostic procedures and hearing tests. Allergy was diagnosed on the basis of a family history which revealed positive findings, a clinical history, physical findings, nasal smears, and confirmation by positive cutaneous reactions to scratch or intradermal tests.

Since 1956 the American Academy of Ophthalmology and Otolaryngology has been concerned with a long-term study of hearing problems in children. Last year Eagles and Wishik[1] reported preliminary findings indicating that the normal hearing levels are significantly more acute in children than in adults. Therefore, a child can have a considerable hearing loss without its being detected by the 15- or 20-db. screening levels currently employed. We define a hearing loss in children as a drop of acuity of at least 15 db. for at least two test tones in either ear.

During the diagnostic procedures and before therapy was given, each patient participated in a series of at least three audiometric tests, given at intervals ranging from one week to one month apart. The details of procedures and precautions employed to ensure the validity of test results have been reported[2] and need not be repeated here.

A total of 456 hearing tests were made on 120 patients. The results of these audiometric series, their explanation, interpretation, and integration with other known bodies of fact are the concern of this presentation. Of the total group, 50 of the 120 patients (42 per cent) suffered some disturbance of hearing sensitivity. Thirty-nine of the 69 patients who were under nine years of age (57 per cent) in contrast with 11 of 51 patients (22 per cent) who were nine years or older showed hearing loss, indicating the greater frequency of hearing loss in the younger children. Of the 101 patients who had either seasonal or perennial allergic rhinitis, only 8 of the 44 over nine years of age (18 per cent) showed disturbed acuity, while 37 of the 57 (65 per cent) who were less than nine years old were so affected.

In only 16 of the 50 patients who showed a loss was this loss demonstrable on every test of the series. In other words, more than two thirds of the loss cases showed intermittent loss of hearing which might or might not have been discovered, had only a single test been made. Twenty-eight of the 34 cases of intermittent loss occurred in children under nine years of age.

The National Conference on Identification Audiometry[3] defined the medical, social, and educational justifications for programs of identification audiometry thus:

> . . . to locate children who have even minimal hearing problems so that they can be referred for medical treatment of any active ear conditions discovered to be present and so that remedial educational procedures can be instituted at the earliest possible date. Programs should be designed to identify not only children with a chronic disability, but also children who have difficulty during only certain times of the year or under certain conditions.

Our findings demonstrate the high proportion of allergic youngsters who may fall within this group. Their physicians should be constantly aware of this. That such is not necessarily the case is suggested by a study of referral diagnoses which has been made at The New York Hospital of a group of preschool children on whom the hospital made the finding of hearing loss. At least 60 per cent were referred as mentally defective, aphasic, or emotionally disturbed. Less than 40 per cent were referred with even the possibility of a hearing loss cited in the referral.

For an adult whose vocabulary is well

established and who has a normal reservoir of language experience, the partial, scattered, fluctuating obliterations of sound which mark hearing disturbances may be annoying, but they are seldom incapacitating. He is able to make up for them by an understanding of the context of the situation, by a memory of and familiarity with customary language usage. The young child has no such reservoir to draw on. Daily he is subjected to a bombardment of new experiences and unfamiliar words. Thus the degree of hearing loss, which may be of little practical significance to an adult, may be a substantial handicap to the academic progress of a child.[4] We feel that an investigation for the presence of allergic disease may establish etiologic conditions for many presently inexplicable problems of speech and language deviation.

Eustachian tube

We speak of simple physical maturation. Our findings and those of other investigators point to some significant changes in the child's otologic status as he grows older. Armstrong[5] states that 78 per cent in a series of 1,016 patients with ears containing fluid were children of eight years of age or under. Davison[6] reports that over 65 per cent of middle-ear effusions occur in children under ten years of age, in contrast to 16 per cent which occur in the eleven-to-twenty-year age group. Among 1,726 children five through seven years of age who failed their first tests, Wishik found that 48.4 per cent failed later tests. Therefore, 51.6 per cent of these children overcame or outgrew their hearing disorders within the eight-year follow-up covered by this report.

To understand these changes it is necessary to review briefly the anatomy of the eustachian tubes. The eustachian tubes in the infant differ considerably from those in the older person. We have not been able to find anywhere in the literature a description of the intermediate steps showing the descent of the eustachian tube. In the infant the eustachian tube is shorter than in the adult, being less than half the adult length, about 14 mm. compared with about 35 mm. The tympanic orifice and the caliber of the tube are quite as large as in the adult; therefore, the tube as a whole is relatively much wider. The osseous and cartilagenous portions of the infant tube are very much the same, in a straight line, whereas in the adult they form an obtuse angle at the junction. The direction of the tube is almost horizontal in the infant, the tympanic orifice being practically at the same level as the pharyngeal opening, while in the adult the orifice is 15 mm. higher. The pharyngeal opening of the tube at birth is opposite the edge of the hard palate, while in the adult it is at least 10 mm. above this level.

Such maturational changes are significant in a consideration of hearing loss because physiologically the eustachian tube is a combined ventilating and drainage channel. It is normally closed, opening periodically to ventilate the tympanic cavity. Its chief function is to maintain equal air pressure on each side of the tympanic membrane, that is, in the external and the middle ear. This is essential to a free-swinging lever system, since a marked difference in pressure between the outer canal and the tympanic cavity tends to lessen the effectiveness of sound vibrations on the ossicles. Visualizing the position, width, and straightness of the immature eustachian tubes, we can recognize the decreased opportunity for tubal drainage and the increased opportunity for the collection of nasopharyngeal secretions in and about the tubal orifice.

What are the mechanisms and effects of eustachian tube dysfunction? Birrell[7] points out that the result of an obstruction of the eustachian tube is that oxygen is absorbed in the middle ear, and the negative pressure develops because the air thus lost cannot be replaced until the tube opens. Since the air in the external meatus remains at atmospheric pressure, the tympanic membrane is drawn in. This differential loading of the two sides of the membrane results in a conductive deafness which is called vacuum otitis, the main symptom of which is hearing loss, usually painless. A sequela may be the exudation of seromucus into the tympanic cavity, its outstanding symptom being a sensation of fullness in the ear, with transitory tinnitus and hearing loss. This condition is called secretory or serous otitis media. It is a disease entity commonly encountered in otologic practice, and myringotomy is frequently employed to relieve such middle-ear congestion and to re-establish efficient sound conduction.

Comment

The relationship between upper respiratory allergy and a heightened incidence of hearing disturbance is, of course, well known to both allergists and otologists. It is the high degree of previously unsuspected loss, demonstrated in our cases, which is noteworthy.

Solow[8] states that one third of all cases of serious otitis which he has investigated are due to allergy, and that one of its main symptoms is fluctuating hearing loss. Kuhn[9] has emphasized the need to search out hearing disorders which are due to allergy. He stated, as did Solow after him, that the best clue is variability in both the presence and intensity of hearing changes from day to day. Canfield[10] has pointed out that not only infections but also allergic reactions of the nose, throat, and ears can cause a hearing loss. Allergy is implicated as the causative agent of such symptoms because the mucous membrane of the eustachian tube is identical in structure and function with the mucous membrane of the nasopharynx of which it is an extension. Derlacki[11] reports that an allergic involvement of the middle ear is a part of the generalized allergic reaction of the respiratory epithelium, with a selective emphasis on the mucous membranes of the eustachian tube and of the tympanic cavity. The intermittency of allergy-connected hearing loss is associated directly with the more observable fluctuations in the severity of allergic symptoms. It may be considered as a first-degree otologic involvement which sometimes subsides as a result of anatomic maturation, but which can also develop that second degree of severity characterized by persistent loss. These are the cases with which all otologists are familiar.

Summary

We have described a syndrome which we call allergic paracusis of childhood. It is most prevalent in the early years of life, affecting the hearing of 65 per cent of the children who present symptoms of allergic rhinitis and who are under nine years of age. Allergic paracusis is initially associated with vacuum otitis, is unaccompanied by pain, and is most frequently characterized by an intermittency of hearing loss. Even in those cases where loss is persistent, it fluctuates in intensity. Because paracusis occurs so often in the very young and is variable, its presence is rarely suspected and behavioral disturbances attributable to it are frequently charged to immaturity, inattentiveness, dullness, and emotional insecurity.

General physicians and pediatricians must be more concerned with the etiologic evaluation of the child who "always has a cold." The necessity for a consultation with allergists may be indicated more frequently. For children with chronic upper-respiratory symptoms who may also demonstrate disorders of speech and language development, scholastic underachievement, or behavior deviations such as inattentiveness, dullness, and daydreaming, the physician should seek allergic, as well as otologic, consultation and a series of hearing tests should be considered part of the diagnostic work-up.

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Discussion

Dr. Siegal: Thank you, Dr. and Mrs. Szanton. I know we are all grateful for a provocative presentation of a very important subject. Sidney S. Feuerstein, M.D., Assistant Attending of the Otolaryngology

Service at The Mt. Sinai Hospital will open the discussion on this subject of impaired hearing in children in relation to allergy.

Sidney S. Feuerstein, M.D., *New York City*. Dr. and Mrs. Szanton should be complimented for spearheading our thinking in their direction.

We see patients from fifteen to twenty-five years of age who have a certain amount of deafness. Their troubles started perhaps when they were two or three years old. Their physicians or pediatricians failed to recognize that these children had a certain type of otitis media, and whether or not it was on an allergic or inflammatory basis, these children were allowed to grow up without the proper treatment. They developed a conductive deafness which at the age of fifteen or twenty years required hearing aides and possibly ear surgery for rehabilitation later in life.

Paracusis means abnormal hearing. Abnormal hearing can mean many things. What has been stressed this evening is conductive paracusis. The nerve and the inner ear are normal; the mechanical area of transmission of sound, which is the middle ear, is abnormal. What can cause an abnormality in the middle ear? Allergy, chronic upper respiratory infection, tumors of the nasopharynx, adenoiditis, sinusitis, and so forth. All these things can cause middle-ear deafness.

There is nothing characteristic about an allergic type of otitis media. In most reports in the literature eosinophils are rarely found in the middle-ear fluid. Some physicians report 2 per cent, others 10 per cent, and some 20 per cent of cases.

Joseph Goldman, M.D., Chief of the Ear, Nose, and Throat Service at The Mt. Sinai Hospital, has done about 150 aspirations. In none of them has he found any significant increase in the number of eosinophils. The middle-ear problem is not primarily an allergic one. The allergic problem is in the adenoid region of the nasopharynx. Similarly, an upper-respiratory infection which causes an otitis media will present the same symptoms.

An examination of the tympanic membrane in these children is of extreme importance. The average practitioner who looks at an ear drum may not recognize that it is abnormal. A marked injection is not noted. Usually seen are a thickening of the drum, a dulling of the light reflex, and either a slight bulging or a slight retraction. Usually there is retraction because, as Dr. Szanton pointed out, a vacuum type of otitis develops.

So-called allergic otitis may be accompanied by an inflammatory otitis and both should be treated. The nasopharynx should be examined very carefully for any infected adenoid mass which may be obstructing the eustachian tube. This should be removed, surgically, if necessary, and the proper antibiotic should be given, in addition to the allergic work-up and desensitization.

Dr. Siegal: Thank you, Dr. Feuerstein.

Question: Dr. Szanton, what allergens are usually incriminated in allergic paracusis? Are they primarily inhalants or have foods also been involved? Do you find prompt remission with the institution of therapy?

Dr. Szanton: All of the cases that we have presented have had pollen or house dust sensitivity. We have not, as yet, had the opportunity to look into food allergy cases.

Question: Do you have controls on this, doctor?

Dr. Szanton: No. We do not have to use controls on this. We know the figures on hearing loss are usually about 7 to 10 per cent in a population and we do not require controls here any more than we would on, for instance, white blood cell counts and differentials.

Murray Dworetzky, M.D.: Would you say something about the response of hearing acuity to adrenalin as a differential point in the diagnosis of allergic paracusis.

Mrs. Szanton: This is the Kuhn test. We have done this on some of the youngsters when we were trying to establish the differential diagnosis, and it has been very interesting. Of course, this is short-lasting. First we do threshold audiometry, then administer an injection of adrenalin, and finally, a half-hour later, do an audiometric retesting. This is, of course, in addition to conductive testing. We find there is better acuity a half-hour later.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
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Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by MAX TESSLER, M.D.

Diarrhea, Constipation, and a Lesion in the Cecum

Case history

MACKENZIE VERDREHEN, M.D.: A forty-seven-year-old unmarried white woman was admitted to Knickerbocker Hospital for the first time in 1953 because of urinary frequency and burning on urination accompanied by suprapubic pain. She had had a similar attack about one month previously, apparently associated with her last menstrual period. On both occasions she noted that her urine was cloudy. She had been in good health previously. The menarche had been normal, and the menses were regular. She had never had symptoms referable to the urinary tract before. The system review disclosed no further information.

A physical examination was unrevealing except for suprapubic tenderness. A pelvic examination was not performed. She was afebrile.

The urine was acid, had a specific gravity of 1.020, a very faint trace of albumin, no sugar, and 1 or 2 white blood cells per high power field in the sediment. The hemoglobin was 12.8 Gm. per 100 ml., and the white blood cell count was 5,900 with 51 per cent polymorphonuclear leukocytes, 42 per cent lymphocytes, 5 per cent eosinophils, and 2 per cent monocytes.

A cystoscopy revealed some redness of the trigone. Both ureteral orifices appeared normal. Retrograde pyelography showed both kidneys to be fairly large and low in position. No calculi were demonstrable. There was marked dilatation of both renal pelves and calyces and very narrow ureteropelvic junctures. Following the withdrawal of the catheters the urinary outflow tract emptied slowly. An irregular calcified shadow was seen overlying the midsacrum.

The patient was treated with analgesics and was discharged improved on the third hospital day.

Five years and ten months later she was readmitted for the second time because of heartburn and postprandial regurgitation of three months duration. She now stated that she had had intermittent episodes of epigastric pain crossing to the right flank for about twenty-five years. She had passed the menopause three to four years previously, and during the past two or three years these episodes had become more frequent. There had been no vomiting except for a single episode six months previously. There had been no hematemesis, melena, or loss of weight. She did not smoke, and she denied drinking. Her family physician had treated her with a bland diet and some medicine which had not relieved her symptoms.

She also stated that one month previously she had had an attack of bursitis in the right shoulder which had been treated with several injections of cortisone followed by the oral administration of a corticoid.

She was afebrile, and her vital signs were normal. A physical examination was unrevealing except for epigastric tenderness on deep pressure. A pelvic examination was not performed.

The urine had a specific gravity of 1.017 and was free of sugar, acetone, albumin, or cells in the sediment. The hemoglobin was 10 Gm. per 100 ml., and the white blood cell count was 5,150 with 83 per cent polymorphonuclear leukocytes, 13 per cent lymphocytes, and 4 per cent monocytes. The fasting blood sugar was 107 mg. per 100 ml., and the nonprotein nitrogen was 37 mg. per 100 ml. The total protein was 5.2 Gm. per 100 ml. with 3.8 Gm. albumin and 1.4 Gm. globulin. A gastric analysis revealed 56 units of total acid and 40 units of free hydrochloride, rising to 90 units of total acid and 78 units of free hydrochloride after histamine. An electrocardiogram disclosed no specific abnormality.

A chest roentgenogram showed no abnormality of the heart or lungs. There was no evidence of soft tissue calcification in an x-ray film of the right shoulder. A large, homogeneous, sharply-defined calcific deposit was found along the palmar aspect of the right wrist. An upper gastrointestinal series revealed some smoothing of the gastric rugae, a constant deformity of the prepyloric area encroaching on the greater curvature, and a niche in the first portion of the duodenum.

A subtotal gastrectomy was performed. Radiotherapy was given for the lesion in the right wrist. The patient was discharged on the twenty-third hospital day.

One year and five months later she was readmitted for the third time because of a painless mass in the right breast. During the interval she had lost about 15 pounds in weight and had become anemic. The mass was about 1 cm. in size, located just lateral to the nipple. A physical examination was not revealing. A pelvic examination revealed no abnormal findings.

The urine had a specific gravity of 1.010, contained a very faint trace of albumin and many bacteria, but was free of sugar or acetone. The hemoglobin was 10.9 Gm. per 100 ml., and the white blood cell count was 8,000 with 59 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes, and 1 per cent eosinophils. A chest roentgenogram revealed normal heart and lungs. A routine skeletal survey showed no evidence of metastatic disease.

An operation was performed on the fourth hospital day. She received 2 units of whole blood.

One year and ten months after the breast operation, she was readmitted in March, 1962, for the fourth time, now stating her age as sixty-one years. During the interval between hospital admissions she had noted episodes of intermittent constipation and diarrhea increasing somewhat in frequency over the last year. Occasionally, flatulence and abdominal distention accompanied this change in bowel habits, but there was no vomiting and no hematemesis or melena.

On admission, the vital signs were normal. Specifically, the abdomen was soft, without guarding, and free from palpable organs or masses. There was no costovertebral tenderness. A pelvic examination was not performed. The patellar reflex was exaggerated bilaterally.

A urinalysis revealed a specific gravity of 1.010, no sugar or albumin, and occasional white blood cells. The hemoglobin was 12.3 Gm. per 100 ml. The white blood cell count was 7,100 with 52 per cent polymorphonuclear leukocytes, 45 per cent lymphocytes, 1 per cent eosinophils, and 2 per cent monocytes. The nonprotein nitrogen was 25.5 mg. per 100 ml. The stool guaiac test showed negative findings.

A chest roentgenogram showed borderline cardiac enlargement with prominence of the aortic knob. There was no evidence of an intrapulmonic disease. A sigmoidoscopy was unrevealing. A barium enema showed a deformity in the wall of the cecum which had a smooth outline and sharp margins. It appeared globular in outline, and the mucosal markings were smooth but not effaced or destroyed. An operation was performed.

Discussion

Max Tessler, M.D.*: In the case of the woman now under discussion we are faced with four admissions to the hospital with essentially widely separate problems. There is meager laboratory data but fortunately some excellent roentgenographic studies which I shall use as a point of departure in attempting to unify one or more of these admissions under a common diagnostic entity in the best traditions of CPCmanship or perhaps to arrive at a number of widely separate and distinct diagnoses.

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The first admission in 1953 was apparently for a mild nonspecific cystitis. While a fairly extensive urologic investigation was carried out, no specific conclusions were reached. Apparently no bacterial studies were done at the time. Since we are able to follow this patient's course over the next nine years, and there is no recurrence of this problem, we can leave it safely. However, there is one negative point which merits comment, and that is that no renal calculi or interstitial calcification was noted during this workup. This datum may be of importance in light of the following discussion.

The second admission to the hospital in 1958, five years and ten months later, apparently was precipitated by a three-month history of heartburn and postprandial regurgitation. We also are told that during the previous twenty-five years the patient had had occasional episodes of epigastric pain which crossed to the right flank. There is no further description of either of these pains, such as whether they were related to any specific types of food or as to their temporal occurrence. The remainder of her gastrointestinal history shows essentially negative findings. However, we are also given the information that she had an attack of bursitis approximately a month before her admission and that she had been treated with intramuscular and oral corticosteroids. The exact type, dosage, and duration of this medication is unknown to us. Her positive physical findings apparently are limited to epigastric tenderness. The laboratory data at our disposal are essentially unremarkable with the exception of the fact that she had an anemia with 10 Gm. of hemoglobin and that a gastric analysis revealed 56 units of total acid with 40 units of free hydrochloride on what I assume is an overnight fasting specimen. These latter values rose to 90 units of total acid with 78 units of free hydrochloride following histamine stimulation. An upper gastrointestinal series was done with some striking findings, and it is undoubtedly as a result of this examination that the subtotal gastrectomy was performed.

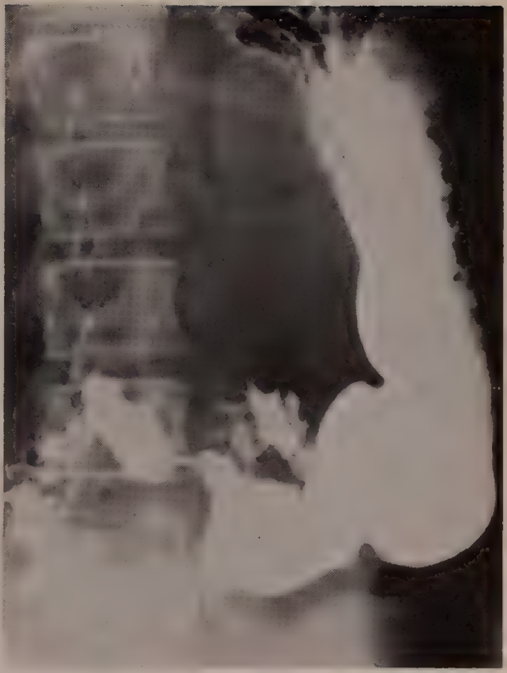

FIGURE 1. Upper gastrointestinal series showing a deformity in the pyloroduodenal region. The roentgenographic landmarks are obliterated, and the line of demarcation between pylorus and duodenum is obscure.

For the purposes of discussion we can separate the gastrointestinal series into two parts. Turning our attention to the duodenum first, I think everyone will agree that we have obvious evidence of peptic ulcer disease in the bulb (Figs. 1 and 2). While it would be difficult to point to any one spot with certainty and identify a definitive crater (with the exception of perhaps one spot in the center), the bulb is certainly irregular and somewhat deformed. There is marked postbulbar spasm of the descending duodenum. The pyloric canal is somewhat eccentric with regard to its entrance into the bulb, and there are coarse folds in the bulb, all secondary signs of duodenal ulcer disease. The ob-

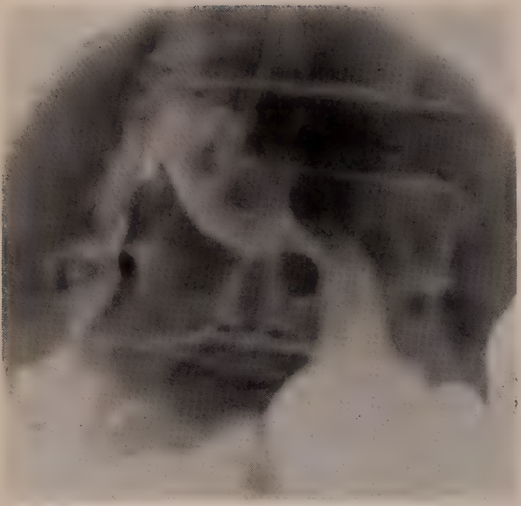

FIGURE 2. Spot film of the duodenal bulb showing detail of the deformity with a possible ulcer crater.

vious double density at the apex of the bulb I feel represents only the superimposition of the apex of the bulb on the most proximal portion of the descending duodenum, giving the appearance of a double density.

While the historical data provided are certainly not sufficient to make a diagnosis of duodenal ulcer disease, certainly the laboratory data point most strongly in this direction, since the levels for free and total acid in both the fasting and histamine-stimulated specimens are markedly elevated for a woman in this age group. Normally 10 to 20 units of free acid in a total of 20 to 36 exist in a fasting specimen, and following histamine the free acid component could rise to as high as from 35 to 50 units of free acid in a total of 45 to 60 units. Our patient goes from 40 units of free acid in a total of 56 units to as high as 78 units of free acid in a total of 90 units following her histamine-stimulation, a marked hyperchlorhydria. Unfortunately, we are given no information concerning the volumes of the acid secretion, since it is well known that in patients with duodenal ulcer the overnight volume as well as the acid can be elevated markedly.

The interesting question is what part, if any, did steroid therapy play in her peptic ulcer disease. It is well established that the therapeutic administration of adrenal cortical hormones has resulted in an increased incidence of peptic ulcer disease or an exacerbation of known peptic ulcer disease. Cooper *et al.*[1] have shown that while there is not a direct dose relationship, gastric acidity tends to be increased with larger cortisone dosages. But, second and more important, in certain circumstances cortisone has been found to render the gastric mucosa more susceptible to acid peptic digestion. In animals who are pretreated with corticosteroids there is a definite mucosal susceptibility or decreased resistance to acid pepsin digestion. When those disease processes for which long-term corticosteroid therapy is most frequently used have been studied, the higher incidence of peptic ulceration has been found only in patients with rheumatoid arthritis rather than in those with ulcerative colitis or with skin disorders treated with steroids.[2] The pattern of the disease is different in those individuals. For example, the usual sex difference in duodenal ulcer disease disappears. It has been shown that ulceration may occur as soon as after one week of therapy and that the larger the dosage of steroid and the longer the dosage the greater is the increase in the incidence of peptic ulcer disease. It is true that in steroid-induced ulcer a higher proportion are gastric ulcers than would be found normally in proportion to duodenal ulcer disease.

While we have no information concerning the stool guaiac on this admission, it is of interest that a patient with bursitis may very well have taken aspirin as part of her therapeutic regimen. Aspirin has been shown in various dosage levels to be responsible for a flare-up of peptic ulcer disease in individuals with the ulcer diathesis. It is true, however, that the most common manifestation in these individuals is bleeding rather than pain or heartburn.

We now turn our attention to the lesion in the stomach. We find that the pathologic findings are confined pretty much to the immediate prepyloric region along the greater curvature aspect of the stomach (Fig. 1). The lesion shows itself as a smooth intrusional mass into the lumen of the stomach with no evidence of overlying mucosal destruction. There is some smoothing out of the folds in the distal antrum in this area. In the center of the lesion there is a thin projection of barium which extends into it (Fig. 3). There is some question in my mind as to whether or not there is some element of fixation of the opposite wall in this area, but this is a question which could be answered better by the fluoroscopist. Could this lesion represent a simple benign ulcer in the immediate prepyloric region? If this were so, it certainly would be an ulcer surrounded by a great deal of edema to cause this intrusional mass, and I doubt this on a second basis, that the protrusion of barium is much too thin and much longer than what ordinarily would be seen in an ulcer crater. With so much edema and inflammation in this area surrounding an ulcer I would have expected that the patient would have had signs or symptoms of obstruction. Furthermore, in view of the fact that the patient was subjected to surgery for relatively minor complaints, it is unlikely that the staff considered this to be simple benign ulcer disease.

I doubt that this lesion represents primary carcinoma in the area. First, although this diagnosis is not excluded by the presence of duodenal disease, it is certainly unlikely. The extremely high acid secretion values militate strongly against this diagnosis. If it is a malignant process, it is certainly not a mucosal lesion, since this x-ray picture fits fairly well the criteria for a submucosal lesion. In discussing submucosal tumors the first question that arises is whether this could be a metastatic lesion either by contiguous spread from the adjacent pancreas or from carcinoma elsewhere in the body. While the classically described iceberging of the greater curvature of the stomach is not present, it is true that we have seen more and more carcinomas infiltrate the stomach from the pancreas without this roentgen sign. However, in view of the fact that the patient has lived at least four years following her subtotal gastrectomy with apparently no surgical attack on the pancreas, I feel that this diagnosis is extremely unlikely. I will put aside for the moment the discussion of metastatic disease from other areas and discuss it later in relation to the patient's breast and colon disease. One of the more common submucosal tumors in the stomach is the leiomyoma. However, these tumors usually give rise to ulceration, often an eccentric ulceration which may bleed. No positive guaiac test findings are reported in this case. Furthermore, the umbilication (Fig. 3) is rather central as opposed to the usual eccentric location. One must discuss two other submucosal tumors in this area. Both arise from the pancreas, the first being due to a noninsulin-producing beta cell tumor which, as you know, may give rise to what we now consider the Zollinger-Ellison syndrome. It is well known that these tumors may be extrapancreatic, occurring most frequently in the duodenal and stomach wall. The hallmark of the Zollinger-Ellison syndrome is extreme hyperacidity. It is always accompanied by an extremely high volume of secretion, anywhere from 1,000 to 4,000 cc. in overnight specimens. Information regarding the volume is not available. Furthermore, the symptomatology of the ulcer disease is usually more rapid than we find in this case, and a markedly atypical

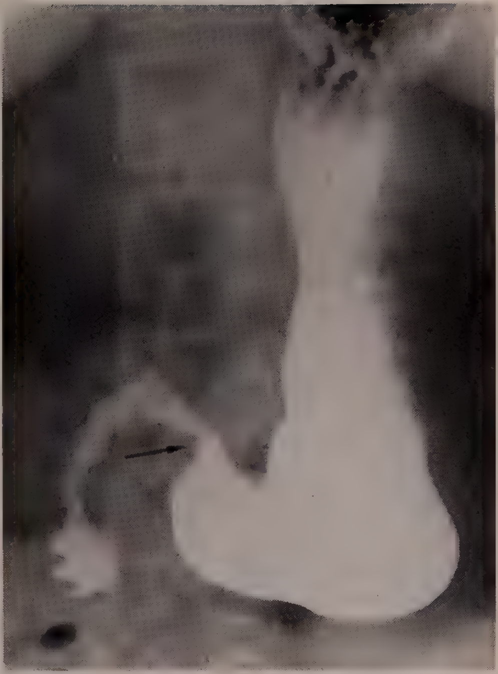

FIGURE 3. Upper gastrointestinal series showing a small collection of barium (arrow) which might be a ductal structure leading into aberrant pancreatic tissue.

location of the ulcer is extremely common. The explanation of this latter phenomenon is that the extremely acid gastric juice reaches a point farther along in the duodenum or proximal jejunum without having been properly neutralized, and it is well known that the farther one gets from the duodenum the less is the mucosal resistance to acid pepsin digestion. The mention of the Zollinger-Ellison syndrome of course must bring to mind the possibility of the polyglandular adenoma syndrome or Werner's syndrome, and this by a somewhat devious route brings us to the parathyroid gland. In the presence of hyperparathyroidism from any one of a number of causes the incidence of duodenal ulcer has been noted to be as high as 26 per cent, although Ostrow, Blanshard, and Gray,[3] in a carefully controlled study, reported an incidence of 9.1 per cent. Duodenal disease associated with hyperparathyroidism is noted to be more aggressive and has been correlated with a marked increase in gastric secretion as shown by Donegan and Spiro.[4] These authors also showed that the hypocalcemia which may occur in hypoparathyroidism is accompanied by a marked decrease in gastric secretion with a rise in pH. I brought this disease into the discussion because of the previous episode of urinary tract disease and the presence of what was apparently a calcified tendonitis in the wrist of this individual. However, the extensive bone surveys which we have at our disposal reveal no other changes of demineralization, and, as I indicated earlier, there was no evidence of calcification of the kidneys. We have no information concerning the blood calcium in this patient, and I think this diagnosis is not tenable on the data at hand.

Returning to aberrant pancreatic tissue in the gastric wall, the variety which deserves serious discussion here is that which arises from rests of pancreatic tissue in the embryologic gastrointestinal tract. Barbosa *et al.*[5] point out that these are most common in the pyloric area of the stomach, most often on the greater curvature toward the posterior wall, sometimes associated with gastric hyperacidity. They range in size from 0.2 to 5 cm., and actually 50 per cent of the aberrant pancreatic tissue located throughout the entire gastrointestinal trace is found within the stomach and duodenum. The diagnosis cannot be made roentgenographically unless a ductal structure can be identified. Even when this structure is present, it can resemble a tumor with an ulcer crater within it. I think that this is a very real possibility to be strongly considered in this particular case.

One year and five months later the patient was readmitted because of a painless mass in the right breast. Unfortunately, we have no further information as to whether this mass was hard or soft or whether it was fixed to adjacent or overlying skin. We are told that during the interval from the previous admission the patient had lost 15 pounds and had become anemic. However, we are given no information concerning the patient's dietary habits or postsubtotal gastrectomy problems, if indeed she had any. From the nature of the lesions in the stomach and duodenum one would presume that at least a Billroth II type of procedure was performed, and weight loss following such a procedure is not at all uncommon. By comparing the set of chest x-ray films which were kindly put at my disposal one can see that breast shadows are present bilaterally on all films including those taken after the surgery was performed on the breast. Ergo, I feel it is safe to assume that a radical mastectomy was not performed, and I would conclude that the lesion in the breast was removed locally and in all probability was benign.

The patient's final admission one year and ten months after the breast operation was brought about because of episodes of intermittent constipation and diarrhea which had increased in frequency in the year prior to her admission. She also was subject to flatulence and abdominal distention which accompanied this change in bowel habits. Unfortunately, there is no description of the type of diarrhea which the patient had so that we cannot relate it to her gastric surgery as opposed to the colon lesion which was demonstrated on the barium enema. This lesion is located in the cecal cap toward the medial wall below the entrance of the terminal ileum

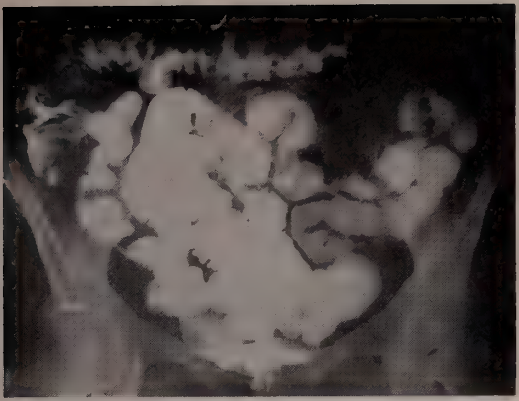

FIGURE 4. Barium enema postevacuation showing a rounded, sharply circumscribed defect in the cecum without evidence of mucosal destruction.

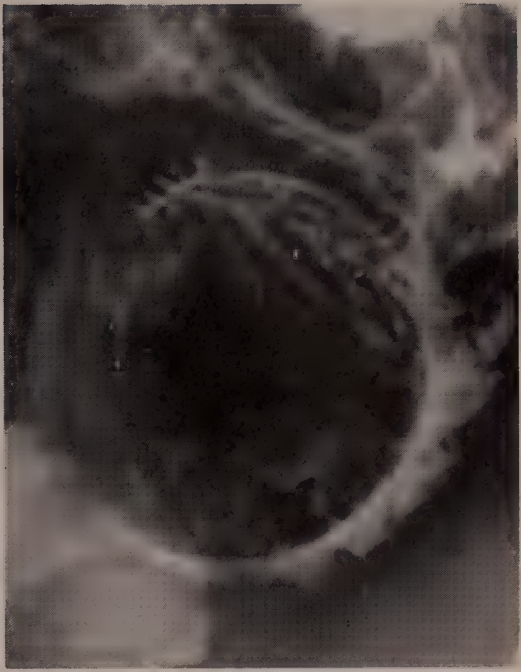

FIGURE 5. Spot film of cecum under pressure showing detail of the sharply defined defect with a spherical contour. The preservation of thinned mucosal folds is clearly visible.

(Fig. 4). On one of the spot films (Fig. 5) we can clearly see the lips of the ileocecal valve which are not involved. The lesion is round and symmetrical in shape, most definitely radiolucent, and from the sharp angulation which it makes with the wall of the cecum one can surmise that the tumor is submucosal in location, or, less likely, subserosal and growing into the lumen of the cecum. The mucosal pattern in the immediate area of the cecum surrounding the lesion, while somewhat effaced, is not at all disrupted. The problem thus evolves into a differential diagnosis of submucosal, benign lesions of the cecum. First one must give thought to metastatic disease to the bowel which can occur, of course, anywhere in the intestines. Herein exists the only association which conceivably could be made between the stomach, breast, and colon lesions. Indeed, if this patient had carcinoma of the breast as opposed to a benign process, this calls to mind the fascinating study by Hartmann and Sherlock[6] which demonstrated most conclusively that there was a significant increase in metastatic disease to the stomach and duodenum in patients with breast carcinoma who were being treated with adrenal steroids. They showed that metastases were six times as frequent to this area in patients treated with adrenal steroids as compared with a control group. Again, the same hypotheses that are presented as the explanation for the increased incidence of peptic ulceration in steroid therapy with, for example, rheumatoid arthritis become pertinent here, and lower local tissue resistence in the mucosa and submucosa may give rise to a more fertile "soil" for the implantation of the rapidly disseminating tumor "seeds." The fact that the gastric lesion was discovered a year and a half before the breast lesion became clinically manifest does not alter this postulate. However attractive this entire triad may be, I am forced to dismiss it because I feel that the mass in the breast was not malignant, and furthermore the cecal lesion is certainly not a typical one for a subserosal metastatic lesion.

Another lesion which occurs frequently in this area and which may be associated with a lesion in the stomach is a carcinoid tumor. We would have to postulate the presence of two independent carcinoids, because, were either of these lesions metastatic from the other, one would have expected additional manifestations of the carcinoid syndrome which this patient did not have. Gastric carcinoids do occur as a primary lesion, 77 cases having been reported in the literature. However, this colonic lesion is not typical for carcinoid, since the tumor rarely reaches this size without having caused more severe symptoms either locally or due to distant metastases.

We do not know whether or not this patient had an appendectomy, but on these x-ray films one cannot demonstrate appendiceal filling. The possibility of a mucocele of the appendix growing into the cecal wall arises. This is not likely because of the radiolucency of the tumor and because a mucocele occurs as the result of an obstruction in the appendix and therefore would be more likely to be found in the distal portion of the organ. Had this woman had an appendectomy, I could not exclude this diagnosis. In fact, the location of the lesion would be more likely because mucoceles can arise in an appendiceal stump.

Last, one would have to consider most strongly the tumor which causes a round radiolucent appearance and which often is found in the cecum; in fact 75 per cent of these tumors in the gastrointestinal tract occur in the colon. The tumor I have in mind is a lipoma. These are usually solitary tumors which may be submucosal or subserosal and which on rare occasions may ulcerate. Constipation is the commonest symptom accompanying this lesion although in general the symptoms are vague. Intermittent intussusception occurs in about 35 per cent of the cases and may be accompanied by abdominal distention. In most cases it is almost impossible to differentiate with certainty on x-ray films from either carcinoma, polyp, spindle cell tumor, lymphosarcoma, or carcinoid. However, it rarely involves the entire cecal wall, is frequently lobulated, and causes a smooth filling defect (Fig. 5), forming a sharp angle with the bowel wall. On rare occasions a radiolucency with multiple, fine, strandlike areas due to a fibrous stroma can be identified, and this in conjunction with a dense capsule may lead one to the definitive diagnosis of a lipoma. Leiomyoma again must be considered, but because of the smooth globular shape of the tumor I think it is more likely to be a lipoma.

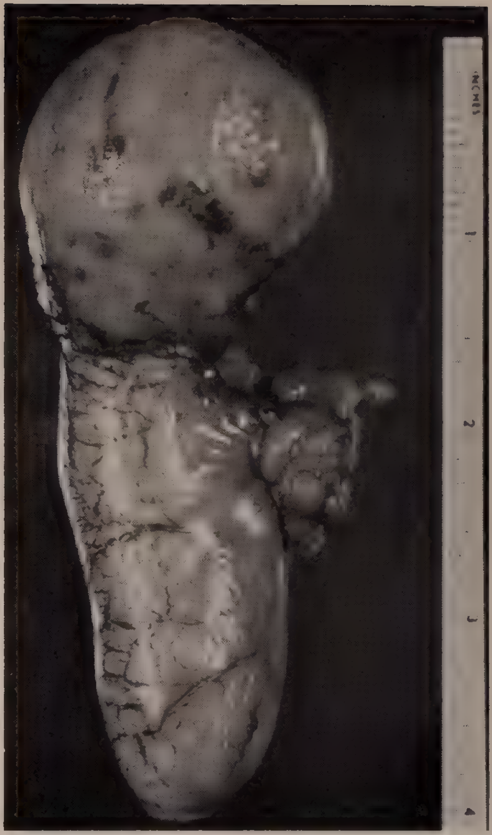

FIGURE 6. The appendix is distended, and its proximal third is covered by a cap of cecal mucosa.

MARDOQUEO I. SALOMON, M.D.: With respect to the Zollinger-Ellison syndrome, a recent report by Helimskii[7] in the Russian literature confirmed that the cell type in the islet cell adenoma is not the insulin-secreting beta cell but rather gamma and delta cells. Have you any further information about this?

DR. TESSLER: No. I am not familiar with this report.

DR. SALOMON: With regard to the question of a carcinoid tumor in this patient's cecum, one would not expect the carcinoid syndrome unless there were extensive metastases to the liver.

DR. TESSLER: Quite so. Serotonin must escape the action of monoamine oxidase in the liver and escape into the peripheral circulation, producing hyperserotoninemia, for the syndrome to occur. The liver metastases are usually massive, and there is no evidence of liver metastases in the patient at all. Therefore, I would have to postulate two separate carcinoids, one in the pyloric area and one in the cecum. This is not very probable, albeit multiple carcinoids do occur.

Marcel Tuchman, M.D.: Cannot lipomas in the gastrointestinal tract be multiple even as in the skin?

Dr. Tessler: That is quite so. Also, there is an increased association between lipomas in the skin and ones in the gastrointestinal tract.

Dr. Tuchman: Could the lesion seen on the upper gastrointestinal series be a lipoma?

Dr. Tessler: I doubt it. The x-ray picture is not really that of a submucous tumor.

Clinical diagnosis

1. *Cystitis, nonspecific*
2. *Duodenal ulcer*
3. *Benign tumor of breast*
4. *Mucocele of appendix*

Dr. Tessler's diagnoses

1. *Urinary tract infection, nonspecific*
2. *Duodenal ulcer, possibly activated by steroids*
3. *Aberrant pancreatic tissue, prepyloric area*
4. *Benign tumor of breast*
5. *Benign submucous tumor of cecum, probably lipoma*

Pathologic Report

William B. Ober, M.D.: During the past three years we have received three specimens from this patient. The first specimen was from a subtotal gastrectomy. We were unable to demonstrate the lesion in the duodenum, for that area was not resected. At the pylorus the gastric mucosa was thinned, chronically inflamed, and did show a focal superficial erosion. There was no aberrant pancreatic tissue. We made multiple sections because of the preoperative suspicion of an infiltrative lesion.

The second specimen was an intraductal papilloma of the breast, a benign lesion as Dr. Tessler predicted. One of the pitfalls that was neatly dodged in the discussion was the possibility of metastasis to the ovary from the breast tumor with subsequent extrinsic pressure on the cecum. Ovarian metastases from a primary breast cancer occur much more frequently than is usually thought. Turksoy[8] found ovarian metastases from breast cancer in 42 per cent of 19 autopsied patients and in 30 per cent of 26 patients subjected to prophylactic castration. The metastases were bilateral in all autopsy cases and in 5 of 8 surgical cases.

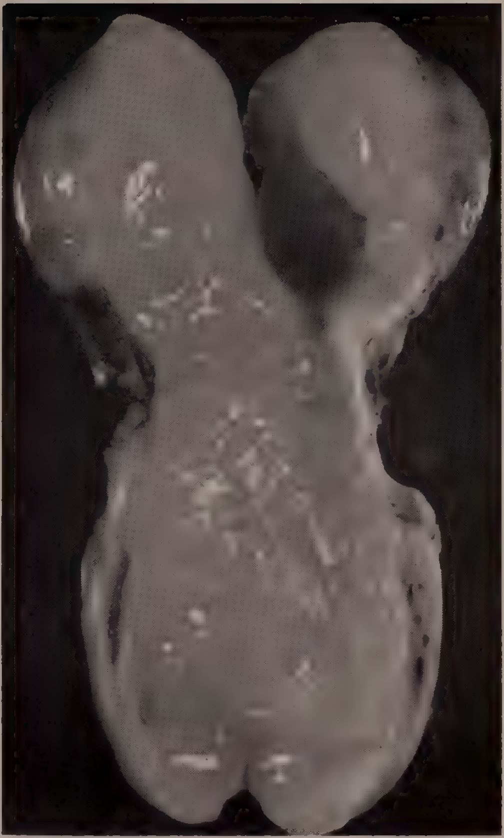

FIGURE 7. The appendix is opened to show the mucoid contents.

The third specimen proved to be a mucocele of the appendix (Fig. 6). It measured 10 by 3.5 cm. and had partly intussuscepted into the cecum. The resected specimen was capped with thinned, flattened cecal mucosa which had become adherent to the serosa of the distended appendix. It is easy to visualize how this partly intussuscepted

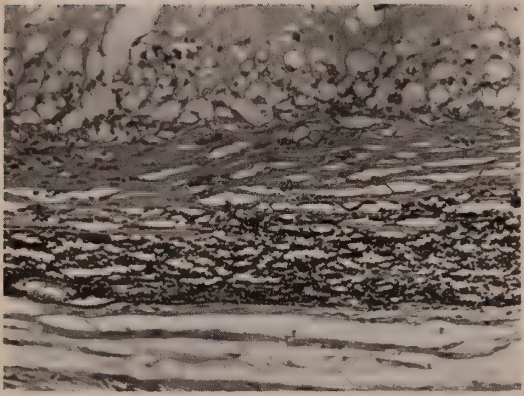

FIGURE 8. Section of the appendix showing loss of mucosa and atrophy of submucosa. Mucus is adherent to the luminal surface.

sausage-like structure produced the sharply outlined defect seen in the barium contrast study. The lumen of the appendix was filled with partly coagulated mucus with an opalescent sheen (Fig. 7), and the mucosa was flattened, atrophic, and even destroyed (Fig. 8). The submucosa and muscular coats showed typical atrophic changes secondary to a persistent increase of intraluminal pressure.

Anatomic diagnoses

1. *Chronic gastritis, pyloric area, with healing erosion*
2. *Intraductal papilloma, breast*
3. *Mucocele of appendix, partly intussuscepted into cecum*

Michael S. Bruno, M.D.: I would like Dr. George Haddad, who has been taking care of this patient, to close the discussion.

George H. Haddad, M.D.: I was pleased to hear Dr. Tessler's analysis of this patient and to listen to his technic of ferreting out the different ailments she had. I think I might say a word about the gastroduodenal lesion. Dr. Tessler was quite correct in inferring that I performed a Billroth II subtotal gastrectomy. The decision to explore was based on the opinion of two consultants, a radiologist and a surgeon, both of whom felt that the distortion in the prepyloric area might indicate an infiltrative carcinoma. This was prior to the gastric analysis which demonstrated increased free acid. When this determination was reported, I felt much relieved, and I did not expect to find a tumor when I operated. Fortunately, my expectations were justified, and a limited procedure was done. After the subtotal gastrectomy the patient did have trouble eating and maintaining her weight. This was why we gave her the blood transfusions at the time of the breast operation. Although the protocol does not really describe the breast lesion as it appeared clinically, it was not very alarming when I felt it. However, in this area, discretion is the better part of valor, and one biopsy is worth five guesses, so we removed the small mass and again were relieved to find that it was benign.

The mucocele of the appendix must have developed during the four-year interval since the gastrectomy because it was not there when I explored the abdomen at that time. The diagnosis of mucocele was made very firmly by Dr. Moynahan on the basis of his barium enema films, and he had no difficulty in persuading me that this was the case.

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Nutrition
Excerpts

*Prepared with the cooperation of the faculty
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DAPHNE A. ROE, M.D., Editor

Possible Control of Cholesterol Biosynthesis with Uncouplers of Oxidative Phosphorylation

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A CONSIDERABLE NUMBER of recent studies have been concerned with the significance of cholesterol in the etiology of atherosclerosis. One approach to the control of atherosclerosis has been to obtain a greater understanding of the reactions involved in the biosynthesis of cholesterol with the expectation that such knowledge would lead eventually to effective means of regulating biosynthesis and tissue levels of the sterol.

Essential reactions

Prominent among the reactions essential in the biosynthesis of cholesterol is a series of sequential phosphorylations.[1] These reactions are the phosphorylation of mevalonic acid mediated by mevalonic acid kinase to yield mevalonic acid-5-phosphate, the phosphorylation of mevalonic acid-5-phosphate mediated by phosphomevalonic acid kinase to yield mevalonic acid-5-pyrophosphate, and the phosphorylation of mevalonic acid-5-pyrophosphate mediated by pyrophosphomevalonic acid kinase to yield the hypothetical mevalonic acid-3-phosphate-5-pyrophosphate. In these reactions ATP (adenosine triphosphate) serves as the high-energy phosphate donor or driving force. The biosynthesis of cholesterol is, therefore, intimately associated with ATP and absolutely dependent on metabolic reactions that yield ATP.

As far as the animal kingdom is concerned, ATP can originate by either of two processes —substrate phosphorylation or oxidative phosphorylation. In substrate phosphorylation certain intermediates in the utilization of carbohydrate such as 1,3-diphosphoglyceric acid or phosphoenolpyruvic acid possess sufficient energy in themselves to form the high energy ATP from ADP (adenosine diphosphate). In oxidative phosphorylation the transfer of electrons (and hydrogen) from the oxidation of an energy source is "coupled" to the generation of ATP by a process that is not well understood, and for every pair of electrons (and hydrogens) abstracted from a nutrient, 1 mol of oxygen is consumed and 2 to 3 mols of ATP are formed.

Studies by Wright and coworkers [2-5] have demonstrated that when liver homogenates that are highly active in the biosynthesis of cholesterol are treated with reagents that interfere with metabolism in such a way that a level of ATP is not maintained, cholesterol biosynthesis comes to a halt. Cholesterol biosynthesis in homogenates is effectively inhibited by: (1) preincubation of homogenates with ribonuclease, an enzyme that hydrolyzes a polynucleotide essential in oxidative phosphorylation; (2) preincubation with certain inorganic salts such as those of vanadium or calcium that interfere with or precipitate inorganic phosphate; (3) preincubation under anaerobic conditions that do not permit normal oxidation by free oxygen; and (4) preincubation with certain uncouplers of oxidative phosphorylation such as 2,4-dinitrophenol, azide, methylene blue, 1,1,3-tricyano-2-amino-1-propene, or carbonyl cyanide p-chlorophenylhydrazone. These latter compounds probably stimulate the breakdown of ATP by activating specific ATPases. Many of these compounds are quite active as inhibitors of cholesterol biosynthesis in homogenates. The classical uncoupler of oxidative phosphorylation, 2,4-dinitrophenol, for example, is active in the order of 10^{-5} M. Carbonyl cyanide p-chlorophenylhydrazone, one of the newer uncouplers of oxidative phosphorylation, is even more active.

Cholesterol biosynthesis is not the only process inhibited by interference with the level of ATP maintained in homogenates. Thus it is possible to show, for example, that homogenates preincubated with ribonuclease do not convert glucose-1-C^{14} to $C^{14}O_2$ presumably because of the unavailability of ATP for the enzyme hexokinase that must convert glucose to glucose-6-phosphate before it is further metabolized in reactions catalyzed by glucose-6-phosphate dehydrogenase, lactonase, and finally gluconic acid-6-phosphate dehydrogenase to yield finally ribulose-5-phosphate and CO_2.

Hypothesis

Since ATP is essential for a number of synthetic and degradative reactions it is apparent that kinases (those enzymes that catalyze phosphorylations) must have either the same or different affinities for ATP. The possibilities for the selective control of cholesterol biosynthesis in vivo exist if the mevalonic acid kinases have less affinity for ATP than do other "more essential" kinases. Stated in another way, it seems certain that there must exist an affinity series of the kinases for ATP. If the mevalonic acid kinases should be near the bottom of such a list, then in a condition of marginal tissue levels of ATP, such as might be brought about by the administration of an uncoupler of oxidative phosphorylation, cholesterol biosynthesis would be inhibited in preference to the other more essential reactions.

As early as 1934 Cutting, Rytand, and Tainter[6] showed that the administration of 2,4-dinitrophenol to rats is not accompanied by any reduction in blood levels of cholesterol. This finding does not necessarily mean that 2,4-dinitrophenol is without effect on cholesterol biosynthesis since it is well known that the blood level of cholesterol is the resultant of the operation of a number of variables. More direct information on the effect in vivo of an uncoupler of oxidative phosphorylation has now been obtained in this laboratory.[7] Young rapidly growing rats were divided into two groups. One group received a standard stock diet while the other group received the same diet plus 0.25 per cent of 2,4-dinitrophenol. During the next six days the rats which were fed the stock diet gained an average of 12 Gm. while the rats which were fed the stock diet plus the drug lost an average of 25 Gm. of weight. The loss in weight of the drug-fed rats is considered a reflection of uncoupling of oxidative phosphorylation. In other words, the drug-fed rats consumed their diet and metabolized it with the consumption of oxygen and the production of carbon dioxide, but were unable to derive useful energy (ATP) from it. After six days all rats were given an intraperitoneal injection of mevalonic acid-2-C^{14}. Two hours after the injection the rats were killed, and the livers (main site of cholesterol biosynthesis) were removed, saponified, and the nonsaponifiable fraction (mainly cholesterol) was isolated and counted. The livers from the rats which were fed the stock ration alone had an average of 6,620 counts per minute, while the livers from the rats fed the stock ration plus 2,4-dinitrophenol had an average of 6,520 counts per minute. It would appear therefore that the mevalonic acid kinases must be well up on the priority list for ATP, since, under conditions of what must have been marginal levels of tissue ATP, cholesterol biosynthesis did not appear to be adversely affected. Stated in another way, it would appear that cholesterol biosynthesis must be considered as one of the more essential reactions of the body.

In retrospect, since cholesterol is considered to be a precursor of the sex hormones, the hormones of the adrenal cortex, the

D vitamins, and other steroid metabolites of vital importance in the economy of the body, it is understandable why cholesterol biosynthesis seems to have high priority for ATP. The findings described in this discussion provide little support for a research program designed to find drugs useful in the treatment of atherosclerosis and other diseases characterized by hypercholesterolemia involving an interference with cholesterol biosynthesis. Cholesterol biosynthesis may be a series of reactions that are so vital that they cannot be interfered with without widespread deleterious effects.

Examined in another way, if, in fact, a priority list for ATP exists where the more essential reactions of the body have first call on available ATP then it may be possible that nontoxic uncouplers of oxidative phosphorylation may be devised that will bring about weight reduction without interfering with the more essential reactions of the body. Actual control of weight is possible with 2,4-dinitrophenol, but unfortunately this drug is too toxic for use. Conceivably, useful uncouplers of oxidative phosphorylation could be found with utility in the control of obesity. Ultimately, control of obesity may be of more significance in the therapy of atherosclerosis than inhibition of cholesterol biosynthesis.

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Number thirty-one in a new series of Nutrition Excerpts

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Scientific Program

Any State Society member who wishes to present a paper before a scientific section or a general session is requested to write to Bernard J. Pisani, M.D., Chairman, Convention Committee, 170 West 12th Street, New York 11, New York, before October 15, 1962. A short abstract of the proposed presentation should accompany the letter.

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

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Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Intoxications Due to Tranquilizing Drugs and Plants

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Substance Ingested	*Age*	*Sex*
Tranylcypromine, a monoamine oxidase	$1^1/_2$ years	Female

This one and one-half-year-old female was admitted to a hospital because of the alleged ingestion of antidepressive tablets. This apparently occurred about 11:00 A.M. on the day preceding her admission. According to the mother's account, the child was normal throughout the day, took feedings well, and played as usual. About 10:30 P.M. when the parents returned home, they found that the bottle of pills was empty, and the pills could not be found. The child was brought to the hospital emergency room, and her stomach was lavaged. The mother related that the child had acted peculiarly, her eyes appeared to roll, and she was noncommunicative.

No returns were obtained from the stomach lavage twelve hours after the supposed ingestion. Following the lavage, however, the child appeared normal. She was responsive and alert and was sent home. On returning home she became agitated, semistuporous and had eye-rolling. The parents were then advised to return the child to the hospital. The child was comatose on the second admission. The laboratory workup produced essentially negative findings except for a leukocytosis (16,500) with 56 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes, 3 per cent eosinophils, and 1 monocyte.

Supportive therapy was given, including intravenous fluids, and the child gradually awakened. After two days of hospitalization the patient was discharged symptom-free.

This case is noteworthy because of the massive ingestion of a drug not too frequently reported in a child of this age.

INCIDENT 2

Substance Ingested	*Age*	*Sex*
Prochlorperazine Dimaleate Suppository	5 years	Male

The reporting physician relates as follows:

The pharmacist substituted 50 mg. of prochlorperazine dimaleate for 50 mg. of chlorpromazine hydrochloride. The drug was administered rectally at 7:30 A.M. on

February 6, 1962. At 12:00 NOON the patient began to have tightening of the jaw which pulled over to the left. At 6:00 P.M. he developed rigidity and hyperextension of the upper and lower extremities. There was clonus present in both lower extremities. His orientation was good, and there was no paralysis or Kernig or Brudzinski signs. Improvement was slow, and there was no marked improvement until February 8, 1962, at 3:00 P.M. The lips improved first and then the arms. He was still having spasms of the jaw on February 10, 1962, five days following the administration of the drug. On February 13, 1962, he was perfectly normal.

Because of the alarming side-effects sometimes encountered following the use of some tranquilizing drugs, the physician and particularly the pediatrician have an obligation to use such drugs only when there is a definite indication for such use. Only the least hazardous and those with a minimum of side-reactions should be chosen.

INCIDENT 3

Substance Ingested	*Age*	*Sex*
Prochlorperazine Dimaleate	23 years	Female

The patient took one 10-mg. tablet of prochlorperazine dimaleate in the morning. She began feeling a general stiffness. By 8:00 P.M. this was localized to the jaw. She was given phenobarbital 130 mg. and atropine 0.4 mg. She returned to the emergency room at 10:30 P.M. because of pain in the upper jaw and was given codeine 65 mg. and told to take Benadryl 50 mg. at bedtime. She was asymptomatic the next morning.

This case is cited to illustrate the fact that even an initial therapeutic dose of one tablet of some tranquilizers can produce undesirable symptoms.

INCIDENT 4

Substance Ingested	*Age*	*Sex*
Chlorpheniramine Maleate	14 years	Female

This patient took eight 8-mg. capsules of chlorpheniramine in a suicidal gesture. She took the medication at 4:15 P.M., but it was not reported to the parents until three and one-half hours later at which time she was taken to a hospital emergency room. The only findings on admission were marked restlessness and slight drowsiness. The stomach was lavaged with water. The patient was observed for about a day and was sent home symptom-free.

The New York City Poison Control Center receives frequent reports from private physicians, hospitals, and schools of attempted suicides by adolescents by means of chemicals and drugs.

INCIDENT 5

Substance Ingested	*Age*	*Sex*
Plantab (fertilizer tablet)	$1^1/_2$ years	Female

The child ingested a fertilizer tablet which was obtained from a high-level drawer that failed to elude the efforts of this very young but mobile child. The mother called the Poison Control Center and was advised to call a physician but was assured that the only likely hazard involved was the presence of nitrate as a fertilizer ingredient.

This Center has received many calls following the ingestion of similar products, since they are frequently used in the home by household horticulturists. The current belief is that the ingestion of nitrate is not particularly dangerous but that the formation of nitrite in the intestinal tract by bacterial reduction creates the hazard of nitrite methemoglobinemia. Because of this possibility, gastric lavage or an emetic is frequently recommended.

One approach, which as far as we know has not been recommended, would be to use either a sulfonamide or an antibiotic to suppress the bacterial activity. This suggestion is not based on clinical experience but on theoretic grounds. It is always advisable, whenever possible, to avoid the hazard associated with an emetic or the traumatic experience of a gastric lavage.

INCIDENT 6

Substance Ingested	*Age*	*Sex*
"Dogwood" Plant	5 years	Female

This incident was reported from a hospital in Suffern, New York, which requested information on dogwood berries. The child reportedly ate some dogwood and four hours following the ingestion was found unconscious. While the child denied ingestion, her playmate insisted that the child had ingested the dogwood.

Vomiting was induced, and the patient was taken to the hospital. On admission the child was stuporous and in a coma. The physical examination revealed essentially negative findings. The laboratory findings revealed a leukocytosis, and the urine contained acetone, diacetic acid, and an albuminuria. A spinal tap produced negative findings.

The patient remained in the hospital for two days. She was treated symptomatically and was discharged home symptom-free.

"Poison dogwood" is actually not dogwood but poison sumac and is a name apparently limited to certain localities. The well-known dogwood berries are nontoxic and are actually used in the preparation of certain fruit desserts. This case is not cited as an authentic dogwood poisoning but is used to emphasize the need for confirmation in the reporting of plant poisonings. Local museums, botanical gardens, or educational institutions may provide such verification. This Poison Control Center makes an effort, not always successful, to obtain such verification.

INCIDENT 7

Substance Ingested	*Age*	*Sex*
Jack-in-the-Pulpit	14 years	Female

A call was received from an Upstate high school nurse for advice concerning two fourteen-year-old girls who had been mischievously given pieces of jack-in-the-pulpit plant and were suffering from intense irritation of the mouth and throat. The irritating agent has been ascribed both to an "acrid principle" and to sharp calcium oxalate crystals. Calls concerning jack-in-the-pulpit are received here most often in the fall when the attractive bright red berries are frequently ingested by children, since this plant is widely distributed in this area. The ingestion of the stalk is reported less commonly.

When one consults the popular Muenscher's *Poisonous Plants of the United States*,[1] one finds this plant listed. Naturally, if the plant is ingested, great concern follows, and overalarm and overtreatment may ensue. On the other hand, *Edible Wild Plants of Eastern North America*[2] discusses the food use of this plant after proper processing. The treatment is palliative, and the burning sensation disappears after varying intervals.

We recently have received a communication from the Food and Drug Administration, Department of Health, Education, and Welfare, which we think should be of interest, especially to pediatricians, and merits wide publicity. The communication is reproduced in part as follows:

> Over-the-counter preparations for minor sore throats: warning statement for throat preparations for temporary relief of minor sore throat: lozenges, troches, washes, gargles, etc.
>
> Warning—Severe or persistent sore throat or sore throat accompanied by high fever, headache, nausea, and vomiting may be serious. Consult physician promptly. Do not use more than two days or administer to children under three years of age unless directed by physician.

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Number ninety-nine in a series of Accidental Chemical Poisonings

Case Reports

Survival with Normal Growth Following Massive Resection of Small Intestine in Newborn Infant

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THE REMARKABLE ADVANCES in surgery, anesthesia, and pre- and postoperative care of the newborn infant have resulted in increasing numbers of infants surviving massive resection of the small and large bowels and even of the stomach. Gastroschisis, multiple areas of atresia, midgut volvulus, and meconium ileus have all necessitated extensive resections. The surgeon and the pediatrician, caring for the infant surviving this type of procedure, are beset with many problems and doubts as to the long-term prognosis.

The purpose of this paper is to present a case of massive resection of the small bowel with a twelve-month follow-up. The survival and subsequent normal growth and development of this infant, after many difficulties encountered in the postoperative period, should encourage perseverance and hope in confreres faced with similar situations.

Case report

A white female was born at term by normal spontaneous delivery. The birth weight was 5 pounds, $11^1/_2$ ounces. The physical findings shortly after birth were within normal limits.

Twelve hours after birth, feedings were instituted and taken fairly well. Normal meconium stools were passed at that time. On the second day of life the infant began to vomit every feeding and that evening passed a large, bloody stool. An examination at that time revealed the abdomen to be slightly distended but not tense. There were no masses palpable, and a rectal examination gave completely negative results. The hematocrit was 31. The child was given 10 mg. of vitamin K and a fresh blood transfusion of 40 cc. on the assumption that this might be a hemorrhagic disease of the newborn infant. A flat film of the abdomen revealed distention of loops of small bowel with air-fluid levels. No air was seen in the large bowel (Fig. 1).

The child was operated upon on the third day of life. At operation the stomach, duodenum, and proximal jejunum were markedly distended, and the latter ended blindly in a complete atresia. The remainder of the small bowel was involved in a volvulus around a shortened mesentery and was gangrenous. The cecum was incompletely rotated and was located in the epigastrium.

A resection of the gangrenous small bowel as well as the distal 5 cm. of the dilated proximal jejunum was performed, and the jejunum was anastamosed to the remaining 5 cm. of terminal ileum in end-to-end manner. Approximately 50 cm. of jejunum and ileum were left in situ, an estimated 65 per cent of the small bowel being excised. The mesenteric defect was closed, and the abdomen was closed in layers.

The pathologic report described two specimens. One consisted of approximately

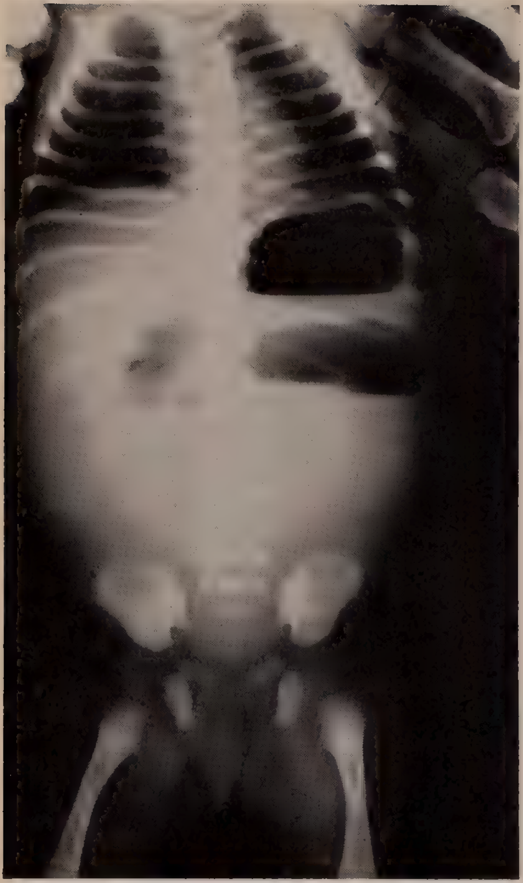

FIGURE 1. Flat film of abdomen at two days of age showing distended loops of small bowel with air-fluid levels; no air seen in colon. Classic findings of intestinal obstruction in newborn infant.

60 cm. of small bowel with hemorrhagic infarction, and the other was a portion of dilated intestine measuring 5 cm. in length.

Following the procedure the child did fairly well on intravenous fluids. The abdomen remained soft without distention. She was alert and active with a good cry. On the second postoperative day the infant passed a small stool and was started on small amounts of glucose water by mouth.

After seven or eight feedings were taken well, the baby vomited twice. She appeared dehydrated, and therefore intravenous fluids were reinstituted and a Levin tube passed. For the next three days she had no stools, and there were increasingly larger amounts of gastrointestinal drainage. There were occasional episodes of projectile vomiting.

An x-ray examination showed distention of the small bowel. The child's condition was deteriorating, and so a re-exploration was performed on the fourteenth day of life. At laparotomy adhesions were found running from the stomach over the ileum distal to the previous anastomosis. The small bowel proximal to these bands was markedly dilated. After transecting the bands, air was seen to pass freely into the colon. The abdomen was closed in layers.

Following the second procedure, the child was in poor condition. On the first postoperative day she was started on oral fluids but did not tolerate them. Diatrizoate sodium (Hypaque sodium) was given by mouth and was seen to pass into the colon. On the fourth postoperative day her weight was down to 1,700 Gm. She passed 2 small stools at that time.

The child was started on small amounts of a high-protein formula with banana powder (Probana) in addition to receiving intravenous fluids. She tolerated the feedings well and began to have good bowel movements. Intravenous therapy was discontinued. She now began to have very frequent, watery stools and rapidly became dehydrated. She was started on intravenous fluids again, but oral feedings were continued.

The child continued to have 15 to 20 stools per day over the next week. She was kept on intravenous fluids and oral feedings. In addition, she was given occasional infusions of plasma and blood to maintain her serum proteins. The charcoal transit time at one month of life was two hours and twenty minutes, and her weight was still 1,700 Gm.

Soon after the child began to have frequent twitchings. The serum calcium was 7 mg. per 100 ml., and calcium gluconate was added to her feedings.

Over the next month she began to show some improvement. Her weight increased slowly, and she began to take more formula by mouth. She still had many watery stools each day and occasionally became dehydrated. At these times intravenous fluids would be given until the dehydration was corrected, but oral feedings were never discontinued. She received blood and plasma on several occasions when her condition deteriorated.

In the third month of life her weight gain continued, and her stools became less frequent and more formed. A repeat charcoal transit time was five hours and fifty minutes. Solid foods were added to the diet, and she tolerated them well. She was finally discharged at the age of three months and ten days weighing 3,140 Gm.

On a subsequent admission at age nine months, the baby weighed almost 20 pounds, and although she was having very large stools, they were not frequent and were well formed. An upper gastrointestinal series on this admission showed dilatation of the jejunum proximal to the anastomosis. Barium was seen in the colon on the sixty-minute film. The estimated length of remaining small bowel approximated the surgeon's evaluation at operation.

Comment

Until recently, reports in the literature were very discouraging as to the long-term prognosis of infants surviving massive resection of the intestinal tract. Gross,[1] Ulfelder,[2] Kiesewetter,[3] Jackson,[4] and Clark and Booth[5] all reported severe problems with nutrition, anemia, and chronic diarrhea. Such experiences tend to dissuade surgeons from resecting large portions of the small bowel in infants and children. Pilling and Cresson,[6] Benson and others,[7,8] and Berman[9] have all reported survivals of newborn infants after extensive resections of the small and large bowel with subsequent normal growth and development. Finney, Schnaufer, and Stafford[10] have reported normal nutrition following a total gastrectomy in an eighteen-month-old infant. Boley, McKinnon, and Marzulli[11] found normal growth and development following a subtotal gastrectomy and a subtotal colectomy in an eleven-year-old girl. Apparently, the prognosis following massive resections of the gastrointestinal tract is better than was previously believed.

The most significant fact to be gained from the case reported here is that if one can carry an infant over the first few months following massive resection, there is good reason to hope for subsequent normal nutrition. The remarkable development of this infant after the initial three-and-one-half-month hospitalization is most encouraging. This sequence of events was also found by Boley *et al.*[12] in extensive resection of the small bowel in dogs. Animals who could be nursed over the first few postoperative months survived 90 per cent resections with subsequent normal nutrition.

Various suggestions as to the dietary management of these infants have been made. Breast milk, intravenous Lipomul, Nutramigen, Hi-Pro, and a high-protein formula with banana powder have all been used. Pilling and Cresson[6] emphasized frequent feedings with high calorie and volume intake. In our case the formula with banana powder was chosen, but the utilization of any low-fat, high-carbohydrate formula, with supplementation with vitamins, parenteral electrolyte solutions, and blood and plasma transfusions as indicated, should prove as successful. Meticulous attention to fluid and electrolyte balance is essential, as demonstrated by the multiple episodes of dehydration in our case. The passage of one large bowel movement in a $3^1/_2$-pound infant can result in clinical dehydration approximating 10 per cent. Intravenous fluid therapy, in addition to the oral intake, is necessary when these episodes occur.

The occurrence of tetany in patients with a limited small bowel has been attributed to the loss of calcium and a deficiency of fat-soluble vitamins.[13] In our patient, tremors and low serum calcium levels were present for over a month in spite of the daily oral administration of calcium gluconate. Intravenous calcium was required on several occasions to control the symptoms of hypocalcemia.

We feel that the liberal use of blood and plasma transfusions played a significant role in the survival of the infant. The absence of any demonstrable anemia may be due to this therapy, although Pilling and Cresson's[6] cases had no anemia and received no transfusions.

The dramatic course of events in the case reported here is best demonstrated in Figure 2. There were many times when it appeared that this child would not survive, but although her weight fell from 5 pounds, 11 ounces at birth to 3 pounds, 8 ounces at her low point, today she is normal for her age. This should encourage surgeons and

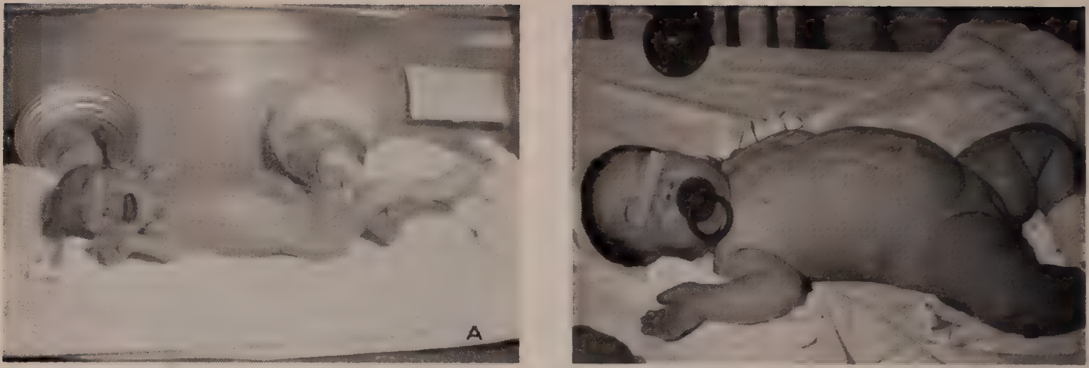

FIGURE 2. (A) Infant at lowest weight of 3 pounds, 8 ounces following second operation. (B) Child at age nine months, weight 20 pounds.

pediatricians to persevere in the care of such cases, as full recovery and growth are possible.

Summary

A case of massive resection of the small bowel in a newborn infant with survival and normal growth and development is reported.

The first few months of life present the greatest difficulties, but if the child can be carried through this period, normal nutrition is possible.

A dietary regimen consisting of a high-carbohydrate, low-fat formula, with supplementation with intravenous fluids, vitamins, and blood and plasma transfusions, is recommended.

The close surveillance of fluid and electrolyte balance is stressed.

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Primary Cutaneous (Ulceroglandular) Infection Due to Pasteurella Hemolytica

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PASTEURELLA HEMOLYTICA is a well-known pathogen of domestic animals, associated with shipping fever in cattle[1] and septicemia in lambs and newborn pigs.[2-4] Henriksen and Jyssum[5] encountered a new and unusual variant of Past. hemolytica in the flora from the respiratory tract of man, but they were not convinced it induced any infection. This variant, Past. hemolytica variant ureae, was again isolated from cases of sinusitis by Omland and Henriksen,[6] and it was sensitive to tetracycline hydrochloride. Jones and O'Connor[7] isolated this variant from the sputum of 17 persons, most of them elderly, who were suffering from chronic bronchitis or bronchiectasis. Whether this bacterium aggravated the disease or acted as a mere commensal when it was growing in damaged tissues was not clear.

This is a report of a case of primary cutaneous, ulceroglandular infection in a woman from whom Past. hemolytica was isolated in a pure culture from the exudate of a lesion on the finger. As far as can be determined, this is the first report of such an infection.

Case report

A forty-three-year-old woman, living in Horseheads, New York, shot and dressed a buck deer in the field about 11 : 00 A.M. on November 24, 1960. While she was hunting, she acquired a number of lacerations of the skin on the back of both hands. She was seen by one of us (C.K.S.) in the late evening of November 25 at which time the lacerations were inflamed and there were "red streaks running up her arms." She had a moderate fever for several days, never rising above 100 F. The multiple lesions of the hands were linear scratches that were elevated and erythematous. On the middle finger of the right hand there was a papule resembling the cutaneous lesions of ulceroglandular tularemia.[8] Exudate from the lesion was obtained for culture.

After surgical cleansing the lesions were treated daily locally with tetracycline hydrochloride. Streptomycin, 0.5 Gm., and 400,000 units of procaine penicillin were given intramuscularly. This was repeated for four days. On November 29 the patient was started on a daily dose of 1 Gm. of streptomycin. In addition, because the possibility of glanders was considered, sulfadiazine therapy was included. On November 30 her temperature became normal, and streptomycin was discontinued on December 2.

Specimens of blood were taken on November 28, December 8, December 22, 1960, and on March 6, 1961, for serologic evidence of tularemia. The cutaneous lesions responded to therapy and disappeared promptly. Epitrochlear and axillary lymphadenopathy of both arms was seen early, but this did not enlarge or suppurate during therapy. The patient was seen several times subsequently and is well.

Although the majority of cases of tularemia in New York State have been of the ulceroglandular form[9] and tularemia was definitely considered in the differential diagnosis of this case, none of the specimens of blood showed serologic evidence of antibodies to Pasteurella tularensis. Therefore, a thorough study of the strain of bacterium isolated from the lesion of the finger was undertaken.

Materials and methods

Strains. Strain OM 6187/60 was isolated from the exudate of the lesion on the right finger of this patient. It was identified as Past. hemolytica at the Communicable Disease Center of the U.S. Public Health Service. It was not the variant ureae. Strain 1870/61, of bovine origin, was obtained from the Ontario Veterinary College of Guelph, Canada, through the cooperation of Dr. G. R. Carter and served as a standard control strain in studies of the human isolate.

Antisera. Antisera were prepared in rabbits by the intravenous injection of killed culture suspension of the standard control strain.

Serology. The antigens for the agglutination tests were spectrophotometrically standardized suspensions of twenty-four-hour agar cultures in 0.5 per cent phenolized salt solution. The tests were incubated in a water bath at 37 C. for four hours and continued overnight at from 3 to 6 C. The reactions were read as plus to 4 plus, based on the degree of agglutination observed. The titers recorded represent the reciprocal of the highest serum dilution exhibiting a minimal reaction of 2 plus.

Complement-fixation tests were performed with antigens recovered from living culture suspensions by ether treatment according to the method of Ribi, Milner, and Perrine.[10] The technic of the test followed the principles employed at the Division of Laboratories and Research of the State of New York Department of Health for examinations for evidence of syphilis.[11]

The agar diffusion plate test which was used was an adaptation of the Ouchterlony[12] method, with an antigen prepared as for complement-fixation tests. The indirect fluorescent antibody technic for the demonstration of an antigen was that described by Cherry, Goldman, and Carski.[13]

Mouse pathogenicity. Mouse pathogenicity was determined by an intraperitoneal injection of twenty-four-hour agar cultures suspended in a phosphate-buffered salt solution to a standard optical density corresponding to approximately 14 billion microorganisms per milliliter.

Tissue preparations for histologic examination. Skinned carcasses were dropped in Bouin's solution promptly after obtaining cultures of the heart blood.

Results

Serologic tests for the confirmation of identity were made with rabbit antiserum to strain 1870/61. Results of agglutination (with unabsorbed and absorbed serum) and complement-fixation tests are presented in Table I. The homogeneity of strains was demonstrated by cross-absorption studies. In agar-diffusion precipitin and also in indirect fluorescent antibody tests[12] the antigen of strain 6187/60 exhibited reactions with antiserum to 1870/61. No reactions occurred with the normal serum which was used as a control for each serologic procedure.

Both strains were similar in mouse pathogenicity, requiring somewhat in excess of 2 billion microorganisms to induce death. This is in line with the experience of Smith[14] in the studies of Past. hemolytica. Following the infection, animals survived only from sixteen to forty-two hours in most instances, although one mouse lived for two and one-half days. On autopsy Past. hemolytica was recovered from the heart blood of animals with but 1 exception. The relatively brief period of survival is strongly indicative of a toxic process in the disease. A histopathologic examination of tissues of infected mice revealed only generalized congestion of the viscera and serous membranes of cavities. There was no evidence of acute inflammation or abscess formation.

Summary

The first known human infection induced by Past. hemolytica has been reported. It occurred in a forty-three-year-old woman who acquired numerous lacerations on the hands from berry bushes while hunting and dressing a deer in the field in November, 1960. Her lacerations became inflamed and she developed lymphangitis and regional lymphadenitis. From the exudate of a papular lesion of the finger Past. hemolytica was isolated in a pure culture. Ulcerogland-

TABLE I. Serologic tests of identity with antiserum to strain 1870/61, Past. hemolytica

	Agglutination Test*			
	Serum			Complement-Fixation Test[11]
Antigens	Unabsorbed	Absorbed 1870/61	with 6187/60	
1870/61	80	0	0	170
6187/60	80	0	0	60

* Titer expressed as reciprocal of highest serum dilution exhibiting definite agglutination.

ular tularemia was considered, but several serial specimens of blood taken within a four-month period failed to reveal any agglutinating antibodies to Past. tularensis. A definite serologic identification of the strain as Past. hemolytica was made. Virulence studies in mice did not reveal any pathognomonic lesions; death was rapid and appeared toxemic in nature. Infections due to Past. hemolytica in domestic animals, especially cattle, lambs, and newborn pigs, have been known for many years.

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Orange juice as cause of allergic reactions in infants

The common belief that orange juice frequently causes allergic reactions, such as rashes, in babies, is questioned in a recent study by two University of Rochester researchers, Ruth A. Lawrence, M.D., and Estelle E. Hawley, Ph.D., reported in the February, 1962, issue, of the *American Journal of Clinical Nutrition.* A three-month test was made of 114 infants. One group of babies received orange juice; another received a commercial instant breakfast drink containing vitamin C; and a third group received a control solution which contained dextrose and was colored to resemble orange juice. Neither the babies' parents nor their pediatricians knew which infants received each solution; as an extra check on results, the babies were switched from one solution to another during the last part of the three-month test period.

The statistical tests failed to indicate a significant difference in the incidence of untoward reactions to the three solutions employed, although some rashes developed in infants, without apparent cause, before any of the solutions could be administered. Babies with a history of family allergy accounted for a considerable proportion of the reactions: Of 32 babies with a history of family allergy, 56 per cent showed an undesirable reaction during the study.

The lowest percentage of side-reactions occurred with the instant breakfast drink. Most of the babies seemed to like the taste of whichever "juice" they received; least popular with the discriminating small fry was the control solution.

Role of Nursing Home In Over-All Program Care of the Aged

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WE ARE HERE to help educate ourselves and educate each other as to the needs each one of us faces if we are to provide the best possible care for the aged. It has been said often that education only begins when one gets out of school; in other terms, most of our knowledge comes from the sharing of experiences. Through this sharing we have an opportunity to increase our information and our care.

To set the stage for my later remarks I would like to give to all of you some background information on the role of nursing homes in the over-all program of care for the aged.

Nursing homes are among our most effective tools for the care of the convalescent and rehabilitable patients. However, these facilities have not been employed advantageously for these purposes as compared with their utilization in long-term care. The nursing home can play an ever-increasing part in geriatric and chronic disease programs by being the bridge between the community and general hospitals, chronic disease hospitals, or rehabilitation centers.

Traditionally, nursing homes have been considered a one-way street. For years, in the great majority of cases, the entire medical policy was based on the assumption that the patients were hopelessly ill and that medical treatment beyond nursing care to keep them comfortable was unnecessary and extravagant. Homes that worked with extremely handicapped patients and achieved some improvement which allowed the patients' return to the community were few.

It has been apparent for some years that nursing homes and homes for the aged were assuming an increasingly important role in the care of the long-term patient. However, the extent and composition of that role was largely a matter of conjecture. We did not know the number of homes, total number of available beds, or the extent of the services offered. Much confusion resulted from the multiplicity of ill-defined terms, such as nursing home, convalescent home, convalescent hospital, home for the aged, rest home, boarding home, and so forth. The facilities ranged from small boarding homes housing two or three people to large institutions serving several hundred persons. Although many states had licensing laws, the regulating agencies usually were allocated insufficient funds to provide staffs for the enforcement of these regulations.

Nursing homes wishing to improve their services had no guides as to the direction in which they should move. The most charitable thing we can say for this period is that most nursing homes had a minimum idea of care, met a minimal interpretation of the licensing regulations, and they filled a need in the community.

Development of skilled nursing homes

Four major factors influenced the development of skilled nursing homes as we know them today:

1. The organization in 1948 of the American Association of Nursing Homes,

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Presented at the Joint Council on Health Care for the Aging, Buffalo, New York, September 21, 1961.

with the elevation of standards as one of its primary goals.

2. The first National Conference on Aging, in August, 1950. This conference, sponsored by the Federal Security Agency, brought 816 leaders in the field of aging together and led to the next step, which was

3. The appointment, in 1951, of a committee to study standards for sheltered care. This group, sponsored by the National Committee on Aging of the National Social Welfare Assembly, in 1953 published three volumes on standards of care for older persons in institutions. These suggested standards for nursing homes were the first uniform guide lines available to nursing home administrators and licensing agencies.

4. Last and most important was the revision in the Federal Social Security Act which became effective on July 1, 1953. Under the terms of this Act states wishing to extend their participation in the old-age assistance program were required to establish and maintain standards in sheltered care facilities.

I review this background to emphasize the very short period of time, twelve years, in which nursing homes have emerged from custodial care to skilled nursing care. It is not my intention to dwell on the many difficulties nursing homes have faced during this period. Changes have occurred in operators' attitudes and technics as well as in the opinions of the public and attitudes of the paramedical groups. Sufficient to say, they have changed and continue to do so—for the better!

Just as we saw an improvement in the facilities and standards of care after Federal legislation in 1953, so we expect to see gains in the extension of services and implementation of legislation providing for medical care for the aged. Even without such legislation nursing homes are now mature enough to take their proper place in the health picture.

Place of nursing home in community

What is that place? What are we, as nursing home administrators, doing to improve the level of care to the aged and chronically ill patient? More important, what can we do that we are not now doing?

In a comprehensive community program it is possible for nursing homes to develop closer working relationships with community hospitals, rehabilitation centers, voluntary health agencies, and other community groups. Such relationships will promote integrated medical care and improvements in standards of all medical services to both the patient and the community.

We believe that the nursing home as part of this total health scheme should be utilized in three ways:

1. In its traditional function for care of the subacute chronically ill patient who does not need to occupy a general hospital bed.

2. As a restorative training service for the older patient who will benefit from learning simple activities of daily living, but who does not require the skills and specialized services of a wide variety of professional disciplines.

3. As an intermediate step from the general hospital, chronic disease hospital, or rehabilitation center to the patient's return to the community.

If the nursing home is to fulfill this new mission, it must look beyond its own internal operation. It must coordinate its activities with other institutions and services in such a way that its full potential will be realized. The need for and expected results of this closer relationship will improve the quality of health services, promote the continuity of care, permit the easy transfer of patients as medical need indicates, and facilitate the education of personnel.

What additional services will be necessary in this new role?

With planned programs it has been shown that many hospitalized patients can be rehabilitated to such a degree that many can be returned to their homes or to boarding facilities. Most of us think of rehabilitation only with the younger-age group. This is why I prefer the term "restoration" when speaking of older patients. Restoration of the elderly sick can occur. However, it takes longer at that age. It is here that nursing homes have the greatest opportunity to contribute.

General hospital care is expensive, and it will become more so as greater services are demanded. In a lesser degree, care is also expensive in chronic disease institutions and rehabilitation centers. Additionally, these beds are in short supply and must be utilized by those patients who will benefit most from the services. When a patient no longer needs the complete battery of services offered in these specialized settings, but still has not completely mastered new technics, his transfer to a nursing home is the obvious solution. In making this transfer we do not wish the patient to lose the newly acquired skills but rather we seek to improve them to their maximum benefit. Therapy must be continued.

Long-term restoration

Long-term restoration, as practiced in nursing homes, is for the most part similar to chronic disease hospital or rehabilitation center therapy, differing only in the simplification of technics and the use of nursing aides working under the supervision of registered nurses or registered therapists. Thus, every patient may be provided with daily restorative activities. The patients may be treated in a variety of settings providing the principles of treatment remain the same in all areas.

Dental care, when it is carefully integrated into the restorative program, can broaden considerably the base of general supportive therapy. Not only will it implement nutritional treatment, but also it will contribute to better speech capacity and general aesthetic appearance. The best-intentioned planning for good nutrition is to no avail if the patient is unable to eat the food. Dental care in most nursing homes will be directed principally to the maintenance of teeth. However, dentures can be made, and patients can be educated in their use.

Pilot programs in dental care for the institutionalized and home-bound patient have been started in several states. A compact, portable dental unit has been developed and will be for sale shortly. The Connecticut Dental Society and the Connecticut Medical Society recently have sponsored a series of dental-medical conferences in dental care of the chronically ill and aged. Nursing home facilities were used as teaching units. Our Association hopes to make available films on new technics and teaching methods of the conference as soon as copies can be obtained, and we shall be happy to share them with any interested groups.

In nursing homes, the basic team of physician and nurse is already available for the restorative program, since all accredited nursing homes must have a consulting physician on call, as well as the individual physicians treating patients in the home, together with a staff nurse. The physician will serve as the chief of the restorative team. He will receive data from referring agencies as well as his own information. With this background and with the recommendations made by the other members of the team, he will prescribe the necessary therapy. The final responsibility for all decisions will be the physician's, although the therapy will be directed and administered by others.

The nurse, next to the patient, is the most important person in a nursing home. She not only renders general nursing care, but also is alert to the patient's need to help himself. She assists in the self-care planning and helps patients over difficult periods in therapy. She is the person who observes the patients' level of function and encourages the mastery of technics. It is also the nurse who must see that the patient maintains the gains that have been made. Having reviewed the background and the status of nursing homes as they are related to the total picture of care for the aging, we are now ready to consider their needs. At this time I would like to discuss with you, from the standpoint of a nursing home administrator, some specific things which each of the other professional groups here today might do, so that nursing homes may do the best possible job in caring for the aged.

Role of doctors

As nursing home administrators we recognize that doctors face many problems: busy schedules, long hours, study required to keep up-to-date on advances in the field of medicine, and many other things which are necessary parts of a doctor's life. However, from the viewpoint of a nursing home administrator, the following items are important if we are to do a complete job of care for our patients.

To begin with, doctors should know the differences in the types of facilities and the services which each facility provides. This may be, or seem to be, an elementary statement, but I would like to call your attention to the results of a survey made of Central New York doctors in April, 1958. Nineteen per cent, or nearly one fifth of the participating physicians replied that they were not familiar with the types of care for the aged which were available in their areas. Six per cent did not reply. Only three out of every four doctors answered that they were aware of the local facilities.

For the benefit of all present at this meeting, let me quote from the New York State Social Welfare Law, which lists these definitions:

> PRIVATE PROPRIETARY NURSING HOME. A private proprietary nursing home shall mean a facility operated for the purpose of providing therein lodging, board, and nursing care to sick, invalid, infirm, disabled, or convalescent persons, for compensation and profit.
>
> PRIVATE PROPRIETARY CONVALESCENT HOME. A private proprietary convalescent home shall mean a facility operated for the purpose of providing therein lodging, board, and bedside care or hygienic attention, but not including medical or nursing care to sick, invalid, infirm, disabled, or convalescent persons, for compensation and profit.
>
> PRIVATE PROPRIETARY HOME FOR ADULTS. A private proprietary home for adults shall mean a facility operated for the purpose of providing suitable care therein, for compensation and profit, to two or more adult persons who, though not requiring medical or nursing care, are in such condition by reason of their age, infirmities, or disabilities as to require, in addition to lodging and board, the services of attendants to assure their safety and comfort and to enable them to be bathed, dressed, fed, or to move about.

Lest there be confusion, it must be noted that the designation of convalescent home is no longer given to new facilities, but there are still some homes within our area that provide this type of service.

It must be noted, too, that the Social Welfare Department has established a category known as "private homes for the aged," which are corporately owned and usually church or fraternally operated.

Once the doctor is familiar with the various facilities which are available, his next step is to recognize when a patient needs hospital care and when nursing care is sufficient for the patient's needs. To make this evaluation it will be necessary for the doctor to be familiar with the specialized services which the nursing homes can render in his immediate locality.

If nursing home care is desirable, the doctor should attempt to "sell" the patient on the benefits of nursing home placement, considering the care received and the costs involved as compared with those in the hospital. Again, to do this properly, a doctor must be familiar with nursing home costs and the services provided for these costs.

When a patient is admitted to a nursing home, the doctor should give the home a complete medical history, diagnosis, and orders for nursing care. The doctor should visit the patient as often as the patient's condition requires, but at least once a month.

Verbal orders should be kept to a minimum and should be confirmed in writing as soon as possible.

We need prompt service on emergency calls. Doctors who will be unavailable on weekends or on particular days should provide for an answering service or should designate an alternate physician, so that we may carry out the doctor's desires in this matter.

In cases of death the nursing home needs the cooperation of the doctors in obtaining a pronouncement of death.

Finally, we want the doctors to recognize the nursing home as an important part of the medical care team. The nursing home administrator needs the doctor's full cooperation in all phases of care and treatment. We would like the doctors, through their medical societies, to recognize the role of the nursing home and to educate their members in the nursing home's effective and proper use in the care for the aged.

Role of hospitals

Next we turn to the hospitals to discuss what the nursing homes need from them to fulfill properly their role in health care.

First, nursing homes would like recognition by hospitals as bona fide members in the program of care for the aged. Many hospitals have accorded this recognition to nonprofit homes but have denied equal status to proprietary nursing homes.

Hospital administrators, like doctors, should be familiar with the various types of care facilities and the availability of these facilities in the local community.

Patients no longer in need of hospital care should be transferred as soon as possible to nursing homes if nursing home care is indicated. Hospital personnel, like doctors, should know what services are available and again should "sell" the patients on the desirability of nursing home care, particularly from a financial standpoint.

When patients are being transferred to nursing homes, complete referral sheets should accompany each patient to assure good nursing care. These should include the patient's medical history, diagnosis, medication and time of day to be taken, special diets, behavior problems, and special nursing care needs.

Finally, we ask the indulgence of hospital administrators in understanding and accepting nursing homes and their services. We do not claim that all nursing homes are perfect; we do claim that many nursing homes are providing excellent care and comfortable living for thousands of patients. Good homes should be given credit for the job that they are doing and should not be subject to unfavorable criticism by generalities.

Role of dentists

Finally, we turn to the dentists in the consideration of their role in care for the aged. Here we are on difficult ground. There has been too little contact and experience with dental care in nursing homes. However, as nursing homes progress and place greater emphasis on restorative services, of necessity there will be a greater liaison between them and the dentists. Recently more activity has been noticeable in this area, such as a dental workshop held in Utica recently and the dental-medical conference held in Connecticut to which I alluded previously. I am confident that these and similar programs will result in better dental care for nursing home patients. Specifically, we suggest the following:

1. That the dentists, as well as the doctors and hospital administrators, become familiar with the facilities offered by nursing homes in their areas, so that they will know exactly what they will have to work with when they are called to a nursing home.
2. We urge more study and research by dentists on dental problems of the aged.
3. We urge the development of a list of simple oral hygiene procedures which would improve the appearance and add to the comfort of nursing home patients.

Conclusion

Surveys indicate that each year the life span of the American citizen grows longer, bringing ever-increasing problems in the care of the aged. Medically, it is only through the use of the integrated services offered by the doctors, the dentists, the hospitals, and, as we firmly believe, the nursing homes, that maximum care will be given for minimum cost. Let us continue to meet with one another, study with one another, and grow with one another, so that we can make restoration a promise rather than a hope, for the "golden years."

BILLSBORD

My Lady Godiva gained fame and renown,
  Riding a white horse through Coventry town
Clad only in skin and hair golden brown,
  'Twas a gesture of protest to drive taxes down.
Today tax relief is a dream sadly forlorn,
  And one doubts any note of an absence of gown
Unless by some chance her tresses were shorn,
  And the steed she bestrode was a real unicorn.

* * *

The old frontier had Billy the Kid;
The new frontier has Billy Sol Estes!

* * *

The thin difference between success and failure is well illustrated by the implications of these hackneyed expressions: "Riding to the Hounds" and "Going to the Dogs."

* * *

Reference manual for ladies

We must admit to an occasional twinge of conscience at the generally aimless character of this column and the emphasis on foam rather than beer. So, we are happy to announce the proposed development of a reference manual for ladies. The arrival of winter signals the usual cycle of meetings which affright all of us but must be devastating to women. In every community, club after club plans lecture after lecture and tea after tea, either in the afternoon for women only or at night when they are pressured to bring their husbands. Our own wives seek escape by accompanying us to a medical meeting or convention, but they find themselves right back on the lemon or sugar merry-go-round, as they run into the Ladies Committee and are faced with a get-acquainted tea, a fashion show and tea, a garden tour and/or a tour of historic homes and a tea. This is not the fault of the committee—what else can they do? They have the task of entertaining a group of women they don't know and who don't know each other.

Some day, there will be a medical meeting where a physician's wife will be made welcome and can go where he goes. A meeting where she will not have to contend with a special ladies program. A meeting where she can feel wanted and not suffer the indignity of the usual poorly camouflaged adult baby-sitting program designed to get her out of the way. Here she will drink what she wants (even tea!) and go where and with whom she wants. A meeting that would provide release from the monotony of cultural meetings that beset her at home. Of course, such a meeting might well present special problems. For instance, the committee on arrangements would probably have to add a precautionary note something like this to the announcement:

"It is expected that wives and husbands will arrive together and the committee will do all it can to see that the same arrangement prevails at time of departure; however, it can assume no responsibility for the interim period."

Realistically, it must be recognized that society is not prepared for such a revolutionary procedure as of the present. Intriguing as it may seem it must await a future time and a different attitude. We considered what could be done now and decided a compilation of the roster of available lecturers with a short critical summary was the answer. With such information she no longer need be deluded by challenging or provocative titles or slanted descriptions of the lecturer's personality. Provided with factual information she no longer will be lured into poorly ventilated, makeshift halls only to face an oft repeated conflict between sleepiness engendered by the monotonous monotones of a deadly boring speaker and wakefulness stimulated by the devilish discomfort of a chair designed to fold rather than to be sat upon. Obviously the whole listing cannot be reproduced here but a few excerpts will, I am sure, indicate the fundamental utility of this proposed manual.

1. Leander and the Hellespont. This lecturer is a relict of the debunking school of the twenties. Clothes, appearance, and speech are all a little too precise, and the result is ineffectual, somewhat like the too vigorous fluorishing of an unloaded gun—a sort of sheep in aging wolf's clothing. The lecture will follow the usual debunking technic by claiming Leander not only did not swim the Hellespont on the tragic night that Hero threw herself into the sea

but that he never did swim it. By a process of phantasy which defies logic and ignores contradiction he will prove Leander used a well-hidden dinghy. He will also claim that Keats was mistaken when he penned:

> "Dead—heavy; arms and shoulders gleam awhile,
> He's gone; up bubbles all his amorous breath!"

Rather he will claim the truth was found in Byron's lines:

> "And clouds aloft and tides below,
> With signs and swells forbade to go."

Hero jumped not because she saw him drown but because her torch was extinguished by the wind. (What a spot for an Ever-Ready Battery ad!) Leander was forced to wander disguised. He avoided other love affairs and was in fact really Hippomenes chosen to judge the races between Atalanta and her suitors because of his known indifference. When the beauty of the cursed Atalanta aroused him he was helped by Venus (the three golden apples) not because of his supplications but as a means of revenge because Hero had been a priestess of the goddess.

Such thinking is not associated with schizophrenia. It is a well-planned exercise in the art of the dropping of learned facts that coincides with name dropping in theatrical circles. It provides a camouflage of erudition so that no matter how boring or how wrong one might be one gains a reputation of great learning and extensive knowledge.

2. THE BACKYARD CHEF. This lecturer is a sort of junior edition of the preceding. He is younger but no more masculine. There will be many rather poor witticisms about man, his backyard, and his barbecue. This is a subject few women find humorous because of painful association. He will probably prove somewhere in his speech that Johnny Appleseed planted the tree that shades Columbia coffee, that there is a difference between goulash and hash, and that wild rice is not really feral but basically a tame variety that has been irritated synthetically.

3. THERE ARE NO BULLS IN OUR CHINA SHOP. Actually there is no such title on the lecture list. We just inserted it as a plug for artificial insemination.

4. THE GORDIAN KNOT. Beware of this one. It sounds as if it concerned some vital decision such as nuclear testing or the abandoning in New York State of adultry as the single reason for grounds for divorce. Actually it is about the knot tying program of the Boy Scouts and will end with an appeal for funds.

5. OUR PROBLEM CHILDREN. This will feature different lectures dependent on the size of the honorarium or how well known the chairman of the program committee might be. But it makes no difference whether it is a professor of psychiatry or a junior instructor in psychology from a state teachers college; they will say the same thing as to the child's basic need for love and security. When they start fixing the blame they will change the content of their talk to suit the audience. With an audience of teachers, the parents will be caustically castigated; with an audience of parents, the teacher and the school system will be pilloried; with an audience of grandparents, both the parents and the teacher will be criticized and a few words about discipline will be thrown in; and of course with an audience composed of a mixture of all of these, the violent television program will become the whipping boy.

This gives some idea of the content of the proposed manual. Of course it will include many other items also, such as the various types of critics, with particular attention to the amateur psychologist who finds psychologic significance in the ordinary as well as in the extraordinary event. (The sort of fellow who will hint that the reason for the sacrifice of Sidney Carton was really his love of Charles Darnley rather than his love of Lucie.)

We hope we have not given the impression that we are completely opposed to the idea of cultural lectures. There are things we like about them of course. On occasion we are sure the ladies even enjoy attending them although offhand Ogden Nash is the only lecturer we know of that could make a woman impervious for a period of an hour to the joint discomfort of a discarded undertaker's chair and a too-tight girdle.

WRC

Medical News

Postgraduate courses offered

The University of Buffalo School of Medicine announces the following postgraduate courses to be given during 1962 and 1963.

Obstetrics and gynecology, October 3 and 4; endocrine disease, October 17 and 18; pediatrics, November 7 and 8; introduction to electrocardiography, November 12; clinical cardiology, November 13 through 15; angiography, November 16; fluid and electrolyte therapy and parenteral nutrition, November 28 and 29; minor surgery and office orthopedics, December 5 and 6; physical medicine and rehabilitation in clinical practice, December 12 and 13; allergy, March 5 through 7, 1963; obstetrics and gynecology, March 27 and 28, 1963; arthritis, April 3 and 4, 1963; and anesthesia, April 17 and 18, 1963.

Applications and registration information may be obtained from the Department of Postgraduate Education, University of Buffalo School of Medicine, 3435 Main Street, Buffalo 14, New York.

Postgraduate rhinoplasty course

An intensive postgraduate course in rhinoplasty, reconstructive surgery of the nasal septum, and otoplasty will be given January 12 through 25, 1963, by Irving B. Goldman, M.D., and staff at The Mount Sinai Hospital, in affiliation with Columbia University.

Candidates for the course should apply to the Registrar for Postgraduate Medical Instruction, The Mount Sinai Hospital, Fifth Avenue and 100th Street, New York 29, New York.

Study of hereditary defects

A study to uncover new hereditary defects in infants and to determine how these interfere with normal development is being undertaken at Columbia University under a new grant of $39,992 from The National Foundation.

The project will be under the direction of Orlando J. Miller, M.D., of the Department of Obstetrics and Gynecology. The study will center chiefly on intensive analysis of the number and types of chromosomes in blood cells from a number of newborn babies suspected of having congenital defects, as well as from some stillborns.

Dr. Miller's study is of particular importance in view of the recent finding that all normal human beings have 46 chromosomes in each cell, instead of 48, as formerly believed. Any number above or below this is abnormal and likely to be reflected in some unusual trait.

His project is concentrating on one phase of The National Foundation's expanded program aimed at unraveling the causes of congenital malformations, one of the leading medical problems of today.

Blindness research grants

Four New York State institutions have received unrestricted grants from Research to Prevent Blindness, Inc., a new national voluntary health foundation. They are: Columbia University, New York City; Cornell University, Ithaca; New York University, New York City; and Eye Bank for Sight Restoration, New York City.

Postgraduate ophthalmology course

The Department of Ophthalmology of the State University of New York Upstate Medical Center at Syracuse will present its thirteenth annual postgraduate course in ophthalmology at the Hotel Syracuse, November 30 and December 1.

The course is limited to 70 members. Inquiries regarding the course may be addressed to James L. McGraw, M.D., at 766 Irving Avenue, Syracuse 10, New York.

Poliomyelitis immunization

The New York State Department of Health has announced that it will recommend the continued use of oral poliomyelitis vaccine within the State. The Department said that at the present time its own scientists' recommendations, after a review of currently available information, were in general agreement with those of the Polio Advisory Committee to Luther L. Terry, M.D., Surgeon General of the U.S. Public Health Service, who concluded that it was not possible to establish that any of the cases studied were due to vaccine virus.

Clinical pathology

Appraisal of practical clinical laboratory methods and newer diagnostic technics will be the emphasis of the postgraduate course, "Clinical Pathology in Medical Practice," October 23 through 25, to be held at the Medical College of Georgia.

Topics and technics selected have been considered from the standpoint of interest to the practicing physician and of application in small hospital laboratories. Lectures, panels, open discussions, and laboratory demonstrations will be used. The subjects encompass the following divisions of clinical pathology: biochemistry, blood banking, hematology, microbiology, and surgical pathology.

Each course is acceptable for eighteen hours credit by the American Academy of General Practice. Registration is limited to a small group for close faculty-participant communication. Applications and information may be obtained from Claude-Starr Wright, M.D., Director, Department of Continuing Education, Medical College of Georgia, Augusta, Georgia.

Northeastern New York Radiological Society

At a recent annual meeting of the Northeastern New York Radiological Society, the following officers were elected for the 1962–1963 term: Donald H. Baxter, M.D., Albany, president; Lester I. Citrin, M.D., Troy, vice-president; and Anthony J. Tabacco, M.D., Albany, secretary-treasurer.

Glorney-Raisbeck Fellowship

The Glorney-Raisbeck Fellowship in the Medical Sciences for the academic year beginning July 1, 1963, will be awarded by the Committee on Medical Education of The New York Academy of Medicine for one year of research and/or study in any field of medicine or its allied sciences. Under circumstances deemed appropriate by the Committee, the Fellowship is renewable on a year-to-year basis for two additional years.

The Fellowship, which carries a stipend of $6,000, is open only to holders of a doctor of medicine degree who have demonstrated a potential for productivity in research and teaching. In general, preference will be given to physicians from the Greater New York area.

Deadline for receipt of applications is December 1, 1962. Requests for application forms and additional information should be addressed to: Aims C. McGuinness, M.D., Executive Secretary, Committee on Medical Education, The New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Course on psychiatric problems in medical practice

A 10-session course on psychiatric problems in medical practice will be given by the American Institute for Psychoanalysis at the Karen Horney Clinic Building, 329 East 62nd Street, New York 21, New York. Sessions will be held on Wednesdays at 8:30 P.M. and will begin on October 3.

The course is designed to present the general practitioner with those fundamentals of theory and practice which he requires for the diagnosis, treatment, and referral of the psychiatric problems he meets in his practice. There is no fee for the course.

Applications should be sent to: Harold Kelman, M.D., Dean, American Institute for Psychoanalysis, 329 East 62nd Street, New York 21, New York.

Course on surgical rehabilitation

New York University Medical Center will offer a full-time, four-day course on surgical rehabilitation of arthritic deformities from November 13 through 16 under the direction of Robert L. Preston, M.D., clinical professor of orthopedic surgery, in cooperation with Currier McEwen, M.D., and Edward F. Hartung, M.D., of the Department of Medicine.

The symposium is designed for the experienced orthopedic surgeon interested in technics for surgical correction of arthritic deformities and rehabilitation of patients handicapped by the disease. The course also will include current information on the systemic management of rheumatic diseases and is open to a limited number of experienced rheumatologists.

Applications and further information may be obtained from the Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, New York.

American Board of Obstetrics and Gynecology

The next scheduled Part I (written) examination of this Board will be held at various examining centers in the United States and Canada, and military centers outside the continental United States, on December 14.

Current bulletins may be obtained by writing to Robert L. Faulkner, M.D., Executive Secretary and Treasurer, 2105 Adelbert Road, Cleveland 6, Ohio.

Diabetes symposium

The tenth all-day symposium of the Clinical Society of the New York Diabetes Association will be held on October 13 at the Barbizon Plaza Hotel, 58th Street and Sixth Avenue, New York City.

Physicians, medical students, and other professional personnel interested in diabetes are invited to attend this program. Advance registration is required and may be made by calling or writing the New York Diabetes Association, 104 East 40th Street, New York 16, New York, OX 7-7760.

Clara Thompson Lecture

The William Alanson White Institute of Psychiatry, Psychoanalysis & Psychology announces that the fifth annual Clara Thompson Memorial Lecture will be held at the Academy of Medicine, 2 East 103rd Street, New York City, on Friday, November 2, at 8:30 P.M.

Bruno Bettelheim, Ph.D., will discuss "The Struggle for Self in Autistic Children."

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis will present Martti Siirala, M.D., lecturing on "Schizophrenia: a Human Situation," on October 24 at 8:30 P.M. at the New York Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Dr. Siirala, professor of psychiatry, Helsinki University, Helsinki, Finland, is a training analyst and an active member of the Society for the Promotion of Psychoanalysis of Helsinki.

Southern Medical Association

The section of ophthalmology of the Southern Medical Association announces that Arthur Gerard DeVoe, M.D., New York City, will be the guest speaker at their annual meeting at the Fontainebleau Hotel, Miami Beach, Florida, the week of November 12 through 15.

For further information, contact the secretary of the Association, Albert C. Esposito, M.D., Suite 1212, First Huntington National Bank Building, Huntington, West Virginia.

Dermatology lecture

The Department of Dermatology of the New York University Schools of Medicine announces that the eleventh Sigmund Pollitzer lecture will be given by Thomas B. Fitzpatrick, M.D., on Tuesday, November 20, at 8:45 P.M. in classroom B of Alumni Hall, 550 First Avenue, New York 16, New York.

Dr. Fitzpatrick, Edward Wigglesworth Professor of Dermatology at Harvard Medical School, will speak on: "Melanin: Biosynthesis and Selected Disorders in Man."

International Council of Group Psychotherapy

The International Council of Group Psychotherapy announces that 46 countries are now represented in the Council, with a present total of 138 members. Elected officers include: J. L. Moreno, M.D., Beacon, New York, president; S. H. Foulkes, M.D., Great Britain, first vice-president; Serge Levovici, M.D., France, second vice-president; A. Friedemann, M.D., Switzerland, treasurer; and Berthold Stokvis, M.D., Netherlands, secretary.

Inquiries about the Third International Congress of Group Psychotherapy should be sent to: P.O. Box 311, Beacon, New York.

Medical librarianship leaflets

Two leaflets describing the educational and personal qualifications of a medical librarian, the variety of jobs in medical libraries, and the rewards of medical librarianship may be obtained from the Medical Library Association, 919 N. Michigan Avenue, Chicago 11, Illinois. *Be A Medical Librarian* is addressed to high school students, and *Choose Medical Librarianship* is intended for use with college students.

Personalities

Elected. Samuel L. Berson, M.D., Brooklyn, as president of the Association of Private Hospitals, and Julius Edward Astrachan, M.D., Queens; Eugene Sole, M.D., Kings; Anton Notey, M.D., Nassau; Imre Weitzner, M.D., Manhattan; and Isadore Yasuna, M.D., The Bronx, as vice-presidents.

Appointed. Goran C. H. Bauer, M.D., associate professor in experimental orthopedics at the University of Lund, Sweden, as director of research at The Hospital for Special Surgery, New York City . . . Harry L. Draker, M.D., assistant director of the Bureau of Dental Health of the New York State Department of Health, as program evaluator in the Health Department's Public Health Research, Development and Evaluation Group . . . Theodore G. Klumpp, M.D., Sands Point, president of Winthrop Laboratories and a vice-president and director of Sterling Drug Inc., by President Kennedy to the Health Resources Advisory Committee, newly-formed unit of the Office of Emergency Planning . . . Harry S. Lichtman, M.D., chairman of the public health committee of the Kings County Medical Society, as director of public health of that Society . . . Walter B. Stankewick, M.D., as director of the Department of Pediatrics of St. Vincent's Hospital, West New Brighton, Staten Island.

Speaker. George T. Pack, M.D., New York City, before the University of Götesberg, Götesberg, Sweden, on "Primary and Metastatic Cancer of the Liver, Moles and Melanomas and Sarcomas of the Soft Somatic Tissues," July 31 through August 2.

Medical Meetings

Division of Dermatology, Downstate Medical Center

The Division of Dermatology of the Department of Medicine, State University of New York Downstate Medical Center, will present a discussion on "Electron Microscopy of Eczematous Skin" on October 5, from 10:00 to 11:30 A.M., in the E building auditorium, Kings County Hospital, 451 Clarkson Avenue, Brooklyn.

Philip Prose, M.D., associate professor of pathology, New York University School of Medicine, will be the speaker, and Lawrence Frank, M.D., professor of dermatology, State University of New York Downstate Medical Center, will be the moderator.

Women's Medical Society

The 56th fall meeting of the Women's Medical Society of New York State, Inc., will be held on October 13 at the Corinthian Club, 930 James Street, Syracuse. A scientific paper on "Studies of Catecholamine Metabolism in Neuroblastoma" will be presented by Mary L. Voorhess, M.D., from the Upstate Medical Center in Syracuse.

American Public Health Association

More than 6,000 public health practitioners are expected to attend the 90th annual meeting of the American Public Health Association at the Fontainebleau Hotel in Miami Beach, Florida, October 15 through 19.

Registration is open to persons professionally interested in public health, including nonmembers of the Association. In addition to scientific discussions, scientific and technical exhibits are being planned.

Further information may be obtained from Schless and Company, 59 East 54th Street, New York 22, New York.

Industrial medicine

A joint session of the New York State Society of Industrial Medicine and the Section on Occupational Medicine of the New York Academy of Medicine will be held on October 24 at 5:00 P.M. at the Academy of Medicine, 2 East 103rd Street, New York 29, New York.

Dr. Jean S. Felton, professor of occupational health at the University of California Medical Center, will speak on "Health and Human Behavior in Industry." Discussion will follow.

American Society of Anesthesiologists

The annual meeting of the American Society of Anesthesiologists will be held at the Statler Hilton Hotel, New York City, October 20 through 26.

Among the subjects to be covered by the scientific papers are: the metabolic fate of the new barbiturate, methohexital; the management of barbiturate coma; the use of an electronic device to predict uptake and distribution of anesthetic agents in patients, anesthesia for open heart surgery, management of cardiac arrest, hypothermia; electronic monitoring of patients under anesthesia; and recent advances in equipment used as automatic ventilators to breathe for patients under anesthesia.

Solomon G. Hershey, M.D., New York City, director of anesthesiology, Beth Israel Hospital, and clinical professor of anesthesiology, New York University Medical School, is chairman of the committee on annual session arrangements.

Louis R. Orkin, M.D., New York City, director of the Department of Anesthesiology, Bronx Municipal Hospital Center, and professor and chairman of the Department of Anesthesiology, Albert Einstein College of Medicine, is in charge of programs.

Local arrangements are being made by Robert G. Hicks, M.D., New York City, director of anesthesiology, St. Vincent's Hospital.

Albert M. Betcher, M.D., New York City, director of anesthesiology, Hospital for Joint Diseases, and assistant clinical professor of anesthesiology, Albert Einstein College of Medicine, is president-elect.

Mid-Hudson Society of Internal Medicine

The Mid-Hudson Society of Internal Medicine will hold its annual meeting October 31 to November 1 at Grossinger's, in Liberty, New York.

Rachmiel Levine, M.D., Martin Goldner, M.D., Thomas Frawley, M.D., and Harold Rifkin, M.D., will participate in a panel discussion of diabetes at 2:00 P.M. on October 31. Dinner and entertainment will follow.

On November 1 Harold Berger, M.D., president of the New York State Society of Internal Medicine, will speak on "Recent Economic Developments"; and Robert Schwinger, M.D., secretary of the Society, will speak on "Mechanics and Functions of the New York State Society of Internal Medicine."

Registration forms and further information may be obtained from David S. Gerbarg, M.D., 169 Washington Avenue, Kingston, New York.

Symposium on diabetes mellitus

The New Jersey State Department of Health in cooperation with the New Jersey Diabetes Association will present a symposium on "Diabetes Mellitus in Children and Young Adults," to be held in the Prudential Insurance Company of America, main auditorium, Gibraltar Building, 763 Broad Street, Newark, New Jersey, on October 31.

Further information may be obtained from Arthur Krosnick, M.D., Coordinator, Diabetes Control Program, Division Chronic Illness Control, State of New Jersey Department of Health, Trenton 25, New Jersey.

American College of Gastroenterology

The 27th annual convention of the American College of Gastroenterology will be held at the Morrison Hotel in Chicago, October 29 through 31.

I. Snapper, M.D., Brooklyn, will be a moderator of the annual course in postgraduate gastroenterology given at the Morrison Hotel and at the Cook County Hospital on November 1 through 3, immediately following the convention.

Copies of the program and further information concerning the postgraduate course may be obtained by writing to the American College of Gastroenterology, 33 West 60th Street, New York 23, New York.

Doctors' business problems to be discussed

The first national convention on medical practice management, sponsored by the National Committee on Medical Practice Management, will be held November 1 and 2 at the Flamingo Hotel, Las Vegas, Nevada.

Aid to the physician in solving low-cost medical care problems, financial problems, and relations with his patients and employes will be discussed. Nonclinical aspects of the doctor's practice will be stressed.

For further information, contact: National Committee on Medical Practice Management, 6043 Hollywood Boulevard, Los Angeles 28, California.

New England Postgraduate Assembly

The nineteenth annual New England Postgraduate Assembly will be held November 6 through 8 at the Statler Hilton, Boston, Massachusetts.

The Assembly is sponsored by the Council of New England State Medical Societies in cooperation with the New England State Chapters of the American Academy of General Practice.

The Assembly is open to all physicians. For further information write to: Mr. Getty Page, Secretary, 128 Merchants Row, Rutland, Vermont.

The unexpected in new drug research

The most challenging problems in the field of drugs center mainly on diseases which are not yet clearly understood. The research efforts required for their resolution will entail basic understanding and a close integration of many disciplines. The problems still with us are difficult and complex. No one can state with certainty what the future holds. Indeed, in the field of research and new products we are often puzzled—or even astonished—at the least expected point.—*Dr. Ernest H. Volwiler, former president, Abbott Laboratories, to Senate Subcommittee on Antitrust and Monopoly, December 9, 1961*

Abstracts

Lerman, S.: Radiation cataractogenesis, New York State J. Med. **62:** 3075 (Oct. 1) 1962.

The eye is unusually sensitive to many forms of the two major types of radiation: the electromagnetic spectrum and corpuscular radiation. Radio waves, long-wave diathermy, and visible rays usually do not produce cataracts, but short-wave diathermy and infrared and ultraviolet radiation have a definite cataractogenic potential. While grenz rays, beta radiation, and cosmic rays may produce cataracts, they are of little significance in comparison with other forms of radiation cataractogenesis. Neutrons, roentgen rays, and gamma rays possess the most serious cataractogenic potential. The cataracts produced by these three forms of radiation are similar in appearance and structure, consisting initially of posterior subcapsular and cortical opacities, requiring latent periods before becoming visible, and occurring with doses that do not necessarily produce any other clinically evident lesions. One of the earliest chemical changes observed in the lens following exposure to x-radiation is a rapid fall in the level of SH (sulfhydryl) groups. Experiments on rats have suggested that the initial direct effects of x-radiation of the lens may be due to its action on RNA (ribonucleic acid) and DNA (desoxyribose nucleic acid) within the lens.

Schwartz, M. J., Hopewell, W. S., and Piotrowski, S. F.: Prepared saccharin solution for study of circulation time, New York State J. Med. **62:** 3086 (Oct. 1) 1962.

A study was made of a new intravenous saccharin solution, suitable for storage in ampule form, to determine the arm-to-tongue circulation time in 27 normal subjects and 13 patients with congestive heart failure. The technic was safe, and the results were accurate with a reproducible end point; no systemic reactions occurred. The data are comparable to those obtained using sodium dehydrocholate but with none of the allergic reactions frequently reported with the latter.

Knox, W. G., and Coletti, L.: Symptomatic abdominal aortic aneurysm; need for accurate diagnosis and prompt surgery in improving surgical salvage rate, New York State J. Med. **62:** 3089 (Oct. 1) 1962.

An analysis was made of 14 patients with ruptured or rapidly expanding abdominal aortic aneurysms. The cause of death in the 14 cases, all subjected to emergency surgery, was hemorrhage with renal shutdown and continued shock in 11, coronary occlusion in 2, and cerebral vascular accident in 1. Unnecessary delay occurred in almost every instance, and early, accurate recognition of the lesion and prompt surgical intervention might have improved the salvage rate. Over a period of five years the mortality rate for elective resection of these lesions, when intact, was 9 per cent, whereas with those lesions treated after rupture or rapid enlargement, the mortality rate was 80 per cent.

Lyons, A. S.: Pyloric stenosis due to lye ingestion, New York State J. Med. **62:** 3093 (Oct. 1) 1962.

Whereas ingestion of corrosive acid causes damage primarily to the stomach, ingestion of caustic alkali (lye) causes severe damage to the esophagus and may produce pyloric obstruction. The factors responsible for the gastric insult are: the amount reaching the stomach, the degree of pylorospasm produced, and the extent of neutralization in the stomach. Pain is a constant feature of pyloric stenosis. Radiologic evidence of virtually complete obstruction is usually obtainable. The treatment is surgical with gastroenterostomy and tube gastrostomy the preferred procedures.

Nash, D. T.: Chronic alcoholism treated via half-way house and citrated calcium carbimide, New York State J. Med. **62:** 3098 (Oct. 1) 1962.

A study was made of 79 homeless severely addicted alcoholic males treated at a "half-way" house by conventional methods and 46 severely addicted alcoholic patients, including 10 women, who were seen in private practice and treated with a daily 50-mg. tablet of citrated calcium carbimide (Temposil). The results in the 46 patients in the citrated calcium carbimide group were: excellent, 7; good, 12; fair, 16; and poor, 11. The results in the 79 patients in the half-way house group were: excellent, 18; good, 6; fair, 6; and poor, 49. The drug-treated group had significantly higher worthwhile results, and there was a lack of serious toxicity.

Byron, H. M.: Ophthalmic survey of 162 mentally retarded children, New York State J. Med. **62:** 3102 (Oct. 1) 1962.

An ophthalmic survey, including external and orthoptic evaluations, cycloplegic refractions, and adequate funduscopy through dilated pupils, was undertaken of 162 mentally retarded children. High refractive errors and strabismus were the most frequent abnormalities detected. Others included: conjunctivitis, subalbinism, optic atrophy, ptosis, nystagmus, colobomas, congenital glaucoma, congenital cataracts, and papilledema. The incidence of ophthalmic defects was higher than in the population at large. The long-term therapeutic effects have not yet been determined, but an ophthalmic examination is recommended as an integral part of the multiphasic diagnostic approach to the retardate.

FIFTY-SIXTH ANNUAL

District Branch Meetings

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Eighth District Branch

Thursday, October 4, 1962

Bartlett Country Club, Olean, New York

Morning

Golfing facilities available (see pro shop)
11:00 A.M. Registration

Afternoon

12:00 NOON Advisory Council Luncheon Meeting
2:00 P.M. *Panel Discussion:* **Toward Better Understanding of Deafness: Etiology, Diagnosis, Treatment;** panelists are from the University of Buffalo School of Medicine, Buffalo, New York
Irwin A. Ginsberg, M.D., Clinical Associate in Surgery
Harold Brody, Ph.D., Associate Professor of Anatomy
Elmo Knight, Audiometrist
5:00 P.M. Business Meeting

Evening

6:30 P.M. Cocktails
7:30 P.M. Dinner Dance
Introduction of Officers
Remarks: Joseph A. Lane, M.D., President, Medical Society of the State of New York
Remarks: Mrs. Herbert J. Ulrich, President, Woman's Auxiliary to the Medical Society of the State of New York

Officers—Eighth District Branch

President	Irwin Felson, M.D., Wellsville
President-Elect	John D. Naples, M.D., Buffalo
Secretary	Myron E. Williams, Jr., M.D., Batavia
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Allegany	George E. Taylor, Jr., M.D., Cuba
Cattaraugus	Leo J. Murphy, M.D., Olean
Chautauqua	Ernest Homokay, M.D., Silver Creek
Erie	Clarence A. Straubinger, M.D., Buffalo
Genesee	David B. Johnson, M.D., Batavia
Niagara	William H. Vickers, Jr., M.D., Niagara Falls
Orleans	Harvey J. Blanchet, Jr., M.D., Medina
Wyoming	C. Stanley Baker, M.D., Castile

Abstracts in Interlingua

Lerman, S.: Cataractogenese per radiation (*anglese*), New York State J. Med. **62:** 3075 (1 de octobre) 1962.

Le oculo es inusualmente sensibile pro multe formas del duo major typos de radiation, i.e. del spectro electromagnetic e de radiation corpuscular. Undas de radiophonia, diathermia a longe undas, e radios del spectro visibile usualmente non produce cataractas, durante que radiation infrarubie e ultraviolette possede definitemente potentialitates cataractogene. Ben que radiation Bucky, radiation beta, e radiation cosmic pote producer cataractas, illos es de pauc signification in comparation con altere formas de cataractogenese per radiation. Neutrones, radios roentgen, e radios gamma possede le plus serie potentialitate cataractogene. Le cataractas producite per iste tres formas de radiation es simile in apparentia e structura, consistente initialmente de posterior opacitates subcapsular e cortical, requirente periodos de latentia ante que illos deveni visibile, e occurrente con doses que non necessarimente produce altere clinicamente evidente lesiones. Un del plus precoce alterationes chimic observate in le lente post exposition a radiation X es un rapide declino del nivello de gruppos sulfhydrylic (SH). Experimentos con rattos ha indicate que le directe effectos initial de radiation X in le lente consiste possibilemente in un affection de acido ribonucleic e de acido disoxyribonucleic.

Schwartz, M. J., Hopewell, W. S., e Piotrowski, S. F.: Pre-preparate solution de saccharina pro le studio del tempore de circulation (*anglese*), New York State J. Med. **62:** 3086 (1 de octobre) 1962.

Esseva executate un studio de un nove solution de saccharina, magasinabile in ampullas, al uso intravenose in determinationes del tempore de circulation bracio-lingua. Le subjectos esseva 27 normales e 13 patientes con congestive discompensation cardiac. Le technica se provava salve. Le resultatos esseva accurate, monstrante un reproducibile puncto terminal. Occurreva nulle reactiones constitutional. Le datos es comparabile a illos obtenite con le uso de dishydrocholato de natrium, sed nulle del reactiones allergic superveni le quales es frequentemente reportate post le uso de iste ultime agente.

Knox, W. G., e Coletti, L.: Symptomatic aneurysma del aorta abdominal; le necessitate de accuratia diagnostic e promptitude del intervention chirurgic in le interesse de un meliorate superviventia (*anglese*), New York State J. Med. **62:** 3089 (1 de octobre) 1962.

Esseva analysate un serie de 14 patientes con rupturate o rapidemente expansive aneurysmas del aorta abdominal. Le causas de morte in le 14 casos—omnes subjicite a chirurgia de urgentia—esseva hemorrhagia con suspension del function renal e choc continue in 11, occlusion coronari in 2, e accidente cerebro-vascular in 1. Retardos innecessari habeva occurrite in quasi omne le casos, e un accurate recognition del lesion sequite de un prompte intervention chirurgic haberea potite meliorar le procentage del superviventes. Un statistica pro cinque annos revela pro elective resectiones de iste lesiones un mortalitate de 9 pro cento quando le aneurysma esseva intacte e de 80 pro centro quando le aneurysma esseva rupturate o habeva comenciate expander se rapidemente.

Lyons, A. S.: Stenosis pyloric causate per le ingestion de alcali caustic (lixivia) (*anglese*), New York State J. Med. **62:** 3093 (1 de octobre) 1962.

Durante que le ingestion de acido corrosive causa un damnification de primarimente le stomacho, le ingestion de lixivia causa sever damnification del esophago e pote producer obstruction pyloric. Le factores responsabile pro le insulto gastric es (1) le quantitate que arriva al stomacho, (2) le grado de pylorospasmo producite, e (3) le potentia neutralisatori in le stomacho. Dolores es un constante characteristica de stenosis pyloric. Evidentia radiologic de un virtualmente complete obstruction es usualmente obtenibile. Le tractamento es chirurgic, con gastroenterostomia e gastrostomia a tubo como manovras preferite.

Nash, D. T.: Chronic alcoholismo, tractate (1) a un "casa de medie via" e (2) con citratate carbimido de calcium (*anglese*), New York State J. Med. **62:** 3098 (1 de octobre) 1962.

Esseva effectuate un studio de 79 severmente toxicomane alcoholicos mascule sin domicilio qui esseva tractate a un "casa de medie via" per methodos conventional e de 49 severmente toxicomane patientes alcoholic, incluse 10 feminas, qui esseva tractate in un practica private con citratate carbimido de calcium (Temposil) a un mesura de un tabletta de 50 mg per die. Le resultatos in le gruppo del 46 patientes tractate con citratate carbimido de calcium esseva excellente in 7 casos, bon in 12, satis bon in 16, e non bon in 11. Le resultatos in le gruppo del subjectos tractate in le "casa de medie via" esseva excellente in 18 casos, bon in 6, satis bon in 6, e non bon in 49. Le gruppo a tractamento pharmacotherapeutic monstrava significativemente plus incoragiante resultatos. Serie toxicitate esseva absente.

Byron, H. M.: Un studio ophthalmic de 162 mentalmente retardate juveniles (*anglese*), NEW YORK STATE J. MED. **62:** 3102 (1 de octobre) 1962.

Un studio ophthalmic—incluse evalutationes externe e orthoptic, refractiones cycloplegic, e adequate fundoscopia via dilatate pupillas—esseva executate in un gruppo de 162 mentalmente retardate juveniles. Alte errores refractive e strabismo esseva le plus frequente anormalitates detegite. Altere anormalitates esseva conjunctivitis, subalbinismo, atrophia optic, ptosis, nystagmo, colobomas, glaucoma congenite, cataractas congenite, e papilledema. Le incidentia de defectos ophthalmic esseva plus alte que in le population in general. Le effectos therapeutic a longe vista ha non ancora essite determinate, sed il es recommendate que un examine ophthalmic es includite como parte integral in le multiphasic programma diagnostic pro casos de retardamento mental.

Drop in disabilities lasting eight days or more

Disabilities lasting eight days or more dropped to the lowest level in five years during 1961 among employes of Metropolitan Life Insurance Company, it is reported by company statisticians.

New cases of disability among employes covered by Metropolitan's group insurance program occurred at the rate of 148 per 1,000 employes, 5 per cent below each of the preceding three years and appreciably under the rate of 169 per 1,000 recorded in 1957, when influenza outbreaks were widespread.

Among males in the seventeen to sixty-four age range, the disability rate decreased only slightly between 1960 and 1961: from 107 to 105 per 1,000. The decrease among females in the seventeen to fifty-nine age group was much greater: from 237 to 211 per 1,000. Despite this favorable trend, the disability rate among women was twice that for men, reflecting the higher rate among women for each cause of disability except heart disease.

A good part of the decrease in disability among women was due to the reduced incidence of diseases of the respiratory system, from 94.8 to 81.8 per 1,000.

Diseases of the respiratory system continued to be the leading cause of disability among both men and women, accounting for 2 out of every 5 cases among women. Diseases of the digestive system ranked second as a cause of disability in each sex, followed by accidental injuries. Diseases of the circulatory system ranked fourth among men, while diseases of the genitourinary system and tumors, mostly benign, turned up as a relatively important cause of disability among women.

Necrology

Benjamin Robert Bass, M.D., of Buffalo, died on May 18 at Millard Fillmore Hospital at the age of sixty-eight. Dr. Bass graduated in 1915 from Long Island College Hospital Medical School. He was a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Theodor Blum, M.D., of New York City, died on July 24 at his home at the age of seventy-nine. Dr. Blum graduated in 1911 from the University of Pennsylvania School of Medicine, after having received his Doctor of Dental Surgery from there in 1909, and in 1912 received a medical degree from the University of Vienna. He was the founder of the Institute of Clinical Oral Pathology and was one of the first dentists to use x-ray for dental diagnosis and procaine for block anesthesia. Dr. Blum was a Fellow of the American College of Surgeons and a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Walter J. Craig, M.D., of Albany, died on August 12 at St. Peter's Hospital at the age of seventy-four. Dr. Craig graduated in 1921 from Yale University School of Medicine. From 1927 until his retirement in 1944 he had been associated with the State Department of Health and was director of the Department's division of orthopedics. Dr. Craig was a consulting physician in orthopedics at St. Peter's Hospital.

Joshua H. Friedman, M.D., of Brooklyn, died on August 19 at Long Island Jewish Hospital at the age of seventy-eight. Dr. Friedman graduated in 1908 from Long Island College Hospital Medical School.

Arthur Frucht, M.D., of Hempstead, died on August 15 at South Nassau Communities Hospital, Oceanside, at the age of sixty-four. Dr. Frucht graduated in 1932 from New York Homeopathic Medical College and Flower Hospital. He was a founder and a past-president of the Nassau Radiological Society and a founder of the Radiological Society of New York State. Dr. Frucht was a Diplomate of the American Board of Radiology (Roentgenology) and a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Ferenc Grossman, M.D., of the Bronx, died on July 18 at the age of sixty-four. Dr. Grossman received his medical degree from the University of Budapest in 1925. He was a clinical assistant attending surgeon in proctology at Lebanon Hospital. Dr. Grossman was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Henry Hodas, M.D., of New York City, died on August 15 at The Mount Sinai Hospital at the age of fifty-eight. Dr. Hodas graduated in 1929 from New York University and Bellevue Hospital Medical School. He was an attending physician at City Hospital at Elmhurst and Columbus Hospital, a consulting physician at Misericordia Hospital, and an honorary consulting cardiologist to the New York Police Department. Dr. Hodas was a Fellow of the American College of Cardiology, a Fellow of the American College of Chest Physicians, and a member of the American Geriatrics Society, the Association of Military Surgeons of the United States, the New York Cardiological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Quentin McAdam Jones, M.D., of Utica, died on June 12 at the age of fifty. Dr. Jones graduated in 1938 from Cornell University Medical College. He was a senior attending surgeon at St. Luke's Memorial-Hospital Center. Dr. Jones was a member of the Utica Academy of Medicine, the Oneida County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Leo Leonard Klein, M.D., of New York City, died on July 23 at the age of sixty-four. Dr. Klein graduated in 1924 from the Medical College of Virginia and interned at Montefiore Hospital. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Otto Knina, M.D., of Staten Island, died on July 5 at Richmond Memorial Hospital at the age of seventy-nine. Dr. Knina received his medical degree from the University of Vienna in 1909. He was a member of the Richmond County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Paul Liebesny, M.D., of Arlington, Virginia, formerly of the Bronx, died on August 11 at the Washington Hospital Center, Washington, D.C., at the age of eighty-one. Dr. Liebesny received his medical degree from the University of Vienna in 1905. He was a consulting physician in physical medicine at the Bronx Hospital. Retired in 1950, Dr. Liebesny was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Abraham Benjamin Pemsler, M.D., of Miami, Florida, formerly of the Bronx, died on August 11 at the age of seventy-two. Dr. Pemsler graduated in 1912 from New York University and Bellevue Hospital Medical School. Retired, he had formerly served as an attending orthopedist at the Bronx Hospital. Dr. Pemsler was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Solomon Siker, M.D., of Miami Beach, Florida, formerly of Port Chester, died on July 1 at Miami Beach at the age of sixty-nine. Dr. Siker graduated in 1917 from Long Island College Hospital Medical School. He was a member of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical Schools

Albert Einstein College of Medicine

Research career awards. Stanley M. Levenson, M.D., professor of surgery, and Dr. Alex B. Novikoff, research professor of pathology, have been awarded Research Career Awards by the United States Public Health Service. The awards offer life-time support to distinguished investigators to aid them in any research they may wish to pursue.

New York Medical College

Post-Doctoral Fellowship. A post-doctoral fellowship has been established for studies of the nutritional problems associated with hyperthyroidism with special emphasis on vitamin factors by Vitamin Products, Inc. The fellowship will be in the Department of Medicine, Division of Metabolism.

Dr. Jose Jiminez is the recipient and will receive $5,500 annually for three years of work in the field and will work with Dr. Rachmiel Levine, chairman of the Department.

State University of New York Downstate Medical Center

Appointments. Paul Dreizen, M.D., research associate in biophysics, Massachusetts Institute of Technology, as assistant professor; Hyman Solovay, M.D., as clinical assistant professor; Nathaniel F. Nelson, M.D., lecturer in ophthalmology; James M. Byrne, M.D., lecturer in urology; and Irwin Polk, M.D., lecturer in environmental medicine and community health, all in the Department of Medicine.

Retired. Charles A. Weymuller, M.D., professor of pediatrics, and Samuel A. Wolfe, M.D., clinical professor of obstetrics and gynecology, retired from the faculty at the end of the summer.

Grants. The receipt of 16 research grants totaling $376,825 have been received by the Center during June and July. In addition to the research grants, the Department of Medicine received $25,000 from the National Institutes of Health to support an undergraduate heart training program and $3,325 from the Arthritis and Rheumatism Foundation to support an arthritis laboratory, and the Dean received $3,450 from the Health Research Council of the City of New York for student research fellowships.

State University of New York Upstate Medical Center

Appointments. Peter H. Byles, M.D., and Murray Mendelson, M.D., assistant professors, Department of Anesthesiology; Wilfred A. Cassell, M.D., and Francis J. Durgin, M.D., instructors, Department of Psychiatry; Alfredo M. Garcia, M.D., assistant professor, Department of Anatomy; John A. Meyer, M.D., assistant professor, Department of Surgery; Lawrence H. Port, M.D., clinical instructor, Department of Medicine. John F. Keighley, M.D., has received a change of title from fellow to instructor, Department of Medicine.

Fellowships and research assistants. Richard H. Aubry, M.D., research fellow, Department of Obstetrics-Gynecology; Agnes S. de Leon, M.D., research fellow, Department of Pediatrics; William A. Vincent, M.D., fellow, Department of Medicine; and Rolf Zurbrugg, M.D., research fellow, Department of Pediatrics.

New and renewal grants. Nearly $1,700,000 in new and renewal grants have been received by the faculty. New grants totaling $918,726 have been issued to William H. Bergstrom, M.D., associate professor, Department of Pediatrics, from the National Kidney Disease Foundation; Fred T. Caldwell, Jr., M.D., assistant professor, Department of Surgery, Seymour Fisher, M.D., professor, Department of Psychiatry, Dr. William B. Kinter, professor, Dr. Maxwell M. Mozell, assistant professor, Dr. Otto H. Muller, professor, Dr. James B. Preston, professor and chairman, all from the Department of Physiology; Dr. Charles F. Reed, assistant professor, Department of Psychiatry (psychology), Dr. William R. Ruegamer, associate professor, Department of Biochemistry, and George A. Sisson, M.D., clinical associate professor, Department of Otolaryngology, grants from the U.S. Public Health Service; Robert H. Eich, M.D., associate professor, Department of Medicine, from the New York Heart Assembly; and Dr. Tracy B. Miller, post-doctoral fellow, Department of Pharmacology, from the American Heart Association, Inc.

Renewal grants in the amount of $682,174.52 have been received for: J. A. Abildskov, M.D., associate professor, Department of Medicine; Dr. Richard J. Doisy, assistant professor, Department of Biochemistry; Lytt I. Gardner, M.D., professor, and George S. Husson, M.D., assistant professor, Department of Pediatrics; David B. Jones, M.D., associate professor, Department of Pathology; Richard H. Lyons, M.D., professor and chairman, Department of Medicine; Dr. Samuel Mallov, associate professor, and Dr. Alfred E. Farah, professor and chairman, Department of Pharmacology; Dr. Americo A. Marucci, assistant professor, Department of Microbiology; C. Barber Mueller, M.D., professor and chairman, Department of Surgery; Dr. Dan A. Richert, professor, Department of Biochemistry; David H.P. Streeten, M.D., associate professor, Department of Medicine—two renewals; Dr. Akira E. Takenori, assistant professor, Department of Pharmacology, and Dr. W. W. Westerfeld, professor and chairman, Department of Biochemistry, all renewals from the U.S. Public Health Service. Dr. Henry DiStefano, associate professor, Department of Anatomy, from the Population Council, Inc.; and Lloyd S. Rogers, M.D., associate professor, Department of Surgery, from the American Heart Association, Inc., as well as a renewal from the U.S. Public Health Service.

University of Rochester School of Medicine and Dentistry

Three-year grant. A three-year grant of $56,751 from the National Foundation-March of Dimes has been awarded for the studies of a newly-discovered class of antibodies. John H. Vaughan, M.D., associate professor of medicine, will direct the project and John P. Leddy, M.D., will conduct basic studies on the nature of a kind of antibody known as beta 2A.

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Sources of medical school loan assistance monies

According to the August, 1962, issue of *Datagrams*, published by the Association of American Medical Colleges, the private sector of the economy contributes about two thirds of the fiscal support for medical school loan funds while the public or governmental sector contributes about one third. With respect to the private sources, philanthropic support by individuals and agencies, outside of medicine, accounts for about 40 per cent of all monies available to the schools for loan purposes. It is noteworthy, however, that foundation support decreased slightly (7 per cent) between 1960 and 1961 while memorial funds and other nonalumni contributions increased substantially (20 per cent). Medical alumni giving, in keeping with the profession's tradition of supporting itself, amounts to 10 per cent per year. Next, only eight medical schools carry an item in their budgets for student loans. Also, the average dollar volume per school of these items is quite small relative to other sources. Nevertheless, this source, within the schools having it, showed a dramatic increase (74 per cent) in dollar volume from 1960 to 1961, thus indicating the largest shift of any source. Industry provided only a small fraction of the total direct support for medical school loan funds.

Support from the public sector of the economy is considerable at the Federal level but miniscule at the state and local level. The Federal government, through the medium of the National Defense Education Act, provided the largest proportion of total funds (31 per cent) of any single source. The amount of this support has increased 20 per cent since 1960. In contrast, the state and local levels of government provided only about 2 per cent of the available loan monies, and there was only a slight increase from 1960 to 1961.

Not included in the report is the Medical Education Loan Guarantee Program of the American Medical Association which started in February, 1962. This is a significant new source of loan funds to medical students and already more than 2,300 applications for loan assistance have been received from medical students of which 68 per cent are from undergraduates and the remainder from interns and residents.

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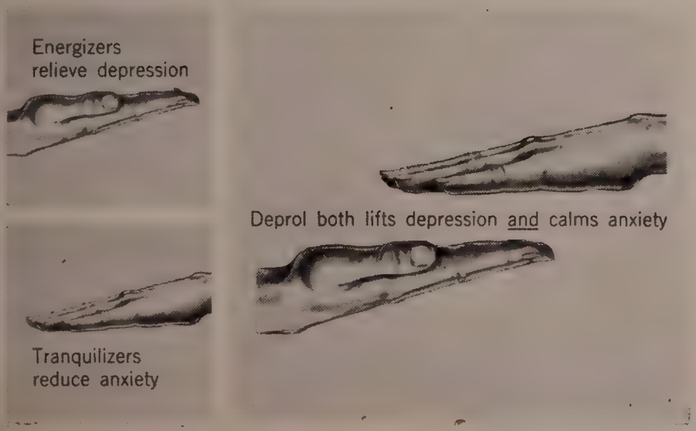
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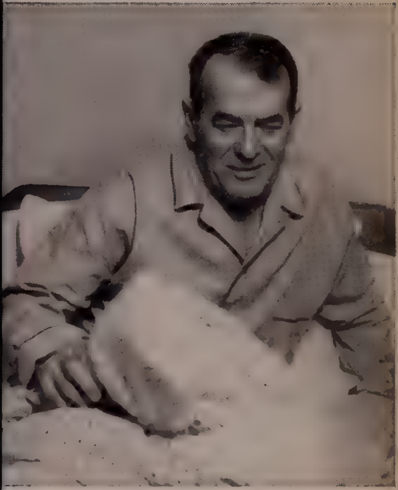

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1. Ford, R. V.: Clin. Res. Notes 2:1 (Dec.) 1959. 2. Ford, R. V.: Cur. Therap. Res. 2:92 (Mar.) 1960. 3. Elliott, J. P., Jr., and Goldman, A. M.: South. M.J. 54:794 (July) 1961.

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1. Cohen, B. M.: M. Times 88:855 (July) 1960. 2. Cohen, B. M.: Méd. et Hyg. (Genève) #494, p. 210 (Mar. 15) 1961.

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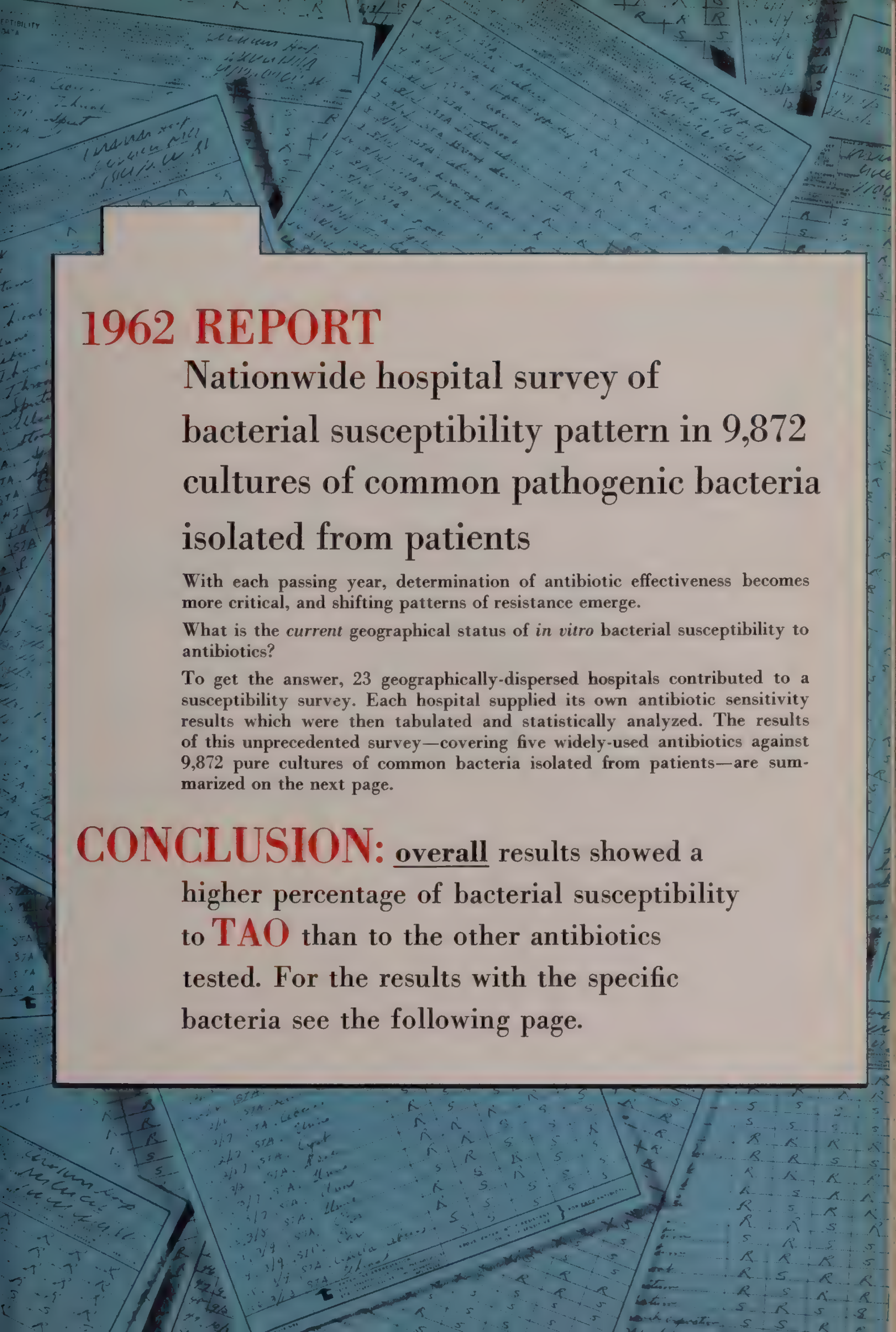

1962 REPORT

Nationwide hospital survey of bacterial susceptibility pattern in 9,872 cultures of common pathogenic bacteria isolated from patients

With each passing year, determination of antibiotic effectiveness becomes more critical, and shifting patterns of resistance emerge.

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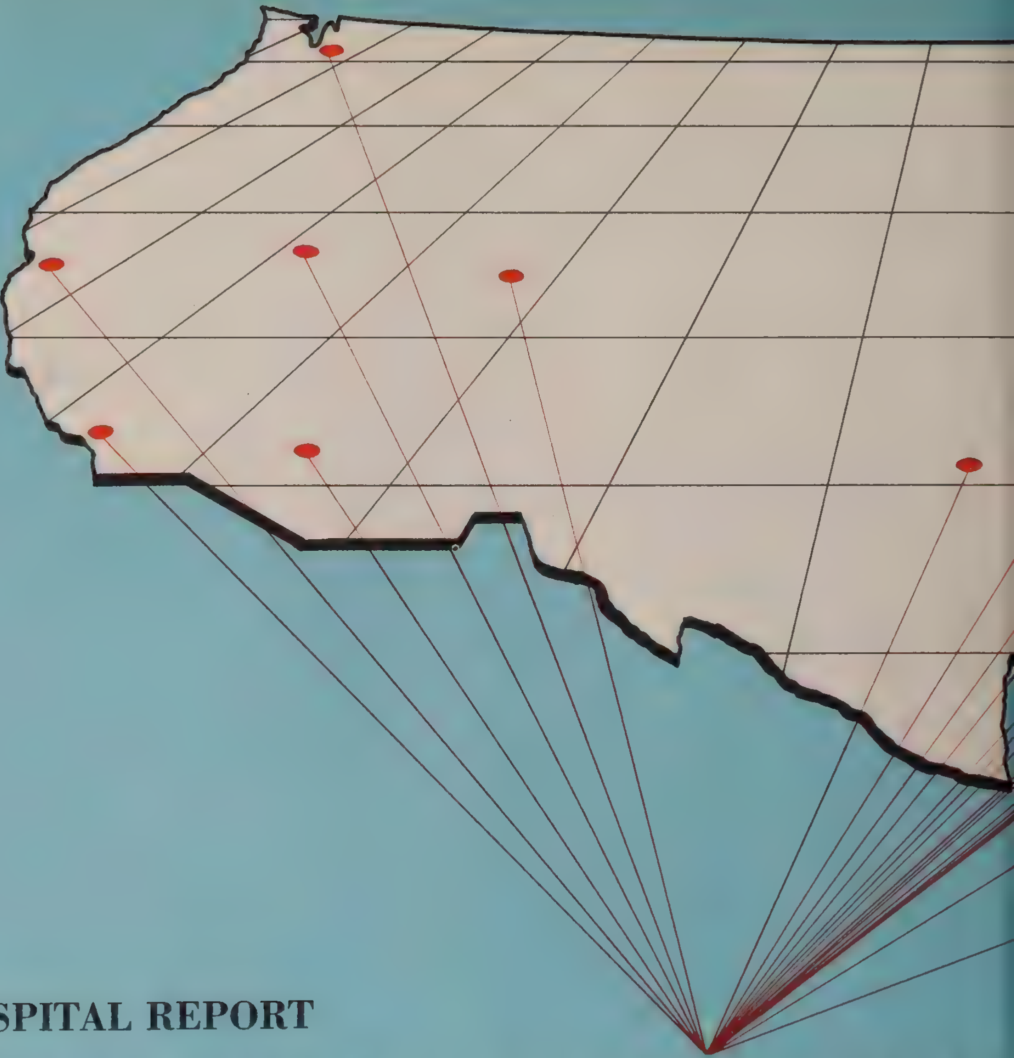
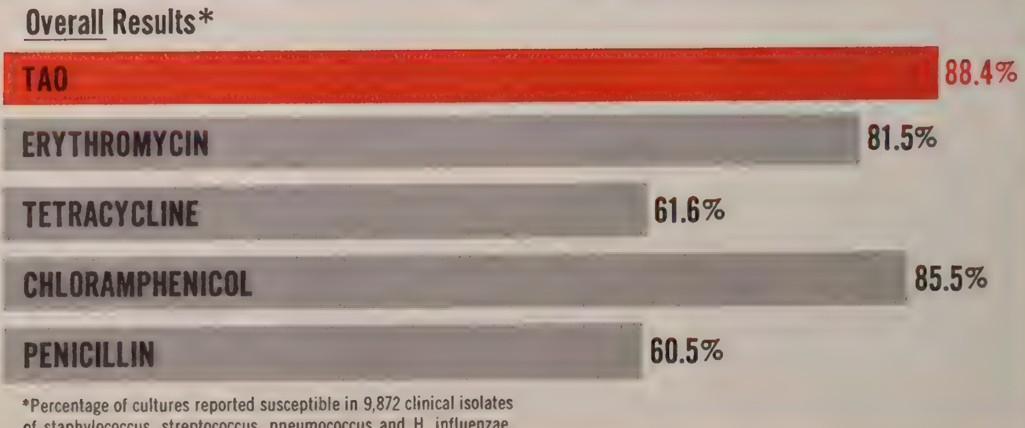
CONCLUSION: overall results showed a higher percentage of bacterial susceptibility to **TAO** than to the other antibiotics tested. For the results with the specific bacteria see the following page.



1962 HOSPITAL REPORT

RESULTS FROM A NATIONWIDE



*Percentage of cultures reported susceptible in 9,872 clinical isolates of staphylococcus, streptococcus, pneumococcus and H. influenzae.

Of 6,725 staphylococcal isolates tested TAO showed a clear superiority; of 2,488 streptococcal and 463 pneumococcal isolates tested results were about equal. Of 196 H. influenzae isolates tested TAO was less effective.

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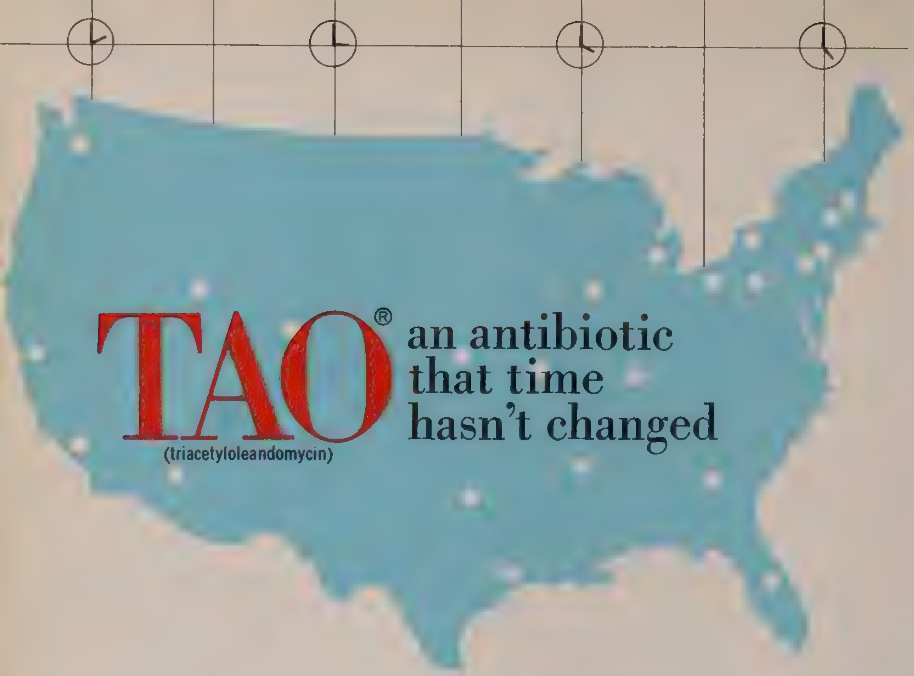
1. "Bacterial Susceptibility Patterns: A Geographic Survey." Fowler, J. Ralph, M.D., and Watters, John L., M.D. Scientific Exhibit presented at the Annual Meeting of the American Society of Clinical Pathologists, Chicago, Ill., August 31 to September 8, 1962.



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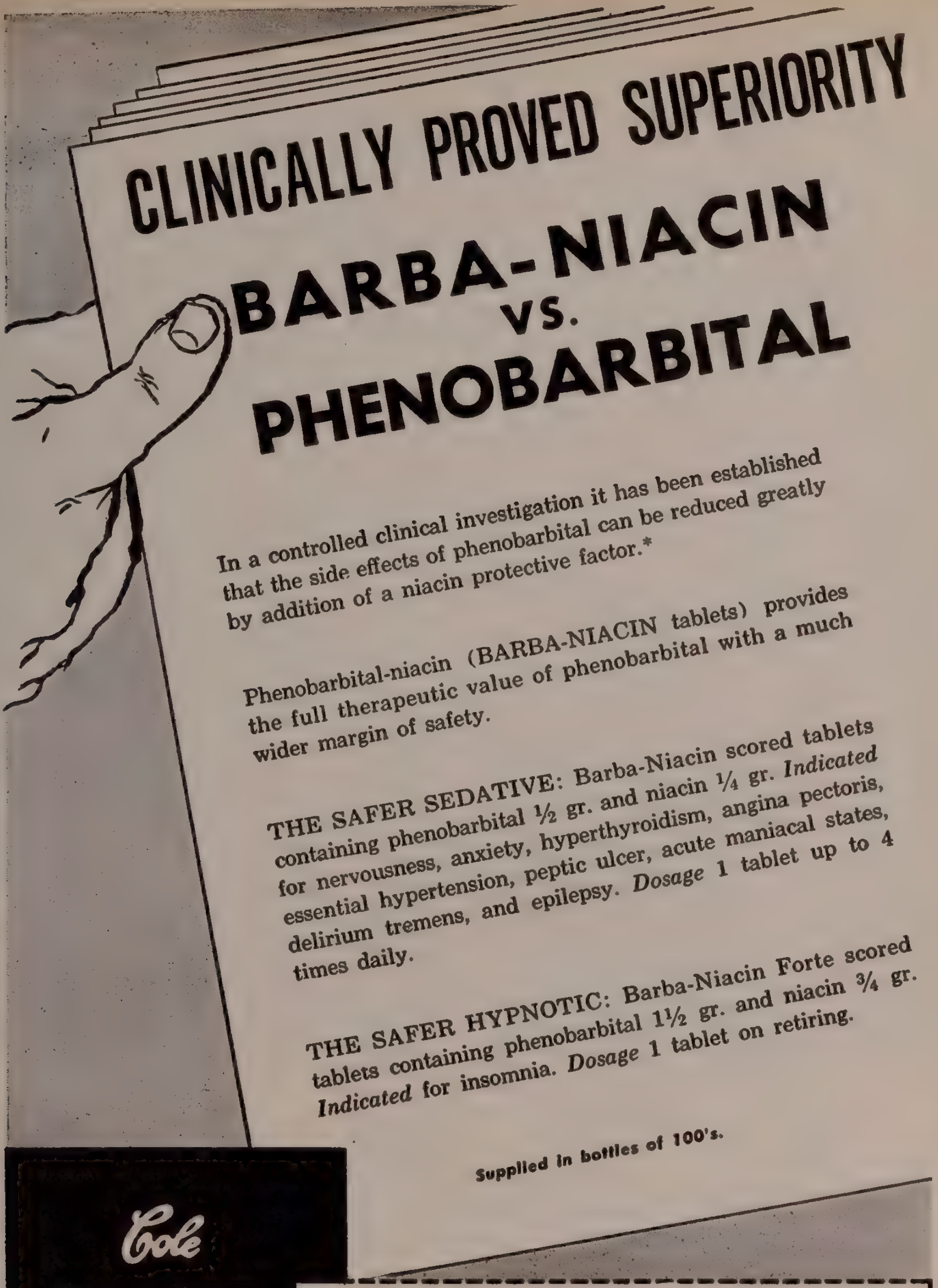

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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1. Berger, R.A., Clinical Medicine, Sept. 1961.

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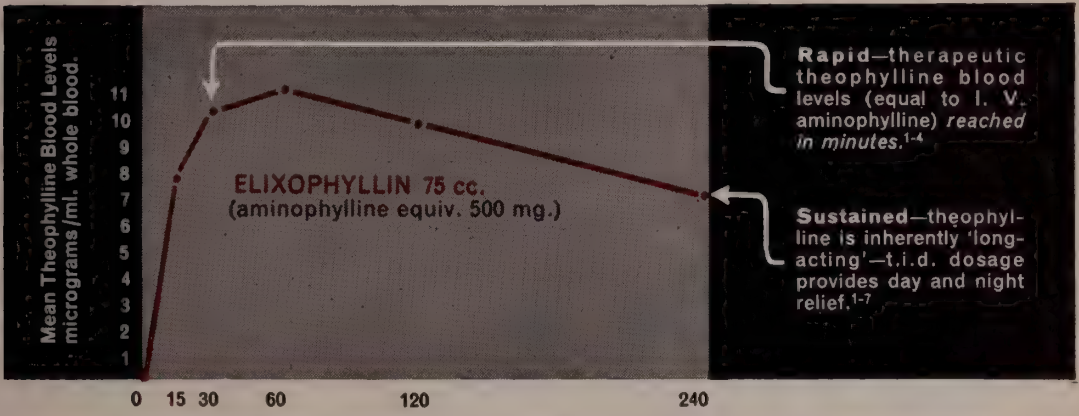

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diminished itch
decreased
inflammation"
in dry, pruritic
skin disorders
SENILE DERMATOSES
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To answer many inquiries; the 1961 Medical Directory is still available.

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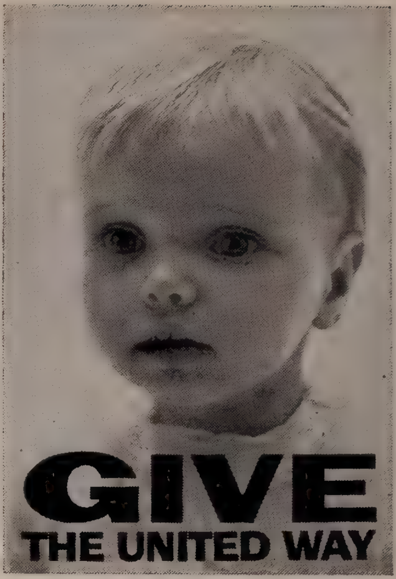

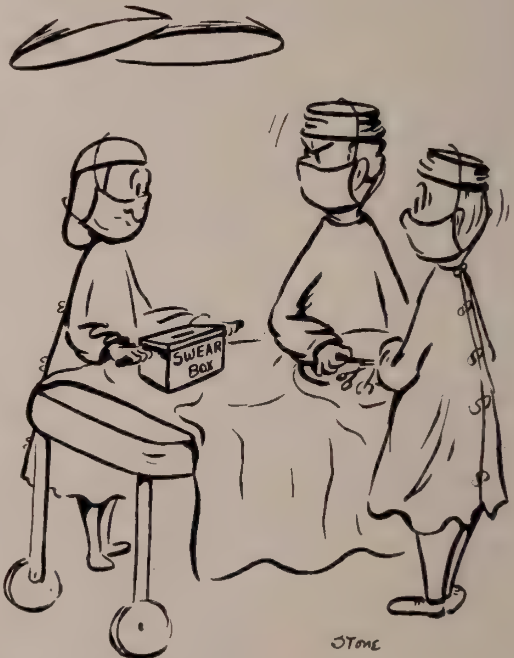

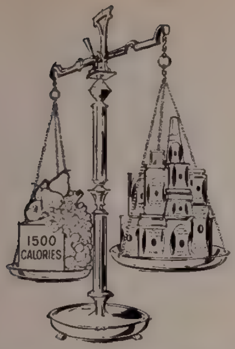

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60 DELICIOUS FOODS THAT CUT CALORIES, FAT AND CARBOHYDRATES!

How often do you sit across the desk from a patient whose problem is overweight, and wonder whether the directions you give for diet will be followed accurately—or at all?

A pleasant and efficient solution to this problem is to recommend the new Mott's Figure Control Foods. This line of over 60 different items has been developed through the latest scientific knowledge in the field of nutrition—and provides foods lower in calories by an average of 50%. Figure Control Foods take the guesswork out of menu-planning. Calorie cutting can be made pleasant and accurate, while eating normal-size portions of the kinds of food people enjoy every day.

Low carbohydrate, low fat: Meat products have most of the hard fats removed (these are the saturated type) in a way that cannot be done at home. Sauces and dressings are prepared with a high proportion of non-fat milk solids, vegetable colloids; all are delicious and appetizing. Fruits, juices, desserts and sauces are prepared with non-caloric sweetener—natural fruit values are intact. The carbohydrate, protein and fat content appears on each label, along with calorie counts. Useful for diabetics, too.

Easy medical tool for doctors: No possible dangerous side effects, not even temporary dislocation of meal patterns. Figure Control Foods in supermarkets include: Soups, Meats, Poultry, Sauces, Salad Dressings, Preserves, Syrup, Fruits, Drinks, Desserts, Sweeteners.

New Mott's Figure Control® Foods offer Good Eating at Half the Usual Calories

	Quantity	Figure Control Calories	"Regular" Food Calories
Apple-Grape Drink	½ cup	20	52
Five-Fruit Juice Breakfast Drink	½ cup	20	52
Braised Beef and Vegetables	6½ oz.	184	380
Meat Balls in Brown Gravy	3½ oz.	84	280
Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
Cherry Pie Filling	1 oz.	20	60
Chocolate Topping	1 tbsp.	8	63
Preserves (Peach, Strawberry)	1 tbsp.	9	55
"Maplette" Syrup	1 tbsp.	9	55
Liquid or Powder Sweetener	(to equal 1 tbsp. sugar)	0	16

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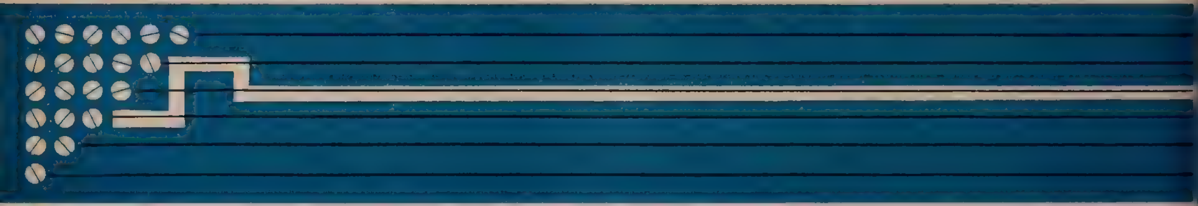

Orinase dosage 1 Gm.= ⊘⊘

Mrs. C. S., a youthful 50-year-old, is a busy clubwoman and civic leader. Her mother was a diabetic, and so is her daughter. In November 1956, she was transferred to Orinase after 16 years on insulin. Following a period of adjustment, her Orinase dosage was stabilized at 2 Gm. daily.

Mrs. S. has no need for increased Orinase in the course of her extensive social activities. For instance, she can and often does arrange for impromptu entertainment at her home without requiring additional dosage.

The patient is frequently oblig
to travel in connection with he
social, philanthropic, and civic
responsibilities. She needs
no increase in Orinase on thes
occasions, and finds her trips
enjoyable now that she is free
of the fears and difficulties tha
accompanied insulin injection

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5 years of control

Mrs. S. did, however, need more Orinase when pyorrhea and other dental problems necessitated oral surgery, beginning late in 1959. During the five-month course of dental treatment, the patient's Orinase requirement was 3 Gm. daily. Thereafter, she was well maintained on 2 Gm.

When her daughter went to live abroad in 1961, the stress of the parting had an adverse effect, and Orinase had to be increased to 3 Gm. for 2 months. Mrs. S. then resumed her routine dosage.

Apart from temporary, stress-induced changes, Mrs. S. gets along very satisfactorily on 2 Gm. daily. With Orinase control, she has been leading an active and gregarious life for 5½ years.

Among oral agents for the treatment of diabetes, Orinase* (tolbutamide) stands in a unique position. It alone has had five years or more of day-to-day routine clinical use in the hands of thousands of physicians throughout the country. Accordingly, there are by now a considerable number of truly long-term Orinase-treated patients. This series of Orinase five-year case histories has been prepared to illustrate and exemplify some aspects of actual experience in management. Patient data made available to us by physicians have been factually incorporated; however, patients' identities have been concealed. Any inquiries regarding this Orinase case history series should be addressed to: Medical Department, The Upjohn Company, Kalamazoo, Michigan.

Orinase is supplied in bottles of 50 and 200 tablets.
Each tablet contains: Tolbutamide ... 0.5 Gm.

Reminder advertisement. Please see package insert for detailed product information.

Upjohn

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the right combination

. . . *safe, effective antihypertensive therapy*

Rauprote

(Rauwolfia serpentina and Protoveratrines A and B combined)

Rauprote combines two effective antihypertensive agents—*Rauwolfia serpentina* for moderate tranquillizing and gentle hypotensive effect, and Protoveratrines A and B for faster, more potent lowering of blood pressure and bradycrotic action. The combination produces a therapeutic hypotensive effect which is superior to larger doses of either drug alone; reduced dosage of both components minimizes or eliminates toxic side effects completely.[1,2]

Clinical studies show the majority of patients suffering from significant elevation of blood pressure achieve an excellent response to this combination.[2]

Rauprote is indicated in management of moderate to severe essential hypertension.

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1. Goodman, L.S. and Gilman, A.: The Pharmacological Basis of Therapeutics, 2nd Ed., Macmillan & Co., New York (1955).

2. Roberts, E.: Four Year Evaluation of an Antihypertensive Agent, J. Am. Med. Women's Assn. *13*:349 (1958).

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The modern, non-staining therapy for vaginal trichomoniasis, non-specific vaginal discharges, vaginal pruritis and malodorous lesions.

Low surface tension assures uniform coating of the vaginal mucosa... permits deep penetration of all areas. Kills most offending pathogens and re-establishes normal vaginal flora. Prescribe economy size Nylmerate Jelly, 5 oz. tube with applicator. (Also available in refill tubes.) Use twice daily, morning and night.

Active Ingredients: Polyoxyethylenenonylphenol 0.10%, Boric Acid 1.0%, Phenylmercuric Acetate 0.02%, in a gum base with pH adjusted to 4.

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More effective than vinegar, Nylmerate Antiseptic Solution is ideal for therapeutic and prophylactic use as a vaginal douche.

Simple to use: One capful in two quarts of water. Prescribe in pint bottles.

Active Ingredients: Phenylmercuric Acetate 0.2% in a buffered solvent of Alcohol 50%, Acetone 10% and de-ionized water q. s., added certified color with pH adjusted to 4.9.

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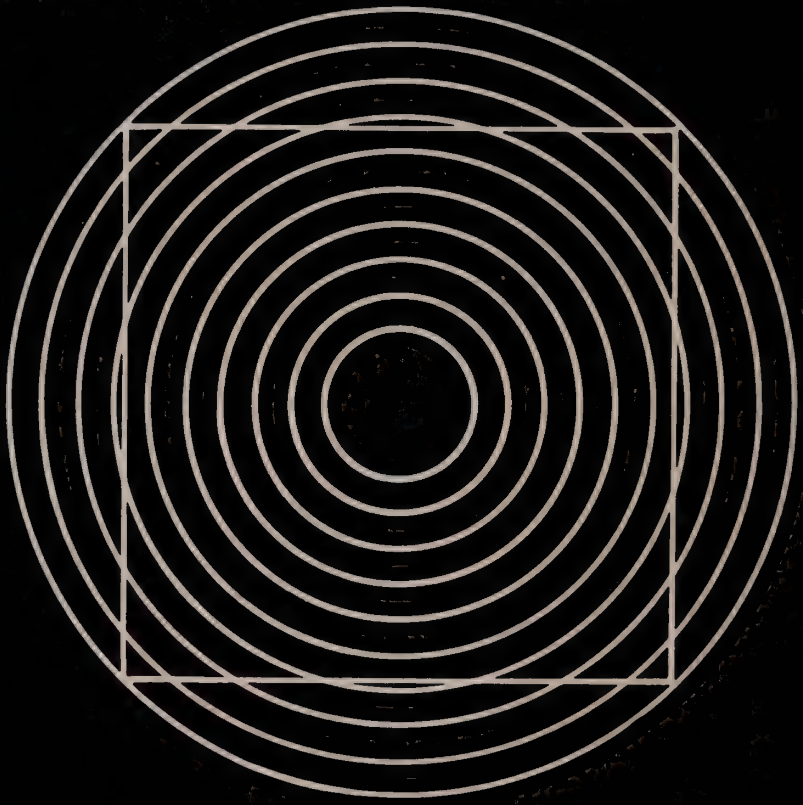

If the confusing array of concentric circles were removed, it would be easy to see that the sides of the square are perfectly straight.

Likewise, when claims of "price" and "blood level" advantages are viewed in proper perspective, it becomes clear that it's what a drug *does* that counts.

V-Cillin K® achieves two to five times the serum levels of antibacterial activity (ABA) produced by oral penicillin G.[1] Moreover, it is highly stable in gastric acid and, therefore, more completely absorbed *even in the presence of food.* Your patient gets more dependable therapy for his money . . . and it's therapy he really needs.

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prescribe V-Cillin K in scored tablets of 125 and 250 mg. or V-Cillin K, Pediatric, in 40 and 80-cc.-size packages. Each 5-cc. teaspoonful contains 125 mg. crystalline potassium penicillin V.

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1. Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.

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New York State Journal of Medicine

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Editorials

The tragedy of thalidomide

Alpha (N-phthalimide) glutarimide looked like the perfect sedative-hypnotic. Its toxicity in the usual testing procedures was so low that not even LD50 could be established. In heavy dosage it did not depress respiration or affect cardiac function. Thus it seemed an ideal drug in that it could not be used for suicidal purposes—in fact the record shows one intended suicide ingested 144 times the normal dose without effect.

Synthesized in 1953, after the usual animal and clinical testing, it went on the market in West Germany in 1957. The first inkling of toxicity in practice came from England in February, 1961, where peripheral neuritis was reported as a possible toxic effect of long-term use of thalidomide. Not until November, 1961, did it become apparent to the original manufacturer in West Germany that the drug had a teratogenetic effect when taken during the first trimester of pregnancy. Children born of mothers who had taken the drug early in pregnancy were being born with the congenital deformities of phocomelia, ectromelia, and amelia. The manufacturer immediately alerted his licensees on the continent and abroad.

Fortunately for us, the F.D.A. had not yet released this drug to the American market. Deliberation and caution on the part of this government bureau worked this time in our favor. Although the drug had been dispersed for clinical trial in this country only 10 known cases of congenital defect have been reported to date.

Much research now needs to be done to extend animal testing of drugs to include teratogenic effects. Unfortunately we may learn that these results may occur in man but not in lower animals. There is, however, a lead in regard to thalidomide. It has been reported that pregnant rabbits tested with the drug failed to produce viable offspring.

We are prying so close now to the hidden secrets of life that our scientists must literally look before they leap. Added safety factors are already under study by scientists in both industry and government. The Coggeshall Commission created by the Pharmaceutical Manufacturers Association is charged with broadening scientific knowledge regarding the predictability of action in humans of the potent drugs likely to emerge in the future. The objective of the Commission is to reduce danger to the lowest possible degree without discouraging imaginative research from which stems increasing release from disease.

Our sympathy goes out to all concerned with this dreadful tragedy. We condemn no one. We have learned a bitter lesson but take renewed strength for the continuing task of developing safe and useful drugs.

Influenza immunization

Once again attention is called to the importance of immunization against influenza with the generally available polyvalent killed-virus preparation, effective against types A, A_1, A_2, and B.

This may seem like crying wolf for we had no epidemic in this country in 1960 or 1961, but since we cannot predict with certainty when an epidemic may strike it would seem sensible to persist in routine immunization each year. Any physician who served through a serious outbreak of the disease would strongly endorse this program.

The Surgeon General's Advisory Committee recommends that this year all persons over age forty-five and particularly those over age sixty-five; persons of any age who have chronic cardiovascular, pulmonary, renal or metabolic disease; and pregnant women be immunized since experience has shown that such patients have experienced the highest mortality rates in former epidemics. Those not immunized previously should receive a subcutaneous 1 cc.-dose (500 units) of the vaccine this fall and a second 1 cc.-dose two months later. Persons immunized previously should receive a single dose of 1 cc. The vaccinations should be completed by mid-December.

Reports indicate that one dose of the vaccine is 60 to 75 per cent effective.

Current preparations do not contain penicillin. The principal contraindication is a known allergy to egg or chicken, since the virus is grown on an egg media.

Comment on McDermott versus Manhattan Eye, Ear and Throat Hospital*

In a recent malpractice case, the plaintiff subpoenaed one of the defendant physicians to testify and then sought to ask him questions calling for expert or opinion testimony. The trial court ruled, on the objection of the defendant's counsel, that the questions were improper. Thereafter, the plaintiff did not produce any independent expert, and at the close of the plaintiff's case the complaint was dismissed. On appeal it was argued that the plaintiff should have been permitted to elicit opinion evidence from the defendant since he was a hostile witness.

In a well-reasoned decision, the Appellate Division of the Supreme Court of the State of New York, First Judicial Department, held that the defendant, having been subpoenaed, could not be compelled to give expert testimony. The defendant could properly testify to the facts concerning his examination, diagnosis, and treatment of the plaintiff, but he could not be required to give an opinion as to the proper standard of medical care.

After reviewing the law in other states, the Court said:

> The New York rule is that a witness may not be compelled to give expert testimony. . . . An additional reason against the compulsory expert testimony of an adverse party such as the defendant is that by the commencement of this action the plaintiff's position is to the effect that said defendant did not conduct himself in accordance with accepted medical practice. In requiring the expertise of defendant relating to usual and customary medical procedures concerning the standard by which the jury is to judge the conduct of the defendants, the plaintiff invites the jury to be guided by a standard furnished by a source condemned by her.

The Court's ruling that witnesses may not be compelled to give expert testimony is a sound one. Moreover, it is certainly fair to require a plaintiff who has charged a doctor with malpractice to supply independent expert testimony rather than to rely on the expertise of the defendant physician.

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* 228 N.Y.S. 2d 143

President's Page

JOSEPH A. LANE, M.D.

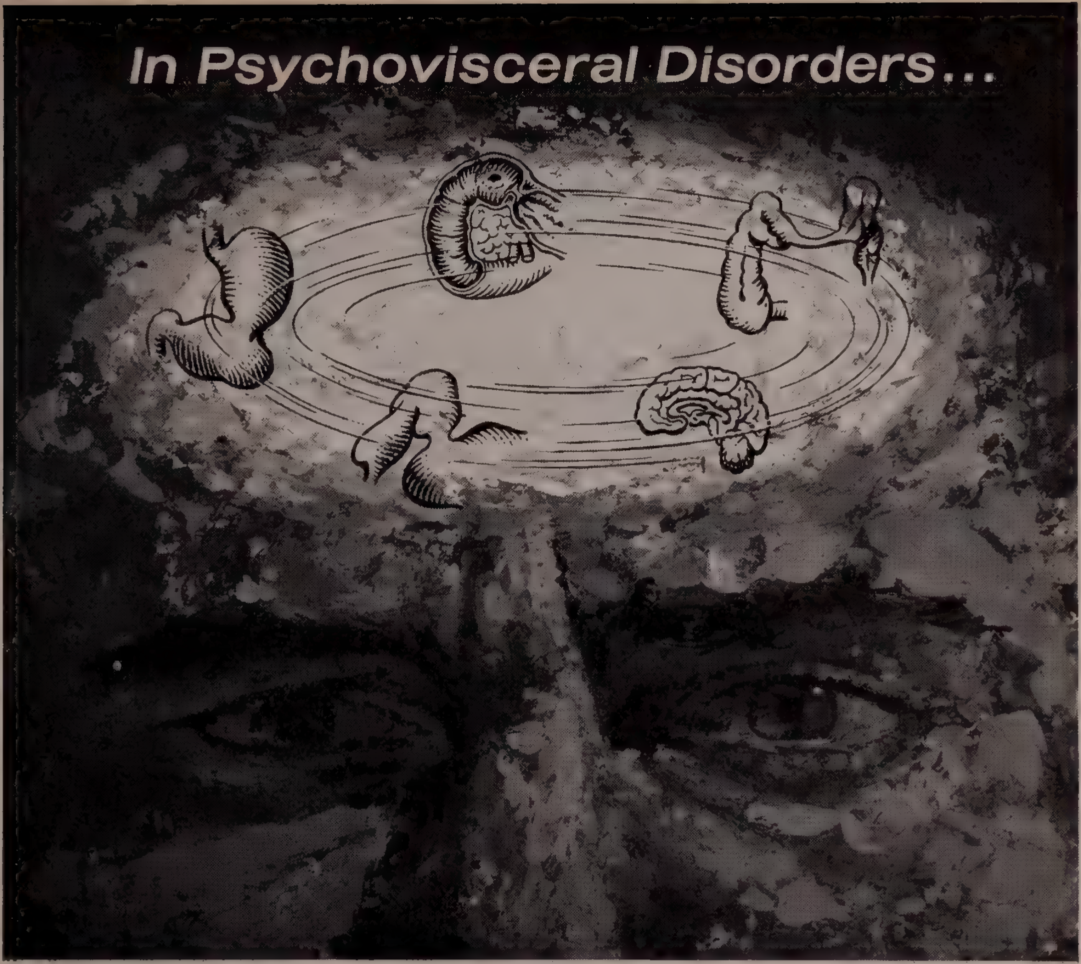
Within a few weeks of the publishing of this issue of the JOURNAL we will have another election day, specifically, Tuesday, November 6, and I wish to urge you all as citizens to get out and vote. I have reason to believe that many election days pass with a rather large number of physicians failing to exercise their constitutional right. Your failure to vote could be the cause of a valuable legislator being defeated or a new candidate not being elected. Either one of these individuals could be a friend of medicine, and his absence in whatever branch of the legislature to which he aspires could be a serious detriment at a time when his help would be needed to protect the private enterprise type of medical practice. This is not a plea for any particular individual but a strong appeal to each of you to vote on November 6. Mark your calendar accordingly, vote early, do your day's work, and then play golf or whatever else your heart desires.

* * *

Representatives of your State Society recently had a meeting with one of the top executives of a popular magazine that had published an article that was very critical of medicine. The article was an excerpt from a book written by a doctor quoting many instances that made medicine appear in a very bad light. The picture on the magazine cover was very dramatic, and I am sure many of you recall it. Our discussion resulted in a recommendation that articles of a favorable nature would be composed and submitted to the magazine for publication, and this is under consideration.

However, the article did bring to light the fact that any one of our profession should be extremely careful in his comments in publications that have an extensive distribution to the public. This should be borne in mind especially by the physician who speaks of his profession in public or allows himself to be quoted in the lay press. Overstating and overgeneralizing the problems of medicine in public and unwittingly allowing these comments to reach nationwide readership by the newspapers and other media can do great disservice and sometimes irreparable harm to the physician image. I cannot urge you too strongly to keep these comments in mind. If you have an idea that things should be corrected, we have the means within our own organization (the Commission on Public Affairs) to handle such matters, and this should be the proper procedure.

JOSEPH A. LANE, M.D., *President*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Scientific Articles

Merit H. Cash Prize Essay

The Use and Value of Extension in Volkmann's Ischemic Contracture

JOSEPH K. SURLS, M.D.
New York City

WHEN IT IS *a question of whether or not to operate in a case of suspected Volkmann's contracture, immediate manual extension of the digits and wrist may be done, with maintenance of this extension by a plaster splint and daily removal of the splint for active and passive motion. When a definite diagnosis has been made, an operation should be done immediately. Interference with circulation is the cause of Volkmann's contracture; the nature of interference may vary, but most often the injury is incidental to maintaining the reduction of a supracondylar fracture of the humerus. A case is reported in which there was an interval of two months between onset of symptoms and periarterial sympathectomy. The patient had muscular weakness in the affected forearm for years following Volkmann's contracture but eventually regained full power; this is explained by the assumption that new muscle fibers developed.*

IN A CASE of suspected Volkmann's contracture, when it is a question of whether or not to operate, immediate manual extension of the digits and wrist may be done, with maintenance of this extension by a plaster splint and daily removal of the splint for active and passive motion. Such was the treatment in the case herein reported. A search of the literature does not reveal previous employment of the preceding treatment in the manner stated. This procedure contrasts sharply with the current concept of immediate operation in the case of suspected Volkmann's contracture. The writer appreciates that the current concept is far superior to waiting and doing nothing.

In the case herein reported, there was an interval of two months between the onset of the symptoms and periarterial sympathectomy. This is the longest interval on record in a patient who was cured completely. I suggest that the cure can be explained only on the basis of the previously mentioned nonoperative treatment during this interval.

When I employed manual extension in this case, which was a clear-cut case of Volkmann's contracture, my only purpose was to restore the anatomic position so that the hand would be useful if active motion should be regained. Horn and Sevitt[1] explain just how new muscle fibers are formed, making it possible to regain active motion even though the original muscle tissue has been destroyed. Griffiths[2] in his editorial on Volkmann's ischemic contracture sums up their contribution as follows:

> Horn and Sevitt have given us a series of observations of real importance, and the fact that such striking muscle recovery can occur still further emphasizes the need to prevent contractures. The new fibers that develop must not be allowed to adapt themselves to the shrunken and useless length of a damaged muscle.

The case herein reported of a patient with years of muscular weakness in the affected forearm following Volkmann's contracture, but with eventual full power, can be explained best on the assumption that new muscle fibers developed. Fortunately she was only two years old when the Volkmann's contracture was produced and so had the tremendous ability of the very young to develop new tissues.

Additional benefits from full extension have been found: The gradual onset of sclerosis in the blood vessels after forty-eight hours, as pictured by Fontaine and Dany,[3] may be delayed or prevented. Similarly the strangulation of the median and ulnar nerves to the point of no return after several weeks, as described by Goldner,[4] may also be delayed or prevented.

In some cases whether or not to operate is a big question. The four cardinal features may not all be present: pulselessness, pain, pallor, and paralysis. The features present may vary in degree and even vary at different times. Pulselessness, for example, may change to a clearly felt pulse, only to fade out again.[5] It is a benefit to the patient and the surgeon if the decision does not have to be made under such circumstances. No harm has been reported from an immediate operation, even the most extensive, in suspected Volkmann's contracture, but surely it must be called meddlesome surgery if it can be avoided safely, as will be set forth.

The preceding remarks are based on the benefit to the patient, of the nonoperative approach, but this approach also helps the surgeon, saving him from the dilemma of whether or not to explore further. All of us, in every specialty, have been up against the decision of whether or not to operate, and that is the time when we wish we had studied law instead of medicine. With the previously cited approach the surgeon can safely delay operation until he is sure what he wants to do.

The earliest record of Volkmann's contracture that I have come across is a drawing, with no caption, of a patient pursuing his doctor in the street, holding aloft his withered hand. The doctor is running his hardest and is clearly unhappy. From the literature it is evident that this picture has been repeated often, in one form or another. "The medical literature in all languages has recorded innumerable cases of Volkmann's Ischemic Paralysis."[6] I suggest that it is high time to eliminate Volkmann's contracture except those cases in which the original injury has damaged the vascular tree so extensively that medical science cannot correct the damage.

One must look out for the antecubital fossa. I believe that this warning should be uttered when the fossa is first demonstrated to the student. If he is also warned by the traumatic surgeon never to be satisfied with a cyanosed or blanched hand unless he can explain it, nor with increasing pain in the member, the student will be well armed against Volkmann's contracture.

Case report

The patient, a two-year-old girl, was first seen at the Presbyterian Hospital outpatient department, in New York City, on July 17, 1927, complaining of pain in her right elbow, which was markedly swollen and ecchymosed. She had fallen a distance of 10 feet. An x-ray film showed a T-shaped fracture of the distal end of the humerus.

The fracture could be reduced easily under the fluoroscope but could not be retained with customary splints. Internal fixation was considered unjustified under the circumstances. For these reasons a pad was placed in the antecubital fossa, and the elbow was flexed acutely.

It was realized that such action might cause a Volkmann's contracture, and there was disagreement about taking the risk. Because the reduction was excellent, it was decided to retain the dubious pad and elbow flexion but to have the patient watched for increasing pain or a change in the color of the hand.

Within twelve hours the child was brought to the emergency ward for increasing pain in the elbow, forearm, and hand. An ulcer had developed in the antecubital fossa; flexure was present in the digits and wrist; active flexion and extension of the little finger was possible, but not of the other digits; the hand was cyanotic and cool; and the radial pulse was small. Volkmann's contracture was diagnosed.

The pad was removed from the antecubital fossa, and the acutely flexed position was given

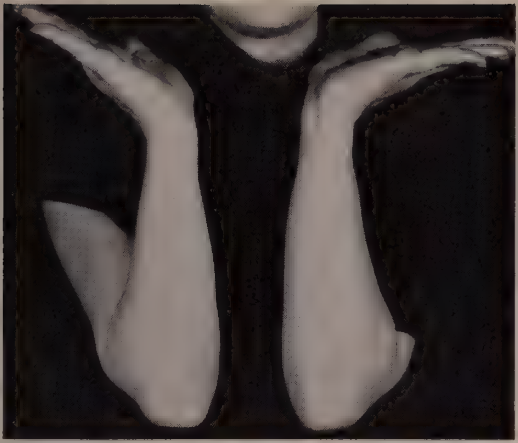

FIGURE 1. Hyperextension of digits slightly limited, as is extension of wrist.

up. Anteroposterior plaster splints were applied, which did not interfere with the antecubital fossa. The digits and wrist were slowly extended manually and maintained by a plaster splint; complete extension could not be obtained. The cyanosis of the hand became less marked.

The next day, the removal of the extension splint was followed promptly by flexure of the digits and wrist to the same degree as the day before. Manual extension was performed twice for the sake of exercise, and nearly complete extension was obtained. A new plaster splint was applied to maintain the increased extension.

For a month this routine was followed daily. The pain subsided rapidly and disappeared after several days, but the other features remained stationary: recurrent flexure as soon as the extension splint was removed, paralysis of the digits except for the little finger, coolness of the hand, and small radial pulse. The residual cyanosis gradually changed to pallor.

Beginning with the second month, manual extension was changed from daily to every other day. During this month there was an increase in the range of active motion of the little finger; active extension of the other digits began, but there was no active flexion. Complete passive extension of the digits and wrist was obtained by the end of the month.

At the end of the second month a neurosurgeon examined the patient. There was a complete loss of sensation in the area supplied by the median nerve. Ulnar sensation was intact in the little finger but was only partial on the ulnar side of the ring finger.

A periarterial sympathectomy of the brachial artery in the antecubital fossa was done. There was no improvement in the succeeding four months except an increase in the range of active motion of the little finger and in active extension of the other digits, but there was still no active flexion in them. During this period manual extension was being done every other day, as during the second month; the splint was left on constantly.

Six months after the onset of Volkmann's contracture and four after sympathectomy, the spasmodic flexure of the digits and wrist began to improve; the flexure did not recur so promptly when the splint was taken off. The pallor of the hand was improved also, but the coolness and weakness of the pulse remained the same as formerly. By the end of this period there was a good range of motion in the little finger; the extension of the other digits had increased; and active flexion had begun.

Seven months after onset the spasmodic flexure had improved so much that the splint was taken off during the day. Motion in all the digits had improved still more. Nine months after onset the hand could be used for ordinary purposes, but the grip was weak. There was also an improvement in pallor, coolness, and radial pulse. There was still a tendency to flexure, on which occasions the splint was applied at night.

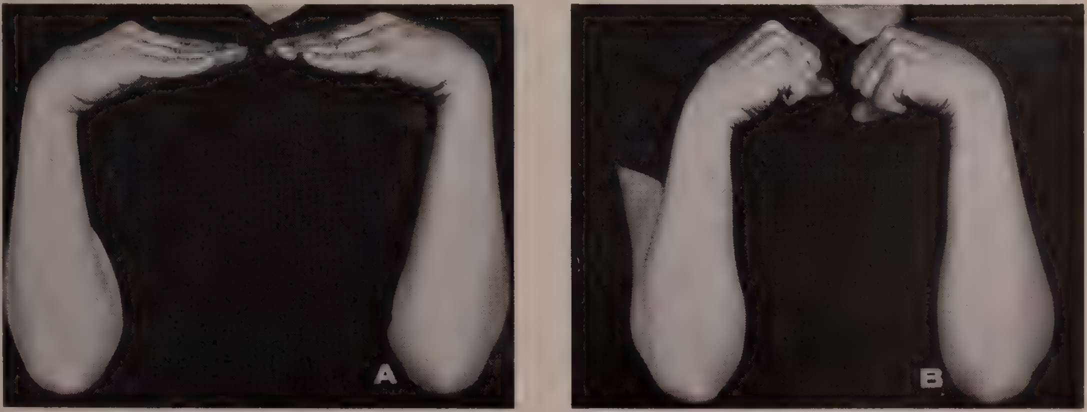

FIGURE 2. (A and B) Flexion of wrist slightly limited.

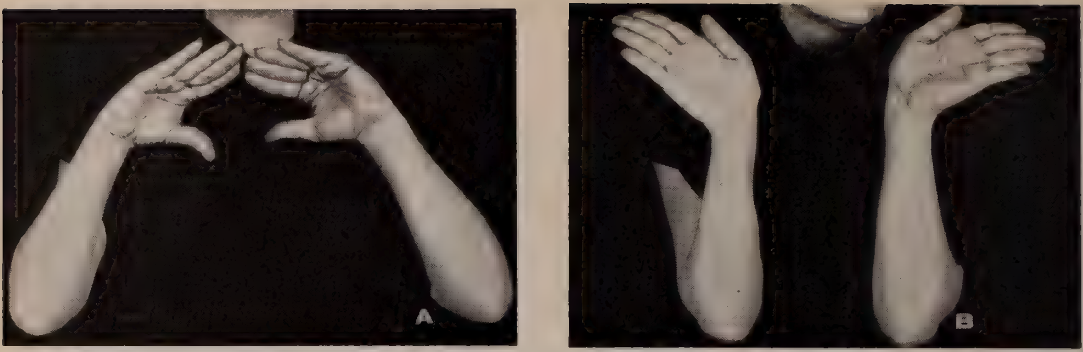

FIGURE 3. (A) Radial deviation normal. (B) Ulnar deviation normal.

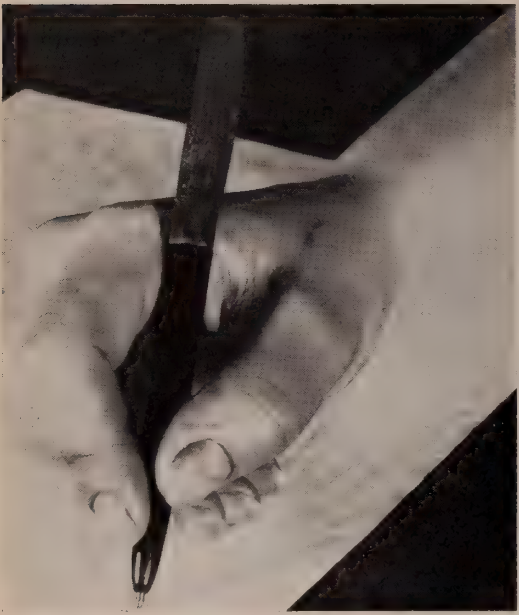

FIGURE 4. Grip: right, 58; left, 60. No anesthesia or paresthesia of hand or forearm.

Three years after onset the grip of the right hand was good but not so strong as that of the left. The pallor and coolness had disappeared; the radial pulse was equal to that of the left. The patient was discharged.

Follow-up. Twenty-eight years later the patient invited the writer to her wedding, as being partly responsible for her enjoying a normal life. The photographs of the result (Figs. 1 to 5) were taken at that time, thirty-one years after the onset of Volkmann's contracture. Until she went to college she had found the right hand normal except for extremely active use, such as tennis, when she felt some weakness.

On physical examination at college entrance her grip was: right, 30, and left, 60. Exercises, such as squeezing a rubber ball, improved her grip over the years. After graduation she worked as a technician in a medical laboratory. Her grip is normal: right, 58, and left, 60. The oscillometric readings in the right hand were: wrist, 1; below elbow, 1.25; and above elbow, 1.50. In the left hand they were: wrist, 1; below elbow, 1.50; and above elbow, 1.50. The Allen test showed in the right hand normal findings in the radial and ulnar arteries and in the left hand slight filling delay in the radial artery and normal findings in the ulnar artery.

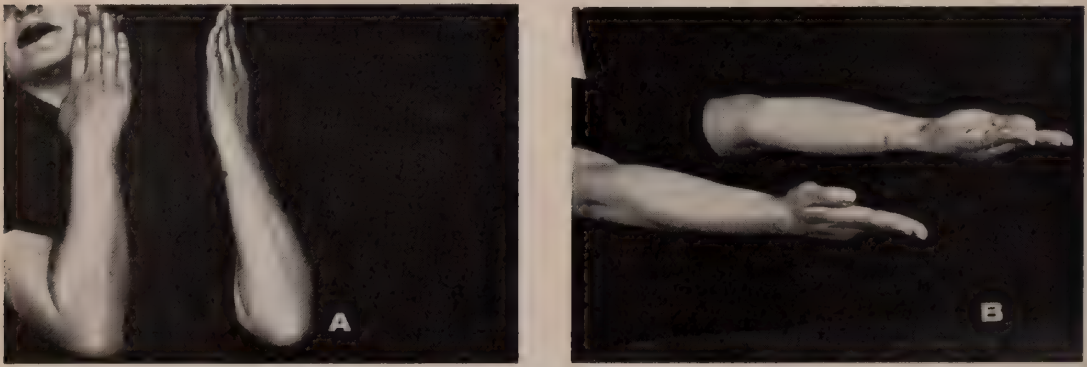

FIGURE 5. (A and B) Result in supracondylar fracture in spite of makeshift retention, employed when effective retention produced Volkmann's contracture. Elbow has full flexion and extension but no hyperextension.

TABLE I. Skin temperature of patient's hands*

Area	Right C.	Right F.	Left C.	Left F.
Digit				
1	34.4	96.0	35.2	96.0
2	37.4	99.5	36.0	97.0
3	36.8	98.2	35.5	96.3
4	36.2	97.1	35.6	96.3
5	35.0	95.0	36.2	97.5
Dorsum hand	36.8	98.2	36.8	97.8

* Room temperature: 25 C.; 77.5 F.

The skin temperature is recorded in Table I.*

Etiology and pathology

Interference with circulation is the cause of Volkmann's contracture; there is agreement by the majority on this point. There is not agreement on the nature of the interference, but in most cases it is attributed to arterial spasm. Occasionally, a thrombus has been found at operation, with rapid recovery following thrombectomy. In some cases the interference may consist of silting in the arterioles and capillaries; in some it is evidently due to venous congestion. Mechanical interference caused by the original injury has been found at operation.[5,7] But most often the injury is incidental to maintaining the reduction of a supracondylar fracture of the humerus, as illustrated by the case reported herein. In such a case trauma usually damages the brachial artery in the antecubital fossa, with consequent segmentary spasm of the artery and its collateral circulation.

Nontraumatic interference with circulation was produced by chlorpromazine hydrochloride in one case; the drug had been injected into the perivascular tissues in the course of an intravenous injection, in the opinion of Pernet[8] who reported the case.

Also, interference may be produced by trauma to the forearm distal to the fossa, as part of the original injury. In such a case extravasation extends into the fascial planes, with intrinsic compression of the muscles and choking of their circulation. In regard to this phenomenon Benjamin[9] says:

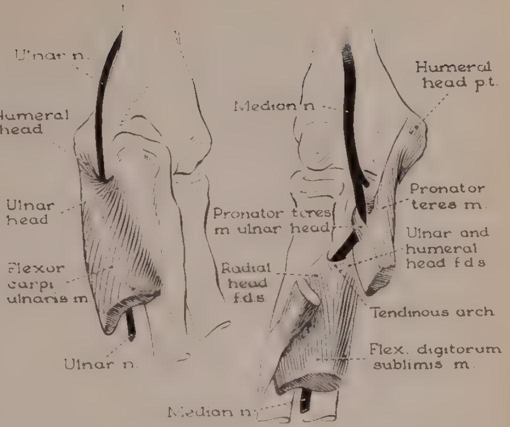

FIGURE 6. Anatomic "slings" in which median and ulnar nerves lie are potentially dangerous if muscles involved go into spasmodic contracture. (Reproduced through the kindness of Paul R. Lipscomb, M.D., Mayo Clinic, Rochester, Minnesota.)

> It is suggested that tension in a fascial compartment may provide the stimulus that maintains arterial spasm, and that the consequent ischaemia aggravates the oedema, so that a vicious circle is established.

Injury to the median and ulnar nerves in Volkmann's contracture has been reviewed by Goldner[4] who recognizes two kinds of injury: (1) direct injury to the nerve and (2) indirect injury to the nerve from ischemia, owing to the nerve's anatomic position (Fig. 6). The median nerve lies in a sling as it passes between the two heads of the pronator teres and under the tendinous arch formed by the two heads of the flexor digitorum sublimis; the ulnar nerve lies in a similar sling as it passes between the two heads of the flexor carpi ulnaris.

Goldner's[4] thesis is that the contracture of these muscles tightens the slings and so strangulates the nerves. He adds that, although the nerves might survive ischemia from arterial damage and resultant spasm, in many instances they cannot survive this additional insult. Goldner demonstrates that the nerves often will regenerate if the strangulation is reduced even several weeks after the onset of Volkmann's contracture. Brower[6] believes that these observations are so important that they should be applied clinically.

I suggest that perhaps the time limit for regeneration may depend on the degree of injury to the pathway down which new axones may grow to replace those destroyed. Eventually the nerve trunk distal to the injury loses its structure, becomes merely a cord of scar tissue, and so is impassable to new axones.

---

* The laboratory data were recorded by Ellen McDavitt, M.D., Vascular Research Laboratory, Cornell University Medical College, New York City.

The observations of Horn and Sevitt[1] on the development of new muscle fibers in the damaged muscle and the gradual onset of sclerosis in the blood vessels after forty-eight hours, as described by Fontaine and Dany,[3] have already been mentioned.

Diagnosis

It is the patient's hand that holds the key to the diagnosis of Volkmann's contracture. The diagnostic alliterations of pulselessness, pain, pallor, and paralysis, all of which are found in the hand and wrist, have been mentioned previously. Their uncertainty also has been referred to—uncertainty in incidence and, if present, their variation in degree among patients and, in the same patient, their variation at different times. If the nerve damage is severe, the pain, which is our best diagnostic guide, may be minimal. Variations in the pulse are quite suggestive. The hand is usually pallid, although this pallor may be preceded by cyanosis from pressure at the elbow or forearm level. Flexure of the digits and wrist, if present, is marked, with partial or complete paralysis.

It is the total clinical picture on which the diagnosis rests in Volkmann's contracture, as is the case with most diagnoses.

Treatment

Because this paper is concerned essentially with the treatment of the suspected Volkmann's contracture that does not clearly demand surgery, this feature of treatment will be taken up first.

In such a case immediate manual extension of the digits and wrist should be done, using only so much force as the patient will bear without much complaint. To get the maximum extension is a long, slow job. This extension is maintained by a plaster splint which is removed frequently enough to guard against undue pressure on the skin, especially of the terminal phalanges. Active motion, supplemented by passive motion, should be carried out often enough and long enough at each session to get the maximum results thereby. If the patient is ambulatory, the forearm and hand are kept horizontal in a sling.

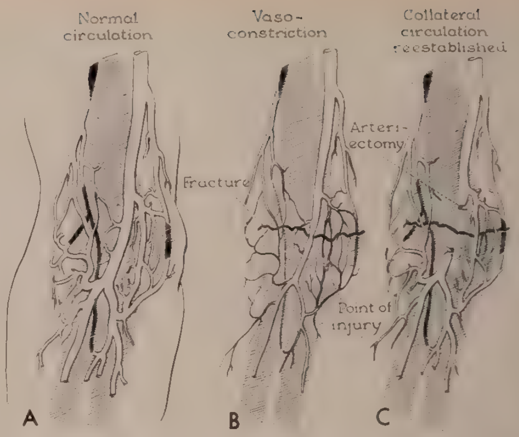

FIGURE 7. (A) Rich collateral circulation. (B) Spasmodic vasoconstriction consequent on injured brachial artery. (C) Collateral circulation re-established following arteriectomy of injured portion. (Reproduced through the kindness of Paul R. Lipscomb, M.D., Mayo Clinic, Rochester, Minnesota.)

When a definite diagnosis has been made an operation should be done immediately, and it should be done even without a definite diagnosis if there are unusual indications. As stated previously, no damage has been reported from an exploratory operation. Usually the antecubital fossa is explored first, with an inspection of the artery that has received the most trauma, which is most often the brachial. The median and ulnar nerves are also inspected as occasion demands. If clinical evidence localizes the trouble distal to the antecubital fossa, of course the localized area is the elective site.

If arterial injury is found, with spasmodic or fibrotic constriction, and if no thrombus is seen, the traumatized portion of the artery should be resected. The collateral circulation, which is rich (Fig. 7A), will be relieved of any resultant spasmodic vasoconstriction (Fig. 7B and C). If a thrombus is seen, its removal alone may re-establish the collateral circulation.

If there is no obvious arterial injury, an exploration should be carried far enough to make sure that there is no injury to the radial or ulnar artery, even if the incision has to be carried well down the forearm. Brower[6] recommends that, in the face of an impending Volkmann's contracture, the median nerve be freed from its course between the heads of the pronator teres, to protect it from further constriction and ischemia. Goldner's[4] views on this point have already been given.

If no injury to the arteries or nerves is found, and if general swelling exists in the antecubital fossa or distal to it, the incision should be carried into the fascial planes of the forearm extensively enough to release any intrinsic compression of the muscles. The wound should be closed loosely to avoid undue tension; a delayed closure can be revised several days later when the swelling has gone down.

If a pathologic condition sufficient to explain the clinical picture has not been found, the stellate ganglion should be blocked by Novocain after the operation. If the circulation still appears precarious, Lipscomb[7] recommends: (1) slow, intravenous infusion of 5 per cent alcohol; (2) heating of the other three extremities and the remainder of the body, but not of the injured extremity; and (3) avoidance of elevation of the injured extremity.

If there is flexure of the digits, the manual extension routine should be followed, as described previously, starting extension before the patient is out of anesthesia.

218 EAST 79TH STREET

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Scientific Program

Any State Society member who wishes to present a paper before a scientific section or a general session is requested to write to BERNARD J. PISANI, M.D., Chairman, Convention Committee, 170 West 12th Street, New York 11, New York, before November 1, 1962. A short abstract of the proposed presentation should accompany the letter.

Management of Acute Respiratory Failure in Patients with Chronic Respiratory Disease

Practical Considerations

J. HOWLAND AUCHINCLOSS, JR., M.D.
Syracuse, New York
ROBERT GILBERT, M.D.
Syracuse, New York
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From the Department of Medicine, State University of New York Upstate Medical Center

THE PROLONGATION of life through the use of mechanical aids to ventilation is assuming increasing importance as a result of the prevalence of chronic respiratory disease in our aging population. However, there is no agreement on such fundamental points as the best type of apparatus and the indications for tracheostomy. This report deals with the management of respiratory failure in 15 cases of chronic pulmonary emphysema and 1 case of kyphoscoliosis, using an intermittent positive pressure apparatus without a negative phase (IPPBI).

The first patient was treated in September, 1959, and the last one in January, 1961. Prior to the treatment of the first patient, we had been reluctant to use the positive pressure apparatus in respiratory failure because of the technical problems involved. The greatest of these problems was the uncertainty that adequate ventilation was provided in patients with enlarged alveolar dead space who tended to breathe with high respiratory frequencies and low tidal volumes. Our past experience had been largely with the tank respirator. Although a number of patients had been saved with this machine, deaths continued to occur, and in some of these failures it was felt that adequate ventilation had not been achieved. The decision to investigate the potentialities of the positive pressure apparatus more thoroughly was largely dominated by the availability of automatic cycling and cuff tracheostomy. During the period of the study the tank respirator was used in 4 cases and we still employ it in individual instances. Aside from these 4 cases, the present series represents all of those instances of respiratory failure due to emphysema and kyphoscoliosis which occurred during the study period in which our assistance was requested. Our service provides about 40 consultations each year on hospitalized patients with respiratory problems and provides pulmonary functional testing where necessary.

Selection of patients

Table I provides vital statistics on the 16 patients. Case 1 presented the picture of pure kyphoscoliotic cardiorespiratory failure. Cases 5 and 11 had radiographic evidence of pulmonary fibrosis as well as emphysema. The clinical course of these 2 patients in the years prior to admission, as well as that of the remaining 13 patients, was characteristic of progressive chronic obstructive disease of the airways accompanied by anatomic pulmonary emphysema. A subsequent observation of the course of the survivors in no way changed this evaluation. Thirteen of the 16 patients were believed to have cor pulmonale on the basis of electrocardiographic or radiographic findings or because of a prior episode of right heart failure. Five

Supported in part by Grants H-2800 and PN-2014 from the United States Public Health Service, Bethesda, Maryland.

* National Institutes of Health Research Fellow in Cardiology.

patients were in cardiac failure during the admission in which the episode of respiratory failure occurred. Complicating respiratory infections were clearly present in 8 patients and were possibly present in 3. Acute hemorrhage from a duodenal ulcer was the precipitating event in Case 2, and self-administered sedation was probably responsible for respiratory failure in Case 3. The precipitating cause of acute respiratory failure was not always clear, and it was often felt that earlier and more vigorous treatment of the complications of emphysema might have obviated the need for the therapy here described.

The decision to set up a resuscitation program was made immediately on admission in only 6 cases. In the remainder of the cases efforts were made to improve the patients with more usual measures such as oxygen therapy, bronchodilators, digitalis, diuretics, and a varied use of the positive pressure apparatus. The investigators were usually not in charge of the patient's care from the beginning of the episode and entered the case when the patient appeared to be deteriorating or was making unsatisfactory progress. From the viewpoint of the present study, therefore, respiratory failure was a situation in which we believed that hypoventilation endangered life, and progressive deterioration in the face of hospital treatment was given great emphasis in case selection. The likelihood remains that some of the cases would have survived without mechanical aids to ventilation, but it was felt impossible to select such cases with precision.

All 16 patients had recently become irrational or lethargic except for Case 12 in whom the cause for concern was the appearance of intolerable dyspnea and severe cyanosis. The presence of carbon dioxide retention was documented in all instances by venous carbon dioxide content determinations of 30 mEq. or more and in 5 cases by arterial carbon dioxide tension values (Pa_{CO_2}) of from 66 to 75 mm. Hg.

During the study period 4 emphysematous patients who required hospitalization were found to have arterial carbon dioxide tension values of from 60 to 67 mm. Hg. They were treated electively with the positive pressure apparatus or without mechanical assistance and made uneventful recoveries of a degree sufficient to permit discharge. These patients are not included in the study because at no time were they believed by us to be in danger of death due to hypoventilation. By contrast, the 16 patients of the study were believed to be deteriorating rapidly. Thus, the selection of patients for mechanical assistance was primarily by clinical rather than laboratory methods of examination, and this remains our policy. Where doubt exists as to the need for mechanical aids, we adhere to a policy of watchful waiting or perform arterial blood gas determination for its value in aiding clinical judgment.

FIFTEEN CASES *of chronic pulmonary emphysema and 1 case of kyphoscoliosis were treated using an intermittent positive pressure apparatus without a negative phase (IPPBI). Respiratory failure was a situation in which hypoventilation was believed to endanger life, and progressive deterioration in the face of hospital treatment was given great emphasis in case selection. Six patients died; there was no consistent relationship between survival and the type or intensity of therapy, and the deaths therefore were most likely related to complicating factors in individual patients. The importance of the following factors is stressed: possibility of avoiding tracheostomy in some cases; establishment of a ventilatory control by means of properly designed automatic cycling devices; monitoring of tidal volume on a routine basis; and use of arterial blood carbon dioxide measurements to determine the correctness of settings once a stable state has been achieved.*

Therapeutic programs with intermittent apparatus

As can be seen from Table I, there was a considerable variation in the type of resuscitative program instituted and in the consistency of its maintenance. This can be explained by the following considerations: (1) The duration of the study was sufficiently long so that standards were improving; (2) the patients varied widely in their

TABLE I. Vital statistics on 16 patients during resuscitative program*

Case number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Age	50	53	67	70	59	54	72	58	69	47	65	74	65	76	42	63
Sex	M	M	M	M	M	M	M	M	M	F	M	F	M	M	M	M
Diagnosis	K	E	E	E	F + E	E	E	E	E	E	F + E	E	E	E	E	E
Similar previous episode	0	0	0	0	0	0	0	1	0	1	0	0	0	0	1	1
CV_{CO_2} (mEq. per liter) highest value obtained during hospital course	38	40	35	44	37	38	40	39	38	37	35	38	30	39	42	35
Pa_{CO_2} (mm. Hg) highest during entire admission while unassisted	. . .	. . .	66	. . .	. . .	. . .	. . .	. . .	70	. . .	. . .	. . .	75	. . .	74	67
Pa_{CO_2} (mm. Hg) lowest during entire admission while assisted	. . .	35	. . .	. . .	. . .	. . .	. . .	41	. . .	. . .	. . .	40	47	48	44	49
Pa_{CO_2} (mm. Hg) lowest value after treatment with respirator	45	47	44	. . .	. . .	46	. . .	. . .	. . .	. . .	. . .	44	52	. . .	. . .	. . .
Sa (per cent) before treatment	. . .	. . .	76	. . .	. . .	. . .	. . .	. . .	37	. . .	. . .	. . .	40	. . .	46	50
Tracheostomy with inflated cuff	+	+	0	0	0	0	0	+	0	+	0	0	+	+	+	+
Nature of program	A	SC	A	SC	A,TC	SC	SC	SC	A	SC	A,TC	SC	SC	SC	SC	SC
Respiratory frequency while on respirator	24 32	20 24	20	20	20	10	15	20	. . .	10	12	12	12 16	12	12	12 18
Highest and lowest values of tidal volume while on respirator (milliliter)	. . .	500 640	. . .	400	600 1,000	700	300 800	950 1,000	. . .	600 1,000	600 800	600 1,000	500 700	600 800	400 700	500 800
Greatest peak mask pressure utilized (centimeter of water)	. . .	20	20	35	20	20	. . .	. . .	. . .	40	. . .	. . .	20	30	40	26
Aided mechanically more than 50 per cent of time during acute phase	+	+	0	+	+	+	+	+	0	+	0	+	+	+	+	+
Total duration of mechanical aid (days)	4	28	2	17	<1	<1	7	2	9	38	<1	<1	10	18	10	3
Living (L) or dead (D) at end of hospitalization	L	L	L	L	D	L	L	D	L	L	D	L	L	D	D	D

* K = kyphoscoliosis; F = pulmonary fibrosis; E = chronic pulmonary emphysema; CV_{CO_2} = concentration of carbon dioxide in peripheral venous blood (normally less than 30 mEq. per liter); Pa_{CO_2} = partial pressure of carbon dioxide in arterial blood (normally less than 46 mm. Hg); Sa = arterial oxygen saturation (normally 93 per cent or greater); A = program purely of ventilatory assistance (no control of respiratory frequency); SC = program of sustained control of respiratory frequency and tidal volume; A,TC = program predominantly of assistance but in which control of respiratory frequency and tidal volume was temporarily established. Peak mask pressure refers to reading on "mask pressure" gauge of the intermittent positive pressure apparatus.

recovery potential; (3) the programs were carried out, with few exceptions, on the service where the problem presented itself, not only in different parts of a single institution, but also in three separate hospitals. Before discussing the causes of death, it is necessary to review the variables in therapy with the positive pressure apparatus which seem to us most important and which can be controlled to detect any effect of variations in therapy on survival.

Tracheostomy with inflated cuff versus mask or mouthpiece

A tracheostomy with an inflated cuff was performed only when the patient would not tolerate a mask or mouthpiece or when we were convinced that retained secretions were exerting a prominent effect. The reduction of anatomic dead space caused by a tracheostomy is only of importance in the rare instance in which adequate effective tidal volume cannot otherwise be achieved, and it was never a consideration in this study. The fact that 6 of 8 cases treated without tracheostomy survived has demonstrated to us the need for a patient and skilled effort to persuade the patient to accept the discomfort of a mask or mouthpiece rather than to accept any generalization that respiratory failure by itself requires a tracheostomy. Tracheostomy with the positive pressure apparatus requires the use of an inflated cuff. This cuff became detached or protruded over the end of the tube in 2 cases (2 and 15), with fatal consequences in 1 instance (Case 15).

Ventilatory assistance versus ventilatory control

In a ventilatory assistance program the positive pressure apparatus senses the initial inspiratory effort of the patient and furnishes mechanical assistance immediately. This is the only form of positive pressure apparatus use which is practicable with the earlier apparatus available to us (Bennett Model TV-2P) and can still be readily accomplished with the improved machine (Model PR1A) used in all but 2 patients of the present study. In a ventilatory assistance program, therefore, the respiratory frequency is determined entirely by the patient. Of 5 cases treated entirely or predominantly by this method (Table I), 3 survived. In 2 survivors (Cases 1 and 3) satisfactory arterial carbon dioxide tension values were obtained following therapy. Earlier experience, however, has led us to distrust this form of therapy as a standard for all patients, inasmuch as occasional patients appear to become more lethargic while positive pressure ventilation is being administered. The use of compressed air instead of 100 per cent oxygen makes therapy more complex and fails to relieve hypoxia where intrapulmonary gas exchange is severely impaired, as is usually the case. In the controlled ventilatory assistance study of Fraimow, Cathcart, and Goodman[1] there were 7 instances in which the arterial carbon dioxide tension value was greater than 54 mm. Hg. In 3 of these patients the fall of the arterial carbon dioxide tension value was less than 9 mm. Hg during the period of positive pressure breathing. Ventilatory assistance, therefore, cannot be regarded as a reliable method of achieving the correct ventilation for all patients.

An alternative program may be termed "ventilatory control" and implies the freedom of the physician to control both the tidal volume and the respiratory frequency within limits. The Bennett PR1A positive pressure apparatus contains a built-in automatic cycling mechanism which limits the duration both of inspiration and expiration. With such a mechanism, leaks can exist without rendering the machine unusable, an important feature when a mask is used. A more important advantage of this type of automatic cycling mechanism, however, is that it enables the physician to perform the maneuvers illustrated in Figure 1. When the automatic control was disengaged (A), a period of apnea ensued which was followed by the resumption of patient-activated respirations at a rapid rate (B). This can be regarded as a transition from control to assistance. The transition from assistance back to control was readily accomplished by the "capture" of the respiratory frequency (C) at a relatively fast rate, much as an ectopic focus in the atrium captures the heart beat. With the engagement of the automatic cycling device it is possible to

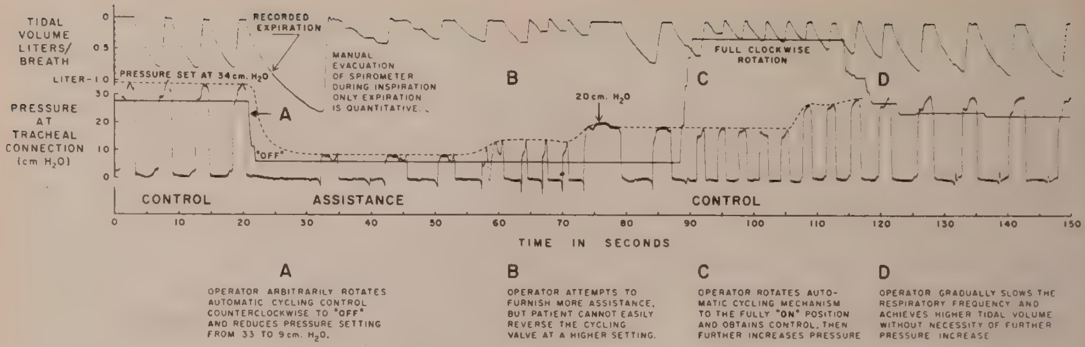

FIGURE 1. Continuous recording of tidal volume (top tracing), degree of rotation of automatic cycling control (solid middle tracing), and pressure at tracheal connection (lowest tracing) made on patient 15 to demonstrate feasibility of converting from ventilatory assistance to control and vice versa. At onset patient is under ventilatory control at rate of about 10 cycles per minute and peak mask setting of 34 mm. water. At point A operator arbitrarily rotates automatic control to full counterclockwise position and reduces mask pressure setting to about 10 cm. water. Necessity of reducing pressure during assistance is shown in B where increasing pressure to 20 cm. water results in delay in reversal of cycle. Capture of respiratory frequency is shown at points C and D by process of accelerating frequency with automatic control and elevating pressure, then later reducing frequency to allow as much time as possible for expiration. No sedation was used in this demonstration.

employ higher inflating pressures to increase the tidal volume. Finally, the reduction of the machine-controlled frequency (D) permits a longer period for expiration. This prolonged expiration in a patient with airway obstruction results in a higher tidal volume (Fig. 1). Tidal volumes of 500 cc. or greater can be achieved except where the impedance to ventilation is overwhelming. A capture of the respiratory rate with a subsequent controlled slowing has been performed by us many times; as a rule, it does not require sedation. We presume that the facility with which it can be performed with the apparatus used is largely the result of the lowering of the arterial carbon dioxide tension value during the period of "capture." Where the machine is used for the first time on a patient who is hypoxic, the rapid rise in the arterial carbon dioxide tension value may also be of importance in reducing the output of the respiratory center. An important advantage of a ventilatory control program is that the ventilation achieved tends to be steady. The constancy of the respiratory frequency and the tidal volume enhances the value of determination of body carbon dioxide tensions (arterial or mixed venous rebreathing) in that they can confidently be related to long periods of time. Finally, the constancy of ventilation can be monitored, and many complications can be identified quickly before they become apparent by more serious effects such as shock, convulsions, or cardiac arrest. Eleven patients were treated with sustained control programs, with 7 survivors. In 2 others the feasibility of ventilatory control was demonstrated but control was not maintained; both of these patients died.

Percentage of time on respirator during acute phase

A patient with emphysema or kyphoscoliosis who is believed to require mechanical assistance for survival deserves to receive respirator aid for more than 50 per cent of the time, yet he differs from the totally paralyzed patient in being able to remain without such assistance for brief periods without definite harm. Short periods of interruption for nursing care, eating, and certain laboratory procedures can and must be accepted in the majority of cases. The positive pressure apparatus is often used in hospitals on a treatment basis to facilitate deep breathing postoperatively or in aerosol administration. These two facts are essentially unrelated, yet together they can easily result in a misunderstanding between the supervising physician and other personnel. A program which to the physician is intensive and continuous can be turned into a totally inadequate effort, purely in the time sense. The result of this misunderstanding will be undertreatment. The criterion of 50 per cent of the time is arbitrary and retrospective. It serves, however, to identify 3 patients (Table I) who were treated inadequately. Happily, 2 of them survived. Currently we require nursing personnel to keep records of the amount of time during which the respirator is functioning and to make a total estimate at the end of each eight-hour period. The need for intensive therapy requires constant reiteration and supervision and is basically an educational problem.

Duration of therapy

It can be seen from Table I that the total duration of therapy varied widely in both survivors and fatal cases. Therapy in the surviving patients was reduced gradually below the intensive level as the patient improved, and no effort was made to achieve any given value of the arterial carbon dioxide tension during the unassisted state. In 2 instances intensive therapy was discontinued in less than twenty-four hours without apparent harm. In Case 5 this dramatic improvement was explained readily by prior self-medication with a sedative drug which had been depressing the respiratory control system. The need for prolonged therapy in other cases requires no explanation, since some patients were at or near the terminal phase of their disease.

Operation of positive pressure apparatus and control of therapy

The Bennett PR1A apparatus is modified by the attachment of a heated reservoir nebulizer. This was not available in its present form during the period of this study, but it is now considered an important adjunct in the management of secretions. A modified exhalation manifold is used to measure the expired air volume. The tidal volume is measured with a spirometer because this equipment is available, accurate, rugged, and too large to be mislaid easily. Ventilation meters have also been used where portability and small size are critical considerations. The spirometer is connected to the exhalation manifold by wide-bore tubing which is normally vented to the air of the room by a "tee" connection (Fig. 2). The physician or nurse can easily measure the tidal volume by placing the palm of the hand over the side opening of the "tee." After collecting a few breaths in the spirometer, the hand is removed. The side opening of the "tee" is sufficiently large so that it can easily serve both to empty the spirometer and to vent the patient's expired air when the hand is removed. The spirometer empties by the weight of its own bell. The bell is normally in the empty position because its resistance to filling is greater than that provided by the side opening of the "tee." Such a system is readily explained to the house staff and nurses, cannot easily become obstructed by moisture or confused operation, and is fairly inexpensive since it avoids the use of respiratory valves and gear mechanisms. Expired air volume is measured so that inspiratory leakage is not counted. Furthermore, leaks about the connections are minimal during expiration, since the system is under atmospheric pressure. It is important that the flow of gas through the nebulizer be turned off during the measurement or else falsely high values are obtained. The question arises whether or not the value of tidal volume obtained is equal to that which the patient receives when the nebulizer is in operation. Since under most circumstances a reversal of the respirator cycle from inspiration to expiration occurs because the respirator setting pressure has been achieved, tidal volume should usually be independent of the nebulizer flow. If an error exists, it should be an error of underestimation of the tidal volume,

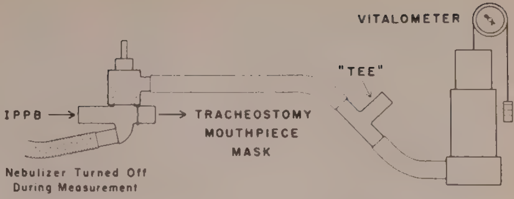

FIGURE 2. Diagram of simple arrangement for measuring tidal volume. Measurements are made at any time by turning off nebulizer and occluding opening of "Tee" connection with palm of hand.

and this possibility is accepted as being without an appreciable hazard. Tidal volume only is measured on the spirometer and the respiratory frequency, usually from 12 to 20 breaths per minute in control programs, is counted separately. After the program is in operation, measurements are made every fifteen to twenty minutes, and the nurse is instructed to regard the tidal volume and peak airway pressure readings as vital signs along with the pulse, blood pressure, and respiratory frequency. This is now accomplished regularly by individual instruction of medical and nursing personnel assigned to the patient. Considerable improvement in efficiency can probably be realized by incorporating such instruction into medical and nursing educational programs. Before accepting respirator settings for prolonged maintenance, an arterial carbon dioxide tension value is obtained. We currently seek an arterial carbon dioxide tension value of about 50 mm. Hg promptly after instituting the program and have encountered no difficulty in achieving this in the 4 instances where the measurement was made specifically for this purpose (Cases 13 to 16, Table I). Early experience with the rebreathing method of measuring mixed venous arterial carbon dioxide tension values, as described by Campbell and Howell,[2] is encouraging and promises to reduce the need for arterial sampling.

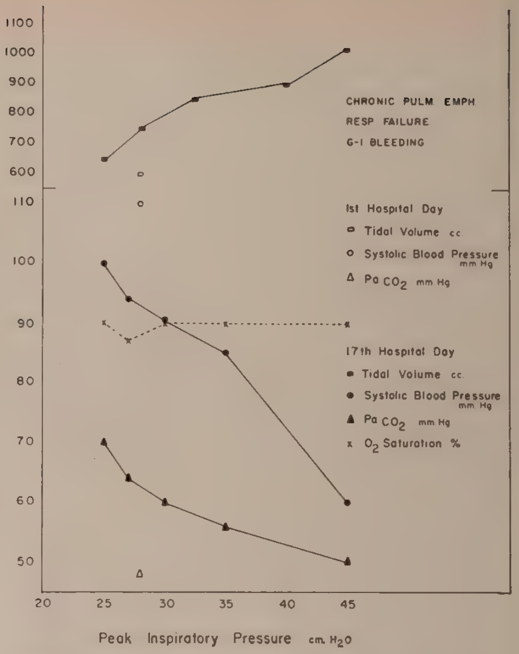

FIGURE 3. Case 14. Measurements of tidal volume, systolic blood pressure, and arterial carbon dioxide tension made on first hospital day and same measurements plus oxygen saturation on seventeenth hospital day to demonstrate increasing difficulty in obtaining settings which satisfied both respiratory and circulatory requirements. All measurements made while patient breathed 100 per cent oxygen.

Unfortunately, there are occasions when satisfactory respirator settings are not possible with the apparatus described. Evidence in support of this statement was achieved in Case 14, a seventy-six-year-old man with advanced emphysema. On the first hospital day (open symbols, Fig. 3) the positive pressure apparatus was set at a frequency of 12 breaths per minute (not recorded graphically) and a peak pressure of 27 cm. of water (recorded on the horizontal axis). These were considered satisfactory settings when the arterial carbon dioxide tension value was found at that time to be 47 mm. Hg, with a tidal volume of 600 cc. per breath. The patient improved sufficiently to have discontinuous respiratory assistance but did not recover fully. On the seventeenth hospital day his over-all condition had deteriorated, respiratory control was established again, and the four determinations connected by lines were made for the purpose of determining the optimum settings. The same respiratory frequency of 12 breaths per minute was employed, but now it was necessary to use a peak pressure of 45 cm. of water to achieve an arterial carbon dioxide tension value of 50 mm. Hg. This setting could obviously not be maintained, since the systolic blood pressure fell promptly to 60 mm. Hg. It was therefore necessary to accept a higher value for the arterial carbon dioxide tension for maintenance. The patient died on the following day. An autopsy revealed advanced emphysema, bronchopneumonia of both lower lobes with intra-alveolar hemorrhage, and an acute gastric ulceration with massive hemorrhage. The relative importance of these unfavorable complications is difficult to assess, but the data demonstrate at least two problems of importance: first, the greatly increased resistance to lung inflation and, second, the

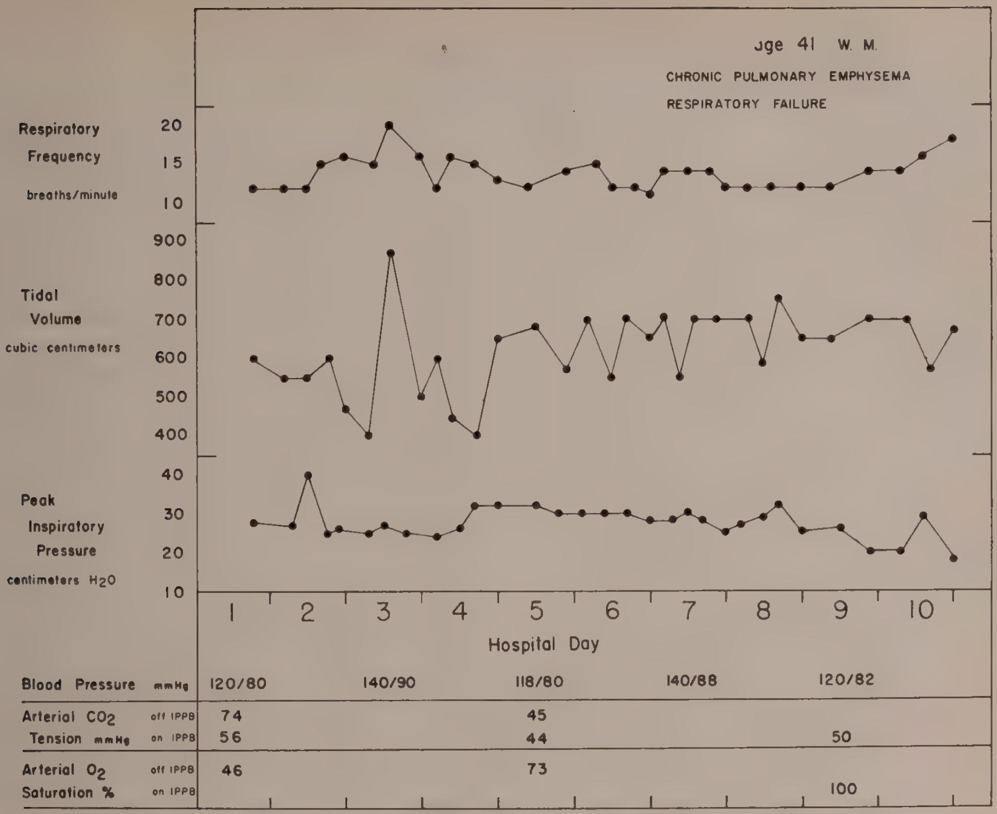

FIGURE 4. Case 15. Ventilatory variables and arterial blood values to show that given tidal volume may be maintained with decreasing values for peak mask pressure.

inability to maintain blood pressure with the positive pressure apparatus at higher settings. Thus, it cannot be claimed that truly desirable respirator settings are always possible, and it seems likely that when circulation is unstable and the resistance to lung inflation is for any reason extreme, these difficulties together may be more decisive than the refinement of apparatus or the amount of human skill or effort expended.

As a rule, the pressure necessary to maintain any given tidal volume will decrease as treatment progresses. This is illustrated in Figure 4 where the data from Case 15 are plotted chronologically. From the fourth through the tenth hospital day, there is an irregular fall in the peak inspiratory pressure observed to be necessary to maintain the tidal volume in the 500 to 700 cc. range. This fall amounts to about 10 cm. of water (that is, from about 30 to 20 cm. of water). We do not hesitate to use inflating pressures up to 30 cm. of water if necessary and if the blood pressure is well maintained, as was the case in this patient. After a stable and adequate level of ventilation is obtained, a rapid fall in the tidal volume or the need for a higher inflating pressure usually indicates either the development of a leak or the need for the removal of secretions from the airway. The cuff itself may be the cause of obstruction. A frequent measurement of the tidal volume is essential to insure a rapid identification and correction of these difficulties. A mechanical breakdown of the positive pressure apparatus is not uncommon and makes it essential to have a second machine available.

Cause of death

Inasmuch as the foregoing discussion of treatment fails in itself to provide an explanation for death among the nonsurvivors, the following facts are considered pertinent.

Case 5 was desperately ill and was in shock when he was first seen; death occurred in less than twelve hours. Case 8 was in his second episode of respiratory failure and died suddenly shortly after an arterial carbon dioxide tension value of 41 mm. Hg was obtained and the program was judged satisfactory. Case 11 died suddenly during treatment which was inadequate; a supraventricular tachycardia was present, and this may have been caused by large doses of digoxin given on the day of death. Case 14 died of hypoventilation and gastric hemorrhage as described earlier. Case 15 was in his second episode of respiratory failure and was under satisfactory ventilatory control (Fig. 4) when the cuff of the tracheostomy tube apparently detached from the tube and obstructed the airway; this was recognized before death, but cardiac arrest supervened. Case 16, also in his second episode of respiratory failure, had several grand mal seizures while he was under satisfactory ventilatory control, and thereafter he became comatose until death. Autopsy permission was denied, so that the clinical suspicion that a cerebrovascular accident had occurred could not be proved.

We are therefore unable to obtain a consistent relationship between survival and the type or intensity of therapy and must conclude that death is most likely related to complicating factors in individual patients. These may be related to therapy; as when a cuff obstructs a tracheostomy tube, but must be differentiated from the over-all inadequacy of treatment. Second episodes of respiratory failure appeared to carry a poor prognosis, although even here recovery was possible (Case 10).

Survival bore no relationship to the presence or absence of clinical evidence of bronchopulmonary infection or of cardiac failure. The absence of known precipitating factors does not therefore appear a justifiable basis for accepting an episode of acute respiratory failure as the logical end point of chronic respiratory disease. Only when the patient repeatedly requires mechanical aid to ventilation on a semicontinuous basis can such an end point be inferred to exist, and even then the decision may be far from clear.

Comparison with results of others

While a complete review of the therapeutic approach to respiratory failure in emphysema and kyphoscoliosis is beyond the scope of this communication, it is necessary to comment briefly on some of the reported experiences which appear particularly relevant to our own. It is at once apparent that the choice of respiratory aid and the use of tracheostomy are related problems. While tracheostomy has received considerable emphasis in most articles, Harvey and Ferrer[3] do not recommend it and currently advocate the use of the tank respirator without tracheostomy. Under such circumstances therapeutic bronchoscopy must be readily available for the removal of secretions.

By contrast, Mollaret *et al.*,[4] on the basis of experience with 420 tracheostomies, believe that complications, however serious they may be when they occur, are uncommon and are greatly outweighed by the advantages. Although this group has employed a variety of respirators, the machine which they prefer to use in this type of case under discussion is the Engstrom respirator. This device is volume-cycled and therefore delivers a fixed volume irrespective of leakage, that is, it does not compensate for leaks. Since leakage can be prevented or minimized by the use of a cuffed tracheostomy tube and a cuffed endotracheal tube is not suitable for prolonged use, it is apparent that the choice of this machine obliges the physician to perform a tracheostomy. Once this has been accomplished, the patient can be sedated if he offers appreciable opposition to the fixed cycle of the respirator. Under these circumstances, the Engstrom is by all accounts a remarkably effective respirator and undoubtedly is a more reliable means of achieving steady ventilation over prolonged periods of time than the positive pressure apparatus used in this study. It is, however, many times more expensive than the positive pressure apparatus and is therefore unlikely to be available in most institutions. The experience of Mollaret *et al.*[4] extends to all forms of respiratory failure and is detailed in numerous articles; their review of four years of experience is especially valuable for its comprehensiveness. They also place considerable emphasis on the importance of ventilation measurement. However, of a group of 15 patients with bronchopulmonary disease with arterial carbon dioxide tension values of from 78 to 110 mm. Hg, there were only 10 survivors. Of the 5 deaths, 2 were attributed to cerebrovascular accidents and 1 was sudden and unexplained.

In a study by Gierson *et al.*[5] the respirator was more comparable to the one used by us. In 8 episodes treated with tracheostomy plus the automatically cycled positive pressure apparatus there were 7 survivals. Munck, Kristensen, and Lassen[6] treated 23 cases of acute ventilatory failure due to bronchopulmonary disease and kyphoscoliosis with intermittent positive-negative pressure breathing via a cuffed tracheostomy tube at a constant respiratory rate and ventilation with a survival of 15 through the crisis. Thus, the percentage of survivors in the different series of this admittedly incomplete review varies from 65 to almost 90 per cent. It will be of great interest to see whether or not this variation decreases as larger series are obtained and technics for providing mechanical assistance improve, or whether, as suggested by the present study, other factors which limit survival are already playing an important role. We expect that ultimately there will be a greater degree of agreement as to the methods of mechanical assistance and procedures for their evaluation. This will be important mainly as it simplifies the problem for the physician and institution who only on occasion are called on to handle such a serious and complex problem. At the present time it appears reasonable to state that with the positive pressure apparatus containing the automatic frequency control feature used here a better than 60 per cent survival rate can be achieved in a consecutive series without the benefit of a tracheostomy in every case and without the benefit of a centralized respirator service. However, it is important that laboratory facilities for blood-gas analysis be available, not only to solve individual problems, but also as aids to the development of improved clinical judgment. Furthermore, reliance on a regular house staff plus ward and private duty nurses of varied experience presupposes that a continuous educational effort is made during the period of time when each patient is seriously ill.

Summary

We have discussed the treatment of respiratory failure with the positive pressure apparatus in 16 cases. Emphasis has been placed on (1) the possibility of avoiding tracheostomy in some cases, (2) the establishment of a ventilatory control by means of properly designed automatic cycling devices, (3) the monitoring of tidal volume on a routine basis, and (4) the use of arterial blood carbon dioxide tension measurements to determine the correctness of settings once a stable state has been achieved. The death of 6 of the 16 patients could not be related simply to the quality of the effort expended on their care but appears rather to be determined by other factors or by acute obstruction to the airway in 1 instance.

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Care and Management of the Ureteroileostomy Patient

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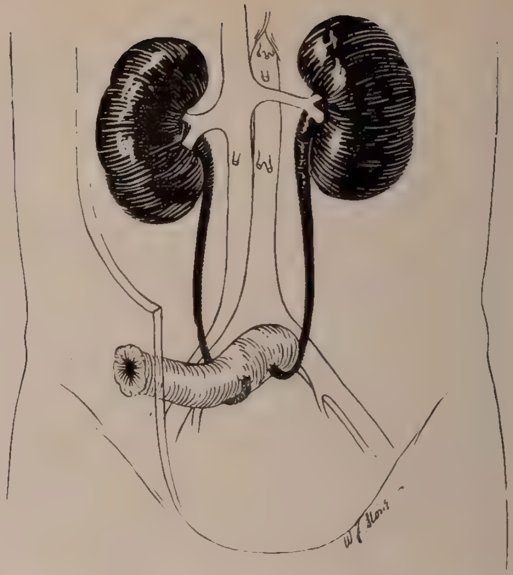

FIGURE 1. Schematic diagram of ureteroileostomy.

THE DIVERSION of the urinary stream by means of a ureteroileostomy was reintroduced by Bricker in 1950 (Fig. 1). Since that time this surgical procedure has been utilized for supravesical diversion in a variety of diseases of the urinary system including bladder neoplasia, vesicovaginal fistulas, and neurogenic bladders.

The popularity of the procedure of ureteroileostomy is due in part to the complications of other methods of diverting the urine. Following ureterosigmoid transplants, a significant occurrence of postoperative hyperchloremic acidosis and pyelonephritis has been noted. Neither does ureterosigmoidostomy lend itself to situations where appreciable ureteral dilatation has taken place, since retrograde renal contamination by the fecal stream occurs more readily. Cutaneous ureterostomies are frequently attended by a postoperative stricture of the ureteral stomas and usually require indwelling ureteral catheterization for optimal drainage. Finally, although a nephrostomy affords efficient drainage because larger caliber catheters can be inserted directly in the renal pelves, the presence of a foreign body in the collecting system invariably leads to pyelonephritis.

During the past five years, 81 ureteroileostomy procedures for bladder neoplasia have been performed at Roswell Park Memorial Institute. The proper adaptability of the patient to the ileal conduit apparatus has been in our experience a most necessary aspect to the success of the procedure. The psychologic and educational preparation of the patient is directed by the urology nursing team. Instructions as to the proper use and care of the ileostomy apparatus are given not only to the patient but also to the immediate members of the family who will be in close contact with the patient when he leaves the hospital.

It is the purpose of this paper to describe the preparation and care of the ureteroileostomy patient and to indicate the active and important role of the nursing staff in the successful result of this procedure.

Preoperative preparation

The decision for performing a cystectomy for bladder neoplasia is based primarily on the results obtained from a cystoscopy, a bladder biopsy, and pyelography. The preoperative evaluation includes a chest roentgenogram, an electrocardiogram, and a hemogram. Renal function determinations are performed including the fifteen-minute phenolsulfonphthalein and serum creatinine determinations. The base line electrolyte status of the patient is determined by obtaining the carbon dioxide-combining power and by the results of serum sodium, potassium, and chloride studies. The patient's blood is typed and cross-matched. If the hemogram reveals an anemia, preoperative transfusions are given.

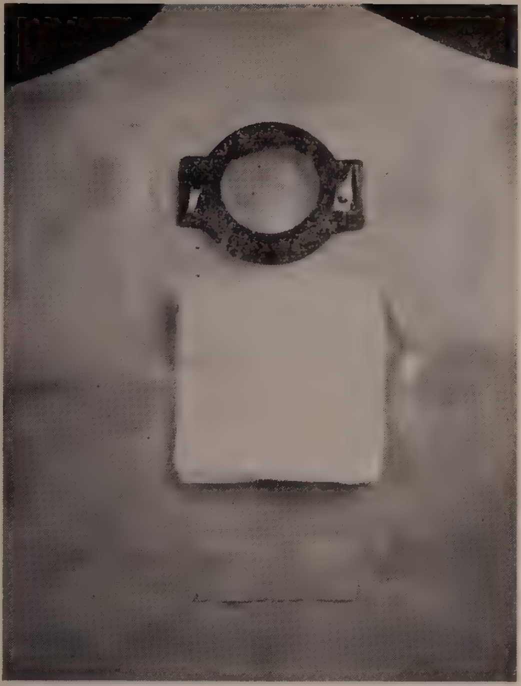
FIGURE 2. Skin testing for allergy to components of ureteroileostomy device including rubber ring, skin cement, and collecting condom.

DIVERSION OF THE *urinary stream by means of a ureteroileostomy is used in such diseases as bladder neoplasia, vesicovaginal fistulas, and neurogenic bladders. Proper adaptability of the patient to the ideal conduit apparatus is necessary to the success of the procedure. Preoperative preparation includes psychologic and educational preparation, outlining of the skin creases and skin testing, and bowel preparation. Postoperative care includes selection of a urinary collection device, skin care, patient rehabilitation, and follow-up. The role of the nursing staff is important in affecting proper patient adjustment and successful surgical results.*

The psychologic preparation of the patient for the ureteroileostomy is of prime importance. A frank discussion by the physician with the patient concerning the intended surgery is necessary. The nurse must be well informed as to the surgical plan so that she may answer questions as they arise. Frequently she may further reinforce the physician's discussion, possibly in terms more readily understandable to the patient and his family. The patient must fully understand the importance and necessity of the operation. His psychologic adjustment to the idea of urinary diversion and the external apparatus involved enhances successful postoperative rehabilitation. Other patients with similar surgery are sometimes asked to speak with the patient preoperatively. The anxious patient may not be as apprehensive and reluctant if he meets other individuals who have had the same procedure and are progressing well. The family is included in the discussion of the operation also. Their understanding and acceptance of the problem will enable them to bolster the patient's confidence when he returns to his home environment.

Further preoperative preparations are then made. The skin creases and folds of the abdomen are located, marked, and the area for the intended stoma is chosen. By initially outlining the skin creases, they may then be avoided at the time of surgery, resulting in a lesser chance for leakage of urine due to the poor apposition of the urinary collection apparatus to the abdominal wall. The patient is also skin tested for any allergy to the cement, rubber ring, and collecting condom (Fig. 2). If an allergy to any of the constituents of the collecting apparatus exists, a substitution is made.

A bowel preparation is necessary to cleanse the gastrointestinal tract of fecal content and reduce the bacterial count. The preparation is performed over a three-day period as follows:

1. The patient is fed a low-residue diet.
2. Every four hours 1.5 Gm. of Sulfathalidine is administered.
3. An intramuscular injection of 10 mg. of vitamin K is given daily.
4. Fleet Phospho-Soda enemas are given daily.
5. Neomycin is administered, 1 Gm. an hour for four doses, then every four hours during the twenty-four hours prior to surgery.
6. On the evening prior to surgery plain water enemas are given until clear results are obtained.

A Levin tube is inserted on the evening prior to surgery and attached to a suction apparatus for preoperative decompression of the stomach and small bowel. The preparation of the skin of the abdomen is performed during the day prior to surgery. The urinary collection apparatus is made available for application in the operating room immediately on the completion of surgery.

Postoperative care

The patient is taken to the recovery room at the completion of surgery. When the vital signs are stable, the patient is returned to the urology ward where he is observed closely for the next twenty-four hours. Careful fluid intake and output measurements are recorded. The amount and color of the urinary output during the first twenty-four hours may vary. The urinary output may be decreased and somewhat blood-tinged during the first postoperative day. The Levin tube is kept patent and attached to low suction until peristalsis is noted. Because of the manipulation of the bowel and the resection of the ileum peristalsis may be slow in returning, and a paralytic ileus can occur. The Levin tube usually is removed when peristalsis returns, generally on the third or fourth postoperative day. Once the Levin tube is removed, the patient advances from clear liquids to a diet as tolerated over the next seventy-two hours. Oral fluids are encouraged since the maintenance of a hypotonic urine may reduce the likelihood of electrolyte disturbance secondary to increased reabsorption. Supplemental hydration by intravenous fluids is determined by the daily intake and output records and serum electrolyte studies. The results of the serum chemistries can reveal an electrolyte abnormality before clinical symptoms of irritability, nausea, drowsiness, and weakness appear.

To help prevent pulmonary and vascular complications, the patient is turned frequently, stimulated to cough, and given deep-breathing exercises. Early ambulation is started for short periods on the first postoperative day.

Urinary appliances

Several types of urinary collection devices for the ureteroileostomy patient are available. We have found the Lapides apparatus most satisfactory (Fig. 3). Some of the advantages of this device are: (1) It can be applied in the operating room immediately on completion of surgery; (2) the condom portion can be changed frequently, making the apparatus less odoriferous; (3) many patients can wear this apparatus with the support of the belt alone thus eliminating the use of skin cement; and (4) the leg bag can be positioned out of sight beneath the patient's clothing and can be easily emptied.

Ileostomy skin care

To help prevent skin excoriation and pressure necrosis, we have instituted the policy of repositioning the apparatus daily during the first week. The skin immediately surrounding the stoma is cleaned with soap, water, and ether. The area is then dried, and tincture of benzoin is applied. When the skin is thoroughly dry, the apparatus is reapplied in a location adjacent to the previous application. In this manner the entire area surrounding the ileostomy stoma is utilized, and the breakdown of skin is avoided.

Patient rehabilitation

Demonstrations of the use of the urinary appliance are generally started on the sixth postoperative day. The acceptance of the ureteroileostomy and the accompanying urinary collection apparatus is the first step toward the patient's rehabilitation. The

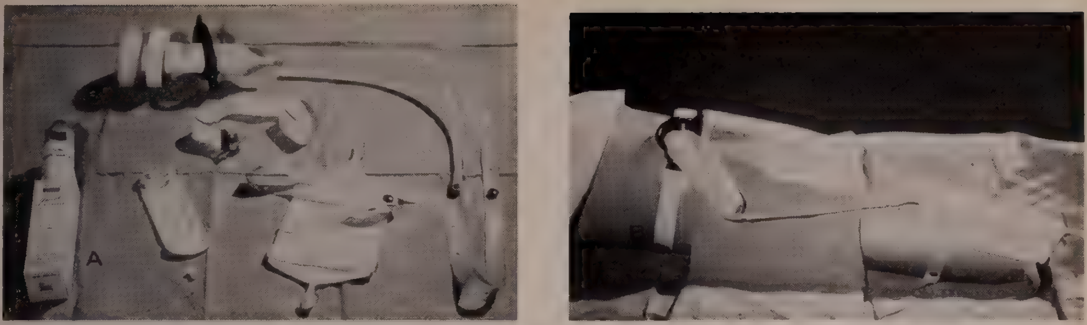

FIGURE 3. (A) Components of Lapides ureteroileostomy collection apparatus. (B) Assembled ureteroileostomy device in proper position.

nurse has the responsibility for teaching the patient how to assemble and apply the urinary collection device. The manner in which the leg bag is emptied constitutes the first demonstration. Next, the importance of skin care and rotation of the ring is stressed. Gradually the patient assumes the responsibility for the care and maintenance of the apparatus with the nurse always close at hand to give assistance. Only when the patient displays thorough ability to apply and care for the apparatus correctly is he considered ready for discharge from the hospital.

Follow-up

A nursing referral is sent to the community public health agency along with printed instructions for the care of the collection apparatus. The patient is informed that a public health nurse will visit him periodically to assist with any problems that may arise. A return date for a follow-up clinic appointment is given to the patient on discharge. During these subsequent visits to the clinic, the patient will have serum chemistry determinations performed as hyperchloremic acidosis may ensue latently. The skin surrounding the ureteroileostomy is examined for any breakdown, and the stoma is checked for stricture. If a stricture has developed, digital dilatation of the stoma is taught. Long-term follow-up in the outpatient clinic is carried out at three-month intervals.

Summary

The nursing and surgical preparation and management of the ureteroileostomy patient is reviewed.

Emphasis is placed on the importance of the role of the nursing staff in affecting proper patient adjustment and successful surgical result.

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Percutaneous Renal Biopsy

Its Importance in Research and Clinical Medicine

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DESPITE THE PROFUSION of recent papers on renal biopsies in diverse, apparently unrelated maladies, or perhaps because of them, the practicing physician is still confronted with the following problems: What is the importance of this procedure in, and its contribution to, the progress of scientific medical investigation? What are the indications for this novel procedure in "practical" cinical medicine?

This paper represents an attempt to delineate the importance of this procedure as a research, diagnostic, and prognostic tool.

Two prefatory remarks appear to be in order: First, there is the notion that a series of necropsies can solve the same problems in pathogenesis or anatomic substratum that the biopsy is supposed to solve. This notion is untenable, for at the autopsy tables the lesions are too far advanced and too complex to be of much use in the process of deciphering the morbid process in evolution, before the moment of "doom" and extinction; this is especially true in glomerulonephritis and nephrotic cases.[1]

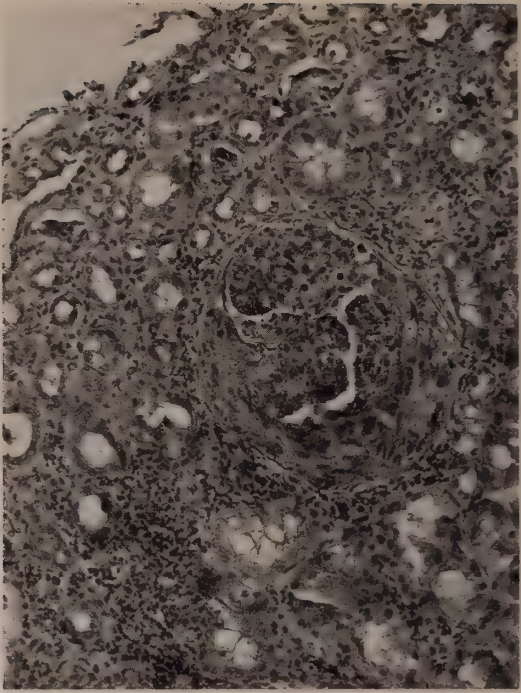

FIGURE 1. Renal biopsy showing damaged glomerulus with adhesion of tuft to parietal layer of Bowman's capsule. Epithelial crescent is prominent, and there is inflammatory exudate in interstitial tissue.

Second, there is the problem of the reliability of the biopsy findings in the over-all diagnostic picture. In strictly diffuse lesions, for example, nephrosclerosis, the problem hardly exists. But even in "patchy" diseases, such as pyelonephritis, a good biopsy specimen, while it is not always representative, has a good chance of "hitting" the spot. In very many of our biopsies, 50 to 75 glomeruli are found, thus enhancing rather markedly the probability of hitting the lesion.

Glomerulonephritis

It is probably in the field of the rational classification and identification of the com-

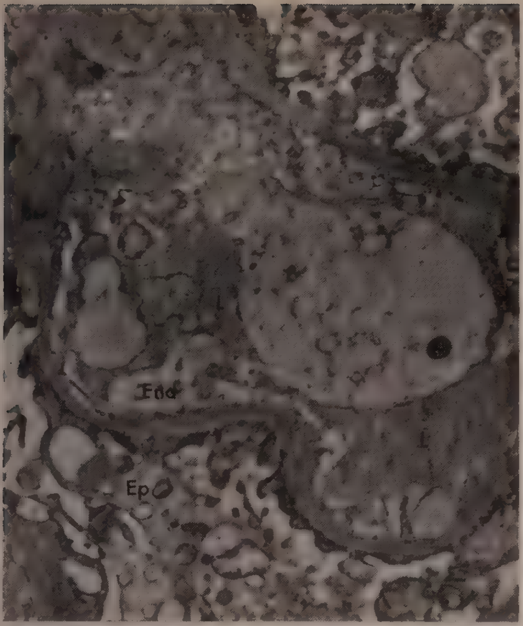

FIGURE 2. Electron micrograph of nephrotic syndrome of childhood showing capillary with patent lumen (L) surrounded by endothelium in part attenuated, in part swollen (End). Basement membrane lying between endothelium and epithelium (Ep) is normal in thickness and density but in focal areas shows changes suggestive of splitting. Epithelium is applied directly to basement membrane as a sheet, although in some areas it shows a suggestion of former foot process structure (× 5,800).

RENAL BIOPSY *is an important research, diagnostic, and prognostic tool which has contributed greatly to the knowledge of glomerulonephritis and nephrosis. It has also been extremely useful in hypertension and pyelonephritis and in other conditions such as diabetic nephropathy, toxemia of pregnancy, lupus erythematosus, and sickling. Its potential in many other diseases of the kidney is great. Contraindications include: diseases in which a sudden loss of blood could be dangerous; bleeding tendencies; and presence of only a single kidney.*

plex entity of glomerulonephritis that renal biopsy has achieved the most brilliant successes.[1] It is owing only to the close cooperation between the clinician who observes a patient with subacute glomerulonephritis and the pathologist who examines the biopsy specimens that the hitherto obscure correlation between the specific anatomic substratum and the disturbed renal function in this malady becomes apparent.[2] This problem has been very well described by Baldwin and McCluskey[1]; our own experience with similar cases fully corroborates their findings. Figure 1 depicts a renal biopsy in such a case in which the advent of renal insufficiency and of the anatomic abnormalities appeared practically simultaneously.

Furthermore, the very problem of the nosographic entity of the acute, subacute, and chronic glomerulonephritis, which are considered by some not as different phases but as different diseases altogether, has been settled by Baldwin and McCluskey[1] who observed on serial biopsies the transition of one of these forms into the other. Thus, there can be no more question, for example, of chronic glomerulonephritis being usually anything other than a late phase of the acute form. Our own experience also amply confirms this viewpoint and rules it out as a disease de novo in most cases.

Nephrosis

Our knowledge of nephrosis, the enfant terrible of nephrology, also has benefited immensely from the advent of renal biopsy, especially when it is coupled with an electron microscopic examination. In this field, Farquhar's [3-5] research has opened entirely new vistas. We shall refer the interested reader to her splendid papers on the fine structure of the kidney in the wide spectrum of nephrotic disorders. Indeed, the relations between the nephrotic stage of glomerulonephritis, the de novo nephrosis, and the "pure" nephrosis, assuming that there are such entities, are being investigated[1] and are developing into a rational concept. The correlation between the anatomic substratum and the clinical parameters of the disease is being elucidated. Finally, the relation between these forms of nephrosis and those representing renal complications or manifestations of lupus erythematosus, diabetes mellitus, and so forth, is gradually being explained. The electron microscopy of the renal glomeruli in the nephrotic syndrome of childhood often shows only the fusion of foot processes, while in the adult there are usually basement membrane changes. Figure 2 will give the reader an idea of these findings.

Hypertension

In the field of hypertension the contribution of renal biopsies have again been quite substantial. Our own group has demonstrated the practically inevitable damage which is inflicted on the kidneys by long-standing hypertension, namely, nephrosclerosis[6]; we have also demonstrated the lack of parallelism between the clinical parameters of hypertension and the degree of renal damage; we have even described 1 case of clinically benign hypertension in which the kidney on which a biopsy was done turned out to be afflicted with what is considered the hallmark of malignant hypertension, that is, necrotizing arteriolitis. At the present time we are continuing our research on the impact of drug treatment on the renal lesions as mirrored in serial biopsies.

Pyelonephritis

Pyelonephritis is an extremely controversial subject, particularly of late when the diagnostic criteria for anatomic diagnosis started to undergo some drastic reevaluation. Indeed, it would appear that many cases which hitherto have been diagnosed as pyelonephritis do not fit into the modern concept of this malady.[7] Again, the relation between the acute and the chronic forms of this disease is being elucidated. As far as our own group is concerned, it has been our experience that the cultures of tissue which are obtained by renal biopsy frequently yield different germs from those which are obtained by urine culture. The etiologic and therapeutic implications of these findings are self-evident.

Renal amyloidosis is another condition in which the physician can benefit greatly from the advent of renal biopsy. Indeed, the very diagnosis of the disease frequently can be made with certainty only by biopsy. Nevertheless, at this writing, not much progress has accumulated in this field.

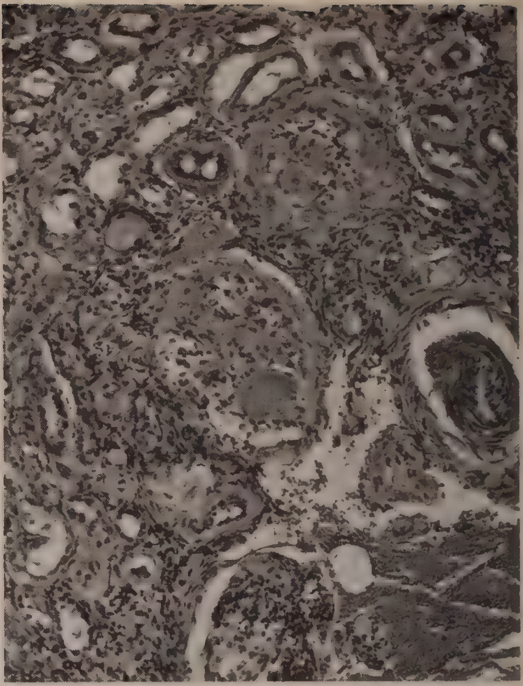

FIGURE 3. Renal biopsy showing extensive arteriolar and glomerular sclerosis. Nodular hyaline aggregates are seen within damaged glomeruli.

Other conditions

Diabetic nephropathy. Diabetic nephropathy is certainly a most fascinating subject to study. It is in this condition that renal biopsy coupled with electron microscopy has afforded quite a substantial amount of data.[8-10] The studies by Farquhar[3-5] and Hatch *et al.*[10] have made the physiopathology of this puzzling lesion more comprehensible.

Some important facts which have been elucidated by renal biopsy are that the basic lesion appears to be an accumulation of abnormal glycoprotein in the basement membrane of the glomerulus and that the lesion does not progress pari passu with the progress of diabetes but is quite independent in its development. The controversial issue of the diffuse versus the nodular lesion is on the verge of being solved (Fig. 3).

Electron microscopy demonstrates that

the basic lesion is a thickening of the basal membrane; it is often accompanied by the intercapillary deposition of a basement membrane-like material. Further details will certainly be forthcoming in the next few years, indubitably with the help of renal biopsy. We are now studying a sizable group of these patients with the aid of electron microscopic inspection of renal biopsies.[11]

TOXEMIA OF PREGNANCY. Toxemia of pregnancy has emerged in a new light since Altchek's[12] studies on this important subject had the benefit of a large number of renal biopsies examined under the electron microscope. Indeed, the histopathologic criteria for differentiation from concomitant essential hypertension seem near to a final delineation. In toxemia of pregnancy, the endothelial cells, as seen under the electron microscope, are swollen, often in the absence of any membranous or foot process changes. These differences, incidentally, suggest that the electron microscope examination is often useful in the early differentiation of these nephropathies.

LUPUS ERYTHEMATOSUS. The renal lesion in lupus erythematosus is sometimes difficult to diagnose in the absence of a renal biopsy.[13] Indeed, the very diagnosis of lupus occasionally can depend on the renal lesion. Curiously enough, a recent paper on the subject tends to equate lupus with chronic glomerulonephritis on the basis of renal biopsy studies.[14] While we share the author's enthusiasm for the study, we feel that the pathologic vocabulary of the glomerulus is limited; hence the clinical difference of the two maladies is such that their identification appears to be premature, to say the least. Perhaps an analogy between multiple myeloma and primary amyloidosis, established on the basis of similar bone marrow findings (a condition also possessing a limited vocabulary for the expression of minutiae), is a good example of a similarly rash identity postulation based on the convergence of appearances. Be that as it may, in systemic lupus erythematosus there is a thickening of the basement membrane as seen under the electron microscope, the proliferation of the fine intercapillary basement membrane branches being its characteristic feature.

SICKLING. In people who sickle—no matter whether they are heterozygotes or homozygotes—hyposthenuria is a well-established and well-known functional abnormality, for which no explanation has been found, notwithstanding a thoughtful paper by Levitt *et al.*[15] Currently we are engaged in the study of renal biopsies in this fascinating disorder, the results of which so far appear to be promising.

Comment

This paper does not pretend to be an encyclopedic review of indications for renal biopsy. We have endeavored to show the many fields in which kidney biopsy has contributed or is about to contribute, a substantial amount of data of scientific interest. If we did not mention, for instance, dermatomyositis, scleroderma, Wegener's granulomatosis, angiokeratoma, diffusum universale, and a host of other diseases, it is only because the research in these fields, from the viewpoint of renal biopsy, is still rudimentary. On the other hand, we are convinced that in de Toni-Fanconi syndrome, in the hereditary nephropathies with or without deafness, in the nonglycosuric meliturias, and in many other conditions, renal biopsy is able to afford a tremendous amount of useful information. We hope that in the near future its apparently little-used potential for research will gain its well-deserved place.

In two fields we feel strongly that renal biopsy is destined to play a most important role in shedding light on the puzzling functional behavior of the kidney. We are convinced that renal biopsies leading to a histochemical investigation of the tubules will contribute immensely to explain the perplexing physiologic puzzle of renal tubular acidosis. The second of these conditions is subacute bacterial endocarditis; the problem of transition, if any, between the embolic focal phenomena in the kidney and the generalized picture of glomerulonephritis will certainly be illuminated by serial renal biopsies coupled with renal function studies. We omit mention of renal hemosiderosis in some hemolytic anemias, for example, paroxysmal nocturnal hemoglobinemia. Indeed, Leonardi and Ruol performed some interesting work in this field.

From the viewpoint of clinical application, renal biopsy also offers a very broad field of indications. The physician faced with glomerulonephritis can frequently be in doubt concerning the very nature of the disease. Is it a chronic glomerulonephritis with an acute flare-up or a de novo entity? Many times, in the absence of a reliable history, or even in the presence of a reliable but obscure anamnestic set of data, the diagnosis cannot be established by any means short of renal biopsy. The importance of this procedure from a prognostic viewpoint is obvious.

The diagnosis of pyelonephritis is frequently difficult. We feel, contrary to the usual belief, that the disease is frequently overdiagnosed. A biopsy often can establish the correct diagnosis.

It is unnecessary to dwell on the importance of a needle biopsy in cases of lupus nephropathy; indeed, the prognostic gravity of the disease has recently again come into focus rather sharply.[13] What's more, the very diagnosis of lupus can sometimes hinge on the procedure.

In diabetes mellitus, because of the unpredictable renal findings in this disease, it is frequently impossible to tell whether the presence of clinical signs pointing to renal involvement is due to some intercurrent, trivial pyelonephritis or whether it is the heralding sign of diabetic glomerulosclerosis. There is no reliable sign to differentiate the two, short of a biopsy. Prognostically, the distinction is of paramount importance.

In hypertension, a knowledge of the presence of renal involvement is of great importance. In view of the great strides achieved in the therapy of this serious disease, it would be inexcusable to leave a hypertensive patient untreated "until or unless he becomes symptomatic." The efficacy of reserpine, guanethedine sulfate, and so forth, and their relative lack of toxicity is so marked that no patient should be denied their use and benefits. Again, a renal biopsy is of great imoprtance.

We shall avoid the re-enumeration of other, more esoteric disorders in which a kidney biopsy is definitely useful or even necessary. Every physician worthy of his title certainly feels thrilled when he unravels what appeared to be a complex, incomprehensible, or most unusual case. He who solved such a problem by performing an appropriate procedure will think highly of it. Renal biopsy is frequently such a procedure.

Contraindications

It would be quite erroneous to conclude from the foregoing disquisition that renal biopsy is an innocuous procedure with ecumenic indications or some short cut to a sound clinical judgment. Such is not the case. In the presence of diseases in which a sudden loss of blood could be dangerous, for example, recent coronary thrombosis, cerebrovascular insufficiency, marked hypovolemia, and so forth; in the presence of bleeding tendencies; or in a patient with a single remaining kidney, even the usually insignificant hematuria that follows a renal biopsy occasionally could be dangerous. Even in very experienced hands this procedure carries a certain risk of morbidity; perirenal hematomas have been known to occur occasionally after a carefully performed biopsy. Very rarely nephrectomies have had to be perfomed after a renal biopsy caused severe intrarenal laceration. A complication related to the local anesthetic employed recently occurred in a patient of ours. This was manifested as a severe hypersensitivity reaction to the procaine that was injected to anesthetize the region to be biopsied. The patient recovered uneventfully. Thus, before a biopsy is embarked on, the factors mentioned must be weighed carefully. On the other hand, we do not favor procrustean rules in this respect.

Technic

We shall not go into the details of the different technics that are being used by some authors in the performance of percutaneous renal biopsy; instead, we shall limit ourselves to a brief outline of the technic that we used and described elsewhere.[6] Briefly, it consists in having the patient in a prone position, with a sandbag under his abdomen to bring the renal region nearer the dorsal surface. On an intravenous pyelogram, or a good flat plate, at least, the lower

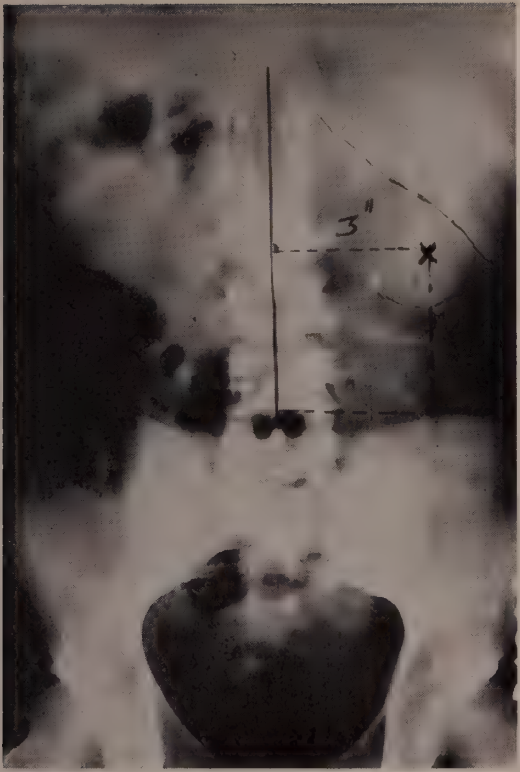

FIGURE 4. Intravenous pyelogram showing measurement for selection of strategically located point for percutaneous renal biopsy.

pole of the kidney is repaired, and a point is chosen that would be strategically located, that is, far from the hilus, as near the lower pole as possible, and as far from the outer border of the kidney as would seem necessary to avoid a "miss" caused by the distortion of the organ on the x-ray image. The distance of that point is measured both from the midline of the lumbar spine and from the uppermost point of the iliac crest.

Figure 4 gives a good idea of what we mean. The same distances are repaired on the patient's back with a pencil. The intersecting point is infiltrated with some local anesthetic, as are also the deeper structures, but not the practically insensitive subcutaneous tissue.

A thin spinal tap needle is then introduced until the depth of the kidney is ascertained, rather by the feeling of the rubbery consistency than by the respiratory movements of the needle. The thin needle is then withdrawn, and the biopsy needle, usually some modification of the Vim-Silverman, is introduced to the same length as the exploring needle. Actually, we introduce it a little less then the exploring needle, for the inner needle is naturally about 1 inch longer than the outer one; thus we practically always are sure of obtaining cortical tissue. We almost always prefer the left kidney, while most authors biopsy the right one.

Be that as it may, in the approximately 120 biopsies which we have performed so far, we have found the previously described method as most useful. Needless to say, before the procedure is embarked on, we investigate the bleeding, clotting, and prothrombin time of the patient. After the biopsy is over, a bandage is applied and left in place for two hours. The patient is left in a supine position on the sandbag for a few hours and altogether in strict bed rest for twenty-four hours. The vital signs are checked at frequent intervals for twenty-four hours and not so frequently for the ensuing twenty-four hours.

Summary

The contribution of percutaneous renal biopsy to the understanding of several nephropathies has been reviewed briefly. The progress in our knowledge of the natural history of glomerulonephritis, the correlation of the histologic findings with the physiopathologic changes in the different phases of the disease, and the knotty problem of the nosographic concept of the disorder have been evaluated as related to renal biopsy.

In nephrosis, the knowledge which has accumulated through the electron microscopic study of biopsy material has been described briefly. The important changes seen in the hypertensive kidney have been mentioned. In diabetes mellitus, in lupus erythematosus, and in several other diseases the correlation, or lack of it, with diagnostic and prognostic data has been brought out. The importance of kidney biopsy in the diagnosis of some disorders which are not primarily renal has been mentioned. The contraindications to and hazards of the procedures have been enumerated. A short description of the technic as used by the authors was included.

ACKNOWLEDGMENT. The authors wish to express their grateful appreciation to J. Churg, M.D., and William Mautner, M.D., for their valuable help in reviewing the electron microscopic data. Our thanks are also due to Eli Goldstein, M.D., for his valuable suggestions.

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The Warm-Up and Autogenous Injury

THE WARM-UP *in the living organism is concerned with safety features for the organism and its component systems. The basic activity occurs in the central nervous system where the necessary kinetic patterns are reinforced and the chief initiation of the proper hemodynamic patterns comes about. Factors in the process include joint innervation, proximal body set, and circulation, both peripheral and central. Proper warm-up is important not only in improving the level of performance of physical activity, but also in prevention of autogenous injuries.*

HARVEY P. KOPELL, M.D., F.A.C.S.
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From the Department of Orthopedic Surgery,
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AUTOGENOUS INJURIES, those that are self-induced, are common but often are not recognized as such. Their prevention is concerned not only with the determination of the preaccident state, but also with the mechanism of the trauma. The facts in these cases are colored by the different levels of origin of the initiating causes. At one end of the scale the concept of "accident proneness" implies a subliminal volitional nature. At the other end is the unintentional trauma of an unknowingly inadequate warm-up. It should be noted that an inadequate warm-up also may be a function of "accident proneness." The warm-up is defined as a series of maneuvers that closely precede the performance of a related specific action to prepare for the execution of that action. The general feeling is that the warm-up is important to assure excellence of performance, but equally important is the prevention of an autogenous injury through the elimination of a malfunction of some portion of the action.

Examples of the warm-up as distinct from the training period are familiar in the external world. A pilot taxies his plane to the runway; he stops and guns up each motor in turn. He checks the response to the controls, the power, the measurements of the response, and the interlinkage of the controls. He is checking the efferents, afferents, end organs, and the intersystem modulation. By simulated load conditions, he is bringing components up to optimum temperature and pressure ranges.

Such a routine seems to be an obvious safety measure. The warm-up in the living organism in a similar fashion is concerned with safety features for the organism and its component systems. There are divergent views on the purpose and mechanics of the warm-up. It would seem that the generally accepted belief that it functions to loosen up the muscles by lowering viscosity or stimulating local circulation is too restricted a view. The basic activity is primarily central in initiation. The factors to be considered in an understanding of the process are joint innervation, proximal body set, and the circulation, both peripheral and central.

Joint innervation

The movement of a joint requires more than an individual muscle action. These elements are concerned:

1. Innervation of the direct motor muscle, the prime mover.
2. Innervation of the synergists to the direct motor muscle.
3. Innervation of the antagonists.

The synergists not only assist the prime mover of the joint, but they also have another extremely important function; the maintenance of the joint's mechanical integrity. They keep the bearing surfaces in the correct relationship, or establish the fulcrum. The synergists must work together in a concerted fashion. If the prime mover starts to pull before the synergist stabilizes the joint, unusual stress will be brought to bear on the joint's ligaments and capsule, which may result in a sprain or even a tear. If the synergists contract too hard before the prime mover acts, the joint will tend to freeze or to present an abnormal resistance to motion. Inappropriate action then by the prime mover may result in an abnormal muscular strain, either in the prime mover or at its attachments. As the prime mover acts, the antagonists must relax at a proper rate by the inhibition of their tension which is accomplished by the progressive decrease in the discharge rate along the motor neurons. All this action is metered by the proprioceptive awareness. The higher centers that must attune the action to the load, or expected load, determine whether or not the relayed proprioceptive stimuli serve to provide a positive or negative feed-back to the internuncial pool. This is not a peripheral function but is carried out by the central nervous system in the internuncial pool which terminates in the activity of the ultimate motor neurons.

Proximal body set

To complete a final action the proximal lever of the joint must be fixed by a stable platform. The stable base must provide the proper amount of inertia even though it is in motion. The inertia is determined by the proximal mass and the forces directed against the acting limb. If there were not sufficient mass and force directed against the functioning limb, then the limb action would result in an inappropriate body motion rather than a purposeful action of the limb. It is not a forearm and arm swinging a racket, but rather an extremity's action against a body set that makes the action. A paraplegic patient playing basketball from a wheel chair illustrates a difficulty in body set.

In baseball and golf the preliminary to the body set for the action is called the stance. It is the appropriateness of this posture to the final act that determines grace and often excellence in action. When it is not properly related, or the component parts of the posture do not act in unison, then either the final act will be faulty or some joint apparatus proximal to the end-directed one may be overstrained. The body set is all directed from the central nervous system. It is capable of modification through learning. We can envision the warm-up as altering or facilitating these various pathways. The various proprioceptors send back the impulses of "too much force here," or "insufficient stabilization of a somatic segment there." On the next trial the impulses going down to the internuncial pool will be requantitated for a better preparation toward the expected load. A better kinetic pattern is then set up for the whole organism.

Peripheral circulatory factors

There are two main factors to be considered about the circulatory activity during the warm-up. The first is peripheral, and the second is proximal, or central.

PERIPHERAL. The warm-up does provide for the accumulation of metabolic by-products which can cause local vasodilation. The majority of intense endeavor is carried out in either a recurrent or acute local oxygen deficit. The circulatory increase that a warm-up induces provides a larger reservoir for the energy requirements of the muscles. The oxygen and fuel indebtedness that are created in the muscles and their local reservoirs ultimately must be satisfied by an increased cardiac output and pulmonary ventilation. The build-up of metabolic products and possibly adrenaline-type substances provides the basis of the "second wind" phenomenon, the nature of which is still under investigation. Its effects may be through a more efficient use of the output of the right side of the heart when better gaseous exchange is obtained through the dilation of the pulmonary capillary network. This may occur through the direct active dilation of the arterioles and their capillaries or passively because of the closure of the extrapulmonary shunts. When this happens, the cardiac output of each side of the heart feeds into load characteristics suited to its needs. Therefore, there is a better utilization of the heart energy expenditure in terms of the total cardiac output. The changes do not occur instantly, but require time. The period when this condition obtains—when the local oxygen debt, or carbon dioxide build-up, matches its pulmonary relief as a steady state—is the time for the "second wind" to come about. This is more important in continued activity, such as running, than in a one-shot activity, such as weight lifting. The warm-up properly timed and executed will provide the setting for an earlier satisfaction of peripheral demands. It must be emphasized that the warm-up action is important only as it influences a more central function.

Central circulatory state. There is general recognition of three central aspects of hard activity: raised pulse rate, elevated cardiac output, and increased pulse pressure. The latter is a variable resultant of three factors: cardiac output, cardiac rate, and total peripheral resistance. There is a fourth factor, absolute blood volume change, but this factor, first positive, then negative, does not play a significant role in the pulse pressure determination of most normal activities. The aspect of peripheral resistance that concerns us here is the amount of dilation in the visceral and parietal vascular beds. The blood volume can be shunted to its region of need by a change in the resistance of the vascular networks. The stimulus of food or its symbol will increase the flow of the digestive juices. This means that there has been an increased blood flow in the visceral vascular network and, therefore, a drop in resistance in that portion of the system. Some large organs, such as the brain, kidney, and perhaps the liver, may maintain fairly fixed levels of resistance under most conditions of daily life as compared with the changes in the intestinal wall. The closing down of the visceral bed in response to motor activity, whether it is mediated through direct autonomic nervous system elements, circulating hormones, or tissue metabolism products, takes a certain amount of time. The completion of the volume shift requires different periods depending on the circumstances. It will occur in a shorter period after a meal is mostly digested than it will just after the start of the digestion of a heavy meal. If the activities of the musculoskeletal system initiate parietal vasodilation when the visceral bed is still open, then abnormally low total peripheral resistance is presented. A relative hypovolemia ensues. An increase in the pulse pressure will result because of a lowered diastolic value which may not achieve adequate compensation through increases in stroke volume and rate.

The coronary blood supply is related directly to the diastolic pressure. The lowering of this value means a decreased pressure head to the coronary arteries which can bring about ischemia. Therefore, decreased resistance in the musculoskeletal network while there is still visceral network dilation can result in cardiac muscle ischemia at the time when there is a demand for an increased cardiac output to meet the extra work requirements.

A few cases will be presented that illustrate these aspects of the warm-up. Although they are dissimilar in medical content, they all bear a relation to the problem.

Case reports

Case 1. A college athlete was late in getting to a track meet. He undressed in a hurry and reported to the starting line without a warm-up. Two or three steps after the start he collapsed to the track, unable to move. An examination disclosed that he had ripped off a portion of his iliac crest.

Comment. The athlete did not have a warm-up that was adequate either in time or in intensity. It might be argued that because of the lack of a warm-up, the gluteal and tensor fascia muscles were contracting in a state of relative ischemia. Then when a forceful contraction was called, the muscles went into a tetanic spasm and avulsed the bone. However, this happened so soon after the start that the central nervous system was more likely the origin of the trauma rather than the rapid onset of a circulatory deficit. The fault was one of a lack of reinforcement of the pattern of synergistic action between the agonists and antagonists. In the faulty kinetic pattern there was either an overcontraction of agonists and antagonists too close together, or a strong pull on one side of the iliac crest without a properly timed bracing pull on the other, as from the abdominal and flank muscles.

It must also be noted that a warm-up may help to dispel part of the tenseness of an impending competitive situation, since tension can interfere with the establishment of smooth kinetic patterns.

Case 2. A man arose one morning and immediately bent over the sink to wash. As he started to get up, he developed an acute pain in his back and was unable to complete his trunk extension. He had sustained an acute low back derangement.

Comment. Here it seems obvious that a local vascular inadequacy or lack of intramuscular fluidity cannot be blamed. For the mechanism we must note the action of a true joint. There is a myoligamentous system which stabilizes the joint or maintains its bearing surfaces in relation to others. This is usually separate from the prime mover or motor muscle. The relationship also exists in the spinal joints. If a dyssynergia is present at a joint, a fault in the timing of either muscle class will result in abnormal stress applied to basic ligamentous joint structures. The action of the contiguous spinal joints above and below the distressed joint participating in the action causes further local aggravation. There is normally no way to compensate fully for or bypass a poorly stabilized joint when function is demanded of the whole spinal column.

Thus, in Case 2 the patient suddenly performed an act which demanded a concerted action at many joints without a significant preliminary recall of a kinetic pattern. It does not vitiate this explanation to ascribe a pre-existing structural weakness or the residual of some trauma. Even though additional force is needed to "set" such a segment, its stabilization must have the proper timing both with relation to itself and to other segments. The fact that it occurred right after the patient arose is indicative that the patterns of stabilization did not have time to be reestablished. The episode might have been avoided had he walked around a bit and had some preliminary graduated activity of his trunk musculature.

CASE 3. A man came home from work. He ate his supper and immediately went out to start vigorous snow shoveling. Within the next twelve hours he developed a coronary infarction.

Comment. In this case we are dealing with the circulatory aspects of the warm-up. Following the meal there was a dilation of the visceral bed. The patient started to shovel snow within a half hour after eating. He attacked a heavy-effort job which rapidly called forth dilation in the musculoskeletal bed without allowing time for visceral constriction. Without this compensation he undoubtedly had a large fall in the diastolic pressure because of a low peripheral resistance. This was responsible for the inadequate coronary filling. The situation was aggravated by warm clothing which prevented heat loss. This opened up cutaneous and subcutaneous networks which further dropped the peripheral resistance. A properly timed warm-up would have brought about the interruption of the digestive activity. The closure of the visceral bed probably would have prevented the diastolic lowering which caused relative coronary ischemia when his activity demanded an increased cardiac output for the work load.

CASE 4. A high school basketball player sustained a broken ankle in a pile-up during an important game. As the x-ray films were being taken, he vomited his last meal one-half hour after the trauma, and six and one-half hours after the meal. It appeared to be completely undigested.

Comment. The significance of this case is in the demonstration of the influence of the central nervous system on visceral action. The patient did not perform any physical activities relevant to a warm-up for several hours after his meal. However, the tension or excitement in anticipation of the impending competitive exercise prevented the proper digestive action. Therefore, the blood was shunted out of the visceral network from an initiating stimulus originating first at a cortical level. This caused an interruption of the normal involuntary digestive action that should follow a meal.

There was very little evidence of chemical alteration of the food after all that time. This is an aspect of the warm-up phenomenon even though its onset was six hours prior to the action. It further illustrates the central nature of the warm-up process.

Summary

The warm-up has significance to the physician as a participant in physical activities, in the treatment of injuries that may result from them, and in his advisory capacity to prevent such injuries. A proper warm-up is important not only in improving the level of the performance of activity, but also in the prevention of autogenous injuries. Although not generally considered so, the chief site of warm-up activity is in the central nervous system. It is here that the necessary kinetic patterns are reinforced and the chief initiation of the proper hemodynamic patterns comes about.

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Serum Flocculation Test for Diagnosis of Obstructive Jaundice*

A STUDY *was made of the Jirgl serum flocculation test for the diagnosis of obstructive jaundice in 111 patients and controls. The test gave a positive reaction in 87 per cent of 31 patients with obstructive jaundice and negative results in 89 per cent of 54 patients with jaundice that was not due to biliary obstruction and in all of the healthy controls. False negative results were obtained in 1 case of porta hepatis obstruction, 2 cases of complete bile duct obstruction by carcinoma of the pancreas, and 1 case of common duct stone. Eleven patients tested after successful treatment of obstructive jaundice gave negative test reactions.*

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THE DIFFERENTIATION of jaundice due to biliary tract obstruction from other types not infrequently presents a difficult problem. Existing technics of clinical and laboratory evaluation do not always lead to correct answers, and serious errors may be made in some cases. In 1957 a new test for obstructive jaundice was described by Jirgl,[1] who observed flocculation in the sera of patients with obstructive jaundice while performing determinations of serum mucoprotein levels. He studied this reaction in the sera of 691 patients with various hepatic and nonhepatic diseases, including 46 patients with obstructive jaundice. Positive results were obtained in 95 per cent of obstructed patients, and no positive results were found among the rest. A confirmatory clinical report by Daikos, Mattheou, and Athanasiadou appeared in 1959.[2] Ninety sera were studied; positive reactions were obtained in 23 of 25 patients with obstructive jaundice, and false positive reactions were seen in 10 per cent of the group with hepatocellular jaundice.

The mechanism of the test is still not clear. Although the reagents used are those for the determination of serum mucoprotein,[3] the reacting material in jaundiced serum is said not to be mucoprotein.[1]

The reported results appear to indicate the superiority of Jirgl's flocculation test over other tests of jaundice in the differentiation of obstructive jaundice, but it has not yet become popular nor well explored. The following is an evaluation of it in 96 patients, most of whom were jaundiced.

Methods and materials

The following procedure was used: To 1 ml. of serum in a test tube is added 2 ml. of 0.1-normal sodium hydroxide. After mixing it well, this mixture is left for forty-five minutes, and then 2 ml. of 20 per cent sulfosalicylic acid are added. After mixing, the contents are filtered through Whatman number 1 or 2 filter paper into a centrifuge tube. To this filtrate, 0.5 ml. of 5 per cent phosphotungstic acid in 2-normal hydrochloric acid is added; the mixture is allowed to stand from ten to fifteen minutes. This is centrifuged and the supernatant fluid discarded. The inside wall of the tube

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* A more detailed report of this study has been published in the *A.M.A. Archives of Internal Medicine* **109:** 270 (Mar.) 1962.

TABLE I. Results of serum flocculation tests

Diagnostic Category	Number of Patients	Positive Reactions
Jaundice due to biliary obstruction	31	27 (87 per cent)
Same, after relief of obstruction	11	0
Jaundice not due to biliary obstruction	54	6 (11 per cent)
Miscellaneous diseases, without jaundice	7	1
Healthy individuals	15	0

is wiped, and the precipitate is dissolved in 3 ml. of 10 per cent sodium carbonate, transferred to a 10- by 75-mm. test tube, and 0.25 ml. of Folin-Ciocalteu's phenol reagent diluted 1:3 in water is added. The result is read after the reaction mixture stands overnight and graded according to Jirgl: A clear blue color is negative, opacity plus, flocculation double plus, and precipitates triple plus. All steps are carried out at room temperature.

One hundred twelve sera were obtained from 96 medical and surgical patients at the Veterans Administration Hospital and the Roswell Park Memorial Institute, Buffalo, New York. The majority of cases were selected from records of bilirubin determinations in the clinical biochemistry laboratories of these institutions without knowledge of the clinical data. After the flocculation tests had been completed and recorded, each case was reviewed, using all the available clinical and pathologic data. In 66 patients, diagnoses were confirmed by needle or surgical biopsy of the liver and/or by autopsy.

There were 31 patients who were judged to have obstructive jaundice, 54 patients with jaundice that was not due to biliary obstruction, and 7 patients who had no jaundice. In addition 11 patients were evaluated after the relief of biliary obstruction. Fifteen healthy individuals served as controls.

Results

Table I presents the results of Jirgl's test by major diagnostic categories. The flocculation test gave a positive reaction in 87 per cent of patients with biliary obstruction. The results were negative in 89 per cent of patients with jaundice that was not due to biliary obstruction and in all of the healthy controls.

Table II presents cases of obstructive jaundice according to diagnosis. The false negative test results were obtained in 1 case of porta hepatis obstruction, 2 cases of complete bile duct obstruction by carcinoma of the pancreas, and 1 case of common duct stone.

All of the 11 patients tested after successful treatment of the obstructive jaundice gave negative Jirgl flocculation test reactions. Ten of these had surgical therapy; 1, whose obstruction was caused by a metastatic tumor, had a dramatic response to chemotherapy. Flocculation tests had been

TABLE II. Results of serum flocculation tests in patients with jaundice due to biliary obstruction

Diagnostic Category	Before Treatment		After Relief of Obstruction	
	Number of Patients	Positive Reactions	Number of Patients	Positive Reactions
Metastatic carcinoma				
Intrahepatic	7	6	...	...
Extrahepatic	9	9	3 (1)*	0
Carcinoma of gallbladder	1	1	1	0
Carcinoma of head of pancreas	8	6	2 (1)*	0
Carcinoma of papilla of Vater	2	2	...	...
Choledocholithiasis	4	3	5 (2)*	0
TOTAL	31	27	11 (4)*	0

* The numbers in parentheses represent cases not tested prior to treatment. All of the others had positive test reactions before relief of obstruction.

TABLE III. Results of serum flocculation tests in jaundiced patients without biliary obstruction

Diagnostic Category	Number of Patients	Positive Reactions
Hepatic neoplasms	10	1
Cirrhosis and fatty liver	21	1
Hepatitis, toxic and viral	10	3
Miscellaneous	13	1
TOTALS	54	6

performed before the relief of obstruction in 7 of these patients; all the results were strongly positive. The test results became negative within a few days after the obstruction was relieved.

Table III summarizes the results in 54 jaundiced patients without biliary obstruction. This is shown according to diagnostic categories, and there were 6 false positive results.

Seven patients without jaundice were studied because they had one or more of the following: hepatomegaly, high serum alkaline phosphatase activity, presumably of bone origin, high serum mucoprotein level, or elevated and abnormal serum proteins. Primary diagnoses included polycythemia vera, osteoblastic metastasis to the bone, multiple myeloma, disseminated lupus erythematosus, and rheumatoid arthritis. All gave negative serum flocculation reactions except 1 patient with polycythemia vera, who had only hepatosplenomegaly. His liver function test results were within normal limits.

Table IV presents a comparison of Jirgl's flocculation test with other tests used in the differential diagnosis of jaundice. In obstructive jaundice, the serum alkaline phosphatase level is usually above 30 King-Armstrong units,[4] the serum transaminase (SGOT) value seldom exceeds 300 units,[5] the cephalin flocculation test remains within normal limits, and urobilinogen is absent from the urine. The results of these tests and of the serum flocculation reaction are shown for comparison of two groups. It is apparent that the discriminatory value of the Jirgl test, on an over-all basis, is at least as good as that of any of these other tests.

TABLE IV. Comparison of the Jirgl flocculation test and other laboratory tests in jaundiced patients

Diagnostic Category	Jirgl Flocculation Test		Serum Alkaline Phosphatase		Urine Urobilinogen		Serum (SGOT) Transaminase		Cephalin Flocculation	
	Patients Tested	Positive	Patients Tested	Over 30 King-Armstrong Units	Patients Tested	Negative	Patients Tested	Under 300 Units	Patients Tested	Negative or 1 plus
Biliary obstruction	31	27 (87 per cent)	27	23 (85 per cent)	10	8 (80 per cent)	22	22 (100 per cent)	27	21 (78 per cent)
No biliary obstruction	54	6 (11 per cent)	39	8 (21 per cent)	26	4 (15 per cent)	43	33 (77 per cent)	36	6 (17 per cent)
Neoplasm of liver	10	1	9	3	4	1	7	5	7	3
Cirrhosis	21	1	16	0	12	1	17	15	14	2
Hepatitis	10	3	10	4	7	1	10	4	10	0
Miscellaneous	13	1	4	1	3	1	9	9	5	1

Comment

Our results are not quite as striking as those of Jirgl,[1] who reported only 5 per cent false negative reactions and no false positive ones; they are in good agreement with those of Daikos, Mattheou, and Athanasiadou.[2] The "diagnostic efficiency index" which was recently introduced by Maclagan[6] is a simple statistical method to evaluate the efficiency of a test to differentiate one disease from the other, and is calculable by the following formula by percentage:

$$100 - \frac{\text{false positives} + \text{false negatives}}{2}$$

The figure expressed represents only the probability of arriving at a correct diagnosis, if one particular test is used as the sole criterion for a differential diagnosis. When our results in Table IV are examined by this method, they are found to be 88 per cent for Jirgl's test, 82 per cent for alkaline phosphatase, 83 per cent for urinary urobilinogen, 62 per cent for transamine (SGOT), and 81 per cent for cephalin flocculation. These figures indicate that Jirgl's test is as good as alkaline phosphatase or urine urobilinogen determinations in the differentiation of obstructive jaundice.

The mechanism of the positive reaction in this test is still not clear. It may depend on a complex interprotein reaction, as do other flocculation tests.[7] However, our animal experiments suggest that the factor responsible for a positive reaction may be excreted through the biliary tract under normal conditions.[8] This would suggest that it is a physiologic substance which may accumulate in the circulation when the biliary system is occluded.

Although the mechanism of the Jirgl test is unknown, it appears to be different from that of other tests used in the differential diagnosis of jaundice. Since this reaction discriminates relatively well between biliary obstruction and other causes of jaundice, it should be useful in the evaluation of difficult cases when routine tests give equivocal or contradictory results.

Summary

A serum flocculation test for the diagnosis of obstructive jaundice was evaluated in 111 patients and controls. Positive reactions were obtained in 87 per cent of 31 patients with bile duct obstruction and negative reactions in 89 per cent of 54 patients without biliary obstruction. This test appears to be of value in evaluating the status of the hepatobiliary system during jaundice.

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Carcinoma of Breast in Community Hospital

A FIVE-YEAR REVIEW *was made of 78 patients with carcinoma of the breast. The majority of patients were from forty to fifty-nine years old. Seventy-one patients underwent curative procedures. The operability rate was 91 per cent. The absolute five-year survival rate was 53.8 per cent, varying from 90.9 per cent in patients who had a radical mastectomy with the axillary nodes histologically negative to 27.3 per cent in patients with positive axillary nodes.*

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COMMUNITY HOSPITALS care for three quarters of the American people when they require hospitalization. It is apparent that a major share of surgery is being done in such hospitals.

To assay the effects of treatment of carcinoma of the breast in a community hospital it was thought worth while to review the cases admitted to St. Vincent's Hospital of the Borough of Richmond during the years 1950 through 1954 with a diagnosis of carcinoma of the breast. The 78 patients who were seen comprise this report. These patients had not received any previous therapy.

Clinical material

Seventy-three of the 78 patients, 93.7 per cent, presented symptoms of a mass in the breast. Other symptoms were bleeding or discharge from the nipple in 3 patients, a painful breast mass in 4 patients, a mass in the axilla in 1 patient, while in 2 patients the mass was detected by a physical examination. Fifty-one patients were aware of a mass in their breast for three months or less. Four patients stated that a mass was known to be present for over two years, and in 1 patient it was present for seven years.

Forty-three patients had tumors situated in the left breast, while 35 patients had a tumor in the right breast. The upper outer quadrant of the breast was the most common site of predilection for the tumor, noted in 35 of the 78 patients. The tumor was located in the inner quadrants of the breast in 24 patients. It was located centrally in 11 patients, and in 6 patients the tumor was localized to the lower outer quadrant. In 2 patients the mass was so extreme that it completely replaced the breast.

The prognosis of cancer of the breast is directly proportional to the presence or absence of axillary metastasis. In this series 43 patients had axillas that indicated clinically negative results for malignant disease; however, in 5 patients the nodes proved positive on histologic examination. This difference is important to appreciate because if nodes are not cleared pathologically a prognosis should not be given. Table I shows the size of the primary lesion relative to the state of the axillary nodes both clinically and histologically in patients undergoing radical mastectomy. It is of interest to note that some patients whose primary lesions were 1 cm. or less had positive histologic axillary nodes, while in other patients whose lesions were over 10 cm. the axillary nodes were negative. This is further evidence that the size of the lesion by itself should not be the primary consideration as to whether or not patients have operable lesions.

A vexing problem present constantly in patients with a tumor in the breast is the

TABLE I. Size of lesion in patients in relation to nodal involvement determined pathologically

Size of Lesions (Cm.)	Total Number of Patients	Radical Mastectomies Nodes Negative	Radical Mastectomies Nodes Positive
1	7	6	1
2	11	7	2
3	14	10	2
4	11	3	6
5	17	4	10
6	3	1	1
7	8	1	6
8	4	2	2
9	1	1	..
10	2	1	..

extent of the investigation patients should receive preoperatively. Many of the laboratory and radiologic examinations result in a paucity of information that fails to aid the clinician in determining the operability of the lesion. Physicians and surgeons alike are prone to suggest operations for diagnosis and treatment without a proper evaluation of the patient. In this series 38 patients had chest x-ray films, and 1 had positive evidence of metastatic disease. The importance of bone surveys in patients with suspected carcinoma of the breast is evident in this series. Nineteen patients had bone surveys and 4 had evidence of bony metastasis. Routine liver chemistries were not performed in the majority of patients.

The age group in this series ranged from 2 patients in the twenty-to-twenty-nine-age group to 1 patient who was eighty-four years of age. However, the majority of patients were in the fourth and fifth decades of life. Seventy-one patients underwent curative procedures. Radical mastectomies were performed on 62 patients, while a simple curative mastectomy was performed in 9 patients. Two patients had a palliative simple mastectomy, and 3 patients had a local excision of the tumor. Two patients received hormonal therapy because of the advanced stage of their disease.

The operability rate in this series was 91 per cent, 71 of 78 patients. If this clinic adhered rigidly to criteria, as outlined by Haagensen and Stout,[1-4] the operability rate would have been 80 per cent which is within the range of the majority of clinics reporting cases. The triple biopsy technic was not performed in this series. If this procedure, which is espoused by Haagensen and Stout, had been performed, the operability rate would probably have been from 50 to 60 per cent.

TABLE II. Ages of patients with curative surgery

Ages (Years)	Number of Patients	Survived (Per Cent)
20 to 29	2	...
30 to 39	6	83.3
40 to 49	20	70.0
50 to 59	18	61.1
60 to 69	14	42.8
70 to 79	10	50.0
80 to 89	1	100.0

The types of tumors seen in this series were carcinoma simplex in 30 patients and scirrhous carcinoma in 26 patients. Eight patients had a medullary type of carcinoma, and 6 patients had a duct-cell carcinoma. Three patients had a mucinous-cell carcinoma, and 3 patients had a carcinoma in situ. One patient had an anaplastic tumor, and the last an adenocarcinoma. The follow-up in this series is 98.7 per cent, with 1 patient lost to follow-up, and she is presumed dead from cancer of the breast.

Results

Of the patients who received primary treatment, 59.1 per cent were alive after a five-year period. The absolute five-year survival rate in this group of patients was 53.8 per cent. Thirty-five of 62 patients (56.4 per cent) had a five-year survival rate following radical mastectomy, while after a simple mastectomy and radiation therapy 7 of 9 patients or 77.7 per cent survived. The number of patients who had a simple mastectomy were too few in number to compare statistically with the radical mastectomy group. There were no five-year survivals in patients undergoing palliative procedures.

Table II is of interest in that it shows that the five-year survival rates were not influenced by the age of the patient, as reported by many clinics.[5-7] Table III notes the time of death after a curative radical mastectomy. This excludes the 1 postoperative death. Twenty-three patients (57.5 per

TABLE III. Time of deaths following radical mastectomy (excluding 1 death postoperatively)

Months of Survival	Number of Patients	
3	2	57.5 per cent
5	3	
9	2	
14	3	
15	1	
16	3	
18	1	
20	1	
22	2	
24	2	
30	1	
36	2	
39	2	
42	1	
48	1	
54	2	
56	3	
57	1	
70	1	
78	2	
84	1	
91	1	
104	1	

cent) were dead within thirty-six months of the operation, while 1 patient survived eight years and eight months and died of metastatic disease.

The times of death in 2 patients after a curative simple mastectomy were three years, two months and one year, nine months. Patients who had a palliative mastectomy survived one year, and patients who had hormonal therapy survived two months, and eleven months, respectively.

In 8 patients the disease extended to a degree that if Haagensen and Stout's[1-4] criteria of inoperability had been followed, no operation would have been done, and these patients would have received other modes of therapy. Table IV is a composite study of patients who fell within these criteria of inoperability. It shows the age of the patient, the reason for being in this category, the clinical and pathologic state of the axillary nodes, the type of operative procedure, and the survival rates. It must be reiterated that not all clinics adhere to Haagensen's criteria of inoperability. Seven of these patients underwent a radical mastectomy, and none survived a five-year period. These 7 patients who had radical mastectomies survived the following periods of time: three, five, nine, fifteen, seventeen, and twenty-two months and three and one-half years.

It is well known that during surgery, manipulations result in emboli of tumor cells into the general circulation, causing generalized metastatic implants and hastening the progression of the disease. Haagensen and Stout[1-4] state unequivocally that if clinics are to attain the best results, their criteria must be followed. The policy of operating on all patients without considering the stage of their disease is decried.

Comment

To elucidate the factors in patients who survived five years, the following information is available:

TABLE IV. Haagensen's criteria not adhered to

Patient's Age (Years)	Reason	Axillary Nodes		Operation	Length of Survival
		Clinically	Pathologically		
58	Far-advanced local disease	Positive	Positive	Radical	5 months
72	Local disease	Positive	. . .	Simple	3 years, 4 months
79	Bone metastasis	Positive	Negative	Radical	22 months
57	Local disease	Positive	Positive	Radical	9 months
50	Far-advanced local disease	Positive	Positive	Radical	$3^1/_2$ years
29	Inflammatory disease	Positive	Positive	Radical	17 months
65	Bone metastasis	Positive	Positive	Radical	15 months
56	Far-advanced disease	Positive	Positive	Radical	3 months

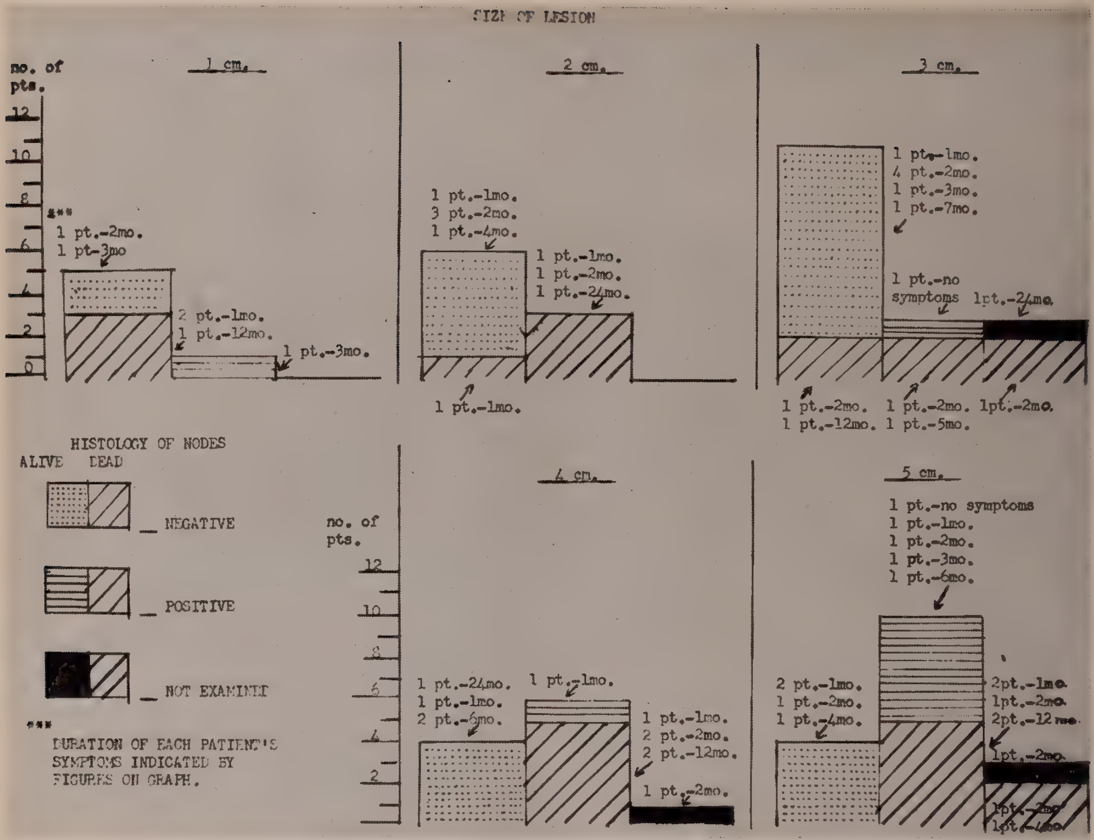

FIGURE 1. Evaluation of lesions (1, 2, 3, 4, and 5 cm. in size).

THE RELATION OF THE SIZE OF THE LESION TO SURVIVORS. Thirty-two patients had lesions measuring 3 cm. or less and 19 of these patients survived (59.3 per cent). Thirty-one patients had lesions measuring from 4 to 6 cm. with 17 survivors or 54.8 per cent. Fifteen patients had lesions from 6 to 10 cm., and 5 patients survived (33.3 per cent).

THE RELATION OF DURATION OF TUMOR MASS TO SURVIVORS. In the 42 patients who survived five years, a breast mass of less than three months duration was present in 29 patients (66.7 per cent). Eight patients had a mass between four and eight months, and 2 patients had a mass for one year. Two patients had masses for two years, and the last patient had a mass for four years.

THE RELATION OF THE SIZE OF THE LESION, DURATION OF SYMPTOMS, AND THE PRESENCE OR ABSENCE OF METASTASIS TO THE AXILLA TO THE FIVE-YEAR SURVIVALS. Figures 1 and 2 show that 9 of the 42 patients had positive axillary nodes. The size of the lesion in these 9 patients and the duration of symptoms were as follows: (1) One patient's lesion measured 1 cm. in size, and this tumor was known to be present for three months; (2) another patient had a tumor 3 cm. in size, and this was detected by a physical examination; (3) the third patient's tumor was 4 cm. in size, present for one month; (4) 5 patients had lesions 5 cm. in size and their symptomatology was of one, two, three, and six months duration, while in 1 of these patients the tumor was undetected until the patient was examined by a physician for other reasons; and (5) one patient's lesion measured 7 cm., present for one month.

Figures 1 and 2 also reveal that in 32 patients the lesions measured less than 3 cm., and 25 of these patients had axillary nodes that were negative, with a cure rate of 68 per cent, compared with 7 patients with positive

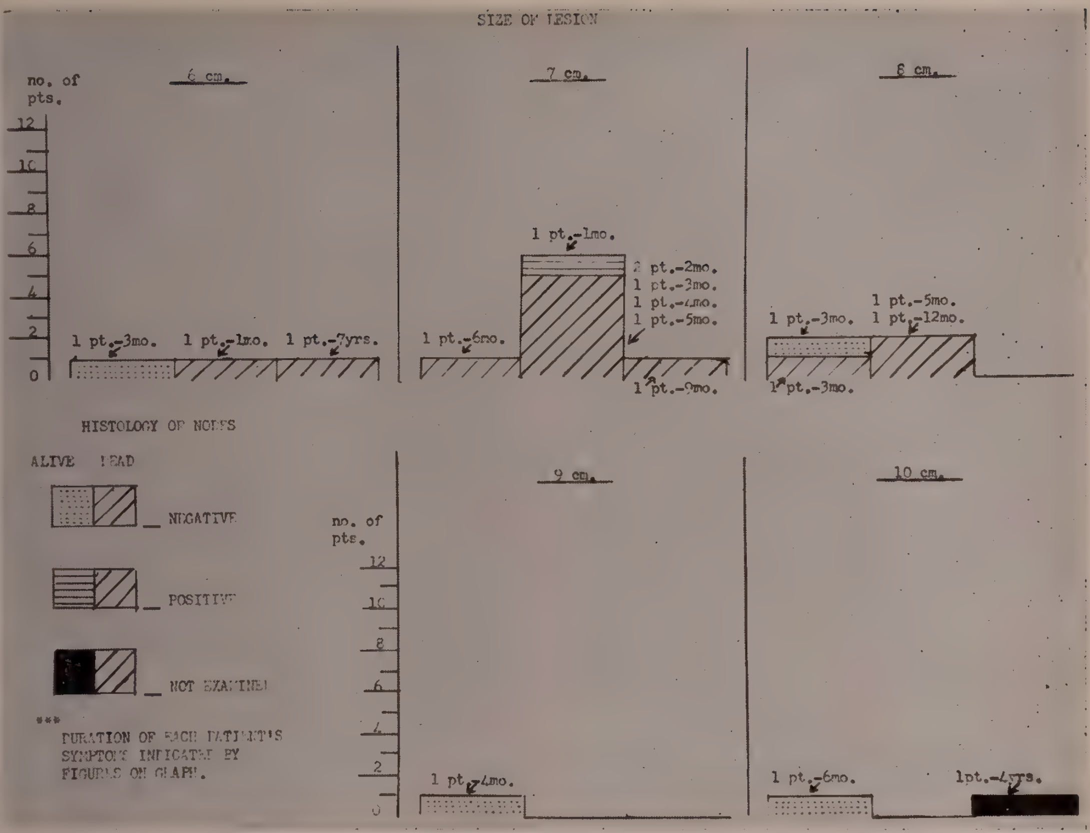

FIGURE 2. Evaluation of lesions (6, 7, 8, 9, and 10 cm. in size).

nodes who had a 28.5 per cent survival rate for five years or more. Thirty-one patients had lesions of from 4 to 6 cm. In this group 14 patients had negative axillary nodes and the survival rate was 78.5 per cent compared with the 17 patients with positive nodes who had 6 survivors or 35.2 per cent. Fifteen patients had lesions from 7 to 10 cm. in size, and 8 had positive nodes with a survival rate of 12.5 per cent, compared with a survival rate of 57.1 per cent in 7 patients whose axillary nodes were negative.

THE LOCATION AND TYPE OF TUMOR AND THE CONDITION OF THE AXILLARY NODES IN RELATION TO SURVIVALS. Some reports state that the location of the tumor is an important factor in the five-year survival rates.[8] It was thought important for us to investigate this facet of the problem. The results show that lesions in the outer quadrant of the breast had a slightly better prognosis than lesions in the inner quadrant, namely, 58.1 versus 56.8 per cent. It is thought that lesions in the inner quadrant metastasize via the internal mammary chain: hence, the controversy between the extended radical mastectomy as proposed by Urban,[9] Wangensteen,[10] and Urban and Baker[11] versus the conservative management outlined by McWhirter,[12,13] Haagensen,[4] and Garland.[14] The 2 patients with an inflammatory type of carcinoma had lesions that completely encompassed the breast. An investigation was made as to what histologic type of tumor carried the best prognosis. In the commonly seen tumors in this series, namely, the carcinoma simplex and the scirrhous, the five-year survival rates were 56.9 per cent with the carcinoma simplex, while the scirrhous type had a 42.3 per cent five-year survival rate. As is usually reported in most series,[15-18] duct-cell carcinoma, mucinous cell carcinoma, and carcinoma in situ carry the best prognosis. In this series the

6 patients with duct-cell carcinoma all survived five years, and the patients with the anaplastic and carcinoma in situ survived a five-year period.

A COMPOSITE STUDY OF THE IMPORTANCE OF THE AXILLARY NODES TO SURVIVORS:

1. In the 22 patients undergoing radical mastectomy with the axillary nodes both clinically and histologically negative, the five-year survival rate was 90.9 per cent or 20 patients.
2. In 11 patients who had radical mastectomies and in whom the axillary nodes were clinically negative, but on pathologic examination were positive, the five-year survival rate was 27.3 per cent or 3 survivors.
3. In 20 patients undergoing radical mastectomy, with the axillary nodes both clinically and histologically positive for metastatic disease, the five-year survival rate was 30 per cent or 6 survivors.
4. In 10 patients with the axillary nodes clinically positive but on histologic examination negative, the five-year survival rate was 70 per cent or 7 patients.
5. In 7 patients undergoing curative simple mastectomy, with the axillary nodes clinically negative, the five-year survival rate was 85.7 per cent or 6 patients.
6. The 1 patient undergoing a curative simple mastectomy with axillary nodes clinically positive did not survive for five years.
7. There were no survivors following other types of therapy.

It is evident that the most important prognostic factor is whether or not the nodes in the axilla are positive or negative for metastatic disease. This has been reported in all series[9,11,17,19,20] reporting on carcinoma of the breast. The size of the tumor and the duration of the disease are of secondary importance.

The minimum follow-up in this series was seven years, and the maximum was eleven years. Seven patients who survived for five years after a curative procedure died subsequently. The following information is available about these patients:

One patient survived six and one-half years and was clinically free of disease at the time of her death. Another patient survived seven years, eight months, and at autopsy no evidence of disease was seen. The third patient survived six and one-half years and at autopsy was free of disease. The fourth patient survived six years, eight months, and died of an intercurrent disease; at autopsy no evidence of metastatic carcinoma was found. In the last 2 patients, 1 survived five years, ten months and at autopsy no evidence of disease was present, while the other patient survived seven years, ten months and showed no evidence of carcinoma at autopsy.

It is evident that one should not speak of five-year cures, since some patients will die in subsequent years of their disease process. From all the previously mentioned data it is obvious that our knowledge of the factors that cause some tumors to grow with extreme rapidity and others very slowly is meager. Perhaps the immunologic aspects discussed recently by Crile[21,22] should be evaluated further. I believe that Tables I through IV also substantiate the theory of biologic predeterminism and host resistance as some biologic factor finally overwhelms the host and then the disease becomes widespread, which has been espoused by MacDonald,[18] Shimkin,[6] Shimkin, Griswold, and Cutler,[23] and Crile.[22] Efforts should be directed to determine if the biologic activity of the tumor cell could be forecast from the beginning rather than in a retrospective fashion as is done now, since we determine this factor by the clinical course of the patient.

Summary

A comparatively small series of cases (78) has been reported with a follow-up of 98 per cent, representing a five-year study of carcinoma of the breast seen in a community hospital. The ages are the usual distribution one sees in this disease. The usual measurements were made detailing the size of the lesion, the position of the tumor, the duration of symptoms, and the presence or absence of axillary nodes both clinically and pathologically. It was shown that the common denominator in regard to prognosis was the presence or absence of pathologically diseased axillary nodes. In patients who had a radical mastectomy with the axillary nodes histologically negative, the survival rate was 90.9 per cent, while the survival rate in patients with positive axillary nodes

was 27.3 per cent. The importance of Haagensen and Stout's[3] criteria of inoperability has been discussed. The importance of biologic predeterminism and host resistance has been noted. A series of this type is important to report, since it points up that good cancer surgery is being performed in the community hospitals in this country.

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The doctors of the U.S.A. are being asked to send their medical journals—after they have read them—to colleagues overseas (Asia, Latin America, and Africa) who wish to have access to current medical literature but, either because of currency regulations or actual cost involved, cannot themselves subscribe to medical periodicals. We can supply you with the name, address, and medical specialty of doctors in these areas who would be happy to receive these much wanted journals, particularly specialty journals.

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Use of Oral Pregnancy Test and Effect on Nonpregnant Endometrium

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THE SEARCH FOR an easy, inexpensive, and yet dependable nonbiologic test for early pregnancy continues. In recent years there has been great interest in tests based on the response of the endometrium to the administration of a progestational hormone. It has been well established that in the nonpregnant woman the endometrium, adequately primed with estrogen, will shed on the administration of progesterone, whereas in the pregnant woman bleeding will not occur. Many different progesterone compounds have been investigated for use in pregnancy testing. The newest of these agents are constituted of both progesterone and estrogen because it has been established that with this combination the incidence of false-positive results in patients with amenorrhea is smaller.

In this article we present a preliminary report of our experience with one of these compounds, an oral hormone combination agent (Pro-Duosterone),* used in the PD test, which contains 50 mg. of anhydrohydroxyprogesterone and 0.03 mg. of ethinyl estradiol per tablet. The purposes of our study of this drug were twofold: (1) to confirm the results reported by others[1-5] regarding its merits in pregnancy determination, and (2) to obtain data as to its effect on the endometrium in various states.

Material and methods

One hundred eighty-five private patients were included in the study. They were grouped according to the following categories:

GROUP 1: CONTROLS. Before the oral hormone dosage was started, each of 12 normal patients was proved by endometrial biopsy, basal body temperature chart, and results of the fern test to be ovulating. These patients took one tablet three times a day from day 5 to day 25 of their cycles. On day 26 or day 27 another endometrial biopsy was performed in each subject, and the results were compared with those of the first.

GROUP 2: DELAYED MENSTRUAL PERIOD. After biopsies disclosed their endometria to be normal, 15 regularly ovulating patients were given four tablets daily, in divided doses, from day 20 to day 40. The results of endometrial biopsies taken immediately post-therapy were compared with those of the pretherapy biopsies.

GROUP 3: SECONDARY AMENORRHEA. Twenty patients with varying degrees of secondary amenorrhea (menses occurring irregularly every sixty to ninety days) were given four tablets daily for three days. Those who failed to have withdrawal bleeding were primed with 0.05 mg. of ethinyl estradiol three times a day for ten days and then given one oral hormone tablet four times a day for three days. After the dosage was completed, endometrial biopsies were taken within one or two days.

GROUP 4: PREGNANCY. One hundred fifty-nine patients, 22 of whom had histories of irregular cycles varying from twenty-six to forty-five days in length, whose expected menstrual periods were delayed from two to ten days were given one oral hormone tablet four times a day for three days. Two weeks after the expected date of menstruation, biologic tests for pregnancy were done on all the patients who did not bleed. If these tests produced negative results, the patients were given 0.05 mg. of ethinyl estradiol three times a day for ten days, then one oral hormone tablet four times a day for three days.

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* The Pro-Duosterone tablets used in the study described in this article were kindly supplied by Andre L. Courtin, M.D., of the Roussel Corporation, New York City.

Results

GROUP 1: CONTROL GROUP. No instances of break-through bleeding in any of the 12 women were noted during the oral hormone therapy. Post-therapy biopsies revealed atypical secretory endometria in all subjects. The stroma was advanced over the glands, with a mild predecidual reaction. An increase in stromal vascularity as well as mild edema were observed (Fig. 1). Menstruation occurred two to four days after the cessation of therapy. Quantitatively and qualitatively, the flow was normal. The basal body temperature was elevated during the medication interval, and no typical fern formations

A STUDY WAS *made of an estrogen-progesterone combination used in the Pro-Duosterone (PD) oral pregnancy test on 185 patients. In 15 normal patients, menstruation was delayed when the hormone combination was given from day 20 to day 40 of the cycle. Nineteen of 20 patients with secondary amenorrhea showed withdrawal bleeding after not more than two courses of treatment. One hundred and twelve of 159 patients given the hormone combination as a pregnancy test failed to bleed, and pregnancy was subsequently confirmed by biologic tests; 21 patients had withdrawal bleeding; and of the remaining 26 patients who had negative biologic test results, 22 bled after a second course of the drug following estrogen priming, and 4 were found to be pregnant. Endometrial changes follow the use of the drug in nonpregnant patients. These changes revert to normal in following cycles. Slight nausea in 8 patients was the only side-effect.*

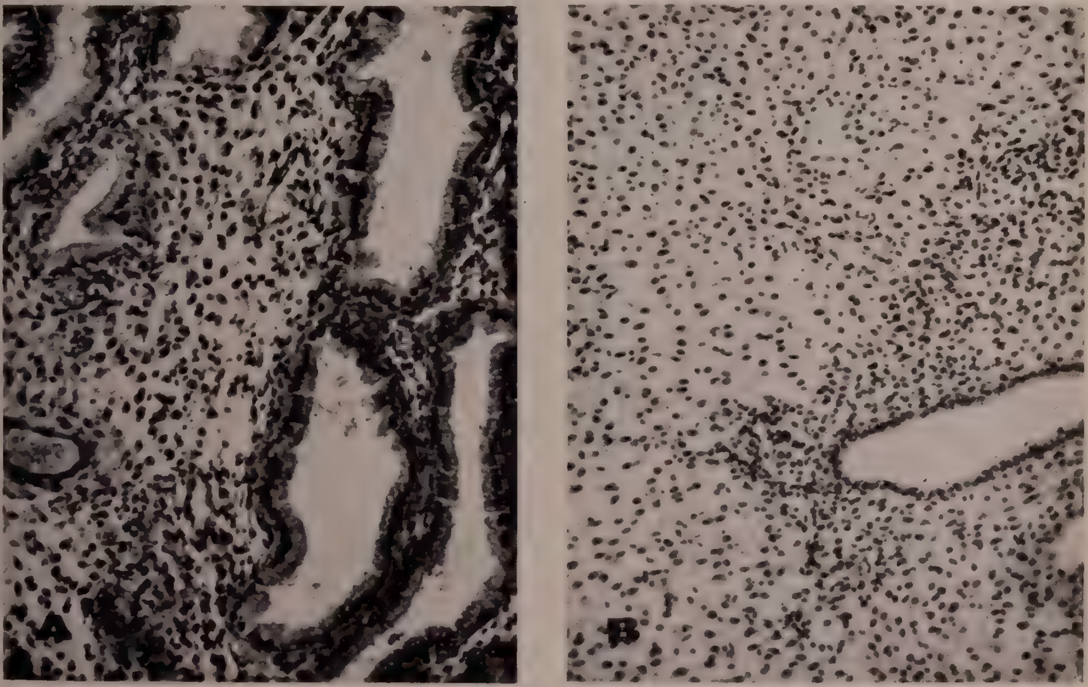

FIGURE 1. (A) Photomicrograph of a premenstrual endometrium showing typical ovulatory glands. (B) Post-therapy endometrium of same patient after three tablets of oral hormone combination daily for twenty days. The stroma is pseudodecidual, and the glands are sparse with no evidence of secretion in the lumen and periglandular round cell infiltration.

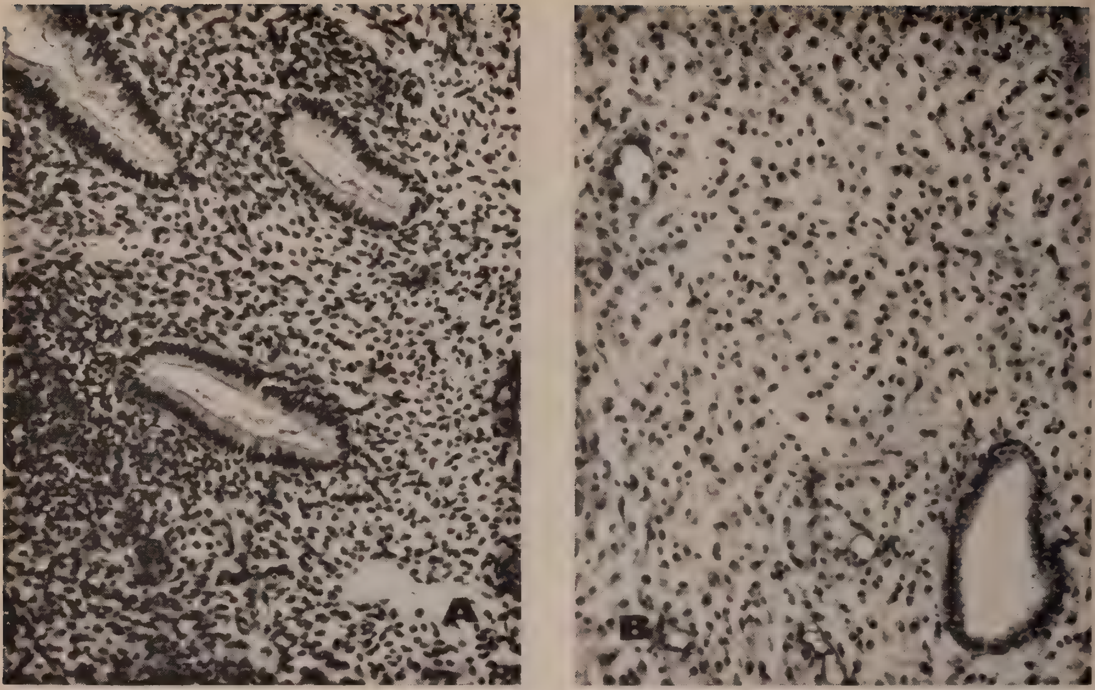

FIGURE 2. (A) Normal pretherapy ovulating endometrium. (B) Post-therapy endometrium of same patient after four tablets of oral hormone combination daily for twenty days. The stroma is pseudodecidual, and the glands are sparse with no evidence of secretion in the lumen and periglandular round cell infiltration.

were observed following the third day of therapy.

Group 2: delayed menstrual period. During the administration of the oral hormone, 4 of the 15 patients had breakthrough bleeding after sixteen days of therapy, 2 patients on day 36, and 2 on day 38. Eleven patients had menstrual bleeding two to four days after the oral hormone administration was stopped (days 42 to 44). The basal body temperature was elevated above 98 F. throughout the period of therapy. Random endometrial biopsies taken on days 38 to 44 showed, in all cases studied, sparse glands without cellular activity or luminal secretion. The stroma was characterized by very definite advancement to a mild pseudodecidual type (Fig. 2). Two to three days after the dosage was stopped, 11 patients had what they considered to be normal periods. The subsequent menses were normal.

Group 3: secondary amenorrhea. Of the 20 patients in this group, 14 had withdrawal bleeding two to four days after the cessation of therapy. The other 6 were given additional estrogen and the oral hormone combination, as described previously. All but 1 responded with bleeding. The patient who failed to bleed had had a bilateral subtotal resection of the ovaries and manifested symptoms similar to those of the menopause. Endometrial biopsies taken from a random sampling of the 14 patients disclosed a progesterone effect, namely, secretory glandular activity and a mild predecidual stromal response.

Group 4: pregnancy. Twenty-one patients had menstrual bleeding two to five days after the cessation of therapy. Withdrawal bleeding was not seen in 112 of the 159 patients in this group. These 112 subjects all had positive results on biologic pregnancy tests subsequently. The 26 patients who did not bleed after the oral hormone administration was stopped (22 of whom had histories of irregular cycles, as mentioned before) all had negative findings on biologic tests. These patients were primed with ethinyl estradiol, and the oral hormone administration was repeated, as described. Twenty-two patients had withdrawal bleeding within ten days after the completion of the second course of treatment; the remaining 4 were found to be pregnant. The PD test was thus accurate in 84.1 per cent of the patients in this group.

Side-effects

Eight patients in the series complained of nausea but of so slight a degree as not to warrant interrupting the hormone administration. Eleven of the 32 patients who took ethinyl estradiol alone after a course of the oral hormone (6 patients in Group 3 and 26 in Group 4) also complained of nausea, but not to the extent that discontinuation of the drug was indicated. Six patients in Groups 1 and 2 complained of slight breast engorgement during the treatment. No allergic reaction was noted in any patient.

Comment

Our findings confirm previous reports of the value of the PD test in the determination of early pregnancy, and we recommend its use. On the basis of the results presented here, as well as those of other investigators, this oral hormone combination appears to have the proper estrogen-to-progesterone ratio to cause withdrawal bleeding in the majority of patients whose menstrual cycles have been fairly regular. The biologic tests, while accurate when giving positive results, yield false-negative results in about 10 per cent of patients. The sources of error in biologic tests have been amply reviewed.[1-4] Some of these errors are related to the type of sample used (urine or serum), the species of the test animal, the technic of the injection, medication taken concurrently by the patient, and a false interpretation of positive findings in the test.

The use of this oral hormone combination in pregnancy testing eliminates many of these sources of error. It can be assumed reasonably that a patient who has menstruated regularly is pregnant if withdrawal bleeding does not occur after the third day of this therapy. In the series presented, the 27 patients who required additional estrogen priming before they responded to the PD test (5 in Group 3 and 22 in Group 4) all had histories indicative of ovarian dysfunction; in these patients the cycles varied in length from twenty-six to forty-five days.

The use of the oral hormone combination in pregnancy testing makes unnecessary the delay of two weeks after the expected date of menstruation that is required before a biologic test is likely to give an accurate result.

In some instances, the PD test may fail to bring on withdrawal bleeding. These instances include: (1) the patient who recently has had a spontaneous abortion, (2) the patient with a retained dead fetus, (3) the patient with persistent corpus luteum activity, (4) the patient taking progestin therapy, and (5) the patient with an irregular cycle, as exemplified by the 22 in Group 4 who bled after estrogen priming and repeated oral hormone dosage. Any of these factors may be a source of error. In patients who fail to bleed and about whom there is doubt, biologic tests may be indicated for the accurate evaluation of their status.

The effect of the oral hormone on the endometrium, as shown in the patients in Groups 1 and 2, did not appear to be deleterious. Cycles after the hormone combination administration was halted appeared to be normal. In most of the patients in whom menstruation was delayed for from fourteen to sixteen days by the oral treatment (11 of the 15 subjects in Group 2), the endometrium after treatment was well preserved and manifested pseudodecidual reaction.

Fourteen of the 20 patients with secondary amenorrhea had withdrawal bleeding following the third day of the drug's administration. Five responded after additional exogenous estrogen priming. The 1 patient who did not respond had had a bilateral subtotal resection of the ovaries and evidently had very low levels of endogenous estrogen. This finding would indicate that in a very poorly primed endometrium (as in severe ovarian dysfunction) more estrogen than that supplied by the oral hormone is needed to effect withdrawal bleeding.

Summary

1. Of 159 women given an oral hormone combination agent (Pro-Duosterone) in a

direct pregnancy test, 112 failed to bleed, and pregnancy was subsequently confirmed by biologic tests. Twenty-one patients did have withdrawal bleeding following the medication. Of the remaining 26 patients who had negative biologic test results 22 bled after a second course of the drug following estrogen priming, and 4 were found to be pregnant.

2. Nineteen of 20 patients with secondary amenorrhea showed withdrawal bleeding after not more than two courses of treatment. The patient who failed to respond evidently had a very low endogenous estrogen level.

3. In 15 normal patients, menstruation was delayed when the hormone combination was given from day 20 to day 40 of the cycle.

4. The oral hormone combination causes an elevation of the basal body temperature.

5. Endometrial changes follow the use of the drug in nonpregnant patients. These changes revert to normal in following cycles.

6. The hormone combination caused no major side-effects under the conditions of the study.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963,* and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Memorial Hospital for
Cancer and Allied Diseases
New York City
October 13, 1961

Conducted by RULON W. RAWSON, M.D.

Discussed by THOMAS P. ALMY, M.D., and
ALLYN LEY, M.D.

Liver Disease, Hematologic Disorder, and Infection

Case history

Charles La Monte, M.D.: A sixty-one-year-old Brazilian woman of Italian descent was first seen at Memorial Hospital for weakness of about four months duration and was followed subsequently in the clinic and in the hospital until her death three years later.

She had been studied at another hospital three months prior to her admission because of weakness and pallor of a few weeks duration. At that hospital she was found to have an enlarged liver and an enlarged spleen. The hemoglobin was 5 Gm. per 100 ml., and the white cell count was 1,000. The red blood cells showed polychromatophilia and many target cell forms. Osmotic fragility tests showed initial hemolysis at 0.62 per cent and complete hemolysis at 0.34 per cent. Direct and indirect Coombs tests produced negative results as did agglutination tests for auto- and iso-antibodies. Tests for hemorrhagic tendency showed findings within normal limits. Repeated bone marrow aspirations showed megakaryocytes and platelets, numerous smudge cells, and one report of 51 per cent normoblasts. A liver biopsy showed fatty metamorphosis and glycogenation of the nuclei. Persistent anemia with hemoglobin as low as 4.5 Gm. per 100 ml. required transfusions. Because of a positive serologic test result for lues, 47 million units of penicillin were administered. She was discharged three weeks before coming to Memorial Hospital with a diagnosis of chronic lymphocytic leukemia in an aleukemic phase.

When the patient was studied at this hospital, it was ascertained that there was no family history of anemia, no history of exposure to halogenated hydrocarbons, no alcoholic intake, no treatment with any drug or medication prior to the present illness, and no ingestion of fava beans. A physical examination disclosed a well-developed, pale, white woman weighing 146 pounds. The vital signs were unremarkable. There were no spider angiomas on the skin and no palmar erythema; the tongue was well papillated. The heart was not enlarged, but there was a Grade II precordial systolic murmur. The lungs were clear. The liver was firm, nontender, and palpable 3 fingerbreadths below the costal margin. The spleen was hard, thick, nontender, and extended 4 fingerbreadths below the umbilicus and medially to the midline. The extremities were free of edema, cyanosis, or clubbing. A few shotty lymph nodes were felt in both inguinal areas. A neurologic examination was unrevealing.

On admission the hemoglobin was 6.4 Gm. per 100 ml.; the red blood cell count 2.3 million; hematocrit 21; and the white blood cell count 4,000 with 54 per cent neutrophils, 43 per cent lymphocytes, 2 per cent basophils, and 1 per cent monocytes. The platelet count was 112,700, and reticulocytes were 7.5 per cent. Tests for hemorrhagic tendency showed findings within normal limits. The blood sugar was 105 mg., urea nitrogen 13 mg., cholesterol 116 mg. with 34 mg. esterified, and serum bilirubin 2.65 mg. per 100 ml. The urinary urobilinogen was 0.28 Ehrlich units; the sulfobromophthalein sodium (Bromsulphalein) retention was 7 per cent. The thymol turbidity was 3.3 units, alkaline phosphatase 2.5 units, and cephalin flocculation 4 plus. The total protein was 5.7 Gm. per 100 ml. with 3.4 Gm. albumin. A glucose tolerance test was of the diabetic type. A direct Coombs test produced positive findings, but negative results were obtained by the indirect technic using trypsin-treated cells. A Mazzini test gave a 4 plus reaction, but complement fixation tests for lues showed negative findings. The osmotic fragility was normal. A cold agglutinin test gave negative results, and a sickle-cell preparation did also. Electrocardiographic studies revealed normal findings. Roentgenographic studies confirmed the presence of an enlarged spleen.

The etiologic background of the patient's anemia was investigated. Several bone marrow aspirations revealed erythroid hyperplasia at the normoblast level and slight lymphocytosis. The stools showed intermittently positive guaiac test results. A gastric aspiration contained no free acid but also showed positive guaiac test results. Roentgenographic studies of the upper and lower portions of the gastrointestinal tract revealed no intrinsic lesion. A bruit was heard over the spleen by two observers, but most other observers questioned whether the bruit were not transmitted. A therapeutic trial of vitamin B_{12} 15 micrograms intramuscularly daily for one week did not produce an elevation of hemoglobin or reticulocytes. Transfusions were given to raise the hemoglobin to normal levels. When this was achieved, corticoids were administered. On cortisone 50 mg. twice daily, continued hemolysis was reflected by a fall in the hemoglobin to 4.8 Gm. per 100 ml. and by twenty-four-hour urinary urobilinogen levels of between 40 and 80 mg. (Normal is 3 mg.). On cortisone 100 mg. twice daily, the hematologic status improved, so that the hemogram was normal three days after the steroids were discontinued and the ACTH medication was begun. The hemoglobin was 14 Gm. per 100 ml.; red blood cell count 4.3 million; hematocrit 40; and the white blood cell count 4,300 with 81 per cent neutrophils, 17 per cent lymphocytes, and 2 per cent monocytes. Progressively diminishing doses of ACTH were given for four weeks. During the first week of treatment she developed a felon of the right thumb. This was incised, and hemolytic Staphylococcus aureus was cultured. Despite x-ray changes consistent with osteomyelitis, the finger infection gradually cleared. On discharge, after four and one-half months in the hospital, the hemoglobin was 13.3 Gm. per 100 ml. The discharge diagnosis was acquired hemolytic anemia.

She was readmitted six weeks later because the hemoglobin level had declined progressively to 5.3 Gm. per 100 ml. despite the institution of cortisone therapy on an outpatient basis. A liver biopsy performed in the clinic had shown considerable fatty metamorphosis. On readmission the patient was icteric. The spleen was 18 cm. below the left costal margin. The liver was 8 cm. below the right costal margin. There was no ascites, and otherwise the physical examination was unchanged from previous observations. In addition to anemia, laboratory tests of liver function gave abnormal values, such as serum bilirubin 4.3 mg. per 100 ml., cholesterol 97 mg. per 100 ml. with 33 mg. esterified, alkaline phosphatase 11.5 units, thymol turbidity 5.2 units, cephalin flocculation 4 plus, total protein 5.8 Gm. per 100 ml. with 3.9 Gm. albumin. She was treated with transfusion, cortisone, and later ACTH. The hemoglobin rose to 11.9 Gm. per 100 ml., the white blood cell count to 4,600 with 29 per cent lymphocytes, reticulocytes were 5.8 per cent, and the platelet count was 121,000. Splenectomy was performed four weeks after the patient's admission. One week later, without postoperative transfusions, the hemoglobin was 16.7 Gm. per 100 ml., white cell count 10,600 with 15 per cent lymphocytes, reticulocytes 1.3 per cent, and platelets 418,000.

A histopathologic study of the spleen showed evidence of acquired hemolytic anemia. There was no evidence of chronic splenic vein hypertension. There was no positive evidence on which to base a diagnosis of chronic lymphatic leukemia, nor could this diagnosis be excluded. The patient was discharged ten days after the splenectomy. Her postoperative course had been uneventful.

She remained in good health for about a month, but then developed anorexia, nausea, fever, and deep jaundice. The abdomen was distended and tympanitic. Rales were heard at the base of the left lung. The liver was palpable 4 to 5 fingerbreadths below the right costal margin. The hemogram remained unchanged except for a lymphocytosis of 57 per cent. The fasting blood sugar was 92 mg., urea nitrogen 10 mg., and total serum bilirubin 15.2 mg. per 100 ml., with 12 mg. direct, alkaline phosphatase 15.2 units, thymol turbidity 11.1 units, cephalin flocculation 4 plus, and total protein 7.6 Gm. per 100 ml. with 3.1 Gm. albumin. The total cholesterol had risen to 234 mg. with 169 mg. esterified. The direct Coombs test still showed positive results, but the indirect reaction was negative as was the reaction with trypsinized cells. Over a three-month period, on a regimen of bed rest and supportive measures, the symptoms abated, icterus diminished, and liver function tests gradually returned to normal values. At the time of the patient's discharge, the thymol turbidity was still 9 units and the globulins 4 Gm. per 100 ml.

She was readmitted two months later because of ascites. Her physical and laboratory status were unchanged. She was discharged following paracentesis.

Ten months later she had a single episode of hematemesis. She had been maintained during this interval with a normal hemoglobin and platelet count. Leukocytosis between 11,000 and 36,000 with an absolute lymphocytosis persisted during the year. On admission, she was not in shock, since the episode of hematemesis had been minor. Esophagoscopy and an esophagogram failed to disclose the source of the bleeding. An upper gastrointestinal series showed a deformity of the duodenum, but this could not be demonstrated on a second examination. The sulfobromophthalein sodium retention was 26 per cent. The Coombs test showed positive results by the direct technic only. The Mazzini test reverted to negative findings. The aspiration of sternal marrow showed moderate mature lymphocytosis, normal hematopoiesis, and normal megakaryocytes.

During this fifth hospital admission, she developed further ascites, edema of both legs, palmar erythema, and spider angiomata. She lost weight. The ascites responded to paracentesis and diuretics supplemented by ion-exchange resins. She was discharged after five weeks in the hospital.

Six months later she was readmitted for the sixth and last time because of progressive jaundice, progressive liver enlargement, and fluid retention. The hemoglobin was in the range of 8 to 10 Gm. per 100 ml., the white blood cell count 30,000 with a marked shift to the left, reticulocytes above 10 per cent, and platelets 160,000. The sulfobromophthalein sodium retention was 39 per cent, serum bilirubin 9.4 mg. per 100 ml., thymol turbidity 16 units, and total protein 8 Gm. per 100 ml. with 4.5 Gm. globulin and 3.5 albumin.

Steroid therapy resulted in an improvement of the jaundice, but the problem of fluid retention was aggravated. She responded temporarily to intravenous glucose, tetracycline, and a high carbohydrate, low protein diet. Five weeks after admission she developed a urinary tract infection which was treated with Gantrisin. Two days later she lapsed into an hepatic coma from which she was never roused. The aspiration of gastric contents yielded coffee ground material. The hemoglobin was 10 Gm. per 100 ml., and the blood urea nitrogen was 76 mg. per 100 ml. The following day she developed melena, and the hemoglobin fell to 7.8 Gm. per 100 ml. The prothrombin time was 26 seconds. Transfusions were administered. Tetracycline was discontinued, and penicillin and streptomycin were given instead. However, she expired the following day, three years and three months after her first admission.

Clinical discussion

Thomas P. Almy, M.D.*: There are

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one or two items of information I would like to have if they are available. First, did she have any clinical history of syphilis?

Dr. La Monte: There is no comment on this point in the chart.

Dr. Almy: Do we have a uric acid determination anywhere in the record?

Dr. La Monte: There is no report of any.

Dr. Almy: When she was admitted about a month after the splenectomy with jaundice, anorexia, and fever, was her liver tender?

Dr. La Monte: This point is not recorded.

Dr. Almy: Let me see if I can get any useful information from the x-ray studies.

Ruth Snyder, M.D.: We have a series of chest films taken during her six admissions. All of them show moderate cardiac enlargement and a little prominence of the hilar markings, particularly during the last admission. A film taken during her last admission shows a slight pleural effusion. We never were able to demonstrate esophageal varices, but one of the films shows some degree of posterior displacement of the esophagus which might lead one to suspect a mediastinal enlargement. Films of the abdomen show a very striking degree of splenic enlargement. The spleen extends below the iliac crest. In a pyelogram the left kidney is seen to be pushed to the right of the midline. Even the outline of the aorta is deviated to the right at the level of the renal arteries and then returns to a normal position in the pelvis.

Dr. Almy: Isn't that unusual—for a spleen to push the kidney right across the midline?

Dr. Snyder: Not necessarily; we see it occasionally. This is a very large spleen. Most of them push nearby structures downward, but medial displacement can occur as well. There was some mention of an infection of the thumb. An x-ray film taken at this time shows a little erosion of the terminal tuft and some soft tissue swelling. I believe this is secondary bone involvement.

The most interesting part of the roentgenographic studies lies in the gastrointestinal series. The stomach is displaced anteriorly by the large liver, and the cardia is displaced downward; it is almost a transverse stomach. There is a tapered narrowing of the gastric antrum in most of these films. It varies in width, so that it is not fixed, but its relative contours remain similar. On some of the films there is a suggestion of tiny ulcerations or erosions. One cannot be sure, but it is suggestive. I do not believe this is a normal stomach. There may be an ulcerative gastritis; there may even be an infiltrative tumor. However, we have no later films.

Allyn B. Ley, M.D.:* I think we have to remember that this patient was first seen here some eleven years ago. At that time the differentiation of hematologic disorders in general, and specifically the hemolytic anemias, was nowhere near so well defined as it is today. However, let us not be overly proud. Someone else will say the same thing about our present state of knowledge eleven years from now. I think it is fairly evident that this patient did have a hemolytic anemia. It was associated with a warm-dependent antibody that gave a positive direct Coombs test reaction persistently and a positive indirect Coombs test result occasionally during the early stages of her illness.

We can classify patients with acquired hemolytic anemia into three major groups:

1. Patients with a cold-dependent auto-antibody or auto-agglutinin. These patients usually have a definite but not strongly positive Coombs test reaction. In these instances, standard antiglobulin serum reacts not with the antibody itself but with complement. Characteristically, the Coombs test result is more weakly positive than in patients with warm antibodies.

2. Patients with a warm-dependent antibody. This is readily detectable with a Coombs test, and both direct and indirect reactions are usually positive, although the indirect reaction may be variable, as in this case. The way in which antiglobulin serum is prepared is of some importance because of the type of reaction obtained in these two classes. In general, the standard antiglobulin sera are particularly avid for gamma globulin, the usual antibody fraction, and

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less avid for complement, which is not a gamma globulin. Special sera, the so-called nongamma-antiglobulin sera, give strongly positive reactions with cells coated with cold antibody and complement. Indeed, there are occasional reports of cases in which a cold antibody can be demonstrated readily with nongamma-antiglobulin serum and cannot be demonstrated at all with the usual gamma-containing antiglobulin.

3. The third class of hemolytic anemia is the unusual type in which we are not able to demonstrate an abnormal antibody or an abnormal protein either on the red cell or in the serum. These may be pathogenetically different from the cold and warm types of auto-immune hemolytic anemias, but there is no way of being certain. All we can say is that we cannot demonstrate an immune substance by present methods.

Any of these three classes of acquired hemolytic anemia may be an apparently primary process, that is, "idiopathic," or may be associated with another primary illness. In this hospital, the usual primary illness is a lymphoma, particularly chronic lymphocytic leukemia or Hodgkin's disease. In other hospitals the primary disease might more likely be systemic lupus, sarcoidosis, or a number of other diseases in which there is a disturbance of protein synthesis.

It is clear that this patient had a warm antibody acquired hemolytic anemia. Whether or not it was really associated with an underlying disease is far from clear. This morning I reviewed the bone marrow aspirations taken during her illness, and there are clearly increased numbers of lymphocytes in the peripheral blood and to a lesser extent in her bone marrow. This is somewhat unusual in patients with idiopathic acquired hemolytic anemia of the warm antibody type. On the other hand, the principal evidence against a diagnosis of chronic lymphatic leukemia is the pathologist's report of the splenectomy specimen. The spleen was removed almost a year and a half after the onset of her illness. It was a very large spleen. I find it difficult to believe that chronic lymphatic leukemia of this duration should not be readily apparent in a spleen of this size. To be sure, she had been treated with high doses of corticoids for some time prior to the splenectomy, and this undoubtedly modified some of the features of her disease. Nevertheless, I doubt that the corticoids would have been so effectively lympholytic as to abolish all evidence of leukemia in this patient's spleen.

Let us return to her clinical course. Initially, she did have a good response to cortisone at high doses. The splenectomy became indicated, however, because it became necessary to use unduly high doses of cortisone to control the hemolysis and because eventually, even with these dosage levels, she had a relapse. The splenectomy, it is clear, was very effective in controlling her hemolytic process. As you know, the results of a splenectomy in any individual case of acquired hemolytic anemia are unpredictable. About 50 to 60 per cent of patients will have a complete or nearly complete hematologic remission following a splenectomy, but so far we do not have any accurate way of selecting those patients who will benefit from the operation from those who won't. The results with corticosteroids are in some ways even better. We can achieve satisfactory hematologic remission in as high as 80 per cent of the patients with acquired hemolytic anemia by the use of corticoids. However, it is impossible to continue patients indefinitely on large doses of steroids for reasons that are clear to all of us. If one is confronted with hemolytic anemia of such severity that it can be controlled only by large doses of corticoids, one must look for some other way of controlling the process, and a splenectomy is the next choice.

So, as happens frequently in our experience in this hospital, by one means or another we were able to alleviate substantially the hemolytic anemia which this patient had, if indeed we did not cure it. Yet, in the course of therapy, certain iatrogenic complications arose, notably those involving her liver, which led to her demise. Perhaps her death was hastened by the additional use of steroids and antibiotics; perhaps not. I will leave it to Dr. Almy to discuss her liver disease and the final outcome of the case.

Dr. Almy: I'm glad you brought up the question of iatrogenic complications of disease. I am sure that there is hardly a case that is presented in these conferences in which the question cannot be properly raised or in which we are not obliged to think of it.

The first piece of information we have about this patient's liver is that it was enlarged when she was first seen at another hospital and that a biopsy showed fatty metamorphosis and glycogen vacuoles in the nuclei. It is, perhaps, comforting to learn that her liver was diseased before she came to this hospital, but I think that in the long run we managed to make it worse rather than better.

We usually consider that a fatty liver is the result of a nutritional deficit, most commonly associated with alcoholism. However, we can exclude alcohol and poor diet in this patient, unless she had some peculiar dietary habits. We do know that her blood sugar tended to be at the upper limits of normal and that she had a diabetic type of glucose tolerance curve. She did not have glycosuria, and frank diabetes mellitus had not developed. Nonetheless, diabetes mellitus is merely the overt expression of a congenital metabolic defect, and it is perfectly possible for a patient to have some other manifestations of the diabetic state before frank glycosuria appears. Not uncommonly, we see unexplained hepatomegaly in diabetic patients and patients with prediabetes. Some of these livers do contain increased amounts of intracytoplasmic fat; some contain increased nuclear glycogen. This patient showed both phenomena, and I am tempted to lay considerable stress on the nuclear glycogen.

Another factor contributing to this patient's liver abnormalities could well be hemosiderosis as the result of the many transfusions she received. Individual tolerance to multiple transfusions is quite variable, and we have no information that her ferritin mechanism was abnormal. However, she did receive many transfusions over a short period of time, and to some extent the deposition of iron in the reticuloendothelial system in the liver and elsewhere has a dose-time relationship. Even patients with a normal iron turnover can accumulate iron in the liver if one gives them a lot of blood in a few weeks or months. Whether or not such a deposition of iron leads to functional damage or to morphologically irreversible scarring is another question.

The third and most significant aspect of this patient's liver disease is the episode of jaundice, anorexia, and fever which developed about a month after the splenectomy. That is a reasonable incubation time for the virus of serum hepatitis, and I am reasonably confident that she acquired this disease in this hospital, probably from a transfusion given preoperatively, although I cannot exclude injections of other types. She was seriously ill with this disease and required three months of hospital care. I don't think her liver fully recovered from this insult. Her subsequent course was that of progressive liver disease, despite the good hematologic remission. She probably had considerable destruction of the liver parenchyma at the time, and she went on to postnecrotic scarring which terminated in death due to liver failure about two years later.

Perhaps I should introduce a modifying factor in this analysis of her liver condition. I think we can state unequivocally that when she was first admitted here she must have had some degree of functional impairment of the liver. Her serum bilirubin was slightly elevated, 2.65 mg. per 100 ml., and clinically she bordered on icterus. You cannot get jaundice on a purely hemolytic basis. The reserve capacity of the normal liver permits it to excrete more bilirubin in twenty-four hours than can possibly be released by hemolysis in the course of a single day. Thus, I must postulate some functional impairment of the liver, and I suggest that the existence of chronic hemolytic anemia in itself was one of the primary factors in liver injury.

One last point. Two days before she lapsed into a hepatic coma, the protocol states, she developed a urinary tract infection. Some studies have been made at the Boston City Hospital on the effect of urinary tract infection in increasing the available ammonia in the blood stream of patients with hepatic disease. I don't have their calculations at my fingertips, but the point of their argument is that a serious urinary tract infection can provide as much ammonia as a diet containing 100 Gm. or more of protein per day. So you cannot reduce the sources of ammonia in a patient with hepatic coma by following the usual rules if he also has an infection of the urinary tract.

Dr. Ley: How much bilirubin can the normal liver excrete in a day?

Dr. Almy: I was afraid you would ask me that. I think it is about 1,500 mg., but I would have to check that figure.

Meyer Davidson, M.D.: That would imply, then, that in any hemolytic anemia you would not see jaundice unless the anemia itself damaged the liver?

Dr. Almy: Well, there is the supposition that it produces ischemic damage to the liver.

Dr. Ley: It certainly has been noted for half a century or more that patients with acquired hemolytic anemia are much more anemic than they are jaundiced, and that frequently patients with severe hemolytic anemia have little if any elevation of the serum bilirubin. Around the turn of the century the distinction was noted between acquired hemolytic anemia and congenital hemolytic jaundice, as it used to be called, where, in the latter, jaundice was more prominent than the anemia, which was relatively mild. This has never been explained satisfactorily, but I think the basic point is a good one; namely, that in acquired hemolytic anemia jaundice is not prominent unless there is marked anemia. It may be stretching it a bit, however, to say that jaundice doesn't occur at all.

Dr. Almy: Perhaps I may be stretching too far for this point too, but I think that there is a corollary in that, so far as I know, one does not see pure unconjugated bilirubin in the serum in any of the common examples of hemolytic anemia; some conjugated bilirubin is always present as well. To me this implies that there is some disturbance in liver function, or else it would be merely a matter of retaining the unconjugated material.

William B. Ober, M.D.: Does that line of reasoning apply to the acute, massive type of hemolysis one occasionally sees in bacterial infections? For example, in some patients with Bacillus welchii infection associated with septic abortion, the serum bilirubin can rise to 10 or 15 mg. per 100 ml. in a few hours, and the patients become deeply jaundiced almost under one's eyes. Does the rate of hemolysis have anything to do with the development of jaundice?

Dr. Almy: We think of liver function as being impaired in any acute ischemic process; acute hemorrhage, for example. Possibly, in patients with septic abortion there is some impairment of the circulation to the liver. Many such patients are in shock, and the clearance of bilirubin is impaired as a result of a decreased hepatic blood flow.

Dr. Ley: At a recent conference I tried to emphasize that the urine urobilinogen test, which follows the same pattern really, is not a test of hemolysis but a test of liver function. I must confess that there was considerable reluctance to accept this point.

Dr. Almy's and Dr. Ley's Diagnosis

1. *Chronic lymphatic leukemia* (?)
2. *Acquired hemolytic anemia, warm-dependent antibody type, in remission*
3. *Postnecrotic cirrhosis, liver*

Pathologic report

Robert V. P. Hutter, M.D.: The pathologic evidence in this case stems from three sources. First, we have a series of liver biopsies taken during the course of the progression of her disease. Then we have the spleen which was removed two years and four months before the patient's death, and finally we have the autopsy observations.

The first liver biopsy (Fig. 1) was taken at another hospital three months before the patient was first seen here. It shows an essentially normal architecture; there is no scarring. We did see, as did the pathologists at the other hospital, a slight degree of fatty metamorphosis and some nuclear vacuolation presumably due to glycogen. One does see such livers in diabetic patients, particularly in patients with mild diabetes who never needed rigid control. The changes are not specific for diabetes; they are merely consistent with it. I do not know whether or not one finds these minor changes in prediabetic patients. However, it is not unreasonable to infer as Dr. Almy

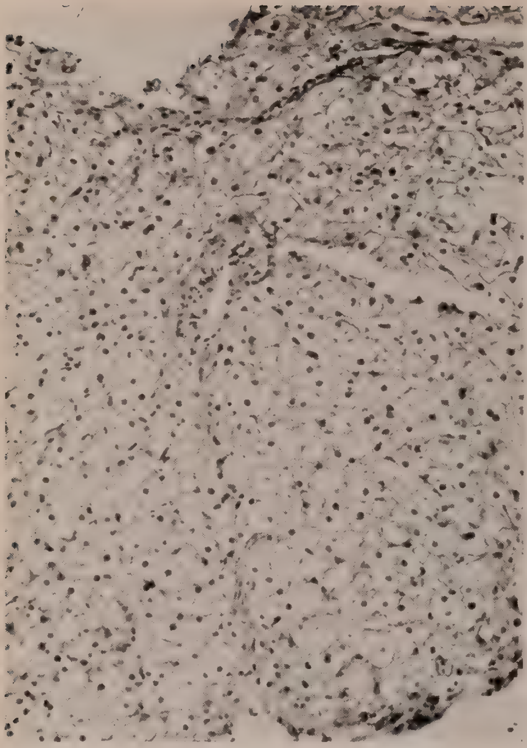

FIGURE 1. First liver biopsy. Essentially normal architecture devoid of scars. There is very slight fatty metamorphosis and nuclear vacuolation.

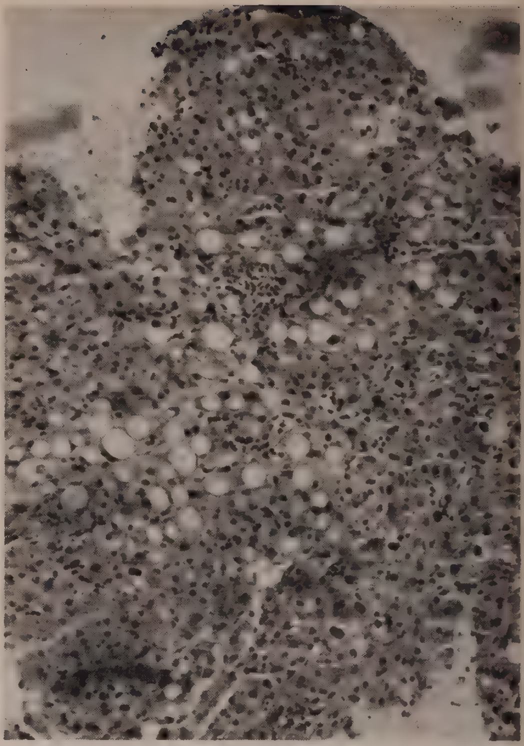

FIGURE 2. Second liver biopsy one year after that seen in Figure 1. There now are minute stellate scars, more evident fatty metamorphosis, and focal round cell accumulations.

did that they can occur in this type of individual. The second liver biopsy (Fig. 2) was performed here about a year after the first one and about three months before the splenectomy. It shows a more evident degree of fatty metamorphosis, an occasional focus of round cell infiltration, and minute stellate scars. This is clear-cut evidence of an intrinsic liver disease prior to the splenectomy, prior to the episode which clinically resembled serum hepatitis. Whether or not this picture is related to her hemolytic process is not clear. The third liver biopsy (Fig. 3) shows dense fibrosis circumscribing nodules of disturbed liver parenchyma. Thus, we have been able to trace over a three-year period the transition from an essentially normal-appearing liver to postnecrotic cirrhosis.

The spleen was removed about three months after the second liver biopsy because of progressive hemolytic disease. It weighed over 1,000 Gm. and showed diffuse hemosiderosis in macrophages and in the interstitial tissue as well as the larger siderotic nodules called Gandy-Gamna bodies (Fig. 4), which are deposits of iron and calcium salts on the collagenous elements in the spleen. These findings are consistent with any hemolytic process of some severity. There was no evidence of leukemia in the spleen. The malpighian corpuscles were of normal size, even slightly reduced. No clusters of abnormal lymphoid or myeloid cells were seen.

At the postmortem examination, the patient weighed 90 pounds and was 5 feet tall. She was deeply icteric. The abdomen was protuberant, and there was pitting edema of the legs. The peritoneal cavity contained 6 L. of yellow-green fluid. The peritoneal surfaces were thickened and studded with 0.5-cm. gray-white, purulent nodules over all the surfaces.

The liver weighed 1,950 Gm., was coarsely nodular and greenish-brown. A microscopic

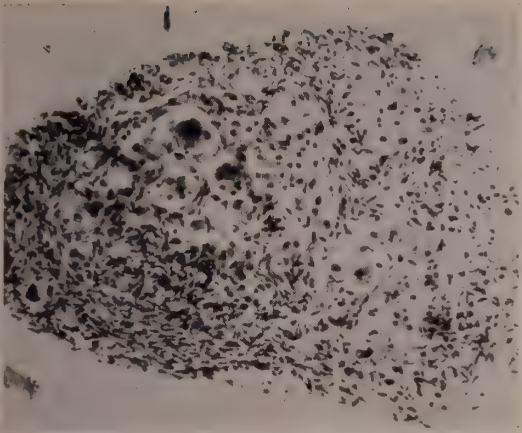

FIGURE 3. Third liver biopsy approximately three years after that seen in Figure 1. Dense fibrosis surrounding nodules of parenchyma is now evident.

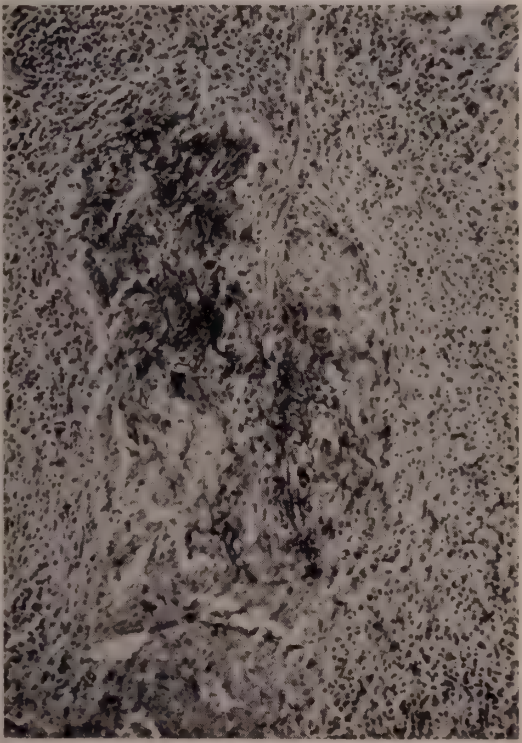

FIGURE 4. Spleen with Gandy-Gamna body. These are siderotic nodules formed by the deposition of iron and calcium salts on the collagenous elements of the spleen. These are seen associated with severe hemolytic processes.

examination (Fig. 5) showed the typical picture of postnecrotic cirrhosis with broad bands of fibrosis subdividing lobules of liver parenchyma, bile duct proliferation, and round cell infiltration. Bile stasis was evident in some areas. Iron stains revealed hemosiderin in macrophages, in liver cells, and interstitially. Thus, we have a liver with both posthepatic cirrhosis and hemosiderosis secondary to chronic hemolytic anemia.

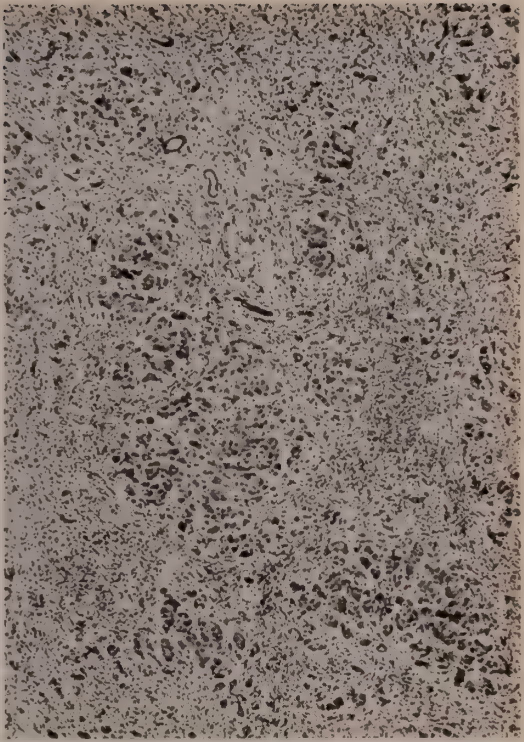

FIGURE 5. Liver at autopsy showing diffuse alteration similar to that in Figure 3.

The bone marrow demonstrated hyperplasia of erythroid elements, chiefly at the normoblast level (Fig. 6). There was no significant lymphocytosis, nor cellular forms to suggest leukemia of any type.

The lungs had a combined weight of 1,030 Gm. Both lower lobes contained a number of abscess cavities filled with grayish-yellow pus. The abscesses were about 2.5 cm. in diameter and essentially uniform in size and age; they were not confluent. Routine sections showed zones of central necrosis exudation of polymorphonuclear leukocytes and surrounding edema (Fig. 7). Sections stained for microorganisms by the Brown-Bren stain, a modified gram stain for tissue, showed a number of branched filamentous organisms about 1 micron in diameter in

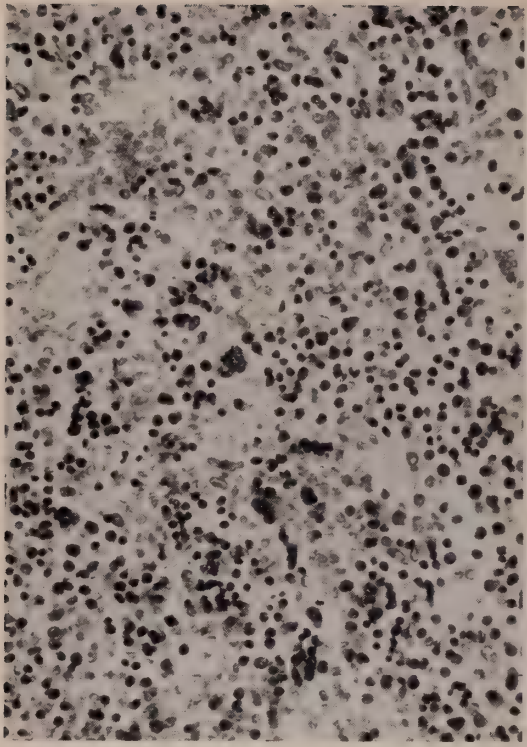

FIGURE 6. Bone marrow shows hyperplasia of erythroid elements, particularly at the normoblast level.

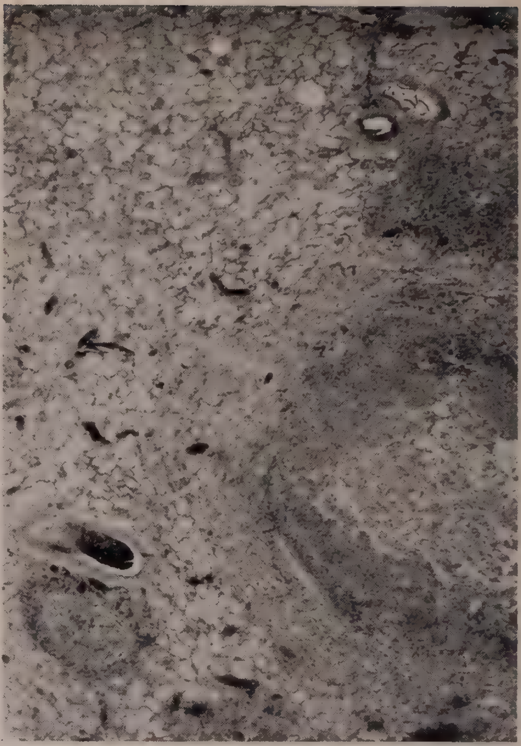

FIGURE 7. Lung, low magnification, demonstrating large abscess and edema. Organisms cannot be identified with routine hematoxylin and eosin stain.

these abscesses (Fig. 8). Morphologically, these are consistent with the actinomycetes, either Nocardia or actinomyces. We cannot distinguish one from the other on a structural basis alone.

The brain weighed 1,300 Gm. and had numerous abscesses about 2 cm. in size scattered throughout. These abscesses were located in the left postcentral gyrus, left corona radiata, right anterior central gyrus, supramarginal gyrus, and right fastigial nucleus of the cerebellum. These areas all contained acute, purulent exudate, and no microorganisms were seen on a routine stain (Fig. 9). However, a Brown-Bren stain again demonstrated many organisms similar to those found in the lungs (Fig. 10).

The stomach contained three ulcers ranging from 3 to 4.5 cm. in size, and the duodenum contained a single ulcer 1.5 cm. in size. The ulcers were acute, and a Brown-Bren stain again demonstrated actinomycetes in the exudate lining their craters. Sections of the purulent nodules studding the peritoneal surfaces also revealed acute inflammatory exudate admixed with actinomycetes.

Lymph nodes, in areas unaffected by abscess formation, showed extramedullary hematopoiesis with numerous megakaryocytes, immature granulocytes, and erythropoietic cells (Fig. 11).

The kidneys showed lesions of intercapillary glomerulosclerosis (Fig. 12) in a few glomeruli and some "basement membrane" thickening in many more. These lesions can appear prior to the onset of overt diabetes mellitus. There was also a good deal of sclerosis of afferent and efferent arterioles. Brownish granules were found in the renal tubular epithelium; iron stains proved this pigment to be hemosiderin (Fig. 13).

Morphologically, the actinomycetes are identifiable as gram-positive, branching filaments 1 micron in diameter. The actinomyces generally form mycelial masses with

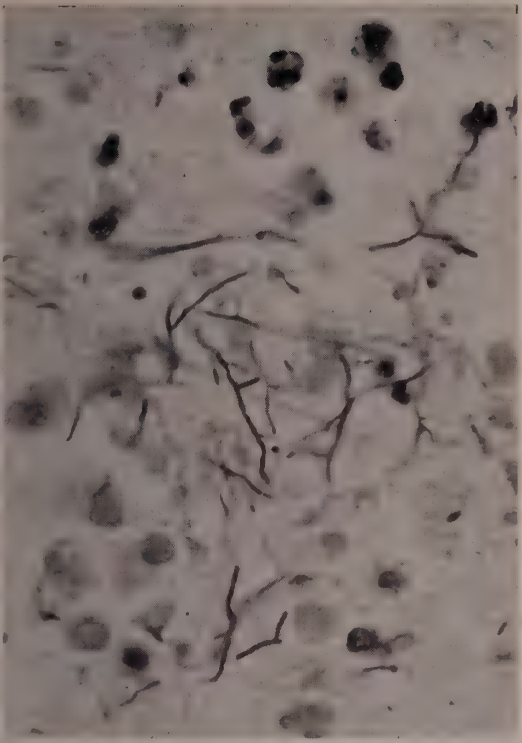

FIGURE 8. Lung, Brown-Bren stain, demonstrating actinomycetes. These are branching filaments 1 micron in diameter.

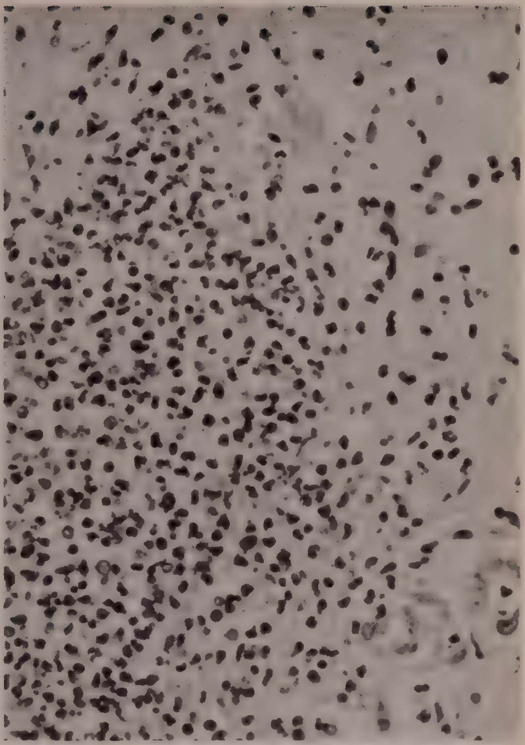

FIGURE 9. Brain. A large abscess is demonstrated. There is acute necrosis, but no organisms are identifiable by routine hematoxylin and eosin stain.

sulfur granules, whereas the Nocardia are less prone to do this. The organisms do not stain well, if at all, with hematoxylin and eosin or with Schiff's periodic acid reagent, but they do take the tissue gram stain (Brown-Bren) very well. They form minute abscesses and suppurate chronically. The lesions are seen clinically as discrete granulomas in the jaw, oral cavity, tongue, lungs, and abdominal organs. Occasionally, the infection becomes disseminated.

We have been interested in fungus diseases in general, and in knowing how this hospital, which is a somewhat specialized institution with a selected high distribution of neoplastic disease, compares with more general hospitals in terms of the incidence of fungal disease and with the specific fungi involved. In 1956, Keye and Magee[1] reported on 88 cases of fungal infection in 15,845 autopsies from Washington University in St. Louis. Their report covered a thirty-six-year period from 1919 to 1955, and they were able to show a gradual rise from about 0.1 to 1.1 per cent over this period.

Recently, we had occasion to review one particular type of mycosis, namely mucormycosis, in the world literature.[2] When the data were arranged in chronologic sequence, it was clear that the increasing incidence in recent years seemed to be true the world over. In fact, almost two-thirds of the reported cases occurred during the years 1952 to 1958 in the era of multiple antibacterial and anticancer agents. When we compare a general hospital with ours, we find that the most frequent fungal pathogen in both types of institution is Candida. In a general hospital population, the next two most frequently encountered fungi are Histoplasma and Cryptococcus. However, in our institution we had fewer of these organisms and more of aspergillus and actinomycetes. Of course, in a general hospital, many of the patients are admitted primarily for their fungus infection, most

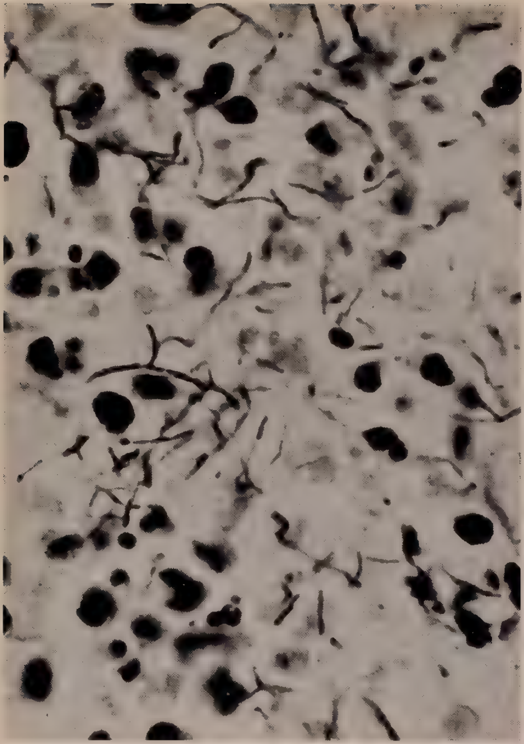

FIGURE 10. Brain, Brown-Bren stain, demonstrating actinomycetes similar to those seen in Figure 7.

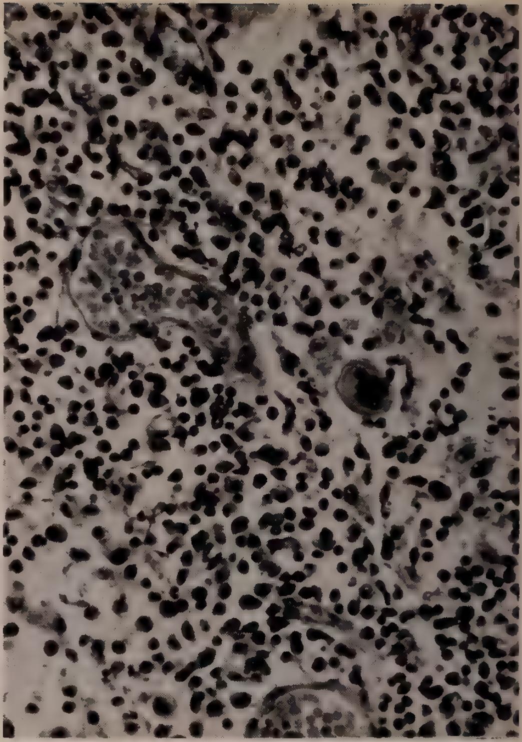

FIGURE 11. Section of lymph node with extramedullary hematopoiesis. Note large megakaryocyte.

usually actinomycosis, blastomycosis, or coccidioidomycosis. In our hospital, the fungal infection is almost always superimposed on an underlying disease; we see very little blastomycosis or coccidioidomycosis, and the actinomycosis that we do see, such as in the present case, is a secondary infection. In our hospital, the secondary mycotic infections are caused by Candida in a majority of cases, then actinomycetes, aspergillus, Cryptococcus, Geotrichum, and Mucor in that order.

There is an interesting side light related to mucormycosis. This infection is described in the literature as a complication of diabetes mellitus. Actually, when the world literature was reviewed, we found that the incidence in diabetic patients was essentially the same as in cancer patients, about 20 per cent. However, in cases involving only head and neck structures, almost 75 per cent of the patients had diabetes. These often were associated with a clinical triad of uncontrolled diabetes, orbital infection, and meningoencephalitis. In 202 cases of mycoses at Memorial Hospital the incidence of diabetes mellitus was 2 per cent.

There are a number of factors in a given patient which may predispose the patient to an infection by a fungus. These include altered metabolic states producing a loss of phagocytic ability, ketosis in diabetic patients, devitalization of tissue, alteration of the bacterial flora of the gastrointestinal tract by antibiotics, even actual irritative tissue injury by antibiotics, ulceration of mucosal surfaces by cancer chemotherapeutic agents, and agranulocytosis. Any or all of these may be combined in a patient with neoplastic disease, and the rapid invasive growth of opportunistic fungi is facilitated when more than one of these factors is present.

Epicrisis

Harvey S. Collins, M.D.:* Actually, my own presentation is going to take a very

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* Associate Physician, Memorial Hospital; Assistant Professor of Medicine, Cornell University Medical College.

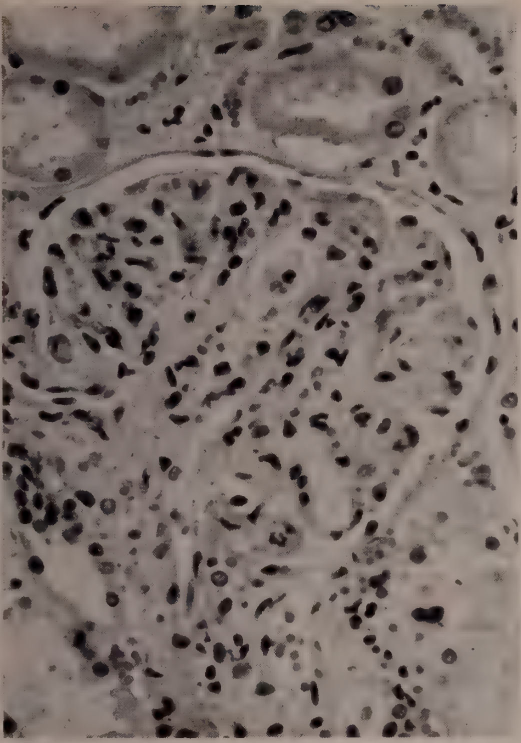

FIGURE 12. Kidney with intercapillary glomerulosclerosis in glomerulus. Note also the thickening and smudgy appearance of afferent arteriole.

different form from what you might expect. I think it is still appropriate in this setting. We have had 2 cases of systemic mycoses presented here recently, and Dr. Hutter has covered the major aspects. In addition, Donald B. Louria, M.D., recently gave a splendid discussion about nocardiosis and actinomycosis. So I thought that instead I would take up the fundamental aspects of the actinomycetes and find out what they are in broad terms. I am taking the group of actinomycetes as a whole so that, in the time allotted, many of the statements will be half-truths for individual strains, but they are fundamentally true for the group.

Now, first of all, to get out of the way the basic taxonomy. This is a bit of review of mycology. What are the actinomycetes? You see the statement that they are transitional forms between bacteria and fungi. Well, this may be one way of looking at it. On the other hand, it might be appropriate to put them off in a third category all by themselves, not belonging to a continuum between bacteria and fungi.

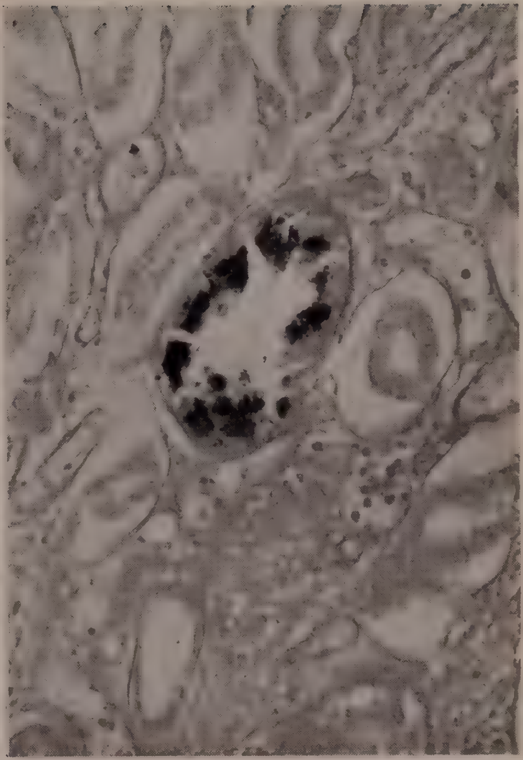

FIGURE 13. Kidney. Iron stain demonstrating pigment granules in tubules.

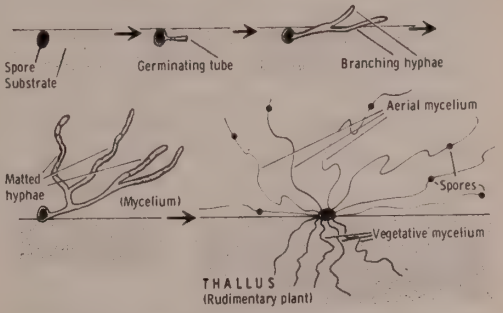

FIGURE 14. Schematic formation of a "thallus."

In the broadest terms, whether you have bacteria, or actinomycetes, or fungi, growth starts as follows (Fig. 14): Here is a nutrient substrate. Here is a spore, or perhaps a fragment of a hypha. When one of these decides to germinate, it sends out a germinating tube which elongates. This tube in turn may or may not segment; it may or may not branch; at times it forms sexual or asexual spores. The original structure is also sending out "roots," the vegetative mycelium, into the substrate for nourishment, and, on the other hand, it is sending up the branch which may or may not divide, until you get the whole aerial mycelium coupled with the vegetative mycelium. This whole structure is a rudimentary plant called a "thallus." Microorganisms which do this in any measure fall into the general division of Thallophyta; or, stated backwards, this is why Thallophyta include bacteria, actinomycetes, and true fungi, since the latter conform in structure and growth pattern to this plan.

Now, there are variations here. As I say, morphologically, there may be segmentation; there may or may not be spores. Some bacteria don't even go this far. Instead, they are rather primitive and just multiply by repeated divisions so that when you look at a whole colony of bacteria, you are looking at innumerable cells which are derived from a parent cell.

Certain others, for instance the actinomycetes, may or may not develop the aerial mycelium. For instance, the anaerobic Actinomyces bovis doesn't develop an aerial mycelium. It just develops a small colony on the plate, but it does sink roots. It is rather hard to shove on the plate when you push the colony with a wire loop. Somewhat more typical, the Nocardia may or may not get a little rudimentary fuzz on top. Last, the streptomyces in general belong here. They tend to have well-developed aerial hyphae. So, those are the three groups in the actinomycetes: the actinomyces, the Nocardia, and the streptomyces. At least we have them in with the division of thallophytes, but we haven't yet given the evidence by which they are or are not to be considered transitional forms between bacteria and fungi.

Now to go back historically, the true fungi are much larger than bacteria, so of course they were the first things to be spotted. They were classed according to the colonial structure as it appeared on a plate, and according to the septation, spore forms, and the appearance of the aerial mycelium in general. That is classical botanic classification.

However, by 1900 there was utter chaos in taxonomy. The same organisms had been described independently in many different places, many different laboratories, by different workers. Then, add to that the fact that the media were not standardized. As you know, they worked with beef broth and so forth, of different compositions and different salt concentrations. These factors often alter the structure of fungi enormously. And there are so many other technical details which went into it. So, one can appreciate why even as late as 1914 Güssow, who was working on potato scab, which is caused by an actinomycete, commented: "On endeavoring to place the organism in its proper genus, we found ourselves confronted by one of the most perplexing problems of botanical nomenclature, which promises a rich harvest to those who are fond of such study."[3]

Well, to get out of this mess, a Committee on Characterization and Classification set up by the Society of American Bacteriologists, started in 1917 to try to bring into being a system of classification of bacteria into families, tribes, and genera. This culminated in 1923 in the first edition of Bergey's *Manual of Determinative Bacteriology* which is the bible, in a sense, in this country.

A few years ago the seventh edition of Bergey appeared, and I can assure you that over the years virtually every bug which ever has been found has changed places at least once, sometimes several times. They have been dropped from editions, they have been reincorporated into different families in other editions, and it is still pretty tough going.

The present status is much better, however, based on such matters as the standardization of media. Investigators now use pure carbon sources and pure nitrogen sources and achieve control of their media ever so much better. There is, moreover, much new knowledge based on cytology, life cycles, mutations, adaptations, enzymology, biochemical activities, and intermediary metabolism.

Thallophyta is the general division (Fig. 15). This is subdivided into the algae, which have chlorophyll, and those which are the nonchlorophyll-bearing ones. Please follow down the nonchlorophyll-bearing line into the true fungi, or, on the other hand, down into the bacteria. These are

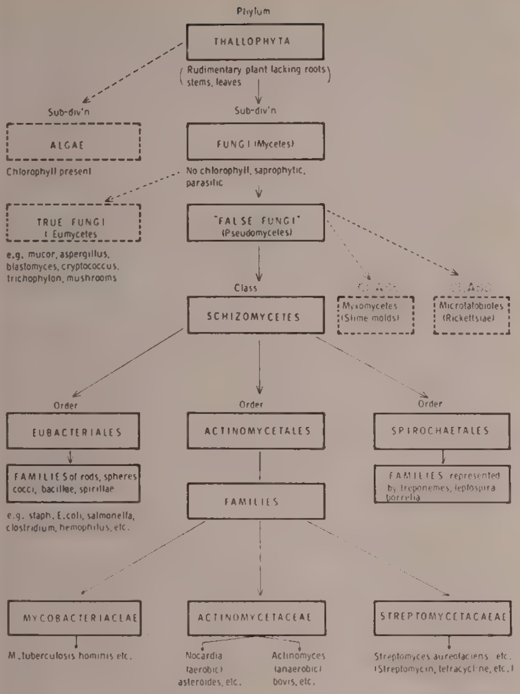
Phylum
THALLOPHYTA
(Rudimentary plant lacking roots stems, leaves)
Sub-div'n
ALGAE
Chlorophyll present
Sub-div'n
FUNGI (Mycetes)
No chlorophyll, saprophytic, parasitic
TRUE FUNGI (Eumycetes)
e.g. mucor, aspergillus, blastomyces, cryptococcus, trichophyton, mushrooms
"FALSE FUNGI" (Pseudomycetes)
Class
SCHIZOMYCETES
CLASS
Myxomycetes (Slime molds)
CLASS
Microtatobiotes (Rickettsiae)
Order
EUBACTERIALES
FAMILIES of rods, spheres cocci, bacillae, spirillae
e.g. staph, E.coli, salmonella, clostridium, hemophilus, etc.
Order
ACTINOMYCETALES
FAMILIES
Order
SPIROCHAETALES
FAMILIES represented by treponemes, leptospira borrelia
MYCOBACTERIACEAE
M. tuberculosis hominis etc.
ACTINOMYCETACEAE
Nocardia (aerobic) asteroides, etc.
Actinomyces (anaerobic) bovis, etc.
STREPTOMYCETACAEAE
Streptomyces aureofaciens etc. (Streptomycin, tetracycline, etc.)

FIGURE 15. "Geneology" of an actinomycete.

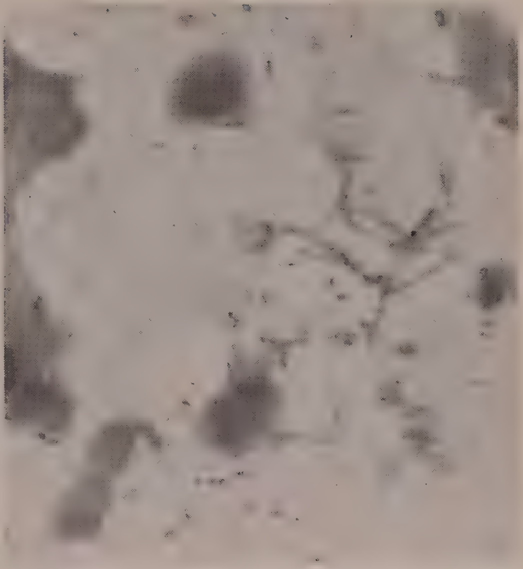

FIGURE 16. Nocardia and pneumococci in purulent sputum.

simple rods and other forms, simple bacteria, and allied with these are the actinomycetes which we are talking about.

Now to take the actinomycetes by themselves: Are they bacteria or fungi, or neither? The actinomycetes which Dr. Hutter showed resemble bacteria in many ways.

This is a Nocardia asteroides in the sputum from a patient (Fig. 16). These little things here are pneumococci which were present at the same time. This illustration shows the general dimensions of one of these branching forms alongside the pneumococcus. You also note that the parenchymal diameter, which Dr. Hutter mentioned, is about 1 micron. The diameter of the hyphae and the spores of the actinomycetes are similar to those of bacteria, but quite dissimilar to those of proved fungi, such as aspergillus. They may be acid-fast, faintly acid-fast, but you can pep up this feature a little bit by putting them into milk for growth. You can still see them in the same sputum specimen after it has been stained with an acid-fast technic. They resemble in morphology and physiology the Mycobacteria. This is especially true of the Nocardia. We had a one-day-old culture of this same Nocardia stained with an acid-fast technic. Certain of the forms were branching. On the other hand, many of them were fragmented. It is easy to see how in certain sections or under certain preparations one might have taken these to be mycobacteria.

Often in the actinomycetes there is no extensive aerial mycelium. There is no true nucleus, no true mitosis, in the sense that there is in the fungi; nor is there in bacteria for that matter. This is brought out in various ways, such as nuclear staining, phase microscopy, vital staining, and other technics. (Debatable issues are involved here.)

A very interesting thing is that the cell walls of the fungi have cellulose or chitin; on the other hand, the cell walls of the actinomycetes show amino sugars, amino acids, and certain other sugars. They have the same structure, the same chemical composition as you find in the cell walls of gram-positive bacteria. The chemical composition of the internal part of the cell, too, has been found to resemble that of bacteria rather than that of fungi.

The phenomena of lysis and phage activity establishes a relationship to bacteria rather than to fungi. This includes autolysis, bacteriolysis, and bacteriophage lysis. All of these are quite distinctive.

I can refer you to the definitive monograph of Selman A. Waksman, Ph.D., *Actinomycetes: Nature, Occurrence, Activities.*[4] I assure you it is stupendous reading, some 300 pages of fascinating detail, and each topic that I mention is discussed at great length.

There is another point; that the actinomycetes in general are sensitive to certain antibiotics active against the usual bacteria, whereas the fungi are not.

On the other hand, what about the resemblances to fungi? Well, there are certain resemblances of some actinomycetes to fungi, but they are chiefly of historical interest, especially from the morphologic viewpoint. I think it is easier to align these actinomycetes in your mind with bacteria. This is especially true of those forms which are pathogenic for man and animals. These are very few out of the many actinomycetes. I counted 300-odd species of actinomycetes falling into these three groups: actinomyces, Nocardia, and streptomyces. In the last twenty years a fantastic amount of information has been developed on these organisms. This came about, of course, because industry was looking for antibiotics.

As a group, many of the actinomyces are capable of profound biologic stunts. First, they can utilize cellulose. This may not seem important at the moment. Second, they can utilize, as the sole sources of energy, carbon, nitrogen, and a diverse bunch of compounds, so diverse as to include phenols, pyrimidines, steroids, paraffin, moth balls, lipids, and fats. And I might say that they are hungry enough to convert compound S into compound F.

They can reduce nitrates to ammonia, but they cannot fix nitrogen, and so they have to depend on a preformed source of nitrogen for their nitrogen supply.

There is one curious phenomenon: they can use carbon monoxide, hydrogen, and volatile aliphatics out of the air.

Next there are three items which we can lump together: They can live in a dried state for thirty years, they can function in the absence of light, and they can withstand wide temperature ranges.

Now a word about the wide temperature ranges. Actinomyces are found every place from the bottom of the sea to as high as men have gone in the mountains and in the soil of the whole globe. Those in the sea usually are 0 to 20 C. at their optimum. Those which are pathogenic for man in general are about 28 to 38 C. Those which are thermophils you will find existing at as high as 65 to 70 C. perfectly comfortably. Thermophils are found in hot springs and in composts where the degradation of organic matter is taking place. Moist heat at 70 C. will often kill them in ten minutes. On the other hand, you can have them in dry heat and dry soil, for prolonged periods of time. For instance, in the Sahara Desert you have only to dig into the soil a bit and you will find plenty of actinomycetes, at a blistering temperature, alive.

They do not need light to carry out their reactions. On the other hand, if you were to have infrared light, which is heat, or red light, you might kill the organism simply by cooking it to pieces. To go to the other end of this extreme, ultraviolet light from about 2,500 to 2,800 angstroms causes a retraction from the cell wall and plasmolysis, which is lethal to the organisms. However, if you raise the number of wave lengths to about 3,500 to 4,900 angstroms, it does delightful things to these organisms: It causes them to mutate and they begin to form more and more antibiotics. This is one of the tricks used by the industrial people to develop mutants which may provide antibiotics.

They also can go through an extreme of osmotic change without being harmed. They may utilize carbon dioxide. This has been explored and developed through Warburg, "tracer," and other technics. It has been of particular use to industry.

They can decompose keratin and chitins, which as a result break down to ammonia and to nitrates. This gets rid of hair, skin, the shells of small arthropods in the soil, and so forth.

They decompose rubber. Natural rubber is actually destroyed this way, largely by Nocardia. Also, marine petroleum deposits, the hydrocarbons, are destroyed by Nocardia.

They exhibit a wide range of proteolytic activity. I am not going to say very much about the lytic mechanisms against live and dead forms, nor "phages," except that they are of great importance in fermentation studies. I don't know whether or not you realize how much it means to a manufacturer to find that his vat is going sour on him and he is not getting the proper antibiotic out of it.

A curious thing about these "phages" and these lytic mechanisms is that there are even actinomycetes which produce antibiotics which protect the strain involved against actinomycetes which produce actinophages directed against the actinomycetes!

The actinomycetes produce a wide variety of extra- and intracellular enzymes. I will just list a few of them to give you an idea: proteases; rennet, which coagulates milk; urease; deguanidase; amylases; polysaccharidase; invertase; lipase; catalase, which incidentally parallels streptomycin production; penicillinase, trypsinase, things which enzymatically change steroids; and it goes on and on.

Next you see that actinomycetes can produce vitamins and growth factors. This is quite true. Breeders feed them to animals and stock to enhance fertility and growth. There are other outlets, even in the field of plant growth. I might mention that citrovorum, vitamin B_{12}, and thiamine are all created by actinomycetes.

These organisms seem to have inherited the earth. In soil they run into the millions of colonies per gram of soil. They are found in large numbers in sea water, fresh water, and sludge.

Such wonderful organisms—saprophytes! parasites! pathogens! nonpathogens! givers! takers! but on a magnificent scale.

They abound in stable manure and composts, and these are decomposing, as I said, at temperatures as high as 70 C. The waste products of animal and plant life on land, in sea, and in the air are largely recycled and put back into useful forms by the actinomycetes.

Moreover, they spoil our foods, give rise to musty odors, give us potato scab, matted wool in sheep, and toothaches in elks who go around in the winter chewing on trees. They make the water of the River Nile impotable because of the stench, and the same goes, so I read, for the River Moscow in the autumn months. Worse than that, they even spoil rum! On the other hand, as I pointed out, they enhance growth and fertility of livestock, give us antibiotics, and thereby please the manufacturer.

Anatomic diagnoses

1. *Acquired hemolytic anemia with:* (*a*) *status postsplenectomy* (*two years, four months*), (*b*) *hemosiderosis of liver, spleen, and kidneys*, (*c*) *extramedullary hematopoiesis, lymph nodes*
2. *Postnecrotic cirrhosis, liver* (*viral type*)
3. *Disseminated actinomycetosis with multiple abscesses in brain, lungs, mesentery, peritoneum, and ulceration of stomach and duodenum*
4. *Intercapillary glomerulosclerosis* (*diabetes mellitus, mild*)
5. *Icterus, severe*
6. *Ascites, 6,000 ml.*

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Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Pediatric Ambulatory Endotracheal Anesthesia

SUBGLOTTIC EDEMA is a serious complication following endotracheal intubation in children. In a mild form it may be characterized by hoarseness or a croupy cough. In the more severe cases signs and symptoms of respiratory obstruction, such as suprasternal retraction, intercostal retraction, use of the accessory respiratory muscles, and finally restlessness and anxiety appear.* The first signs usually are manifest within one-half to three hours following the extubation, while the child may still be in a recovery room where treatment can be instituted promptly. Occasionally, however, the development of a significant degree of edema may be delayed for several hours, at which time diagnostic skill and therapy may not be available readily.

Case report

A four-year-old boy was brought to the emergency room because of stridor and respiratory distress. The child had been entirely well until forty-eight hours previously, when he had undergone extensive dental repair under endotracheal diethyl ether-oxygen anesthesia. The mother stated that the child had been observed in the dentist's recovery room for three hours before being sent home. In the evening the child developed a croupy cough and a "heavy" voice. The next morning he had rapid respirations and a more severe croupy cough. He was afebrile. Throughout the first postoperative day the signs of respiratory distress increased in severity. The mother used a vaporizer but without apparent benefit. Late in the afternoon the parents called the dentist who suggested contacting the family physician. This, however, was not done until noon of the second postoperative day when the child exhibited restlessness and irritation in addition to the cough and rapid respiratory rate. The family physician immediately referred the child to the hospital.

On admission, the child was restless and upset with inspiratory and expiratory stridor, a respiratory rate of 36 per minute, and substernal retraction. The rectal temperature was 99.6 F. Cyanosis was not apparent, and the voice was only slightly hoarse. A physical examination revealed the posterior pharyngeal wall to be reddened and edematous. A few coarse rhonchi were heard scattered over the chest, but essentially both lungs were clear. A chest radiogram did not show any abnormality. A laryngeal examination was deferred.

The boy was placed in a high-humidity oxygen tent, and phenobarbital 30 mg. was administered intramuscularly. However, no improvement occurred, and one hour after his admission

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Presented and discussed at a conference held at Bellevue Hospital, New York City, June 4, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

* Deming, M. V., and Oech, S. R.: Steroid and antihistaminic therapy for post intubation subglottic edema in infants and children, Anesthesiology 22: 933 (Nov.-Dec.) 1961.

surgery and anesthesiology consultations were requested as emergencies.

The anesthesiologist responded immediately and noted that the parents removed the child's head from the oxygen tent at frequent intervals. They also prevented the fatigued child from resting by continuously talking to him. The anesthesiologist decided to take the child to the recovery room for further care, leaving the understandably apprehensive parents on the pediatric ward.

In the recovery room the boy cried for a brief period and then fell asleep. His respiratory rate declined to 28 per minute, and the inspiratory stridor vanished while the expiratory stridor diminished in severity. It was decided by the departments of anesthesiology, pediatrics, and surgery that the child should be watched closely in the recovery room under the constant supervision of an anesthesiology resident. At the earliest sign of deterioration, laryngoscopy, bronchoscopy, or tracheostomy could be accomplished.

Accordingly, an anesthesia machine was set up at the bedside in the recovery room with the proper size endotracheal intubation equipment ready for use. Two senior anesthesiology residents took turns watching the child during the night. Mild sedation and the use of oxygen and moisture were continued, 50 mg. of Solu-Cortef were injected intravenously, and the pharynx was sprayed with Neo-Synephrine.

The boy improved steadily. He was kept in the recovery room for a total of thirty-six hours during which time an anesthesiology resident was in constant attendance.

After another forty-eight hours on the pediatric ward, the child was discharged.

It was felt that in the absence of fever or leukocytosis, bacterial infection was improbable and that the most likely possibility was subglottic edema secondary to endotracheal intubation.

Comment

The dictum, tracheostomy should be performed as soon as it is seriously considered, probably should be modified in children because the care of a tracheostomy is more difficult than in adults, and the immediate and later complications present a greater hazard.

Postanesthesia care does not end with the discharge of a patient from a recovery room. In the case of ambulatory anesthesia, the family must be alerted as to the potential dangers, they must be instructed concerning warning signs, and they must inform the anesthesiologist at the earliest sign of trouble. It is the duty of anyone who attempts elaborate anesthetic procedures, such as those described, to be prepared and competent to manage those complications which inevitably will occur.

Number one hundred twenty-nine in a series of Clinical Anesthesia Conferences

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Gluten bread not a calorie reducer

There is no advantage in using gluten bread on a weight-reduction program, according to an article by Dr. Philip L. White in the July, 1962, issue of *Today's Health*. Gluten bread contains about the same number of calories as ordinary bread, but it should contain at least 25 per cent gluten, an important wheat protein. For this reason, such bread has a high protein content.

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Glue Sniffing*

GLUE SNIFFING, particularly among teenagers, has been reported with increasing frequency to the New York City Poison Control Center. Since the beginning of the year until May 15, 1962, 15 cases have been reported in individuals between the ages of nine and eighteen years, 10 males and 5 females. A few cases are cited here.

INCIDENT 1

Toxic Agent	*Age*	*Sex*
Airplane Glue	12 years	Male

This twelve-year-old child was in a group of boys who were assembling a model airplane in the school yard when they decided to smell the glue which they were using. This practice was soon discovered by school authorities who referred the children to Kings County Hospital for observation and indicated treatment. On their admission to the hospital the patients were entirely asymptomatic. One twelve-year-old patient was referred to the State Hospital where he remained for forty-five days for further psychiatric observation.

INCIDENT 2

Toxic Agent	*Age*	*Sex*
Glue (toluene solvent)	16 years	Male

This sixteen-year-old was sniffing glue cement. He developed nausea and vomiting and was referred to a hospital emergency room. On admission the patient vomited spontaneously; no other symptoms were noted. This patient made an uneventful recovery after two days of hospitalization.

INCIDENT 3

Toxic Agent	*Age*	*Sex*
Plastic Cement	14 years	Male

This patient related that he and several other boys were smelling airplane glue which they had bought from the candy store. After using it for three weeks, two to three times daily, one of the boys read in the newspaper about the danger of glue sniffing and its possible harm to the kidneys. They discontinued its use, and the patient was taken to his physician for treatment. The patient related that he was sniffing the airplane glue "for kicks" and that it was quite a common practice among his teen-age friends. He remained asymptomatic and did not develop any ill-effects after discontinuing the use of the drug. The laboratory work-up, including blood and urine tests, showed negative findings.

INCIDENT 4

Toxic Agent	*Age*	*Sex*
Airplane Glue	14 years	Male

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* Since the submission of this brief, another discussion on "Glue Sniffing in Children" appeared in the July 28, 1962, issue of the *Journal of the American Medical Association*, volume 181, page 300.

The boy's mother, who brought the child to the hospital, related to the physician in the emergency room that the patient was reported by the class monitor as being "groggy" after inhaling airplane glue. She had been called to the school to take the child home. The mother was certain that her child's interest was aroused after listening to a news broadcast. The symptoms on admission were lethargy and stupor. The patient was admitted to the hospital for observation and after several days was referred to the psychiatric division for further observation.

At the time of this writing a child psychiatrist assigned to the Children's Court called the Poison Control Center for information on the medical aspects of "glue sniffing." He was in the process of studying a child who was referred to him by a judge because of "glue sniffing." Some children are being held by the police authorities under the penal regulation regarding impairing the health and morals of minors. On the other hand, the sale itself of this product is not prohibited.

INCIDENT 5

Toxic Agent	*Ages*	*Sex*
Airplane Glue	11,11, and 12 years	Female

A public health nurse working in the School Health Services called the Poison Control Center for information on "glue sniffing," since it is not an uncommon occurrence among school-age children, and she was totally unfamiliar with the problem. She also reported as follows:

> Three girls were found by the teacher dancing, giggling, and in general demonstrating inappropriate behavior. Two of the girls were eleven and one was twelve years old. They admitted to sniffing airplane glue containing a toluol polystyrene plastic cement.
>
> The first girl said she felt dizzy, that things were turned around instead of straight, and that she had a funny feeling in her forehead. She also felt "silly" and wanted to dance.
>
> The second girl said she felt happy at first, and later she felt sleepy.
>
> The third girl had difficulty focusing. Her eyes appeared somewhat crossed, and she heard a steady ringing in her ears for about one hour.
>
> The girls stated that they put the glue in a paper bag, cupped it over their nose, and then breathed in. There was conflict as to where they got the glue. One of them said at first that a boy gave it to her so she "would do things." But she told the Juvenile Aid Bureau officers that she bought it at a store. One of the other girls substantiated this. Then, in the afternoon the first girl came to the medical room and said that a boy did give it to her and that she had lied to the Juvenile Aid Bureau officer because the boy would hurt her if she told.
>
> The girls' period of elation lasted from about 10:00 to 11:30 A.M. Some of this elation was "put on." When their mothers came to the school, the girls quickly "sobered up." At 1:00 P.M. all of them were examined by the school physician who found no visible effects.

Comment

This product is used in what appears to be a widespread practice promoted either by word of mouth or through the news media. The glue is usually injected into a small brown paper bag and then held over the nose for a sniffing session.

The plastic glues are variously formulated. One of the most frequently used products contains methyl isobutyl ketone 50 per cent and monomethyl ether of ethylene glycol acetate 50 per cent. The median lethal dose of each ingredient is 0.5 to 5 Gm. per kilogram. They are dangerous by all routes. The maximum allowable concentration of methyl cellosolve is 25 parts per million. The plastic bases include polyvinylacetate, nitrocellulose, and others. The solvents include toluene, trichlorethylene, cyclohexanol, ethylenedichloride, and other solvents having suitable physical and chemical properties.

Symptomatology

While many patients presented no symptoms, a few have evidenced such symptoms as nausea, vomiting, and diarrhea, and some have reported central nervous system depression or excitement including giggling, dancing, and "feeling high." On the other hand, some were drowsy and in a stupor. "Glue sniffing" may cause excitement or delirium and unconsciousness. Damage to the hematopoietic system, kidneys, and liver also must be considered in addition to the central nervous system manifestations.

Treatment

The treatment is merely supportive and symptomatic. It is important, however, that even in asymptomatic cases such children be referred for the indicated psychiatric guidance. It is to be emphasized, particularly in cases of chronic usage, that tests should be done to determine the blood, bone marrow, liver, and kidney damage. Of the cases reported to the New York City Poison Control Center, no serious toxicity was observed resulting from the use of airplane glue. The chief problem, however, relates not to the use per se, that is, not only to the immediate problem but to the underlying factor which drives the adolescent to use this product. We believe that the same child who resorts to this practice also will resort under given circumstances to the use of alcohol, ether, or addicting drugs, including barbiturates and heroin, to get a "kick." Therefore, it is strongly urged that all such cases be referred for psychiatric follow-up.

A proposal has been made recently to add disagreeable, malodorous substances to the formulation to discourage its misuse. On the basis of our experience, however, we do not believe that this would act as a deterrent, nor is it commercially practical. One is apprehensive about the publicity given to the misuse of this product as was indicated by one parent. We are of the opinion that the usage is increased following undue publicity. The usual results which follow public health information apparently misfire when they are directed to thrill-seeking minors. On the basis of our experience we have reason to believe that the wide publicity given to this practice has increased rather than decreased the practice.

"Glue sniffing," we believe, is not an isolated event and cannot be placed in a vacuum. It is part of an over-all family and community health problem. "Glue sniffing," like alcoholism, gasoline inhalation, and drug addiction, is not a disease entity in itself but is symptomatic of an underlying emotional disturbance, a basic personality disorder. It is not the addiction or use per se which is important but what causes the adolescent to engage in this practice.

Number one hundred in a series of Accidental Chemical Poisonings

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Population growth greatest in small cities

Population growth in the United States between 1950 and 1960 was fastest in small cities, according to statisticians of Metropolitan Life Insurance Company.

Cities with 10,000 to 15,000 residents in 1950, as a group, increased their population more than 35 per cent in the decade, while cities with 100,000 or more residents gained only 7 per cent.

In each group of cities, however, population growth varied widely from one geographic area to another. Relative gains were largest in the West and Southwest and smallest in the Northeast.

The smaller cities in the Pacific states, for example, showed gains of up to 85 per cent, during the decade, while the corresponding rise in the Middle Atlantic area was only 5 per cent.

One fifth of the 1,086 cities in the country with populations of 10,000 or more in 1950 actually lost residents during the ten years, and the relative number of cities with losses rose with the size of city.

In most sections of the country a large part of the population gains in the cities resulted from the extension of city boundaries. In fact, outside the Middle Atlantic and Pacific states, at least 70 per cent of the population increase in cities of 10,000 residents and over was due to annexation.

In spite of the low rate of growth in cities of over 100,000 their combined populations in 1960 still comprised 59 per cent of the total in cities of 10,000 and over.

The Sacroiliac Twist

Inoperable Chondrosarcoma Rendered Resectable by Hemipelvectomy

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THE PRESENT REPORT concerns a patient with a massive chondrosarcoma arising from the left ileum which had extended to fill the entire lateral and midportion of the pelvis. It had been declared inoperable by others and was found to be almost inoperable at surgical exploration. The procedure of the sacroiliac twist, which is to be described, permitted the visualization of all the structures necessary for the deep pelvic dissection of hemipelvectomy. In fact, it is the belief of the authors that, had the procedure of the sacroiliac twist not been utilized, there would have been little or no chance of performing the hemipelvectomy.

Case report

The patient, a twenty-eight-year-old Puerto Rican male, had been admitted to the Hospital for Joint Diseases in December, 1958, because of a mass involving the left groin and pain in the left groin radiating to the leg, of two years duration. A biopsy was diagnosed as chondrosarcoma of the ileum. Amputation was advised, but the patient refused for two years, and was admitted to the Metropolitan Hospital on December 21, 1960. He had suffered severe pain in the region of the left hip and progressive constipation. He had not moved his bowels for nine days preceding admission. There was also difficulty in urination, consisting of frequency, dysuria, and difficulty in starting and controlling the urinary stream.

The physical examination showed normal findings except for a mass which involved the left groin, measured approximately 10 by 6 cm., and was fixed to the soft tissues of the inguinal region (Fig. 1). On digital examination, the rectum was found to be markedly compressed by extrinsic pressure from this large, firm mass. An attempted sigmoidoscopy was unsuccessful because of this constriction. All laboratory data, including blood count, serum calcium, phosphorus, alkaline and acid phosphatases, thymol turbidity, bilirubin, and serum transaminase, were within normal limits.

Roentgenograms of the chest showed no evidence of metastasis. Roentgenograms of the pelvis revealed that the lower portion of the iliac bone, extending to the acetabulum and the pubic ramus, had been destroyed by an osteolytic process, and there was marked evidence of extension of a mass into the soft tissues of the pelvis. An intravenous pyelogram revealed nonvisualization of the left kidney and ureter and marked displacement of the bladder toward the right (Fig. 2). Many members of the surgical staff who examined this patient declared him inoperable.

OPERATIVE PROCEDURE. The technic utilized is a modification of the one described by Pringle[1] and Gordon-Taylor and others.[2,3]

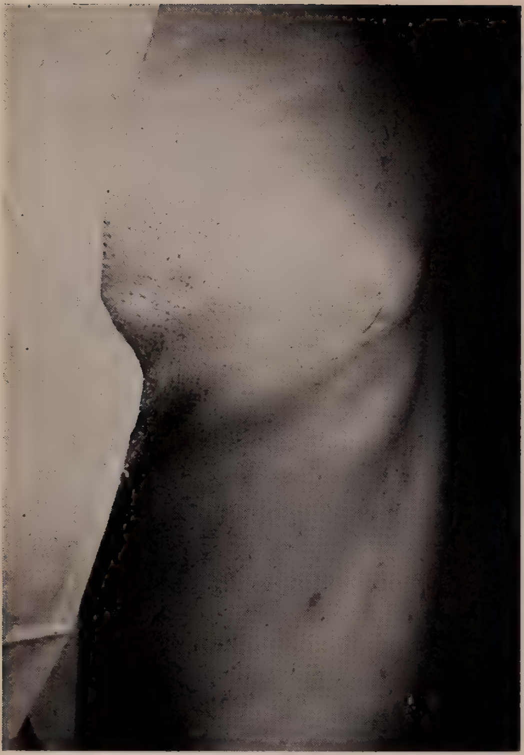

FIGURE 1. Chondrosarcoma filling left pelvic cavity. Note fullness and lateral protrusion caused by underlying tumor.

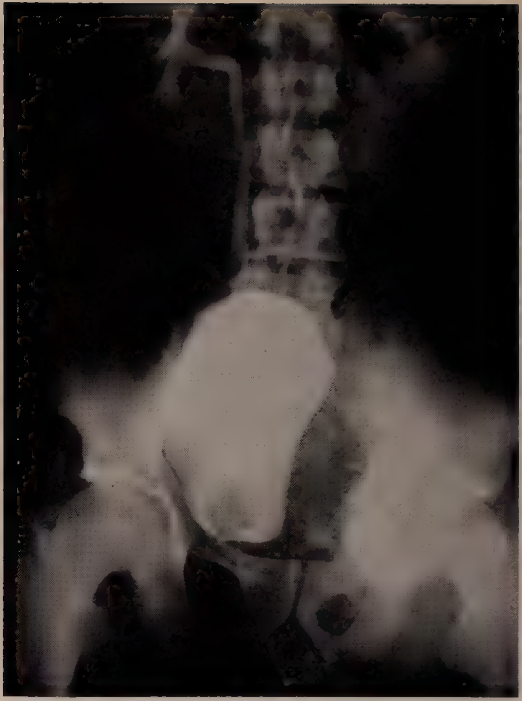

FIGURE 2. Intravenous pyelogram demonstrating nonfunctioning left kidney, displacement of bladder, osteolytic alterations of left innominate bone, and cartilaginous extension of neoplasm into left pelvic cavity.

A Foley catheter was inserted into the bladder, and the anal sphincter was closed with a purse-string suture. The incision extended from the symphysis pubis upward and outward (excising the biopsy scar) to a point about 5 cm. superior to the iliac crest. The anterior incision was then deepened through the subcutaneous tissue and fascia. The rectus abdominis muscle was divided at its insertion into the pubic bone, the external and internal oblique muscles were transected, and the inguinal ligament was severed at its lateral attachment to the pubis (Fig. 3). The spermatic cord is ordinarily retracted out of the field at this point, but in this instance the spermatic cord was incorporated into the tumor mass and the cord was transected accordingly.

The huge chondrosarcoma, which completely filled the left half of the pelvic cavity, was encountered. The peritoneum, which was not invaded by cancer, and its abdominal contents were retracted superiorly and medially. The exposed tumor compressed and extended over the bladder and pressed against the sigmoid colon (Fig. 4). The iliac artery and vein crossed anteriorly to the tumor, but the ureter was posterior to the mass. A portion of the ureter proximal to its constriction by the neoplasm measured somewhat more than 2 cm. in diameter. The common iliac artery and vein were ligated easily between clamps and secured with number 00 black silk.

It was realized that, under the circumstances, the deep pelvic dissection, with danger of hemorrhage from the presacral venous plexus and the hypogastric vein, would render the performance of hemipelvectomy most hazardous. Attention was directed, therefore, to the resection of the symphysis pubis. The bladder was dissected from the pubis in the space of Retzius. The incision was extended inferiorly and laterally to the posterior gluteal fold. The insertions of the ischiocav-

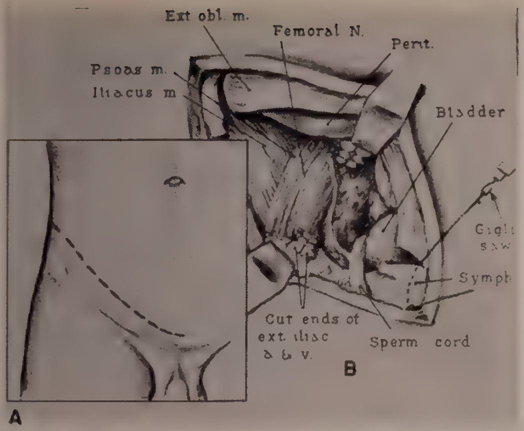

FIGURE 3. Anterior dissection of routine right hemipelvectomy. (A) Incision extends from symphysis pubis superiorly and laterally to a point about 5 cm. superior to iliac crest and paralleling inguinal ligament. (B) Retroperitoneal space has been exposed after serving rectus abdominis muscle at its insertion into pubic bone, external and internal oblique muscles, and inguinal ligament. External iliac artery and vein have been divided and symphysis pubis skeletonized preparatory to transection with Gigli saw. Bladder must be retracted carefully during this phase of operation.

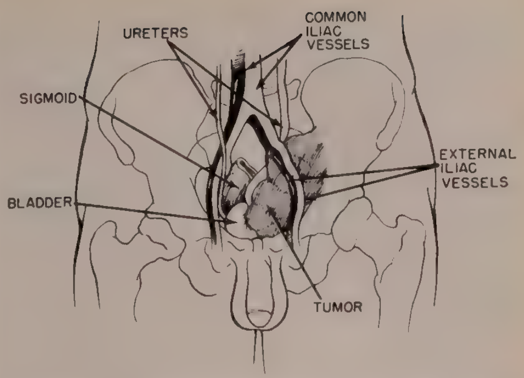

FIGURE 4. Illustrates chondrosarcoma of patient in this report which displaces bladder and rectum and fills left half of pelvic cavity. Its extent prevented dissection shown in Figure 3.

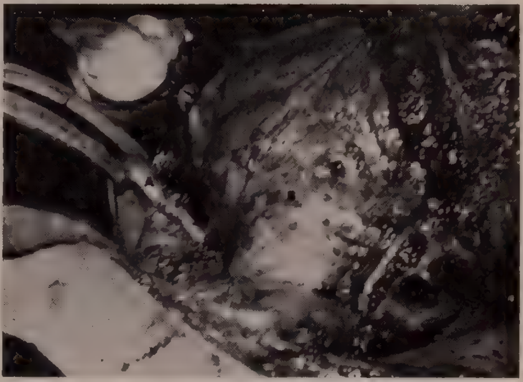

FIGURE 5. Photograph at operation, demonstrating dissection of ureter from chondrosarcoma. (A) Ureter. (B) Chondrosarcoma. (C) Severed symphysis pubis.

ernosus and pubocavernosus muscles were severed and the innominate bone skeletonized. A Gigli saw permitted the transection of the symphysis pubis. Next the crest of the ileum was skeletonized by severing the attachments of the quadratus lumborum muscle. The iliacus, piriformis, gemelli, and levator ani muscles are usually divided next in the performance of a hemipelvectomy. The tumor obscured all the landmarks except the iliopsoas muscle, which was transected, and the upper portion of the iliacus, which was also transected. The other muscles, including the piriformis, gemelli, and levator ani muscles, were obscured by the huge chondrosarcoma which was overriding and fixed to the muscles and to the posterior pelvis (Figs. 5 and 6).

Accordingly it was decided to abandon this phase of the operation momentarily, and the posterior dissection was performed. This consisted of carrying the incision posteriorly and inferiorly, extending from the superior junction of the anterior incision over the buttock to join the inferior border of the anterior incision. A thick skin flap was developed, and the posterior attachment to the gluteal muscles was divided. Then the limb was sharply flexed and abducted, and by transecting the major ligament to the sacrum and the great nerve trunk, the extremity was partially mobilized. The superior gluteal and obturator arteries were identified, ligated, and severed.

Sacroiliac twist. Attention was then directed to the dissection of the deep pelvis. An attempt to dissect the tumor off the bladder resulted in brisk bleeding. Efforts to expose the sacroiliac articulation by sharp dissection also resulted in brisk bleeding. The sacroiliac articulation was obscured by the tumor, which extended beyond the midline and was attached

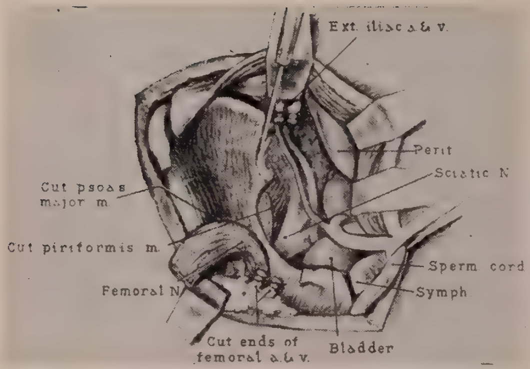

FIGURE 6. Dissection of deep pelvis and separation of sacroiliac joint as performed in routine hemipelvectomy.

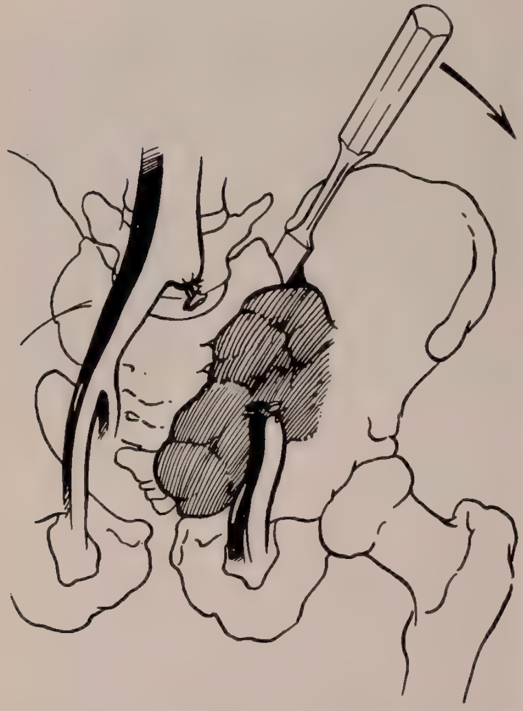

FIGURE 7. Dissection shown in Figure 6 was not possible in this case because of size of tumor. Sacroiliac joint is weakened by a few strokes with a mallet against a chisel inserted at superior border of joint.

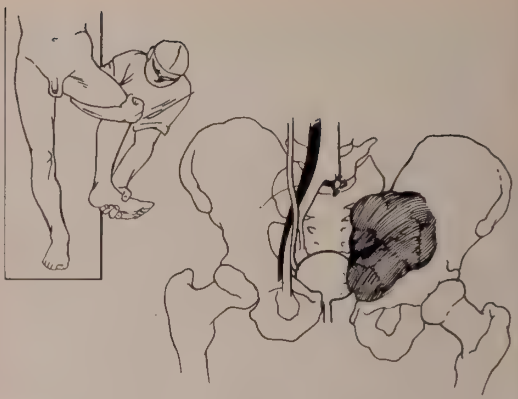

FIGURE 8. Insert: sacroiliac twist. Forceful external rotation and abduction fracture the joint. Tumor is shown after sacroiliac disarticulation. Neoplasm has "rolled" away from bladder and sacrum.

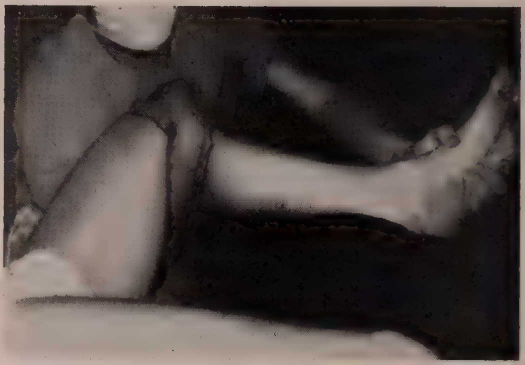

FIGURE 9. Performance of sacroiliac twist.

to the sacrum (Fig. 7).

The sacroiliac twist was then attempted. The extremity was abducted and rotated externally, and forceful pressure was exerted on the sacroiliac articulation. By means of forceful external rotation and abduction, it was possible to fracture the sacroiliac joint. After the disarticulation of the joint, the external rotation of the tumor mass resulted in a cleavage plane that permitted the dissection of the tumor from the bladder and the severance of the piriformis, gemelli, and levator ani muscles. With this accomplished, the limb was removed (Figs. 8 to 11). The posterior flap was tailored, removing some redundant skin, and a repair was obtained. A catheter was inserted into each end of the wound and attached to a suction apparatus. The temporary scrotal and anal sutures were removed, and a bulky pressure dressing was applied.

Comment

Chondrosarcomas metastasize much less frequently than do most malignant neo-

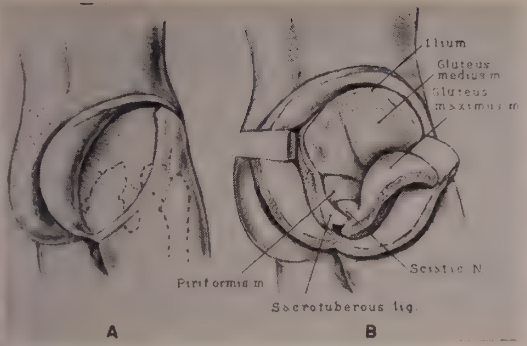

FIGURE 10. Posterior dissection. (A) Skin incision. (B) Deep dissection.

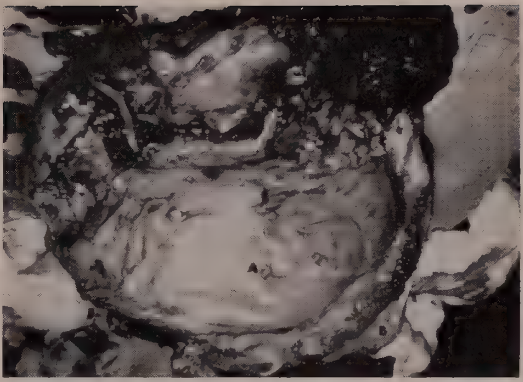

FIGURE 11. Surgical specimen. Neoplasm extends over severed sacroiliac joint. (A) Tumor. (B) Severed sacroiliac joint.

plasms of the bone. In Dahlin and Henderson's[4] series from the Mayo Clinic, metastases occurred in less than 10 per cent of 212 patients. Most deaths are the result of local infiltration. It therefore behooves the surgeon to make every effort to resect a chondrosarcoma. No other modality is available for treating these tumors; hence, if surgery fails, the patient is doomed.

With this in mind and realizing that in the patient of the present report the chondrosarcoma filled most of the pelvic cavity, the procedure of hemipelvectomy was attempted. The operation progressed in a routine manner except for the dissection of the adherent cancer from the bladder, rectum, and deep pelvic wall. By sharply abducting and externally rotating the involved extremity—the sacroiliac twist—it was possible to rotate the neoplasm externally away from the bladder and away from the sacroiliac synchondrosis. This technic permitted good exposure of the synchondrosis and allowed dissection under direct vision of this region. This simple procedure should be kept in mind when one has difficulty in performing the sacroiliac dissection. In this instance, the technic made the operation possible and removed the hazard of blind dissection in this region. Miller[5] has used the procedure of sacroiliac twist routinely in performing hemipelvectomies and has reported his experiences with 32 cases.

The patient has done well postoperatively. The nonfunctioning left ureter is now functioning. Bowel and bladder functions are normal.

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Wegener's Granulomatosis Treated with Nitrogen Mustard

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THE TRIAD of necrotizing granulomas of the respiratory tract, disseminated necrotizing vasculitis, and focal or diffuse glomerulonephritis characterizes the disease entity, Wegener's granulomatosis.[1] The cause of this rare, usually rapidly fatal disease, is unknown. However, many authors feel that the disease represents a state of hypersensitivity, and some have suggested that antibiotics, sulfa drugs, or products of infection may be the inciting agent.[2,3]

Radiation therapy to local lesions,[4,5] adrenocorticosteroids,[1,3,6,7] antibiotics, and in 1 case nitrogen mustard[1] have been used as treatment. In a few cases one agent, or a combination of agents, has resulted in remissions of varying degrees and durations. However, in most cases treatment has been without effect on the rapid dissemination and final fatal outcome of the disease.

The case presented here illustrates the pertinent clinical and pathologic manifestations of the disease. The illness began with localized lesions in the nasal cavity and progressed rapidly to the involvement of multiple organs. Transient but definite improvement was obtained with nitrogen mustard after steroids had failed to control the disease. Attempts to sustain the remission with chlorambucil and then combinations of prednisone, ACTH, and chloroquine were unsuccessful. The patient expired of a wound infection due to Clostridium welchii following the excision of an omental infarction.

An incidental finding in this patient was the very rare hereditary trait, bisalbuminemia.

Case report

This twenty-two-year-old white male barber was admitted to Roswell Park Memorial Institute on May 5, 1960, complaining of nasal obstruction, weakness, and joint pains. In January, 1960, he first noted right nasal obstruction. Despite symptomatic treatment, this symptom became worse. In February he noted weakness and anorexia, and he was admitted to another institution where a biopsy of the lesion in the right nostril revealed a granuloma. Local hydrocortisone therapy resulted in some shrinkage of this lesion. However, in March he was hospitalized again with complaints of severe frontal headache, photophobia, pain in the throat, and a purulent drainage from the right ear. At about the same time he noted pain, with limitation of motion, in several joints, beginning in the shoulder. These symptoms of arthritis were migrating in nature and intermittently involved the shoulders, wrists, elbows, fingers, knees, ankles, and toes. The pain was accompanied by swelling but without associated redness of the regions involved, and it lasted for as short a period as a few hours and usually not over two days.

In April he was admitted to the Lahey Clinic, where a review of the biopsy slides confirmed the diagnosis of Wegener's granulomatosis. Studies of renal function, including urinalysis, urinary concentration, blood urea nitrogen, and a phenolsulfonphthalein excretion test showed normal findings. The sedimentation rate was 77 mm. in one hour. A lupus erythematosus cell preparation showed negative findings. An x-ray examination of the paranasal sinuses revealed hyperplastic sinusitis, and a chest roentgenogram showed a well-rounded area of infiltration in the upper lobe of the right lung. Sputum, nose, and ear cultures contained Staphylococcus aureus, coagulase positive. The sinusitis and otitis media improved on tetracycline therapy. Four weeks prior to his admission to our hospital, because of persistent arthritic symptoms, the patient was given methylprednisolone (Medrol) 40 mg. daily in divided doses; this was followed by some improvement of the joint symptoms. Three weeks prior to his admission he noted subcutaneous nodules on the ulnar surface of his elbows, an acneiform rash on his forehead, and a slight nonproductive cough. One week prior to his admission he developed postprandial epigastric pain. Because of these symptoms, the methylprednisolone therapy was discontinued, and within three days there was a recurrence of the arthritis, weakness, malaise, sore throat, and dysphagia. These symptoms persisted until the day of his admission. He had lost 30 pounds of weight since the onset of his illness.

The past history was noncontributory except for an episode of gonorrhea while he was in the Army. There was no history of allergy, tuberculosis, or rheumatic fever.

A physical examination on admission revealed an acutely ill white male with a temperature of 100.6 F. and blood pressure of 130/90 mm. Hg. The pulse rate was 84, and respirations were 18 per minute. There was dullness of the right tympanic membrane without evidence of scarring. The conjunctivas were injected bilaterally. The optic fundi appeared normal. There was a complete obstruction of the right nostril and partial obstruction of the left. The mucous membrane of the pharynx was reddened and was partially covered by a small amount of yellow exudate. No lymph nodes were palpable. The heart and lungs were normal. Tenderness with a slight muscle spasm was present in the mid-epigastrium. The liver and spleen were not palpable. There was limitation of motion of the right shoulder, knee, and elbow, and pain on motion of the wrists. A punctate, hemorrhagic rash was noted on the buttocks and nodular, hemorrhagic, and partially necrotic lesions, measuring 1 cm. in diameter, were found on the ulnar surfaces of both elbows. The neurologic examination showed normal findings.

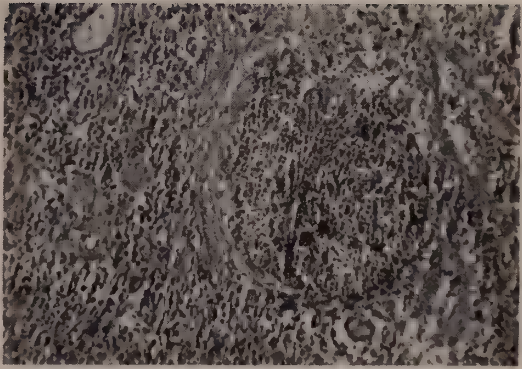

FIGURE 1. Photomicrograph of biopsy from right nostril. In the center is a microabscess containing degenerating leukocytes, erythrocytes, neutrophils, some eosinophils, and some large hyperchromatic binucleate macrophages. To the left are multinucleated giant cells, and surrounding the abscess are numerous plasma cells and eosinophils (hematoxylin and eosin stain, × 105 diameters).

HOSPITAL COURSE. The initial chest x-ray film showed a density with a central radiolucent area in the upper lobe of the right lung. X-ray films of the paranasal sinuses showed chronic maxillary sinusitis without evidence of bone destruction. Roentgen studies of the barium-filled stomach, duodenum, and small intestine did not reveal any abnormalities. The blood urea nitrogen, fasting blood glucose, alkaline phosphatase, uric acid, calcium, and phosphorus values were all within normal ranges. The hemoglobin was 13.5 Gm. per 100 ml., the platelet count was 230,000, and the white blood cell count was 12,000 with a normal differential. The urine contained no protein and no red blood cells. The phenolsulfonphthalein excretion was normal. An L.E. cell preparation showed negative findings, and the C-reactive protein was 2 plus. The alligator erythrocyte hemagglutination test for the rheumatoid factor was 2 plus. An electrocardiogram revealed no abnormalities. The bone marrow was of normal cellularity but contained a considerable number of plasma cells, histiocytes, eosinophilic myelocytes, and mature granulocytic cells. A review of the slides of the original nasal biopsy revealed a severe inflammatory reaction in which the mucosa and submucosa could scarcely be identified. Blood vessels could not be identified as arteries or veins. The inflammatory cells consisted of eosinophils, plasma cells, and some neutrophils; in some areas there were

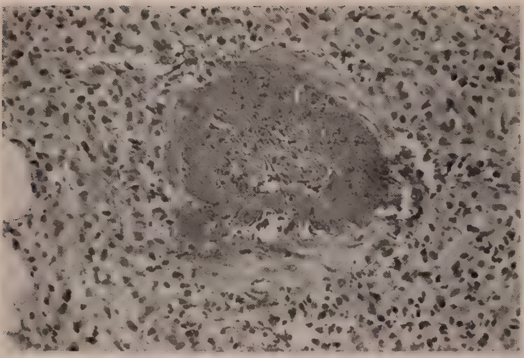

FIGURE 2. Photomicrograph of biopsy from right gastrocnemius muscle demonstrating the vasculitis. The lumen of the artery is occluded by an organizing thrombus which has obliterated the tunica intima. Much of the tunica media is involved with focal necrosis, and the tunica adventitia is infiltrated with inflammatory cells (hematoxylin and eosin stain, × 131 diameters).

multinucleated giant cells as well as a microabscess (Fig. 1). Stains for acid-fast bacilli were negative. A biopsy of the skin and muscle in the region of the right gastrocnemius revealed a severe obliterating vasculitis (Fig. 2). Cultures from the pharynx revealed Staph. aureus, coagulase positive. Several blood cultures were sterile. Paper electrophoresis of the serum proteins showed an increase in the gamma globulin fraction and a double albumin band. The total protein was 6.23 Gm. per 100 ml. of which the serum albumin was 3.8 Gm. per 100 ml.

The patient was treated with 2 Gm. of erythromycin daily over a period of five days without any effect on the temperature, which persisted at levels of 101 to 102 F. On May 7, 1960, the third hospital day, small punctate hemorrhagic lesions, confluent in some areas, became visible on the dorsum of the feet and gradually extended over the lateral aspects of the legs (Fig. 3A). At the same time mucosal ulcerations appeared bilaterally at the junction of the hard and soft palates (Fig. 4). Epigastric pain continued intermittently, and the patient developed melena and then grossly bloody bowel movements. On the fourth hospital day a rectosigmoidoscopy revealed petechial lesions in the mucosa of the rectum and lower sigmoid colon. At this time the urine contained 1 plus protein without microscopic hematuria. On the sixth hospital day ankle edema was noticed. Nitrogen mustard therapy was instituted at this time because of the rapid progression of the disease process. Our plan was to try to maintain any remission obtained with the oral alkylating agent, chlorambucil. The patient received intravenously 0.1 mg. per kilogram of body weight of nitrogen mustard daily for four days, May 11 through May 14. There was a gradual diminution of the arthritic symptoms during the treatment period, and on May 14 they disappeared completely. The ankle edema and conjunctivitis disappeared, and by May 15 the skin lesions had begun to fade. However, concurrently with the therapy, proteinuria increased, and hematuria appeared. Rectal bleeding persisted, and the abdominal pain became more severe. Nausea and vomiting, which had occurred during the nitrogen mustard therapy, persisted on the day after therapy, and on May 15 he had clinical and roentgenographic evidence of a small bowel obstruction. A laparotomy revealed three areas of perforation in a 10-cm. segment of the distal ileum. The lumen of the small bowel contained 750 cc. of clotted blood. A 45-cm. segment of the ileum was resected, and an end-to-end anastomosis was performed. A pathologic examination revealed that the serosa was covered with a fibrinopurulent exudate. In the segments adjacent to the perforations the bowel wall was paper thin. Proximal and distal to these lesions the intestinal wall showed congestion, flattening of the plicae, and areas of polypoid hypertrophy. On microscopic examination necrosis, hemorrhage, and ulceration were seen, and leukocytic infiltration and granulation tissue in the area near the perforation were found. At the lines of surgical resection there was a thickening of the submucosa, scarring, mononuclear cell infiltration, and inflammatory reaction in the serosa. Chronic arteritis and phlebitis were evident.

Because the patient had received steroid therapy for a period of three weeks prior to surgery, he was given hydrocortisone intravenously before, during, and after surgery, in daily doses of 100 to 200 mg. This was followed by oral medication with 20 mg. of prednisone daily. For five days after surgery he received 9 million

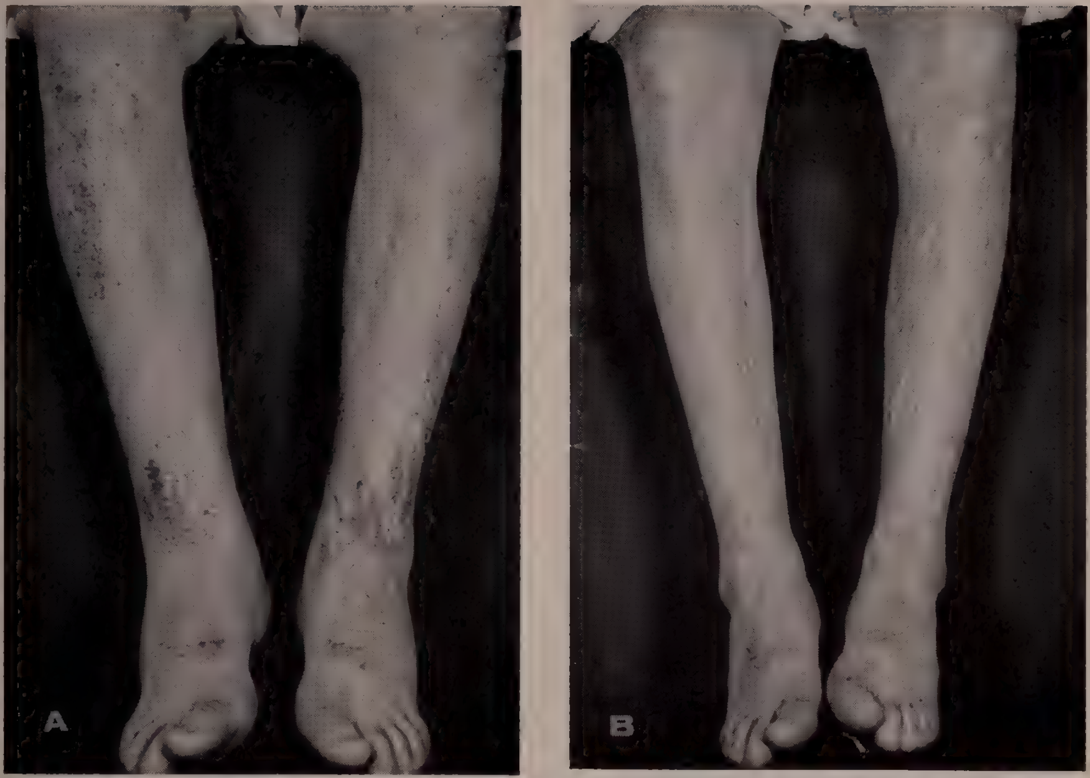

FIGURE 3. (A) Photograph of patient's legs showing symmetrical punctate hemorrhagic rash and ankle edema just prior to nitrogen mustard therapy. (B) Photograph of patient's legs showing early recurrence of skin lesions on lateral aspects of legs and ankles fifteen days after completion of nitrogen mustard therapy.

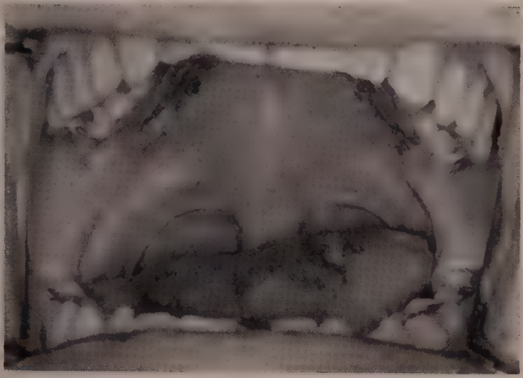

FIGURE 4. Photograph of oral cavity showing symmetrical ulcerations at junction of hard and soft palates.

units of penicillin and 2 Gm. of streptomycin daily. The antibiotic therapy was then changed to chloramphenicol 500 mg. every six hours which was discontinued after six days.

Five days after surgery, on May 20, 1960, proteinuria and hematuria disappeared temporarily for five days. A chest x-ray film at this time revealed a diffuse infiltration in the left lung in addition to the previously described infiltrate with cavitation in the upper lobe of the right lung (Fig. 5A). Subjectively the patient was feeling better than at any time during his illness. However, on May 23, nine days after the completion of the nitrogen mustard therapy, intermittent slight stiffness of the first interphalangeal joints was noted, followed by migratory arthralgia which, however, was not as severe as it had been on his admission. At this time, oral chlorambucil therapy, 6 mg. per day, was instituted. The patient continued to have a slight fever, which, after May 26, rose to 102 F. On May 29 a recurrence of the skin lesions on the lateral aspects of the ankles became evident (Fig. 3B). After three days there was some clearing of these lesions. However, new lesions then appeared on the anterior

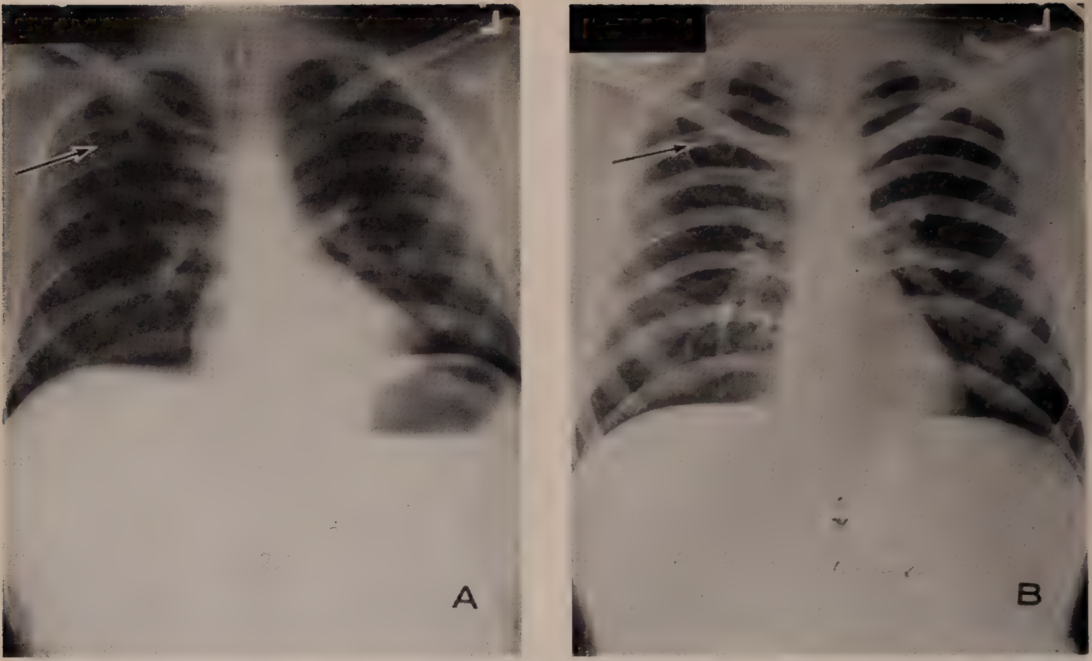

FIGURE 5. (A) Chest x-ray film taken five days after completion of nitrogen mustard therapy. There is diffuse infiltration in periphery of left lung in addition to infiltration with cavitation in upper lobe of right lung which was present prior to therapy. (B) Chest x-ray film taken June 1, 1960, showing complete disappearance of infiltrate in left lung and improvement in infiltrate in upper lobe of right lung.

abdominal wall in the area from which the adhesive tape was removed.

On May 31 the chlorambucil dosage was increased to 12 mg. daily. A chest x-ray film showed a complete disappearance of the infiltrate in the left lung and marked improvement in the lesion of the upper lobe of the right lung (Fig. 5B). By June 2 the patient again complained of a sore throat, and the areas of ulceration on the soft palate showed an increase in size. He also complained of epigastric and paraumbilical pain, but there was no tenderness or spasm on abdominal palpation. The prednisone dose was increased to 60 mg. daily without any beneficial effects.

At this time we decided to use other therapeutic agents which have been of some benefit in various "hypersensitivity" diseases. Because of the critical state of the patient and the rapid progression of the disease, it was felt that reliance could not be placed on a single agent, and therefore several agents were given simultaneously. Thus, on the following day, ACTH 80 units was administered by an intravenous drip over a six-hour period, and on the same day 2 Gm. of chloroquine were given. There was an immediate drop in the patient's temperature to normal levels. Intravenous infusions of ACTH and 1 Gm. of chloroquine were given daily thereafter.

On June 6, 1960, the abdominal pain became more severe. There was diffuse tenderness over the abdomen and occasional nausea and vomiting. On June 8 pain, tenderness, and spasm became localized to the right lower quadrant of the abdomen. A second laparotomy was performed, and a small infarct in the omentum was resected. Following surgery, hydrocortisone in doses of 100 mg. three times a day was given intravenously. The first postoperative day was uneventful except for a rise of the temperature to 102 F. The following morning the patient was found in shock. A physical examination revealed decreased breath sounds and dullness in the base of the right lung. The abdomen was diffusely tender. After the bandage was removed from the wound, gas bubbles were noted in the incision. The skin adjacent to the left margin of the wound was necrotic in an area measuring 5 by 10 cm.

A smear of material removed from the wound revealed spore-bearing, gram-positive rods. Thirty million units of penicillin and nine vials of gas gangrene antitoxin were administered intravenously over a period of ten hours. The skin and subcutaneous tissue were excised from a 20- by 20-cm. area of the abdominal wall. Six hours later the patient had a grand mal seizure and died. The diagnosis of Cl. welchii infection was confirmed by appropriate bacteriologic studies.

Postmortem findings. The autopsy revealed two symmetrical ulcers in the larynx just beneath the true vocal cords. Both lungs had numerous areas of hemorrhagic pneumonia measuring about 2 cm. in diameter. A 2.2-cm. diameter cavity with coarse margins, containing light tan friable debris, was noted in the upper lobe of the right lung. There was a 2.2-cm. infarct in the left lobe of the liver, and the surface of the spleen contained multiple minute infarcts. The kidneys had several small areas of congestion measuring 0.4 to 0.6 cm. A 2.5-cm. area of hemorrhage was present in the left testicle.

A microscopic examination revealed hemorrhagic pneumonia in the lungs. There was no evidence of vasculitis or chronic granuloma in sections from the region of the cavity. The liver showed fatty metamorphosis. The serosa of the stomach and small intestine showed acute inflammation secondary to generalized peritonitis. Sections of the spleen revealed coalescent infarcts, hyperemia, and several foci of acute and subacute periarteritis. There was a vasculitis involving the coronary arteries (Fig. 6) and rare foci of periarteritis and/or phlebitis in the gallbladder, pancreas, and testes. The kidneys showed an acute glomerulitis with rare granulomas. There were numerous red cell casts and evidence of degenerative and regenerative changes in the tubules (Fig. 7).

Comment

Lesions of the upper respiratory tract are usually, but not always, the first manifestations of Wegener's granulomatosis. Nasal obstruction; rhinitis; sinusitis; otitis media; and ulcerations of the tongue, gums, or oral mucous membranes are common. The involvement of the nasal septum may progress to a saddle-nose deformity. Frequently the first symptoms are cough, hemoptysis, or chest pain.[8] Roentgenograms of the chest may demonstrate single or multiple infiltrates of varying density which sometimes show cavitation. At any time during the course of the disease multiple organ involvement may occur, such as pericarditis, pleuritis,[9] prostatitis,[10] orchitis, conjunctivitis, parotitis,[5] migratory arthralgia or arthritis, neuritis,[3] and skin lesions. Chemosis, papillitis, perilimbal keratitis,[3] exophthalmos,[6] and blindness[7] have been described. Abdominal pain may indicate the involvement of abdominal viscera, and bloody stools result from gastrointestinal tract disturbances.[3] The course of the disease is usually characterized by fever, weakness, malaise, and weight loss. The symptoms may be episodic with exacerbations and remissions which are not related to therapy. Finally, evidence of renal damage appears in the form of proteinuria, hematuria, casts, and uremia. Death usually results from uremia or bronchopneumonia.[4] The average survival time from the onset of symptoms is six months. Only a few patients have survived for over two years.[1,11]

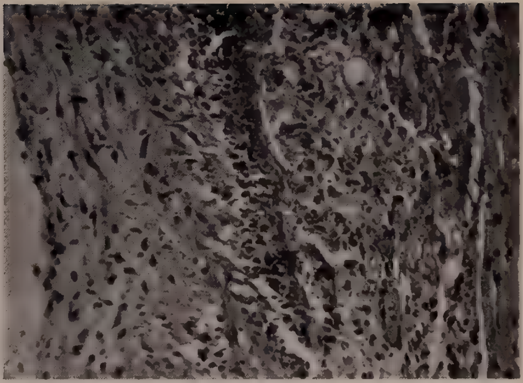

FIGURE 6. Photomicrograph of section through the wall of a branch of a coronary artery. Arterial lumen is at left. There is fibroblastic reaction involving all layers and acute degenerative changes in a few myocardial muscle fibers on the right. The circumference of this segment of artery showed early inflammatory changes as well as areas of healing (hematoxylin and eosin stain, × 138 diameters).

The present case shows several clinical features which we feel warrant emphasis.

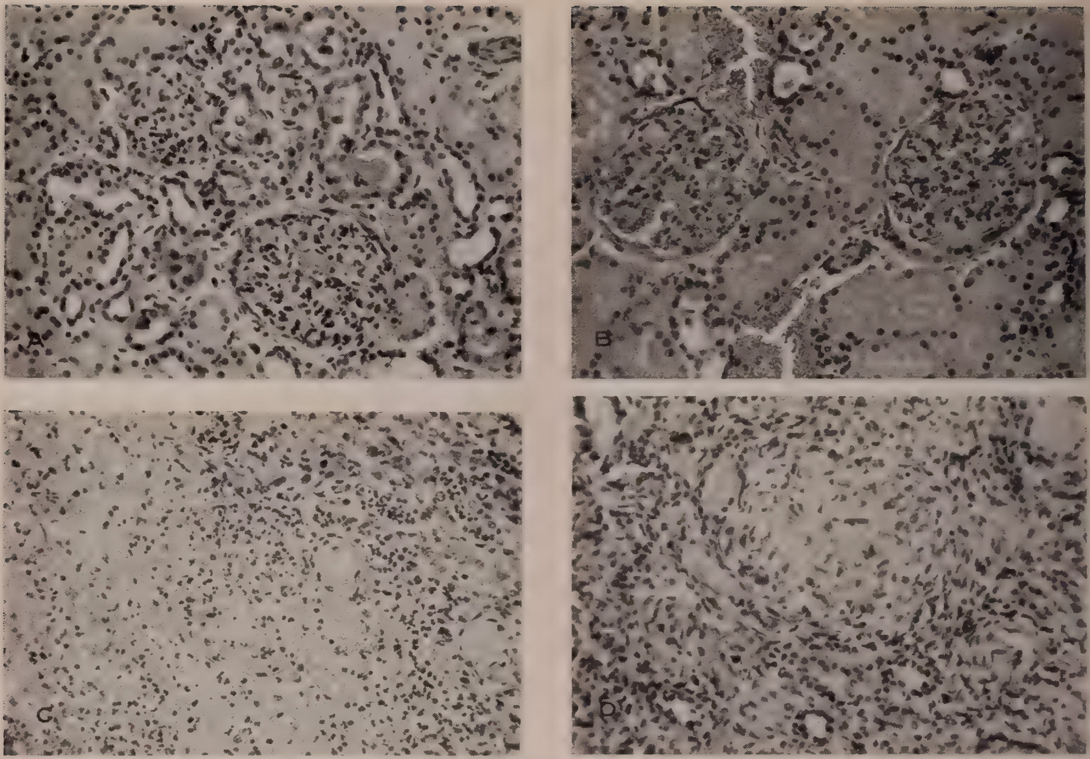

FIGURE 7. (A) Photomicrograph of kidneys showing acute hemorrhagic glomerulonephritis with mild proliferative changes in the glomeruli as well as a thrombus in the lower glomerulus. There are early degenerative changes in the cytoplasms of some tubules (× 156 diameters). (B) This photomicrograph illustrates some of the best preserved glomerular and tubular structures remaining in the patient's kidney. However, there is epithelial proliferation lining Bowman's capsule as well as red blood cells free in Bowman's space (× 164 diameters). (C) Photomicrograph showing edge of recent infarct in kidney. Polymorphonuclear leukocytes in glomerulus and around tubules were fragmenting. Cross sections of two large cases are seen at right of the field (× 142 diameters). (D) Photomicrograph of microgranuloma in area presumably where glomerulus previously was present. There are a few fibroblasts, histiocytes, and lymphocytes in a fibrinoid matrix (× 160 diameters). (Hematoxylin and Eosin Stain)

The ulcerations of the soft palate and the pharynx, the nodules at the elbows, and the skin lesions were remarkably symmetrical in their appearance. Some of the skin lesions seemed to develop in pressure areas. They were noted first on the buttocks, then around the ankles, on the lateral aspects of the legs, in a band corresponding to the area where the blood pressure cuff had been applied, and on the abdominal wall in the area under the adhesive tape of the surgical dressing. The lesions were hemorrhagic with some areas of necrosis. In other areas they were petechial in appearance, although extensive studies of clotting factors did not reveal any abnormality. The arthritis was very migratory with pain and swelling frequently remaining for only two hours in any one joint.

Vascular lesions of the intestines were found in 24.1 per cent of 54 autopsied cases of Wegener's granulomatosis reviewed by Walton.[4] In our case, intestinal involvement with a perforation of the ileum represented a major clinical problem. This was followed three weeks later by localized peritonitis due to omental infarction. Cardiovascular collapse due to the complication of wound infection by Cl. welchii was the immediate cause of death in our patient.

The histopathologic findings in our case demonstrate all of the typical features of the disease as set forth by Godman and Churg[12] in their detailed study of 7 cases of Wegener's granulomatosis. There were necrotizing granulomatous lesions of the upper air passages or lower respiratory tract, generalized focal necrotizing vasculitis involving both arteries and veins, and glomerulitis. Although no material was obtained from the pharynx, nasal cavity, or sinuses at autopsy, previous biopsy material demonstrated a necrotizing granulomatous process with angiitis in the nasal mucosa. Vasculitis was evident in the muscle biopsy as well as at autopsy. Even though there was little clinical evidence of azotemia at the time of death, there was a marked glomerulitis and rare granuloma formation in the kidneys.

The laboratory findings in this patient were similar to those found in other reported cases of Wegener's granulomatosis. There was a slight leukocytosis and anemia and an increased erythrocyte sedimentation rate. The urine revealed microscopic hematuria and albuminuria. However, the blood urea nitrogen was not elevated except on the day of death. The laboratory finding of especial interest was the paper electrophoresis of the patient's serum. At first we thought that the pattern represented a decrease in serum albumin associated with an increase in the alpha-1 globulin fraction. Further investigation by immunologic technics revealed that the band which was considered to be alpha-1 globulin was, in fact, a second albumin.[13]

Bisalbuminemia has been reported previously as a familial trait.[14] Thus far, no known disease has been found to be associated with this anomaly, with the possible exception of a peculiar acrocyanotic lesion which has been described in two members of one family having the trait.[15] We have found this trait in five members of the patient's family at the time of this writing. All of them are in good health.

An abnormality of the serum protein pattern in Wegener's granulomatosis has been described. Lindholm and Nilsson[3] found that in 3 of 6 patients there was a decrease in albumin, a large increase in alpha-1 and alpha-2 globulin, and a less marked increase in the gamma globulin. Similar changes in the alpha globulin fractions have been reported recently by Budzilovich and Wilens.[16] We are grateful to Dr. Nilsson, who sent us the electrophoretic patterns of his 3 patients, none of which showed any evidence of a double albumin. It is likely, therefore, that the presence of bisalbuminemia and Wegener's granulomatosis in our patient is a coincidence. Others have reported abnormalities of the serum proteins in Wegener's granulomatosis, including reversal of the albumin globulin ratio,[6,7] hyperglobulinemia,[1] and an increase in gamma globulin.

The treatment of Wegener's granulomatosis has been unsatisfactory. ACTH and adrenocorticosteroids have been used with varying success. In some cases they have caused prolonged remissions of the disease process,[1] but in others there was a progression of the disease during therapy.[17] Radiation therapy to localized areas of involvement in the nasal cavities and lungs has been of benefit in some cases[4,5] but has produced no results in others.[1] There is one report of a temporary improvement following nitrogen mustard therapy.[1] The indication for antibiotic therapy is the frequent occurrence of bacterial infection of the upper and lower portions of the respiratory tract.

Prior to his admission to the hospital our patient observed an improvement of his joint symptoms and nasal stuffiness while he was receiving methylprednisolone in daily doses of 40 mg. However, the abdominal symptoms, skin rash, and nodules on the forearm appeared during this treatment. Because the disease was progressing on steroid therapy, and nitrogen mustard had been reported to produce temporary benefit, we decided to try therapy with alkylating agents. Nitrogen mustard also has been reported to produce improvement in other "hypersensitivity" diseases.[18]

Our hope was to obtain a rapid remission with nitrogen mustard and then to attempt to maintain such a remission by continuing the therapy with the oral alkylating agent, chlorambucil. The necessity to administer adrenocorticosteroids when major surgery had become mandatory makes difficult an exact evaluation of the nitrogen mustard therapy. Besides, spontaneous remissions also may occur. Nevertheless, we believe that nitrogen mustard did produce an improvement of some manifestations of the disease. The arthritis, ankle edema, nasal stuffiness, and conjunctivitis had disappeared completely, and the skin lesions had begun to fade prior to the administration of hydrocortisone. The improvement in the abdominal pain, hematuria, and proteinuria five days later may have been coincidental or may represent a slower response to nitrogen mustard therapy. It is also possible, however, that this improvement was produced by hydrocortisone, even though the disease was resistant to methylprednisolone. This also may be true in regard to the pulmonary lesions which, following the nitrogen therapy, at first progressed and then improved.

It is our impression that any favorable response which may have been obtained with nitrogen mustard was of a very short duration. It is unfortunate that the effects of maintenance therapy with chlorambucil could not be tested fully.

Summary

A case of Wegener's granulomatosis is presented with a comment which emphasizes the clinical aspects and treatment. The illness began with a lesion in the nose and then progressed to the involvement of multiple organs including the lungs, joints, skin, larynx, oral mucosa, and small intestine. After steroids had failed to control the progression of the symptoms, nitrogen mustard was administered and caused a short but definite improvement. The attempts to maintain the improvement with chlorambucil and then with combinations of prednisone, chlorambucil, ACTH, and chloroquine were apparently unsuccessful; however, an evaluation of this phase of the therapy is difficult because of the very short period of observation before the patient's death from a postoperative wound infection.

The course was complicated by two surgical emergencies, perforation of the ileum and omental infarction. A postoperative Cl. welchii infection was the immediate cause of death.

Of further interest in this patient was the presence of a rare familial trait, bisalbuminemia.

ACKNOWLEDGMENTS. We are indebted to Benjamin Volk, M.D., Department of Otolaryngology, Albany General Hospital, for permission to use the photomicrograph of the nasal biopsy; to Ira LeFevre, M.D., of Coeymans, New York, for referring this interesting patient to us; to John Hubbard, M.D., Department of Pathology, Roswell Park Memorial Institute, for his assistance with the pathologic material; to Gerald S. Spears, M.D., Department of Pathology, Johns Hopkins Hospital, for his review of the pathologic material; and to Joseph E. Sokal, M.D., and Leon Stutzman, M.D., for their critical review and helpful suggestions.

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Special Articles

Words, Words, Words*

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College of Medicine, State University of Iowa

RECEIVING A FORMAL AWARD, eulogy, or commendation is so pleasing that I for one have never had the experience of rejecting one. Beholden as I am to you and your committee and grateful too, commitments for a trip to Washington for the dedication of the new building for the National Library of Medicine keep me from being here. An award received in absentia resembles being asleep at a dream of one's own funeral and missing all the fun. In this uneasy dreamlike way I cannot savor the varied reactions of those in attendance at my expression of pleasure in receiving this honor. I planned to have Dr. Erwin Di Cyan, my surrogate, display for this company selections from various things which I have written. This is not completely satisfactory or satisfying for it becomes in effect a form of eulogizing oneself. I thought I might have added up for your entertainment the literally thousands of manuscripts I have read in review and expatiated on the monstrous regiment of errors, or the hundreds of books I have read and reviewed, or the errors in the large body of papers I have published even though I have labored over them long and lovingly, if not always effectually. I shall marshall for you excerpts from a series of papers which bear witness to my long interest in medical writing. They are examples which embody precept.

Although there is some repetition of ideas, the quotations I make from my publications are given unchanged. More than twelve years ago at a medical convocation for students embarking on a career in various branches of medicine and the health science, I had these words to say:[1]

* * *

Let us consider a few instances where a high regard for excellence will be tested. First of all in the daily use of language, the spoken and written word, if you are like most students today, somehow in your rush to acquire preprofessional techniques, many of you have neglected that vital technique of clear command of your native tongue. Comprehension of ideas depends on language which, as the medium of your learning, must serve as the framework on which your special training is built. Perhaps because it has been unfashionable to aim for excellence in school, many of you have failed to attain even bare competence in expression. In contemporary American life there is generally a fear of culture as though it were a perversion of normal. You cannot do an effective job in a profession unless you sweep aside the childish notion that culture correlates with effeminacy. For those who have made some progress along the road to culture and for that larger band which now determines to make the pilgrimage, it is done best by gaining familiarity with the thoughts and words of the finest members of the human race through all the ages. You must read and become familiar with what they have left us in the way of literary treasures. Much lost ground can be made up by the habit of even brief daily reading in some extracurricular field. This can be done in the face of the overwhelming burden of study upon which you are about to launch only by a profound determination to attain excellence. If you achieve it you will avoid the prevailing sin of obscurity and confusion of ideas which vexes us in so many aspects of our daily existence, and you will enrich your own lives.

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* Acceptance in absentia of the Award for Distinguished Service in Medical Communication of the Metropolitan New York Chapter of the American Medical Writers' Association, New York City, December 13, 1961.

* * *

As president for the Central Society for Clinical Research at the annual meeting in Chicago, November 2, 1951, I delivered an address entitled "A Testament of Duty: Some Strictures on Moral Responsibilities in Clinical Research."[2] Among the topics I touched on was the moral responsibility to be intelligible.

* * *

Clinical research is predicated upon the belief that its significant results should be communicated and used by others. How miserably this is accomplished is any contemporary editor's tale of woe and any thoughtful reader's sorrow. The pseudo prestige of long and difficult words transcends the useful scientific term and diffuses widely through our papers. Simple things are made complicated, and the complex is made incomprehensible. Chaos reigns. The so-called medical literature is stuffed to bursting with junk, written in a hopscotch style characterized by a Brownian movement of uncontrolled parts of speech which seethe in restless unintelligibility. Every day we realize that the iron curtain which disbars us from sampling in adjacent fields of science is not so much the erudition of our colleagues as the tropical jungles of verbiage and gobbledegook in which this erudition lurks, unobserved save by the initiated. Has this unfortunate situation any corrective? If some small fraction of the time and effort which goes into the techniques of research were spent on study and perfection of the simple techniques of writing and speaking clearly, paths could be made in the jungle. Those who start late must read and study good models of exposition. Learn the simple rules: write, rewrite, delete, polish. For sage advice, Allbutt's *Notes on the Composition of Scientific Papers* has lost none of its cogency, and elegantly combines precept with example. For a contemporary view Gower's *Plain Words* is equally good. With such guides our scientific writing must improve. Correct grammar, thoughtfully combined with rhetoric, might lead through grace to that elusive quality style and make a worthy medium for telling of significant work.

* * *

This general theme was continued a week later at a conference dedicated to "Preparing for a Medical Education."[3] Here I commented on the role of liberal arts in preparation for a medical education. I was critical of some of the deficiencies in preprofessional training which I observed, particularly when undergraduate medical students first came on the wards and got into close relationship with sick people, house officers, consultants, and nurses.

* * *

The first and major difficulty is in talking to patients, finding out what is wrong with them, and analyzing it and expressing it in ordinary sensible language. Part of this difficulty results from the necessity of making several translations in thought and speech processes. First, it is necessary to use the vernacular or ordinary everyday language to find out what is troubling people. Their symtoms then have to be translated into our understanding of the mechanisms by which things go wrong, in other words the pathologic-physiology. This includes using all the basic science information we have in anatomy, chemistry, physiology, and the like. We hope to arrive at a conclusion which we call the diagnosis; and the success of our efforts depends on arriving at the correct one.

The next problem is explaining our medical formulations to the patient in language which he can understand and which gives him enough information to make him a willing, indeed an active co-operator in the program of restoration to health. These difficulties of ideas and speech are very real and are so great that some physicians never completely overcome them. If I had to choose among necessary qualities in the student I would put capacity to organize ideas and to express them readily and to interpret them far ahead of the most complete accumulation of factual data.

A great deal can be added to any physician's usefulness by those cultural achievements which unfortunately have come to be looked upon as somewhat perverse in our contemporary society. When I interview students applying for admission to medical school, I usually ask them what great doctors they know in their own community, what famous doctors now or from the past they know in their own state, in their own country, and in the world. I am sorry to have to announce that such knowledge is often very meager, depressingly so in those who are planning to spend their lives in this great profession. Perhaps nowhere better than in knowing the lives of great physicians can the premedical student fruitfully contemplate greatness and largeness of spirit.

* * *

One of the hardest transitions that undergraduate students in medicine make is the shift from basic science to patients and clinical problems. Far more than most of them realize these difficulties are difficulties in expression and in the interchange of ideas. In a paper entitled "A Soliloquy for House Officers," published in the *Journal of the Student American Medical Association* in June, 1956,[4] I dealt with the problem of vocabulary, the choice of words which reveal so many besetting weaknesses of the undergraduate student.

* * *

Though every patient is a test subject and every operation, treatment, regimen, or program is, in the strict sense, an experiment, do not use the word experiment in front of patients and never mention human guinea pigs. Language, the really marvellous development and developer of man's brain, is the hardest tool to use well, the hardest technique to master. In our transactions especially with patients and as models for our students, we should study at all times how we may improve our mutual understanding by the use of language. Words are subtle, slippery, changing chameleons, leaving our lips with one intent, heard with a different meaning or implication, misunderstood, or falsely emphasized. Out of context they may be frightening. They may be clutched at as straws of hope or rejected as messengers of evil. They are sources of anguish when they are interpreted as a sentence of death or invalidism. The long words we may let slip are a great annoyance and frustration to the unsophisticated or even the sophisticated patient. Translate into common terms that a child can understand. Avoid all terror words such as cancer, pernicious, and malignant. Avoid the long and technical words if they are unfamiliar. The patient may be able to take "electrocardiogram" in stride but he may be completely bewildered by "dyspnea." In talking to patients, and especially about patients, avoid the good zoological labels of "male" and "female," accurate though they be. It is just as easy to say man or woman, girl or boy. It avoids the implication of the patient's being a specimen or subject of experiment. At the same time, it removes the subtle, but very real implication, of intellectual or social superiority. We don't refer to our children as three-year-old white males, we call them little boys (or holy devils). Few of us would introduce our mother or Aunt Maggie from Dubuque as a charming fifty, sixty, or seventy-year-old white female. This crude usage is an example of the shocking depersonalization in medicine, so subtle that physicians rarely recognize it and rarely think about it. Patients resent it, though in their quiet acceptance, they say little.

Equally macabre is the reference to patients as cases, at least within their hearing. No doubt, a large element of our thoughtless insults to patients comes because we never quite shake off the physician-cadaver relationship which introduces us to medical school. Much of the public's increasing hostility to physicians results from the unmeant offense in relegating patients to the role of inanimate items or statistics, the physical vehicles (and a nuisance at that) for enchanting processes or beguiling lesions. Even in talking with each other, most doctors have a tendency to use a long word (often erroneously) where a short one, not only is easier, but is correct. We say pathology when we mean lesion, though few say "how fine the astronomy!" when we admire the stars, or "how pleasant the horticulture!" when we look at a flower garden. Though a surgeon may operate his case, if he operates a patient it is to exploit him for gold, not cure his disease. A patient may properly be on a bed or on a bed pan but not on digitalis or on a high fat diet unless he fell into the soup. When we call for consultation, in our unconscious egomania, we say "have dermatology or orthopedics see him." There are a hundred other awkward word usages which are no clearer than the correct and usually simpler American idiom. These high-brow terms annoy and reveal the carelessness of our habits.

* * *

My most recent consideration of words and language was published last summer in the *Archives of Internal Medicine*. It was entitled "Tower of Babel 1961."[5] Among other things it contained a grammatical error: A singular subject failed to get a singular verb. Another error was the alteration of altar into alter by the sometimes bemused and bewildered grammarian from the Archives' headquarters on North Dearborn Street in Chicago. It was missed in the galley proof. Some of you may be glad to know that I have a faithful company of readers who get much pleasure in calling my errors to my attention. Since I have never written a perfect paper, this pack of eager beagles has been able to achieve much merriment and a rich feeling of superiority by showing me my mistakes. I thank them, confessing with contriteness that my misdeeds merely illustrate and embellish the ancient aphorism that those who live in glass houses shouldn't turn the lights on at night, or shouldn't heave stones through their own picture windows, or maybe just shouldn't live in glass houses. It is good clean fun, and I trust that I have managed to learn something from the silent company of errors and infelicities which cannot be expunged from the fair face of the text after the last galley has been returned. I quote, somewhat at random.

* * *

Medical terminology is "the language in which we medical men try to hide our mysteries from the laity and sometimes perhaps our ignorance from ourselves," according to Sir Henry H. Dale. Some further excoriations of language seem to be used so frequently now that they are coming to be accepted. As an example of this we may take the expressions "basis," "type," "level," and "wise." Instead of treating someone as an outpatient we treat him "on an outpatient basis"; surely by adding to the length of this statement we do not add clarity. Instead of something resembling a balloon or being like a balloon, it is a balloon-type thing. Whereas we have come to accept such expressions as lengthwise, we still may be caught up short by hearing that a patient is in trouble, painwise. Finally, I suppose, we will have to learn to put up with such grotesqueries as "this stool has a flatus-type smell, feceswise" or its simpler Anglo-Saxon equivalent.

There are dozens of new usages which must have seemed awkward at first but which have become accepted into the body of orthodox medicalese. Very few are dismayed at the growing ugliness of our language. When one compares them with readily accessible analogies in simple English they still seem awkward. Rarely is the term "dosage" used when dose would not serve the purpose more accurately. Many nouns get converted into verbs by adding -ize. The overuse of -ize, and even more of -ization, has been compared to the proliferation of laboratory fittings, useful in their proper place, but not to be multiplied beyond their judicious employment for practical purposes, and distinctly distracting in the living room. Although "finalize" may still ruffle a feather, "hospitalize," which is especially uncouth to British ears, is quite acceptable to ours. The word beddage is accepted in military medical circles, although we do not "bedize" patients who are hospitalized, and happily few are bedizened.

In recent years I have noted with interest the almost complete disappearance of the word "before." In medical circles it is supplanted by the more cumbersome pseudoelegant "prior to." In case presentations I have frequently heard the expression "prior to" used from twenty to fifty times before the good old Anglo-Saxon word "before" was used. I have no idea what to make of this important observation.

Another example of the cagey coyness which sometimes defaces and deforms our language is the false reference of inappropriate scientific terms, as one may see in the statement that "I am not unaware of a tannish grizzloid ursoid patch," when one had better say "I see a bear" and take appropriate action.

* * *

I hope that this rehearsal of my past efforts justifies my pleasure at the honor you have conferred. Osler has advised us once in a medical lifetime to climb a high mountain and take full inventory of our deeds, soul, and our mind, but not to make it a recurring and, therefore, insignificant pilgrimage. Nonetheless, from time to time in our medical work of various sorts it is a good idea to emulate the artist who backs away from the immediacy of his canvas and changes the light and focus. He looks at his creations differently from a more distant place. He stops the act of embodying his percepts and concepts in the process of painting to get a more general view of his progress to find, in terms of the vernacular, where he is at. So, craftsmen in many fields of medical endeavor, I greet you in spirit and gain the sense of rejoining the world at large. My distress at not being able to receive this distinguished award in person is mitigated by the hope that you may have enjoyed my continuing battle with those who do not make the effort needed to master language, to exchange ideas by reaching for truth and finding a deeper communion with our fellows.

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Birth and death rates in New York State

The birth rate in New York State during the first half of 1962 was the lowest in twelve years, according to statistics released by the State of New York Department of Health. The birth rate was 20.1 per 1,000 population, compared with 21.3 for the first six months of 1961. The number of births, 172,308, was 7,882 below the figure for the same period last year.

There were 92,789 deaths, 1,931 more than for last year. The death rate, 10.9, was the highest in three years.

The infant mortality rate was 26.0 per 1,000 live births (4,481).* The January to June rate for 1962 was 23.5 (4,232).

The maternal mortality rate was 4.7 per 10,000 live births and stillbirths (83), compared with 4.6 (85) for the same period last year.

The death rate from cancer, 186.5 per 100,000 population (15,949), was the lowest in three years. The rate from diseases of the heart was 481.6 (41,187), compared with 478.8 (40,479) in the first half of 1961. The diabetes death rate, 19.9 (1,703), was the highest since 1956.

The rate from vascular lesions affecting the central nervous system, 93.2 per 100,000 population (7,967), was the lowest in seven years. The death rate from diseases of the arteries, 24.6 (2,108), was the lowest since 1957, while the tuberculosis death rate, 6.8 (584), was the lowest on record. The rate from rheumatic fever, 0.3 (24), has been lower only once.

The rate from cirrhosis of the liver was 20.6 (1,758), compared with 19.6 (1,656) for the same period last year. The pneumonia death rate was 44.0 (3,762), compared with 42.6 (3,599).

No deaths from poliomyelitis were reported for the period.

Among the external causes of death, the death rate from motor vehicle accidents, 12.3 (1,048), was the highest since 1953. The suicide rate, 9.3 (792), was the highest since 1952 except for 1960, and the homicide rate, 4.0 (341), was the highest since 1936.

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* Figures in parentheses represent actual number of deaths.

Challenges in Mental Health in New York—1961

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From the New York City Community Mental Health Board

ONE YEAR AGO it was my privilege to speak to this Association for the first time after becoming Director of Community Mental Health Services for New York City.[1] It now becomes my opportunity to speak again, after one year and a few months of service here, and to place before you a set of conditions that must be confronted by greatly expanded efforts if we are to see any hope for advancement or progress in what has been recognized as the foremost health problem in the United States today. The opportunity is welcomed on two counts: first, because this affords me the occasion to give you a brief accounting of the progress which one year ago the Mayor and Board of Estimate authorized by providing additional mental health funds; and, second, because this event allows me to sketch for you programs which will be lost or impaired largely because of the failure of the State legislature to remove the artificial ceiling on City-State sharing in the support of community mental health under the terms of the New York law.[2] These matters may be seen as aggregates which form very complex obstacles to mental health achievement. A confrontation of these provides a series of definable challenges.

Program complexity and the setting of goals

Before proceeding to report something of the progress achieved during the past year, the goals of the Community Mental Health Board should be reviewed briefly. Some of these, it may be seen, are general, rather than specific, in purpose. Therefore, they may be considered to have been operative during the past year, and indeed, being of a general nature, may be applicable for the next several years. Others are couched in somewhat more precise terms; these are readily enough recognized so that specific comment on each is unnecessary.

IN THE FIELD OF MENTAL ILLNESS. To assist in the development and expansion of preventive services which obviate unnecessary hospitalization or commitment, especially in the fields of readily available clinic services and the adjunctive services of day care and night care.

To work with the State of New York Department of Mental Hygiene, for increasing rapprochement between mental hospitals and the community services of New York City and to overcome the isolation which so long has interfered with optimum mental patient care.

To assist in the development and elaboration of new extramural programs aimed at the rehabilitative phase of psychiatric care.

IN SPECIAL CATEGORIES OF NEED. To institute a special program of mental health consultation services to certain caretaking facilities for the aged in New York City; to work for increased availability of psychiatric clinical services to the aged.

To mark for special concern the need for new ventures in the fields of delinquency and correction, embarking on a new study of the former conjointly with both voluntary and official agencies; and developing a revised, more comprehensive approach to correction in collaboration with the department concerned.

To engage collaboratively in the establishment of new approaches in the problem of narcotic addiction, especially as regards the younger victim.

To continue to support and encourage specialized facilities aimed at the care and treatment of the mentally retarded and the

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emotionally disturbed child.

In relation to municipal services. To increase work with other city departments and agencies to improve standards and the scope of psychiatric services, coordinating staff activities with those of the departments of Health, Hospitals, Education, Welfare, and Correction, and those of the courts, among others.

To gather and disseminate information to assist the city agencies in tasks of planning, as related to mental health, and to provide information through *NYCCMHB Reports* about mental health to other departments and agencies of the New York City government.

In respect to voluntary facilities. To stimulate the optimum effective use of the voluntary psychiatric facilities in the community by providing consultative and advisory services to these facilities, by helping them to coordinate programs, and by the judicious use of funds.

To encourage the growth of voluntary psychiatric facilities, in locations and in phases where the need is disclosed to the New York City Community Mental Health Board through its research planning and consultative activities.

In general. To increase work toward making more effective the New York City Community Mental Health Board and various other organizations and systems which are aimed at the reduction of such mental health problems as are of increasing concern to many agencies and professions.

To utilize the information available in this complex and important field as a basis for promoting innovation and new departures, supporting to the greatest extent feasible new directions of effort.

To expand mental health education services to provide responsible key members of the community agencies with better facilities for the handling of mental health problems within their field of endeavor.

To facilitate a greater sharing between all levels of government in the provision of psychiatric care in keeping with the newer knowledge available and to work unremittingly toward a complete removal of per capita limitations on State aid legislation.

This range of goals for the Mental Health Board would suggest that many challenges may be found to program planning and the effort of assigning priorities. A statement in the report, *Action for Mental Health*, points toward a working rule:

> In the matter of establishing priorities as they relate to the broad areas of patient care, recruitment, professional education, and research in mental health, we would sound a note of caution. In the final analysis, our judgment warns us against imposition of a system of priorities. The reason is that we actually have no choice, as humanitarians as well as educators and scientists, but to move as rapidly as possible on all fronts at once . . . .
>
> Indeed, we can see only one matter that takes priority over all others in the program we propose and that is to obtain vastly increased sums of money for its support.[3]

While one may agree that the matter of obtaining sufficient money to support mental health programs dominates all others, the administrator is still left with the problem of program planning in a complex field. These are a substantial group of interwoven challenges to the planner.

Diversification and the implementation of expansion, 1960 to 1961

Another intricate set of challenges must be faced when the execution of a program of expansion is undertaken. Movement toward a number of different objectives is demanded in order that a diversification of the program be achieved. Until the time that clearly established priorities are agreed on, diversity in new developments is demanded. The goals given previously provide a perspective for a review of the accomplishments of the Mental Health Board during the past year. A hint of the formidable task is to be found in the diversified program development that was achieved during 1960 to 1961 in New York City.

Expansions and improvements in existing contracts for outpatient services. With the availability of additional funds, the program in New York City has been improved in the past year by the Community Mental Health Board under contractual arrangements as follows: It has expanded child guidance services on Staten Island, provided additional service in a West Side community center for the treatment of narcotic addicts and juvenile delinquents, established new clinical services in locations in the Rockaways and in North and East Queens where services had been nonexistent or limited, increased contracts with three voluntary agencies in Harlem to assure continuation, at a high level, of services being rendered, supported a special day program for suspended school children in a clinic of the Lower East Side, and promoted two mergers between mental health organizations in Brooklyn to strengthen and improve services to persons of all ages. All of these expansions, covering a considerable variety of services, were made possible by the close continuing cooperative relationships between the city's Board personnel and voluntary clinics already engaged by the Board under the contract program.

INCREASED DIVERSIFICATION OF PROGRAM THROUGH NEW CONTRACTS. With the additional funds, the Board was able also to add five new contracts for much-needed special psychiatric services: Two contracts provide clinical services in day treatment facilities for seriously disturbed children, one increases service in a center for the study and care of the younger retarded children, one establishes a special psychiatric clinic for the aged in a general hospital clinic in the Bronx, and one establishes a new outpatient clinic which is part of a spectrum of community psychiatric services aimed at giving optimal continuity of care.

ADDITIONAL INPATIENT SERVICES THROUGH VOLUNTARY HOSPITAL AGREEMENTS. Furthermore, the Board developed agreements with two additional voluntary hospitals bringing to six the number engaged in the care of inpatients under the Charitable Institutions program, thereby indirectly removing some of the pressure on our overburdened municipal services.

PENDING NEW DEPARTURES AND INNOVATIONS. Finally, the Board has developed other substantial new programs which we believe will soon be placed before the Board of Estimate by the Director of the Budget: the establishment in a health center of a day hospital, emergency clinic, and treatment service under the direction of one of the municipal hospitals; establishment under another city hospital of a clinical service for one of the higher criminal courts; introduction of a new program of day and night care for patients in voluntary general hospitals; and the provision of special clinical services in support of the Youth Board street club workers in their work with teenage groups.

IMPLICATIONS OF EXPANSION. This range of expanded programs testifies to the readiness of New York City to increase its effort and to underwrite new directions of work yet to be initiated. I hope it also conveys to you a sense of accomplishment, the foundations for which were laid over a year ago when the Mayor, supported by interested citizens, won an increase in the per capita formula for State aid for mental health. The foregoing list of achievements gives documentary support to a comment made in the recent Report of the Surgeon General's Ad Hoc Committee on Planning for Mental Health Facilities.

> The burden for the care, treatment, and rehabilitation of the mentally ill has been traditionally borne by the States; however, in recent years, the local communities have begun to accept this responsibility. As a result, local community mental health boards have been established through legislative or administrative action. These boards are concerned with the development of local mental health programs encompassing prevention, community education, early diagnosis and treatment, care of the acute and chronically ill, and aftercare services for those requiring temporary hospitalization. In this perspective the traditional mental hospital becomes only one of the resources needed.[4]

Programming: special interests and jurisdictional problems

In keeping with the effort at identifying the challenges before us, this review has served to tell us most effectively about one great challenge with which we must come to terms: that of program planning for necessary community mental health services. Here boards and directors are held accountable by a substantial number of interests. If one merely recounts special categorical interests, such as the severely emotionally disturbed child, the mentally retarded person, the narcotic addict, the alcoholic patient, the aged, and the ex-mental hospital patient, an almost bewildering set of problems are placed in focus demanding attention. Boards and directors are expected to take account of all of these in the elaboration of plans, or "the master plan."

Here involved is much more than simply the allocating of funds for special direct patient services for each of the categories. Boards and directors must consider how to develop programs of prevention, consultation, education, and rehabilitation. This is a very substantial charge already, and we have not yet considered other dimensions of planning: between disciplines, between agencies, and between governments.

We may be somewhat comforted by the knowledge that we as directors and boards do not bear our responsibilities alone, for we know that other agencies and organizations have had some responsibility for these problems long before the enactment of the Community Mental Health Services Act of 1954. Sometimes the board and director are seen as welcome additions to the whole range of effort. At other times, the influence and effectiveness of directors and boards may be impeded by the agencies having the original responsibility, perhaps because of a perceived "intrusion" of the new agency into the local scene.

Winning legislative support

A review of the first five years of operation in New York State under the Community Mental Health Services Act has been accomplished by Davies.[5] This is a comprehensive study of as complicated a group of issues as exists today in any health field. To me it seems that the study weighs aspiration against accomplishment, expectation against achievement, anticipation against disappointment, and indeed hope against despair. On the whole, Davies concludes, and I heartily agree, that the beginnings toward community mental health under the Act have been in the right directions, especially with respect to more local responsibility assisted by increased State financial aid. He recommends that the limitation on State aid, which is often called the "ceiling," be removed so that local communities may develop programs commensurate with needs, as determined locally.

This year, New York City's mental health program suffered a major setback when the legislature failed to pass any measure for modification or elimination of the per capita formula on State aid. While we may hope that the next session of the legislature will view this situation with more appreciation of the needs of local government, the position of the Mental Health Board is that mental health problems ought not to have to wait for another year before the necessary action is obtained. For this reason the budget estimate of the Board included a supplementary request for an additional $1.3 million, to come from city tax sources. This request was not allowed. The executive budget as adopted by the Board of Estimate provides for a little over $23.8 million for the Community Mental Health Board, an amount some $900,000 more than the budget for 1960 to 1961, as modified. The executive budget will provide for the maintenance of the current and pending programs, although not without some possible slight reduction in services. Possibly one new contract may be developed: a clinic for retarded children, which would expire without the Mental Health Board's support.

Plans which the Board had begun to develop for increasing desperately needed services in a number of special areas must again be postponed and, so far as 1961 to 1962 is concerned, must be assumed to be "lost." Expanded services for the retarded and for the aged, rehabilitation programs for psychiatric patients, day care programs for seriously disturbed children, and expanded clinics in neighborhoods which have little or no service cannot be supported under the proposed budget. The enormity of this challenge can be assessed in terms of loss incurred this coming year as a result of having failed to win legislative support.

Assessing failure: lost plans for mental health, 1961 to 1962

During the winter and spring of 1960 to 1961, the staff of the Mental Health Board and others in the city worked hard and thoughtfully to plan for the immediate future. The urgent needs of all categories of patients in all areas of New York City were weighed carefully. Plans for 1961 to 1962 covered some of the most urgently needed services in the city today.

PROGRAMS IN AREAS LACKING PSYCHIATRIC SERVICES. Although New York City has many psychiatric services,[6] there is a considerable degree of clustering of these in a few areas. Even so, some of these areas are underserved as compared with the needs of the population. Worse yet, other neighborhoods in New York City have little or no local psychiatric service. Such neighborhoods exist in all boroughs and in many parts of each borough.

Of greatest concern to the Community Mental Health Board are the areas lacking in services which also have high admission rates to State hospitals, high rates of juvenile delinquency, narcotic addiction, and other problems which may be indices of emotional disturbance and mental illness. The people living in such areas very often are unable to afford private psychiatric care. They need low-cost or free psychiatric services which are readily available in their own neighborhoods.

Plans to expand existing clinical services and add contracts with new clinical services in many of these unserved and needy areas have had to be abandoned. These programs would cost $400,000.

EXTENSION OF SPECIAL SERVICES. Agencies under contract with the Board now provide, or are prepared to provide, special programs designed to reach groups of patients for whom psychiatric care would otherwise be limited or nonexistent. These special programs include treatment facilities for children, adolescents, narcotic addicts, and prisoners; expansion of evening clinics for working people; and psychiatric consultation services to community centers. Needed to meet the contract agency requests for the extension of these special programs is $425,000. Additional funds could be obligated in new contracts with agencies not now in our contract program.

DAY CARE PROGRAMS FOR SERIOUSLY DISTURBED CHILDREN. For many years the only available solution for seriously disturbed children was institutionalization in a hospital or residential center outside of New York City. That it is possible to maintain some seriously disturbed children in their own community through day care centers strengthened by clinical services has been increasingly recognized. However, there are as yet only five of these centers in existence in the city.

Within the last few months State aid regulations governing community mental health services have been revised to permit the inclusion of day care centers under the Community Mental Health Services Act. Two of the centers are ready to expand their clinical services; one wishes to increase both its clinical and day care facilities. A total of $160,000 was estimated for this purpose.

SERVICES FOR RETARDED PERSONS. Only six psychiatric programs exclusively or mainly for the retarded person exist in New York City; these services are principally for children. The U.S. Children's Bureau has stated that about 3 per cent of the population are retarded. If these figures are correct for New York City, almost 240,000 residents are retarded to some degree. In the year 1959 to 1960 between 9,000 and 10,000 of these were in State institutions, and an unknown number were in private institutions for retarded persons. The six psychiatric services for the retarded patient in the New York City area served about 2,500 children, during the same year. Undoubtedly many more retarded children among the unserved retarded population could have benefited by psychiatric services had they been available.

For the expansion of two existing contracts and for one new contract expenditures of $115,000 were estimated.

SERVICES FOR THE AGED. As elsewhere in the nation the population of New York City above the age of sixty-five is steadily increasing. One result, which is to be deplored, is the increasing numbers of first admissions in the older-age groups to State mental hospitals. There is evidence to suggest that elderly patients are more appropriately given care in other facilities. To do this, new community services are needed in support of nursing homes, homes for the aged, and day centers. Only two psychiatric clinics specifically for the aging now exist in New York City. Other clinics, as has been indicated, take a few aging persons, but their numbers are small in comparison with the persons of other age groups served and in comparison with their numbers in the population. Yet agencies which have attempted work with the aged confirm the fact that in many cases psychiatric treatment can benefit older persons. To provide group consultation and clinical services for the aged persons in one borough and to negotiate a new contract with a clinic for the aged in another, $100,000 was estimated.

REHABILITATION PROGRAMS FOR PSYCHIATRIC PATIENTS. There are only four rehabilitation services for psychiatric patients in New York City today, and three of these are in the same borough. One is a limited clinical service for persons who are clients of the parent agency, one is a vocational rehabilitation service only, one provides social rehabilitation through group activities, and one provides both social and vocational rehabilitation. It is impossible to estimate exactly how many psychiatric patients are served by these four services. However, increasing numbers of patients are being returned to New York City by State hospitals each year. Some of these patients may be ready with a little help to take up their normal activities again. Some can function adequately with only the help provided by the State aftercare clinics. Many others need not only clinical help but also help in readjusting to their family and social groups, help in learning how to find a job, and help in holding it once it is found.

The rehabilitation help which is available is strictly limited geographically. To overcome this in some degree and to expand rehabilitation services would have required $100,000.

URGENT NEED FOR CORRECTIVE LEGISLATION. At the outset, it may seem that the removal of the per capita limitation on State aid would be of importance only to the more densely populated areas and of no consequence to the others. Certainly, from the standpoint of immediate need as seen in the losses that have been recounted, the more populous areas now cry out for this relief. To the extent, however, that all share distress in a common disaster, the less populous areas suffer, too, from the limitation. Perhaps it is only a matter of time before the more sparsely settled regions will also find themselves thwarted by the per capita limitation on State local sharing. In our society we do not withhold relief from areas stricken by flood, drought, unemployment, or other natural and economic troubles, simply because all communities have not been equally affected. In the field of mental illness can we afford to withhold the same compassionate spirit from mentally ill residents who live in the larger metropolitan areas?

In my view, Davies[5] here identifies a major obstacle to our advance in this State and a challenge to our purpose. The time for remedial legislation on this matter is upon us. There appears to be a gathering sentiment throughout the State that the per capita formula is now obsolete and should be discarded. This is the problem of the greatest magnitude, a solution for which is to be sought legislatively.

State and local collaboration

The need for increasingly effective rapprochement between the mental hospital system and the newer community services seems apparent to most observers. The Community Mental Health Board, as an agency of local government, is in a promising position to be helpful. The step, this year becoming law, which was taken by the Commissioner of Mental Hygiene in appointing regional advisory mental health committees would appear to be in the right direction.[7]

There is another type of collaboration which will be required if the greatest combined potential is to be realized between State and local agencies. On this point, I would quote a recommendation of Davies[5]: "More frequent conferences of the boards and directors of counties of comparable size for joint participation in planning are also indicated," (page 61) in addition to consultation from the Commissioner's office. I believe that this point is worthy of being underscored. The directors, by coming together to discuss problems confronting each of them in this complex field of public service, may be able to give invaluable assistance to the Commissioner, which has not been much available up to now, as I understand it. If the directors may be helped to become more articulate, the community mental health services program may move more objectively ahead.

All of this points up the requirement for increasingly effective relations between the

State and local agencies. Local community mental health boards and directors may be, and should be, involved early in planning programs, legislation, regulations, and the like. Procedures toward this end should be developed where they do not now exist. The assistance of the local board staff should be sought in planning which involves other local agencies and State departmental representatives. Both State and local mental health offices need to be as well informed as possible if each is to be in strong partnership with the other. This in all probability will require more State and local personnel to engage in the collaborative planning necessary to the strengthening of the State and local programs.

One more comment on the recommendations in the Davies report will conclude this. The report suggests that an integration of State and community services might begin around the provision of aftercare. There must be a widely distributed number of possibilities for the integration of service at almost any point in the continuum of patient care. The most eloquent arguments favoring an integration of services would appear to be those concerning improved treatment for the individual. Possibly the most telling, albeit not affirmative, ones are those concerning budgets, fiscal policy, or taxation. It will take close working together between local and State offices to achieve the much-needed new directions of program planning, legislative support, and City-State cooperation.

Summary

Challenges may be viewed in accordance with different perceptions of the mental health issues of our times. Viewed administratively, these have been identified as complex obstacles of great importance: program complexity and the setting of goals, diversification and the implementation of expansion, special interests and jurisdictional problems, winning legislative support, assessing failure, and State and local collaboration. These areas of challenge have been related to one year of activities of the New York City Community Mental Health Board.

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7. Mental Hygiene Law, Section 190, as amended by Act of the Legislature of 1961, chap. 281, Albany, State of New York Department of Mental Hygiene.

Patient stays conscious during external heart massage

An unusual case of a man who remained conscious while undergoing closed-chest massage to restart his heart was reported by George M. Bernier, M.D., in the August 4, 1962, issue of the *Journal of the American Medical Association.* It is much more common for a patient to be in a coma during and after external heart massage. The comatose state is believed to be caused by a marked reduction in the flow of blood, and consequently the oxygen supply, to the brain.

However, the sixty-three-year-old patient who did not go into a coma had lived for two years with a pulse rate of 20 to 40 beats a minute. It is considered possible that the cerebral blood flow obtained during closed-chest massage in this patient did not differ much from his usual state. Although there is no information as to whether or not a chronic, mild lack of oxygen can result in decreased oxygen needs of brain tissue, it might be that an adaptive mechanism allows a more effective utilization of oxygen.

Necrology

William Gilford Dickinson, M.D., of Syracuse, died on August 18 at the age of seventy-two. Dr. Dickinson graduated in 1915 from Syracuse University School of Medicine. He was an honorary attending ophthalmologist at University Hospital. Dr. Dickinson was a Diplomate of the American Board of Ophthalmology and a member of the American Academy of Ophthalmology and Otolaryngology, the Syracuse Academy of Medicine, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Harry H. Ebberts, M.D., of Buffalo, died on July 19 at his home at the age of eighty. Dr. Ebberts graduated in 1904 from the University of Buffalo School of Medicine. He was a consulting roentgenologist at the Edward J. Meyer Memorial Hospital and consulting radiologist at Buffalo State Hospital.

Edmund Leo Finley, M.D., of Oneida, died on July 30 at St. Luke's Memorial Hospital, Utica, at the age of seventy. Dr. Finley graduated in 1917 from University of Pennsylvania School of Medicine. He was an attending anesthetist, obstetrician, and junior surgeon at the Oneida City Hospital. Dr. Finely was a member of the American Society of Anesthesiologists, Inc., the Madison County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Julius John Frederick Hayn, M.D., of the Bronx, died on July 5 at the age of seventy. Dr. Hayn graduated in 1921 from the University of Buffalo School of Medicine. He was a senior assistant attending surgeon at St. Vincent's Hospital. Dr. Hayn was a member of the New York County Medical Society and the Medical Society of the State of New York.

Harold Joseph La Tulip, M.D., of Oswego, died on July 21 at his home at the age of sixty-four. Dr. La Tulip graduated in 1924 from Syracuse University School of Medicine. He was an attending surgeon and chief pediatrician at Oswego Hospital and city health officer. Dr. La Tulip was a member of the American Academy of General Practice, the Oswego Academy of Medicine, the Oswego County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Arthur A. Markowitz, M.D., of the Bronx, died on August 29 at Le Roy Hospital at the age of fifty-nine. Dr. Markowitz graduated in 1926 from George Washington University School of Medicine. He was chief of general practice at the Royal Hospital of the Bronx. Dr. Markowitz was a member of the American Academy of General Practice, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Giacomo Orsillo, M.D., of Elmira, died on July 21 at St. Joseph's Hospital at the age of sixty-nine. Dr. Orsillo received his medical degree from the University of Naples in 1920. He was a member of the Chemung County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Reid, M.D., of New Paltz, died on July 19 at the age of sixty-nine. Dr. Reid graduated in 1914 from Albany Medical College. He was attending physician at the New Paltz Central School District, Teachers College, Ulster County Home, and New Paltz Infirmary, and in 1949 and 1958 was elected mayor of New Paltz. Dr. Reid was a member of the Ulster County Medical Society and the Medical Society of the State of New York.

Arthur Porter Squire, M.D., of Rotterdam Junction, died on July 13 at the age of eighty. Dr. Squire graduated in 1906 from the University of Buffalo School of Medicine. He was a member of the Schenectady County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

A.M.A. physical reveals many M.D.'s have ailments

Preliminary analysis of the pathologic tests run at the American Medical Association exhibit laboratory in Chicago in June indicates that two thirds of the physicians tested had significant abnormalities, according to a report issued by Thomas M. Peery, M.D., at a meeting of the American Society of Clinical Pathologists. Dr. Peery is chief pathologist at George Washington University and Hospital, Washington, D.C.

A total of 17 tests were made on each physician. Nine of the tests were blood chemical procedures and yielded the most abnormal results—1,963. The four urinalysis procedures yielded 122 abnormalities; three hematologic procedures also turned up 122 abnormalities.

Elevated blood glucose was found in 21 per cent (378) of the physicians tested, elevated blood cholesterol in 30 per cent (533), and elevated uric acid in 36 per cent (632).

Many physicians had more than one abnormal finding—2,212 abnormal results being reported in the total of 1,771 physicians tested. All physicians whose tests showed significantly abnormal results were sent a letter suggesting that follow-up tests be made by the doctor's own pathologist to see whether or not actual disease is present.

U.S. gets post in Pan American organization

Announcement has been made of the election of Costa Rica and the United States to the executive committee of the Pan American Health Organization. The newly-elected nations replace Colombia and El Salvador whose three-year terms on the committee have expired.

Institute for Advancement of Medical Communication moves headquarters

Richard H. Orr, M.D., director, Institute for Advancement of Medical Communication, has announced that headquarters of the Institute have been moved to 9650 Wisconsin Avenue, Bethesda 14, Maryland. The Institute will continue to maintain offices at 30 East 68th Street, New York 21, New York, and at 1028 Connecticut Avenue, N.W., Washington 6, D.C.

Mount Sinai gets funds for mental health outpatient services

Marvin E. Perkins, M.D., Commissioner, New York City Community Mental Health Board, has announced approval by the Board of an agreement with The Mount Sinai Hospital to provide mental health outpatient services and/or facilities totaling $75,778 for the remaining months of the 1962–1963 fiscal year. On an annual basis, the contract would total $108,490. Mount Sinai already receives Community Mental Health Board funds for psychiatric inpatient services.

Course in laryngology and bronchoesophagology

The Department of Otolaryngology, University of Illinois College of Medicine, will conduct a postgraduate course in laryngology and bronchoesophagology, March 18 through 30, 1963, under the direction of Paul H. Holinger, M.D.

Registration will be limited to fifteen physicians who will receive instruction by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures.

For further information write to: Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

CARE-MEDICO seeks surgeons

In cooperation with The American College of Obstetricians and Gynecologists, CARE-MEDICO is initiating an overseas program to send gynecologists and obstetricians to its hospitals and clinics. The college is developing a list of surgeons who would be willing: (1) to serve for a short period of time—one or two months—without remuneration, paying their own transportation but receiving full maintenance during their stay in the country itself; and (2) to serve for longer periods of one to two years, with salary, transportation, and maintenance provided by CARE-MEDICO.

Countries where such gynecologic services are immediately available are: Afghanistan, Malaya, Cambodia, Haiti, and South Viet Nam.

For further information and applications for foreign service, write to: Richard TeLinde, M.D., The American College of Obstetricians and Gynecologists, Johns Hopkins Hospital, Baltimore 5, Maryland.

Personalities

Honored. Mario F. Tagliagambe, M.D., Brooklyn, with the title "Man of the Year" by the Italian-American Professional Business Men's Association.

Speaker. Leona Baumgartner, M.D., Commissioner, City of New York Department of Health, in Washington, D.C., on September 8, at a forum on venereal diseases.

Awarded. Helmuth Nathan, M.D., New York City, a gold medal as first prize for his oil painting "Seascape" and first prize for his graphic illustration "Chassidic Dancers" at the American Medical Association convention in Chicago in June . . . Leo Wollman, M.D., Brooklyn, an honorary membership in the Argentina Society of Hypnotherapy and in the Brazilian Society of Medical Hypnosis.

Appointed. Goran C. H. Bauer, M.D., Sweden, as director of research for the Hospital for Special Surgery, New York City . . . Irvin J. Cohen M.D., Washington, D.C., as executive vice-president of Maimonides Hospital of Brooklyn . . . Henry I. Fineberg, M.D., New York City, executive vice-president of the Medical Society of the State of New York, as head and Harold P. Graser, M.D., Buffalo, as a member of the new nine-member Advisory Council on Drug Addiction appointed by Governor Rockefeller . . . Charles Murray Gratz, M.D., New York City, as an associate attending in orthopedic surgery on the staff of University Hospital-New York University Medical Center . . . Herman B. Snow, M.D., Ogdensburg, as director of Hudson River State Hospital, Poughkeepsie.

Parental interference linked to child's behavior problems

The degree of parental interference in a child's activities has been linked to the development of juvenile behavior problems, according to a study by Kearsley *et al.* reported in the July, 1962, issue of the *American Journal of Diseases of Children.* Children having major or minor behavior problems had significantly more parental contact and authority and significantly less parental approval than average for their particular age group.

The study was based on questionnaires filled out by parents of 721 children, most of whom were between six and seventeen years of age. A key section of the questionnaire, dealing with the parent-child relationship, was designed to indicate the degree of parental contact with the child, parental authority over his behavior, and parental approval of his conduct.

The results obtained from questionnaires on 207 children whose over-all social and academic performance was judged to be satisfactory by school authorities and physicians were used as the yardstick to measure the other results. While 40 children under professional care for behavior problems were included in the study, most of the children were students at a private school or were seen at a well-baby clinic.

A considerable number of the school and clinic group gave indications of behavioral disturbances, usually in association with parental contact and authority exceptionally higher and parental approval exceptionally lower than found among trouble-free children of comparable age. The possibility that the relationship found between parental attitudes and child behavior has a causal significance is intriguing. The findings support the theory that much of the behavior and personality deviations of children can be linked directly with motivations resulting from parental attitudes.

The questionnaire used in the study, which requires only twenty minutes to complete, may prove suitable for use by practicing pediatricians who now may spend a large percentage of their time dealing with behavioral problems of children. "Although it is recognized that parents might tend to withhold information and thus fail to respond accurately to questions posed, this did not appear to be a factor in more than a few instances. On the contrary, most parents seemed to welcome this opportunity to have the behavioral problems posed by their children given this sort of attention."

Medical Meetings

New York State Chapter, American Academy of General Practice

The fourteenth annual scientific assembly of the New York State Chapter of the American Academy of General Practice will be held in Syracuse, October 15 through 17. High lights of the scientific program will include sessions on edema and related problems; the team approach to the diagnosis, treatment, rehabilitation, and research in cancer patients; and tranquilizers and energizers and virology. The scientific sessions will be held at the Onondaga County War Memorial.

Western New York Chapter of the National Kidney Disease Foundation

The Western New York Chapter of the National Kidney Disease Foundation will present a symposium on "The Kidney in Health and Disease," on October 17, in the Golden Ballroom of the Statler Hilton, Buffalo, New York. The symposium begins at 9:00 A.M.

American Fracture Association

The twenty-third annual meeting of The American Fracture Association will be held at the Huntington Sheraton Hotel, Pasadena, California, October 20 through 25. Attendance at the meeting will qualify physicians for category 2 credit from the American Academy of General Practice.

Augustus B. Wadsworth Lecture

The thirteenth Augustus B. Wadsworth Lecture will be given at the Division of Laboratories and Research, State of New York Department of Health, Albany, on October 25, at 8:00 P.M. Alexander G. Bearn, M.D., of The Rockefeller Institute, New York City, will speak on "Genetic Polymorphism in Human Populations."

Emil A. Gutheil Memorial Conference

The Association for the Advancement of Psychotherapy will present the third Emil A. Gutheil Memorial Conference on Sunday, October 28, in the Empire Room of the Waldorf-Astoria Hotel, New York City. The theme of the conference is 'The Psychotherapeutic Management of the Acting-Out Patient." Speakers will include the following: Frederic Wertham, M.D., New York City; John N. Rosen, M.D., Gardenville, Pennsylvania; Leopold Bellak, M.D., New York City; and Carl Whitaker, M.D., and Thomas P. Malone, M.D., Atlanta, Georgia.

For information contact: Lewis C. Park, M.D., Secretary, The Association for the Advancement of Psychotherapy, 116–66 Park Lane South, Kew Gardens 18, New York.

Division of Dermatology, Downstate Medical Center

The Division of Dermatology of the Department of Medicine, State University of New York Downstate Medical Center, will present a discussion on "Experimental Studies on Penicillin Hypersensitivity" on Friday, November 2, from 10:00 to 11:30 A.M., in the E Building Auditorium, Kings County Hospital, 451 Clarkson Avenue, Brooklyn.

Zoltan Ovary, M.D., associate professor of pathology, New York University School of Medicine, will be the speaker, and Lawrence Frank, M.D., professor of dermatology, State University of New York Downstate Medical Center, will be the moderator.

National disaster medical care conference

"Survival in the Sixties" will be the theme of the thirteenth County Medical Societies Conference on Disaster Medical Care, Chicago, November 3 and 4. The two-day meeting, sponsored by the American Medical Association's Council on National Security, will be held in the Palmer House.

For additional information write to: Mr. Frank W. Barton, Secretary, Council on National Security, American Medical Association, 535 North Dearborn, Chicago 10, Illinois.

Federation of Mental Health Centers

The Federation of Mental Health Centers, Inc., an organization of directors and administrators of psychiatric clinics and mental health centers, will hold its first annual conference at the Barbizon Plaza Hotel, New York City, Sunday, November 4.

Guest speaker at dinner will be Paul H. Hoch, M.D., Commissioner, Department of Mental Hygiene, State of New York Department of Health. Dr. Hoch will stress the strengths and weaknesses of the therapeutic accomplishments of the clinics. Herbert M. Rosenthal, M.D., New York City, will deliver the presidential address.

For further information contact: Mr. Joseph LeBoit, Public Relations, Federation of Mental Health Centers, Inc., 126 Washington Place, New York 14, New York, Telephone CHelsea 3-2313.

New England Postgraduate Assembly

The nineteenth annual New England Postgraduate Assembly will be held November 6 through 8 at the Statler Hilton, Boston, Massachusetts.

The Assembly is sponsored by the Council of New England State Medical Societies in cooperation with the New England State Chapters of the American Academy of General Practice.

The Assembly is open to all physicians. For further information write to: Mr. Getty Page, Secretary, 128 Merchants Row, Rutland, Vermont.

Phlebology Society of America

The Phlebology Society of America will meet on Saturday, November 10, at the Americana Hotel, in New York City. The subject of the meeting will be "Peripheral Vascular Diseases."

For further information contact: H. I. Biegeleisen, M.D., Executive Director, The Phlebology Society of America, Wickersham Hospital Building, 133 East 58th Street, New York 22, New York.

Association for the Advancement of Psychoanalysis

The Association for the Advancement of Psychoanalysis will present a two-day symposium on psychoanalysis as a creative process on November 10 and 11 at the Carnegie Endowment International Center, 345 East 46th Street, New York City, from 9:30 A.M. to 5:00 P.M.

The philosophic, theoretic, clinical, and therapeutic aspects of the relationship of creativity to self- and group development, freedom, artistic growth, and sex will be discussed.

For information contact: B. Joan Harte, M.D., Chairman, Public Relations Committee, Association for the Advancement of Psychoanalysis, Inc., 329 East 62nd Street, New York 21, New York, Telephone PLaza 2-5267.

Symposium at M. D. Anderson Hospital and Tumor Institute

"Viruses, Nucleic Acids, and Cancer" will be the subject of the seventeenth annual symposium on fundamental cancer research sponsored by The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas, February 20 through 22, 1963.

For information write to: Publications Department, M. D. Anderson Hospital, Texas Medical Center, Houston 25, Texas.

American Industrial Health Conference

The 1963 American Industrial Health Conference will be held March 18 through 21, 1963, in Washington, D.C. The conference is comprised of the annual meetings of the Industrial Medical Association and the American Association of Industrial Nurses. For further information write to: American Industrial Health Conference, 55 East Washington Street, Chicago 2, Illinois.

Injury to eye caused by exploding golf ball

Exploding golf balls have caused a number of eye injuries, according to a question in the July 14, 1962, issue of the *Journal of the American Medical Association*, answered by William H. Havener, M.D. The explosion is caused by the sudden release of a liquid rubber compound contained under pressure in the center of the golf ball. A case was described in which such an explosion occurred while a boy was trying to "peel" a golf ball. Particles of the rubber compound became embedded in his eye. The injured eye usually responds to treatment within a week or so.

Abstracts

Surls, J. K.: The use and value of extension in Volkmann's ischemic contracture, New York State J. Med. **62:** 3227 (Oct. 15) 1962.

When it is a question of whether or not to operate in a case of suspected Volkmann's contracture, immediate manual extension of the digits and wrist may be done, with maintenance of this extension by a plaster splint and daily removal of the splint for active and passive motion. When a definite diagnosis has been made, an operation should be done immediately. Interference with circulation is the cause of Volkmann's contracture; the nature of interference may vary, but most often the injury is incidental to maintaining the reduction of a supracondylar fracture of the humerus. A case is reported in which there was an interval of two months between onset of symptoms and periarterial sympathectomy. The patient had muscular weakness in the affected forearm for years following Volkmann's contracture but eventually regained full power; this is explained by the assumption that new muscle fibers developed.

Auchincloss, J. H., Gilbert, R., and Epifano, L. D.: Management of acute respiratory failure in patients with chronic respiratory disease; practical considerations, New York State J. Med. **62:** 3234 (Oct. 15) 1962.

Fifteen cases of chronic pulmonary emphysema and 1 case of kyphoscoliosis were treated using an intermittent positive pressure apparatus without a negative phase (IPPBI). Respiratory failure was a situation in which hypoventilation was believed to endanger life, and progressive deterioration in the face of hospital treatment was given great emphasis in case selection. Six patients died; there was no consistent relationship between survival and the type or intensity of therapy, and the deaths therefore were most likely related to complicating factors in individual patients. The importance of the following factors is stressed: possibility of avoiding tracheostomy in some cases; establishment of a ventilatory control by means of properly designed automatic cycling devices; monitoring of tidal volume on a routine basis; and use of arterial blood carbon dioxide measurements to determine the correctness of settings once a stable state has been achieved.

Damon, J. E., and Woodruff, M. W.: Care and management of the ureteroileostomy patient, New York State J. Med. **62:** 3244 (Oct. 15) 1962.

Diversion of the urinary stream by means of a ureteroileostomy is used in such diseases as bladder neoplasia, vesicovaginal fistulas, and neurogenic bladders. Proper adaptability of the patient to the ileal conduit apparatus is necessary to the success of the procedure. Preoperative preparation includes psychologic and educational preparation, outlining of the skin creases and skin testing, and bowel preparation. Postoperative care includes selection of a urinary collection device, skin care, patient rehabilitation, and follow-up. The role of the nursing staff is important in affecting proper patient adjustment and successful surgical results.

Salomon, M. I., Bruno, M. S., and Ober, W. B.: Percutaneous renal biopsy; its importance in research and clinical medicine, New York State J. Med. **62:** 3248 (Oct. 15) 1962.

Renal biopsy is an important research, diagnostic, and prognostic tool which has contributed greatly to the knowledge of glomerulonephritis and nephrosis. It has also been extremely useful in hypertension and pyelonephritis and in other conditions such as diabetic nephropathy, toxemia of pregnancy, lupus erythematosus, and sickling. Its potential in many other diseases of the kidney is great. Contraindications include: diseases in which a sudden loss of blood could be dangerous; bleeding tendencies; and presence of only a single kidney.

Kopell, H. P.: The warm-up and autogenous injury, New York State J. Med. **62:** 3255 (Oct. 15) 1962.

The warm-up in the living organism is concerned with safety features for the organism and its component systems. The basic activity occurs in the central nervous system where the necessary kinetic patterns are reinforced and the chief initiation of the proper hemodynamic patterns comes about. Factors in the process include joint innervation, proximal body set, and circulation, both peripheral and central. Proper warm-up is important not only in improving the level of performance of physical activity, but also in prevention of autogenous injuries.

Shimaoka, K., and Firat, D.: Serum flocculation test for diagnosis of obstructive jaundice, New York State J. Med. **62:** 3259 (Oct. 15) 1962.

A study was made of the Jirgl serum flocculation test for the diagnosis of obstructive jaundice in 111 patients and controls. The test gave a positive reaction in 87 per cent of 31 patients with obstructive jaundice and negative results in 89 per cent of 54 patients with jaundice that was not due to biliary obstruction and in all of the healthy controls. False negative results were obtained in 1 case of porta hepatis obstruction, 2 cases of complete bile duct obstruction by carcinoma of the pancreas, and 1 case of common duct stone. Eleven patients tested after successful treatment of obstructive jaundice gave negative test reactions.

Mitty, W. F., Jr.: Carcinoma of breast in community hospital, New York State J. Med. **62:** 3263 (Oct. 15) 1962.

A five-year review was made of 78 patients with carcinoma of the breast. The majority of patients were from forty to fifty-nine years old. Seventy-one patients underwent curative procedures. The operability rate was 91 per cent. The absolute five-year survival rate was 53.8 per cent, varying from 90.9 per cent in patients who had a radical mastectomy with the axillary nodes histologically negative to 27.3 per cent in patients with positive axillary nodes.

Roland, M., Smith, J. J., and Schwartz, E.: Use of oral pregnancy test and effect on nonpregnant endometrium, New York State J. Med. **62:** 3270 (Oct. 15) 1962.

A study was made of an estrogen-progesterone combination used in the PD (Pro-Duosterone) oral pregnancy test on 185 patients. In 15 normal patients, menstruation was delayed when the hormone combination was given from day 20 to day 40 of the cycle. Nineteen of 20 patients with secondary amenorrhea showed withdrawal bleeding after not more than two courses of treatment. One hundred and twelve of 159 patients given the hormone combination as a pregnancy test failed to bleed, and pregnancy was subsequently confirmed by biologic tests; 21 patients had withdrawal bleeding; and of the remaining 26 patients who had negative biologic test results, 22 bled after a second course of the drug following estrogen priming, and 4 were found to be pregnant. Endometrial changes follow the use of the drug in nonpregnant patients. These changes revert to normal in following cycles. Slight nausea in 8 patients was the only side-effect.

Crystalline structure of female sex hormone

The crystalline structure of another of the important female sex hormones has been determined by Dr. Dorita A. Norton and others at Roswell Park Memorial Institute, according to the July 2, 1962, issue of the *New York State Department of Health Bulletin*.

The molecular architecture, including bond lengths and angles of the steroid hormone, estradiol, has been established. Estradiol is a hormone which is produced by the ovaries. Normally it controls the development of the female sexual characteristics and initiates the first phase of the menstrual cycle.

The hormone is important in the study and the treatment of cancer. But the relationship between estradiol and cancer is not yet clear. In animal studies, small doses of estradiol cause tumors to grow, while large doses stop the growth of previous tumors. In human beings, estradiol is used chiefly in replacement therapy in cases of estrogen deficiency. It is also used in the treatment of breast and prostatic cancers.

A small single crystal was grown in the Roswell Park laboratories. The crystal was mounted and bombarded with intensive x-ray beams, which were diffracted by the crystal, collected by an automatic scintillation counter, and recorded electronically on charts. The material represented on the charts was fed into complex electronic computers, and the final analysis provided the scientists with a picture of the actual positions of the atomic structure of the crystal.

Although the scientists do not yet know how the positioning of the various atoms affects the behavior of the steroid, future studies will be directed toward a better understanding of the relation of estradiol to its biologic activity.

Month in Washington

A special advisory committee reported to the Public Health Service that the occurrence of 12 cases of poliomyelitis among persons who had taken 38 million doses of oral vaccine did not provide any ground for questioning the safety of the live-virus vaccine.

Reporting on the study by the advisory committee, Luther L. Terry, M.D., Surgeon General of the P.H.S., said: "Following administration of more than 38 million doses of oral vaccine, only 12 cases, outside of the epidemic areas, including 5 from Oregon, have been reported which had their onset of illness within thirty days of vaccination.

"Although the number was very small in relation to the number given vaccine and the diagnosis in certain of these cases seems questionable, I decided to call together members of my advisory committee to examine in detail the diagnosis, laboratory studies, and epidemiologic circumstances relating to each of the cases.

"The group met on two occasions, on August 9 and 16, and after careful consideration of the facts concluded that it was not possible to establish that the vaccine virus caused any of the cases. The advisers emphasized that polio viruses, as well as other viruses, are frequently present in the community and that it can be anticipated that occasionally poliomyelitis or illnesses simulating it may occur following vaccination programs. Illness and injury completely unrelated to polio and naturally occurring cases of polio have continued and, no doubt, will continue to be attributed to the vaccines. Furthermore, it is well known and recognized that any effective medication administered to millions of persons will cause or appear to cause a number of side-effects.

"The committee, in summary, urged the continuation of present and projected programs of immunization looking toward the final elimination of the disease."

As of August 11, the approximate midpoint of the poliomyelitis season, 274 cases of paralytic poliomyelitis had been reported. The total, which included 129 cases in Texas where outbreaks of type I had been occurring, was the same as for a comparable period last year.

* * *

Life expectancy at birth reached an estimated 70.2 years in the United States in 1961, according to the Public Health Service.

The estimate was based on a 10 per cent sample of death records received by the National Vital Statistics Division from all the 50 states.

Deaths totaled about 1,702,000 in 1961—a rate of 9.3 per 1,000 population, only slightly higher than the record low rate of 9.2 for 1954.

Five of the ten leading causes of death showed sharp rate declines as compared with last year. The declines were large enough to make it improbable that they were produced by normal fluctuations due to sampling. The five were vascular lesions; accidents; influenza and pneumonia, except of newborn; general arteriosclerosis; and diabetes mellitus.

The infant mortality rate of 25.3 per 1,000 live births set a record low, about 2 per cent under the previous low of 25.7 recorded in 1960.

Recent statements that citizens of some foreign countries are healthier than Americans were disputed emphatically by the American Medical Association. The A.M.A. statement was prompted by a paper presented at the recent annual meeting of the American Sociological Association in Washington. The paper said that the United States is not as "healthy" as Sweden and England.

"This is like trying to compare apples to oranges," F. J. L. Blasingame, M.D., the A.M.A.'s executive vice-president, said.

"There have been accounts that comparisons of a nation's over-all health can be made on the basis of life expectancy—that the people of Sweden and Britain are healthier because they live longer on the average than Americans.

"This proves nothing, for what you are actually comparing are differences in the makeup of populations. Both of these nations have small, stable, homogeneous populations, whereas that of the United States is a vast mixing from practically every conceivable corner of the globe, including all nationalities and races. . . .What you can prove statistically is that a person of Swedish descent in Minnesota lives longer than a Swede in Sweden and that Mexicans apparently live longer in New Mexico than they do in Mexico. . . .

"The death rate from automobile accidents is much higher in the United States than in any European country because a larger percentage of the population own cars. This is a matter of economics and not medicine. Yet auto fatalities are a large factor in reducing this nation's life expectancy."

Dr. Blasingame also pointed out the economic

Prepared by the Washington, D. C., office of the American Medical Association.

aspect of Americans living at a faster pace, consuming more expensive fatty foods, and dying of heart attacks with much more frequency.

"Communicable diseases, on the other hand, are almost entirely a medical problem and the fact is that the death rate from communicable diseases in the United States is well below that of England or Sweden," he said.

International statistics on infant mortality rates are meaningless, Dr. Blasingame said, because of different definitions for what is a live birth or a still birth.

"As for insinuations that longer life span and lower infant mortality are somehow linked with the socialized medical practices of England and Sweden, there is absolutely no substantiation," he said. "The rate of increase in longevity in England is no different now from what it was prior to the founding of the National Health Service there in 1947 and may actually have declined."

Tranquilizer prevents airsickness

Meprobamate affords significant protection against airsickness, according to an article by John J. Franks, M.D., Lawrence J. Milch, Ph.D., and Elmer V. Dahl, M.D., in the July 21, 1962, issue of the *Journal of the American Medical Association*. While a tranquilizer would not be desirable to prevent motion sickness in pilots or combat personnel, it might be useful for passengers since the drug is noted for its low rate of adverse side-effects. "Furthermore it may not be necessary to prescribe antimotion sickness drugs for passengers receiving meprobamate for other reasons, at least for relatively short flights."

In the study 441 airmen, ranging in age from seventeen to twenty years and with little or no flying experience, were given identical capsules containing either meprobamate, meclizine, a combination of these two drugs, or sugar about two hours before a flight in a C-54. After an hour of straight and level flight, the airmen were subjected to simulated turbulence, in which the plane pitched and yawed, rolled and turned, and climbed and descended for ten to fifteen minutes.

Forty-six per cent of the volunteers who had received the sugar pills became sick during their flights, compared with 26 per cent of those who took meprobamate, 25 per cent of those who took meclizine, and 24 per cent of those who received both drugs.

The effectiveness of meprobamate was surprising. Despite the probable role of psychologic factors in motion sickness, tranquilizers previously tested proved of little value in preventing the syndrome. However, there is a distinct difference between the tranquilizers investigated earlier, all of which affect the involuntary nervous system, and meprobamate, which is classified as a muscle relaxant and does not affect the involuntary nervous system.

Since extensive trials during World War II, antihistamines have emerged as the most effective drugs for motion sickness. Meclizine is an antihistamine, and like other antihistamines it also has a tranquilizing effect. Its mode of action in preventing motion sickness has not been determined.

Meprobamate has no antihistaminic effects, but its tranquilizing effect may be somewhat similar to meclizine. "On the other hand, the exposure of individuals with little previous flying experience to sudden, violent motion of short duration may provide a situation where tranquilization is uniquely effective." The effectiveness of meprobamate against more prolonged motion remains to be determined. It would be interesting to study mephenesin, another muscle relaxant, under similar conditions, since this drug resembles meprobamate but has only a slight tranquilizing action.

Abstracts in Interlingua

Surls, J. K.: Le uso e le valor de extension in contractura ischemic de Volkmann (*anglese*), NEW YORK STATE J. MED. **62:** 3227 (15 de octobre) 1962.

Quando in un caso de suspicite contractura de Volkmann le question de si o non intervenir chirurgicamente se subleva, extension manual del digitos e del carpa pote esser effectuate immediatemente, con mantenentia del extension per medio de un bandage a gypso que es removite omne die pro permitter motion active e passive. Quando le diagnose es definitemente establite, le operation debe esser interprendite immediatemente. Interferentia in le circulation es le causa de contractura de Volkmann. Le natura del interferentia pote variar, sed in le majoritate del casos illo superveni in connexion con le mantenentia del reduction de un fractura supracondylar del humero. Es reportate un caso in que il occurreva un intervallo de duo menses inter le declaration del symptomas e le effectuation de sympathectomia periarterial. Le patiente suffreva de debilitate muscular in le afficite antebrachio durante annos post le contractura de Volkmann, sed in le curso del tempore ille reganiava su fortia complete. Isto es explicate per le supposition que nove fibras muscular se disveloppava.

Auchincloss, J. H., Gilbert, R., e Epifano, L. D.: Tractamento de acute disfallimento respiratori in patientes con chronic morbo respiratori; considerationes practic (*anglese*), NEW YORK STATE J. MED. **62:** 3234 (15 de octobre) 1962.

Dece-cinque casos de chronic emphysema pulmonar e 1 caso de cyphoscoliosis esseva tractate con le uso de un apparato a intermittente pression positive sin phase negative. Disfallimento respiratori esseva un situation in que hypoventilation pareva impericular le vita del patiente, e deterioration progressive in despecto de tractamento hospitalari esseva revestite de grande importantia in le selection del casos. Sex del patientes moriva. Esseva trovate nulle uniforme relation inter le superviventia e le typo o le intensitate del therapia, e le mortes per consequente esseva relationate le plus probabilemente con factores complicatori in le patientes individual. Le signification del sequente factores es signalate: Le possibilitate de evitar tracheostomia in certe casos; le establimento de regulation respiratori per medio de un correctemente construite automatic dispositivo cyclic; surveliantia del volumine de aere currente a base routinari; e le uso de mesurationes del bioxydo de carbon in sanguine arterial pro determinar le correctitude del adjustamento quando un stato stabile ha essite attingite.

Damon, J. E., e Woodruff, M. W.: Tractamento e assistentia pro le patiente de ureteroileostomia (*anglese*), NEW YORK STATE J. MED. **62:** 3244 (15 de octobre) 1962.

Diversion del fluxo urinari per medio de ureteroileostomia es usate in disordines como neoplasia del vesica, fistulas vesicovaginal, e neurogene dysfunction vesical. Un bon adaptation del patiente al apparato del ducto ileal es necessari pro le successo del procedimento. Le preparation pre-operatori include elementos psychologic e educational, le delineation de rugas cutanee e tests de pelle, e le preparation del intestino. Le assistentia post-operatori include le selection de un apparato de collection de urina, hygiene del pelle, rehabilitation del patiente, e examines catamnestic. Le rolo del personal guarda-infirmos es importante como factor in le adjustamento del patiente e assi in le prospectos de bon resultatos chirurgic.

Salomon, M. I., Bruno, M. S., e Ober W. B.: Biopsia renal percutanee; su importantia in le recerca e in le medicina clinic (*anglese*), NEW YORK STATE J. MED. **62:** 3248 (15 de octobre) 1962.

Biopsia renal es un importante instrumento de recerca, diagnostic, e prognostic, le qual ha contribuite grandemente a nostre cognoscentias de glomerulonephritis e nephrosis. Illo se ha etiam provate de extreme utilitate in hypertension e pyelonephritis e in altere conditiones, incluse nephropathia diabetic, toxemia del pregnantia, lupus erythematose, e falciformation. Su potential in multe altere morbos del ren es grande. Le contraindicationes include morbos in que un subite perdita de sanguine poterea esser periculose, tendentia hemorrhagic, e le presentia de un sol ren.

Kopell, H. P.: Le "poner se in forma" del corpore e traumatismo autogene (*anglese*), NEW YORK STATE J. MED. **62:** 3255 (15 de octobre) 1962.

Le processo del "poner se in forma" in le vive organismo es concernite con le securitate del organismo e su componente systemas. Le activitate basic occurre in le systema nervose central. Il es in ille systema que le requirite configurationes cinetic es reinfortiate e que le initiation del requirite configurationes hemodynamic ha in essentia su origine. Factores participante in le processo es innervation articular, disposition del partes proximal del corpore, e regulation del circulation (tanto peripheric como etiam central). Le processo es importante non solmente in meliorar le nivello del performance in un activitate physic sed etiam in prevenir traumatismo autogene.

Shimaoka, K., e Firat, D.: Test a flocculation de sero pro le diagnose de jalnessa obstructive (*anglese*), New York State J. Med. **62:** 3259 (15 de octobre) 1962.

Esseva studiate le test a flocculation de sero de Jirgl pro le diagnose de jalnessa obstructive in 111 patientes e subjectos de controlo. Le test produceva un reaction positive in 87 pro cento del 31 patientes con jalnessa obstructive e un reaction negative in 89 pro cento del 54 patientes con jalnessa non causate per obstruction biliari. Le reaction esseva negative in omne le subjectos de controlo. Un false resultato negative esseva obtenite in 1 caso de obstruction de porta de hepate, 2 casos de complete obstruction del ducto biliari per carcinoma del pancreas, e 1 caso de calculo del ducto commun. Dece-un patientes habeva reactiones negative in tests effectuate post successose therapia de jalnessa obstructive.

Mitty, W. F., Jr.: Carcinoma mammari in le hospital del communitate (*anglese*), New York State J. Med. **62:** 3263 (15 de octobre) 1962.

Esseva facite un revista quinquenne de 78 patientes con carcinoma mammari. Le majoritate del patientes habeva etates de inter quaranta e cinquanta-novem annos. Septanta-un del patientes esseva subjicite a procedimentos de therapia. Le quota del operabilitate amontava a 91 pro cento. Le absolute superviventia quinquenne esseva 53,8 pro cento. Le superviventia variava inter 90,9 pro cento in le gruppo de patientes con mastectomia radical e negativitate histologic de nodos axillari e 27,3 pro cento in le gruppo de patientes con positivitate histologic del nodos axillari.

Roland, M., Smith, J. J., e Schwartz, E.: Le uso del oral test de pregnantia e su effecto in le endometrio non-pregnante (*anglese*), New York State J. Med. **62:** 3270 (15 de octobre) 1962.

Le test de pregnantia a PD oral (Pro-Duosterona, un combination de estrogeno e progesterona) esseva executate in 185 subjectos. In 15 subjectos normal le menstruation esseva retardate quando le combination de hormones esseva administrate inter die 20 e die 40 del cyclo. Dece-novem de 20 patientes con amenorrhea secundari manifestava sanguination de suspension post non plus que duo cursos de tractamento. In 112 ex 159 subjectos recipiente le combination de hormones como test de pregnantia, nulle sanguination occurreva, e le pregnantia esseva confirmate subsequentemente per tests biologic. Vinti-un subjectos habeva sanguination post suspension. Inter le remanente 26 subjectos (qui habeva negative tests biologic), 22 manifestava sanguination post un secunde curso de medication precedite per le uso de estrogeno preparatori, durante que pregnantia esseva constatate in 4. Alterationes endometrial occurre post le uso del droga in patientes non-pregnante. Iste alterationes non recurre in cyclos subsequente. Leve grados de nausea esseva notate in 8 patientes e representava le sol adverse effecto secundari.

Heart disease in older persons

More older men and women are hospitalized for heart disease than for any other nonsurgical condition, according to the statisticians of Metropolitan Life Insurance Company.

A study of the company's retired personnel shows also that the hospital admission rate for heart disease rises with advance in age. In 1959 to 1960, the rate for retired men increased from 18 per 1,000 under age sixty-five to 36 per 1,000 at ages seventy-five and over. The relative frequency of the disease was considerably greater for the men than for the retired women at every age group. Coronary artery disease accounted for about half of all the heart disease cases among both men and women.

Diseases of the digestive system ranked second as a cause of hospitalization for nonsurgical conditions among the retired personnel in both sexes. Other relatively common illnesses were respiratory diseases and cerebral hemorrhage.

Mental disease accounted for a very small proportion of the cases in this experience but was responsible for long periods of hospitalization. Among the retired men, for example, the average hospital stay for psychoneuroses and psychoses increased from forty days per case at ages sixty-five to seventy-four years to one hundred and thirty days at ages seventy-five and over.

Books Received

*The following books were received during the month of August, 1962**

Textbook of Anatomy. By W. Henry Hollinshead, Ph.D. Quarto of 1,047 pages, illustrated. New York, Harper & Row, Publishers, Inc., 1962. Cloth, $16.

System of Ophthalmology. Edited by Sir Stewart Duke-Elder. **Vol. VII. The Foundations of Ophthalmology.** Quarto of 829 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $30.

Psychosomatic Medicine. The First Hahnemann Symposium. Edited by John H. Nodine, M.D., and John H. Moyer, M.D. Octavo of 1,002 pages, illustrated. Philadelphia, Lea & Febiger, 1962. Cloth, $16.50.

Treatment of Cancer and Allied Diseases. Second edition. Volume VI. Tumors of the Female Genitalia. By twenty-seven authors. Edited by George T. Pack, M.D., and Irving M. Ariel, M.D. Quarto of 381 pages, illustrated. New York, Harper & Brothers, Publishers, 1962. Cloth, $16.50.

Child Psychiatry and the General Practitioner. Edited by Adam J. Krakowski, M.D., and Dante A. Santora. Octavo of 190 pages, illustrated. Springfield, Ill., Charles C Thomas, 1962. Cloth, $5.75.

Humors, Hormones, and Neurosecretions. By Chandler McC. Brooks, Ph.D., Jerome L. Gilbert, M.D., Harold A. Levey, Ph.D., and David R. Curtis, M.D. Octavo of 313 pages, illustrated. New York, State University of New York, 1962. Distributed by University Publishers Inc. Cloth, $7.50.

Laboratory Manual of Pediatric Micro- and Ultramicro-Biochemical Techniques. Edited by Donough O'Brien, M.D., M.R.C.P., and Frank A. Ibbott, F.I.M.L.T. Third edition. Quarto of 340 pages, illustrated. New York, Harper & Row, Publishers, Inc., 1962. Paper, $6.50.

The Medical Clinics of North America. Mayo Clinic Number. July, 1962. Medical Considerations in Surgical Disease. Octavo. Philadelphia, W. B. Saunders Company, 1962. Published bi-monthly (six numbers a year). Cloth, $18 net; paper, $15 net.

Diabetes and its Long Range Control. By Arthur Krosnick, M.D. Octavo of 41 pages, illustrated. New York, Medical Film Guild, Ltd., 1962. Paper, $1.00.

Age-Grouping Methods in Diptera of Medical Importance. By T. S. Detinova. Octavo of 216 pages, illustrated. Geneva, World Health Organization, 1962. Distributed by International Documents Service, Columbia University Press. Cloth, $5.25.

* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

From test tube to bedside

Each year the pharmaceutical industry in this country makes, discovers, or synthesizes more than 100,000 chemical compounds or substances. Of these perhaps about 2,500 to 2,800 may reach the stage of investigation to determine their usefulness in human beings. And of this latter number perhaps 30 to 40 may eventually appear on the market. Incidentally, to undertake this huge job of searching and testing there are more than 16,000 scientific personnel employed by the pharmaceutical industry. And about five to six years, as an average, intervene from the time an idea is discovered in a test tube and when it finally emerges for general use in sick people.—*Austin Smith, M.D., in Military Medicine, March, 1962*

Books Reviewed

Principles of Public Health Administration. By John J. Hanlon, M.D. Third edition. Octavo of 713 pages, illustrated. St. Louis, The C. V. Mosby Company, 1960. Cloth, $10.50.

Already a tradition among those identified with public health, Dr. Hanlon's great work is now even more worthy of recognition as one of the genuine classics in the broad area of the medical sciences. At a point when single editorship, not to mention single authorship, of a comprehensive text is an increasing rarity, this eminent teacher and administrator, for the third time in little more than a decade, has been the sole author of a unique volume—one which for practical purposes is the equivalent, if not the equal, of multiple works on a subject representing all the sciences, natural and social, basic and applied. As a product of one man's knowledge, experience, and wisdom, this book constitutes the highly improbable creation of a readable, interesting, and well-integrated text.

To be sure, the limitations inherent in any solitary undertaking might have been reduced in part by the critical perusal of sundry suborders of minutia-minded "experts," not excepting proofreader-grammarians who encounter so few Churchillian passages from nonprofessional writers. Even a conservative consensus might find the style too wordy and rambling, the fine print too frequent, numerous figures too small for ready definition, and, perhaps least pardonable, too many older references that do not merit the perpetuity of timeless contributions. Happily some of these limitations also are among the real virtues of this volume, which presents a wealth of material in historical perspective, with themes common to all chapters linking past, present, and future in a manner unknown and impossible among the complex comminuted creations of multiped authorship, wherein each separate, small pseudopodium seems unaware of or indifferent to the interests of the others. In a day when biomedical archeologists are still dusting off the wondrously intact figure of the whole man, it is heartening to suspect, as Dr. Hanlon gives us reason to, that further excavations will also rediscover the whole community.

Although all the traditional areas of public health are dutifully represented in his book, there is an added sense of a single common approach, if not a simple, common solution, to the infinite yet indivisible problems encountered. Here is no list of ready-made answers, no digest of essential facts, no set of universal principles. There is no pretense to computer-like formulations to meet the multifarious needs of preventive medicine. Those looking for the mechanics of management, for a complete, overall program, or for precise plans for every eventuality will gain little help from this book. Those seeking a broader context and a pliable point of view will be well rewarded by this practical projection of thoughts from, about, and on behalf of people—the deeper dimension of demography within which there must somehow soon be sighted the pathway not only to the public health but also to the public survival.—Robert W. Hillman, M.D.

Clinical Chemistry, Principles and Procedures. By Joseph S. Annino. Second edition. Octavo of 348 pages, illustrated. Boston, Little, Brown and Company, 1960. Cloth $8.00.

This is one of the best practical treatises on clinical chemistry. It is particularly valuable for the student training to be a technician. There are excellent chapters on principles and practice including handling of pipets, technics in transfer of solutions, and colorimetry. There is a good review chapter on quantitative analysis and another on the collection of blood sample and a list of normal values.

The second part of the book is devoted to methods in clinical chemistry. They include not only technics, but also a discussion of their significance.

The book is highly recommended.—William S. Collens, M.D.

Anatomy: A Regional Study of Human Structure. By Ernest Gardner, M.D., Donald J. Gray, Ph.D., and Ronan O'Rahilly, M.D. Quarto of 999 pages, illustrated. Philadelphia, W. B. Saunders Company, 1960. Cloth, $15.

The basic facts of structure and function displayed by the anatomy of the human body are as unchanged now as they were in the days when man first struggled to understand them. Knowledge of human anatomy is now, as it must always be, best gained by dissection—with the added help of literal descriptions, drawings, pictures, and diagrams. Thus, modern textbooks of human anatomy differ only with regard to the form and manner of their presentation of anatomic facts.

The present work benefits by the collaboration of three authors, each writing with the authority of experience in his special field and a blending of their talents in those sections of the book where their knowledge is pooled—all to the advantage of the medical student. The study of human anatomy is not easy, and the special value of this book is in the arrangement of the material. It is compact, and its particular helpfulness to the student is visual: The names of principal structures are shown in boldface type, and it is especially to be noted that sections of particular interest in the subject matter of each chapter are clearly set off in paragraphs with titles in boldface type. These details of arrangement are important to the student in his feverish haste to look something up; and it is to the medical student that this book is slanted.

The organization of the material is very sensible: The human body is considered on a regional basis, and each region is treated by descriptions of the skeletal, muscular, nervous, and vascular relationships, with elaborations of special structures. Each section ends with a summary of blood and nerve supply and pertinent radiographic interpretations. Certain relatively common abnormalities of structure (especially those affecting function) are described and illustrated. The drawings are excellent, and the diagrams are particularly understandable. Pertinent references, selected for collateral reading, are scattered throughout the text, and there are occasional references to classic experiments.

One of the pleasant surprises in this book is an outline of the history of anatomy and a brief guide to anatomic literature. The authors have certainly succeeded in presenting the facts of human anatomy in a straightforward manner, directed especially to the needs of the medical student, who, confronted by several other contemporary authoritative publications in this same field, will find in this one a rather refreshing style.—GORDON E. MESTLER

The Gentle Legions. By Richard Carter. Octavo of 335 pages. Garden City, N.Y., Doubleday & Company, Inc., 1961. Cloth, $4.50.

The author is a well-known journalist whose first opus, *The Man Who Rocked the Boat*, was a fearless exposé of the corrupt waterfront rackets. His scathing indictment of the medical profession in *The Doctor Business* stamped him as an iconoclast without peer. *The Gentle Legions*, as epitomized in the subtitle, is "a probing study of the national voluntary health organizations."

With practice born of dissecting the economic innards of waterfront racketeering and the practice of medicine, he slashes ruthlessly away at the inner sanctums of the great gods of philanthropy, exposing their feet of clay. Charity, greatest of all theological virtues, is being shamefully prostituted in the sordid competition to capture a greater share of the donation dollar.

The veracity of these incredible disclosures has recently been confirmed in an independent investigation by the Rockefeller Foundation. Despite its unsavory revelations, it is reporting at its finest.—MILTON B. SPIEGEL, M.D.

Progress in Medicinal Chemistry. Volume 1. Edited by G. P. Ellis, Ph.D., and G. B. West, Ph.D. Octavo of 262 pages, illustrated. London, Butterworth & Co. Ltd., 1961. Cloth, $11.25.

The first volume of this new and valuable work presents the subject of medicinal chemistry as a bridge between biochemistry and pharmacology and as such is of great value to both disciplines. The claim that the survey with which the volume opens is the most detailed treatment of the subject can hardly be held to be an overstatement. The discussion of pharmacologic screening tests is not only a superb reference but a prototype for writing in this field.

The subjects of hypertensive agents, tranquilizers, diuretics, and oral hypoglycemic and antifungal agents are exhaustively reviewed by an impressive group of authorities. This entire book is beautifully written and is intended primarily for experts. In the process of treating specific topics in a highly sophisticated manner the reviews present a wealth of sound clinical material well worth any physician's reading. Succeeding volumes should be eagerly anticipated by a large and enthusiastic audience. —ROBERT W. KIMBALL, M.D.

Eye Symptoms in Brain Tumors. By Alfred Huber, M.D. Octavo of 329 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $16.

This book by a noted Swiss ophthalmologist is based on a series of 1,600 cases of brain tumor observed at the neurologic department of the University of Zurich. It includes chapters on neuro-ophthalmologic examination, the general symptoms of increased intracranial pressure, the local symptoms of brain tumors, and pseudotumors, including subdural hematomas, brain abscesses, and aneurysms. The importance of the eye in the early diagnosis of brain tumor is emphasized by the fact that subjective ocular symptoms were among the initial complaints in over half the cases; in about 60 per cent papilledema was observed, and ocular signs led to fairly accurate localization of the tumor in about one quarter of the cases. This is an excellent textbook that can be studied to advantage by all physicians concerned in any manner with the subject.—JESSE M. LEVITT, M.D.

The Myth of Mental Illness. By Thomas S. Szasz, M.D. Octavo of 337 pages. New York,

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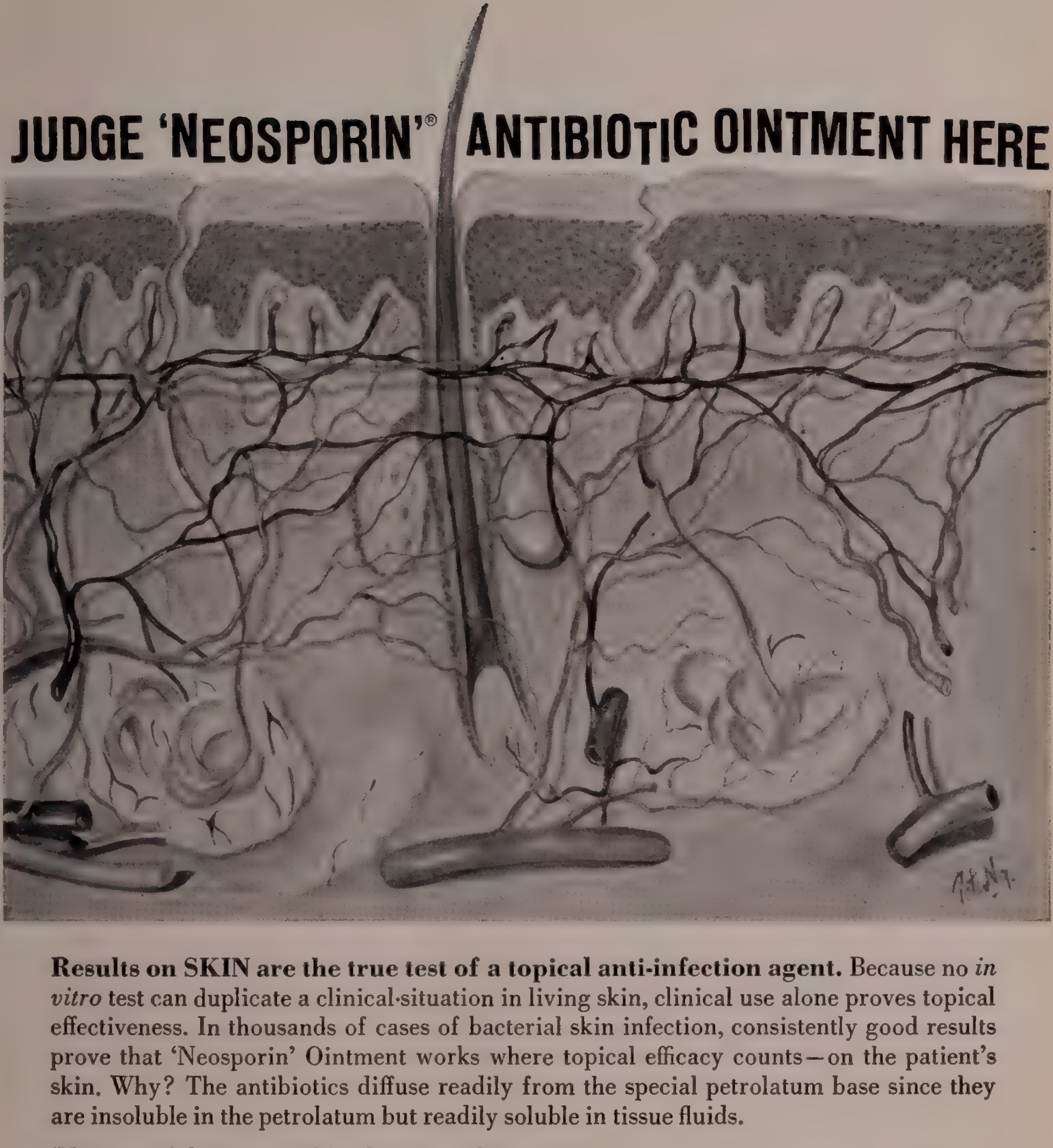

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Paul B. Hoeber, Inc., 1961. Cloth, $7.50.

The author, Hungarian-born, received his academic and medical education in the United States. He is currently professor of psychiatry at the State University of New York Upstate Medical Center in Syracuse. He is well qualified to discuss the topic of this stimulating and provocative book.

The author attempts to present what he considers a more useful concept of mental illness and its corollaries, diagnosis, prognosis, and treatment by dividing his volume into Book One, "The Myth of Mental Illness," with a historical perspective of hysteria in the light of Charcot's contribution and also that of Breuer and Freud, using hysteria in psychosomatic medicine as a pivotal point of reference; and Book Two, in which hysteria is further analyzed, followed by "rule-following analysis of behavior," with reference to the ethics of helplessness, theology, witchcraft, and hysteria; and "game-model analysis of behavior" with special relationships to problems of impersonation and cheating, regarding hysteria as a game, and object relationships.

There follows a summary and conclusions in which it is obvious that the author is out of line with traditional and major psychiatric thinking and practice regarding the definition of psychiatry as a medical specialty concerned with the study, diagnosis, and treatment of mental illnesses. The author considers this a worthless and misleading definition and that mental illness is a myth. It would seem that the author is tilting with the projections of his own mental gymnastics in which his use of semantics is tailor-cut to his theory of personal conduct. The author would do well to review the psychobiologic personality concepts of Adolf Meyer who has done more than any other American psychiatrist to bring order into psychiatric thinking and improvement of psychiatric practice, keeping in mind the individual's life chart and his total environment, which includes social-situational and even ethical problems to which the individual reacts throughout his lifetime. Nothing is foreign to the obligation of the psychiatrist if it affects the individual's emotional and mental well-being and how he might better become socially integrated in "mental health" functioning. This has to show in the integration of the various functions and activities of the total personality with a sound flow of constructive and reactive imagination and phantasy able to reach reality and use it effectively. This involves adequate digestion of the past and anticipation of the future, but particularly measuring up to the duties, responsibilities, and opportunities of here-and-now experience, along with growing harmony in getting along with people with a minimum of unnecessary conflict.

Apparently the author felt, out of ten years of turning the matter over in his mind, that there was a need of such a book. It is doubtful whether or not it will add to the practicing psychiatrist's ability to serve more effectively those to whom he obligates himself. If one will merely glance through the American Psychiatric Association publication, *Diagnostic and Statistical Manual of Mental Disorders*, it becomes apparent that the psychiatrist has a tremendous job on his hands. Nevertheless, this controversial volume should be welcomed as a jolt to complacency and a need for recurrent review of the psychiatrists' ever-growing role in the understanding and treatment of mentally ill persons and the need of a "worksheet" for exploring further research inroads that have practical melioristic possibilities in preventing and alleviating America's number one health problem. The psychiatrist must not forget that he is first, foremost, and always a physician in which his specialist concern is the total "he" or "she" functioning, implicit and explicit, in his social setting. Sharing the responsibility with his fellow physicians in larger measure, as well as with ancilliary helpmates of psychiatry (psychologists, social workers, occupational therapists, and so forth) is of growing importance in the multidisciplinary team approach.

Although the book was primarily written for psychiatrists, it is highly recommended as stimulating and provocative reading for all those interested in better care of mentally ill persons.
—FREDERICK L. PATRY, M.D.

Health Education. Edited by Bernice R. Moss, Ed.D., Warren H. Southworth, Dr.P.H., and John Lester Reichart, M.D. Fifth edition. Washington, D.C., National Education Association of the United States, 1961. Cloth, $5.

This fifth edition of *Health Education* is broad in its scope and well presented. It encompasses all fields of health education from infancy through the various schools of learning, even through college and adult life. It is written under the auspices of the National Education Association and the American Medical Association for improvement in our children's health. It is a companion to *School Health Services* and *Healthful School Living*.

The profound problems are handled only schematically. One would expect the host of eminent and chosen consultants to be just a little more specific and conclusive in their answers to certain pertinent, albeit controversial, matters. While a host of references is advised, which is good, the relative value of each reference is not given. It leaves one with the impression that not only is a great deal still unknown but also one must personally evaluate what is good when a moot question arises. While this book is written for teachers and others in the school health field, including physicians and nurses, and serves a good purpose, it will

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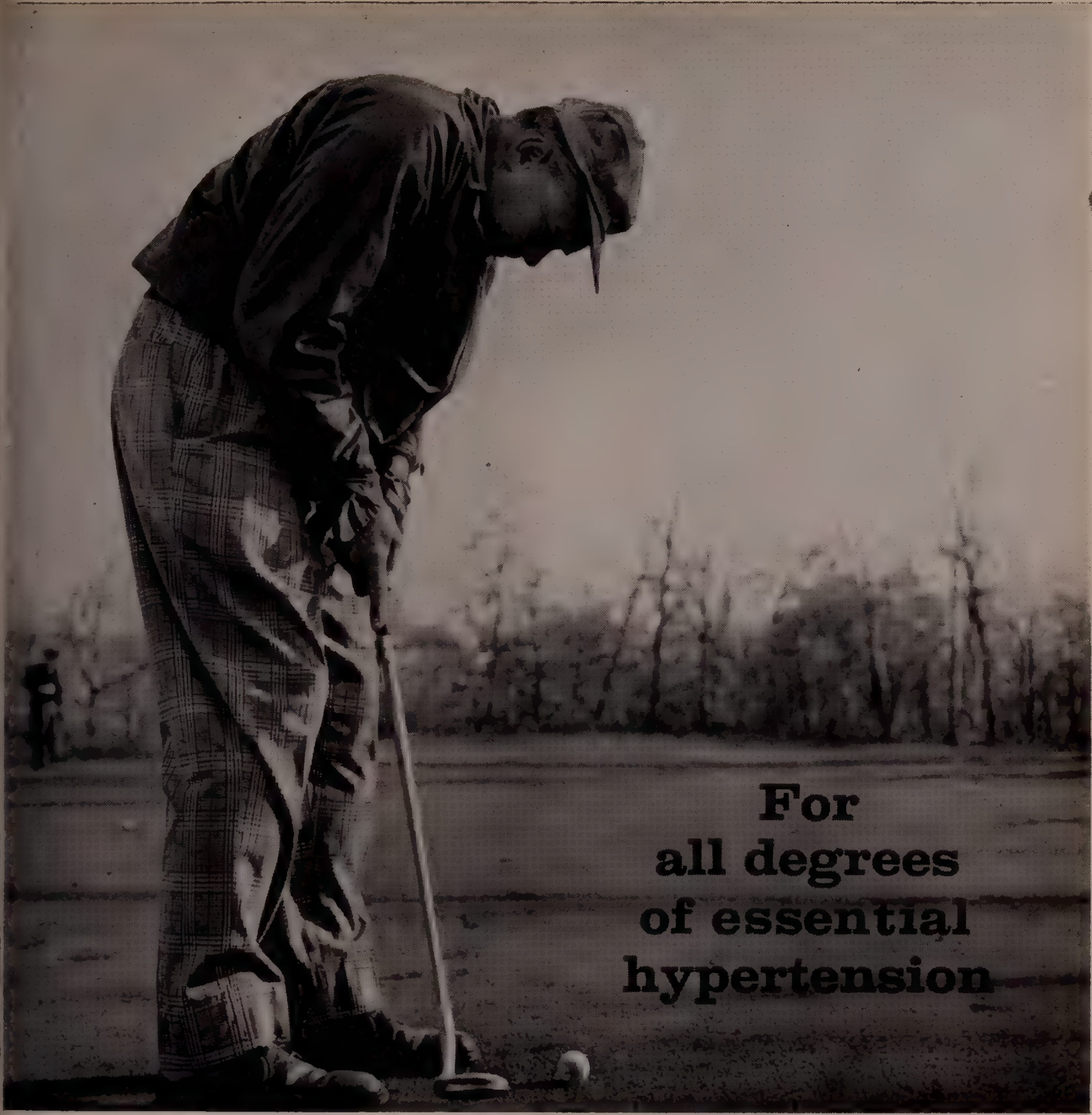

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improve in quality with succeeding editions.—Bernard Seligman, M.D.

Systemic Lupus Erythematosus. By Daniel L. Larson, M.D. Octavo of 212 pages, illustrated. Boston, Little, Brown and Company, 1961. Cloth, $7.50.

This monograph is a review of the experience at Columbia-Presbyterian Medical Center with systemic lupus erythematosus over the twenty-year period from 1940 to 1959. It provides a valuable analysis of the natural history of this syndrome, based on careful clinical study and excellent follow-up data in a series of 200 patients. Many but not all of these patients have been under the personal observation of the author. This material is well organized and presented clearly. The many ramifications of the life history of this protean disease are brought out. The discussions of neuropsychiatric problems, thrombocytopenic purpura, and pregnancy during the course of systemic lupus are particularly valuable.

The monograph is weakest in its discussion of the laboratory abnormalities (serologic, histologic, and cytologic) associated with systemic lupus. Dr. Larson has chosen to put his emphasis on the purely clinical data available to him from the charts of the patients studied, rather than to review at any length the large body of pertinent laboratory work. One other weakness of the monograph is its inadequate discussion of drug-induced lupus erythematosus.

In summary, this volume provides valuable information about the clinical course and prognosis of patients with systemic lupus erythematosus. It should be a useful reference for the medical student, the general practitioner, and the internist.—Stanley L. Lee, M.D.

The Stages of Human Development before Birth. By E. Blechschmidt, M.D. Quarto of 684 pages, illustrated. Philadelphia, W. B. Saunders Company, 1961. Cloth, $23.

This book is a highly desirable and most welcome addition to the library of anyone interested in developmental human anatomy. It is not a textbook but an atlas accompanied by just enough text material to clarify the illustrations and maintain continuity from one illustration to the next.

The illustrations consist of several types: drawings from reconstructions, photomicrographs, and line drawings used primarily to demonstrate movements of groups of cells and organs. In general the quality of the plates is very high. Each drawing and photograph is labeled completely in both English and German.

The text material is given in both English and German and utilizes the Paris nomenclature for adult anatomy. Some of the terms will be new to individuals who are most familiar with the standard English and American texts of human embryology, but most of these terms are not difficult to interpret, and in addition a list of terms with definitions is provided at the beginning of the book.

The first portion of the book consists of a series of illustrations and accompanying text depicting the chronologic development of the body as a whole and the extraembryonic membranes during the first three months of development.

The second portion is made up of a more detailed study of individual organs and structures on a regional basis. Each organ is carried through its critical stages of development with attention paid to both gross and microscopic changes.

This book would certainly be very valuable to any student of developmental anatomy at the graduate level and would be of particular interest to anyone making a detailed study of serial sections of early human or even other mammalian embryos.—George B. Talbert, Ph.D.

Functional Behavior of the Microcirculation. By Benjamin W. Zweifach, Ph.D. Octavo of 149 pages, illustrated. Springfield, Charles C Thomas, 1961. (American Lecture Series) Cloth, $7.00.

The author felt that the area of the dynamic microcirculation because of its inaccessibility has escaped critical investigation. He noted that the only authoritative treatise on blood capillaries is the monograph by Krogh first published in 1926. Since then considerable progress has been made, particularly on a biophysical and chemical basis. This monograph is based on the author's experience in the field for over twenty-five years.

There are 12 chapters covering general concepts, structural basis of the microcirculation, special and regional considerations, endothelium, functional behavior, vascular reactivity, structural considerations in capillary permeability, mechanism of transcapillary exchange, vascular component of tissue injury, mediators of tissue injury, experimental shock, and circulatory homeostasis.

Each chapter is furnished with a concise summary and pertinent references. This authoritative work should be of special interest to pathologists, physiologists, and surgeons as well as to the knowledgable internists and general practitioners.—Maurice Morrison, M.D.

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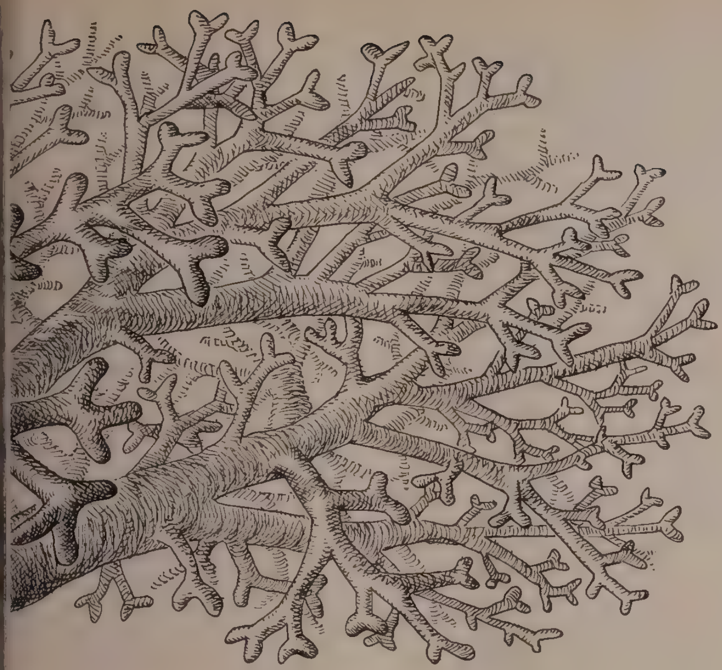

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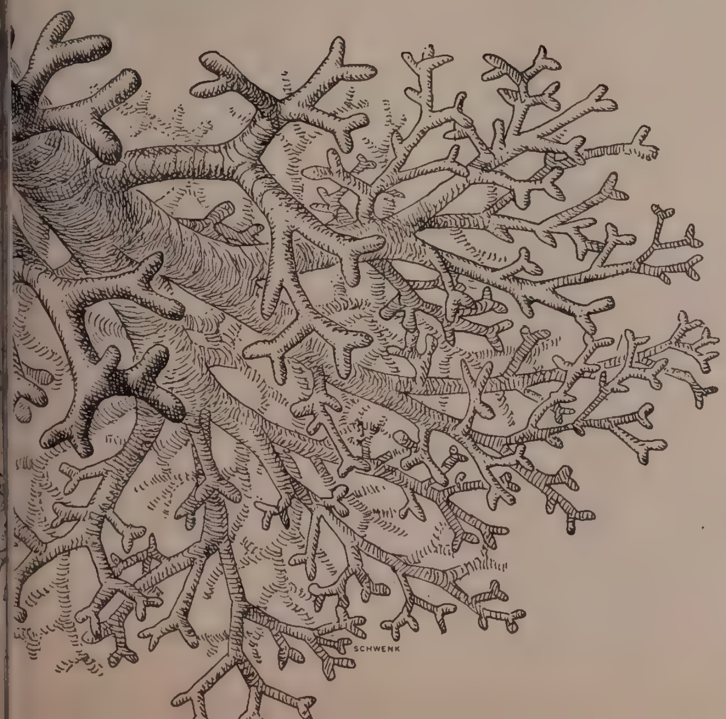

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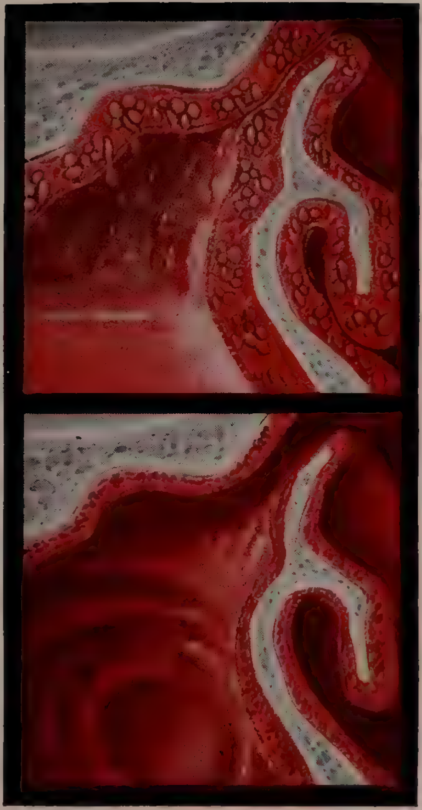

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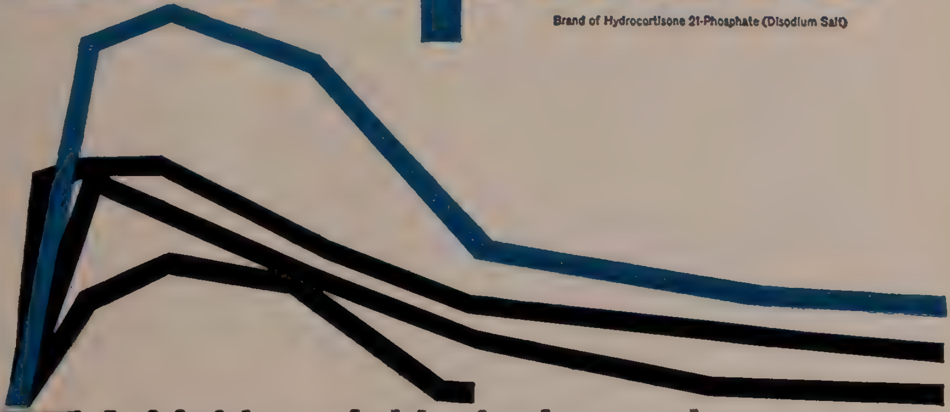

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1. Melby, J. C., and Silber, R. H.: Am. Pract. & Digest Treat. 12:156 (March) 1961. 2. Melby, J. C., and St. Cyr, M.: Metabolism 10:75, 1961

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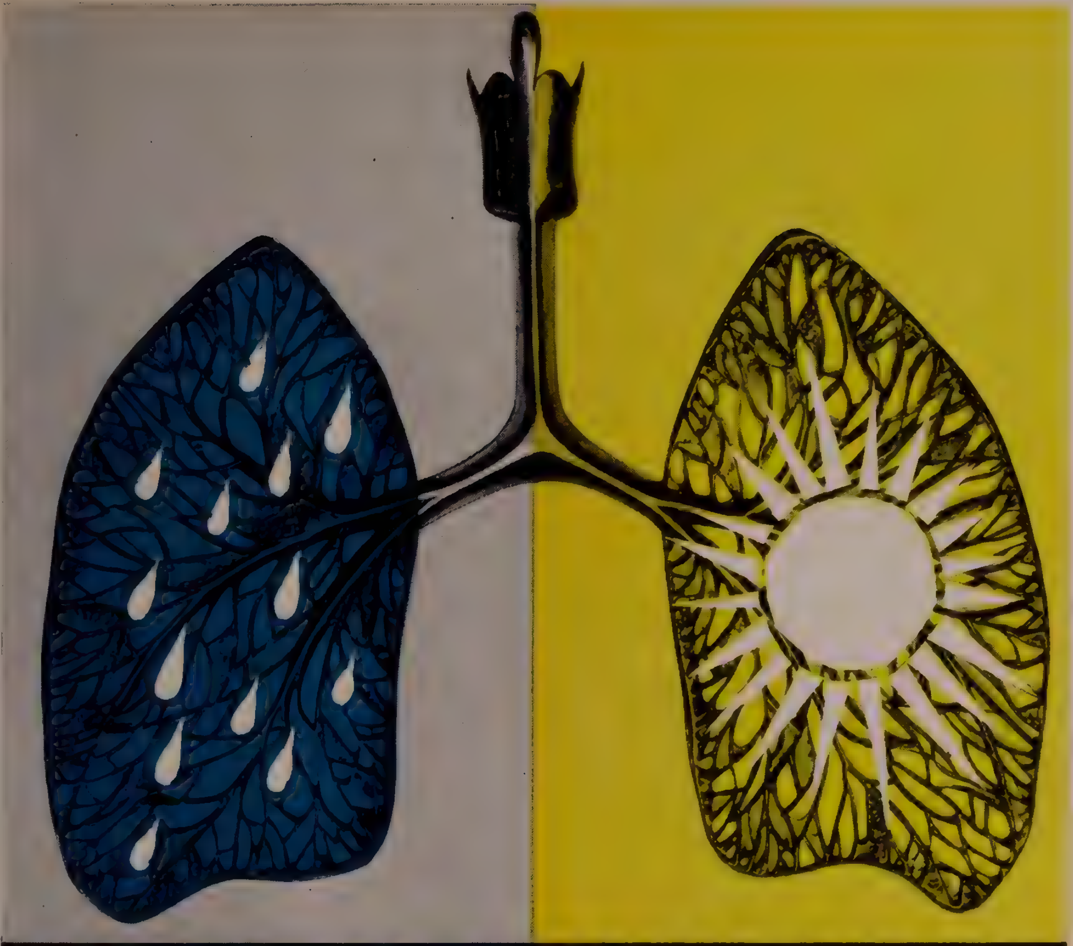

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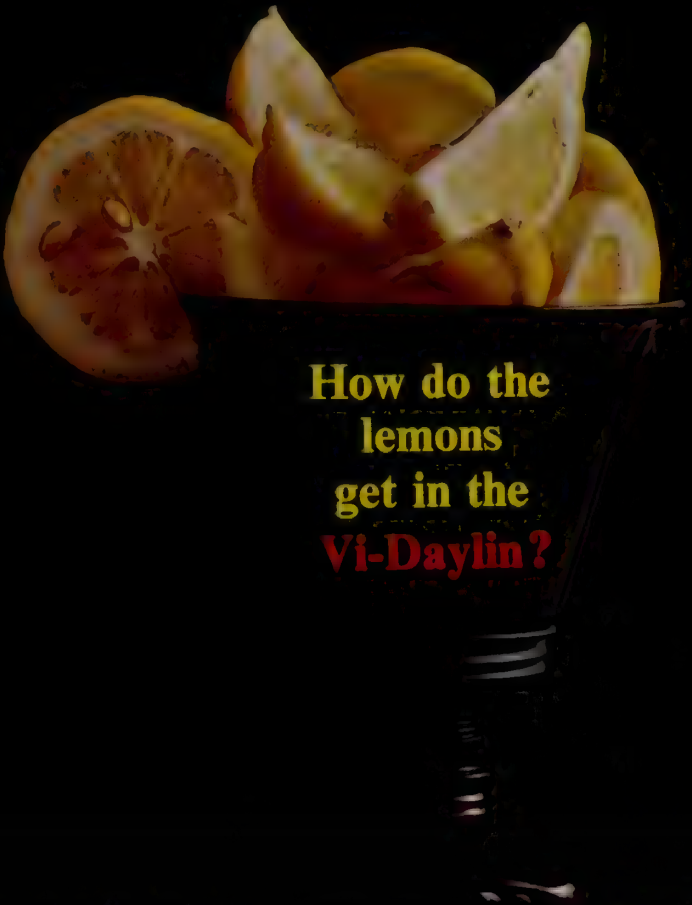

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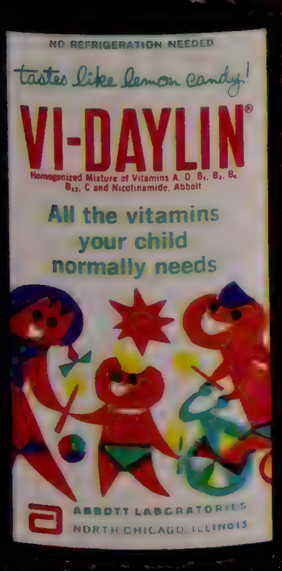
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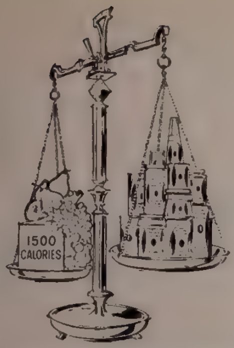

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Five-Fruit Juice Breakfast Drink	½ cup	20	52
Braised Beef and Vegetables	6½ oz.	184	380
Meat Balls in Brown Gravy	3½ oz.	84	280
Chopped Chicken Livers	1 oz.	31	100
Chicken a la King	3 oz.	72	230
French Style Dressing	1 tbsp.	10½	60
Brown Gravy	1 tbsp.	7	21

	Quantity	Figure Control Calories	"Regular" Food Calories
Applesauce	½ cup	48	90
Fruit Cocktail	½ cup	44	90
Cherry Pie Filling	1 oz.	20	60
Chocolate Topping	1 tbsp.	8	63
Preserves (Peach, Strawberry)	1 tbsp.	9	55
"Maplette" Syrup	1 tbsp.	9	55
Liquid or Powder Sweetener	(to equal 1 tbsp. sugar)	0	16

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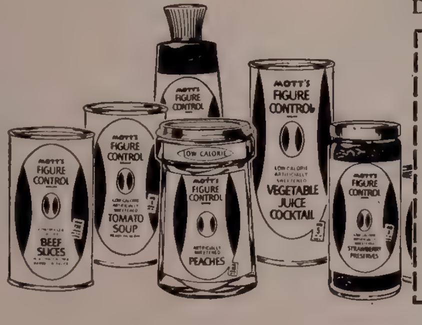
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*McCune, W. G.: M. Clin. North America 44:1479, 1960.

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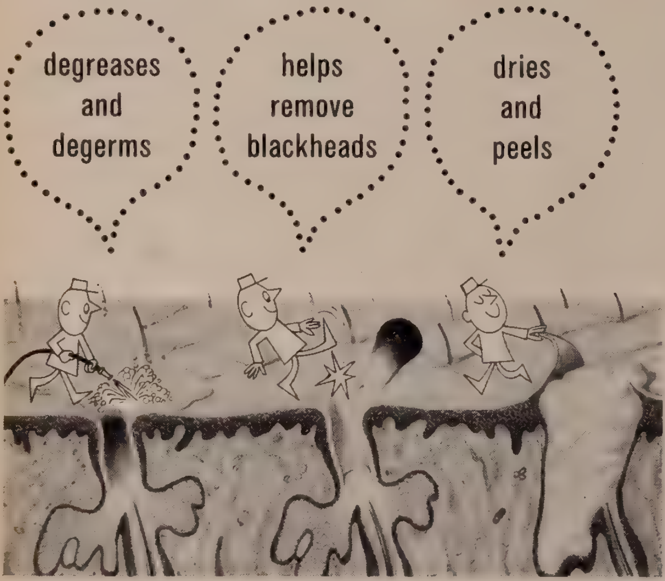

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1. Meyers, G. B.: Ind. Med. & Surg. 26:3, 1957. 2. Murray, R. J.: N. Y. St. J. Med. 53:1867, 1953.

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- Medical staff and research appointments in voluntary, government hospitals in New York State (official titles).

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The next edition will not be published until late in 1963.

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*Alexander, F.: Psychosomatic Medicine, New York, W. W. Norton, 1950, p. 119.

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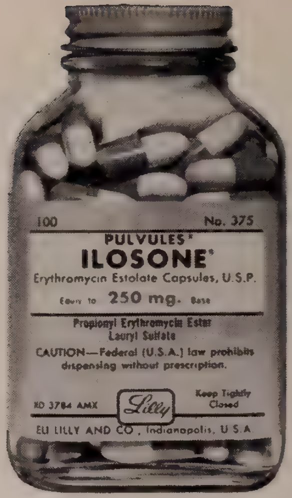
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A far-reaching new medical education loan guarantee program is under way in American medicine. The goal of this program is to help eliminate the financial barrier to medicine for all who are qualified and accepted by approved training institutions. It is designed to provide a means of financing a substantial portion of the cost of a medical education.

The loan program for medical students, interns, and residents is the result of a cooperative effort by American medicine and private enterprise and is administered by the American Medical Association's Education and Research Foundation. The Foundation has established a loan guarantee fund. On the basis of this fund, the bank will lend up to $1,500 each year to students. The Foundation in effect acts as cosigner. For each dollar on deposit in the loan fund, the bank will lend $12.50.

More than 3,300 students, interns, and residents have borrowed over six million dollars since the fund was started last February. Physicians and others have contributed almost $700,000 to the fund, which makes these loans possible. In New York State alone $25,400 was lent to 21 medical students, and $98,700 was borrowed by 82 interns and residents.

Now, however, the guarantee fund is almost depleted. More money is needed immediately to keep up the loan program. Eventually, as loans are repaid, it will become self-sustaining, but right now substantial financial help is needed. Your check will help to keep this important program viable.

Donations should be mailed to: American Medical Association Education and Research Foundation, 535 North Dearborn Street, Chicago 10, Illinois.

Need for semantic synapse

Much of the controversy around colorectal adenomas could be cleared if surgeons and pathologists had a common language and understood each other. There is a great need for each to state precisely the basis for clinical or histologic diagnosis.

Vacillation could be prevented by discarding the term "malignant adenoma" which in truth implies a benign lesion. Similar misleading terms are "atypical" and "carcinoma in situ" and "adenocarcinoma, grade I, benign" which connote benignancy to some and malignancy to others. In the same category are "premalignant" and "precancerous." About the only precancerous aspect of the colon is the colon itself.

The diagnosis of cancer should be emphatically unequivocal. Equivocation leads to frustration for both the patient and clinician. Not all pathologists agree on the criteria for malignancy in adenomas, and some are inclined to render a diagnosis of malignancy for fear of missing one. The true test remains the invasiveness or the noninvasiveness of the lesion, the determining boundary line being the muscularis mucosae. Involvement of the mucous membrane and/or the lamina propria without invasion of the muscularis mucosae is not considered invasive cancer. Of course there are exceptions, however this makes a serviceable guideline for teaching and therapeutic orientation.

To detect invasion in an adenoma it is

important to remove and submit to the pathologist the entire lesion in one piece or in large segments. This means "total biopsy" as against "fractional biopsy" a practice which is to be condemned. Experience has shown that considerable reservation should be entertained for a diagnosis based solely on frozen section technic, since experienced pathologists can be deceived in either direction.

The same applies to adenocarcinoma of the rectum where it is physically possible to remove the entire growth for preoperative microscopy which would make possible the utilization of the Dukes classification. It is now fully appreciated that the prognosis of each grade of tumor varies from bright for grade A to very poor for grade C thus giving substance to the statement that cancer is many diseases. Hence it is misleading to lump the therapeutic results of all grades of adenocarcinoma of the rectum and to state that over 50 per cent of patients with rectal cancer survive for more than five years. This misleading statistic does not begin to show that Dukes A lesions are perhaps universally "cured" by the Miles procedure but instead indicates that at the present time this radical operation is performed as a matter of calm acceptance of an unsatisfactory procedure in the hope that in the future a better solution will be forthcoming. Until we have a means of removing every rectal lesion so that precise involvement of the muscularis mucosae can be established, the justification and necessity for the treatment of Dukes A lesion will remain a legitimate question mark. R. T.

Smoke hazard from burning leaves

The sight and smell of burning leaves is synonymous with autumn. The rising column of smoke, the spicy scent, and the crisp tang of the air combine to climax the summer. This was all well and good when the population was not dense and before the invention of insecticides. Now burning leaves may create a health hazard.

During the fall season a condition exists called inversion. This is characterized by clear windless days when smoke and other air contaminants are held close to the ground. The experience at Donora, Pennsylvania, illustrates the serious effects that inversion and static smoke may have upon those suffering from bronchitis, asthma, and other respiratory diseases. The smoke from burning poison ivy leaves can be deadly serious to persons sensitive to this plant. Residents in built-up suburbs should be urged to save their leaves for the mulch pile to enrich their lawns and gardens and protect themselves and their neighbors from the hazards of air pollution.

Editorial comment

A classification of sickroom visitors. The operation may be a great success but the patient may have a rough time of it because of family or friends.

This artifact, often beyond control of the doctor and sometimes of the hospital administration, is a force to be reckoned with.

In a recent issue of *Hospitals*, journal of the American Hospital Association, Claude L. Brown, M.D., of Mobile, Alabama, described the more pernicious types as follows:

> *Desperately helpful.* They are persuaded that the sight of their face, and theirs alone, will bring hope to the suffering. Once in a sickroom, and they do get in through snow and fog, through cordons of nurses, and red "No Visitors" signs, they fall upon you with the zest of a fox in a hen house. They crank

the bed up and down; they raise the window shades ("How do you see in this room?"); they knock the pillow around, pull the covers off, sit on the bed ("Oh, I'm sorry. I didn't know that was the broken one; its not in a cast.").

Blithe spirit. These are effervescent, thoughtless, usually traveling in pairs as emissaries of some group with which you are casually affiliated. Jokes and fun are the thing, man ("Get out of that bed, we know a goldbricker when we seen one."). These visitors like snappy repartee, a live show, and if you're sick they get uncomfortable and leave.

The mysterious stranger. Even when it becomes clear to the stranger that he is in the wrong room and he apologetically leaves, the experience is still rather unsettling for the patient.

Sadly remembering. There aren't many plainly melancholy visitors. Far more common are those whose dismal turn of mind seeps unwittingly through their surface smiles and small talk. "Your flowers are pretty, but (deep sigh) those bright colors fade so fast." "You're looking more like your father. When I came in I thought for a second it was him, you're aging so."

They are loaded with news of earthquakes, traffic accidents, and medical news, and with one well-chosen phrase they undermine all the confidence you were hopefully trying to work up in your physician: "Dr X is good, I hear, but do you know his wife?"

In addition to the single visitors, Dr. Brown also noted the groups who overrun the patient's room, talking constantly and loudly.

Everyone has seen the "Quiet! Hospital" signs on the streets around hospitals. If the surrounding streets were as noisy as the interior of the hospital, the community would insist that the hospital be moved to a lonely site in the country.

When anyone enters the room of a patient, a demand is put upon that patient, a demand to be responsive. No matter if the sick one's head hurts, if he's nauseated, if he just doesn't feel like talking, or even listening, still he must present a picture of welcoming appreciation to the visitor—a subtly wearying process.

Hospital management must assume responsibility for the problem, for no one else can. The patient is a relatively helpless participant in the process of being visited; he doesn't want to appear less than glad to see visitors; he doesn't want to seem churlishly ungrateful. So he's stuck with them.

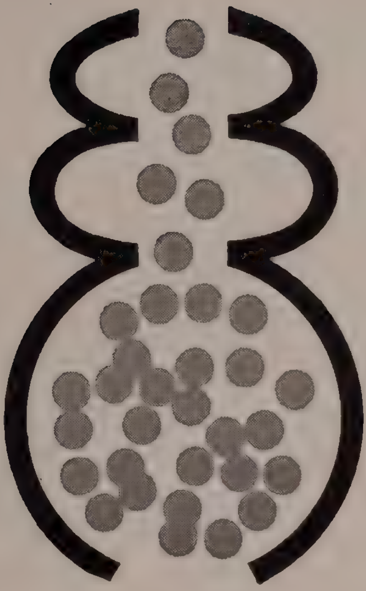
With firm hospital visiting policies, the patient can be protected, and with careful explanation the public will understand the reasons for the policies.

Announcement 1962 District Branch Meetings

Branch	*Date*	*Place*
SECOND	Sunday, Monday, Tuesday November 11, 12 13	Grossinger's Grossinger, New York

LOMOTIL®

(brand of diphenoxylate hydrochloride with atropine sulfate)



ANTIDIARRHEAL
TABLETS and LIQUID

lowers motility / relieves cramping / controls diarrhea

Roentgenographic studies by Demeulenaere[1] established that a single dose of 10 mg. of Lomotil slowed gastrointestinal transit within two hours and that it maintained its decelerating activity for more than six hours.

In diarrhea this lowered propulsion permits a physiologic absorption of excess fluid, lessens frequency and fluidity of stools and gives safe, selective, symptomatic control of most diarrheas. Concurrently, it conserves electrolytes and controls cramping.

Investigators have found the antidiarrheal action of Lomotil not only "excellent"[2] but "efficacious[3] where other drugs have failed. . . ."

DOSAGE: For *adults* the recommended initial dosage is two tablets (2.5 mg. each) three or four times daily, reduced to meet the requirements of each patient as soon as the diarrhea is under control. Maintenance dosage may be as low as two tablets daily. For *children* daily dosages, in divided doses, range from 3 mg. (½ teaspoonful three times daily) for infants 3 to 6 months to 10 mg. (1 teaspoonful five times daily) for children 8 to 12 years. Lomotil is supplied as unscored, uncoated white tablets of 2.5 mg. and as liquid containing 2.5 mg. in each 5 cc. A subtherapeutic amount of atropine sulfate (0.025 mg.) is added to each tablet and each 5 cc. of the liquid to discourage deliberate overdosage. The recommended dosage schedules should not be exceeded.

NOTE: Lomotil is an exempt narcotic preparation.

Descriptive literature and directions for use detailed in Physicians' Product Brochure No. 81 available from G. D. Searle & Co., P. O. Box 5110, Chicago 80, Illinois.

1. Demeulenaere, L.: Action du R 1132 sur le transit gastrointestinal, Acta Gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.
2. Kasich, A. M.: Treatment of Diarrhea in Irritable Colon, Including Preliminary Observations with a New Antidiarrheal Agent, Diphenoxylate Hydrochloride (Lomotil), Amer. J. Gastroent. 35:46-49 (Jan.) 1961.
3. Weingarten, B.: Weiss, J., and Simon, M.: A Clinical Evaluation of a New Antidiarrheal Agent, Amer. J. Gastroent. 35:628-633 (June) 1961.

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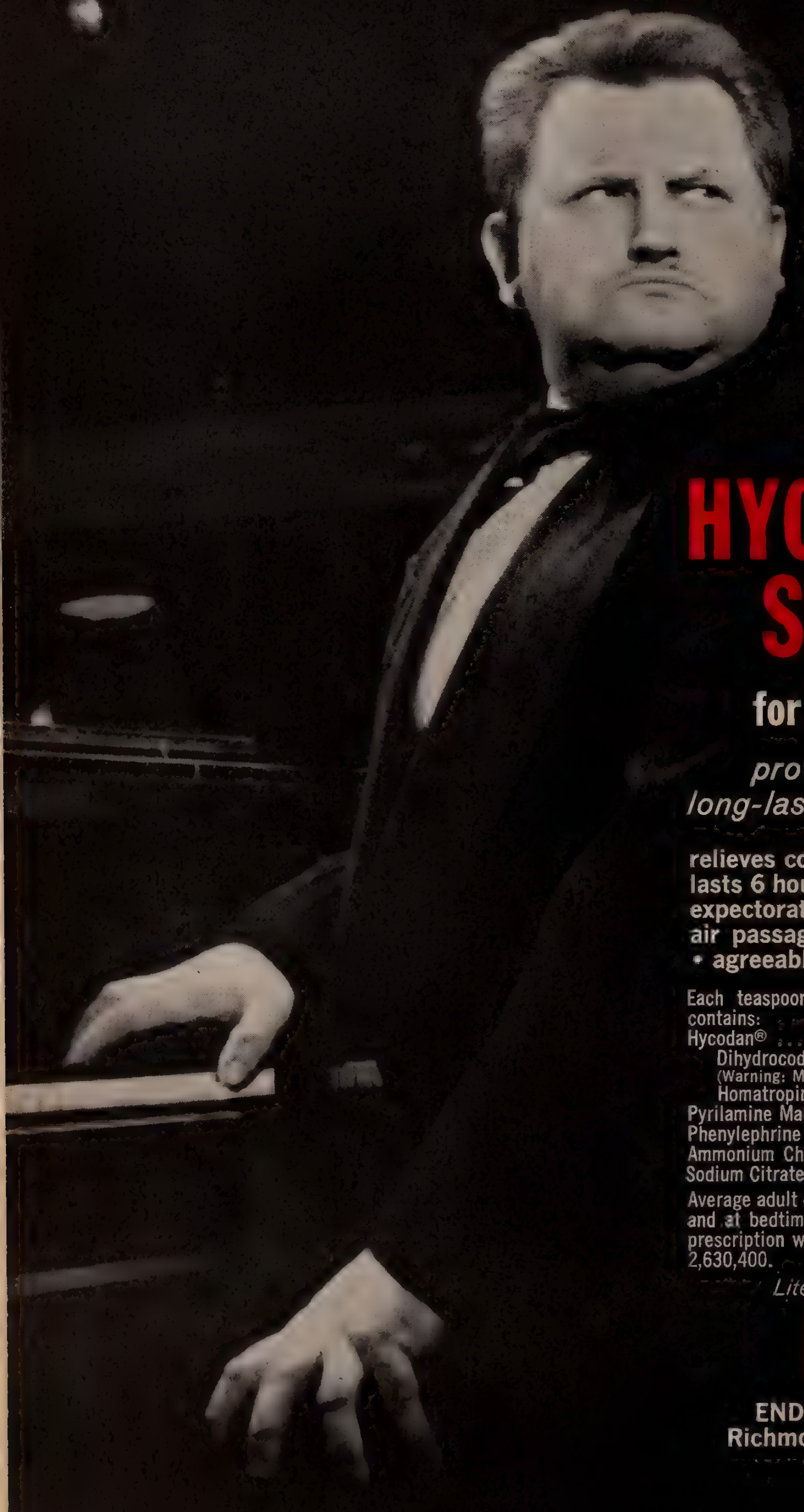
Research in the Service of Medicine



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relieves cough in 15-20 minutes • lasts 6 hours or longer • promotes expectoration and decongestion of air passages • rarely constipates • agreeably cherry-flavored

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Hycodan®	6.5 mg.
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Literature on request

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Preoperative Anticancer Chemotherapy

Preliminary Report

ALVIN L. WATNE, M.D.
Buffalo, New York
GEORGE E. MOORE, M.D., PH.D.
Buffalo, New York
SIGMUND NADLER, M.D.
Buffalo, New York
CHARLES A. ROSS, M.D.
Buffalo, New York

From the Department of Surgery,
Roswell Park Memorial Institute

IN SOME PATIENTS *various anticancer agents have provided excellent tumor regression, with an associated improvement in the patient's condition. This creates a possibility of conversion of the previously nonresectable lesion to a potentially curable situation. Four such cases are described in which the drug appeared equally effective against both the encroachment of the tumor mass and the associated metastases; but whether or not this sterilization of tumor areas by chemotherapy will be permanent, with resultant cure of these patients, must await further follow-up. Although patients of this type are relatively rare and their cure rate is still unknown, many more might appear if treated and observed for this possibility.*

WHILE ADEQUATE PALLIATION is an acceptable result for today's cancer chemotherapist, the cure of the patient remains the ultimate goal of treatment. In some patients, various anticancer agents have provided excellent tumor regression, with an associated improvement in the patient's general condition. When this has occurred, we have evaluated the patient carefully for the possibility of the conversion of the previously nonresectable lesion to a potentially curable situation. Such therapy has been possible in the following 4 patients.

Case reports

CASE 1. A fifty-seven-year-old white man was admitted to the Roswell Park Memorial Institute on February 21, 1957, because of dysphagia of four months duration together with a 13-pound weight loss. A gastrointestinal x-ray study and esophagoscopy performed at another hospital one month prior to admission were reported as showing normal findings. The past history was unremarkable. A physical examination revealed no abnormality. The patient's weight on admission was 51.6 Kg.

An esophagogram taken on February 21, 1957, revealed a marked constriction in the terminal esophagus, with some irregularity of the mucosal pattern in the area of constriction. This was interpreted as carcinoma of the lower esophagus or gastric cardia. Esophagoscopy revealed esophagitis at a level 40 cm. below the upper incisor teeth, but without evidence of tumor on two repeat occasions. A biopsy was reported as gastric mucosa. A Papanicolaou smear was negative for malignant cells.

Because of the persistent dysphagia, a left thoracoabdominal exploration was performed on April 9, 1957. At this time, the thoracic esophagus was found to be normal. A tumor mass was found in the cardia of the stomach, with an infiltration resembling linitis plastica, involving primarily the posterior wall of the stomach and encroaching on the lesser and greater curvature regions. The lesser and greater omenta were diffusely infiltrated with tumor. The liver was studded with grayish, rounded nodules averaging about 1 cm. in diameter, and a biopsy of these revealed metastatic carcinoma (Fig. 1A). Numerous enlarged lymph nodes were found in the upper edge of the pancreas and the area of the celiac axis. The patient was deemed incurable, and no further surgical procedure was performed at that time.

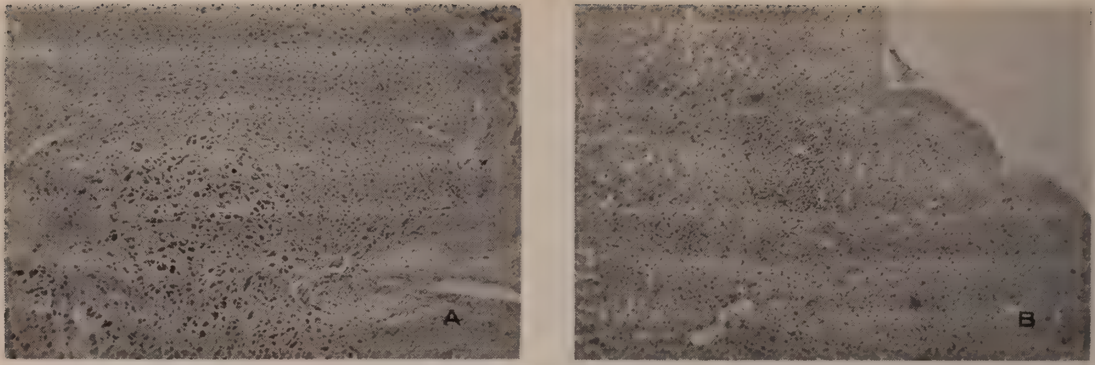

FIGURE 1. Case 1. (A) Gastric carcinoma metastatic to liver. (B) Residual scar in liver after chemotherapy.

Postoperatively he received TSPA (triethylene thiophosphoramide) intravenously, 11 mg. daily (0.2 mg. per kilogram of body weight) for four consecutive days. This was followed by a marked improvement in his swallowing and in his general condition. He was discharged on the fourteenth postoperative day with a normal hematologic picture and body weight of 51.6 Kg.

He was followed in the outpatient clinic at monthly intervals for four months. There was a definite improvement in his ability to swallow and no evidence of advancing disease. He maintained a weight of 50 Kg. during this time.

Although he was asymptomatic, he was readmitted to the Institute on August 28, 1957, for further treatment with TSPA. A physical examination at this time revealed a weight of 51.6 Kg., a liver edge palpable 3 cm. below the right costal margin, and a mass in the epigastrium that was interpreted as an enlarged left lobe of the liver. The rest of the physical findings were essentially normal. He received TSPA, 10 mg. daily, intravenously for five consecutive days, without toxic effects.

After his discharge from the hospital, he was seen in the outpatient clinic at monthly intervals without evidence of further swallowing difficulties. An esophagogram on September 3, 1957, revealed a rigid constriction of the lower esophagus, unchanged from February, 1957.

He was readmitted to the Institute on November 26, 1957, because of progressive dysphagia of one week's duration. His weight on this admission was 48.4 Kg. An esophagogram on this admission showed no change in the filling defect of the cardia. Esophagoscopy did not reveal a tumor. He again received TSPA, 10 mg. intravenously for five consecutive days, without toxic effects and with slight improvement in his ability to swallow.

When the patient was seen at the outpatient clinic on December 12, 1957, he was complaining of severe difficulty in swallowing. Except for gross evidence of malnutrition, his general condition at this time was satisfactory. There was no clinical evidence of progression or dissemination of the disease. A roentgenogram of the chest showed normal findings. The slow progression of the disease led us to readmit this patient, with the idea of performing a palliative bypassing procedure to relieve the dysphagia.

An abdominal surgical exploration was done on December 23, 1957, ten months after the original operation. At surgery, the disease was confined to a 2- by 2.5-cm. movable mass at the gastric cardia. The previously described diffuse tumor infiltrations of the greater and lesser omenta and the superior pancreatic and celiac nodal metastases were no longer evident. The liver, although enlarged to the level of the iliac crest, was free of gross evidence of tumor. Six small, stellate, flat scars measuring 1 to 2 mm. in size were noted on the superior surface of the liver and on biopsy were reported negative for tumor (Fig. 1B). These were presumably the scars of the previously described metastatic nodules in the liver. These findings led us to abandon our plans for a merely palliative procedure, and instead a proximal subtotal gastrectomy with splenectomy was performed, reconstituting intestinal continuity by esophagogastrostomy and pyloroplasty.

The postoperative course was uneventful. Except for occasional epigastric distress after meals, the patient did well after the operation. There was no evidence of recurrence of disease at six months. His weight, which was 41 Kg. postoperatively, increased to 49 Kg. On July 22, 1958, there was no sign of recurrent cancer. The patient died suddenly at his home on August 21, 1958, of unknown cause.

CASE 2. A twenty-eight-year-old woman was first seen at Roswell Park Memorial Institute in May, 1961, with a history of intermittent constipation and gnawing pain in the abdomen for about one year. Her family physician had placed her on a bland diet, but this did not relieve the symptoms. In September, 1960, the pains became more severe, and she was hospitalized for a possible ovarian cyst. On

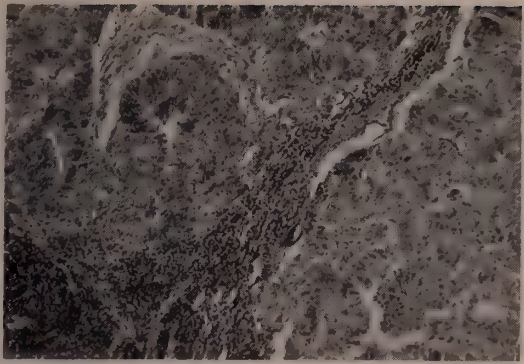

FIGURE 2. Case 2. Colon carcinoma metastatic to gastric lymph node.

September 24, 1960, her abdomen was explored surgically, and she was reported to have a ruptured diverticulitis with peritonitis. Twelve days after this first surgical procedure, a transverse colostomy was performed. On December 13, 1960, she returned to the operating room, and a large adenocarcinoma of the sigmoid colon was removed. Postoperatively she did well until March, 1961, when she developed pain in the wound area, and an abscess was found midway in the healed incision. This was drained, and it became apparent that she had a recurrent tumor in the abdominal wound.

On her admission to Roswell Park Memorial Institute, the patient was thin, with a general appearance consistent with chronic illness. Her pulse was 120 and her blood pressure 102/80. An examination of the head and neck, chest, breasts, heart, and lungs revealed no disease. An abdominal examination revealed no palpable liver, kidney, or spleen. There was a functioning double-barreled midline transverse colostomy. The left paramedian surgical scar was the site of several large tumor masses, the largest being 10 by 15 cm., with an ulcerating surface. There were palpable inguinal lymph nodes on the left, and a pelvic examination showed the recurrent tumor separate from the pelvic organs. A laboratory examination showed: hemoglobin, 11.7 Gm. per 100 ml.; blood sugar, 80 mg. per 100 ml.; and alkaline phosphatase, 5 King-Armstrong units. X-ray films showed a normal chest, an upper gastrointestinal series showed displacement of the stomach and small bowel suggesting masses in the left abdomen, and the electrocardiogram showed normal findings.

The patient underwent an exploratory celiotomy on May 19, 1961. At this time, the recurrent tumor involving the left abdomen was found to be continuous into the area of the pancreas, spleen, and left kidney. The liver and pelvis were free of tumor. A lymph node removed from the greater curvature of the stomach was positive on frozen section (Fig. 2). Numerous other nodes were present in the small bowel mesentery. In view of the extensive tumor spread, the abdomen was then closed.

Postoperatively, the patient did well. The ulcerating lesion is shown in Figure 3A. She was treated with 5-FU (5-fluorouracil), beginning with 500 mg. and continuing with 375 mg. intravenously on alternate days. At the end of this period, the lesions appeared somewhat smaller (Fig. 3B).

The patient was followed periodically in the outpatient clinic, with no marked change in tumor size. On August 2, 1961, she was readmitted to the hospital for another course of treatment with 5-FU. At this time the tumor mass in the left abdomen measured 10 by 21 cm., and the ulcerating area measured 5.5 by 9 cm. No liver masses were palpable, and the chest x-ray film showed normal findings. The laboratory data were as follows: hemoglobin, 7.9 Gm. per 100 ml.; white blood count, 9,360 mg. per 100 ml.; platelet, 462,000 cu. mm.; sulfobromophthalein sodium (Bromsulphalein) retention, 7.5 per cent; alkaline phosphatase, 6 King-Armstrong units; total protein, 6.62 Gm. per 100 ml.; calcium, 7.5 mg. per 100 ml.; phosphorus, 3.1 mg. per 100 ml.; blood urea nitrogen, 9 mg. per 100 ml.;

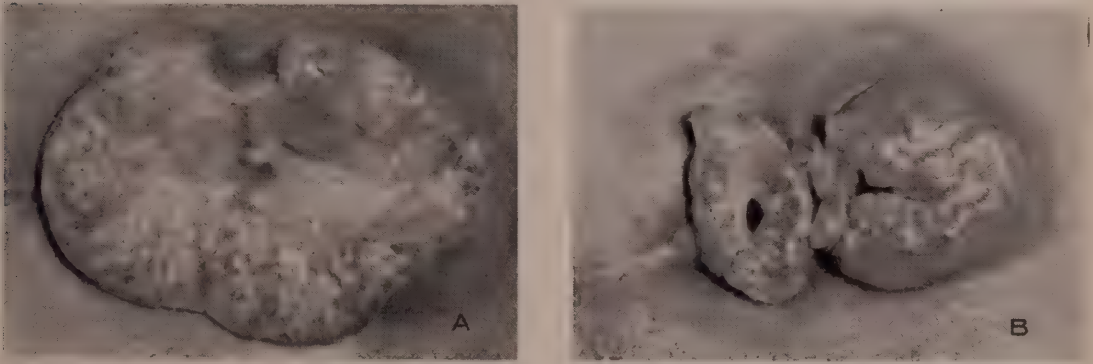

FIGURE 3. Case 2. (A) Colon carcinoma, abdominal wall tumor before chemotherapy. (B) After first course of 5-FU therapy.

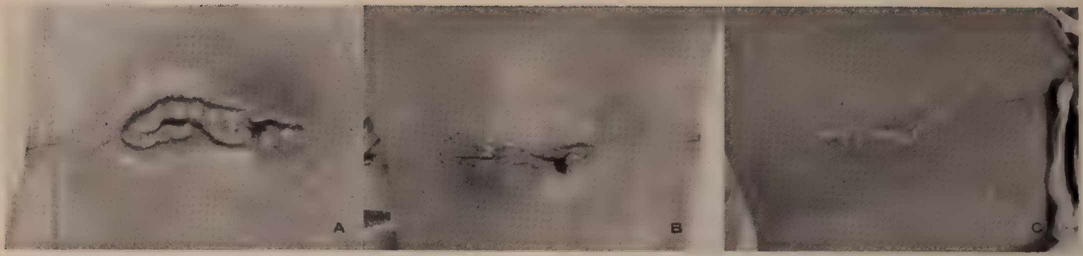

FIGURE 4. Case 2. (A) Tumor after second course of 5-FU therapy. (B) Further regression with 5-FU maintenance therapy. (C) Disappearance of tumor after 5-FU therapy.

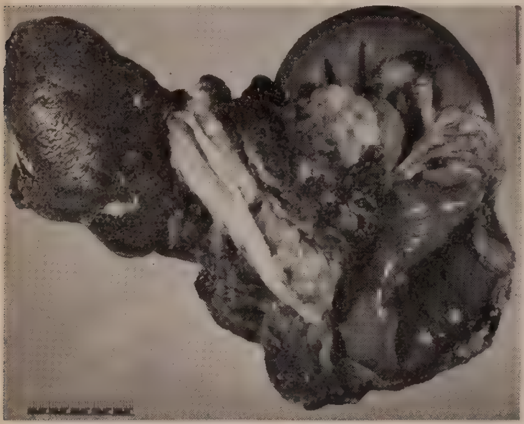

FIGURE 5. Case 2. Surgical specimen showing colon carcinoma with bowel, spleen, and skin scar.

sugar, 89 mg. per 100 ml.; and serum electrolytes, within the normal range.

The patient was given 5-FU intravenously, 15 mg. per kilogram daily for six days, with only slight nausea and vomiting after drug administration. Two days after the last drug administration, the white blood cell count fell to 2,650 cu. mm., and it became apparent that the tumor was decreasing in size, the mass measuring only 3.5 by 10 cm. and the ulcer 7 by 2.1 cm. (Fig. 4A). Four days later, the leukocyte count had returned to 5,780, and the patient was treated with 7.5 mg. of 5-FU per kilogram of body weight on alternate days for three treatments. She was then discharged home, receiving a maintenance dosage of 7.5 mg. per kilogram twice weekly.

This maintenance course was followed until September 5, 1961, with further regression of the tumor (Fig. 4B). At this time, the drug was stopped because of diarrhea. After treatment with Kaopectate and paregoric for one week, the patient was placed on a once-a-week maintenance dosage of 500 mg. of 5-FU intravenously.

Under this regimen, the tumor mass continued to decrease in size. On December 11, 1961, the patient was readmitted for a possible resection of the remaining tumor. At this time, her pain had virtually disappeared, and she had gained 10 Kg. in weight since her previous admission. On physical examination, the liver was not palpable, the colostomy functioned well, the tumor mass in the left flank measured 3 by 3 cm. and was movable, and the skin had healed, leaving no ulcerating tumor (Fig. 4C). The laboratory data were as follows: hemoglobin, 11 Gm. per 100 ml.; white blood count, 5,590 cu. mm.; and platelet count, 135,000 cu. mm.

The patient was taken to the operating room on December 15, and the abdomen was opened through a left paramedian incision. The liver was found to be free of metastases, with no lymph nodes visible or palpable in the mesentery. The tumor itself was then removed, necessitating a multiple organ resection, including the spleen, the tail of the pancreas, a portion of the stomach, a segment of the duodenum at the ligament of Treitz, a loop of the small bowel, the descending colon, muscle, and skin (Fig. 5). The necessary bowel anastomoses were done, including the removal of the colostomy with the anastomoses of the transverse colon to the sigmoid. The patient's postoperative course was complicated by a wound abscess which healed slowly. Multiple sections through the scar that had previously been the site of the ulcer failed to show any tumor (Fig. 6).

On January 7, 1962, after the wound was healed, the patient received 5-FU, 15 mg. per kilogram of body weight intravenously for five days, then one more 15 mg. per kilogram dose two days later. She was discharged on January 14, to be followed in the outpatient clinic. On January 19, the patient was bothered with diarrhea and some alopecia, and no chemotherapy was given in the outpatient clinic.

When she was seen again on February 1, there was a suspicious 3- by 4-cm. mass underlying the umbilicus, and a biopsy of this mass was recommended. For various reasons, the patient was not admitted to the Institute until March 7, 1962. At this time the periumbilical mass measured 4 by 7 cm., but it was freely movable and extended from the edge of the left paramedian incision across the midline. Her weight was 48.5 Kg.; hemoglobin, 11.6 Gm. per 100 ml.; white blood count, 8,240 cu. mm.; platelets, 365,000 cu. mm.; bilirubin, 1.2 mg. per 100 ml.; and alkaline phosphatase, 6.7 King-Armstrong units. A barium enema revealed no recurrent tumor. On March 13 the recurrent tumor in the abdominal wall was

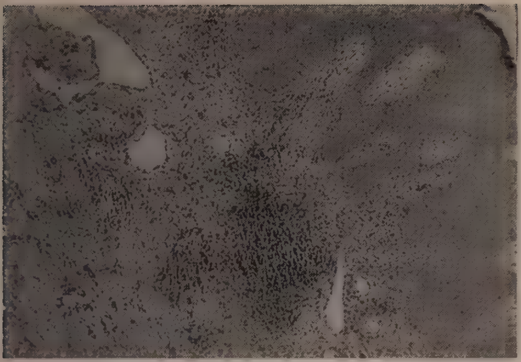

FIGURE 6. Case 2. Skin scar showing no residual adenocarcinoma.

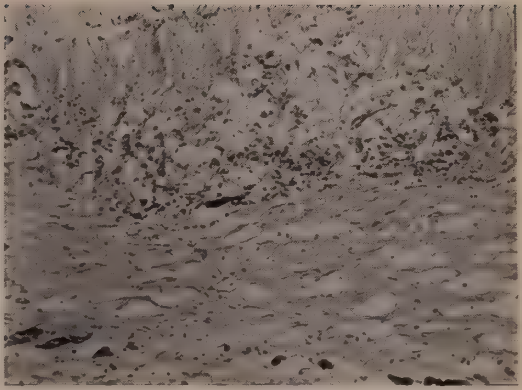

FIGURE 7. Case 3. Diaphragm invaded by mucus-producing adenocarcinoma.

excised en bloc. An exploration of the abdomen at this time revealed no additional tumor masses. Her postoperative course was uneventful. At the present time she is active and tumor-free.

Case 3. A sixty-one-year-old white female was first admitted to Roswell Park Memorial Institute on June 8, 1960, complaining of a vaginal discharge of one month's duration. A report of dilatation and curettage done by her family physician showed positive findings for adenocarcinoma in an endometrial polyp. A vaginal smear report was consistent with adenocarcinoma, classified as Stage I, Group 1 adenocarcinoma of the endometrium. On June 6, 1960, a total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. An exploration revealed no node involvement. Blood samples taken from a uterine vein at the time of surgery were negative for malignant cells. The patient's postoperative course was uneventful, and she was discharged on June 25, 1960. The pathology report concerning the surgical specimen described the lesion as multiple endometrial polyps and a small thecoma, with no evidence of malignant disease.

Follow-up examinations from July 25 to November 28, 1960, were not remarkable except for a hernia at the operative site, which was corrected surgically by her family physician in January, 1961. She continued follow-up visits in our outpatient clinic. In August, 1961, she complained of some gastrointestinal difficulties and stated that she was under her doctor's care at home. In November, 1961, the family physician referred this patient back to Roswell Park Memorial Institute for an esophageal obstruction.

The patient was again admitted to Roswell Park Memorial Institute on November 21, 1961, for study and treatment. At this time, she described a progressive difficulty in swallowing solids for four to five months prior to admission. Her esophagogram and upper gastrointestinal x-ray films showed a lesion of the fundus of the stomach, involving the cardia, with possible involvement and obstruction of the distal esophagus. Esophagoscopy on November 24 revealed a normal esophagus up to and including entry into the stomach, with biopsies negative for cancer. Repeat x-ray films were in agreement with the previous reports.

An exploratory laparotomy was performed on November 28 and revealed a carcinoma of the stomach 5 cm. in diameter on the lesser curvature at the cardia, with shelving along the diaphragm and nodular spread into the diaphragm. A frozen section of the diaphragmatic implants was positive for metastatic carcinoma (Fig. 7). A liver biopsy and peritoneal washings were negative for tumor. The patient was considered inoperable because of the diaphragmatic involvement. Her postoperative period was uneventful, and she was discharged on December 5.

On January 4, 1962, a full course of 5-FU, 15 mg. per kilogram of body weight intravenously daily for five days, was started on an outpatient basis. She then received 7.5 mg. per kilogram of body weight intravenously every other day for four doses, after which diarrhea developed. She developed a mild leukopenia of short duration, after which she was placed on a weekly maintenance dosage of 500 mg. of 5-FU intravenously beginning on January 26. This was continued for four weeks.

For one and one-half months prior to chemotherapy, she was unable to swallow solids, taking only thin liquids, but after chemotherapy she was able to eat solid foods. Because of this clinical improvement, a repeat upper gastrointestinal study was done. It revealed some evidence of a decrease in the esophageal obstruction.

The patient was readmitted to the Institute for the third time on February 27, 1962, for a repeat surgical exploration on the basis of the x-ray film findings and the marked clinical improvement following the 5-FU therapy. At surgery on March 2, 1962, the tumor had decreased to 2 cm. in diameter, and the tumor infiltration of the diaphragm had disappeared. There was still some adherence to the left lobe of the liver, but it was felt grossly that the tumor

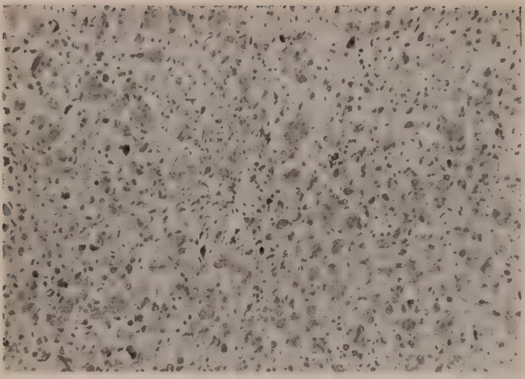

FIGURE 8. Case 4. Osteogenic sarcoma of right femur.

could be excised in its entirety. That being the case, a total gastrectomy, splenectomy, removal of the tail and body of the pancreas, omentectomy, partial removal of the left lobe of the liver, and entero-enterostomy with esophagojejunostomy were performed. The procedure was tolerated well. The patient's postoperative course was uneventful.

Case 4. A fifty-three-year-old white male truck driver was first admitted to Roswell Park Memorial Institute on March 3, 1961, with a past history as follows:

In March, 1960, the patient sustained injury in the left popliteal area. In May, 1960, he noticed a swelling of the injured area about the size of an egg, and he consulted his family physician at this time. In June, 1960, the patient had an excision of a right popliteal aneurysm with insertion of a Teflon artery graft. He was asymptomatic until October, 1960, when he noted a recurrence of the swelling in the right popliteal area.

A biopsy of this mass in November, 1960, gave a diagnosis of undifferentiated sarcoma, and on November 30, 1960, the patient had a right midthigh amputation. The pathology report was an osteogenic sarcoma of the right popliteal fossa (Fig. 8).

On February 10, 1961, the patient was readmitted to the hospital with a complaint of hemoptysis. A chest x-ray film at this time revealed metastatic lesions in the lower lobe of the right lung, one in the right middle lobe, and a possible third lesion anterior to the aortic shadow.

The patient was then referred to Roswell Park Memorial Institute. On admission to the Institute on March 21, 1961, he gave the preceding history, plus the fact that his right hand had been injured in an airplane accident in 1923 and had been amputated at the wrist. A physical examination showed: pulse, 100; respiration, 20; blood pressure, 140/90; and head and neck areas negative for tumor. There was some decrease in breath sounds over the left chest, but no abdominal masses. A chest x-ray film confirmed the presence of pulmonary metastases (Fig. 9A). The laboratory data were: hemoglobin, 13.1 Gm. per 100 ml.; white blood count, 10,300 cu. mm.; platelets, 207,500 cu. mm.; sulfobromophthalein sodium retention, 7 per cent; alkaline phosphatase, 6.5

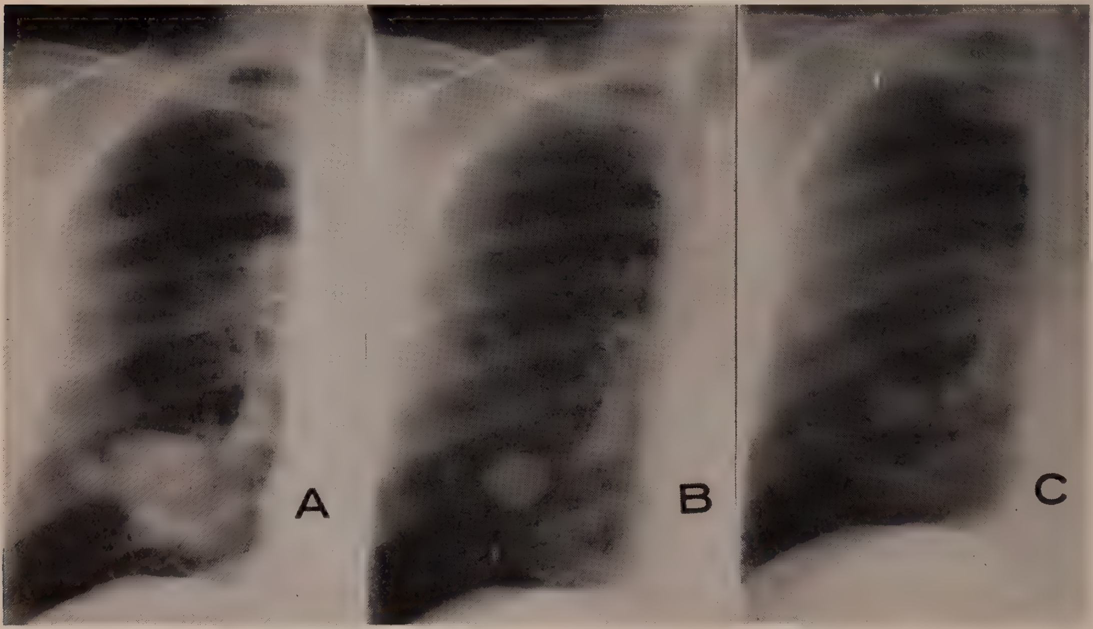

FIGURE 9. Case 4. (A) Pulmonary metastases from osteogenic sarcoma before therapy. (B) Decrease in size of metastases after therapy with AB-132. (C) Persistent lung lesion after AB-132 therapy.

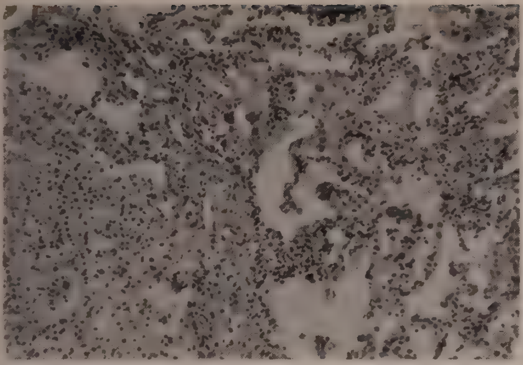

FIGURE 10. Case 4. Lung lesion showing giant-cell and round-cell infiltration.

King-Armstrong units; and total protein, 7 Gm. per 100 ml. The patient was treated with AB-132 (ethylcarbamine) receiving 10 Gm. intravenously over a nineteen-day period in 1- or 0.5-Gm. daily doses. Minimal toxicity of slight nausea and occasional vomiting was controlled with Thorazine. Chest x-ray films taken at the time of discharge on April 11 showed a decrease in the size of the chest lesions (Fig. 9B).

The patient was followed in the outpatient clinic, and was then readmitted to the Institute on June 5, 1961, the chest lesions remaining much the same since his last treatment. At this time, his complaint of hemoptysis had disappeared, his weight had remained constant at 65 Kg., and he was active with gardening and activities around home. At physical examination, his pulse was 70 per minute and his blood pressure 124/62. No tumor masses were evident. The laboratory data were: hemoglobin, 14.2 Gm. per 100 ml.; white blood count, 4,200 cu. mm.; platelets, 320,000 cu. mm.; and total protein, 7.5 Gm. per 100 ml. He was retreated with AB-132, 10 Gm. total dose given daily intravenously in 1- and 0.5-Gm. doses over a sixteen-day period. At the completion of this therapy, a repeat chest x-ray film showed a complete disappearance of the lesions in the left lung and a decrease in the size of the right lung lesions.

He was followed in the outpatient clinic, with no further regression of the chest lesions. He was readmitted to the Institute on August 21, 1961, for treatment with a cultured tumor cell vaccine. This vaccine was prepared from cultured tumor cells arising from an osteogenic sarcoma biopsy from a previous patient. They were attenuated before injection by subjecting them to 5,000 rads of roentgen rays. The cells were then injected subcutaneously twice a week in increasing dosages from 4 times 10^6 to 128 times 10^6 cells over a three-week period. No chemotherapy was given during this admission, and no change in the patient's clinical status was seen. After his discharge from the hospital, he was followed in the outpatient clinic and given weekly vaccine injections. The solitary nodule in the right lung remained stationary throughout this time period.

In view of this solitary identifiable lung lesion, the patient was readmitted on December 4, 1961, for surgical excision of the lesion. At this time, his physical examination gave essentially the same results as on previous admissions. No palpable tumor masses were present. The laboratory tests showed: hemoglobin, 11 Gm. per 100 ml.; white blood count, 7,560 cu. mm.; platelets, 280,000 cu. mm.; alkaline phosphatase, 12.4 King-Armstrong units; total protein, 7.8 Gm. per 100 ml.; blood urea nitrogen, 20 mg. per 100 ml.; and bilirubin, 0.7 mg. per 100 ml. A chest x-ray film revealed the persistence of a solitary right lung lesion (Fig. 9C).

The patient was taken to surgery on December 8, and celiotomy showed the liver and abdomen to be free of tumor. He was then turned on his left side, and a right thoracotomy was performed through the bed of the fifth rib, and the nodule was excised from the lower lobe of the right lung. Frozen and permanent section revealed no tumor, only fibrosis with histiocytes and giant-cell and round-cell infiltration (Fig. 10). The patient's postoperative course was smooth, and on December 13 he was given a booster dose of tissue-culture cell vaccine, and a 6-Gm. course of AB-132 was administered, 0.5 Gm. a day intravenously. This was tolerated well, and the patient was followed in the outpatient clinic and given weekly injections of the cultured tumor cell vaccine.

He was tumor-free on February 26, 1962, when he was readmitted to the Institute for another course of AB-132, which was administered in 0.5-Gm. daily doses for a total dose of 10 Gm. No initial toxicity developed, and he returned home on March 19. He is being given vaccine every two weeks.

Comment

The opportunity to excise surgically a previously unresectable tumor after chemotherapy is rare, but unless the cancer chemotherapist is aware of this possibility, such opportunities may be missed. The timing of the surgical procedure is of great importance. In several patients we have obtained good regression of the tumor after chemotherapy, and then because the patients would not accept additional surgery at that time or because we felt another course of chemotherapy might further improve their condition, additional time was lost, and the tumor became drug resistant and again inoperable. With 5-FU we have been able to maintain remissions for six weeks to three months using weekly or biweekly maintenance therapy. We have not used AB-132 or TSPA in a similar manner. With AB-132 repeated treatment gave additional tumor regression, which is less common with TSPA.

What role the tumor tissue-culture cell vaccine played in the response of the patient with osteogenic sarcoma is unknown. He did show a marked allergic response at the injection sites, with an elevation of the Fraction I gamma globulin, and fluorescent antibody was demonstrated against the tissue-culture cells, all of which is nonspecific and was expected. The complete disappearance of the tumor from the lung, with only the persistence of histiocytes and giant cells, is a phenomenon awaiting further definition. The histiocytes may represent some form of host resistance or may simply be present to phagocytize a necrotic tumor. Although no pretreatment lung biopsy was obtained, from the x-ray picture it seems unlikely that the lesions were some kind of granuloma; and if such was the case, a response to AB-132 would be even less likely. Spontaneous cures of osteogenic sarcoma have been reported,[1] and such a phenomenon cannot be ruled out for this patient.

In each of these patients some tissue appeared to have been sterilized by the drug. Although the surgical scar in Case 2 failed to show any nests of tumor when it was excised after chemotherapy, the recurrence about the umbilicus indicates that some nests of cancer cells did remain. For this reason, we are continuing chemotherapy even after the surgical removal of the gross tumor. The first patient, who underwent gastric resection after therapy with TSPA, died eight months after surgery, without apparent malignant disease. No postoperative drug was given in this case. This patient was described in a previous report[2] by one of us (C.R.) and led to our interest in this possible use of chemotherapy. Case 3, showing the decrease in gastric obstruction after 5-FU therapy, had the repeat gastrointestinal study with the idea of possible surgery, and the regression of the gastric tumor prompted the surgical intervention.

The drugs appeared equally effective against both the encroachment of the tumor mass and the associated metastases. Whether or not this sterilization of tumor areas by the chemotherapy drugs will be permanent with the resultant cure of these patients must await a further follow-up. This paper is not intended to indicate any special drug or drugs for this purpose, but rather to alert our colleagues to the possible change in operable status resulting from chemotherapy. We do not advocate any tumor cell vaccine as an adjuvant to drug therapy at this time.

Summary

In certain patients, anticancer drugs can render a previously inoperable tumor surgically resectable. Four such patients are presented. The value of repeated treatments with chemotherapy and of maintenance chemotherapy to obtain a maximum regression is borne out by the case reports. The possible role of cultured tumor cell vaccines is unknown as yet. We do not advocate any special drug or treatment regimen to gain this end. Although patients of this type are relatively rare and their cure rate is still unknown, we believe that many more such patients will become apparent if they are treated and observed for this possibility. In our opinion, this technic offers a new hope for patients with advanced cancer.

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SYMPOSIUM AND PANEL DISCUSSION

Bacteremic Shock in Obstetrics

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Protocols

Alexander H. Rosenthal, M.D.: Obstetric patients were first admitted to The Long Island Jewish Hospital in May of 1954, and by January 1, 1961, more than 12,000 women had been delivered with only 3 puerperal deaths. Then in February of this year and within twelve days of each other, 2 patients died of bacteremic shock following delivery. These mortalities occurred with frightening speed, and to those at the bedside it appeared as if there were no adequate therapeutic measures available to halt the swift, deadly progress of the infection. One of the 3 previous puerperal deaths had occurred in 1956. This was a thirty-five-year-old woman who was delivered at term ten days after the rupture of the membranes. Fever and chills had preceded the delivery followed by overwhelming sepsis, uncontrollable shock, and death within twelve hours. The histories of our 2 recent cases are similar and are as follows:

Case 1. The patient was a thirty-three-year-old white para 2-0-0-2, thirty-seven weeks gravid, whose expected date of confinement was March 3, 1961. Her past history included pneumonia in 1946 and the excision of a pilonidal cyst in 1952. In 1954 she had hepatitis.

The prenatal course with her present pregnancy was uneventful until 8:00 p.m. on February 9, 1961, when she complained of generalized malaise, fever, nausea, vomiting, and diarrhea. At 1:00 a.m. on February 10, her temperature rose to 105 F. Her family doctor was notified by telephone, and the patient was put on oral antibiotics. A second doctor was contacted during the night, but the patient was first seen at 9:00 a.m. February 10 when she had a temperature of 102 F. At that time she was given an antibiotic intramuscularly. At 2:30 p.m. on that day spontaneous rupture of the membranes occurred along with the onset of labor. At 12:15 p.m. on February 10, three weeks prior to her estimated date of confinement, she was admitted to the hospital in advanced, active labor. On examination she was found to be febrile and toxic. The cervix was fully dilated with the vertex at the spines. Fifty mg. of meperidine hydrochloride (Demerol) and 1/200 grain of scopolamine were given intravenously, and at 2:35 p.m. she was delivered of a stillborn infant weighing 3,850 Gm. The placenta and membranes were delivered intact.

Following the delivery her temperature was 102 F., pulse 160, respirations 36, and the blood pressure 100/70. She appeared toxic and cyanotic, but no petechiae were seen. A paronychia of the right thumb was noted. An intravenous administration of fluids was begun, and a blood culture was drawn. Coagulation studies done at this time showed normal clotting with subsequent good clot retraction. Two hours after the delivery, at 4:30 P.M. on February 10, the blood pressure was 70/0, pulse 140, and respirations 40. Antibiotics were administered. These included penicillin 1 million units intramuscularly with 5 million units of penicillin and 500 mg. of chloramphenicol (Chloromycetin) being added to the intravenous solution of glucose and water. Two ampules of levarterenol bitartrate (Levophed) also were added to the infusion. At 7:00 P.M. 20 cc. of gamma globulin were given intramuscularly. At this time the dosage of penicillin was increased to 15 million units. A total of 2 Gm. of chloramphenicol was added to the infusion, and Staphcillin, 3 Gm., also was given. The dosage of levarterenol bitartrate was increased to 10 ampules, and 1 ampule of Regitine also was added to the intravenous solution. The patient was placed on a cooling mattress and was given Thorazine intravenously to control her chills. Within seven hours after delivery, at 9:30 P.M., the patient had been given 2,600 cc. of intravenous fluid, but no appreciable urinary output occurred. At 10:30 P.M. an additional 20 cc. of gamma globulin were given. At 11:30 P.M. the temperature dropped to 99 F. The blood pressure was now 70/0. At this time jaundice was obvious. Seventeen hours after the delivery, at 7:30 A.M. February 11, jaundice increased, and no blood pressure could be obtained. Although the brachial pulse was not palpable, pulsations were felt over the femoral areas. By this time the total urinary output was only 40 cc. Twenty-three hours after her admission the blood pressure rose to 110/70 for a short interval, but the patient's general condition remained critical. Her cyanosis persisted, and skin petechiae were noted. Scrapings from these petechiae showed gram-positive cocci. Twenty-five hours after the delivery the intravenous administration of steroids was begun. At 10:45 P.M. on February 11, thirty-two hours and fifteen minutes after her admission, the patient expired. A necropsy was performed.

CASE 2. An eighteen-year-old white married para 0-0-0-0, twenty weeks gravid, was admitted to the hospital on February 21, 1961. Her prenatal course had been uneventful until ten days prior to her admission when she began to complain of lower abdominal cramps, fever, and vomiting. A local doctor made a diagnosis of a viral infection. Her fever and other symptoms subsequently subsided, and she was apparently well until February 20 when she again developed fever and generalized malaise. Fetal movements had been noted two weeks prior to her admission and were present until the evening of February 20, 1961. At 2:00 A.M. on February 21, she was awakened from sleep by crampy pains in the lower part of the abdomen. At 6:00 A.M. moderate vaginal bleeding occurred. Intervention was denied, and in fact, the patient was known to be desirous of having a baby.

On admission to the hospital at 8:00 A.M. her blood pressure was 110/70, pulse 92 and regular, and temperature 102 F. The uterus was enlarged to the size of a five-months gestation and was tender. Mild contractions were palpable every three or four minutes. No fetal heart tones were audible. The liver, spleen, and kidneys were not palpable. A foul, bloody, vaginal discharge was noted. The cervix was slightly dilated and effaced, and visualization showed no evidence of trauma. Cervical and blood cultures were taken. An intravenous administration of glucose and water was begun, and penicillin and chloramphenicol were added to it. The patient was in early labor and was sedated with meperidine hydrochloride, scopolamine, and Sparine. At 12:15 P.M. Pitocin was added to the intravenous fluid to speed the emptying of the uterus. The membranes were intact until the cervix was fully dilated, when they were ruptured artificially. This was followed by a shaking chill. Her blood pressure was 155/90, and the pulse was 160. A 400-Gm. stillborn fetus was delivered which showed no maceration, followed by the expulsion of a grayish placenta and membranes. Soon after delivery the blood pressure was 90/50, pulse 160 and somewhat feeble, and the temperature 105.2 F. In addition to the intravenous fluids, 1 unit of whole blood was given without any response of the blood pressure, which remained in the vicinity of 70/50. Blood was noted to be coming from the gums near a cracked carious upper molar, and minimal vaginal bleeding also was noted. An exploration of the uterus showed it to be intact with no evidence of retained tissue. Levarterenol bitartrate medication was started with a return of the blood pressure to 130/90 for a short while. An examination of the blood showed no clotting, the fibrinogen level was 17 mg. per 100 ml., and a fibrinolysin was demonstrated. The patient was given fibrinogen and hydrocortisone intravenously and vitamin K_1 oxide. After 6 Gm. of fibrinogen were given, persistent lysis of the blood clot was still noted, and additional fibrinogen was given for a total of 14 Gm. The patient was put on a hypothermia blanket, and the temperature was reduced from 105.2 to 98.5 F. The blood pressure returned to the hypotensive levels of 70/50, but despite this shocklike state, the patient's sensorium remained clear until just prior to her death. Additional hydrocortisone was given in the amount of 400 mg. The penicillin administration was raised to 50 million units, and streptomycin and vancomycin also were given. Repeated hematocrits remained unaltered. The white blood cell count rose from 6,050 on admission to 60,000 with atypical lymphocytes and toxic granules noted. Smears taken from the blood of the umbilical cord and the patient showed intracellular gram-positive cocci within the leukocytes. Jaundice followed by evidence of septic embolization became apparent. The patient became stuporous and unresponsive and expired at 11:30 P.M. on the day of admission, approximately fifteen and one-half hours after being admitted to the hospital. A necropsy was performed.

COMMENT. Thus, 3 of the 5 puerperal deaths occurring in this hospital have been from bacteremic shock with 2 occurring in patients at or near term. While such puerperal deaths undoubtedly have occurred in the past, it is my impression that this type of catastrophic complication is on the increase, and to support this opinion we have reviewed the data from the Committee on Maternal Mortality of the Kings County Medical Society. This committee was headed by the late Charles A. Gordon, M.D., to whom great credit should be given for his pioneer work in the reduction of maternal mortality. He was one of the first to publicize the value of the analysis of a maternal death with regard to the recognition of controllable factors. In Brooklyn during the years 1937 to 1949, 1,126 puerperal deaths occurred in approximately 650,000 pregnancies. While sepsis was a common cause of death, the pathologic condition generally showed suppurative peritonitis and septicemia with pelvic thrombophlebitis and embolic dissemination to the lungs. In these patients death did not occur within the short interval common to the cases being presented here.

I have spoken with James L. O'Leary, M.D. He and I were the recorders of the committee, and neither of us can recall reports of similar cases. I would presume that death from bacteremic shock probably had occurred, but I submit that the incidence must have been extremely low.

Since this cause of death occurs from infections in organs other than those of the female genitalia, and because the problems encountered in therapy are not purely obstetric in nature, the subject should be of general interest. We are asking our colleagues in other fields to help us in the control of this dread complication, and to this end this symposium has been arranged. We will begin by asking James I. Berkman, M.D., to present data on our 2 recent cases.

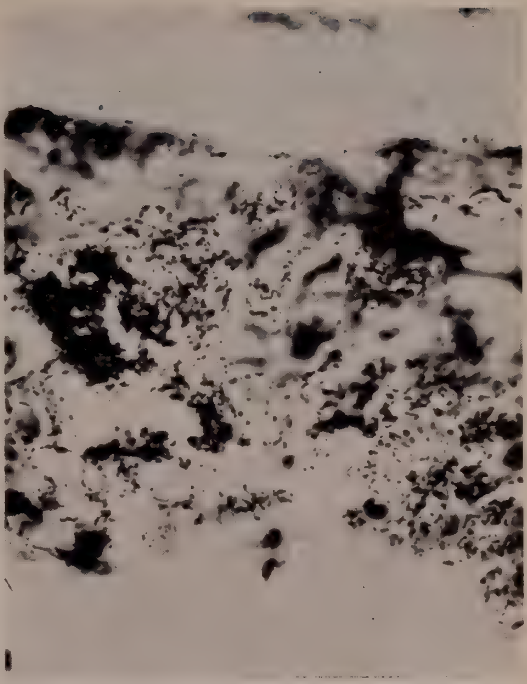

FIGURE 1. Placenta. Gram-positive cocci in small groups and dense clumps are disseminated throughout the amnion and chorion (Brown-Bren stain, ×380).

Comment on data

JAMES I. BERKMAN, M.D.: I'd like first to present such clinical and laboratory data as are not included in the protocols which are available to you, and then I shall present the autopsy findings.

CASE 1. While the placenta and membranes in Case 1 were described as being not unusual both by the attending obstetrician and subsequently by a pathologist, this conclusion was based on a gross examination. As you will see in a moment, significant microscopic changes were found.

Now in regard to pertinent laboratory data which are not listed in the protocol, it should be noted that her hemoglobin never fell below 11 Gm. Her white blood cell count was 30,400 and remained at that level with a marked shift to the left. The blood urea nitrogen, which on admission was 12 mg. per 100 ml., rose to 31 mg. per 100 ml. before her death, and there was a minor reduction of the serum sodium and chloride levels with no significant acidosis.

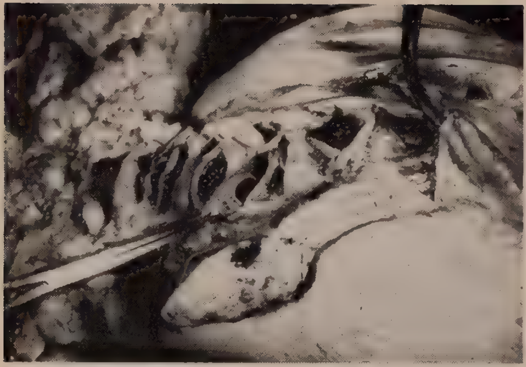

FIGURE 2. Fundus of uterus with left ovary and ovarian ligament: posterior view. The ovarian veins are greatly distended and occluded by fresh thrombus.

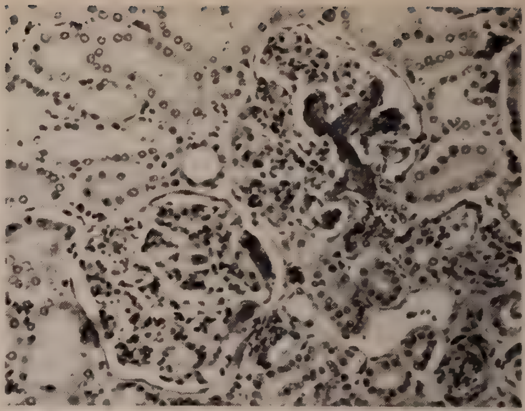

FIGURE 3. Kidney. Glomerular capillaries are occluded by fibrin thrombi, as is the juxtaglomerular arteriole of the glomerulus on the right (hematoxylin and eosin stain, ×120).

Autopsies were performed on both the mother and the baby. I would like to discuss the pertinent anatomic findings and then review the bacteriologic findings.

Anatomic findings. The gross and microscopic findings in the baby revealed nothing really remarkable with the exception of disseminated petechial hemorrhages. We ordinarily lump these together as reflecting the so-called perinatal distress syndrome, or if you will, in this case, as evidence of intrauterine anoxia. A section of the baby's lung showed subpleural hemorrhage.

Along the surface of the chorion and amnion of the placenta was an infiltration of polymorphonuclear leukocytes. An additional section from a different area revealed an acute suppurative process which extended through the membranes, but not into the chorionic villi. In gram stains these tissues were loaded with gram-positive cocci, and there was evidence on culture that these were either staphylococci or an enterococcus, which also were recovered on culture (Fig. 1). We searched high and low but could not demonstrate in the placenta or other maternal tissues a gram-negative organism.

Figure 2 shows what the postpartum uterus looked like. The only remarkable gross feature is to be seen in the left adnexal veins, which are completely occluded by fresh thrombi. From these sections through the uterus it is very clearly evident that we were dealing with acute diffuse myometritis. Let me next direct your attention to the extensive edema and cellular infiltration with separation of the muscle bundles, and pools of polymorphonuclear leukocytes in and around the blood vessels. Many sections through the uterus revealed this change. There were small vessels from the myometrium which revealed a very interesting combination of changes. There were a number of necrotic granulocytes in the lumina enmeshed in material which had all the features of fibrin. In sections through the left cornua of the uterus, there was extensive acute endometritis and myometritis. In sections which border on the uterine veins as they come up into the broad ligament to form or to join with the ovarian plexus, there was severe inflammation of the venous walls, some of which were filled with fresh thrombi. This suppurative thrombophlebitis extended for a considerable distance.

The kidneys of the mother were of considerable interest. They were pale and swollen. We could not visualize grossly anything that looked like the classical picture of bilateral cortical necrosis, and yet there was a suggestion periodically of minute surface hemorrhages. There was pallor of the cortex, not particularly intense, and intense congestion of the medullas. Histologically, the kidney sections were remarkable. The loops of practically every glomerulus were filled with occlusive fibrin thrombi (Fig. 3). There was really no

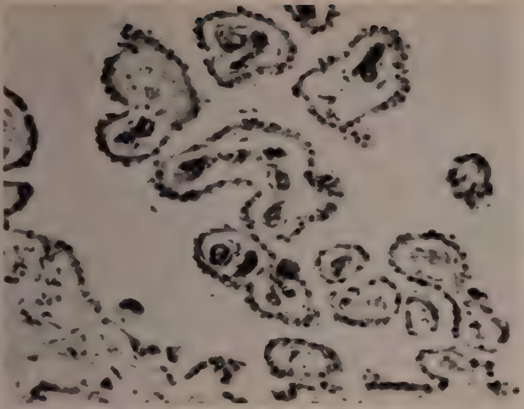

FIGURE 4. Choroid plexus. The capillaries of many villi are occluded by fibrin thrombi (hematoxylin and eosin stain, ×120).

tubular necrosis. There was no "lower nephron nephrosis." Indeed, there was not, as judged from microscopic study of many sections, evidence of lesions other than fibrin thrombi in the glomerular and interstitial capillaries. They were colored by various staining methods. In trichrome preparations they stained as does fibrin; with the phosphotungstic acid-hemotoxylin (PTAH) method, they stained as does fibrin; with periodic acid-Schiff stain, they became colored as does fibrin.

This woman had been jaundiced, and we were considerably interested in what we might find in her liver. It was swollen and weighed 2,400 Gm. We could see no gross features of significance. Microscopically, what we encountered periodically in venules or sinusoids were the same fibrin thrombi which we saw elsewhere. There was perhaps an occasional necrotic liver cell and a small focus of nonspecific hepatitis.

In the myocardium there were interesting findings which we had not anticipated from gross observation, since the heart looked quite normal. There was a patch of suppurative endocarditis along with some myocarditis. In the lungs there was a variety of vascular lesions. In a small arteriole there was a plug composed of fibrin and disintegrating leukocytes. In smaller vessels there were homogeneous fibrin clots. In the PTAH stain, the nature of these plugs in minute capillaries was evident. They were shown as dark distending plugs of fibrin. Even in the skin, corresponding to the petechiae which developed during life, we were able to demonstrate fibrin plugs, as well as an acute diffuse inflammatory process in the corium.

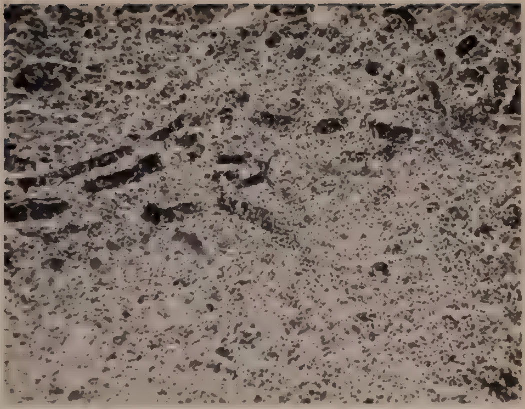

FIGURE 5. Pituitary gland. A rim of intact cells of the anterior lobe remains at the top. The rest of the adenohypophysis is infarcted. Capillaries in the transition zone are occluded by fibrin thrombi (hematoxylin and eosin stain, ×50).

Steered by some past observations of Dr. McKay, we looked at the choroid plexus in this patient. Here was a beautiful example of fibrin thrombi in the capillaries of the choroid plexus (Fig. 4). Belinda Aftalion, M.D., who performed this postmortem examination, pointed out that when she removed the pituitary gland, it didn't seem quite right. It was soft and discolored. Figure 5 shows zones of necrosis in the anterior pituitary. There are intact pituitary cells, surrounded by disintegrating necrotic cells and a zone of hemorrhage and marginating leukocytes. Better demonstrated in this photograph are fibrin plugs occluding many marginal capillaries.

Bacteriologic findings. Now then, what were the bacteriologic findings? Henry Isenberg, Ph.D., our microbiologist, spent long hours with these cases. From cultures of this mother's blood during her life he got a coagulase-negative staphylococcus and an enterococcus. I would remind you that this woman had been receiving large doses of antibiotics. The same organisms were recovered from the paronychia during life and postmortem. Staphylococci and enterococci were recovered from the throat. Remarkably, direct vaginal smears revealed no organisms, and on culture nothing grew

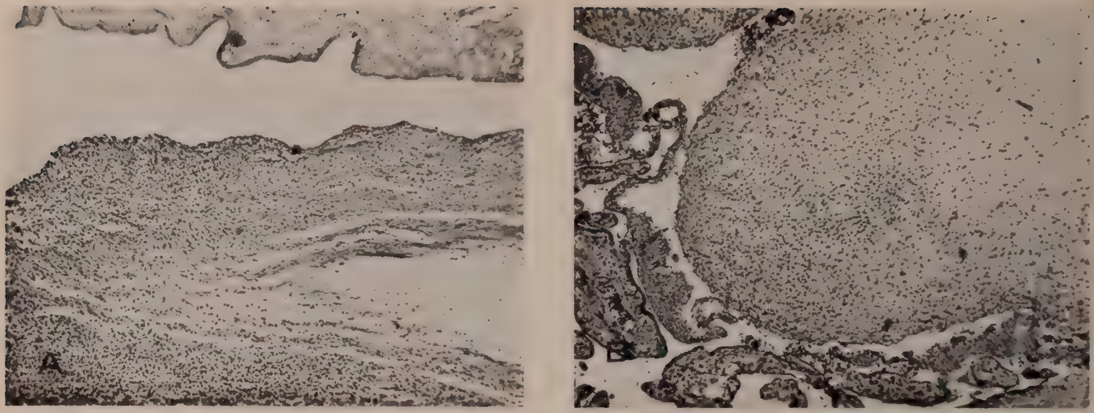

FIGURE 6. Placenta. (A) The amnion is necrotic and the chorion is diffusely infiltrated by fibrinopurulent exudate. (B) There is intervillous accumulation of fibrinopurulent exudate. (Hematoxylin and Eosin Stain, × 50)

from the vaginal discharge. On direct smears from material submitted to the laboratory as a placental clot, Dr. Isenberg was able to see rare gram-negative rods, or at least what he thought were gram-negative rods, but we couldn't get anything to grow that was gram negative. What we got on culture was a hemolytic Staphylococcus aureus and again an enterococcus.

From the tissues of the baby postmortem we got no growth from any organ; that is, we saw no organisms on direct smears; and with the exception of the liver, from which grew a staphylococcus and a hemolytic staphylococcus which was coagulase-positive, the baby's organs were sterile.

Case 2. As Dr. Rosenthal has told you, having been distressed with our experience in this case, we very shortly thereafter encountered another. Now in regard to the second case, despite massive and heroic efforts at therapy, again a successful outcome did not occur. When the patient came into the hospital, and this may be of some interest, her white blood cell count was 6,500. It very rapidly rose to 20,000. Some of us thought that we were able actually to see some gram-positive intracellular cocci in some circulating granulocytes. Arthur Sawitsky, M.D., and his staff, the hematology group in this hospital, investigated her clotting mechanisms rather closely. Her blood did not clot. Her platelets were 60,000. The fibrinogen level was 17 mg. per 100 ml., and Dr. Sawitsky was able to demonstrate, in addition, the presence of a circulating fibrinolysin. She also became jaundiced. There was not time to study the nature of her jaundice chemically before she died, approximately fifteen and one-half hours after her admission to the hospital.

The postmortem examination on the mother was performed at the office of the Queens County Medical Examiner. We are indebted to John F. Furey, M.D., the Deputy Medical Examiner, and Theodore Sard, M.D., a resident on our obstetrical service, for bringing us the tissues from this patient.

Anatomic findings. The 400-Gm. female fetus was deeply discolored but not macerated. I think that what would strike you most are the yellow-gray opacity of the membranes and the fetal surface of the placenta. A microscopic section through the membranes shows a remarkable picture of the chorion and the amnion (Fig. 6). There is an extensive inflammatory exudate in these membranes which extends into some of the chorionic villi as well. Both mononuclear cells and granulocytes are present. A photomicrograph made at higher magnification revealed fibrinopurulent exudate between the chorionic villi. The umbilical cord, too, was infiltrated by inflammatory cells as was the wall of this vessel. An additional section showed the diffuseness of this process and the zones of associated necrosis. Another section stained by the gram method showed topographically the massive encrus-

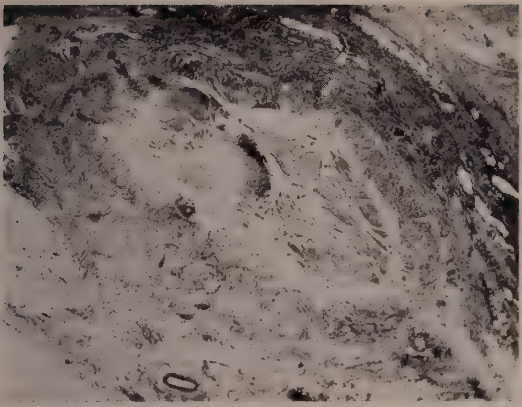

FIGURE 7. Appendix. The mucosa is ulcerated and sloughed into the lumen which is filled with necrotic debris. All layers of the wall reveal subacute inflammation (hematoxylin and eosin stain).

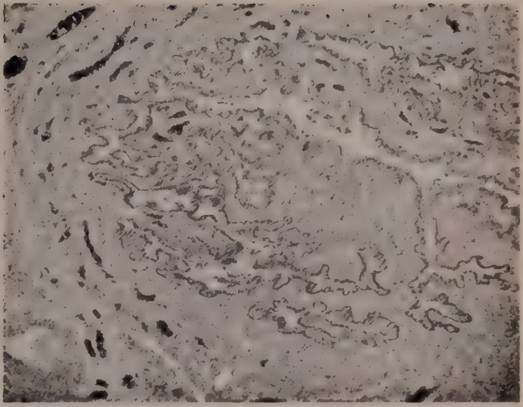

FIGURE 8. Isthmus of fallopian tube. Mucosal folds are clubbed and fused. There is inflammatory exudate in the lumen and in all layers of the wall (hematoxylin and eosin stain, ×20).

tation of these membranes by bacteria. Colonies of gram-positive coccoid organisms mixed with huge groups of gram-negative bacilli could be seen.

Sections of the lungs of the fetus showed that the baby already had an intrauterine pneumonia characterized by groups of alveoli filled with purulent exudate.

Dr. Furey described a remarkably significant finding in the autopsy protocol of the mother. When the pelvic organs were examined, he observed a periappendiceal abscess. The appendix was plastered up against the right tube and ovary, which were inflamed. Figure 7 shows a section of what remained of the appendix. The lumen was filled with necrotic debris. All layers of the wall were infiltrated by inflammatory cells, which were predominantly lymphocytes and monocytes but included granulocytes as well.

A section of the right ovary showed hemorrhage and diffuse inflammation. The fimbriated end of the right fallopian tube was involved in an extensive inflammatory reaction. Figure 8 shows the isthmic portion of the tube. Not only are the mucosal folds clubbed and edematous and filled with inflammatory cells, but in the muscular coats as well there is a diffuse inflammatory process. There are decidual abscesses. There is also diffuse myometritis. We believe the pathway for the infection of this pregnant uterus was clearly through the tube from a contiguous appendiceal abscess.

A microscopic section of the kidney showed findings which recapitulated those seen in the previous case. The capillaries in almost every glomerulus were filled with thrombi, which again in trichrome and PTAH preparations had the characteristic reaction of fibrin. In the lungs were fibrin thrombi in vessels of varying sizes. In the PTAH-stained section they were shown somewhat more effectively.

An interesting finding in a random section of the myocardium was a perivascular focus of necrosis and hemorrhage. There was a zone of necrosis which was infiltrated with mononuclear cells, and a little hemorrhage was alongside it.

The adrenals were of considerable interest. On gross examination they looked as if they were diffusely congested. Actually, they were peppered with hemorrhages. If one looks at sections under a little higher magnification, the explanation for the hemorrhages is obvious. Practically all of the sinusoids are plugged with fibrin thrombi (Fig. 9).

Bacteriologic findings. Before the death of this patient several blood cultures revealed color bacilli. Direct smears revealed gram-negative rods in the vaginal discharge. These were identified on culture as colon bacilli. In the postmortem material we were able to demonstrate in suitably stained sec-

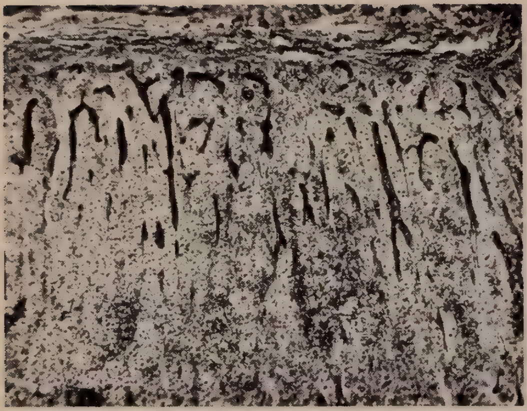

FIGURE 9. Adrenal gland. The sinusoids in the zona glomerulosa and fasciculata are occluded by fibrin thrombi. There are many fresh cortical hemorrhages (phosphotungstic acid and hematoxylin stain, ×50).

tions the presence of colon bacilli in practically all her organs.

The pathologic findings in these 2 tragic maternal deaths are identical with, or closely resemble, the lesions which are seen in experimental animals, rabbits in particular, with the generalized Shwartzman phenomenon. I think that what we have demonstrated to you are 2 cases of maternal death associated with anatomic evidence of endotoxin shock and a generalized Shwartzman phenomenon.

Dr. Rosenthal: The discussion will be opened by Donald G. McKay, M.D.

Discussion

Donald G. McKay, M.D.: These cases that Dr. Berkman has shown you are classic examples of what one may see in maternal deaths in 1961. It is very interesting that obstetrics in the past ten to twenty years has been amazingly successful in reducing maternal mortality to a very small death rate. In just those short years, it has been reduced from a level of about 3 per cent to less than 1 per cent, and we are left now with a residuum of unusual or at least unexpected types of deaths. These deaths, I think, illustrate very well the fact that patients, as human beings, are heir to the generalized Shwartzman reaction.

It's my belief that this reaction has more significance to obstetrics than just those cases in which bacterial endotoxin is known or is likely to have been circulating in the patient's blood. I would like to illustrate this breadth of application by showing you the pathologic background of certain other disease processes in which, I think you will agree, the nature of the disease is very much the same as that which Dr. Berkman has shown you. From this we may, by using the experimental model in animals and by studying the known circumstances of bacterial endotoxin in the circulating blood of human patients, derive a great deal of information in terms of mechanisms with respect to other disease processes.

There is a wide variety of disease processes which exhibit this pathologic process: First, and perhaps most intriguingly, is eclampsia; second, the premature separation of the normally implanted placenta; and third, bacterial infections, whether in terms of abortion in the early part of pregnancy or in terms of the premature rupture of the membranes with marked chorioamnionitis.

There may be other syndromes which are associated with this pathologic process, but these are the outstanding ones, as those of you who practice obstetrics will recognize. Among these types of disease processes are those about which the obstetrician has said for years that there is a degree of shock which is all out of proportion to the patient's loss of blood, and these patients when they are in this condition of shock, look a little bit like "death warmed over."

Pathologic changes. I would like to discuss now the pathologic changes which occur in these patients. I'm going to try to show you a composite picture, not of one disease syndrome, but of all of them as exemplified by individual cases.

The first example of this process is a patient who had multiple fits and who had eclampsia. She had the picture of the classic eclamptic liver. This was characterized by foci of hemorrhage and necrosis, which were visible in the capsule of the liver, but if we had taken a deeper cut we would have seen them down in the substance of the liver also.

The uterus in the patient who has had this condition contains a marked diffusion of blood in focal areas which, if it were to extend through the myometrium, you would say was a Couvelaire uterus. There are hemorrhages and areas of necrosis in the uterine muscle.

The lungs in such a situation contain petechial hemorrhages and a few ecchymoses on the surface. These are characteristic of peritoneal, pleural, and epicardial surfaces in patients with this disease process.

The brain in such a patient contains a diffuse subarachnoid hemorrhage which is not large in volume, but which is extensive in its localization, all over the cerebral cortex. The source of this hemorrhage is in the pons and in the midbrain. Cerebral hemorrhage occurs in about 10 to 15 per cent of these patients.

A section of the kidneys of a patient who died not of eclampsia but of profound shock and renal failure following premature separation of a normally implanted placenta shows bilateral renal cortical necrosis.

Such are the gross findings in these cases. We should mention that not every patient who dies shows this pathologic picture. Some may show no pathologic change whatsoever; others will show a variety and a mixture of pathologic changes that are analogous to these.

Etiology. After having seen the gross alterations, our next question is: What can be causing this kind of pathologic process? We must turn to the microscopic view to determine the cause of these changes.

In a liver from one of these patients, and it could have been from any one of these disease processes, may be seen the hepatic arterioles occluded by the black masses which, as Dr. Berkman has said, are composed of fibrin. These, by obstructing the flow of blood to the peripheral portion of the lobule, will produce a hemorrhage and an area of necrosis in the periphery of the lobule of the liver.

Another example can be seen in the hepatic arteriole occluded by fibrin and the fibrin expanding out into the periportal region causing dilatation of the sinuses and necrosis of the liver cells.

We observed a kidney of a patient who died with toxemia and with a hydatidiform mole. This is an unusual combination, but this patient died in acute shock with a massive loss of blood. Here we found every glomerulus occluded by the masses of fibrin which obstructed the flow of blood into the glomerular capillaries.

The adrenal also participates in this reaction. One adrenal that we observed showed that the occlusive masses may obstruct the lumens of the vessels and produce hemorrhage and necrosis, or they may coat the wall of these small blood vessels, leaving the red cells visible inside. Other areas of the body are involved. For example, the choroid plexus may show multiple capillary fibrin thrombi. One patient had recovered from damage to her pituitary by about seven days. The thrombi were dissolved by a process of proteolytic digestion.

The end result of this process, a fibrosis and almost total destruction of the pituitary, was noted in such a patient who had survived for one year so that the disease, Simmonds' disease, may be the end result of this process.

The posterior lobe of the pituitary also was involved in this case. One may see patients with diabetes insipidus as well as anterior lobe insufficiency following one of these catastrophic events.

Various regions of the brain may be involved, for example, the tuber cinereum with thrombi and foci of necrosis. One may see an involvement of the paraventricular and supra-optic nuclei.

In these disease processes we have an example of a disseminated intravascular coagulation. There have been many demonstrations that this material is fibrin, both by electron microscopy and by the use of fluorescent antibodies, which demonstrate this in a very clear fashion.

Having demonstrated by microscopy that there is intravascular clotting, the question arises: What is the cause of this disseminated clotting episode? In the case of a bacterial endotoxin, I think it is very easy to see why these patients have disseminated fibrin masses because, if we look at the effects of endotoxins in experimental animals, we will see the following results. Usually this requires the injection of two separate doses of a bacterial endotoxin, somewhere between six and seventy-two hours apart, into the animal's vein. As little as 0.2 mg. of the endotoxin will do the trick. In nonpregnant animals, with two spaced doses, in about 60 per cent of the cases we end up with kidneys that contain, for all intents and purposes, bilateral cortical necrosis as we see it in the human being. And, if we look at the kidneys of these animals before the bilateral cortical necrosis becomes obvious, we see that each glomerulus is filled with fibrin.

If we look in other regions of the body, we will find that there are fibrin masses. They are found in the lungs, in the spleen, and in the liver. Therefore, in the experimental animal, an endotoxin produces a process of disseminated intravascular clotting.

Now, having seen in experimental animals the effects of bacterial endotoxin, and having compared them with the cases in human beings, it becomes quite clear that these patients are sharing this reaction. I also would like to suggest that this is not confined to patients who have bacterial infections with gram-negative organisms, but it occurs in other disease processes as well. This offers us a lead as to the pathogenesis and a method of study of the basic mechanisms in these other disease processes, such as the premature separation of the placenta and eclampsia.

Dr. Rosenthal: Thank you, Dr. McKay. Our next discussor is Benjamin W. Zweifach, Ph.D., who has contributed much to our knowledge of the physiology of microcirculation and shock and is an authority in this field.

Benjamin W. Zweifach, Ph.D.: I thought that it might be useful to discuss what we know about bacterial endotoxemia as an entity, and what we know about shock as an entity, and whether the two actually can be combined into a meaningful term, such as "endotoxic shock."

There has been a tendency in the literature, certainly in experimental work, to consider that patients who die for no obvious reason can be lumped conveniently into one basket which we call "shock"; as if to say that all roads lead to Rome and that most people die because of a failure of the circulation which apparently is not myocardial and is not central in origin, but is a form of peripheral failure.

From this point of view, the 2 patients who were discussed here died in shock. Obviously, since they had an associated bacteremia, the term "bacteremic shock" can be applied.

I'd like to review a number of concepts of circulatory failure and then see whether or not I can pull this together with some experimental indications of what the basic elements of shock are and what role bacteremia and endotoxemia may play in shock.

Perhaps the one important aspect of shock which is still unresolved is the fact that, as time progresses and the shock syndrome persists, an irreversible trend develops. The condition becomes increasingly difficult to treat by any known therapeutic management, and indeed this is why the term "irreversible" was coined. The precise cause of this syndrome has been rather controversial. No one seems to be able to place his finger on the sequelae leading to the irreversible trend.

Not too many years ago, information was provided by Fine and his coworkers[1, 2] that the normal trend towards an irreversible outcome in shock could be circumvented by simply introducing antibiotics into the picture. Animals were given antibiotics orally and then subjected to what should have been a lethal shock situation. Most of the animals survived.

This interesting observation led to a great deal of experimentation. Eventually Fine was able to show that he could procure from the blood of animals which were in irreversible hemorrhagic shock a material which, on analysis, seemed to have all the characteristics of bacterial endotoxins. When he carried out the same procedure in animals which had been pretreated with antibiotics, the toxic symptoms and the toxic circulating agent could not be demonstrated.

Several interesting facts in this regard can be assessed in the light of other information. A large body of experimental evidence seemingly does not support a bacteremic concept of shock. Many forms of shock progress to a lethal outcome in the face of antibacterial treatment. Recent experiments were conducted with animals raised in a germ- or bacteria-free environment. Irreversible shock can be induced in such animals by procedures which are identical in every way with the procedures used in normal conventional animals. Germfree animals seemingly develop all the pathologic symptoms of shock.

One can then bring to bear a number of other explanations for the disturbances occurring in shock, other than those attributable to bacterial endotoxemia per se.

The hypothesis advanced by Fine, as might be indicated by the fact that oral antibiotic treatment seems to prevent the development of shock, supposes that the entrance of the bacterial invaders into the systemic circulation is by way of the small intestine. Primarily what was believed to occur in shock was that the circulation through the bowel is reduced to the point where an overgrowth of gram-negative anaerobic forms is favored. In addition, the attrition resulting from the reduced blood flow to the intestinal tract breaks down the normal barrier between the blood stream and the intestinal lumen. Hence the invasion of the bacterial products from the bowel into the circulation is facilitated. In addition, the shocked animal (this is true of shocked patients as well) becomes inordinately susceptible to bacterial agents. For example, an animal which normally would require, let us say arbitrarily, about 100 micrograms of a particular endotoxin to produce a lethal outcome, after a short exposure to hypotension will now react to as small a dose as 1 microgram; in other words, a 100-fold increase in susceptibility.

FACTORS INCREASING SUSCEPTIBILITY. Thus, one of the key questions to be answered here is, what are the factors responsible for this increased susceptibility? In this regard two factors should be brought to your attention. In the patients under discussion here there seemed to be an associated pathologic condition of the liver. There is good evidence that part and parcel of the attrition that developed during the shock syndrome was a breakdown of an important component of our bacterial defense mechanisms, the so-called reticuloendothelial (R.E.) system. A major portion of this mechanism resides in the liver, namely, in the Kupffer elements. One can demonstrate in association with shock a breakdown in the capacity of this system to handle bacteria and to clear colloids from the circulation. One also can demonstrate by histologic inspection the degenerative changes in the Kupffer cells. Foci of inflammatory reactions appear in the vicinity of the Kupffer cells following protracted shock. Therefore what we may have in patients in shock is a general impairment of the bacterial defense mechanisms primarily because of a general impairment of the R.E. system.

Interestingly enough, we have come to look on the R.E. system as primarily a bastion for the clearance of bacteria. There is, however, a good deal of evidence that the R.E. system participates in a wide variety of physiologic reactions. The behavior of the R.E. system can be interfered with by a number of processes other than infection. For example, it is possible to introduce colloids into the circulation to a point where the R.E. system avidly takes up the colloids and then develops what is referred to as an R.E. blockade or insufficiency. Such animals not only show an incapacity to clear the blood stream of colloids or infectious agents, but also a variety of changes in the blood coagulation mechanisms and in circulating enzymes. In some way, interference with the R.E. system interferes with the hemostatic mechanism of the body. The possibility then exists that damage to the R.E. system is associated, indirectly perhaps or directly in some situations, with interference with some factor other than the clearance or removal of endotoxic material from the blood stream.

There is a good deal of evidence in the scientific literature that one can increase the capacity to withstand shock by producing an opposite effect on the R.E. system, namely, by stimulating it. The repeated exposure of the R.E. system to sublethal amounts of trauma or to sublethal amounts of bacterial endotoxins, or to small amounts of any colloid results in the repeated uptake of these materials by the R.E. system, and a stimulation or a state of hypertrophy develops.

These animals develop a resistance to shock. In fact, they can become resistant not only to shock, but also to bacterial endotoxemia. One of the methods by which animals can be made resistant to shock is to expose them repeatedly to small doses of bacterial endotoxins.

Interestingly enough, all of these forms of adaptation or resistance to shock can be circumvented by interfering with the R.E.

system. If, at a stage of the experiment where resistance has been engendered, one introduces a seemingly harmless agent, such as a denatured colloid, and causes the R.E. system to take up the colloid so as to block the R.E. system, the animal will lose completely his resistance to shock. It is therefore evident that resistance to shock in some way depends on the status of the R.E. system.

INTERPRETATION. Now what does this experiment mean, in terms of the particular patients that we have under consideration? These patients seem to die of an endotoxemia, and obviously endotoxemia can result in shock. Acutely lethal doses of a bacterial endotoxin leave in their wake very little in the way of a definitive pathologic condition. The pathologic condition is just as indefinite as it is in most cases of shock. A pathologist examining the organs of animals that have been subjected to hemorrhagic shock finds very little objective evidence, aside from the usual sequelae, of a reduced circulation in various organs.

To produce the type of pathologic condition seen in the patients under discussion, principally the bilateral cortical necrosis of the kidneys and fibrin deposits within the vascular system of the organism, one must in some way sensitize the patient or the animal. Experimentally, we have to give the animal two doses of bacterial endotoxin. After a dose is given on day 1, a period of about eighteen hours must elapse before we can elicit successfully a reaction of this kind with a second dose of endotoxin.

In most instances, the animal does not die of the reaction to the endotoxin. It develops bilateral cortical necrosis and usually dies several days later of renal insufficiency. In the reaction under consideration we have an acutely lethal situation, so that we have to assume that pregnancy, or some antecedent reaction associated with this particular set of patients, in some way sensitized the patients to a single exposure of bacterial endotoxin.

One means by which patients can be sensitized is by exposing them repeatedly to endotoxins in small amounts; another would be to interfere with some component of their defense apparatus, such as their R.E. system; in other words, to blockade, as it were, the R.E. system so that one dose of bacterial endotoxins produces a widespread reaction which terminates in this type of bilateral cortical necrosis.

Unfortunately, we do not know what actually prepares an individual for this reaction. When two doses are given, what does the first dose do to prepare for the second dose? We know that changes occur in what has been called the heparin precipitable component of the blood, although this situation has more or less returned to normal by the time the second dose of endotoxin is given.

There is some evidence that pregnant animals are more susceptible to bacterial endotoxins to the extent that they act like prepared animals. A single overwhelming dose, particularly late in pregnancy, toward the third trimester, can result in the formation of fibrinoid material and its deposition within certain loci, such as the spleen, the liver, and the kidneys. We must confess that no one has studied extensively the background of the pregnant animal so as to be able to define what causes a single dose of bacterial endotoxin to result in a generalized Shwartzman reaction.

Several aspects of the shock syndrome have been developed. The clinical entity which we recognize as shock is not associated with the generalized Shwartzman reaction. Certain predisposing agencies, such as the blockade of the R.E. system with a substance such as Thorotrast, a toxic colloid which is taken up by the R.E. system and which damages the R.E. system, predispose animals so that a single dose of an endotoxin gives rise to a Shwartzman-like reaction. Previous exposure to a sublethal shocklike episode also predisposes to endotoxemia, again seemingly in part because of an effect on the R.E. system.

It is not clear by which mechanism endotoxins alter the coagulation system and give rise to the deposition of fibrinoid. We know that in some way the leukocyte system is involved. The factors associated with fibrinogen and hypofibrinogenemia may be associated with this reaction, but these are only vaguely understood. Any situation associated with bilateral cortical necrosis should be suspected as involving endotoxemia, since this seems to be the sine qua non of the generalized Shwartzman reaction.

In 1 of the 2 patients who were brought to your attention, there was no evidence of gram-negative organisms. The term endotoxin has been used to describe the somatic antigen of gram-negative forms. There is no real evidence that gram-positive organisms have a similar lipopolysaccharide component which could be responsible for this type of reaction. Some consideration should be given to the possibility that tissues may contain polysaccharide components which can combine with lipid or with protein to produce a toxic reaction which is similar to that resulting from bacterial endotoxins.

I bring this to your attention because we cannot explain satisfactorily many of the reactions which occur in animals raised under germfree conditions. Shock develops essentially in the same way in germfree animals despite the absence of bacteria or bacterial products. Hence, we cannot rule out the possibility that under certain circumstances tissue components may be the factors involved in the ensuing collapse of the circulation.

There is no well-defined procedure for treating endotoxic shock. The only definitive therapy that has had any success experimentally has been the use of corticosteroids. Other agents, such as levarterenol bitartrate and adrenergic blocking drugs, have been ineffective.

The fact that bacterial endotoxemia is associated with an alteration in the catecholamine activity should make one hesitant about using large doses of levarterenol bitartrate in a situation where endotoxemia is suspected, even though levarterenol bitartrate may seemingly and heroically raise the blood pressure. Tissue damage may be associated with high levels of catecholamines in the presence of endotoxin; in particular, renal shutdown may occur. This type of therapy should be examined carefully before one utilizes it in such patients.

Dr. Rosenthal: Thank you Dr. Zweifach. The third discussor has a difficult assignment. While Dr. Zweifach touched briefly on therapy, it is the specific task of Edward W. Hook, M.D., to discuss the management of bacteremic shock. Dr. Hook, I wonder if you would be so kind as to include prophylaxis in your discussion of therapy. I have in mind the problem of the premature rupture of the membranes followed by a minor febrile reaction. Would you, for example, give antibiotic therapy to such a woman prior to the onset of labor, or during labor? In some clinics the teaching has been to withhold chemotherapy from such patients. Dr. Hook.

Edward W. Hook, M.D.: Dr. Zweifach summarized my comments in his introductory remarks when he said that the therapy of bacteremic shock was difficult and that its present status was unsatisfactory.

A variety of microbial agents may produce overwhelming infection that leads to vascular collapse.[3] The most common cause of this syndrome is infection with one of the enteric gram-negative bacilli, such as Escherichia coli, Aerobacter aerogenes, Proteus species, or Pseudomonas. However, vascular collapse also may occur occasionally during the course of certain other bacterial, viral, or fungal infections; for example, shock may complicate staphylococcal or pneumococcal bacteremia and has been described in Candida albicans septicemia. Although my remarks are concerned primarily with the therapy of vascular collapse secondary to infection with one of the gram-negative enteric bacilli, at least certain of these comments apply equally well to shock associated with infections caused by other microbial agents.

It has become increasingly clear that the vascular damage observed during the course of infection with gram-negative bacteria is related to the lipopolysaccharide endotoxins elaborated by these organisms.[4–6] Certain of the complex mechanisms where endotoxins damage the blood vascular system and disturb hemodynamic function have been mentioned previously by Dr. McKay and Dr. Zweifach. Despite this vast amount of data pertaining to the mechanisms of the biologic effects of endotoxins, the pathogenesis of bacteremic shock is still unclear. It is reasonable to believe that the further elucidation of the mechanisms of the damaging effects of endotoxins in man will serve as a basis of a more rational pharmacologic approach to therapy.

The therapy of shock due to infection with gram-negative bacilli can be divided into three components: (1) the control of infection, (2) the correction of the hemodynamic disturbance, and (3) attempts to block certain of the biologic effects of endotoxins and prevent additional damage, especially vascular damage.

CONTROL OF INFECTION. In the patient suspected of having bacteremia with a gram-negative bacillus, antimicrobial therapy must be initiated at the earliest possible moment. Blood cultures always should be obtained and, if indicated, other body secretions or excretions should be cultured. However, antimicrobial therapy should be started immediately, before the results of the bacteriologic studies are available.

As is well known, a large proportion of enteric gram-negative bacilli are resistant to the commonly-used antimicrobial drugs.[7] Even within one species there is striking variability in the susceptibility to antibiotics from one strain to another. Since antimicrobial therapy must be initiated prior to a bacteriologic diagnosis, and since no single drug can be relied on to provide effective antimicrobial coverage against the gram-negative bacilli most often responsible for bacteremia, an attempt should be made to provide "broad" coverage by using more than one drug. The use of multiple drugs in the treatment of an infection which would respond just as well to a single drug is to be deplored, but in this particular situation, the presumptive diagnosis of bacteremia with gram-negative enteric bacilli, multiple drug therapy is the only rational approach at the present time. It is our practice to use at least two and frequently three antimicrobial drugs. Chloramphenicol is given intramuscularly in a dose of 3 Gm. per day, most often in combination with streptomycin, 0.5 Gm. intramuscularly every six hours. In addition, penicillin is frequently added in doses of 20 million units by a continuous intravenous infusion each twenty-four hours. At this dosage level one can get concentrations of penicillin into the blood stream which will inhibit the multiplication of the majority of strains of Proteus mirabilis, the most common Proteus species, as well as a number of other gram-negative bacilli.[8] Tetracycline is given occasionally instead of chloramphenicol, but we feel that chloramphenicol provides somewhat broader antimicrobial coverage than tetracycline.[7] If renal insufficiency is present, streptomycin is either discontinued or the dose is reduced after the first twenty-four-hour period. Kanamycin sulfate may be given instead of streptomycin, but the relatively greater ototoxicity and nephrotoxicity of this drug are important deterrents.

When the bacteriologic diagnosis has been established and the results of sensitivity tests are available, the therapeutic regimen is modified accordingly.

It has been shown that the combined use of an antibiotic and gamma globulin in the treatment of certain experimental infections gives a higher survival rate than when either agent is used alone. There are also a few observations which purport to show a beneficial effect of combined gamma globulin and antibiotic therapy in the management of patients with refractory or overwhelming infections.[9] These results are uncontrolled, unimpressive, and unconvincing and do not constitute sufficient justification for the use of gamma globulin in patients with severe or overwhelming infection unless hypogammaglobulinemia is present.

THE CORRECTION OF THE HEMODYNAMIC DISTURBANCE. The present evidence suggests that there is usually no critical reduction of the blood volume during the early stages of uncomplicated bacteremic shock, and an infusion of blood or plasma is rarely sufficient to correct the hemodynamic disturbance.[1,3] However, the blood pressure often is restored to normal levels after the administration of a vasopressor drug, such as norepinephrine or metaraminol bitartrate. In a previously normotensive individual whose systolic blood pressure ranges below 85 mm. of mercury, norepinephrine is infused intravenously at a rate sufficient to maintain the systolic pressure at 100 to 110 mm. of mercury.

Certain investigators have indicated a preference for metaraminol bitartrate instead of norepinephrine.[3] It is true that metaraminol bitartrate can be given subcutaneously or intramuscularly, and its administration probably requires less nursing supervision than the administration of norepinephrine. However, it is less potent than norepinephrine, and in our hands it is less effective in sustaining the blood pressure at satisfactory levels.

Although vasopressor agents may restore the blood pressure to normal levels, their precise value in the therapy of bacteremic shock is unknown. I agree with Dr. Zweifach that the use of vasoconstrictors in this situation represents an interesting paradox, and it is important for us to remain alert to the possibility that additional vascular damage may be induced by these agents. Lillehei and MacLean[10] have shown that the administration of norepinephrine simultaneously with endotoxin enhances the lethality of endotoxin for dogs. It also has been demonstrated by Thomas[11] that bacterial endotoxin "sensitizes" the blood vessels to the action of epinephrine or norepinephrine. For example, if a small dose of epinephrine which produces only transient blanching of the skin of a normal rabbit is given into the skin of a rabbit that has been pretreated with bacterial endotoxin, extensive vascular damage and hemorrhagic necrosis develop at the site of the injection. It is also of interest that Greisman and his coworkers[12] recently have presented preliminary evidence that human volunteers with experimentally induced typhoid fever hyper-react to the vasopressor effects of norepinephrine, not only during the active phase of the disease, but also during convalescence. Additional observations are needed to define the role of vasopressors in the patient with bacteremic shock.

ATTEMPTS TO PREVENT ADDITIONAL DAMAGE BY ENDOTOXIN. The question of therapy with anti-inflammatory corticosteroids frequently comes up when we are considering the management of patients with bacteremic shock. It is true that under certain well-defined conditions, adrenal cortical hormones have been found to be effective against the lethal action of endotoxin in animals.[4] Evidence also has been presented that the dose of the vasopressor agent necessary to sustain the blood pressure in experimentally-induced endotoxin shock is considerably less in hydrocortisone-pretreated animals than in control animals.[3] Despite these observations in animals, there is certainly no definitive evidence that corticosteroids exert a beneficial effect on the course of bacteremia caused by the enteric gram-negative bacilli in man, with the exception of typhoid and paratyphoid fever. The literature contains both favorable and unfavorable impressions relating to the effects of adrenal corticosteroids in clinical infections due to endotoxin-containing bacteria. For example, Kass[13] appears to be doubtful that there is any benefit to be gained by the use of these agents, whereas Spink[3] appears to be convinced that corticosteroids have a definite value in the therapy of bacteremic shock. Spink recommends large doses of these agents, equivalent to 300 to 500 mg. of hydrocortisone immediately, and then 500 to 1,000 mg. daily thereafter for from three to five days.

As far as our own practice is concerned, we have used the anti-inflammatory corticosteroids intermittently and have not been aware of any advantages attributable to their use. Marshall[14] and his associates on the urology service at the New York Hospital have attempted to evaluate their results with corticosteroid therapy in gram-negative bacteremia and have found that the mortality rate was just as high in the steroid-treated group as in the group that did not receive steroids.

A potential disadvantage of the anti-inflammatory corticosteroids resides in the capacity of these agents to enhance bacterial infection. The enhancing action is not apparent if the steroids are administered with an antibiotic to which the infecting organism is sensitive. However, an obvious potential danger is that antimicrobial therapy might be ineffective, thereby permitting the infection-enhancing effect of steroids to proceed unimpeded.

There has been a recent flurry of activity about the possible beneficial effects of hypothermia in the management of patients with gram-negative bacteremia. Cockett and Goodwin[15] described a series of 12 patients with gram-negative bacteremia and shock who had been treated with hypothermia in addition to antimicrobials, vasopressor agents, and anti-inflammatory corticosteroids. The results of this study were extremely impressive in that 11 of the 12 patients treated with hypothermia survived. It is unfortunate that the authors did not give more detailed information on the nature and severity of the illness in each individual patient, since the mortality rate is strikingly influenced by the degree and duration of shock, age, underlying disease, and so forth. Marshall[14] has used hypothermia in 2 patients with gram-negative bacteremia and shock, and both patients died. In my opinion the observations relating to the use of hypothermia are provocative and interesting and call for additional studies. My reaction at present is a conservative one.

There are a number of additional agents which have been shown to exert a protective effect against the lethal action of bacterial endotoxins in animals.[4,5] For example, antihistaminics, adrenolytic agents, and serotonin antagonists have been shown to exert a beneficial effect under well-defined experimental conditions. As far as I know none of these compounds has been shown to be of any value in the treatment of endotoxemia in man.

In summary, the therapy of shock related to an infection with enteric gram-negative bacilli is quite unsatisfactory. The mortality rate at excellent hospitals all over the country still exceeds 50 per cent. Intelligently planned antimicrobial therapy obviously is an important aspect of the management of these patients. Current clinical practice approves the use of vasopressor agents to combat hypotension, but the ultimate value of these drugs is unknown. The use of anti-inflammatory corticosteroids is controversial and certainly of no striking benefit as it is currently employed. Hypothermia has been proposed as an additional measure, and this requires further study. There is no evidence that gamma globulin, adrenolytic agents, serotonin antagonists, or any other agents which protect against experimental infection or intoxication alter the course of the naturally-occurring disease in man. I've avoided any comment about surgical therapy, and I hope that Dr. Rosenthal will have something to say about that.

DR. ROSENTHAL: Thank you, Dr. Hook. Now this brings to a close the formal program for the evening.

Up until now, I have avoided pointedly the possible role of the surgical management of these cases. I have reserved this task for a close colleague of mine. He has had the advantage for many years of being at the Kings County Hospital, a large city hospital where these cases occur with greater frequency than in a hospital such as ours. I introduce to you now J. Edward Hall, M.D.

Surgical management

J. EDWARD HALL, M.D.: It has been asked whether or not there should be a surgical treatment of the entity of bacteremic shock in obstetrics. In an effort to answer this question I would like to present a few statistics illustrating our experience at the Kings County Hospital. Bacteremic shock is associated most frequently with abortions in obstetrics, and our experience is limited to this combination.

About 1,400 abortions are seen each year at the Kings County Hospital. Some of the complications are transitory shock, septic shock, and acute renal failure. These three complications are the most serious, particularly acute renal failure. Our death rate is 1.3 per 1,000 abortions. This is a low rate when it is realized that the number of septic cases is large, 12 to 15 per cent. Seven of the 15 deaths we encountered were caused by renal failure. It is of interest that 10 of the 13 cases of acute renal failure, or 77 per cent, died.

In 5 cases of septic shock no deaths occurred.

We have not done any major surgical procedures, such as hysterectomy. We do not believe that the low death rate of 1.3 per 1,000 abortions would be improved, in most cases, by hysterectomy. However, these cases are few, and those selected for surgical intervention should have this done only after great consideration. These patients are desperately ill, and a major procedure may be fatal.

Our big problem is acute renal failure, and those who have died have not shown the generalized Shwartzman reaction, as was the case in the patients presented here.

We are aware of the difference of opinion about the use of catecholamines. However, it has been our experience that those patients who have been treated with catecholamines and whose blood pressures were maintained, were the ones who survived. Therefore, I would agree with Dr. Hook that these substances may have a beneficial effect.

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Scientific Program

Any State Society member who wishes to present a paper before a scientific section or a general session is requested to write to Bernard J. Pisani, M.D., Chairman, Convention Committee, 170 West 12th Street, New York 11, New York, before November 1, 1962. A short abstract of the proposed presentation should accompany the letter.

Endoscopy of the Major Bile Ducts

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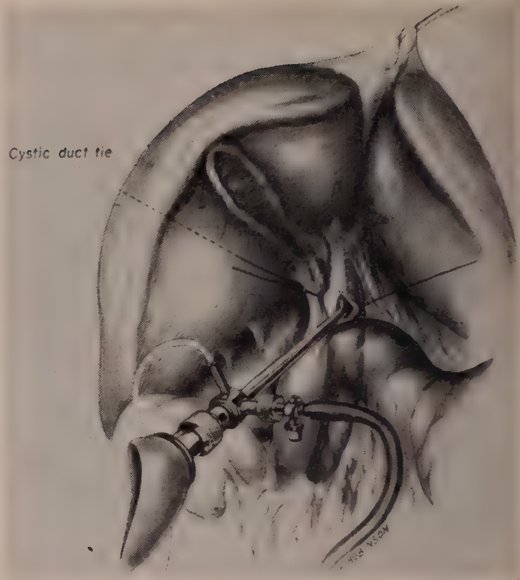

FIGURE 1. Choledochoscope is in common bile duct with lens directed into vestibule, marking bifurcation of common hepatic duct. Side arms are for battery cord and irrigation fluid. Rubber eye socket acts as light shield for operator. Left traction suture is not necessary.

THE CHOLEDOCHOSCOPE employed in the present study was introduced by Wildegans in 1953.[1]* The earliest American description of successful endoscopic visualization of the interior of the common bile duct was reported by McIver in 1941.[2] His instrument was a right-angled observation telescope 45 cm. in length and 1 cm. in width, incorporating an irrigating system in its shaft. McIver's paper included a photograph of an autopsy specimen in which a stone had been placed in the duct. There is, however, no detailed clinical experience, and we have been unable to find a follow-up publication.

Visualization of the interior of the biliary system had been attempted previously by cystoscopic instrumentation of the interior of the gallbladder through a cholecystostomy fistula. Babcock reported such an experience briefly in 1937[3] using a cystoscope or urethroscope. Bartlett stated in 1937[4] that he had used this method of visualization of the gallbladder lumen since 1930; he delayed such observations until six weeks after cholecystostomy. Hollenberg, Eikner, and Springs[5] reported their experience in 1937; they "cystoscoped" the gallbladder as a bedside procedure at the time of the removal of the cholecystostomy tube and were able to extract residual calculi from the lumen of the gallbladder and the first part of the cystic duct. In 1947 Laubersheimer[6] reported a ten-year experience with 30 cases of cholecystic endoscopy performed with a McCarthy foroblique panendoscope or resectoscope. He preferred to defer observation until the fourteenth postoperative day and reported an inability to catheterize the common duct by way of the cystic duct. DeWeese[7] used cholecystoscopy in 6 cases and advocated this as a method of removing residual calculi that might predispose the ducts to fistula or sinus formation following cholecystostomy.

A truly satisfactory visualization of the biliary tract was not achieved until Wildegans developed the choledochoscope.[8]* In his monograph Wildegans reported its use in Europe by numerous surgeons, in-

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Presented before the New York Surgical Society, New York City, January 11, 1961.

* Available from Sass-Wolf and Co., Ritterstrasse 12–14, Berlin S.W. 61, West Germany.

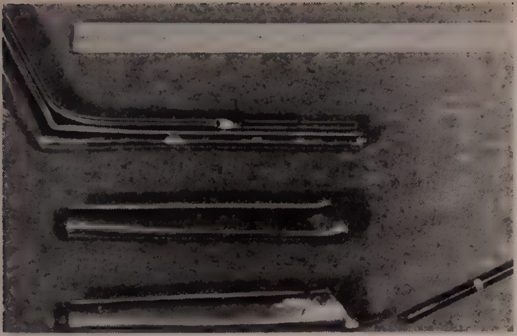

FIGURE 2. Upper figure shows central position of irrigating aperture in relation to butt end which contains bulb and lens. Number 18 shield is used to cover two shafts. Lower figure is that of modified shield which incorporates whip and follower.

cluding Griessman, Fischer, Reimes, Guderley, Lordat-Jacob, Richards, Rathke, and Brocks; no pertinent publications have appeared from this country.[9] Actual experience with this instrument was obtained by one of us (C.J.S.) at Wildegans' clinic in July, 1960, prior to the initiation of the Montefiore series.

Instrument

The choledochoscope, as developed by Wildegans, consists of a head, shaft, and operating angle (Figs. 1 and 2). The head contains an ocular that may be adjusted to suit the operator's vision. The side arms are the sites of attachment for the irrigation system and the battery connection to the light bulb. The shaft is 18.5 cm. long and contains the built-in light carrier, the irrigation channel, and the lens system, so that the operator's view is along a 180-degree axis, that is, the operator looks straight ahead. Wildegans also described a choledochoscope with the same basic optical irrigation principle, containing a larger shield with a side-arm attachment for the introduction of intraductal biopsy forceps, coagulation tips, loops, and curets.[9] This operating choledochoscope can be inserted only into very large ducts and is less useful and more complicated to manage than the instrument that is intended solely for visualization. Technical details regarding the use of the observation choledochoscope are described in a separate publication.[10]

CHOLEDOCHOSCOPY *enables direct visualization of the common bile duct and of any calculi, diverticuli, tumors, and extrinsic duct compressions. It has enabled a more complete understanding of hepatic duct anatomy. Nonoperative methods of evaluation of common bile duct integrity are chemical and roentgenographic; operative methods include palpation, instrumentation, and roentgenography. Operative cholangiography and choledochoscopy complement each other, the disadvantages of one being compensated for by the potentialities of the other. Choledochoscopy is especially useful in demonstrating residual or reformed calculi and may minimize them once they are demonstrated. Motion pictures have been made of endoscopic findings.*

The use of the endoscope entails, in fact, no alteration of standard operating procedure and no elaborate apparatus or additional personnel. It is simply the addition of a visual system to the time-honored methods of probing and irrigating the common duct. There is no more hazard to its use, in competent hands, than to the introduction of the ordinary dilators and probes. It has the advantage of the simplicity that goes with looking at an object directly in good light. Its use and the benefits to be derived from it are under the direct visual control of the operating surgeon. The procedure may be carried out rapidly; visualization is usually accomplished in five minutes. Unlike cholangiography, it does not require a preoperative preparation beyond that of sterilization; as such it may be used immediately in those instances in which choledochotomy was not anticipated in the operative procedure. Its unique features are that it is the only method of demonstrating cholangitis and mucous membrane changes and of observing the action of the sphincter of Oddi directly. It is especially helpful in differentiating functional or edematous from tumor or calculus obstruction at the distal end of the duct.

This form of endoscopy, from both the

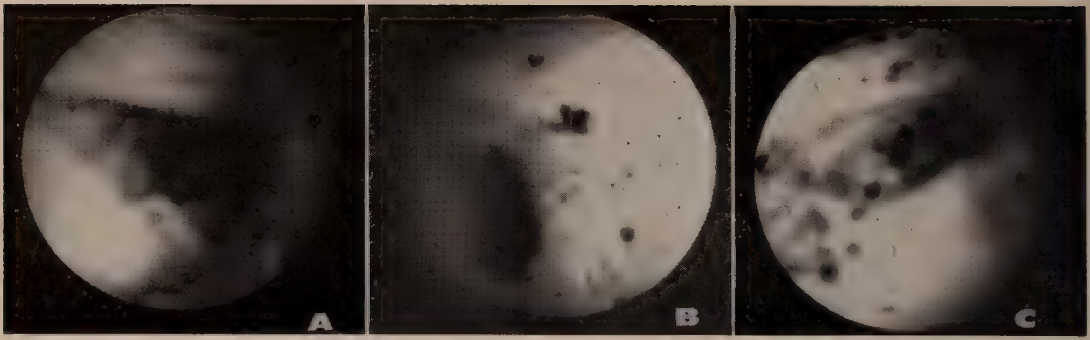

FIGURE 3. These photographs of interior of bile ducts were obtained through ordinary choledochoscope using regular light bulb (×4). All are close-ups to demonstrate details in the wall. (A) Common bile duct in midchannel, looking toward ampulla, showing tubular structure and oval glandular pits. (B) Patulous sphincter looking into void that is duodenal lumen. Small calculi and sludge are seen in lumen. (C) Numerous calculi are seen within lumen of ductal system.

manipulative and interpretive points of view, must be acquired by practice. Its limitations are determined by the experience and skill of the operator. Since calculi, diverticuli, tumors, and extrinsic duct compressions are visualized directly, the need for transduodenal exploration and the occurrence of the residual stone should be decreased significantly.

The advantages of choledochoscopy include: operator control; no contrast medium; direct differential diagnosis; observation of sphincter action; immediate availability; no excessive personnel or equipment; unlimited examinations; "live anatomy"; and the fact that it is the only way to diagnose cholangitis. The limitations of the method include the following: The technic must be acquired; choledochotomy is necessary; the duct may be too small for instrumentation; and the pancreatic duct is not visualized.

Method

The endoscope may be introduced as soon as the duct is opened. Our preference, however, is to carry out the usual investigation of the common bile duct by irrigation, palpation, probing, and dilatation of the sphincter and to perform endoscopy as a final measure, to be certain that the lumen is clear or to clarify palpable abnormalities in relation to the lumen. The general direction of the common duct is defined by the curve of the dilator that has been inserted. In most instances the angle or working end of the instrument is inserted into the duct, the shaft of the instrument being used as a handle. The operator should look while he is inserting the instrument, and not depend solely on withdrawal visualization, even though this often provides the best over-all view. A failure to observe this precaution can result in a slipping past a stone in the blind area between the duct wall and the side of the shield.

We prefer to insert the instrument proximally first, defining the carina and the lumen of the right and left hepatic ducts, and then to pass into each of these divisions. Tertiary and quartinary divisions of the ventral cranial branch are easily seen. The dorsal caudal branch is entered for about 1 cm., and one may see about 2 cm. beyond this. The choledochoscope is withdrawn to the end of the carina, and the left hepatic duct is entered for a short distance. Undescribed and unnamed minor ducts (2 to 3 mm. in diameter) are sometimes visualized in the carinal spur. The instrument is withdrawn and reinserted toward the duodenum. A funneling at the distal end of the duct indicates the approach to the ampulla. The sphincter may be seen to open and close, and the instrument is passed through the sphincter: an end point which is recognized by the changes in color and the thickness of the mucous membrane folds, from the pale reddish-yellow flat lining of the bile duct to the dense thick red mucosa of the duodenum. It is frequently necessary to angle the end of the choledochoscope to the right and anteriorly to reach the sphincter; the lumen is always visualized ahead of the instrument by rotating it slightly from side to side and dorsoventrally. Where there is much mucus or exudate, the rate of irrigation is increased. More fluid is required for irrigation on the duodenal side than on the hepatic side. The best view of the distal end of the duct is obtained on withdrawing the instrument (Fig. 3). The use of the whip and follower is a well-established principle in urology and has been used in the bile ducts by Ferris.[11] It is occasionally of great help in passing through the funnel into the duodenum.

Anatomy of hepatic ducts

The standard textbooks of surgery and anatomy give sparse descriptions of the anatomy of the hepatic ducts beyond the primary bifurcation. For the most part such descriptions either are entirely lacking or are not detailed. Comprehensive studies of the hepatic ducts have, however, been made at the University of Lund. Hjortsjo[12] studied the ducts by means of corrosion preparations and postmortem stereoscopic roentgenograms obtained after the hepatic ducts had been injected with radiopaque red dye. He published a comprehensive definitive monograph in 1951. Norman,[13] also at Lund, studied the hepatic ducts by cholangiography, with a view toward determining the frequency of intrahepatic calculi. In vivo studies correlating the endoscopic and cholangiographic anatomy are in progress in the present series and have been aided by oblique and lateral cholangiograms in addition to the conventional anteroposterior views (Fig. 4).[14]

Although there is considerable variation in the ducts of the third and fourth order, the primary and secondary divisions are fairly constant. However, these ducts vary greatly in length. The orientation considered here is that of the surgical endoscopist viewing the common bile duct in the direction of the liver.

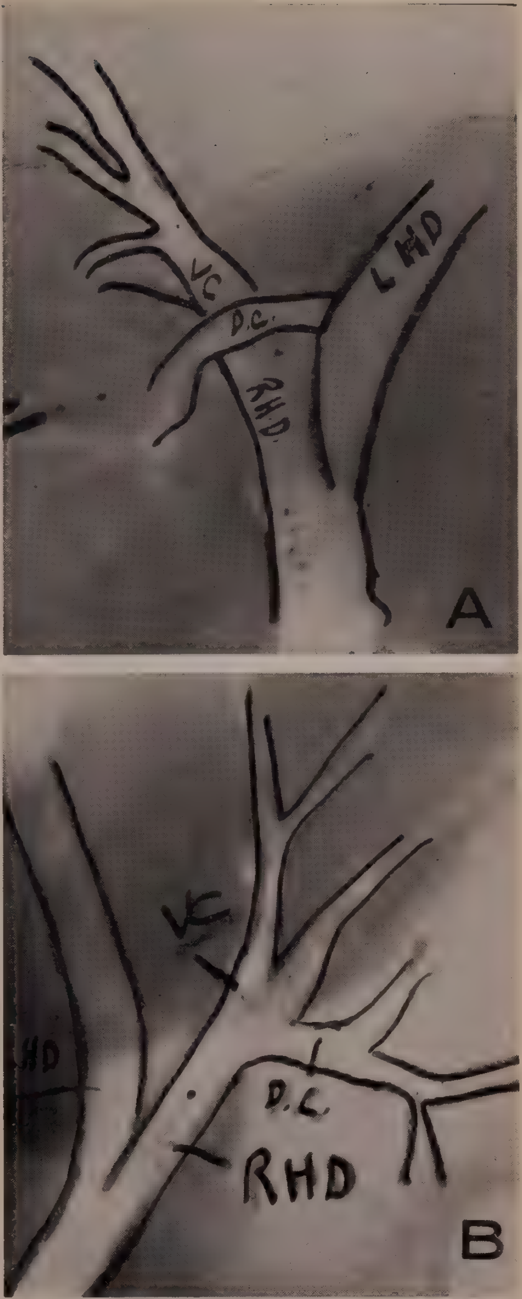

FIGURE 4. (A) Anteroposterior and (B) lateral cholangiograms indicate configuration of major ducts beyond carina. (LHD represents left hepatic duct; RHD, right hepatic duct; VC, ventrocranial division of RHD; and DC, dorsocaudal division of RHD.)

The common duct approaches a vestibule from which the right and left hepatic ducts originate. The common hepatic duct is from 2.5 to 7.5 cm. in length, depending on the site of the insertion of the cystic duct.

The single carina here is vertical. The bifurcation is immediate, with the left hepatic duct going off at a broad angle, although the angle may be acute or actually parallel. The bifurcation of the common hepatic duct is usually extrahepatic and is covered by the posterior surface of the quadrate lobe of the liver. Nuboer[15] reported that in 88 per cent of cases the junction was in the transverse fissure; in only 7 per cent was it within the hepatic parenchyma.

The extrahepatic portion of the right hepatic duct is short, while that of the left is longer. The latter frequently measures 4 to 6 cm. in its extrahepatic course. Our observations, in the presence of biliary ectasia, show the left duct to be somewhat wider than the right. It is probable that, in the presence of obstruction distally, the greater extrahepatic length of the left hepatic duct permits it to dilate earlier and to a greater degree. The left hepatic duct passes anteriorly and cranially, and its major subsequent bifurcation into dorsolateral and ventrolateral branches usually cannot be seen endoscopically, although smaller ostia coming from its lumen can be visualized. The pattern on the right side is more variable than that on the left. The right hepatic duct bifurcates almost immediately into a dorsocaudal division and a ventrocranial division. The latter is a direct extension of the right hepatic duct; the former has its ostium on the left lateral wall of the vestibule, usually within 1 cm. of the common vestibule. The course of the dorsal branch renders exploration and manipulation difficult in this part of the duct because of the sharp angulation which it takes when it crosses over the right branch of the portal vein.

The mucous membrane is yellowish with a white or bright yellow hue. Sometimes the membrane has a reddish-yellow or pink-yellow color. Small reticulated blood vessels are clearly visible, more so at the hepatic than at the duodenal extremity of the duct. The extent of proximal vision is dependent on the degree of choledochal dilatation; the visual depth is increased as a function of the degree of dilatation. The fourth order of hepatic ducts is easily seen if the common bile duct is over 1.5 cm. in diameter.

The common bile duct has an average length of 7.5 cm., ranging between 5 and 15 cm. depending on the site of confluence of the hepatic ducts and the site of entrance of the cystic duct. It is a cylindrical tube, narrowing to a funnel before entering the ampulla. The four portions are best referred to in relation to the duodenum: supraduodenal, retroduodenal, infraduodenal (pancreatic), and intraduodenal. The duct is actually an epithelial-lined tube on a fibroelastic tissue support. Hendrickson[16] has pointed out that the human common bile duct contains relatively little muscle except in its terminal portion. The duct narrows where it passes obliquely through the muscular wall of the duodenum to exit at the ampulla, on the posterior medial wall of the duodenum, 7 to 10 cm. from the pylorus.[17] Endoscopically the mucous membrane has a reddish-yellow or pinkish-yellow color; the papilla is seen as the funnel is passed. The sphincter is observed to open and close. Its shape varies in different individuals and in the same individual at different times. The duct courses obliquely through the duodenal wall for a distance of almost 2 cm.; Boyden[18] has illustrated this portion of the common duct in great detail.

The normal choledochal mucous membrane is smooth and flat and is rarely arranged in large folds. The submucosal blood vessels are thin and arranged in reticular fashion. The lumen normally contains a small amount of mucus. In the hepatic divisions the carinae are all sharp. The glands are seen as small (1 to 3 mm.) oval pits in the mucous membrane. The shape of the sphincter varies individually and during its functioning phases. The endoscopist soon learns to compensate and adjust for the distortion in size which is produced by observation. Stones are seen in a magnified fashion, only the most proximal one being visualized when they are arranged in a tandem fashion. After the stone has been removed there is an increase in the mucous flakes, and the site of the calculus frequently is seen as a localized area of hyperemia which occasionally is ulcerated as a calculus decubitus.

Obstructing papillitis (often suggested by cholangiography) is a rare endoscopic finding. Cholangitis is seen far more often than is suggested by the ordinary choledochot-

TABLE 1. Classification of endoscopic abnormalities

Condition	Type		
Choledochectasia	Obstructive	. . .	. . .
	Nonobstructive		
Cholangitis	Localized	Congestive	. . .
	Diffuse	Catarrhal	
		Suppurative	
Stones	Type	. . .	. . .
	Location		
	Number		
Tumors	Benign	Intrinsic	Location
	Malignant	Extrinsic	
Sphincter	Shape	. . .	. . .
	Function		
Structural abnormalities	Accessory or anomalous ducts	. . .	. . .
	Stricture		
	Diverticuli		

omy. Wildegans[1] reported it in 15 per cent of the cases of chronic cholecystitis and Brocks[19] in one third of the patients on whom he had performed endoscopy. We have observed particularly severe cholangitis in patients with partially obstructed cholecystojejunostomies which were performed previously for distal common duct obstruction. We have also observed severe relatively localized left hepatic duct cholangitis due to a stone blocking at the left orifice. It would appear that the recognition and certainly the demonstration of cholangitis have been delayed until the entire mucous membrane could be visualized. Obviously segmental in vivo biopsies of the common bile duct are impractical. Endoscopy is the only way of visualizing the mucous membrane changes throughout the length of the common duct. A pertinent series of common duct biopsies from this clinic is reported elsewhere.[20] The usual mucosal change is that of edema and congestion; exudative reactions and purulent cholangitis are not uncommon. There is commonly an increased mucus production in association with calculus ectasia. Fat necrosis is seen occasionally in the common duct wall, but on such occasions it is usually very pronounced elsewhere. Extrinsic compression results in a normal mucous membrane, with distortion and/or elevation of one or more walls and resulting luminal eccentricity. The endoscopic findings are recorded according to the classification that appears in Table I.

The extrahepatic biliary passages serve as a simple conduit for the flow of bile from the liver and gallbladder into the duodenum. Peristalsis of this tube has not been demonstrated convincingly. Its dynamics are passive in relation to the secretory pressure of the liver and the contraction of the gallbladder. Therefore the primary changes attributable to its dysfunction are due to the obstruction of its lumen. Such obstruction is usually due to a stone or tumor and less frequently to a primary infection. Iatrogenic obstructions are the result of injury to the duct resulting in stricture or fistula formation. Regardless of the cause, obstruction is followed by dilatation and cholangitis, and their simultaneous effects on the hepatic parenchyma, ranging from dilatation and bile stasis to abscess formation and biliary cirrhosis.

The dilated common duct is an indication of some biliary tract abnormality. Ducts which are larger than 1 cm. in diameter are abnormal, and yet dilatation per se is not a criterion of disease.[21,22] Stones have been found in small ducts. Normal ducts may range up to 1.2 cm. in size, especially in the postcholecystectomy state. In terms of pathology there is no such thing as a "silent stone" or nonmalicious biliary obstruction, although the amplitude of effect on the bile ducts and liver may not correspond or be directly related to the extent of the patient's signs and symptoms. The surgery of the common bile duct is basically that of maintaining its patency, and the diagnostic problems are those of determining whether or not the duct is obstructed, what the etiologic factor is, and how this is reflected in hepatic changes.

Evaluation of common bile duct integrity

The nonoperative methods of evaluating common bile duct integrity are chemical and roentgenographic. Laboratory findings of an obstructive nature (in the presence of jaundice) are reliable early in the obstructive phase; later they may be confused by the addition of changes which are indicative of parenchymal damage. Oral and intravenous cholangiography have proved to be of great value in the nonicteric patient.[23] In the presence of icterus the radiographic evidence of common duct disease depends on the demonstration of changes in the papilla ("papillary sign") or of secondary contour changes in the neighboring viscera.[24] Transhepatic puncture cholangiography is a somewhat risky procedure, but when it is successful, it is of definitive value in demonstrating the site and often the cause of block.[25,26] Once the diagnosis of obstructive jaundice has been made and the patient is subject to a direct evaluation of the common duct, a similar problem exists in determining the site, cause, and extent of obstructive disease and the best surgical approach to its management. The operative methods include palpation, instrumentation, and roentgenography; endoscopy offers real advantages.

The palpation of the duct is aided by mobilizing the second portion of the duodenum and by palpation from the left side. Transduodenal visualization is often necessary.[27] Palpation over a sound is of value, but frequently it leaves the operator with a sense of uncertainty. Patient exploration, with copious irrigation and gentle instrumentation, often produces unexpected stones but is not definitive.

The introduction of operative cholangiography by Mirizzi in 1932[28] provided a distinct advance. This enabled the operating surgeon to see roentgenographically beyond the limits of his direct vision and palpation. It is hard to overemphasize the proved value of this procedure in demonstrating residual calculi. Its value in the operating room has some limitations in regard to shadow interpretation, accuracy, and hazard. With regard to the former, it is frequently difficult or impossible reliably to distinguish a calculus from an air bubble, fibrin, clots, or organic debris. At the distal end of the duct, contrast medium may sometimes fail to enter the duodenum, even on the delayed film, when there is no organic obstruction.

It is almost impossible to make a cholangiographic diagnosis of cholangitis.[29] Usually one may demonstrate only dilatation. Definitive films may be difficult to obtain in the obese patient. Operating room personnel are understandably reluctant to expose themselves repeatedly to the radiation. Occasionally a significant pancreatitis is precipitated by cholangiography.[30] The method is confusing or not diagnostic in about 10 to 15 per cent of cases.[31–34]

The advantages of operative cholangiography include: simplicity of technic; shared responsibility; visualization of pancreatic duct and common channel and of distal hepatic ramifications; and the fact that it requires only needle puncture. Its limitations include: difficulty in interpreting shadows; artifacts; radiation exposure; inaccuracy in small stones or biliary "mud"; drug sensitivity; precipitation of pancreatitis; and limitation of number of examinations.

Recent efforts to obtain increased accuracy employ an image intensifier and a television screen during operative cholangiography. These methods are too new to evaluate. In 1952 Mallet-Guy[35] suggested complementing cholangiography with manometery. Increased pressure in the biliary system is thus demonstrated. The method gives no clue to the cause or to the need for or the type of surgical therapy. It has a limited operative practical usefulness except in evaluating sphincter tonicity.

A state of insecurity and dissatisfaction, especially in reference to the dismaying finding of a residual stone, led to a search for other methods of direct, immediate exploration of the common duct, without transferring the responsibilities to the radiologist. Kirby in 1950[36] introduced a lithophone; the contact of a stone with this instrument gives

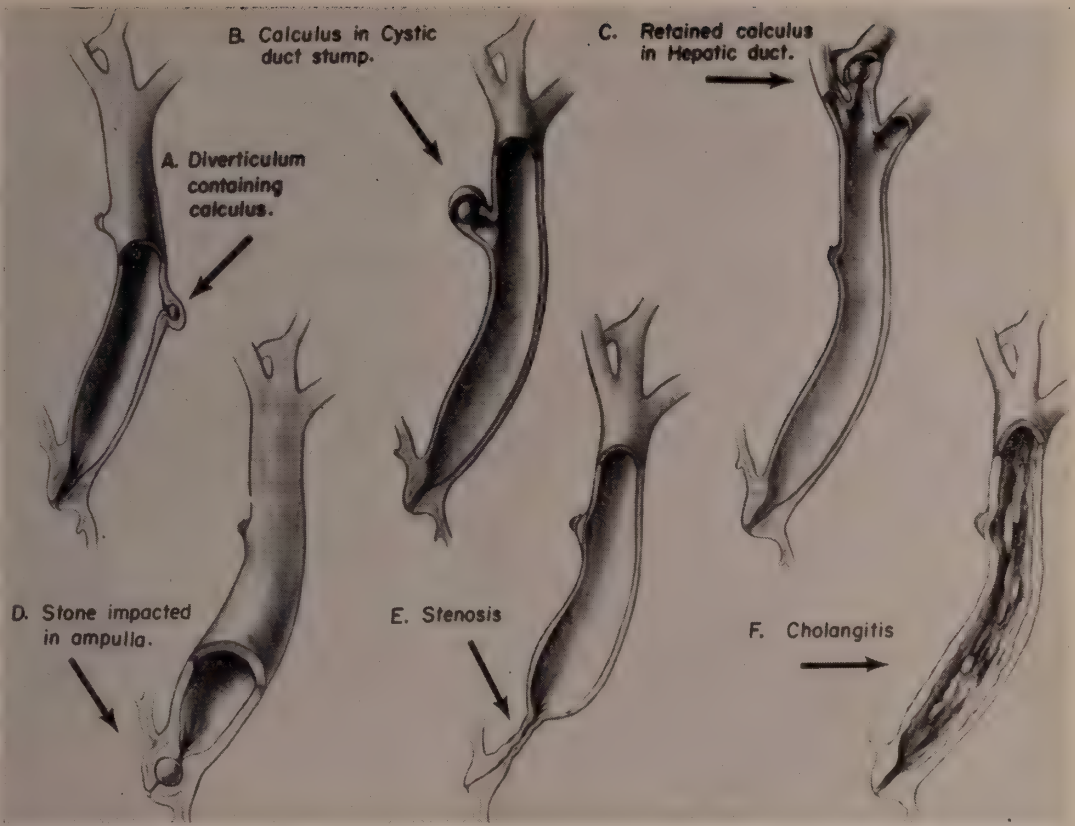
B. Calculus in Cystic duct stump.
C. Retained calculus in Hepatic duct.
A. Diverticulum containing calculus.
D. Stone impacted in ampulla.
E. Stenosis
F. Cholangitis

FIGURE 5. Sites of retained stone and anatomic-pathologic precursors of recurrent calculi are illustrated. Each of these areas may be visualized endoscopically and such pitfalls surgically avoided or managed.

off a recognizable sound that is not elicited in the presence of a normal duct. There have been no further reports of the use of this instrument, and it is impossible to evaluate its practical value on the basis of published data. Air-contrast cholangiography has not solved the problem.[37] None of these methods has the advantage of the direct vision provided by the choledochoscope.

The advantages and disadvantages of operative cholangiography and choledochoscopy have been summarized previously. It is apparent that they do not supplant one another but rather complement each other. The disadvantages of the one are compensated for by the potentialities of the other. From the point of view of practical usage, if only one modality is available, it is apparent that the skilled operator may obtain more information with the choledochoscope than with cholangiography. It enables him to explore directly an 8 to 10-cm. tube through a 1-cm. incision in such a way that obstructive factors may be diagnosed and managed. Particularly, and practically, he may be reasonably certain that all stones have been removed.

Residual or reformed calculi

Retained calculi or reformed calculi are the commonest cause of unsatisfactory results in biliary tract surgery. Such calculi constitute the commonest cause of the postcholecystectomy syndrome in the immediate or late period. These calculi often are first discovered by postoperative T-tube cholangiography. However, the absence of symptoms, or the failure to fistulize, is of itself no proof of the absence of stones. Hicken, McAllister, and Call[38] point out that patients may close their T-tube fistulas in spite of residual stones, the stones becoming symptomatic at some future time. It is fortunately a common experience to find that stones may pass spontaneously or in association with the biliary flush regimens of Pribram[39] and Best.[40] However, 85 per cent of patients harboring residual or reformed calculi in their common bile ducts require secondary operative procedures.[41] The reported incidence of retained calculi in large series is about 10 per cent, with a range of from 2 to 24 per cent. Usually these calculi have been overlooked because the operator did not know that they were there. However, there is good experimental and clinical evidence that new stones may form in the presence of partial choledochal obstruction or cholangitis[42,43] and that they may reform in and pass down from a cystic duct stump.[44] Such stones usually are found in the ampulla or in the hepatic ducts, the areas in which palpation is of least value. In the distal and narrow end of the duct they may become impacted, and it is difficult by palpation to distinguish intraluminal stones from pericholedochal lymphadenopathy and from inflammatory nodular or neoplastic pancreatic disease. Stones may lodge in a diverticulum and be bypassed during irrigation and probing. The narrowed, tapered area in the distal duct is also the most difficult site to evaluate from a cholangiographic point of view (Fig. 5). Kantor, Evans, and Glenn[45] report that on the average this area is 2.23 mm. in width and 13.01 mm. in length. When this is proximal to the site of obstruction, it dilates and permits the choledochoscope to pass through it.

Best[46] reported hepatic stones in about 7 per cent of patients with cholelithiasis, and Norman[13] found them in 23.6 per cent of patients with choledocholithiasis. Choledochoscopy may minimize residual calculi once they are demonstrated, since it is almost always possible to remove them by choledochotomy. In those instances in which choledochoscopy demonstrates distal inflamed, obstructive disease that cannot be corrected by a direct surgical attack, a side-to-side choledochoduodenostomy may be performed to manage the problem by short-circuiting. This is of particular value in patients with chronic recurrent sclerosing pancreatitis involving the common bile duct.

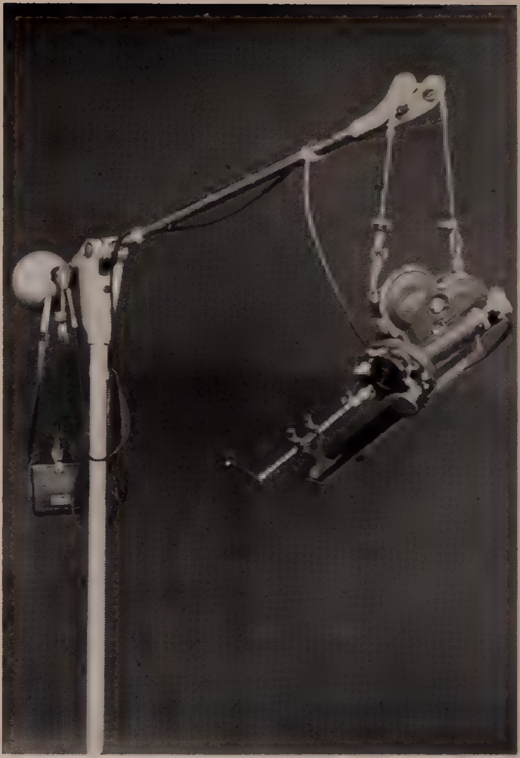

FIGURE 6. Weighted, balanced arm is used to support camera as it is aligned with choledochoscope. Operator's view is from camera eye out endoscopic lens directly into biliary channel.

The surgeon, therefore, need not stop before a satisfactory examination has been obtained and a choice of therapy selected on the basis of direct visualization of the pathologic condition. Kantor, Evans, and Glenn[45] have pointed out a very high incidence (48 per cent) of unsatisfactory operative cholangiograms if strict criteria are used. By the roentgen method it is not possible to distinguish tumors from stones. The poor results obtained with neoplasms are related, in part, to a failure to diagnose them at a stage when resection is feasible and hepatic function is adequate. Endoscopy is the only method of clarifying a bizarre cholangiogram that may reflect a combination of calculus disease, ulceration, cholangitis, and granulomatous change. Choledocholithiasis is not rare in association with obstructing pancreatic lesions. After the removal of the calculi, endoscopy is the most reliable method of demonstrating obstructive intrusion of the enlarged, distorted pancreatic head.

Photographic recording

Endoscopic observations are difficult to document and describe by words alone. A photographic recording of the findings is of obvious value. McIver in 1941[2] showed a black-and-white photograph of an intraluminal stone which was taken in the autopsy room. In 1956 Wildegans[9] reported the possibility of endoscopic photography; his 1960[8] monograph contains two-color photographs obtained with a special bulb and the foroblique choledochoscope. Griessman in 1960[47] reported the development of a "Foto-Choledochoskop."

We have obtained colored motion picture films, in autopsy material, of the bile ducts for their entire course, ranging from the sphincter to the fourth order of intrahepatic ducts.[48] The camera arrangements, as illustrated in Figure 6, consist of a Bakelite support for the endoscope and a heavy balance for the camera. The operator looks from the camera directly out of the endoscope, manipulating the system as one unit. For the motion picture we have used an Arriflex camera with high speed Ektachrome film taken at 8 frames per second. The black-and-white films reproduced here have been obtained with the same system, using a single lens reflex camera and Tri-X film at one fifth of a second. The light source has been that of the bulb which is ordinarily used in direct observation choledochoscopy. Operative color motion films of diseased bile ducts are now being made. This system offers a direct means of correlating cholangiography with endoscopic pathologic anatomy in permanent records.

Choledochoscopy has been utilized in 54 patients in this series to date. In individual patients the instrument has been inserted several times as a procedure to determine patency. On several occasions it has served to include a procedure not originally planned or to lend security to a difficult choledochol toilet. In no case has the procedure been harmful. A detailed analysis of illustrative cases is the subject of a separate report which is in preparation.[49]

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ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963,* and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Residuals of Phlebitis

Clinical Study

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OF 150 MEN *with phlebitis, most were from twenty to twenty-nine years old at the time of their initial attack. The preceding factor was a medical condition in 36 cases, an injury or surgical procedure in 70, physical activity in 16, and no apparent reason in 28. Phlebitis of the lower extremity was most common on the left side. The three most commonly found sequelae were edema, varicosities, and ulceration. Of the complications, 41 per cent were moderate and 20 per cent severe. There were 25 recurrences of phlebitis. At present, combination of bed rest and an elastic support to the involved extremity is the most effective method of preventing or alleviating complications. Extensive use of anticoagulants and fibrolysins requires further evaluation.*

THIS IS A REPORT on the results of a study of the residuals of phlebitis in 150 cases observed in the surgical clinic of the New York Regional Office of the Veterans Administration. These patients were examined and treated during the past two years. The description of the initial treatment, as well as the circumstances surrounding the beginning of their disability, were obtained from the original military records and from reports submitted by Veterans Administration hospitals.

Methods and materials

AGE GROUPS. The ages of these individuals at the time of onset of their disease were divided into ten-year groups as following: 22 men were less than twenty years of age at the beginning of their illness, 83 between twenty and twenty-nine years old, 32 between thirty and thirty-nine years of age, 6 between forty and forty-nine years, and 7 were fifty years old or over. As one would expect in a military service, most of the individuals affected were in the twenty- to twenty-nine-year age group.

PRECEDING FACTOR. It was interesting to note the circumstances which preceded the onset of phlebitis. In 28 cases, or 18.6 per cent, phlebitis occurred without any apparent cause or related incident. In 16, or 10 per cent, a physical activity, such as rapid walking, lifting of weights, immersion in cold water, or swimming, was listed as the precipitating factor. Medical conditions ranging from pharyngitis to typhoid fever preceded the onset of phlebitis in 36 cases, or 24 per cent. Surgical procedures were involved in 37 instances, or 24.6 per cent. Finally, trauma precipitated an attack of phlebitis in 33 cases, or 22 per cent.

PERIOD OF FOLLOW-UP. Eighty-one of these veterans were seen between five and nine years after the onset of phlebitis, 42 between ten and fourteen years, 16 between fifteen and nineteen years, and 11 more than twenty years after the onset of their illness.

SITE OF INVOLVEMENT. Nine of these cases had bilateral involvement at the onset of their disease or at some subsequent period. The most frequently involved side was the left, and 93 individuals were in this group. The remaining 48 had disease limited to the right lower extremity. It is interesting to note that in the major number of cases the left lower extremity was the site of involvement, but there was no apparent explanation for this phenomenon.

INITIAL TREATMENT. The records studied show that very often more than one treatment was utilized. However, in every instance there was one item in treatment which seemed to be the most important element in the individual case. The principal treatment in 84 cases was simple bed rest. Antibiotics were used in 22 cases. During the 1940's sympathetic block combined with bed rest was a common form of treatment, and 18 individuals received this form of therapy. The usual material used for the block was 1 per cent Novocain. Anticoagulants were used in 14 cases, while a combination of bed rest, sympathetic block, and antibiotics was used in 2 instances. Sympathectomy as a principal form of treatment was used once. Anticoagulants and antibiotics as a combined treatment were administered to 2 patients. A femoral vein ligation was performed 4 times and saphenous ligation 3 times.

Sequelae

Classification. To classify the residuals of phlebitis, the cases have been divided arbitrarily into 3 groups. Group 1, the mild cases, comprised those who demonstrated slight swelling of the extremity and a few small varices. Group 2, the moderate cases, included those individuals who had a 1-inch increase in circumference of the leg and who may have had varices also. Group 3, the severe cases, comprised those who had marked swelling of the involved extremity with ulcer and varices. Some of the latter cases also had an extensive system of collateral circulation through varices visible on the abdominal wall. There were 16 patients in this study who demonstrated no residuals at all. Forty-one cases were in Group 1, 62 in Group 2, and 31 in Group 3.

Ulceration. There were 29 cases of ulceration in Group 3. They undoubtedly presented us with the greatest problem as to treatment. Usually, the longer the ulcer was present, the more difficult it was to eradicate. There were 29 cases of ulceration of the lower extremity. Nine of these appeared within two years after the onset of phlebitis, 5 between three and five years, 8 between six and eight years, 2 between nine and eleven years, and 5 between twelve and fifteen years after the initial attack of phlebitis.

It was possible to heal 9 of these cases at varying intervals from the onset of treatment. It is interesting to note that 1 healed finally after fourteen years, and another healed only after the patient changed his occupation from ordinary labor to a more sedentary type of work. The treatment continued for nine years in the latter case.

We have found that the most important element in the treatment of these chronic ulcerations is the use of a supporting apparatus, such as a well-applied elastic bandage or an accurately fitted elastic stocking. It is not sufficient merely to prescribe the elastic bandage, but patients must be painstakingly taught the proper method of application of such bandaging. We are fortunate in having a group of well-trained public health nurses who assist in the instruction and treatment of our patients. The use of elastic stockings must also be supervised carefully, since they have a tendency to become ill-fitting in a rather short time. The second most important element in treatment, in our opinion, is the use of sufficient bed rest. As to the local treatment of the ulcer, there does not seem to be much advantage in any one particular technic. The important factor in local treatment is to assure that nothing is done to injure the tissues during the period of healing. The application of irritating materials or medications is obviously contraindicated. Cleanliness is all important.

Recurrence. Twenty-five of our cases, or 16.9 per cent, had a recurrence of phlebitis in one or both extremities. The second attack occurred at various times following the initial disease, most often within four years after the first incident. Thus, 13 cases occurred within four years, 7 between five and nine years, and 10 between ten and fourteen years after the initial phlebitis. The precipitating factor varied from an ordinary nasopharyngitis to a major operation.

Pulmonary embolus. There were 29 cases of pulmonary embolus. Of these, 4 occurred in the group of recurrent phlebitis mentioned previously. There were 2 cases of pulmonary infarct which occurred while anticoagulant treatment was being given. It is not within the intent of this study to present the reasons for pulmonary embolus, since so much has already appeared in the literature in regard to this serious problem.

Comment

This clinical study of the residuals of phlebitis was concerned with the findings of a follow-up of from five years to more than twenty years after the initial disease. As one would expect in a military service, most of the individuals who were studied were in the third decade of life when they were subjected to the initial attack of the disease. It is interesting to note that the initiating or preceding factor to the phlebitis was a medical condition in 36 men and an injury or a surgical procedure in 70 cases. In 28 instances no apparent reason could be presented for the onset of the phlebitis, while in 16 cases physical activity seemed to be the cause. We also noted that phlebitis of the lower extremity was most common on the left side, although we offer no explanation for this phenomenon. The anatomy of the venous system on this side may have some bearing on this interesting point.

The three most commonly found sequelae were edema, varicosities, and ulceration, although other changes such as subcutaneous fibrosis and pigmentation were also a common result of phlebitis. We concentrated on the three major complications. A classification of sequelae has been offered, and in accordance with the classification, 41 per cent were moderate in nature, and 20 per cent were considered severe. The presence of ulceration constituted a difficult problem in treatment. Most of the individuals who were studied suffered their initial attack during the 1940's, when anticoagulation treatment was still in its infancy. Only 14 of the 150 individuals who were studied had received anticoagulants. Almost all were treated by bed rest during the early period of their disease. Those who received sympathetic block showed no distinct improvement from this treatment.

There were 25 recurrences of phlebitis, usually within the first four years, although 1 patient suffered a recurrence fourteen years after the initial attack. Recurrences were due to a variety of preceding conditions.

The serious complication of pulmonary embolus was present in 29 cases, or 16 per cent. It is possible that the incidence of embolus was actually higher. It is known that the diagnostic accuracy in this condition is only 20 to 50 per cent when it is based on the usual criteria. A recent study showed that the incidence of pulmonary embolus is extremely high, varying from 22 to 41 per cent depending on age.*

Ulceration following phlebitis presented us with the most difficult problem in treatment in an outpatient clinic. There were 29 cases of ulceration occurring anywhere from two to fifteen years after the onset of the illness. We have found that the most effective treatment is a combination of bed rest and the constant use of a supporting elastic device, such as a stocking or bandage, combined with local cleanliness of the ulcer site. In this manner we were able to heal 9 of these resistant cases. Incidentally, 2 were healed after they maintained continuous treatment under supervision following a change in employment from ordinary labor to a sedentary type of work. There was 1 individual whose ulcer healed after eight years of treatment but who suffered a relapse when he decided to discard the use of an elastic support. Another individual, aged twenty-six, succeeded in healing his ulcer by the combination of bed rest and an elastic support but had a recurrence when he discarded the support. Because of the increase in size of the ulcer he was admitted to a hospital, where a sympathectomy was performed on the affected side. Healing did not occur after this operation, but treatment was successful when the patient agreed to wear an elastic support again.

Our study, therefore, indicated that in spite of its simplicity, a combination treatment of bed rest and an elastic support to an involved extremity is the most effective method of preventing the complications of phlebitis or alleviating them when they do occur. It remains to be seen whether or not the extensive use of anticoagulants will change this situation in the future. The recent increase in use of the fibrinolysins also may prove to be of value in preventing such complications.

Summary

A report has been presented on the clinical study of the sequelae of phlebitis occurring in a group of 150 patients. The most effective treatment for the complications of edema, ulceration, and varices in this outpatient clinic consisted of an elastic support, occasional bed rest, and local cleanliness.

252 Seventh Avenue, New York 1

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* Wacker, W. E., Rosenthal, M., Snodgrass, P. J., and Amadore, E.: A triad for the diagnosis of pulmonary embolism and infarction, J.A.M.A. 178: 8 (Oct. 7) 1961.

Abuse of One-Pint Transfusions

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THE CHARTS OF PATIENTS who each received a 1-pint blood transfusion in Saint Vincent's Hospital of the Borough of Richmond from June 1, 1959, to December 1, 1960, were reviewed. During these eighteen months, 272 patients received 1 unit of blood or 9.8 per cent of the 2,855 transfusions administered in the hospital. These 272 transfusions do not include patients with blood dyscrasias where 1 unit of blood was necessary to bring blood volumes to acceptable levels for the maintenance of normal activities.

Table I is a study detailing the age of the patients with the hemoglobin values prior to the transfusions. It is obvious that the practice of giving 1-pint transfusions affects all age groups, thus all physicians are guilty of doing this. A disturbing feature in this table is that 141 patients who received one transfusion had hemoglobin levels of 12 Gm. or more. The table also shows that 218 of the 272 patients had hemoglobin values of 10 Gm. or more.

Forty-nine of the 272 patients who each received a 1-pint transfusion had no operative procedure performed on them. In this nonoperative group 23 patients had hemoglobin values of 9 Gm. or less. Seven patients had inoperable carcinomas. The value of transfusing patients in this category is also open to serious question. The other diagnoses were: fractured hips, 2; bleeding peptic ulcers, 5; incomplete abortion, 1; hypertrophy of prostate, 1; acute tonsillitis with nephritis, 1; diaphragmatic pleurisy, 1; hypertensive heart disease, 1; chronic nephritis, 2; fecal fistula, 1; and acute pelvic inflammatory disease with localized peritonitis to the pelvis, 1.

The following diagnoses were recorded in the 26 patients who had a hemoglobin of 9 Gm. and over without surgery being performed on them: incomplete abortion, 2; cirrhosis of the liver, 3; cirrhosis of the liver with esophageal varices, 1; duodenal ulcer, 1; gastrointestinal hemorrhage, 1; carcinoma of the uterus, 1; carcinoma of the rectum, 1; carcinoma of the testis, 1; abdominal lymphosarcoma, 2; postoperative hemorrhage secondary to hemorrhoidectomy, 1; postpartum hemorrhage, 1; hemorrhage secondary to varicose veins, 1; fractured skull, 1; ruptured viscus, 1; nephrotic

TABLE I. Age and hemoglobin levels

Age	Hemoglobin (Gm.)							
(Years)	3 to 5	6 to 7	8 to 9	10 to 11	12 to 13	14 to 15	16 to 17	None
81 to 90	..	1	3	2	3	1	..	1
71 to 80	1	3	4	5	12	4	1	..
61 to 70	1	..	6	11	19	5	2	1
51 to 60	..	..	6	10	9	8	..	1
41 to 50	..	1	5	23	20	6	2	..
31 to 40	..	1	5	13	17	2	1	2
21 to 30	..	..	9	10	12	2	..	1
11 to 20	..	2	2	2	4	2	1	..
0 to 10	..	1	2	2	2	..	..	..
TOTALS	2	9	42	78	98	30	7	6

TABLE II. Per cent of patients with hemoglobin values of 9 Gm. or over

Departments	Number of Patients	Patients with Hemoglobins of 9 Gm. or Over	
		Per Cent	Number
Surgery	74	74.3	55
Medicine	14	66.6	9
Obstetrics and gynecology	94	69.1	65
Orthopedics	32	81.2	26
Genitourinary diseases	18	88.8	16
Malignant diseases	40	82.5	33

THIS STUDY OF *one hospital's experience reveals that of 272 patients who received 1-pint blood transfusions, 141 had hemoglobin levels of 12 Gm. or more, and 218 had hemoglobin values of 10 Gm. or more. Forty-nine had no operation. Many of these patients could probably have been managed without the use of a blood transfusion. Complications of transfusion include immediate hemolytic reaction, allergic reaction, pyrogenic reaction, bacterial contamination, bleeding tendency, and pulmonary congestion. To avoid complications, indications for transfusion must be reappraised critically and constantly.*

syndrome, 1; acute myocarditis, 1; chronic myocarditis with failure, 1; acute gastritis, 1; osteoporosis of the femur, 1; cerebral vascular accident, 1; thrombotic occlusion of superior mesenteric artery, 1; and cervical tear secondary to delivery, 1.

It is most likely that many of these patients could have been managed without the use of a blood transfusion.

Patients were then segregated by departments and services to which they were admitted in an effort to determine whether or not any pattern was apparent in deciding to give transfusions to patients (Table II). After these patients were subdivided by services, an investigation was made to determine what per cent of patients had hemoglobin values of 9 Gm. or over. Table II reveals this information. This is further evidence that all specialties are indicted in this practice of giving single blood transfusions.

Table III lists the commonly performed operations during which patients with hemoglobin values of 8 Gm. or more received a 1-pint transfusion. A preoperative hemoglobin of 12 Gm. or over was found in 63.4 per cent of the patients, while 94.4 per cent had hemoglobin values of 10 Gm. or more. This is another manifestation of the practice of anesthesiologists and surgeons alike of giving blood transfusions during an operative procedure before estimating the exact amount of blood loss and checking the preoperative values to see if the blood loss need be replaced immediately by transfusions or if the patient's hematopoietic system with the aid of iron could make up the loss in the ensuing weeks. In this group 95 patients received their transfusions during the operation.

If surgeons and anesthesiologists would check on their own practice regarding 1-pint transfusions, I am certain that many radical changes would occur and that the number of 1-pint transfusions would decrease markedly. It is the hope of the author that this report will cause other surgeons and anesthesiologists to pause and think of the inherent dangers that we condone in allowing unnecessary 1-pint transfusions to be given especially in the operating room.

Comment

Many authors have investigated the quantity of blood loss in various operations.[1,2] A study by Saltzstein[3] revealed the average blood losses in various surgical procedures (Table IV). From this list of commonly performed operations, only a few procedures require routine blood transfusions when a normal blood volume exists preoperatively. This of course is predicated on the ability of the surgeon and his meticulousness with hemostasis.

In 1959 approximately 5 million pints of blood were given to patients in the continental United States. The rates of both fatal and nonfatal complications are difficult to ascertain and vary considerably with different investigators. The national mortality rate from transfusions varies from 1 death in 1,000 to 1 death in 5,000 transfusions. In a

TABLE III. Preoperative hemoglobin determination

Operative Procedures	Number of Patients	Hemoglobin (Gm.)				
		8 to 10	10 to 12	12 to 14	14 to 16	16 to 18
Cesarean section	12	. .	6	6	. .	. .
Panhysterectomy	30	1	13	14	2	. .
Vaginal hysterectomy	9	. .	2	7	. .	. .
Laminectomy	4	. .	. .	2	. .	2
Exploratory laparotomy	11	. .	4	2	4	1
Spinal fusion	2	. .	1	1	. .	. .
Cholecystectomy	12	. .	5	6	1	. .
Gastrectomy	10	1	2	4	3	. .
Transurethral resection	11	2	1	5	3	. .
Colon resection	5	. .	1	2	1	1
Radical mastectomy	5	. .	. .	4	1	. .
Dilatation and curettage	10	2	3	3	2	. .
Appendectomy	5	1	1	3	. .	. .
TOTALS	126	7	39	59	17	4

recent study Cole[4] reported a mortality of 0.00046 in 217,000 transfusions. The reported incidence of hepatitis both fatal and nonfatal also varies from 1 death from serum hepatitis for every 500 patients receiving transfusions to 1 death in 5,000 patients.[5,6] Some statistics[5] show that the transfusion mortality for hepatitis alone approximates that for appendectomy for nonperforated appendicitis. The incidence of serum hepatitis with jaundice from professional sources was 7 to 10 times that experienced when all the blood that was given was from family donors.

There is experimental and clinical evidence to show that a patient with a normal blood volume can safely lose as much as 10 to 15 per cent of his blood volume.[7,8] Thus, in an individual weighing 155 pounds, this loss would amount to from 490 to 735 cc. For an 88-pound patient this would be from 240 to 360 cc. If the hemoglobin level, rather than the blood volume, is used as a criterion of blood need, studies indicate that a concentration of 7 Gm. of hemoglobin per 100 ml. is sufficient for tissue oxygenation for most situations in surgery, and a concentration of 10 Gm. at the start of surgery provides adequate leeway. The routine use of blood transfusions to replace anticipated blood loss would seem therefore to be irrational and dangerous in patients who come to operation with adequate blood volumes and hemoglobin levels and who suffer no unusual blood loss during surgery.

TABLE IV. Average blood loss in various surgical procedures[3]

Procedure	Loss (Cc.)
Simple mastectomy	419
Radical mastectomy	1,151
Subtotal gastrectomy for ulcer	865
Subtotal gastrectomy for cancer	1,005
Cholecystectomy	219
Common duct exploration	732
Abdominal perineal resection	2,037
Colon resection	613
Hysterectomy for fibroids	541
Ventral hernia	347
Groin dissection	920
Exploratory laparotomy for inoperable cancer	348
Vein stripping	1,100

Complications

Obviously there are occasions when a transfusion of a single pint of blood may obviate the need for a second pint and may bring the patient's condition to a point where measures other than blood will suffice. The dangers of transfusion cannot be denied, and the recuperative powers of human beings should not be overlooked. The complications of transfusions in general are usually placed under the following categories:[9-11]

IMMEDIATE HEMOLYTIC REACTION. The national average of 5 hemolytic reactions per 1,000 transfusions probably reflects the actual incidence of this dangerous complication. In actual numbers it would represent that 13,500 patients annually have hemolytic reactions. By using a reported mortality for hemolytic transfusion reaction of 50 per cent, the estimated yearly toll is the loss of about 6,750 lives from this one complication of whole blood transfusion. The well-known signs of hemolysis are readily masked in an anesthetized patient.

ALLERGIC REACTION. The incidence of allergic reaction varies from 1 to 3 per cent.

PYROGENIC REACTION.

BACTERIAL CONTAMINATION.

BLEEDING TENDENCY.

PULMONARY CONGESTION.

Immediate complications incident to the methods of transfusion are: (1) air embolism, (2) circulatory overload, (3) cardiac arrest, and (4) thrombophlebitis; and the late complications are: (1) the transmission of disease (influenza, syphilis, hepatitis, malaria, and brucellosis) and (2) isosensitization.

On January 9, 1959, a report issued by the U. S. Vital Statistics Special Department, The U. S. Department of Health, Education, and Welfare, Washington, D. C., stated that the annual mortality from only three complications of blood transfusions, namely, hemolytic reaction, overload, and serum hepatitis, is computed to be 16,500 patients. The computed annual death rate from blood transfusions exceeds that reported for many common surgical diseases, such as rectal carcinoma, appendicitis, diverticulitis, duodenal ulcer, cholecystitis, and intestinal obstruction.

One must certainly consider when he prescribes whole blood that an illness may be inflicted on his patient which is far worse than the retarded recovery which it is assumed but not proved will attend a failure to replace all preoperative red-cell deficits and all operative blood losses. Since certain complications are unavoidable after a transfusion, one's only means of prevention of transfusion morbidity is to avoid transfusion. To make this decision wisely, the validity of the commonly used indications must be reappraised critically and constantly.

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Poor quality of Russian drugs

Every year, there is an increase in the production of various drugs in our country. Many of them are sent for evaluational testing to the Central Pharmacological Research Institute. In the last year, for example, 112 various drugs were sent to us—ampules, tablets, and others. And it is deplorable that 75 per cent of them did not meet the requirements of the official governmental pharmacopoeia and the technical standards. In the first three months of the current year, the Institute received some dozens more of pharmaceuticals, and this time again, from the 74 tested, 58 did not meet the requirements.—*Meditsinskii Rabotnik* (*Moscow*), *July 14, 1961*

Course on Psychiatry for Physicians

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From The New York Academy of Medicine

"I have been treating a girl for obesity; she did very well for a while but now she's having trouble at night. She thinks other people are talking about her and has what I think you might call auditory hallucinations. What should I do?"

"I'm never sure how far I can go with patients when they start telling me about their personal lives. Are there any rules I can follow so I know when not to probe or when to refer them to a psychiatrist?"

"Can I continue to treat a patient of mine who, I've just learned, was formerly in a state hospital with a diagnosis of schizophrenia?"

"What do you do with a patient who refuses to go to a psychiatrist?"

"I find that some patients annoy me more than others. How can we learn to control our own attitudes and reactions in managing our patients?"

THESE QUESTIONS are typical of what doctors ask during courses on psychiatry for the practicing physician and point to one of the many problems which confront medicine today, namely, our need to develop a further understanding of the complicated interaction of social, medical, and psychologic factors in disease.[1] Current inadequacies in medical practice are ascribed, in part, by Whitehorn[2] to an educational system that inculcates a quest for certainty and a phobic avoidance of the many variables and uncertainties that are inherent in human nature. Other elements contributing to the shortcomings are the still-too-rarefied and infrequent encounters between the psychiatrist, the physician most concerned with human behavior, and his medical and surgical colleagues. Deficient communication and understanding result between psychiatrists and other physicians with harmful effects for doctors and patients, as well as for medicine and science generally.[3]

However, throughout the nation today a heartening development is the remarkable increase in courses for physicians on the emotional aspects of medical practice. These teaching projects are organized under the auspices of the American Psychiatric Association with the cooperation of the American Academy of General Practice. They are being supported financially by the National Institute of Mental Health and are sponsored by various county, state, and other medical organizations. The instructors are experienced psychiatrists with a special interest in teaching and in working with their colleagues in medicine.

The form and content of these courses vary with geographic and other factors, such as the character of the local sponsoring organization, the orientation and preferences of the instructors, the previous psychiatric training of the physician-student, and the composition of the groups. In all instances, however, as reported in the National Colloquium of Psychiatrist-Instructors in 1961,[4] the main objective of these programs is to improve the physician's management of clinical cases by an increased awareness of the interrelationships of social, psychologic, and medical elements.

Program of the New York Academy of Medicine*

On October 22, 1962, The New York Academy of Medicine will begin its fourth annual course on Emotional and Psychiatric Problems in Medical Practice. The course is open to both general practitioners and specialists. Basic and advanced sections are organized with from six to ten participants who meet for one and one-half hours at weekly intervals for 14 sessions.

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* Psychiatrist-instructors in the program are: Robert J. Campbell, M.D., Edward W. Kloth, M.D., Alfred Lilienfeld, M.D., Wil J. Tanenbaum, M.D., Manuel D. Zane, M.D., and Howard D. Zucker, M.D.

The basic sections, for those with little or no postgraduate psychiatric training, combine didactic and group discussion methods of instruction. The chief aims are to teach technics of interviewing and some of the essentials in diagnosis, theory, and treatment. Experience has taught us that the physician-students' expectations differ in different years. Accordingly, the subjects dealt with change somewhat each year. The instructors have been asked by their students to cover such areas as how to manage the patient who is overtalkative or the patient who will not follow any prescribed regimen, how to use psychopharmaceuticals, how to distinguish between psychosis and psychoneurosis and between psychotherapy and psychoanalysis, and so forth.

The advanced sections are composed of physicians who have taken the basic course or its equivalent. Small group discussions are utilized to develop a fuller understanding of the principles involved in evaluating and managing patients with pronounced psychopathologic behavior. Verbatim experiences from the practices of the participants and instructors are utilized for study. At most sessions efforts are made to have patients brought in by the students and interviewed. A common basis for discussion and learning is thus provided. Afterwards the group as a whole comes to some recommendation as to management, and consideration is given to the theoretic aspects in similar problems.

An example of the type of problem brought up in the advanced class is shown in the following case report.

Case report

A fifty-one-year-old woman was brought in by her physician who felt he needed help in managing her. She complained of feeling "no good," helpless, and a burden to those around her. A twenty-minute interview by the instructor before the group elicited that she felt hopeless about the future and thought several times a day about committing suicide. Her mind was taken up, obsessively, with self-recriminations over a single, short-term, extramarital affair eight years earlier.

The patient reported difficulty in sleeping and awakened early in the morning filled with a sense of hopelessness. Toward the end of the day, as she lost herself in routine activities, she felt better. Generally, however, almost nothing attracted her interest, not even her grandchildren. Every action was experienced as a great burden. Since the onset of her depression six months earlier, she had consulted with several psychiatrists. One of them had given her a course of electroconvulsive shock treatments, but she felt much the same. With her present physician she found some relief in being able to talk things over, more than had been possible before. She was now on chlorpromazine hydrochloride and benactyzine hydrochloride therapy.

In the patient's family both her mother and maternal grandmother had gone through deyressive episodes during the climacteric period. Her three daughters were married and were fully occupied with their own lives; two of them lived far away. Her husband was an alcoholic patient and was more of a burden than a help. She felt herself becoming less attractive physically, while her age made it difficult for her to anticipate getting a new job.

During the discussion of the case, it was recognized that the physician had a very hard job in treating this woman until conditions might change and alter her feelings. Some reassurance was given by letting her know that most people, including her mother and grandmother, had gone through such bleak episodes at some time in life. It was suggested that she be seen regularly and that the medication be changed.

The doctor felt that he was supported in his effort to help the patient and appreciated better the nature and the size of the task. At the end of the course, four weeks later, the doctor reported that the patient felt better, was sleeping through the night, and had taken more interest in her personal appearance and in life generally. Her ruminations about her earlier indiscretion and about suicide had subsided almost completely.

Such a case suggests the possibility that sometimes a patient may progress better when she is managed by her private doctor, supported and guided by the psychiatrist than by the psychiatrist alone.

Some results of program to date

At the end of each year's course a questionnaire regarding their reactions to the program has been distributed to the participants. Criticisms and suggestions received in this way from the participants and instructors have provided a basis for instituting changes in the organization and in the development of the course. For example, a syllabus* embodying the basic principles and simplified outlines of what is to be taught has been developed, and, in addition, this year audiovisual teaching aids will be utilized.

The information obtained from conducting these courses has not yet been subjected to a systematic evaluation. However, it appears desirable that a preliminary presentation be made of some of the typical reactions, experiences, and ideas observed and developed up to the present time.

Generally, as in similar programs,[5] the participants reported feeling more secure in dealing with patients in whom emotional elements were prominent. Thus, in a tape-recorded session a physician-student, on concluding his second series of seminars with the same instructor, stated:

> What I was looking for primarily in this course was to get the basic things about psychiatry because what we learned when we were in medical school many years ago we have forgotten or is now outmoded. So I felt I was completely at a loss when it came to psychiatry and I wanted to bring myself up-to-date. I wanted to learn some fundamentals, such as why a patient will break down, what will happen, what differentiates a normal from a psychoneurotic person, and so on. Now I feel the course, particularly the second one, has done me a great deal of good. I feel more secure. Before I was following my intuition, so to speak; now I have something authentic to go by, some rules. I know, for example, that a patient with neurosis, under stress, will exhibit an inappropriate action and that he cannot help it. There are patients who still irritate me, even today, but I control myself better, because I realize that this is an illness just like pneumonia or hepatitis over which they have no control. They don't do it because they want to be a nuisance. I realize now that neurosis is a chronic ailment and that I am not going to cure the patient. My job is to relieve their stress just a little bit—to make conditions bearable. I don't shoot for goals I cannot attain. At the same time I know I can do some good by relieving their stress, usually through communication. Generally I feel more competent than before in talking to my patients.

Two other physicians reported recent suicidal attempts in their practices. Both felt the possibility that they might have handled the cases more appropriately had they known better how to conduct an adequate interview and had they recognized that symptoms such as insomnia, poor concentration, eating disturbances, and slowness in speech and movement can signify underlying depression, while a sudden well-being in a depressed person might herald the danger of suicide.

One physician volunteered that talking to the group members, with their acknowledgment of the difficulties confronting them, made him feel less alone and less guilty about disheartening experiences. Another physician pointed out that he felt that he had been enabled to discuss such problems openly and to learn better ways of managing such occurrences in the future because of the fact that others, including the instructor, had reported similar unfortunate occurrences in their practices. This physician also stated that now particularly he recognized the value of seeking psychiatric consultation to help him handle such cases when the possibility of suicide appeared. To the instructor their statements about how they would now act suggested that they had learned to look for, recognize, and tackle the possibility of suicide more directly and effectively. It is also believed that the group activity had enabled the participants to face up better to what they did not know and to learn to act more constructively.

Most physicians indicated that they always had thought an adequate interview would take too much time. A physician in a tape-recorded meeting said:

> As a busy practitioner, I don't usually find the time to listen to these people's complaints. At times I have felt annoyed when they tried to take up too much of my time. Now I have learned to respect their attitudes a little and am somewhat more sympathetic toward them in line with their reasoning. I listen to their problems for ten or fifteen minutes, and if I think the patient needs more time I will suggest another appointment when we will both have more time.

Another doctor often finds the longer interviewing approach difficult financially but feels compensated, nonetheless, by a growing interest in the problem. He observed:

> The stories I get—I never thought they existed—family relationships—and the things

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* Available for $0.75 from the Office of Medical Education, The New York Academy of Medicine, 2 East 103 Street, New York 29.

> that go through these people's minds—things that don't exist, except in their minds. They magnify and make a big to-do about a small thing. I think, though, that once you show them that often it isn't as big a problem as they think, it helps them. Many of them say, "I feel better," even before they leave the office.

During a taped discussion of the problems of psychiatric referral, an example of the kind of exchange that often takes place during the sessions may be given. As one doctor put it:

> When you mention that patients should see a psychiatrist who could give them more time and analyze the problem better, they often stop coming to you. Many times you lose a patient.

Another practitioner then continued:

> I was concerned with a family for many years. The young daughter could not function, wouldn't go to work, and was very depressed. I suggested a referral to a psychiatrist. Her mother got very upset, and I have never seen them since. I found out from another patient that she stopped coming because I suggested psychiatry. On the other hand, another young woman called me at 2:00 A.M., because she had a sort of hysterical excitement that she could not get over. I also suggested a psychiatric consultation. She was very much against it. I said to her on leaving, "Look, here is the name of a psychiatrist anyhow, in case you change your mind." Several months later she called me up. She wanted to thank me for referring her because she did go and got a lot of help. She just had to go for a short time. So those are the calculated risks.

Comment

As an example of the psychiatrist-instructor's role in evoking discussion and elaborating a problem such as the matter of referral, the following question and answers may be cited.

PSYCHIATRIST: Suppose a patient says, "I don't want to go to a psychiatrist. I want to come to you." What would you do then?

PHYSICIAN: Well, I would say I would accept her for a few times to see whether or not I could help her. I would say, "All right, if you want to come to me I'll be glad to take care of you to see whether or not I'm able to help you."

PSYCHIATRIST: Suppose the case is one where you feel there's a danger of suicide?

PHYSICIAN: Then I would come out and say, "I am sorry, but you see I am doing general practice and you need special care. If you needed a gallbladder operation, I would not attempt it, because I do not have the proper training."

PSYCHIATRIST: But suppose the patient says, "I know all that but I don't want to go to a psychiatrist. If I go there I am afraid I will kill myself, but with you I would try to work out my problems."

PHYSICIAN: If I felt that there was a real danger, I would not accept. I would say, "You will have to go because I am just unable to handle it."

ANOTHER PHYSICIAN: I had an instance of this type, but I told the patient, "I'll treat you if the psychiatrist tells me I can do so. Just go there for one visit."

PSYCHIATRIST: A very good point. Did the patient go?

PHYSICIAN: She went and remained with the psychiatrist. But I was happy about it, since she had been a young girl with suicidal tendencies.

Conclusion

The impression gained from the completed questionnaires and comments in class was that, as a result of the course, to varying degrees and at different times, the participants felt more capable in interviewing and managing their patients and found the work more interesting. They allotted their time more efficiently and recognized that patients' involuntary patterns of response to stress affect the organism physiologically and psychologically, just as any other pathogenic agents do. The physician-students pursued more realistic goals and felt more confident. They determined more readily and appropriately when psychiatric consultation or referral was necessary, utilized community resources more frequently, and prescribed drugs with better understanding of their effects and dangers. They appreciated more than ever the powerful role exerted by the doctor in reducing both the degree of the patient's stress in periods of crisis and the patient's associated involuntary reactions. While they were aware of the genuine help they provided, the physician-students also recognized better some of their own shortcomings, as well as the limitations inherent in treating what is, in effect, chronic illness. They appreciated also the immensity of the struggle confronting psychiatry and medicine in fashioning a more effective approach to mental illness* in all of its manifestations.

The psychiatrist also is deeply affected by entering into close collaboration with his fellow physicians. First, he finds it necessary to simplify his language and to attach his concepts to the frames of reference which are accepted by his medical colleagues. Second, he learns that the best way of influencing the physician's behavior favorably is not by analyzing his motivations as much as by providing the physician with sufficient information about what is happening to him and the patient in the clinical situation. Thus, when he is frustrated by the patient's confounding responses, the physician may realize that he, like all other people, reacts to the stress of the situation with anger, withdrawal, excessive demands, indifference, or other involuntary stereotyped approaches. On the other hand, when they are given pertinent information, most physicians can develop more constructive and helpful therapeutic approaches. Thus, doctor and patient are visualized as capable of appropriate or inappropriate responses that are influenced by the adequacy of the information received from other people. Third, particularly in the advanced groups, by encouraging the physician-students to communicate their clinical experiences freely, the psychiatrist submits his findings to observations and conceptions that may conflict sharply with his own. He thus becomes able to examine his beliefs against data which he does not get ordinarily. In time this new experience may lead to valuable changes in psychiatric theory. Similarly, by becoming involved in how the nonpsychiatric physician helps patients who have emotionally-influenced disorders, the psychiatrist may learn to look at his own therapeutic role from a broader perspective. Thus, he may recognize that the main effect of "superficial" psychotherapy, as practiced by every physician, is to relieve severe stress and its disruptive involuntary defensive reactions in a limited area of experience. Therapeutic experiences as disparate as those in medicine, psychiatry, and physical rehabilitation may assume a unified character.[6]

The psychiatrist also may become aware that the distinctive feature of intensive psychotherapy and psychoanalysis is that they go beyond the individual situation and seek to provide the conditions by which the patient learns to behave more appropriately in more of the most important situations in his life most of the time.

Courses such as the one described here do not resolve the problems which confront medicine and behavioral science, but they do contribute toward an interaction which can only have beneficial effects for the involved professions, particularly for psychiatry and the other medical specialties. Up to now, these postgraduate programs have reached a relatively limited number of physicians, and an increasing number should become involved. It is hoped that this preliminary presentation will encourage many workers to take another look at this critical problem and to join in the exciting effort to construct a more comprehensive approach to the practice of medicine.

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* By mental illness is meant the behavior manifested as feeling, thoughts, or actions, which appear inappropriate to the situation in which the patient is observed, and is due to learned patterns of response or organic brain changes.

Vaginal Prosthesis for Control of Complete Urinary Incontinence

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IN 5 PATIENTS *with complete urinary incontinence due to neuromuscular pathologic conditions, fair to good control of the urine has been achieved with the use of an individually fitted vaginal prosthesis. The acrylic mould caused no ulceration of the vaginal mucosa or abnormal vaginal discharge. Its action of compressing the urethra against the symphysis pubis to control urine outflow is similar to sphincteric action.*

COMPLETE URINARY INCONTINENCE due to a neuromuscular pathologic condition has always been and remains a most difficult clinical problem to handle. The neurogenic bladder is devoid of sphincter action, and the retention of urine with overflow incontinence that is due to a vesical neck obstruction is present in most instances. This inability to empty the bladder voluntarily causes many adverse effects on the ureters and kidneys. In many instances this is the direct cause of the shortening of life of patients. The residual urine may be from 300 to 600 cc. or more. The bladder is typically trabeculated and presents evidence of a chronic cystitis.

To relieve this retention, some urologists perform a transurethral vesical neck resection.[1,2] In the patient with the neurogenic bladder, however, this operation will not correct the problem of incontinence but will prevent the development of serious sequelae of residual urine.

In 1907 Giordono reported a successful transfer of the gracilis muscle to obtain sphincter-type control about the urethra.[3] Very few surgeons have been able to gain control with this operation. The bulbocavernosus and pyramidalis muscles have been tried in like manner. In stress incontinence many types of operation have been devised which give fair to good results in the majority of cases. The Kelly plication first done in 1912[4,5] still is the operation most frequently performed to correct simple stress incontinence. The Marshall-Marchetti vesicourethral suspension procedure has proved quite successful in certain cases of stress incontinence.[6] The many fascial sling operations devised by Goebell,[7] Stoeckel,[8] Frangenheim,[3] Miller,[9] and Aldridge[10] may work when there is some urethral sphincter action.[3,11] The object of the sling is to reinforce the inefficient urethral sphincter. The operations are useless and should not be performed on patients with neurogenic bladders. Kegel[12] has done much to help control stress incontinence through strengthening the perineal and vaginal musculature with a definite exercise regimen. He has devised the Kegel perineometer.

In the female patient all methods of attempting to collect urine externally with various receptacles have been inadequate. The use of an indwelling catheter poses many well-known and serious problems such as the introduction of chronic infection and the development of calculi within the bladder. This lack of measures to control the release of urine has compelled the surgeon to perform more serious or radical procedures such

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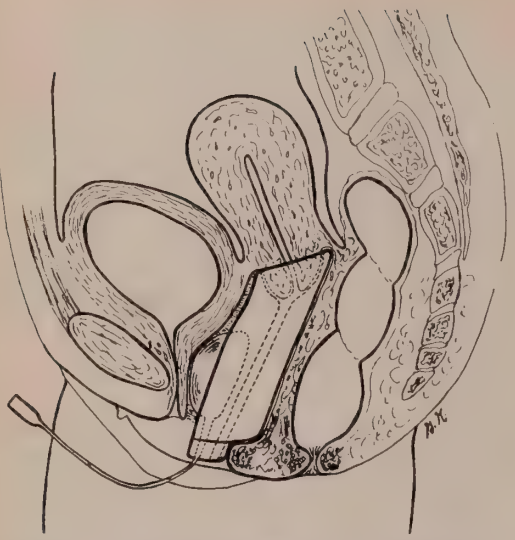

FIGURE 1. A vaginal prosthesis for control of incontinence in patients with neurogenic bladders.

as ureterocutaneous transplants and ileal loop urinary diversion operations.[13]

Method

In 5 patients with complete urinary incontinence due to neuromuscular pathologic conditions, fair to good control of the urine with the use of the vaginal prosthesis has been achieved. This prosthesis conforms to the general contours of the vaginal canal (Fig. 1). Its upper portion receives the cervix in the normal anatomic position within a hemispherical, convex cup as is demonstrated in the illustration. This portion is also cylindrical in form in the long axis.

The lower portion of this acrylic mould is wider in its transverse diameter than in the anteroposterior diameter. It contains a lacunal cavity, which receives a balloon. The opening of this cavity is on the anterior surface. When the balloon is inflated, it bulges out through this opening and compresses the urethra gently against the symphysis pubis.[14] The heel portion of the prosthesis rests on the natural anatomic shelf that is formed by the bulbocavernosus and the transversus perinei muscles at the posterior fourchet. The thick musculature and the integument of this region resist the posterior displacement of the vaginal prosthesis when the balloon is inflated. This positioning and design prevents the rotation of this insert. For normal control from 10 to 25 cc. of air are required to inflate the balloon and compress the urethra. The volume varies with the different sizes of the prostheses and the different capacity of each balloon cavity. These have been made to conform exactly to the patient's specific anatomy. Standardization into several general sizes may be possible after more experience has been gained with this method of therapy.

A brief résumé of the histories of 3 patients in whom the vaginal prostheses were used follows.

Case reports

Case 1. A thirty-eight-year-old married woman had intramedullary cord disease. She had developed a cord bladder with urine retention of 2,200 cc. A resection of the vesical neck was performed to relieve the retention. However, because she had no sphincter control, this resulted in complete incontinence. A vaginal plastic operation was performed but was not successful. The patient was seen, and the intravaginal prosthesis described was made for her. This gave her full control of her bladder content during the day and night. She was able to go about her normal routines without any difficulty. Prior to the use of the prosthesis, she had used small rolls of turkish towels to absorb the urine. She was followed for fourteen months, and no ulcerations or discharge occurred as a result of wearing the prosthesis, and her urinary control was good.

Case 2. A twelve-year-old girl had a congenital spina bifida lesion and a meningomyelocele.[15] She had a saddle area of anesthesia with urinary and rectal incontinence. When she was examined at the age of five years, she had a typical cord bladder with trabeculae and retention of urine. Her dribbling was that found with overflow incontinence. A resection of the vesical neck was done at a large clinic. This relieved the problem of urinary retention, but again since there was no sphincter action, urinary incontinence persisted. At nine years of age a gracilis muscle operation was done in an effort to control the incontinence. This failed. Through the years she had collected urine by using numerous layers of flannel diapers with very frequent changes. The skin about the perineal area became excoriated, fissured, and infected, requiring hospitalization several times a year for treatment.

Twelve months ago a prosthesis was made for her. This gives her excellent control of her bladder contents. She has no discomfort in wearing the prosthesis. The skin has healed and she no longer wears diapers for absorption. Her bladder capacity is now from 12 to 14 ounces. This enables her to sleep throughout the night without urinary leakage. During the day, she empties the bladder every three or four hours by simply deflating the balloon. The conduit incorporated in the prosthesis for menstrual flow functions well. She has no loss of control with walking or any moderate physical activity. An intravenous pyelogram study in October, 1960, showed normal findings. No ulceration of the vaginal mucosa and no abnormal discharge has developed with long use. She wears the prosthesis twenty-four hours per day and takes a cleansing vaginal douche about three times a week.

CASE 3. In 1953 a fifty-year-old married woman had a subtotal hysterectomy because of large fibroids. At this time she also had stress incontinence for which a Kelly plication operation was done. She did not have much relief following this procedure. In 1958 a Marshall-Marchetti vesicourethral suspension operation was performed. This second operation also did not aid in relieving the stress incontinence. She was not able to hold urine for more than one hour and had frequent accidents, especially when she was walking. A prosthesis was made for her. She feels that it gives good support, and she is now able to control the urine over four- to five-hour periods during the day.

Conclusion

The use of an especially designed vaginal prosthesis to control complete urinary incontinence has been described. This acrylic mould thus far has caused no ulceration of the vaginal mucosa and has given rise to no abnormal vaginal discharge. Its action of compressing the urethra against the symphysis pubis to control urine outflow is similar to sphincteric action. It keeps the urine in its normal habitat and helps rehabilitate these unfortunate patients without employing radical procedures that do not eliminate the need of externally applied collection receptacles. With more experience and study perhaps this prosthesis can be standardized and developed so that it may then be available for more general application. It always will, however, have to be fitted individually for all patients.

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The Role of Wine in the Treatment of Obesity

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To ACHIEVE a lasting and substantial loss of weight, rigid adherence to a very low-calorie diet is required. Unfortunately, as many obese subjects have learned, such adherence imposes heavy demands on both the body and the mind of the individual.

When tensions and anxieties are already present, these are generally magnified, with resulting threats to the success of the reducing plan. When these strains do not exist at the start, preoccupations connected with the overuse of food often lead to new anxieties which may become a serious obstacle to successful treatment.

There is little doubt that good results can be achieved when the treatment of obesity is based on the psychotherapy of these emotional difficulties. For the majority of obese patients, however, the time and the cost required by psychotherapy make it practically unavailable. Instead, various pharmacologic agents, such as bulk-producers, appetite-depressants, and tranquilizers, have often been prescribed to make low-calorie diets more acceptable. The indications for the use of such drugs and their respective assets and limitations have been widely discussed. In all cases, it appears that their administration requires close medical supervision, that they cannot be continued indefinitely, and that their usefulness is usually temporary.

Accordingly, an attempt was made to explore the possibility that wine, given in small amounts, might alleviate some of the anxieties and the hunger of obese subjects under prolonged treatment, thus making their reducing diets more tolerable and their weight loss more marked and lasting.

The use of alcoholic beverages in the diet of the obese is seldom recommended, probably because of the apparently high caloric content of these beverages.

While it is true that a gram of alcohol yields 7 calories, it should be noted that an ounce of the average American table wine yields only about 30 calories, and an ounce of the average American dessert wine yields only about 50. If ingested in moderation, for example in quantities of not more than 4 or 6 ounces daily, wine would hardly contribute to the caloric excesses of the obese.

It is needless to emphasize that a most careful investigation of the drinking habits of the obese individual is required prior to the inclusion of wine in his diet. Past or present alcoholic excesses of any kind represent definite contraindications to the dietary use of wine.

Materials and methods

SUBJECTS. All of the subjects were studied in New York and were private ambulatory patients.

A total of 35 individuals, 7 men and 28 women, participated in this study. The high proportion of women in the group does not necessarily indicate a higher incidence of obesity among women. Rather, it appears that more women than men in our culture are interested in losing weight, usually for esthetic rather than medical reasons.

All the subjects had sought medical care previously for their obesity, but without satisfactory results. Their experiments with treatment had usually been fitful and short.

No individual with a past history of alcoholic excesses was included.

Age. The respective ages of the subjects were as follows: twenty to twenty-four years, 3 women; twenty-five to twenty-nine years, 3 women; thirty to thirty-four years, 2 men and 2 women; thirty-five to thirty-nine years, 1 man and 7 women; forty to forty-four years, 2 men and 5 women; forty-five to forty-nine years, 5 women; fifty to fifty-nine years, 2 men and 1 woman; and sixty or more years, 2 women.

It will be noted that 20 of the 35 subjects were between the ages of thirty-five and fifty. This is the period, especially for women, when patients often experience anxieties over their weight and find difficulties in controlling it without help.

Overweight. The degree of obesity, according to the ideal body weight for a given height,* was as follows: 10 per cent or less overweight, 2 women; 11 to 20 per cent, 3 men and 8 women; 21 to 30 per cent, 1 man and 9 women; and 31 to 40 per cent, 2 men and 9 women. One man was found to be more than 60 per cent overweight.

Physical status. Uncomplicated obesity was observed in 2 men and 21 women. In 3 men and 3 women, the obesity was complicated by cardiovascular disease. In 2 men and 4 women, gastrointestinal disease was noted.

DIETARY RECORD. In the initial stages of any reducing treatment, experience has shown that patients find serious difficulties in complying rigidly with the dietary prescriptions. This is particularly true when the suggested daily diet includes not more than 1,000 to 1,200 calories.

In this study, all patients were told at the outset which diet was suited to their individual conditions. All were also told that an immediate and rigid adherence to this "ideal" diet was not expected. Nevertheless, each subject was asked to keep a careful record of his food intake and told that no criticism would be directed at him because of any dietary excesses.

ADMINISTRATION OF WINE. *Dinner use.* Within the framework of our culture, adherence to a rigid dietary program is reasonably easy until 5:00 or 6:00 in the afternoon. Most overweight individuals eat a light breakfast and enjoy it without much anxiety or feeling of deprivation. The same generally holds true for lunch. In the late afternoon, however, fatigue, hunger, and anxiety over hunger all become progressively acute, and the caloric content of dinner in the diet of the obese person is usually excessive. In many of them, after-dinner nibbling adds to the extravagant caloric intake.

AN INVESTIGATION *was made of the possibility that wine in small amounts might alleviate some of the anxieties and hunger of 35 individuals on reducing diets. Past or present alcoholic excesses of any kind constituted definite contraindications to the dietetic-therapeutic use of wine. In 27 patients the best results were obtained when wine was taken with dinner, with an average loss of 0.53 per cent of initial body weight per week, as compared with 0.26 per cent in a control period on the reducing diet alone. A moderate reduction of body weight occurred when wine was taken after dinner or before bedtime, and no detectable benefit was obtained with wine taken more than thirty minutes before dinner. In 8 subjects who demonstrated an urge to eat at night or engage in nighttime refrigerator raids and who likewise suffered from insomnia, the use of wine after dinner or at bedtime resulted in a decrease in frequency of refrigerator raids, a reduction in body weight, and an alleviation of insomnia in 5 subjects.*

For these reasons, attention in 27 patients was focused on the effects of wine taken before, during, and after dinner. Four experimental periods, including a control period, were studied in each subject:

1. Control: reducing diet with no wine or other alcoholic beverage.
2. Reducing diet with wine ingested from thirty to sixty minutes before dinner.
3. Reducing diet with wine ingested during dinner.
4. Reducing diet with wine ingested either from thirty to sixty minutes after dinner or before bedtime.

Several sequences of these four periods were used to minimize the possibility that one experimental condition might affect the following one.

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* In this study, "ideal" was considered the ideal mean weight of a person of medium frame, as given in the Tables of the Metropolitan Life Insurance Statistical Bulletin 24: 6 (June) 1943.

TABLE I. Effect of wine on average daily caloric intake

Case	Control Period		Wine Before Dinner		Wine With Dinner		Wine After Dinner	
	Calories	Per Cent	Calories	Per Cent	Calories	Per Cent	Calories	Per Cent
1	2,400	100	2,000	83	2,400	100	2,500	104
2	1,465	100	1,525	104	1,275	87	1,555	106
3	1,350	100	2,000	148	1,450	107	1,750	130
4	1,250	100	1,250	100	1,900	152	1,000	80
5	2,035	100	1,475	72	1,225	60	2,000	98
6	2,050	100	2,000	98	1,900	93	1,650	80
7	900	100	1,000	111	950	106	900	100
8	1,000	100	1,100	110	1,200	120	1,300	130
9	3,250	100	2,250	69	2,200	68	2,240	69
10	2,175	100	1,400	64	1,000	46	2,100	97
11	900	100	1,050	117	1,100	122	1,050	117
12	1,500	100	1,700	113	1,090	73	1,630	109
13	2,750	100	2,900	105	2,250	82	2,600	95
14	1,475	100	1,675	114	1,600	108	1,300	88
15	2,810	100	2,600	93	2,100	75	2,200	78
16	2,925	100	3,100	106	3,000	103	2,000	68
17	2,200	100	2,300	105	2,150	98	1,700	77
18	1,750	100	1,825	104	1,775	101	. . . *	. . .
19	1,900	100	1,270	67	1,130	59	1,510	79
20	1,425	100	1,750	123	1,000	70	1,500	105
21	1,890	100	2,000	106	1,450	77	1,700	90
22	2,100	100	1,900	90	1,500	71	2,200	105
23	1,600	100	1,800	112	1,700	106	1,400	88
24	1,000	100	1,200	120	1,000	100	1,200	120
25	2,400	100	1,600	67	1,100	46	2,150	90
26	1,950	100	2,250	115	1,050	54	2,000	103
27	2,230	100	2,135	96	1,890	85	1,950	87
Average	. . .	100	. . .	100.4	. . .	87.7	. . .	96.0

* Subject did not participate in this period.

The choice of wine, either table or dessert, was left to the individual subject. Each subject was advised to take approximately 3 ounces each day at the indicated time.

The total daily caloric intake; the caloric intake of the wine; the subjective feelings of fatigue, hunger, and anxiety before dinner; and the weight changes were determined for each subject in each period.

Bedtime use. In the other 8 subjects, the major problem appeared to be an overwhelming urge to eat after dinner and often during the night. All suffered from irresistible impulses to "raid the refrigerator." All likewise suffered from insomnia. In the study of these 8 individuals, only two periods were utilized:

1. Control: reducing diet with no wine or other alcoholic beverage.
2. Reducing diet with wine ingested before bedtime.

The caloric intakes, subjective feelings, and weight changes were noted for each subject.

Results

DINNER USE. In the first phase of this investigation, 26 of the 27 subjects participated for approximately five weeks apiece in each of the four periods. One subject failed to complete the fourth period.

Wine choice. During experimental period 2, with wine ingested before dinner, 15 subjects elected to use table wine and 12 chose dessert wine. During period 3, with wine ingested with dinner, 19 of the 27 subjects used table wine. During period 4, with wine consumed after dinner or before bedtime, 12 of the 26 subjects used table wine, and 14 selected a dessert wine.

No significant differences could be found in the relative effects of table wine and dessert wine on either the reduction of total caloric intake or the loss of weight.

Wine calories. The caloric value of the wines consumed ranged from 60 to 250 per day for each subject. For the overwhelming majority, however, the caloric value of the

TABLE II. Effect of wine on average weekly weight change (per cent)

Case	Starting Weight (Pounds)	Control Period	Wine Before Dinner	Wine With Dinner	Wine After Dinner
1	180	+0.16	−0.11	+0.06	0.0
2	180	−0.56	−0.61	−0.87	−0.50
3	160	−0.94	+0.62	−0.62	−0.44
4	154	−0.65	−0.32	0.0	−1.23
5	180	0.0	−0.56	−1.61	+0.28
6	195	0.0	0.0	+0.26	−0.51
7	177	−1.41	−0.85	−0.85	−1.13
8	178	−0.84	−0.17	−0.39	−0.28
9	180	+1.94	−1.22	−1.00	−1.33
10	205	+0.05	−0.98	−1.32	−0.05
11	184	−1.68	−1.09	−1.14	−1.30
12	200	−0.91	−0.75	−0.85	−0.80
13	193	+0.78	+0.67	−0.52	+0.52
14	190	−1.32	−1.06	−0.47	−0.47
15	240	+0.42	+0.42	−0.67	−0.42
16	280	+0.36	0.0	−0.36	−0.71
17	165	0.0	+0.91	+0.61	−1.03
18	167	−0.54	−0.48	−0.48	. . .*
19	135	−1.11	−0.74	−0.74	0.0
20	144	0.0	+0.07	−0.35	+0.14
21	150	+0.07	+0.13	−0.20	−0.47
22	185	0.0	−0.22	−0.11	0.0
23	140	−0.71	0.0	0.0	−0.71
24	210	−0.81	−0.24	−0.71	−0.24
25	169	+0.59	0.0	−0.89	+0.89
26	189	0.0	+0.26	−1.06	+0.26
27	163	0.0	−0.12	−0.25	−0.18
Average	. . .	−0.26	−0.23	−0.53	−0.37

* Subject did not participate in this period.

wine was kept between 90 and 120, representing about 3 to 4 ounces of table wine daily.

Effect on total caloric intake. The effects of the ingestion of wine at about the time of the dinner meal are indicated in Table I, which presents the average daily intake, as related by the subject, as a percentage of the intake during the control period.

During the control period, with no wine consumed, it is evident that 6 of the 27 subjects achieved their lowest daily caloric intake.

In period 2, with wine consumed before dinner, no significant caloric reduction was reported. Of the 27 subjects, 11 maintained approximately the same intake (within 10 per cent of control values), 10 increased their intake, and 6 reduced it. The average daily caloric intake for the group was the same as that for the control period.

In period 3, with wine consumed with dinner, the most substantial reduction in daily caloric intake was reported, with the average for the group being reduced to about 88 per cent of control values. During this period, 10 subjects maintained approximately the same intake, 3 increased it by more than 10 per cent, and 14 reduced it by more than 10 per cent. It was noted that 4 subjects claimed that they had reduced their dietary intake to less than 60 per cent of control values, and 2 of these reportedly reduced it to less than 50 per cent.

In period 4, with wine consumed after dinner, a slight reduction in caloric intake was reported, with the average for the group reduced to 96 per cent of control levels. In this period, 12 of 26 subjects maintained about the same caloric intake, 4 increased it by more than 10 per cent, and 10 reduced it by more than 10 per cent.

Effect on weight. Actual changes in body weight are presumably more accurate and of more significance to most patients than reported changes in caloric intake. These weight changes are shown in Table II. It is apparent that some but not all subjects actually lost weight most readily in the periods during which they reported the lowest caloric intake.

During the control period 1, when no wine was consumed with a reducing diet, 9 of the 27 subjects demonstrated their greatest weekly weight loss. For the group, the average loss was 0.26 per cent per week of original body weight. In this period, 9 subjects essentially maintained their original weight, 6 gained, and 12 lost.

No significant difference was noted during period 2, when the subjects utilized a reducing diet with wine taken before dinner. The average weight loss was 0.23 per cent per week of original body weight. Only 2 of the 27 subjects achieved their maximum weekly weight loss during this period. Five of the subjects maintained their original weight, 6 gained, and 16 lost.

The maximum weight loss was recorded during period 3, when wine was ingested during dinner. The average weight loss was 0.53 per cent per week of original body weight, with 10 of the subjects achieving their maximum weight loss during the period. Of the 27 subjects, 3 maintained their original weight, 2 gained, and 22 lost.

In period 4, with wine consumed after dinner, the average weight loss was 0.37 per cent per week of original body weight. Six subjects noted their maximum weight loss during these conditions. Of 26 subjects, 4 maintained their original weight, 5 gained, and 17 lost.

In some instances, the loss of weight was substantial and gratifying to the individuals. One subject was a forty-four-year-old woman (Case 9), 5 feet 5 inches tall, who weighed 180 pounds at the start of the program. During the control period, her average daily intake was 3,250 calories, and her weight increased by 3.5 pounds a week. Using approximately 120 calories of a table wine daily, she reduced her total intake to about 2,200 calories daily, lost an average of 2.2 pounds per week during period 2, 1.8 pounds per week during period 3, and 2.4 pounds per week during period 4, and finally reduced her weight to 134 pounds. Thereafter, she continued to maintain her new weight by taking wine when she was hungry or fatigued.

Another subject, a thirty-six-year-old man, 5 feet 9 inches in height and weighing 200 pounds (Case 12), averaged 1,500 calories per day during the control period, during which he lost an average of 1 pound per week. Adding wine to his basic reducing diet, he lost 1.5 pounds per week during period 2, 1.7 pounds per week during period 3, and 1.6 pounds per week during period 4, finally reaching the weight of 165 pounds.

Effect on tension. The study of fatigue, hunger, and anxiety was based on observations limited to the hours preceding dinner. It is well known that at this time most obese individuals on a reducing diet experience discomfort.

Fatigue before dinner was present in 22 of the subjects. It was alleviated by wine in 15 of these individuals. Hunger and anxiety also were present in 22 subjects and were relieved by wine in 12 of them. In general, the relief of these emotional states was most evident in those patients who simultaneously were showing the greatest weight losses.

Later weight changes. After the completion of the formal investigation, with its dietary records, most of the subjects, 25 of the 27, were followed informally for periods varying between two and twenty-six weeks. Of these individuals, 5 regained weight, 9 maintained their weight at about the new levels, and 11 continued to lose weight. All of these subjects continued to use wine either regularly or irregularly after the completion of the dietary records.

BEDTIME USE. The 8 subjects whose overeating was marked by frequent nighttime refrigerator raids were followed only during a control period and a period in which they took wine after dinner or immediately before bedtime.

Five of these subjects elected to drink dessert wine, while the other 3 used table wine. The caloric value of the wine ranged between 120 and 150 per day for each subject.

As shown in Table III, 5 of the subjects demonstrated a decrease in the number of refrigerator raids per week and likewise achieved a greater loss of weight. For the entire group, there were 5.7 raids per week when wine was used, as compared with 7.3 in the control period, and there was a weight loss of 0.46 per cent per week of the initial

TABLE III. Effect of wine on nightly refrigerator raids

Case	Starting Weight (Pounds)	Average Weekly Weight Change (Per Cent)		Average Weekly Number of Raids	
		Control	Wine	Control	Wine
28	199	−0.20	−0.35	5.5	3.0
29	180	0.0	−0.62	4.0	3.8
30	175	+0.57	−0.06	14.0	15.0
31	160	−0.44	−0.37	5.0	6.0
32	167	0.0	−0.36	11.0	6.0
33	218	−0.46	0.0	7.0	7.0
34	163	−0.80	−1.10	7.0	3.0
35	180	−0.56	−0.83	5.0	2.0
Average	...	−0.23	−0.46	7.3	5.7

weight as compared with a loss of 0.23 per cent per week in the control period.

In the 5 patients who experienced a decrease in the incidence of night raids, there was also an improvement in insomnia.

Of the 3 subjects who continued their nighttime eating, 2 nevertheless achieved a modest reduction in weight, and the third maintained his weight at about the initial level.

Summary

In an attempt to explore the possibility that wine given in small amounts might facilitate weight loss in obese patients, the following observations were made:

1. In most of 35 obese subjects on a reducing diet, the ingestion of wine with or after dinner resulted in a lowered daily caloric intake and a gradual but consistent loss of body weight.
2. In a series of 27 subjects on a reducing diet, the best results were obtained when wine was taken with dinner, when an average loss of 0.53 per cent of initial body weight was achieved per week, as compared with 0.26 per cent in a control period on the reducing diet alone.
3. A moderate reduction of body weights was noted when wine was taken after dinner or before bedtime.
4. Wine taken more than thirty minutes before dinner did not prove to have any detectable value in the treatment of obesity.
5. In a series of 8 obese subjects who demonstrated an urge to eat at night or engage in nighttime refrigerator raids, and who likewise suffered from insomnia, the use of wine after dinner or at bedtime resulted in a decrease in the frequency of nightly refrigerator raids, a reduction in body weight, and an alleviation of insomnia in 5 subjects.
6. No differences were detected between the effects of table wines and those of dessert wines in these studies.
7. Past or present alcoholism or alcoholic excesses of any kind represent definite contraindications for this dietetic-therapeutic use of wine.

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Clinicopathologic Conference

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Discussed by HERBERT S. KUPPERMAN, M.D., and
ISRAEL DIAMOND, M.D.

Sexual Precocity in a Four-Year-Old Boy

Case history

U Dong, M.D.: A forty-five-month-old boy was admitted to the hospital because of progressive enlargement of the penis and the appearance of dark pubic hair during the previous nine months. His voice had remained unchanged.

He weighed 6 pounds 7 ounces at birth. During the first five months of his life he had had five hospital admissions for diarrhea and failure to gain weight. On the fifth admission a diagnosis of congenital heart disease was made.

At six months of age he was admitted for an intensive study. He was poorly developed and poorly nourished, weighing 10 pounds 8 ounces. The heart was enlarged to the left. There was a thrill over the pulmonic area, and a continuous "machinery-like" murmur transmitted to the neck. An electrocardiogram showed more strain than normal on the right side of the heart. A fluoroscopy revealed a large pulmonary artery. At twenty-four months of age he weighed $22^1/_2$ pounds and was 35 inches tall. The blood pressure was 96/60. He was thin, sweaty, irritable, and small for his age. After a re-evaluation of his cardiac status, an intrathoracic operation was performed. His postoperative course was uneventful, and he was discharged in good condition. He apparently continued in good health until the onset of premature genital development at three years of age.

When he was admitted at forty-five months of age, he weighed 48 pounds and was 44 inches tall. He was well developed, well nourished, and overly large for his age. The physical findings included a large penis with a normally situated urethral meatus and a moderate amount of coarse pubic hair. The testes could not be palpated in the scrotum or inguinal canals.

The hemoglobin was 11.8 Gm. per 100 ml. The red blood cell count was 4.2 million. The white blood cell count was 9,000 with 19 per cent neutrophils, 70 per cent lymphocytes, 7 per cent monocytes, 3 per cent eosinophils, and 1 per cent basophils. The blood pH was 7.45. The blood carbon dioxide was 20.7 millimols per liter. The chlorides ranged from 99 to 106 mEq., potassium 5.9 to 6.5 mEq., and sodium 134 to 142 mEq. per liter. The urinary 17-ketosteroids were 2.5 mg. per twenty-four hours. His bone age by x-ray determination was five years.

A laparotomy with a complete exploration was performed. Following the operation there was considerable nausea, vomiting, and abdominal distention which disappeared abruptly after the intravenous administration of Solu-Cortef. He was discharged with medication.

One month later the urinary 17-ketosteroids were 1.7 mg. per twenty-four hours.

He was readmitted at forty-nine months of age. At this time he weighed 50 pounds and was 47 inches tall. The blood pressure was 100/70. There were no complaints except for some recent bouts of priapism. His cardiac status was normal; there was no cardiac enlargement, and no murmurs were heard. The blood urea nitrogen was 11 mg. per 100 ml. The carbon dioxide was 19.5 millimols per liter, and chlorides 118 mEq., potassium 5.5 mEq., and sodium 138 mEq. per liter. The urinary 17-ketosteroids were 2.2 mg. per twenty-four hours. His medication was increased.

Six weeks later the urinary 17-ketosteroids were 0.1 mg. per twenty-four hours.

He was readmitted to the hospital at fifty-three months of age. He now weighed $53^{1}/_{2}$ pounds and was $47^{1}/_{2}$ inches tall. A second abdominal operation was performed. The postoperative course was uneventful. At fifty-four months of age the penis measured 7 cm. long and 2 to 3 cm. wide in its flaccid state. Chemical studies of the blood gave values comparable with those previously obtained. In addition, the serum calcium was 6.3 mEq. per 100 ml., phosphorus 4.7 mg., and alkaline phosphatase 2.4 Bodansky units. His radiographic bone age was eleven years. The genetic sex was determined at this time.

Discussion

Herbert S. Kupperman, M.D.*: Despite the presence of a number of discrepancies or contradictions, it is obvious that the patient must be characterized as one with sexual precocity. The following clinical categories associated with sexual precocity must be considered in the differential diagnosis:

1. Constitutional sexual precocity
2. Sexual precocity due to isosexual neoplastic changes of the gonads or adrenals
3. Female hermaphroditism associated with adrenocortical hyperplasia
4. Adrenal gland neoplasia
5. Central nervous system injury, disease, pineal gland tumor, or space-occupying tumor in the area of the mid-brain
6. Exogenous steroid therapy to the mother during her pregnancy
7. A masculinizing tumor of the mother during her pregnancy.

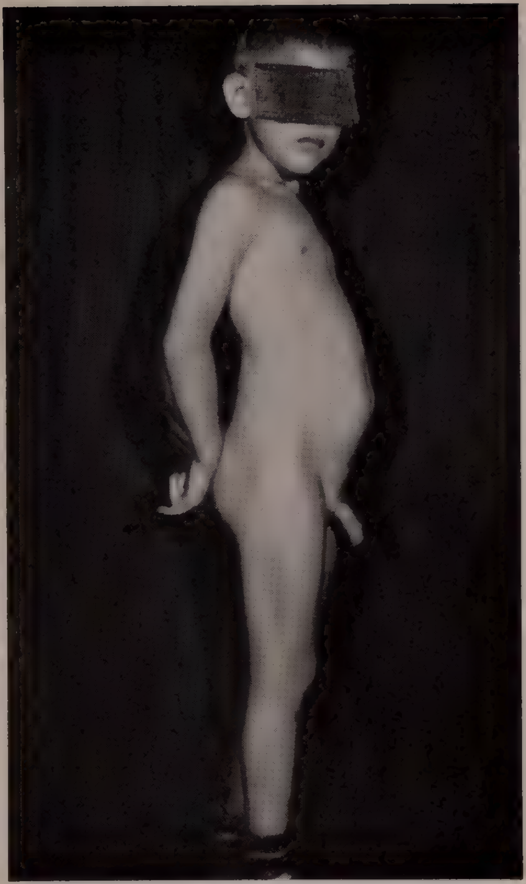

FIGURE 1. Patient at fifty-four months of age.

This list may be whittled soon to one or two possible diagnoses. However, before eliminating the unlikely possibilities, it would be well to review some of the changes which took place during the child's neonatal development, as well as the physical characteristics during the first five years of his life.

During the first five months of his life the infant did poorly with respect to his development and nourishment. He was subject to repeated bouts of diarrhea. This represents an important clinical point and offers a clue

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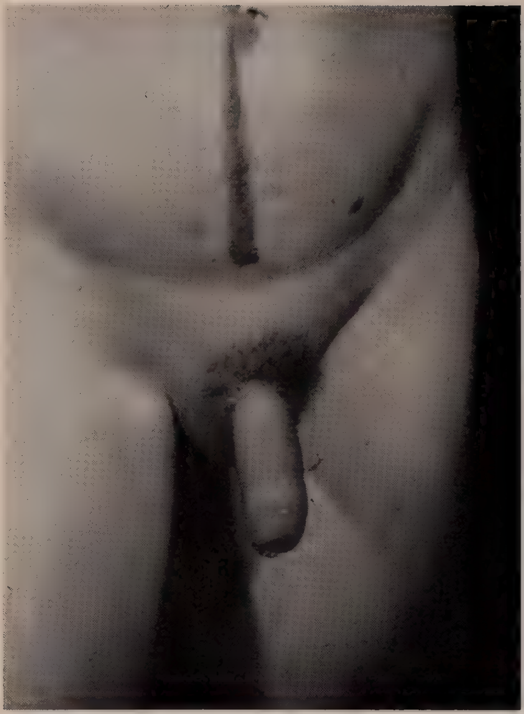

FIGURE 2. Note pigmentation of the abdominal scar.

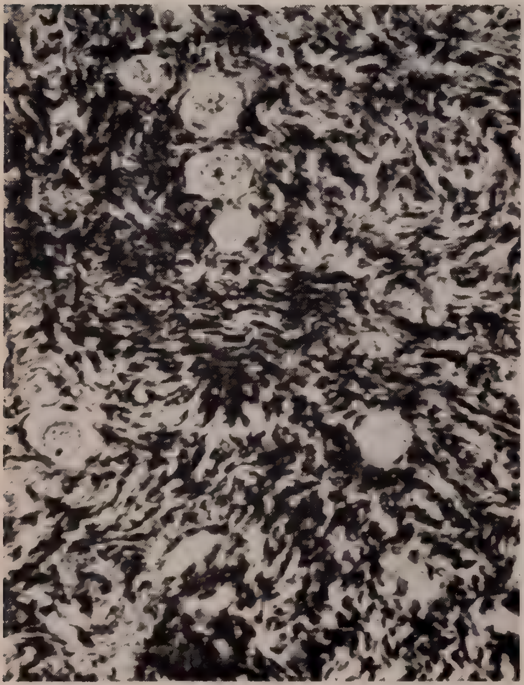

FIGURE 3. Gonadal biopsy at first laparotomy showing typical ovarian stroma and primordial follicles.

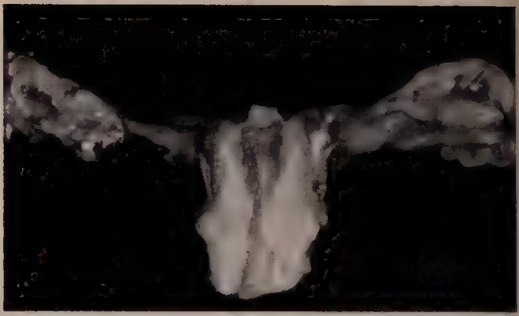

FIGURE 4. Specimen obtained at second laparotomy. The uterus has been opened to show the thickened, slightly hemorrhagic endometrium.

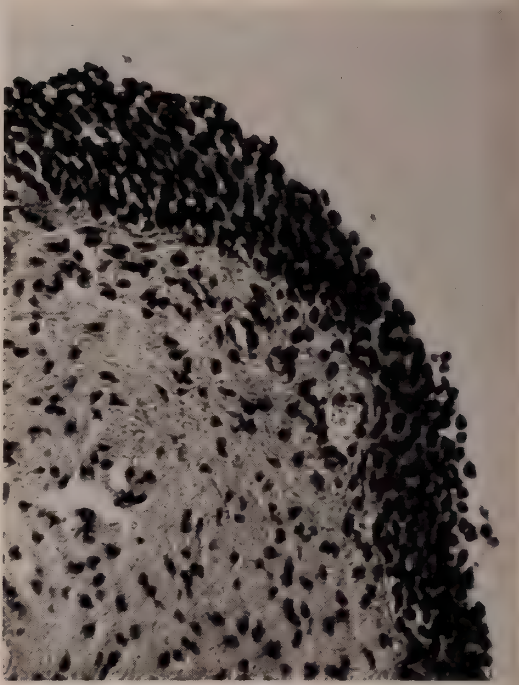

FIGURE 5. The characteristic hyperchromatic transitional epithelium of the urogenital sinus.

as to the most probable diagnosis in light of his further progress at the age of three or four years. At the age of twenty-four months the patient was still underdeveloped and was described as being sweaty and irritable. In addition, it was noted that his blood pressure was low. An intrathoracic operation was done because of a continuous machinery-like murmur and cardiac enlargement. Following successful surgery, the patient apparently thrived and presented

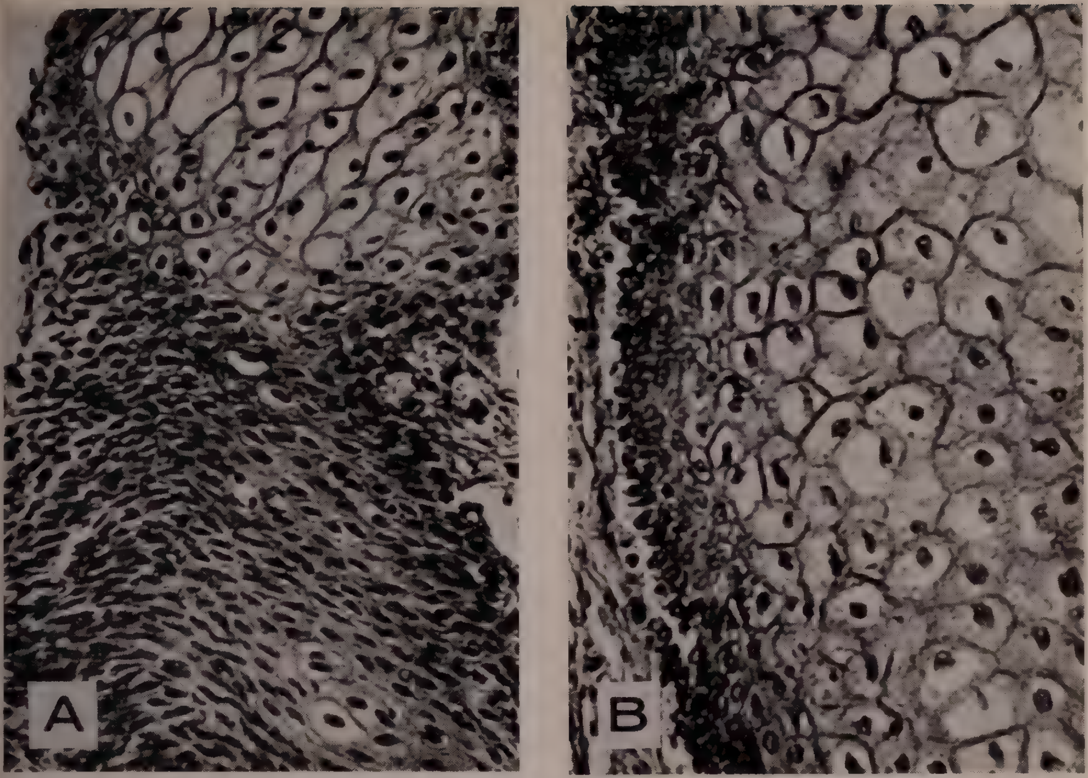

FIGURE 6. (A) The abrupt transitional zone between the urogenital sinus and the vaginal epithelium. (B) The endocervical epithelium showing marked glycogen filling indicative of estrogen stimulation.

no medical problem until sexual precocity developed at three years. At the age of forty-five months sexual precocity was clearly apparent and was expressed by an enlargement of the phallus associated with bilateral cryptorchism. The somatic development was considerably advanced. No comment is made regarding the pigmentation of the scrotum. In view of these findings, one now can rule out the possibility of constitutional sexual precocity. It would be unreasonable to expect an infant with such a diagnosis to have bilateral cryptorchism. At the same time and for the same reason, it would be logical to discard the diagnosis of a central nervous system lesion as a factor in the sexual precocity. In such patients the gonads would be present in the scrotum and would play a role in the child's development. However, at this time, the possibility of a neoplasm of the gonads or adrenals still cannot be eliminated.

The next most important step in a diagnostic evaluation would be to determine the nuclear sex chromatin pattern by examining the polymorphonuclear leukocytes in the peripheral blood or squamous cells from the buccal mucosa. The chromatin pattern is obtained to establish the possibility of female hermaphroditism associated with adrenocortical hyperplasia. At this point we are faced with inadequate or incorrect information. The 17-ketosteroid level reported in the protocol is rather confusing, particularly since the child's bone age definitely was advanced. Normally, an infant will excrete about 0.5 to 1 mg. of 17-ketosteroids per twenty-four hours per year of life. Thus, the values presented must be considered as being normal. If we assume that the reported value of 17-ketosteroids is in error, the advancement of bone age associated with sexual precocity in an apparent male with a scrotum devoid of testes suggests that the most likely diagnosis is that of female hermaphroditism associated with the adrenogenital syndrome. A positive chromatin test would be of the utmost importance to support this diagnosis. The adrenogenital syndrome would explian some of the earlier clinical features which the patient has presented. One must presume, then, that the chromatin pattern in this child would be positive, that is, female.

Before discussing some of the basic disturbances in the enzyme systems in this disease, other etiologic possibilities leading to sexual precocity should include the possibility of cryptorchid testes with a Leydig cell tumor. The possibility of a neoplasm playing a role in the patient's symptomatology may be eliminated promptly by obtaining the results of a urinary pregnanetriol test. This would be most informative, since an elevated 17-ketosteroid associated with a normal pregnanetriol would point either to an adrenal or ovarian neoplasm or, rarely, to those patients with a profound salt-losing adrenogenital syndrome. This latter possibility would be remote, since the child survived the early neonatal period without supplementary salt or adrenocortical hormone therapy. Normally, urinary pregnanetriol is found to range from 0 to 1.8 mg. per twenty-four hours in children and adults alike. Values significantly elevated above this level would be commensurate with the adrenogenital syndrome.

Why is the pregnanetriol elevated, and just what are the metabolic defects in patients with the adrenogenital syndrome? The metabolic defect appears to be inherited as a recessive character. The major defect lies in the adrenal cortex and is concerned with the process of hydroxylation, a process which is essential for normal steroid synthesis. The defect may be one of a deficiency of 17-alpha, 21-, or 11-beta hydroxylation. Wherever the defect lies, a reduced amount of hydrocortisone is synthesized, since some of its vital precursors are not formed completely. The site of the defect in most patients is at the 21 position. As a result of a diminished hydrocortisone output, an increased secretion of pituitary adrenocorticotropic hormone (ACTH) occurs. The elevated ACTH then stimulates the adrenal cortex excessively so that it becomes hyperplastic. Since the defect still persists, little or no hydrocortisone is produced. However, the zona reticularis is stimulated excessively and will synthesize excessive amounts of androgenic steroids or 17-ketosteroid precursors. These substances are responsible for the virilization of patients with the adrenogenital syndrome as well as for the irregular menses, anovulatory cycles, or amenorrhea that may occur.

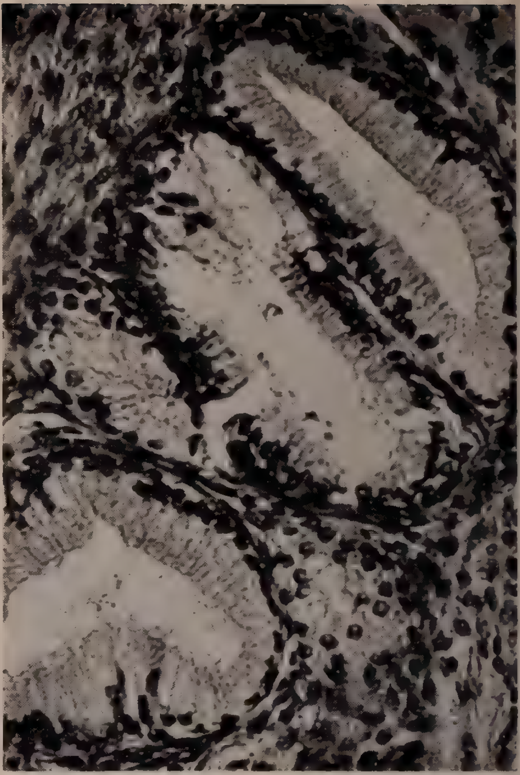

FIGURE 7. Hyperactive mucin secreting glands of the endocervix.

The increase in pregnanetriol is due in part to the excessive amount of 17-alpha hydroxyprogesterone that is being produced. Pregnanetriol is the principal metabolite of 17-alpha hydroxyprogesterone. If 17-alpha hydroxylase is absent, a defect in hydroxylation at the 17 position would occur, and the 17-ketosteroid excretion level would be increased, but there would be little or no elevation in the pregnanetriol excretion. In these infants a profound salt-losing syndrome may prevail. Unless mineralocorticoids are administered to such pa-

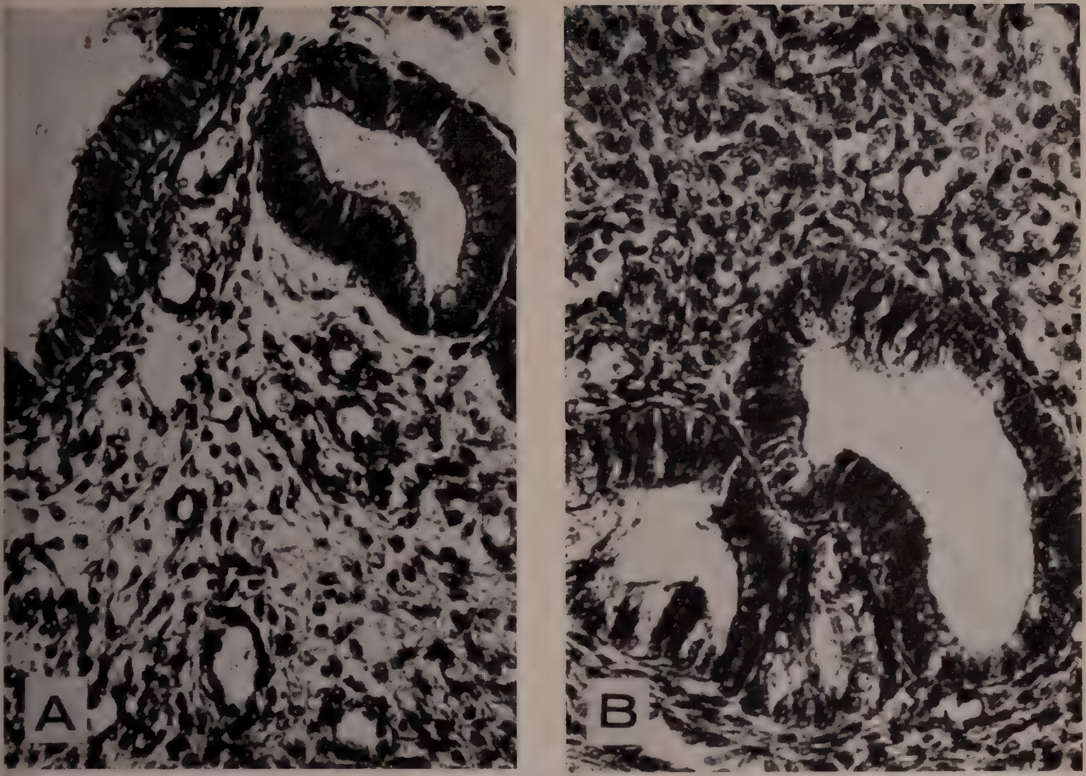

FIGURE 8. (A and B) Superficial and deep endometrium showing proliferating glands and a cellular edematous stroma.

tients, they may succumb. A defect of 11-beta hydroxylase also can result in a modified salt-losing syndrome. This is not so profound as that noted in the patients with 17-alpha hydroxylase defects.

If this patient was one with female hermaphroditism due to adrenocortical hyperplasia, both the urinary pregnanetriol and 17-ketosteroid should be elevated markedly. The laboratory data offered in the history are not helpful on this point. In the history, another factor favoring female hermaphroditism is the fact that at the time a laparotomy was done, the patient had to be maintained on intravenous hydrocortisone because of shocklike blood pressure levels during and following the surgery. This implies an adrenocortical insufficiency of the Addisonian type which is the usual picture that one sees in patients with the adrenogenital syndrome of the congenital type. Indeed, the dehydration which was present at the patient's birth and during the first six months of his life supports the possibility of the adrenogenital syndrome, and the failure to thrive might not have been due primarily to the cardiac lesion. In such patients, the neonatal period may be very critical, and they may die, particularly if they develop an intercurrent infection of the respiratory tract. This is attributed to the relative selective adrenal insufficiency due to decreased glucocorticoid levels.

Another possibility that must be considered is that the child's mother may have taken androgenic steroids during her pregnancy and thereby masculinized the external genitalia of a normal female. This is highly remote, since if this were so, the size of the patient's phallus would not have increased following his operation.

There are several interesting aspects of this syndrome which are worthy of mention. First, there was no comment made as far as hirsutism is concerned. This also would fit into the diagnosis of the adrenogenital syn-

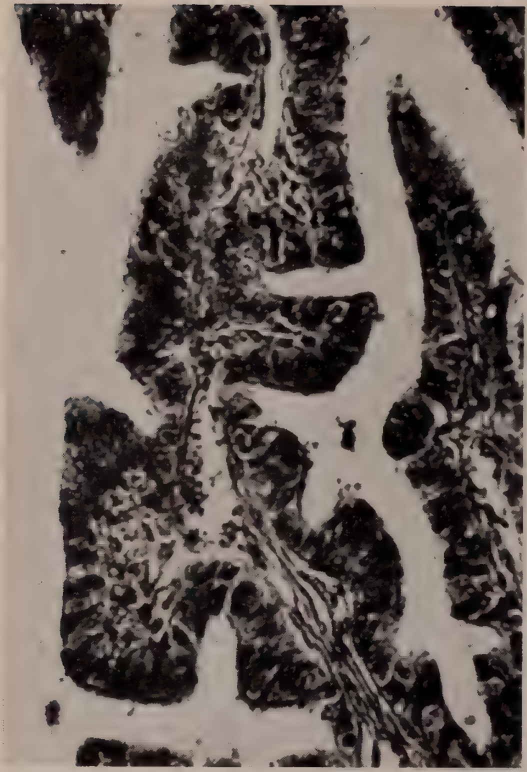

FIGURE 9. Fallopian tube showing active tall columnar epithelium.

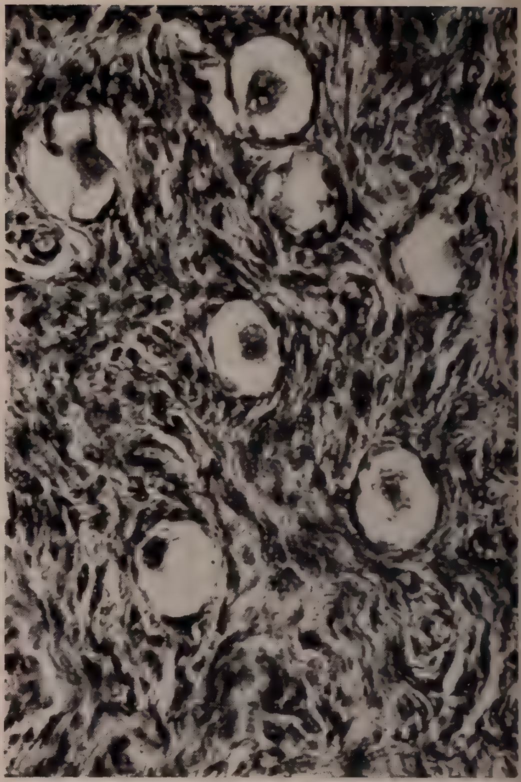

FIGURE 10. Typical cortical ovarian stroma with primordial follicles.

drome since many of these children are not hirsute, despite their high androgen output as measured both by the elevated 17-ketosteroid and phallic enlargement. The hirsutism usually becomes more apparent after puberty or after adulthood has been attained.

The question, of course, must be raised as to how this child should be brought up. Since he was much beyond the eighteen-month age where a reversal of sex may be achieved without adverse effects on the psyche, it would have been very difficult to raise this child as a female. It is most likely that the patient has an intact uterus and ovaries and probably would begin to menstruate while being maintained on corticoid therapy after the age at which puberty normally would occur. It is for this reason that it will be advisable to remove the uterus and ovaries in toto and to bring the child up as a male, his present sex of rearing. Corticoid therapy may be administered up until the time of puberty to permit normal growth and bone maturation to take place. After puberty the corticoid therapy may be discontinued, and endogenous adrenal androgens should be permitted to express their full androgenic effect and maintain secondary sexual characteristics. Obviously, such a patient in his assigned sex will be entirely infertile.

Mardoqueo I. Salomon, M.D.: Virilization and pubertas praecox in prepubescent females also has been reported with ovarian tumors, such as arrhenoblastoma and masculinovoblastoma, even rarely with thecomas, and with such quasi-neoplastic lesions as hyperthecosis. How can one distinguish between adrenal hyperplasia and an ovarian lesion in this context?

Dr. Kupperman: The most useful single laboratory test is urinary pregnanetriol which is almost invariably elevated in adrenal hyperplasia unless there is a failure to hydroxylate at the 17 position. I have never seen the pregnanetriol elevated in an ovarian lesion. Also, in adrenocortical hyperplasia,

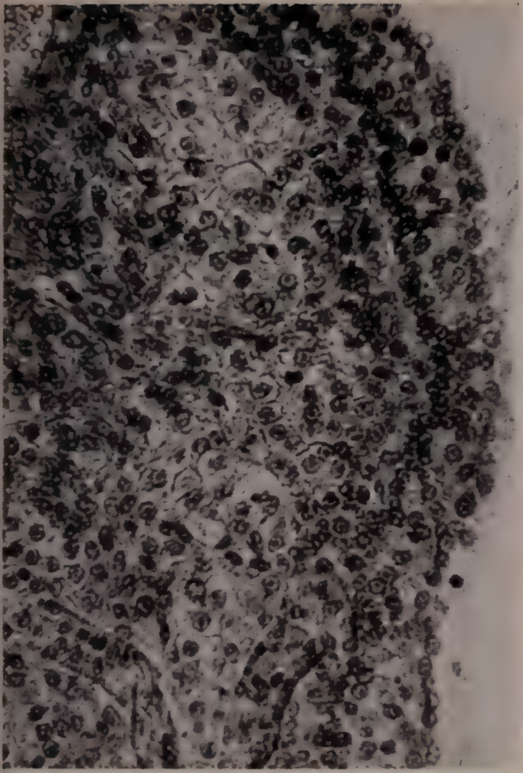

FIGURE 11. Lining of a cystically expanded follicle showing laminated granulosa cells.

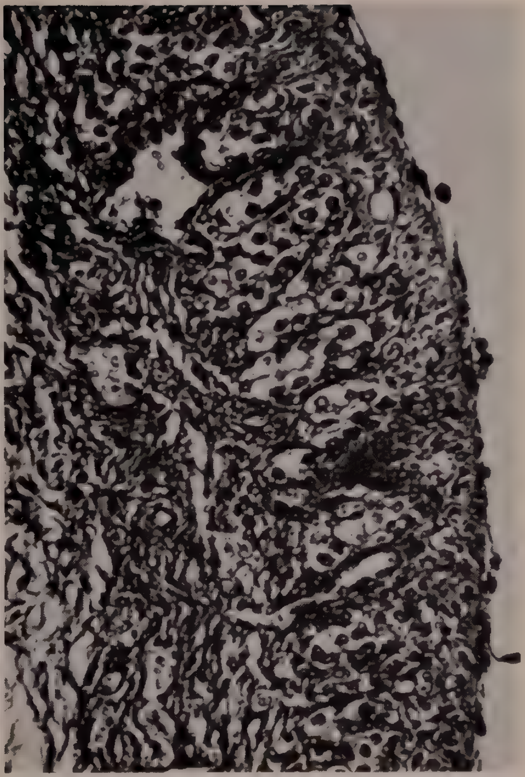

FIGURE 12. The cordlike arrangement of theca interna cells around some of the cystically expanded follicles.

the 17-ketosteroid level will rise with ACTH stimulation and will be suppressed with cortisone. However, if the adrenogenital syndrome is due to an adrenal carcinoma, the lesion may be sufficiently autonomous so that there is no response or only a slight response to provocative or suppressive tests.

Marcel Tuchman, M.D.: What do you think was done or found at the first exploratory operation?

Dr. Kupperman: I would infer that at the time of the laparotomy essentially normal female internal genitalia were found and that the adrenal region was explored for the possibility of a tumor. I also would infer that no tumor was found, and therefore, it was decided to manage the patient by cortisone suppression.

Perry Berg, M.D.: How do you account for the progression of the signs of precocity despite effective cortisone suppression?

Dr. Kupperman: The 3-inch increase in height between forty-five and forty-nine months was probably due to an inadequate dosage of cortisone. When the cortisone was increased, the child grew only one-half inch between forty-nine and fifty-three months of age. The weight increase is not very impressive and is a less sensitive index. I am disturbed by the report of an increase in the bone age from five to eleven years during this eight-month period, but in the absence of x-ray films I cannot really make a constructive comment on this point.

Clinical diagnosis

Adrenogenital syndrome

Dr. Kupperman's diagnosis

Adrenocortical hyperplasia with female pseudohermaphroditism

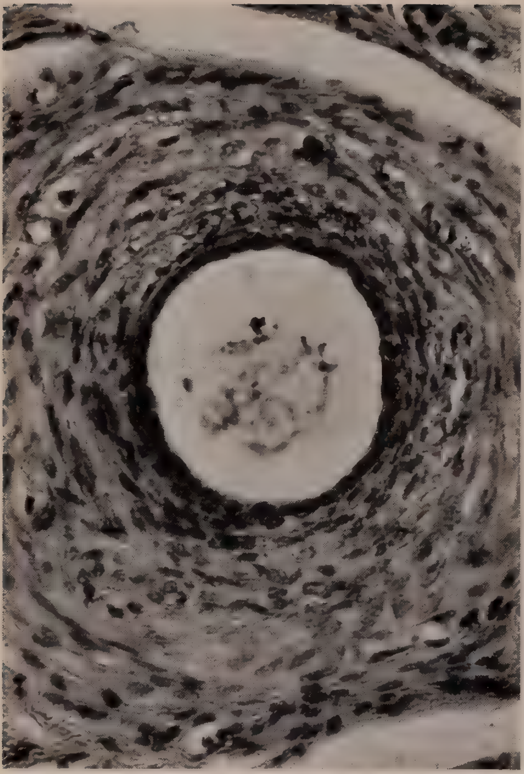

FIGURE 13. A cross section through a wolffian duct remnant lying subjacent to the fallopian tube.

Pathologic report

Israel Diamond, M.D.[*]: As usual, Dr. Kupperman has given us a brilliant analysis of the clinical and endocrinologic aspects of the case, and needless to say, has provided us with the proper diagnosis. We may begin by looking at the patient as he was photographed after the second operation (Fig. 1). The precocious features are the body habitus and muscular development, the enlarged phallus, and the pubic hair (Fig. 2). Worthy of note is the Addisonian-like pigmentation of the abdominal scar. The nuclear sex-chromatin pattern of this patient was female, and the first operation furnished bioptic material from both gonads consisting of immature ovarian tissue with many primordial ova (Fig. 3). At the first laparotomy the surgeon had no difficulty in identifying normal female external genitalia. He also palpated the adrenal glands, which were enlarged.

It is pertinent to locate this case in time, since the management of the adrenogenital syndrome is different today. This patient was seen in 1952 at which time many clinicians still believed that the genetic sex should be the major determinant. Indeed, it was suggested to the parents that the child be raised as a female. The suggestion was received with dismay and horror. In their wisdom the parents appreciated the social penalties of such a reversal to themselves and to their child far more than the well-meaning clinicians. It was only on the parents' insistence that castration was performed so that the child could continue to be raised as a boy.

Following the first laparotomy the child received hydrocortisone therapy but in an inadequate dosage, as demonstrated by the 17-ketosteroid levels. Ultimately, a proper dosage was arrived at, and the urinary 17-ketosteroids were reduced to 0.1 mg. per twenty-four hours. The initial value of the 17-ketosteroids reported in the protocol is much too low for the adrenogenital syndrome caused by congenital adrenocortical hyperplasia. An investigation at the time revealed a common laboratory error. The extraction of the urine with a volatile solvent may yield a frothy interface. Some technologists need to be told which fraction contains the steroid. In this instance the technician discarded the froth and a good deal of the steroid with it.

The castrating operation yielded an immature uterus, tubes, ovaries, and the upper portion of the vaginal canal (Fig. 4). The latter was continuous with the proximal portion of a urogenital sinus. The urogenital sinus was lined by nonglycogenated, compact, transitional epithelium (Fig. 5) as seen in congenital rectovaginal and rectovesical fistulae. There was an abrupt transition from the sinus epithelium to the well-glycogenated, estrogen-stimulated squamous epithelium (Fig. 6A) of the vagina, and the same epithelium was found on the endocervix (Fig. 6B). Continuing up the genital canal, we found an endocervix lined by actively mucin-secreting columnar epithelium (Fig. 7), much in excess of that seen in the juvenescent cervix. The body of the uterus

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[*] Director of Laboratories, Lutheran Medical Center; Associate Professor of Pathology, State University of New York Downstate Medical Center.

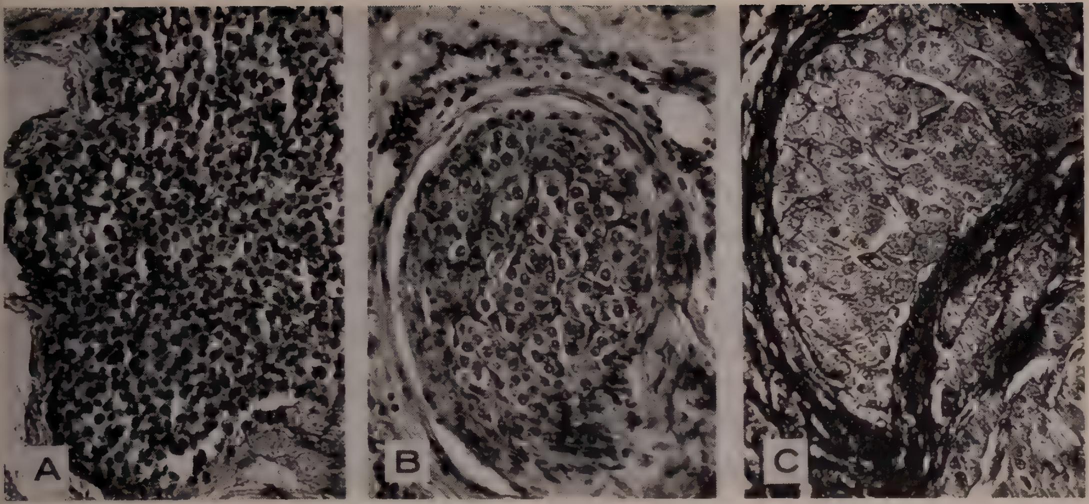

FIGURE 14. (A, B, and C) Typical ectopic adrenal cortical nodules from the ovarian hila and the broad ligaments. Note the variation in cell size. The cells in (C) are identical with those seen in a congenitally hyperplastic adrenal cortex.

was lined by a grossly hyperplastic endometrium (Fig. 4) showing microscopically an increase in stroma and proliferating glands (Fig. 8). The same succulent epithelial appearance continued into the fallopian tubes (Fig. 9) wherein the fronds were draped by tall collumnar cells, obviously stimulated by estrogenic substances.

The ovaries showed numerous primordial follicles (Fig. 10) and cystically expanded follicles, many of which were lined by thickened layers of granulosa cells (Fig. 11). We were intrigued by a number of expanded follicles exhibiting a regular cord-like arrangement of cells (Fig. 12), somewhat reminiscent of the disposition of hyperplastic theca interna in cases of the polycystic ovary syndrome. However, one sees the same configuration in normal juvenile ovaries as well. The broad ligaments contained well-formed wolffian duct remnants (Fig. 13) and a considerable number of accessory adrenocortical nodules, also present in the ovarian hila. There was considerable variation in their morphology (Fig. 14). Some nodules consisted of small cells with pyknotic nuclei and relatively small volumes of clear cytoplasm, not unlike the cells of the zona glomerulosa. Other nodules were composed of large, epithelioid cells with prominent, somewhat irregular nuclei and a generous volume of eosinophilic cytoplasm. There were many nodules with a transitional histologic picture. In some, the cells were indistinguishable from those of an interstitial cell tumor of the testis. Golden-brown intracellular pigment was found, but crystalloids of Reinke were not identified.

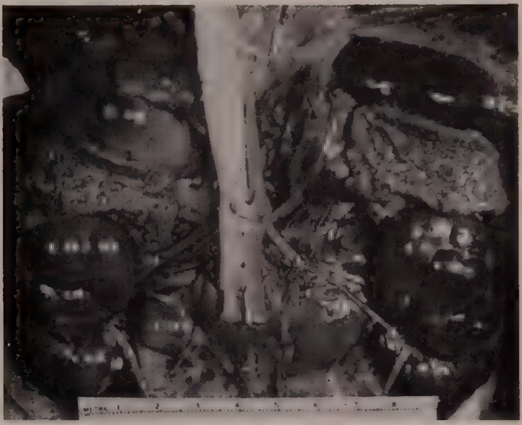

FIGURE 15. The typical appearance of congenital adrenocortical hyperplasia from a neonate dying in an Addisonian crisis.

The operative findings, the clinical appearance, and the chemical studies leave no doubt as to the diagnosis. This female child suffered from congenital adrenocortical hyperplasia. No laboratory determinations were done to determine the urinary pregnanetriol and pregnanediol excretion. We have only to look at the glycogen content of the endocervical and vaginal epithelium to see that there was profound estrogen stimulation. If further evidence were required, it would be provided by the hyperplastic endometrium. The enlargement of the adrenals noted at the first laparotomy undoubtedly was accompanied by excessive corrugation of the surface of the gland (Fig. 15), a finding difficult to detect by palpation.

In congenital adrenal hyperplasia, the enlargement and complexity of the surface configuration is due to an increase in cortical cells similar to those in Figure 14C. On occasion this has been labeled "persistence of the fetal cortex." A study of patients dying in the neonatal period in Addisonian crisis shows that while the cells are similar, the hyperplastic true cortex can be delineated clearly from the involuting fetal cortex.

Anatomic diagnoses

1. *Congenital adrenal hyperplasia*
    - (*a*) *Adrenogenital syndrome in a female*
    - (*b*) *Urogenital sinus with external meatus at tip of phallus (pseudohermaphroditism)*
    - (*c*) *Estrogen stimulation of genital tract*
2. *Tetralogy of Fallot (clinical)*

Human factors in motor vehicle accidents

Repeated arrests for traffic violations, social maladjustments, and various personality traits have been isolated as "human factors" that contribute to motor vehicle accidents, according to statisticians of Metropolitan Life Insurance Company.

Inasmuch as motor vehicle accidents take about 38,000 lives and inflict disabling injuries on an additional 1,400,000 persons in the United States each year, psychologists and other scientists are trying to identify persons most likely to become involved in automobile mishaps.

Social scientists find that drivers who commit traffic violations are particularly likely to have accidents. A study of Iowa drivers, for example, demonstrated that the ratio of actual accidents to the number expected was 134 per cent among drivers with two or three violations. Speeding, improper passing, and failure to observe stop signs were the moving traffic violations which had the highest association with accidents.

The frequency of motor vehicle accidents is more than average among socially maladjusted persons. In this context, socially maladjusted persons include those who have had credit difficulties, a record of juvenile or adult court offenses against persons or property, and truancy from school.

"Behavioral scientists now generally recognize that basic personality characteristics and attitudes of drivers are specific factors in the causation of violations and accidents. Some investigators have reported a considerable degree of success in predicting driver performance by analysis of personality traits such as sense of social responsibility, acceptance of authority, and aggressiveness."

Nutrition Excerpts

Prepared with the cooperation of the faculty of the Graduate School of Nutrition, Cornell University, Ithaca, New York

DAPHNE A. ROE, M.D., Editor

Nutritional Significance of Generalized Exfoliative Dermatoses

DAPHNE ANDERSON ROE, M.D., M.R.C.P.
Ithaca, New York

THE TERM "exfoliative dermatitis" has long been used to denote cutaneous diseases, manifested clinically by generalized erythema and excessive shedding of the horny layer of the epidermis. Included for the purposes of the present discussion are dermatoses in which exudation of serum occurs and those, such as pemphigus foliaceus, in which the cellular part of the epidermis is partially removed.

The pathogenesis of these diseases is still obscure, although the etiologic factors inducing this clinical picture are in many cases well known. These include genetic predisposition, as in ichthyosiform erythrodermia; exogenous irritants of a physical or chemical nature; and such specific dermatologic entities as atopic eczema, psoriasis pityriasis rubra pilaris, and pemphigus, which have a tendency, under certain circumstances, to cause generalized exfoliation. This group may be considered as primary processes of the epidermis.[1] In addition, systemic disease may be associated with exfoliative erythrodermia. Such is the case with drug idiosyncrasy, heavy metal intoxication, malignant reticuloses (l'homme rouge), and rare cases of the malabsorption syndrome. In the large series described by Gentele, Lodin, and Skog,[2] the basic disorder preceding the exfoliation was eczema in 34.8 per cent, psoriasis in 22.9 per cent, and malignant systemic disease (lymphoma) in 15.5 per cent of the cases.

The exact clinical picture varies with the causative mechanism, but the universal erythema, scaling, and, in chronic cases, the loss of hair and nails combine to give these patients a similar appearance. Emaciation, cold intolerance, and, less commonly, peripheral edema are features of the established syndrome.

Two concepts will be considered with regard to the nutritional status of these cases. First, that excessive scaling of the skin may in itself induce malnutrition. Second, that exfoliative dermatitis may occasionally be a result of a specific nutritional deficiency.

Protein loss

The investigation of the metabolic response to exfoliation has been hindered in the past by a lack of accurate methods for the quantitative estimation of desquamated scale. Indeed, published figures for the normal dermal excretion of nitrogen are quite variable (from 179 to 254 mg. per square meter of body surface per day).[3,4] It has been noted that the collection of exfoliated epidermal particles has usually been incomplete. A recent estimate of the dermal excretion of nitrogen, under nonsweating conditions, suggests that a mean figure of 380 mg. per square meter of body surface per day is more realistic.[5] This result was obtained through the estimation of the total daily nitrogen excretion and the subsequent subtraction of the nitrogen excreted in the urine, feces, and exhaled air. It was believed that the remaining nitrogen excretion pertained to the integument. The requirement for epidermal renewal has been calculated to amount to 0.56 mg. per square meter of body surface per day.[6]

An accurate method has now been developed for the collection of scale in exfoliative dermatitis. This involves the use of special clothing which has been designed to prevent the dissemination and loss of material.[7] The application of this technic gave the information that exfoliation of 9 Gm. of scale per square meter of body surface per day produced no clinical or laboratory evidence of a negative nitrogen balance. Indeed, the exfoliation of 17 Gm. of scale per square meter of body surface per day was necessary before a negative nitrogen balance was obtained. Even at this level there was no clinical evidence of protein malnutrition. There was a close correlation between the degree of scaling and the extrarenal water loss.

These results may be compared with those of Pegum, published ten years ago.[8] He studied 10 cases of exfoliative dermatitis, 5 of whom had normal levels of plasma proteins and 5 of whom exhibited hypoproteinemia. In the former group, there was a maximal loss of 6.8 Gm. of scale per square meter of body surface per day, while in the latter group, a minimal loss of 7.15 Gm. per square meter of body surface per day was estimated. Previously, the association of hypoproteinemia with exfoliative dermatitis was thought to be due to liver dysfunction. However, Tickner and Basit[9] showed that in 88 per cent of a total of 36 cases no disturbance of liver function could be demonstrated. These workers obtained experimental evidence of a significant decrease in total serum proteins and in serum albumin with a rise in the serum globulin fractions in their patients. The change most frequently encountered was a fall in serum albumin. It was postulated that the serum albumin is the source from which the skin derives some of its amino acids and, further, that the synthesis of serum albumin by the liver may be increased in exfoliative dermatitis. However, experimental proof of these hypotheses was not attempted.

Clinical experience has shown that in exfoliative dermatitis, uncomplicated by grave systemic disease or serum loss, evidence of protein deprivation becomes apparent only when the disease is prolonged. Malnutrition may be associated not only with protein loss but also with anorexia and intercurrent infection.

Cutaneous mineral loss

The iron content of the body depends on the rate of iron excretion as well as on the rate of iron absorption from the alimentary tract.[10] Approximately 0.5 mg. of iron is lost per day through the normal skin. Accurate reports of iron loss in exfoliative dermatoses are not available, but it may be surmised that iron deficiency anemia, associated with this condition, may be due to the integumentary removal of this mineral. It would be valuable to study the iron requirements of the body under the stress of generalized exfoliation.

Although some cases of exfoliative dermatitis have been shown to be associated with hypocalcemia, no attempt has been made to correlate the blood findings with the amount of calcium lost in the scale.[11]

Vitamin C

Patients with widespread dermatoses exhibit a prolonged saturation time with vitamin C.[12] The blood ascorbic acid levels are low in exfoliative dermatitis. However, it has been demonstrated that this is not due to poor absorption from the intestine. It may be presumed that there is an increased requirement for this vitamin, associated with the reparative function of the skin.

Exfoliative dermatoses in association with malnutrition

Exfoliative dermatitis has been observed in the course of chronic protein deficiency states, more especially in kwashiorkor.[13] A similar widespread dermatosis has also been recorded in the pellagra syndrome.[14] A vicious circle may be established, whereby a dermatosis is initiated by malnutrition and exacerbated by the cutaneous protein, water, and mineral loss. Recently the classification of iatrogenic skin disorders has been enlarged to include generalized scaling dermatoses following the administration of cholesterol-lowering agents, such as triparanol and nicotinic acid.[15,16] Perhaps this may be considered as a deficiency disease due to interference with lipid metabolism. It is apparent that a chemical blockade of cholesterol synthesis may cause interference with the essential biochemical functions of the body and more particularly with the ectodermal structures.[15]

Comment

An attempt has been made to summarize the pertinent data with respect to exfoliative dermatoses and malnutrition. The metabolic responses of the body to the loss of horny material should receive fuller investigation. Basic information concerning the relationship of serum loss to exfoliation in regard to the drain on specific nutrients is essential to such a study. The nutritional requirements of these patients should receive special consideration, since they relate directly to successful therapy. Although nonspecific control of the exfoliative dermatoses by corticosteroids has been effective in many cases, these drugs have also complicated the clinical picture with respect to concomitant malnutrition. Research into the biochemical factors inducing exfoliation should be linked closely to a broad study of the nutritional defects and deficiencies presented by this syndrome.

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Number thirty-two in a new series of Nutrition Excerpts

Clinical Anesthesia Conference

A series of conferences on medical emergencies in the operating room including causes of death during anesthesia

Prepared by the Anesthesia Study Committee of the New York State Society of Anesthesiologists

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Misuse of Thiobarbiturate and of the Recovery Room

Refinements in anesthetic agents and practice require more rather than less skill to insure the patient's safety. The proper use of thiobarbiturates is even today not universally understood. A recovery room may produce a false sense of security.

Case report

A Negro woman, age thirty, was admitted with the chief complaint of excessive vaginal bleeding. She had been pregnant seven times and in 1959 had undergone bilateral tubal ligation at another hospital. She had no other complaints.

A physical examination on admission revealed a blood pressure of 110/76 mm. Hg and a temperature of 98 F. Her lungs were clear to percussion and auscultation. Her admission hematocrit was 32, and her white blood count was 6,300 per cubic millimeter.

She was scheduled for dilatation and curettage. There was no preanesthesia note on the chart.

She was made to fast from midnight of the day of surgery and received $^1/_6$ grain of morphine sulfate and $^1/_{150}$ grain of scopolamine intramuscularly at 8:45 A.M. No note was made of her degree of sedation. Her vital signs were 90/60 mm. Hg, pulse 60, and respiratory rate 20 per minute before induction and were charted as being unchanged throughout the procedure. The anesthetic was 2 per cent thiopental sodium intravenously in divided doses. Five cc. were first administered, followed by 2 and 3 cc. increments, until a total of 15 cc. or 300 mg. had been administered for the dilatation and curettage which was begun at 9:52 A.M. Both the surgery and the anesthesia were terminated at 10:10 A.M. The anesthetist supported the jaw to maintain the airway. No other agent and no oxygen was administered during the procedure.

The patient was placed on a stretcher and was transferred to the recovery room accompanied by a resident in gynecology. She arrived in the recovery room within a minute of leaving the operating room. In the recovery room a registered nurse checked the vital signs and changed the bed linen. The patient did not react to any manipulations. These manipulations consumed about five to ten minutes, whereupon the recovery room nurse went to take care of another patient.

When the patient had been in the recovery room for fifteen minutes, the registered nurse asked the practical nurse to check the vital signs. There had been approximately a five-minute period during which the patient was not observed. The practical nurse could detect no pulse, and the patient was apneic. The practical nurse called the registered nurse, who also found no pulse. A surgeon who was outside the room responded immediately. Closed-chest massage on a soft mattress with a phy-

Presented and discussed at a conference held at Bellevue Hospital, New York City, June 4, 1962. Clinical Anesthesia Conferences are held on the first Monday of each month.

sician exerting counter pressure on the back was begun. The trachea was intubated, and oxygen was administered.

The patient may have been pulseless for about ten minutes. No one knew whether or not the patient had vomited and aspirated, but no vomiting motions were observed.

After about five minutes of closed-chest massage a pulse was detected, and another hour or so later spontaneous respirations returned.

A recovery room nurse first suctioned the endotracheal tube at 4:00 P.M. She removed light green, liquid, nonfoul material. A chest plate taken in the recovery room showed massive pneumonia or atelectasis in the upper lobe of the left lung. The right lung was clear.

That evening a bronchoscopy was done under halothane-succinylcholine. A clear liquid material similar to gastric contents was aspirated.

The following day the patient's white blood cell count was 35,000 per cubic millimeter with 98 per cent polymorphonuclear leukocytes. The blood urea nitrogen was 70 mg. per 100 ml. She remained in a coma and died three days later.

The specimen from the curettage was reported as postabortion endometritis.

An autopsy revealed minimal patchy subarachnoid hemorrhage of the brain, believed to be consistent with an episode of cerebral anoxia.

There was acute suppurative laryngotracheal bronchitis and congestion and partial patchy atelectasis of the lung, thought to be consistent with an infection superimposed on vomiting and aspiration. There was slight rheumatic mitral sclerosis.

Comment

The errors committed in the management of this case are not subtle.

Thiobarbiturates are not primarily analgesic agents. They are sedative and hypnotic agents. To achieve quietus with only thiopental sodium, as was done in this case, a near lethal dose has to be administered. Admittedly, the preanesthetic morphine may have some analgesic potency, but it would have been much safer to have added an analgesic, such as 50 per cent nitrous oxide and 50 per cent oxygen, to the anesthetic management.

The failure to observe the patient in the recovery room is difficult to understand. The area was well staffed. The sole responsibility of the staff is to observe the patients. Yet this patient was unobserved and was permitted to vomit and to aspirate while she was supine.

No general anesthetic nor any surgical procedure, not even a little thiopental sodium or a simple dilatation and curettage can be considered minor.

Number one hundred thirty in a series of Clinical Anesthesia Conferences

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Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
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Poisonings Due to Mistaken Identities of Products

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

Toxic Agent	*Sex*	*Age*
Narcissus Bulbs	Female	76 years

This incident was reported from rural Connecticut. The reporting physician stated that the patient lives alone and was snowed in. Her daughter brought her a week's supply of groceries. She also brought a bag of paper-white narcissus bulbs. The victim prepared a stew that evening and mistakenly used the bulbs in place of onions. About one and one-half hours after eating the meal, the patient experienced a dry mouth and nausea which was followed by repeated and violent vomiting. Later she also had some colicky cramps and abdominal pains. She called her daughter, and the cause of the incident was ascertained. The family physician was called, but by the time he arrived at the house the patient was asymptomatic, and no pathologic findings were manifest. Prior to the physician's arrival the patient took some proprietary antacid preparations as a first-aid measure.

The narcissus plant belongs to the Amaryllidaceae (amaryllis) family, the toxic agent being alkaloidal in nature.

Because of the marked resemblance of narcissus bulbs and other bulbs to onions, incidents resulting from such mistaken identities are not uncommon and have been reported both here and abroad. It would serve the public well if florists and other purveyors of such plant bulbs would warn purchasers routinely of this possibility and to keep such bulbs away from the reach of children.

INCIDENT 2

Toxic Agent	*Sex*	*Age*
Cafergot	Female	$2^1/_2$ years

This two and one-half-year-old child obtained a preparation which apparently was prescribed for the mother and put it in her nose. The patient vomited spontaneously and became nauseated. She soon became drowsy and somnolent for two hours. When she awoke, her face was flushed, and her hands and legs appeared edematous. The upper extremities also were cold and clammy for about thirty hours following the ingestion.

The product is an ethical preparation composed of an ergotamine tartrate combination, belladonna alkaloids, and sodium phenobarbital.

It is believed that the unorthodox nasal route of administration produced symptoms more marked than if the product had been taken orally. The circulatory symptoms with this minimal dosage have not been noted previously.

INCIDENT 3

Toxic Agent	*Sex*	*Age*
Hair Color	Male	$2^{1}/_{2}$ years

This patient obtained a metallic hair-color preparation used by his mother and inhaled an unknown amount of the spray. The physician called the Poison Control Center inquiring about the product. He was informed that it is a residual brass dust with a minor toxicity index, but that there was a possibility of a chemical pneumonia which might develop within twenty-four to forty-eight hours. Therefore, it was suggested that the patient be observed for at least that period. The patient was admitted to the hospital, and twelve hours following his admission he developed a temperature of 104 F. and also dyspnea. The other symptoms noted were vomiting and coughing. Chest x-ray films revealed a bilateral bronchopneumonia. Antibiotics and aspirin also were administered, and after five days of hospitalization the symptoms subsided, and the patient was discharged with a guarded prognosis because of a possibility of a pulmonary granulomatous formation in the lungs. The patient was to be observed at home by the attending physician.

This is another illustration of a long series of cases reported to this Center following the ingestion of metallic hair spray. However, the Center has not received any documentation of pulmonary involvement resulting from the use of polyvinyl pyrrollidine containing hair lacquer which is currently mentioned widely in the medical literature.

INCIDENT 4

Toxic Agent	*Sex*	*Age*
Vial of Liquid from Carpenter's Level	Male	27 years

This incident reveals a suicidal gesture by a twenty-seven-year-old male with a very unorthodox agent, the liquid from a carpenter's level. The patient was admitted to the ward and was treated symptomatically. The Poison Control Center ascertained that the liquid was water. The cause of the rare occurrence of incidents of this type is obscure. Similar occurrences result from the ingestion of the liquid center of golf balls. This patient made an uneventful recovery and was later referred for psychiatric observation because of a depressed state.

INCIDENT 5

Toxic Agent	*Sex*	*Age*
Atropine Eye Drops	Female	40 days

This medication was prescribed for an adult member of the household but was given mistakenly to the infant as nose drops. The patient began to vomit spontaneously and was taken to the hospital emergency room. This child was observed until she became symptom-free. Ophthalmologists always must bear in mind the potential hazards of their products and state it to their adult patients and caution them to keep these drugs away from children.

INCIDENT 6

Toxic Agent	*Sex*	*Age*
Sedative	Male	22 years

The following case was reported by Barbara Parker, M.D.

A twenty-two-year-old heroin addict of five years duration was admitted to the hospital because of a stuporous state apparently induced by the ingestion of an overdose of sedative (phenobarbital or pentobarbital sodium by history). The gastric aspirate contained some white fragments which were not identified chemically. The patient became fully reactive within a few hours after his admission. He was treated with slow phenobarbital withdrawal and was transferred to Manhattan General Hospital for further treatment on the sixth hospital day at which time he was receiving 15 mg. phenobarbital twice daily. In the course of his stay he revealed that he had been taking glutethimide daily for the past six months. No signs of glutethimide withdrawal were observed during his Bellevue stay.

The final diagnosis was mild barbiturate intoxication, acute barbiturate and heroin addiction, and glutethimide habituation.

The danger of addiction to this drug is one that merits wider recognition on the part of the physician as well as the public.

Number one hundred one in a series of Accidental Chemical Poisonings

Case Reports

Postcesarean Large Bowel Obstruction

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THREE YEARS AGO, the late Arthur Beil, M.D.,[1] read a paper before the Brooklyn Gynecological Society in which he presented several cases of an obstruction of the small intestine complicating the early postpartum period. These are usually mechanical in nature and are caused most frequently by adhesions following a previous laparotomy. We have had few, if any, such cases at The Brooklyn Hospital in the past thirty years, but we have had 3 cases of a large-bowel obstruction following a cesarean section in recent years, which were sufficiently serious to warrant reporting.

The rarity of an intestinal obstruction complicating pregnancy is emphasized by nearly everyone writing on this subject, but this observation becomes academic when one's own patient develops this complication. An obstruction of the small intestine occurs more frequently at the fourth to the sixth month of gestation, at or near term, and as previously mentioned, in the early puerperium. An obstruction of the large intestine practically always occurs postpartum, but its occurrence requires just as immediate and intensive therapy as does the small intestinal variety.

The causes of a large-bowel obstruction associated with pregnancy are most frequently (1) a sigmoidal obstruction due to extrinsic neoplasms which become incarcerated in the pelvis, (2) a postpartum uterus which becomes incarcerated in the pelvis, (3) a volvulus of the sigmoid colon or cecum, and (4) intrinsic lesions of the large intestine. Simply stated, a large-bowel obstruction associated with pregnancy occurs because of external pressure, twisting, or intrinsic lesions causing a partial or complete blockage. There are reports in the literature illustrating all of these conditions in patients who had been delivered vaginally as well as in patients who had been delivered by cesarean section.

In the 3 cases to be reported here, the etiology differed from the causes enumerated previously in that the external pressure was presumably exerted by the normally involuting postpartum uterus impinging on the sacral promontory while it was still an abdominal organ.

Case reports

CASE 1. This patient had an uneventful full-term pregnancy, labor, and delivery in 1954. She was admitted to this hospital on February 17, 1959, in the thirty-eighth week of her second pregnancy because of bright-red, painless, vaginal bleeding. A complete placenta previa was found to be present on a vaginal examination, and an immediate low-flap cesarean section was performed.

The operation was completed at 12:15 P.M. The following morning there was moderate, soft, abdominal distention. That night, thirty-six hours postoperatively, the abdominal distention increased considerably. A Harris irrigation resulted in the passage of a moderate amount of flatus and formed stool. The patient was now complaining of nausea and abdominal pain.

The next morning, forty-four hours postoperatively, the abdomen was very tense,

Presented at a meeting of the Brooklyn Gynecological Society at The Brooklyn Hospital, October 19, 1960.

and the patient vomited a large amount of green fluid. Wangensteen suction was instituted, and the parenteral fluids were continued. She was complaining of abdominal cramps and eructations.

A flat plate of the abdomen disclosed marked distention of the large bowel, especially the cecum, which was remarkably dilated and shifted toward the left. There also were noted distended loops of small bowel. In the upright view, air-fluid levels were seen throughout the colon, with the gas being very minimal in the distal sigmoid and rectum. The air-fluid levels in the colon were limited to the level coinciding with the pelvic inlet. The amount of distention in the cecum was more likely on a basis of mechanical obstruction than of paralytic ileus.

A surgical consultant advised an immediate laparotomy. The abdomen was reopened through the cesarean incision. A greatly distended cecum was found with its longitudinal bands already splitting. The remainder of the colon was less markedly distended, and a redundant sigmoid containing feces was found to be occluded by the pressure of the involuting uterus on the promontory of the sacrum. This was released, and the cecum was aspirated to reduce the distention, after which a cecostomy was performed through a stab wound using a catheter encircled with several purse string sutures.

The postoperative course was satisfactory, the cecostomy tube was removed on the fifteenth day after the operation, and the patient was discharged two days later.

In this case, your attention is directed to two features: first, that the sigmoidal obstruction had caused sufficient distention of the cecum to make a perforation or a complete rupture imminent within forty-eight hours of the cesarean section, and second, that the condition was treated successfully by a simple tube cecostomy.

Case 2. This patient was admitted in the thirty-eighth week of her third pregnancy because of the spontaneous rupture of the membranes. She had a small gynecoid pelvis and had been delivered of her first baby, which weighed 2,688 Gm., by a low-forceps extraction after a four-hour second stage of labor. The second baby, which weighed 2,308 Gm., necessitated a rotation and mid-forceps extraction. When the patient was admitted with this pregnancy, the fetus was estimated to be larger than had been her second baby. An elective low-flap section was performed under cyclopropane anesthesia without incident, and a 3,061-Gm. infant was obtained. During the second night postpartum the patient complained of nausea and vomiting. The vomiting continued in spite of the discontinuance of everything by mouth, the administration of parenteral fluids, and a Harris irrigation which was effectual for large amounts of flatus and fecal material. The patient then began belching, complained of spasms of right-sided abdominal pain, and became increasingly more distended.

A surgical consultant found an enlarged cecum on inspection and palpation with exquisite tenderness, diagnosed a mechanical obstruction of the large bowel, and following x-ray confirmation, performed a laparotomy four and one-half days after the section.

No distention of the sigmoid colon was found, but an increasing distention of the transverse and ascending portions of the colon with the cecum tremendously distended, thin, bluish, and with serosal tears was present. No mechanical cause for the obstruction was found other than that the uterus impinged against the promontory of the sacrum.

A transverse colon colostomy was performed with the escape of a tremendous amount of gas and liquid fecal material. This was closed seventeen days later, and the patient was discharged thirty-one days after the section, twenty-seven days after the colostomy, and ten days after its closure.

In this case the obstruction occurred later than in the previous case, but while the postpartum uterus was still an abdominal organ. The treatment was by colostomy rather than by cecostomy.

Case 3. This thirty-five-year-old patient had had three previous cesarean sections performed at other hospitals, the first for a cephalopelvic disproportion. Her first admission to The Brooklyn Hospital occurred on December 2, 1956, in the thirty-ninth week of an uncomplicated pregnancy, for an elective repeat section and Pomeroy sterilization, which were performed the following morning. The operation was complicated by the presence of numerous adhesions. On the second postoperative day there was moderate distention and some vomiting. Parenteral fluids, Wangensteen suction, and the use of a rectal tube were instituted, but the vomiting and distention persisted, with the distention increasing. Increasing tenderness with rebound developed in the right lower quadrant of the abdomen. An x-ray film on the fourth postoperative day disclosed enormous distention of both the transverse and ascending portions of the colon, particularly in the region of the cecum. On the x-ray film the diameter of the cecum measured 15 cm. There was no gas in the pelvis, and immediate surgery was advised.

As with the other 2 cases, an exploration disclosed no point of obstruction to the large bowel other than the pressure of the postpartum uterus. There was tremendous dilatation of the cecum with serosal tears, and perforation seemed imminent.

A transverse colostomy was performed, following which the patient made a good recovery. She was discharged thirteen days after the colostomy and was readmitted two weeks later for its closure, which was accomplished successfully.

Comment

All of these patients exhibited the cardinal symptoms of an acute mechanical obstruction of the large bowel. The x-ray film in each instance disclosed an alarming degree of distention of the cecum. For example, in Case 3 the diameter of the cecum was 15 cm. Lowman and Davis[2] state that an x-ray film taken with the patient in the prone position disclosing a cecal diameter of 9 cm. or more indicates that a perforation is impending, and immediate surgical intervention is urgent.

That these cases might have been treated successfully without surgical intervention is suggested by the report of 10 cases cited by Cannell and Tovee in 1957,[3] in which a postpartum large-bowel obstruction was caused by the involuting uterus becoming incarcerated in the pelvis. Eight of these cases followed cesarean sections, and the remaining 2 followed vaginal deliveries. They were successful in treating some of these cases early in their course by means of the knee-chest position plus the gentle manipulation of the uterus with a rectal tube in place. As soon as the pressure was relieved, gas was passed, the symptoms subsided dramatically, and the patient was cured.

The surgical procedure indicated for the obstruction depends on the findings at the time of an exploratory laparotomy. The problem resolves itself into first, decompression, and second, the treatment of the underlying pathologic condition. If no intrinsic pathologic condition is found, as in the 3 cases reported here, decompression of the bowel alone is all that is necessary, and a cecostomy is generally considered to be sufficient. Some surgeons, however, still prefer a colostomy because of (1) a lower mortality rate; (2) more effective decompression; (3) less tendency toward chemical imbalance; (4) subsequent surgery, if indicated, can be performed earlier and with better bowel preparation; and (5) cecostomy is frequently followed by fistula formation and hernia. The proponents of a cecostomy prefer it because (1) the area of bowel most likely to perforate soonest is decompressed first, (2) a transverse colostomy may overlook an impending or actual perforation of the cecum, (3) handling of the transverse colon may cause a cecal perforation, (4) cecostomy is easier to perform, and (5) no major procedure is required to close it.

The cases of postcesarean section large-bowel obstructions reported in recent years include 1 case due to a pelvic abscess[4]; 1 due to a ruptured pseudomucinous cystadenocarcinoma behind the uterus[5]; 10 due to pressure of the postpartum uterus in the pelvis[3]; 1 very similar to our cases in which no obstruction was found, and the diagnosis was considered to be a segmental ileus of the large bowel[6]; and 2 others considered to be due to a severe adynamic ileus definitely limited to segments of the colon with the etiology unknown.[7]

We would like to add our 3 cases, all of which followed ordinary cesarean sections with the distention of all segments of the colon proximal to the rectosigmoid junction and all apparently due to pressure from the normal postpartum uterus while it was still an abdominal organ. It would appear that these cases, had they been recognized sufficiently early, might have been relieved by the conservative treatment suggested by Cannell and Tovee.[3]

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Annular Pancreas in a Premature Infant

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Annular pancreas is a rare cause of neonatal intestinal obstruction. In Gross'[1] series, annular pancreas was present in less than 1 per cent of the neonatal obstructions. Of obstructions localized to the duodenum, annular pancreas was present in less than 5 per cent of the cases.

A ring of pancreatic tissue encircling the duodenum most commonly produces an incomplete or intermittent obstruction, requiring an operative correction in childhood or in adult life. Only rarely does the obstruction occur in the neonatal period, requiring surgery during the first few days of life. In a review of the literature from 1944 to 1959, Hays, Greaney, and Hill[2] analyzed 40 cases with acute neonatal obstruction of the duodenum due to annular pancreas. Twenty-two of these patients survived. Thirteen of the 40 had associated major anomalies or were premature, with 4 survivors. Four of the 40 were premature, with 1 survivor, a 1,984-Gm. infant with no associated anomalies.[2–6]

The case reported here is a 1,750-Gm. premature infant with malrotation of the midgut and annular pancreas. The surgical management was successful.

Case report

A white male was born in Maimonides Hospital of Brooklyn on August 9, 1960, after a thirty-four-week gestation. Maternal hydramnios was present. One previous pregnancy had terminated in the delivery of a normal full-term infant. The patient was normal in appearance at birth, and a physical examination revealed no abnormality. The birth weight was 1,750 Gm. When feedings were started, frequent vomiting occurred. There was no bile in the vomitus, and daily meconium stools were noted. On August 13, 1960, slight upper abdominal distention was present. The infant's weight was 1,450 Gm. X-ray studies were performed, and surgical consultation was requested.

An examination revealed a lethargic premature infant with a depressed fontanel and poor skin turgor. The rectal temperature was 37 C. There was slight upper abdominal distention with tympany; no abnormal masses were palpable; the abdomen was soft. The gastric aspirate consisted of milk curds with no bile staining. A digital rectal examination produced negative findings. A routine blood count and urinalysis were within normal limits.

The scout film of the abdomen revealed marked distention of the stomach and proximal duodenum. No gas was present distal to the first portion of the duodenum. Barium studies revealed a normal esophagus. A dilated stomach and greatly distended duodenal bulb were noted with no distal passage of the contrast medium (Fig. 1).

It was felt that an atresia of the duodenum was present, and the infant was prepared for surgery with continuous gastric suction and the administration of parenteral fluids through an ankle cut-down. Several hours later a laparotomy was performed under local infiltration anesthesia with 0.25 per cent procaine. The peritoneal cavity was entered through a transverse incision in the right upper quadrant of the abdomen. The cecum was present in the right upper quadrant, and several peritoneal bands were noted coursing over the duodenum between the cecum and the liver. These bands were sectioned, and the right side of the colon was mobilized freely and placed in the left side of

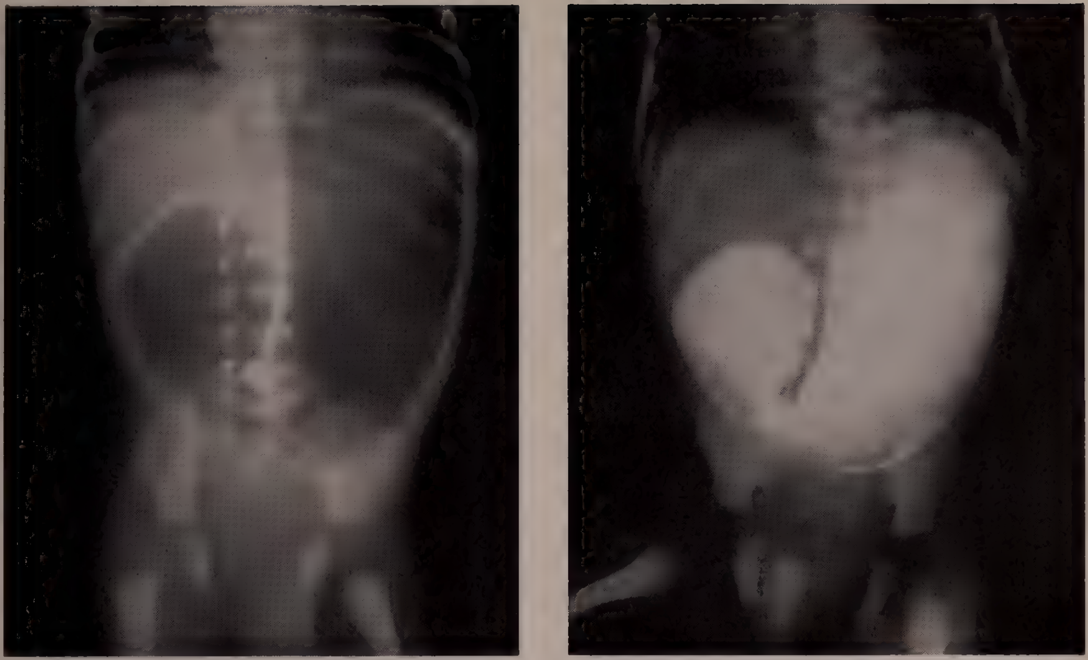

FIGURE 1. (A) "Double bubble" demonstrated in film taken with patient in supine position. (B) Barium swallow.

the abdomen (Ladd procedure). An inspection of the duodenum then revealed a band of pancreatic tissue completely encircling the bowel just distal to its first portion. Proximal to this level the bowel was markedly distended; distally it was completely collapsed. The gallbladder was not distended. A two-layer, side-to-side duodenojejunostomy was established between the duodenal bulb and the first loop of the proximal jejunum. Interrupted 5-0 silk sutures were placed as a seromuscular suture; a continuous suture of 4-0 chromicized gut was placed through all the layers as an inner suture. The wound was closed without drainage with interrupted 4-0 silk to appose the peritoneum and fascia and a continuous 4-0 plain gut subcuticular suture. Collodion was applied to seal the skin edges.

Parenteral penicillin and streptomycin were given postoperatively; the gastric suction and intravenous fluids were continued. Gavage feedings were started on the third postoperative day. The patient was discharged on the thirty-sixth postoperative day weighing 2,350 Gm. His health was excellent, and he took normal feedings with no difficulty. At six and one-half months of age his weight was 5,573 Gm.

Etiology

Annular pancreas is a congenital developmental anomaly in which a ring of pancreatic tissue encircles the descending portion of the duodenum. Kie, Wittebol, and Lundig[7] state that the condition was first described by Tiedmann in 1818, named by Ecker in 1862, with the first infant case reported by Vidal in 1905.

The pertinent embryology relates to the dual origin of the normal pancreas. Dorsal and ventral anlage arise as independent outpouchings of the primitive gut. Normally they fuse and come to lie within the curve of the duodenum. The failure of the coordinated rotation and fusion of these segments may produce a partial or complete ring of pancreatic tissue encircling the duodenum. The ring itself consists of functioning pancreatic tissue with its own duct system.

Not infrequently stenosis or atresia of the encircled bowel is also present.[1,7-9]

Clinical picture

Of all the individuals with annular pancreas, it is estimated that only about one-third ever have any symptoms.[7] Most of the symptomatic individuals have a partial or intermittent duodenal obstruction. A much smaller group of patients has obstructive symptoms at birth.

It is obvious that when symptoms start at the time of the first neonatal feedings, a high degree of obstruction is present. Vomiting is the predominant symptom. Bile may or may not be present in the vomitus, depending on the level of the ring. The majority of cases is associated with hydramnios during the last trimester. Lloyd and Clatworthy[10] reported maternal hydramnios in 66 per cent of the cases of newborn infants with duodenal or jejunal obstructions. Abdominal distention is an inconstant finding and may disappear intermittently as the stomach empties with vomiting. X-ray studies of the abdomen with the patient in the supine and erect positions reveal the characteristic picture of duodenal obstruction: the double bubble. One bubble represents the dilated stomach, and the other represents the proximal duodenum. The injection of a small quantity of air into the stomach through a nasogastric tube may help to demonstrate this finding. Contrast media add little information when the characteristic picture is present. However, if such material is given, it should be removed immediately to prevent aspiration into the tracheobronchial tree. Contrast visualization of the colon may be performed to demonstrate colonic patency and the possibility of malrotation.

The exact mechanism of the obstruction can be determined only at the time of a laparotomy. The most common causes of duodenal obstruction are atresia, stenosis, and malrotation, with abnormal peritoneal bands obstructing the duodenum; rarely an annular pancreas is present. Infrequently, an annular pancreas may constrict the common bile duct, causing obstructive jaundice.[4]

Treatment

Preoperative gastric suction and parenteral fluid replacement are essential. The division of the ring of pancreatic tissue has been followed by a high incidence of pancreatic fistulas.[3] Furthermore, even if the ring were sectioned, an underlying stenosis or atresia of the duodenum might be left uncorrected. For these reasons, Gross and Chisholm in 1944[11] performed a duodenojejunostomy successfully. This operation is now considered the most acceptable procedure. The risk of a fistula is avoided, and any intrinsic duodenal obstruction is simultaneously bypassed. To avoid a long jejunal loop, a side-to-side retrocolic anastomosis is preferred. A gastroenterostomy may be performed if local conditions prevent a satisfactory duodenojejunostomy. However, a gastroenterostomy may not adequately drain the proximal duodenum, thereby causing biliary reflux into the stomach. In addition, a marginal ulcer may develop as a late complication.

At operation a search for other correctible visceral anomalies should be made. If an obstruction of the common bile duct is present, a cholecystenterostomy should be performed.[4] A temporary tube gastrostomy may be added to avoid nasogastric intubation in the postoperative period.

Comment

The successful treatment of neonatal intestinal obstruction depends primarily on an early diagnosis. Maternal hydramnios or neonatal vomiting should alert the physician to the diagnosis. With hydramnios there is a 14 per cent chance that the infant will have intrinsic intestinal obstruction.[10] In most cases, simple roentgenograms with the patient in the supine and erect positions are diagnostic. In doubtful cases the instillation of air into the stomach through a nasogastric tube may clarify the picture. A routine barium swallow should be avoided. While the infant is still in the x-ray department, the films that have been taken should be reviewed by the radiologist. If they are not diagnostic, he should then request immediate contrast studies of the colon or upper portion of the gastrointestinal tract as the situation warrants. An unnecessary barium ingestion exposes the patient to the risk of the aspiration of barium and may leave barium at the site of a bowel anastomosis. If a gastrointestinal study is indicated, a water-soluble agent should be used; if this proves unsatisfactory, a thin barium mixture may be given. Fluoroscopy should be performed only if it is indicated, and minimum exposure time should be allowed.

The constant awareness of the symptoms of obstruction by the staff pediatrician, house staff, and nursing staff can eliminate a delay in the diagnosis. An early surgical intervention offers the only chance of survival. Associated major anomalies are present in 75 per cent of the neonates with annular pancreas.[3] The surgical procedure of choice is a duodenojejunostomy. A temporary tube gastrostomy is a useful adjunct.

Summary

A successfully treated case of annular pancreas producing an acute neonatal obstruction in a 1,750-Gm. premature infant is reported. An associated malrotation of the midgut was present. A review of the literature since 1944 reveals one other premature infant surviving surgery for annular pancreas.[2]

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Blue and yellow safest colors for cars

From the standpoint of motoring safety, blue and yellow are the best car colors, according to an article in the September, 1962, issue of *Today's Health.* In fact, a two-tone blue and yellow automobile appears to be one of the safest combinations.

Studies at the University of California at Los Angeles showed that the color of an approaching automobile definitely influences a driver's judgment of how far away it is. Judged at a distance of 200 feet, objects of some colors appeared to be up to 6 feet closer than objects of other colors. A distance of 6 feet in judging distance may easily mean the difference between a serious accident and no accident.

Of the various colors tested on 164 subjects, blue and yellow made distant objects seem closest under both daytime and nighttime conditions. Gray shades made objects appear to be the farthest away. Blue was ranked safest in daylight and fog and yellow safest at night.

Colors have both a physical and psychologic effect. Red, green, and blue have a very definite physical effect. Tests show that when red predominates in a room it increases blood pressure, quickens muscular reactions, excites emotions, tends to produce restlessness, and makes time appear to pass much more slowly. On the other hand, green has been shown to have a calming effect, and time tends to slip by faster for a person in a blue room.

Happiness also can be linked to room color. Persons surrounded by dull gray walls experience monotony, fatigue, headache, discontent, irritability, and hostility, while those in a colorfully decorated room had feelings of comfort and well-being.

Women are more affected by color than men, and psychologists believe that persons who dislike color or fail to respond to it are emotionally repressed.

Sleep Paralysis

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SLEEP PARALYSIS is a term first used by Wilson[1] to describe short periods of inability to move while the consciousness is clear. These attacks may occur just prior to falling asleep or on awakening. Originally characterized as "night palsy" by Mitchell,[2] it has also been called "delayed psychomotor awakening" in the German literature[3] and "cataplexy of awakening" in the French literature.[4]

Sleep paralysis is frequently associated with the narcolepsy syndrome which consists of four parts: (1) uncontrollable, excessive, and persistent sleepiness, narcolepsy proper; (2) cataplexy or episodes of muscular weakness induced by emotion; (3) sleep paralysis; and (4) hypnagogic hallucinations which are vivid, realistic visual or auditory sensations occurring during the drowsy state.[5] In 400 patients with narcolepsy Yoss and Daly[5] found cataplectic attacks in 64 per cent and sleep paralysis in 28 per cent. There are also several case reports of sleep paralysis alone.[6-11]

The attack consists of a period of almost complete paralysis just prior to falling asleep or on awakening. It lasts from many seconds to a few minutes during which the patient is able to breathe, although at times the rate may be altered. Occasionally a patient may be able to open his eyes or grunt or moan, so that others in the environment are made aware of the attack. During the attacks the patients are conscious and may be aware that they are having an attack of sleep paralysis and that the incident is temporary, will be of short duration, and will end spontaneously. Others do not have the intellectual awareness during the episode and with each attack go through the mental anguish associated with the struggle to move or speak. Usually the patient is fully aware of his surroundings and of people entering the room. The attacks end abruptly with the initial regaining of the capacity to move some part of the body. This may be spontaneous or be initiated by someone touching the patient. Some people have their episodes associated with hypnagogic illusions or hallucinations, like dream states. These may be terrifying and may add to the anguish of the attack.

The incidence of sleep paralysis is equal in males and females. In sleep paralysis alone the family history usually reveals negative findings, unlike that associated with narcolepsy where the family incidence may be increased. Most of the patients have the onset in the teens, but cases have been reported in narcoleptic children[12] and in older-age groups. The attacks then continued to occur from a few times weekly to a few times each year. The neurologic examination and skull x-ray films are normal. The electroencephalograms have been reported as normal.[7] The tracings obtained during the attacks show patterns of alternating drowsiness and wakefulness but no evidence of abnormal electrical activity.[5]

Some authors suggest that the incidence of sleep paralysis is much more common than most of us recognize.[5,7,9] In discussion with some of my medical colleagues I have ascertained that most of them have not encountered such cases. My psychiatrist acquaintances, however, tell me that they have had occasional patients describe such attacks. Schneck[10] suggests that it is usually a secondary complaint which may be overlooked because it is insufficiently stressed.

I shall describe 4 cases which illustrate most of the features of sleep paralysis. They also afford the opportunity to record the patients' observations during the attacks.

Case reports

Case 1. A forty-two-year-old white female authoress consulted me on October 20, 1960, because of recurrent attacks of sleep paralysis. She had the attacks for several years, at times daily for a few weeks, and then would be free of them for several months. She usually had no trouble falling asleep in a few minutes and never took sleeping medication at night or other medication during the day. She usually awakened eight or ten times nightly and would fall asleep in a few minutes after looking at her clock or changing the position of her dogs at the foot of the bed. She slept alone and usually awakened spontaneously or was aroused by her dogs at 7:00 A.M. She had no history of narcolepsy, cataplexy, or hypnagogic illusions. At my request for a description, she wrote the following:

> It is like a little defect in the transmission, so that the gearshift from waking to sleep, and from sleep back to waking, does not function smoothly. At the very moment of passing from waking into sleep, I start up with the very unpleasant sensation that I have forgotten to breathe and am unable to resume it. I try to sit up, to facilitate breathing, but notice that I am unable to move. I want to open my mouth to resume breathing, but notice that my face is likewise paralyzed.
>
> This situation lasts probably no longer than a second, probably less; but it takes me several seconds, perhaps a minute, to recover from the shock. If I try to go back to sleep after that, the same phenomenon may repeat itself three or even four times, so that I am actually scared to fall asleep. Usually I get quite annoyed with myself at this point, and then, finally succeed in falling asleep. This may happen several days in a row, afternoon and evening, or there may be weeks of intermission during which I fall asleep quite normally.
>
> The same thing happens when somebody wakes me up, especially if it is very soon after I have fallen asleep. I say "somebody," not "something": There is no disturbance if I am awakened by an alarm clock, but only if I am awakened by a person or by the telephone; in other words, when I am somehow aware that an immediate wake response is expected of me.
>
> I cannot remember how far back I first noticed this particular disturbance. Certainly it goes back some years. I know that it was simply "to forget to breathe" at the moment of falling asleep or the sensation that my heart was getting out of place and was falling into my back, a feeling which I could avoid by trying to fall asleep on my stomach; or a feeling that I was falling which would make me start up just at the moment of falling asleep.
>
> I also know that this particular disturbance was part of a syndrome of related disturbances, such as difficulties in breathing or in swallowing in claustrophobic situations. Such disturbances go back to my fourteenth year and have been greatly relieved by psychoanalysis when I was eighteen, and by the general process of growing up.
>
> I also know that my father must have suffered from similar symptoms. I remember that he referred to his afternoon nap jocularly as "little terror naps" ("Ich habe nicht geschlafen, nur schreckhaft genickt") and that, especially in his younger years, he had similar difficulties in swallowing (which I found out, however, only after I had already pretty well overcome my own difficulty), and that he suffered slightly from claustrophobia and from agoraphobia.

The patient's general physical examination, neurologic examination, chest x-ray film, electrocardiogram, blood count, urinalysis, protein-bound iodine, and serum potassium indicated normal findings. The nature of the attacks was explained to the patient and I received a note from her two months later.

> I have had very few attacks since I left you, perhaps two or three altogether. For a first, very brief phase I have the impression that the whole thing is as rapid as a dream; that is, I am aware only of the struggle to move. It is a new struggle each time. But then intellectual awareness interferes. I think, after I left you, I invented a new trick: I tell myself, "Don't move, there is no reason why you should." So I give up the struggle as soon as it starts, and then, after a minute, everything is over anyway. This seems to be a very efficient method to deal with the problem.

Case 2. A twenty-five-year-old white male attorney was seen by me on February 2, 1961. His sleep paralysis began in May, 1954, at the age of eighteen years. The attacks always came on falling asleep, from about ten to twenty-five minutes after lying down and seemed to correspond with periods of increased tension. In the first few months the patient had about three or four attacks. The attacks became more frequent in the fall of 1954 and the spring of 1955 while he was in his first year of law school. At that time they came every third night for three weeks, then, intermittently, they occurred about every six weeks. For the past few months the attacks have come every two weeks. They seem to be increased by anxiety and by lack of sleep. The patient usually sleeps for seven hours. Should he sleep for only four hours, he would be likely to have an attack the next night. The attacks come while he is lying in bed with his eyes closed. They start with a feeling of heaviness and weight around the head. He thinks that he opens his mouth to get air because of a feeling of suffocation. At times, at this point, he is able to jump up and put on the lights and thus abort the attack. But, later that evening, he is certain to have another episode. As the attack proceeds, he has the feeling of water rushing through his head and this lasts while he counts for about twenty-five seconds. At this time he cannot move, feels that he cannot open his mouth, and his nose occasionally gets stuffed. This is associated with a fear of being caught under the covers and suffocating. The patient knows that the attacks will end and counts to somewhere from 15 to 160 before the episode ends spontaneously. He knows whether the lights are on or off and can see, if he can get his eyes open. During an attack no one has ever entered the room nor has the phone rung. He has not had narcolepsy or cataplexy, but he describes three types of hallucination which accompany the attacks: (1) He thinks he is moving and crawls out of bed with difficulty and gropes about on the floor, (2) he thinks people are coming into the room, and (3) he has the fantasy of driving a car, and when he steps on the brakes they do not slow the car, and he has great fear of an accident. At times the attacks seem to come in two "waves"; initially, there is a sense of weight in the head, then a period of feeling nothing but an inability to move, followed by a recurrence after a fifteen- to twenty-second interval. If he attempts to move or call for help, the second wave begins immediately. So he has learned that it is best to lie still and try to relax. The diagnosis was made originally at the Massachusetts General Hospital in 1954 where, the patient says, his work-up, including an electroencephalogram taken during an attack provoked by a sedative, was normal.

Case 1 represents a case of sleep paralysis alone. Case 2 is one of sleep paralysis with hypnagogic hallucinations. The following 2 cases are associated with narcolepsy, cataplexy, and hypnagogic hallucinations.

Case 3. In 1950, at the age of twenty-three years, this white male (a private patient of Edward Tolstoi, M.D., and Henry Carr, M.D.) was admitted to The New York Hospital. He stated that starting as a high school student, he occasionally fell asleep in class during study periods. Once or twice weekly he would go to bed on coming home from school and sleep until the next morning.

He entered the navy at the age of eighteen years for a period of twenty-seven months. During this period he fell asleep on watch on a few occasions. In 1946 his basal metabolic rate was minus 15, and he was given thyroid. Between 1948 and 1950 there was a worsening of the narcolepsy, with attacks of drowsiness and a heavy feeling of the eyelids followed by falling asleep about 10:00 to 11:00 A.M. and 1:00 to 2:00 P.M. daily. This began even while walking or driving his car. In addition, there were attacks lasting from one to three seconds during which all the strength would seem to go out of his body, and he would feel limp but would not fall. During the six to eight months prior to his admission to the hospital, the patient had four or five attacks of sleep paralysis after going to bed and closing his eyes. The attacks were ushered in by a loud ringing in the ears and then followed complete paralysis, with a numbness and tingling of the extremities and an inability to speak. The attacks were described as lasting about half an hour and were terminated when someone, attracted by his groaning noises, came in and woke him. His general physical and neurologic examinations were normal. The complete blood count, urinalysis, Mazzini test, and an electroencephalogram showed normal results.

The patient was readmitted for a month in 1958 for a myocardial infarction from which he made an uneventful recovery.

When he was last contacted in December, 1960, he still had narcoleptic episodes once or twice daily for a few days at a time, and then he would be free of attacks for from one to two weeks. He continues to have attacks start while driving, but has not had any accidents. The episodes of sleep paralysis come every few months for a few nights in a row or in the afternoon if he lies down to sleep. He says that, as he is falling asleep, he notices a roaring in the ears, a pressure sensation in the head, sensations of pins and needles in his face, and a complete inability to move and talk. If he can open his eyes, the spell is broken. If he cannot, the spell lasts until he falls asleep. He describes it "like a hypnotic spell."

Case 4. This patient, now forty-nine years old, was admitted to The New York Hospital in 1950. Narcoleptic attacks started when he was thirty-seven years old. Typical cataplectic episodes began the following year, and sleep paralysis started at thirty-nine years of age. He continues to have many narcoleptic episodes daily and infrequent cataplectic attacks, lasting a few seconds, when he falls to the floor. These attacks are always brought on by emotional stress, for example, when he tries to tell a joke or laugh. Sleep paralysis occurs a few nights in a row, and then he is usually free of attacks for a few weeks or months. They always occur on awakening from sleep. His wife recognizes them by the groans that she hears, and she then, with difficulty, pulls the patient to a sitting position and the attack ends. The attacks last about a minute from the time his wife hears the groaning. She says that he is "limp from the shoulders up, but the rest of his body is as stiff as a board." The patient is fully conscious during the attack, but is not aware that the attack will end soon and puts up a marked battle each time to talk and move. With each attack, he suffers not only the agony of the feeling of paralysis but has hallucinations such as "a tiger is about to catch me" or that he is "pinned up against a wall and the savages will get me." In 1950 his hospital work-up, including an electroencephalogram, was normal.

Comment

There is no effective therapy for sleep paralysis. Sedation to shorten the interval before falling asleep has been suggested, but in Case 2 sedation was used successfully to provoke an attack. It is of importance that the condition be recognized, so that the patient may be reassured about the nature of the attacks. In Cases 1 and 2 this was of value in reducing the anguish experienced during the episodes. This intellectual awareness was of no benefit in Case 4 nor in the patient reported by Levin[8] where there was no recognition during the attack that these were transitory periods that would soon pass.

Summary

Sleep paralysis consists of short periods of motor paralysis while consciousness is maintained, coming on just prior to falling asleep or on awakening. It may exist by itself or be associated with narcolepsy, cataplexy, and hypnagogic hallucinations. Four cases have been reported, exemplifying most of the features of the disorder. There is no effective treatment, but an explanation of the nature of the attacks may alleviate, in some patients, the emotional suffering experienced during an attack.

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Adolescents at a Family Court

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In dealing with difficulties of adjustment among adolescents, the need to consider the family and community as well as the adolescent has been recognized. New York City has therefore developed a family court which has jurisdiction over all family disputes other than those involving financial support and felonies. It is important to recognize emotional disorders and to arrange treatment as soon as the adolescent comes to attention, whether within the family or through school, church, social agencies, hospital clinics, police precincts, or city courts. Families, when they think that an adolescent is beginning to get out of hand, often seek help from the local courts. In this report, the experimental approach of a new family court system toward adolescents and their families will be presented in its diagnostic, therapeutic, and preventive aspects. The need for additional specialized treatment facilities will be emphasized.

Cases of adolescents, aged sixteen to twenty-one, involved in family conflict in New York City are heard in two specialized courts having auxiliary professional services, including psychiatric clinics. Adolescent girls in difficulty with their families or with the community are seen at Girls' Term Court.[1] Male adolescents who encounter difficulty with their families are seen at the Home Term Court. The majority of cases at the latter court are conflicts between married couples, but problems involving male and occasionally female adolescents are seen also.[2] Families having difficulty come to the court through their own action or are referred by local police precincts, other city courts, and community social agencies.

Male adolescents are brought to court by a parent or other family member on a summons or warrant and charged as wayward minors. The difficulties behind this charge are usually that the adolescent is in conflict with another family member, is disobedient, stays out late, runs away, is truant from school, keeps undesirable company, drinks excessively, refuses to work, or caused scenes and disorder at home. The court offers the litigants a choice between legal action and the use of its social services. Most choose voluntarily or can be persuaded to accept the ancillary services of the court. Initially the parents want to use the authority of the court to force the adolescent to behave, to punish him, or to effect placement outside the home. The focus of the court is not on the offense, but on the offender and his family. The object is not to punish, but to explore, understand, and alleviate the family difficulties in the hope of preventing family disruption, delinquency, criminal activities, and serious emotional disorders. The probation department at the court has an active role in helping adolescents remain out of jail and in working with their families.

Since 1955 the court has had an attached psychiatric clinic, and many of the cases involving adolescents are now referred there by the judges and probation officers for study. The adolescent and the parent involved in the court hearing, and sometimes other family members, are seen in separate interviews at the clinic by the psychiatric social worker and then by the psychiatrist. Psychologic testing is done on a large number of the adolescents referred to the clinic. A summary report of the total clinic study of the adolescent and his family is prepared by the psychiatrist for the use of the judge and probation officer on the case. Appropriate patients are taken on for treatment at the clinic where social case work, supportive psychotherapy, and dynamically oriented psychotherapy are available. Treatment is offered to the adolescent and one or both parents, and any one or all of these may receive treatment.

Psychiatric findings

All the adolescents and parents in the present study were seen in psychiatric consultation by the writer during the period from December 4, 1956, to September 1, 1961. The number represents a little less than half the adolescent cases studied at the clinic during that time. The diagnoses follow the American Psychiatric Association classification wherever possible. In most instances they are the result of at least two hours study on each individual patient, but they might be qualified with more exploration.

There was a total of 100 adolescents given one or more appointments for psychiatric consultation, and 66 of these came. Sixty-nine diagnoses were made on these patients, since a few required more than one diagnosis. There were 31 patients with psychoneurotic reactions, presenting a diversity of symptoms. Twelve patients with schizophrenic reactions were seen, of whom 2 required prompt psychiatric hospitalization. There were 9 patients with sociopathic personality disturbances, and 3 of these were hospitalized for heroin addiction. Personality pattern and personality trait disturbances occurred in 8 patients. One had a mild, chronic brain syndrome secondary to trauma. Eight suffered from mental deficiency, and 2 of these required institutionalization.

Seventy-nine of the 100 adolescents were single male defendants, while there was 1 married female defendant. Eighty of the total were male, while 20 were female.

Fifty-five mothers brought adolescent sons to court, and 41 of these mothers came for psychiatric consultation. Eleven fathers and 1 stepfather brought 14 sons, and 8 of these parents kept their appointments. Siblings and grandparents brought a few male adolescents to court. An effort was made to see many parents who were not directly involved in the litigation. The diagnostic impressions on the parents varied. On the whole, it was thought that most parents were more disturbed emotionally than were their adolescents. Frequently adolescents suffered from psychopathologic symptoms and defense mechanisms similar to those of one or both parents, but often they differed markedly and appeared to be in reaction against the parents.

An interesting and unexpected occurrence was that of 6 adolescents each summoning a parent to court, all of the parents being charged with disorderly conduct. Four fathers were brought to court: 2 by male adolescents and 2 by adolescent daughters. One male adolescent and one adolescent girl brought their mothers to court. All these parents were rather seriously disturbed, while their adolescents had only minor emotional disturbances.

A recent development during the past two years has been the referral of 21 married adolescents to the clinic. Eleven of these were teen-agers married to an adult, of whom 6 came for psychiatric consultation. Ten of these were involved in five teen-age marriages. Both parties in two of the teen-age marriages and 1 party in one teen-age marriage kept their appointments. These cases were adolescent wives bringing a husband to court on charges of assault or disorderly conduct. Only 1 adolescent wife was brought to court by her adult husband on charges of disorderly conduct. The few married adolescents who were seen appeared to be more disturbed emotionally and tended to act out more than the unmarried group.

Two cases, involving 3 male adolescents, will be presented briefly to illustrate the kinds of problems seen and their management.

Case reports

Case 1. A forty-six-year-old father, who had been married for twenty-six years, brought his 2 sons to court as wayward minors. The eighteen-year-old son was untidy at home to such a degree that he had been assigned a separate room in the rear of the house. The father brought in snapshots to illustrate the disorder there. The son was well endowed intellectually and gifted in electronics but had dropped out of school, refused to work, was friendless, and spent all his time alone in his room attempting to build space rockets. On examination he appeared to be suffering from a simple schizophrenic reaction with grandiose ideas about himself.

The sixteen-year-old son also had quit school and refused to work. His history revealed late hours, undesirable companions, and several encounters with law enforcement agencies because of antisocial activities. He failed two psychiatric appointments and came one hour late for the third. He appeared to show an early schizophrenic reaction with antisocial tendencies.

The father seemed to have a compulsive personality and to be openly hostile toward both sons, but more rejecting of the younger one. He was preoccupied with cleanliness, order, and good citizenship. On several occasions he telephoned the writer, insisting that the court get both sons out of his sight because he thought that neither could ever be a decent human being.

The mother was a forty-four-year-old woman who spent the interview time discussing her medical history and various somatic symptoms. She was entirely preoccupied with her health and seemed unconcerned that her entire family was in court. Her understanding of the situation and her emotional reactions were limited. Less well-organized than the father, she was less rejecting of the sons but seemed detached from them. The impression was that she suffered from a chronic undifferentiated schizophrenic reaction.

Probably as a result of the encouragement and exploration of his abilities at the clinic, as well as of the fear of the authority of the court, the elder son improved his appearance and secured a position as a television repairman. Later he joined his father in the refrigeration business and continued living at home. He remained under the supervision of the court through the probation department.

The younger son's previous pattern continued, with increased overt rebellion. Along with a group of male adolescents, he was convicted of transporting a stolen car across state lines and is serving a three-year sentence in a Federal penitentiary.

Case 2. A seventeen-year-old male adolescent brought his father to court on a charge of disorderly conduct, complaining that the house was dirty and full of junk. A highly intelligent, ambitious, and personable young man, his conflict with his father interfered seriously with his study and school performance. By coming to court he hoped to replace his father as head of the household and to take care of his mother and twelve-year-old brother. He expected to work part time and to attend a city college. He appeared to be having an anxiety reaction and began psychotherapy at the clinic.

His father, a fifty-five-year-old immigrant, who had been married for twenty-one years, had a paranoid reaction. For several years he had thought that his landlady and neighbors were organized against him and had urged his family to avoid contact with them. In the hope of appeasing the court and holding his family together, he painted the apartment and discarded some of the litter he had collected. Soon he was summoned to a higher court by his landlady, charged with assault.

The mother, a forty-five-year-old immigrant, suffered from multiple psychoneurotic symptoms. She was an anxious, passive, dependent, and compliant person, unable to take action without support. It was recommended to the court that the parents separate temporarily and the two sons remain with the mother, who planned to resume full-time employment. Because of complicating circumstances, this recommendation was not effected, and the family remained together. The son and mother are receiving psychotherapy, and the father has periodic psychiatric examinations at the clinic.

Comment

Bringing an adolescent to court on the part of parents probably indicates anxiety about him, as well as punitive and rejecting attitudes toward him. Relatively few fathers brought their sons, which probably is related to the father's being outside the home every day and his unwillingness to take time off from work to come to court several times and is not a sign that he is less interested or less punitive than the mother.

Perhaps there are sources of strength available to the adolescents in the community which caused them to show less disturbance than did their parents. It is possible, however, that the stresses of adult life will make disturbances in the adolescents more apparent at a later date.

The need for further study and the increasing interest in young people and their families lead the court to refer larger numbers of them to the psychiatric clinic. The adolescent group often requires extended study to reach a diagnosis and to gain sufficient understanding and rapport to help with their problems.

About two thirds of the adolescents and their parents kept appointments for psychiatric study, and some of these voluntarily began psychotherapy at the clinic. It has been found that often the adolescent can be treated in a court setting. Often treatment must be on his terms. Sometimes the authority of the court can be used constructively in motivating the adolescent to attend treatment sessions at the clinic. The success of his treatment does not necessarily depend on the simultaneous treatment of his parents.

The specialized family court represents a distinct advance in the handling of problems with adolescents. These cases are now heard in one court with experienced judges and probation officers, and the services of the attached psychiatric clinic are available at any time for any case. Punitive attitudes toward male adolescents are rapidly being resolved at this court, but a problem remains in that a few of them are confined to jail for a few days before the case is heard. Outpatient psychotherapy is now offered to the wayward minor, predelinquent group through the court. The psychiatric clinic makes psychiatric impressions and recommendations available to the court and probation department. Thus the court can commit seriously disturbed adolescents to hospitals for observation and treatment, and the probation department can supervise closely those who are less disturbed.

There is a most serious problem regarding placement when it is desirable as part of the treatment program to remove an adolescent from an unsuitable home environment. The present policy is to attempt to avoid sending the adolescent to a public psychiatric hospital or to a state training school for lack of other facilities. For those adolescents who are ready and who should live away from home, residence centers must be established in the community to provide a home from which they might receive psychotherapy and participate in a treatment program, and from which they could attend school or work. If such facilities were readily available, the younger son in Case 1 might have been removed from his home and neighborhood in time to prevent his criminal activity and prison term.

Conclusion

It is important to recognize the need for special lower courts to handle minor legal problems with adolescents. Psychiatric clinics attached to such courts demonstrate that such adolescents and their families suffer from emotional disorders. Through their diagnostic and treatment facilities young people in difficulty with their families can be reached before they cause difficulty in the community. There is an increasing need, however, for residence-treatment centers for selected adolescents.

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References

1. Bromberg, N., and Rose, J. V.: Experiences with psychotherapy of adolescent delinquents in a clinic attached to a court, American Psychiatric Association meeting, Atlantic City, New Jersey, 1955.

2. Ferguson, G. R.: An experimental psychiatric clinic in a family court: with diagnostic impressions, Internat. J. Social Psychiat. 4: 108 (Autumn) 1958.

A grateful physician

There is obviously a great difference between academic investigation and the industrial research problems which must be solved before a new therapeutic substance can be produced in large amounts. Methods must be perfected and standardized. Large scale clinical tests must be organized and the results appraised. The product must be introduced to physicians and trustworthy information supplied to them. The ethical and competent promotion of a new and vitally necessary substance plays a very important role in the saving of lives. It is frequently very important to make drugs quickly and generally available. I am not competent to discuss the obvious financial risks which an industrial company must take under these conditions, but there have been several occasions when I have been, as a physician and as a human being, profoundly grateful to them for accepting these risks.—*Charles H. Best, M.D., Director, Banting and Best Department of Medical Research, University of Toronto, to Senate Subcommittee on Antitrust and Monopoly*

Doctor's Role in the Social Security Disability Program*

JOSEPH J. OLIVA, M.D.
New York City

Chief Medical Consultant,
Bureau of Disability Determinations,
State of New York Department of Social Welfare

EVERY PHYSICIAN will want to have a good understanding of the Social Security disability program, principally because he is asked at one time or another to furnish medical evidence in connection with a patient's claim for disability benefits. The cooperation of claimants' physicians has been indispensable in administering this program. Last year physicians submitted about 100,000 medical reports for residents of New York State.

Social Security disability benefits are payable to persons who lack the physical or mental capacity to perform substantial gainful activity. This is not an occupational definition; it includes any work within the applicant's vocational experience and educational background. His inability to engage in continued work must be due to a medically determinable impairment or a combination of impairments. Thus, the illness must be demonstrable through the diagnostic technics of medicine. It must have prevented work for six months and must be expected to be of long-continued and indefinite duration in spite of therapy.

Applying for disability benefits

In New York State persons with significant impairments may apply for disability benefits at one of 50 Social Security district offices scattered throughout the State. The district office gives the disabled applicant information about his rights, helps him to fill out his application, and advises him as to the proofs and documents he may need to support his application. Each claimant must furnish medical evidence in support of his claim to the district office. He is given a medical report form to be completed by his attending physician. His physician's report, together with supplemental reports from other physicians, hospitals, or clinics are then forwarded with his application by the district office to the Bureau of Disability Determinations of the State of New York Department of Social Welfare, which evaluates claims on behalf of the Federal Social Security Administration.

Who makes the determination

Physicians are employed by the New York State Bureau of Disability Determinations (located in New York City) to serve on teams with experienced lay disability evaluators to make the disability decision. The State agency physician reviews and evaluates the medical evidence to ascertain whether or not the clinical facts adequately describe the onset and cause of the impairment, its severity, and how it limits the applicant's physical and mental capacities. In addition, consideration is given by the team as to whether or not the impairment, when considered with the claimant's education, skills, and vocational experience, so limits his ability to perform significant functions—such as, moving around, handling objects, hearing, speaking, reasoning, and understanding—that it prevents him from doing any substantial work.

In over half of the disability claims filed in New York State, the extent of residual functional capacity can be determined by the State agency based on the initial evidence submitted. However, in about 25 per cent of the remaining claims it is necessary to recontact the claimant's own medical sources to obtain specific clinical facts which were not submitted initially. In the other one quarter of the cases, additional evidence not obtainable from the claimant's medical sources is needed to assure a sound decision or to resolve conflicts in the evidence. In such cases, the Bureau of

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* Reprinted, by permission, from New York Medicine **18:** 336 (May 5) 1962.

Disability Determinations is authorized to purchase from specialists, at Government expense, independent medical examinations and special tests to supplement information already in file.

It therefore becomes clear that by submitting a carefully documented and complete medical report initially, including a detailed and carefully dated history, specific physical findings, as well as laboratory data and clinical course, the doctor contributes to his patient's welfare by facilitating a prompt decision by the State agency.

Diagnosis vs. function

A good medical report enables the State agency to evaluate the claimant's remaining physical or mental capacity. As a rule, to evaluate the severity of impairments, the same kind of history, physical findings, and laboratory data are needed that the attending physician requires in making his diagnosis and planning his treatment. Certain medical facts, however, have greater physical capacity relevance than diagnostic and therapeutic relevance. For example, a ventilatory study or a determination of the patient's oxygen consuming capacity is more significant for evaluating physical capacity than for diagnostic purposes. A carefully detailed and dated medical report, including the clinical course, enables the reviewing physician to assess the applicant's remaining physical and mental capacity and, thereby, eliminates the need to write back to the reporting physician or purchase specialist examinations.

About 1 out of every 3 New Yorkers found disabled was awarded disability insurance benefits on the basis of cardiovascular disease. If you are describing heart disease in your patient, general terms such as mild, moderate, or severe are helpful, but unless supporting facts are included the reviewing physician does not have the precise data he needs to measure remaining capacity for work. The medical report should include heart size as determined by the point of maximal impulse and by a roentgenographic examination. Serial blood pressure readings in patients with hypertension are often helpful. Electrocardiographic interpretations should be accompanied by descriptions and actual tracings. Comment should be included as to the presence and extent of edema as measured by physical findings, weight change with diuretics, and so forth. The report also should show the amount of exertion that results in dyspnea and/or angina and the clinical characteristics of these symptoms.

Where dyspnea is present, it is necessary to know characteristics of this symptom to accurately evaluate disability. When was it first noticed? Is it persistent or intermittent? Is it progressive? How does it relate to exercise? Dyspnea should be expressed in terms of the number of steps that can be mounted or the distance in blocks that the patient can walk and the speed at which these activities can be performed. In diagnostic, prognostic, and therapeutic medicine, precise measurements of exertional dyspnea are not always crucial, since the degree to which this sensation is present does not necessarily affect diagnostic conclusion and therapeutic regimen. To evaluate loss of function and remaining capacity for work, however, the State agency needs sufficiently detailed information to decide whether or not the applicant's dyspnea is so severe that it is unreasonable to expect him to work. Because of their prognostic significance, it is extremely important to include paroxysmal nocturnal dyspnea and orthopnea if they are present.

Where chest pain is the patient's principal complaint, it is important for the physician to indicate the character and severity. The attending physician's report of angina should include its location, whether it radiates, the frequency of attacks, the duration, and how it responds to medication. The severity of angina should be related to specific activity, eating, emotional stress, and the effects of the vicissitudes of climate.

The reports received from New York State physicians indicate that we are well on our way to establishing good communications between the attending physician and the Social Security disability program as to what is required to evaluate functional capacity. Through this improved understanding will come prompt and equitable disability decisions for all applicant-patients.

BILLSBORD

As for my doctor, it seems strange as hell
When I am sick, he makes me well
But then by some mysterious trick
When I am well, he makes me sick!

* * *

A good teacher must earn respect not demand it.

* * *

Criteria differentiating amateur and professional based on voluntary ptosis:

An amateur closes her eyes when kissing.

An amateur closes his eyes when singing "When Irish Eyes are Smiling."

An amateur closes his eyes and swings on a three and two count.

An amateur closes his eyes when he ducks a right cross.

An amateur closes his eyes when he is paid.

* * *

Whether there is or is not such a thing as originality is a question which philosophers have debated since man started to communicate one with the other. We do not presume to even attempt an answer. We recognize that a lifetime of reading, listening, and watching might well represent the source or even the prototype of what we may say or write and which we assume is original because it apparently comes from ourself without recognition of previous contact. However, all of us have memories of some thought pungently expressed by someone else which so impresses us that we never forget that person or where he came from. The following from my memory represent quotes I wish I could claim.

Heard at a trimester in psychiatry and neurology at the Columbia-Presbyterian Medical Center some twenty-eight years ago, it was said by Dr. Ward Millias now of Rome, New York.—"The superego (conscience) is that part of the personality readily soluble in alcohol."

Another example came from a lifetime friend, Tom Lomasney, writing from an unnamed camp shortly after his induction in the early years of the second world war.—"The dining room or quarters is unbelievably large, filled with tables of the same size each seating ten men, and completely occupied at mealtime without an empty chair. Their idea of basic training here is to put a platter with nine pork chops on each table."

* * *

There was an old woman who lived in a shoe
She had so many children she didn't know what to do
For sad to relate
She lived in the state
Of Connecticut, where birth control was taboo.

* * *

Summary of some fifty centuries of progress: From the fig leaf of Eve to the bikini.

* * *

We must admit to a lack of enthusiasm for the fallout-shelter program. It strikes us as the type of defensive program which history suggests is doomed to failure as was the chastity belt and the Maginot Line.

* * *

Someone has asked the age of ole Doc. Apparently this information is classified; at least, we can't find out. However, he is of an age that if he overheard some young fellow at an adjoining night-club table saying 36-30-34, he would figure he was a quarterback doing his homework.

* * *

Memory Lane

Remember the questionable humor of college days? In medical school it frequently evidenced itself by merging the medical specialty board with tin-pan alley—a conception that might distort the chromosomes of the most tolerant geneticist but which, by the small miracle of juxtapositioning, produced an effect we considered humorous; and maybe it was. We will leave it to you.

Obstetrician: "Baby It's Cold Outside!"

Gynecologist: "I'm (not) accustomed to her face."

Orthopedist: "As The Backs Go Moaning By."

Psychiatrist: (Oedipus movement) "I Want a Girl, Just Like the Girl, That Married Dear Old Dad."

Psychiatrist: (Interpretative mood) "You Tell Me Your Dream."

Urologist: "By The Waters of Minnetonka."

WRC

Letters to the Editor

Destruction of our natural environment

To the Editor: I read with interest Dr. Glenn Seaborg's commencement address to the students of Northern Michigan College reported in your issue of August 1, 1962.

I am forced to take issue with one of his points. He states that atomic energy will have certain peaceful uses, among them the leveling of the passes over the Sierra Nevada in California and the deepening of the Gibraltar Straits.

In past years I lived in California, and I have traveled a great deal in that state. I know the Sierra Nevada well. The range is the highest in the south, with gradually decreasing elevations toward the north. About seven major roads cross the most accessible passes in the northern Sierra Nevada. They are well built two-lane roads which lead through some of the most beautiful scenery found anywhere in this country. Some of them are well known—the road through Yosemite Park over Tioga Pass and the road from San Francisco to Reno over Donner Pass, for instance.

Further south the passes are steeper and more forbidding. At most, they may be crossed by trail, on foot, by mule train, or on horseback. Here is preserved one of the most splendid wilderness regions in the United States, comprising great portions of Kings Canyon and Sequoia National Parks.

Now comes Dr. Seaborg and, no doubt, other advocates of progress with similar ideas. He proposes to "level" the passes of the Sierra Nevada. To what level would he like to reduce them, one may ask? Perhaps not to sea level; but probably he would like to eliminate some annoying tight turns and switchbacks which now impede rapid traffic over this outdated natural obstacle. After all, it would be in keeping with our increasingly total disrespect for nature to build one or several superhighways across the Sierra Nevada, perhaps as beautiful as the New Jersey Turnpike or some of the Los Angeles freeways. Naturally, to relieve the monotony of mountain crag and pine forest, they should be interrupted at frequent intervals by gas stations and stereotyped chain restaurants. Motor hotels with several hundred rooms would also be needed to accommodate the intrepid traveler who is caught far from civilization at dusk. And who wants the wilderness of the National Parks, anyway? Why not a four-lane highway from Owens Valley right past Mount Whitney, so that everyone can enjoy the sublime sights of nature without taking his foot off the gas pedal?

And what means are to be used to accomplish these beneficial purposes? This is to be a peaceful application of atomic energy! Atomic explosions will bring down the mountain fastnesses efficiently and at relatively small expense. Again, no one will count the smoke and the noise, the destruction of plants and wildlife, the desecrated, wounded earth.

I think the proposal is an outrage, and I am shocked that a highly placed and responsible person such as Dr. Seaborg, who presumably has no axe to grind for lumber or mining interests, would market such an idea. I do not have the Straits of Gibraltar to dispose of and, thank God, neither does Dr. Seaborg. But I raise my voice as an American and former Californian against those who in the name of soulless material progress will stop at nothing to destroy the natural environment that is man's common heritage and is at present entrusted to us to pass on to future generations. The parts of our country where man can still know nature relatively undisturbed are small enough already. The legitimate demands of transport and industry can surely be met without leveling the mountains and poisoning the countryside with the debris of "peaceful" atomic excavations.

THOMAS F. LEO, M.D.

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Jamaica 14, New York

Reply

To the Editor: In reply to Dr. Thomas F. Leo's concern that I am strongly advocating the destruction of the scenic beauty of the Sierra Nevadas by the application of nuclear explosives, I can say that in the past I have generally placed myself in that group of California citizens interested in the preservation of such natural beauty.

I am afraid that Dr. Leo took my statement made in the commencement address to the graduating class of Northern Michigan College too literally. I meant to give examples of possible future uses of nuclear explosives—uses in which they might conceivably be substituted for conventional explosives at a cost savings.

Just as conventional explosives today find proper use in road building of mountain passes and, in fact, have been used extensively in the construction of many of the California roads, so several decades from now small nuclear explosives may find similar application.

From my experience over the past two years as Chairman of the Atomic Energy Commission, let me add one further thing; any use of peaceful nuclear explosives will be carefully evaluated by the Government prior to use to insure that there is no danger to the public health and welfare. At that time, all interested persons will have an opportunity to voice any and all opinions.

Glenn T. Seaborg, Ph.D.,
Chairman, United States Atomic
Energy Commission

Washington 25, D.C.

Incidence of side-effects of ergotamine

To the Editor: I note in the article "Effectiveness of Aerosol Administration of Ergotamine Tartrate in Migraine Headache" by Lawrence Meyers, M.D., and George S. Craft, M.D., in the July 1, 1962, issue of the Journal, that I and my colleagues were quoted as stating that the incidence of side-effects of ergotamine given to patients with migraine headaches was 10 per cent. I would call attention of the authors to our article "Ergotamine Tartrate: Its History, Action, and Proper Use in the Treatment of Migraine" (Friedman, A. P., Von Storch, T. J. C., and Araki, S.: New York State J. Med. **59:** 2359 [June 15] 1959) in which we state as follows:

> In the past four years in our clinic over 1,200 patients have been given ergotamine *plus caffeine* either orally or rectally for the treatment of migraine. Side-reactions occurred in approximately 10 per cent of this group, while they occurred in approximately 16 per cent of a series of 108 patients who were given ergotamine tartrate parenterally for symptomatic treatment of migraine.

Arnold P. Friedman, M.D.,
Physician-in-Charge, Headache
Unit, Montefiore Hospital

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New York 67, New York

Critical period in resuscitation following apnea

To the Editor: I would like a brief résumé of data concerning the longest periods of apnea that have been followed by successful resuscitation. Is there a significant difference in the critical period for children and adults? Does the critical period differ significantly for drowning, suffocation, and electric shock? The physician is often forced by social pressures to attempt resuscitation even when a person has been submerged for thirty or more minutes. It would be helpful if physicians had pertinent "official" information to use in educating rescue workers, first-aid groups, news reporters, and the general public.

George E. Moore, M.D.

Roswell Park Memorial Institute
Buffalo 3, New York

Type of hand not related to talent or strength

The size of a person's hand is not significantly related to its strength or ability, according to an article by Evan McLeod Wylie in the July, 1962, issue of *Today's Health.* "Among musicians, physicians, artists, athletes, and all others who depend on their hands to earn a living there is an infinite variety of stubby fingers, slender fingers, large hands, and small hands."

Directed by a disciplined, determined brain, human fingers can be trained to perform amazing feats. A master pianist can strike 120 notes per second, and a skilled surgeon can tie strands of silk thread into tight knots inside the human heart with two fingers.

The hands are the busiest, most complex instruments of the entire body, and the thumb is the busiest and most important of its digits. "Because of the thumb's unique ability to cross over and link up with any of the other fingers for a pinch, grab, or squeeze, we can get along with one thumb and one other finger. In a serious hand injury, surgeons try first to save the thumb."

The other fingers are markedly different in strength. "In the average person, the middle finger is the strongest, followed in order by the index finger, the fourth finger, and the little finger. Fingers two and three are the fastest of the five. The little finger is the slowest, but finger four is considered by teachers of music and typewriting to be the least responsive to training because of an innate muscular weakness."

FIFTY-SIXTH ANNUAL

District Branch Meetings

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Second District Branch

Sunday, Monday, and Tuesday, November 11, 12, and 13, 1962

Grossinger's, Grossinger, New York

Sunday, November 11

Registration (all day)

Evening

7:30 P.M. Dinner

Monday, November 12

Afternoon

12:30 P.M. Luncheon
2:00 P.M. Address: **Diagnosis and Treatment of Female Infertility**
David J. Wexler, M.D., Bay Shore, Chief, Department of Gynecology, Southside Hospital

Evening

6:30 P.M. Cocktail Party (Courtesy of the Grossinger Family)
7:30 P.M. Dinner
Introduction of Officers
Greetings: Mrs. Herbert J. Ulrich, President, Woman's Auxiliary to the Medical Society of the State of New York
Address: William L. Wheeler, Jr., M.D., President-Elect, Medical Society of the State of New York

Tuesday, November 13

Morning

9:00 A.M. Business Meeting: Election of Officers

Afternoon

12:30 P.M. Luncheon
2:00 P.M. Address: **Newer Concepts in the Etiology of Cancer**
Luigi Ferraro, M.D., Rome, Italy, Visiting Professor of Pathology

Officers—Second District Branch

President	Charles W. Shlimbaum, M.D., Bay Shore
First Vice-President	Paul H. Sullivan, M.D., Great Neck
Second Vice-President	John P. Ruppe, Jr., M.D., Islip
Secretary	Albert M. Biglan, M.D., Central Islip
Treasurer	George C. Erickson, M.D., Hempstead

Presidents—Component County Societies

Nassau	Jeff J. Coletti, M.D., Old Westbury
Suffolk	L. Barrett Davis, M.D., Westhampton Beach

Abstracts

Watne, A. L., Moore, G. E., Nadler, S., and Ross, C. A.: Preoperative anticancer chemotherapy; preliminary report, New York State J. Med. **62:** 3387 (Nov. 1) 1962.

In some patients various anticancer agents have provided excellent tumor regression, with an associated improvement in the patient's condition. This creates a possibility of conversion of the previously nonresectable lesion to a potentially curable situation. Four such cases are described in which the drug appeared equally effective against both the encroachment of the tumor mass and the associated metastases; but whether or not this sterilization of tumor areas by chemotherapy will be permanent, with resultant cure of these patients, must await further follow-up. Although patients of this type are relatively rare and their cure rate is still unknown, many more might appear if treated and observed for this possibility.

Schein, C. J., Hurwitt, E. S., and Herskovitz, A.: Endoscopy of the major bile ducts, New York State J. Med. **62:** 3412 (Nov. 1) 1962.

Choledochoscopy enables direct visualization of the common bile duct and of any calculi, diverticuli, tumors, and extrinsic duct compressions. It has enabled a more complete understanding of hepatic duct anatomy. Nonoperative methods of evaluation of common bile duct integrity are chemical and roentgenographic; operative methods include palpation, instrumentation, and roentgenography. Operative cholangiography and choledochoscopy complement each other, the disadvantages of one being compensated for by the potentialities of the other. Choledochoscopy is especially useful in demonstrating residual or reformed calculi and may minimize them once they are demonstrated. Motion pictures have been made of endoscopic findings.

Strenger, G.: Residuals of phlebitis; clinical study, New York State J. Med. **62:** 3423 (Nov. 1) 1962.

Of 150 men with phlebitis, most were from twenty to twenty-nine years old at the time of their initial attack. The preceding factor was a medical condition in 36 cases, an injury or surgical procedure in 70, physical activity in 16, and no apparent reason in 28. Phlebitis of the lower extremity was most common on the left side. The three most commonly found sequelae were edema, varicosities, and ulceration. Of the complications, 41 per cent were moderate and 20 per cent severe. There were 25 recurrences of phlebitis. At present, a combination of bed rest and an elastic support to the involved extremity is the most effective method of preventing or alleviating complications. Extensive use of anticoagulants and fibrolysins requires further evaluation.

Mitty, W. F., Jr.: Abuse of one-pint transfusions, New York State J. Med. **62:** 3426 (Nov. 1) 1962.

Of 272 patients who received 1-pint blood transfusions, 141 had hemoglobin levels of 12 Gm. or more, and 218 had hemoglobin values of 10 Gm. or more. Forty-nine had no operation. Many of these patients could probably have been managed without the use of a blood transfusion. Complications of transfusion include immediate hemolytic reaction, allergic reaction, pyrogenic reaction, bacterial contamination, bleeding tendency, and pulmonary congestion. To avoid complications, indications for transfusion must be reappraised critically and constantly.

Kulick, G.: Vaginal prosthesis for control of complete urinary incontinence, New York State J. Med. **62:** 3435 (Nov. 1) 1962.

In 5 patients with complete urinary incontinence due to neuromuscular pathologic conditions, fair to good control of the urine has been achieved with the use of an individually fitted vaginal prosthesis. The acrylic mould caused no ulceration of the vaginal mucosa or abnormal vaginal discharge. Its action of compressing the urethra against the symphysis pubis to control urine outflow is similar to sphincteric action.

Lolli, G.: The role of wine in the treatment of obesity, New York State J. Med. **62:** 3438 (Nov. 1) 1962.

An investigation was made of the possibility that wine in small amounts might alleviate some of the anxieties and hunger of 35 individuals on reducing diets. Past or present alcoholic excesses of any kind constituted definite contraindications to the dietetic-therapeutic use of wine. In 27 patients the best results were obtained when wine was taken with dinner, with an average loss of 0.53 per cent of initial body weight per week, as compared with 0.26 per cent in a control period on the reducing diet alone. A moderate reduction of body weight occurred when wine was taken after dinner or before bedtime, and no detectable benefit was obtained with wine taken more than thirty minutes before dinner. In 8 subjects who demonstrated an urge to eat at night or engage in nighttime refrigerator raids and who likewise suffered from insomnia, the use of wine after dinner or at bedtime resulted in a decrease in frequency of refrigerator raids, a reduction in body weight, and an alleviation of insomnia in 5 subjects.

New technics in study of brain

Technologic developments in medicine, pharmacology, and electronics have brought exciting advances in brain-mapping, according to an article in the August, 1962, issue of *Today's Health*. Tiny electrodes can be pushed deep into the human brain without damaging its tissues through holes buried in the skull. Scientists with probing electrodes have discovered and mapped emotional centers deep in the midbrain: pinpoints of tissue that control pleasure, pain, hunger, thirst, sex, and other basic drives. By stimulating these centers electrically in animals and human beings, scientists have produced a gamut of emotional responses and are learning how these centers color and govern our behavior: how they remember, how they act under stress, and how, as a last resort to control disease, some of these tissues can be destroyed without damaging the rest of the brain.

Neurologists formerly believed that man's enlarged cortex gave him superior intelligence because it could encompass highly specialized regions for the control of highly specialized activities beyond the capacity of animal brains. They were also convinced that if the use of one of these regions of the cortex was lost through injury or disease, the ability it controlled was permanently lost.

However, recent exploration of the brain made possible by depth electrodes shows that instead of strict specialization, the reverse is true.

"Our enlarged cortex permits dispersal of function control. It provides sheets of nerve tissue in which various regions play some part in many different activities. True, there are focal centers for control; but if one section is knocked out or destroyed, another will try to compensate for the loss. Thus it is apparent that our cortex, complex and delicate as it is, has remarkable powers of reorganization and recovery."

Research efforts in this area have bold objectives: to control the basic drives in human beings and to correct imbalances that result in mental and emotional disorders and in all kinds of psychosomatic disease.

Medical News

County society appoints woman executive

The appointment of Miss Hazel Spadafora as executive director of the Medical Society of the County of Kings has been announced by Leo S. Drexler, M.D., Brooklyn, president. The first woman director in the one hundred forty-year history of the Brooklyn physicians' group assumed office on October 1.

Miss Spadafora has been associated with the Kings County group for twenty-five years and was assistant director since 1950. In private life she is Mrs. Daniel F. Colonna.

Blue Cross will have "open enrollment" for older persons

Walter J. McNerney, president of the Blue Cross Association, has announced that notice of open enrollment periods for people sixty-five years of age and older will be given by Blue Cross Plans across the country in the last quarter of 1962.

Dates for the periods will be announced locally by individual Blue Cross Plans. No physical examination will be required. The benefit programs will be adapted to available local health facilities and will be priced in accordance with local economic conditions.

Maimonides Hospital offers lectures on pediatrics

The Department of Pediatrics of Maimonides Hospital of Brooklyn, 4802 Tenth Avenue, Brooklyn 19, New York, is offering a series of conferences to be held on Tuesday mornings at 10 A.M. in the Solarium of the Kronish Pavilion at the hospital.

Specialists from medical centers, teaching institutions, and hospitals in the Metropolitan New York area will be guest lecturers. For a complete list of the lectures write to Howard Setleis, M.D., Department of Pediatrics, at the above address.

Grants given for eye research

The National Council to Combat Blindness, Inc., has awarded 73 grants and fellowships, totaling $250,802 in support of eye research during the year 1962-1963. Included are 36 grants-in-aid; 15 postdoctoral research fellowships; and 22 student fellowships.

The Council is a voluntary health agency founded in 1946 with the primary objective of supporting eye research to discover the causes and cures of the eye problems resulting in defective vision and partial or total blindness.

Applications for the 1963 group of awards are now being invited by the office of the National Council to Combat Blindness, Inc., 41 West 57th Street, New York 19, New York. March 1, 1963, is the closing date for receipt of completed applications.

St. Vincent surgeons win prize

Five surgeons associated with St. Vincent's Hospital in New York City have won first prize for 1962 in the annual Speidel Awards offered by the United States Section, International College of Surgeons. The prize was given for the paper "A Direct Evaluation of the Ability of the Portal Vein to Assume the Role of an Accessory Outflow Tract in Cirrhosis of the Liver." The authors are:

Albert R. Burchell, M.D.; S. Frederick Slafsky, M.D.; Augusto H. Moreno, M.D.; Louis M. Rousselot, M.D.; and Rudolph F. Bono, M.D.

Two New York City physicians have been named honorary fellows by the College. They are: Gustav Bucky, M.D., and Milton Helpern, M.D.

Allergy course in Philadelphia

A two-week course in clinical allergy is being offered by the Departments of Allergy and Applied Immunology of the Temple University Medical Center and the Graduate School of Medicine of the University of Pennsylvania, from February 18 through March 1. The subject matter has been selected to serve as an introductory course for those entering the field or as a review course for practicing allergists.

For information write to: George I. Blumstein, M.D., Temple University Medical Center, Philadelphia 40, Pennsylvania.

Telstar transmits data from England to U.S.

An historic medical program in which physicians in the United States exchanged information on the treatment of psoriasis with physicians in England by way of Telstar television communication took place during the twelfth international congress of dermatology in Washington, D.C., in September. The satellite was on its 587th pass over the Atlantic Ocean when the telecast began.

During the broadcast, a panel of British dermatologists presented clinical data on 7 psoriasis patients. Some 2,500 dermatologists attending the congress in Washington were able to see detailed photographic studies of psoriatic lesions on the British patients.

Arthritis subject of course in Georgia

The Medical College of Georgia, Department of Continuing Education, has announced a course, "Diagnosis and Practical Management of Arthritis," to be held November 13 through 15. The course is acceptable for 18 hours of credit by the American Academy of General Practice.

For registration write to: Claude-Starr Wright, M.D., Director, Department of Continuing Education, Medical College of Georgia, Augusta, Georgia.

Annual Health Conference elects officers

At a recent meeting of the Annual Health Conference, Inc., the following officers were elected: William A. Brumfield Jr., M.D., White Plains, Commissioner, Westchester County Health Department, as president; Morris J. Frank, M.D., Newburgh, president of the New York State Health Officers Association, as vice-president; Granville W. Larimore, M.D., Albany, Deputy Commissioner, State of New York Department of Health, secretary; and Marion L. Henry, Delmar, Assistant Commissioner for Administration and Management, State of New York Department of Health, as treasurer. James J. Quinlivan, M.D., Albany, was reappointed as assistant secretary; and Clifford M. Hodge, Chatham, was reappointed as executive secretary.

Annual Health Conference Inc., is a nonprofit organization chartered by the Secretary of State.

The fifty-ninth Annual Health Conference will be held in June of 1963 in New York City.

Postgraduate medical seminar cruise

The Washington Post Graduate Medical Faculty is sponsoring a medical seminar cruise to the Caribbean aboard the Holland-American Line flagship, *S. S. Rotterdam*, January 5 through 20. The course will present a wide variety of topics of interest to the practicing physician and will stress diagnosis and treatment. Instruction will be by lecture and panel.

For further information write to: Allen Travel Service, Inc., 565 Fifth Avenue, New York 17, New York.

Personalities

Appointed. Leona Baumgartner, M.D., Commissioner, City of New York Department of Health, as Assistant Administrator of the Agency for International Development, by President Kennedy . . . Saul B. Gusberg, M.D., New York City, as director of the Department of Obstetrics and Gynecology at The Mount Sinai Hospital.

Speakers. Donald G. Anderson, M.D., Rochester, the presidential address at the annual meeting of the Association of American Medical Colleges, on October 29, on the subject "Some Pertinent and Impertinent Comments on Medical Education" . . . William T. Lhamon, M.D., New York City, on September 21, on the topic "Some Aspect of Perception of Time" at a staff meeting of the Veterans Administration Hospital, Northport, Long Island . . . Helmuth Nathan, M.D., New York City, at the University in Marburg, Germany, on the topics "Physiologic Consideration in Gastric Surgery" and "Art and Medicine" . . . Juan Negrin, Jr., M.D., New York City, on the subject "Recent Advances and Perspectives of Neurological Surgery" on October 8 at a meeting of The Society of Medical Jurisprudence . . . John Romano, M.D., Rochester, at the annual meeting of the Association of American Medical Colleges, on October 30, on the topic "Requiem or Reveille—The Clinician's Choice" . . . Robert Turell, M.D., New York City, on September 19, before an audience of third-year medical students at the University of Vermont School of Medicine on the topic "Proctologic Examination" and on September 20 at a meeting of the Vermont Division of the American Cancer Society at Montpelier, Vermont, on the subject "The Story of the Polyp."

Medical Meetings

Morgagni Lecture

The Morgagni Society of Brooklyn announces that its annual Morgagni Lecture will be given on October 31 at 8:30 P.M. in the McNaughton Auditorium, Kings County Medical Society Building, 1313 Bedford Avenue, Brooklyn 16, New York.

Arthur R. Sohval, M.D., associate attending physician, The Mount Sinai Hospital, New York City, and clinical associate professor of medicine, State University of New York Downstate Medical Center, will speak on the topic "Chromosomes and Clinical Medicine."

National Society for Crippled Children and Adults

The National Society for Crippled Children and Adults will hold its annual convention November 16 through 20 at the Hotel Fontainebleau in Miami Beach, Florida. The care, treatment, and rehabilitation of crippled children and adults will be the subject of the meeting. Specialists from the Caribbean area will participate in a special session in Spanish on services for the handicapped in their countries.

For information contact: National Society for Crippled Children and Adults, 2023 West Ogden Avenue, Chicago 12, Illinois.

New York Allergy Society

The New York Allergy Society will hold a meeting on November 28 at the Beekman Tower Hotel, 49th Street and First Avenue, New York City. The meeting will be preceded by cocktails and dinner at 6:15 P.M. The scientific session, which is open to the medical profession, will begin at 8:30 P.M.

The theme of the scientific session will be "Immunization Procedures—Present Status." Geoffrey Edsall, M.D., of the Harvard School of Medicine will speak on "Tetanus Toxoid and Antitoxins"; Saul Krugman, M.D., of New York University School of Medicine will discuss "Measles and Poliomyelitis Vaccines"; and Glenn O. Lease, M.D., from Parke, Davis & Company will consider "Influenza, Adenovirus, and Common Cold Vaccines."

For information contact: Bernard B. Siegel, M.D., Secretary, The New York Allergy Society, 20 Plaza Street, Brooklyn 38, New York.

Symposium on cerebral palsy

The City of New York Department of Health, The New York Academy of Medicine, and the Professional Advisory Council of United Cerebral Palsy of New York City, Inc., are sponsoring a two-day symposium on the recognition and management of cerebral palsy, on Thursday and Friday, November 29 and 30, at the New York Academy of Medicine, 2 East 103rd Street, New York City.

All practicing physicians are welcome to attend, but since attendance is limited, early application is requested. Interested physicians should write to: Harold Jacobziner, M.D., Assistant Commissioner, The City of New York Department of Health, 125 Worth Street, New York 13, New York.

Symposium on cosmetic aspects of dermatology

The relationship of modern day cosmetics to skin disorders will be analyzed at a one-day symposium on cosmetic aspects of dermatology on December 4 in Chicago. The symposium will be sponsored by the Committee on Cosmetics of the American Medical Association as a part of the program of the annual meeting of the American Academy of Dermatology.

Symposium on nutrition, oral health, and disease

Dr. Rachel Larson, of the National Institutes of Health; Dr. James Shaw, of the Harvard School of Dental Medicine; and Dr. Abraham Nizel, of the Massachusetts Institute of Technology, will be among the speakers at a symposium on nutrition, oral health, and disease to be held on Saturday, December 8, at the New York University College of Dentistry, 421 First Avenue, New York City, at 9:00 A.M.

The symposium is sponsored by the National Vitamin Foundation. Members of the medical, dental, and allied professions are invited to attend.

New York Heart Association

"Infectious Diseases of the Heart and Circulation" will be the theme of an all-day conference at the Waldorf-Astoria Hotel in New York City, on Tuesday, January 22, under the auspices of the New York Heart Association. The meeting will highlight the Association's program of professional education which has as its purpose the dissemination of specialized information to representatives of the medical and professional community.

For information contact: New York Heart Association, 10 Columbus Circle, New York 19, New York.

Eastern Conference of Radiology

The Eastern Conference of Radiology will be held at the Bellevue-Stratford Hotel in Philadelphia, April 4 through 6. The program will include refresher courses sponsored by the Radiological Society of North America. There will be a special lectureship on Friday, April 5.

For further information contact: Luther W. Brady, M.D., Secretary, Eastern Conference of Radiology, The Hahnemann Medical College and Hospital of Philadelphia, 230 North Broad Street, Philadelphia 2, Pennsylvania.

Glue-sniffing potentially harmful

Glue-sniffing, increasingly popular among adolescents who want to get "high," is potentially harmful, according to an article by Helen H. Glaser, M.D., and Oliver N. Massengale, M.D., in the July 28, 1962, issue of the *Journal of the American Medical Association*. The inhalation of plastic cements and airplane glue produces effects ranging from mild intoxication to disorientation and coma if exposure is prolonged.

"Certainly the practice is symptomatic of social illness in the individual habitué and appears to be closely associated with other forms of juvenile asocial behavior. That it can lead the young person to more serious and lasting forms of misbehavior such as alcoholism, drug addiction, and criminal activity is implicit in the nature of the practice. Although it is doubtful that true addiction to glue occurs, it is clear that children do acquire psychologic dependency on the sensations induced and physiologic tolerance to the vapors."

Although there is no documented evidence of serious physical harm resulting from glue-sniffing, the solvents contained in glues can be harmful to organ systems, such as the liver, kidneys, brain, and bone marrow. Among unconfirmed accounts of serious effects due to glue are reports of mental deterioration, acute liver damage, and death following kidney failure.

A study of children who make a habit of glue-sniffing has been started by the authors to determine the possible organic effects. In the Denver area, it is now considered to be the most serious problem among youngsters involved in law violations. In the city of Denver the number of arrests for glue-sniffing increased from 30 in 1960 to 134 in 1961. The 134 youngsters involved in these arrests ranged in age from seven through seventeen, and all but 6 were boys. Eighty per cent were of Spanish-American origin and lived in low-income neighborhoods. Additional offenses for which some glue-sniffers were charged included primarily burglary and larceny but also truancy, drinking, car-prowling, running away, and curfew violation.

The most common method of inhaling the fumes is to squeeze out a tube of cement into a handkerchief which is held near the nose. At first "a few whiffs" will produce a "jag," but habitual users may have to inhale as many as five tubes to produce the desired results. The immediate effect is one of mild intoxication, exhilaration, and a sense of well-being. Then the child begins to act "drunk," exhibiting a loss of muscular coordination and slurring his speech. At the same time double vision and a buzzing in the ears are likely to occur during this phase lasting thirty to forty-five minutes. Drowsiness, stupor, and unconsciousness may follow with the child remaining unresponsive for as long as an hour or more. Subsequently the child cannot remember his actions during this final phase.

The habitual glue-user suffers from unpleasant breath and excessive salivation resulting from irritation to the membranes of the nose and mouth. They also experience nausea, loss of appetite, and loss of weight. School authorities have noted irritability and inattentiveness on the part of student glue-sniffers, who may fall asleep in the classroom or even lose consciousness.

Plastic cement and model airplane glue contain different combinations of solvents which evaporate easily, including chloroform and alcohol. These solvents are used so widely in lacquers, paint thinners, and enamels that they are not considered poisonous in general use. Legislation to prevent the sale of potentially poisonous cements has been suggested, and certain manufacturers have been experimenting with the idea of giving the cement an unpleasant odor. It is hoped that public awareness of the seriousness of glue-sniffing will lead to its ultimate control.

Abstracts in Interlingua

Watne, A. L., Moore, G. E., Nadler, S., e Ross, C. A.: Chimotherapia pre-operatori anti cancere; reporto preliminari (*anglese*), New York State J. Med. **62:** 3387 (1 de novembre) 1962.

In certe patientes, varie agentes anti cancere ha effectuate un excellente regression del tumores, con associate melioration in le condition del patiente. Isto crea le possibilitate del conversion de un previemente non resecabile lesion ad in un stato de curabilitate potential. Es describite quatro casos in que le pharmaco pareva esser equalmente efficace contra le foco primari del tumor e contra le associate metastases. Tamen, si o non iste sterilisation del areas de tumor per agentes chimotherapeutic va esser permanente e va resultar in le curation del patientes remane un question usque futur observationes de controlo provide le responsa. Ben que patientes de iste typo es relativemente rar e ben que le incidentia de curationes inter illes es ancora incognoscite, multe simile casos va possibilemente apparer si le tractamento e le observation pro iste possibilitate deveni plus general.

Schein, C. J., Hurwitt, E. S., e Herskovitz, A.: Endoscopia del major ductos de bile (*anglese*), New York State J. Med. **62:** 3412 (1 de novembre) 1962.

Choledochoscopia rende possibile le directe visualisation del ducto biliari commun, incluse calculos, diverticulos, tumores, e intrinsec compressiones del ducto. Illo ha resultate in un plus complete comprension del anatomia del ducto hepatic. Le methodos non-chirurgic pro le evalutation del integritate del commun ducto biliari es chimic o roentgenographic. Le methodos chirurgic include palpation, instrumentation, e roentgenographia. Le methodos chirurgic de cholangiographia e de choledochoscopia complementa le un le altere. Le disavantages del un es compensate per le potentialitates del altere. Choledochoscopia es specialmente utile in demonstrar residue o re-formate calculos e pote servir a reducer lor signification post lor demonstration. Cinematographias esseva obtenite ab le constatationes endoscopic.

Strenger, G.: Residuos de phlebitis; un studio clinic (*anglese*), New York State J. Med. **62:** 3423 (1 de novembre) 1962.

De 150 masculos con phlebitis, le majoritate habeva vinti a vinti-novem annos de etate al tempore de lor attacco initial. Le factor immediatemente etiologic esseva un condition medical in 36 casos, traumatismo accidental o chirurgic in 70, activitate corporee in 16, e nihil apparentemente causative in 28. Phlebitis del extremitate inferior esseva le plus communmente sinistro-lateral. Le tres sequellas trovate le plus communmente esseva edema, varicositate, e ulceration. Le complicationes que occurreva esseva moderate in 41 pro cento e sever in 20 pro cento del afficite casos. In 25 patientes il occurreva recurrentia del phlebitis. In le stato presente del arte, un combination de reposo al lecto con le uso de un supporto elastic pro le extremitate afficite es le plus efficace methodo pro prevenir complicationes o pro alleviar los. Le extense uso de anticoagulantes e de fibrinolysinas require un plus extense evalutation.

Mitty, W. F., Jr.: Abuso del transfusion de sanguine in pintas (*anglese*), New York State J. Med. **62:** 3426 (1 de novembre) 1962.

De 272 patientes qui recipeva transfusiones de sanguine in quantitates de 1 pinta, 141 habeva nivellos de hemoglobina de 12 g o plus, e 218 habeva nivellos de hemoglobina de 10 g o plus. In 49 nulle operation esseva effectuate. In multes de iste casos, il es probabile que le patiente haberea potite remaner sin transfusion de sanguine. Complicationes associate con transfusion de sanguine es immediate reaction hemolytic, reaction allergic, contamination bacterial, tendentia hemorrhagic, e congestion pulmonari. Pro evitar tal complicationes, le indicationes pro transfusion de sanguine debe esser re-evalutate criticamente e constantemente.

Kulick, G.: Prosthese vaginal pro retener un complete incontinentia urinari (*anglese*), New York State J. Med. **62:** 3435 (1 de novembre) 1962.

In 5 patientes con complete incontinentia urinari causate per conditiones pathologic neuromuscular, un grado satisfacente o bon de regulation del urina esseva obtenite per medio de un individualmente adaptate prosthese vaginal. Le modulo acrylic causava nulle ulceration del mucosa vaginal e nulle anormal discarga vaginal. Su action de comprimer le urethra contra le symphyse pubic in regular le effluxo de urina es simile a un action sphincteric.

Lolli, G.: Le rolo del vino in le tractamento

de obesitate (*anglese*), New York State J. Med. **62:** 3438 (1 de novembre) 1962.

Esseva investigate le possibilitate que vino in micre quantitates allevia certes del anxietates e le sensation de fame in 35 individuos qui sequeva un regime dietari anti obesitate. Excessos alcoholic de non importa qual genere, tanto in le passato como etiam in le presente, esseva reguardate como un definite indication contra le uso dietetico-therapeutic de vino. In 27 patientes le melior resultatos esseva obtenite quando le vino esseva prendite con le dinar, con un perdita medie per septimana de 0,53 pro cento del peso initial, in comparation con 0,26 pro cento in un periodo de controlo con le dieta anti obesitate sin le adjunction de vino. Un moderate reduction del pesos corporee esseva obtenite quando le vino esseva prendite post le dinar o ante le ir al lecto, e nulle detegibile beneficio esseva effectuate quando le vino esseva prendite plus que trenta minutas ante le dinar. In 8 subjectos characterisate per le tendentia de mangiar durante le nocte o de attaccar le refrigerator durante episodios de insomnia, le uso de vino post le dinar o ante le ir al lecto resultava in un reduction del frequentia del visitationes del refrigerator, un reduction del peso corporee, e un alleviation del insomnia in 5 casos.

Blood abnormalities and smoking habits linked

A significant relationship between smoking habits and two blood abnormalities has been reported in an article by Heiskell *e al.* in the August 25, 1962, issue of the *Journal of the American Medical Association.* The blood abnormalities have been associated previously with various diseases and are revealed by chemical tests showing the appearance of substances not found in normal blood.

The findings resulted from a study of 1,500 men and women over the age of twenty-five living in an agricultural community who volunteered for blood tests. The study showed that both blood abnormalities increased with age in men and women. However, when the effect of age was held constant, there was a significant correlation between the incidence of the abnormalities and increased cigaret smoking. The correlation was significantly closer in men than in women.

One of the two blood factors studied is the C-reactive protein which has been found in patients with such inflammatory diseases as rheumatic fever and in cancer patients.

The other factor is an abnormal dispersal of chemical particles in the blood determined by a seroflocculant test. This abnormality has been found frequently in patients hospitalized for cancer as well as a variety of noncancerous diseases.

While these blood abnormalities are subtle evidence of disease, they are not indicators of specific diseases. However, smoking has been associated with a wide variety of causally unrelated diseases.

Medical Schools

Albany Medical Center

Regional center. A regional center for the diagnosis and treatment of children born with birth defects has been established to serve patients in 29 counties of eastern New York and western New England. The Center is supported by the National Foundation and will be known as the March of Dimes Birth Defects Center. William A. Petersen, M.D., was appointed director. The Birth Defects Center will accept only those patients who have been referred by a physician. All patients will be evaluated first in the outpatient clinic. Those patients with adequate financial resources will be charged the prevailing clinic rate and by agreement with the National Foundation no patient will be denied service for any financial reason.

In addition to the full-time services of Dr. Petersen as director, the Center will have a full-time medical social worker, Mrs. Heidi Freund of Slingerlands, and a part-time staff which will consist of a child psychologist, Dr. N. Dale Bryant of Rensselaer, and a pediatric neurologist, Robert Cassidy, M.D., of Schenectady, and a secretary.

College of Physicians and Surgeons

Appointed. Donald P. Swartz, M.D., was appointed October 1 as clinical professor of obstetrics and gynecology and director of the combined service of obstetrics and gynecology at Harlem Hospital. Other new appointments to the faculty are: Aubre de L. Maynard, M.D., as clinical professor of surgery, Frederick R. Randall, M.D., assistant clinical professor of surgery, Herbert G. Cave, M.D., assistant clinical professor of anesthesiology, and Elizabeth Bishop Davis, M.D., assistant clinical professor of psychiatry.

Grant. The National Foundation-March of Dimes has awarded a grant of $44,492 to continue studies on how viruses grow inside cells. Harry M. Rose, M.D., John E. Borne Professor of Medical and Surgical Research as well as chairman, Department of Microbiology, is in charge of the study and associated with him are Drs. Councilman Morgan, Arline D. Deitch, Gabriel C. Godman, and Herbert Rosenkranz, and Calderon Howe, M.D.

Cornell Medical Center

First-year class. Eighty-five entering students chosen from among 988 applicants were welcomed at the opening exercise at which Wallace W. McCrory, M.D., professor and chairman, Department of Pediatrics, spoke. Dean John E. Deitrick pointed out during the opening exercises that the scholarship awards for this academic year were the largest ever made in the history of the College. One hundred and six students are sharing $130,000 and of this amount $21,900 has been awarded to 19 first-year students. Dr. Deitrick also announced that the Herman L. Jacobius Prize in pathology had been won by Donald Catino and the William C. Thro Prize in clinical pathology by John D. Van Der Decker, both members of the third-year class.

Distinguished service award of A.M.A. Russell L. Cecil, M.D., emeritus clinical professor of medicine, was the 1962 recipient of the Distinguished Service Award made annually by the American Medical Association to a doctor "who has made a notable contribution to the advance of medical science."

New York University Medical Center

Appointed. Joseph Goodgold, M.D., director of the electrodiagnostic service at the Institute of Physical Medicine and Rehabilitation, has been appointed associate professor of physical medicine and rehabilitation and director in the organization of electrodiagnostic service at Bellevue Hospital Center, Goldwater Memorial Hospital, and Elmhurst General Hospital. Nathan Kaplan, M.D., a former fellow at the Institute, has been appointed to the staff to assist Dr. Goodgold in the organization of electrodiagnostic service. Fred Frieden, M.D., has been appointed an instructor in the School of Medicine, a member of the Institute staff, and assistant attending physician in physical medicine and rehabilitation at University Hospital. Arnold S. Zentner, M.D., has been made director of the Consultation Center for Alcoholism.

Neurological in-patient service. University Hospital will open a new neurological in-patient service on February 1, 1963. The unit will consist of 18 beds for private patients with acute or chronic disease of the nervous system and all patients admitted will be under the care of members of the faculty of the Department of Neurology.

New York Medical College

Soviet visitor. Bernard M. Wagner, M.D., chairman, Department of Pathology, left October 5 for an indefinite visit to the Soviet Space Chief, Dr. Vassili V. Parin, for a cooperative exchange of data in the space program which will include information obtained from the Russians' history-making tandem orbital flights.

Heart Institute. Formation of the Heart Institute has been announced by the College. The Institute will be the only hospital of its kind in this country to be devoted entirely to research and treatment of cardiovascular disease. It will educate and train members of the medical profession in the areas of both research and clinical cardiology. Robert A. O'Connor, M.D., assistant dean, will be administrative director. Atop the hospital will be a helicopter landing to facilitate the arrival of emergency cases from airports.

State University of New York Downstate Medical Center

Expanded postgraduate program. An expanded postgraduate program for physicians was announced in September by Robert A. Moore, M.D., president of the Center. Eleven courses and three intensive conferences have been scheduled for the 1962–3 academic year. Courses in pediatrics, psychiatry, rehabilitation medicine, respiration, obstetrics and gynecology, gynecological pathology, and internal medicine began in October and in November a two-day conference on "Fundamentals of Vascular Grafting" and a one-day conference on "Systemic Lupus Erythematosus" will be held. After January 1 courses to be offered will include functional anatomy, dermatology, progress in internal medicine, heart failure, and a three-day conference on pediatrics. The postgraduate program is under the direction of Schuyler G. Kohl, M.D., an associate dean of the Medical School. Information may be obtained by writing the Office of Postgraduate Education, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

Visiting professor. Dr. Lloyd Stocken, Department of Biochemistry, Oxford University, England, was visiting professor of pathology during September. Dr. Stocken is in charge of teaching graduate students in biochemistry at Oxford and is a Fellow of St. Catherine's College, Oxford, and a consultant to the Atomic Energy Radiation Group at Harwell, England.

Sabbatical leaves. Dr. Robert F. Furchgott, professor and chairman, Department of Pharmacology, left August 1 for a full year's leave to work with Dr. J. Pasternak, chairman, Department of Physiology, University of Geneva, Switzerland. They will work with radioautography as a technic for localizing drugs in tissues and with electron microscopy for the study of peripheral autonomic neuro-effector systems. As a visiting professor, Dr. Furchgott will also do some graduate teaching at the University of Geneva.

Harry Mellins, M.D., professor and chairman, Department of Radiology, began a full year's leave on October 1. For the first nine months Dr. Mellins will work in the research laboratories of the Department of Radiology, Johns Hopkins University, and the last three months at the Institution of Urology, London, England.

Herbert C. Lichtman, M.D., associate professor of medicine, will spend a year in research and study in the field of human genetics at the Galton Laboratory, University College, London, England, under a Commonwealth Fund Fellowship.

A leave of six months has been granted to Dr. Eustace E. Suckling, associate professor of physiology, to work with a research team at the Marey Institute, Paris, France, in the field of sensory physiology and, more specifically, on brain control of sensory receptor sensitivity. Dr. Suckling will also visit scientists in London and Moscow who are interested in ultrasonics.

Visiting professor. Robert J. Kellar, professor of obstetrics and gynaecology, University of Edinburgh, Scotland, was visiting professor in the Department of Obstetrics and Gynecology for the month of October.

State University of New York Upstate Medical Center

Freshman medical students. One hundred entering students were welcomed by the faculty and staff in September. This is the largest number ever enrolled at the College.

Speakers. Julius B. Richmond, M.D., professor and chairman, and William J. Waters, M.D., clinical associate professor, Department of Pediatrics, addressed the general assemblies of the Tenth International Congress of Pediatrics, held in Lisbon, Portugal, September 9 to 15. Also participating were Lytt I. Gardner, M.D., professor, and Mary L. Voorhess, M.D., assistant professor, Department of Pediatrics, and Lawrence Pickett, M.D., clinical associate professor, Department of Surgery.

Prior to attending the International Congress of Pediatrics, Dr. Gardner attended the meeting of the European Society for Pediatric Research, Barcelona, Spain, as representative of the American Society for Pediatric Research of which he is president, and Dr. Pickett attended the annual British Pediatric Surgical Association meeting in London.

Promotions and additions to faculty and staff. James G. Derr, M.D., clinical associate professor to clinical associate professor emeritus; John B. Stevens, M.D., clinical professor to clinical professor emeritus (orthopedic), and Robert Becker, M.D., assistant professor to associate professor (orthopedic), all in the Department of Surgery; Ernest Becker, M.D., from instructor to assistant professor, Department of Psychiatry (anthropology); William H. Bergstrom, M.D., from associate professor to professor, and Sterling P. Garrard, M.D., from assistant to associate professor, Department of Pediatrics; William R. Chaffee, M.D., from instructor to assistant professor, Department of Medicine; David B. Jones, M.D., from associate professor to professor, Department of Pathology; Robert O. Jensen, M.D., from instructor to assistant professor, Department of Surgery; Chauncey W. Kenney, M.D., from clinical associate to clinical professor, Department of Obstetrics and Gynecology; David B. Robinson, M.D., from assistant professor to associate professor, and Shirley Rubert, M.D, from instructor to assistant professor, Department of Psychiatry; Stephan S. Wang, M.D., from instructor to assistant professor, Department of Preventive Medicine; Charles W. Lloyd, M.D., formerly professor in the Department of Obstetrics and associate professor, Department of Medicine, to lecturer, Department of Medicine. Also: David G. Murray, M.D., as assistant professor, Department of Surgery (orthopedics); John Sipple, M.D., clinical instructor, Department of Medicine; Richard J. Gillis, M.D., clinical instructor, Department of Ophthalmology; William V. Delaney, Jr., M.D., clinical instructor, Department of Ophthalmology; Frank A. Johnson, M.D., instructor, Department of Psychiatry; and Anthony Markarian, M.D., clinical instructor, Department of Surgery.

Internal Medicine courses. Two postgraduate courses in internal medicine began October 4, "New Measures for Medical Emergencies" and "Basic Principles of Electrocardiography." Both courses when completed will be applicable for Category I credit of the American Academy of General Practice.

University of Rochester School of Medicine and Dentistry

Appointed. Abraham A. Lurie, M.D., formerly assistant professor of anesthesiology, Tufts University, has been appointed professor of anesthesiology and an associate anesthesiologist in Strong Memorial Hospital.

Space Sciences Center to be established. Dr. Wallace O. Fenn, senior professor of physiology, will be the director of a Center for the Space Sciences to be established at the University. The Center is expected to facilitate the work currently being carried out in separate departments and also will encourage new experiments related to space exploration.

Opening Ceremonies. Dr. Donald G. Anderson, dean, attended the opening ceremonies of the University of Lagos Medical College and its teaching hospital in Lagos, Nigeria, on October 3. While in Lagos Dr. Anderson was the guest of the Council of the Lagos Medical School and the Lagos Hospital Board.

International Union of Physiologists. Dr. Wallace O. Fenn, senior professor of physiology, attended the meetings of the International Union of Physiologists in Leiden, the Netherlands, September 10 to 17. Dr. Fenn is secretary of the union and also presided at a symposium on "The Mechanics of Respiration." Also attending were Albert B. Craig, Jr., M.D. assistant professor, and Dr. Edward F. Adolph. professor emeritus, of the physiology department.

Heart drug used for glaucoma

Digitalis, long used for heart failure, has been found to be useful in treating several types of glaucoma, according to an article by Kenneth A. Simon, M.D., and Sjoerd L. Bonting, Ph.D., in the August, 1962, issue of *Archives of Ophthalmology.* Digitalis was used to treat 16 patients with chronic simple glaucoma and 5 patients with congenital and juvenile glaucoma.

Digitalis alleviates the main characteristic of glaucoma, intense pressure within the eye, by reducing the production of the fluid which fills the eye cavity. The drug inhibits an enzyme involved in the formation of the fluid, cutting fluid production by 45 per cent.

This is comparable to the effect produced by acetazolamide. Digitalis could be used when side-effects or sensitivity preclude the use of acetazolamide.

A.M.A. Committee on Nursing

Objectives and Program*

The program of the American Medical Association's Committee on Nursing is based on three general assumptions: (1) that nurses have a separate and distinct professional status, and their contributions are those of coworkers; (2) that nursing should expect the medical profession to support and endorse high standards of nursing education and service; and (3) that each of the various levels of academic and technical accomplishment in nursing makes its own unique contribution to the total health care of the public.

Objectives

On the basis of these broad assumptions, the Committee has adopted the following objectives:

To expand and strengthen liaison activities between organizations representing the medical and nursing professions at the national, state, and local levels.—Liaison has been established with all the major nursing organizations (including the American Nurses' Association, the National League for Nursing, the National Federation of Licensed Practical Nurses, the National Association for Practical Nurse Education and Service, and others) as well as with constituent and component medical associations, medical specialty groups, and several national organizations with a collateral interest in nursing.

The Committee feels that one of its major contributions is to promote interprofessional conferences between physicians and nurses. A committee composed of American Medical Association and American Nursing Association representatives is now planning a conference on nurse-physician aspects of professional practice. The Committee on Nursing will also encourage the inclusion of nurses on programs of national and state medical meetings and attempt to remedy the scarcity of positively oriented, unbiased material on nursing in the medical literature.

To study and report to the medical profession on current practices and trends in nursing and on developments among nursing auxiliary personnel.—Through its headquarters staff, the Committee is collecting information on nursing matters vital to physicians. A file of abstracts, excerpts, and reprints is available for quick reference.

To stimulate, initiate, and, where feasible, support research in areas pertinent to the nurse-physician relationship in professional practice.—Such research requires the collaboration of many disciplines. Several nurse-physician teams are now engaged in extensive research projects. These include studies of interdisciplinary participation in planning care; the nursing needs of chronically ill ambulatory patients; and the amount and type of nursing service which makes the maximum contribution to maternal and infant welfare.

To offer advisory services to both professions on interprofessional matters.—The secretary and chairman of the Committee serve at present on the committee on careers of the National League for Nursing. The secretary is also a member of the advisory council of the National Federation of Licensed Practical Nurses, the National League for Nursing's committee to study costs of nursing education, and the hospital advisory council of the National Association for Practical Nurse Education and Service. The Committee will also serve as a consultant group to committees, councils, and departments within the A.M.A. Similar services have been offered to constituent and component medical associations.

To provide support and assistance to the nursing profession and its nonprofessional auxiliary personnel in their efforts to maintain high standards.—Nursing, like medicine, is faced with pressing demands for change if high standards are to be maintained in our present environment of rapid scientific and social advances. Nursing is now engaged in a continuous re-evaluation of its educational system, its scope of services, its legal responsibilities, and other phases of its practice which reflect in the quality of patient care. This Committee supports the efforts of the nursing profession in maintaining high standards and offers its cooperation and assistance.

To encourage physicians to accept invitations to serve on nursing school faculties.—In view of growing pressures on the professional nurse to assume responsibilities of a medical nature, the teaching role of the physician warrants re-evaluation. At the present time, some nursing schools are finding it necessary to assign nurse faculty members to lecture on medical subjects.

Comment

If the medical and nursing professions are to make the fullest use of their joint potential, they must have not only a common denominator of interest in the patient and a comparable body of knowledge, but also the kind of relationship that derives from a deeper appreciation of, and respect for, each other as allies working toward the same goals.

Arthur A. Kirchner, M.D., *Chairman*
Clarence H. Benage, M.D.
Elias S. Faison, M.D.
W. Benson Harer, M.D.
Charles L. Leedham, M.D.
William R. Willard, M.D.

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Necrology

Paul M. Ajosa, M.D., of Rockville Centre, died on December 9, 1961, at the age of sixty-seven. Dr. Ajosa graduated in 1924 from General Medical College, Chicago. He was an assistant attending physician at Metropolitan Hospital and a former physician with the New York City Department of Health.

Carmen Louis Albano, M.D., of Mount Vernon, died on March 6 at the age of fifty-seven. Dr. Albano received his medical degree from the University of Rome in 1933. He was a clinical assistant attending obstetrician at Mount Vernon Hospital. Dr. Albano was a member of the Westchester County Medical Society and the Medical Society of the State of New York.

Stanley C. Babcock, M.D., of Buffalo, retired, died on February 11 at the age of ninety-five. Dr. Babcock graduated in 1890 from the University of Buffalo School of Medicine.

George Edward Barnes, M.D., of Utica, retired, died on August 27 at the age of ninety-one. Dr. Barnes graduated in 1899 from Columbia University College of Physicians and Surgeons.

Philip Borst Becker, M.D., of New Rochelle, died on April 23 at the age of seventy-one. Dr. Becker graduated in 1918 from the University of Vermont College of Medicine. He was a clinical assistant attending surgeon at New Rochelle Hospital. Dr. Becker was a member of the Westchester Academy of Medicine, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Zelman Moseij Berman, M.D., of New York City, died on May 6 at the age of seventy-four. Dr. Berman received his medical degree from the University of Leipzig in 1914. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Lazarus Blaustein, M.D., of Goshen, died on September 16 at the age of sixty-six. Dr. Blaustein graduated in 1919 from Fordham University School of Medicine. He was a member of the American Geriatrics Society, the Orange County Medical Society, and the Medical Society of the State of New York.

Jacob Buckstein, M.D., of New York City, died on September 18 at the age of seventy-two. Dr. Buckstein graduated in 1915 from Cornell University Medical College. He was a consulting physician at Trafalgar and Good Samaritan (Suffern) Hospitals, a consulting physician in gastroenterology at Grand Central Hospital, a former visiting roentgenologist in the Alimentary Tract Division of Bellevue Hospital, and for more than twenty-five years had been an assistant professor of clinical medicine at Cornell University Medical College. Dr. Buckstein was a Diplomate of the American Board of Internal Medicine (Gastroenterology) and a member of the American Roentgen Ray Society, the New York Academy of Medicine, the New York Gastroenterological Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

James E. Burns, M.D., of Glen Cove, died on May 10 at Palm Island, Florida, at the age of eighty-eight. Dr. Burns graduated in 1899 from New York University and Bellevue Hospital Medical College. Dr. Burns was the first mayor of the City of Glen Cove, the first vice-president and a founder of the First National Bank of Glen Cove (now Franklin National), and from 1934 to 1949 was postmaster of Glen Cove.

Gustav Einstein, M.D., of New York City, died on May 2 at the age of seventy-seven. Dr. Einstein received his medical degree from the University of Munich in 1909.

Bernard Hyle Eliasberg, M.D., of New York City, died on September 12 at the age of seventy-six. Dr. Eliasberg graduated in 1906 from Cornell University Medical College. He was a consulting anesthetist at The Mount Sinai and Jewish Memorial Hospitals and an emeritus anesthetist at Montefiore Hospital. President of Mount Sinai's medical alumni association, he was the recipient of the Hospital's Jacobi Award in 1958. Dr. Eliasberg, a founder of the Phi Delta Epsilon fraternity at Cornell, was a Diplomate of the American Board of Anesthesiology (of which he was a founder), a Fellow of the American College of Anesthesiologists, and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

E. Scott Francis, M.D., of Middleport, died on May 6 at the age of thirty-six. Dr. Francis graduated in 1953 from Western Reserve University School of Medicine. He was a member of the medical staff of Medina Memorial Hospital. Dr. Francis was a member of the Orleans County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Gitzelter, M.D., of Brooklyn, died on December 13, 1961, at the age of fifty. Dr. Gitzelter graduated in 1939 from the University of Edinburgh. He was an associate attending physician at Kings County Hospital Center, Goldwater Memorial Hospital, and the Jewish Chronic Disease Hospital Dispensary, and director of diabetes at Kings County Hospital Center Outpatient Department. Dr. Gitzelter was a Fellow of the American College of Angiology, an Associate Fellow of the American College of Chest Physicians, and a member of the Brooklyn Society of Internal Medicine, the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

John Michael Griffin, M.D., of Glens Falls, died on April 5 at the age of eighty-five. Dr. Griffin graduated in 1901 from Albany Medical College. He was a consulting surgeon in ear, nose, and throat at Glens Falls Hospital. Dr. Griffin was a member of the Glens Falls Academy of Medicine, the Warren County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

George Eugene Hayunga, Jr., M.D., of New York City, died on April 28 at the age of sixty-two. Dr. Hayunga graduated in 1940 from Queens University Faculty of Medicine, Kingston, Ontario. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Jakob Josef Hellman, M.D., of Brooklyn, died on March 24 at the age of seventy-four. Dr. Hellman received his medical degree from the University of Vienna in 1915. He was a member of the Brooklyn Academy of Medicine, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Herman Leon Hessel, M.D., of Brooklyn, died on December 9, 1961, at the age of thirty-four. Dr. Hessel graduated in 1953 from New York University College of Medicine and interned at Kings County Hospital Medical Center and the Veterans Administration Hospital, the Bronx. He was an assistant attending physician at the Jewish Chronic Disease Hospital and the Kings County Hospital Medical Center. Dr. Hessel was a member of the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Allen Hirst Hirsch, M.D., of Forest Hills and Brooklyn, died on March 4 at the age of sixty-five. Dr. Hirsch received his medical degree from the University of Frankfurt in 1920. He was a clinical assistant attending physician at Cumberland Hospital. Dr. Hirsch was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harold Booth Judd, M.D., of Rumson, New Jersey, formerly of New York City, retired, died on May 6 at the age of eighty-two. Dr. Judd graduated in 1904 from Cornell University Medical College and interned at City Hospital, at Elmhurst. He was a consulting surgeon in otolaryngology at City Hospital at Elmhurst and an honorary surgeon at the New York Eye and Ear Infirmary. Dr. Judd was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Aron Arnold Kaplun, M.D., of New York City, died on May 20 at the age of sixty-five. Dr. Kaplun received his medical degree from the University of Giessen in 1925. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William George Keens, M.D., of Albany, died on March 25 at the age of eighty-one. Dr. Keens graduated in 1904 from Albany Medical College. He was a member of the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph A. Le Pener, M.D., of Syosset, died on March 26 at the age of sixty-nine. Dr. Le Pener received his medical degree from the University of Vienna in 1918. He was a member of the Nassau County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Karl J. Lowe, M.D., of New York City, died on April 12 at the age of ninety. Dr. Lowe received his medical degree from the University of Vienna in 1904. He was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Sebastiano Mauro, M.D., of Mount Vernon, died on February 12 at the age of thirty-nine. Dr. Mauro received his medical degree from the University of Catania in 1948. He was a staff physician at the Montefiore Hospital. Dr. Mauro was a member of the Westchester County Medical Society and the Medical Society of the State of New York.

Alan Miller Moodie, M.D., of Schenectady, died on April 8 at the age of forty. Dr. Moodie graduated in 1948 from Albany Medical College. He was a junior attending surgeon at Bellevue Hospital, New York City and an assistant attending surgeon at Ellis and St. Clare's Hospitals. Dr. Moodie was a Diplomate of the American Board of Surgery, a Fellow of the American College of Surgeons, and a member of the Schenectady County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Leo Ambrose Parker, M.D., of Hollis, died on March 29 at the age of eighty-two. Dr. Parker graduated in 1905 from Columbia University College of Physicians and Surgeons and interned at St. Mary's Hospital.

Harry D. Pasachoff, M.D., of the Bronx, died on September 20 at the age of sixty-five. Dr. Pasachoff graduated in 1918 from Columbia University College of Physicians and Surgeons. Clinical professor of pediatrics at New York Medical College, he was a consulting pediatrician at Morrisania and Sydenham Hospitals and medical director of the Shield of David. Dr. Pasachoff was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Bronx Pediatric Society, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Martin Reid, M.D., of St. Albans, died on May 21 at the age of eighty. Dr. Reid graduated in 1911 from the University of McGill Faculty of Medicine. He was a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Ben-Henry Rose, M.D., of the Bronx, died on September 16 at the age of sixty-five. Dr. Rose graduated in 1920 from New York University and Bellevue Hospital Medical College. He was a Fellow of the International College of Surgeons and a member of the American Geriatrics Society, the American Association for Research in Psychosomatic Problems, the New York Academy of Medicine, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Albert Aaron Rosner, M.D., of Crestwood, died on March 3 at the age of fifty-two. Dr. Rosner graduated in 1935 from the University of Pennsylvania School of Medicine and interned at the Neurological Institute. He was an associate attending physician in psychiatry at Presbyterian Hospital and an attending neuropsychiatrist at Veterans Administration Hospital, the Bronx. Dr. Rosner was a Diplomate of the American Board of Neurology and Psychiatry, a Fellow of the American Psychiatric Association, and a member of the American Psychoanalytic Association, the American Academy of Neurology, the New York Neurological Society, the New York Psychoanalytic Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

David N. Rudin, M.D., of Baltimore, Maryland, formerly of New York City, died on March 18 at the age of fifty-seven. Dr. Rudin graduated in 1936 from the University of Minnesota Medical School and interned at Goldwater Memorial Hospital. A Member of the American Psychiatric Association, he held memberships also in the New York County Medical Society and the Medical Society of the State of New York.

John Howard Stewart, M.D., of Norwich, died on September 8 at the age of seventy-nine. Dr. Stewart graduated in 1908 from Syracuse University College of Medicine. He was an attending otolaryngologist and rhinologist at Chenango Memorial Hospital. Dr. Stewart was a member of the Chenango County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Alfred Andrew Trivilino, M.D., of Jamaica, died on March 26 at the age of fifty-eight. Dr. Trivilino graduated in 1927 from Long Island College Hospital School of Medicine. He was a consulting pediatrician at Queens Hospital Center and Mary Immaculate Hospital, Jamaica. Dr. Trivilino was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Brooklyn Academy of Pediatrics, and the Queens Pediatric Society.

Hyman Wohl, M.D., of New York City, died on May 14 at the age of fifty-eight. Dr. Wohl graduated in 1927 from New York Homeopathic Medical College and Flower Hospital. He was an adjunct urologist at the Hospital for Joint Diseases. Dr. Wohl was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Books Reviewed

Practical Pediatric Dermatology. By Morris Leider, M.D. Second edition. Quarto of 437 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $13.75.

This book was written primarily for the busy pediatrician and general practitioner. As the author explains in his preface, emphasis is placed on common conditions and usable therapy. Common conditions happen commonly, but most teaching texts do not recognize this obvious truism. There is some room devoted to the rare and exotic, but most nondermatologists prefer to refer these conditions to the dermatologist. Where the author feels it is necessary, he has delved into theory. Often he states his own opinion, with which all dermatologists may not agree. Be that as it may, Leider's opinions are worth hearing. Especially stimulating and provocative are his ideas in the field of bacterial allergy. He does not hesitate to take a clear stand about controversial topics, such as the role of food in the production of dermatoses.

This is a second edition, in which therapy, which is always in a state of flux, is brought up to date. However the time-proved principles of treatment are still emphasized.

Probably the single most important chapter in the book is the one devoted to principles of dermatologic therapy. Leider states that "the entire purpose and goal of medical practice is prophylaxis or effective treatment of disease and that in the field of dermatologic therapy it is possible to be a fairly good therapeutist without being a superlative diagnostician. This is especially true in the case of pediatric dermatology." Recent statistics show that skin conditions constitute 10 to 20 per cent of cases seen in general practice, and a large part of skin diseases (at least 50 per cent) are inflammations (dermatitis-eczema group). The pediatrician and the general practitioner, who carefully digest this chapter, will obtain a thorough and well-rounded course in therapy, which can be put to good practical use.

The book contains numerous clear and well-arranged tables and diagrams and an excellent glossary of terms and definitions. Where possible, adequate black-and-white pictures aid descriptions and instructions.

The author writes forcefully, with sparkle and wit. There is no doubt that he adds color and flair to that which is notoriously dull and monotonous.

Sir William Osler strongly advocated and urged periodic brain dusting to his physician students. Even the experienced dermatologist will find the means in this book for this valuable exercise.—LIONEL A. DICK, M.D.

A Manual of Neurology and Psychiatry in Occupational Medicine. By Ralph T. Collins, M.D. Octavo of 244 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $6.50.

The *Manual of Neurology and Psychiatry in Industrial Medicine* appears rather hastily written. Neurologic problems are given a sketchy and superficial treatment. The psychiatric discussion deals with problems well within the scope of general practice. A large portion of the volume consists of diagrams and figures available in any standard text interspersed with worth-while counsel, for example, advice in draping a female patient and bits of misinformation, such as ascribing the Hoffmann's sign to pyramidal tract disease. This work is likely to be received by a rather restricted audience.—ROBERT W. KIMBALL, M.D.

Stapes Surgery for Otosclerosis. By Victor Goodhill, M.D. Quarto of 212 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $11.50.

The author is eminently qualified to prepare and present his views and technics in a book of this kind. Besides his many other accomplishments he is clinical professor of otology at the University of California School of Medicine. In this monograph Dr. Goodhill "presents the basic fundamentals and highlights of recent progress in the field of otosclerosis." He acknowledges that "there are many conflicting attitudes on the subject and that new techniques are continually being introduced." The book is based on the author's experiences with approximately 3,000 patients, and he presents 29 case histories. The format is excellent, and the text is amply illustrated with photographs, drawings, and audiograms. Photomicrographs are also included. The illustrations of surgical technic are particularly clear. There is an ample bibliography and an informative index. At this time there is a definite need for this publication, and it is wholeheartedly recommended to otologists and others, who may be interested in the problem of otosclerosis.—SAMUEL ZWERLING, M.D.

The Medical Clinics of North America.

Nationwide Number. September, 1961. Arthritis and Rheumatism. J. Sydney Stillman, M.D., guest editor. Octavo. Philadelphia, W. B. Saunders Company, 1961. Published bi-monthly (six numbers a year). Cloth, $18 net; paper, $15 net.

In this day of rapid developments throughout medicine it is little books like this one which keep the practicing physician informed on present-day developments long in advance of changes in the textbooks. An excellent group of authorities in the field of arthritis and rheumatism have covered the broad field of rheumatic disease in the light of present-day knowledge.

Some of the information presented will be of immediate importance to the general practitioner such as the section on therapy, particularly the cautious comments of Dr. Slocumb on steroids and the encouraging comments of Dr. Bayles on the use of gold. Some of the information such as that on serologic tests and pathology may be on a somewhat elementary level for workers in the field, but nevertheless present the broad picture to other internists and generalists. Osteoarthritis, although the most prevalent form of rheumatic disease, is given only a very brief mention, and the section on rheumatic fever likewise could be expanded. However, rheumatoid arthritis and gout are well covered, and the chapter on periarteritis and related diseases is excellent. Lupus erythematosus could be the subject of a volume in itself, and this perhaps may be why it is not discussed except in passing in this volume. The problem of vasculitis in rheumatic disease which is such a vexing clinical problem is mentioned only briefly.

This volume has a great deal to recommend it to internists, general practitioners, and medical students and can be recommended as an up-to-date and authoritative collection of papers.—Charles M. Plotz, M.D.

Boys in White, Student Culture in Medical School. By Howard S. Becker, Blanche Geer, Everett C. Hughes, and Anselm L. Strauss. Octavo of 456 pages, illustrated. Chicago, The University of Chicago Press, 1961. Cloth, $10.

Although one can quibble with the authors' selection of a title (calling twenty-three-year-old and over males, boys), *Boys in White* must be regarded as a pioneer in the desert. The authors, by their piece of motivation research which is ubiquitously applicable, have demonstrated the metamorphosis of actions and ideas among medical students at the University of Kansas Medical School.

There have been numerous discussions and articles by educators on what medical education is and should be. Since this book is written through the eyes of the medical student, the other half is heard for the first time.

This study has been performed by observing the normal daily routine of different groups of medical students at different levels in their medical education. The authors, who are sociologists, have put the emphasis on the word student, rightly stating that the opportunities and disabilities of the student role are decisive in shaping the perspectives these students develop and which condition them for the future.

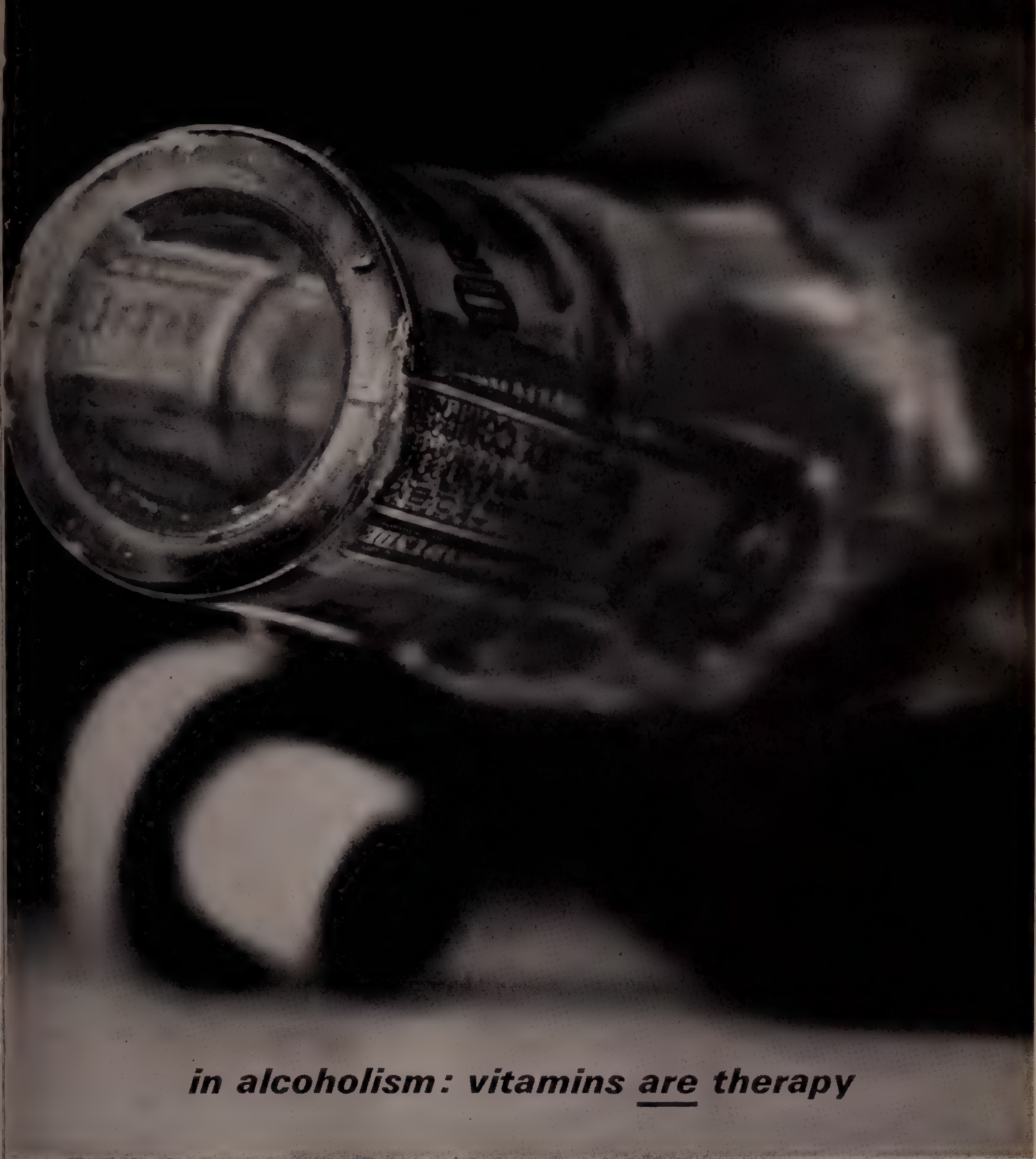
The book opens with the freshman student on his first day of school and ends with a group of senior students. In the interim the authors have skillfully shown the temporary shelving of idealism by the student and his acceptance of shorter-range, less idealistic goals which are necessary to survive the rigors of school duties and pressures. The student's reaction to exams, courses, and different methods of teaching and how he adapts to them is well described. His ambivalence at being called "doctor" while he is not, his thoughts, and relationships with patients and faculty are clearly depicted. This is accomplished through the use of direct excerpts of conversations with and among medical students and expresses their thoughts and ideas far more convincingly than a third-person description.

There are several small failings in the text. The charts and tables are superfluous as all the material presented in graphic form is described completely and clearly in the text. Such graphs and tables may tend to frighten off many nonscientifically oriented people. Also, the authors tend to gloss over certain pertinent factors before arriving at their conclusions. They attribute the dominance of the "I'll-study-what-they-want-us-to-know" philosophy on the part of the student to the influence of the fraternity in student culture. That is not the case: During the first year students cannot embrace the "I'll-study-what-I-will-need-as-a-doctor" philosophy because it is unworkable; the first-year student still has a lay outlook on medicine and is not in a position to discriminate among areas of importance in medical practice.

This book is recommended to the medical student as an aid in self-evaluation and to the medical educator as it may give him the first realization of what his students are faced with, although I earnestly hope this will not be the case. For a laity, saturated with the stereotypes and unrealistic propaganda about the medical student from motion pictures, novels, and television, it is the first real glimpse into medical education.—Lawrence Hessman, M.D., '62, State University of New York Downstate Medical Center

Diagnosis and Therapy of the Glaucomas. By Bernard Becker, M.D., and Robert N. Shaffer, M.D. Octavo of 360 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $18.

continued on page 3502



A full "comeback" for the alcoholic is partly dependent on nutritional balance...aided by therapeutic allowances of B and C vitamins. Typically, the alcoholic patient is seriously undernourished...from long-standing dietary inadequacy, from depletion of basic reserves of water-soluble vitamins. Supplied in decorative "reminder" jars of 30 and 100.

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Vitamin C (Ascorbic Acid)	300 mg
Vitamin B_6 (Pyridoxine HCl)	2 mg
Vitamin B_{12} Crystalline	4 mcgm
Calcium Pantothenate	20 mg

Recommended intake: Adults, 1 capsule daily or as directed by physician, for the treatmen of vitamin deficiencies.

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STRESSCAPS®

Stress Formula Vitamins Lederle

continued from page 3500

Glaucoma, like cancer and hypertension, has become a source of increasing public concern through mass screening tests. Hence the need for books which will help to dispel needless alarm. From the standpoint of diagnosis, this means especially the doubtful or borderline case. The authors rightfully warn us that "The true intraocular pressure in the completely undisturbed eye is difficult to determine, for the methods of measurement alter it" and furthermore that "a definite diagnosis of glaucoma cannot be made unless the increased pressure has produced damage to the optic nerve." Because of the anxieties encountered in mass screening, ways and means are sought constantly to render a positive and conclusive evaluation for the questionable or borderline case.

Gonioscopy, tonography, applanation tonometry, and provocative tests have posed trying problems for the clinician who seeks simple methods of diagnosis. It remains to be seen whether or not these measures or others to follow can prove sufficiently objective and conclusive. The subject of glaucoma has become vast and unwieldy, and its many varieties and problems are discussed in an authoritative manner in this valuable book. For the present the practitioner is advised to adhere to the time-honored methods, which include Schiotz tonometry, study of the optic disk, perimetry, and tangent screen tests, and to rely on refined measures in the selected case.—EMANUEL KRIMSKY, M.D.

Symptoms and Signs in Clinical Medicine. By E. Noble Chamberlain, M.D. Seventh edition. Octavo of 569 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1961. Cloth, $9.00.

This is the seventh edition of what has now become a standard introduction to clinical medicine. It covers the material usually taught as physical diagnosis in the United States and covers it well, as in previous editions. The photographs and x-ray films, the latter all new, are particularly fine. Many of the chapters have been revised. A commendable addition is an introductory chapter on the medical history of this branch of medicine. The section on taking a patient's history is skimpy or barely adequate.—MILTON PLOTZ, M.D.

Cerebral Vascular Diseases. Transactions of the Third Conference. Edited by Clark H. Millikan, Robert G. Siekert, and Jack P. Whisnant. Octavo of 247 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $5.75.

This volume is a compilation of the transcribed proceedings of the third conference on cerebral vascular disease held in January, 1961, at Princeton, New Jersey, under the auspices of the American Neurological Association and the American Heart Association. The reports include contributions from the disciplines of physiology, neurology, neuropathology, and surgery. Cerebral arterial disease is divided, for convenience, into three clinical groups: (1) impending stroke, (2) progressing stroke, and (3) completed stroke.

The material in this book represents the newer knowledge and problems of cerebral vascular disease. It is a compendium of short presentations, each on a particular phase of the problem. The stenographically recorded discussions follow the presentations. The index to this volume makes it useful as a reference text.

Approximately one half of the conference is devoted to the impending or incipient stroke—focal ischemic attacks or focal intermittent insufficiency in which treatment might reverse the process. The diagnostic characteristics of the involvement of the vertebral-basilar and carotid systems are presented. The indications and contraindications for arteriography are delineated clearly, and the decreased incidence of complications are attributed to better nontoxic contrast media and to better selection of patients. Atherosclerosis of extracranial and intracranial vessels, microthrombi and emboli, and the effect of hypotension and occlusive disease on the collateral circulation are stressed as pathogenetic factors in impending stroke. This prepares the reader for the discussion of the status of anticoagulant treatment and surgical therapy. The importance of recognizing and treating occlusive disease in the carotid artery is stressed.

The pathogenesis of progressing stroke centers around the problem of cerebral artery thrombosis, its mechanism and recognition by the pathologist. The treatment of an acute cerebral infarction with anticoagulants is considered dangerous. The benefits of anticoagulants in progressive stroke are mitigated by the very real danger of cerebral hemorrhage. Thrombolysis therapy of cerebral arterial thrombi has had a very limited experience. Surgical treatment of progressive stroke is again directed at the removal of the clot from a carotid artery which is readily accessible.

A discussion of the well-established stroke completes the volume.—IRVING G. KROOP, M.D.

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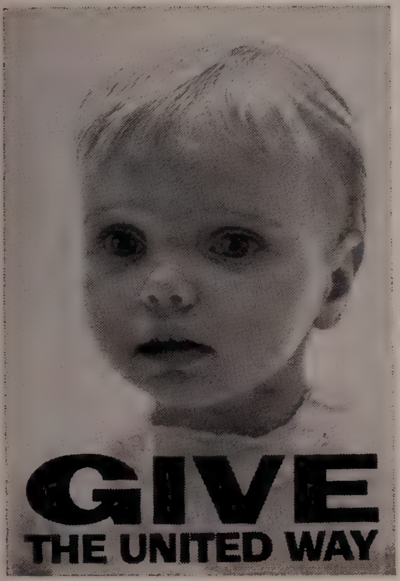

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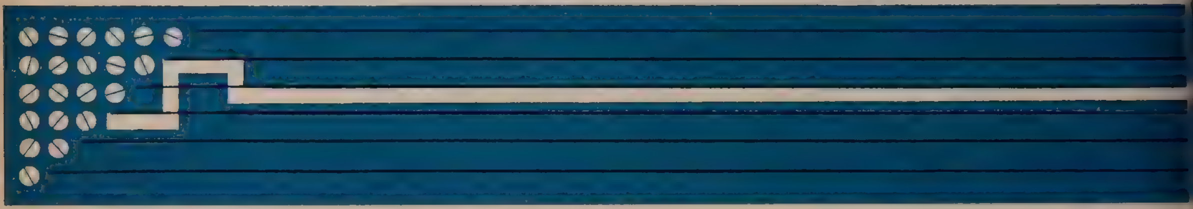

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*Schwartz, I. R.:
Current Therap. Res. 3:29, Feb., 1961.

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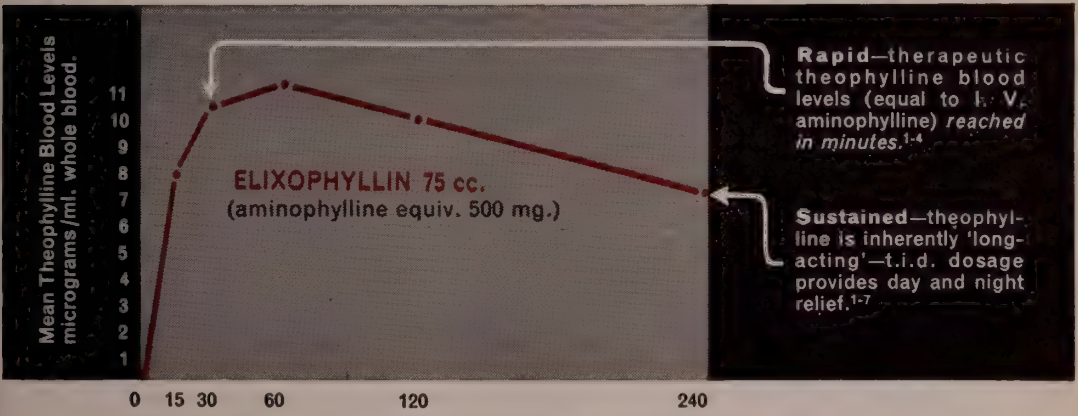

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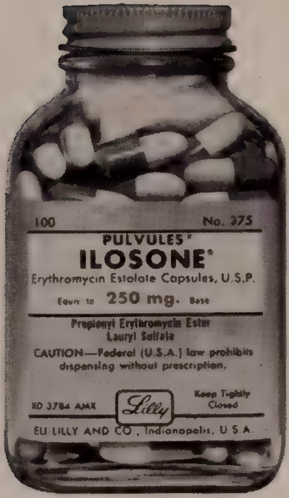
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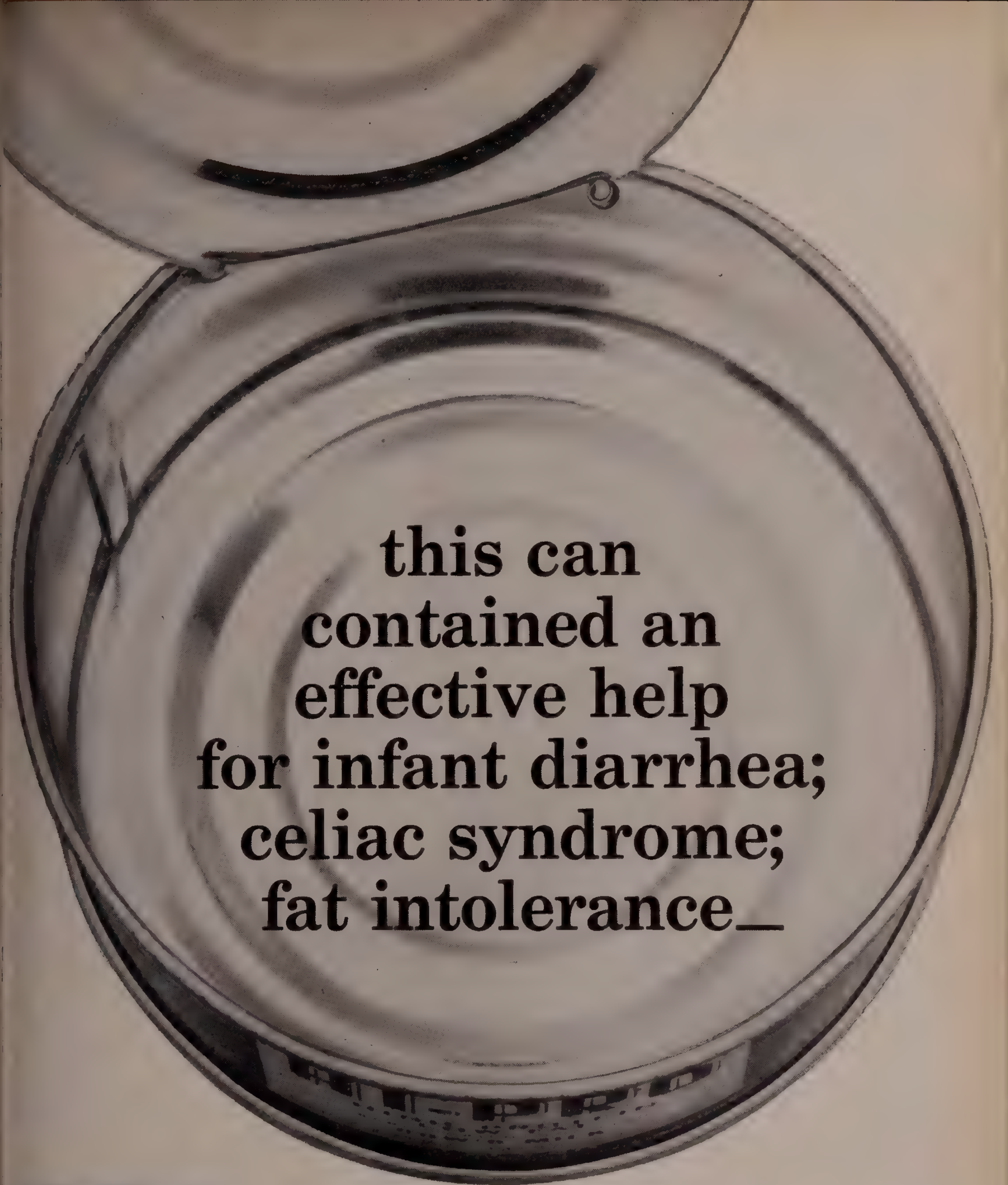

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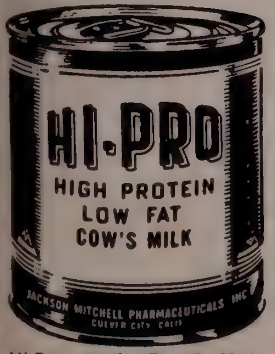
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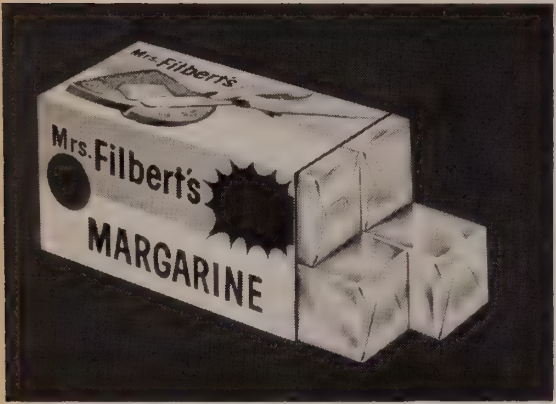
*AMA Council on Foods and Nutrition: The Regulation of Dietary Fat, *JAMA* 181: 411-423 (August 4, 1962).



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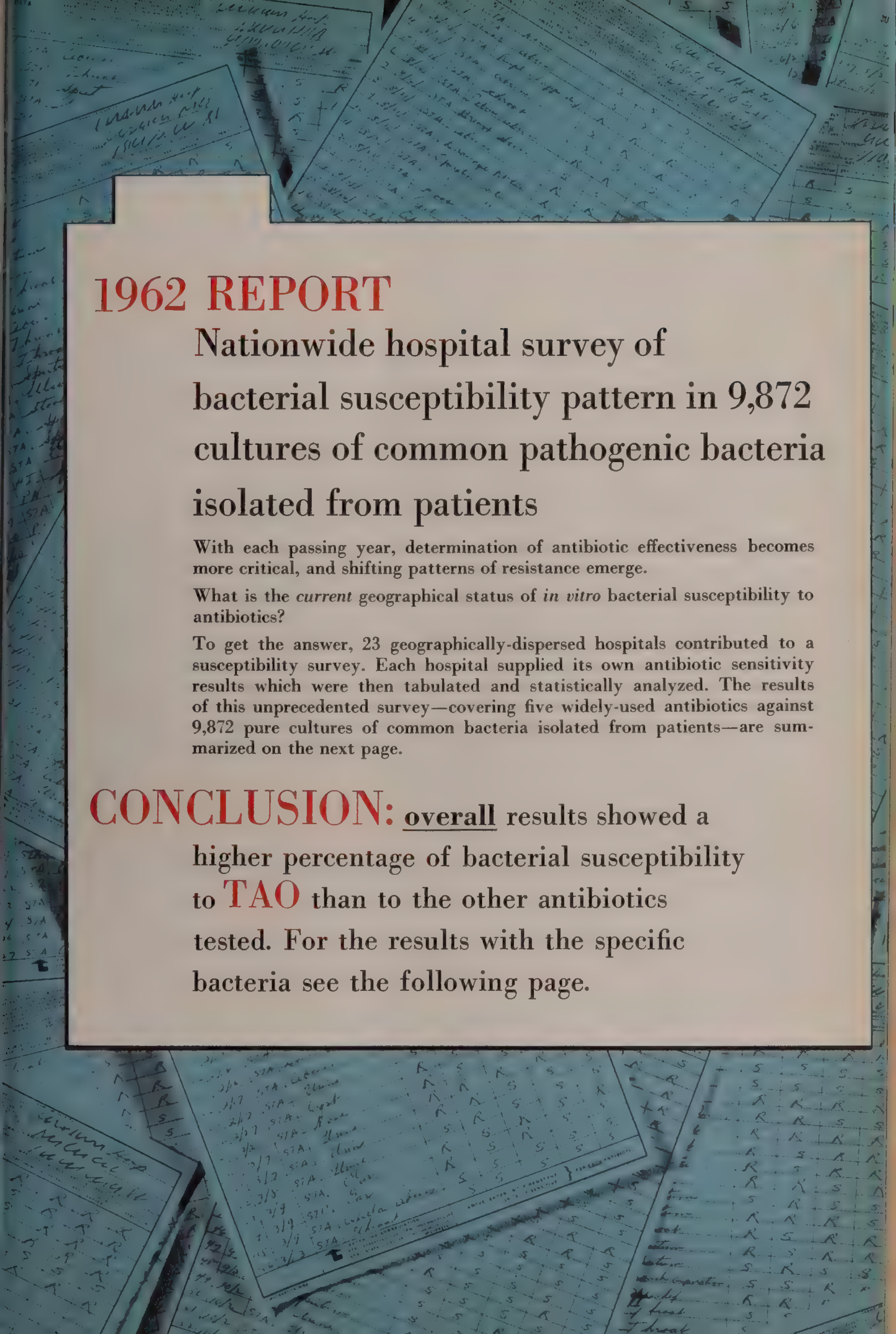

1962 REPORT

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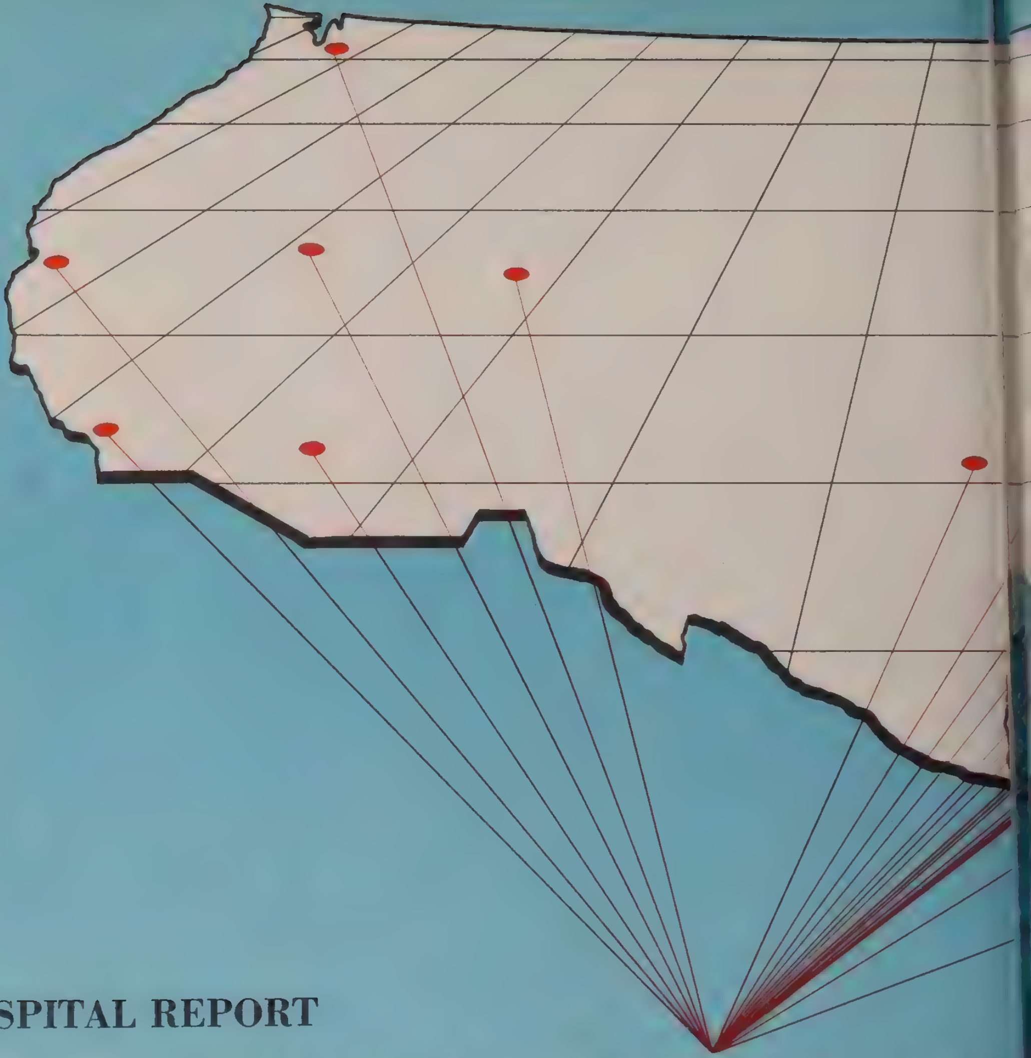
With each passing year, determination of antibiotic effectiveness becomes more critical, and shifting patterns of resistance emerge.

What is the *current* geographical status of *in vitro* bacterial susceptibility to antibiotics?

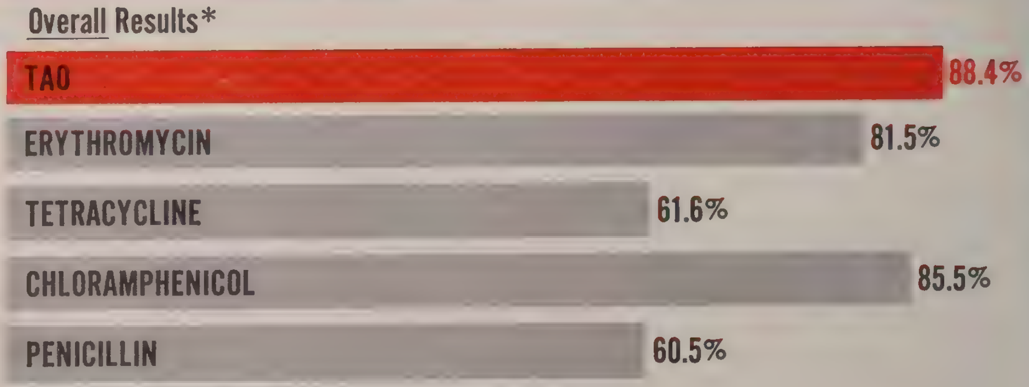
To get the answer, 23 geographically-dispersed hospitals contributed to a susceptibility survey. Each hospital supplied its own antibiotic sensitivity results which were then tabulated and statistically analyzed. The results of this unprecedented survey—covering five widely-used antibiotics against 9,872 pure cultures of common bacteria isolated from patients—are summarized on the next page.

CONCLUSION: overall results showed a higher percentage of bacterial susceptibility to TAO than to the other antibiotics tested. For the results with the specific bacteria see the following page.



1962 HOSPITAL REPORT

RESULTS FROM A NATIONWIDE



Overall Results*

*Percentage of cultures reported susceptible in 9,872 clinical isolates of staphylococcus, streptococcus, pneumococcus and H. influenzae.

Of 6,725 staphylococcal isolates tested TAO showed a clear superiority; of 2,488 streptococcal and 463 pneumococcal isolates tested results were about equal. Of 196 H. influenzae isolates tested TAO was less effective.

SURVEY OF ANTIBIOTICS

Staphylococcus, streptococcus, pneumococcus and H. influenzae isolated from patients were the organisms challenged by five widely used antibiotics. All the antibiotics have been in clinical use at least five years: penicillin, erythromycin, triacetyloleandomycin, tetracycline and chloramphenicol. Only results of susceptibility studies on pure cultures were considered valid; the disc testing technique was utilized.[1]

Active against common pathogenic bacteria. Even after five years of general use, triacetyloleandomycin (TAO) is highly active against common pathogens. For specific information on the many TAO dosage forms, its uses in acute pediatric, skin and soft tissue, and respiratory infections, turn the page.

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(triacetyloleandomycin)
an antibiotic
that time
hasn't changed

[1] "Bacterial Susceptibility Patterns: A Geographic Survey." Fowler, J. Ralph, M.D., and Watters, John L., M.D. Scientific Exhibit presented at the Annual Meeting of the American Society of Clinical Pathologists, Chicago, Ill., August 31 to September 8, 1962.

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Acute pediatric infections: particularly streptococcal.

Other acute genitourinary, gastrointestinal and miscellaneous infections: pyelonephritis, pyelitis, ureteritis, cystitis, urethritis (including gonococcal urethritis), acute salpingitis, endometritis, bartholinitis, staphylococcal enterocolitis, osteomyelitis, septic arthritis.

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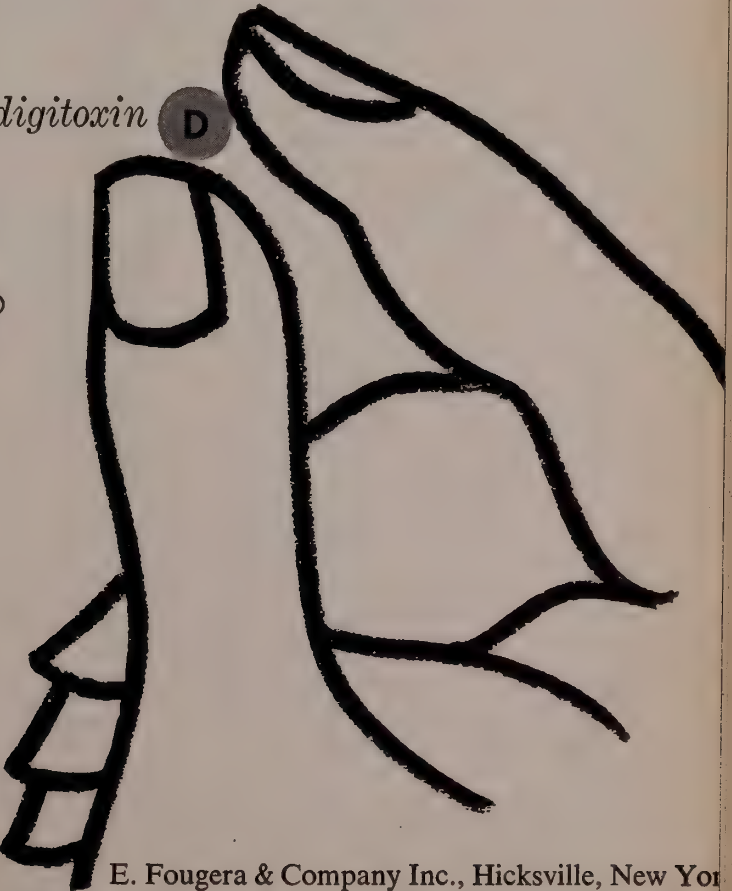

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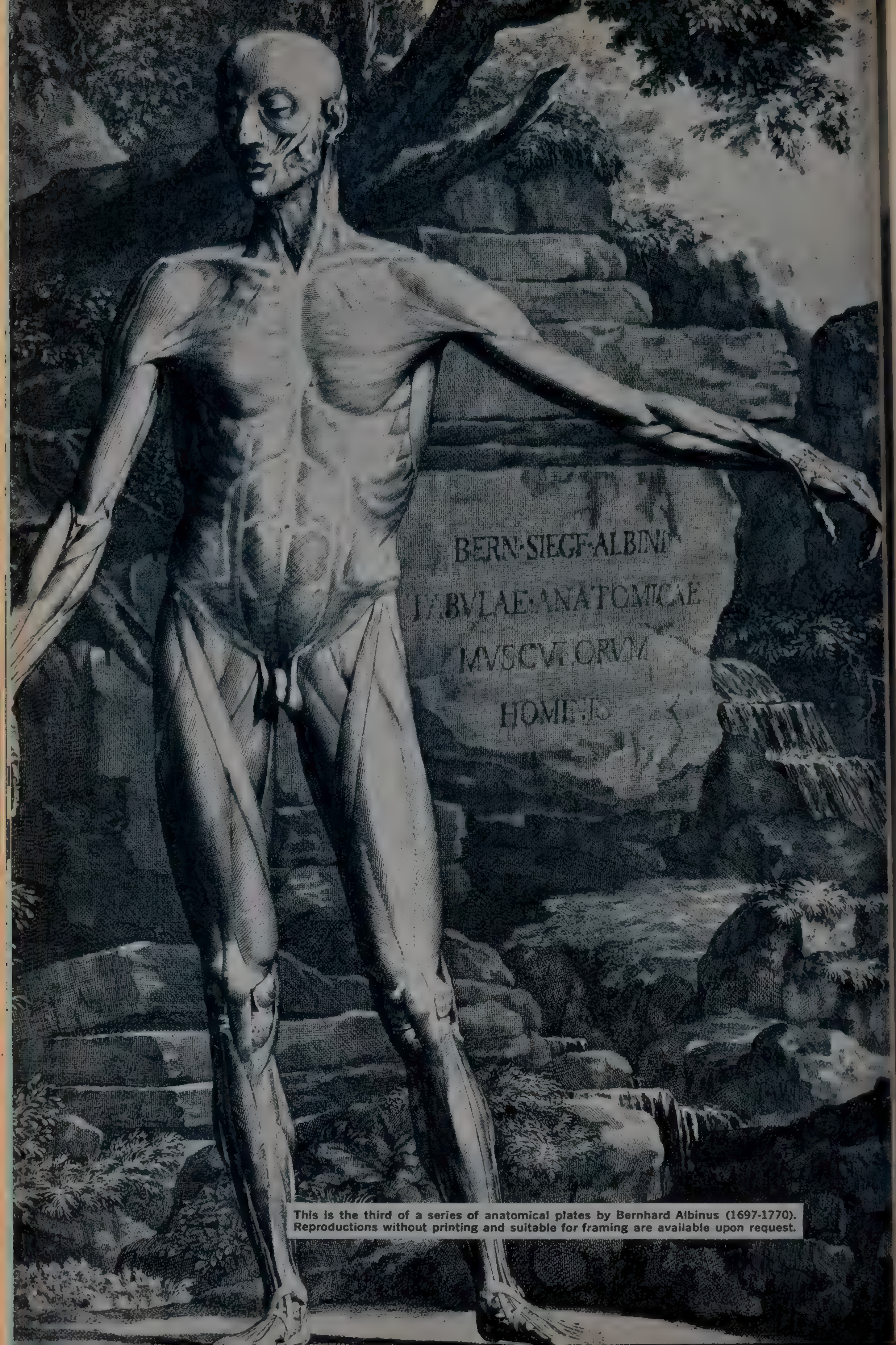
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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin. *New York State J. Med.* Vol. 62: 221-223, 1962.

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1. Borota, A., and Grinell, R. N.: J. Amer. Geriatrics Soc., 10:413, 1962.
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3. Lubowe, I. I.: Western Med. 1:45, 1960.
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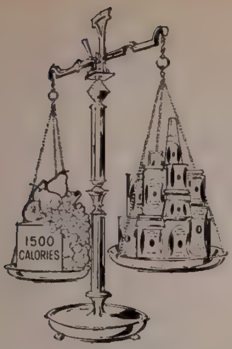

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Pyloric Channel Ulcer	6	3	1	0	2	2	1	1	0	0
Pyloric Ulcer	4	2	1	1	0	1	1	0	0	0
Gastric Ulcer, bleeding	3	1	2	0	0					
Gastric Ulcer	48	31	11	1	5	12	5	7	0	0
Gastric Ulcer, penetrated	1	0	1	0	0	1	1	0	0	0
Gastric Ulcers, multiple	1	1	0	0	0					
Duodenal Ulcer	494	220	195	48	31	99	41	38	13	7
Duodenal Ulcer, bleeding	38	19	15	3	1	2	1	0	1	0
Duodenal Ulcer, obstruction	13	4	3	1	5					
Duodenal Ulcer, perforated	5	2	1	0	2	6	0	3	1	2
Gastric and Duodenal Ulcer	4	2	2	0	0					
Peptic Ulcer, unspecified	25	19	4	0	2	18	8	7	2	1
TOTALS	653	307	239	57	50	142	58	57	17	10
		83.6%					81.0%			

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Bibliography of recent articles on Robinul: **1.** Abbott, William E., et al.: "Effect of Glycopyrrolate (Robinul) on Basal and Histamine- or Insulin-induced Gastric Secretion," Annals of the New York Academy of Sciences, 99:163, Feb. 28, 1962. **2.** Alphin, R. S., et al.: "Action of Glycopyrrolate (AHR-504) on Gastric Secretion in Dogs," Federation Proceedings, 20:251, March, 1961. **3.** Epstein, Jerome H.: "Clinical Observations with a New Anticholinergic, Glycopyrrolate," The American Journal of Gastroenterology, 37:295, March, 1962. **4.** Franko, Bernard V., et al.: "Pharmacodynamic Evaluation of Glycopyrrolate in Animals," Annals of the New York Academy of Sciences, 99:131, Feb. 28, 1962. **5.** Franko, Bernard V., and Lunsford, C. D.: "Derivatives of 3-pyrrolidinols-III. The Chemistry, Pharmacology and Toxicology of some N-substituted-3-pyrrolidyl α-substituted Phenylacetates," Journal of Medicinal and Pharmaceutical Chemistry, 2:523, May, 1960. **6.** Moeller, Hugo C.: "Physiological Effects and Clinical Evaluation of Glycopyrrolate in Peptic Ulcer," Annals of the New York Academy of Sciences, 99:158, Feb. 28, 1962. **7.** Sun, David C. H.: "Comparative Study of the Effect of Glycopyrrolate and Propantheline on Basal Gastric Secretion," Annals of the New York Academy of Sciences, 99:153, Feb. 28, 1962. **8.** Young, Robert, and Sun, David C. H.: "Effect of Glycopyrrolate on Antral Motility, Gastric Emptying, and Intestinal Transit," Annals of the New York Academy of Sciences, 99:174, Feb. 28, 1962.

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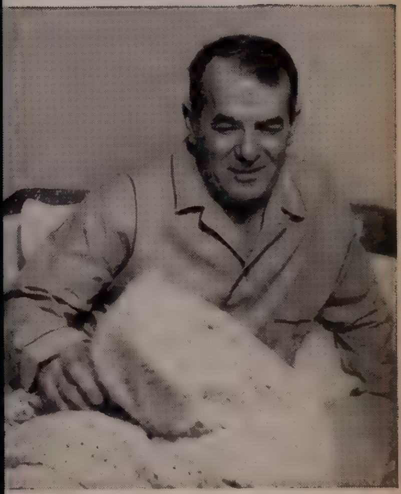

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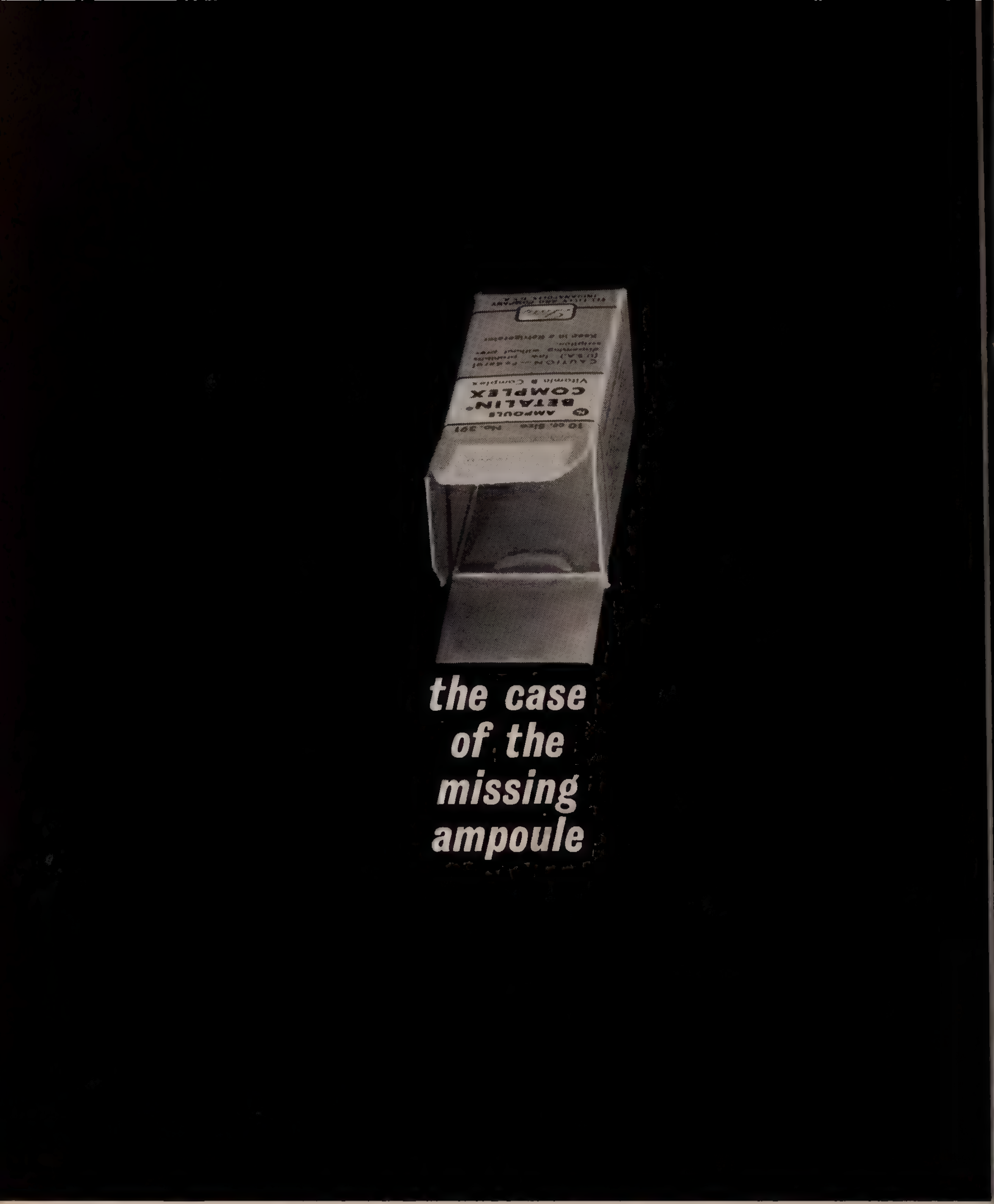
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New York State Journal of Medicine

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Editorials

Shadow and substance

Today's clinician rarely stands alone. He has two invaluable partners ready and able to add precision to his diagnosis. The services of the radiologist and the pathologist are often an integral part of the diagnostic work-up and are of particular importance when the problem is difficult.

Precision in interpretation from these two departments is an accepted commonplace. We owe this not so much to advancement in technics as to the superb training and experience of the interpreters.

By bringing these two disciplines together in dialogue in the series inaugurated in this issue, Correlation Conferences in Radiology and Pathology, we hope to show how these two branches of medicine complement each other.

We hope also that this tying together of the shadow and the substance may prove as valuable to our readers as the well-tried clinicopathologic conference.

The conferences will come alternately from the State University of New York Upstate Medical Center, Syracuse, conducted by Paul A. Riemenschneider, M.D., professor of radiology, and Howard Ferguson, M.D., professor and chairman, Department of Pathology, and from St. Luke's Hospital, New York City, conducted by Nathaniel Finby, M.D., director of radiology, and Charles F. Begg, M.D., director of laboratories.

Every effort has been made to make the reproduction of the accompanying radiographs and photomicrographs as fine as we can possibly obtain.

Suggestions as to subjects to be discussed or improvements in the presentation will be welcomed.

Adjudged best of breed

At the nineteenth annual meeting of the American Medical Writers' Association held in Washington, D.C., on October 12 this JOURNAL was the recipient of the honor award for distinguished service in medical journalism in the class of state medical journals. The award reads as follows:

> The NEW YORK STATE JOURNAL OF MEDICINE has been selected as the 1962 recipient of the honor award for distinguished service in medical journalism—class state medical journals—of the American Medical Writers' Association for accuracy, clarity, conciseness, and newness of information; for excellence of design, printing, and illustrations, and for distinguished service to the medical profession.

The citation reads as follows:

> A committee of five reviewed thirty-four individual state journals. Evaluation of the journals was on a seven-point scale which included five basic yet detailed criteria. These were: general appearance; front material; advertising; scientific articles, and general contents. The NEW YORK STATE JOURNAL OF MEDICINE, as a unique semimonthly publication, smaller in page size than the average medical journal, presents a wealth of diversified material. Professional articles and items of general and local interest are timely, succinct, and easily read. The general format meets the popular standards of an excellent medical publication.

Despite the title of this editorial, the JOURNAL is not a dog.

President's Page

JOSEPH A. LANE, M.D.

This month I would like to discuss some of the problems of malpractice insurance.

First I believe it is important to remind you that your State Medical Society has a unique arrangement in that it has the only setup in the world in which the carrier agrees to abide by the recommendations of a committee (the State Society's Malpractice Insurance and Defense Board). The carrier accepts the Board's recommendations for the cancellation of a subscriber's insurance as well as for the approval of applicants, not only for insurance itself but also for specific types of insurance, such as cosmetic plastic surgery, electroshock therapy, superficial and deep x-ray therapy, and/or isotope teletherapy. Any subscriber who has been having repeated claims against him is interviewed by the Board before any recommendation for cancellation, continuation, or a change in the classification of his insurance is made.

It is important for all subscribers to realize that the Legislature of the State of New York has approved a change in the law that now allows a period of three years to expire from the time an incident occurs to the time a suit can be instituted, thereby extending the statute of limitations from two to three years. This change in the law becomes effective on January 1, 1963.

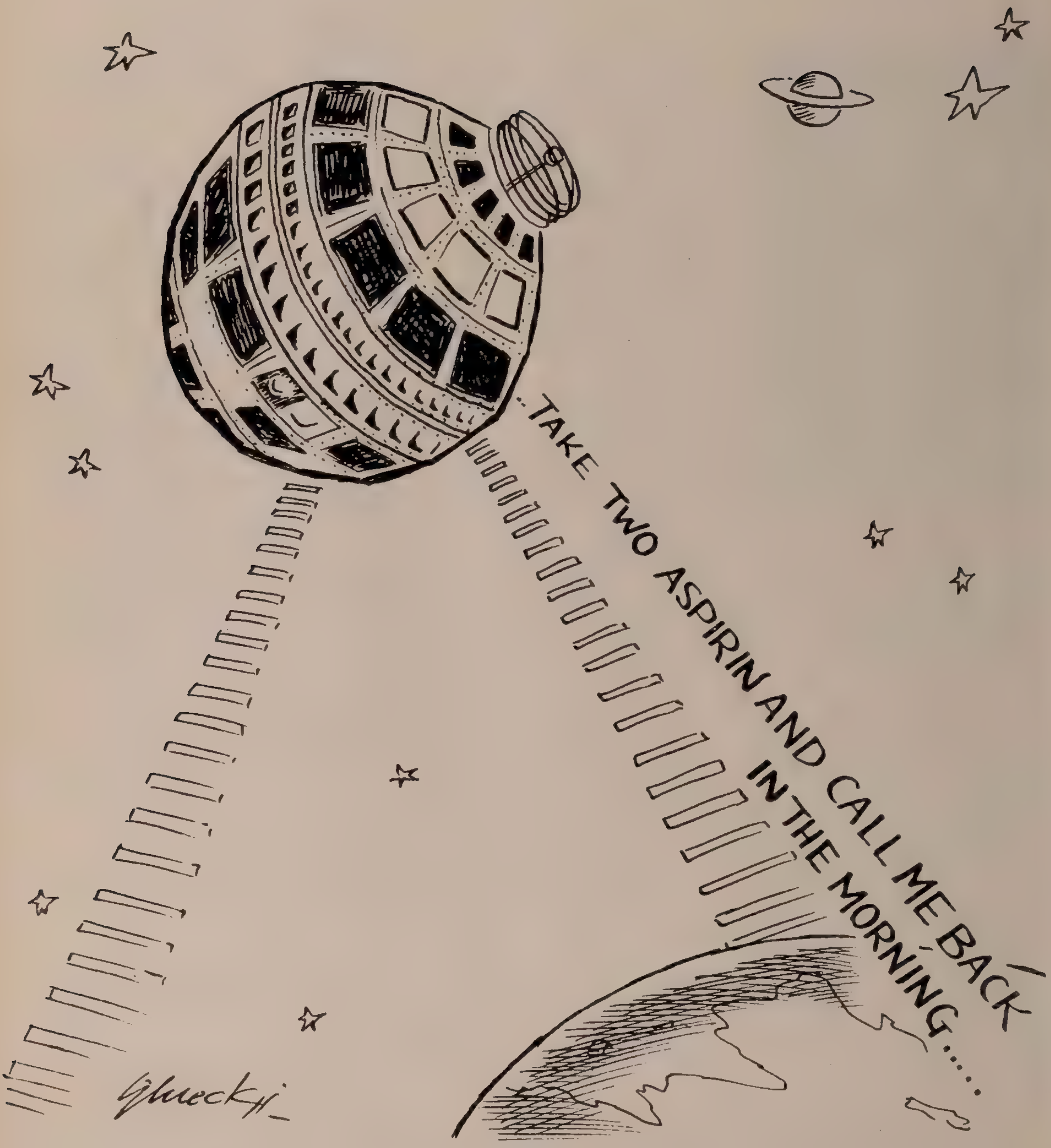
I am sure that you know your premium is based on several factors including geographic location—metropolitan, surburban, and upstate. It is based also on your type of practice, your compensation rating and specialty board certification, and on your hospital appointments. The annual premium is based on the loss ratios, which are computed annually, and these losses are studied by expert actuaries.

The law firm of Martin, Clearwater and Bell has had vast experience in the field of malpractice insurance and does its utmost to resolve problems in the best manner possible considering the facts developed after investigation of a claim.

You are strongly urged to continue your insurance with your State Society or, if you are not under the Group Plan at present, to subscribe to it on the expiration of your present policy.

Joseph A. Lane, MD

JOSEPH A. LANE, M.D., *President*



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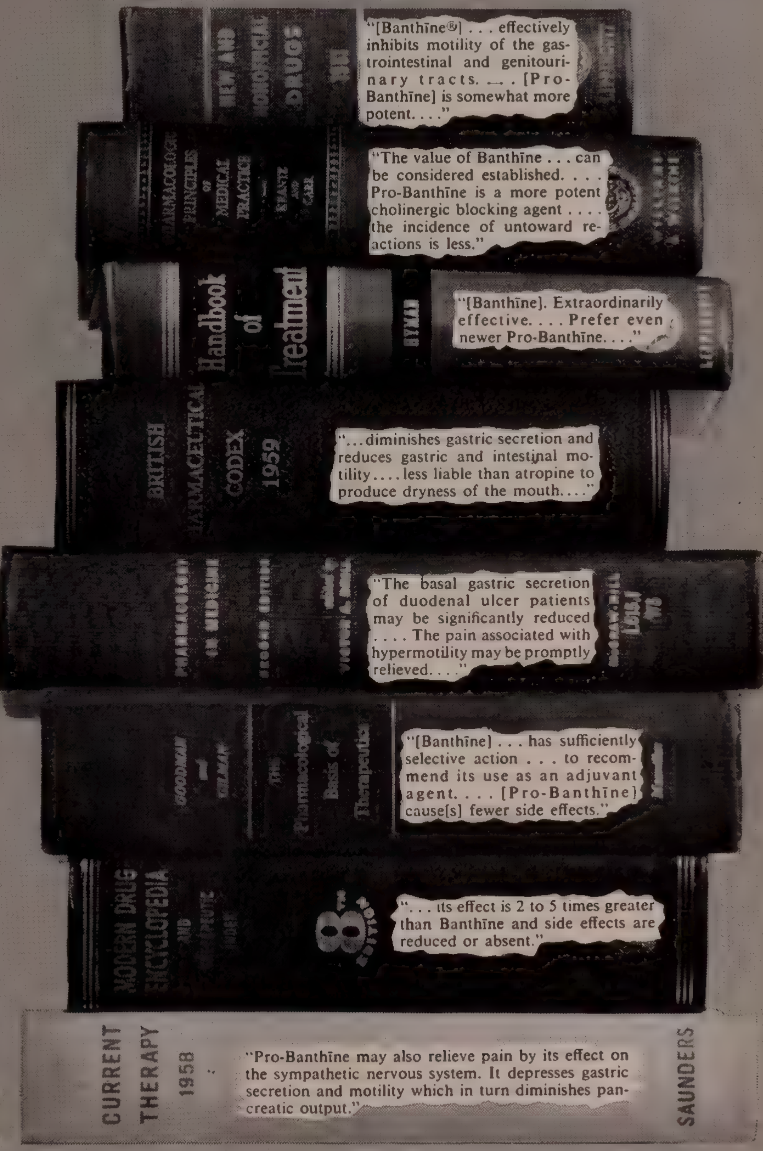
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Results of Treating Patients with Ovarian Cancer with Radioactive Isotopes

IRVING M. ARIEL, M.D., F.A.C.S.
New York City

From the Division of Radioactive Isotopes,
Hospital for Joint Diseases, and Pack Medical Group

SEVENTY PATIENTS *with ovarian cancer were given combinations of a radioactive isotope of a short half-life and one of a longer half-life, which is believed to be the preferable manner for intra-abdominal administration. Of the 70 patients, 57 have died; of the 13 who are living, 5 received isotopes prophylactically after a surgical resection of an isolated ovarian cancer, 3 have evidence of residual cancer, and 5 have no evidence of cancer even though there was widespread cancer at the time of treatment. Of the patients who received the isotopes for palliation, the results were good in 20, fair in 22, equivocal in 6, and of no benefit in 18. There were no serious complications of the regimen. Radioactive isotopes, alone and in combination with other means, are useful in destroying intraperitoneal seedings and small omental masses arising from ovarian cancer, in treating both smaller and larger masses of ovarian carcinomatosis, and in irradiating pelvic cancer. They are contraindicated in patients with intestinal obstruction and those severely debilitated from extreme carcinomatosis.*

THIS REPORT DESCRIBES the response of 70 patients bearing ovarian cancer who have been treated with radioactive isotopes for one or more of the following reasons: (1) intra-abdominally as a prophylactic procedure after an apparently successful resection of an ovarian cancer (5 cases); (2) intra-abdominally for the control of ascites (22 cases); (3) intra-abdominally in patients with evidence of dissemination of their ovarian cancer without ascites (8 cases); (4) interstitially into pelvic masses (4 cases); and (5) miscellaneous: isotopes administered intrapleurally to control hydrothorax (2 cases), patients who were treated both intra-abdominally and intrathoracically (4 cases), intra-arterially as a means of determining the effects of isotopes administered into the arterial supply of the cancer (4 cases); or a combination of these procedures.

The patients ranged in age from sixteen to seventy-five years. The breakdown by decades reveals that there was 1 patient between ten and twenty years of age, 1 twenty to thirty years of age, 4 thirty to forty years of age, 26 forty to fifty years of age, 24 fifty to sixty years of age, 12 sixty to seventy years of age, and 2 seventy to eighty years of age. This is the usual age distribution for patients with ovarian cancer.

The types of cancer from which the patients suffered consisted of cystadenocarcinoma, 37 patients; anaplastic carcinoma, 9 patients; adenocarcinoma, 11 patients; granulosa cell carcinoma, 3 patients; pseudomucinous carcinoma, 1 patient; teratoma, 1 patient; and type of cancer not stated, 10 patients.

The anatomic extent of the cancer was as follows: generalized abdominal metastasis

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Presented at the 8th Annual Meeting of the Society of Nuclear Medicine, Pittsburgh, Pennsylvania, June, 1961.

in 60; evidence of intestinal obstruction, 23; metastases to skin and brain in addition to extensive abdominal metastases in 1 patient; metastasis to liver, 13; metastasis to lung, 9; metastasis to cervical lymph nodes, 5; large pelvic deposits, 7; and metastasis only to the opposite ovary, 5. These values are not mutually exclusive inasmuch as a patient may have generalized abdominal metastasis and in addition have metastasis to the lung or evidence of intestinal obstruction. Several features of this breakdown become evident: Metastasis throughout the abdomen was the most frequent condition. A rather high incidence of intestinal obstruction was observed. Relatively few patients had metastasis to the lung, and a few had localized large pelvic deposits. Five patients had involvement of both ovaries as the only evidence of the cancer.

Types of isotopes and dosages

Three isotopes were used: Au^{198} (colloidal radioactive gold); Y^{90} (radioactive yttrium) as the chloride with 250 mg. of Y^{89} (nonradioactive yttrium) as the carrier[1,2]; and $CrP^{32}O_4$ (colloidal radioactive chromic phosphate). Combinations of these isotopes were often administered as part of an investigation studying the effects of combining an isotope of a short half-life with one of a longer half-life. Usually, either radioactive gold or yttrium was administered as the short-lived isotope, combined with P^{32} (radioactive chromic phosphate) as the longer-lived isotope. The number of combinations of isotopes used were as follows: chromic phosphate (alone), 21 patients; chromic phosphate and yttrium, 11 patients; yttrium and gold, 2 patients; chromic phosphate and gold, 16 patients; yttrium (alone), 3 patients; and miscellaneous mixtures consisting of P^{32} (5 millicuries), rose bengal I^{131} (20 millicuries), used for the treatment of liver metastasis,[3] and Ir^{172} administered interstitially.

The dose varied from 50 to 150 millicuries of radioactive gold and from 10 to 20 millicuries of radioactive chromic phosphate. The dose was determined by considering all factors, including the size and weight of the patient, her general metabolic state, the hematopoietic reserve, and the previous therapy. If only gold was to be used, the patient usually received from 100 to 150 millicuries of the isotope intra-abdominally; on the other hand if she was to be treated by a combination of gold and chromic phosphate, she would then receive between 50 and 100 millicuries of gold and from 10 to 20 millicuries of chromic phosphate.

When they were administered intra-arterially, 50 millicuries of gold were given into the aorta via a polyethylene catheter threaded through the femoral artery to the level of the celiac axis and from 5 to 10 millicuries of radioactive chromic phosphate were administered through this catheter.

Results

Longevity. Of the 70 patients treated, 57 have died—55 from ovarian cancer and 2 from other reasons, 1 from a cerebrovascular accident and 1 from a coronary thrombosis. Thirteen are alive. Of these there are 5 who received isotopes prophylactically after a surgical resection of an isolated ovarian cancer, who are alive and free of evidence of cancer from two to five years after their operation and isotopic regimen. Of the additional 8 living patients, 3 have evidence of residual cancer. The additional 5 are surprisingly well with no evidence of cancer even though there was widespread cancer involving the abdominal cavities at the time the isotopes were administered (Table I).

An analysis of the time of death after the isotope regimen revealed that 19 patients died immediately or within two months after the administration of the isotopes. There were no complications in these patients as a result of the isotopes. Rapid death after the therapeutic regimen focuses on the fact that these patients were in terminal stages and the isotopes were administered as a very last resort in the hope that something heroic might be accomplished. The failure of accomplishment emphasizes the futility of administering radioactive isotopes to such patients. Of all the patients who died, including the 19 who died within two months after isotope therapy, the average duration of life was 7.5 months. Fifteen patients died between the

TABLE I. Clinical data of patients with disseminated ovarian carcinoma living after treatment with radioactive isotopes

Age of Patient (Years)	Pathologic Diagnosis	Extent of Cancer	Previous Treatment	Isotope and Dose	Course	Comment
53	Papillary anaplastic carcinoma	Primary carcinoma, right ovary, metastatic to left ovary and peritoneum	Panhysterectomy, bilateral salpingo-oophorectomy (Sept. 10, 1957)	Chromic phosphate 10 mc. (Sept. 16, 1957) Yttrium 50 mc. (Sept. 20, 1957) Chromic phosphate 5 mc. (Sept 25, 1957)	Laparotomy and gastrectomy for duodenal ulcer (Apr. 8, 1959) No evidence of carcinoma	Patient well and free of cancer $5^1/_2$ years after therapy
44	Granulosa cell carcinoma, right ovary	Adherent to sigmoid and pelvic wall	Right oophorectomy followed by panhysterectomy and omentectomy (Apr. 18, 1961)	Radioactive gold 50 mc. Chromic phosphate 20 mc. (Apr. 20, 1961)	Patient well.	No evidence of cancer 13 months after isotope therapy
50	Papillary cystadenocarcinoma	Carcinoma involving both ovaries	Hysterectomy and bilateral salpingo-oophorectomy (May 26, 1959)	Radioactive gold 50 mc. Chromic phosphate 20 mc. interstitially into pelvic mass	Pelvic recurrence (July 17, 1960) Thio-TEPA and methotrexate given intravenously. No benefit from chemotherapy	Patient well 6 months after interstitial injection of isotopes into pelvic mass with evidence of cancer
62	Papillary cystadenocarcinoma, right ovary	Generalized, peritoneum and omentum	Hysterectomy and bilateral salpingo-oophorectomy, postoperative x-ray therapy August, 1958. Omentectomy (Dec. 14, 1960)	Radioactive gold 100 mc. Chromic phosphate 10 mc. (Dec. 16, 1960)	Patient received external x-ray therapy to pelvic mass after isotope therapy: 200 kv. 50 cm. Target skin distance: 1,500 r in air in 3 weeks.	Patient well 17 months after isotope therapy
58	Papillary cystadenocarcinoma, right ovary	Peritoneal metastasis, ascites	Bilateral oophorectomy (Apr. 12, 1960)	Radioactive gold 100 mc. Chromic phosphate 10 mc. (June 3, 1960) Chromic phosphate 15 mc. (Nov. 10, 1960)	Fluid reaccumulation (Oct. 20, 1960). None since	Patient asymptomatic, evidence of pelvic cancer 2 years after isotope therapy. Associated therapy: vaginal cobalt colpostat 1,232 mg. hours radium equivalent (Aug. 4, 1960)
58	Papillary cystadenocarcinoma, left ovary	Direct extension to pelvic structures, sigmoid and mesocolon	Excision carcinoma, left ovary and sigmoid (Jan. 26, 1959)	Radioactive gold 50 mc. (Jan. 28, 1959)	Patient well; symptoms of psychosis (Dec. 1, 1961)	Hysterectomy 1946 for fibroids, right oophorectomy 1950 for cyst. Patient received vaginal cobalt colpostat: 1,232 mg. hours radium equivalent. Well 3 years after therapy
22	Papillary cystadenocarcinoma, right ovary	Metastases to left ovary, general peritoneal and omental	Left oophorectomy (July 2, 1959)	Radioactive gold 75 mc. Chromic phosphate 20 mc. (Aug. 14, 1959) Chromic phosphate 20 mc. (Feb. 27, 1960)	Pregnancy with delivery of normal child Sept. 18, 1960, via cesarean section. No carcinoma found on exploration.	Patient well without evidence of carcinoma 3 years after isotope therapy
45	Cystadenocarcinoma, left ovary	Disseminated peritoneal implants	Hysterectomy-bilateral oophorectomy (Apr. 10, 1956) Ascites: 6,000 cc. clear fluid and cancer cells identified in fluid (Oct. 1, 1956)	Chromic phosphate 11 mc. (Oct. 1, 1956)	No evidence of cancer (May 1, 1962)	Control of cancer for over 5 years
16	Malignant teratoma, right ovary	Metastasis to left ovary and peritoneum	Panhysterectomy and omentectomy	Y^{90}, 25 mc. Chromic phosphate 1 mc.	No evidence of cancer $2^1/_2$ years later	Patient received mild x-ray therapy to abdomen in foreign country. Factors not known

third and fifth month; 13 patients died between the fifth month and one year after isotope therapy. One patient lived thirteen months, 2 for sixteen months, 1 for thirty-two months after isotope therapy; and 1 who lived for four years succumbed from metastases to the brain.

Palliation. Of the patients who received the isotopes for palliation, a good result accrued in 20, fair in 22, an equivocal result was noted in 6, and no benefit occurred in 18.

The symptoms which responded were as follows: 36 of the patients stated they enjoyed a feeling of well-being. Pain subsided in 35, and in 16 there was a definite shrinkage of a palpable mass. Of the 22 patients who received the radioactive isotopes for the control of ascites, the control was complete in 2, partial in 10, and in 10 patients no benefit accrued. When the isotopes were administered for the control of hydrothorax, benefit was observed in 1 of the 2 patients so treated. Cancer cells were identified in the fluid of each patient before radioactive isotopes were administered.

No patient who had evidence of severe intestinal obstruction benefited from the regimen of radioactive isotopes given intra-abdominally. The intra-abdominal administration of isotopes is accordingly considered not indicated in the presence of severe intestinal obstruction.

The duration of palliation varied from one month to four years. When a recurrence of symptoms occurred, a second course of isotope therapy usually had little effect.

Complications. No patient suffered any serious complications from the administration of the isotopes, such as the perforation of a bowel or the infiltration of a solid viscus. Three patients suffered from infiltration of the isotopes into the abdominal wall, which resultant reaction persisted for from one to three months (Fig. 1). In 2 there was seepage of isotopic-containing fluid from the abdominal cavity after the administration of the isotopes. This caused an erythematous reaction of the skin about the puncture wound where the isotopes were administered, which subsided spontaneously in from five to fifteen days.

Two patients developed severe paralytic ileus which resulted in marked intestinal distention after the administration of the radioactive isotopes. One patient received 100 millicuries of radioactive gold and the other a combination of Au^{198} and $Cr\ P^{32}O_4$. In these instances it is believed that the isotopes produced a form of chemical peritonitis resulting in ileus. In both these instances the ileus subsided after medical management with no severe residuum. One patient suffered severe pain at the site of the injection of the radioactive isotopes; the pain was intra-abdominal and it is interpreted that the material may have been injected directly into the omentum which was the cause for the painful reaction.

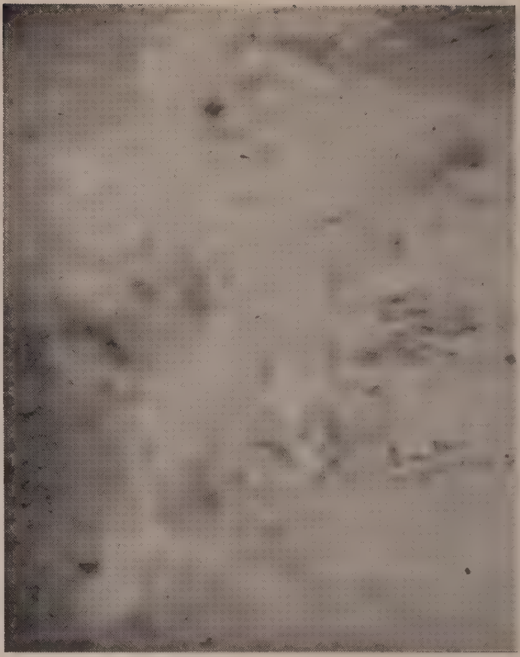
FIGURE 1. Radiation reaction of abdominal wall following administration of radioactive chromic phosphate.

Pancytopenia was observed in 2 patients. These patients however were subjected to a complicated and rigorous course of therapy before the isotopes were administered. In 1 patient who had received chemotherapy previously with thio-TEPA (triethylene thiophosphoramide) the blood count dropped significantly, with all elements participating in the drops but rose rapidly after the transfusion of 1,000 cc. of fresh whole blood. The other patient suffered a fatal aplasia from combined x-ray therapy and isotopes administered intra-abdominally; subsequent to a course of chemotherapy (thio-TEPA) the combination of teletherapy and intra-abdominal isotopes appears to have greater damaging ability to the hematopoietic system than either modality alone. Accordingly, great care must be exercised when both methods of radiation are given.

Comment

Large doses of superficial irradiation can be administered by giving radioactive isotopes intra-abdominally. The poor cure rate from ovarian cancer, averaging about 25 per cent of five-year cures, emphasizes the need for improved treatment methods. A large number of recurrences from ovarian cancer are probably due to the rupture of cysts containing fluid in which float cancer cells which produce deposits of cancer throughout the peritoneum. Such seeding produces a situation which is favorable for treatment by the intra-abdominal administration of radioactive isotopes. The fact that 5 patients treated by postoperative isotopic administration are doing well from two to five years after the excision of their ovarian tumors suggests that the isotopes were beneficial in helping to control growth from possible seedings. This is speculative and one cannot make a definite statement pertaining to the effects of the isotopes in controlling recurrences in these 5 patients. Rose[4] reported 24 patients treated prophylactically postoperatively for ruptured cystadenocarcinoma. Eighteen (75 per cent) were alive and well six to seventy-six months after treatment. Weed and Barraza[5] report favorable results from the prophylactic administration of isotopes intra-abdominally after the operative removal of ovarian cancer. The observation that approximately 75 per cent of patients with primary ovarian cancer develop postoperative intra-abdominal cancer, which often starts as tiny growths resulting from the adherence of cancer cells to visceral and parietal peritoneum, suggests strongly that isotopic administration is indicated prophylactically after the resection of ovarian cancers.

The observation that 1 patient with extensive intra-abdominal metastases including an omentum solid with cancer, who revealed no evidence of cancer of the abdomen as evidenced by inspection eleven months after the intra-abdominal administration and who delivered a normal baby, indicates the efficacy of the intra-abdominal administration of isotopes in controlling certain cancers.[6]

CASE REPORT. The patient was a twenty-two-year-old woman with extensive inoperable ovarian carcinomatosis. She was treated with one course of 75 millicuries of radioactive gold and 20 millicuries of P^{32} (radioactive chromic phosphate) that was delivered on August 14, 1959, and a second course of isotopes consisting of 20 millicuries of P^{32} that was administered on February 27, 1960, which has apparently controlled all evidence of extensive intra-abdominal ovarian carcinomatosis to the time of writing.

This first course of radioactive isotopes did not prevent the patient from becoming pregnant and supporting the pregnancy. A second course of radioactive isotopes administered intra-abdominally at a time when the patient was one month pregnant had no visible effects on the fetus. The child is now over two years of age and is normal in every respect (Fig. 2).[6]

CONCLUSIONS. The fact that such seeding may be an important factor in the production of fluid makes the intra-abdominal administration of isotopes a favorable method for destroying the cancer cells and controlling fluid. Other studies from this clinic have demonstrated that fluid accumulates in the abdomen owing to peritoneal cancer seedings or to obstruction to circulation. It has been this author's policy that if a patient does not respond to isotopic administration intra-abdominally on two occasions, further isotopic therapy should be abandoned and reliance placed on irradiating by external means the region of the porta hepatis. Evidence has accumulated demonstrating that ascites results from a circulatory compromise in this region.

Certain patients may have large masses involving the abdomen as well as seedings. Intra-abdominal isotopic administration will control the smaller-sized tumefactions scattered throughout the abdomen but will have very little if any effect on the large masses because of the superficial nature of the irradiation. It is accordingly our policy to give radioactive isotopes intra-abdominally for the control of the seedings and to depend on external irradiation given over more

FIGURE 2. Mother and child, at age eighteen months, after intra-abdominal isotope therapy for ovarian cancer.

limited ports to aid in the control of larger masses. That interstitial isotopic irradiation can be extremely effective is evidenced by a five-year "cure" of a malignant melanoma of the vagina by radioactive isotopes administered interstitially.[7]

When patients have pelvic deposits, palliation can often be obtained by the judicious use of isotopes injected interstitially into these pelvic masses. This has been done in a number of patients whose masses were observed to be inoperable and who received interstitial isotopic irradiation at the time of operation or postoperatively via the intravaginal route. The procedure is atraumatic, nontime-consuming, and often effective. It is realized that the dose of irradiation given by this technic usually lacks homogeneity, but the treatment is given for palliation, and uniform dosage distribution is not an absolute essential. Experiments are in progress to improve the logistics of the administration of isotopes interstitially to assure a more homogeneous dose.

The observation that omental masses disappeared after isotope therapy suggests that the omentum which is known to concentrate cancer cells as part of its function of being a "catch-all" also concentrates colloidal radioisotopes administered intra-abdominally and thereby affords an effective measure for destroying cancer within the omentum.

The results from administering radioactive isotopes intravascularly into the abdominal aorta as a means of having them delivered via the arteries to the tumors are too meager from the experiments herein reported to warrant any conclusion. Metastases of the liver are treated by this route via a catheter threaded into the aorta to the level of the celiac axis or into the hepatic artery for metastases that are discovered to be inoperable at the time of surgery. These patients have also received injections of isotopes directly into the hepatic cancer, the site of the cancer being determined by scintiscanning direction.[8] The fact that patients with intestinal obstruction do not benefit from radioactive isotopes suggests that the administration of isotopes is not indicated in such instances. Furthermore, the observation that patients in a severely debilitated state with far-advanced cancers in no way benefited indicates also that radioactive isotopes are contraindicated in such instances. The intra-abdominal administration of combined radioactive isotopes offers a satisfactory means of irradiating superficially most of the abdominal cavity, and evidence indicates that superficial cancer deposits will be destroyed. The vagaries of the natural history of ovarian cancer are reflected by the variation in response to isotopes given intra-abdominally. In some patients a dramatic response may occur; in others no response can be noted. The ease and rapidity with which isotopes can be administered makes this a preferred method of treating patients with intra-abdominal dissemination of ovarian cancer.

Summary

1. The intra-abdominal administration

of radioactive isotopes can destroy intraperitoneal seedings and small omental masses arising from ovarian cancer.

2. Its use appears indicated prophylactically after an operation for ovarian cancer has been performed.

3. Ascites was controlled completely in 5 per cent of the patients, partially controlled in 47 per cent, and no effect was observed in 47 per cent after the intra-abdominal administration of radioactive isotopes.

4. Combined radioactive isotopes were used, one with a short half-life (Y^{90} or Au^{198}) and another with a longer half-life ($CrP^{32}O_4$). This combination is believed the preferable manner for the administration of isotopes intra-abdominally.

5. The intra-abdominal administration of isotopes combined with teletherapy is indicated to treat both smaller and larger masses of ovarian carcinomatosis.

6. The interstitial administration of radioactive isotopes is a useful means of irradiating pelvic cancer.

7. Complications with this type of therapy are minimal.

8. Patients with an intestinal obstruction and those severely debilitated from extreme carcinomatosis respond poorly. Radioactive isotopes are contraindicated in such instances.

139 East 36th Street

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SYMPOSIUM
AND PANEL
DISCUSSION

PROCEEDINGS

NEW YORK ALLERGY SOCIETY
MURRAY DWORETZKY, M.D., Editor

Insect Sting Allergy

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SHEPPARD SIEGAL, M.D., New York City
Moderator
JAMES H. BARNARD, M.D., Attending Physician,
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Introduction

Sheppard Siegal, M.D.: The subject about to be presented is insect sting allergy. We are fortunate in having some outstanding speakers who will participate in our panel. As you know, all of these people have made significant contributions to this subject. James H. Barnard, M.D., our moderator, is regional representative of the Committee on Insect Sting Sensitivity of the American Academy of Allergy. I now take pleasure in turning the meeting over to Dr. Barnard.

James H. Barnard, M.D.: The problem of sensitivity to insect stings has gained a great deal of prominence in recent years. As recently as August, 1954, the following question appeared in a medical periodical directed by a physician to an expert: "A twelve-year-old boy was stung by a wasp and within fifteen minutes a generalized urticaria developed with moderate edema of the glottis. How can he be desensitized? Might this sensitization recur after he has once been desensitized?" The reply was: "It is doubtful whether desensitization is necessary in this case unless exposure to wasp stings is of more than average frequency. Most people go through life without a wasp or a bee sting. Since desensitization is slow, this patient would have to go through years of injections for protection against a wasp sting that he might never experience again."[1]

In contrast, today it is the responsibility of the physician to explain to the patient or

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Presented at the Hotel Beekman Tower, New York City, May 9, 1962.

the parents that there may well be subsequent stings and that there may be a more violent reaction the next time, so that immunization should be attempted with proper emergency measures available until immunity has been shown to be adequate by a subsequent sting.

Case reports. To stress the dangers of these reactions, three fatalities which occurred last year will be described. The first two will be presented by George Hatzel, M.D.

George Hatzel, M.D.: The first of these cases is that of a middle-aged white female of Italian extraction, approximately forty-four years of age, who was sitting at a table set on a grass lawn. She apparently dropped something and when she reached down to pick it up and her hand touched the grass, she was stung by an insect, the nature of which was never ascertained. She screamed, crying out that she had been stung by a "bee." She became hysterical, frequently mentioning a death from a bee sting which had occurred in New Jersey only a few days before. This presumably was on her mind because of a recent news article.

She was rushed to the hospital where she was treated by an internist who found her semicomatose and in shock, with irregular heart rate and rhythm. An electrocardiograph machine was immediately attached to the patient, and a graphic record of the cardiac impulse was obtained until she expired. Emergency treatment at the time consisted of cortisone acetate, oxygen, and epinephrine (Adrenalin) placed directly within the heart, but death occurred about forty-five minutes after the sting.

At autopsy the body of a middle-aged, well-developed, well-nourished white female was seen, measuring five feet and ten inches in length and weighing 160 pounds. In the right posterior triangle of the neck there were two slightly raised, bluish-black areas. Subsequent information indicated that these marks probably represented the sites of the sting, since witnesses claim she immediately had held her hand to the right side of the neck after crying out that she had been stung by a "bee."

The remainder of the autopsy revealed a marked degree of congestion of the thoracoabdominal viscera. There was no evidence of coronary artery disease. The death certificate read: "anaphylactic shock due to bee sting." Microscopic sections added nothing to the gross findings.

I have considerable reservation in this case. I am still not convinced that this patient was not frightened to death, although we could never prove it. I say this in all sincerity because of the time interval, the type of death, the marked arrhythmia, and the reported symptoms of hysteria associated with the other signs and symptoms. The second case was more convincing.

This was the case of an elderly white male who lived in retirement with his wife. A physician was called late in the morning to see the patient's wife, at which time the physician asked about the health of the patient who answered that he felt quite well. About two hours after the physician had left, the patient was in the yard picking up some things around the lawn when a swarm of yellow jackets attacked him. He was stung twice on the left ear lobe. According to reliable witnesses, he was not unduly alarmed, waved his arms to fight off the insects, and then went into the house accompanied by relatives and friends. From fifteen to twenty minutes later, he suddenly developed a marked dyspnea and expired within minutes.

At autopsy the body was found to be that of a poorly nourished white male measuring five feet and nine inches in length and weighing about 125 pounds. In the left ear lobe there were two puncture sites about $^1/_8$ inch apart. The larger of these sites was located medially and was surrounded by a zone of ecchymosis $^1/_2$ inch in diameter. The smaller of the two sites had a slight but distinct zone of ecchymosis.

The lungs showed no evidence of edema. The heart was enlarged with fibrosis of the aortic cusps and patchy areas of fibrosis on the mitral leaflet. The coronary arteries were of good size, tortuous, and patent throughout. The most serious area of narrowing occurred in the anterior descending branch $^1/_2$ to 1 inch from its origin. The lumen here was from $^1/_8$ to $^3/_{16}$ inch in diameter, and there was no evidence of recent or old infarction of the myocardium. The brain was unremarkable except for a pia-arachnoid edema.

A microscopic study added nothing of significance. The final diagnosis was anaphylactic shock due to a yellow jacket sting. A number of the insects which stung the deceased, collected from low areas about the base of the porch, where shown to an entomologist who identified them as yellow jackets.

Dr. Barnard: Thank you very much, Dr. Hatzel. There is another type of fatal reaction to a sting which may be overlooked. This is demonstrated by a case in Connecticut which came to autopsy ten days after a single sting. We are fortunate in having with us tonight Nilo Herrera, M.D., who will describe the case.

Nilo Herrera, M.D.: This case suggests a delayed hypersensitivity type of reaction to a bee sting.

Case report. A fifty-year-old white male apparently was in his usual state of health until approximately ten days prior to his admission to the Danbury Hospital. While he was on a picnic, he was bitten by an insect which was thought to be a bee. We learned subsequently that this man had been stung by a bee about a week before. The first sting was on the front of his neck and the second one was on the back of his neck.

There was no immediate reaction to either sting, other than local swelling. About three days after the second sting he consulted his family physician because of blood in his sputum, and at that time the physician found that he had a purpuric discoloration in the neck and applied ice cold packs to the back of the neck. Three days later, or about a week after the second sting, he continued to bleed, and by this time a yellow, purpuric rash had appeared over more of the skin. The patient saw a second physician who put him on vitamins C and K and gave him some methylprednisolone acetate (Depo-Medrol). On methylprednisolone acetate therapy, the hemoptysis ceased in a few days, but the purpura remained. A few days later he was admitted to the hospital for study.

My first contact with the patient was when I was told that there was an Irish patient who was a heavy drinker and who was brought in with bleeding from secondary hypoprothrombinemia due to cirrhosis. However, he had a peripheral platelet count of only 10 to 20,000 per cubic millimeter. Liver function studies were normal except for a positive cephalin flocculation rate. An electrophoretic study of the patient's serum revealed a rather abnormal peak in the gamma globulin region.

By this time, in addition to his purpura and hyperglobulinemia, we also had evidence of a moderate anemia (10 Gm. per 100 ml. hemoglobin), jaundice (approximately 3 mg. per 100 ml. bilirubin), and his urine, during a period of twenty-four hours, contained red and white cells and small casts. Within twenty-four hours after his admission to the hospital, he developed coma and other evidence of central nervous system involvement and expired

A postmortem examination revealed a gross evidence of hemorrhage in most organs including the heart and kidneys, but the major cause of death was massive intracranial hemorrhage which was thought possibly to be the result of several bouts of small petechial hemorrhages which had coalesced to produce a single massive hemorrhage.

Dr. Barnard: Thank you very much indeed, Dr. Herrera.

The United States Public Health statistics for 1959 showed 17 deaths reported from bee stings and 16 deaths reported from wasps. There is no classification for yellow jackets, and so they probably are included in these figures.

A thorough review of the literature reveals numerous reports of autopsy findings which are fairly uniform in character. They include studies from England, Germany, and France, in addition to those in the United States and Canada. The positive features reveal marked visceral congestion, frothy, often blood-tinged mucus in the bronchi, scattered areas of marked edema in various organs and skeletal tissues, and diffuse petechial hemorrhages in the viscera and other body tissues.

The Committee on the Study of Insect Sting Sensitivity of the American Academy of Allergy has accumulated over 1,000 cases. Twenty-six per cent of these cases had a positive family history of allergy, 20 per cent had a history of drug sensitivity, and many reported an absence of excessive local reactions from previous insect stings. Thirty-five per cent had no recollection of previous stings at all, and 31 per cent had had two or more previous reactions to stings. One case had over twenty previous systemic reactions, and 1 patient reported that he had had approximately 50 mild systemic reactions.

Syncope has occurred in some cases with each sting. Sixty-two per cent showed an increase in the amount of local reaction with each subsequent sting, 28 per cent were unchanged, and 10 per cent thought that subsequent reactions had decreased. While I stress that this is an early evaluation of the data which may not be entirely accurate, 80 per cent of the patients immunized reported a decrease in reactions after treatment.

Eloise Kailin, M.D., of Washington, Chairman of our Committee, has kindly sorted out a list of 11 patients who did not show protection after receiving immunization therapy. It will be our task this year to try to find out the reason for the failures. There were 4 cases from California, 1 from Kentucky, 2 from Pennsylvania, 1 from Texas, 2 from Ohio, and 1 from the state of Washington.

This brings us up to our panel, and the first speaker will be Mary Loveless, M.D.

Immunology involved in insect sting allergy*

MARY H. LOVELESS, M.D.: Tonight's program, devoted entirely as it is to the subject of insect sting allergy, contrasts strongly with the situation in 1946. At that time I was pushed reluctantly into this field by a physician's mother who had been near death on one occasion after the sting of a honeybee and on another after the sting of a yellow jacket wasp. In those days the only preventive suggestions the medical profession would give were to avoid the insects and, if stung, to inject epinephrine. Neither suggestion was pertinent for my patient who was stung, on the second occasion, as a bee flew into her car while she was driving. She collapsed so quickly that she was unable to stop the car which crashed into a tree. She pleaded with me to try to immunize her, experimental and inherently dangerous as this would certainly be.

DEVELOPMENT OF IMMUNIZATION PROCEDURES. At that time the only antigen available on the market was lyophilized bee sting-and-venom sac which was used for the treatment of arthritis. Cautious and prolonged injection therapy was carried out at weekly intervals for seven months with this preparation.

After a total preseasonal dose of twenty-three sacs, I ventured to challenge the patient's forearm with two lively honeybees. A suggestive lowering of the blood pressure and a transitory, mild tingling of the fingers were the only consequences. She had no accidental encounters that summer. By the next spring I had acquired a second anaphylactic patient with a history that clearly incriminated yellow jackets. The lyophilized bee sting antigen was no longer available, and so I procured a nest of live yellow jackets, etherized a cupful, and made my first whole-body extract. Annual preseasonal courses with whole-body extracts were gradually cut down until 1950 when a total of 15,000 protein nitrogen units were given, and the first planned sting tests with live yellow jacket wasps were carried out. Seven months later the accidental sting of a Polistes wasp caused 1 of the 2 subjects only mild localized discomfort.

By 1953 the experimental group had acquired new members, and it seemed more logical to use venom as an antigen rather than whole-body extract. Consequently, venom sacs were extirpated from living worker wasps under light anesthesia and with sterile precautions. When the venom was to be stored under refrigeration through the ensuing fall and winter, the sacs were preserved in glycerin. On the day of use, the venom was released by trituration of the sacs with a sterile rod and diluted with an isotonic saline solution.

Over the years the experimental group has grown to about 60, and the preseasonal immunization of these violently allergic individuals has been linked systematically with deliberate stingings to test our success. At the same time the standard annual treatment has been reduced from about 20 sacs in four visits to a single two-and-one-half-hour visit and a total dose of six sacs of venom.[2] Only one type of venom is chosen, that of the wasp which has been incriminated by comprehensive history taking. Usually yellow jackets or Polistes wasps are used. Adverse reactions are rarely engendered and have been of significant intensity in only 2 individuals, both Polistes-allergic. The latter have required four or five visits for the completion of the standard annual allotment of six sacs of venom. For the rest of the group, three quarters of whom have submitted to sting tests after therapy, a high order of resistance has been induced, with stings by from one to four wasps in the field or in the hospital causing no adverse developments in the large majority and trivial sequelae in others.

In an effort to simplify further the therapeutic procedure for the patient, since 1960 I have been trying out mineral oil emulsions of venom as a single-injection repository. Since I had discovered earlier that glycerin, added to pollen antigen as a preservative, exerted a deleterious effect on the delaying action of mineral oil, it has been found necessary to have at least ten live wasps on hand on the day of repository treatment. The freshly-removed venom sacs then served as the source of antigen for the emulsion which was made, as it were, "while the patient waited." It would, of course, prove far more convenient if stored, glycerinated material could be used, since the procurement of live wasps is difficult, if not at times impossible, outside their summer season of abundance.

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Furthermore, the interval between repository treatment and induced immunity is from six to ten weeks. This fact forced us to abandon the idea of utilizing yellow jackets for venom repositories, since they are rarely available before their season, July 1 through October. Polistes wasps, on the other hand, hibernate in more or less accessible places and can be procured perennially.

Consequently, the pioneering attempts with repository venom in 1960 and 1961[3,4] involved Polistes-allergic persons, 8 of whom not only showed complete tolerance of the six sacs of Polistes venom which were given to them in a single subcutaneous injection of 1.2 ml. of emulsion, but also exhibited trivial sequelae in only 2 instances when they were stung by from one to three Polistes, either in the field or at the hospital, as long as seven and one-half months after therapy. There were no abscesses, cysts, or new growths. A ninth member, who had to be given his emulsion in divided doses during two visits and who took only half the allotted dosage of six sacs because of mild, adverse developments, refused to be sting-tested.

Encouraged by the demonstrated effectiveness of emulsified venom, we devised a means of applying the principle to yellow jacket-reactive patients. It rested on an earlier finding in the laboratory that Polistes venom neutralized all the passive transfer activity of yellow jacket-allergic serum (the reversed test was only partially negated).[2] It was assumed that Polistes venom would not only react with yellow jacket reagins, as demonstrated, but would probably also elicit mutual blocking antibodies for the two venoms. On this premise 24 individuals with unequivocal and severe sensitization toward yellow jacket stings were immunized with a six-sac repository of Polistes venom.[5] Three fourths of them accepted our invitation to undergo a challenge with from one to three yellow jackets from two to six months after treatment. There was only one adverse reaction, sharp hypotension and near collapse in a sixty-nine-year-old man five minutes after the first yellow jacket sting. Fortunately, he responded promptly to 0.5 mg. of phenylephrine which was injected into the tubing of the intravascular glucose drip which we employ routinely throughout these tests. The hospital's resuscitation crew, when they arrived a few minutes later, merely applied an oxygen mask intermittently to discourage cerebral hypoxia. Since this patient had tolerated the stings of two yellow jackets applied to his forearm several months after a routine course of fluid yellow jacket venom had been completed two years earlier, we were disconcerted and puzzled by the current startling developments. To determine whether the explanation lay in this rather elderly man's failure to maintain immunity for as long as five months, as in the present instance, or whether Polistes venom had failed to protect him against the other wasp, we gave him a standard course of fluid Polistes venom during a two-hour period a month after the collapse reaction. To our delight, a challenge with two lively yellow jackets thirteen days later was fully tolerated, thus substantiating the conclusion derived from all the other sting tests that cross protection was regularly achieved with Polistes immunization.

Having established this finding, we were in a position to immunize against or to the sting test for either type of wasp allergy any month in the year. As a matter of fact, most patients who have exhibited satisfactory resistance during their sting tests have since been on a regimen of intermittent, deliberate stings by two insects throughout the year. The first such treatment usually takes place a month after the initial test, intervals being gradually lengthened until four or even six months or more elapse between sessions. The procedure appears to serve not only as a periodic test of resistance, but also as a probable means of maintaining immunity. This approach carries the advantage of simplicity for the physician, in addition to great economy of immunizing material and of treatment time. Its ultimate worth must await further trials. Occasionally adverse developments have been encountered when the interval is great, but, without exception, they have been trivial or mild in intensity.

Two premises of immunization. Before closing, I should like to remark that my insistence on venom in contradistinction to whole-body extract as the agent for immunization rests on two premises.

The first premise is that only venom participates in the sensitizing process that stems from accidental stings. The female wasp does not, like scabies, introduce her whole body into her victim. There is merely a brief penetration of superficial nature which involves the stinger through which the droplet of venom is injected. Therefore, to force patients to build up antibodies against numerous other, nonparticipating proteins which are present in the body of the insect seems pointless and dissipatory.

Far more commanding is the second premise which states that these extraneous proteins may set up over a long term such antibody responses as theoretically underlie periarteritis and similar disorders of obscure origin. Indeed, wasp venom allergies belong in the same category as foreign serum allergies, penicillin allergy, and so forth. For these allergies no genetic predisposition seems necessary as a handmaiden to their development—we are all candidates, so to speak. Let us then restrict all therapy, indeed all tests, to the absolute minimum and let us employ only the indispensable antigen, venom. During my many years of live wasp hunting, I, myself, have gradually acquired a wasp sting allergy, and I can assure you that I am avoiding immunization until the situation is essentially life threatening, as in the case of my patients. Under no circumstances would I submit to treatment or even to any type of test including the scratch variety with whole-body extract. And to use a mixture of whole-body extracts is only to compound the hazards. Such preparations deserve no better designation than "junk."

Conclusion. One can only hope that the efforts which I have been making, and perhaps others as well, to bring pure venom into commercial availability will materialize before long. Hundreds of physicians have been seeking this for may years. Until that time comes, we shall have to take the trouble to catch our own insects, dissect them, and preserve the venom sacs which our patients need and merit.

Dr. Barnard: Our next panelist is Harry Mueller, M.D.

Diagnosis and testing for insect sting allergy

Harry L. Mueller, M.D.: The diagnosis of systemic reactions to insect stings usually presents no difficulty from the history, and, as a rule, the patient has had the diagnosis made before he ever sees the allergist. We believe that a differentiation should be made between local reactions and systemic reactions. Although systemic reactions are frequently preceded by increasingly large local reactions from previous stings, a great many people have large local reactions accompanying successive stings for many years without ever having systemic sensitivity. We do not recommend treatment for local reactions regardless of the extent, and indeed, there are so many of these reactions that we could not possibly treat them.

Local and systemic reactions. In most instances we believe that the local reaction is a toxic one, and it does not respond to desensitization. If we only had some method of determining which local reactions are the prelude to or the beginning of systemic reactions, it would be helpful in doubtful cases, but we do not have any way of determining this. In this type of patient, when we are not sure if there has been a systemic reaction, we do serial intracutaneous testing. I am not sure that this is a reliable criterion, but it is the best we have at the present time.

It must be remembered that systemic reactions can also be on a toxic basis, and if it is possible and time allows, it is useful to make this differentiation. Symptoms of toxicity are usually delayed. They are accompanied by edema without urticaria. Headache, fever, drowsiness, involuntary muscle spasm, and sometimes convulsions are signs of toxicity. Patients who have had ten or more stings at one time should be suspected of having a toxic reaction, but in any situation involving a question of anaphylactic shock, this is so serious that measures to combat it should be taken without delay, regardless of whether or not toxic symptoms are suspected.

IMPORTANCE OF DIAGNOSIS. I am convinced that a great many systemic reactions to insect stings, particularly fatal ones, are misdiagnosed, and it should be noted that stings are not confined to warm weather. The paper wasp is an indoor dweller at times and wakes up very easily when the heat is turned on. We have many examples of this, such as the physician who visited her summer home during Christmas vacation, turned on the heat, went to bed after the house was warm, and was stung, experiencing an almost fatal reaction.

One of the most interesting diagnostic problems was that of a young couple who had dinner with friends. On leaving, as the man put his arm through the sleeve of his coat which had been taken from a warm closet, he felt what seemed to be a scratch on his wrist, which he ignored. As they started to drive off, he told his wife that he felt badly and thought that he had indigestion. They started down the road, but within a few minutes he fortunately stopped the car as he lost consciousness. His terrified wife drove to a nearby community hospital where the nurse on duty called a physician and told him she had a man in the emergency room who seemed to be dying of a heart attack. On arrival, the physician examined the patient and found that he had a swelling from the right wrist to the right elbow and urticaria across the chest and back. Believing that this was an anaphylactic reaction probably due to an insect sting, the physician administered epinephrine. The patient recovered and is now under treatment. This diagnosis could well have been missed by a less alert physician.

TESTING. For purposes of study in our clinic, we have classified these patients into four groups according to the severity of symptoms, ranging from a Grade I or a slight general reaction to a Grade IV or a shock reaction.

Our most recent figures from approximately 275 patients show a higher percentage of slight general reactions than our previous reports. This, we believe, merely represents a dissemination of information. Ten years ago most physicians regarded this as a medical curiosity, and usually only the more severe cases found their way to the allergist. I use the phrase "found their way" because I am still surprised to see the large number of patients who seek treatment because of information from lay periodicals while their doctors are unaware that such treatment is available. I think this is a very important point, and this criticism is not necessarily directed at the practitioner.

Some time ago a professor in a medical school joined us at lunch, and in the course of conversation he said, "Don't you fellows know something about insect stings? My daughter has had reactions to three different stings, and each one is becoming more severe. She was unconscious with the last one. Is there anything that can be done about this?"

Most patients and their parents are sure they know exactly what stung them and become quite indignant about this when the identification of the insect is questioned. One of our main differences with Dr. Loveless in the approach to treatment hinges on this point. I do not believe that one knows what actually stung the individual patient in 10 out of 100 cases. It is practically impossible to know unless the insect which caused the sting is brought in. The color and size of the insect are of no value, since there are many variations of these factors in the various species of all the bees and wasps.

Patients come in and tell us that they were stung by a "hornet." We ask them how they knew it was a hornet, and often they will say, "Someone was with me and said it was a hornet." Frequently they did not even see the insect. Dependence on the patient's interpretation is, in our opinion, entirely worthless. A correlation of the circumstances at the times of the sting with the nesting habits, which are, of course, very definite, and the presence or absence of a stinger may give presumptive evidence, but in no case can this be certain unless the insect is captured. Since multiple cross sensitivities exist in most patients and there is no reliable way to determine the exact situation in a given patient, identification of the insect, in our opinion, is of little or no importance.

About 90 per cent of our patients, out of approximately 275 cases, show sensitivity, by the skin test at least, to more than two insects, and over 60 per cent of them show sensitivity to three or four insects. We are still quite cautious about testing these patients, and we usually start our intracutaneous testing at the 1:100 million level of dilution. We use whole insect extracts. Refrigerated saline dilutions may retain their potency for twelve weeks and possibly longer, but we do not recommend using solutions that are over twelve weeks old, and every four weeks we make fresh solutions for testing.

Scratch tests with high dilutions are entirely unreliable in our experience, but if we are in doubt from the history that the patients had a systemic reaction, we do scratch testing with concentrated 1:10 whole-insect extract. If the results are negative, we will start our intracutaneous testing at 1:10,000 in such patients. If the scratch-test results are positive, we go back to the 1:100 million for intracutaneous testing. We do not have enough of these cases to feel that this is an acceptable general procedure. It must be remembered that once systemic sensitivity develops, it usually becomes increasingly severe as time passes, although the patient does not have interval stings, and the speed of this increase varies with the individual patient.

One cannot predict what is going to happen with these patients. We do serial intracutaneous testing with extracts of bee, Polistes wasp, hornet, and yellow jacket because we are collecting data, but for practical purposes a mixed extract should be satisfactory for clinical use. Our experience to date still indicates that, generally, the shorter the time interval from the sting to the onset of symptoms, the more severe the reaction will be, and that the more severe the reaction, the higher will be the dilution that will give an initial positive result on serial testing. However, there are exceptions to both of these generalizations.

DR. BARNARD: Thank you very much, Dr. Mueller. At this time I would like to introduce Eugene Walzer, M.D.

Basic treatment of insect sting allergy

EUGENE H. WALZER, M.D.: Monroe Coleman, M.D., of Stamford, Connecticut, and I studied 140 patients with clinical sensitivities to the bee, wasp, yellow jacket, and/or hornet, and the clinical results of therapy were evaluated. These patients ranged in age from two to sixty-five years, and there were 101 males and 39 females. A survey of the patients' histories revealed 102 atopic patients with either a positive family history, a personal history of allergy, or both. There were 38 patients who gave no history of allergy.

The patients' reactions to stings were divided arbitrarily into three categories: mild, severe, and shock (Table I). The 74 patients in the mild group developed either generalized urticaria or angioedema. In 24 patients with severe reactions the major symptom, in addition to urticaria and angioedema, was a feeling of constriction of the chest which was associated with wheezing and dyspnea in 17 patients. Other severe reactions included abdominal pain, nausea and vomiting, glottal edema, fever, or purpuric urticaria. There were 42 patients who went into shock. In 7 of these patients there were no additional symptoms. Thirty-five of them had urticaria and angioedema, and of the latter 3 had asthma as well.

The skin testing of these patients will not be discussed except to say that they were tested intracutaneously with serial dilutions of aqueous or glycerinated extracts of individual whole insects, starting with a 1:1 million dilution. The results showed that with the materials used 61 per cent of the patients had positive skin-test results, and 39 per cent had negative results.

Most reactors whose skin-test results were positive showed sensitivity to more than one insect on skin testing, corroborating the findings of other workers.[2,6] Loveless and Fackler,[2] in human beings, and Foubert and Stier,[7] in animal experiments, have shown cross sensitivity to the various insects in this group. Among the patients under discussion here, many of whom were children, few were able to identify the insects which stung them, and they used the terminology of bee, yellow jacket, hornet, and so forth loosely. Many of those who thought they could identify the insects changed their minds or became confused when confronted with pictures. Although it was thought

TABLE I. Classification according to severity of reaction

Reaction	Number of Patients	Description of Reaction
Mild	74	Generalized urticaria and/or angioedema.
Severe	24	Above plus either constriction of chest, wheezing, abdominal pain, nausea, vomiting, glottal edema, fever, or purpuric urticaria.
Shock	42	Any of above plus usual signs of shock: fall in blood pressure, weakness, thready or absent pulse, collapse or unconsciousness.

that identification might be established by the circumstances of the stings, that is, the type of area or the nesting habits of the insect, identification was rarely certain. Moreover, the fatal potential for this type of allergy placed it outside the area of speculation. For all of these reasons, it was decided to treat the patients with a mixture of all four of the insects.

Method of treatment. Treatment consisted of the weekly subcutaneous administration of increasing amounts of glycerinated extracts of whole insects, using a mixture of bee, wasp, hornet, and yellow jacket to a maximum tolerated dose or to 0.8 ml. of a 1 : 100 dilution. The dosage was started arbitrarily with a 1 : 1 million dilution except in the more sensitive patients. In these patients two criteria were considered: the degree of sensitivity in the reactors with positive test results and the severity of clinical reaction to a sting in the severe and shock groups of the patients with negative test results. These more sensitive patients were started on 1:100-million- or 1:10-million dilutions. After a maximum dosage was attained, the patients were maintained on a top dosage at monthly intervals up to three years. Of 140 patients, there were 38 who were stung 51 times after adequate dosage had been attained or after therapy had been completed.

In Table II the clinical response of 38 treated patients to 51 stings after treatment is compared with the responses of these patients before treatment. After 40 stings, which represented 80 per cent, there was a minimal response in the patients. This meant that they experienced no more than the ordinary small local reaction seen in nonsensitive individuals.

In this group there were 16 stings in patients who had previously experienced mild reactions. Twelve of these stings occurred in atopic patients and four occurred in nonatopic patients. Eleven stings occurred in atopic patients who had previously experienced a severe reaction. Thirteen stings occurred in patients who had initially had a shock reaction; of these, nine were atopic and four were nonatopic.

The responses to six stings after therapy were classified as unknown because these patients panicked and took prophylactic medication which included adrenergics

TABLE II. Clinical response of 38 treated patients to 51 stings

After Treatment		Before Treatment			
			Patients		
Response After Stings in Treated Cases	Number of Stings Sustained	Severity of Original Reaction to Stings	Atopic (31)	Nonatopic (7)	
			Number of Stings		Totals
Minimal	40	Mild	12	4	16
		Severe	11	0	11
		Shock	9	4	13
Unknown (Prophylactic Medication)	6	Mild	2	0	2
		Severe	0	0	0
		Shock	4	0	4
Unchanged	5	Mild	2	1	3
		Severe	0	0	0
		Shock	2	0	2
Totals	51	. . .	42	9	. .

and/or steroids. All of these reactions were minimal after therapy. Two occurred in the atopic mild group and four occurred in the atopic shock group. The responses of five stings after therapy remained unchanged. Three stings occurred in patients whose pretreatment response had been mild, two in the atopic group and one in the nonatopic. Two of these stings occurred in atopic shock patients, and the response after treatment remained that of shock.

If the unknown group is omitted, this type of therapy had been proved successful in 89 per cent of the stings, and it had failed in 11 per cent. All of the failures occurred in patients with positive test results, with four stings occurring in the atopic group and the other occurring in the nonatopic group. During immunization therapy a few patients developed large, local reactions on relatively low doses of extract. Generally, it was possible to pass this low level by increasing the dosage slowly. Several patients could not tolerate more than 0.1 or 0.2 ml. of a 1:1,000 dilution of the four-extract mixture. Two cases developed constitutional reactions while they were being desensitized. They had not attained top dosage but were brought to higher levels by reducing the dosage and gradually increasing it at a slower rate. A dose in the 1:100 dilution was always considered a good immunizing level.

How long should insect-sensitive patients be treated? The criterion of three years is based on equivocal evidence, but at the present time it is suggested that all patients should be treated for at least three years. The mild group may be discharged at the end of this time. The severe and shock groups should be maintained on therapy indefinitely, and, where possible, the time intervals between injections should be spread out. It is hoped that further investigation will clarify this problem and give us more scientific criteria for terminating treatment.

Dr. Barnard: Thank you very much, Dr. Walzer. This matter of how long to continue treatment is far from being settled, but I received an interesting communication about a man who had a severe reaction with shock from a sting in 1954. He received 18 treatments, after which treatment was discontinued, and it was felt that he would be all right from then on. In 1958, however, the man had a near-fatal shock reaction after one sting and remained in coma for sixteen days. He was left with a hemiplegia and a Parkinsonian type of tremor and has not improved since. The letter was sent for the purpose of stressing the point that until we know otherwise, it would, perhaps, be better to continue treatment indefinitely rather than take a chance on such an occurrence.

The meeting is now open for discussion or questions from the floor. I believe that Everett Gaillard, M.D., has something to tell us of his experience with treatment with whole-body extract.

Question and answer period

Everett Gaillard M.D.: We have used a mixture of bee, hornet, wasp, and yellow jacket in emulsion. We treated 54 cases in 1960 and 108 in 1961. Of these, there were 38 repeats, so that the total number of cases treated by this method was 124. The patients were classified according to their degree of sensitivity as mild, moderate, severe, and shock types, of which we had 31, 34, 42, and 18 patients respectively. We found a dose of 2,500 protein nitrogen units adequate while producing fewer and less severe local reactions than larger doses. We had no systemic reactions, 13 immediate local reactions which lasted as long as seven days, and 3 delayed local reactions which began a week or a month later and lasted for several days. There were a few firm masses, but no cysts.

Of the patients, 16.5 per cent were stung in the field after treatment. Among these we had no systemic reactions. There was no positive identification of the insect in any case. This year, for the first time, we have begun to treat a few patients with emulsions of the venom.

Vincent James Fontana, M.D.: Are there blocking antibodies or any antibody studies?

Dr. Loveless: Yes, we did serologic studies by passive transfer some years ago, not only for reagins, but also for a blocking factor, both of which were demonstrated in the post-treatment sera. However, we discontinued both types because of the risk of transmitting homologous serum jaundice to the normal test subjects. At the present time Thomas Nall, M.D., and I are engaged in "auto" blocking tests which employ the patient's heated serum, admixed with graded amounts of venom in his own allergic skin and eye. I first described this auto-immune test in 1940[8] for pollen-blocking antiserum. The end points of the patient's serum before and after specific therapy are compared. We expect to have enough data for publication before long.

Dr. Siegal: What is the significance of a delayed skin-test reaction to insect extracts without the presence of an immediate reaction?

Dr. Loveless: This is exactly what one would expect and, indeed, often sees, in insect allergy. It is also typical of serum disease. The first contact may well evoke no local or general reaction. From ten to fourteen days later, however, a classical serum disease syndrome may arise—urticarial eruption associated perhaps also with fever, adenopathy, malaise, headache, and so forth. Normal students whom I used for passive transfer studies showed no immediate wheal and flare responses in their initial control sites because very dilute venom was employed to avoid the customary "irritative" reactions which are always associated with injected venom of high concentration. Over half of the test subjects, however, developed definite itching and urticaria in the many sites which I had tested earlier. Quite a few of the patients also had regional adenopathy, while some of them experienced malaise. They also had acquired a reactivity to testing solutions of venom which were previously inactive in normal skin. In short, I had induced venom allergy in them, at least locally. Incidentally, although there is an incubation period which gives the impression of a delayed reaction, the antigen-antibody reaction is actually immediate in type, once both participants are present in the body. During the incubation period only the antigen, venom, was in existence. Once reagins had been formed, combination was immediate, and a wheal and flare resulted. This incubation period distinguishes the whole group of allergies from classical atopy, just as does the lack of a familial predisposition in serum, drug, and venom allergies.

Dr. Mueller: We have seen a good many twenty-four to forty-eight-hour delayed reactions to skin tests. We do not know for sure what these mean. One immunologist whom we consulted on this problem believes that this is a sign of delayed sensitivity which may become immediate, and he has advised us that these patients should be protected.

We have 5 patients who have not had immediate systemic reactions but have had typical serum sickness which developed from seven to ten days later with polyarthritis, fever, urticaria, and so forth. Of these patients, 4 out of 5 have shown only delayed reactions. In 1 out of 5 patients we had a very large immediate reaction at a dilution of 1:100,000, as well as a delayed reaction. We have treated these patients.

Physician: Please comment on newspaper articles sponsored by the Red Cross recently.

Dr. Loveless: The Red Cross-sponsored article stated that I had recently reported on a single injection of serum that afforded year-round protection against wasp stings. Actually, the article was released before the Red Cross had time to corroborate its accuracy, and they have taken steps to correct the situation. The reference should have stated that an emulsion of venom was being employed in a single, annual injection and that protection appears to last at least from four to six months and, in some instances, for over seven months. They intend also to emphasize that severe, generalized reactions to stings are the exception, and that localized responses are normal rather than dangerous. After reading this article, many mothers were alarmed by these local reactions and hurried to physicians with their children for immunization.

Speaking of local reactions brings me to my final comment. Insect preparations, at least whole-body extracts and venom, characteristically produce wheal and flare reactions. A negative response merely means that a more concentrated solution must be used. This is because the agents are primary irritants. For this reason, all my normal subjects exhibited responses to yellow jacket venom, not only in the skin by the endermal route with serial dilutions, but also in the eye by instillation. A deliberate sting done on the same day also promptly elicited a wheal and flare. A positive reaction in itself is, therefore, of no diagnostic value unless one determines with serial dilutions the minimal reactive strength. This, as I have written, will usually serve to distinguish a normal from an allergic response. However, one should depend on a carefully-taken history to unfold clinical evidence of susceptibility to venom. After coming to a diagnosis by the latter door, tests are carried out not to make a diagnosis of sting allergy and the type of insect, but rather to get a clue to what will be a safe, starting therapeutic dose of venom. Tests are occasionally useful to decide which of two, equally likely suspects is actually the offender. Routine and broadscale testing with insect antigens should be condemned strongly for reasons I have mentioned earlier. On the other hand, skillful immunization with an established offender's venom in roughly minimal protective amounts, associated with the fewest possible tests, can be dramatically successful in saving life.

DR. MUELLER: We tested 50 medical students, and of these only 2 showed positive reactions to skin tests. Subsequent histories revealed that these 2 patients had had systemic reactions to insect stings when they were children, but did not remember that they had ever been stung since.

The venom contains not only a good many different allergens, but also a number of other constituents, possibly including viable, infectious organisms, and actually the particular allergen that might affect the patient may be diluted quite a bit in the venom. Whether it is "junk" in the extract of the whole insect or whether it is "junk" in the venom, we are dealing with a multiplicity of substances. We feel that we are giving better protection by using the mixed extract than we are by using the individual venom. Again, we cannot tell in most instances what has stung the patient.

PHYSICIAN: Are there any cases of anaphylactic shock reported from mosquito bites?

DR. MUELLER: There have been cases of systemic reactions to mosquito bites, but to my knowledge there is no record in the literature of any fatal reaction to a mosquito bite. Beyond that, I do not know.

PHYSICIAN: Must a patient who suffers a systemic reaction following a sting react at least as violently when stung again by the same species?

DR. MUELLER: No, this is not necessarily so. We have had patients who have been stung by an insect and have had a systemic reaction and have subsequently been stung by what we think was the same insect without having a reaction or with less reaction. These cases are rare in our experience.

DR. DWORETZKY: Are you familiar with any cases of fatal reactions which were not preceded by constitutional reactions in the past?

DR. MUELLER: Yes, we are. We have records of patients who have had fatal reactions in whom no known previous systemic reaction had occurred.

PHYSICIAN: Do you give yearly booster doses after basic immunization?

DR. MUELLER: We follow these patients now. There are some patients whom we have followed for eleven to twelve years since we first gave them their three-year immunizing treatment. We have patients who have gone as long as eight years after stopping a three-year treatment series and who have been stung and have had no reaction. As a matter of fact, we have had no one who has completed three years of treatment and has subsequently been stung two, three, five, and up to eight years later who has had a systemic reaction, but this does not prove it cannot occur because we have a large number of treated patients who have not been stung. We do not know what is going to happen to these patients and whether we ought to give them booster doses or not.

We have shortened our period of treatment a great deal, and we have got it down now, in the second year, to every two months, and in the third year to every three months. I have the feeling that eventually we can make this a very simple treatment.

Physician: How do you manage a patient who cannot tolerate the usual desensitizing doses without a constitutional reaction?

Dr. Mueller: Frankly, we have been able to build all our patients up to a protective dose if we do it slowly.

Physician: Without subjecting a patient to an actual sting, how do we know when to stop hyposensitization?

Dr. Walzer: I do not know. Monroe Coleman, M.D., and I have advised continuing treatment on patients for more than three years. We do not feel that with the severe shock cases we should ever stop. I do not think that I have the courage to do so.

Physician: Is a history of associated allergies of the patient and familial allergies a determining factor for mandatory hyposensitization in a patient with a history of insect sting with at least a minor local reaction?

Dr. Walzer: I think that if the reaction is local, desensitization is not warranted. The immunologic aspects of this subject are far from understood. For example, we have found that patients can have positive test reactions on some occasions and have negative skin reaction at other times. We have also found that we cannot transfer all of the large reactions that one gets on skin testing. In patients with a multiplicity of sensitivities on skin testing, you can transfer some with the psychokinesis technic and you cannot transfer others. With so much that is unexplained about the immunologic mechanisms involved in pathogenesis, diagnosis, and treatment, there are as yet no criteria for discontinuing therapy after three years.

Dr. Barnard: I am sure that I speak for the members of the Society in thanking the panelists for the excellent presentations they have given. I will now turn the meeting back to Dr. Siegal for closing remarks.

Dr. Siegal: I wish to thank the members of the panel and all of those who participated on behalf of the membership and the guests for an outstanding evening.

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Psychiatric Evaluation of Premenstrual Tension

A STUDY OF *the menarche and menstrual symptoms, with emphasis on attitudes relating to feminine sexuality, was made in 103 women. A correlation was found between freedom from symptoms and a good mother-daughter relationship, including a favorable introduction to the menstrual experience. Menstrual symptoms can be divided into the physiologic and the ancillary; the latter can be understood in terms of loss of self-esteem and ego defense. Dysmenorrhea was found to have a physiologic basis in some patients and a large psychogenic component in others. Psychogenic factors seemed to be largely responsible for amenorrhea, which had occurred in 30 per cent of the patients.*

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THIS REPORT is an outgrowth of a study of menstruation started in 1958. The study of 103 women was undertaken because of its relevance to problems of feminine psychology and particularly the so-called female castration complex. The psychologic background will be reviewed briefly in the following paragraph to set the study in its proper context.

Just as the Biblical fathers believed God made man in his image, Freud[1] and his early workers (as do some classical psychoanalysts today) adhered to the view that man is the prototype of humanity and that women are defective in their structure because they lack a penis. He believed that many women felt castrated as a result of this lack and developed the theory that women suffered from "penis envy" on a biologic basis and that because of this many were driven to emulate men and developed a "masculinity complex." In some instances, they suffered from a so-called "castration complex." He also believed that women were more passive than men, had weaker consciences, and were in general more narcissistic and shallower than men. From a theoretical standpoint, Freud[2] tried to balance his equation with something positive on the side of femininity, by considering the childbearing function as a compensation for the lack of a male organ. There are, of course, many who have challenged these views—notable among them are Karen Horney and Clara Thompson. Thompson[3-5] stressed the cultural aspects of women's envy of men, and Horney[6] emphasized the importance of the feminine creative function.

Onset of menstruation

In reviewing the theoretical considerations, which have already been dealt with in a previous report,[7] the onset of menstruation was chosen as an area for study, since it is an experience universal to all women at approximately the same period of life. A careful menarchal and menstrual history was taken, and some unexpected findings were brought to light as a result of the study. This is, of course, a difficult area to explore since the most extensive work-up of each individual from both a physical and psychologic standpoint would still leave it to some degree problematic where the physiopathologic area ends and the psychogenic begins. Nevertheless, it is possible to arrive at some etiologic generalizations.

For students of other disciplines, the intangibles with which the psychiatrist deals often seem confusing and unreliable at best. The psychiatrist and analyst, insecure in his relatively recently developed discipline, has perhaps been defensive in response to criticisms pointed in this direction. There has been a growing tendency to do research involving large numbers of individuals in an attempt to draw conclusions from statistical studies, and this report comprises one such study. Yet, although the study is based on quantification and controls, it is the author's belief that if the psychiatrist is to be of value, this will come not from statistical studies, which can be misleading, but from thought and inference about individuals, who follow certain broad patterns but also are essentially unique, and whose behavior, responses, and emotions require careful interpretation, often leading to postulates which are valid only until more appropriate ones can be found. This, of course, applies to all empiric clinical research.

Dyspareunia

Perhaps this approach will be clearer if some questions are raised about the use of the word dyspareunia, a common term to all physicians including the gynecologist, a term that suggests something "tangible," and also a blanket term for many things. What does dyspareunia mean? Coital pain as a manifestation of a pathologic condition of the pelvis? And if so, at what site? Pain and discomfort as a result of some physiologic incompatibility between sexual partners? Pain on intercourse in a woman who desires intercourse? (And, might she acquiesce consciously while rejecting it unconsciously?) Discomfort in a woman who is unable to be aroused? Pain as the result of submission to an experience that may amount to a hostile attack? Pain with her husband but not with a casual partner? Pain with a casual partner but not with her husband?

Is there not much information about the personality and physical status of the woman and the nature of the intercourse and relationship of the partners that would be necessary to understand it? Can one, therefore, generalize easily about it or feel readily satisfied with statistical computations of it? The gynecologist or general practitioner, of course, is concerned largely with his patient's physical health and cannot spend his time in detailed inquiry. Yet his understanding of emotional and psychologic factors can be helpful in many ways.

Premenstrual tension

It is generally acknowledged that a large proportion of women suffer premenstrual tension, many being seriously disabled by symptoms relating to the menses. Some estimate that as high a proportion as 70 per cent of all women are incapacitated in one way or another. In this study, it was found to be as high as 85 per cent.[7] I would define premenstrual tension as that group of symptoms recurring periodically in relation to the menses, usually appearing within a time span of from one week before until the third or fourth day after the onset of menstruation. It includes a wide variety of symptoms, prominent among them a feeling of tension, irritability, and quarrelsomeness; swelling of body parts; headache, nausea, and vomiting; depression; hunger; a desire for sweets; extreme lassitude; and a wish to call mother.

I would raise the following questions in relation to premenstrual tension:

1. Why should one accept premenstrual tension and pelvic pain or discomfort as almost an inevitable of feminine experience —what other organ system seems to share the same degree of physiologic aberration?

2. Why is there not the same pain, discomfort, and tension for the first menstruation and generally the next few times?

3. Why are so few complaints centered around breast engorgement and nipple tenderness, even though these are acknowledged as uncomfortable?

4. What meaning can we impute to the marked clarity of recall in relation to the circumstances of the first menstruation?

5. How can one account for such varied symptoms as hunger, depression, craving for sweets, nausea, vomiting, and tiredness, to cite a few, on the same physiologic basis?

In 1958, Goldfarb[8] reported that premenstrual tension is not well understood and enumerated the symptoms included under this rubric. He reported on medical treatment involving the use of estrogen and diuretic, antispasmodic, and analgesic agents. Notable in his paper was the implication, although not so categorized by him, that while the symptoms referable to the emotional state did at times improve under treatment, the physical signs of water retention and endocrine change did not improve, even though treatment for these conditions was presumably specific.

Pelvic pain

In June, 1960, Gidro-Frank, Gordon, and Taylor[9] reported on a study of pelvic pain. Here, pelvic pain, rather than menstrual symptoms per se, was the focus of attention. But it was observed that pain is quite prominent in the female sexual and procreative functions, and that the pain of dysmenorrhea is not necessarily related to the pain of "pelvic congestion." It was recognized that pain is often a psychosomatic expression, and that women suffering pelvic pain to such extent as to seek relief seemed to be ambivalent toward marriage and homemaking, uncomfortable during pregnancy, frequently hostile to the mother, and had a higher rate of fertility problems, as a group, than the majority of women. In short, they recognized profound conflicts in the area of femininity. However, the study was directed more toward an observation of symptoms and their relation to personality types than to etiologic considerations.

This is the point at which the present report starts: A study of the onset of menstruation focuses on attitudes relating to feminine sexuality. It is the start of the reproductive function, but also contains a summation of all the feminine feelings and attitudes to that point. It is something experienced by every girl at approximately the same age, and memories relating to this experience frequently contain a few drops of the distillate of the mother-daughter relationship. It is, therefore, a nodal point in the development of femininity and part of a sequence of experiences influencing the development and awareness of the self.

Case report

Before going into a detailed report on the study, I will give a brief example from the analysis of a forty-year-old woman. As an eleven-year-old girl who had had no preparation for her menses, she awoke early one morning feeling wet. She threw off her bedclothes and on observing blood ran in panic to her mother's room. Her mother seemed annoyed at being awakened, slapped her face, and then explained that the blood was her period, which had really

FIGURE 1. Questionnaire on menstrual experiences submitted to 103 women.

Present age: Marital Status:

Age at marriage: No. of children:

Educational background—
high school, college, etc.:

Vocation, if any:

Mother's birthplace:

1. How old were you at onset of menstruation?
2. Did you look forward to menstruation, pleasantly or otherwise? Explain in full:
3. What preparation did you have for it—
   a. From mother
   b. From anyone (sister, friend, etc.)
4. How did you discover your first menstruation (all the circumstances you recall)?
5. How did you feel—(your immediate and subsequent reactions)? What did you do?
6. What was your mother's reaction—
   a. What did she say or do?
   b. How did she help you?
7. Did you have pain or cramps then or since: If yes, did they persist after having a child (or did you have a D and C—and what result)?
8. What is your menstrual cycle (number of days from onset to onset)?
9. How many days does it last?
10. Is there much variability in your cycle?
11. How heavy a flow would you estimate? Are you aware of the flow—are there manifestations of gushing, blood clots, etc.?
12. Do you limit your activities during menstruation? To what extent?
13. Are you aware of premenstrual tension—describe?
    For how many days are you aware of premenstrual breast fullness?
14. Have you had any prolonged period of absence of menstruation? If yes,
    a. How long? Can you relate this to any emotional disturbance before or at the time?
    b. Was there any change in your life (a trip, etc.)?
    c. Was a physical disorder diagnosed—describe?

Any other comments:

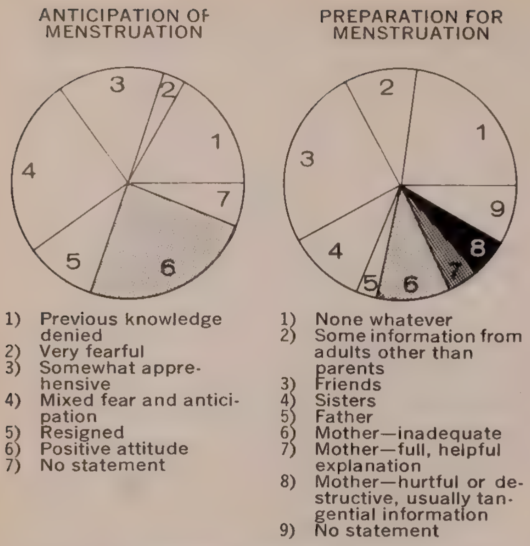

FIGURE 2. Findings relating to preparation for menarche.

started too soon, and added as an afterthought that it was a natural occurrence. The girl was told what to do for herself hygienically, then she was advised to take to her bed for the day since she would be uncomfortable; but she was given no other information.

At fourteen she had the following experience: She had been the favorite grandchild of her maternal grandfather, an orthodox Jew. On his death, she was denied admission to the cemetery to participate in the burial ceremony. She was told that a menstruating woman is "unclean" and cannot set foot on holy ground. Thus, not only was she cut off from her grandfather by death but also from the last meaningful experience in relation to him, and a structured occasion to work out her grief. She developed a deep feeling of resentment about being a girl. It seemed to her that people viewed a girl as a sickly, inferior creature and that her function of menstruation was something undesirable and abasing. Here we can see directly the cultural aspect of her self-devaluation as a woman and the role of her mother and social group in contributing in these instances to its development.

These were the observations from a psychiatric point of view, but it is of interest from a gynecologic vantage point to note that this girl suffered from premenstrual symptoms of anxiety, irritability, tiredness, intense hunger, and depression and also took to her bed for the first day of her period. Although no direct inferences can be drawn from this, can one fail to be impressed by the relationship between history and symptoms? These symptoms, incidentally, ran the true course of the traumatic neurosis entity, taking from three to four months to develop after the traumatic incident—the onset of menstruation.[10]

Materials and method

In the present study, a questionnaire was devised covering brief background data; a detailed menarchal history, including anticipation of menstruation, the circumstances of its discovery, and the responses to its discovery by both mother and daughter; and, finally, a detailed current menstrual history including questions relating to premenstrual tension, dysmenorrhea, and amenorrhea (Fig. 1). This questionnaire was submitted to a total of 103 women who were divided into five comparable groups located in different areas. My patients constituted one group, a control group of 22 women whose attitudes about femininity had been studied and were well known to me. Of the other four groups, one was constituted largely of college students, one was a group of women in Pennsylvania, and two were groups located on Long Island. Except for the student group, most women were married and of relatively high economic and educational levels. It was anticipated from this that the data would be relatively reliable and that the women who had made a "good adjustment" would probably have less than average difficulty. The extent of the symptoms was therefore quite surprising. No attempt was made to focus selectively on premenstrual tension and dysmenorrhea, the interest being largely in what the prevalent experience of a small cross section of women would be.

Results

Of the women, 21 per cent had no advance preparation for their menarche (Fig. 2). In general, the clarity with which menarchal experience can be recalled is quite striking; and many in this group recalled with intense feeling the terror of this discovery, which several associated with the fantasy of having been damaged or cut. Of those who had some advance knowledge, 75 per cent anticipated menstruation with anxiety, fear, and dread (Fig. 3). A startling fact became apparent in evaluating the maternal responses

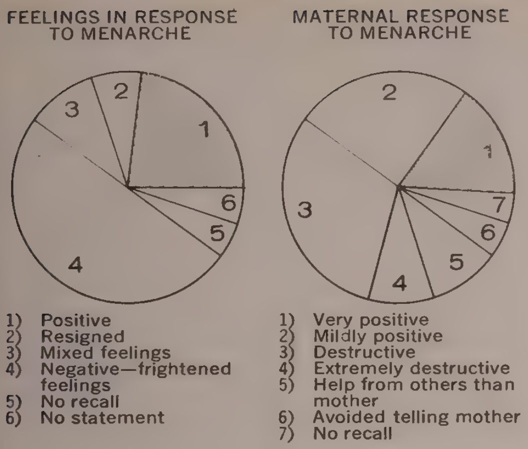

FIGURE 3. Findings resulting from questionnaire on menstrual experiences.

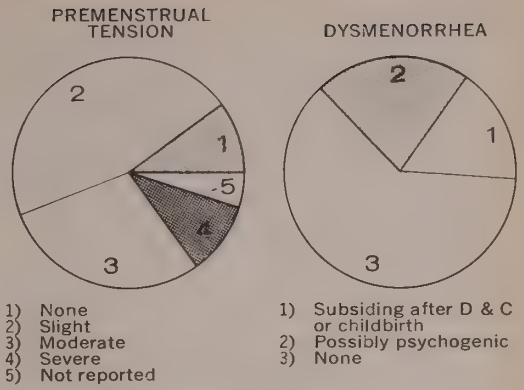

FIGURE 4. Symptoms of premenstrual tension and dysmenorrhea.

to this event: Only 15 per cent of all the mothers reacted with pleasure to this sign of maturation in their daughters; 60 per cent showed responses that were negative and damaging; and 10 per cent were extremely destructive.

Contrast the statement of a symptom-free woman who was well prepared for her menarche and whose mother responded well to this event: "My mother was thrilled and expressed joy at having a grown daughter. She had prepared me with the necessary equipment and now showed me how to use it. We congratulated each other on my entering womanhood"—with the following statement by a woman who had had no preparation for her menses, was greeted with a slap on the cheek (unexplained), and reported: "My mother told me only that if a man came near me I could get pregnant. I felt an enormous fear and was afraid to stand near my brother." It is interesting to note that in addition to symptoms of premenstrual tension, this woman had difficulty in conceiving and carrying a baby to term, although no direct relationship is necessarily inferred.

Of the total group, only 13 per cent of the women were consistently free of symptoms of premenstrual tension (Fig. 4). These were the same whose mothers had prepared them adequately for menstruation and received the news of its occurrence with pleasure. A study of the patients in the control group, and other observations, suggests that this freedom from symptoms indicates an acceptance of their femininity. The remaining 87 per cent experienced symptoms of premenstrual tension, and 15 of these suffered severe, disabling tension. As might have been anticipated, the incidence of premenstrual tension in the psychiatric group was higher than in the others, and it was also more severe and disabling.

While physiologically, the endocrine and water-balance changes probably account for a feeling of tension, weight gain (in part), breast engorgement and nipple tenderness, and, to some degree, headache, all other symptoms comprise an ancillary group that is psychogenic in origin. It is likely that many headaches are psychosomatic expressions as well. It was found that the ancillary premenstrual symptoms could be placed in two categories from a psychiatric viewpoint: one includes hunger and a desire for sweets, a wish to call mother, anxiety, depression, and insomnia. All of these can be considered to represent a yearning for love and a state of helpless defenselessness. These symptoms were found in girls whose lack of preparation for menarche left them feeling "motherless and abandoned" and who were further shattered by a hostile or cruel response from the mother as a reaction to menarche. The second category includes irritability, quarrelsomeness, tension, headache, nausea, and vomiting. These suggest an angry, defensive reaction to an anticipation of attack and feelings of vulnerability.

The women in this group could be considered to have some "implements" with which to fight back, in contrast to those in the first, whom one might consider psychologically empty-handed. While the second may involve a higher order of adaptive potential than the first, both represent an impoverishment of the ego, particularly relating to feminine self-acceptance, and in the patient control group the symptoms were related specifically to the concept of self as sexually undesirable.

Thus, at a time when the body physiologically recapitulates the experience of menarche, there is a compulsive repetition of the emotional climate of the experience, especially in relation to the mother. There is also implicit in this reaction a compulsive obedience to the demands and expectations, conscious or unconscious, of the mother, which has interesting similarities to the posthypnotic suggestion and compulsive triad in hypnosis.[11] But again, if it is inferred that the menarchal experience and interaction are unique, special, and set apart from the rest of the mother-daughter relationship, this will be a misconception. They are best understood as a link in a chain of similar experiences, but a particularly strong and at the same time revealing link. Here, incidentally, are some of the seeds of the frigidity which manifests itself later on.

As has previously been mentioned, breast discomfort, while frequently present, is rarely a source of serious concern or dramatization. One could speculate that the late development of this organ accounts for this, since the girl's personality is already quite well structured by the time of its appearance, and it has played no part in the early mother-daughter struggle.

Dysmenorrhea is a more difficult symptom to evaluate because of the possibility of a large physiologic component. Yet Gidro-Frank, Gordon, and Taylor[9] have reported that pelvic pain often appears in the absence of physical findings and that it is often increased in the premenstrual period and may disappear with the onset of menstruation. There is, of course, always the possibility that a pathologic condition of the pelvis may be causing pain, but otherwise it is assumed here that menstrual cramps occur as the result of uterine contractions to help shed the endometrial decidua and send it through the cervical canal. It might be expected that the first such occurrence would be, if anything, more painful, even though the discharge is slight. Yet only 1 woman in the total study was aware of discomfort during her first menstruation. A total of 39 per cent reported dysmenorrhea, and 19 of these indicated it had subsided after childbirth or dilatation and curettage, suggesting a small cervical outlet as its cause. In the remainder, there was assumed to be a large psychogenic component (Fig. 4). Several patients in the control group, suffering severe dysmenorrhea with ancillary symptoms, had had frightening introductions to the menarche and had been led to expect it to be painful. In each instance, it took a period of several months for dysmenorrhea to develop. It seemed to be a somatization of anxiety in women with hypochondriacal tendencies, whose attitudes were characteristic of those traditionally considered masochistic and passive.

Of the total, 30 per cent experienced amenorrhea of varying lengths at one time or another. It has been reported that functional bleeding occurs from any histologic type of endometrium and the same with amenorrhea, which may occur with endometrial hyperplasia.[12] Psychogenic factors have long been acknowledged to play a part here, and women seem to be aware of this. Many recalled a precipitating event with intense affective response; several related extreme changes in weight to this occurrence, difficulties with their mothers, or a sense of guilt about some sexual experience.

Comment

The onset of menstruation heralds the possibility of motherhood, which, like all creative experiences, is inextricably linked with vulnerability. It is not surprising, therefore, if a certain amount of anxiety inevitably accompanies the menarche. Yet excessive anxiety is reflected in menstrual symptoms, which indicate the quality of the new awareness of self as a woman and are an outgrowth of the mother-daughter relationship.

For many years, women have often been subjected to inattention, ridicule, or even cruelty, by those to whom they have turned for help in areas where they are uniquely vulnerable. Fortunately, in our culture, with the growth of understanding, there has been considerable change. Of what value is a delineation of menstrual symptoms (other than the physical) to the gynecologist or general practitioner? Often a tactful, sympathetic inquiry about the conditions of the menarche, in the context of a warm doctor-patient relationship, may be enough to alleviate periodic suffering, through a ventilation of the psychic wound, enhancement of self-esteem, and encouragement thereby of a more hopeful attitude toward others. But whether an inquiry in this area is therapeutic or not, it is in many instances likely to be quite revealing and of great help in suggesting whether or not the patient should be referred to a psychiatrist for further study and help.

Summary

1. A study of menarche and menstrual symptoms was undertaken, focusing on attitudes relating to feminine sexuality.

2. A definite correlation was found between freedom from symptoms and a good mother-daughter relationship, one aspect of which was a favorable introduction to the menstrual experience.

3. Menstrual symptoms can be divided into the physiologic and the ancillary. The ancillary symptoms can be understood in terms of loss of self-esteem and ego defense.

4. It is proposed that the ancillary menstrual symptoms suggest psychologic damage mediated by the mother.

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Predisposing causes of pneumonia

According to an article by William Allen Riley, M.D., in the February, 1962, issue of the *North Carolina Medical Journal*, the pulmonary condition usually referred to as pneumonia often is a symptom of another underlying disorder rather than a pathologic entity of its own. Antibiotic treatment, therefore, is in the nature of a palliative, and unless the underlying cause is identified and treated, the pulmonary symptoms may be expected to recur.

Among the conditions which lower patient resistance and predispose to pneumonia are: anemia; endocrine or exocrine gland dysfunction (diabetes, hypo- or hyperthyroidism, or hyperadrenocorticism); emphysema; alcoholism; psychosomatic illnesses; allergies; cardiac conditions; dietary deficiencies; hemodystrophies or other hemopathy; bacillary or viral infections; and so forth.

Pneumonia must bring into play a wide range of medical knowledge in general, and in particular an understanding of the individual patient.

Head Pain of Temporomandibular Joint Origin

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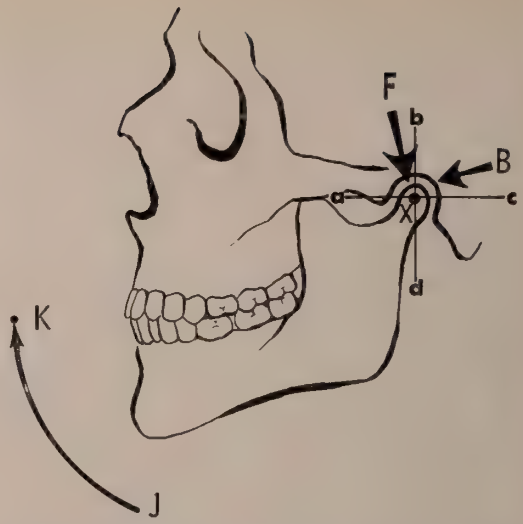

FIGURE 1. Correct interdigitation of the teeth, in harmony with the neuromuscular closure of the mandible and the temporomandibular joints. The mandible has described the arc of closure, JK. X, the center of condyle, is the pivotal point. Note that the joint gap, F, is evenly spaced in the glenoid fossa, B. This even spacing of the joint gap can be verified by comparison with F in the roentgenogram of the normal temporomandibular joint (Fig. 4). (By permission, see reference 2.)

FROM THE DIAGNOSTIC point of view, head pain is one of the most baffling entities encountered by the medical profession. Depending in large measure on the anatomic location of the pain, a particular case will be seen by one of a variety of medical specialists. For example, an otolaryngologist would be apt to be consulted for symptoms focusing on the ear, the sinuses, or deglutition. The orthopedist might be called in because of symptoms of limitation of movement of the temporomandibular joint. Vague but persistent head pains would be referred to the neurologist. And in the absence of any physical findings, the catchall of the medical profession, the psychiatrist, might be called on to evaluate a case of possible psychosomatic origin.[1]

Any one of these specialists may be the first medical consultant whose help is sought by the patient. However, it is much more likely that the patient will have been referred by the general internist who was consulted initially. Although the writer by no means believes that all head pain is caused by temporomandibular joint dysfunction, he does feel that a considerable number of patients with such symptoms make the medical rounds before their ailments are diagnosed accurately. The purpose of this paper is to alert the general practitioner to the existence of head pain caused specifically by temporomandibular joint dysfunction and to emphasize the need for competent dental management.

Figure 1 is a profile view of a normal centric-relation occlusion, showing the correct interdigitation of the teeth, and is included in the series of illustrations for purposes of comparison with the diagrams of pathologic occlusion.

Pathologic closure

"Temporomandibular joint arthrosis (dysfunction) is a noninfectious, trophic, degenerative affection of the joint tissues initiated by intrinsic trauma and causing abnormal changes in the function of the joint."[2] In 90 per cent of the cases, this is caused by the pathologic occlusion of the teeth. Figures 2 and 3 show the initial and terminal stages of pathologic closure involving an occlusal contact of only one upper and one lower tooth. An interfering contact (Figs. 2E and 3E) causes deflection of the mandible, malpositioning of the condyles within both temporomandibular

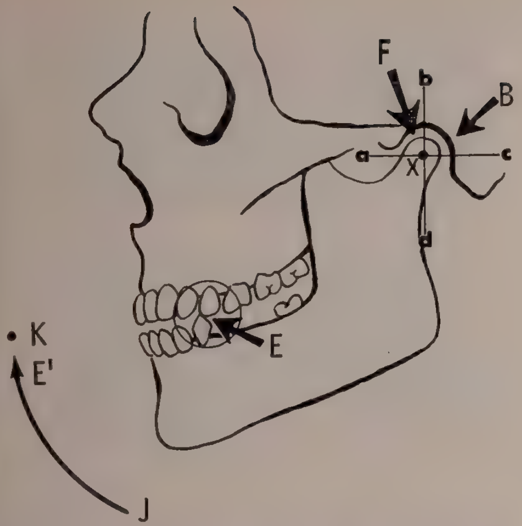

FIGURE 2. First stage of pathologic closure involving an occlusal contact of an upper and a lower tooth. The pathologic interfering occlusal contact at E has prevented the mandible from completing closure. The mandible has described the arc JE′; the condyle has rotated on X.

joints, and upsets the equilibrium of the muscles and ligaments that control condylar movement within the joints. This is the basic cause of temporomandibular joint dysfunction and its associated symptomatology.

Roentgenograms in diagnosis

The diagnosis of temporomandibular joint dysfunction can be confirmed by roentgenograms, which accurately depict the position of the condyles within the fossae.[3] Figure 4 is an oblique-lateral transcranial projection of a roentgenogram of normal left and right temporomandibular joints; it should be compared carefully with Figure 5, which is a similar view of an abnormal joint, illustrating a case of temporomandibular joint arthrosis, or dysfunction.

Differential diagnosis

> TEMPOROMANDIBULAR *joint dysfunction is a noninfectious degenerative affection of the joint tissues which is caused in 90 per cent of the cases by pathologic occlusion of the teeth. The condition should be suspected in the presence of the following symptoms: clicking, crackling noise, crepitation, tenderness, pain in and around the temporomandibular joint, and occasional locking of the jaw. The pain may affect numerous areas of the head, the neck and shoulder regions, the arms and fingers, and even the lumbar spine. Treatment calls for close medical-dental coordination.*

The fundamental problem confronting the general internist is one of a differential diagnosis. It is obviously not within the province of the writer to instruct the physician. It is, however, pertinent to underline the fact that pathologic occlusion results not only in the impairment of function of other parts of the masticatory system, but also produces dysfunction of the neuromuscular system and neural symptoms in such seemingly unrelated areas as the neck, shoulders, and arms. In the absence of any

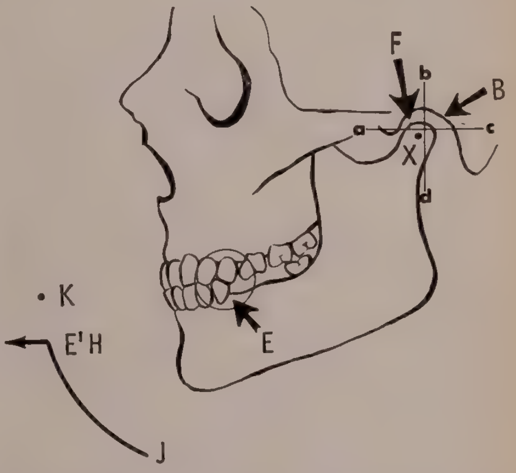

FIGURE 3. Completion of pathologic closure involving an occlusal contact of an upper and a lower tooth. The pathologic interfering occlusal at E has brought about a deflection of the mandible and malpositioning of both condyles. As the mandible described the arc of closure JE′ it struck the interfering contact at E, causing the mandible to shift forward and complete the arc E′H. The center of the condyle, X, has shifted inferiorly and anteriorly from the point of intersection of a, b, c, and d. Note that the joint gap, F, is narrow anteriorly and wider superiorly and posteriorly. Compare with F of Figure 1. This uneven spacing of the joint gap can be verified by comparison with F in the roentgenogram of the pathologic temporomandibular joint (Fig. 5). (By permission, see reference 2.)

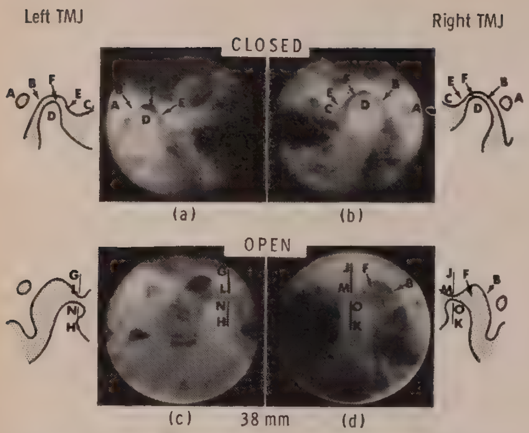

FIGURE 4. Temporomandibular joint roentgenogram (oblique-lateral transcranial projection) of a normal right and left temporomandibular joint in the closed (a, b) and open (c, d) positions. In the closed position, A: external auditory meatus; B: glenoid fossa; C: articular eminence; D: condyle; E: posterior wall of articular eminence; F: joint gap. Note that right and left joint gaps are equidistant (in temporomandibular joint arthrosis, these joint gaps are dissimilar).

In the open position, lines NH and OK (condyle centers) should appear beneath lines GL and JM (centers of articular eminences).

A state of hypomobility exists when condylar lines NH and OK do not quite approach lines GL and JM. A state of hypermobility exists when lines NH and OK have passed lines GL and JM. (By permission, see reference 2.)

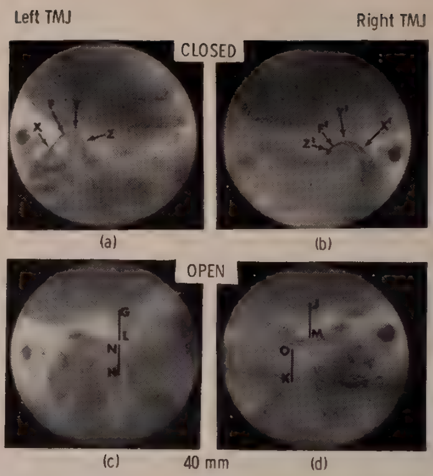

FIGURE 5. Roentgenograms (oblique-lateral transcranial projection) of abnormal left and right temporomandibular joints in the closed (a,b) and open (c,d) position. In the closed position (a) note that the left joint gap, F, is wide posteriorly at X and almost obliterated superiorly at Y and anteriorly at Z. In (b) the right joint gap, F′, is narrow anteriorly at Z^1, and wider superiorly at Y′ and posteriorly at X′. Compare these dissimilar joint gaps with F in Figure 4a and b.

In the open position (c), the center of the left condyle, line NH, is directly under the center of the eminence, line GL. In (d), the center of the right condyle, line OK, is anterior to the center of the eminence, line JM. A state of hypermobility exists in (d) because line OK is 10 mm. anterior to line JM.

overt disease state, such as the arthritides, infections of the head or ear, migraine, or eye disorders, to name but a few, the medical practitioner who is confronted with a case of head pain of unknown origin should be on the "qui vive" for the possibility of temporomandibular joint dysfunction.[4,5]

The existence of temporomandibular joint arthrosis should be suspected if the following manifestations are evidenced: clicking, crackling noise, crepitation, tenderness, and pain in and around the temporomandibular joint. The clicking may or may not be accompanied by pain, but if clicking or crepitation occurs, the implication of the temporomandibular joint is indicated. Pain can vary from a dull, constant ache to one of such intensity as to simulate the pain of tic douloureux. Another manifestation is the occasional locking of the jaw. At first this is easily reducible, but eventually it becomes increasingly irreducible and results in the restriction of the jaw opening. This is followed by recurrent subluxation of the joint opposite the painful, restricted joint. It is especially important to note the type of pain—whether it is lancinating, paroxysmal, or dull, and what specific type of mandibular movement produces the pain.[6]

The vicious cycle of muscle spasm—pain—spasm is usually initiated by a state of pathologic occlusion, which in turn creates neuromuscular dysfunction. Through the mechanism of referred pain, temporomandibular joint dysfunction is frequently accountable for innumerable areas of pain in the head, in many instances radiating into the neck and shoulder regions, down the arms into the fingers, and even into the lumbar spine.[7–9] This is schematically represented in Figures 6 and 7.

Therapy

In many of these cases there exists a

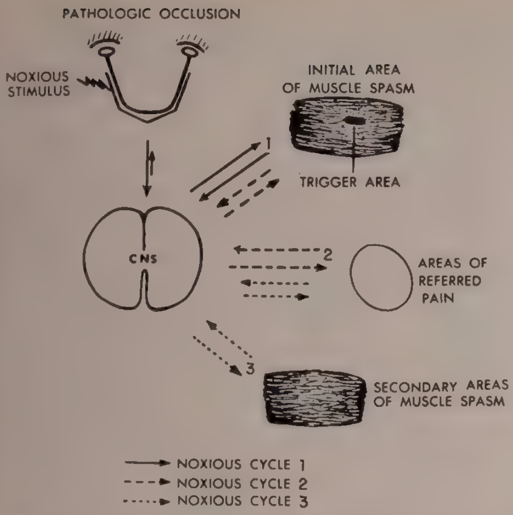

FIGURE 6. Diagrammatic representation of the direct neural relationship between pathologic occlusion, as the noxious stimulus, and the resultant feed-back cycles of muscle spasm, trigger areas, and referred pain, all distant from the primary noxious stimulus. (By permission, see reference 2.)

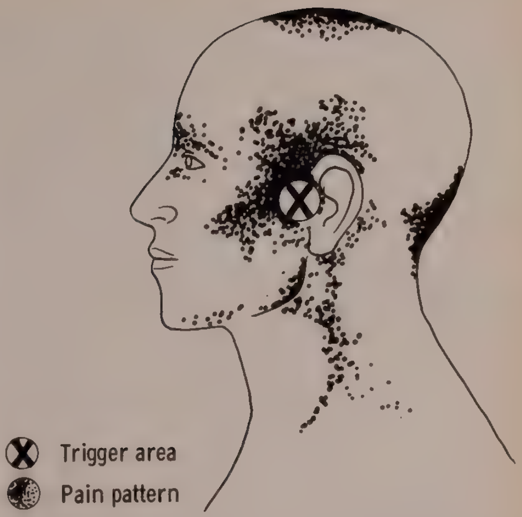

FIGURE 7. Schematic diagram illustrating areas of referred pain from the temporomandibular joints. (By permission, see reference 2.)

strong psychogenic factor. The careful evaluation on the part of the physician as to what proportion of the symptomatology is due to neurotic components often poses a challenging and even baffling diagnostic problem.[10-12]

The therapeutic approach to cases of temporomandibular joint disorders calls for close medical-dental coordination. The dentist is prepared to assume the responsibility for managing the pathologic occlusion of the teeth. It is the physician's task to evaluate the psychogenic and nutritional status of the patient and to treat him accordingly.

Once the physician has established the diagnosis and has referred the patient to a dentist competent to deal with this particular syndrome, the results are dramatic. With the remission of the pain and the restoration of mandibular movement, the dentist, with the aid of the physician, can successfully treat the existing pathologic occlusion and forestall any return of the symptoms.

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Serum Carotene Concentration in Normal Individuals and Its Clinical Interpretation

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Steatorrhea and other evidence of malabsorption due to primary or secondary bowel disease is but slowly acquiring recognition. This stems in great part from the fact that the definitive diagnosis of steatorrhea hinges on a quantitative stool fat determination. Such a chemical analysis is a specialized procedure usually not available in routine clinical laboratories. A simpler procedure, readily performed, indicating in very many instances the presence of steatorrhea, and possibly indicating malabsorption of other substances as well, is the determination of the serum carotene concentration. This study presents the normal values in the largest group of individuals thus far reported in the literature.

The reliability of this single, easily performed determination as an indicator of small-bowel dysfunction depends on a variety of factors. The lack of ingestion of a proper diet containing foods rich in carotene such as spinach, lettuce, carrots, tomatoes, liver, and kidney will depress the serum carotene levels even in the presence of normal gastrointestinal function. Abnormal bowel continuity will have the same effect because of the bypassing of a proper absorbing surface, even in the presence of a proper diet. Fever, hyperthyroidism, liver disease, and chronic illnesses tend to lower the serum carotene values. Other diseases such as hypothyroidism, diabetes, nephrosis, and hyperlipemia cause increased serum levels. Excess carotene intake has the same effect on raising serum concentration. It thus becomes important to know the normal serum carotene levels and the range, to use this as a simple screening procedure to detect suspected malabsorption. A 75 per cent correlation between increased stool fat and decreased serum carotene concentration was indicated in a recent study.[1] This is indicative of the value of a simple serum determination as a guide to uncover malabsorptive states and would seem to warrant its more widespread use in clinical medicine.

Method and materials

The method used in this study was that of Yudkin.[2] This procedure was carried out as follows: 2 ml. of 95 per cent ethyl alcohol were added by drops and with shaking to 2 ml. of serum, followed by the addition of 4 ml. of petroleum ether (boiling point 30 to 60 C.). A glass-stoppered 15-ml. tube was used. The contents were shaken vigorously for ten minutes and then centrifuged for five minutes at 1,800 revolutions per minute. An aliquot of the colored supernatant petroleum ether solution containing the extracted carotene was removed and transferred to a suitable cuvette, which was immediately stoppered with a clean cork. The optical density was determined at 440 millimicrons, using the Coleman Jr. spectrophotometer with a 12-mm. cuvette. Its equivalent in micrograms of carotene per 100 ml. serum was evaluated by reference to a standard curve, which was prepared by reading the optical densities of petroleum ether solutions con-

SERUM CAROTENE *levels may be used as a simple screening procedure to detect suspected malabsorption. The normal range for serum carotene in 227 apparently healthy individuals on a normal mixed diet was found to be 70 to 300 micrograms per 100 ml. with a mean of 153 and a standard deviation of ± 57. No statistical variation was found according to sex, age, or season. For a proper interpretation of serum carotene values it is important to know the patient's dietary intake for at least the preceding two weeks.*

taining known concentrations of carotene (90 per cent beta, 10 per cent alpha).

As a rule, the blood samples were collected between 5:00 and 6:00 P.M. and stored in the refrigerator until the following day, when they were analyzed. Harris *et al.*[3] and Kimble[4] have shown that ordinary meals do not cause a measurable increase in carotene within two to six hours. Yudkin[2] demonstrated that samples of blood may be stored in the refrigerator for forty-eight hours without change. He also showed that slight hemolysis had no effect on the results.

Subjects included in this study were selected at random from a cancer detection clinic. All received a complete physical examination as well as routine blood and urine examinations during their cancer detection investigation. With a few exceptions there was no evidence to indicate disease states which are known to influence the serum carotene level. The exceptions were 9 subjects who were essentially healthy and asymptomatic but whose low serum carotene levels resulted in establishing in 5 a diagnosis of steatorrhea. The remaining 4 were unwilling to submit to further study.

Of the 227 individuals examined, 91 were males and 136 females. These were further subdivided into five-year age groups ranging from fifteen to seventy-five years. Arithmetic means, standard deviations, and medians were calculated for the whole group, for males and females alone, and

TABLE I. Summary of values (micrograms per 100 ml. of serum) found in the present study

Age Group	Sex	Number	Median	Mean	Standard Deviation
..	Total group	227	145	153	±57
..	Females	136	152	158	±50
..	Males	91	132	137	±49
15 to 20	F	0	..	..	...
	M	2	..	145	...
21 to 25	F	1	..	162	...
	M	3	104	100	...
26 to 30	F	14	142	144	±32
	M	6	127	125	±23
31 to 35	F	9	148	150	±32
	M	11	109	120	±42
36 to 40	F	11	178	171	±45
	M	8	134	134	±24
41 to 45	F	17	148	147	±37
	M	13	132	139	±32
46 to 50	F	21	172	169	±36
	M	12	160	166	±57
51 to 55	F	23	157	172	±55
	M	10	158	150	±34
56 to 60	F	14	138	146	±47
	M	13	116	125	±33
61 to 65	F	9	125	132	±55
	M	3	132	126	...
66 to 70	F	8	160	182	±50
	M	2	..	150	...
71 to 75	F	2	..	147	...
	M	3	156	139	...

TABLE II. Seasonal variation in normal serum carotene (micrograms per 100 ml. of serum)

Sex and Season	Number of Cases	Mean	Standard Deviation	Median
Males				
Spring	36	138	±37	132
Summer	20	152	±47	148
Fall	30	139	±43	135
Females				
Spring	54	162	±46	152
Summer	35	163	±51	150
Fall	40	159	±48	154
Total group				
Spring	90	152	±44	146
Summer	55	159	±49	150
Fall	70	150	±47	149

for each age group (Table I). Since it has been demonstrated that serum carotene concentrations vary with the season,[2,3,5,6] the values for the entire group were divided into the observations made in the spring, summer, and fall, and the same values were calculated as for the age groups (Table II). Finally, the values were arranged according to the number of observations in each 10-microgram range, starting with 51 to 60 and going up to 411 to 420 micrograms. These data are presented graphically in Figure 1.

Results

Of the 227 values in Figure 1, 215 or 95 per cent fall between 70 and 300 micrograms per 100 ml. There are five values (1.8 per cent) in the 51 to 60 range and seven values (3.1 per cent) between 311 and 470 micrograms. The mean for the total group is 153 micrograms per 100 ml. serum, with a standard deviation of ±57 (Table I). It therefore seems reasonable to exclude from the normal range the five lowest values, which are almost 2 standard deviations below the mean, and the seven highest values, which are 3 to 5 standard deviations above the mean. In calculating the mean, standard deviation, and median for the total group as shown in Table I, all the values were used. However, in calculating these figures for males and females and for the various age groups, these twelve extreme values were omitted. In addition, there are data which indicate that the persons in whom the five low values were found have gastrointestinal disease.[7] In some groups the number of individuals was too small to calculate medians, means, and standard deviations.

The results obtained in the spring, summer, and fall are seen in Table II. The values for females and for the total group in each season are the same, while the mean for males in the summer is somewhat higher than that found in the spring and fall. However, the difference is only one-half a standard deviation and is not significant.

Table III lists the results of other investigations in which the normal serum carotene was determined. Our values agree most closely with those reported by Kimble,[4] Harris *et al.*,[3] and Yudkin,[2] if one excludes Yudkin's winter observations.

Comment

In a study which aims to establish the range of serum carotene in normal individuals, such factors as age, sex, diet, and season must be considered as possible determinants. It can be seen from the data in Table I that between the ages of fifteen and seventy-five, age apparently does not play a role in influencing the level of serum carotene. No important differences in the means for the various age groups are seen. Yarbrough and Dann[8] studied 197 persons between the ages of five months and sixty-eight years. These authors do not present their data so that one may see whether or not any differences related to age were found.

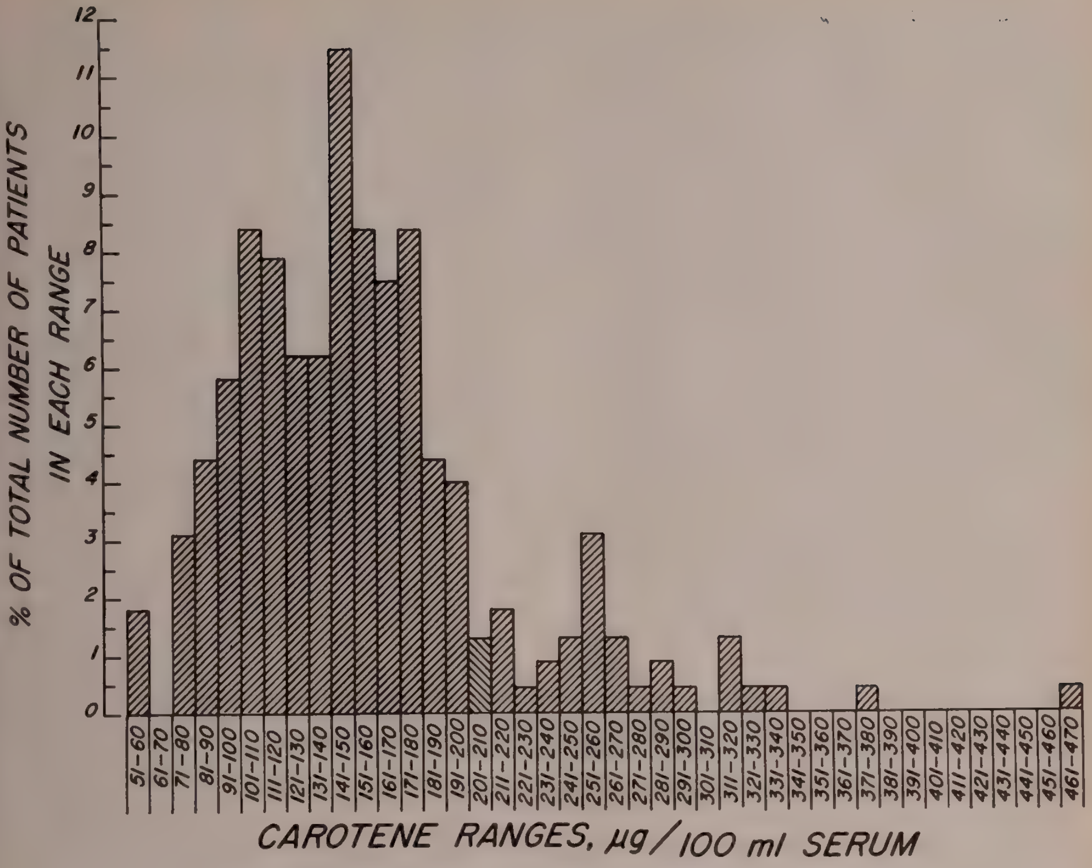

FIGURE 1. Carotene ranges (in micrograms per 100 ml. of serum).

TABLE III. Serum carotene values (in micrograms per 100 ml. of serum) as reported by other investigators

Investigator	Range	Mean	Standard-Deviation	Comment
Murrill *et al.*[11]	100 to 348	199	. . .	25 males
	136 to 420	227	. . .	20 females
Harris *et al.*[3]	80 to 370	210	±31	70 subjects
Haworth, Moschette, and Tucker[14]	49 to 202	120	±34	40 females 15 to 22 years of age
Kimble[4]	50 to 300	166	±59	30 males
	90 to 340	187	±77	34 females
Yudkin[2]	117 to 241	158	. . .	11 subjects, summer
	50 to 118	85	. . .	12 subjects, winter
Wenger, Kirsner, and Palmer[1]	70 to 282	123	±47	110 subjects
Caveness, Satterfield, and Dann[15]	18 to 278	138	±62	71 healthy persons, chiefly college students on ordinary diet
Yarbrough and Dann[8]	34 to 422	131	. . .	197 subjects 5 months to 68 years
Kirk and Chieffi[9]	200 to 320	. .	. . .	155 middle-aged and old individuals; 47 younger subjects
Highman[6]	110 to 370	207	. . .	20 European males
	113 to 340	244	. . .	20 European females
	100 to 310	162	. . .	11 Indian males
	30 to 260	131	. . .	8 Bantu males

Their results are merely stated as a mean for the entire group, with the standard error and range. One may perhaps assume that no differences were found. Kirk and Chieffi[9] investigated 155 middle-aged and old persons and 47 younger ones, and found that while individual values varied greatly, there were no statistically significant differences between different age groups. Their values ranged from 200 to 320 micrograms per 100 ml. May *et al.*[10] studied serum carotene in infants and children ranging in age from four days to twelve years. Their results are expressed in "440 units," which is directly related to the optical density (measured at 440 millimicrons in an Evelyn photoelectric colorimeter) of the petroleum-ether-extracted carotene solution. For this reason, their figures are not quoted. These authors, however, did show that the serum carotene in infants up to five months of age is only about 20 per cent that of infants of nine months and of children up to twelve years. Age, then, seems to be a factor in serum carotene levels only in infants up to about nine months of age.

As Table I shows, the mean for females is 25 micrograms higher than that for males. However, the difference is less than one-half a standard deviation and is probably not significant. Murrill *et al.*,[11] Kimble,[4] and Kirk and Chieffi[9] found similar differences and also concluded that they were of doubtful significance. It would seem, therefore, that there is no important difference between the sexes in carotene concentrations.

Although serum carotene is not subject to important variations as a result of diet in any one day, concentrations may drop sharply within one week as a result of a markedly deficient intake of carotene-containing food. Thus Wald, Brouha, and Johnson[12] have demonstrated that shortly after one week on a diet deficient in carotene, the serum level was found to have decreased from 100 to 200 micrograms per 100 ml. to almost 50 micrograms per 100 ml. and in some instances to traces which could not be measured accurately. Similarly, Brenner and Roberts[13] found, on placing 6 subjects (4 females and 2 males, aged twenty to twenty-four years) on a low carotene diet for twenty to thirty-one weeks, that the values which were 139 to 310 micrograms at the start fell steeply during the first week to low values and then decreased slowly until a plateau was reached. Even at the end of the experimental period, however, the serum was not completely free of carotene, containing, as it did, 30 to 44 micrograms per 100 ml. The diet used provided some carotene, and perhaps this is why the depletion was not more complete. These data seem to indicate that in the normal individual the serum carotene concentration reflects to a great extent its daily intake, and that carotene is not stored to any extent in the body. This is probably what one sees in the seasonal variations found by many investigators.[2,3,5] Harris *et al.*,[3] quote a personal communication from Clausen and McCord, who found that serum carotenoids rose from a May low of 154 micrograms per 100 ml. to a maximum of over 280 micrograms per 100 ml. in September and gradually returned to a minimum the following May. In the present study, no seasonal differences between April and October were found (Table II). This would seem to indicate that in New York City during this period a supply of carotene-containing foods was obtained at all times. For a proper interpretation of serum carotene values it is, therefore, important to know the patients' dietary intake for at least the preceding two weeks.

Summary

1. The normal range for serum carotene in an apparently healthy adult population on a normal mixed diet was found to be 70 to 300 micrograms per 100 ml. of serum with a mean of 153 and a standard deviation of ±57. No seasonal variations were noted in this group from spring into the fall.

2. No statistical variation was found between males and females.

3. Age did not influence the serum carotene concentration in adults.

4. Dietary history is important in the proper interpretation of the serum carotene levels.

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Yellow Pigmentation Associated with Novobiocin Therapy

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DRUG-INDUCED JAUNDICE has been the subject of numerous reports in recent years, coincident primarily with the advent of the diverse tranquilizing agents which are now utilized so extensively.[1] The occurrence of jaundice associated with antibiotic therapy has been less frequent, and, indeed, aside from the hepatotoxicity induced by pyrazinamide, erythromycin lauryl sulfate, and para-aminosalicylic acid (PAS), few antibacterial agents have been significantly incriminated.

Although the manufacturers and clinical investigators have been aware of a yellowish pigmentation accompanying novobiocin administration,[2] only a mere handful of reports have been concerned with the recognition, characterization, and pathogenesis of the pigmentation.[3-9] The American Medical Association Council on Drugs apparently has been satisfied with the presumptive metabolic explanation for this phenomenon.[10] The experience of observing patients with yellow pigmentation secondary to novobiocin administration prompted a review of currently available pertinent literature. The present report is likely to focus attention on rather than resolve the controversy regarding whether or not novobiocin exerts a hepatotoxic effect in addition to the well-documented innocuous yellowish pigmentation.

Case reports

CASE 1. A thirty-eight-year-old white male was admitted to the Surgical Service of the Elizabeth A. Horton Memorial Hospital on July 25, 1960, after having sustained a comminuted fracture of the right elbow. Aside from a series of "poison ivy shots" six to eight weeks previously, there was no significant antecedent history. An open reduction was performed on July 25, 1960, utilizing nitrous oxide and halothane to produce anesthesia.

Preoperatively, he was given hydroxyzine hydrochloride, 25 mg.; promazine hydrochloride (Sparine hydrochloride), 25 mg.; and atropine sulfate, $^{1}/_{150}$ grain. Postoperatively, he was started on novobiocin and received a total dose of 3.25 Gm. when yellowish pigmentation was noted four days later. He had also received buccal streptokinase-streptodornase (Varidase). A physical examination was unremarkable except for yellowish scleral pigmentation.

The hemogram, aside from a leukocyte count of 12,000 showed entirely normal findings. The urinalysis was not unusual and showed negative findings for bile. Urobilinogen was present in a dilution of 1:20. The SGOT (serum glutamic oxalacetic transaminase) was 45 (1 to 40) units and the SGPT (serum glutamic pyruvic transaminase) 31 (1 to 45) units. The serum alkaline phosphatase was 2.5 Bodansky units (1.5 to 4). The total bilirubin was 0.7 mg. per 100 ml. The cholesterol and esters were normal, as was the thymol turbidity and cephalin-cholesterol flocculation test. The sulfobromophthalein retention was 6 per cent in forty-five minutes.

Aside from an irregularly febrile course to 101 F. over seven days, the clinical course was entirely uneventful on the cessation of antibiotic therapy.

CASE 2. A seventy-six-year-old female was admitted to the Surgical Service of the Elizabeth A. Horton Memorial Hospital on February 23, 1960, following an intertrochanteric fracture of the left hip. There was no pertinent previous history.

A physical examination demonstrated the hip fracture, which was confirmed by a radiographic study.

On February 24, 1960, the fracture was treated by a Richards sliding hip screw fixation. During surgery 500 ml. of whole blood were administered. Chlorpromazine hydrochloride, 12.5 mg., was given intramuscularly preoperatively. Nitrous oxide-oxygen anesthetic was utilized. Postoperatively she was started on novobiocin, 250 mg. four times a day and had received 750 mg. when "icterus" was noted the following day. A large hematoma was noted at the wound site, for which buccal streptokinase-streptodornase was prescribed. The total dose of novobiocin that was administered before it was discontinued was 3.5 Gm.

Four days after yellowish pigmentation was

TABLE I. Blood chemistry values in Case 3

Date	SGOT	SGPT	Sulfobromophthalein Retention (Per Cent)	Thymol Turbidity	Total Cholesterol	Esters	Alkaline Phosphatase (Bodansky Units)	Icterus Index	Van den Bergh Test	Cephalin Flocculation
July 30	68.5	52	45	1.65	139	81	6	...	...	...
August										
1	46	45	...	...	...	...	...	...	0.68/1.1	...
3	88	95	37.5	...	...	...	...	8	...	4 plus
7	...	...	...	...	...	...	...	...	...	Negative
24	...	...	...	...	...	...	...	...	...	Negative
27	139	290	31.5	...	...	...	...	...	...	...
29	...	...	...	1.1	...	...	9.9	...	...	...
September										
30	...	...	3.5	...	...	...	...	...	...	...

A YELLOWISH *pigmentation accompanying novobiocin therapy was observed in 4 patients. In 3 there was evidence of pigmentation and an elevation of the icterus index without a corresponding hyperbilirubinemia. There was chemical evidence of hepatocellular involvement in the other case. Caution should therefore be used in the administration of novobiocin until further study determines its hepatotoxicity.*

observed, a hemoglobin of 8.3 Gm. per 100 ml. was recorded. The icterus index was 41.9, while the serum bilirubin was 9.7 mg. per 100 ml. The alkaline phosphatase was 13.9 Bodansky units, the SGOT 26 units, and the SGPT 13 units. A study of the serum and the urine showed negative findings for hemolysis by spectrophotometry. The total cholesterol was 221 mg. per 100 ml., and the cholesterol esters were 140 mg. per 100 ml. Five days later the SGOT and SGPT were 22 and 10, respectively. The cephalin-cholesterol flocculation was 2 plus in forty-eight hours. The alkaline phosphatase had fallen to 4.3 Bodansky units, and the serum bilirubin was 1.52 mg. per 100 ml.

There was no other evident cause for the jaundice other than the administration of novobiocin, and, following the withdrawal of novobiocin, the pigmentation gradually subsided.

CASE 3. A forty-two-year-old white female was admitted to the Surgical Service of the Elizabeth A. Horton Memorial Hospital on July 20, 1960, with a fracture dislocation of the ninth and tenth dorsal vertebrae following an automobile collision. On July 26 she had a spinal fusion of the eighth to eleventh dorsal vertebrae, using autogenous iliac crest bone, after which she was placed on a Stryker frame. Six units of whole blood were administered. Three days postoperatively her scleras were noted to be yellow. She had been started on chloramphenicol and novobiocin postoperatively and had received 3.25 Gm. of the latter by the onset of the yellowish pigmentation. At that time, the liver was not palpable, nor were there other pertinent findings. Bile was absent from the urine, and urobilinogen was present in a dilution of 1:80. Serum protein electrophoresis was revealing only of a modest diminution of the alpha-1 globulin.

On August 24 she sustained a pulmonary embolus to the right lung with a radiographic parenchymal shadow and an elevation of the right leaf of the diaphragm. She recovered from these mishaps and made an otherwise uneventful recovery. Her blood chemistries are summarized in Table I. Of particular note are the elevated sulfobromophthalein retention, serum transaminase values, and cephalin-cholesterol flocculation. A needle biopsy of the liver was considered but could not be accomplished because the patient was immobilized in a Stryker frame. After rehabilitation, she was discharged to her home on October 2, 1960. More extensive blood chemistry studies were not permitted by the patient, but it should be noted that the sulfobromophthalein retention returned to a normal value.

It must be noted that some of the chemical abnormalities might have been related to the pulmonary embolus. However, while hyperbilirubinemia is commonly a sequela of pulmonary infarction, chemical evidence of hepatocellular damage is not usually observed. Persistently demonstrated abnormalities in transaminases, alkaline phosphatase, and cephalin-cholesterol flocculation, accompanied by sulfobromophthalein retention, lend support to the suggestion that hepatotoxicity followed the administration of novobiocin in this instance.

CASE 4. A forty-year-old white female was admitted to the Surgical Service of the Elizabeth A. Horton Memorial Hospital on November 16, 1960, for the fusion of a severely osteoarthritic left hip. The procedure was performed without incident. On November 27 she developed a wound abscess with a fever spike to 103 F., and 2.5 cc. of creamy pus and blood were evacuated. A culture revealed Escherichia coli and Micrococcus pyogenes, aureus variety. Blood cultures were negative. Therapy was begun with novobiocin and oleandomycin, each in a dosage of 500 mg. four times a day, with supplementary kanamycin sulfate later. On December 5 she developed a diffuse morbilliform eruption and jaundice with fever, after having received 15.5 Gm. of novobiocin. There were no other pertinent findings. The few laboratory studies which the patient would permit revealed an icterus index of 8.1 with a total bilirubin of 0.55 mg. per 100 ml. The SGOT was 22 units. The rash and fever gradually subsided. No further venipunctures were permitted by the patient.

Comment

The development of painless icterus in a patient under medical observation for an unrelated disease suggests the possibility of an iatrogenic cause. The increasing use of novobiocin has focused attention on the bacteriologic indications as well as on the generally benign untoward effects. An over-all incidence of toxic reactions has been estimated at 12.7 per cent by Bridges, Berendes, and Good[3] in their survey of the literature, while Welch *et al.*[11] and Finland and Nichols[12] reported side-reactions with the following frequency: mild diarrhea, 37 per cent; skin rashes, 8.9 per cent; fever, 2 per cent; eosinophilia, 1.47 per cent; gastrointestinal irritation with nausea, 1.3 per cent; and leukopenia, 0.6 per cent. A yellowish pigmentation of the skin and scleras is said to occur in 0.6 per cent of cases.

Bridges, Berendes, and Good[3] reported a fatal case of a fourteen-year-old boy with rheumatoid arthritis who developed icterus and a pruritic rash while he was receiving novobiocin, 2 Gm. orally twice a day for eight days. Despite cortisone therapy, he expired, and a necropsy revealed diffuse hepatic necrosis and generalized lymphoid hyperplasia, attributed by the authors to novobiocin therapy.

Hughes[4] described a seven-month-old child who developed an apparent sensitization to novobiocin with a clinical picture resembling the Stevens-Johnson syndrome.

Controversy surrounding the potential of novobiocin to induce hepatotoxicity was stimulated by the report of Cox *et al.*,[6] who studied a twenty-five-year-old physician with a staphylococcal abscess. Their patient had been found previously to have normal findings in liver function studies in the course of a drug evaluation in which he participated. His sulfobromophthalein retention was noted to be 17.5 per cent in forty-five minutes during the active phase and 4 per cent one month subsequently. Absorption spectrums were obtained and were identical with those of bilirubin. The pigment could not be extracted by 3 volumes of chloroform at pH 7.4, in contrast to the behavior of the lipochrome reported by the manufacturers to represent a metabolic product of novobiocin. The direct serum bilirubin was 0.34 mg., and the total was 6.8 mg. per 100 ml. by the Evelyn-Malloy procedure.

From these data, the authors deduced that a definite hepatic abnormality existed which was confined to defective bilirubin and sulfobromophthalein conjugation. They further speculated that selective interference with bilirubin-glucuronate conjugation was the mechanism, suggesting only speculatively that an abnormality of sulfobromophthalein conjugation with aminoacetic and glutamic acids might be implicated.

Studies on a second patient demonstrating icterus on novobiocin therapy failed to reveal hepatic abnormalities. Editorial comment in the *New England Journal of Medicine*[13] raised serious doubts regarding the validity of the chemical observations of Cox *et al.*[6] The defective conjugation of bilirubin by the liver was rejected for the following reasons. Decreasing serum bilirubin values were observed in spite of continued novobiocin administration. Furthermore, an increased serum retention of sulfobromophthalein without a study of sulfobromophthalein metabolites[14] does not allow specific characterization of the defect.

Sutherland and Keller[9] described an outbreak of apparent increased neonatal jaundice associated with the administration of novobiocin in controlling a newborn nursery staphylococcal outbreak. They noted that the administration of novobiocin to newborn infants produced a threefold increase in neonatal hyperbilirubinemia. However, liver necrosis was not observed in any of the patients who were studied, nor could abnormal hemolysis be excluded. Since newborn infants have a known decreased hepatic glucuronide-conjugating mechanism, a novobiocin-induced enzymatic blockade could interfere with the bilirubin metabolism in inducing hyperbilirubinemia. It would appear that the utilization of novobiocin need not be restricted because of untoward side-effects. However, the clinical usefulness is sufficiently circumscribed that unwarranted administration should be condemned.[15] The need to consider hepatotoxicity as a deterrent to its use is as yet unproved, and further study will be required before this problem is settled.

Conclusions

While special studies could not be undertaken to ascertain the mechanism of hepatotoxicity, it is a fact that chemical evidence of hepatocellular involvement is apparent in Case 3. In each of the 3 other cases, there was evidence of pigmentation and an elevation of the icterus index without a corresponding hyperbilirubinemia. One would have been most interested in a liver biopsy in Case 3, but the precarious state of the patient made this impossible. That one consultant could observe 4 such cases in a short period points up the potential for untoward reactions associated with novobiocin therapy. Certainly if further reports substantiate the potential hepatotoxicity which was first observed by Cox *et al.*,[6] even more caution should be exercised in the utilization of novobiocin.

Summary

A yellowish pigmentation which was thought at first to be jaundice has been observed in 4 patients who were treated with novobiocin. The pigment appeared to be distinct from bilirubin, but in one instance defective sulfobromophthalein excretion and chemical findings of hepatocellular damage were observed. The toxicity of novobiocin has been reviewed, along with previous arguments relating to its possible hepatotoxic effect.

27–31 RIDGE STREET

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Cerebellar Pressure Cones

Postmortem Study

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THE STANDARD textbooks of pathology and the literature state that when swelling of the brain occurs the brain is pressed downward against the rigid structures of the foramen magnum, and the cerebellar tonsils are molded into a cone shape.[1-8] This process has been called the coning of the cerebellum. This mechanism of formation has been widely accepted since Alquier first proposed it in 1905,[9] and in consequence the presence of the deformity has been accepted as indicating the existence of increased intracranial pressure. In our experience this morphologic finding is seen frequently in brains which do not contain any expanding lesion. For the purpose of clarifying the significance of these pressure cones, a study of the in situ appearance of the cerebellum in autopsy material has been performed and correlated with the findings of the examination of the brain. This report concerns these findings.

Materials and methods

One hundred and thirty-three consecutive autopsies were used in the present study. This group of cases included 56 females and 77 males. With the body in a prone position and the head flexed, a skin incision at the base of the dorsal surface of the skull was made. A triangular wedge of the occipital bone and of the first two vertebrae was removed. The vertex of this triangular excision was caudal. The meninges were removed carefully in the same manner, and a clear view of the foramen magnum and the base of the cerebellum was obtained (Fig. 1). The relationship of the cerebellar tonsils to the lip of the foramen was noted, and a photograph was taken. After the completion of this procedure the brain was removed by the usual technic, preserved by an injection of the middle cerebral vessels with 12 per cent formalin, and examined after three or four days of formalin fixation. At the time of the sectioning the brains were searched for pathologic changes, and at the same time the cerebellar tonsils were carefully evaluated for cone formations. Falx and hippocampal herniation were recorded when present. The data obtained were placed on

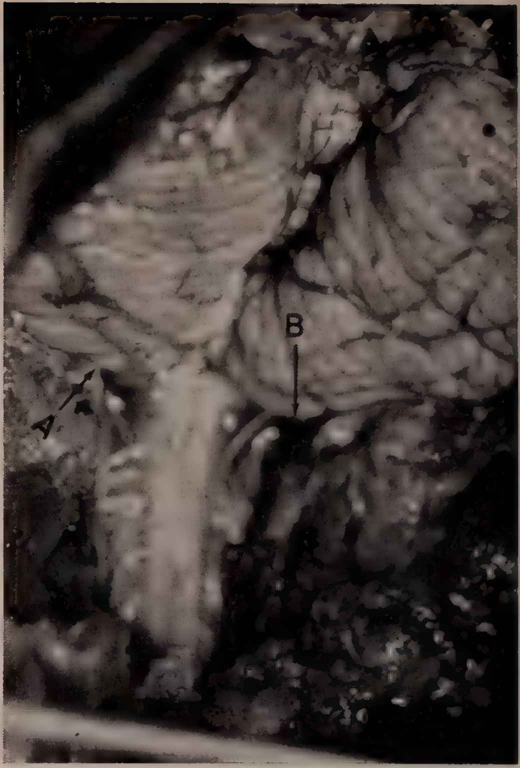

FIGURE 1. Normal brain with no herniation; in situ appearance of base of cerebellum and its relationship to foramen magnum. (A) shows edge of foramen magnum; (B) shows cerebellar tonsils at same level as edge of foramen.

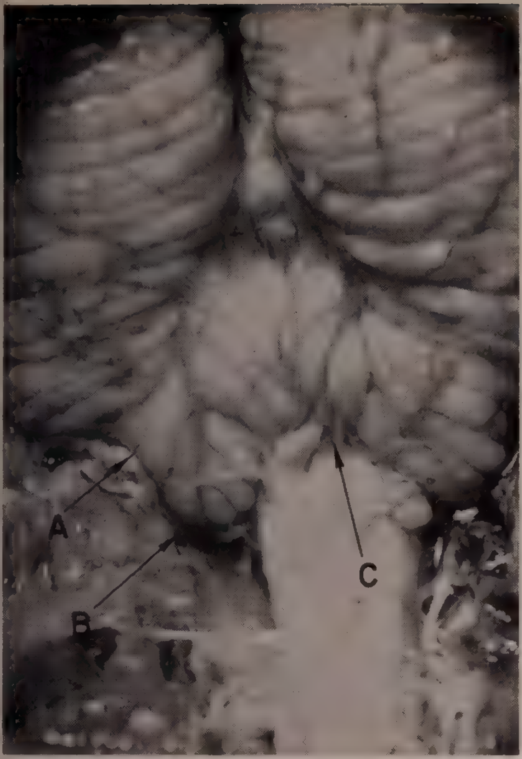

FIGURE 2. Normal brain with cerebellar tonsillar herniation. (A) shows edge of foramen magnum; (B) shows tip of tonsil herniated through foramen, with herniation mostly unilateral; (C) shows preservation of normal angle formed by tonsils (see Fig. 3).

IBM index cards and correlations were carried out.

Results

The brains were divided into two groups: normal and abnormal. For our purposes an abnormal brain was one in which the brain contained a primary or metastatic tumor, hemorrhage, encephalomalacia, inflammation, or any other clearly-defined pathologic lesion. A normal brain indicated that no significant focal or diffuse changes were found.

The in situ study of the cerebellar tonsils was extremely interesting. The relationship between the cerebellum and the foramen magnum was inconstant. In some cases the tips of the cerebellar tonsils were far above the orifice, in others they touched the edges of the foramen, and in a fewer number the tonsils herniated into the spinal canal. In the cases with herniations the cerebellar substance extended as far as 5 mm. beyond the foramen magnum. These herniations were not always bilateral, but they occurred unilaterally (Fig. 2).

ALTHOUGH CEREBELLAR *tonsillar herniations and/or cerebellar pressure cones can be caused by expanding brain lesions, they may occur in the absence of such lesions. In a study made in 133 consecutive autopsies, pressure cones were present in 18 per cent of the normal brains and in 27 per cent of the abnormal brains. Herniation and pressure cones were more frequent in cases with primary brain tumors than in metastatic brain tumors, indicating a relationship to the size of the lesion. There is a loose relationship between the presence of cerebellar tonsillar herniation and cerebellar cones, but one may occur without the other. Falx and hippocampal herniation were observed only in abnormal brains.*

Table I shows a comparison of normal and abnormal brains in the presence or absence of cerebellar tonsillar herniation. Only 14 per cent of the normal brains were associated with herniation, but 25 per cent of the abnormal brains had such association. Table I also indicates that those brains which contain primary malignant tumors have a higher incidence of cerebellar tonsillar herniation than brains containing metastatic brain tumors. It shows that benign tumors and encephalomalacia are not often associated with herniation of the tonsils. Why? The data in Table II may answer the question. The herniation of cerebellar tonsils occurs much more frequently when the lesions are large than when they are small. Most of the primary brain tumors were large ones, but many of the metastatic tumors were small. Most of the benign tumors and encephalomalacia were small. It is also interesting to note that those brains with large lesions were associated not only with herniation, but also with an elongation of the tonsils so that their tips tended to approach each other, causing an obliteration of a view of the medulla (Fig. 3). The extent of herniation itself was not appreciably different.

TABLE I. Relationship of tonsillar herniation to brain findings

Brain Findings	Number of Cases	Herniation: None	Herniation: Bilateral	Herniation: Unilateral
Normal	96	83	4	9
Abnormal	37	28	4	5
Benign tumors	2	2	0	0
Primary malignant tumors	7	3	3	1
Metastatic malignant tumors	19	17	1	1
Hemorrhage	3	2	0	1
Encephalomalacia	5	4	0	1
Other	1	0	0	1
TOTALS	133	111	8	14

TABLE II. Size of brain lesions compared with tonsillar herniation

Size of Lesion (Mm.)	Number of Cases	Herniation: None	Herniation: Bilateral	Herniation: Right	Herniation: Left
Unknown size	11	9	...	1	1
No brain lesion	96	83	4	6	3
10	2	2	...	...	...
15	2	2	...	...	...
20	1	1	...	...	...
25	1	1	...	...	...
40	3	3	...	...	...
50	3	3	...	...	...
60	5	3	1	1	...
70	2	1	1	...	...
80	3	3	...	...	...
99 or more	4	...	2	1	1

Pressure cones

A molding of the cerebellum into a shape called a pressure cone presumably results from the herniation of the tonsil into the spinal canal, with a resultant pressure of the lip of the bone on the cerebellar substance. In this study the defect called pressure cones was present in 18 of 96 normal brains or 18 per cent and in 10 out of 37 abnormal brains or 27 per cent (Table III). It was more commonly present in the abnormal (Fig. 4) than normal (Fig. 5) brains. Again, unilateral defects were present, for in 2 cases only the right tonsil was considered abnormal.

Pressure cones were found more frequently in those cases with primary brain tumors than in metastatic brain tumors (Table III). Benign tumors, encephalomalacia, and hemorrhage were infrequently associated with pressure cones (Table III). The size of the brain lesion is related to the presence of pressure cones, since a higher frequency is seen in those cases with larger lesions (Table IV).

The question arises whether or not a relationship exists between the presence of herniation of cerebellar tonsils and the presence of cerebellar cones. The data in Table V indicate that a loose relationship is present, but the ratio is nowhere near 1:1. Cerebellar tonsillar herniation may occur without formation of cerebellar cones, and cerebellar cones may be found without tonsillar herniation. However, in 50 per cent of cases with herniation of the tonsils the cerebellum has a cone configuration. This percentage is significantly higher than that found in patients without herniation. On the other hand, cerebellar cones are more frequently found alone than with herniation. The data indicate that cone formation is not indicative of either increased intracranial pressure not of tonsillar herniation, but it may occur as a result of either or both.

Falx and hippocampal herniation were observed only in abnormal brains. However, all brains containing abnormalities did not show these defects. These herniations

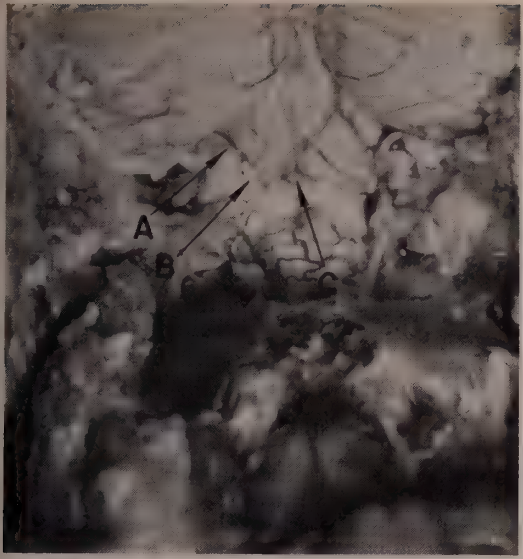

FIGURE 3. Astrocytoma of brain with bilateral herniation. (A) shows edge of foramen magnum; (B) shows tips of tonsils seen below edge of foramen; (C) shows loss of intertonsillar angle due to backward displacement of tonsils.

appear to occur more regularly with primary malignant brain tumors than in other lesions including metastatic brain tumors, but again the size of the lesion rather than the histologic type is the most significant factor.

Finally, a notching of the crus, as described by Kernohan and Woltman,[10] was observed in only two brains. Both cases had metastatic tumors.

Summary

From this study several conclusions can be stated:

1. It can be reconfirmed that large expanding brain lesions cause cerebellar herniations and cerebellar pressure cones.
2. However, the presence of cerebellar tonsillar herniations and/or cerebellar pressure cones does not in itself mean that an expanding brain lesion is present. These findings occur frequently when no anatomic brain lesion is evident.

TABLE III. Relationship of cerebellar cones to brain findings

Brain Findings	Number of Cases	Pressure Cones Absent	Pressure Cones Bilateral	Pressure Cones Unilateral
Normal	96	78	17	1
Abnormal	37	27	9	1
Benign tumors	2	2	0	0
Primary malignant tumors	7	4	3	0
Metastatic malignant tumors	19	13	5	1
Hemorrhage	3	3	..	0
Encephalomalacia	5	4	1	0
Other	1	1	..	0
TOTALS	133	105	26	2

TABLE IV. Size of lesion compared with prominent tonsils

Size of Lesion (Mm.)	Number of Cases	Prominent Tonsils None	Prominent Tonsils Bilateral	Prominent Tonsils Right
Unknown in size	11	10	...	1
No brain lesion	96	78	17	1
10	2	2	...	...
15	2	2	...	...
20	1	1	...	...
25	1	1	...	...
40	3	2	1	...
50	3	3	...	...
60	5	3	2	...
70	2	1	1	...
80	3	1	2	...
99	4	1	3	...

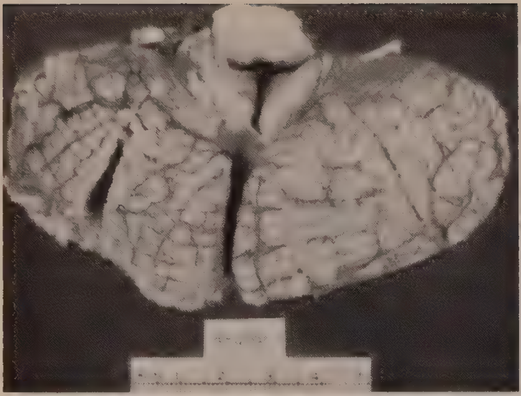

FIGURE 4. Cerebellum of Figure 3 with typical pressure cone. This is type frequently found in cases of large expanding lesions of brain.

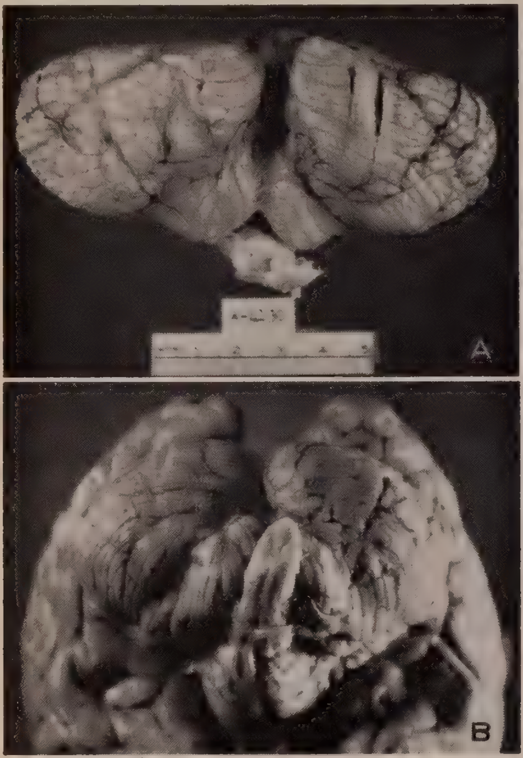

FIGURE 5. Normal brains. (A) No herniation. Note extreme prominence of tonsils giving typical appearance of "pressure" cone in case in which increased intracranial pressure was absent. (B) Cerebellum of Figure 2. Tonsils are markedly prominent on both sides.

TABLE V. Relationship of tonsillar herniation and cerebellar cones

Condition	Tonsillar Herniation	—Cerebellar Cones—	
		Absent	Present
Absent	111	94	17
Present	22	11	11
TOTALS	133	105	28

3. The ratio between the presence of cerebellar tonsillar herniations and cerebellar pressure cones is not a positive one. Either lesion may be found in the absence of the other one. Therefore, the interpretation that the presence of cerebellar cones means tonsillar herniation is false and erroneous.

4. Herniation of the falx and/or the hippocampal gyri indicate a space-occupying lesion.

5. Herniation of the cerebellar tonsil may cause death if the tonsils are of sufficient size, so that during the herniation they surround and press the brain stem. To identify this anatomic finding it is necessary to expose and view the in situ brain which can be done by a triangular incision at the base of the skull. Unfortunately, after the brain is removed, the relationship is obscured.

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Clinicopathologic Conference

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Conducted by STANLEY M. ARONSON, M.D.

Discussed by ANNE C. CARTER, M.D.

Infantile Form of Gaucher's Disease

Case history

A six-year-old white female child was admitted to Kings County Hospital because of intermittent, severe nose bleeds of about fifteen days duration.

The patient's parents had emigrated from Italy shortly before her birth in Brooklyn. The parents were healthy; there was a fourth-cousin relationship between the mother and the father.

The patient was born after an unusually prolonged period of labor of sixty-five hours. The delivery was effected with forceps. The patient's birth weight was 7 pounds, 2 ounces. The patient was breast-fed for eight months and then was fed by spoon. The mother noted that the baby encountered difficulty in swallowing semisolid foods at this age, and she therefore withheld meat and most vegetables until her baby was eighteen months of age. The infant's motor development was probably retarded. The mother stated that the infant could not rotate her head at the age of eight months. The mother felt that the patient was physically underdeveloped at one year of age, and she brought the infant to another hospital, but records are not available. The patient sat at thirteen months of age and began to walk at approximately fourteen months of age. She spoke a few words at this time.

At the age of eighteen months the patient had a convulsion involving the face and hands and accompanied by body rigidity, cyanosis, salivation, and unconsciousness. In the succeeding three years the convulsions increased in frequency, occurring as often as a few times each hour. However, the duration of each convulsion had diminished to but a few seconds.

The patient had exhibited nocturia, with a frequency of up to 10 times per night, since the age of two years. The mother stated that the urine frequently had a strong odor and was occasionally red.

The patient was admitted to Kings County Hospital at the age of four years as a boarder, accompanying her mother who was admitted independently because of an incomplete abortion. The child at this time was described as a mentally retarded and physically underdeveloped female. She was capable of speech, but it was difficult to understand her. Her gait was normal. A convergent strabismus was present. The pupils reacted to light promptly. The ocular fundoscopy was normal. The tonsils were enlarged markedly. A diffuse, cervical lymphadenopathy was present; no chest abnormalities were recorded. The abdomen was distended markedly, and the liver was considerably enlarged. A midline scar was noted.

A neurologic examination noted a marked

intention tremor; the speech was an unintelligible jargon. The patient's hearing was unaffected. Most observers felt that there was diminished visual acuity. While in the hospital, the patient developed a mild otitis media accompanied by some fever. The mother removed the child after two days of hospitalization.

The hemoglobin was 12 Gm. per 100 ml., and the white blood cell count was 11,500 per cubic millimeter with polymorphonuclear leukocytes 31, lymphocytes 66, monocytes 2, and basophils 1 per cent. A sickle cell preparation produced negative findings. A urinalysis gave essentially unremarkable findings. The total protein was 8.3 Gm. with 4.2 Gm. albumin and 4.1 Gm. globulin. The serum glutamic oxalacetic transaminase was 147 units. The total cholesterol was 88 mg. per 100 ml., and the free cholesterol was 26 mg. per 100 ml. The thymol turbidity was 3.3 units, and the acid phosphatase was 2.8 King-Armstrong units.

The patient was readmitted to Kings County Hospital at the age of four and one-half years, again as a boarder, accompanying her mother who was undergoing a spontaneous miscarriage. An interval history suggesting periodic fevers in the child was obtained at this time. The child was described as a mentally and physically retarded female. The head was normocephalic. A convergent strabismus was present. The pupils were round and equal, responding to light and accommodation. The teeth showed some irregularity in arrangement. The palate was unusually high. The neck was supple. An examination of the heart and lungs showed no abnormalities. There was a large mass, believed to be the right lobe of the liver, approximately 10 cm. below the right costal margin. The muscle tonus in all the extremities was increased. The abdominal reflexes were absent. The tendon reflexes were hyperactive. No pathologic reflexes were found. The patient's weight at this time was 27 pounds.

At this admission the hemoglobin was 9 Gm. per 100 ml., and the white blood cells were 23,000 per cubic millimeter with polymorphonuclear leukocytes 40, lymphocytes 50, monocytes 9, and basophils 1 per cent. A lumbar puncture produced clear spinal fluid; 2 leukocytes were noted microscopically. The Pandy test produced negative findings. The sugar was 66 mg. per 100 ml., and the protein was 20 mg. per 100 ml. A culture of the spinal fluid was sterile. The blood sugar was 59, calcium 8.8, and phosphorus 3.6 mg. per 100 ml. The alkaline phosphatase was 5.3 units, and the total protein was 8.5 Gm. The thymol turbidity was 11.6 units, and the blood urea nitrogen was 41 mg. per 100 ml. An additional fasting blood sugar on the following day was 58 mg. per 100 ml. The patient was discharged after two days in the hospital at the request of her mother.

The patient was admitted for the third time to Kings County Hospital at the age of five and one-half years because of severe epistaxis beginning two weeks before admission. It was not accompanied by trauma.

In the interval between hospitalizations the patient's seizures had continued. She had been sleeping poorly and her appetite had diminished. A vague history of multiple limb fractures was obtained at this time with an indication of severe, continuing pain in the knees and right shoulder. The mother stated that the patient's neck was "paralyzed" and that she could not rotate her head.

The patient was a small, underdeveloped and undernourished white female breathing heavily and with an oral odor of acetone. Her temperature was 102 F., pulse 120 per minute, respirations 40 per minute, body weight 33 pounds, height 87 cm., head circumference 41 cm., and chest circumference 60 cm. The skin was pale and clear except for numerous superficial blood vessels over a distended abdomen. A generalized lymphadenopathy was present, particularly in the neck. Internal strabismus was present. The patient displayed a photophobia, but her vision was apparently normal. The ears showed no abnormalities. A bloody exudate was noted within the nose. The teeth were largely carious. The throat could not be visualized because the patient was unable to open her mouth fully. The neck was slightly rigid. An examination of the heart and lungs showed no abnormalities except for a Grade I systolic murmur over the apex. The abdomen was considerably enlarged, and the liver was palpated 21 cm.

below the costal margin. The edge was smooth and not tender. The legs were thin and atrophic, and there was a bilateral contracture of the Achilles tendons. All the limbs were moderately rigid. Ankle clonus was elicited. The patient could not walk.

The patient exhibited numerous very brief convulsions during the course of the admission examination.

The laboratory data at this time revealed that the hemoglobin was 3.5 Gm. per 100 ml., and the white blood cells numbered 38,350 per cubic millimeter, with polymorphonuclear leukocytes 51, band forms 2, lymphocytes 43, monocytes 3, and basophils 1 per cent. The platelet count was reduced. A urinalysis showed unremarkable findings. The blood urea nitrogen was 9 mg. per 100 ml., total cholesterol 88 mg. per 100 ml., total protein 6.8 Gm. per 100 ml. with 2.8 Gm. albumin and 4 Gm. globulin, alkaline phosphatase 11.9 units, and acid phosphatase 65.2 units.

Nasal packs were inserted, and small, multiple transfusions were administered, raising the hemoglobin level to 5.8 Gm. per 100 ml. Following two days of transfusions, the patient appeared noticeably improved, and she was able to feed herself. The epistaxis persisted. The temperature was 102.2 F., and rales were noted in the base of the right lung. The fever persisted, and the child expired on the seventh hospital day.

Discussion

ANNE C. CARTER, M.D.: This case is that of an Italian child whose illness was stated to have begun at eight months of age with difficulty in swallowing. The patient was underdeveloped and had progressive neurologic deficits as well as signs suggesting the involvement of the reticuloendothelial and osseous systems. At the time of her death at six years of age, she was profoundly anemic, had epistaxis, and possibly a terminal infectious process. It is my impression that the patient had Gaucher's disease of the infantile type with neurologic involvement. The obvious involvement of somatic tissues reasonably excludes such diagnostic considerations as infantile amaurotic family idiocy, spongy degeneration of infancy, and the various leukoencephalopathies. This patient's illness must also be distinguished from Niemann-Pick disease and gargoylism.

The child's parents were fourth cousins, of Italian origin, and not Jewish. Although the majority of the reported cases of Tay-Sachs and Niemann-Pick diseases are of Jewish extraction, most of the recorded children with the infantile form of Gaucher's disease are not Semitic. It is important to note that the mother had at least two miscarriages, a common finding in the obstetric histories of mothers bearing infants with Gaucher's disease.

Gaucher's disease is clearly a familial disorder.[1] At the present time it is thought that there are three genetically distinct variants: a minority of instances in which the gene is transmitted as an autosomal dominant; the majority of cases in which the gene is transmitted as an autosomal recessive (splenomegalic, non-neurologic variety); and a group of cases in which neurologic involvement is always present and in which the gene acts as an autosomal recessive. It is not known whether these genes represent a system of separate alleles at one locus or whether they are located at separate loci. If my diagnostic impression is correct, then this child would fall into the last-mentioned form of Gaucher's disease. The frequency of consanguinity in families with Gaucher's disease is greater than in the general population. A low degree of consanguinity is present in the background of this patient.

The patient's birth was assisted by forceps extraction after a prolonged labor of sixty-five hours. Her birth weight was normal, and the infant's development apparently was normal until eight months of age. There is no information in the protocol to suggest that her subsequent symptoms resulted from the difficult labor. Difficulty in swallowing semisolid foods, the child's first symptom, appeared at eight months of age. In the light of later clinical developments this symptom was probably of neurologic origin, possibly due to some form of brain stem involvement, rather than representative of primary enteric disease.

On the basis of the recollections of the patient's mother, the child's motor development was retarded. Head rotation was not accomplished until eight months of age, and the child did not sit until thirteen months of age, at least six months later than the usual attainment of this developmental milestone. She walked at fourteen months of age which is not very abnormal, and she also was able to speak a few words at this time.

At eighteen months of age the patient had generalized seizures occurring as frequently as a few each hour. It does not seem likely that these seizures were the result of hypoglycemia, such as might be associated with glycogen storage disease, although she did have hepatomegaly and, on two occasions, slightly depressed blood sugars (59 and 58 mg. per 100 ml.). Her blood cholesterol also was low.

We know that at the age of four years the child was mentally retarded, that her speech was incoherent, and that she had a convergent strabismus and an intention tremor. Subsequently it was noticed that she had increased muscle tone in all her extremities, hyperactive tendon reflexes, ankle clonus, and absent abdominal reflexes. It is difficult to explain the absence of abnormal reflexes. Her neck was described as "paralyzed" and slightly rigid. This may represent the characteristic retroflexion of the head, sometimes called pseudo-opisthotonus, so often found in children with Gaucher's disease. Her vision and hearing were normal, and ophthalmoscopic examinations produced unremarkable findings. These collected neurologic findings are in contrast to what would be anticipated in Niemann-Pick disease wherein muscle hypotonicity, progressive blindness (often with macular degeneration), and the absence of strabismus would be expected.

The patient was physically underdeveloped. At the time of her terminal admission she weighed 33 pounds (normal is 37 to 46 pounds), her height was 35 inches (normal is 43.5 to 46.5 inches), and her head circumference was 16 inches (normal is 20 inches) without evidence of microcephaly.

Incidently, because of her underdevelopment, she was hospitalized at another institution at the age of one year. We know nothing about that admission except that when she was first seen here she had a midline abdominal scar, and the spleen was never palpated. I think that we may surmise that a splenectomy was performed at the age of one year.

The protocol describes hepatic, tonsillar, and cervical lymph node enlargement, but no mention is made of any skin lesions. This would likely exclude such reticuloendothelioses as histiocytosis X, Letterer-Siwe disease, or Hand-Schüller-Christian disease. Hurler's syndrome also can be discarded from consideration in the absence of typical skeletal deformities, corneal opacification, and deafness.

We also learn that the child suffered from bone pain and sustained multiple limb fractures. I suspect that if an x-ray film of the lower ends of the femurs were available, we would see the typical Erlenmeyer flask lesion which is so suggestive of Gaucher's disease.

During the brief terminal admission the patient had profuse nasal bleeding and was severely anemic. The platelets were reduced, and the white blood cell count was elevated. No information is given about the presence of normoblasts. In spite of such limited hematologic data, I would like to suggest that the child had a myelophthisic anemia due to bone marrow replacement with Gaucher cells. The anemia of Niemann-Pick disease is rarely as severe as this and is not generally associated with bleeding tendencies. Further, I would expect the cholesterol to be somewhat increased in Niemann-Pick disease.

There is one laboratory finding which I believe truly confirms the diagnosis of Gaucher's disease. The acid phosphatase was considerably elevated to 65.2 King-Armstrong units. This method of determining the acid phosphatase, as well as the method of Gutman and Gutman, employs phenylphosphate as a substrate at pH 5. The method of Bodansky uses beta-glycerophosphate as a substrate. The acid phosphatase in Gaucher's hydrolyses phenylphosphate but not beta-glycerophosphate, and shows other preferential substrate activity serving to distinguish it from the acid phosphatase of prostatic origin.[2] Isolated examples of osteogenesis imperfecta have been associated with an elevated acid phosphatase in serum. Very rare cases of Niemann-Pick disease also have been re-

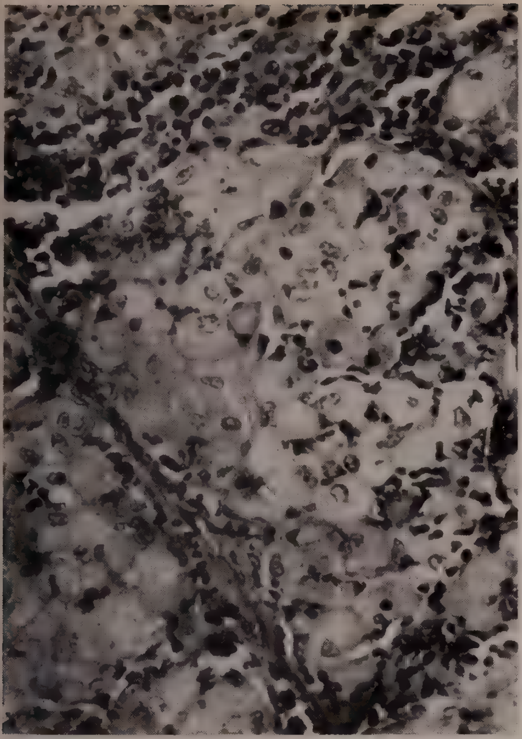

FIGURE 1. Photomicrograph of mediastinal lymph node with collections of Gaucher cells (hematoxylin and eosin stain). (×230)

ported to have high serum acid phosphatase, although this has not been confirmed invariably.

Dr. Carter's diagnoses

1. *Gaucher's disease of the infantile type with neurologic involvement, primarily of the brain stem, and involvement of osseous, hepatic, and reticuloendothelial tissues*
2. *Status—postsplenectomy for Gaucher's disease*
3. *Myelophthisic anemia*
4. *Terminal pneumonia*

Pathologic report

STANLEY M. ARONSON, M.D.: A complete autopsy was performed. The body was that of a proportionately but poorly developed white female, weighing 36 pounds and measuring 87 cm. in length. The head circumference was 41 cm. The abdomen was protuberant and contained a healed midline scar. No further abnormalities of the skin were noted. The following salient features were described within the thorax and abdomen: The lung parenchyma (weighing 300 Gm.) exhibited a diffuse brownish-yellow discoloration and patchy, focal areas of increased consistency. There was no suffusion of fluid or exudate from the cut pulmonic surfaces. The trachea, bronchi, and pleura were grossly unremarkable. The liver was symmetrically enlarged, weighing 2,100 Gm. The hepatic parenchyma was firm and uniformly pale brown. The lobular architecture was obscured. The spleen was absent, as a consequence of a previous surgical resection. Scattered lymph nodes within the mediastinal, retroperitoneal, and para-aortic regions were discretely enlarged and on cross section were pinkish-gray in color and soft in consistency. Cross sections through the available bones showed a diffuse pallor of the marrow, conspicuously so within the vertebrae, sternum, and ribs. A slight swelling of the distal shafts of the humeri, femurs, and tibias also was seen.

Histologic preparations disclosed the existence of large numbers of distended, spherical cells about 20 to 45 microns in diameter, generally mononuclear, and characterized by a voluminous cytoplasmic mass containing numerous, faintly visible striae. The cytoplasmic accumulations were minimally acidophilic with routine stains, showed an intensely positive reaction with the periodic acid-Shiff procedure, both in frozen and paraffin sections, a moderate sudanophilia, and a negative reaction with Luxol fast blue. The cytoplasmic striae were more strikingly visible with phase contrast microscopy. These Gaucher cells were particularly abundant in the liver, the bone marrow, and the lymph nodes (Fig. 1). Within the lung tissue there was a diffuse thickening of the alveolar septums caused by contiguous Gaucher cell infiltration between the central capillaries and the adjacent alveolar lining, resulting in an obvious reduction of the air space.

The brain weighed 1,079 Gm., representing a moderate reduction in weight. The cerebral hemispheres nevertheless were of approximately normal volume and symmetry. The external configuration of the brain stem and cerebellum also was normal. The leptomeninges appeared grossly un-

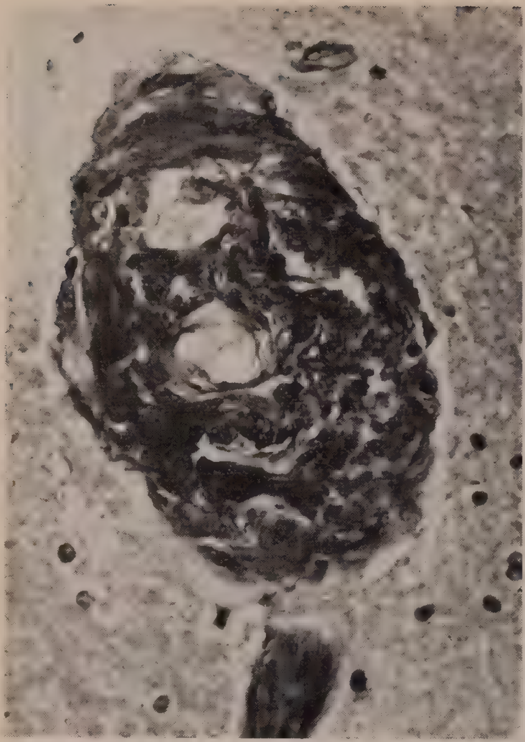

FIGURE 2. Photomicrograph of cerebral white matter; perivascular accumulations of Gaucher cells show intensely positive staining reaction with periodic acid-Schiff procedure. (×360)

remarkable. The dissection of the intracranial contents failed to show any gross abnormalities of the cerebral cortices, white matter, or deeper gray matter nuclei. The ventricular system was of normal dimension throughout. Multiple histologic sections from the cerebral cortex showed patchy areas of neuronal loss, particularly in the deeper lamina, provoking foci of neuronophagia and associated with a more diffuse gliosis and interstitial rarefaction. The extent of the supratentorial nerve cell destruction was greatest in the cortical mantle, less severe in the thalamus, and least evident in the basal ganglia. Widespread neuronal loss, with attendant glial response, was seen throughout the brain stem and cerebellum.

In the subcortical white matter of the cerebrum and throughout the brain stem and cerebellum there were moderate numbers of vessels completely surrounded by collections of oval or spindle-shaped cells characterized by an abundance of pink, reticulated cytoplasm (Fig. 2). These perivascular cells exhibited all the staining reactions of the Gaucher cells described previously and were seen to arise from, or infiltrate within, the vascular adventitia. Some reactive astrocytosis of a nonspecific form was found occasionally in the areas of cortical rarefaction as well as within some zones of white matter adjacent to the involved perivascular spaces. In general, however, the myelin within the white matter was preserved.

Tissue lipid analyses were performed through the courtesy of A. C. Crocker, M.D. There was a significant increase in the water-insoluble glycolipid content of the lung tissue and a borderline increase within the hepatic tissue (Table I). A comparison is made in this table with the biochemical levels noted in some previously published cases of infantile Gaucher's disease, described by Banker, Miller, and Crocker.[3] The appreciable elevations of the water-insoluble reaction of the glycolipids would indicate that the accumulating storage substance was a cerebroside. A further biochemical identification of the tissue cerebroside was not undertaken. The normal cerebroside molecule, constituent to tissues, is composed of a sphingosine base, a fatty acid (mainly lignoceric, behenic, and palmitic acid), and sugar moiety (galactose). Various investigators have observed that the cerebroside complex in Gaucher's disease differs from the normal cerebroside molecule in that glucose replaces the galactose.

The neuropathologic changes recorded in the case under current consideration correspond closely to the alterations described in most of the published cases of infantile Gaucher's disease. The present and previously published cases differ from the remaining members of the family of sphingolipidoses by the relative absence of any cytoplasmic storage within the nervous system neurons. The neuronal changes in infantile Gaucher's disease are more of a lytic type suggesting, in accordance with Banker's notion, that if cytoplasmic storage were present this process might be cytotoxic, causing rapid cell death and the lack of any demonstrable intracellular accumulation. Certainly neuronophagia is very prominent, particularly in the cerebral cortex and brain stem (Fig. 3). It should be noted that

TABLE I. Glycolipid studies of liver and lungs

Organ	Present Case	Case 1[3]	Case 2[3]	Case 3[3]	Normal Range
Liver					
Total lipids*	2.56	4.47	4.25	4.65	3 to 4.5
Glycolipids*	0.64	1.24	1.50	1.29	0.2 to 0.6
Lung					
Total lipids	3.12	5.58	7.19	3.16	2 to 3.5
Glycolipids	0.99	0.91	1.47	0.57	0.2 to 0.6

* All values expressed as per cent of fresh weight.

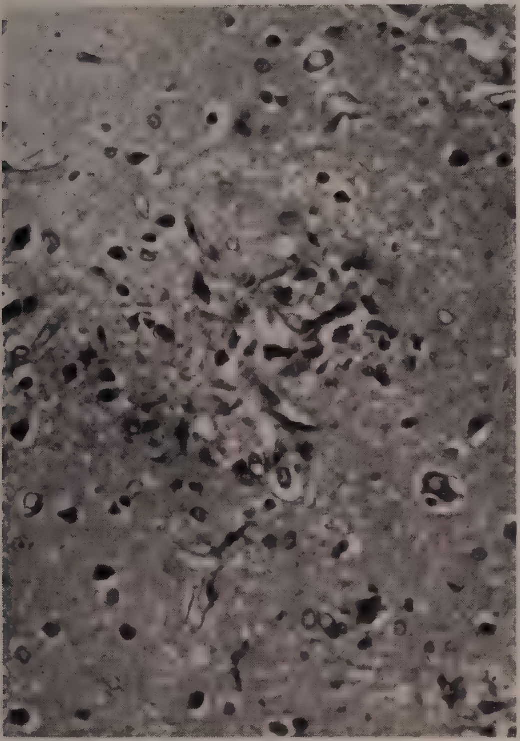

FIGURE 3. Photomicrograph of cerebral cortex; typical focus of neuronophagia (hematoxylin and eosin stain). (×230).

conspicuous cytoplasmic accumulations of cerebroside within neurons have been seen in very rare instances of juvenile Gaucher's disease.

The most singular changes found in the nervous system are clusters of oval or polygonal cells surrounding the deeper blood vessels, particularly within the central white matter of the cerebral hemispheres. The cytoplasmic accumulation within the cells presents the histochemical characteristics of a glycolipid, and a negative Bial reaction further narrows the possibility to a cerebroside.

Last, I should like to return very briefly to some of the clinical aspects of the present case. The number of fully documented and pathologically verified instances of infantile Gaucher's disease with neurologic involvement is sufficiently meager to permit some general comparisons. The evolution of the clinical events in the current case is certainly similar to those described before. The retardation of development, the hepatosplenomegaly, and the curious, decerebrate posturing, similar to opisthotonus have been noted with remarkable constancy in all cases. Similarly, progressive dysphagia, dysarthria, strabismus, and trismus have been equally documented. The bulk of nervous system symptoms therefore points to the predominance of brain stem damage. Perhaps the most unusual feature in the case under present consideration is the unusual longevity, despite no active therapy other than the splenectomy performed about four years prior to death.

Anatomic diagnosis

Infantile Gaucher's disease, with involvement of nervous system, reticuloendothelial system, lungs, liver, and other tissues

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Correlation Conferences in Radiology and Pathology

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Backache with Mass in Right Sacroiliac Area

Case history

A sixty-nine-year-old white male entered the Syracuse Memorial Hospital with a chief complaint of backache. About eighteen months before admission he had noticed a sore spot in his lower right back. He had also had pain in other areas, in particular the right shoulder and arm, the left thumb, and the left knee. He was treated with heat and aspirin at that time with relief in all areas except his back. Ten weeks prior to admission, he noticed the onset of muscle aching with radiation down both legs which was worse late in the day. This was relieved by local heat. He had noticed swelling over his right lower back for the past five or six months. He had had no constitutional symptoms such as weight loss or fever.

He had been having digitalis for five years, had been taking thyroid, the reason for which was obscure, and had had an old fracture of the scapula. His physical examination was unremarkable except that his liver was palpated 2 fingerbreadths below the right costal margin, his prostate was slightly enlarged, and there was a 5- to 6-cm. soft tissue swelling over the upper portion of the right sacroiliac joint.

Radiologic discussion

Edward Carsky, M.D.*: The chief complaint of this patient was backache together with a mass in the right sacroiliac area.

On the plain film of the abdomen (Fig. 1) we see normal liver and spleen shadows. The kidney shadows appear to be of normal size and of normal configuration. I do not see any opaque calculi. Looking at the soft tissue density in the abdomen, I wonder whether or not there is a little more density of soft tissue in the general area of the right sacroiliac joint.

There is an area of destruction in the posterosuperior part of the wing of the ilium near the right sacroiliac joint. It extends to the sacroiliac joint, but there is no definite evidence that it crosses it. I think that the transverse process in that area is intact. I think that the sacrum is probably intact as well. On the urogram, the calyces are entirely normal in appearance. There is no dilatation of either ureter. There is no displacement of the right ureter in the frontal projection. We don't know whether it is

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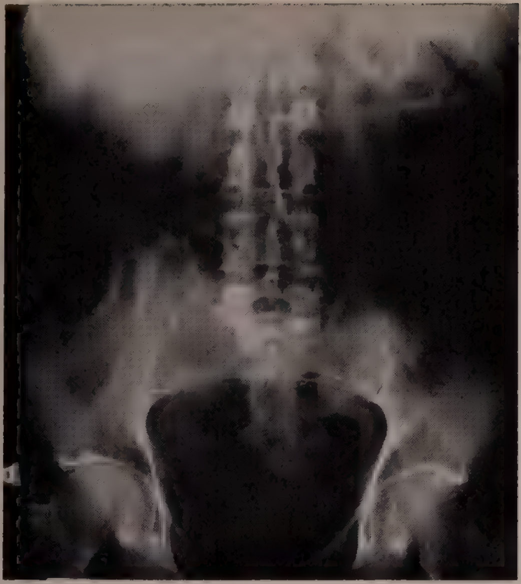

FIGURE 1. Anteroposterior film of abdomen. Destructive area in right ilium suggesting overlying gas.

displaced forward in this area without a high right posterior oblique film.

I think the bladder is within normal limits and I don't see anything abnormal in the lower pelvis. At this point, I am left with a destructive lesion in the right wing of the ilium with a normal pyelogram, although the possibility that the ureter has been displaced forward has not been entirely excluded.

Clayton H. Hale, M.D.: We have some detailed films of the right sacroiliac joint (Fig. 2).

Dr. Carsky: I don't think that with these films I would alter or add anything. So we have a sixty-nine-year-old man with a destructive lesion in the right side of his pelvis which is a solitary lesion to the best of our knowledge. The most likely cause of bone destruction at this age is metastatic neoplastic disease. Metastatic carcinoma of the prostate would be essentially excluded by the lack of sclerosis. Carcinoma of the lung would be the most likely primary site. Thyroid would have to be considered as would kidney except that we don't see anything abnormal in either kidney. Carcinoma of the gastrointestinal tract goes to the bone rather rarely. At least, this is true when you first see a radiographic study on a patient. Its incidence is about 20 per cent at autopsy, but this figure is certainly high for findings on a patient when he is first examined. As far as primary bone tumors are concerned, reticulum cell sarcoma would be high on the list, and multiple myeloma would have to be strongly considered. The possibility of chondrosarcoma should be considered, but

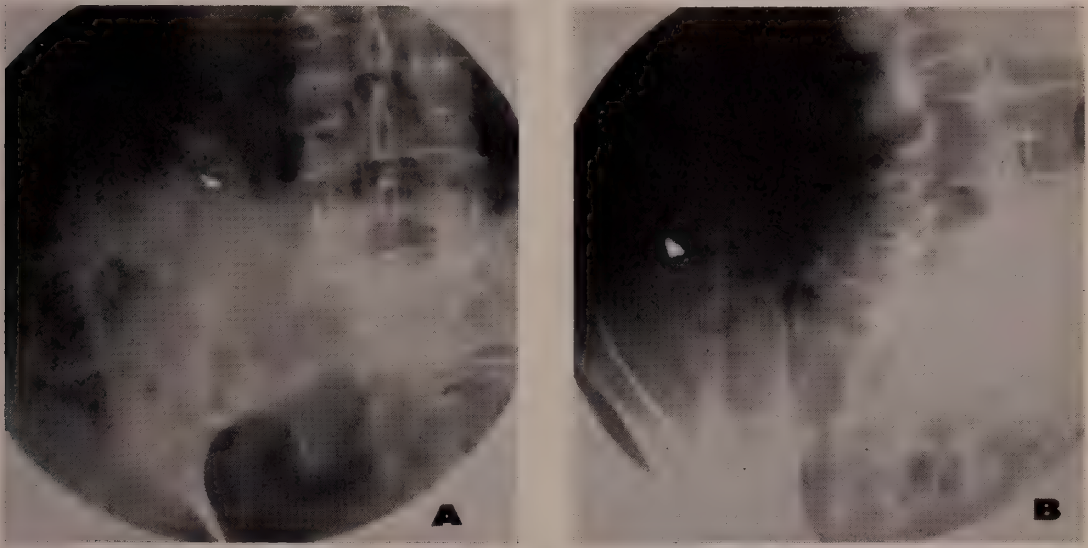

FIGURE 2. (A) Anteroposterior spot radiograph of right sacroiliac joint. Metal marker placed over palpable soft tissue mass. (B) Oblique spot film emphasizing destruction of right sacroiliac joint.

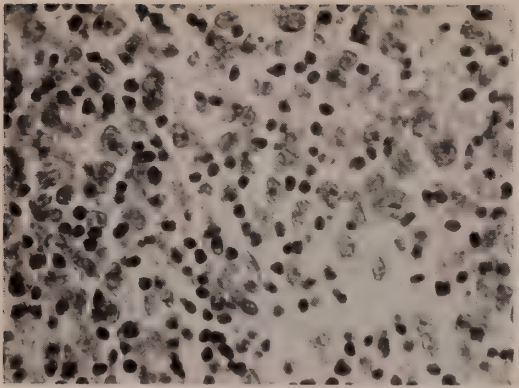

FIGURE 3. Typical distribution of malignant reticulum cells and lymphoid cells (hematoxylin and eosin stain, ×400).

the type of calcification which is so characteristic of it is not present here. At this point, I would like to see a chest radiograph, but even if that showed negative findings, I would still feel that metastatic disease is the most likely possibility, followed closely by reticulum cell sarcoma and multiple myeloma.

Dr. Carsky's diagnosis

Metastatic lesion probably from carcinoma of the lung

Dr. Bender: A biopsy study of the patient was done.

A physician: There is no question but that he had had a fracture of the scapula to explain the deformity that we see?

Dr. Bender: That is correct.

Pathologic discussion

J. Howard Ferguson, M.D.: The biopsy consists of a small piece of tissue. There is fairly uniform replacement of the entire structure by a massive growth which is made up of a combination of two different types of cells (Fig. 3). There is a scattering of lymphoid cells through various areas, but most of the mass is a collection of large, somewhat pale, very pleomorphic cells. In some of the sections there are a few fragments of bone. It was felt that microscopically this was a reticulum cell sarcoma.

Histologic diagnosis

Reticulum cell sarcoma

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Bunions not congenital

Bunions, thought by some experts to be congenital in nature, are actually due to the weakened muscles caused by the stress and strain of adult living, according to a report by Dr. Donald A. Schubert at the American Podiatry Association meeting, August 16, 1962. The uneven pull of small muscles in the foot results in the deformities known to most people as bunions. If congenital factors were as predominant as many think, one would expect to see many more bunions in children.

Instead, most of those seeking treatment are adults, which leads to the conclusion that muscle weakness, brought on by age and stress, produces faulty weight-bearing. This, in turn, leads to the development of bunions.

There is a surgical procedure which restores normal muscle balance without immobilizing the patient for an excessive period. Practically permanent correction of the bunion is achieved within three weeks, and the patient is able to walk with a cut-out, hard-soled shoe in two to four days. Regular exercise therapy assists in restoring full strength to the affected muscles.

Maternal Welfare

Prepared by the Subcommittee on Maternal and
Child Welfare, Committee on Public Health and
Education, Medical Society of the State of New York

EDWARD C. HUGHES, M.D., Syracuse, Editor

Progress in Reduction of Perinatal Mortalities

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According to a report issued by the National Vital Statistics Division, there has been a reduction of more than a third in the perinatal mortality rate from 1940 to 1959. The data are based on vital statistic reports and concern fetal deaths, stillbirths of twenty or more weeks gestation, and early neonatal deaths, those deaths occurring during the first week of infancy, (Fig. 1).

This is an encouraging note, but it is generally agreed that there is still a need for continuing attention to the perinatal problem, especially since there has been practically no change in early neonatal death rates in the past three or four years. It is, likewise, generally felt that more nationwide data are needed on the causes of fetal and neonatal deaths, and considerable effort has been made in obtaining this information in the past few years. This type of information, needed to direct research for preventive and treatment technics, is obtained generally from two sources: vital statistic certificates and final diagnoses on hospital charts.

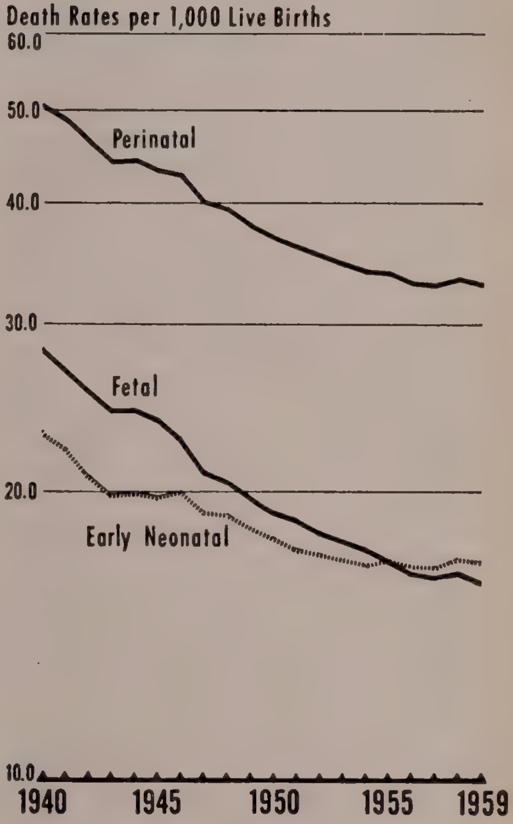

FIGURE 1. Perinatal mortality; United States, 1940–1959; semilogarithmic scale (Reproduced from Statistical Bulletin—Metropolitan Life Insurance Company, May, 1962, vol. 43).

Evaluation of data

The data obtained from birth, stillbirth, and death certificates are frequently publicized, and there is reason to suspect that many discrepancies are involved. It has been our experience that the diagnoses placed on death certificates on occasion do not correspond with hospital diagnoses. Recently we surveyed 300 deaths associated with pregnancy which occurred in Upstate New York. It was not at all unusual to find that the death certificate diagnosis, especially if it is written before the autopsy reports are completed, is completely inaccurate. This situation is exemplified often in situations where the preautopsy clinical diagnosis is some type of emoblism which is not confirmed by the autopsy. No supplementary postautopsy diagnosis is submitted to vital statistic offices and, therefore, the case is categorized as an embolism death, although postmortem examinations showed the cause of death as undetermined or due to some other cause. Our experience is that this same situation occurs frequently in stillbirths and neonatal deaths.

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Accuracy of causes of stillbirths and neonatal deaths is complicated further by the fact that comparatively few diagnoses are based on autopsied cases. We were able to analyze our maternal mortality series on the basis of questionnaires giving specific data on each case. The final diagnosis was made at autopsy in more than 75 per cent of the cases, and of the remainder all but about 2 or 3 per cent were confirmed clinical diagnoses. It is our impression that the causes of death would have been quite different and quite inaccurate if we had depended solely on death certificate diagnoses.

It is our feeling that published data on stillbirths and neonatal deaths may be relatively inaccurate, particularly if they are based on vital statistic information. A study of 237 neonatal and postneonatal death certificates and 159 stillbirth certificates submitted to the Vital Statistic Office in Syracuse, New York, during 1961 showed that approximately 40 per cent of the records did not show whether or not an autopsy had been performed. Other surveys conducted during the same year, however, show that autopsies had been performed in approximately 30 to 40 per cent of early neonatal deaths, and a slightly smaller percentage of stillbirths were posted. Thus, in our area the final diagnoses of neonatal deaths and stillbirths are based in more than half the cases on clinical diagnoses. Our survey of records of perinatal mortality committees reveal that clinical diagnoses can often be unreliable. One case, in point, involved a neonatal death. The working clinical diagnosis was a respiratory distress syndrome. The baby expired and a postmortem examination revealed that death was due to major congenital anomalies, none of which appeared externally. It is a virtual certainty that this case would have been classified as a respiratory distress syndrome fatality if the autopsy had not been performed. Comparable situations are encountered repeatedly and point up the definite requisite for autopsies of neonatal mortalities and stillbirths if an accurate picture of causes is to be obtained. There is little question that most clinical diagnoses of these fatalities are accurate, but some of them are little more than educated guesses.

There is a constant effort to improve the accuracy of information placed on birth and death certificates. One must accept their limitations, however. The National Vital Statistics Division recently published the results of matching and comparing birth certificates and census information on babies who were born in the first three months of 1960. Of these, 8.7 per cent showed a lack of agreement between the two records in the number of children reportedly born alive to the mother. Inconsistencies in the age of the mother were noted on 20.1 per cent of the cases. The realization of such inaccuracies in this very simple category of factual information leads to a conjecture of comparable inaccuracies in the much more complicated facets of the causes of death.

Conclusion

It is felt that conclusions on the subject under consideration are much more realistic when they are based on hospital diagnoses, particularly those conclusions resulting from hospital perinatal mortality committee analyses. It is accepted, however, that the material based on vital statistic records will continue to be used to designate causes of mortalities.

The physician is required to complete birth, stillbirth, and death certificates.

It would seem reasonable to point out that he should use every means at his disposal to be certain that the cause of death is recorded as accurately as possible. This can be accomplished best if the diagnosis is based on autopsy findings. Circumstances may be such that it is necessary to complete certificates before the final autospy diagnosis is available. In such instances, if the original diagnosis is not confirmed by an autopsy, a supplemental form ("Correction of Certificate and Record of Death") should be filed. On occasion, with or without autopsy, it is impossible to determine the actual cause of death and it would seem advisable to record the cause of death as "unknown," rather than to record an unverified diagnosis. Finally, it is our intention to point out that the attending physician is not only responsible but is also in the best position to correlate all data and record the cause of death.

Summary

The completion of vital statistic records is not a particularly pleasant duty; however, it is a necessary one. The information recorded is put to constructive use. The physician can aid in helping to direct research and other efforts designed to help in reducing fetal wastage and perinatal mortality by recording the cause as accurately as possible.

Glossary

The following terms are defined to facilitate a better understanding of perinatal mortalities:

Perinatal mortality (National Vital Statistics interpretation): fetal deaths with gestation given as twenty weeks or more, oı not stated, and deaths occurring in the first week of infancy.

Fetal death and stillbirth: these terms are synonymous.

Neonatal death: death from birth to the twenty-eighth day of life.

Postneonatal death: death from one month to one year of age.

766 Irving Avenue, Syracuse 10

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963,* and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

HAROLD JACOBZINER, M.D., Assistant Commissioner,
The City of New York Department of Health;
Medical Director, Poison Control Center
HARRY W. RAYBIN, M.S., Technical Director, Poison Control Center

Barbiturate Poisonings

THE FOLLOWING INCIDENTS were reported recently to the New York City Poison Control Center.

INCIDENT 1

TOXIC AGENT	*Age*	*Sex*
Phenobarbital	1 year	Female

Gertrude Stern, M.D., the Poison Control Officer of The New York Hospital, reports the following:

> This retarded, brain-damaged child, who has cardiac heart disease and seizures, was on phenobarbital daily for two months. In the ten days prior to her admission she was receiving 30 mg. three times a day, which caused the seizures to be less severe. Four days before her admission she developed an infection of the respiratory tract. She took minimal amounts of fluids and on the day of admission was listless and flaccid. The day after admission the barbiturate level was reported as 2.7 mg. per 100 ml. The phenobarbital was discontinued. She was given intravenous fluids, received suction treatment, and gradually became more alert. On April 12, 1962, two days following her admission to the hospital, she was started on Dilantin. She also was found to have pneumonia, which responded to antibiotics. She was discharged on April 20, 1962.

The suggested dosage of phenobarbital for sedation is 6 mg. per kilogram every twenty-four hours, to be divided in three doses. Assuming that this child weighed between 20 and 25 pounds, or approximately 10 Kg., the dose should have been about 68 mg. However, she actually received a minimum of 90 mg., which is rather excessive.

Phenobarbital is a long-acting barbiturate but is not more toxic and may be even less potent than the shorter-acting barbiturates.

The chief symptoms of barbiturate poisoning are progressive central nervous system depression, headache followed by depression, confusion, hallucinations, excitement, drowsiness, stupor, and coma.

The respirations are rapid, the pulse becomes rapid and weak, and there also may be cyanosis, cold and clammy skin, and cardiovascular disturbances. Paresthesia, analgesia, ataxia, and slurred speech also occur. The pupils are generally constricted, and the reflexes are weak. Since bronchopneumonia is not an infrequent complication of barbiturate poisoning, one must be particularly cautious about administering this drug to patients with already existing pulmonary conditions.

The treatment consists of the removal of the drug through gastric lavage, emesis, and catharsis. Emesis should not be attempted if the patient is unconscious. It is most important to establish and maintain an adequate airway and to keep the air passages free of mucus by frequent aspirations of the accumulated secretions. Oxygen for the associated hypoxia is of value. Artificial respiration may be necessary if spontaneous breathing is impaired. The cautious use of an analeptic drug may be indicated, but it must be used selectively. An analeptic drug is generally beneficial if shock occurs. If pulmonary complications develop, the administration of an antibiotic is advisable. Replacement fluids to prevent dehydration also should be administered. In the main the treatment is supportive and symptomatic, and good nursing care is essential in all cases of barbiturate poisoning.

Incident 2

Toxic Agent	*Age*	*Sex*
Amobarbital Sodium	11 years	Female

This child awoke in the morning and decided not to go to school. She swallowed 6 or 7 tablets of amobarbital sodium prescribed for a parent. While eating her breakfast, she became semiconscious and fell down some steps into the living room. The family physician was called immediately and referred the child to a hospital for emergency treatment.

The symptoms on admission were abdominal pains, nausea, and stupor. The stomach was lavaged in the emergency room with water, two hours following the ingestion. After several hours of observation the child was discharged as asymptomatic. The public health nurse who interviewed the household indicated that the child appeared average physically but was classified by the parents as being "lazy," although mentally alert. Psychiatric consultation was advised. Frequent reports of this nature indicate the advisability of parents being discrete about the use and presence of sedatives in the home.

Incident 3

Toxic Agent	*Age*	*Sex*
Vitamin-Fluoride Combination	$4^{1}/_{2}$ years	Male

This incident was reported by the family.

The child had been told that the tablets were to be given to him only by an adult, but he was feeling resentful that he had been left outside to play while the mother was at the supermarket a few blocks away and decided to "punish" her by doing something he knew was forbidden. That evening he was acting very uneasy and couldn't eat his dinner. Although the reason was unknown, it was thought that he was coming down with something. The rest of the night he was very upset and couldn't sleep, in general behaving like a sick child. The next morning brought a return to his normal good spirits. It wasn't until that afternoon that the empty bottle of vitamin tablets was discovered and his illness was connected with it. A doctor was called but was not available immediately, and then the Poison Control Center was called. The child had not eaten all the pills, because some were found in the play area. It is not known how many he actually did consume, but it is believed that had they been smaller he would have eaten more. No medical treatment was administered since the parents were advised that there wouldn't be any further effects.

The parents were very grateful for the prompt and considerate attention to their phone call.

This multivitamin combination also contains fluoride. Such preparations are now used widely, and parents should be alerted to keep them away from the reach of children to prevent therapeutic misuse.

Incident 4

Toxic Agent	*Age*	*Sex*
Methapyrilene Combination and Triple Bromide Preparation	64 years	Female

This patient was admitted to the hospital because of bizarre behavior. She was under psychotherapy and had been taking a methapyrilene combination and a triple bromide preparation for a long period of time. The patient's initial bromide level on her admission to the hospital was 300 mg. per 100 ml. Five days later the bromide level was reduced to 250 mg. per 100 ml. On the sixth hospital day the patient was started on intravenous saline, mercurial diuretics, and ammonium chloride. Two weeks following her admission her sensorium became clearer, and two days afterward the bromide level was 75 mg. per 100 ml. Three weeks following the admission there was only a trace of bromide present. The patient was then discharged symptom-free.

Since bromides still are readily available over-the-counter preparations, poisonings resulting from overdosage by self-medication are not infrequent. Physicians therefore are advised in all cases of erratic behavior or lethargy to consider the possible ingestion of bromide preparations. Fortunately, the chlorides are an effective antidote for bromide poisoning.

INCIDENT 5

Toxic Agent	*Age*	*Sex*
Yellow Pills	$2^1/_2$ years	Female

This patient was watering plants in the living room while the mother was in the bedroom. The child went into the kitchen, moved the chair quietly, and climbed up and managed to remove a small box of pills from the spice rack. She swallowed a mouthful of tablets. The mother became suspicious at the child's quietude and went to look for her. When she learned what happened, she called the family physician who advised that the child be watched carefully and taken to a hospital if any symptoms appeared. While the child was at first symptom-free, played, and was very active, she finally fell asleep two and one-half hours following the ingestion while she was watching television. She also started to groan and became stuporous. She was taken to a hospital where the stomach was lavaged in the emergency room, and four hours following the ingestion she was admitted to the inpatient service where she remained for eight days and was treated supportively and symptomatically.

She finally made a complete recovery. The nature of the "yellow pills" is still unknown, since they were prescribed for the mother in a prenatal clinic without any identifying data. We strongly support the rising conviction that all therapeutic medications should be identified appropriately unless there is good reason for anonymity by the prescribing physician. The traditional secrecy attached to pharmaceutical prescriptions is an outmoded concept in this era of frank and informative labeling.

INCIDENT 6

Toxic Agent	*Age*	*Sex*
Aspirin	22 years	Female

This patient ingested 22.5 Gm. of aspirin, most likely with a suicidal intent. She vomited spontaneously several times and was taken to St. Luke's Hospital.

The symptoms on admission were abdominal pains, nausea, vomiting, and dyspnea. The blood salicylate level on admission was 52.2 mg. per 100 ml. which later was reduced to 42 mg. per 100 ml. There was also acetonuria and glycosuria which persisted for four days. After six days of hospitalization and intensive therapy the patient made a full recovery. Glycosuria is not an infrequent finding in reported cases of aspirin poisoning. It also should be pointed out that this Center receives many reports of massive ingestions (100 5-grain tablets by adults) which result in a rapid favorable outcome after emergency treatment.

Number one hundred two in a series of Accidental Chemical Poisonings

Primary Hyperparathyroidism and Coexistent Parathyroid Hyperplasia Secondary to Independent Renal Lesion

Some Diagnostic Radiologic Features

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THE COEXISTENCE of renal insufficiency and osteitis fibrosa cystica, when it is encountered clinically, may present a difficult diagnostic problem. A differentiation has to be made between skeletal changes with renal damage caused by primary hyperparathyroidism and protracted kidney disease with metabolic acidosis and compensatory parathyroid hyperfunction leading to skeletal demineralization. The differentiation between the two disease entities is not of mere academic interest but has therapeutic importance. The surgical removal of a parathyroid adenoma may arrest or even partly reverse the disease process in a patient who at the onset may have primary hyperparathyroidism, even when it is complicated by considerable kidney damage (Case 5[1]), while in secondary hyperparathyroidism initiated by renal disease surgical intervention is contraindicated.[2] An accurate differential diagnosis becomes increasingly difficult as the secondary changes in either disease process increase in severity. These changes may become so pronounced that they distort or mask the primary disease, and the usually acceptable diagnostic criteria of primary hyperparathyroidism—characteristic changes in the levels of calcium and phosphorus in the serum and in the urine—are no longer valid.

The interrelation of renal disease, hyperparathyroidism, and osteitis fibrosa is well known. The association between skeletal abnormalities and the parathyroid bodies was known to pathologists,[3–6] even before Mandl's[7,8] classic therapeutic parathyroidectomy. Jaffe and others[9,10] were able to produce the pathologic changes observed in von Recklinghausen's disease experimentally by inducing a state of chronic hyperparathyroidism with parathyroid hormone injections in susceptible young animals. Renal involvement is the most frequent complication of primary hyperparathyroidism, and conversely, chronic renal failure, irrespective of its cause, is associated with secondary hyperplasia of the parathyroid glands.[11–21] Furthermore, secondary parathyroid hyperplasia may be induced by renal insufficiency which is itself secondary to primary hyperparathyroidism.[1,22–28]

The association of osseous derangement and renal disease was recognized as early as 1883,[29] and in recent years observations on hyperplasia of the parathyroid glands in the course of renal disease with osteopathy have been reported with increasing frequency.[15,17–20,24,30–39] Berner[40] found a definite positive correlation between the severity of the renal insufficiency and the intensity of the osteopathy.

Renal osteopathy has been reported in the literature under a profusion (and confusion) of terms, having been designated, among others, as renal rickets, renal dwarfism, renal fibrocystic osteosis, osteodystrophia fibrosa, and renal osteodystrophy. Albright, Drake, and Sulkowitch[18] suggested the term renal osteitis fibrosa generalisata, a term more precise and more descriptive of the essential etiologic and pathologic characteristics of the disease process. This term is preferred but should be applied only to those cases in which (1) it can be established definitely that renal disease precipitated the entire disorder and (2) the histologic bone changes are like those which are seen in osteitis fibrosa generalisata owing to hyperparathyroidism. The more general term "renal osteodystrophy"[41] should be used in cases in which histologic data are not available.[42]

In a recent review of cases of primary hyperparathyroidism,[1] interest was revived in the present case which presented some interesting radiologic features and which also appeared to satisfy the previously mentioned criteria of renal osteitis fibrosa generalisata. However, a postmortem examination disclosed the presence of a primary parathyroid adenoma with osteitis fibrosa generalisata and an independent chronic pyelonephritis with secondary parathyroid hyperplasia. These radiologic features and the combination of primary parathyroid disease and primary renal disease with secondary hyperparathyroidism form the basis of this report.

Case report

A thirty-eight-year-old white woman presented herself in November, 1946, complaining of headache and weakness. Two months previously she had a slight pneumonitis which cleared spontaneously in a week without the use of sulfonamides or antibiotics. One month previously, she complained of pain in the back of the neck radiating to both shoulders. An x-ray examination of the cervical segment of the spine indicated no evidence of osteoarthritic changes. The pain disappeared completely in one month with local applications of heat. The weakness had been coming on gradually during the past few months. There were no complaints of dyspnea, vomiting, or other gastrointestinal disturbances. No nocturia, polyuria, bone pain, or edema was present. Her weight had been constant. The tonsils were removed in infancy and again when she was twenty years old. There was no history of sore throats, systemic infections, or scarlet fever. She had had two normal pregnancies and one pregnancy which terminated spontaneously at six months with the delivery of a macerated fetus. The blood pressure and urine examinations showed normal findings during her three pregnancies.

A physical examination disclosed a well-developed, well-nourished, white woman who appeared chronically ill. There was a pallor of the face and of the mucous membranes. The ocular fundi showed myelinated nerve fibers, but no arterial changes, hemorrhages, or exudates. The thyroid isthmus was palpable, but no nodules could be felt. The lungs and heart were normal. The blood pressure was 170/90 mm. Hg. The liver, spleen, and kidneys were not felt. There was no bone or costovertebral angle tenderness. The tendon reflexes were physiologic. The dorsalis pedis pulsations were good. There was no edema. A pelvic examination showed normal findings. There was no significant lymphadenopathy.

LABORATORY DATA. The urine contained a trace of albumin, a few white blood cells, and a very occasional finely granular cast. The specific gravity was 1.008 and remained fixed between 1.008 and 1.010 when a Fishberg concentration test was performed. A hematologic examination revealed: bleeding time and coagulation time, within normal limits; hemoglobin, 8 Gm. per 100 ml.; erythrocytes, 3.8 million per cubic millimeter; leukocytes, 11,000 per cubic millimeter with 75 per cent polymorphonuclear cells; platelets, adequate; and morphology of cells, normal. The bone marrow was entirely normal. The blood urea nitrogen was 18 mg. per 100 ml.; creatinine, 1.9 mg. per 100 ml.; and glucose, 112 mg. per 100 ml. The serum calcium

TABLE I. Representative chemical determinations of the blood

Date	Urea Nitrogen (Mg. per 100 Ml.)	Nonprotein Nitrogen (Mg. per 100 Ml.)	Creatinine (Mg. per 100 Ml.)	Chloride (mEq. per Liter)	CO_2 Combining Power (mM per Liter)	Calcium (Mg. per 100 Ml.)	Inorganic Phosphorus (Mg. per 100 Ml.)	Alkaline Phosphatase Activity	Cholesterol (Mg. per 100 Ml.)	Total Protein (Per Cent)	Serum Albumin (Per Cent)	Remarks
1946												
November	18	..	1.9	..	..	..	..	..	..	..	..	Low-salt diet
1947												
January	20	..	2.0	..	..	..	..	..	..	..	..	
March	26	..	2.5	..	..	..	..	..	..	..	..	
1948												
January	55	..	..	..	..	..	..	..	..	..	..	Kempner rice diet
February	130	146	..	93.0	9.9	6.3	14.0	18.4*	200	7.6	5.3	
March	52	..	..	99.1	27.6	10.1	4.2	..	..	6.5	..	Liberal sodium chloride, calcium gluconate, and aluminum hydroxide gel
April	31	..	..	107.3	..	9.0	4.0	10.4*	..	..	..	
May	42	..	..	..	..	8.1	3.8	..	..	..	..	
June	42	..	..	..	..	11.7	4.0	..	..	7.0	..	
July	65	..	..	..	..	11.7	5.2	..	..	6.3	..	
August	..	96	..	105.2	17.4	9.1	6.0	41.0*	355	6.8	3.7	On sodium bicarbonate plus above
September	..	87	..	90.2	33.9	10.4	..	54.0*	..	..	..	
	..	113	..	95.2	19.6	11.8	3.2	16.8†	..	..	..	
	..	31	..	..	..	..	..	..	..	..	..	
	..	110	..	96.7	15.5	13.6	4.3	..	..	..	..	
November	90	186	..	96.7	24.1	10.4	4.0	..	..	..	..	
	..	246	..	96.7	22.5	8.6	4.7	11.3†	..	..	..	Low salt
December	..	266	13.6	87.0	15.5	..	..	..	..	..	..	Liberal sodium chloride and sodium bicarbonate
1949	116	..	10.8	97.3	14.9	7.0	10.2	75.0†	..	6.1	3.5	
January	120	..	..	90.5	15.8	7.9	8.3	133.0†	..	6.9	3.85	Potassium bicarbonate (4 Gm.)

* Bodansky units.
† King-Armstrong units.

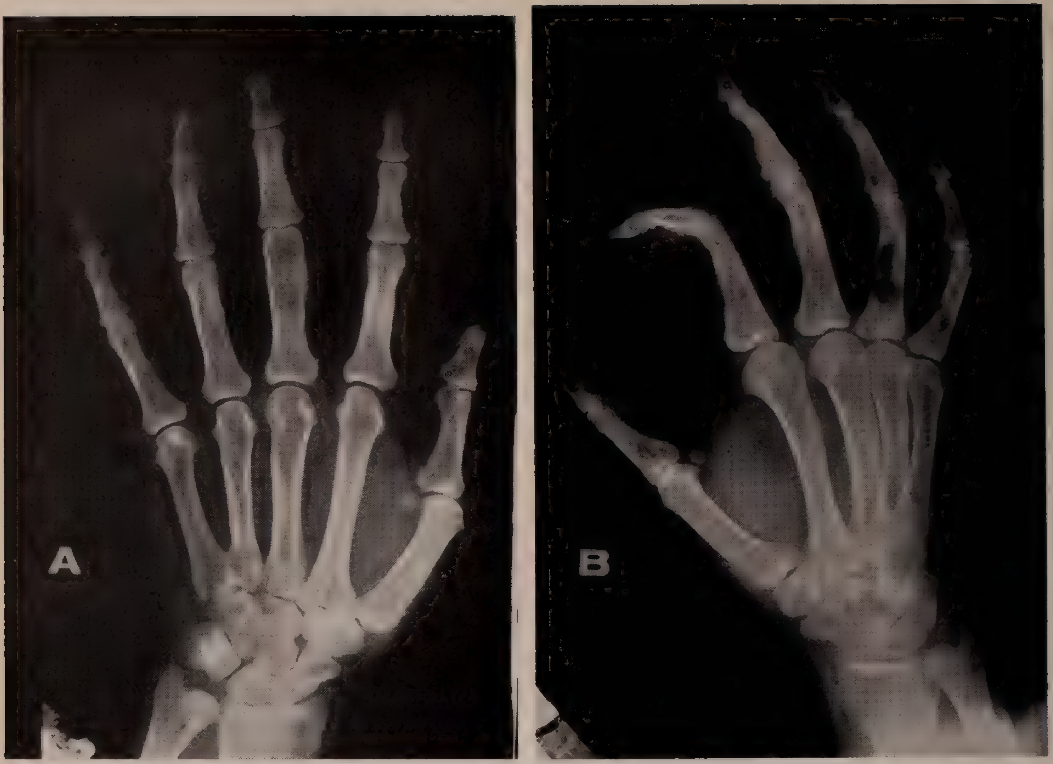

FIGURE 1. Roentgenograms of hands, showing expanding multilocular cystlike bone lesions involving proximal phalanges of left middle (A) and right ring (B) fingers.

and phosphorus were not determined. The electrocardiogram showed only left axis deviation.

The patient was placed on a low-protein, low-salt diet and on intensive liver, iron, and multivitamin therapy. The anemia failed to respond to these measures, and in March, 1947, she received a transfusion of 500 cc. of whole blood with only slight temporary improvement. In the next few months the blood nitrogen level rose slightly (Table I). Eight months after the onset of her illness she began to exhibit transient ankle edema and exertional dyspnea. The systolic blood pressure ranged between 140 and 160, and the diastolic blood pressure between 80 and 90. In January, 1948, she was placed on a Kempner diet of rice and raisins. She became markedly worse, lost her appetite, vomited, and became weaker. This diet was discontinued, and she was given another transfusion of 500 cc. of whole blood.

First hospital admission. The patient was hospitalized in February, 1948, and during the first hospital day she had several generalized clonic convulsions without localizing signs. A physical examination on admission showed essentially the same findings as were noted previously. The blood pressure was 140/80 mm. Hg and remained normal during her hospital stay. An inconstant soft systolic apical murmur was heard.

Laboratory data and diagnostic procedures.* The urine contained 2 plus albumin, 4 to 5 red blood cells, and an occasional granular cast per high power field. The specific gravity was 1.009. Bence Jones protein was not present. The hemoglobin was 9.5 Gm. per 100 ml., red blood count, 3.39 million per cubic millimeter, hematocrit, 29.6, and white blood count, 5,950 with 78 per cent polymorphonuclears. The chemical determinations of the blood on admission and subsequent determinations are tabulated in Table I. The phenol-

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* We are indebted to William G. Speed, III, M.D., of Baltimore, for supplying us with a detailed report of these studies which were carried out at the Johns Hopkins Hospital.

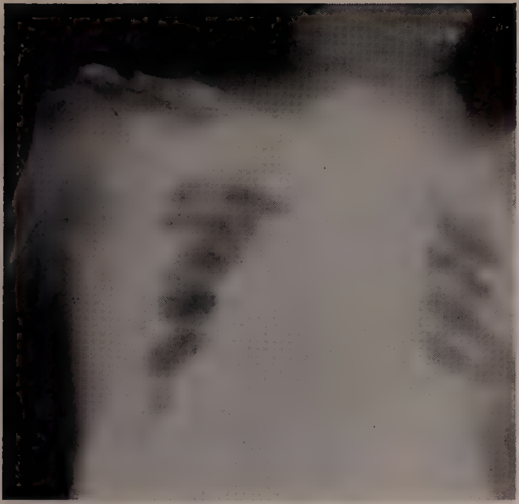

FIGURE 2. Roentgenogram of right acromioclavicular region, showing cystlike changes in lateral portion of clavicle, fraying and irregularity of outer end of clavicle, widening of acromioclavicular joint space, and fraying of articular surface of acromion process.

sulfonphthalein test showed no excretion in two hours. The Congo red test showed 65 per cent retention. The electrocardiogram showed auricular fibrillation. One week later, the electrocardiogram showed left axis deviation and reversion to a normal sinus rhythm. Cystoscopy revealed bilateral ureteral strictures. Retrograde pyelography showed small kidneys, normal calyces, and no calculi or hydronephrosis. Urine cultures grew out alpha nonhemolytic streptococci on two occasions and coli-aerogenes group on two other occasions. An x-ray film of the chest showed no abnormalities of the lungs, heart, and great vessels. An x-ray examination of the bones revealed punched-out areas in the skull, a pathologic fracture of a rib, and erosion of the distal portion of the left clavicle. These bone lesions were interpreted as suggesting multiple myeloma, but a biopsy of the sternum and of the left clavicle showed areas of osteitis fibrosa.

The patient was treated with intravenous fluids and sedation and later with a low-phosphorus, low-protein diet with liberal amounts of sodium chloride, calcium gluconate, sodium bicarbonate, and aluminum hydroxide gel. She received several transfusions of whole blood during her six weeks stay in the hospital. On her discharge, the electrolyte pattern had returned to normal, but the azotemia and the anemia persisted.

The patient did fairly well for the next six months on the preceding regimen and several transfusions of whole blood. In June, 1948, she developed a tender swelling of the left middle finger. An x-ray examination showed considerable rarefaction and cystlike loculation of the proximal phalanges of the left middle and right ring fingers (Fig. 1). The blood pressure ranged between 150 and 180 systolic and 80 and 100 diastolic. The eyegrounds showed minimal vascular sclerotic changes. In November, 1948, the patient complained of severe headache. The blood pressure was 230/100 mm. Hg, and the eyegrounds showed exudates in both eyes. She was placed on a low-salt diet. This diet was badly tolerated, and the nitrogen retention increased, although the blood pressure level dropped to 150/80 mm. Hg.

The patient was admitted to hospitals for short periods in July and again in November for an adjustment of the acid-base pattern with intravenous fluids. A bedside roentgenogram of the chest showed cupping, fraying, and irregularity of the outer ends of the clavicles, widening of the acromioclavicular joint spaces, and fraying of the articular surfaces of the acromion processes (Fig. 2). A roentgenogram of the skull showed diffuse decalcification with numerous scattered nodular densities (Fig. 3).

Final hospital admission. The patient was readmitted to the hospital in January, 1949, in a comatose state. Five days before this last admission, the patient received inadvertently, instead of sodium bicarbonate, 4 Gm. of potassium bicarbonate in four divided doses over a twelve-hour period. Thirty-six hours later she suddenly became dyspneic and complained of palpitation. An examination revealed a few pulmonary basal rales, a protodiastolic gallop with a heart rate of 140 per minute, and a blood pressure of 180/100 mm. Hg. The face became puffy, and the patient became progressively more restless. On the day of admission she had a generalized convulsion and became disoriented.

The pertinent physical findings at this

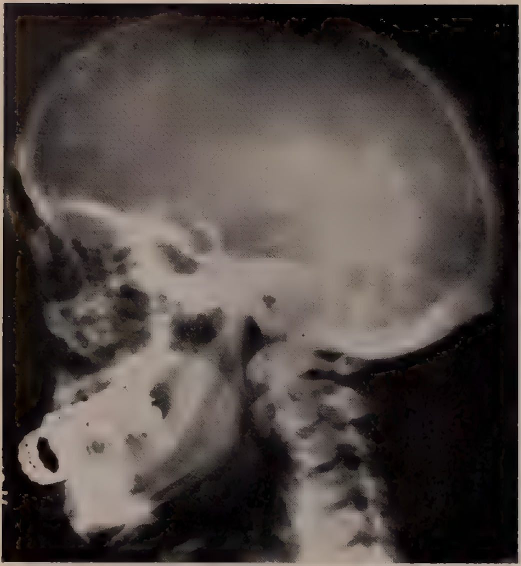

FIGURE 3. Roentgenogram of skull, showing diffuse decalcification, with dense scattered nodular densities.

time were: poor skin turgor; face puffy; heart slightly enlarged; blood pressure, 180/100 mm. Hg; old and fresh hemorrhages in the fundi with some blurring of the disk margin; and negative Trousseau and Chvostek signs. An examination of the urine showed 2 to 4 plus protein, 4 to 5 red blood cells, and 6 to 8 white blood cells per high-power field. The red blood cells numbered 2.5 million per cubic millimeter, and the hemoglobin was 7 Gm. per 100 ml. On the fourth hospital day she developed signs of pleural effusion. The patient died on the eighth hospital day with evidence of cardiac and renal decompensation. An autopsy was performed three hours after death.

Clinical diagnosis. The clinical diagnosis was chronic glomerulonephritis or chronic pyelonephritis with secondary hyperparathyroidism.

Autopsy observations

Gross findings. The peritoneal cavity contained 250 cc. of yellow, clear fluid. The right and left pleural cavities contained respectively 75 and 250 cc. of straw-colored fluid. The heart weighed 400 Gm., and there was thickening of the left ventricular wall and its papillary muscles. The lower lobes of both lungs were atelectatic. The liver weighed 1,485 Gm. and was unremarkable. The gallbladder was filled entirely with a soft white calculus which on chemical analysis was found to be composed of calcium carbonate. There was a cystitis and a subserous fundal myoma of the uterus. The pituitary gland measured 1.2 by 0.8 by 0.3 cm.

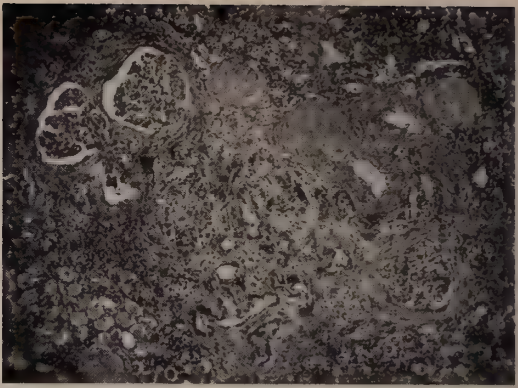

FIGURE 4. Photomicrograph of section of kidney, showing periglomerular fibrosis, hyalinization of glomeruli, and adhesion of capillary loops to each other.

Kidneys. Both kidneys were markedly contracted, the right weighing 25 Gm. and the left 30 Gm. The cortical surfaces were coarsely granular and gray-yellow. The cortex was irregularly narrow with a fine dewdrop appearance. The medullary pyramids were intact. The pelves and ureters were unremarkable, and there was no evidence of calculi, stenosis, or intrinsic or extrinsic strictures. No dilatation of the pelves or ureters was found. An x-ray film of the removed kidneys showed no calcifications. The glomeruli showed considerable periglomerular fibrosis, and many glomeruli were hyalinized (Fig. 4). Tubular atrophy and interstitial fibrosis with mononuclear cell collections were noted. Rare glomeruli showed epithelial proliferation with crescent formation. The intimal thickening of arteries and arterioles was moderate. No calcinosis was noted.

Parathyroids. At the inferior border of the right lobe of the thyroid, a mass 3 by 2 by 1.3 cm. was found lying in loose areolar tissue. The mass was pale yellow-brown,

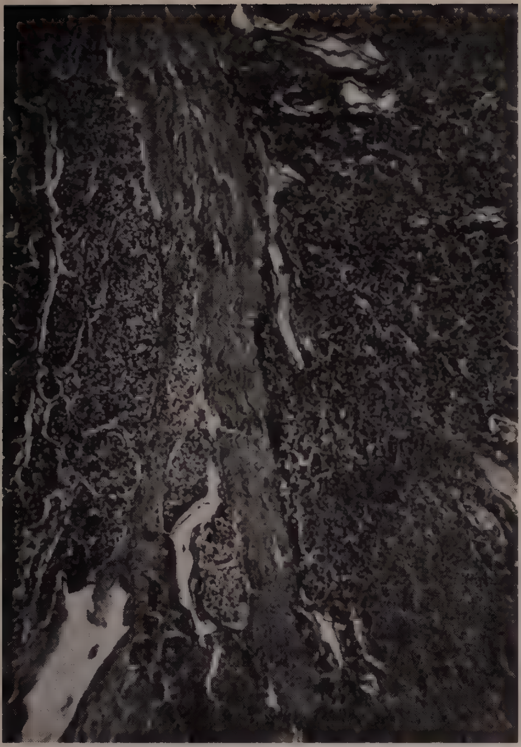

FIGURE 5. Photomicrograph of section of right inferior parathyroid gland, showing junction of adenoma at lower right with hyperplastic parathyroid tissue.

firm, and encapsulated and weighed 10 Gm. The right superior parathyroid was a gray-yellow nodule measuring 1.4 by 0.3 by 0.3 cm. The left parathyroids were similar nodules measuring 1 by 0.5 by 0.5 cm. A few sections of the right inferior parathyroid mass revealed a peripheral remnant of "normal" parathyroid gland in which isolated and scattered fat cells persisted (Fig. 5). The remnant and the other three parathyroids exhibited a similar histologic picture of sheets of normal-size chief cells (Fig. 6). Pale oxyphil cells were rare and never occurred in more than 3-cell clusters.

The right lower parathyroid mass itself presented a heterogeneous picture of cell types in diverse portions of the lesion (Fig. 7). Some fields were composed entirely of chief cells which could be traced readily into other fields of frank aggregations of obvious oxyphil cells. On the other hand, transition stages were frequently encountered from chief cells to extremely vacuolated cells resembling "wasserhelle" cells except for their lack of enlargement. The most striking histologic feature of the mass was the enormous number of large eosinophilic cells in solid pseudoglandular clusters, sheets, or tortuous ribbons. These cells were unlike any normal parathyroid cell because of nuclear enlargement, hyperchromatism, and pleomorphism. No

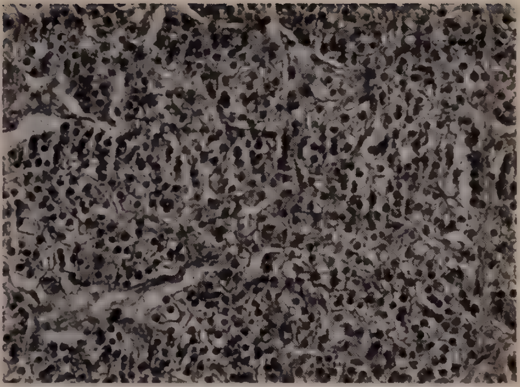

FIGURE 6. Photomicrograph of section of right superior parathyroid gland, showing sheets of chief cells with only scattered fat cells.

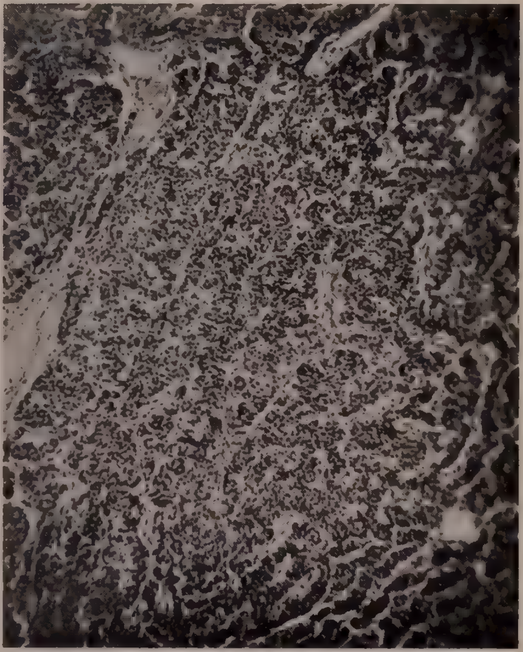

FIGURE 7. Photomicrograph of parathyroid adenoma showing multiplicity of cell types from normal size chief cells in center to giant oxyphilic cells in pseudoglandular pattern at periphery.

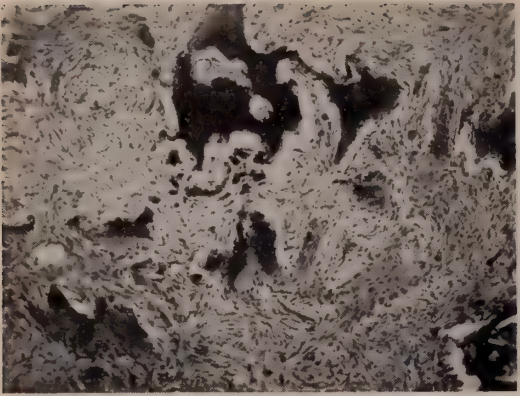

FIGURE 8. Photomicrograph of vertebra, showing osteitis fibrosa cystica, with bone destruction and formation, and fibrosis.

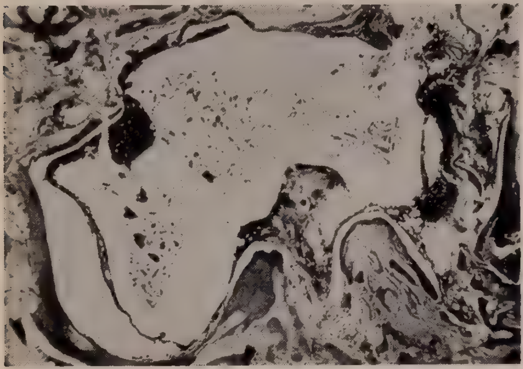

FIGURE 9. Photomicrograph of clavicle, showing osteitis fibrosa cystica with true cyst formation.

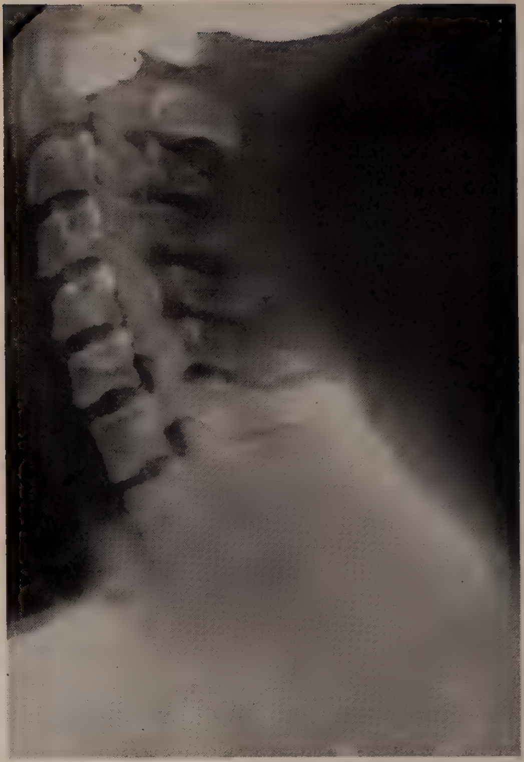

FIGURE 10. Roentgenogram of cervical segment of spine, showing localized radiolucent area with suggestion of pathologic fracture in spinous process of sixth cervical vertebra.

mitoses were found. Even these atypical cells could be evolved, however, from regions of identifiable chief cells. The mass possessed a dense collagenous capsule which contained nests of chief cells here and there. In one high-power field beneath this capsule, the chief cells formed true acini. Several vascular channels contained nests of epithelial cells from the tumor mass, but no mural invasion of the vessels could be found.

Bones. The skull, sternum, ribs, clavicles, and lumbar vertebrae all revealed on cross section an almost homogeneous yellow-gray surface with obliteration of the cortical and medullary patterns by a relatively soft and poorly calcified tissue. These bones cut readily with a knife. Firm pressure on the removed calvarium easily distorted its shape. In the clavicles and skull were found round cystic areas measuring up to 0.5 cm. in diameter and containing a gray sticky material. Similar cysts in the sternum contained red marrow. Except for the abundant dense callus formation at the site of the left fifth rib fracture, none of the examined bones were thickened or grossly distorted. Specimens of the long bones were not obtained. Bone sections revealed marked fibrosis of the marrow and lacunar absorption of the spongiosa and cortex. Throughout the bone sections, simultaneous osteoclastic and osteoblastic activity were taking place (Fig. 8). True cysts were present in several bones and were lined by compressed rims of hematopoietic marrow (Fig. 9). The ribs especially exhibited large cystlike cavities entirely filled with myeloid elements.

Anatomic diagnoses. The anatomic diagnoses were: chronic pyelonephritis; right inferior parathyroid adenoma; secondary hyperplasia of the other three parathyroid glands; osteitis fibrosa cystica; left ventricular hypertrophy; and cholelithiasis.

Following the necropsy, the roentgenograms of the cervical spine which were made in October, 1946, (Fig. 10) were re-examined carefully, and a localized area of radiolucency with a suggestion of a pathologic fracture could be seen in the spinous process of the sixth cervical vertebra. In the light of subsequent bone findings, it is reasonable to assume that the lesion in the cervical spine during the early phase of the patient's illness was also due to hyperparathyroidism.

Pathologic considerations

The basic problem in the analysis of the sequence of events in this case is the determination of the nature of the parathyroid disturbance. All four parathyroid glands were enlarged. Three glands were composed microscopically of broad sheets of normal-appearing chief cells with a sharp increase in fat cells expected on the basis of the patient's age. These features constitute a clear-cut histologic picture of parathyroid hyperplasia secondary to renal insufficiency. The right lower gland was of relatively massive size and of a different histologic picture. Dreskin and Fox[35] reported a case of renal osteitis fibrosa in which there was predominant hyperplasia of one gland, which was easily palpated on physical examination, and typical hyperplasia microscopically of the other parathyroid glands. Six other reports in the literature of cases of secondary parathyroid hyperplasia with massive enlargement of one parathyroid gland are listed in Table II. In view of these reports it is pertinent to consider the possibility that the massively enlarged right lower gland in the present case might similarly represent solely hyperplasia. Sections of the gland, however, revealed the presence of all the criteria suggestive of an adenoma as originally laid down by Castleman and Mallory[15]: (1) a localized proliferative process with the demonstration of a rim of "normal" parathyroid tissue on one margin of the tumor; (2) nuclear hyperchromatism, pleomorphism, and occasional gigantism; (3) protean cytology and histology as compared with the monotonous uniformity of the hyperplasia as a group; and (4) irregular character and distribution of the stroma and vascular channels. For these reasons, the present case is considered to present the coincidental occurrence of both neoplasia and hyperplasia in the parathyroids.

No attempt was made to assay the parathyroid hormone content of any of the parathyroid glands. The dispute concerning which cells of the parathyroid are capable of producing parathyroid hormone is not yet adequately settled. Selye[45] states categorically that "adenomas of either oxyphil or chief cells may cause hyperparathyroidism in man"; on the other hand, Black and Ackerman,[24] among others, accept no reported cases of functioning oxyphil adenoma. The adenoma in the present case, while possessing abundant oxyphil cells, still exhibited a sufficiently distinct heterogenous mixture of cell types to indicate the capability of secreting parathyroid hormone.

The serum level of alkaline phosphatase activity in cases of hyperparathyroidism with definite skeletal changes is said to be increased 1.5 to 15 times the normal maximum.[46] The increase in phosphatase activity is related to the extent of osteoblastic activity and is not a diagnostic criterion of hyperparathyroidism per se. In the present case, the serum alkaline phosphatase activity was consistently increased and rose to markedly high levels in the late stages of the disease. This event would indicate an intense attempt at bone repair, concomitant with extensive bone destruction—simultaneous osteoblastic and osteoclastic activity as noted histologically throughout the bone sections.

Clinical considerations

It may be extremely difficult clinically to arrive at a conclusion about the pathogenesis of hyperparathyroidism in cases of an advanced degree of osteitis fibrosa coupled with renal insufficiency. Shelling and Remsen[17] rightly stress the chronologic sequence of events in the differential diagnosis: The evidence of renal disease precedes the skeletal changes in secondary hyperparathyroidism, and the clinical evidence of parathyroid hyperfunction precedes

TABLE II. Summary of reported cases of parathyroid "adenoma" in secondary hyperparathyroidism

Case	Pathology			Calcium (Mg. per 100 Ml.)	Phosphorus (Mg. per 100 Ml.)	Nitrogen Products (Mg. per 100 Ml.)	Remarks
	Parathyroids	Kidneys	Bones				
MacCallum[43]	Right lower 2 cm. in diameter; other 2 glands normal	Advanced chronic diffuse nephritis	Not recorded (later reviewed by Albright *et al.*[12] and true osteitis fibrosa found	. . .	. . .	. . .	After review of case with Albright, concluded that this was case of primary parathyroid adenoma in a patient with coincidental chronic nephritis.
Bergstrand[13] Case 6	Right upper size of small hazelnut, left lower size of plum; compact, fat-free; wasserhelle cells; other glands normal	Subacute glomerulonephritis and nephrosis	Not recorded	. . .	. . .	. . .	No rim of "normal" parathyroid tissue. (1) Clinical data very meager in Case 6, none in Cases 8 and 9. (2) No mention of the examination of bones in any of the 3 cases. (3) Except for enlarged glands, all other parathyroid glands normal in size and structure, which does not accord with secondary hyperparathyroidism in which hyperplasia is diffuse throughout all the glands.
Case 8	Right upper 600 mg.; left upper 90 mg.; left lower 40 mg.; both upper enlarged, demarcated from "normal" parathyroid tissue	Nephrocirrhosis	Not recorded	. . .	. . .	. . .	
Case 9	Right lower 230 mg., fat-free, well demarcated from remainder of gland which is normal; other 3 glands normal	Arteriosclerotic nephrocirrhosis	Not recorded	. . .	. . .	. . .	
Lindsay[44]	In 1 gland true "adenoma" of very marked chief-cell hyperplasia, surrounded by rim of less hyperplastic tissue.	Not given	Not recorded	. . .	. . .	. . .	Not adequately documented. Character of "adenoma"? No description of the other parathyroid glands.
Black and Ackerman[24] (Case 13)	At operation, all parathyroid glands enlarged to twice normal size; oxyphil adenoma 3 by 3 by 1.3 cm. removed	Chronic nephritis (by history)	X-ray film showed osteolytic changes in vertebrae, sacrum, and ilium	10.6 to 13.8	3.9 to 6.3	Nonprotein, 23 to 50	Interpreted by the authors as fortuitous nonfunctioning oxyphil adenoma in case of nephritis with secondary parathyroid hyperplasia. No pathologic examination of the other "hyperplastic" glands.
Dreskin and Fox[35]	Predominant hyperplasia 1 gland; hyperplasia other glands	Megaloureter and hydronephrosis	Healing osteitis fibrosa generalisata	10.4	8.7	Blood urea, 150	No rim of "normal" parathyroid tissue described.
Morgan and MacLagan[36] (Case 1)	Hypertrophy right upper; "adenoma" 1.1 Gm. right lower but microscopically resembled right upper, consisting mainly of chief cells (only 2 glands found)	Contracted pyelonephritis; calcification in parenchyma along corticomedullary junction	Advanced osteofibrosis; fracture femur below large cyst	9.9 to 7.8	5.3 to 8.8	Blood urea, 177 to 580	No rim described.
Goldberg and Torack[28] (Case 1)	Adenoma 1 gland; secondary hyperplasia of other 3 glands	X-ray film suggested calcinosis, but no calcium deposits found; glomeruli fibrotic, tubules atrophic	Not recorded	10.5 to 11.1	4.8 to 8.3	Blood urea, 70 to 97	No rim described.

TABLE III. Summary of reported cases of renal osteitis fibrosa generalisata with gross bone cysts

Case	Parathyroids	Kidneys	Bones	Calcium (Mg. per 100 ml.)	Phosphorus (Mg. per 100 ml.)	Nitrogen Products (Mg. per 100 ml.)
Castleman and Mallory[15] (Case 23a)	1 normal size, 3 glands enlarged; very little fat tissue; no wasserhelle cells	Marked chronic pyelonephritis	Osteitis fibrosa; x-ray film of skull, ribs, and hands showed definite cysts	8.0	9.0	Nonprotein, 150
Herbert, Miller, and Richardson[32]	Chief cell hyperplasia all 4 glands, very little fat	Renal hypoplasia with advanced renal sclerosis	Soft lobulated fluctuant swelling above acromioclavicular joint, cavitation terminal phalanges fingers	11.7	7.8	Blood urea, 300
Jackson *et al.*[34]	All 4 glands enlarged to 2 cm. in diameter; chief cell hyperplasia	Congenital polycystic hypoplasia	4 by 2 cm. fluctuant cystic mass each acromioclavicular joint and in lumbar region	10.0 to 14.7	2.0 to 13.1	Nonprotein, 78 to 250
Morgan and MacLagan[36]	2 glands found: chief cell hyperplasia; 1 gland appeared macroscopically like an "adenoma"	Contracted pyelonephritis; calcification in parenchyma	Advanced osteitis fibrosa; large "cysts" right femur containing fat, hemopoietic tissue, and hemorrhage	9.9 to 7.8	5.3 to 8.8	Blood urea, 177 to 580
Pollak *et al.*[39] Case 1	All glands enlarged; chief cells, few oxyphil cells	Pyelonephritis	Osteitis fibrosa cystica; (cyst in clavicle by x-ray film)	10.4	11.7	Blood urea, 208
Case 4	All 4 glands enlarged	Polycystic; acute and chronic pyelonephritis	Osteitis fibrosa cystica; (pseudocystic changes metacarpal noted by x-ray film); expanded maxillary bone	9.9	6.7 to 9.4	Blood urea, 79 to 142

the manifestations of renal disease in primary hyperparathyroidism. Such a reliable history, however, is not always obtainable. Nathanson and Slobodkin[47] described distinctive roentgenologic findings in hyperparathyroidism, findings which had been noted but not stressed previously by other observers.[32,42,48] These consist of "cupping of the outer end of the clavicle with fraying due to irregular absorption of the articular surface, with or without similar changes in the articular surface of the acromion process and widening of the acromio-clavicular joint space."[47] Some radiologists claim that these acromioclavicular changes are pathognomonic of hyperparathyroidism, and, in one small series, these bone resorptive changes were present in 4 out of 5 cases of primary hyperparathyroidism with skeletal manifestations.[1] The roentgenographic demonstration of such acromioclavicular changes readily excludes various other clinical conditions which may mimic hyperparathyroidism. But, as was pointed out by Nathanson and Slobodkin,[47] these changes are observed in both primary and secondary hyperparathyroidism and are, therefore, of no aid in the differentiation between the two types. However, in cases which exhibit these acromioclavicular changes and in which bone "cysts" can also be demonstrated by x-ray films, a diagnosis of primary hyperparathyroidism should be seriously considered. There have been very few reports of gross bone "cysts" demonstrated at roentgenologic examination or at gross pathologic examination in cases of secondary hyperparathyroidism. With very few documented exceptions (Table III), cysts when present were determined only by microscopic examination. Albright[49] is not sure that he has ever seen cystlike lesions in secondary hyperparathyroidism. Gilmour[50] in his detailed studies of 90 cases, with careful correlation of the pathologic changes in the bones and in the parathyroid glands attributable to renal disease, found no cysts in any case in the series. The demonstration roentgenographically therefore, of lytic bone defects coupled with the characteristic acromioclavicular changes quoted previously favors a diagnosis of primary hyperparathyroidism.

Summary

The clinical course and autopsy observations of a case of primary parathyroid adenoma with extensive bone involvement and coincidental hyperplasia of the other three parathyroid glands secondary to an independent chronic pyelonephritis are presented.

Gross bone cysts are exceedingly rare in secondary hyperparathyroidism. Distinctive acromioclavicular resorptive changes were described by Nathanson and Slobodkin[47] in hyperparathyroidism, primary or secondary. The demonstration of bone cysts by x-ray films or at gross pathologic examination, coupled with these characteristic acromioclavicular changes, favors the diagnosis of primary hyperparathyroidism.

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Executives no more prone to illness than nonexecutives

Business executives are no more subject to the stress diseases of high blood pressure, heart disease, and ulcers than nonexecutives, according to a study conducted at E. I. Du Pont de Nemours & Co. and reported by Allan J. Fleming, M.D., in *Advanced Management—Office Executive.* Comparing the blood pressure, body weight, serum cholesterol, and smoking habits of executives and nonexecutives in a study group of 1,585 salaried employes, forty to sixty-four years of age, there was no significant difference in the prevalence of high blood pressure, overweight, and excessive cholesterol.

"As a result of our studies we feel that we can assure the up-and-coming young executive that the risk of developing stress disease as he climbs the executive ladder is in no way increased by the climb. In fact, the statistical risk of developing such disease is slightly decreased the higher he climbs."

Considerations on Autism in Infancy and Childhood

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THE PATIENT was two years old when she was initially observed psychiatrically and the diagnosis of early infantile autism was given. A home visit was made for the purpose of obtaining the diagnostic advantages of studying the child in her natural environment and to glean the additional advantage of observing her without the increased degree of anxiety concomitant with a visit to the doctor's office.

She was a beautiful child with long blonde hair and expressive facial features. There was no air of sadness in her facial expression. Her movements were quick, agile, and even rather graceful.

She had not yet begun to walk or say words, which state of affairs evoked the mother's overwhelming concern and fear that she was retarded. There were other important concerns, however, which will be described subsequently.

After her pediatrician found no physical basis for the delayed motor and speech development, she was examined thoroughly by a child neurologist, who also found nothing organically wrong. He told the mother that, based on the clinical picture, the child had the emotional and intellectual level of a fourteen-month-old child and was unamenable to psychologic testing.

During the course of the lengthy home visit, the child's general behavioral characteristics and responses were studied. There was the opportunity to see her behavior toward her father and her four-year-old sister, but the focus of the observations was on the vital mother-child interactions.

An attempt will be made to describe a series of events during the home visit. It is obvious, however, that only certain specific behavioral areas could be concentrated on because of the limitations of the powers of human observation in the face of the multiple complex emotional processes that are in operation at any one given moment.

Home visit

On my entering the home, the child was noted to be dressed neatly and comfortably and was alone in the corner of the room. She had no toys and was lying on the floor, uttering vocal sounds of an unintelligible nature. She did not turn about to evince any interest as I entered the household. The mother perceived this and remarked that her behavior was unpredictable, as she sometimes exhibited a fear reaction toward visitors.

The child's mother picked her up. There was no withdrawal response. In fact, the child cuddled in and clung to her mother. The mother remarked that the neurologist did not believe that the child was autistic because of this emotional responsivity which he had observed in his office. When I smiled and made other verbal overtures to her, the child returned the smile and responded in a coy and almost charming fashion. This was elicited only when her mother held her. When she was given to me to hold, she quickly became tense, cried, and pushed me away promptly and forcibly. She lunged for her mother and stopped crying when her mother retrieved her. On being handed to her father, she did not panic but pulled away gently and leaned toward her mother.

Excessive mouthing activity predominated throughout the entire observation period. As she crawled quickly and agilely along the floor and came on multiple objects, such as toys, furniture, and so forth, she invariably placed her mouth to the object or, if it was small enough, grabbed the object and put it in her mouth. Occasionally she pulled herself up to her feet to bite or suck parts of furniture which she could not reach otherwise. Table tops, arms of chairs, and the ivory teeth of the piano were mouthed in this way. Her mother revealed that she definitely preferred cold, hard objects to soft or cloth objects. She especially enjoyed being in the kitchen where she could mouth pots, pans, strainers, and other cold, hard objects.

During one interval she pounded vigorously and rhythmically on the top of a table. This muscular activity alternated with placing her mouth on the table top for a brief moment. Her mother revealed that she had begun this rhythmic pounding activity only recently.

The room in which we remained primarily had two doorways, each with a wooden accordion-type gate. The child screamed if the gates were closed; she wanted freedom to crawl about the entire house. It was noted that just prior to the closing of the gate the child was content and preoccupied absorbingly in mouthing a wooden toy object. However, the closing of the gates alerted her and was a stimulus for her to wish to go into the room beyond. She scrambled frantically to a gate, screaming.

Generally speaking, I would say that the child was rather unaware of my presence except for the time of my active overture to her while she was in her mother's arms. There was no curiosity or desire to get into any sort of physical or emotional contact with me. On the other hand, a fear of me was apparent on the one occasion when I held her momentarily.

During the early part of the home visit, her mother carried her. Once, when she was placed on her feet, an interesting series of events followed: The change seemed to be too sudden for her. She appeared startled and trembled with anxiety, and fear was clearly on her face. She stood perplexed for a few seconds and then screamed. Her mother responded by picking her up, whereupon she quieted down. This terror response was quite impressive.

On one occasion her sister came over to give her a hug. There was little response. It was almost as if she ignored this activity. It was obvious that there was an intense longing for physical and emotional stimulation from her mother to the exclusion of everybody else.

The child's mother was responsive, solicitous, and perceptive. If the child cried, her mother went to her, spoke to her in a soothing fashion, and usually picked her up. The child responded by clinging, by being comforted, and by stopping from crying. The child's mother revealed that this behavior was atypical and that she ordinarily was self-absorbed and rather disinterested in body contact, but that she had become much more demanding of ministrative attentions recently. The gradual change from autistic to symbiotic behavior had coincided with a changed approach toward her which will be described subsequently and which had been in effect for about four weeks at the time of the home visit.

Developmental history

In discussing the child's developmental history it was elicited that she was a desired and planned-for child. Her sister was two years old when she was born. The parents would have preferred a son, but the evidence indicates that she was accepted lovingly. The gestational period, labor, and delivery were uneventful. Natural childbirth was experienced, and breast feeding was instituted.

The child's mother noticed lethargy from almost the very outset. There were no breast-feeding disturbances. As a matter of fact, it was accomplished with greater ease than for her first baby, who had some difficulties at the breast.

The child was a quiet, contented, and nondemanding baby. This was accepted with relief by the parents, since their first baby had been fretful, hyperactive, and demanding. The parents' approach to the first daughter had been to indulge her and keep her as free from tension as possible. Therefore, they had devoted themselves completely to the baby. This program required a tremendous outlay of energy. The mother described herself as a reactor rather than an initiator in her upbringing philosophy. If the baby's demands were great, the reactions of the mother were equivalent. On the other hand, if she was quiet, she seldom approached her to minister or initiate emotional interplay. This philosophy had resulted in a fine, sturdy, emotionally healthy responsive first child.

The passivity and quietness of the patient were not perceived as stimuli but as a lack of stimuli. Maternal ministrations toward her, therefore, were much less than with the first baby.

As with the first baby, a pacifier was soon initiated, but the patient desired it less than her sister. There was a lack of energy and spark. The mother remembers that the smiling response commenced rather late, "certainly later than my first baby." The mother noted that "she was not a baby you could warm up to." Furthermore, the mother said that "she tended to be aloof and cool." Also, "she wasn't much fun to take care of."

Her physical development was delayed. She sat with support no sooner than eight months. She did not make attempts to stand. "She seemed to be frightened of anything new."

When the child was one year of age the mother developed a series of upper respiratory infections which moderately incapacitated her. It was stated by the mother that at about this time a new maid was "not warm and affectionate. She took care of all the physical needs, but seemed to be more affectionate to my older child."

The inauguration of new foods was always reacted to with anxiety and difficulty. At about one year with the mother's active encouragement, the child attempted to drink from a cup. But, according to the mother, she became frightened at the liquid at the bottom of the cup. From that time on she refused to drink from the cup but mouthed it instead. The child's mother generally tried rather hard to institute new functions, but her efforts were met consistently with enraged crying and aggressive balking. The insistence on sameness was tremendous. New foods were met with violent resistance. Her mother recalled that "she became confused and couldn't make up her mind whether or not to put a new food in her mouth. She showed frustration and screamed."

The child never exhibited any interest in other children. She had no fear or shyness and would approach them, but no emotional contact would be made. She reacted to them as impersonal objects.

She evinced no interest in building things, putting rings on sticks, or stringing beads. All objects were mouthed, and she rigidly preferred the same corners, shoes, plates, or kitchen utensils. She approached the world with her mouth, which functioned as a kind of sensory organ.

At about one and a quarter years, activity in walking became manifest. In addition, there appeared some greater language proclivities. She began to say "Nana" and "Mama." However, both maturational advances were soon forsaken, and she regressed to crawling and uttering unintelligible sounds.

Disturbances prevailed in practically all developmental areas. Physical development, eating, playing, emotionality, language, and even sleeping were atypical. Regular routines were never achieved. She became hungry or tired at different hours on different days. It could never be predicted, for example, whether or not she would be tired and nap on any particular day. Active attempts by her mother to regulate her were reacted to by fantastic rages, crying, and resistances.

The changed approach commenced when the mother actively introduced cuddling, loving, and anaclitic contact in spite of the lack of demand for it. She held the child often, walked around the apartment with her, and devoted the greater part of the day to playing and being in contact with her. Guilt and worry as well as a constructive effort to see if this would be beneficial prompted this changed approach. The child responded by changing gradually from self-sufficiency to clinging demandingness. The response was cogwheel-like; that is, a very definite initial resistance (autism) was present, but once it was overcome, it was followed by an opposite reaction (symbiosis).

Toward her father, who incidentally was consistently very attentive, the child remained cool. At the time of the home visit he had been home one week after a two-week hospitalization for elective surgery. He stated that he was "tremendously hurt" when the child reacted with coldness and an apparent lack of recognition on his return home. He revealed, however, that she began to warm up to him a little following an extraordinary amount of active playing, hugging, loving, and cuddling. The focus of her recent demanding, symbiotic behavior, nevertheless, was on her mother, who accepted this change and was somewhat encouraged.

Comment

The syndrome of early infantile autism, as described by Kanner,[1–3] is characterized by a lack of need for emotional contact. This results in isolation and delayed or absent speech development, for the urge for emotional contact is the driving force behind the need for acquisition of communication, that is, speech. In addition, obsessive-compulsive symptoms, extreme inflexibility, and an obsessive insistence on sameness, characterized by an aversion to anything new, are prevalent. The prospect for adequate adjustment in later life is generally poor, but the degree of attainment of speech appears to be the most sensitive indicator as to the prognosis.[1] The cause of the syndrome is believed to be based on certain innate constitutional deficiencies in conjunction with a rejecting, cold environment. The mothers of autistic children have been described as distant and cool.[2,3]

Mahler[4] has described another type of infantile psychosis, symbiotic infantile psychosis, in which the infant cannot separate the mental representation of its body ego from the mother, which results in a delusion of oneness with the mother and consequently in an overwhelming separation anxiety. The perception of separateness from the mother precipitates attempts at restitution characterized by bizarrely distorted reality testing, hallucinations, and deviant maturation. At a later stage, autistic mechanisms superimpose themselves on the symbiotic process and vice versa. Thus, there is a definite relationship between autism and symbiosis.

In a recent publication Mahler and Furer[5] have postulated that there are three phases in normal development: (1) a normal-autistic phase in which the infant has not yet become aware of anything beyond his own body; (2) a "symbiotic phase" in which "the mother is still a part of his own representation"; and (3) a "separation-individuation" phase in which "the infant gradually becomes aware of his separateness." Thus the infant or child with an autistic infantile psychosis has not developed beyond the autistic phase, and the infant or child with a symbiotic infantile psychosis remains primarily fixated in the symbiotic phase. The treatment endeavor is to engage and maintain the child in a "corrective symbiotic experience." It is hoped that current research will throw additional light on this area.

Let us focus and concentrate our attention on this one case of autism. The patient was not an undesired child. Her coming was pleasantly anticipated. She was breast-fed. Her mother was not a cold and rejecting person. In fact, she and her husband lavished considerable love and affection on their first child who subsequently developed normally and sturdily. The mother believed that a baby required a great deal of "putting into" but that after about three months "the baby would begin to become an emotional being." This expected affectionate responsivity never occurred in the patient in spite of the close physical contact of smooth breast feeding. The smiling response was late and sluggish. "She was no fun to take care of," and "She was passive." Moreover, at three or four months the usual anticipatory posture preparatory to being picked up was absent.

Why was the child passive and quiet? Why didn't she begin to cry or demand to be held, comforted, changed, fed, and so forth? Why didn't she reach, stretch, yearn, pull, yell, gaze, and vociferate more actively and vigorously? The child's older sister had demanded things, and her mother had responded promptly and had felt personally gratified with these ministrations. A strong series of emotional interaction experiences had existed between the mother and the first baby. This first baby's smiles had evoked feelings of warmth and love from the mother. Her cry of discomfort had brought a quick maternal response of trying to discover and eliminate its source. When the baby was happy and contented, the mother tended to be less tense, and the converse was true.

With the second child there were no discernible mother-baby interaction problems during the breast-feeding phase. Sucking behavior was adequate and was accepted pleasurably by the mother. Actually, the routine ministrations of caring for her were not resented in any way. However, there was a relative lack of strong affectionate outflow from the mother toward the child, probably owing to the baby's deficient emotional responsivity, for, as emphasized by Coleman, Kriss, and Provence,[6] the attitudes, feelings, and behavior of the mother toward her child are influenced and affected enormously by the reactions, emotionality, and personality of the child. They state:

> The child that readily accepts the cuddling of the mother will elicit different responses in her than the child that refuses such intimacy, is difficult to comfort, and does not adapt to the mother's body. Observations which would take such differences into account are few; they have to cope with a large number of variables. To illustrate opposites, we refer only to two approaches in current child psychiatry: the one considers severe childhood disturbances largely, if not solely, as the product of the behavior of certain mothers, and here the term "schizophrenogenic mothers" has arisen; the other views the mother's behavior also as response to a child that does not or cannot adequately respond to her. Obviously both factors interact, and their interaction has to be studied.

My contacts with the present case left me with a necessarily impressionistic but definite opinion, namely that this child must have been innately endowed with some sort of vaguely incomprehensible emotional deficiency or maturational defect which was interfering with her capacity to yearn for affection or to feel loved and which was associated with a fantastic degree of crippling anxiety.

Mahler[4] writes:

> In regard to the question of heredity versus early frustrational traumatic etiology of infantile psychosis, we may say that it is very difficult to ascertain whether the grave disturbance in the case of early infantile psychosis has been caused by the mother's pathology and lack of empathy or by the infant's great innate ego-deviation, be it an inherent lack of contact with his living environment or an inordinate need for symbiotic parasitic fusion with the adult. It is a fact that time and again we see schizophrenic children whose mothers appear not to lack warmth, genuine love or acceptance of the individual child, nor do they appear to be exceptionally possessive, infantilizing and restrictive. Human nature provides a mutuality between the infant and his mother by which, on the one hand, severe traumatization, chronic emotional starvation on part of the environment, seems to damage a constitutionally sound baby only if the baby is very young; on the other hand (as the famous Dennis experiment has shown and as every-day life experience demonstrates), the constitutionally sound baby, beyond the fourth, fifth or sixth month automatically coerces the adult's empathy.[7] The infant's contact-seeking gestures appeal to women's most basic biological longing. Hence emotional gratification as well as food are readily given unless maternal psychopathology has rendered the adult partner unable to respond. In other words, it seems that such basic damage to the ego which results in infantile psychosis, occurs in children who have a hereditary or constitutional "Anlage" for it, or in whom an intrinsic factor is prevalent.[4]

In the present case the clinical evidence supports the view that the mother was capable of a warm responsivity, was not an icy person, and would have emoted more had the baby expressed sufficient signs of wanting.

Assuming that a constitutional "anlage" for autism was present, could this defect have been ameliorated or reversed had the child's mother acted in an extraordinarily loving way, that is, had handled her, picked her up, and cuddled her during those first few months of life? In other words, could this silently operating malignant process have been reversed by extra maternal loving behavior? This is a very important issue, since the child's mother would certainly have indulged her had she been alerted. We have seen how her recent indulgent activities resulted in a beginning change from autistic to symbiotic behavior.

What are the behavioral characteristics of neonates who later develop autism? The answer to that question is unknown since, as a rule, the autistic process is not discovered before two to three years of age. We do not know the essential nature of the neonatal behavioral responses: sensitivity thresholds to auditory, visual, tactile, and kinesthetic stimuli; degrees of crying; general tension levels; muscle tonus; grasping reflexes;

sucking behavior; rhythmicity of muscular movements; and general activity levels. These observations, I believe, are essential for a total understanding of the condition.

Once having established itself, the autistic position is violently defended by catatonic-like temper tantrums and rages.[8] This results in the obsessive insistence on sameness and the preoccupation with the old and tested. Any innovations are anathema. The child exhibited this phenomenon via her refusal to allow her mother to introduce new foods, mouthing behavior (oral fixation), and her preoccupation with particular toys, shoes, plates, and even specific locations or corners in the home. She tenaciously fought her mother's attempt to initiate the drinking cup and to wean her from the bottle.

If, as Mahler[4] believes, autism develops because the infantile personality "is unable to cope with external stimuli and inner excitations which threaten from both sides its very existence as an entity," this obsessive insistence on sameness is understandable. The child's delayed walking can be explained on this basis, as evidenced by the panic reaction when she was placed on her feet unexpectedly by her mother.

The child's mother was loaded with guilt. She blamed herself for her daughter's maturational delay and mental difficulties. "If only I had picked her up and fondled her more often, she probably wouldn't be this way now. She must have been a depressed infant," she mourned. Her self-accusations and suffering were acute, and she found ample popular literature which emphasized the thesis that a child's personality is mainly the result of the environment and especially of the maternal responses. Her main concerns, however, were constructive. They consisted of wanting to enlighten herself on measures to help or correct the situation. This was additional evidence of her nonrejecting nature.

Conclusion

Many therapists believe that the basic autistic process can be reversed in infancy and childhood with a therapeutic regimen based on the attainment and maintenance of an anaclitic relationship with a consistent love object. However, this is unproved. Perhaps this position is preferred to capture and sustain the atmosphere of therapeutic optimism which is so necessary for the tremendous treatment effort which these cases demand. It is true that a case seldom presents itself in which the mother is excessively indulging, stimulating, or cuddling, but is it not likely that it is impossible to cathect maternally and libidinally an unreciprocating object for a consistent period of time?

The child's mother plans to continue the active, loving, and indulgent approach. She will require great support and encouragement from everyone around her, as this task is unbelievably difficult. Of course the results are unpredictable, for the outcome is probably unique in every case.

Finally, if it is true that there is an intrinsic factor in children who develop autism, the child's mother should be enlightened of this, if only to alleviate the burden of her enormous guilt. Perhaps then she will be freer possibly to help the child. For, an anaclitic regimen based on excessive guilt inevitably must have a hostile matrix.

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Volvulus of the Splenic Flexure and Tension Pneumoperitoneum Complicating Routine Cesarean Section

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FATAL COMPLICATIONS of elective cesarean section are no longer as frequent as they were prior to the era of modern surgery and antibiotics. Yet, today, complications of a less serious nature continue to plague the obstetrician. D'Esopo,[1] reporting on 1,266 cesarean sections performed at the Sloane Hospital for Women during the period 1942 to 1947, found no maternal deaths, but a morbidity* of 48.5 per cent. A review of the same statistics for 1953 to 1957 shows 1,670 sections, again with no maternal mortality. Morbidity, however, remains high, being 47.5 per cent on the ward service, and 18 per cent on the private service, giving a combined morbidity of 35 per cent. Other work has shown that the primary elective section is accompanied by almost twice the morbidity of repeat sections.[2] Among the most common complications are uterine or abdominal sepsis, adynamic ileus, urinary tract infection, hemorrhage, wound infection, dehydration, thrombophlebitis, and rarely pulmonary embolism. Gastrointestinal complications, with the exception of adynamic ileus, are rare, and acute obstruction in the immediate postoperative period requiring exploration is as yet unreported. Pneumoperitoneum complicating an intestinal obstruction without demonstrable perforation, particularly when following a routine cesarean section, is equally uncommon.

The purpose of this article is to report a volvulus of the splenic flexure of the colon, followed by a spontaneous tension pneumoperitoneum in the absence of bowel perforation, both occurring in the immediate postoperative period of an uneventful tertiary cesarean section and bilateral tubal ligation. Although the likelihood of such events occurring again following a cesarean section is remote, the paucity of operatively proved splenic flexure volvuli in the literature makes a report of this case worth while. In addition, the occurrence of a spontaneous pneumoperitoneum adds to the interest and provokes speculation.

Case report

A thirty-one-year-old Negro, gravida 3, para 2, was admitted to the Obstetrical Service of the Sloane Hospital for Women on December 1, 1958, for an elective tertiary cesarean section and bilateral tubal ligation. Her last normal menstrual period had been March 6, 1958, giving her estimated date of confinement as December 13, 1958. Her antepartum course, other than for a weight gain of 37 pounds, had been benign. Her pelvis had been typed previously as flat-gynecoid. The past history revealed that she had always been obese, weighing 251 pounds in her second pregnancy. Gastrointestinal symptoms were denied. In 1951 she underwent her first uneventful Phaneuf cesarean section because of a borderline cephalopelvic disproportion complicated by a face presentation. Her second section in 1955 also was uneventful except for a postoperative pyrexia lasting for six days and attributed to pulmonary atelectasis.

A physical examination revealed an obese, gravid Negro female weighing 207 pounds. Her blood pressure was 84/62. The cardiorespiratory system was normal. The abdomen was markedly obese with the uterine fundus extending to within 5 cm. of the xiphoid and a term-size infant in the vertex

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* Morbidity is defined by the United States Committee on Maternal Welfare as a temperature of 100.4 F. occurring on any two days of the first ten days postpartum, exclusive of the first twenty-four hours.

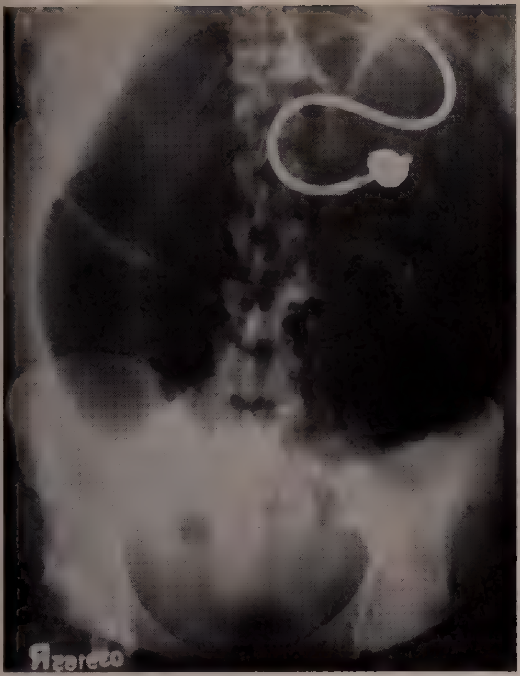

FIGURE 1. Flat film of abdomen six days following section showing massive distention of proximal large bowel with what appears to be a distended redundant transverse colon. No gas is seen in sigmoid or rectum.

presentation. No abnormalities were noted in the remainder of the physical examination. The blood and urine studies were reported as showing normal findings.

On the third hospital day she underwent an uneventful tertiary low-flap cesarean section under nitrous oxide and succinylcholine anesthesia, giving birth to a 3,030-Gm. living female infant. The uterus was closed in two layers, and the visceroperitoneum was closed over it with catgut. A bilateral Pomeroy tubal ligation also was accomplished. At no time was the bowel handled, nor were any abnormalities noted. Postoperatively, the patient ran a low-grade fever attributed to pulmonary secretions which were cleared poorly. The bowel function was returning slowly with the passage of flatus, and a spontaneous bowel movement followed a colon lavage. On the afternoon of the sixth postoperative day her temperature spiked to 102 F., and she had increasing abdominal distention with crampy pain. There were marked tympany and hyperactive bowel sounds, but minimal tenderness. A pelvic examination produced unremarkable findings. The white cell count was 11,300 with 79 per cent neutrophils. A Miller-Abbott tube was inserted. A flat film of the abdomen (Fig. 1) revealed massive distention of the proximal colon. An emergency barium enema was performed showing a normal descending and sigmoid colon, but there was no good filling of the large gas shadow proximal to the splenic flexure, although a small amount of barium did reach the cecum. Attempts at decompression from below were unsuccessful, and an exploratory laparotomy was performed without further delay.

At surgery, the large bowel proximal to the splenic flexure was distended markedly with a redundant U-shaped segment of transverse colon. At the splenic flexure there were adhesions extending to the inferior surface of the diaphragm and the lateral parietal wall, resulting in an axial volvulus with but a slight twisting of the flexure itself, giving rise to a nearly complete obstruction. The adhesions were lysed, the volvulus reduced, and the colon decompressed from below by means of a rectal tube. The bowel was inspected carefully, and no areas of necrosis or ischemia were recognized, but the transverse colon remained redundant on a long mesocolon. The pelvic organs were seen to be healing normally. The incision was closed using wire and retention sutures, while the skin and subcutaneous tissues were packed open with china silk.

Following this operation the patient was started on chloramphenicol (Chloromycetin), although subsequently the cultures were reported as being negative. A continuing low-grade temperature up to 100.4 F. persisted, again attributed to the pulmonary secretions detected on the physical examination. The white blood cell count ranged around 11,500 with 81 per cent neutrophils. The Miller-Abbott tube was removed on the fourth postoperative day following the return of normal bowel sounds and the passage of flatus. By the sixth postoperative day the patient was taking a soft diet, having spontaneous bowel movements, and generally feeling well. However, her temperature again spiked to 102 F., and her abdomen was becoming increasingly

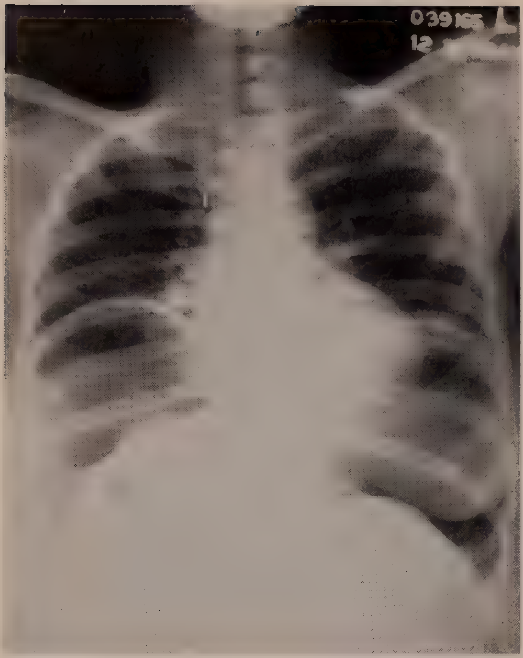

FIGURE 2. Anteroposterior chest film six days following laparotomy showing a large accumulation of free intraperitoneal air and bilaterally elevated diaphragms with a great amount of air between liver and diaphragm.

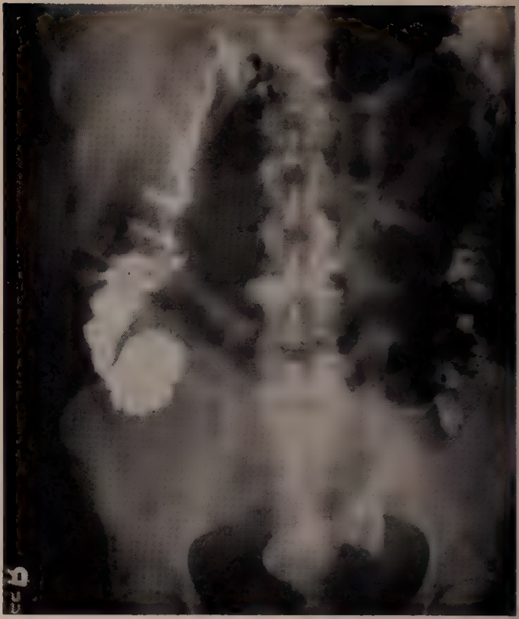

FIGURE 3. Flat film of abdomen six days after laparotomy demonstrating Rigler's sign, with essentially normal colon as outlined by residual barium. Suggestive but not a conclusive demonstration of pneumatosis cystoides intestinalis.

distended despite the normal bowel sounds and the absence of tenderness. Marked tympany and distention with compromised respirations were the predominant physical findings. No evidence of peritonitis could be elicited. An x-ray film of the chest (Fig. 2) on two successive days showed increasing amounts of subdiaphragmatic air. A flat film of the abdomen (Fig. 3) demonstrated Rigler's sign* of pneumoperitoneum but an essentially normal-appearing colon. An upper gastrointestinal series was performed using Renografin, but no perforation or other abnormality was noted. An examination of the operative wound showed 50 per cent healing with a clean granulating base.

Because of increasing distention and the patient's discomfort, a paracentesis was performed which released from the peritoneal cavity approximately 3,000 cc. of odorless gas, initially under some pressure. Chest and abdominal films taken the next day (Fig. 4) showed no reaccumulation of gas, but there was a left pneumonitis, presumably accounting for her fever. Throughout the entire episode the patient felt well and never showed the septic signs of intestinal perforation.

Following the release of the accumulated gas, the chloramphenicol was discontinued, and on penicillin and streptomycin therapy her temperature returned to normal. She was discharged asymptomatic on the twenty-seventh day following the cesarean section.

Comment

The course of events in this case is certainly unusual and warrants discussion under two headings.

Volvulus of the splenic flexure. A review of the literature reveals only 5 previously reported cases. Buenger in 1954[3] reported the first 2, both females, one of which was somewhat similiar to this case in that adhesions were found extending from the splenic flexure to the parietal wall. His

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* Rigler's sign: The bowel wall is clearly delineated by air appearing on both sides in double contrast. Diagnostic of pneumoperitoneum.

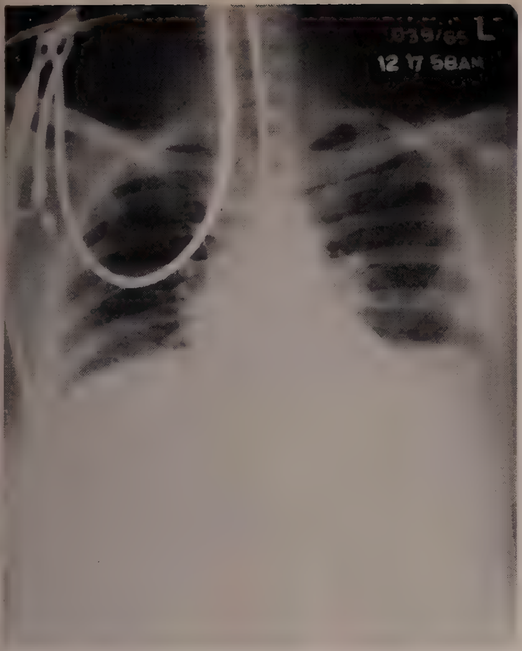

FIGURE 4. Anteroposterior film of the chest one day following abdominal air paracentesis showing no reaccumulation of air and a left basilar infiltrate, presumably accounting for the patient's fever.

second case was diagnosed by x-ray examination, but the patient did not undergo surgery. Young[4] reported another case with adhesions to the lateral portion of the diaphragm, causing an axial torsion in a male who previously had a cecal volvulus reduced. Poppel, Zeitel, and Abrams[5] added 2 more cases in 1956. One was secondary to agenesis of the gastrocolic ligament with lateral peritoneocolic attachments, and the second had a short mesocolon with a benign stricture in the sigmoid. Both were treated successfully by partial colectomy. The case reported here is thought to represent the sixth reported case.

Gerwig, in 1950,[6] reviewed the literature on colonic volvuli and found that only 3 per cent of large-bowel obstructions in the United States were due to torsion. (Enigmatically, this figure may be as high as 30 per cent in Scandinavia.) The most common point of rotation is the sigmoid colon, being twice as common as that of the cecum. Gerwig reports no case of volvulus of the transverse colon or its flexures. To have conditions conducive to volvulus there must be: (1) an elongated mesentery with movable bowel, (2) the absence of the mesentery with mobile bowel, (3) closely approximated points of attachment, or (4) two limbs of bowel close together. Thus, the rarity of flexure volvuli is understood readily when one considers the normal shortness of the mesocolon in the region of the transverse colon and the widely separated points of attachment of the hepatic and splenic flexures.

However, in the transverse colon and its flexures there is a second possibility for volvulus—axial rotation. As Figiel and Figiel[7] have suggested, this is probably the main mechanism involved, and only when redundant limbs of the transverse colon on a long mesocolon are present can true rotation about one another occur. One of the pathognomonic signs of volvulus in this area is a gas-distended proximal transverse colon with conization both proximally and distally which fits with axial rotation about a fixed posterior point. In every torsion of the bowel about its mesenteric axis there is also a component of axial torsion of the bowel itself about a point of posterior fixation, and the axial torsion is twice as great as the torsion of the mesentery. Thus, with only a slight torsion initiated by adhesions of the splenic flexure, the accompanying axial rotation of the redundant colon on a long mesocolon could result in partial to complete obstruction.

It would seem, then, that a volvulus of the splenic flexure can occur in two methods: either true rotation of the colon or by axial torsion, and neither of these can occur in this area without associated abnormalities. In the case presented here, the redundant mesocolon and the adhesions provided an ideal setting for axial torsion. The descending colon was naturally attached, but the adhesions provided a fixed point about which the transverse colon could twist axially, producing an obstruction. The relative fixation of the large bowel in its midportion precludes frequent volvulation, but with the continued increase of abdominal surgery and the formation of postoperative adhesions, this entity may become more frequent.

The symptoms of colonic volvulus are those of any large-bowel obstruction except volvuli of the cecum, when the symptoms are naturally those of small-bowel obstruction. The treatment is mainly operative by surgical intervention and should be prompt when the obstruction is complete, since the mortality may be as high as 23 per cent in total colon obstruction.[8] The resection of the bowel is mandatory when irreversible vascular changes have occurred, but otherwise the success of the operation depends on the fixation of the mobile portion to prevent a repeated volvulus. When the twist is in the transverse colon, one should search distally for the obstruction.

SPONTANEOUS TENSION PNEUMOPERITONEUM. The occurrence of the tension pneumoperitoneum in this case is not explained so easily. Pneumoperitoneum, per se, is not uncommon and may be seen with a variety of conditions. The perforation of some portion of the gastrointestinal tract is the most common cause, and perforating peptic ulcers account for roughly 90 per cent of all pneumoperitoneums.[9] Among other causes are: (1) residual air following laparotomy (usually absorbed in from four to seven days), (2) perforating abdominal wall injuries, (3) rupture of the urinary bladder, (4) diagnostic pneumoperitoneum, (5) subdiaphragmatic abscess, (6) pulmonary-peritoneal fistula, (7) entrance of air through the female genital tract,[10,11] and (8) pneumatosis cystoides intestinalis. A tension pneumoperitoneum presupposes a ball-valve type leak, and may occur with any of the previously mentioned causes. Hinkel[12] and Cunningham[13] reported a total of 6 cases of spontaneous pneumoperitoneum, 1 of the tension variety, for which they could find no cause. However, in only Cunningham's case was there no suggestive evidence for a cause, and this he termed idiopathic spontaneous pneumoperitoneum.

In the case herein reported, there is no absolute cause discernible, but by elimination one condition seems to explain most adequately the sequence of events. LeWald[14] demonstrated the reabsorption of up to 1,500 cc. of gas from the peritoneal cavity from four to eight days, so that air trapped at laparotomy and compressed by returning muscle tone could hardly explain the 3,000 cc. found in our case. An operative examination showing no compromised bowel, an x-ray examination, and the clinical picture militate against a visceral perforation. With a recent tubal ligation, the entry of air through the fallopian tubes seems unlikely, and the absence of urinary symptoms with the constant siphon action of a Foley catheter exonerate a ruptured bladder. A uterine air leak twelve days following the section seems at best a remote possibility. Conceivably, the wound which had been packed open to the fascia was acting as a sucking ball-valve fistula, but a careful examination showed a clean granulating base with no evidence of communication with the peritoneal cavity.

The explanation of this tension pneumoperitoneum, then, must remain labeled as idiopathic unless one accepts the statement made by several investigators that pneumoperitoneum, particularly tension pneumoperitoneum, in the absence of visceral perforation is pathognomonic of pneumatosis cystoides intestinalis.[15-17] The quantity of air seen here is compatible with the diagnosis, since Urban in 1910[18] reported a case with recurrent tension pneumoperitoneum in a thirteen-year-old girl requiring constant drainage of air for several days.

Pneumatosis cystoides intestinalis is a condition characterized by the appearance of multiple gas-filled sessile or pedunculated cysts involving portions of the gastrointestinal tract, which, as noted previously, may rupture, causing pneumoperitoneum. The disease may be primary, but more frequently is secondary to a pathologic condition elsewhere in the alimentary tract. The first case in a human being (a similiar disease was long known in swine) appears in Ruyish's *Anatomical Museum* dated 1737,[19] but the first well-documented clinical report is attributed to Bang in 1876.[20] Since that time approximately 250 additional cases have appeared in the literature. Since this case fits the criteria for diagnosis, the remainder of this report will be devoted to a discussion of gas cysts of the intestine.

Gas cysts of the intestine

Koss in 1952[21] cogently reviewed the literature reporting a total of 213 cases ranging in age from infancy to the eighth decade, with a peak incidence at age thirty to fifty in males and in the sixties for females, males outnumbering the females 3.5 to 1. In 85 per cent of the cases there is a pathologic condition in other portions of the intestinal tract, classically of a stenotic type with partial to complete obstruction, 58 per cent being a constriction at the pylorus due to gastric or duodenal ulcer. While the primary lesions are obstructive in most instances, gas cysts may follow appendicitis, enteritis, colitis, diaphragmatic hernia, intestinal parasites, peritonitis, and after end-to-end anastomoses. Most frequently the cysts are found in the small intestine, usually the ileum, but may be seen anywhere in the abdomen, including the mesentery. Usually they are subserosal in location, but may be submucosal which is characteristic in children. Pathologically, the lesion consists of multiple thin-walled cysts of varying size, filled with odorless gas under tension but no fluid. Endothelial cells, frequently seen to coalesce into multinucleated giant cells, line these cysts, and the impression is that of a foreign body reaction with acute and chronic inflammatory cells, often of the histiocytic group, present. Briggs, Sifre, and Overholt[22] advance the theory, based on microscopic studies, that these cysts are dilated lymph channels. An analogy has been drawn to the cysts seen in emphysematous vaginitis and cystitis.[21]

The etiologic background of this condition remains to be settled, but four main ideas persist.

Neoplastic origin. Gas is formed by malignant cells, but as yet none have been found.

Bacterial origin. The gas arises secondary to the activity of the organisms, but cultures fail to yield any consistent results, and the rupture of these cysts does not result in peritonitis.

Dietary origin. The theory of dietary origin has been quite popular, since in most instances cases have been reported in patients with altered nutritional states. Masson in 1925[23] theorized that the normally soluble carbon dioxide in the lymphatics of the bowel was released by a shift of bowel alkalinity to acidity through abnormal fermentation in the intestine, and that the carbon dioxide bubbles so released produced embolic effects resulting in obstruction and the accumulation of the gas. In addition, similar lesions can be produced in swine fed on nutritionally deficient diets. An analysis of the gas, however, fails to support this theory.

Mechanical origin. Perhaps the theory which has gained the greatest enthusiasm presupposes a break in the integrity of the bowel mucosa due either to overdistention or to an eroding process. With an increase in intraluminal pressure secondary to hyperperistalsis or obstruction, gas is forced through the mucosal defects into the lymphatic spaces with a rapid spread to distant parts of the bowel, forming cysts which not infrequently rupture either intra- or retroperitoneally. The tissue reabsorption of this gas is inhibited by obstruction and local inflammatory changes within the bowel wall, and accumulation continues. In instances where these changes are minimal or reversible the condition resolves spontaneously, following the alleviation of the inciting cause. This theory explains adequately why the cysts are associated more commonly with other gastrointestinal lesions, and it is supported by the microscopic picture. That the gas by direct analysis is not comparable to that of the intestinal lumen[18] does not invalidate the theory, for as Wright[24] has demonstrated, gases have a differential adsorption rate from subcutaneous tissues, which also may be true of the intestine. Furthermore, his microscopic studies show a similarity to the intestinal air lesions. Straus, by producing a closed-loop obstruction in dogs and then introducing air into the loop, found that this air made its way into the lymphatics where cysts appeared, some of which ruptured into the peritoneal cavity.[25] Yet, the mechanical theory does not explain the cysts so commonly seen either distal to or in the absence of obstruction or ulceration. Perhaps hyperperistalsis, so frequently noted in conditions associated with gas cysts, may play more of a role than is generally realized. In our present state of knowledge, however, it cannot be said that any one cause explains all the variations seen.

The diagnosis of the disease should suggest itself whenever idiopathic pneumoperitoneum is seen, particularly when an obstruction or ulceration of the intestinal tract without perforation is or has been present. Occasionally, tension pneumoperitoneum may be the first symptom. No specific symptoms can be ascribed to these cysts. Usually, they are those of the inciting cause. When primary pneumatosis has occurred, in addition to pneumoperitoneum, a complete spectrum of gastrointestinal symptoms has been reported, even to the occlusion of the bowel lumen either by the cysts themselves or by a volvulus caused by them. In most instances the diagnosis is rarely suspected but is discovered at laparotomy or by x-ray examination. A small percentage may show the characteristic radiographic appearance of translucent areas (gas in the cysts) lying within the contour of the normal bowel. When barium is used, the cysts may appear as multiple filling defects.

The treatment is nonspecific. In general, it consists of alleviating the predisposing intestinal abnormality, usually an obstruction or ulceration. Occasionally, as in the case reported here, it is necessary to relieve the symptoms secondary to the cysts themselves, that is, the tension pneumoperitoneum or obstruction. In all but a few cases the cystic condition is benign and self-limited, even though chronic and progressive courses have been reported.[21]

Summary

A report of a routine elective cesarean section and bilateral tubal ligation complicated by a volvulus of the splenic flexure and tension pneumoperitoneum without evidence of intestinal perforation is presented. While obviously a chance occurrence, the component complications are of sufficient importance to be reported.

The literature concerning splenic flexure volvulus is reviewed with a discussion of the principles involved. This case is thought to be the sixth reported to date.

The differential diagnosis of spontaneous pneumoperitoneum is considered in general and as it pertains to this case.

The evidence led to the conclusion that this was a case of pneumatosis cystoides intestinalis, and the literature is reviewed briefly.

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Chronic Constrictive Pericarditis (Pick's Disease)

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THE MISDIAGNOSIS of the symptoms of chronic constrictive pericarditis is still a frequent occurrence. Patients with the typical features of this syndrome still are being operated on for nonexistent hepatic disease or presumed gynecologic problems or treated for chronic congestive heart failure. It is of vital importance to recognize the basic difficulty in these patients because the myocardium in constrictive pericarditis remains intact, and after the removal of the constricting layer, the function of the heart returns to normal.

A basic reason for the frequent failure to make the correct diagnosis is the uncommon occurrence of this syndrome. The relative rarity of constrictive pericarditis is emphasized by the fact that Dalton, Pearson, and White[1] reported a total series of only 78 cases over a period of some twenty-six years, an average of about 3 cases yearly. However, it should be recalled that more than forty years ago reliable clinical methods were available to recognize the circulatory disturbances caused by constrictive pericarditis. The advances that modern research tools have made in the intervening years are necessary only to verify the diagnosis which is still made best at the bedside.

In the following patient, the development of ascites was the initial sign and was the cause of the patient's hospital admission to the gynecology department.

Case report

This was the first hospital admission of a forty-four-year-old white female with the chief complaint of a progressively enlarging abdomen for the previous four or five months. A weight loss of 7 pounds had occurred. She also complained that she had become more tired and slightly short of breath. She was admitted to the gynecologic service of the hospital with the impression that ascites, possibly due to ovarian carcinoma, was present. A cardiac murmur was discovered prior to surgery, and a medical opinion was requested.

There was no history of any previous illness, operation, or hospitalization. Rheumatic fever or any other cardiac disease was denied. The family history was not contributory, and a review of the systems was unremarkable.

The patient was a well-developed, thin, sallow, white female who did not appear to be in any distress. The blood pressure was 120/80, and the pulse was 88 and slightly irregular. The respirations were 20 per minute. The neck veins were distended, and there was further engorgement on inspiration. The lungs were clear. An examination of the heart revealed no enlargement and no thrill. Frequent premature contractions were present, and a loud third heart sound, the so-called pericardial knock, was heard early in diastole (see Comment). The first mitral sound was louder than the second mitral sound, and the second pulmonic sound was louder than the second aortic sound.

The abdomen was protuberant. The liver edge, palpable 4 cm. below the right costal margin, was smooth, sharp, and extended across the midline. The left lobe was relatively more prominent. The spleen was not palpable. No other organs or masses were felt, but shifting dullness and a fluid wave were present. There was no peripheral edema and no cyanosis or clubbing of the fingers. The patient was then transferred to the medical service for studies to verify the clinical impression that the ascites was due to a constrictive pericarditis.

On admission, her urine had a specific gravity of 1.020 with a trace of albumin. The hemoglobin was 12.3 Gm. per 100 ml., and the white blood cell count was 6,350

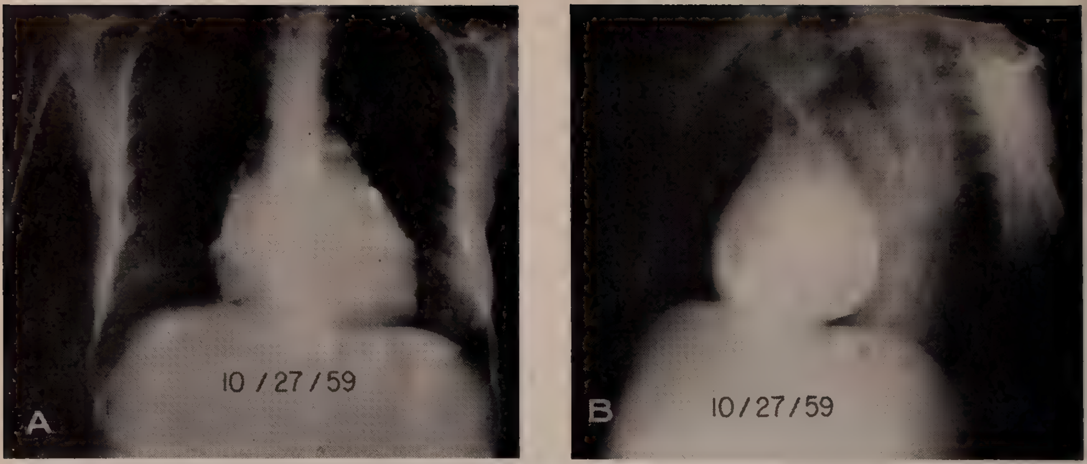

FIGURE 1. Chest x-ray films. (A) Prior to surgery showing clear lung fields and extensive pericardial calcification. (B) Oblique view showing the calcification like an eggshell around the anterior diaphragmatic and posterior surface of the heart.

with a normal differential. The hematocrit was 46, and the sedimentation rate was 18 mm. per hour (Wintrobe). The total serum protein was 7.8 Gm. per 100 ml. with 4.1 albumin and 3.7 globulin. The cephalin flocculation test produced negative findings, the thymol turbidity was 1.6, the alkaline phosphatase 5 Bodansky units, bilirubin 0.9 mg. per 100 ml., and SGPT (serum glutamic pyruvic transaminase) 20. A Bromsulphalein test revealed 21 per cent retention after forty-five minutes. The venous pressure measured 290 mm. and the circulation time 27 seconds (Decholin).

The roentgen examination of the chest did not reveal any enlargement of the heart. However, there was a fullness of the pulmonary artery segment and a double density in the region of the left atrium. Extensive calcifications were noted overlying the left lateral heart border and extending across the apex down to the diaphragm. The lung fields were clear without evidence of congestion (Figs. 1 and 2). An x-ray film of the abdomen revealed gaseous distention of the bowel "plus a haze possibly due to fluid."

An abdominal paracentesis was performed, and 2 L. of straw-colored fluid were removed. A cell block revealed no lymphocytes or malignant cells. The culture was sterile, and the protein content was 4.8 per cent. At a repeat gynecologic examination of the pelvis after the removal of the fluid, a normal uterus and adnexa were palpated.

The pressures recorded at cardiac catheterization are shown in Figure 3 and Table I.

All pressure curves were qualitatively abnormal with a significant diastolic plateau. The right atrial curve showed an "M" shape, and the ventricular pressure revealed an early diastolic dip and a rapid rise to a plateau which was equal to one half of the systolic pressure. The right atrial pressure was elevated. The wedge pressure at the right pulmonary vessels was reported as elevated with a prominent V wave and a slow Y descent. It was the opinion of the catheterization team that the abnormalities of the pressures registered in the right side of the heart confirmed the clinical diagnosis of constrictive pericarditis.

The electrocardiogram (Fig. 3) revealed a regular sinus rhythm, at a rate of 70, with a vertical axis. The P wave resembled a P mitral.

During this time the patient felt well, but it was noted that the abdominal fluid was reaccumulating, and so she was placed on diuretics, with an excellent response. The purified protein derivative showed negative findings at intermediate strength. Repeated examinations for a paradoxic pulse revealed equivocal findings with a fall never greater than 10 mm. Hg at the end of inspiration.

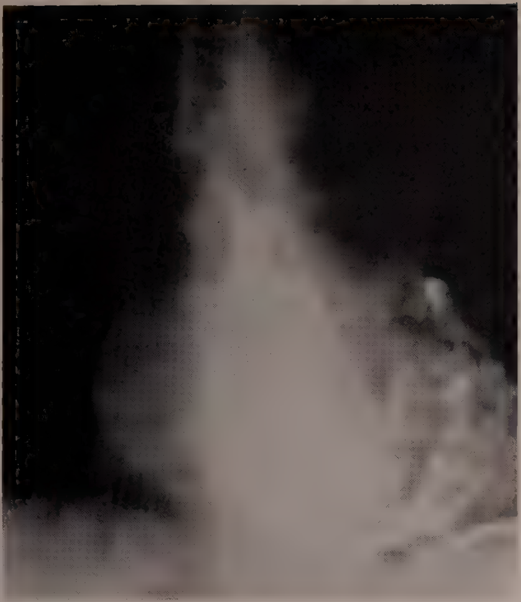

FIGURE 2. Spot film taken during fluoroscopy.

On the completion of the diagnostic studies, the patient was operated on by Charles Ripstein, M.D. The heart was completely surrounded by an adherent calcified pericardium, especially in the region of the right ventricle, with increasing calcification over the left ventricle. A very heavy calcific area was present at the auriculoventricular groove, and a heavy plaque covered the apex of the heart. The right auricle was enlarged markedly, and it was opened and explored. The tricuspid valve was normal. The venae cava were found to be completely free. No thrill was felt over the left side of the heart, and the left auricle was normal in size.

The entire anterior surface of both ventricles, as well as the diaphragmatic portion, was freed. Bone rongeurs were necessary in some regions for the decortication. Many necrotic areas were present.

The specimens sent for bacteriologic and microscopic studies revealed no acid-fast bacilli or pus cells. In one area a pseudoabscess cavity containing detritus entered into the myocardium. Some posterior plaques and a calcific plaque near the apex that penetrated into the myocardium were left because of technical difficulties. The pathologic report was "calcified pericardium with inflammation."

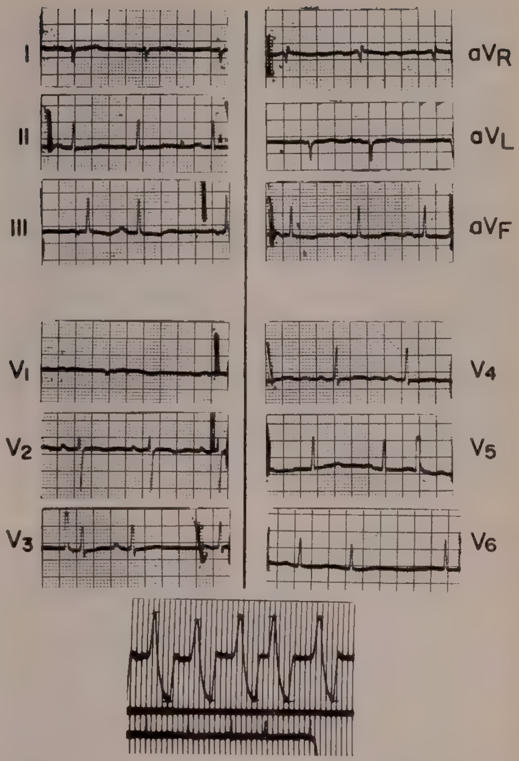

FIGURE 3. Electrocardiogram and pressure curve from the right ventricle at catheterization, showing the characteristic early diastolic dip and rise to a plateau.

TABLE I. Pressures recorded at cardiac catheterization

Site	Pressure
Right auricle	(21 mean)
Right ventricle	25/3
Main pulmonary artery	26/17 (19 mean)
Right pulmonary artery	(23 mean)

The postoperative course was complicated by jaundice which appeared to be due to hepatic insufficiency. Although 4 units of blood had been given during the course of the operation, no hemolytic reaction could be found. The pericardial "knock" disappeared following surgery, but the premature contractions remained. At the time of her discharge, two weeks after surgery, the lungs were relatively clear, no ascites was present, and the neck veins showed much less distention (Fig. 4). The liver edge was only 1 fingerbreadth below the right costal margin, and the left lobe of

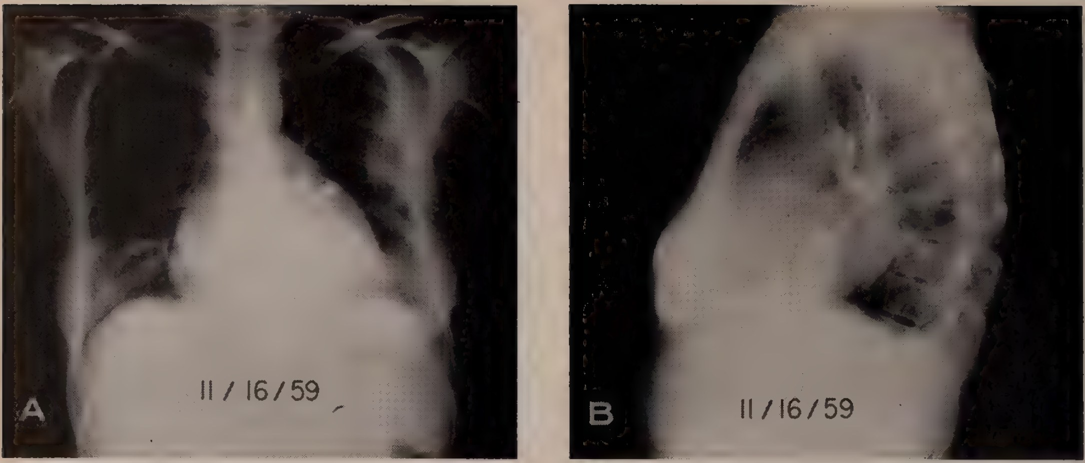

FIGURE 4. Chest x-ray films. (A) Following surgery. (B) Lateral view of chest with most of the calcification removed.

the liver was no longer palpable. The venous pressure was 210 mm. of saline.

Three months after surgery the patient stated that she "felt better than she had in several years." There was no dyspnea, even on moderate exertion, and the patient no longer complained of fatigue. There had been no recurrence of the ascites, and the liver had receded to the costal margin. The previously prominent left lobe had returned to normal size, and the venous pressure had decreased to 180 mm. of saline.

Comment

This patient's primary disease was recognized in time to prevent an unnecessary abdominal laparotomy. Reports of other patients with constrictive pericarditis who undergo unwarranted surgery continue to appear. If the syndrome of constrictive pericarditis were kept in mind, particularly the occurrence of ascites without dyspnea, these errors of diagnosis would not occur.

The causes of constrictive pericarditis rarely can be ascertained. With the declining incidence of tuberculosis the number of cases where microscopic and bacteriologic studies are unrevealing has increased rapidly.[2,3] At the present time, the nonspecific, idiopathic causes are responsible for the largest percentage of cases.

Increasing reports of the viral causation of these cases of so-called "benign idiopathic pericarditis" are appearing. Gillett[4] has compiled 20 cases in which the presence of a viral agent was confirmed. Sixteen were associated with Coxsackie virus B, type 5. Three cases were related to Coxsackie group B, type 3; and 1 case was found to be Coxsackie group A, type 1. Nine patients have been reported to have had pericarditis as a manifestation of infectious mononucleosis.[5] Eight cases associated with influenza virus A and B were reported by Adams.[6]

At the same time, it should be noted that some cases of benign pericarditis do not resolve, but progress to constriction.[7,8] Constrictive pericarditis as the end result of unrecognized acute hemorrhagic pericarditis has been reported as having a viral etiologic background.[9] These studies strongly suggest that a large number of cases may be related to an unknown and possibly asymptomatic viral infection.

Rheumatic fever is not a cause of this syndrome. Already known for many decades, this was re-emphasized by White[10] in the St. Cyres lecture in 1935. Nevertheless, textbooks continue to list rheumatic fever as a cause. The pericarditis in rheumatic fever does not go to constriction, but may leave an adherent, even fibrotic, pericardium which does not lead to the hemodynamics of constrictive pericarditis.

As a sequel to bacterial and suppurative pericarditis this disease has become infrequent since the advent of antibiotics. Occasionally, a traumatic hemopericardium will organize and result in constriction.[11] Exceptionally, cancer en cuirass, Hodgkin's disease, and histoplasmosis will give similar findings.[12]

Constrictive pericarditis (Pick's disease) consists of a heart imprisoned in a rigid cage that impairs diastolic relaxation, causing an "inflow stasis." The circulatory dynamics are determined mainly by the involvement of the right or left ventricle.

The symptoms are a progressive increase in the size of the abdomen due to ascites and enlargement of the liver.[13] Mild exertional dyspnea and early fatigue often are present, and palpitation and cardiac irregularities occasionally are found. Swelling of the lower extremities may be prominent. A loss of weight is usual. Although in typical cases ascites develops before marked peripheral edema is present, nevertheless in one series of cases studied, the symptoms listed in order of frequency were dyspnea, ankle edema, and abdominal swelling.[1]

Physical signs are plentiful. The nontender, nonpulsatile liver with ascites and engorgement of the jugular veins with or without evident pulsation are present in almost all patients. The venous pressure ranges from 250 to 350 mm., and generally the values are higher than those ordinarily seen in congestive heart failure. The circulation time is prolonged in both the systemic and the pulmonary circulation. Textbooks suggest that the size of the heart is small, but most patients have a normal or slightly enlarged heart. Dalton, Pearson, and White,[1] in reviewing the 78 cases previously mentioned, found hepatomegaly in 89 per cent, neck vein distention in 86 per cent, pleural effusion in 50 per cent, and ascites in 47 per cent. The heart size was normal in 46 per cent, minimally enlarged in 36.5 per cent, and definitely enlarged in 16.5 per cent. Normal cardiac pulsations were found in 21 per cent, and calcification of the pericardium was present in 60 per cent.

A very suggestive extra sound has been described in more than 50 per cent of the cases with or without calcification.[14] This extra sound, known as a pericardial knock, occurs early in diastole, during the period when, in the normal heart, the rapid diastolic filling of the ventricles takes place. It is believed generally that the knock is related to the restriction of the diastolic filling caused by the constricting pericardium. This knock is heard at the same time, or slightly after, the opening snap of a mitral stenosis.

The electrocardiogram may show low voltage with a slight elevation of the S-T segments. The T waves are isoelectric or inverted in leads I and II and may resemble the inverted T waves of a myocardial infarction. In 50 per cent of the cases broad, notched P waves are found with the second notch taller than the first. Perhaps this accounts for the P mitral reported in the electrocardiogram of the present patient.

Certain x-ray findings are highly significant. These include pericardial calcification best seen on lateral views of the chest and most striking in the dependent diaphragmatic portion of the pericardium and in the auriculoventricular groove.[15,16] These are also visualized on the x-ray films (Figs. 1 and 2). The heart shadow may appear small or somewhat enlarged because of atrial dilatation, since the atria usually are not constricted as much as the ventricle.[17,18] On fluoroscopy and roentgen kymography, the decreased cardiac pulsations of a heart which is unable to relax or contract completely may be seen.[19] Quite often the pulsations may be ample, as they were in our patient. The superior venae cava shadow is usually widened, representing the elevated venous pressure.

Cardiac catheterization has yielded new insight into the physiologic mechanisms involved. The characteristic right ventricular pressure curve[20] consists of a slightly elevated systolic pressure followed by a rapid diastolic dip with a high diastolic plateau.[21,22] This plateau is usually at a pressure which is greater than one third of the ventricular systolic pressure. It ranges from 6 to 32 mm. Hg. Further, there is an elevation of the pulmonic, systolic, diastolic, and pulmonary wedge pressures.[23,24]

There is no increase in the pressure gradient between the venae cava and the right atrium or between the right atrial mean pressure and the diastolic pressure of the right ventricle, excluding significant constriction of the auriculoventricular groove. The systolic contraction of the right ventricle usually is not impaired significantly unless there is myocardial atrophy. It is the diastolic relaxation which is interfered with and markedly decreased in constrictive pericarditis. This is responsible for the inflow stasis with an increase in the systemic and pulmonic venous pressure. With the prolonged increase of venous pressure, the circulatory blood volume increases.

It was thought previously that the constriction of the venae cava at their entrance into the right atrium played a significant role in the hemodynamics of constrictive pericarditis.[25] However, it has been shown by cardiac catheterization and measurement of the pressure within the venae cava and the right atrium that this is not an important factor in the circulatory disturbance.[21,24] Further, it was found experimentally by Isaacs, Carter, and Haller[26] that the constriction of the right ventricle in dogs produced ascites, hepatomegaly, and systemic venous hypertension, while the constriction of the right atrium produced no effect. If the left ventricle is constricted, signs and symptoms of pulmonary congestion develop.

An operation leads to a cure, or, at least, to a marked improvement in 50 to 75 per cent of the cases.[17] The over-all mortality is about 15 to 20 per cent. In most cases it takes from three to six months for the hemodynamics to return to normal.

Summary

The case presented was that of a forty-four-year-old white female with ascites which was found to be due to a chronic constrictive pericarditis, the cause of which could not be determined. There had been no history of tuberculosis, chest trauma, or acute pericarditis. An immediate clinical impression of constrictive pericarditis avoided an unnecessary abdominal laparotomy, and a pericardiectomy led to an excellent result.

A discussion of this disease entity is presented with special emphasis on the importance of the clinical diagnosis as well as the pathophysiology and etiologic background. The possible relation of chronic constrictive pericarditis to a pre-existent but unknown acute viral pericarditis is suggested.

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Hypoglycemic Cardiac Arrhythmia in Early Diabetes Mellitus

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CARDIAC IRREGULARITIES have been known to be associated with hypoglycemia, whether of endogenous or exogenous origin. This phenomenon has been attributed to hyperepinephrinemia,[1] myocardial anoxia,[2] and, less frequently, to the hypokalemia which accompanies peripheral glucose utilization.

Spontaneous hypoglycemia may be an early manifestation of diabetes mellitus, and this disease may herald itself by symptoms of hypoglycemia such as syncope, diaphoresis, mental confusion, and cardiac arrhythmias before overt manifestations of diabetes develop.[3,4] The following case, we feel, illustrates the aforementioned concepts.

Case report

This was the first admission to the Jewish Hospital of Brooklyn of a sixty-year-old white male clothing worker on December 10, 1959, because of recurrent episodes of syncope during the past five years.

The patient had been in good health until five years prior to admission, at which time he experienced an episode of syncope lasting several minutes following a large meal. He was asymptomatic for the next three and one-half years except for occasional, moderate, nonradiating precordial pain and mild dyspnea associated with exertion. In September, 1957, he experienced another episode of syncope following the ingestion of a heavy meal. These postprandial syncopal episodes were characterized by a sudden loss of consciousness, profuse sweating, and pallor. A spontaneous recovery usually occurred within a few minutes.

In May, 1958, after the completion of a heavy meal, the patient again experienced another episode of syncope accompanied by profuse diaphoresis. He was seen immediately by a physician who made a clinical diagnosis of myocardial infarction. This was not confirmed during the hospital observation. Four weeks prior to admission there was one other episode of postprandial syncope, but this was mild and lasted for only two to three minutes. The remainder of the patient's past history was otherwise completely noncontributory.

A physical examination demonstrated a well-developed, slightly obese white male who weighed 195 pounds. The pulse was 66 per minute and regular. The blood pressure was 140/80. Respirations were 18 per minute. The entire general physical and neurologic examinations were within normal limits. The electrocardiogram revealed nonspecific primary T-wave changes.

The laboratory studies were as follows: The hemoglobin was 14.7 Gm. per 100 ml.; the white blood cell count was 6,650 per cubic millimeter, with a normal differential count; the sedimentation rate was 13 mm. per hour (by the Wintrobe test); the hematocrit was 44; studies of the urine showed a specific gravity of 1,020, with negative findings for albumin, sugar, and acetone and with a sediment containing from 2 to 3 white blood cells per high-power field; the stool did not contain occult blood; the Mazzini test yielded negative findings; the blood urea nitrogen was 15 mg. per 100 ml.; the fasting blood sugar was 65 mg. per 100 ml.; calcium was

9 mg. per 100 ml.; phosphorus was 3.6 mg. per 100 ml.; the alkaline phosphatase was 3.6 Bodansky units; the acid phosphatase was 1.9 Gutman units; the total cholesterol was 254 mg. per 100 ml., with a normal ester fraction; the uric acid was 4.5 mg. per 100 ml.; the cephalin flocculation was 0; the thymol turbidity was 8 MacLagan units; the protein-bound iodine was 5.5 micrograms per cent; the total protein was 7.1 Gm. per 100 ml.; the albumin was 4.5 Gm. per 100 ml.; the globulin was 2.6 Gm. per 100 ml.; and the albumin-globulin ratio was 1.7.

An intravenous pyelogram revealed a possible right renal cyst. A gastrointestinal series revealed normal motility. The oral cholecystogram and skull roentgenograms showed negative findings. A chest x-ray film revealed a slight cardiomegaly with normal lungs. An electroencephalogram indicated negative results. A Master two-step test did not contribute to the diagnosis. A carotid sinus stimulation produced no symptoms.

On the eighth hospital day a one-dose, 100-Gm., six-and-one-half-hour glucose tolerance test was performed. At the fourth hour the patient became stuporous with severe diaphoresis and was pallid, with a rapid regular pulse in excess of 200 per minute. An electrocardiogram was not obtained. The blood pressure was 80/60. The patient soon recovered spontaneously. The blood sugar tests performed by the glucose-oxidase[5] method resulted in the following: fasting, 95 mg. one-half hour, 148 mg.; one hour, 176 mg.; two hours, 115 mg.; four hours, 32 mg.; four and one-half hours, 29 mg.; five hours, 47 mg.; and six and one-half hours, 77 mg. per 100 ml.

The patient was discharged on the thirteenth day and was instructed to adhere to a high-protein, low-carbohydrate diet. He remained symptom-free during the following ten months.

On March 24, 1959, the patient returned to the hospital for a repeat glucose tolerance test. At the third hour he again became faint, pallid, and diaphoretic. An electrocardiogram revealed a nodal rhythm and later a wandering pacemaker. This episode persisted for thirty minutes with no change effected by a carotid sinus pressure. The blood sugar was 66 mg. per 100 ml. Thirty minutes later 25 Gm. of glucose was administered intravenously, with a prompt return on the electrocardiogram to a regular sinus rhythm and an improvement in the patient's weakness. The results of this test were as follows: fasting, 100 mg.; one-half hour, 142 mg.; one hour, 206 mg.; two hours, 156 mg.; three hours, 66 mg.; and three and one-half hours, 55 mg. per 100 ml. This curve was interpreted for the first time as diabetic in type.

FASTING BLOOD SUGAR

TIME HOURS		BLOOD SUGAR MG. PER 100 ML.	
15	—	70	
19	—	129	
23	—	98	
27	—	91	
30	—	57	NO SYMPTOMS
39	—	54	
43	—	51	
48	—	85	

FIGURE 1. Blood sugars taken between fifteen and forty-eight hours following onset of fast and associated with physical activity. Blood sugar method—glucose oxidase of Saifer. No symptoms at levels between 57 and 51 mg. per 100 ml.

Following his discharge, the patient remained asymptomatic and was readmitted on May 5, 1959, for a seventy-two-hour fast and repeat studies to consider the possibility of a functioning islet-cell adenoma. Over the next seventy-two hours he ingested nothing but water. His blood sugars are shown in Figure 1.

The patient remained asymptomatic during the fast and stated that he had "never

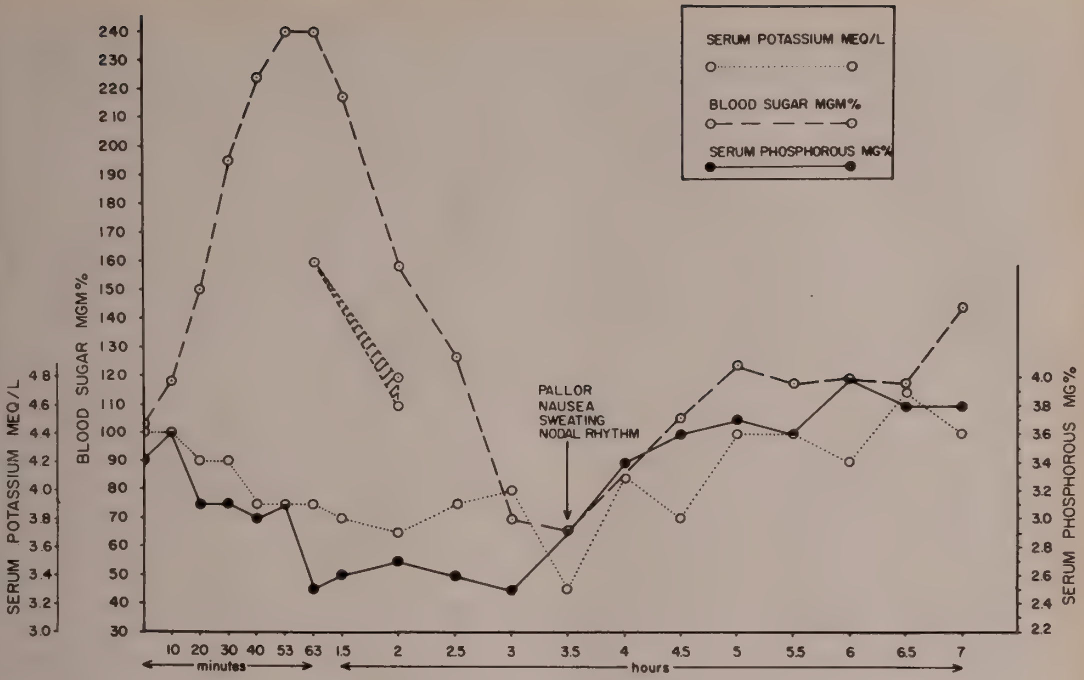

FIGURE 2. Seven-hour oral glucose tolerance test demonstrating sustained hyperglycemia up to and including two-hour period followed by rapid drop to level of 66 mg. per 100 ml. at three-and-one-half-hour period. Also shown is progressive hypokalemia and hypophosphatemia followed by concomitant return to normal of blood glucose, potassium, and phosphorus beyond three-and-one-half-hour period.

felt better." During this time he ambulated freely. Following this study, he was placed on a high carbohydrate diet in preparation for another glucose tolerance test. On May 27, 1959, an intensive glucose tolerance test was performed, with determinations of blood glucose and serum potassium and phosphorous obtained every ten minutes for the first one and one-half hours, then every half-hour until seven hours had elapsed.

The curve revealed a one-hour blood sugar level of 240 mg. and a two-hour level of 159 mg. per 100 ml. (Fig. 2). At three and one-half hours the patient began to complain of weakness and nausea. He perspired profusely and his pulse became irregular. An electrocardiogram at this time revealed a nodal rhythm at a rate of 55 beats per minute, interrupted by unifocal premature ventricular contractions. The blood pressure and pulse remained normal. After five minutes the rhythm reverted spontaneously to normal. During this episode the blood sugar had dropped from 159 mg. per 100 ml. at two hours to 66 mg. per 100 ml. at three and one-half hours and was accompanied by a drop in potassium from 4 mEq. per liter at two hours to 3.3 mEq. per liter at three and one-half hours. Within one-half hour the blood sugar had risen to 86 mg. per 100 ml., and the potassium had risen to 4.1 mEq. per liter spontaneously. The patient became asymptomatic.

The following day, three and one-half hours after breaking a fourteen-hour fast in preparation for a basal metabolic rate, the patient developed profuse diaphoresis, weakness, and a rapid pulse of 190 per minute. An electrocardiogram revealed a nodal tachycardia. Two blood sugars drawn during the attack showed levels of 99 and 107 mg. per 100 ml. The patient was given 25 Gm. of glucose intravenously without change, followed by 20 mEq. of potassium intravenously after which the cardiac rate decelerated and the rhythm gradually reverted to a regular sinus at the end of fifteen minutes.

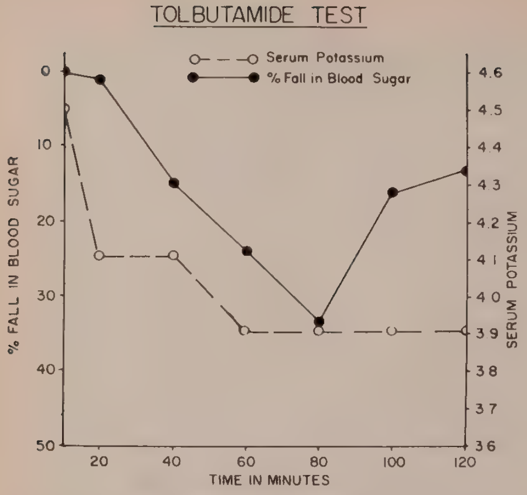

FIGURE 3. Tolbutamide tolerance test demonstrating 2 and 15 per cent blood sugar fall at twenty- and forty-minute periods respectively following intravenous injection of sodium tolbutamide. Greatest blood sugar fall occurred at eighty minutes followed by minimal hypoglycemic responsiveness. This is diabetic response curve.

On May 29, 1959, an intravenous tolbutamide tolerance test was performed (Fig. 3). The response was diabetic in type. We felt that on the basis of: (1) absent fasting hypoglycemia, (2) absent symptomatic hypoglycemia on prolonged fasting and exercise, (3) no demonstrable organic liver disease, and (4) persistent hyperglycemia at the end of two hours following 100 Gm. of glucose given orally, organic hyperinsulinism was excluded and that the patient demonstrated a delayed stimulative hypoglycemia of the early mild diabetic type. He was discharged on a low-calorie, low-carbohydrate diabetic diet.

Comment

Cardiac arrhythmias, as present in this patient, can accompany the hypoglycemic state. Hypoglycemia is associated with two major biochemical alterations which are hyperepinephrinemia and hypokalemia, both or either one of which may influence cardiac action. The plasma concentration of epinephrine can increase as much as 25 times the normal resting value during insulin-induced hypoglycemia.[6,7] The known cardiac responses to epinephrine include sinus tachycardia, unifocal and multifocal ventricular premature contractions, and, occasionally, ventricular tachycardia.[8] Under similar circumstances some elevation in plasma norepinephrine also occurs; however, the mentioned cardiac effects have not been noted.

Some of the hypokalemic effects on cardiac function have been demonstrated to be those of supervening arrhythmias including nodal tachycardia, supraventricular tachycardia, atrial and ventricular premature beats, and various conduction disturbances.[9] The cardiac effects of hypokalemia have been observed during the correction of diabetic acidosis,[10] in hemodialysis,[11] and with the administration of exogenous carbohydrate to patients who were digitalized previously,[12] as well as in acute potassium depletional states accompanying a variety of disease syndromes. In our patient with coronary artery disease it would seem that both phenomena of hyperepinephrinemia and hypokalemia induced the observed cardiac arrhythmias. His clinical appearances at the time of these episodes clearly reflected a state of epinephrine hyperactivity including diaphoresis, nausea, tachycardia, pallor, and a cold skin, as well as marked apprehension. The serum potassium at the beginning of the last glucose tolerance test was 4.2 mEq. per liter. At the three-and-one-half-hour period it had reached a nadir of 3.3 mEq. per liter. This is a significant decrease in serum potassium, and alterations of this magnitude have been known to be associated with cardiac irregularity. The blood phosphorus paralleled the fall in serum potassium. It began at 3.4 mg. per 100 ml. and reached a depth of 2.5 mg. per 100 ml. at one hour and then continued at that level up to three hours. Subsequently it rose parallel to the blood glucose and potassium, finally reaching 3.8 mg. per 100 ml. at the end of the test period. We have found it interesting to note that the initial fall of both phosphorus and potassium occurred while the blood sugar was still rising. Since the drop in blood phosphorus and potassium following glucose administration represents the withdrawal of these elements during the phosphorylation process, it is suggested that the latter began as soon as the blood sugar rose.

Recent studies on plasma insulin concentration following the administration of glucose to both normal and diabetic patients indicate a rise in the insulin levels within the first half-hour of the test.[13,14] Inasmuch as the phosphorylation process is dependent on an insulin effect, our observation is consistent with the alterations in plasma insulin concentrations that have been demonstrated. No effect of hypophosphatemia has ever been noted on cardiac rhythm. The serum-potassium determinations demonstrated clearly that a hypokalemic state existed. The absence of T- and U-wave, Q-T, and P-R interval changes, which are seen with marked hypokalemia, does not necessarily deny the influence of the low-serum potassium on the myocardium, inasmuch as it is recognized that changes in the electrocardiogram do not always accompany even marked potassium depletion.[15]

Myocardial anoxia which presumably occurs during the reduction in blood sugar would seem to be less of an influence in the production of cardiac arrhythmia, inasmuch as the heart can obtain an adequate oxygen supply from noncarbohydrate sources.[16]

The nature of the demonstrated defect in carbohydrate metabolism deserves comment. The existence of a stimulative delayed hypoglycemic response in mild diabetic patients has been reported as early as 1924 by Harris[4] who called it dysinsulinism. This phenomenon, more recently described by Seltzer, Fajans, and Conn,[3] is characterized by fasting normoglycemia, delayed hyperglycemia up to and including two hours, and then, significant hypoglycemia. It was their opinion that these patients were already diabetic, although they demonstrated no overt manifestations of this disease. Subsequent follow-up of their patients revealed that a number of them had developed obvious diabetes, with persistent fasting hyperglycemia. Recent determinations of plasma insulin levels have revealed that such patients have higher circulating levels at the end of two hours after glucose ingestion than do normal patients who manifest their highest levels at one-half hour.[17] This is consistent with the present concept that part of the earliest defect in diabetes is a delay in the insulin release before the phase of absolute insulin deficiency supervenes. In our patient the nadir of blood glucose was 66 mg. per 100 ml. at the three-and-one-half-hour time period. Although this is not an absolute level of hypoglycemia, the change from 159 mg. per 100 ml. at two hours to 66 mg. per 100 ml. is significant. Sudden fluctuations from high to low blood sugar levels can produce symptoms of hypoglycemia without necessarily attaining absolute hypoglycemic levels.[18]

The intravenous tolbutamide tolerance test, recently advanced as another parameter for diabetes detection, helped confirm our diagnosis of diabetes mellitus in this patient.[19-23] Tolbutamide-induced hypoglycemia, principally through betacytotropism, stimulates the release and/or synthesis of endogenous insulin. Following the intravenous injection of 1 Gm. of sodium tolbutamide into a diabetic patient, the blood sugar tends to drop minimally and slowly so that the normal pattern characterized by a rapid maximal fall which occurs within the first forty minutes is not seen. The blood sugar in the former tends to fall so that there is a persistent downward curve for as long as eighty to one hundred and twenty minutes. Our patient's initial response within the first forty minutes was significantly less than is seen in the normal patient. The latter part of the curve demonstrated a persistent fall for as long as eighty minutes. The minimal hypoglycemic responsiveness at the one-hundred- and one-hundred-and-twenty-minute period is not inconsistent with a diabetic response. Progressive hypokalemia accompanied the changes in the blood sugar; however, no cardiac irregularity occurred during this test. It is possible that a final absolute level of 3.9 mEq. per liter prevented cardiac irregularity.

The first glucose tolerance test was performed in May, 1958. Although it was not absolutely diabetic in type, it indicated a trend in that direction. A true blood glucose greater than 160 mg. per 100 ml. at the one-hour period plus a true blood glucose of 115 mg. per 100 ml. at the two-hour period strongly suggests the diagnosis of probable diabetes. The subsequent two glucose tolerance tests were interpreted as truly diabetic responses. All three of the responses demonstrated the delayed stimulative hypoglycemia beyond the two-hour period. The results of these tests and the abnormal tolbutamide response indicate to us that this patient has early mild diabetes mellitus. His family history for diabetes indicated negative findings. The patient has been treated with a low-calorie, low-carbohydrate diet. No further cardiac arrhythmias or syncopal episodes have reccurred, nor has he developed overt diabetes mellitus.

Summary

A sixty-year-old man had intermittent episodes of cardiac arrhythmias and syncope. A clinical study demonstrated mild diabetes mellitus with a delayed reactive hypoglycemia associated with transient hypokalemia and hypophosphatemia. The tolbutamide response test confirmed the diagnosis of diabetes. The role of hyperepinephrinemia and hypokalemia has been discussed. The patient has been treated as mildly diabetic, with no further recurrence of his initial complaints.

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Historical Backgrounds for Disease Concepts in Medicine and Psychiatry

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PHYSICAL DISEASE is as old as man. Mental disease is at least as old as civilization. Psychiatry, growing historically out of medicine, bears the imprint of its origins. This article attempts to show that Western thought about mental disease has borne a somatic emphasis which only recently has begun to change toward psychologic and social orientations.

Primitive culture and antiquity

Man has always had notions about illness, its causes, and what to do about it: treatment. In all cultures, disease is considered to be abnormal. Sigerist[1] affirms Virchow's definition: "... disease is nothing else but life, life under changed circumstances." The responsibility for illness may be projected to other men ("he worked bad magic on me"), to evil forces, or to gods. With the development of societal organization, the concept of personal responsibility appears in the form of breach-of-taboo disease ("I have fallen sick because I broke a taboo").

Two trends, magico-religion and empirico-rationalism, constitute the main intellectual currents of medical history. Elemental concepts in magico-religious tradition are concerned with the soul, with spirits or gods in the environment, with totem and taboo, and with magical technics for control. Empirico-rational tradition is concerned with the body, with what is going on in the body, and with the effect of environmental influences and of empiric (that is, trial and error) technics of management. These two trends constantly overlap, making the pattern of medical and psychiatric history complex.

The causes of disease fall into three broad categories: supernatural agency, human agency (employing magical power), and natural causes. All three categories occur among both civilized and primitive peoples, but the latter is the most prominent among the civilized peoples of Europe and America today. The first two categories are the prevailing ones in primitive culture and in our own antiquity as indicated in Figure 1. Clements,[2] who has examined closely primitive concepts of disease in space and time, narrows these categories down to five main types of primitive concepts of disease: (1) disease-object intrusion, (2) soul loss, (3) spirit intrusion, (4) sorcery, and (5) breach of taboo.

This list is arranged in order of relative antiquity starting with the oldest concept of which we have any knowledge. Clements locates disease-object intrusion in the Old World paleolithic period, with the subsequent concepts developing prehistorically until breach of taboo, which is reached in the Semitic civilizations of Mesopotamia, the land between the rivers in Western Asia. A brief discussion of these concepts follows.

DISEASE-OBJECT INTRUSION. Disease-object intrusion includes all theories which attribute disease to the presence in the body of "some malefic foreign substance" which is tangible: a dart, a piece of bone, a pebble, worms, or insects. Moreover, as Clements[3] points out, "Among certain people... the disease-object is reported to contain... a

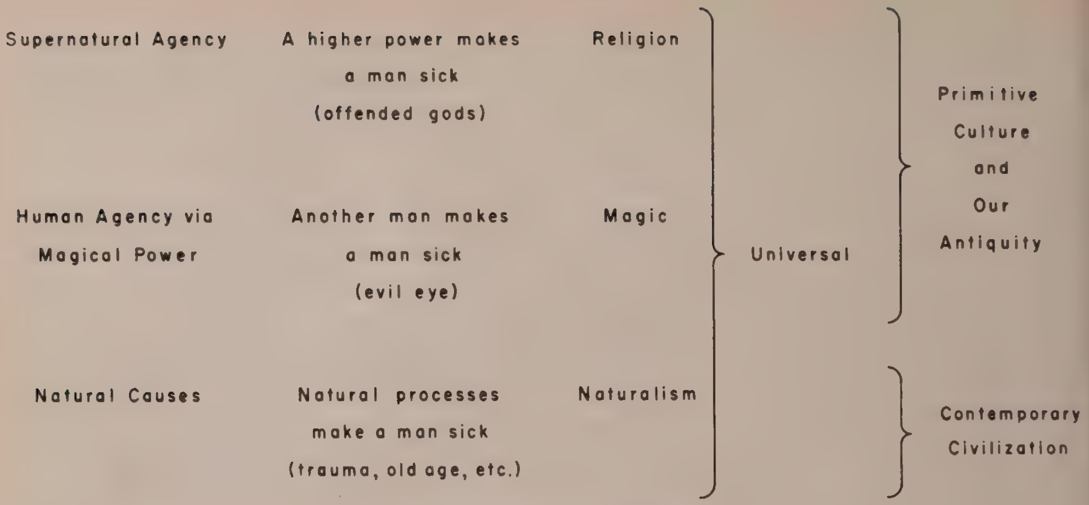
Supernatural Agency
A higher power makes a man sick (offended gods)
Religion
Human Agency via Magical Power
Another man makes a man sick (evil eye)
Magic
Natural Causes
Natural processes make a man sick (trauma, old age, etc.)
Naturalism
Universal
Primitive Culture and Our Antiquity
Contemporary Civilization

FIGURE 1. Causes of disease.

spiritual essence which is the real cause of the sickness. All peoples with the disease-object concept have been said to believe in this essence, the disease-object being used merely to give the spirit tangible form in the primitive mind. Accordingly, the real cause would be a spirit in the body. . . ."[3]

SOUL LOSS. A second class of theories about disease is included under soul loss: A person's soul (his shadow or tenuous double) is abstracted by ghosts or sorcerers or, having left the body during sleep, meets with some accident on its nocturnal rambles and does not return.[4] Soul loss is sometimes used to explain insanity, and witches can steal the soul.

SPIRIT INTRUSION. As we have seen, spirit intrusion cannot be clearly separated from disease-object intrusion. And here we have the prototype of our own medieval demonology: "This class includes all those etiologies which hold that disease is due to the presence in the body of evil spirits, ghosts, or demons."[3] When these spirits become vocal, we arrive at the concept of possession, which is probably the oldest and most widespread concept of mental illness: ". . . the utterances of the insane person (are) interpreted as the voice of the resident spirit."[5] Hysteria and epilepsy, among primitive people, also are explained in terms of possession. Mental suggestion, as Clements[6] points out, "plays an enormous part in the cures as well as the sicknesses,"[6] an observation which was corroborated by Charcot and Bernheim in nineteenth century France.

SORCERY. Sorcery, our fourth category, introduces the human element more specifically in that a human agency is required to wield supernatural power. This includes all cases of imitative magic (sticking pins in an effigy), contagious magic (that is, burning a victim's excrements to cause diarrhea), witchcraft, and the evil eye.

BREACH OF TABOO. Breach of taboo, category five, explains sickness as

> . . . a punishment sent by the gods for breach of religious prohibitions or social prohibitions having divine sanction . . . . The breach may be quite unintentional and even unknown to the sufferer but it is none the less regarded as the real cause of the sickness. In such cases confession often serves as a means of treatment.[7]

COMMENT. What are the common elements in these concepts, and what light can analysis throw on later concepts of illness, including our own?

We note that a "plus" or a "minus," a "too-much" or a "not-enough," principle seems to be involved in the conceptual scheme,[8] as well as the implication of intrusiveness or a "things-in-the-wrong-places" principle. Sigerist,[8] in his history of medicine, regards the "plus" or "minus" and "too-much" or "not-enough" notions as the

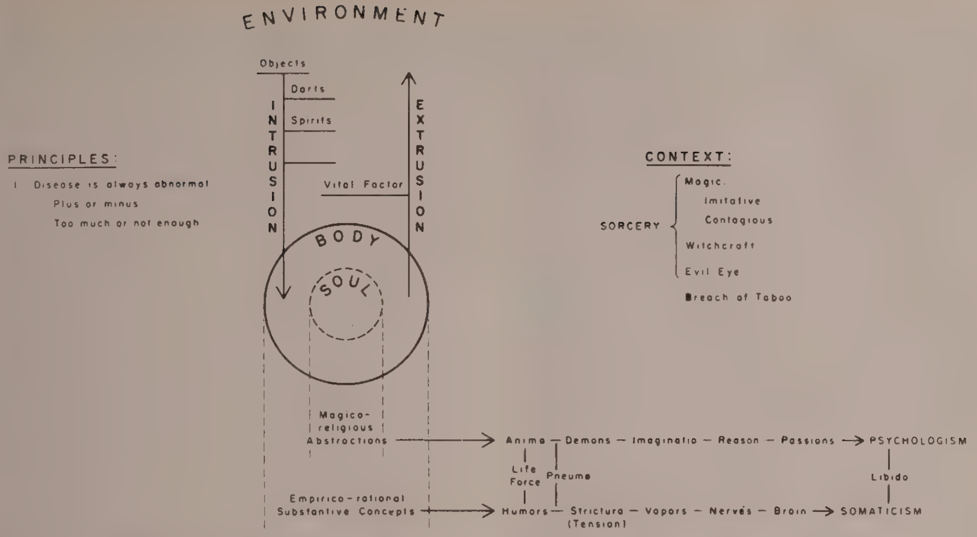
ENVIRONMENT
PRINCIPLES:
I Disease is always abnormal
Plus or minus
Too much or not enough
Objects
Darts
Spirits
INTRUSION
Vital Factor
EXTRUSION
BODY
SOUL
CONTEXT:
SORCERY
Magic.
Imitative
Contagious
Witchcraft
Evil Eye
Breach of Taboo
Magico-religious Abstractions
Anima — Demons — Imaginatio — Reason — Passions → PSYCHOLOGISM
Life Force
Pneuma
Libido
Empirico-rational Substantive Concepts
Humors — Strictura (Tension) — Vapors — Nervés — Brain → SOMATICISM

FIGURE 2. Disease concepts of primitive cultures and our own antiquity.

two oldest and most basic concepts of disease. Perhaps it is logical to assume, then, that "just right" defines health, a state of wholeness and soundness, which, indeed, the etymology of the word "health" confirms. These ideas cannot be dismissed as archaic, primitive logic, without first taking a look at our own tradition. For example, "The arrows of the Almighty were within Job and their poison drank up his spirit. Apollo punished the people with pestilence by shooting his darts at them."[9] Intrusion causes disease. But what is intruded, what serves to reify the concept, varies with the historical time and place: evil spirits in Egypt, gods in Greece, demons in the Bible and in Medieval Europe, and germs after Pasteur and Koch. Incubus and succubus demons of the Middle Ages, by the way, were not far removed categorically from sexual impulses, as anyone who has read the *Malleus Maleficarum* knows. And, metaphorically, repressed impulses and demons are similar, as Reider[10] has pointed out. The "plus" or "minus" and "too-much" or "not-enough" principles apply here also. Moreover, treatment methods, such as exorcism, purgation, bleeding, and catharsis, imply the extrusion and removal of excess.

Primitive cultures use the concept of object intrusion to explain sudden, acute illness and pain, whereas soul loss is used to explain fainting and chronic, wasting diseases. The soul is a universal, elemental concept, paleolithic in origin and antedating its connection with disease. Here, again, in soul loss, the "too much" or "not-enough" principle is applied and also the notion of soul-body integrity: The body sickens or dies if the soul wanders or is stolen, and health is restored when the soul rejoins the body. Primitive theories seem to echo ideas found in our own past and present. We still hear mental illness referred to as "losing one's mind" or "being out of one's mind." (Clifford Beers' autobiography was entitled *A Mind That Found Itself*.[11]) The earliest psychologic theories were concerned with locating the seat of the soul, and soul-body integrity is expressed in the ancient maxim "mens sana in corpore sano." Certainly one of the most influential deficiency concepts was put forward by George Miller Beard whose point of view was so successful that neurasthenia became known as morbus Americanus. In his book, *A Practical Treatise on Nervous Exhaustion* (1880),[12] Beard stated:

> In regard to the pathology of neurasthenia, my view, as expressed in my first paper on the subject, [1869] is that there is an impoverishment of the nerve-force, resulting from bad nutrition of the nerve-tissue on the metamorphosis of which the evolution of nerve-force

> depends; as in anaemia, there may be a deficiency in quantity or impairment of quality of the blood; so in neurasthenia there is, without question, deficiency in quantity or impairment in quality of the nerve-tissue; hence the exhaustion, the positive pain, the unsteadiness, the fluctuating character of the morbid sensations and phenomena, to which the term neurasthenia is applied."[12] "Nervousness," he adds, "is really nervelessness."[13]

Such ideas still haunt us today in terms such as neurocirculatory asthenia, fatigue syndrome, and perhaps even "tired blood"! Often, vitamins, stimulants, or "shots" are prescribed, thus affirming the widespread notion of depletion or deficiency as a cause of disease.

We will bring this section to a close with an illustrative model of disease concepts of primitive cultures and our own antiquity (Fig. 2).

Greco-Roman changes

Magico-religion is relatively more characteristic of primitive and ancient cultures, while empiricism and rationalism, although prominent in Egypt, are more highly developed in later civilizations. Nevertheless, history confronts us with a tangled picture of continuously overlapping magical, religious, naturalistic, and scientific ideas and practices. The emphasis changes, but neither magico-religion nor empirico-rationalism ever prevails completely.

It was precisely a change in emphasis which was ventured by the Greeks. As Ackerknecht[14] points out,

> While the great cultures of old, such as those of Egypt and Mesopotamia, vacillated between naturalistic and supernatural explanations of diseases, the Greeks declared themselves outspokenly in favour of naturalistic explanations and thus became the founders of scientific medicine and of psychiatry.

The foundation which the Greeks provided to scientific medicine and psychiatry was, of course, the physical model of disease. Inasmuch as the Greek physicians struggled less with mind-body dualism than the philosophers did, this model was generalized to include insanity. Those who addressed themselves to mental illness (Hippocrates and Galen left only occasional accounts) were extreme somaticists: Celsus (30 A.D.), Aretaeus (150 A.D.), and Soranus (100 A.D.).[15] From their work we can abstract two disease models which provide a historical background for the modern medical model: one based on the classical theory of the four humors and the other on later "solidistic" concepts. Sick persons who were formerly thought to be possessed by spirits, demons, or gods, were now thought to have a physical disease. Whereas primitive medicine tends to be monistic on a supernatural basis, that of the relationship between the body and supernatural objects, Greek medicine tends to be monistic on a naturalistic basis, that of disequilibrium in the juices or tension in the tissues of the body.*

The application of solidist ideas is best exemplified by Soranus, the most outstanding representative of the methodist school of medicine. His two major works on acute and on chronic diseases have survived in the Latin translation of Caelius Aurelianus.[17] Soranus begins his book on acute diseases, because the order of presentation is "a capite ad calcem" (from head to toe), with a discussion of a mental disease, phrenitis, a disturbance of reason with fever (febrile delirium?) which is to be diagnosed differentially from mania, a disturbance of reason without fever, which he views as a chronic disease.[17] The former is due to both status strictus and status laxus, the latter, or agitated insanity, to status strictus. Melancholia, or quiet insanity, is due not to black bile but to black rage, says Soranus, who, citing Cicero and Virgil, goes on to present his skeptical departure from humoralism: "... for those suffering from melancholy seem always to be downcast and prone to anger and are practically never cheerful and relaxed."[19] Although he sees the relevance of emotion, Soranus does not depart from solidist dogma; he maintains orthodoxy by asserting that melancholia is due to "strictura" (a dry, tense, stringent state) and that the seat of the disease is in the esophagus. As one of the signs of melancholy he describes: "... a sharp pain in the esophagus or cardia extending even to the region between the shoulder blades ... ."[19] To modern ears this suggests esophageal regurgitation. Thus melancholia, like phrenitis and mania, the other two mental diseases which he recognizes, is a physical disease. Only homosexuality is described as a disease of the psyche.[20]

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* The classical theory of disease, that of Hippocrates and Galen, is the theory of the four humors with their corresponding four elements and qualities. The body is composed of four juices: blood, yellow bile, black bile, and phlegm, which correspond to the four elements of the universe: air, fire, earth, and water. Each humor is characterized by two of the four qualities: hot, moist, dry, and cold. Sanguine (excess blood), choleric (excess yellow bile), melancholic (excess black bile), and phlegmatic are the four temperaments which are accounted for in humoral theory.[16] Theories, however, leap ahead of factual knowledge, and after 300 B.C. classical theory found itself in competition with other schools of thought: dogmatists, empirics, and methodists. These schools, particularly the latter two, were rooted philosophically in skepticism, a disbelief in unobservable entities and causes such as humors.[17] Their thinking diverged from humoral pathology toward solidist pathology, which was an empirico-rational step forward. Disease, which formerly was thought to be caused by humors, was now attributed to changes in the solid components of the body. The basic types of disease became: (1) an excessive dryness and tension (status strictus), (2) an excessive fluidity and relaxation (status laxus), and (3) a mixture of both (status mixtus).[18] Familiar principles, such as disease is abnormal, and it involves excess, are now hypostatized as fluid and tonal tissue changes.

We are indebted to the methodists for their skeptical attitude, particularly toward humoralism, although this attitude contributed to their downfall. The teleology of traditional Galenism was much more congenial to the mental attitude of the Middle Ages.[21] Galen became the "Roman dictator" of medicine, the "True Physition," for a thousand years. Classical humoralism, as modified by him, prevailed. To traditional humoralism Galen added a regressive emphasis, which was reminiscent of spirit intrusion, on pneuma: a spirit "which invaded every part of the body, the active cause of disease: in the nervous system, the *pneuma* became 'animal spirits,' in the liver, 'natural spirits,' and so on."[22]

Renaissance and Enlightenment

It is impossible to compress into a short review the vast changes which occurred in man's view of himself after the inchoate survival struggles of the Dark Ages, during the faith-dominated Middle Ages, and in the intellectual reawakening of the Renaissance, characterized as it was by the struggle for secular knowledge and science leading to our own Scientific Age. Certainly each period of intellectual history has left its stamp on medicine and psychiatry in the form of modified concepts of disease, treatment, and physician-patient relationships.[23]

In medieval times, for example, we are not surprised to find that religious faith and deference to authority, the organizing principles of medieval life and mind, manifested themselves on the one hand in faith healing, which was practiced by kings, priests, and laymen, and on the other by inquisitional campaigns against heretics. On the medical scene, Galen, whose writings survived the Dark Ages essentially intact despite errors of Latin and Arabic translations, was the authority. Galenic orthodoxy and Catholic orthodoxy ruled together. Greek naturalism, then, existed side by side with primitive supernaturalism as supported by the Church. As we would expect, physicalistic and demonologic concepts prevailed, with the latter more closely related to psychiatric history. Many mentally ill persons were thought to be witches. The concept of possession as a model for mental disease was restored to a place of respect and power on the unstable medieval social scene. In the stigmata, the marks of possession, one sees the juncture of physicalism and demonology. Nevi, pigmented spots, and areas of anesthesia indicated the presence of devils in the body. Great emphasis was laid on describing various skin and mucous membrane anesthesias: anal, pharyngeal, and corneal. Inquisitors were accompanied by assistants known as prickers who used pins to perform a kind of demonologic forerunner of cutaneous mapping. Much later, as Zilboorg[24] points out, stigmata diaboli "... were incorporated in the latter part of the nineteenth century almost without change into Charcot's clinical picture of major hysteria. The facts observed were the same; their interpretation was different."

The epithet "age of contrasts" applies to the Renaissance as it does to other, perhaps all other, periods of history. Although the demonologic furor tended to obscure it, rational progress in medicine and psychiatry continued. Johann Weyer, whom Zilboorg has named the first psychiatrist, spoke rationally in this period. Weyer did not fully repudiate the prevailing belief in witchcraft, but he dared to raise questions about it, which was dangerous enough. In his *De Praestigiis Daemonum* (On the Trickery of Demons)[25] he took the side of the accused witches, categorizing them as sick and stating that their sickness rendered them unduly susceptible to the machinations of the devil. Weyer was a careful clinical observer, adept at exposing imposture or malingering and desirous of establishing communicative relationships with patients. He was willing to make a patient part of his household for a time to improve his knowledge, as in the case of Barbara Kremers. He recommended that witches first be examined by physicians and then receive what we today would call pastoral counseling: consultations of a re-educational nature with the parish priest. But Weyer's rational approach was out of keeping with his time. Social evolution had proceeded only to the point that the world resembled "a gigantic insane asylum," as Weyer's biographer put it.[26]

About two hundred years separated this period from the Enlightenment of the seventeenth and eighteenth centuries which culminated, on the psychiatric scene, in Pinel's daring act of removing the chains from inmates of the Bicêtre, initiating a liberal trend in which insane persons became patients in a medical sense, legitimate subjects of study by nineteenth century physicians.

Nineteenth century backgrounds for today

On the intellectual scene it was the philosophic and scientific enlightenment of the seventeenth and eighteenth centuries and on the social scene "the shot heard 'round the world'" which set the stage for the modern period. An Age of Reason and Revolt, of changing intellectual and social values, of violent conflict of ideas and men, this period engendered a number of distinct trends in nineteenth century European and American psychiatry: (1) humane reform, moral treatment, and experiments with freedom for patients in mental hospitals (the "open door") after Pinel; (2) increasing nosologic orderliness throughout the century culminating in the Kraepelinian system; (3) differentiation of organic from functional psychoses; (4) hospital building; and (5) a steadily increasing interest in the so-called neuroses.[27] This latter interest in noninsane persons which was to have such great implications for modern psychiatry had been stimulated, of course, by the public demonstrations of Mesmer and the controversies over mesmerism. Although a magician like Mesmer was out of place on the enlightened intellectual scene of eighteenth century France, the trend he stimulated resulted, a century later, in the beginnings of modern psychotherapy.

During the nineteenth century two trends in disease theory became gradually clearer: somaticism, the body-oriented point of view, and psychologism, the psychologic point of view. Needless to say, the former, firmly rooted in a long cultural tradition, predominated.

The heir of empirico-rational humoralism and solidism, somaticism now received support from pathology (that is, general paralysis and senile psychosis), physiology, and neurology, as well as from the nineteenth century fashion in biology under Darwin's influence. These influences, perhaps enhanced by Gall and Spurzheim's popularization of phrenology, led to a new somatic emphasis, localism: the attempt to correlate the nervous system, generally, and certain areas of the brain, specifically, with behavior.[28] We may call the solidism of the nineteenth century neosolidism because, although it continues to express behavior in the somatic idiom, new ingredients were added: physiologic studies of the nervous system, localism, psychosomatic correlations, and the differential diagnosis of organic versus functional disorders. Contributions to the latter two can be found in the works of George Ernst Stahl who, early in the eighteenth century, emphasized the effect of passions and affects on the body and discussed the differential diagnosis of organic from functional delirium.[29]

In regard to the focus of interest on the nervous system, it had been, of course, VonHaller's discovery of nervous and muscular irritability in 1752 which had stimulated William Cullen,[30] professor of medicine at Edinburgh, to coin the term "neurosis" which, from the Greek work "neuron" for nerve, means a diseased condition of nerve. This eighteenth century somatic concept, with its popular counterparts "nerves" and "nervousness," prevails today. It will still be with us in 1969, the two-hundredth anniversary of the publication of Cullen's textbook of medicine.[30]

Unfortunately, nineteenth century contributions to somatic theory got caught up in a semimoralistic theory of hereditary predisposition to degeneration, a subject which has been succinctly presented by Ackerknecht.[31] Degeneration theory, essentially a renewed search for physical signs of mental illness, now in biologic terms of heredity and deterioration toward extinction rather than demons and stigmata, dominated French psychiatry for decades. Charcot used it to explain hysteria. "Dégénérescence," as an explanatory concept in psychiatry, spread to Germany, England, and America. The degeneration theory coincided with Darwinism; it endeavored to make dégénérescence an explanatory concept in psychiatry equal to evolution in biology. As a panchreston,[32] or explain-all concept, dégénérescence, if taken literally, merely classified mentally ill persons, who had been social outcasts and were now patients, as organic degenerates headed for extinction. The influence of this theory on Kraepelin is apparent in his basic concept of dementia praecox.

By the end of the century somaticism had failed to fulfill the hope of its followers that mental illness could be explained in terms of heredity, degeneration, localism, and neurology. Psychologism, the heir of magicoreligious soul, demon, and possession concepts, vitalism, Cartesian rationalism, psychosomatic concepts after Stahl, and the psychologic theories of Enlightenment philosophers, opened the way for further psychologic, social, and psychoanalytic approaches to human behavior, creating a background for the modern scene. Given impetus by the social performance of Mesmer, the clinical work of Liébeault and Bernheim at Nancy, and the researches of Charcot in Paris, psychologism was furthered by Freud. Demon concepts were discarded, dégénérescence was considered inadequate, and, in their place, psychologic concepts such as suggestion (Bernheim) and dissociation of consciousness (Freud) were offered. In his eulogy for Charcot, Freud[33] wrote:

> Let no one object that the theory of dissociation of consciousness as a solution of the enigma of hysteria is too far-fetched to suggest itself to the untrained and unprejudiced observer. In fact the Middle Ages had chosen this very solution, in declaring possession by a demon to be the cause of hysterical manifestations; all that would have been required was to replace the religious terminology of those dark and superstitious times by the scientific one of to-day.

Such formulations, followed by concepts of repression, the unconscious, transference, and mental mechanisms, marked a new departure in Western thought about disease and the mind. Although early concepts did not always depart from traditional somatic views, but translated them into neosomatic concepts such as dammed-up libido, psychoanalysis appears historically to be part of psychologism, a trend which it has advanced until, with later developments in psychosocially oriented psychiatry (Meyer and Sullivan), contemporary concepts in psychiatry are focusing more on interpersonal problems in human living than on physical disease.

Summary

A brief overview of concepts of disease found in the history of medicine and psychiatry, from ancient times until the recent past, has been presented in support of the view that psychiatric thinking has borne the imprint of broadly cultural and specifically medical origins. Recently, historically speaking, disease concepts in psychiatry have moved from a traditional somatic focus toward psychologic and social views.

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Most mothers pleased at first sight of baby

The reaction of most mothers to the first sight of their baby is to smile weakly, according to a study of 500 deliveries reported by Niles Newton, Ph.D., and Michael Newton, M.D., in the July 21, 1962, issue of the *Journal of the American Medical Association.* While more than half of the mothers demonstrated a weak accepting reaction by smiling a little, another 30 per cent were obviously greatly pleased. Only 14 per cent appeared indifferent or displeased.

Three-fourths of the mothers were fully conscious at the time of delivery. The physical experiences of labor, including the use of forceps and the length of labor, were not found to be related to the mother's reaction.

"The mother who was most likely to be very pleased at the first sight of her newborn infant was the mother who had stayed calm and relaxed in labor and who cooperated with her attendants. She had received more solicitous care as indicated by having back pressure applied more frequently for backache. She more frequently had a good emotional relationship with her attendant and particularly desired to breast feed her baby. She was more likely to be pleased if she was a white woman with a tenth grade education or more. The findings suggest that mother love in human beings, insofar as it is visible the first time the mother sees the baby, may be more closely related to her own personality, social class, and inner calm, and to the kindness and friendliness of her attendants, than to traumatic physical experiences in the production of a baby."

What causes a mother to accept or reject her newborn child is just beginning to be investigated, and knowledge on the subject is extremely fragmentary. Under some circumstances consciousness at birth may influence the mother's acceptance of the offspring. Some investigators have found a suggestive relationship between lack of pain-relievers and greater enjoyment of rooming-in care of the baby.

Animal studies have shown that disruption of innate behavior patterns may cause rejection of the newborn. Whether or not this holds true in human beings is not known. "It is difficult to determine any normal human patterns in the highly artificial birth situation in modern hospitals."

Other factors which may be involved include separation immediately after birth, previous childbirths, an abnormality in the mother or infant, and personality factors.

Month in Washington

Influenced strongly by the thalidomide incident, Congress approved legislation giving the Food and Drug Administration more control over the prescription drug industry.

The Kennedy Administration and Sen. Estes Kefauver (D., Tenn.), chief sponsor of ethical drug legislation, successfully exploited the thalidomide incident after prospects of passage of a strong drug bill waned.

However, they were unable to get all they wanted in the legislation even with the impact on Congress of the widespread publicity about the clinical testing of thalidomide in this country coupled with reports from Europe of births of malformed children by women who had taken the drug during pregnancy.

One Administration proposal rejected by Congress would have given the Secretary of Health, Education, and Welfare authority to require physicians to report directly to him on their clinical tests with new drugs.

The new law empowers the F.D.A. to require "substantial evidence" of the efficacy, as well as the safety, of new drugs before licensing them for marketing. The A.M.A. had warned Congress that this might lead to a test of relative efficacy which could result in potentially helpful drugs being barred from sale. The A.M.A. contended that the old F.D.A. requirement that a drug live up to its label claims was a sufficient test of effectiveness.

The Pharmaceutical Manufacturers Association also warned that drug research might slow down as a result of the new law.

"Some provisions of the new law may not be helpful to the public," the P.M.A. said. "In fact, unless there is the wisest administration of the law harm can be done. For example, medical research may slow down, and the costs of medications may increase."

Physicians will be required to get the consent of the patient, or a close relative, for treatment with experimental drugs except in instances where the physician feels that it would not be feasible or would be contrary to his professional judgment. Consent already is a part of the code of ethics of the American Medical Association.

Some other major provisions of the new law are: Authorizes the F.D.A. to swiftly suspend any drug which it suspects is dangerous; requires that the generic name of a drug be printed on the label in type half as large as that for the trade name; extends the time during which F.D.A. may review a new drug application before it must be approved or disapproved; authorizes the H.E.W. Secretary to establish generic names for new drugs; authorizes the H.E.W. Secretary to prevent testing of drugs on human beings if he determines there has not been sufficient preclinical testing; requires batch certification of all antibiotics.

* * *

Congress passed a bill authorizing a $36 million three-year program for Federal aid for intensive vaccination programs against polio, diphtheria, whooping cough, and tetanus.

The vaccination campaigns are to be aimed primarily at children less than five years old. The U. S. Surgeon General was given broad authority in deciding the amount and terms of Federal grants under the program.

Grants will be made to states or, when approved by state officials, to cities or other local governmental units.

Also on the immunization front, a Special Advisory Committee twice recommended to the Public Health Service that Type III oral polio vaccinations be continued for preschool and school age children but not for adults for the time being.

The Public Health Service accepted the recommendation and urged that communities proceed with planned mass vaccination campaigns using Type III for children. But some communities decided to hold up their mass immunization programs at least temporarily or to suspend Type III doses for children, as well as adults.

The Advisory Committee first made its oral polio vaccine recommendation at an emergency meeting on September 15. The meeting was called after Canada suspended use of oral polio vaccine. The Health Ministry action in Canada, where all three types of the oral vaccine had been given in one dose, was prompted by the occurrence of a few cases of Type III polio. The three types of vaccine are given in separate doses in this country.

There also were at that time a few Type III cases reported in this country among adults who had taken the oral vaccine.

After an October 2 meeting, Luther L. Terry, M.D., Surgeon General of the P.H.S., said: "The recommendation that Type III be confined to children has raised the question of spread from vaccinated children to adults, especially family members. The evidence does not indicate a hazard to adults exposed in this way."

"The level of this risk can only be approxi-

Prepared by the Washington, D.C., Office of the American Medical Association.

mated but clearly is within range of less than one case per million doses. Since the (Type III) cases have been concentrated among adults the risk to this group is greater whereas the risk to children is exceedingly slight or practically nonexistent."

* * *

President Kennedy signed into law H.R. 10 permitting physicians and other self-employed persons to take a Federal income tax deduction for private pension plans.

The President signed the legislation less than six hours before the midnight October 10 deadline that he had to act on the measure. If he had not signed it by then, it would have become a law without his signature. It appeared certain that a presidential veto would have been overridden.

Physicians represent less than 3 per cent of employed who could benefit under the new law.

Enactment of the legislation into law climaxed a twelve-year battle in Congress. The House passed it twice, in 1958 and 1959, but it died each time in the Senate with adjournment. This year the House passed it with a 361 to 0 vote. The Senate vote was 70 to 8.

The new law authorizes a self-employed individual, such as a physician, to contribute up to 10 per cent of his earned income or $2,500, whichever is less, toward a retirement plan, provided he includes all of his employes with three or more years of service under the plan. A tax deduction of half of the contribution to the self-employed person's retirement plan would be allowed.

The contributions made on behalf of employes would be fully tax deductible. The measure prohibits drawing on the retirement funds without penalty before age fifty-nine and a half except in case of disability or death.

Tumors in mice caused by standard and filter-tip cigarets

Filter-tip cigarets contain enough tar to cause skin tumors and eventual cancer in mice, according to an article by Bock *et al.* in the August 25, 1962, issue of the *Journal of the American Medical Association*. Six brands of cigarets, including two filter-tip types, were studied in an effort to determine if the cancer risk had been eliminated from cigarets or reduced by modifications in recent years.

During the one-year study with mice, tumors were induced by all six brands even though the filter cigaret smoke yielded only one-third the amount of tar in standard cigaret smoke. However, there were fewer tumors and a slower onset of tumors among the filtered cigaret group. Tar yields among standard cigarets differed by less than 20 per cent.

Skin tumors were produced in 41 of 76 mice in the standard brand group and in 15 of 60 mice in the filter group. In both groups of mice, a total of 19 skin tumors progressed to cancers within the one-year period.

The experimental procedure consisted of condensing the smoke from machine-smoked cigarets to obtain the tar. Each cigaret was puffed 10 times at one-minute intervals at the same pressure, although an individual might puff harder on filtered cigarets because of their increased resistance. The tar was dissolved in a solvent, acetone, and applied to the shaved skin of the mouse in amounts equivalent to 8.3 smoked cigarets per day.

The first tumor was observed nineteen weeks after the start of the experiment. For comparison, 66 mice were painted with acetone alone, and 65 mice were left untreated while kept under the same living conditions as the tar-treated mice. No skin tumors developed in the acetone-treated or untreated mice.

The smoke of all of the six brands of cigarets proved capable of causing cancer, but the total amount of smoke delivered to the target area resulted in a reduction in the incidence of tumors. "A parallel reduction in dose could be accomplished by smokers through smoking fewer cigarets. Studies of human populations have shown that men who smoke fewer cigarets have a lower lung cancer incidence. A reduced intake of smoke also could be accomplished by a smoker through taking fewer puffs or through smoking the same number of cigarets which, by means of filters or other devices, give rise to smaller yields of inhaled tar. The ideal of course, however, would be to stop smoking altogether."

Necrology

William Harrison Barlow, M.D., of Staten Island, died on September 21 at his home at the age of fifty-three. Dr. Barlow graduated in 1935 from Columbia University College of Physicians and Surgeons. He was an attending surgeon and director of surgery at the Staten Island Hospital. Dr. Barlow was a Fellow of the International College of Surgeons and a member of the Richmond County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Martin Brandt, M.D., of Norfolk, died on August 28 at St. Luke's Hospital, Utica, at the age of sixty-eight. Dr. Brandt received his medical degree from the University of Breslau in 1921. He was a staff physician at the Potsdam Hospital. Dr. Brandt was a member of the St. Lawrence County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Cleatus Carhart, M.D., of Bay Shore, died on July 26 at his home at the age of sixty-four. Dr. Carhart graduated in 1929 from New York University and Bellevue Hospital Medical College. He was a senior attending obstetrician and a member of the medical staff of Southside Hospital. Dr. Carhart was a member of the Suffolk County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Benjamin Colton, M.D., of Flushing, died on April 29 at the age of sixty. Dr. Colton graduated in 1926 from New York University and Bellevue Hospital Medical College. He was a Diplomate of the American Board of Radiology (Diagnostic Roentgenology) and a member of the Queens County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

William Brick Cullinan, M.D., of Depew, died on June 11 at the age of fifty-two. Dr. Cullinan graduated in 1937 from Georgetown University School of Medicine. He was an attending physician at Mercy Hospital in Buffalo. Dr. Cullinan was a member of the Erie County Medical Society and the Medical Society of the State of New York.

Martin Fischer, M.D., of Lynbrook, died on September 14 at St. Clare's Hospital, New York City, at the age of sixty-five. Dr. Fischer received his medical degree from the University of Breslau in 1922. He was a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Hugh Frail, M.D., of Cortland, died on July 21 at Cortland Memorial Hospital at the age of sixty-six. Dr. Frail graduated in 1923 from Syracuse University Medical School. He was an attending physician at Cortland Memorial Hospital. Dr. Frail was a member of the Cortland County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Henry Blacklidge Gillen, M.D., of Cohoes, died on September 24 at Cohoes Memorial Hospital at the age of seventy-eight. Dr. Gillen graduated in 1909 from Albany Medical College. He was an honorary attending physician at Cohoes Memorial Hospital. Dr. Gillen was a member of the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Goldman, M.D., of Brooklyn, died on May 11 at the age of seventy-two. Dr. Goldman graduated in 1911 from Long Island College Hospital Medical School. For many years he had served as a senior assistant house physician and surgeon for the New York City hospital and school systems. Dr. Goldman was a member of the American Proctologic Society, the New York Academy of Medicine, the Brooklyn Surgical Society, the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Benjamin Israel, M.D., of the Bronx, died on May 17 at his home at the age of fifty-two. Dr. Israel graduated from the University of St. Andrews Conjoint Medical School in 1933. He was an attending physician and director of chest service at Fordham Hospital. Dr. Israel was a Fellow of the American College of Chest Physicians and a member of the American Association for Thoracic Surgery, the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

John Francis Keating, M.D., of New York City, died on May 26 at St. Vincent's Hospital at the age of sixty. Dr. Keating graduated in 1929 from Jefferson Medical College of Philadelphia. He was an attending physician at St. Vincent's Hospital. Dr. Keating was a member of the hospital's executive board and vice-president of its executive committee, a past-president of the Celtic Medical Society, and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Charles Herbert Keene, M.D., of Kenmore, retired, died on August 31 at the age of eighty-seven. Dr. Keene graduated in 1902 from Harvard University Medical School. He was a former University of Buffalo professor and head of the University of Buffalo's Department of Health and Education. Dr. Keene was a member of the American Public Health Association, the American School Health Association, the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Heman Royce Marvin, M.D., of Lyon Mountain, died on August 25 at the St. Lawrence State Hospital at the age of seventy-nine. Dr. Marvin graduated in 1908 from the University of Vermont College of Medicine. Retired, he was a member of the Clinton County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Milton Plotz, M.D., of Brooklyn and New York City, died on October 1 at his home at the age of fifty-seven. Dr. Plotz graduated in 1928 from Columbia University College of Physicians and Surgeons. He was an attending physician at Kings County Hospital Center, Long Island College and Brooklyn State Hospitals, a consulting cardiologist at Wyckoff Heights and Kings Highway Hospitals, and a consulting physician at Goldwater Memorial, Manhattan General, and Lefferts General Hospitals. Dr. Plotz was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Cardiology, a Fellow of the American College of Physicians, and a member of the New York Academy of Medicine, the Brooklyn Society of Internal Medicine, the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Walter F. Preusser, M.D., of Albany, died on September 16 at the age of sixty-six. Dr. Preusser graduated in 1920 from Albany Medical College. He was a member of the New York Colon and Rectal Society, the Albany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Allan Rossby, M.D., of New York City, died on March 1 at the age of sixty-one. Dr. Rossby graduated in 1931 from New York Homeopathic Medical College and Flower Hospital. He was an assistant attending ophthalmologist at Lincoln Hospital and an associate attending surgeon in ophthalmology at Manhattan Eye, Ear and Throat Hospital. Dr. Rossby was a Diplomate of the American Board of Ophthalmology and a member of the American Academy of Ophthalmology and Otolaryngology, the New York County Medical Society, and the Medical Society of the State of New York.

Clarence Leonard Russell, M.D., of Utica, died on September 27 at his home at the age of eighty-three. Dr. Russell graduated in 1909 from Albany Medical College. A former pathologist at Utica State Hospital, he retired from this post in 1947. From 1947 to his retirement in 1949 he served as head of the laboratory at the former St. Luke's Hospital. Dr. Russell was a member of the Utica Academy of Medicine, the Oneida County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Louis Morton Silverstein, M.D., of Brooklyn and Forest Hills, died on May 11 at Terrace Heights Hospital, Hollis, Queens, at the age of fifty-one. Dr. Silverstein received his medical degree from the University of Zurich in 1936. He was an attending obstetrician and gynecologist at Brooklyn Women's Hospital, an adjunct obstetrician and gynecologist at Beth-El Hospital and Beth-El Hospital Outpatient Department, and an associate attending obstetrician and gynecologist at Coney Island Hospital and Coney Island Hospital Outpatient Department. Dr. Silverstein was a Diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Obstetricians and Gynecologists, a Fellow of the International College of Surgeons, and a member of the Brooklyn Gynecological Society, the Medical Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Wilhelm E. Stern, M.D., of Brooklyn, died on May 2 at the age of seventy-eight. Dr. Stern graduated in 1909 from Long Island College Hospital Medical School. He was an adjunct surgeon in otolaryngology at Brooklyn Eye and Ear Hospital. Dr. Stern was a Diplomate of the American Board of Otolaryngology and a member of the American Academy of Ophthalmology and Otolaryngology, the Medial Society of the County of Kings, the Medical Society of the State of New York, and the American Medical Association.

Liborio A. Volino, M.D., of Yonkers, died on June 7 at the age of sixty-two. Dr. Volino graduated in 1928 from Eclectic Medical College, Cincinnati. He was a member of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

New York physician to lecture at Karolinska Institute

Rachmiel Levine, M.D., chairman of the Department of Medicine at New York Medical College, has accepted an invitation to deliver the annual "Jacobeus Lecture" at the Karolinska Institute in Stockholm, Sweden.

The invitation, issued annually for the last fifteen years by a four-man committee from Scandinavia's four ranking medical schools—Copenhagen, Stockholm, Helsinki, and Oslo—is in the nature of an international accolade since only the top men in the medical profession are chosen to appear at the Institute.

The subject of Dr. Levine's address, which will be given on March 15, will be "Critical Analysis of the Theories of Insulin Action."

Screening method for detection of phenylketonuria

A State-wide demonstration program to determine the reliability on a routine basis of a new screening method for the early detection of phenylketonuria, known as the Guthrie technic, has been announced by Herman E. Hilleboe, M.D., Commissioner, State of New York Department of Health.

The test has been used successfully in individual hospitals but has not been fully tested on a mass scale. The screening program will be conducted by the State Health Department's Bureau of Maternal and Child Health, in cooperation with Robert Guthrie, M.D., the Buffalo physician who developed the test, and hospitals and laboratories throughout the State.

Phenylketonuria is an inborn error of metabolism which results in mental retardation unless detected and treated early in life. The Guthrie technic requires only a few drops of blood obtained from infants immediately prior to their discharge from hospital nurseries. Urine specimens are also required when the infants are between four and six weeks of age.

The demonstration program is scheduled to run for two years but may be terminated earlier if sufficient numbers of specimens are received to evaluate properly the procedure.

Drug from Canada found harmful

Sufferers of arthritis have been warned by the Food and Drug Administration that the drug Liefcort, which is being obtained from Canada, is dangerous and may not be imported legally into the United States.

F.D.A. Commissioner George P. Larrick said that Federal officers are detaining importations by persons who are obtaining the drug in Canada as a result of reading about it in a national magazine article last May. Reports of serious reactions are reaching the Food and Drug Administration. These include severe uterine bleeding.

Liefcort contains potent hormones including estradiol, prednisone, and testosterone. An F.D.A. analysis showed that the product contains ten times the therapeutic dose of estradiol.

Appointments to Workmen's Compensation Board

Colonel S. E. Senior, Chairman, New York State Workmen's Compensation Board, has announced the following appointments to the Board: George S. Deaver, M.D., New York City, as impartial specialist in rehabilitation; Lewis Dickar, M.D., Brooklyn, as compensation medical consultant in rehabilitation; and Edwin W. Roberts, M.D., Watertown, as associate compensation examining physician in the Syracuse office of the Board.

Medical publications cited

At the recent annual meeting of the American Medical Writers' Association held in Washington, D.C., five medical publications were cited for "distinguished service in medical journalism to the medical profession."

The journals honored were: *Archives of Internal Medicine*, published by the American Medical Association, as outstanding in the category of specialty and research journals; the *Bulletin of San Diego County Medical Society* (California), as the best in its category; and *Medical Science* as best among many controlled circulation journals distributed without subscription charge to the medical profession; *The New England Journal of Medicine*, as the best national or regional general medical journal in 1962; and the NEW YORK STATE JOURNAL OF MEDICINE as the outstanding state medical journal for 1962. William Hammond, M.D., Scarsdale, editor, accepted the award for the NEW YORK STATE JOURNAL OF MEDICINE which was presented by Col. John B. Coates, MC, USA.

Drug firms give aid to earthquake victims

More than $210,000 worth of drugs was contributed by member firms of the Pharmaceutical Manufacturers Association for victims of the recent disastrous earthquake in Iran.

The drugs, consisting of a variety of antibiotics, sedatives, antiseptics, and vitamins, were donated in response to an emergency appeal from the American Red Cross. More than 7,500 people were reported dead and 60,000 to 70,000 were left homeless in the wake of the disaster.

State reveals new program for care of addicts

Governor Rockefeller has announced specific plans for the initial implementation of the comprehensive new State program for the treatment of narcotic addicts. Under the law, the program will become effective January 1, 1963.

The three-pronged program, which is medically oriented and backed by law enforcement, will provide for treatment, aftercare, and intensified research. Under the plans developed by Paul H. Hoch, M.D., and the State of New York Department of Mental Hygiene, four new inpatient units will be added to existing facilities to give the State a total of 555 beds with a treatment capacity of over 2,200 patients yearly. This phase of the program will cost 3.4 million dollars, including construction costs, during its first year of operation.

The new treatment facilities include: 175 beds to be located at Manhattan State Hospital, New York City; 165 beds at Pilgrim State Hospital, West Brentwood; 35 beds at Middletown State Hospital, Middletown; and 25 beds at Buffalo State Hospital, Buffalo. The units will include wards for adolescents and for women. More than 400 trained personnel will furnish the necessary services.

Medical assistants convention

Nearly 450 medical assistants attended the American Association of Medical Assistants sixth national convention held in Detroit in September. Among the major actions taken at the convention were the formation of certification and self-improvement programs and a plan to divide the Association into six districts with one trustee elected from each district.

Mildred Taylor, Albany, was installed as treasurer of the Association, and John C. McClintock, M.D., Albany, was elected to the Association's national physicians advisory committee.

New unit for emotionally disturbed blind children

A 20-bed unit for the treatment of emotionally disturbed blind children was opened October 15 at the Fairmount Division of Syracuse State School.

Children up to age sixteen from the Upstate area will be cared for in the new unit which will be under the direction of Marc H. Hollender, M.D., director of Syracuse Psychiatric Hospital. The program will provide psychotherapy, drug, and other therapies as necessary. A full educational program will also be provided.

Pamphlet on drug safety

To help answer patients' questions concerning drug safety, the Pharmaceutical Manufacturers Association has made special leaflets on the subject available to physicians for their waiting rooms.

The leaflet, entitled "Safety of Prescription Drugs," was prepared by a group of prominent industry scientists. A major portion of the pamphlet is devoted to a chronologic outline of steps in testing drugs before they are marketed.

Copies of the pamphlet are available without cost from: Pharmaceutical Manufacturers Association, 1411 K Street, N.W., Washington 5, D.C.

Orthopedics course in Georgia

The Department of Continuing Education of the Medical College of Georgia will present a postgraduate course on "Orthopedics in General Practice" December 4 through 6 at the College in Augusta. Emphasis will be placed on the diagnosis and conservative treatment of orthopedic disease and injury, primarily in the ambulatory patient. The course is acceptable for 18 hours of credit by the American Academy of General Practice.

For information write to: Claude-Starr Wright, M.D., Director, Department of Continuing Education, Medical College of Georgia, Augusta, Georgia.

Personalities

Retired. Harold W. K. Dargeon, M.D., New York City, as chairman of the Department of Pediatrics at Memorial Hospital for Cancer and Allied Diseases.

Appointed. Stanley E. Bradley, M.D., and Harry Eagle, M.D., New York City, as members of the board of scientific consultants of the Sloan-Kettering Institute for Cancer Research. . . George James, M.D., New York City, as Commissioner of the City of New York Department of Health . . . H. Houston Merritt, M.D., New York City, as chairman of the Doctors' Division of the Manhattan-Bronx Hospital Trustees Division of the United Hospital Fund campaign.

Honored. Howard A. Rusk, M.D., New York City, with the title of "Commander of the Royal Order of the Phoenix" by King Paul of

Greece for his work in the training of Greek physicians and paramedical personnel in the field of physical medicine and rehabilitation and in the treatment of disabled patients from Greece.

Awarded. Edward A. Burkhardt, M.D., New York City, a Pfizer Award of Merit for his contributions in the field of civil defense and disaster preparedness . . . Ludwik Gross, M.D., Bronx, and Peyton Rous, M.D., New York City, cash awards from the General Assembly of the United Nations in honor of their contributions to cancer research.

Speakers. Martin Cherkasky, M.D., New York City, at a forum at the New York Academy of Medicine on October 4 sponsored by the Citizens' Committee for Children of New York . . . Harold Jacobziner, M.D., New York City, Assistant Commissioner, The City of New York Department of Health, on October 23 at the Vassar Brothers Hospital, Poughkeepsie, on the topic "Accidental Poisoning in Childhood"; on October 24 at Columbia Presbyterian Hospital, New York City, on the subject "Poison Control-Cooperative Program by Physicians and the New York City Health Department"; on October 25 at the Orange Memorial Hospital in Orange, New Jersey, on Grand Rounds; and on November 21 at Long Island College Hospital, Brooklyn, on the subject "Accidents and Poisonings". . . Richard H. Lyons, M.D., Syracuse, on the subject "The Evaluation of the Hypertensive Patient" at the Rochester Academy of Medicine on November 8 . . . Nathaniel E. Reich, M.D., Brooklyn, on November 10, in New York City, at the annual meeting of the Phlebology Society of America on the topic "Diseases of the Abdominal Aorta" and on November 15 in Waterbury, Connecticut, before the Waterbury Area Heart Association and the Connecticut Academy of General Practice on the subject "Cardiac Complications of Systemic Diseases."

Mortality rate from heart disease

The mortality from heart disease in the past decade decreased at every period of life except early childhood and the older ages, according to statisticians of Metropolitan Life Insurance Company.

Although there was an over-all rise in the recorded death rate from all forms of heart disease combined—from 358 per 100,000 in 1949 to 373 in 1960—it merely reflected the growing ratio of older persons in the country. When allowance is made for this aging, the mortality from heart disease actually showed a 5 per cent drop.

It is believed that the appreciable increase in heart disease deaths at preschool ages partially reflects the fact that a larger proportion of babies with congenital heart lesions benefit by modern treatment methods and survive beyond infancy but then succumb during early childhood. Furthermore, a greater number of such cases are being diagnosed.

Besides taking a heavy toll of life, heart disease is responsible for a large amount of illness and disability. The National Health Survey estimates that there are more than 675,000 heart disease patients discharged each year from short-stay hospitals and that they spend approximately 11 million days annually in hospitals. This is actually an understatement, since the Survey is based on data collected only in household interviews and excludes persons residing in long-stay institutions.

Similarly, heart disease accounts for a large amount of time lost from work. For example, in the survey year ended in June, 1960, a daily average of 52,000 men and 10,000 women were absent from work because of heart conditions. More than 15 million days were lost from gainful employment during the year.

Medical Meetings

Brooklyn conference on pulmonary disorders

"Recent Advances in Clinical Pulmonary Disorders" will be the subject of a conference sponsored jointly by the Kings County Chapter of the American Academy of General Practice, the Brooklyn Tuberculosis and Health Association, and the Medical Society of the County of Kings in cooperation with the City of New York Department of Health on Tuesday, November 20, from 9:00 A.M. to 5:00 P.M. at the State University of New York Downstate Medical Center. Harold A. Lyons, M.D., professor of medicine at the Downstate Medical Center, is the conference chairman.

The morning session will deal with pulmonary emergencies and the afternoon session with management of pulmonary disorders. Floyd M. Feldmann, M.D., assistant professor, Cornell University Medical College, will deliver a special address entitled "The Practicing Physician and the Tuberculin Test."

Interested physicians are requested to make application to: Brooklyn Tuberculosis and Health Association, Inc., 293 Schermerhorn Street, Brooklyn 17, New York.

American Medical Women's Association

The American Medical Women's Association will hold its annual meeting at the Ambassador Hotel, Los Angeles, California, on November 29 and 30. "Medical Aspects of Marriage and the Family" will be the subject of the scientific portion of the meeting.

For information contact: American Medical Women's Association, 1790 Broadway, New York 19, New York.

Medical Services Conference

The fifth annual medical services conference sponsored by the Council on Medical Service of the American Medical Association will be held at the Biltmore Hotel, Los Angeles, California, Sunday, November 25. The topic of the program will be "Kerr-Mills in Action—1962."

Schoenberg Memorial Lecture

"Some Mechanical Approaches to Glaucoma" will be the subject of the annual Schoenberg Memorial Lecture to be delivered by John M. McLean, M.D., professor of clinical surgery (ophthalmology), at Cornell University Medical College, on December 3 at 8:15 P.M. at the New York Academy of Medicine, 2 East 103rd Street, New York City.

Following the Schoenberg lecture, George Gorin, M.D., associate attending surgeon, Manhattan Eye, Ear, Nose and Throat Hospital, New York City, will discuss "Deep Chamber Glaucoma after Cataract Extraction."

The annual lecture series is cosponsored by the National Society for the Prevention of Blindness and the New York Society for Clinical Ophthalmology.

American College of Chest Physicians

The American College of Chest Physicians in cooperation with the Industrial Medical Association will present a postgraduate course on cardiopulmonary diseases and occupation at the Statler Hotel in Detroit, December 3 through 7.

For information write to: American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Lecture on psychoanalysis

The Association for the Advancement of Psychoanalysis will present a talk by Harold Kelman, M.D., New York City, on the subject "Training Analysis: Past, Present, Future," on Thursday, December 6, at 8:30 P.M., at the New York Academy of Medicine, 2 East 103rd Street, New York City.

Diabetes Association, District of Columbia

The Diabetes Association of the District of Columbia, Washington, D.C., will present a one-day symposium on the current aspects of diabetes on Thursday, December 14, at the Washington Hospital Center.

Speakers and their subjects will be as follows: "Introduction," Thomas W. Mattingly, M.D., Washington Hospital Center; "Neuropsychiatric Aspects of Juvenile Diabetes," Reginald S. Lourie, M.D., George Washington University School of Medicine; "Diabetic Nephropathy," Max Ellenberg, M.D., The Mt. Sinai Hospital, New York City; "The Course of Juvenile Diabetes Treated with Unmeasured Diet," Harvey C. Knowles, M.D., University of Cincinnati School of Medicine; "Diabetic Microangiopathy," J. M. B. Bloodworth, M.D., University of Wisconsin School of Medicine; "Insulin Resistance and Insulin Antagonists," George W. Hamwi, M.D., Ohio State University; "The Hypoglycemias," Jerome W. Conn, M.D., University of Michigan; "Iatrogenic Diabetes," Rachmiel Levine, M.D., New York Medical College; "Oral Hypoglycemic Agents," Alexander W. Marble, M.D., Joslin Clinic, Boston.

For further information contact: Adolph Friedman, M.D., Vice-President, Diabetes Association of the District of Columbia, 1712 Eye Street, N.W., Washington, 6, D.C.

Pan American Medical Association

The Pan American Medical Association announces that its thirty-eighth anniversary congress will be in the form of a fourteen-day medical cruise on board the liner *S.S. Independence* of the American Export Lines, departing from New York City on Tuesday, February 26, and returning Tuesday, March 12.

The scientific program will include papers to be read at sea and at medical meetings in San Juan, Puerto Rico; Caracas, Venezuela; and Panama. Medical motion pictures will be shown and scientific and technical exhibits will be displayed on the ship.

For information contact: Pan American Medical Association, Inc., 745 Fifth Avenue, New York 22, New York.

American College of Allergists

The American College of Allergists will hold its nineteenth annual congress and graduate instructional course March 24 through 29, 1963, at the Americana Hotel, New York City. For further information write to: John D. Gillaspie, M.D., Treasurer, American College of Allergists, 2141 14th Street, Boulder, Colorado.

Gill Memorial Eye, Ear and Throat Hospital

The Gill Memorial Eye, Ear and Throat Hospital will hold its thirty-sixth annual spring congress in ophthalmology and otolaryngology April 1 through 5, at the Hospital in Roanoke, Virginia.

For further information write: Superintendent, The Gill Memorial Eye, Ear and Throat Hospital, P.O. Box 1789, Roanoke, Virginia.

Hair spray toxicity

Reports suggesting that the inhalation of hair sprays can cause a new lung disease were questioned in an article by Dr. G. W. H. Schepers in the August 18, 1962, issue of the *Journal of the American Medical Association.* Thesaurosis, the term used to describe the excessive retention of certain chemical elements in the lungs, has been attributed to heavy exposure to hair spray. However, there are many points of similarity between thesaurosis and pulmonary sarcoidosis, which may imitate many diseases.

Sarcoidosis is quite prevalent in the United States, and its manifestations in the lungs are often transient and occur with marked prevalence in women in their thirties and forties.

"On a statistical basis alone, it seems not unlikely, therefore, that pulmonary sarcoidosis will from time to time appear in women who use hair cosmetics abundantly since this practice is the current, well nigh universal vogue. It would seem that a more specific criterion should be found by means of which to differentiate between true thesaurosis and sarcoidosis coincidental to hair spray exposures."

The appearance of lung tissue, which forms the basis for a diagnosis of thesaurosis, is the same in many cases of sarcoidosis, including men who have not been exposed to hair sprays.

Attempts to reproduce thesaurosis in experimental animals have been unsuccessful thus far.

Abstracts

Ariel, I. M.: Results of treating patients with ovarian cancer with radioactive isotopes, New York State J. Med. **62:** 3553 (Nov. 15) 1962.

Seventy patients with ovarian cancer were given combinations of a radioactive isotope of a short half-life and one of a longer half-life, which is believed to be the preferable manner for intra-abdominal administration. Of the 70 patients, 57 have died; of the 13 who are living, 5 received isotopes prophylactically after a surgical resection of an isolated ovarian cancer, 3 have evidence of residual cancer, and 5 have no evidence of cancer even though there was widespread cancer at the time of treatment. Of the patients who received the isotopes for palliation, the results were good in 20, fair in 22, equivocal in 6, and of no benefit in 18. There were no serious complications of the regimen. Radioactive isotopes, alone and in combination with other means, are useful in destroying intraperitoneal seedings and small omental masses arising from ovarian cancer, in treating both smaller and larger masses of ovarian carcinomatosis, and in irradiating pelvic cancer. They are contraindicated in patients with an intestinal obstruction and those severely debilitated from extreme carcinomatosis.

Shainess, N.: Psychiatric evaluation of premenstrual tension, New York State J. Med. **62:** 3573 (Nov. 15) 1962.

A study of the menarche and menstrual symptoms, with emphasis on attitudes relating to feminine sexuality, was made in 103 women. A correlation was found between freedom from symptoms and a good mother-daughter relationship, including a favorable introduction to the menstrual experience. Menstrual symptoms can be divided into the physiologic and the ancillary; the latter can be understood in terms of loss of self-esteem and ego defense. Dysmenorrhea was found to have a physiologic basis in some patients and a large psychogenic component in others. Psychogenic factors seemed to be largely responsible for amenorrhea, which had occurred in 30 per cent of the patients.

Shore, N. A.: Head pain of temporomandibular joint origin, New York State J. Med. **62:** 3580 (Nov. 15) 1962.

Temporomandibular joint dysfunction is a noninfectious degenerative affection of the joint tissues which is caused in 90 per cent of the cases by pathologic occlusion of the teeth. The condition should be suspected in the presence of the following symptoms: clicking, crackling noise, crepitation, tenderness, pain in and around the temporomandibular joint, and occasional locking of the jaw. The pain may affect numerous areas of the head, the neck and shoulder regions, the arms and fingers, and even the lumbar spine. Treatment calls for close medical-dental coordination.

Ross, G., and Parker, J. G.: Serum carotene concentration in normal individuals and its clinical interpretation, New York State J. Med. **62:** 3584 (Nov. 15) 1962.

Serum carotene levels may be used as a simple screening procedure to detect suspected malabsorption. The normal range for serum carotene in 227 apparently healthy individuals on a normal mixed diet was found to be 70 to 300 micrograms per 100 ml. with a mean of 153 and a standard deviation of ±57. No statistical variation was found according to sex, age, or season. For a proper interpretation of serum carotene values it is important to know the patient's dietary intake for at least the preceding two weeks.

Lazar, H. P.: Yellow pigmentation associated with novobiocin therapy, New York State J. Med. **63:** 3590 (Nov. 15) 1962.

A yellowish pigmentation accompanying novobiocin therapy was observed in 4 patients. In 3 there was evidence of pigmentation and an elevation of the icterus index without a corresponding hyperbilirubinemia. There was chemical evidence of hepatocellular involvement in the other case. Caution should therefore be used in the administration of novobiocin until further study determines its hepatotoxicity.

De La Pava, S., and Pickren, J. W.: Cerebellar pressure cones; postmortem study, New York State J. Med. **62:** 3594 (Nov. 15) 1962.

Although cerebellar tonsillar herniations and/or cerebellar pressure cones can be caused by expanding brain lesions, they may occur in the absence of such lesions. In a study made in 133 consecutive autopsies, pressure cones were present in 18 per cent of the normal brains and in 27 per cent of the abnormal brains. Herniation and pressure cones were more frequent in cases with primary brain tumors than in metastatic brain tumors, indicating a relationship to the size of the lesion. There is a loose relationship between the presence of cerebellar tonsillar herniation and cerebellar cones, but one may occur without the other. Falx and hippocampal herniation were observed only in abnormal brains.

Books Received

*The following books were received during the month of September, 1962**

Cancer. By Lauren V. Ackerman, M.D., and Juan A. del Regato, M.D. Third edition. Quarto of 1,296 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $29.50.

Peripheral Vascular Diseases. By Edgar V. Allen, M.D., Nelson W. Barker, M.D., and Edgar A. Hines, Jr., M.D. Third edition. Octavo of 1,044 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $18.

Biopotentials of Cerebral Hemispheres in Brain Tumors. By N. P. Bekhtereva. Authorized translation from the Russian by Basil Haigh, M.B. Octavo of 183 pages, illustrated. New York, Consultants Bureau, 1962. Cloth, $12.50. (The International Behavioral Sciences Series. Edited by Joseph Wortis, M.D.)

Correlative Neuroanatomy and Functional Neurology. By Joseph G. Chusid, M.D., and Joseph J. McDonald, M.D. Eleventh edition. Octavo of 384 pages, illustrated. Los Altos, Calif., Lange Medical Publications, 1962. Paper, $5.50.

Medical Department, United States Army. Surgery in World War II. Activities of Surgical Consultants. Volume I. Editor-in-chief, Colonel John Boyd Coates, Jr., MC. Editor for Activities of Surgical Consultants, B. Noland Carter, M.D. Associate editor Elizabeth M. McFetridge, M.A. Octavo of 621 pages, illustrated. Washington, D.C., Office of the Surgeon General, Department of the Army, 1962. Cloth, $6.50.

Medical Department, United States Army. Wound Ballistics. Editor-in-chief, Colonel John Boyd Coates, Jr., MC. Editor for Wound Ballistics, Major James C. Beyer, MC. Octavo of 883 pages, illustrated. Washington, D.C., Office of the Surgeon General, Department of the Army, 1962. Cloth, $7.50.

Pharmacology and Patient Care. By Solomon Garb, M.D., and Betty Jean Crim, R.N. Duodecimo of 344 pages, illustrated. New York, Springer Publishing Company, Inc., 1962. Paper, $4.00.

Surgery of the Chest. Edited by John H. Gibbon, Jr., M.D. Octavo of 902 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $27.

Thanks for a better memory. By Samuel Kahn, M.D. Duodecimo of 176 pages. New York, Vantage Press, 1962. Cloth, $3.00.

Pharmacogenetics, Heredity and the Response to Drugs. By Werner Kalow, M.D. Quarto of 231 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $8.00.

Handbook of Psychiatric Treatment in Medical Practice. By Nathan S. Kline, M.D., and Heinz Lehmann, M.D. Octavo of 124 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $3.50.

One Hundred Years of Psychiatry. By Emil Kraepelin. Octavo of 163 pages, illustrated. New York, Philosophical Library, 1962. Cloth, $4.75.

Novak's Gynecologic and Obstetric Pathology. By Edmund R. Novak, M.D., and J. Donald Woodruff, M.D. Fifth edition. Quarto of 713 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $16.

Treatment of Cancer and Allied Diseases. Second edition. Volume VII: Tumors of the Male Genitalia and the Urinary System. By thirty authors. Edited by George T. Pack, M.D., and Irving M. Ariel, M.D. Quarto of 397 pages, illustrated. New York, A Hoeber Medical Book, Harper & Row, Publishers, 1962. Cloth, $18.

The Cholera Years. The United States in 1832, 1849, and 1866. By Charles E. Rosenberg. Octavo of 257 pages. Chicago, The University of Chicago Press, 1962. Cloth, $5.95.

Ciba Foundation Study Group No. 12. Curare and Curare-like Agents. Editor for the Ciba Foundation, A. V. S. de Reuck, D.I.C. With 26 illustrations. Duodecimo of 103 pages. Boston, Little, Brown and Company, 1962. Cloth, $2.95.

Ciba Foundation Symposium on The Exocrine Pancreas, Normal and Abnormal Functions. Editors for the Ciba Foundation A. V. S. de Reuck, D.I.C., and Margaret P. Cameron, M.A. With 91 illustrations. Octavo of 390 pages, illustrated. Boston, Little, Brown and Company, n.d. Cloth, $11.50.

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* Books received for review are acknowledged promptly in this column. No other obligation is assumed for the courtesy of those sending them for this purpose. Selection for review is made on the basis of merit and reader interest.

General Pharmacology. By Jean Sicé, Senior Research Fellow of the U.S. Public Health Service. Octavo of 593 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $11.50.

Hypertension—Neural and Renal Mechanisms. Volume X. Proceedings of the Council for High Blood Pressure Research, American Heart Association, Cleveland, November 17, 18, 1961. Edited by Floyd R. Skelton, M.D. Quarto of 95 pages, illustrated. New York, The American Heart Association, Inc., 1962. Paper, $2.50.

Doctors, Patients, and Health Insurance. By Herman Miles Somers and Anne Ramsay Somers. Abridged edition. Duodecimo of 544 pages, illustrated. Garden City, N.Y., Anchor Books, Doubleday & Company, Inc., 1962. Paper, $1.95.

Progress in Neurology and Psychiatry. Volume XVII. Edited by E. A. Spiegel, M.D. Octavo of 607 pages. New York, Grune & Stratton, 1962. Cloth, $14.

The Thyroid. Edited by Sidney C. Werner, M.D. Second edition. Octavo of 873 pages, illustrated. New York, A Hoeber Medical Book, Harper & Row, Publishers, 1962. Cloth, $24.

Artificial Respiration, Theory and Applications. Edited by James L. Whittenberger, M.D. Octavo of 276 pages, illustrated. New York, Hoeber Medical Division, Harper & Row, Publishers, 1962. Cloth, $10.

Advances in Rheumatic Fever 1940–1961. By May G. Wilson, M.D. Quarto of 249 pages, illustrated. New York, A Commonwealth Fund Book, Published by Hoeber Medical Division, Harper & Row, Publishers, 1962. Cloth, $10.

Nutrition in a Nutshell. By Roger J. Williams. Duodecimo of 171 pages, illustrated. Garden City, N.Y., Dolphin Books, Doubleday & Company, Inc., 1962. Paper, $0.95.

Electrocardiography, Fundamentals and Clinical Application. By Louis Wolff, M.D. Third edition. Octavo of 351 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $8.50.

New Antibiotic Drug Termed "Promising"

An antibiotic drug, generically termed oxacillin, has been designed to fight penicillin-resistant strains of staphylococci and has produced good results, it has been reported in the Sept. 1 issue of the *Journal of the American Medical Association.*

Studies have shown that strains of staphylococci are resistant because they produce penicillinase, the biologic antagonist of penicillin.

Oxacillin is a synthetic penicillin which resists destruction by penicillinase, William M. M. Kirby, M.D., Lona S. Rosenfeld, M.D., and Jean Brodie, B.S., Department of Medicine, University of Washington School of Medicine, Seattle, wrote in the *Journal.*

On the basis of laboratory tests and a study of 68 patients, the researchers concluded that oxacillin is a potent and effective drug when administered orally for the treatment of penicillin-resistant infections. Side-effects were minimal. Good results were obtained in 61 of the 68 patients and rated indeterminate in the other 7.

At the time treatment with oxacillin was started, 18 patients were considered seriously ill, the authors said, and in each of these "there seemed a clear-cut response to the antibiotic, and the patient was cured." The seriously ill included 6 patients with pneumonia, 5 with severe head and neck infections, and 3 with infected burns.

In laboratory tests, oxacillin was compared with three other synthetic penicillins and found to be five to eight times more active than one of them (methicillin), against penicillin-resistant staphylococci.

Books Reviewed

Immunity. By Sidney Raffel, M.D. Second edition. Octavo of 646 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $10.

This is a 600-page dissertation on immunity in all the aspects of its relationships to medicine. The exposition is nontechnical but is philosophically thorough and complete. The flow of ideas, reasonings, and judgments are free from interruption by laboratory detail.

The book is apparently written with a view toward serving the needs of the alert, intelligent, progressive general practitioner, internist, allergist, pediatrician, surgeon, or other specialist in whose daily work a better-than-average knowledge of immunology is basic but who would be repelled by a volume encumbered by technical discussion.

The author states that this second and larger edition has been made necessary because of the enormous increase in experimental knowledge over the past few years. Older hypotheses and theories have been outgrown or sharpened and extended with astonishing speed in diseases of the blood, infectious diseases, and the mechanics underlying the rejection of skin grafts and organ transplants, as well as in the elucidation of the pathophysiologic events related to the initiation of diseases such as rheumatic fever, lupus erythematosus, arteritis nodosa, and rheumatoid arthritis. The rapidly growing science of medical genetics likewise is intimately associated with immunity.

The exposition of the subject is divided into four sections. The first treats the fundamental principles of immunity; the second develops the concepts of hypersensitivity and hypersensitivity-like states and their relationship to immunity; the third section applies basic principles to our practical knowledge of acquired immunity as found in specific infectious diseases; and the fourth encompasses the serology and antigens of microbes, tissues, immunologic dysplasias and the A, B, and O, Rh, and other blood type systems.

A summary placed at the end of almost every chapter greatly enhances the reader's ability to recall, reflect on, and understand their contents.

In auditing the recent progress made in each subdivision, the author points out the direction experimentation must take to complete our knowledge so that the text is replete with suggestions for further experimentation.

The bibliography is extremely generous; the index is excellent.

This volume will undoubtedly find a place as a reference book in every medical library of significant size, but it might well be read from cover to cover by a large segment of the medical profession for profit and pleasure.—KENNETH G. JENNINGS, M.D.

Frontiers in General Hospital Psychiatry. Edited by Louis Linn, M.D. Octavo of 483 pages. New York, International Universities Press, Inc., 1961. Cloth, $10.

In recent years psychiatry has taken a tremendous leap forward in breaking down the isolation of the mental patient and bringing him into the functioning of the general medical hospital. Thus, the fact was accentuated that psychiatry was a function of medicine; that psychodynamics operated, pari passu, with organic physiology; and that the body and mind were inseparable components of the human being. However, the integration of psychiatry into the general hospital brought forth new and challenging problems, such as: the physical arrangement for the handling of mental patients, special precautionary measures, training of personnel, prevention of acting-out behavior, methods of therapy, rehabilitation, follow-up measures, interpersonal reactions between the mental and nonmental patients; and the destruction of traditional prejudices.

To seek elucidation and to provide a basis for further development, Dr. Linn, who has previously written on the subject of mental hospitals, has gathered together in this excellent book the views and experiences of about 40 prominent workers in this field from many parts of the world. The methods and views reported are diverse, original, and stimulating. Interesting, indeed, is the fact that the integration of psychiatry into the general hospital is not solely an American phenomenon, nor is it a recent innovation.

This book should be read not only by the psychiatric professional but also by all other physicians who are concerned with general hospital administration or policy. This book is well written, ably edited, and a delight to read.—THEODORE MELTZER, M.D.

Clinical Radiology of the Oesophagus. By Marcel Brombart. Translated by Sheila Kenny, M.D. Octavo of 383 pages, illustrated. Bristol, John Wright & Sons Ltd., (Baltimore, The Williams & Wilkins Company), 1961. Cloth, $15.

Dr. Brombart has long been interested in diagnostic radiology of the esophagus. The meticulous detail with which he has examined so many thousands of esophagi make him almost uniquely qualified to discuss the radiologic exploration of an organ which frequently is neglected because of the apparent ease of examination. This text is the author's attempt to detail his experiences and to establish a guide for esophogography. To do so he has divided his text into several chapters on technic, anatomy, physiology, roentgen anatomy, functional disorders, changes due to extrinsic factors, diverticula, esophagitis, ulcer of the esophagus, cancer, varices, and hiatus hernia. In each chapter there is a brief review of pertinent literature with an addended bibliography and then a statement of the author's own experience. Unfortunately, there is no chapter devoted to congenital anomalies of the esophagus, but the section on esophageal displacements secondary to congenital malformation of the aortic arch is outstanding.

The typography and reproduction detail are excellent. Additional line drawings, of equal excellence, are used freely where necessary.

To the average radiologist it may seem that there is little to be said about the esophagus that has not already been said. Dr. Brombart has produced a volume containing a wealth of information and providing a stimulus to all concerned for more detailed examination of the esophagus. The text is strongly recommended for all concerned with esophageal disease, but it is particularly suited for the radiologist.—SOLOMON SCHWARTZ, M.D.

Medical Genetics 1958–1960. By Victor A. McKusick, M.D., and contributors. Quarto of 534 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $14.50.

This is really three books combined in a single binding, that is, three yearbooks for 1958, 1959, and 1960. The plan in each of the three parts of the book is the same: First there are brief reviews of books published during the year, listings of journals, and brief descriptions of symposiums and congresses held during the year. The bulk of each section is devoted to brief abstracts of papers, arranged according to subject, namely, history, methods, biochemical genetics, congenital malformations, and then the various systems of the body. The editor sums up the advances of the year in an epilogue, and at the end of each section there is an alphabetical listing of the publications quoted. At the end of the entire volume there is a subject index, and for convenience of reference each paragraph is numbered; it is these numbers that are used for cross-reference purposes in the list of references and subject index.

In general the abstracts are descriptive rather than critical, and in some cases merely the title is listed. For example, the numerous reports of associations between blood groups and disease, for example, group O and duodenal ulcer, group A and carcinoma of the stomach, and so forth, are cited as if they were established facts. There is no indication of the existence of other critical articles pointing out certain fallacies in such studies, even though these more critical articles appeared during the period covered by the yearbooks. In contrast, the author does not hesitate to be harshly critical at times of other work; for example, Alvarez's book is listed in paragraph 2 only "to condemn it" and is characterized as "medical fiction."

The interest and usefulness of the volume is enhanced by the inclusion of some 70 figures and a number of tables, and there are occasional more detailed reviews of articles of more general interest, as well as editorial comments, such as the discussion of reports on the heredity of cancer on page 459. Nevertheless, the volume shares the limitations of other yearbooks and hardly constitutes a textbook on human genetics.

Obviously complete coverage of this rapidly expanding subject would have been too great an undertaking, so that the reviews are limited almost entirely to work published in English, and even here no attempt has been made to be complete. Still the coverage is remarkably comprehensive, and this volume would be a valuable addition to the library of any one interested in human heredity, as a helpful key to the literature for the period from 1958 to 1960.—A. S. WIENER, M.D.

Anatomy of the Coronary Arteries. By Thomas N. James, M.D. Quarto of 211 pages, illustrated. New York, Paul B. Hoeber, Inc., 1961. Cloth, $18.

The author of this beautifully illustrated book has succeeded in presenting clearly the gross anatomy of the coronary vessels. The vessels were visualized by an injection technic using a suitably colored plastic medium. The course and distribution of the arteries and veins are demonstrated by reproductions, in black and white and in color. Each coronary artery and its branches are described in separate chapters. A detailed description is given of the blood supply of the interventricular septum, the atrioventricular node, and the sinus node. Individual chapters are devoted to the coronary veins, arterial anastamoses, and the differences between human and canine coronary arteries. The book should prove to be a valuable source of anatomic information for the cardiologist, radiologist, pathologist, and surgeon.—IRVING G. KROOP, M.D.

Clinical Diagnosis. By Rustom Jal Vakil, M.D., and Aspi F. Golwalla, M.D. Octavo of 412 pages, illustrated. New York, Asia Publishing House, 1961. Cloth, $12.

This excellent textbook is a major step in recovering the balance in modern medicine which has swung so far in the direction of instrumental and electronic investigation. It recognizes, or rather reaffirms, the fact that a physician and a patient are involved and that the former must be able to assess illness without expensive and time-consuming equipment.

Both authors are distinguished practitioners in Bombay. The senior author, Dr. Vakil, will be remembered by many Americans as the recipient of the Lasker Award for Medical Research a few years ago. They have collaborated in producing a text which realizes fully their aim of providing a comprehensive handbook of clinical diagnosis for students and practitioners. While it is undoubtedly intended for residents of India, physicians of any nationality can read the book with profit.

A noteworthy feature is the inclusion of very many superb photographs, well chosen and exactly to the point. As far as I know, the illustrations are better than those included in any other similar volume published in this country. The authors are to be congratulated.—MILTON PLOTZ, M.D.

Modern Concepts of Hospital Administration. Edited by Joseph Karlton Owen, Ph.D. Quarto of 823 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $16.

In 1935, the late Malcom T. MacEachern, M.D., Director of the American College of Surgeons, published a text entitled *Hospital Organization and Management.* This was the first such work on the subject, and for many years it was considered the leading text in its field, although since then there have been many volumes published dealing with the nature of hospital organization and management, each in its own way offering evidence of the dynamic growth of hospitals and the new concepts which have developed in their administration.

In this work entitled *Modern Concepts of Hospital Administration*, Joseph Karlton Owen, Ph.D., has presented a unique approach to the subject by collecting in one volume material furnished by leading authorities on particular aspects of hospital operation, and the result is most effective. Of all the volumes since Dr. MacEachern's, this is the most comprehensive.

Dr. Owen received his master's degree in hospital administration from the School of Public Health and Administrative Medicine of Columbia University, and his doctorate of philosophy in hospital administration from the State University of Iowa. He is well-qualified to direct and edit the volume, having served in various administrative and teaching capacities in the field of hospital administration for many years.

The volume deals with operational specifics and community factors involving hospital care, and it should provide stimulating reading for all hospital administrators. Many chapters dealing with the organization of clinical departments would be most helpful to physicians who play a role in hospital medicoadministrative matters.

Chapter 15 on "Organizing the Medical Staff," which was written by Robert S. Myers, M.D., F.A.C.S., of the executive staff of the American College of Surgeons, is particularly well done. It is recommended reading for all physicians with medical staff appointments.—J. V. TERENZIO

Psychiatry. Volume 1. Principles. By E. Eduardo Krapf, M.D. Octavo of 244 pages, illustrated. New York, Grune & Stratton, 1961. Cloth, $6.50.

This book is the first volume of what may become a series of books in psychiatry. It is subtitled "Principles" but is essentially a presentation of the author's viewpoints. While arranged in textbook fashion, it is not at all a text. It is difficult to know for whom this book is intended. The author states in the preface that someone preparing for an examination will benefit from its reading. That is doubtful. To understand it requires a rather comprehensive knowledge of the subject such as that which a specialist possesses. To the student it can be exceedingly confusing.

Being a believer in the "essential unity of the human person," the author attempts to present a "multidimensional" approach to psychiatry. This is commendable but it seems to this reviewer that such a goal cannot be reached merely by putting together little pieces borrowed from several schools of thought. Truth cannot be arrived at through compromise. Truth in psychiatry will result from the application of scientific methods of research as has been the case in other branches of medicine. To this end, the book contributes nothing. The author presents much philosophy, many opinions, too little science, and no experimental data.—THEODORE MELTZER, M.D.

Early Detection and Diagnosis of Cancer. By Walter E. O'Donnell, M.D., Emerson Day, M.D., and Louis Venet, M.D. Octavo of 286 pages, illustrated. St. Louis, The C. V. Mosby Company, 1962. Cloth, $12.

Initially the authors discuss the cancer problem and the cancer detection examination. There then follows chapters devoted to cancer of the skin, head and neck, lungs, breast, female genital tract, gastrointestinal tract, genitourinary tract, and blood and blood-forming organs. Each chapter contains a brief statement of the epidemiology of the particular malignant condition under discussion and the etiology, pathology, and special diagnostic approaches that can be used. Each of these procedures is discussed clearly and simply. Line drawings are commonly employed to aid in the understanding of these technics.

The experience of the authors at the Strang Cancer Prevention Clinic more than justifies this effort to bring cancer detection into the realm of a practical office examination. Each physician's office should be a cancer detection clinic. With the help of this text, this is feasible. Physicians who deal specifically with cancer will find nothing new, but the text is not meant for them. It is meant for that large body of doctors who either through ignorance or lack of time fail to perform the basic studies herein described. The text might well be made part of medical school curriculums.—SOLOMON SCHWARTZ, M.D.

Logan Turner's Diseases of the Nose, Throat, and Ear. Edited by John P. Stewart, assisted by R. B. Lumsden. Sixth edition. Octavo of 524 pages, illustrated. Baltimore, The Williams and Wilkins Company, 1961. Cloth, $11.

The authors have brought the subject matter in this edition up to date, with the inclusion of the stapes mobilization, tympanoplasty, and ultrasonic treatment of Ménière's disease.

The contents are very comprehensive and are written in very clear, concise, and interesting style. Illustrations have been employed unsparingly.

This book is highly recommended for the senior student and the general practitioner who is interested in the field of otolaryngology.—SYDNEY SHAPIN, M.D.

Clinical Diagnosis by Laboratory Examinations. By John A. Kolmer, M.D. Third edition. Octavo of 543 pages, illustrated. New York, Appleton-Century-Crofts, Inc., 1961. Cloth, $10.

The author, Professor Emeritus of Medicine and Director of The Institute of Preventive Medicine and Public Health, Temple University School of Medicine, is eminently qualified to write on the subject of clinical pathology. This book deals with a new and rising specialty, that of the clinical pathologist. There was a time when the pathologist was confined to the necropsy room. The idea of examining a live patient was anathema. Thus he gave out his information and decreed the diagnosis without attention to the changes which took place during the lifetime of the diseased person.

The events of recent years have shown that with every disease there is an accompanying change in the various systems of the body which can be reflected by laboratory diagnosis. The dichotomy of clinical examination and laboratory or pathologic examination was continued, and there was no merging of the art of the physician at the bedside and the science of the physician in the laboratory. This emphasis on the place where the examination was made caused a continued divorce of the laboratory and the clinical picture.

More recently the clinical pathologist has emerged in his proper light. No longer is there emphasis on where the examination takes place. The diagnosis is always made on the basis of all available facts whether they came from the bedside or the laboratory. It is to merge and discuss these facts properly that is the role of the clinical pathologist. There is really but one diagnostic technic, that is, the technic which includes all the facts.

This book was written in an attempt to show how the laboratory and the physician can work together. In this object it succeeds admirably. Every physician, if he wishes to make use of the most modern diagnostic technics, must himself assume the attitude of a clinical pathologist in correlating all the facts which science today can make available to him.—THEODORE McG. FEINBLATT, M.D.

Physical Diagnosis. By Ralph H. Major, M.D., and Mahlon H. Delp, M.D. Sixth edition. Quarto of 355 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $7.50.

Major's classic *Physical Diagnosis*, in its completely revised sixth edition, continues to have the excellence of earlier editions. The reviewer knows of no other such work that he would prefer to this as an introduction to the subject for medical students. The section on medical history taking is especially good.

The illustrations and figures are numerous and relevant. An unfamiliar complaint on the part of a reviewer is that there may be, if anything, too many illustrations. Is it really necessary to have three pictures of kyphosis, five of emaciation, and eight of ascites? Either figure 93 or 94 could have been omitted and either 89 or 90. Does even the most downy-faced novice need figure 30? Despite these extra riches, the volume is well printed and remains reasonable in price.

In short, it is highly recommended.—MILTON PLOTZ, M.D.

Rehabilitation of A Child's Eyes. By Herbert M. Katzin, M.D., and Geraldine Wilson, R.N. Third edition of Scobee's "Rehabilitation of A Child's Eyes." Octavo of 107 pages, illustrated. St. Louis, The C. V. Mosby Company, 1961. Cloth, $3.75.

Rehabilitation of the eyes in this book is limited to only one disorder, namely, cross-eye. One hundred pages are devoted to informing parents of problems confronting the ophthalmologist. Because rehabilitation must be handled by the eye physician, he cannot very well direct the parent what to do but instead involves himself in a theoretical and often technical discussion. Also, in a book intended for the layman positive statements usually are taken to mean that they represent the thinking of all ophthalmologists. Not every ophthalmologist will agree with the statement (page 61) that "practically every child will benefit from eye exercises." Also, one finds contradictions. For example (page 50) one notes that "children who have reading problems should be carefully checked for cross-eye." And on page 55 one reads that "The cross-eyed child seeks solace in books because of psychologic complexes and becomes an excellent student."

The problems of eye surgery, patching of an eye, eye exercises, and eyedrops are subject to differences of opinion. Whatever the merits of this book, it should be clearly understood that it represents one point of view and would help, therefore, to explain teachings emanating from this school of thought.—EMANUEL KRIMSKY, M.D.

Electrodiagnosis and Electromyography. Edited by Sidney Licht, M.D. Second edition. Octavo of 470 pages, illustrated. New Haven, Elizabeth Licht, Publisher, 1961. Cloth, $12.

This second edition (the first edition was published in 1956) represents a marked improvement of the first. The volume is almost twice as long as the initial edition. The original chapters have been revised and five new chapters added. Many colored photographs and numerous charts are incorporated in this edition. In addition to the outstanding specialists in the field of physical medicine, physiology, neurophysiology, and electrophysiology, who were contributing authors in the first edition, the present edition has utilized the skills and knowledge of an electrical engineer and a neuropathologist as well. The chapters on the fundamentals of electromyography and the clinical application of electromyography are outstanding and, in themselves, would constitute an excellent text. In addition, a chapter on electroencephalography and electroretinography have been included.

As previously recommended, a text of this type is essential in the library of every physiatrist, orthopedist, neurologist, and neurosurgeon, and it can and should be of tremendous value to general practitioners utilizing medical rehabilitation in their daily procedures. It is strongly recommended as a reference book in every medical library of every active hospital and teaching institution. Eighteen individual contributors, most of whom enjoy high national and international reputations, and the excellent contributions and editing by Dr. Licht deserve particular commendation.—S. G. FEUER, M.D.

Ciba Foundation Symposium on Somatic Stability in the Newly Born. Editors for the Ciba Foundation, G. E. W. Wolstenholme, M.B., and Maeve O'Connor, B.A. With 63 illustrations. Octavo of 393 pages. Boston, Little, Brown and Company, 1961. Cloth, $10.

This important symposium was accomplished by Ciba Foundation in cooperation with the Neonatal Society; 27 international authorities were gathered to consider the question of somatic stability in newly born infants. The discussion included considerations of kidney function and the excretion of water and solutes, metabolic effects of fasting and food, the stability of the cardiovascular system, the endocrine function of the newborn infant, the relevance of anencephaly, and problems of somatic stability. This book is well written and should be of special value to students in neonatology.

It was of interest to note that in the mid-stage of pregnancy, nutrition is obtained by the active agency of the trophoblastic cells and is unrelated to the nutrition of the mother. In the later stage, when the trophoblasts degenerate, the nutrition is by the placenta and by transfusion. During this fetal stage the nutrition of the mother plays an important part in the development and the stability of the newborn animal.

The kidney function of the neonate shows low glomerular filtration rate and low values of tubular functions. The kidney has a low concentrative ability which is due partly to shortness of the loops of Henle and partly to the low urea excretion which is due to the retention of nitrogen for growth. The ability to dilute the urine is as good as in adults, but the maximum urine flow is lower in the infant in comparison with the adult.

In discussing carbohydrate metabolism and the role of the liver, Zellerstram pointed out that only recently has hypoglycemia in the newborn infant become a syndrome of clinical interest. Biochemical changes occurring during asphyxia and some effects on the heart were discussed by James and Bernhard. Usher discussed the metabolic changes in respiratory distress syndrome of prematurity in infants weighing less than 1,000 Gm. and the fact that those having respiratory distress often die from the metabolic side-effects of asphyxia rather than directly from asphyxia itself. They have toxic degrees of acidosis and hyperkalemia, and he feels that this is related to the inability of the premature infant's kidney during the first few days of life to increase its excretion of solutes and to conserve base. Metabolic therapy consists of the intravenous infusion of glucose and sodium bicarbonate from birth onward which results in the prevention and treatment of metabolic side-effects. This therapy can often be lifesaving but does not affect the underlying asphyxia. Many investigators have tried to reproduce the results obtained by Usher and have been unsuccessful with this therapy. Reardon, at the University of Pennsylvania, uses glucose and sodium chloride. It was surmised that very likely the fluids given expedite renal function and for that reason may be successful.—JOHN A. MONFORT, M.D.

Therapeutic Communication. By Jurgen Ruesch, M.D. Octavo of 480 pages. New York, W. W. Norton & Company, Inc., 1961. Cloth, $6.50.

The author of this volume is professor of psychiatry at the University of California School of Medicine. For over twenty years he has interested himself in the fundamental problem of communication between the patient and the doctor. One can readily agree with him that the ability to communicate is the central ingredient in all forms of mental healing, regardless of the training or the background of the therapist. This is the kernel responsible for the improvement of the patient, and in essence, according to the author, all psychopathologic conditions are a disturbance in communicative behavior. Therefore, in therapy, one should attempt to correct this defect.

In this book, as well as in previous works of the author, he has set himself the task of bringing some degree of clarity out of the confusion which has existed in this fundamental concept of human behavior.

It is an important psychologic investigation, and should be read carefully by all who seek further information and knowledge of the instrument which makes all therapy possible.—Joseph L. Abramson, M.D.

Tumours of the Oesophagus. Edited by Norman C. Tanner, M.D., and D. W. Smithers, M.D. Octavo of 352 pages, illustrated. Edinburgh, E. & S. Livingstone, (Baltimore, The Williams & Wilkins Co.), 1961. Cloth, $13.

In 1944 a group of postgraduate teaching hospitals in London started a scheme for joint consultation and cooperation in the treatment of patients with certain tumors. The purpose of the monographs is not strictly confined to the hospital group, but includes wide clinical experience wherever it may be found and enlists expert help whenever it is available.

The writers present through clear, concise x-ray photographs every phase of esophageal pathology. The excellent geographic maps show the effect of certain rock, as granite and syenite, as a causative factor in carcinoma because of a high concentration of radioactive elements. The statistical analyses cover: age, sex, seasonal effects, marital, economic, occupation, and geographic factors, and a comparison of mortality in selected countries.

It is apparent to most physicians that the cardia has always been a battlefield of physiologic controversy. The relation to the vestibule and ampula of the esophagus, along with the angle of the esophagus at the cardia, acts as a barrier to gastric reflux.

The descriptions of surgical procedures and the illustrations are so literal that they leave no doubt in the reader's mind how to proceed.

This is an outstanding monograph compressed in a small volume. All surgeons, radiologists, and internists should keep it handy.—John J. Lille, M.D.

Ophthalmic Pathology. An Atlas and Textbook. Edited by Michael J. Hogan, M.D., and Lorenz E. Zimmerman, M.D. Second edition. Quarto of 797 pages, illustrated. Philadelphia, W. B. Saunders Company, 1962. Cloth, $30.

This beautifully illustrated and descriptive atlas on ophthalmic pathology published under the combined sponsorship of the American Academy of Ophthalmology and Otolaryngology and the Armed Forces represents an outgrowth of a compressed atlas originally emanating from the old Army Medical Museum. More than 700 eye-appealing illustrations, many covering a full page, help to make this subject most intriguing. The legends are descriptive and comprehensive. The approach is clinical. The text is comprehensive, and the reader constantly discerns the close correlation between clinical ophthalmology and applied pathology.—Emanuel Krimsky, M.D.

First International Conference on Congenital Malformations, London, England July 18–22, 1960. Compiled and edited for the International Medical Congress, Ltd. Quarto of 314 pages, illustrated. Philadelphia, J. B. Lippincott Company, 1961. Cloth, $7.50.

This volume comprises the proceedings of the First International Conference on Congenital Malformations under the sponsorship of the International Medical Congress. It is the fruit of the first concerted approach to a problem which, far from hopeless as it was thought until recently, is beginning to be recognized as being susceptible of study and possible prevention.

There were eight sessions devoted to incidence, genetics, environmental factors, general developmental mechanisms, abnormal developmental mechanisms, maternal-fetal interactions, physiologic and medical problems, and perspectives. Of these, the discussion of environmental teratogenic influences is probably the most important. Up to the revolutionary findings of Gregg with regard to rubella in 1941, congenital malformations had been regarded by physicians as God-determined or at least egg-determined, although most lay people were prepared to place the blame on "shocks" and other emotional aberrations which disturbed the pregnant woman. The session discussed the little authentic current information which is available and the directions for future investigation.

Obstetricians, pediatricians, experts in public health, enlightened physicians, and lay persons will find much to interest them in this volume.—Milton Plotz, M.D.

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Abstracts in Interlingua

Ariel, I. M.: Resultatos del uso de isotopos radioactive in le tractamento de patientes con cancere ovarian (*anglese*), New York State J. Med. **62:** 3553 (15 de novembre) 1962.

Septanta patientes con cancere ovarian esseva tractate con combinationes de un isotopo radioactive a curte periodo de medie valor con un altere a plus longe periodo de medie valor, lo que es reguardate como le procedimento de election in applicationes intra-abdominal. Ex le serie total de 70 patientes, 57 ha morite. Inter le 13 qui vive, 5 recipeva isotopos prophylacticamente post resection chirurgic de un isolate cancere ovarian; 3 manifesta evidentia de cancere residue; e 5 ha nulle evidentia de cancere ben que extense lesiones esseva presente al tempore del tractamento. Inter le patientes qui recipeva le isotopos pro objectivos de palliation, 20 monstrava bon resultatos; le resultatos esseva satis bon in 22, equivoc in 6, e non benefic in 18. Le regime produceva nulle serie complicationes. Isotopos radioactive—sol o in combination con altere modalitates therapeutic—es utile in destruer seminationes intraperitonee e micre massas omental que prende lor origine in cancere ovarian, in le tractamento tanto de micre como etiam de plus grande massas de carcinomatosis ovarian e in le irradiation de cancere pelvic. Lor uso es contraindicate in patientes con un obstruction intestinal e in patientes con sever debilitate in consequentia de carcinomatosis extreme.

Shainess, N.: Evalutation psychiatric de tension premenstrual (*anglese*), New York State J. Med. **62:** 3573 (15 de novembre) 1962.

Esseva effectuate un studio del menarche e del symptomas menstrual in 103 feminas, con attention particular prestate al attitudes relationate con le sexualitate feminin. Esseva constatate un correlation inter absentia de symptomas e un bon relation de matre a filia, incluse un favorabile introduction al experientia menstrual. Le symptomas menstrual pote esser dividite in symptomas physiologic e symptomas ancillari. Le symptomas del secunde de iste gruppos pote esser comprendite a base de factores de perdita de auto-respecto e de defensa del ego. Esseva trovate que dysmenorrhea ha un base physiologic in certe patientes e un forte componente psychogene in alteres. Factores psychogene pareva esser grandemente responsabile pro amenorrhea, que es un condition que habeva occurrite in 30 pro cento del patientes.

Shore, N. A.: Dolor de capite a origine in le articulation temporomandibular (*anglese*), New York State J. Med. **62:** 3580 (15 de novembre) 1962.

Dysfunction del articulation temporomandibular es un non-infectiose affection degeneratori del tissus articular que es causate in 90 pro cento del casos per un occlusion pathologic del dentes. Le condition deberea esser suspicite in le presentia del sequente symptomas: Crepitation, cliccamento, hyperesthesia, dolor in e circum le articulation temporomandibular, e occasionalmente serratura del mandibula. Le dolor pote afficer numerose areas del capite, del collo, e del espalda, le bracios e digitos, e mesmo le region lumbar del columna vertebral. Le tractamento presuppone un intime coordination medico-dental.

Ross, G., e Parker, J. G.: Le concentration seral de caroteno in subjectos normal e le interpretation clinic de illo (*anglese*), New York State J. Med. **62:** 3584 (15 de novembre) 1962.

Le determination del nivello seral de caroteno pote esser usate como un simple test de triage in le detection de suspicite malabsorption. A base del examine de 227 apparentemente normal subjectos recipiente un normal dieta mixte il pote esser asserite que le area de valores normal cade inter 70 e 300 microgrammas per 100 millilitros de sero. In le gruppo studiate le valor medie esseva 153 e le deviation standard ±57. Esseva constatate nulle statisticamente significative variation secundo sexo, etate, o saison. Pro le correcte interpretation del valores de caroteno seral il es importante que on cognosce le ingestion dietari del patiente pro al minus le precedente duo septimanas.

Lazar, H. P.: Pigmentation jalne, associate con therapia a novobiocina (*anglese*), New York State J. Med. **62:** 3590 (15 de novembre) 1962.

Un pigmentation jalnastre esseva observate in 4 patientes sub therapia con novobiocina. In 3, evidentia esseva presente de pigmentation con elevation del indice de ictero sin correspondente hyperbilirubinemia. Evidentia chimic de affection hepatocellular esseva notate in altere casos. Le administration de novobiocina, per consequente, require circumspection usque

continued on page 3682

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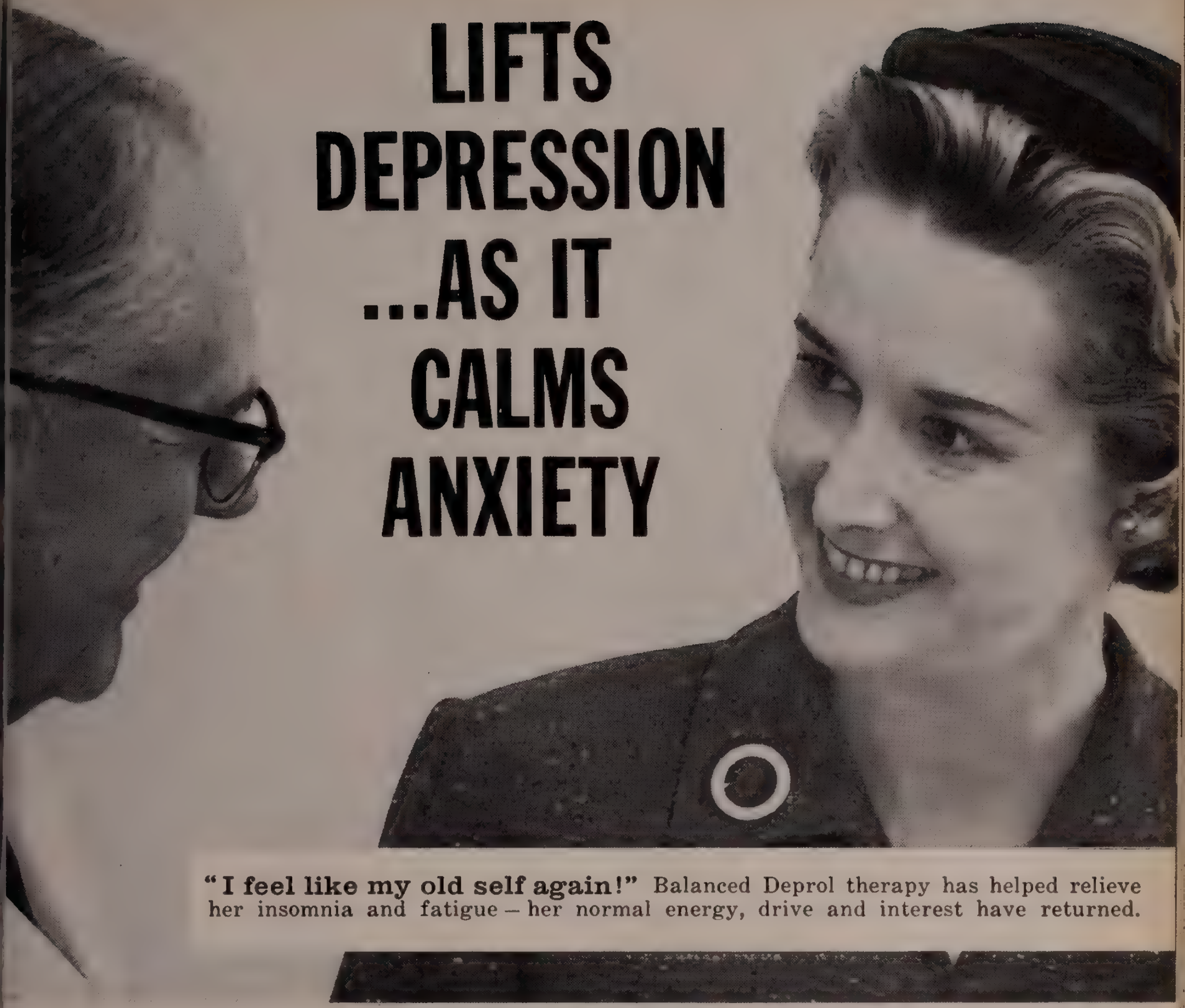

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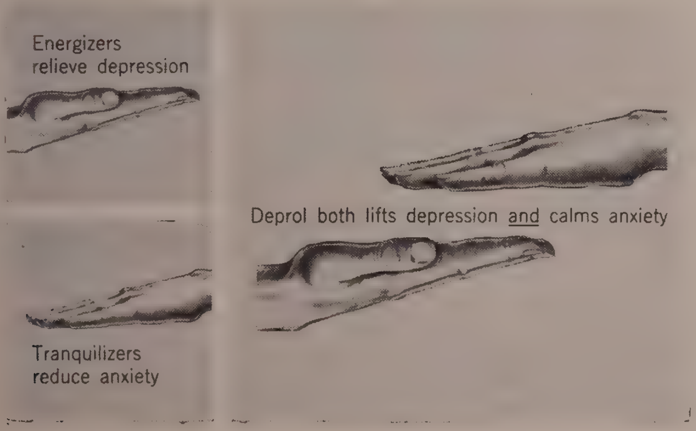
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continued from page 3680

studios additional pote clarificar su hepatotoxicitate.

De La Pava, S., e Pickren, J. W.: Conos cerebellari de pression; un studio post morte (*anglese*), NEW YORK STATE J. MED. **62:** 3594 (15 de novembre) 1962.

Ben que herniationes cerebello-tonsillari e/o conos cerebellari de pression pote esser causate per le expansion de lesiones cerebral, illos etiam pote occurrer in le absentia de tal lesiones. In un studio de un serie consecutive de 133 necropsias, conos de pression esseva presente in 18 pro cento del cerebros normal e in 27 pro cento del cerebros anormal. Herniation e conos de pression esseva plus frequente in casos de primari tumores cerebral que in casos de metastatic tumores cerebral. Isto pare indicar un correlation con le dimensiones del tumor. Il existe un laxe coordination del presentia de herniation cerebello-tonsillari con illo de conos cerebellari, sed le un pote occurrer sin le alteres. Herniation de falce e herniation hippocampal esseva observate solmente in cerebros anormal.

Body storage of surplus protein

Scientific evidence does not support the theory that the body stores surplus protein in the way it stores sugars, starches, and fats for emergency demands, according to an article by L. Emmett Holt, Jr., M.D., Elias Halac, Jr., M.D., and Charlotte N. Kajdi, A.B., in the August 25, 1962, issue of the *Journal of the American Medical Association.*

Protein is a "currently glamorous nutrient," and enthusiasm for protein food is widespread in the United States today. A major factor in encouraging a liberal protein intake is the concept that reserve protein can be built up in advance to offset protein shortages that may develop later due to privation or illness. However, the existence of protein stores has not been established.

Two studies were undertaken to determine if a protein surplus enabled rats to withstand a subsequent deprivation of protein. In the first study, there was no difference in survival between a group of rats fed a moderate protein diet and then deprived of protein and a group of rats fed a high protein diet and then deprived of protein.

In the second study the previous findings were confirmed, and it was found also that the percentage of protein in fat-free tissues did not differ significantly between rats fed a normal protein diet and those given a high protein diet. Thus, neither study supports the concept of protein stores.

Protein deprivation cannot be taken care of in advance. As a general rule, it is after the event that shortages are made up. However, "nutritional requirements in convalescence are very different from those in health. The convalescent is a different animal. At this time he needs and should have more protein than the minimal requirement for health."

On the basis of short-term studies, there is not evidence that there is harm in giving more protein than the minimum adequate requirement to healthy persons. However, the possibility that long-term differences may occur cannot be denied.

Although large areas of the world are suffering from protein deficiency, this disorder is encountered only rarely in the United States in a port or border city with a population from a less favored foreign country.

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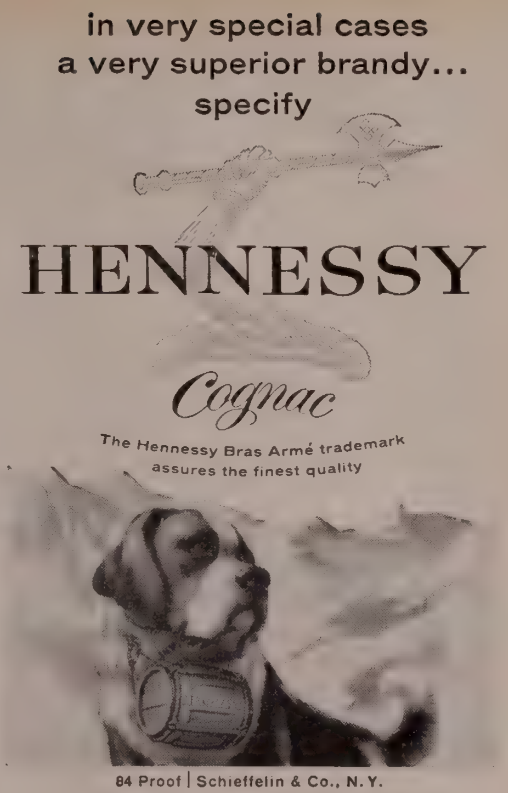

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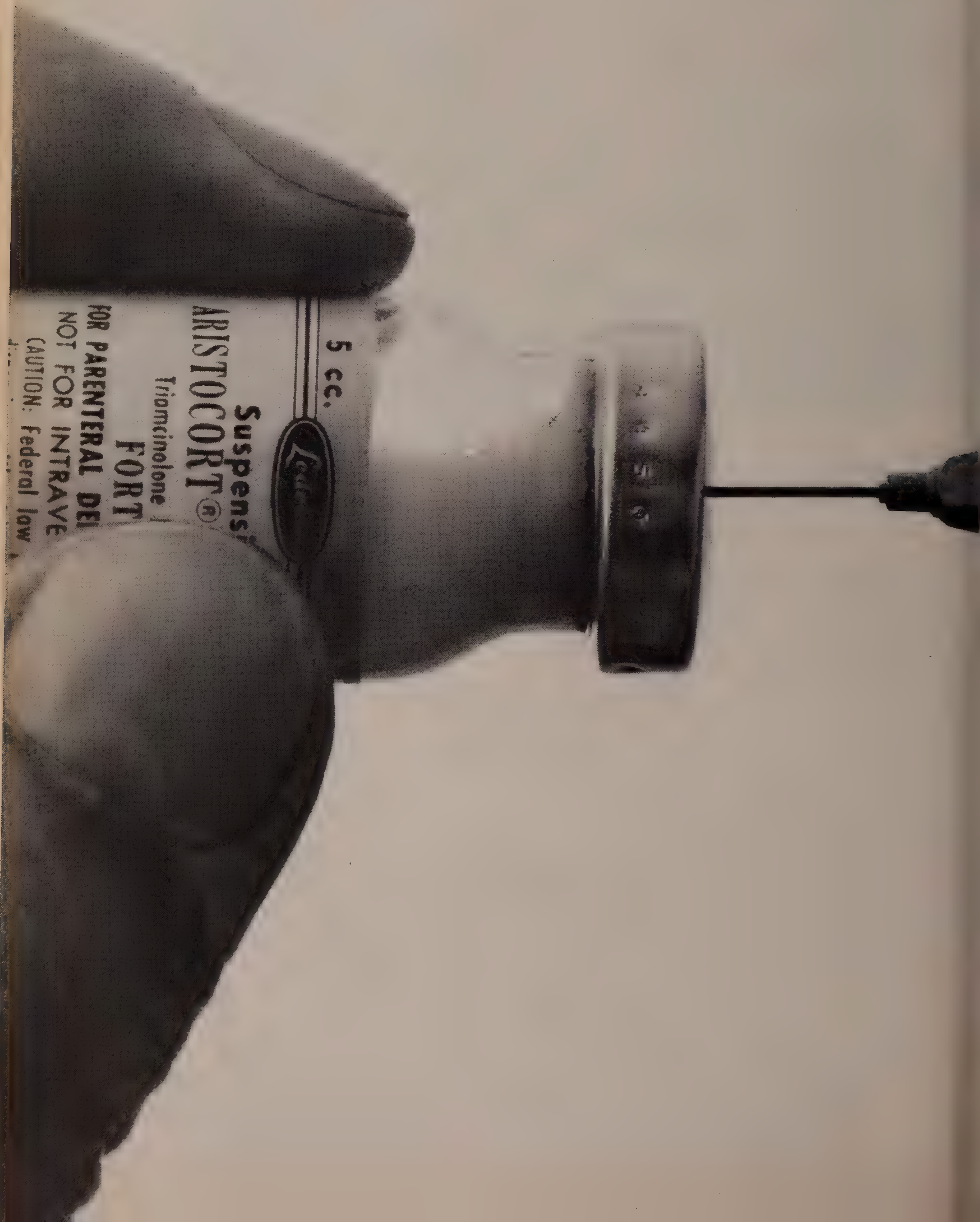
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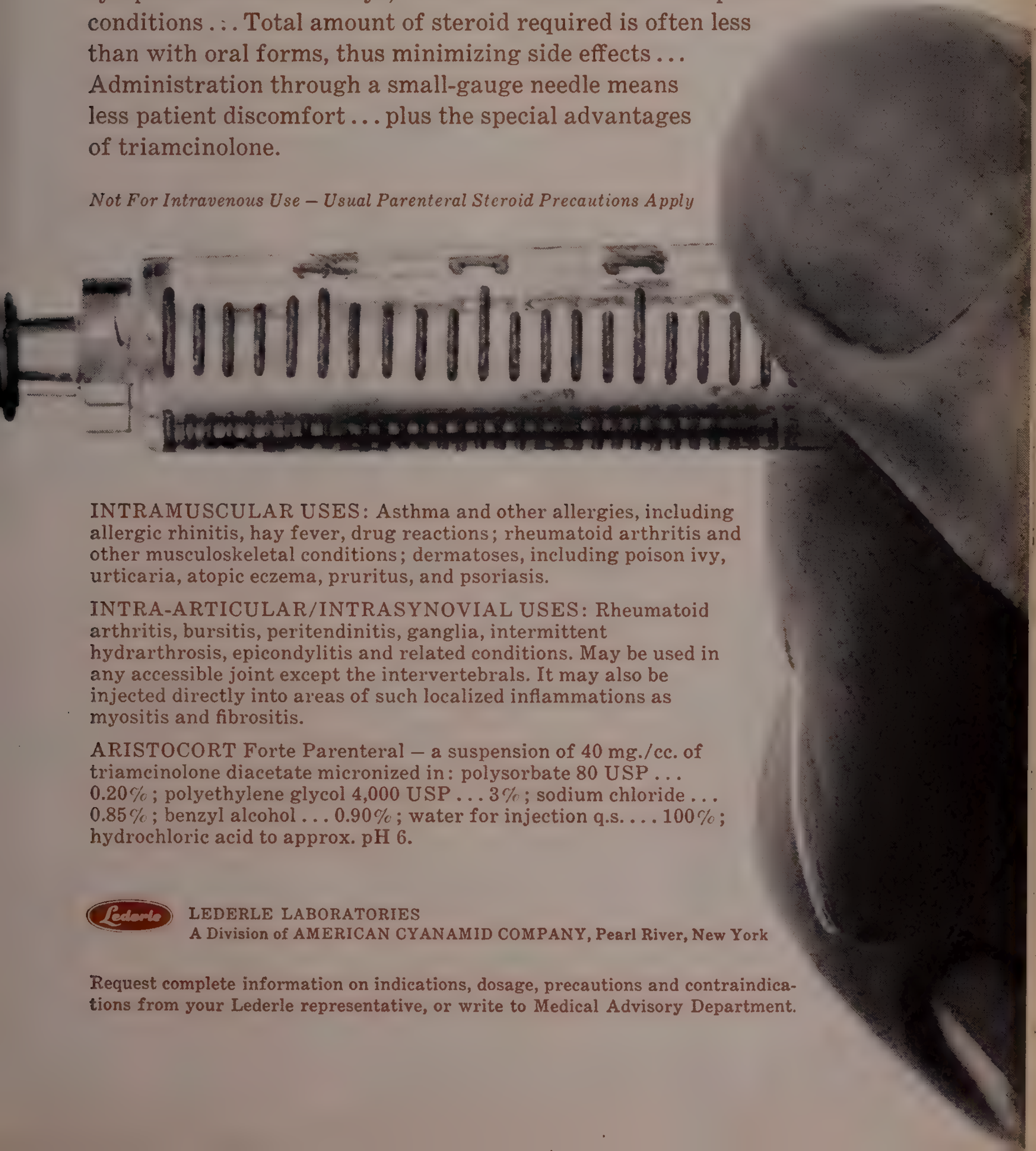

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956.
2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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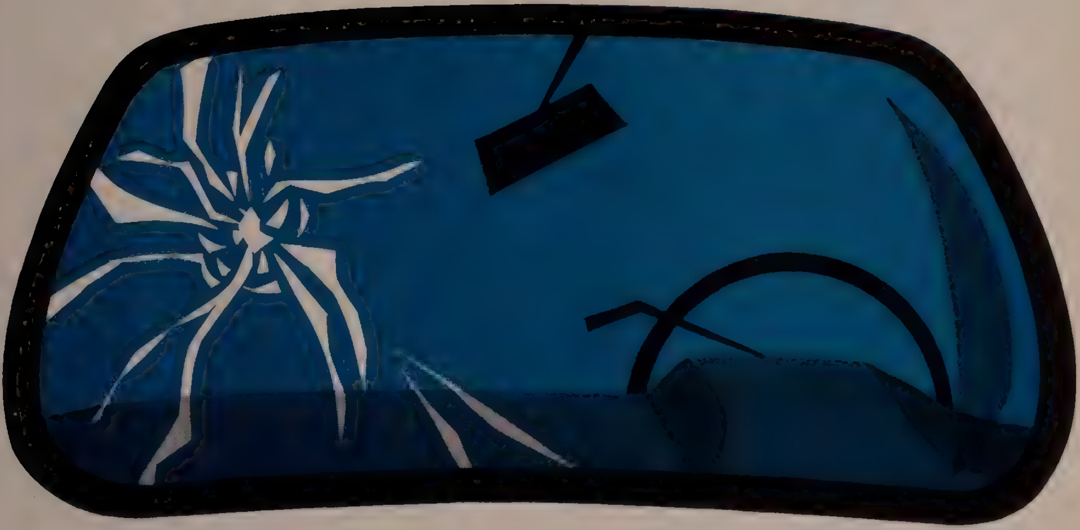

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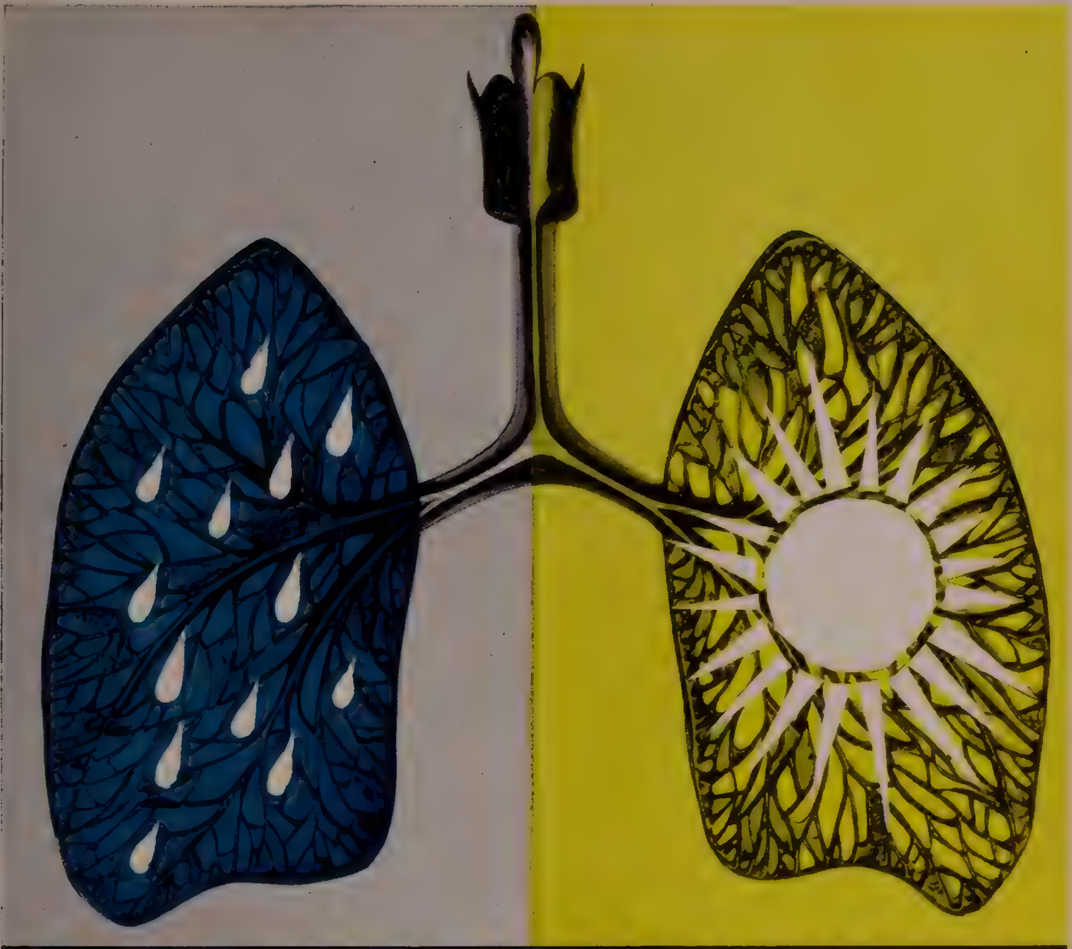

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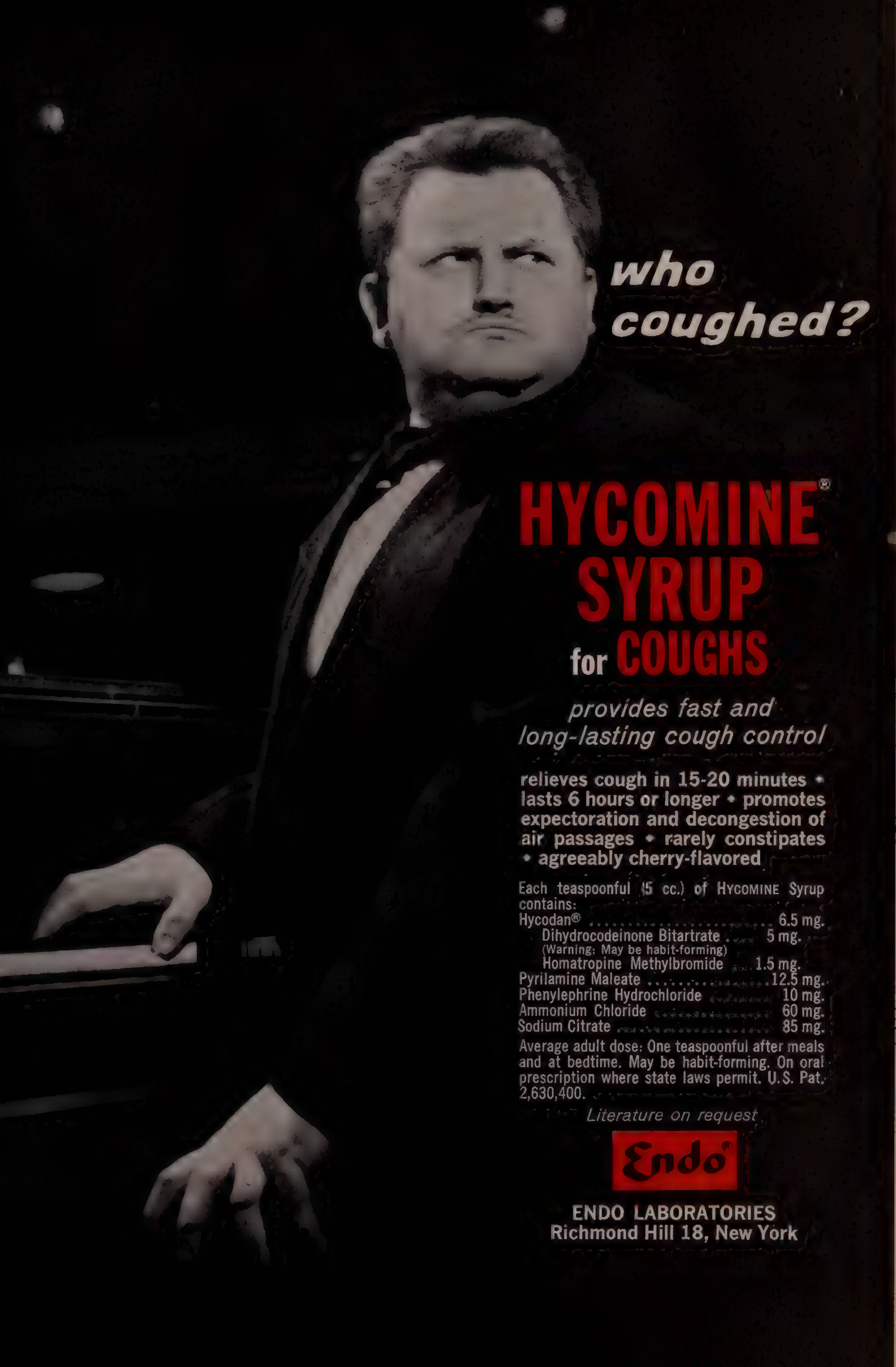
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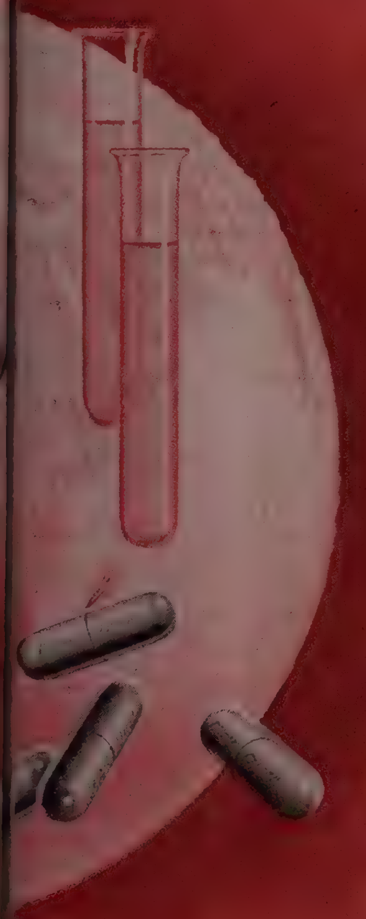

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1. J.A.D.A. ***62:*****466 (April) 1961. 2. J.A.M.A.** ***180:*****94 (April 7) 1962.**

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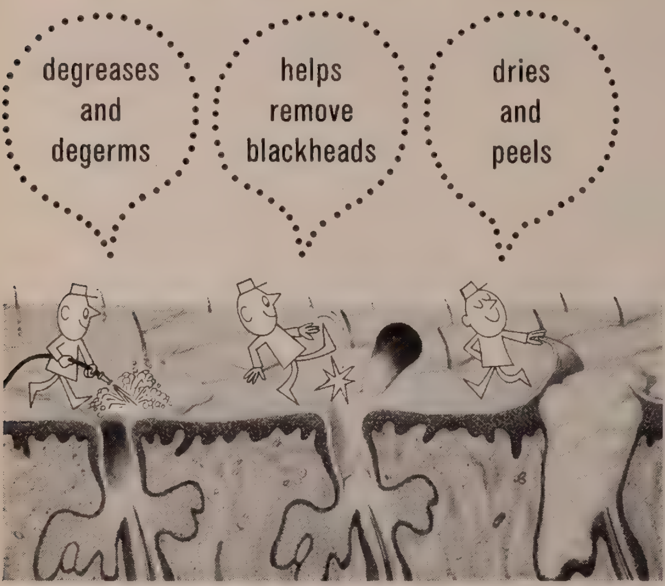

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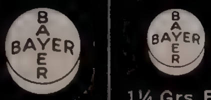

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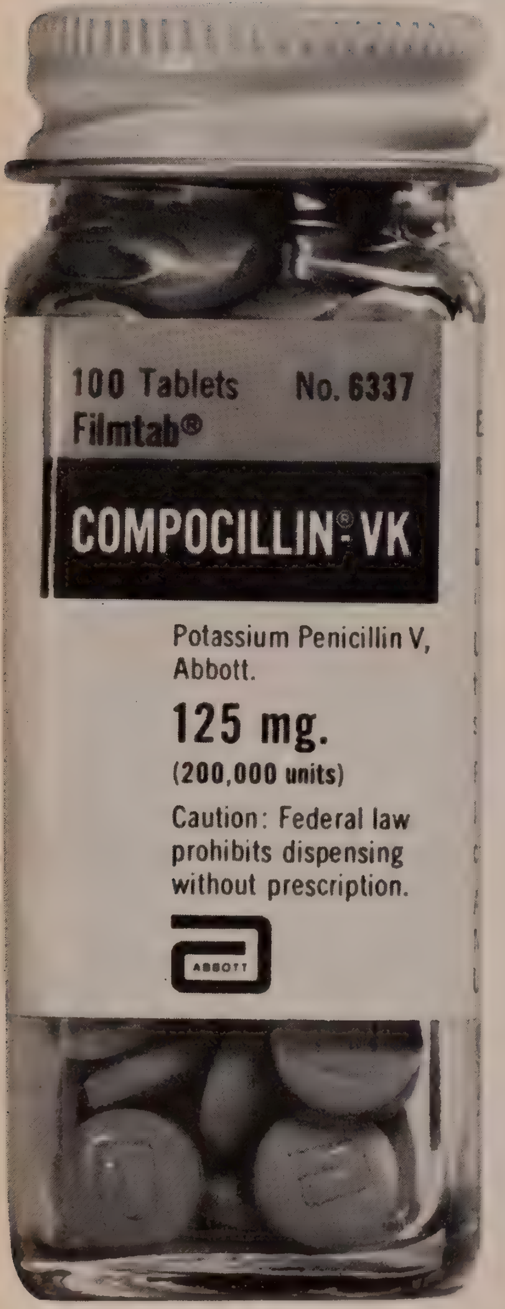

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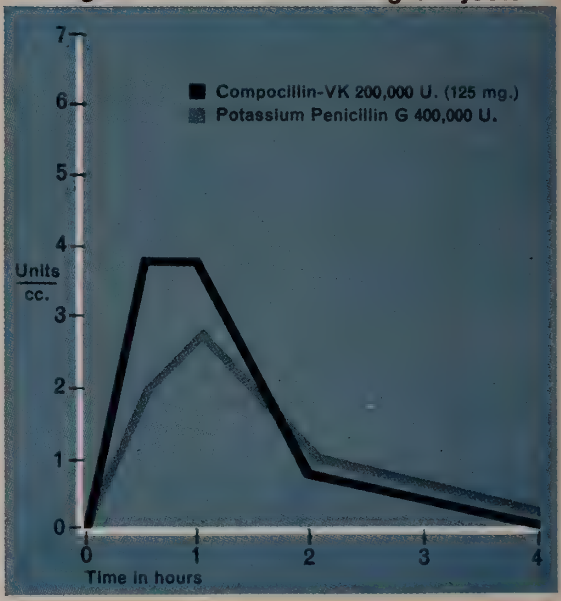

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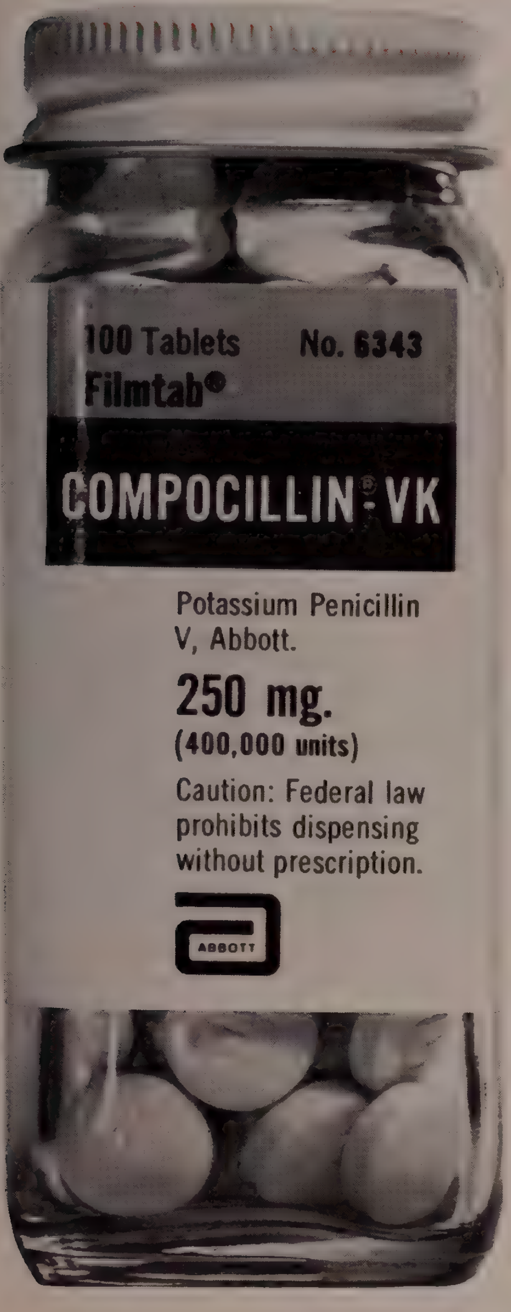
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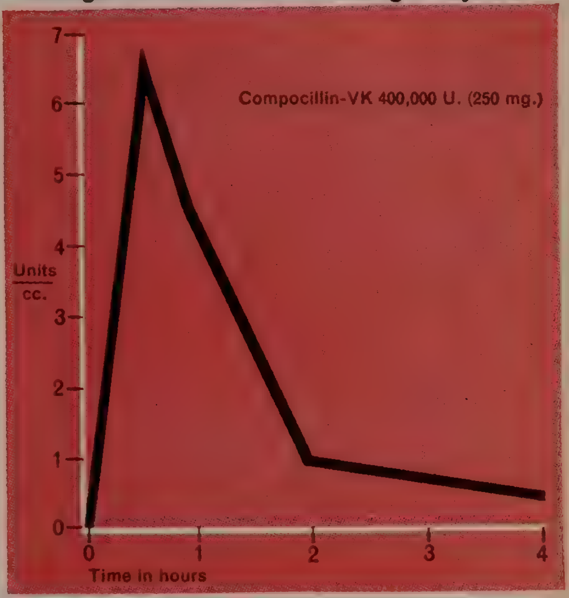
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*Chart data from two separate studies completed by the Microbiologic and Medical Departments of Abbott Laboratories.

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To answer many inquiries; the 1961 Medical Directory is still available. The next edition will not be published until late in 1963.

Many physicians save time by regularly consulting their Directory for telephone listings, a colleague's address or office hours, as well as information about their State Society. You, too, will find your Directory a valuable source of information when you use it often.

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Editorials

A nose for trouble

In times past when coal was used universally for fuel it was not uncommon for a doctor entering a patient's house to smell coal gas and to announce the fact. These warnings undoubtedly saved many lives.

Heating systems have changed, but they are still largely based on combustion, and the danger of carbon-monoxide poisoning is still present. Last year there were 67 deaths from carbon-monoxide poisoning reported in this State.

Although accidental carbon-monoxide poisoning is a hazard throughout the year, the incidence of such poisoning is greater during the winter months.

Here are a few simple precautions that will remove most of the dangers of carbon-monoxide poisoning:

1. Any abnormal condition such as a stove that smokes or the observance or smell of smoke in living quarters is a danger signal and the cause should be investigated. Homes today are more nearly airtight because of storm windows and modern construction technics. This increases the possibility of carbon-monoxide poisoning if furnaces and hot water heaters are not operated properly and adjusted.

2. All fuel-fired hot water heaters should be connected to a flue leading outside the house. Space heaters should also be vented, unless approved for unvented use. This applies to both oil and gas-fired appliances.

3. If a kitchen exhaust fan or any other exhaust fan is used in the house, the fan should be checked during its operation in order to see that proper draft is maintained. An exhaust fan may cause a back draft through the furnace flue. It is possible to pull smoke and fumes through the furnace if the house is sealed too tightly and if a furnace room window is not open slightly.

4. Automobile exhaust systems should be checked regularly to eliminate conditions which might result in the leakage of carbon monoxide. When driving, a leaking exhaust may allow carbon monoxide to accumulate inside the car. Always keep a window open, even in cold weather.

We may have progressed to the point of "overkill" in weatherizing and insulating our houses. The little brown house in the valley was the devil to heat but it certainly was ventilated.

Professional courtesy—a curious twist

New York's highest court in June, 1962, refused to adopt the rule followed in most other states that payments from collateral sources do not reduce the amounts recoverable in a personal injury action.

This decision of the Court of Appeals is of particular interest because it involved a physician who sustained a whiplash injury when his automobile was struck in the rear by another car. Inasmuch as he was a practicing physician and surgeon, he received medical treatment, physiotherapy, and care from his professional colleagues and his nurse and incurred no out-of-pocket expenses therefor. Nevertheless, in his bill of particulars he stated that his special damages for medical and nursing care and treatment amounted to $2,235. The trial court ruled that the value of these services was not a proper item of special damages, and that no recovery could be had therefor, since they had been rendered gratuitously. He thus excluded evidence as to their value. The jury's verdict was for the physician on the question of liability for the accident, but he appealed from the trial judge's ruling concerning the gratuitous services rendered to him by his confreres and his nurse.

The Court of Appeals reviewed the law as followed in New York citing an eighty-year-old case which held that a plaintiff was entitled to recover only his pecuniary losses of which wages gratuitously paid while incapacitated were not an item. And further that he must show what he paid the doctor and could recover only as much as he paid or was bound to pay. It also pointed out that as recently as 1957 the Legislature declined to change this principle even though the Law Revision Commission had advocated the change.

The Court reiterated the long-standing maxim that "(t)he Legislature and not the judiciary is the proper body to decide such a policy question involving the accommodation of various interests. We should not now seek to assume their powers and overrule their decision not to change the well-settled law of this state."

It went on to state that it found no merit in the physician's contention that the medical and nursing services for which he sought damages were supported by consideration. He had testified that he did not have to pay for the physiotherapy treatments (since they were rendered by a nurse employed by him during the usual office hours), and his counsel confirmed the fact that "these various items were not payable by the doctor nor were they actual obligations of his and that he will not have to pay them."

The Court observed that:

> Plaintiff's colleagues rendered the necessary medical services gratuitously as a professional courtesy. It may well be that as a result of having accepted their generosity plaintiff is under a moral obligation to act for them in a similar manner should his services be required; such need may never arise, however, and in any event such a moral obligation is not an injury for which tort damages, which "must be compensatory only" may be awarded.

In another case the Court distinguished its ruling that it had been an error to permit the defendant to establish that the plaintiff was a member of a health insurance plan and that he was receiving increased disability pension benefits. In that case the plaintiff had given value for the benefits he received; he paid a premium for the health insurance and had worked for eighteen years to be eligible for the disability retirement benefits. It went on to state that insurance, pension, vacation, and other benefits which are contracted and paid for were not relevant to the physician's case and to reiterate the New York rule that gratuitous services rendered by relatives, neighbors, and friends are not compensable.

One judge vigorously dissented from the majority view and said in part:

> (T)he defendant should not be given credit for an amount of money, or its equivalent in services received by the plaintiff from other sources. "The rationale of the collateral source doctrine in tort actions," it has been said, "is that a tortfeasor should not be allowed to escape the pecuniary consequences of his wrongful act merely because his victim has received benefit from a third party."

He went on to say that he failed to see any real difference between the instant case and the one distinguished by the majority:

> In neither case was the injured person burdened with any charges for the medical services rendered and, accordingly, when the defendant is required to pay as "damages" for those services or their value, such damages are no less "compensatory" in the one case than in the other. Nor do I understand why a distinction should be made depending upon whether the medical services were rendered gratuitously or for a consideration. What difference should it make, either to the plaintiff or to the defendant, whether an injured plaintiff has his medical bills taken care of by an insurer or by a wealthy uncle or by a fellow doctor? Certainly, neither the uncle, who acted out of affection, nor the doctor, impelled by so-called professional courtesy, intended to benefit the tortfeasor.

President's Page

JOSEPH A. LANE, M.D.

New York 65, an important forward step in providing comprehensive, low-cost health and major medical insurance for New York residents sixty-five years old and older, is now a reality. A group of 47 private insurance companies, banded together in the nonprofit New York 65 Health Insurance Association, offered this insurance throughout the State during its first enrollment period, October 15 through November 15.

This undertaking represents prompt response by the insurance industry to enabling legislation passed in March, 1962, by the New York legislature.

The New York 65 program has been approved in principle by the House of Delegates of the Medical Society of the State of New York. And the Council of your Society has been instructed to cooperate in implementing the law.

This new, state-wide form of more extensive health insurance coverage for the State's residents sixty-five and older affords physicians of New York an unparalleled public service opportunity. At the same time the success of the program will have a further importance. A demonstration that private voluntary plans can effectively meet the health insurance needs of a large number of persons over sixty-five would certainly be timely and significant in view of the wide public interest in this vital subject. New York 65 deserves your cooperation and active support.

The New York 65 Regular and Optional Basic Plans include a schedule of allowances for physicians which is substantially the same as that of the United Medical Service for New York City for those having family incomes up to $4,000. The New York 65 Major Medical does not carry a schedule of allowances for physicians but uses the $6,000 Blue Shield Schedule applicable in the area where the patient resides. It is well known to all of us that the majority of retired people in New York State have less than a $6,000 family income. For those in this income range, physicians are encouraged to determine their fees with this in mind, as they now do for Blue Shield subscribers. Patients with larger family incomes should be made to realize that New York 65 Major Medical Benefits may be only a partial payment because benefits are limited to the $6,000 Blue Shield Schedule.

JOSEPH A. LANE, M.D., *President*

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1. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 6, Baltimore, The Williams & Wilkins Company, 1955, p. 578.

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*McCune, W. G.: M. Clin. North America 44:1479, 1960.

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Lysis of Intravascular Blood Clots

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Fibrinolysin Therapy

Indications, Contraindications, and Results*

EUGENE E. CLIFFTON, M.D.
New York City

From the Sloan-Kettering Institute for Cancer Research

THE MAINTENANCE of the balance between the fluidity and the coagulation of the blood is obviously a major homeostatic mechanism. An adequate blood flow is essential to life in the highly developed animal organism. Coagulation is important in the prevention of excessive bleeding, and fibrin undoubtedly is a factor in maintaining the integrity of the vascular wall. Excessive coagulation, on the other hand, can result in a major failure of the circulation. A constant balance between regional or marginal coagulation and dissolution of the coagulum is necessary to maintain vascular integrity with unrestricted blood flow.

The process of clotting is complicated, and understanding has not been furthered by the failure to agree on terminology. The same semantic arguments seem to be taking place in the field of clot dissolution. This is particularly unhappy since, in my opinion, we stand on the threshold of a new concept of treatment, not only of thrombosis, but also of many other disease processes. From the information which has been gained in the studies related to clot lysis, a new concept of the mechanism of progressive thrombosis and the intra- and extravascular results of changes in the clotting mechanism is being developed.

Fibrin is produced by the enzymatic hydrolysis of fibrinogen by thrombin, with the release of a fibrinopeptide. In vivo the interlacing fibrin network traps serum proteins and blood cells in its meshes, forming a thrombus. The fibrin then contracts (clot retraction), squeezing out serum. The clot becomes progressively more dense and resistant, and after a varying period of time, depending on inflammation and vessel wall damage, fibrous tissue invades the clot, and endothelium is formed.

An injury to the endothelium and a slowing of the blood flow with clumping of

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Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, General Session, May 8, 1961.

* The A. Walter Suiter Lecture.

the platelets precede the development of the thrombus. Some have suggested that injury makes the endothelium wettable like glass.[1] Others maintain that thromboplastic substances are present in the wall and are released at the injured surface to start the process of clot formation.[2] Still others envisage with injury a change in the electric charge or the pH, either of which may cause the platelets to adhere, clump, and degenerate, thereby freeing thromboplastin. Many attempts have been made to find increased prothrombin, thrombokinase, or other factors necessary for thrombin formation in conditions in which thrombosis commonly occurs. All have been unsuccessful.

If the fault is not in the prothrombin-to-thrombin-to-fibrin mechanism, why does excessive clotting occur and propagate to produce clinical thrombosis? Our concept is that fibrin formation and clotting are occurring regularly to maintain vascular integrity and prevent hemorrhage with the innumerable small and large traumas of daily life. Normally when the purpose of fibrin has been fulfilled, it is removed by the normal fibrinolytic activity of the blood. If there is either excessive clotting or a decrease in fibrinolytic activity, thrombosis will persist.

Thrombosis occurs most commonly in patients with chronic illness or who have had recent trauma, including surgery and delivery. In these conditions there are increases in fibrinogen, platelet counts, and fibrinolysin-inhibitor levels. The high platelet count and fibrinogen level tend to increase clot retraction which squeezes out serum with excess thrombin faster than it can be neutralized. This results in further platelet agglutination, fibrin formation, and thrombosis. Also it has been shown both in vitro[3] and in vivo[4] that increased fibrinogen concentration produces a more dense clot and fibrin that is more resistant to lysis by fibrinolysin.

Once fibrin has been formed it can be removed physiologically only by dissolution. Thrombin itself, being a proteolytic enzyme, can dissolve fibrin. This does not occur in vivo under normal circumstances since excess thrombin is inhibited by antithrombin or is fixed by the clot. Physiologically the proteolytic enzyme plasmin is responsible for clot lysis in vivo.

General considerations

The blood of human beings and many, perhaps all, animal species contains an enzyme precursor called plasminogen. When this is activated, it becomes plasmin.

It has been recognized since the time of Morgagni and John Hunter that a mechanism existed to maintain the fluidity of the blood. They observed that with sudden death the blood clotted but later became liquefied. Hunter[5] demonstrated this experimentally when he had two deer run to exhaustion and found that their blood clotted but liquefied very rapidly. Dastre in 1893[6] first used the term fibrinolysin to describe an enzyme that dissolved the clots in dog blood. Several investigators in the early 1900's showed that fibrinolysis was a physiologic process, and Jobling, Peterson, and Eppstein[7] at Columbia University correlated fibrinolysis with the crisis in pneumonia, the liquefaction of the exudate. They also demonstrated an inhibitor process of tuberculosis. It was in 1933 that Tillett and Garner[8] at Bellevue Hospital, New York City, discovered that a filtrate of beta hemolytic streptococcus dissolved human blood clots. Unfortunately they called this fibrinolysin. Milstone in 1941[9] showed that a human fraction was necessary for the streptococcal agent to produce fibrinolysis. The inactive precursor was called plasminogen, and the proteolytic enzyme produced by its activation is plasmin. The activators are kinases. This proteolytic enzyme (plasmin) digests fibrin, fibrinogen, factors V and VII, prothrombin, and other proteins.[10] The enzyme may be activated in vivo by trauma, shock, cyanosis, anxiety, severe exercise, injection of epinephrine, and many other means.[11] Tissue and plasma activators have been isolated, and activators have also been found in human milk, saliva, seminal fluid, and tears.[12]

It is probable that small amounts of the active enzyme are being produced constantly and are inactivated rapidly by inhibitors which are present in the plasma. At least three such inhibitors have been isolated and characterized.[13] There are probably inhibitors for the active enzyme plasmin and for the activator. Inhibitors are of fast and slow types.

Plasminogen may be activated in vitro by chloroform, alcohols,[14] trypsin and other enzymes, and autocatalytically.[15] Certain bacteria also produce activators (kinases). Of these, streptokinase or SK[8] has been studied most extensively, and staphylokinase or STA[16] has aroused some interest. Human urine also contains an activator called urokinase or UK,[17] which is under investigation as a possible therapeutic agent. It is not known whether this is an excreted plasma activator or a kinase produced by the kidney to keep the tubules clear.

In vivo activation has been observed with many drugs. This activation may be a secondary effect of the chemicals rather than a direct activation of the plasminogen by chemical action. Pyrogens have been studied extensively, and it has been reported that the activating principle can be separated from overt pyrogenic reaction.[18] The activity produced by pyrogens is short-lived and for this reason may not be expected to be effective. Other agents, such as nicotinic acid[19] and derivatives thereof, have been shown to produce minimal or short-lived and nonreproducible fibrinolytic activity. It is conceivable that combinations of these drugs with other means of activation may be useful. Other drugs, including the sulfonylureas, have been reported to produce fibrinolytic activity, but there is little indication that this is significant or that they will be found to be useful clinically. Even beer has been reported to produce fibrinolysis in human beings. One interesting method of producing activity locally and at times systemically is by controlled local venous stasis.[20] This can be of sufficient degree and duration to be effective clinically.[21]

Streptokinase has an unusual dual effect on plasminogen in vitro and in vivo. It produces plasmin and also an activator not only for more human plasminogen, but also for the plasminogens of many other species which are not directly activated by streptokinase. This duality has led to most of the disagreement about the mechanisms of fibrinolysis, and since SK has been our best activator, at least until recently, it has led to some of the more bitter disagreements between investigators. One school has maintained stoutly that SK acts on a proactivator to produce the activator which then acts on plasminogen to produce plasmin.[22] The other school has insisted that plasminogen is acted on by SK to produce both the activator and the enzyme.[23] They have not been able to make up their minds whether plasmin or the activator comes first.

We have used the term fibrinolysin for the combination of the activator and the enzyme which is produced by streptokinase. This same combination is produced in vivo and is called plasma fibrinolysin.

Selective thrombolysis

As we have noted, plasmin is a proteolytic enzyme which will destroy fibrinogen, prothrombin, and other blood proteins. The concept that plasmin can dissolve the fibrin from a thrombus without destroying the proteins while it is in the circulation has been difficult to explain.

The method by which fibrinolysin or the activator manages this feat of magic is still not completely understood. The most acceptable theory presumes that the activator which is introduced as fibrinolysin (SK-plasminogen complex) or produced in vivo by the activation of the patient's own plasminogen diffuses into the clot.[24] The plasminogen, which is in close contact with the fibrin molecule, is then activated in the thrombus to plasmin which depolymerizes the fibrin, liquefying the clot. It is also presumed that the inhibitor does not function in the clot, as it does in the plasma. The inhibitor in the circulating blood inactivates the enzyme plasmin and prevents the proteolysis of fibrinogen and other blood proteins.

It has been suggested that the enzyme-inhibitor complex is reversible[25] and that when the complex comes in contact with fibrin the plasmin is freed, permitting the depolymerization of the fibrin and the dissolution of the clot.

It is also possible that the slow inhibitor permits the activator or enzyme to circulate long enough to be absorbed on the clot. The concept that the enzyme-inhibitor complex is reversible or that the inhibition is incomplete is confirmed by the fact that the euglobulin fraction obtained by acid fractionation from plasma or serum at pH 5.4 contains the activator and plasmin while the supernate contains the inhibitor.[26] In many disease states, particularly chronic infections and cancer, the inhibitor level may be extremely high. After streptococcal infections there is usually a marked increase in antistreptokinase.

Factors affecting resistance to lysis of a thrombus

The ability to lyse a clot depends on many factors, both intrinsic and extrinsic. Several of these have been studied:

1. The age of the clot is important. As the clot becomes older it becomes more difficult to lyse. In experimental animals clots up to seven days of age have been dissolved in vivo by a single course of treatment, but it becomes progressively more difficult after three days.[27] This increasing resistance to lysis apparently is due to the solidification of the clot. The formation of endothelium occurs somewhat later in the process.

2. The plasminogen content of the clot obviously will be of great importance. If a clot is formed without plasminogen, it is extremely difficult to dissolve with fibrinolytic agents.[28]

3. The fibrinogen concentration of the blood plasma at the time the clot is formed is also significant. Clots which are formed with fibrinogen concentration above the normal 250 to 300 mg. per 100 ml. become progressively more difficult to lyse, both in vivo and in vitro.[3,4] The importance of this factor is easily understood when we recognize that patients with chronic disease or in the postoperative state have very high fibrinogen levels.

4. Increasing concentrations of lipid in the blood also tend to make the clot or thrombus which is formed more difficult to lyse.[29] Whether this is the result of an increase in the inhibitor or a mechanical effect of the trapped lipids in the thrombus has not been established.

5. Mechanical factors will affect the delivery of an effective concentration of the fibrinolytic agent to the thrombus. The mass and extent of the thrombus itself are important, as with large venous thrombi in which the collaterals as well as the main channel may be obstructed. Not only is it more difficult to get the enzyme to the thrombus, but also diffusion through its mass may take many hours.

6. In arteries, a lack of collaterals makes it necessary to diffuse the enzyme through a stagnant column of blood. Atherosclerosis further complicates the problem by narrowing and distorting the channel, and atherosclerotic material may be inhibitory to fibrinolysin.

7. Normal endothelium also may have a part in the fibrinolytic mechanism as noted by Kwaan, Lo, and McFadzean.[30]

Animal studies

Investigations in animals preceding clinical trials included in vivo activity, toxicology, effects of the enzyme activity itself, and last in vivo effectiveness against artificial clots or thrombi.

ACTIVITY IN VIVO. It was shown that strong fibrinolytic activity can be induced in animals such as rats, dogs, cats, monkeys, and rabbits by the infusion of SK-activated human fibrinolysin. If inhibitor activity is high, as in the pig, a greater quantity of fibrinolysin must be administered. With concentrations producing strong fibrinolytic activity there were decreases in the fibrinogen level and the concentration of other clotting factors. With a greater concentration a marked fall of these proteins to negligible levels could be obtained.

TOXICOLOGY. In animals no significant toxic effects were observed with adequate concentrations. There were no obvious gross or microscopic effects on the liver, kidney, heart, blood, or other tissues and no sensitization or anaphylactic reactions. Mild temperature rises of 1 or 2 degrees were observed in a few animals.

EFFECTS OF ACTIVITY. Toxic end products might be produced by proteolysis, but this was not observed. The lysis of thrombi might be expected to produce hemorrhage if thrombosis is a major factor in the control of bleeding. Even with fresh open wounds severe hemorrhage did not occur, although there was excessive bleeding during the strong fibrinolytic phase of treatment. This excessive oozing ceased quickly, within twenty to thirty minutes after the cessation of the infusion or if the wounds were closed. The wounds healed normally. By the infusion of excessive amounts of fibrinolysin it is possible to produce massive fatal hemorrhage, associated with the decrease of fibrinogen, prothrombin, and factors V and VII to very low levels.

LYSIS OF EXPERIMENTALLY PRODUCED THROMBI. Clots which are produced in the veins and arteries of dogs, cats, and rabbits by sodium morrhuate, thrombin, electric current, heat, and by the Wessler technic of homologous serum injection can all be lysed either by local administration, which is more rapid, or by the systemic infusion of fibrinolysin.[27,31] To obtain lysis it was necessary to maintain a significant lytic activity for from one to three hours. This lytic activity could usually be reached and maintained for the necessary time with about 1,000 units per kilogram per hour. For arterial thrombi a more active fibrinolysis for a longer period was necessary, probably because of mechanical factors. Clotted venous segments usually have collaterals by which blood containing fibrinolysin can be brought to bear on the thrombus from several points at one time. With arterial thrombi the enzyme is probably effective only at the proximal end and by diffusion through a static column of blood. The importance of this mechanical factor was shown by another series of experiments in which the veins were stripped prior to the formation of thrombi, and here the lysis time of venous and arterial thrombi was identical.[32]

Available clinical materials

Two preparations of SK-activated plasminogen are now available for clinical use.

Plasminogen is prepared from Cohn fraction III by the method of Kline or modifications of this method.[33] Fraction III-3 (Cohn) is also used as a source of plasminogen by acidification to pH 5.2. The plasminogen is heated to 60 C. for ten hours to destroy hepatitis virus.

Streptokinase is prepared from cultures of beta hemolytic streptococcus and purified chemically.

One manufacturer indicates that free streptokinase has been removed from the compound (Actase) leaving only the activator. This has been challenged by Fletcher and his group.[34] The recommended dosage does not produce lytic activity in patients.[35] A high incidence (45 per cent) of reactions, some severe, have been reported.

The other compound (Thrombolysin) is known to contain excess streptokinase. Reaction rates are at present about 5 to 10 per cent with the recommended dosage.

Both products by label contain 50,000 units per vial, but it must be remembered that the units used are different.

Other products under investigation

Several materials are under investigation. At least two companies have produced purified streptokinase. With these materials the reaction rates have varied from one reported to be without reaction to 35 per cent.[36]

Urokinase has been in process of development for several years. It was first produced commercially in Scandinavia. More recently it has been produced in this country for investigational use, in combination with purified plasminogen. It has been reported to be effective as a thrombolytic agent in doses of 50,000 to 100,000 plough units.[37] We have also found urokinase alone to be an effective thrombolytic agent. Spontaneously activated fibrinolysins which were tested were found to contain only plasmin without any significant activator. As expected they were inactive in quantities far in excess of effective amounts of streptokinase-activated fibrinolysin.

Bovine fibrinolysin (plasmin) activated with chloroform has been available for several years. It was reported to be effective in a small number of patients with cerebral thrombosis by Herndon *et al.*,[38] but this has not been confirmed. Reactions occurred in 6 of 13 patients. In our experience bovine plasmin in adequate concentrations causes excessive destruction of fibrinogen without significant effect on thrombi. In clinical trials in our hands pyrogenic reactions rarely occurred, but allergic reactions occurred in 2 of 10 patients.

These two factors in our opinion contraindicate the intravenous use of this material as a lytic agent.

Pyrogens have been used to produce fibrinolytic activity. Meneghini[39] has reported cases of clinical thrombosis treated effectively by this means. In view of the short duration of fibrinolysis it seems doubtful that it would be effective in any condition other than the most susceptible of clots.

Local venous obstruction has been found to produce very good results in a few patients with thrombophlebitis.[21] This will be effective only in a pathologic condition which is limited to the extremities and possibly only the distal two thirds of an extremity because of the pain produced by the cuff pressure in the area of thrombophlebitis. We are investigating the combination of other agents with this means. The alternate use of more than one extremity may also be effective.

Pharmacology and toxicity

Human plasminogen does not produce reactions in patients. It is the kinase which has been responsible for most reactions and the most difficult to purify. This is particularly true of streptokinase. Pyrogenic reactions were the rule with the early preparations.[40] More recent preparations of fibrinolysin and streptokinase have been improved consistently until reactions are rarely severe.

Originally it was thought that the reactions were caused by protein breakdown products. This has been disproved since with purification increased activity has been obtained with fewer reactions.

Hemorrhage was a real fear when fibrinolysin was first used clinically, since the oozing associated with accidents of pregnancy, massive surgery, trauma, and carcinoma of the prostate was considered to be due to increased fibrinolysin.[41] Bleeding with fibrinolysin treatment has not been a problem for us and should not be if proper dose schedules and precautions are taken. It is essential to determine that other clotting factors are not abnormal before fibrinolysin is administered. Excessive bleeding was reported with SK treatment by Fletcher and his coworkers.[36] It should be remembered that they used large doses of SK for long periods of time. The cessation of the infusion is usually sufficient to reverse the process if bleeding occurs. Other methods of control will be discussed later.

Using proper precautions we have treated patients immediately postoperatively and patients with peptic ulcers, positive guaiac stool reactions, and other possible sources of oozing, without serious consequence.

It has been suggested that fibrinolysin would cause partial lysis of a thrombus with embolus formation. When fibrinolysin is administered, the fresh propagating thrombus will dissolve first, and the old fixed portion of the thrombus will be the last to lyse. If the infusion were placed behind the thrombus it is conceivable that an embolus could be produced by rapid local dissolution of the fixed portion of clot. For this reason, we have recommended general systemic treatment of venous thrombosis. We have never seen a proved pulmonary embolus in a patient treated adequately with fibrinolysin. Ambrus *et al.*[37] reported 1 patient among 62 treated. We have seen pulmonary emboli in 3 patients with the recurrence of thrombosis at some time after fibrinolysin therapy.

Sensitivity reactions

Sensitization to foreign proteins in the impure SK will occur. For this reason repeated courses of treatment should not be considered except for very strong indications. Antihistamines and corticosteroids should be administered before and during the repeat course of treatment. Patients who have significant allergic histories or who have or have had recent streptococcal infections should be treated with the same precautions even with the initial course of treatment. Ambrus *et al.*[37] have reported one anaphylactic reaction with a second course of treatment. We have not seen such a reaction, but in our experience the pyrogenic-type response has been much more severe with repeated courses.

Formed elements of the blood, white blood count, platelets, and red blood count are not significantly effected by therapeutic doses of fibrinolysin. A temporary leukopenia has been seen in animals and some patients.[42]

Electrocardiograms have not shown any changes attributable to the fibrinolysin in large numbers of patients, both without evidence of coronary disease and with definite coronary occlusion.[43]

Urinalyses have shown no significant change in albumin, blood urea nitrogen, sugar, white blood count, specific gravity, or pH. In about 3 per cent of patients red blood cells appear or increase in number. A rare patient will have obvious bleeding in the urine, most often after prostatic operations.[42]

Liver function tests have shown no consistent change.[42]

Clotting factors may change during very active or prolonged treatment or in patients who have a damaged liver or deficiencies in the clotting factors before the treatment is started. Such patients should be followed very closely, and if there is a sharp change in the prothrombin time or the percentage of factor V or VII or prothrombin the infusion should be stopped or decreased in rate.[42]

Antithrombin formation has been said to occur with fibrinolytic therapy.[44] It has been shown that the digestion of fibrinogen by plasmin or trypsin could result in the formation of an anticoagulant if the digestion was permitted to go to a certain point.[45] We have found measurable antithrombin only one time. It would seem to be less important than alterations in clotting factors and the low fibrinogen level produced by active fibrinolysis.

Indications

The indications for fibrinolysin therapy at present are phlebothrombosis and thrombophlebitis, pulmonary embolus, and peripheral artery thrombosis or embolus. The method of treatment and the dosage will vary for each of these. It is probable that cerebral and coronary thrombosis eventually will be the prime indications, but at the present they are considered investigational. This is particularly true of cerebral thrombosis in which the difficulty in distinguishing hemorrhage from thrombosis could lead to serious difficulties.

Contraindications

There are two absolute contraindications of fibrinolysin therapy. These are: (1) active bleeding and (2) sensitivity to the agent to be used.

There are many relative contraindications. The degree of contraindication will be dependent on the purity of the materials available, the experience of the administrator, and the laboratory facilities available. For maximum safety one should be able to determine quickly and at frequent intervals the plasma fibrinolytic activity, the concentration of the various clotting factors, including fibrinogen, prothrombin, and factors V and VII, and the presence of anticoagulants. We consider the minimal control to be prothrombin time, clotting time, and whole clot lysis time before and at intervals of two hours during the treatment.

The contraindications of a relative nature include (1) recent operations, particularly on the prostate, (2) positive guaiac stool reactions, (3) abnormal prothrombin time, (4) low platelet counts, (5) history of sensitivity or allergy, and (6) high fever. We have treated patients within a few hours of operation and patients with a 4 plus guaiac stool and known ulcer, prothrombin times as high as 25 seconds, and platelet counts as low as 7,000 without serious consequences. Very strict control is essential.

High fever was originally considered a serious contraindication because a dangerous pyrogenic response might occur. More recently we have treated patients with recurrent fever of above 103 F. without serious difficulty. As a matter of fact, on several occasions fever of long duration has regressed after a few days of treatment. Two explanations are apparent: The diffusion of antibiotics may be improved, and chronic infections have liquefied and drained after fibrinolysin treatment.

Methods of treatment

Continuous systemic infusion has been the most commonly used method of treatment. The duration and rate of infusion has varied tremendously from group to group of investigators.

The Fletcher groups[36,44] have used large quantities of SK in continuous infusions of from twenty-four to forty-eight hours. The disadvantages of this method of treatment include the following: Hemorrhagic phenomena are more common, and as a result corticosteroids were administered to prevent complications. An even more serious result is that all plasminogen present in the patient's blood may be used up. If clots are reformed after treatment, they will be without plasminogen and extremely resistant to lysis.

Moser[46] on the contrary, has used treatment which some would consider completely ineffective (50,000 to 100,000 units in four hours). The largest number of investigators stand between these extremes.

It is important to remember that Moser[46] and others used fibrinolysin with full doses of anticoagulants. The effect of the combination of anticoagulants and fibrinolytic agents has not been investigated thoroughly. In vitro studies indicate that there is no accentuation of fibrinolytic activity by anticoagulants, but this does not prove that such a complimentary activity does not occur in vivo. As a case in point, heparin in high concentration inhibits fibrinolysin in vitro, but low concentrations seem to increase its activity in vivo. The clearing effect of heparin might be expected to diminish the inhibitors of fibrinolysin and so decrease the necessary dose. We now recommend 25 to 50 mg. of heparin every six hours with fibrinolysin.

Preliminary evaluations

The duration and activity of the process must be established. Swelling, inflammation, cuff pressure tests, arterial pulsations, sensation, and color should be observed carefully and recorded for objective evidence of improvement with treatment. For the evaluation of thrombophlebitis we prefer the cuff pressure tests as an objective measurement of the activity and evidence of improvement in the process.

Before beginning treatment blood is drawn for the following tests: fibrinogen, prothrombin time, prothrombin and factors V and VII content, spontaneous fibrinolytic activity, inhibitors of plasmin activity, whole clot lysis, and a dose prediction. This latter gives an accurate indication of the dose of fibrinolysin, streptokinase, or other activator which is needed to produce a significant fibrinolytic activity in the individual at the particular time. The estimated dose is given in the first twenty to thirty minutes and then hourly for the duration of the infusion.

Venous thrombosis

If the duration of the venous thrombosis is less than three days, a six-hour infusion is given daily for two or three days. If a dose prediction test cannot be done, the empiric rate of treatment we have advised has been 1,000 units per kilogram per hour with a minimum of 50,000 units and a maximum of 150,000 units per hour. This rate of infusion should be altered according to the effectiveness of the treatment as determined by the euglobulin fibrinolytic test, whole clot lysis, and increase in prothrombin time. Ideally the euglobulin fibrinolytic activity should be about thirty minutes, but a lysis time of up to four hours may be considered effective. The following day's infusions must be varied in accordance with the test results each day. With present materials our maximum dose is 300,000 units per hour. As soon as the cuff test approaches normal and the edema has regressed significantly, the patient is mobilized with elastic bandages or stockings. If for other reasons the mobilization of the patient is impossible, anticoagulants should be started when the fibrinolysin course is completed.

If the thrombosis is of longer duration, the therapy must be prolonged progressively. For a thrombus of five to seven days duration, four to five days of treatment will be indicated. For thrombosis of over three weeks, from seven to ten days of treatment may be necessary. We have had a successful result in patients with continuous symptoms of more than six months. Patients with cancer or other chronic disease, especially those with true migrating or progressive thrombophlebitis, will be much more resistant to treatment than the usual acutely ill or postoperative patient. Even with a thrombosis of short duration they may need a higher concentration of enzyme and extra days of treatment to eradicate the thrombus completely. Fortunately larger doses generally can be given with safety in these patients.

If a very severe acute iliofemoral thrombosis is to be treated, it may be necessary to treat more actively the first day, and both systemic and local infusion may be used to reverse the process quickly and prevent its secondary effects, including evidences of arterial obstruction.

Pulmonary embolus

Massive pulmonary emboli which are not immediately fatal are prime indications for fibrinolysin therapy. Pulmonary emboli vary in size and in the degree of involvement of cardiopulmonary function. A massive pulmonary embolus may cause death in only a few minutes, or small pulmonary emboli may occur repeatedly with severe delayed pulmonary complications. Previous pathologic conditions or abnormal physiology and spasm will alter their effect.

In patients with massive emboli large amounts of enzyme should be given rapidly and in a small volume of solution. Treatment should be started immediately when blood is drawn for the dose prediction test, and the rate should be altered to the proper dose when the laboratory reports are available. Ordinarily we start with 100,000 to 150,000 units per hour in such a patient. In 1 patient with a known high inhibitor level, we used 400,000 units per hour at the start. Antihistamine and corticosteroids may be used to counteract any reaction in such a patient. The infusion should be continued for two to three hours after the patient has shown definite improvement. There should be a return to normal of blood pressure and a relief of pain and symptoms of acute pulmonary and cardiac dysfunction. Usually this will mean a six- to eight-hour course of treatment. On subsequent days repeated infusions are given for the number of days indicated by the age of the original thrombosis to eradicate the source of the embolus. If the source is pelvic thrombophlebitis, treatment may be less successful because infection may continue as a cause of rethrombosis. Pelvic thrombophlebitis, by involving the iliac veins and inferior vena cava, may produce edema of the legs which may be misleading. In these individuals Heparin and warfarin sodium (Coumadin sodium) should be added at the end of the fibrinolytic therapy to help prevent recurrence. In a rare patient vena cava ligation may be necessary if there is recurrence despite adequate treatment.

Arterial thrombosis and embolus

Arterial thrombi are a more difficult problem in management than venous thromboses. There are several reasons for this: (1) An exact diagnosis is difficult, and many times it is impossible to distinguish between thrombosis, embolus, or atherosclerotic plaque as the cause of obstruction. (2) There is frequently a narrowing of the artery which is due to atherosclerosis and which makes the delivery of an effective dose difficult. (3) When thrombosis occurs, it produces what is essentially an end artery with a column of static blood above the thrombus. The enzyme must be diffused through this static column of blood from the nearest branch. (4) It is necessary to obtain a return of circulation rapidly to prevent irreversible destruction of tissue.

For these reasons a high concentration of enzyme for a long period of time is necessary. It is in just these circumstances that the harmful side-effects, pyrogenic reactions, and proteolytic digestion of fibrinogen and the prothrombin clotting factors are seen most commonly.

For the reasons noted previously we feel that local treatment generally is most useful for arterial obstructions. If the thrombosis is fresh and the vessels seem reasonably normal, a trial of systemic treatment may be justified. Under these conditions a lysis time of fifteen minutes in the systemic blood is desirable. Treatment is maintained until adequate circulation has been obtained and is continued for two or three hours beyond this point. The earliest we have seen a good return of circulation has been in seven to eight hours, and rarely we have continued treatment for eighteen to twenty-four hours. On subsequent days short courses (six hours) of therapy are given to assure the complete removal of any residual thrombus.

For local treatment the surgical exposure need only be adequate to control bleeding from the artery during the course of treatment and manipulation. A preliminary angiogram is made. A small polyethylene catheter is then inserted, and fibrinolysin is instilled and allowed to remain in contact with the clot. As the clot is lysed, the catheter can be advanced, and more enzyme is introduced. The catheter should be passed in both directions to assure complete patency of the artery. When a good flow is obtained both centrally and by back flow, a small amount of fibrinolysin and/or heparin is introduced, and a repeat angiogram is made to determine the adequacy of the channel. Fifty to 100,000 units are usually enough for a recent thrombus, and lysis will occur in fifteen to thirty minutes. For old or very large thrombi as much as 300,000 units may be necessary over a period of from thirty to sixty minutes.

If an obstruction is reached which fails to lyse, this indicates either an embolus or an atherosclerotic obstruction. This is then removed with an endarterectomy instrument, and the procedure of instillation of fibrinolysin is continued. The arteriotomy must be closed with more care than usual since clotting which ordinarily closes the small surgical defects will not occur for some time.

If the obstruction is primarily atherosclerotic in nature, the proper surgical treatment may be instituted. This may be endarterectomy or bypass. The results of either will be improved by instilling fibrinolysin after the main channel has been reopened, to dissolve propagating thrombi in the run-off area.

Even if local treatment is planned, it may be wise to use general fibrinolysin treatment during the period of preparation prior to surgery. A propagating fresh thrombus will be opened, permitting a return to relatively good circulation and preservation of the limb during the preparation for surgery. Several patients with emboli have been treated in this way, and it has been very satisfying to find the embolus unattached to the wall of the artery and without a propagating thrombus.

After surgical intervention systemic fibrinolysin therapy may be used to prevent a reaccumulation of thrombus at the areas of intimal damage. We usually advise two to three days of treatment of from four to six hours each.

Cerebral thrombosis

The treatment of cerebral thrombosis with fibrinolysin cannot be considered an established therapeutic procedure. The main problem is diagnosis, although some clinicians feel that they can distinguish between hemorrhage and thrombosis. If hemorrhage has occurred, fibrinolysin is contraindicated.

Although we have treated 9 patients by systemic infusion without serious consequence and with a few satisfactory results, we feel that the diagnosis should be established by cerebral angiography. The fibrinolytic agent can then be administered directly into the carotid on the involved side.

By direct instillation we have obtained a complete return of circulation in 3 cases. Unfortunately 2 failed to show functional improvement because of irreversible damage, and the third succumbed to tracheal obstruction after showing marked improvement. One patient with atherosclerotic obstruction failed to show good blood flow after endarterectomy until fibrinolysin was instilled to lyse propagating thrombus. After two days of systemic treatment he began to show marked improvement which progressed to good function rapidly.

With systemic treatment 2 patients, 1 with thrombosis and 1 with multiple emboli, showed rapid unexpected recovery. We then had bad luck with the latter patient since he died of an obstructed bronchus, caused by aspirated food.

Coronary occlusion

Coronary thrombosis probably will be the major indication for fibrinolytic therapy. Our own clinical experience has been limited, but we have been privileged to assist Isaac H. Richter, M.D. We felt that detailed investigations in animals should precede clinical use. One would certainly wish to prove that myocardial hemorrhage, myocarditis, as has been noted with trypsin, or even dissolution of the infarcted area with rupture would not occur.

As reported by Ruegsegger and others in our group,[47] the results of the treatment of induced infarction in dogs have been very promising.

The thrombi were produced in a major coronary vessel by a modification of Wessler's technic. All treated animals showed a complete return of circulation in five to six hours. Only 1 control showed lysis of the thrombus, and it was found that this animal had lytic activity in his blood equal to that in the treated animals. Dogs have particularly labile fibrinolytic systems, and an occasional animal (about 1 in 10) will show marked lysis with trauma, cyanosis, and anxiety, as originally reported by Tagnon.[48] The possibility that patients with severe coronary occlusions might lyse their own thrombi as a result of anxiety, pain, or cyanosis with sudden death must also be considered.

In the animals treated with fibrinolysin a significant decrease in the size of the infarcts was also noted. In addition, when the microscopic slides were checked it was observed that there were no thrombi in the arterioles, capillaries, and venules and that the fibrin in the tissue spaces and the interstitial edema present in the controls were not seen in the treated animals. These effects were noted most prominently in the marginal part of the infarct.

From this study it seemed possible that fibrinolysin was effective by altering the tissue fluids and microcirculation in the marginal area of the infarct. This permitted peripheral circulation during the critical period of blockage, until the major vessel was reopened.

To test this hypothesis, the mechanical obstruction of a coronary vessel by a clamp was used for the test system. It has been shown in large series of experiments by many investigators that an obstruction of this type for thirty minutes results in an irreversible infarct even if the clamp is released at that time.

In this series of experiments the clamp was left in place for one hour, and fibrinolysin was infused into the treated animals, starting before the release of the clamp and continuing from four to six hours.[49] The treated animals had much smaller and less complete infarcts than did the controls. Even if the animals survived and were not sacrificed for from twenty-four hours to several days after infarction and treatment, the results were equally dramatic. The controls, even without any thrombosing agent being used, showed thrombi in the small vessels. The treated animals showed inflammatory infiltrates but no thrombi.

The treated animals showed no serious hemorrhage in the infarct areas, nor was there any evidence of weakness of the wall which might lead to increased herniation.

More recently we have investigated the effect of coronary obstruction and tissue anoxia on the coagulability of the blood. Blood samples have been collected from the coronary sinus at intervals after coronary occlusion. By this means it has been possible to show that a marked hypercoagulability of the blood occurs within a very few minutes after the release of the obstruction. This probably is related to tissue breakdown products washed out in the circulation or to changes in pH. The importance of this change has yet to be established.

Experience with clinical cases of coronary occlusions using fibrinolytic agents has been recent and is still too limited to warrant any conclusion.

We ourselves have treated 10 patients with coronary disease to the present time. Our first case was treated in 1954 after cardiac arrest. She was improved markedly by a short course of treatment, and we were on the way to give her a second course when she had a second severe attack and died.

The second patient had a third severe coronary occlusion in addition to status anginosis. Complete relief of pain, which had not been obtained previously by large doses of morphine, was obtained after six hours of treatment. He was essentially well for twelve hours when he had a second attack. We were not called to treat him again. He died six hours later.

Three of our more recent patients were suffering with severe angina of long duration. All have been markedly improved after a course of several days of treatment.

Additional experimental studies are indicated, and a large controlled series of cases showing the value of fibrinolysin must be available before its general clinical use can be justified.

To treat coronary thrombosis we will face all of the disadvantages of arterial thrombosis, accentuated in degree. Prolonged treatment with a very high therapeutic range of activity will be necessary to give the hoped-for results. Ten to twelve hours of treatment as soon as possible and no longer than six hours after occlusion would be desirable. Whether treatment should be given for several days or anticoagulants should be administered after the first course to prevent rethrombosis will have to be established by detailed animal and clinical trials.

Fibrinolysis and atherosclerosis

Few people would quarrel with the opinion that atherosclerosis is the real villain in coronary disease and infarction and in many cases of peripheral artery occlusion. This may result in gradual narrowing with successive layers of atherosclerotic material, or there may be a sudden rupture of an atherosclerotic plaque with or without secondary thrombosis. Although tremendous efforts have been expended in the investigation of this entity, we seem no nearer a definitive understanding of the mechanism now than we were a number of years ago.

I should like to outline the possible relationship of fibrinolysis to the production of atherosclerosis. At the moment these are just interesting thoughts.

You are aware, I am sure, of the theory of Duguid,[50] that atherosclerosis results from thrombus or embolus being attached to the endothelium, incorporated in the wall, and ultimately replaced by lipids. They have described human vessels obtained at postmortem in which these changes were observed. In experimental animals, emboli injected into the pulmonary circulation were incorporated into the wall in the same manner.

The differential in fibrinolytic and thromboplastic activity of the various layers of the arterial wall may be of significance in the production of atherosclerosis. Astrup[12] has reported that the fibrinolytic activator activity is greatest in the outer coats of the artery and least in the endothelium and that the reverse is true with thromboplastic activity, which is greatest in the endothelium and least in the outer coats.

Our own studies have been related to the effect of lipids on thrombus formation and lysis. In these experiments it was shown that lipids in the blood inhibit fibrinolytic activity. Clots formed in hyperlipemic animals were remarkably more resistant to lysis than were the clots in normal lipemic animals. Whether this is owing to an actual increase in inhibitors or to an alteration of the clot so that the activator or enzyme is prevented from working on the fibrin has not as yet been established. Additional in vivo studies would lead to the opinion that both factors are important. Hyperlipemic clots were produced in normolipemic animals and the reverse. The clots in the hyperlipemic animals were more difficult to lyse and the hyperlipemic clots far more difficult than the normolipemic in both.

As was mentioned before, the fibrinogen content of the blood is also important. Clot density affects lysis with increasing resistance as density increases. Density is dependent on the fibrinogen content and age of the clot. Increasing age and increasing concentration of fibrinogen both result in the decreasing lysability of clots and thrombi with fibrinolysin.

The importance of these factors in coronary and other arterial diseases must be further evaluated. However, several clinical facts may be correlated with these experimental findings.

1. Fibrinolysis (spontaneous) is produced by hard physical activity which is considered to limit the development of thrombi and atherosclerosis.
2. Fibrinogen levels are high in chronic disease and increase rapidly after the acute onset of a coronary infarct. Perhaps this increases the severity of thrombosis in chronic disease and makes secondary thromboses more difficult to clear by the spontaneously active fibrinolysis.
3. Chronic diseases result in increased inhibitor levels. Patients with diabetes and other high cholesterol diseases have an increased incidence of vascular and coronary diseases.

Summary

Fibrinolytic activity can be produced in animals and patients by many means. At present the infusion of activators of plasminogen or the activator plasmin complex is the best method available. With increased fibrinolytic activity in the blood it is possible to lyse thrombi produced experimentally in animals and clinical thromboses in patients. The importance of the inhibition of fibrinolysis and the effects of increased fibrinogen and inhibitor levels in the production and persistence of thrombi has been shown.

The present indications for fibrinolytic therapy are venous and peripheral arterial thrombosis or embolus and pulmonary embolus. Cerebral and coronary thromboses are still considered subjects for clinical investigation.

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Clot Formation and Dissolution*

Basic Considerations

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ONE OF THE ADVANCES in hematology in recent years is the realization that the blood clotting system is not alone responsible for maintaining hemostasis and hemofluidity, but that other systems such as the retractozime system and the fibrinolysin system have to work in harmony with the clotting system to maintain a homeostatic balance.

It was suggested by several investigators[1-3] that the clotting out of fibrinogen is a continuous process which is in dynamic balance with the continuous lysis of fibrin. As a result of this balance, a thin, possibly monomolecular layer of fibrin is continuously present on the endothelial surface of blood vessels. This is an important factor in maintaining vascular resistance. An overbalance of the fibrinolytic system may lead to hemorrhagic tendencies; overbalance of the clotting component may result in a thickened fibrin meshwork which then will tend to trap large molecular-size lipoproteins, thus initiating the formation of atheromatous plaques.[4-7]

Biochemistry of fibrinolysin system

The fibrinolysin system is not only of physiologic importance, but more recently several of its members have entered the therapeutic armamentarium.

Figure 1 shows a simplified diagram of the fibrinolysin system. Most human tissues contain activators which are able to convert plasminogen, a normal plasma component, to the active enzyme, plasmin. Similar activators are found in some bacteria and fungi. Plasmin is able to digest fibrin and other proteins, including such nonspecific proteins as casein. There are other normal plasma components which we will call antiplasmins, which are able to form a complex with plasmin. Fibrin can compete for plasmin with antiplasmins, absorbing plasmin to its surface.[8,9] This phenomenon explains the specificity of plasmin for fibrin and the fact that fibrin clots can be dissolved with doses of plasmin which will produce little change in other clotting factors and plasma proteins.

Astrup[10] in explaining the mechanism whereby SK (streptokinase), a bacterial enzyme, can activate plasminogen, suggested that another plasma protein called proactivator is involved, which is changed by SK to an activator, and this is then able to act on plasminogen. Human blood seems to contain a great deal of this proactivator, while animal plasmins contain much

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* Dedicated to Professor H. Fischer, M.D., for his seventieth birthday.

† By invitation.

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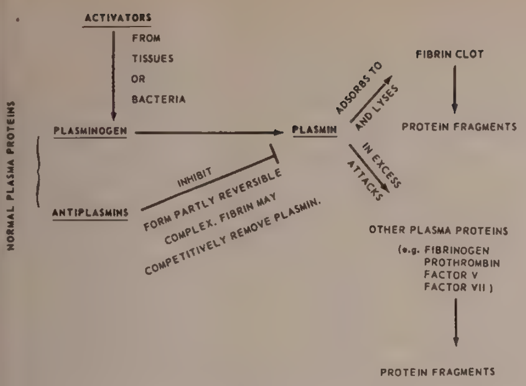

ACTIVATORS
FROM
TISSUES
OR
BACTERIA
NORMAL PLASMA PROTEINS
PLASMINOGEN
PLASMIN
ANTIPLASMINS
INHIBIT
FORM PARTLY REVERSIBLE
COMPLEX. FIBRIN MAY
COMPETITIVELY REMOVE PLASMIN.
ADSORBS TO
AND LYSES
FIBRIN CLOT
PROTEIN FRAGMENTS
IN EXCESS
ATTACKS
OTHER PLASMA PROTEINS
(e.g. FIBRINOGEN
PROTHROMBIN
FACTOR V
FACTOR VII)
PROTEIN FRAGMENTS

FIGURE 1. Simplified scheme of fibrinolytic system.

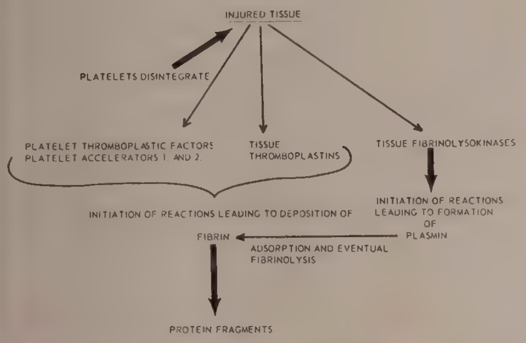

INJURED TISSUE
PLATELETS DISINTEGRATE
PLATELET THROMBOPLASTIC FACTORS
PLATELET ACCELERATORS 1 AND 2.
TISSUE
THROMBOPLASTINS
TISSUE FIBRINOLYSOKINASES
INITIATION OF REACTIONS LEADING TO DEPOSITION OF
INITIATION OF REACTIONS
LEADING TO FORMATION
OF
PLASMIN
FIBRIN
ADSORPTION AND EVENTUAL
FIBRINOLYSIS
PROTEIN FRAGMENTS

FIGURE 2. Relationship between clotting and fibrinolytic processes.

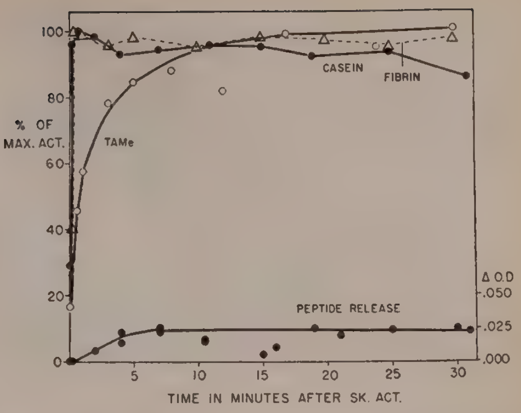


FIGURE 3. Time course of development of proteolytic and TAMe-esterase activities after streptokinase (SK) activation; 1 per cent plasminogen in 0.1 M Tris buffer, pH 8.5, 24 C. SK, 100 units per milligram of plasminogen.

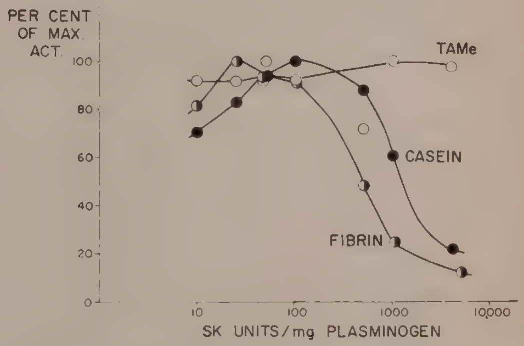


FIGURE 4. Inhibiting effect of high SK concentrations on fibrinolytic and caseinolytic activity but not on TAMe esteratic activity.

less, and some species, for example cattle, seem to contain practically none.

Figure 2 shows a diagram of our hypothesis on the significance of the fibrinolysin system in hemostasis and wound healing. When tissues are injured, thromboplastins are liberated, partly from the injured tissues and partly from the platelets which disintegrate on the rough surface of the wound; they will produce rapid clotting and thus cessation of hemorrhage. At the same time, tissue activators, which will activate plasminogen to plasmin, are liberated from the tissues. Plasmin is then adsorbed to the fibrin clot while it is formed, while in turn any free plasmin will be neutralized by antiplasmins. Endothelial regeneration will commence, and soon the continuity of the blood vessels will be re-established. The blood clot will become intravascular and is responsible for preventing the re-establishment of the circulation. In the meantime, however, the slow fibrinolytic effect of plasmin will result in recanalization and possibly the complete elimination of the clot. Teleologically the rapid action of the clotting system and slow action of the fibrinolysin system is readily understandable.

Figure 3 shows some of the features of the activation of plasminogen with SK. In addition to its fibrinolytic and caseinolytic activity, plasmin also has an esteratic effect and is able to split such synthetic esters as TAMe (tosyl-arginine methylester). If SK is added to human plasminogen, maximal fibrinolytic and caseinolytic activity develops very rapidly. As time passes, the enzyme acquires an esteratic activity as well.[11]

Figure 4 shows an interesting phenome-

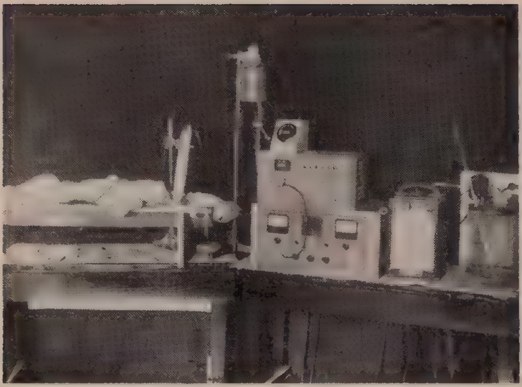


FIGURE 5. Method of assaying fibrinolytic enzymes in vivo.

non which proved to be a useful tool in studying the biochemical characteristics of the fibrinolytic system. If increasing amounts of SK are added to a certain amount of plasminogen, the fibrinolytic activity first increases until a maximum is obtained, and further amounts of SK will then be inhibitory.

The same phenomenon is observed as far as the caseinolytic effect of plasmin is concerned: Namely, with the increase in SK concentration we get first increased and then decreased activity. However, if plasmin is measured by its TAMe esteratic activity, it is evident from Figure 4 that the inhibiting effect of high SK concentrations does not manifest itself.

Time does not permit a discussion of other experiments pertinent to this question. We have concluded that plasmin is not a single enzyme; there are several molecular species of plasmin which possibly transform continuously into each other. At least three related enzymes—alpha, beta, and gamma plasmin—have been characterized in our laboratory.[11] This may be an analogous situation to the activation of chymotrypsinogen into chymotrypsin through a series of molecular forms.

In vivo experiments

Figure 5 shows a method of assaying fibrinolytic enzymes in vivo. Fibrinogen is labeled with I^{131},[12,13] and clots are prepared with this fibrinogen in the large vessels of dogs. Radioactivity is then measured continuously over the clot with the aid of a scintillation counter and radiation ratemeter and recorded with an Esterline recorder.

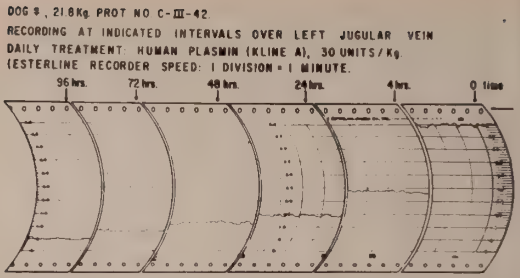


FIGURE 6. Cutouts of record of radioactivity of clot following treatment with fibrinolytic enzymes in vivo.

Figure 6 shows cutouts from such a record; approximately four hours after the injection of plasmin, a decrease in radioactivity becomes appreciable, and maximal lysis is obtained at twenty-four to forty-eight hours later. The fibrin is broken down into small peptides which are excreted chiefly in the urine. Opening of the thrombosed vein can then be demonstrated phlebographically.

Figure 7 shows the results of the following experiment: Dogs were carrying clots of four different ages in four different blood vessels. At the time the plasmin treatment was initiated, these clots were respectively half an hour, one day, two days, and three days old. As shown in Figure 7, all clots dissolved, but the three-day-old clots showed only a small degree of lysis. This seems to indicate that changes which occur in the clot with increasing age may restrict therapy with plasmin to fresh clots as the most promising indication.

We have also observed occasionally that while radioactivity disappears after the injection of plasmin, phlebographically the veins remain obstructed; thus it seems that while the original radioactive clot gradually lysed, a new nonradioactive clot was formed by apposition. The combination of heparinization with plasmin therapy will produce clot lysis and prevent new clot formation at the same time. We have shown clinically in cases of thrombophlebitis that this indeed is the most promising form of therapy.

Figure 8 shows the following experiment: Nonradioactive clots were formed in dogs, and the dogs were infused with I^{131}-labeled plasmin. The plasmin activity disappeared

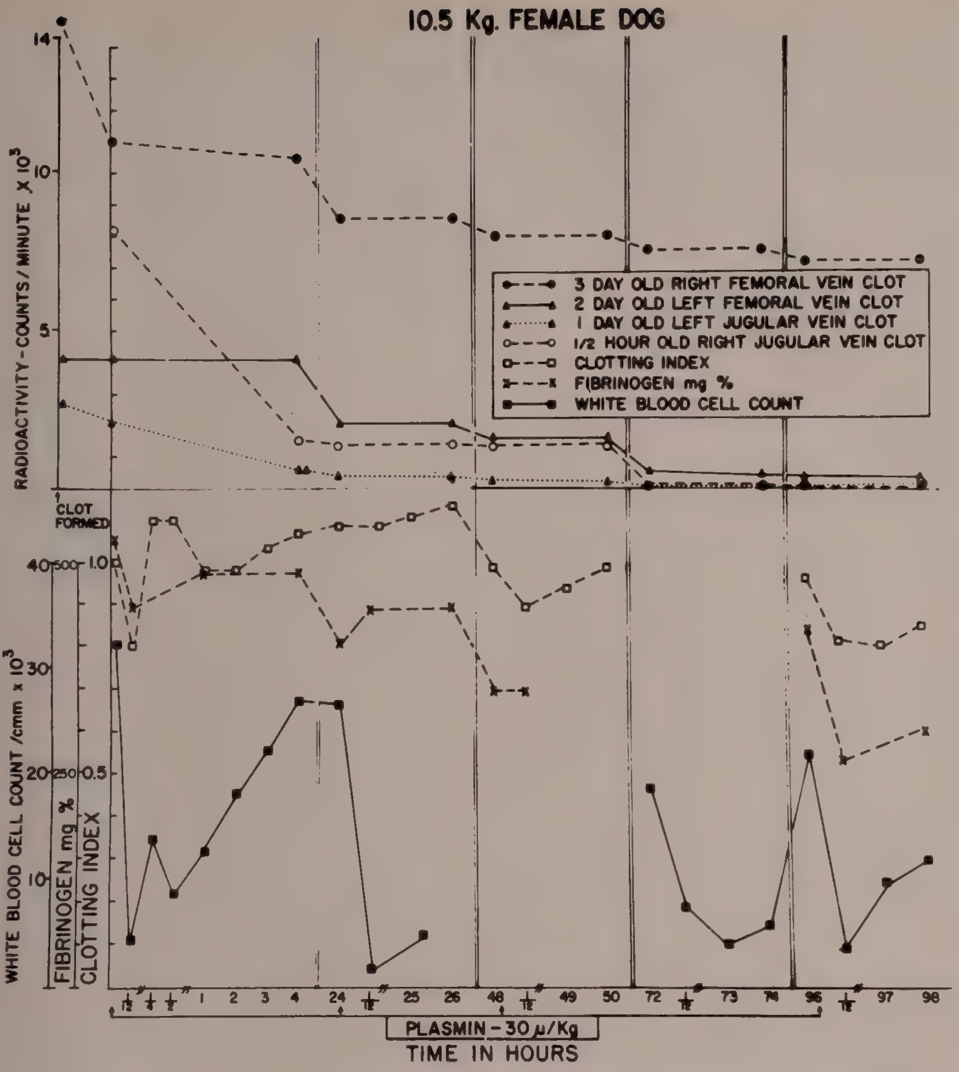


FIGURE 7. Results of experiment with plasmin therapy in dogs showing changes in clots with increasing age.

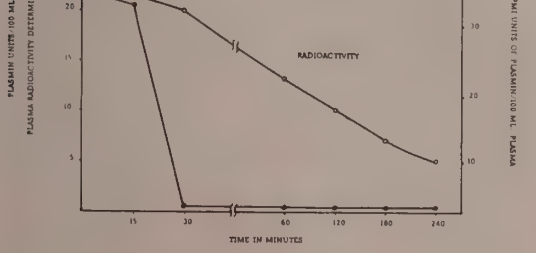


FIGURE 8. Disappearance of plasmin activity in dogs after injection with I^{131}-labeled plasmin but persistence of radioactivity.

rapidly after injection, but radioactivity persisted for a longer period of time. Presumably, plasmin at this point has been present in a complex form with antiplasmin.

After plasmin activity disappeared from the circulating blood, localization of plasmin can be demonstrated on the fibrin clots as shown in Figure 9.[9] Good localization was obtained with SK-plasmin and UK (urokinase) -plasmin whether the plasminogen or the activator part of the enzyme was labeled. However, the activators themselves, SK or UK alone, showed only a meager localization on the fibrin clots.

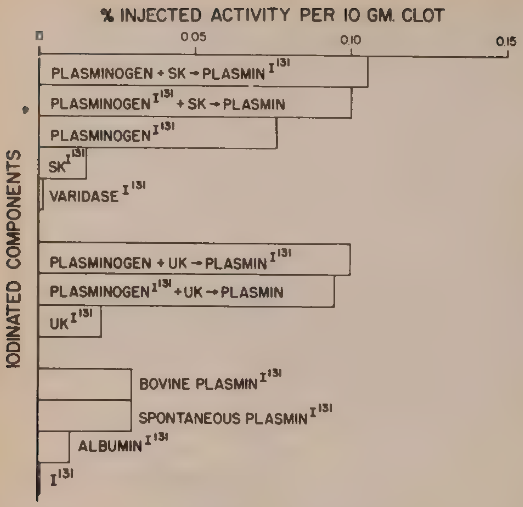


FIGURE 9. Localization of I^{131}-labeled components of fibrinolysin system on clots in dog one hour after injection.

A theory has been advanced by Sherry and his coworkers[14] that the most important mechanism of thrombolysis is the so-called intrinsic activation of the small amount of plasminogen which may become trapped in the fine meshwork of the clot.

To investigate the validity of this theory, we have produced three fibrin clots in three different blood vessels of each experimental dog. One clot in these dogs consisted of human fibrin heavily contaminated with plasminogen, which, therefore, should be dissolved by intrinsic activation. The second clot consisted of bovine fibrin which may contain bovine plasminogen, but the latter is known not to be activated by SK, and, therefore, this clot should not dissolve if the intrinsic activation theory is correct. The third clot was made with highly purified human fibrin, which contains only traces of plasminogen and, therefore, should occupy an in-between position. Figure 10 shows the results. None of the clots dissolved with any concentrations of SK; on the other hand, all dissolved equally well with SK-activated plasmin.

In vitro experiments

We have attempted to explain the mechanism of thrombolysis by a series of in vitro experiments.[8] To a unit of human plasmin, increasing amounts of antiplasmin were added, and each member of the series was assayed for both fibrinolytic and caseinolytic activity.

It is evident from Figure 11 that caseinolytic activity decreases gradually with increasing amounts of antiplasmin until it completely disappears. Fibrinolytic activity, however, disappears much more slowly.

We have explained this phenomenon by suggesting that fibrin can compete much more effectively for plasmin with antiplasmin than can casein or other proteins. If this is true, one would expect that clots can be dissolved in vivo with plasmin-antiplasmin complexes which have no caseinolytic effect at all. Figure 12 shows an experiment performed on the basis of this hypothesis.[15] Plasmin was mixed with antiplasmin in sufficient amounts to abolish completely the caseinolytic activity and also the activator activity on the dog system. Nevertheless, the plasmin-antiplasmin combination produced clot lysis comparable to plasmin alone, while the controls, saline alone and antiplasmin alone, produced no

	TREATMENT				
		SK u/Kg		Human plasmin - SK, acid treated or spontaneously activated. 30 u/Kg	Human plasmin - SK 30 u/Kg
Fibrinogen used to prepare clot	Control	25000	100,000 - 250,000		
Bovin, impure	16.2 (6)	29.6 (5)	26.5 (4)	100 (3)	74 (5)
Human, purified	11.7 (4)	12.7 (5)	1.66 (3)	30.6 (8)	100 (2)
Human, impure	7.8 (4)	10.2 (4)	8 (3)	32.9 (5)	100 (2)

FIGURE 10. Lysis of I^{131}-labeled fibrin clots (in per cent) in dogs within seventy-two hours after treatment (number of clots in parentheses).

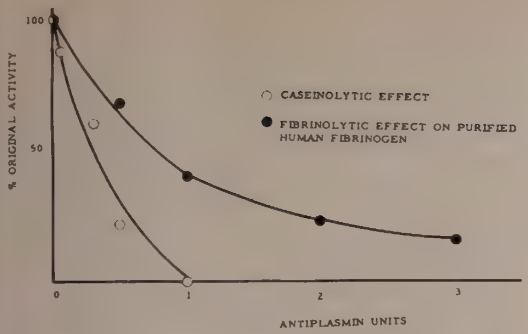


FIGURE 11. Comparison of caseinolytic and fibrinolytic activity of 1 unit of urokinase-activated human plasmin mixed with various amounts of human antiplasmin.

lysis at all, and SK, which was infused in the same amount as contained in the plasmin infusion, also showed very little effect.

So far, I have discussed chiefly SK-activated human plasmin. There is another activator of interest, which can be isolated from human urine, called urokinase or UK. In comparative clinical studies, we have found that SK-activated plasmin is about equally effective in the therapy of thrombophlebitis as UK-activated human plasmin. On the other hand, in the therapy of hyaline membrane disease of infants, UK plasmin appears to be superior. Since my assignment was to cover only "basic considerations" I will not go into the details of our clinical studies which are or will be published elsewhere.[16-18] Because of the difficulties in producing UK, presently only SK-activated human plasmin is available for general use.

Anaphylactic reactions

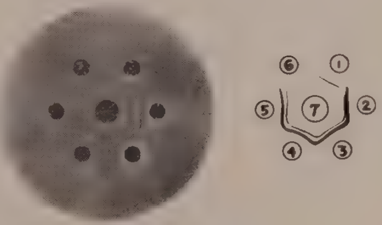
SK is known to be antigenic. We have seen at least three serious anaphylactic reactions in patients who had to be retreated with SK-activated plasmin within several weeks after an initial course because of recurrent thrombotic episodes.

Figure 13 shows the demonstration of the presence of precipitating antibodies against SK up to twenty-two weeks following an initial course with SK-activated human plasmin.

We have followed some patients now up to two years and have found still some anti-SK antibodies present. We do not have quite enough data available at this time to be sure of the statistical danger of retreatment with SK-activated preparations, given at various time intervals after the original treatment. However, we have not seen a single allergic reaction following retreatment with UK-activated plasmin.

No. of dogs	No. of clots	Treatment i. v.	Mean % decrease in radioactivity of clot	
			4 hrs.	24 hrs.
2	6	Saline	6.6	12.6
4	9	Antiplasmin alone	6.3	11.5
2	6	120 U SK/Kg.	2.1	28
4	12	15 U/Kg. plasmin	22.2	63
6	18	15 U/Kg. plasmin + antiplasmin	29	60

FIGURE 12. In vivo fibrinolytic effect of plasmin-antiplasmin complex in dogs carrying I^{131}-labeled purified human fibrin clots.



WELL #	CONTENTS
1	M.B. SERUM PRE-TREATMENT
2	M.B. SERUM 4 WEEKS POST SK PLASMIN 30 RPMI u/kg. IN 1 DAY
3	M.B. SERUM 8 WEEKS POST SK PLASMIN 30 RPMI u/kg. IN 1 DAY
4	M.B. SERUM 14 WEEKS POST SK PLASMIN 30 RPMI u/kg. IN 1 DAY
5	M.B. SERUM 22 WEEKS POST SK PLASMIN 30 RPMI u/kg. IN 1 DAY
6	SALINE CONTROL
7	MS & [redacted] STREPTOKINASE 10,000 u/ml.

FIGURE 13. Presence of precipitating antibodies against SK up to twenty-two weeks following initial course with SK-activated human plasmin.

Conclusion

By necessity, I have presented to you a rather complex system, and I am quite sure that if present trends continue in this field, this system will become even more complex in the years to come. In the meantime, however, we hope to draw useful conclusions to the therapeutic application of plasmin.

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Fibrinolysis in Thromboembolic Disease

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ARTERIAL LESIONS are quite different from venous thromboses since the arterial thrombosis generally is superimposed on arteriosclerosis obliterans, and arterial emboli may contain necrotic debris other than a pure blood clot.

In our institution we have tended to use the fibrinolytic agents as an adjunct to surgical treatment and not as a substitute. Our experience has been mainly with human fibrinolysin.

We became interested in the fibrinolytic agents when it became apparent that small vessels of coronary size had a tendency to rethrombose after thromboendarterectomy. Hugo L. Deaton, M.D., and I[1,2] have recently published two papers in this regard. In evaluating the various antithrombotic agents and the prevention of rethrombosis of intimectomized small arteries in the dog, it became apparent that human fibrinolysin was effective in 85 to 100 per cent of the animals in preventing rethrombosis. Heparin was effective only 20 per cent of the time.

Materials and methods

Our clinical experience with human fibrinolysin now totals 74 patients. Thirty-four of these patients had arterial lesions that could be evaluated objectively by the return of pulses, photography, as in the funduscopic views, or arteriography. In the majority of the patients the return of pulses and of sensation and warmth to the extremity was regarded as sufficient criteria of the re-establishment of circulation.

The most dramatic case was that of a seventy-year-old woman who awoke one morning and while doing her knitting suddenly went blind in the right eye. She was brought to us within six hours of her retinal arterial thrombosis. She was given a twenty-four-hour course of fibrinolytic therapy, and within the twenty-four-hour period there was a complete re-establishment of the arterial circulation in her eye. Before-and-after photographs have been published elsewhere. She did not regain her vision with the re-establishment of the circulation.

On the other hand, three internal carotid occlusions at the common carotid bifurcation with before-and-after arteriograms were

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* By invitation.

TABLE I. Results of treatment in 34 patients with acute arterial occlusions

Vessels Involved	Number of Patients	Results			
		Good	Fair	Poor	Undetermined
Carotid artery	4	..	3	1	..
Brachial artery	1	..	..	1	..
Digital artery	1	..	1	..	..
External iliac artery	1	1	..	..	..
Femoral artery	10	8	1	1	..
Popliteal artery	4	2	..	2	..
Tibial artery	1	..	..	1	..
Retinal artery	2	1	..	1	..
Radial artery	1	1	..	..	..
Aorta	3	1	1	1	..
Coronary	3	..	..	..	3
Skin grafts	3	3	..	..	..
TOTALS	34	17	6	8	3

dismal failures in fibrinolytic therapy. In these 3 cases one lesion was of four days duration, the second of forty-eight hours duration, and the third of approximately twelve hours duration. By and large, thrombotic lesions of over twenty-four hours duration did not seem to respond to fibrinolytic therapy in our hands.

It was also interesting that our experience with arterial embolism was unsatisfactory in that the emboli tended to have necrotic debris; the results of fibrinolytic therapy were poor.

Whereas we performed rather elaborate coagulation studies on the patients receiving human fibrinolysin, we found that the one-stage prothrombin level was a good minimum safeguard for the use of these agents by surgeons and clinicians in general. The euglobulin clot lysis time gives some indication of the enhancement of fibrinolytic activity in the patient but is not absolutely necessary as a safeguard in administration. It should be noted too that with the fibrinolytic therapy there tended to be a drop in the prothrombin level, as well as the fibrinogen level; these changes were not critical in any of our patients. With the doses used up to a million units per day, the euglobulin clot lysis time tended to decrease from over eight hours to less than one hour. We have found that approximately twenty-four hours of fibrinolytic therapy is optimal, and therapy beyond this point did not seem to be of additional benefit.

The fibrinolysin was administered as follows: 100,000 to 150,000 units were given within the first half-hour, intravenously, mixed in saline or 5 per cent dextrose in water, provided that a base-line control one-stage prothrombin level was 80 per cent or above. For the next two hours 100,000 units were administered per hour by intravenous drip. For the remaining twenty-two hours the fibrinolysin was administered at the rate of 50,000 units every two hours. Prothrombin levels and euglobulin clot lysis times were rechecked at six- to eight-hour intervals. In the event of a drop in the prothrombin level below 40 per cent of normal, the rate of administration was decreased. Table I lists the arterial lesions treated to date and the results obtained in this series.

Results

One difficulty in evaluation is that controls would be difficult to obtain, and in the treated cases one cannot be sure that the same result might not have been obtained without fibrinolytic therapy. On the other hand, in instances such as the retinal arterial thrombosis, our ophthalmologist states that in his thirty-five years or more experience he had never seen the complete re-establishment of retinal arterial circulation within twenty-four hours.

In this series we have also had our disappointments and complications. Certain fresh thromboses which might have been expected to respond to treatment have been failures. Approximately 15 per cent of our patients have experienced a febrile reaction which in the great majority has been mild with an elevation to 38.5 C. or less.

We have experienced only 1 case of moderate bleeding in a woman who received the fibrinolysin in the full therapeutic dose described previously at the same time as a 50-mg. dose of heparin intravenously. She had just undergone a femoropopliteal thromboarterectomy and sympathectomy. She developed ecchymoses in both wounds but did not have any hypotension or require transfusion.

One real danger has been to rely on the drug as a crutch and not to follow the usual indications for surgery. This lesson was learned early in our series when another woman who had just undergone femoropopliteal thromboarterectomy showed evidence of popliteal arterial occlusion. On the basis that this might be a rethrombosed segment, she was treated with fibrinolysin. When she did not improve within twelve hours she was re-explored and found to have a dissection of the intima at the distal suture line with the development of a false passage. Hence, it is extremely important to use the fibrinolysin as an adjunct and not as a substitute for surgical operations.

Following the use of fibrinolysin for the initial twenty-four-hour period our patients have been maintained on heparin to prevent rethrombosis. We have found that patients are exquisitely sensitive to heparin and have usually started them on heparin, 25 mg. subcutaneously every four to six hours with daily checks of the clotting time.

More recently, we have been in the process of evaluating the possible use of regional perfusion of areas bearing thrombi. It is as yet too early to state whether or not this method of administration is more advantageous than systemic administration.

Conclusion

Finally, it is our feeling that the fibrinolytic agents provide a useful addition to the surgeon's entire thrombotic armamentarium. We feel that the fibrinolytic agents should be used with the same indications that apply currently for the use of heparin.

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Fibrinolysin Therapy in Thromboembolic Diseases

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In exercises commemorating the centennial of the founding of the Massachusetts Institute of Technology, its president, Julius A. Stratton, said, "the world into which we were born is gone, we have little or no idea of the world into which our children grow into maturity. It is this rate of change, even more than the change itself, that I see as a dominant factor of our time."[1] This statement certainly applies to many fields of medicine and especially to the cardiovascular diseases. However, the management of coronary artery disease has lagged behind. Following the delineation of the clinical picture of myocardial infarction and its recognition by Herrick in 1912,[2] progress in management has been rather slow. The advent of anticoagulant therapy has been a step forward but still is not definitive, and its beneficial features remain controversial. To enable a direct approach

TABLE I. Age and sex distribution in patients with myocardial infarction treated with fibrinolysin

Age (Years)	Males	Females
30 to 39	4	. .
40 to 49	18	3
50 to 59	24	7
60 to 69	25	17
70 to 79	17	12
80 to 89	4	4

TABLE II. Time from onset of myocardial infarction to beginning of fibrinolysin therapy

Hours	Males	Females
1 to 5	32	10
6 to 10	36	14
11 to 20	10	14
21 to 49	11	1
50 to 59	1	. .
60 to 80	1	3
80 to 120	1	1

to the dissolution of a thrombus in situ in a blood vessel would be a major advance in the therapy of thromboembolic diseases. For this purpose a satisfactory agent would be a thrombolytic drug that would increase the clot-dissolving capacity of the blood and be free from harmful side-effects; this should be controlled by a simple, readily standardized, laboratory procedure.

Previous studies have been reported on the use of thrombolytic agents in cerebral thrombosis,[3,4] pulmonary infarction,[4] peripheral arterial occlusion,[4,5] myocardial infarction,[6–8] and thrombophlebitis.[4,9] We have treated 180 patients with various types of thromboembolic diseases. These include 4 patients with cerebral thrombosis, 15 with peripheral arterial occlusion, 22 with thrombophlebitis, 4 with pulmonary infarction, and 135 with myocardial infarction. Of the latter group the last 71 cases were treated with a control alternate case group receiving heparin and warfarin sodium.

The age distribution and time from onset of symptoms are shown in Tables I and II respectively. Table I shows that there were 46 men and 10 women in the age group of thirty to fifty-nine, 25 men and 17 women in the age group of sixty to sixty-nine, and 21 men and 16 women in the age group of seventy to eighty-nine. Forty-six men and 19 women had anterior wall infarction, and 46 men and 24 women had posterior wall infarction. Table II shows the time at which fibrinolysin therapy was started in relation to the onset of symptoms. The majority of patients received therapy within twenty hours after the onset of the attack.

Fibrinolysin administration

All the patients received fibrinolysin* by continuous intravenous drip. The dosage which was given to most patients was approximately 750 to 1,000 units per kilogram of body weight per hour for eight hours per day from one to four days. The diluent was 5 per cent glucose in water, 150 cc. for each two-hour period. The prothrombin time and euglobulin fibrinolytic activity studies were done each day before and during therapy. An electrocardiogram, serum transaminase determination, sedimentation rate, blood count, and urinanalysis were obtained frequently in all patients with myocardial infarction. The last three tests were done in all other patients with various thromboembolic diseases. Diphenhydramine hydrochloride (Benadryl hydrochloride) was given to all patients before and during therapy. Heparin and warfarin sodium were started a few hours after the last dose of fibrinolysin.

Results

Table III shows the results of therapy in the various thromboembolic diseases excluding myocardial infarction. Of 4 cases with cerebral thrombosis, 2 died, and 2 recovered. One of the 2 who recovered showed slight improvement in the hemiplegia. Of the 15 patients with peripheral arterial occlusion, 7 had complete recovery of the limb and return of arterial pulsation, 5 died, and 3 required amputation. Of the 7 recoveries, there were 2 of the bifurcation of the aorta and 5 of artery occlusion: 2 femoral, 2 brachial, and 1 popliteal. Of the 5 who died, 3 were occlusion of the bifurcation of the aorta and 1 of the popliteal and 1 of the brachial artery. The ampu-

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* Supplied by Merck, Sharp & Dohme, West Point, Pennsylvania.

TABLE III. Various thromboembolic diseases treated with fibrinolysin

Disease	Number of Patients	Recovered	Died	Gangrene and Amputation
Pulmonary infarction	4	3	1	. .
Cerebral thrombosis	4	2	2	. .
Thrombophlebitis	22	22	. .	. .
Peripheral arterial occlusion	15	7	5	3
Bifurcation of aorta	5	2	3	. .
Femoral artery	4	2	. .	2
Popliteal artery	3	1	1	1
Brachial artery	3	2	1	. .

TABLE IV. Comparison of myocardial infarction in 71 patients treated with fibrinolysin and 72 control patients treated with anticoagulants

Classification	Fibrinolysin	Anticoagulants
Males	50	50
Females	21	22
Anterior wall infarction	37	45
Posterior wall infarction	34	27
Survived	45	46
Died*	26	26
1 day	14	10
2 days	5	. .
3 to 16 days	6	10
21 to 46 days	1	2
2 to 5 months	. .	4

* Mortality of the whole group of 135 fibrinolysin-treated patients was 38 (26 males and 12 females).

TABLE V. Side-reactions during fibrinolysin therapy

Type	Number
Superficial ecchymosis	2
Abdominal pains	3
Nausea and vomiting	7
Chills	6*
Rectal bleeding	2
Hematuria	3
Bleeding from gums	1
Bleeding from carbuncle	1
Hematemesis	2
Subdural hematoma	1

* Three of these patients were treated with premarketed fibrinolysin.

TABLE VI. Highest rectal temperature of 70 fibrinolysin-treated patients and 72 control patients with myocardial infarction

Temperature (F.)	Fibrinolysin-treated Patients	Control Patients
96 to 99	21	12
100	14	19
101	15	21
102	10	10
103	6	7
104	4	2
106	. .	1

tations were 2 in femoral and 1 in popliteal artery involvement. Treatment was instituted from two to ten hours after onset in 3 patients, after eleven to twenty hours in 8 patients, and after twenty-one to twenty-six hours in 4 patients.

All the 22 patients with thrombophlebitis recovered. Treatment was instituted in 3 patients on the first day of illness, 5 on the second or third day, 11 on the fourth to seventh day, 1 on the eighth day, 1 on the twenty-eighth day, and 1 at the end of three months. Three of the 4 patients with pulmonary infarction recovered. In those instances with recovery, improvement occurred before anticoagulant therapy was started. Of the 135 patients with myocardial infarction, 97 survived, and 38 died, 26 of whom were males and 12 females. Comparing the results of the last 71 patients of the treated group with the control group of 72 (Table IV) we see that of the treated group 45 survived, and 26 died; and of the control group 46 survived, and 26 died.

Side-effects

The side-reactions observed in all patients treated with fibrinolysin are listed in Table V. Significant gross bleeding occurred in 10 patients. Two bleeding episodes occurred on the first day of thrombolysin therapy, 1 on the second day, 5 on the third day, and 2 on the fourth day of therapy. Two of these patients with bleeding died. One had metastatic carcinoma of the urinary bladder, and 1 had a subdural hematoma which probably was related to trauma as-

TABLE VII. Highest prothrombin time obtained in all patients with thromboembolic diseases

Prothrombin Time (Seconds)	Number of Patients
11 to 17	27
18 to 20	65
21 to 25	66
26 to 30	19
31 to 60	3

sociated with syncope and fall at the onset of myocardial infarction. The highest rectal temperatures reached in the alternate case series of myocardial infarction are shown in Table VI. In 70 fibrinolysin-treated patients, as compared with 72 control patients, there was no significant difference in the degree of temperature elevation. (One treated patient died before the temperature could be taken.)

Prothrombin time

Table VII shows the highest prothrombin time obtained during fibrinolysin therapy. It should be noted that a majority of patients had a prothrombin time elevation of eighteen to twenty-five seconds. Euglobulin fibrinolytic activity studies have been done on 60 patients (Table VIII). Of 54 patients with fibrinolytic activity of from one-half to three hours, 40 had a significant rise in prothrombin time. This small number suggests a possible correlation of the results obtained by these two procedures.

Comments

A consideration of the preceding data involves the basic physiologic pattern which governs the response of tissues to acute arterial or venous occlusive processes. The nature of collateral circulation is an important governing factor. The vasospastic responses in different vessels and their effects on different organs are important. For example, following the ligation of a major branch of a dog's coronary artery, Tennant and Wiggers[10] and Prinzmetal *et al.*[11] have shown that changes in the myocardium are reversible in the first fifteen minutes and irreversible after twenty-five minutes. Ruegsegger *et al.*[12] have shown that in experimentally produced infarcts in dogs, total lysis of coronary thrombi occurred in from three to seven hours in 4 out of 8 dogs on fibrinolysin therapy. Therefore, although we cannot initiate treatment within the first twenty-five minutes of an episode of coronary thrombosis, theoretically we can lyse the coronary thrombi by therapy. In the current series, 42 patients received fibrinolysin from one to five hours from the onset of the acute coronary episode, 50 patients from six to ten hours, and 43 patients from eleven to one hundred and twenty hours.

TABLE VIII. Comparison of euglobulin clot lysis time and prothrombin time in 60 patients with various thromboembolic diseases

Fibrinolytic Activity (Hours)	Number of Patients	Prothrombin Time (Seconds)	Number of Patients
1/2 to 1	29	18.5 to 26	23
		15 to 17	6
1 1/2 to 3	25	18 to 26	17
		Less than 18	8
4	2	11.2	1
		15.3	1
6 1/2	2	18	1
		16.8	1
9	1	12.2	1
20	1	14.2	1

Peripheral arterial occlusion without treatment usually is not followed by a return of pulsations. In this small series, 7 patients had a complete recovery of the limb and a return of pulsation. It is noteworthy that 2 of these patients had an acute occlusive process at the bifurcation of the abdominal aorta. The group of patients with thrombophlebitis included 3 patients with a duration of illness of longer than seven days. In spite of the comparatively late use of fibrinolysin in some patients, recovery ensued in all patients prior to the addition of anticoagulants to the therapeutic regimen.

Summary

Fibrinolysin was administered to 180 patients with various thromboembolic diseases. Of 22 patients with thrombophlebitis, all recovered. Of 4 with pulmonary infarction, 1 died. Of 4 patients with cerebral vascular occlusive disease, 2 recovered. Of 15 patients with peripheral arterial occlusion, 7 recovered, 5 died, and 3 required amputation. Of 135 patients with myocardial infarction 97 recovered, and 38 died.

The efficacy of fibrinolysin therapy in thrombophlebitis, pulmonary infarction, and peripheral arterial occlusion is encouraging.

In myocardial infarction, there was no demonstrable clinical benefit in this series of 135 patients.

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Lysis of Cerebrovascular Blood Clots

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RECENT IMPROVEMENTS in medical care have increased the proportion of the population suffering from diseases of old age. This has resulted in a great increase in the number of cases suffering from cerebrovascular disease. Eventually cerebrovascular disease may become the commonest cause of chronic disability and become a commoner problem of public health than schizophrenia.

In spite of this increased number of patients that we see and the acceleration of interest in the pathogenesis and treatment of vascular disease of the brain in recent years, until about ten years ago the medical treatment of acute progressive thrombosis of cerebral vessels remained unchanged from the conservative therapy of time immemorial.

Dr. Cliffton has described the recent advances in enzyme chemistry which have resulted in a better understanding of the fibrinolytic systems and which make possible the administration of enzymes which enhance the fibrinolytic activity and permit lysis of intravascular thrombi.

It is well established that clot lysis can and does occur spontaneously in some cases of thrombosis or embolism, and there are already enzymes available, such as streptokinase and various plasmin preparations, which are of value in phlebitis and phlebothrombosis of peripheral vessels.

The value of therapeutic thrombolysis in cases of arterial thrombosis is as yet not established. In the treatment of cerebral arterial occlusion, adequate and carefully planned evaluation of a large number of well-classified cases has not yet been completed.

Cerebral thrombosis

A few introductory remarks about the problems peculiar to cerebral thrombosis are in order. The metabolic demands of the brain are great; they are about forty times that of muscle, and if the brain is completely deprived of its oxygen supply for more than six to ten minutes, it will become damaged almost totally and irreversibly.

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* By invitation.

Experimental evidence, however, indicates that the cerebral collateral circulation is much more efficient than was previously believed, and nervous tissue with a sluggish circulation which provides about 20 to 80 per cent of its normal oxygen tension may remain alive but nonfunctional for considerable periods of time. Sluggish cerebral circulation, particularly with venous thrombosis, may result also in the accumulation of acid metabolites, a reduction of cerebral pH, and metabolic paralysis. Such a state of metabolic paralysis due to the accumulation of acid waste products in the brain remains reversible for much longer periods than does paralysis from ischemic anoxia and probably may remain reversible for several weeks.

These data suggest that the restoration of the circulation into thrombosed cerebral vessels may be of value in some cases by salvaging brain tissue that otherwise would remain functionless, in which instance irreversible damage would occur eventually.

We have investigated the possible therapeutic value of thrombolysis in the acute progressive cerebrovascular thrombosis. This communication presents the results of treatment of 70 cases of cerebrovascular thrombosis with several fibrinolytic enzymes.

Data to date appear to be sufficient to indicate that this method of therapy is feasible. Eventually, double-blind studies are planned which may establish its true therapeutic usefulness.

Methods and materials

Regarding methods and materials, we have used chloroform-activated bovine plasmin, streptokinase-activated human plasmin, and the urokinase-activated human plasmin that we are using at the present time. Both of the latter were supplied for intravenous injection. The material was dissolved in 1,000 ml. of 5 per cent glucose and distilled water which had been cooled to approximately 4 C., and the solution was kept cool with a refrigerant during infusion.

The material was given intravenously in most cases over a four-hour period of each of the three successive days.

In 3 cases, the first dose was administered intra-arterially at the time of arteriography.

Patient selection

The selection of cases is very important in the treatment of cerebrovascular thrombosis. I would like to define what cases were considered eligible:

All patients were acutely ill and showed gross objective neurologic deficits which were clearly attributable to severe focal cerebral ischemia.

Lumbar puncture was performed in all patients. This is vitally important. Any evidence of intracerebral bleeding, such as xanthochromia or erythrocytes in excess of 3,000 per cubic millimeter, which was not clearly attributable to traumatic tap, was considered a definite contraindication to therapy. The big danger is treating a cerebral hemorrhage with fibrinolysin in error.

In the first group of patients who would receive the bovine material, a skin test was performed to determine if the patient was allergic to the bovine material, and if sensitivity was found, it was considered a contraindication to therapy. However, we no longer use bovine preparations.

Whenever possible the diagnosis was confirmed by arteriography prior to treatment. In some cases, arteriography was repeated after treatment to establish whether or not there had been restoration of circulation in the occluded vessels.

Severe uncontrolled hypertension was considered a contraindication, and I think that this is very important also. However, several of our very severely hypertensive patients were treated with hypotensive drugs until the blood pressure had been lowered to levels below 180 systolic, and then they were treated with plasmin. I think that the dangers of hemorrhage are extremely great in patients with severe hypertension.

All patients received anticoagulants, either heparin and bishydroxycoumarin (Dicumarol) or warfarin sodium, during and after therapy to prevent the reformation of any thrombi once they were dissolved, and I think that in the brain this is an important consideration. The vessel wall is severely damaged, and if a concomitant anticoagulant is not used, I think that the thrombus reforms as soon as the fibrinolytic therapy is discontinued.

We have shown experimentally in animals that cerebral arterial thrombi reform once the fibrinolysin is discontinued unless anticoagulants are given concurrently.

Routine laboratory studies included hemaglobin, total and differential white counts, fasting blood sugar, plasma and urea nitrogen, daily prothrombin time, and Lee-White clotting times; special laboratory studies were performed on specimens drawn immediately prior to therapy at intervals of two, four, six, and eight hours after therapy had been begun. The latter specimens were centrifuged and the plasma frozen immediately for special hematologic studies at a later date. The hematologic studies which were performed on these specimens included euglobulin clot lysis time, fibrinogen level, prothrombin time, prothrombin units, and plasma recalcification time.

Clinical results

Because of the variable clinical course of patients suffering from cerebral thrombosis or embolism, no statistically significant conclusions regarding the efficacy of therapy can be made from the present series.

We discontinued the use of bovine fibrinolysin because the number of reactions was high; 14 per cent showed urticaria and other complications. We now use streptokinase-activated or urokinase-activated human plasmin.

Our results indicate in the series so far that between 50 and 60 per cent of the cases show improvement.

The arteriographic surveys before and after therapy show the recanalization of occluded vessels in several cases. For example, in 2 cases an occluded middle cerebral artery as demonstrated arteriographically was shown to be patent after treatment.

These patients in whom we have shown vascular recanalization do not necessarily recover functionally because there may have been sufficient ischemia so that the brain damage was irreversible, even though the vessel was "opened up."

In 2 cases of occlusion of the internal carotid artery we have shown recanalization after therapy.

The euglobulin clot lysis time in our series of cases showed a significant reduction during the administration of plasmin with a rapid return toward normal after the cessation of therapy. The fibrinogen levels were reduced in our series of patients. The prothrombin units were often reduced during therapy.

In a typical case with thrombosis of the basilar artery, for example, with treatment the euglobulin clot lysis time was diminished, the prothrombin time was prolonged, the prothrombin units decreased, and the fibrinogen level also decreased during the time of administration of plasmin.

In our series of cases only 4 per cent showed progression of the neurologic deficit after the institution of plasmin therapy.

In assessing these preliminary results, it should be borne in mind that because of the experimental nature of this form of therapy and the nature of our acutely ill population of patients, the majority of the patients treated were all seriously and often critically ill.

Complications of therapy

We have not seen febrile reactions in a single case in our series, although we know that other people have recorded this. We have seen extracerebral hemorrhagic phenomena, and I have seen intracerebral hemorrhage in 2 cases, but in 1 case there was a mistaken diagnosis, and we were actually treating a small cerebral hemorrhage. In the other case the hemorrhage resulted from a hemorrhagic softening.

Two patients developed gastrointestinal hemorrhages, neither of which was considered serious. Four patients reacted with hemorrhages from the site of recent tracheostomy. The bleeding of tracheostomy wounds proved to be a major problem in our series and necessitated the temporary discontinuation of therapy in 2 cases.

In 2 cases, epsilon-aminocaproic acid was given in a dose of 1 Gm. intravenously, and the bleeding ceased promptly without clinical evidence of further cerebrovascular thrombosis, which was a matter giving us grave concern at the time we gave it.

Our experience thus far suggests that if tracheostomy is done with very close attention to hemostasis and a patient is closely observed for signs of hemorrhage, plasmin therapy can still be given despite recent tracheostomy which is so commonly used in patients with severe cerebral thrombosis.

What about failures of therapy? In 3 cases who were not improved, we asked the surgical service to perform a reconstruction of the occluded carotid artery. Thereby we obtained a biopsy specimen of the site that we were trying to lyse. In all 3 cases, the clots were old and organized.

A microscopic study of the clots showed that not only were they endothelialized but also fibrosed, and, obviously, fibrinolysin could not benefit such a situation. However, such patients with organized thrombi may have such a sudden onset of neurologic deficit and mimic acute thrombosis. The reasons for this phenomenon are multiple, but I will mention one: Acute blood loss and hypotension, for example, may decompensate the collateral circulation in such a chronic occlusion.

Conclusion

Alfred P. Ingegno, M.D.: I would like to ask one question. How much does fibrinolysin treatment cost?

Dr. Cliffton: It is extremely expensive at the present time. I think that all of us would agree on that, at least in the dosage that we are talking about now, and I think that it is reasonable to say that in many individuals with deep thrombi, who do not have cancer or other chronic diseases which have been treated or heart disease, much smaller doses can be used.

I think that when we prove that fibrinolysin therapy is a useful tool and enough of it is on the market, the price will become reasonable; and we will find better methods of doing it also. Eventually, some of these activators will turn out to be material that will be less expensive and more reasonable.

Popular Media Discussed

Television and radio are gaining recognition as methods of communication in the medical field, according to *Patterns of Disease*, a monthly Parke, Davis & Company publication for physicians. The Albany Medical College's two-way radio conferences, for example, which have grown steadily since the programs began six years ago, have been attended by more than 33,000 physicians. Had they gone to Albany to attend, these physicians would have travelled more than 1,500,000 miles. Similar conferences have been started in Pennsylvania and in North Carolina.

Diabetes Teaching Manual for Patients and Hospital Personnel

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DIABETES MELLITUS is an hereditary disease due to a relative or absolute lack of insulin, resulting in an inability to utilize carbohydrate properly for normal body energy. The term itself is descriptive, and the word diabetes is derived from the Greek, meaning "to siphon or run through." Mellitus is Latin for "honey." The major symptom of the disease is the passage of large volumes of sweet urine; hence, the name is useful in describing the disease.

HISTORY. In 1889 a young German scientist, Oscar Minkowski, removed the pancreas from dogs (pancreatectomy) and noted that the dogs became thirsty and urinated frequently. The urine contained glucose (sugar) and the level of glucose in the blood was elevated. In 1921 a thirty-two-year-old Canadian, Frederick Banting, with the help of a sophomore medical student at the University of Toronto, Charles Best, isolated a substance from the pancreas which abolished all the symptoms of diabetes and restored the blood glucose level to normal. This substance was extracted from a particular area of the pancreas called the islets of Langerhans and was originally named "isletin." Shortly after discovery, however, the name was changed to "insulin," and that is as we know it today.

SYMPTOMS AND THEIR CAUSE. Carbohydrate is the main source of food energy for the body. It is derived from foods such as breads, cereals, rice, fruits, vegetables, milk, sugar, and sweets. It ordinarily supplies from 50 to 60 per cent of the calories in our diet. The remaining calories are supplied by foods containing protein such as meat, milk, cheese, eggs, and fat. The protein is used for body-tissue building, and the fat is used as a reserve source of energy. Under normal circumstances carbohydrates are converted to glucose (a type of sugar) in the intestinal tract, and the glucose is absorbed into the blood stream where it circulates to the body cells which utilize it for energy. In diabetes the glucose cannot be utilized and accumulates in the blood (hyperglycemia). As the glucose levels rise, the kidney, which ordinarily acts as a dam, is unable to hold the glucose back, and it spills over into the urine (glycosuria). The high glucose content in the urine attracts water from the tissues and large amounts of urine are passed (polyuria). The loss of water produces thirst (polydipsia). In addition, since the glucose is not being utilized, a large amount of the food taken in is wasted, resulting in weight loss. To correct the loss of calories, the appetite is stimulated and food intake is increased (polyphagia), but since this food also cannot be utilized, it does not correct the weight loss. The cardinal symptoms, therefore, are excessive thirst, frequent urination, and weight loss despite a large food intake. These symptoms all result from the basic inability of the body to utilize carbohydrate.

As the disease progresses, the energy needs of the body must be met by other foods. Body fat and protein are burned, but when fat is burned in large quantities, substances called ketones accumulate in the blood (ketosis). If the ketones accumulate to such an extent that the normal chemical balance in the body is disturbed, an acid condition develops (diabetic acidosis). If the acidosis is uncorrected, it proceeds to coma (diabetic) and eventually to death. The protein breakdown results in a loss of muscle strength and generalized weakness. The need for this breakdown of fat and protein is abolished as soon as proper equilibrium is restored and carbohydrate once again is burned in the normal fashion.

Types of diabetes

Modern technics have allowed us to delineate two major types of diabetes. The most common is the adult type which is usually accompanied by obesity (overweight) and which has a normal amount of insulin present in the pancreas and in the blood. For some unknown reason, however, the insulin is no longer effective. Since insulin is present, this group is apt to respond to the oral drugs for diabetes.

The second type is the juvenile type of diabetes which usually occurs in children but may also occur in adults. In this group no insulin is present, obesity is uncommon, and diabetic ketosis occurs readily. This group cannot use any of the oral drugs for diabetes unless insulin is also administered.

Heredity

Almost all patients with diabetes have some member of their family who has also had the disease. Often this fact is obscured by insufficient knowledge of distant relatives and the failure to diagnose diabetes properly in former years. Although there are instances where there is no history of diabetes in the family, usually, if a detailed family history can be obtained, there is a positive history for diabetes. Because of the increased incidence of the disease in patients with a positive family history, it is evident that the disorder is transmitted genetically (that is, genes determine the color of the hair, eyes, and so forth, and transmit certain metabolic diseases such as diabetes). Since only a small number of patients develop diabetes in a given family, it is probably transmitted as a recessive trait. Although we know that the disease is transmitted by inheritance, we do not know what makes the disease become manifest, that is, become active and produce symptoms. Certain members of a family will carry the genetic background for diabetes, but they themselves never develop the disease.

DIABETES MELLITUS, *a hereditary disease due to a relative or absolute lack of insulin which results in inability to utilize carbohydrate properly for normal body energy, may be of the adult type, which usually is accompanied by obesity and responds to the oral drugs; or of the juvenile type, in which obesity is uncommon, diabetic ketosis occurs readily, and insulin administration is necessary. Prediabetes often may be detected during pregnancy. Although there is no cure for diabetes, remission may occur. Good treatment means the maintenance of normal weight, normal activity, absence of glycosuria, and as normal a blood sugar as can be achieved without hypoglycemia; it consists of diet, insulin, exercise, and oral hypoglycemic drugs. Complications of diabetes include: diabetic retinopathy, nephropathy, and neuropathy. Insulin reactions may cause cerebral and adrenal symptoms; the treatment is rapid administration of glucose, or glucagon if the patient is unconscious. Diabetic acidosis may occur as the result of failure to take insulin or of severe infection which greatly increases the need for insulin, and the patient's physician should be contacted immediately. Urine testing for glucose is useful in achieving diabetic regulation. Proper care of syringes and needles, careful foot care, and identification tags are essential in patients with diabetes.*

Prediabetes

Since members of a family may carry the tendency toward diabetes without developing the disease, is there any way to detect diabetes in this earlier stage? During pregnancy diabetes often makes itself known for the first time. The full symptoms of diabetes, such as excessive thirst and frequent urination, may not be present, but there is often mild glycosuria, excessive fluid retention, and a history of frequent miscarriages, toxemia of pregnancy, and stillbirths. A glucose tolerance test (a special test with a large oral dose of glucose and hourly blood sugar tests for from three to four hours) will be abnormal during the pregnancy, but it usually reverts to normal after the pregnancy.

For some unknown reason large babies are also associated with prediabetes. The birth of a baby weighing more than 10 pounds often suggests that the mother has diabetes or prediabetes. Any mother who gives birth to a baby of such a weight should be evaluated for diabetes.

There are other medical conditions which may also indicate the prediabetic state, but these are not as well worked out as in the case of pregnancy. Among these are renal glycosuria (sugar in the urine due to a low kidney barrier to glucose), cataracts, and premature arteriosclerosis (hardening of the arteries).

A test has been devised which may indicate the prediabetic state. Based on the knowledge that pregnancy and certain stress situations often precipitate frank diabetes or make a known diabetes worse, cortisone (an adrenocortical hormone) has been administered in a carefully standardized fashion to bring out an underlying diabetic abnormality. It has been found that the glucose tolerance test after cortisone is more frequently abnormal in close relatives of diabetic patients than it is in relatives of nondiabetic patients. Although the test is still experimental, an abnormal cortisone glucose tolerance test may mean that the prediabetic state is present.

Cures and remissions

The new patient with diabetes often asks about cures for diabetes. Unlike many diseases, such as pneumonia, typhoid fever, and so forth, there is no penicillin to eradicate the disease. Insulin, diet, and the newer oral hypoglycemic (hypoglycemia means low blood sugar) drugs are all forms of treatment which have to be continued. The abnormal gene cannot be cured with medicine, but nature, in extremely rare instances, does what medicine cannot do. There are well-documented cases of patients who have had clear-cut diabetes, usually associated with acute diabetic acidosis, whose diabetes has improved and then disappeared completely. Even after many years, there is no evidence of diabetes either clinically or after glucose tolerance testing. These cases, although rare, indicate that diabetes is not always an inherited disorder but may in some instances be acquired and may occasionally disappear completely.

What is more common is to have a remission which means that after treatment the disorder improves. Unlike the situation with cures, diabetes can always be demonstrated with special testing and usually gets worse after a period of poor treatment. A remission is a much-sought goal of therapy. It is most common with diabetes associated with obesity after a reduction to normal weight. In juvenile diabetes early intensive therapy often leads to a remission. Careful treatment may prolong this improved state, making the management of the diabetes simpler.

Treatment goal

The treatment of diabetes is aimed at the restoration of the disturbed carbohydrate, protein, and fat metabolism to normal. Good treatment means the maintenance of normal weight, normal activity, absence of glycosuria, and as normal a blood sugar as can be achieved without hypoglycemia. When the diabetes is mild enough to require no insulin, the aim is a normal blood sugar, since hypoglycemia is not a problem. At the famous Joslin Clinic in Boston there is a plaque which summarizes the treatment for diabetes. It reads, "diet, insulin and exercise." Since the plaque was made, the oral hypoglycemic drugs have also been made available. We shall discuss each factor, starting first with diet.

Diet

Probably for the large majority of adult diabetic patients the most important point in diet treatment is the elimination of obesity, since, as we have pointed out previously, obesity is often the main factor in producing the diabetes. The removal of the excess weight is achieved by using a diet with fewer calories than are needed, forcing the body to burn its own fat as a source of energy. Usually a diet of from 1,000 to 1,500 calories is prescribed to restore the body weight to normal. Once normal weight has been achieved, the calories are increased to a level that will maintain ideal body weight. The most common failure in the management of adult diabetes is the failure to restore the weight to normal or, having restored it to normal, allowing it to increase again at a later date.

In nonobese patients or in patients in whom the restoration of body weight to normal does not correct the disturbed metabolism, carefully calculated measured diets must be used. In the diabetic diet 40 per cent of the calories are supplied as carbohydrate, whereas in the usual American diet from 50 to 60 per cent of the calories come from carbohydrate.

There are two reasons for reducing the amount of carbohydrate in the diabetic diet. First, experimentally it has been shown that high glucose diets which are given to animals who have had part of their pancreas removed make the diabetes worse. Second, unlike the normal person, the diabetic patient cannot increase and decrease his output of insulin according to his blood sugar level. Therefore, to counteract high carbohydrate intakes such large doses of insulin are needed that hypoglycemia is a constant threat.

The protein content of the diet is prescribed according to body weight, with approximately 1 or 2 Gm. of protein supplied for each 2.2 pounds of ideal body weight. The remaining calories are given in the form of fat. At the present time, because of the association of high animal fat diets with high cholesterol blood levels and arteriosclerosis, efforts are made to supply fats of vegetable rather than animal origin when possible.

In former days once the diet was calculated, foods were weighed carefully, but a simple system using standard household measures has largely replaced weighed diets. This system is known as the "exchange system." Foods are broken down into basic units as follows: milk, 1 cup; fat, 1 teaspoon; meat, 1 ounce; bread, 1 slice; fruit, 1 portion; vegetable A and B, 1 and $^1/_2$ cup respectively; and foods that need not be measured. All foods have been placed in these seven basic categories. The amounts have been predetermined, and any food in each category can be substituted for another food in that category by following the amounts given on food lists supplied by the American Diabetic Association and the American Dietetic Association. Experience has shown that patients often have difficulty in estimating ounces of meat, chicken, or fish, since these are the only foods that cannot be estimated with standard household measuring devices. Often the use of an inexpensive scale to weigh the meats after cooking is helpful in the early stages of treatment so that the patient gets a good idea of how much meat, chicken, or fish makes up the 4 or 6 (or however many) ounces of meat that have been ordered. By using the exchange program, the patient has a more varied diet and is able to pick out his prescribed menu even when he is eating away from home.

The diet is often divided so that feedings are given in the middle of the afternoon and at bedtime. Of course, these feedings can always be planned if that is the patient's preference. But they are essential for proper treatment in children and in patients who require a dose of insulin at night. All children should have a snack in the afternoon to avoid the great risk of hypoglycemia. In patients who require a dose of insulin at night and those patients who still use protamine zinc insulin (see section on insulin) as the only insulin, a bedtime feeding is necessary to prevent hypoglycemia during the night.

What about alcoholic beverages? Moderate drinking of straight liquor is not harmful and can be properly calculated into the diet. Liquor should be taken straight or with water or soda. There should be an absolute limit of from 2 to 3 ounces under any circumstances. The heavy consumption of alcoholic beverages is absolutely contraindicated. It is generally advisable to avoid beer. Remember that a hangover with an upset stomach in a nondiabetic person results in a day or two of misery, but in the diabetic patient it can lead to disaster with either diabetic acidosis or severe hypoglycemia.

Insulin

Insulin was discovered in 1921. The original pancreatic extract was called regular or crystalline insulin. This insulin was quick acting and lasted for a short period of time (eight hours) and had to be given prior to each meal. In the 1930's insulin was combined with a protein, protamine, and later with globin, another protein. Protamine zinc insulin was the first long-acting insulin available, but it acted slowly and failed to correct hyperglycemia which occurred after meals. Globin insulin was an intermediate insulin, but it did not quite last twenty-four hours. In 1949, NPH (neutral protamine Hagedorn) insulin (Iletin), a stable mixture of protamine zinc insulin and regular insulin, was introduced by H. C. Hagedorn, M.D. This insulin had prolonged action as did protamine zinc insulin, but, in addition, because of the regular insulin which was present, it frequently corrected the postprandial hyperglycemia (blood sugar elevation occurring after meals). In 1954 the lente insulins were developed. It was found that by a careful control of the acidity when insulin was combined with zinc, the action could be prolonged without adding protein. Semilente insulin, a quick-acting form resembling regular insulin, and ultralente insulin, a slow-acting derivative similar to protamine zinc insulin, were produced. Lente insulin is a mixture of the two and has an action similar to NPH insulin.

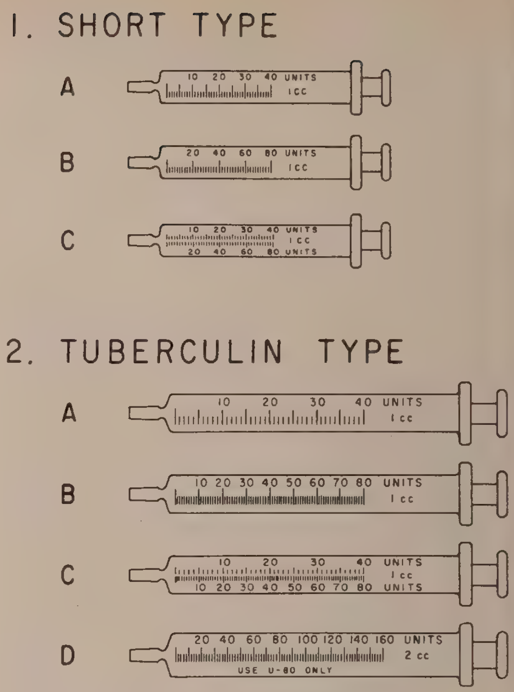


FIGURE 1. Insulin syringes.

For routine use, the most satisfactory insulins are NPH, lente, and globin insulin since they last approximately twenty-four hours but still have a fast-acting component to correct postprandial hyperglycemia. In the presence of diabetic acidosis or acute infection a more rapid-acting insulin is needed. In these instances the insulin of choice is regular or crystalline insulin. When a single dose of insulin produces insulin reactions before the fasting blood is controlled, a second smaller dose, usually of the same type of insulin, is given in the evening. This procedure is most frequently needed in juvenile diabetic patients or in adult patients whose diabetes is difficult to regulate. The use of the two doses allows control of the overnight blood sugar rise and reduces the risk of daytime insulin reactions. When the fasting blood sugar is reasonably normal but postprandial hyperglycemia is still a problem, a more rapid acting insulin such as regular or semilente is added. This is done by drawing up the short-acting insulin and then the long-acting insulin in the same syringe and giving them as a single injection.

All insulin comes in bottles containing 10 cc. and the strength of the insulin is expressed in units. A unit is the amount of crystalline insulin which produces a specific fall in the blood sugar in a laboratory animal. There are two strengths: U-40, in which there are 40 units of insulin per cubic centimeter, and U-80, 80 units per cubic centimeter. The latter is used when patients require more than 40 units of insulin per day. Insulin syringes are calibrated for U-40 or U-80 insulin. There is less chance for error if the syringe which has U-40 or U-80 markings only is used rather than a syringe with both. The syringes in Figure 1 illustrate those that are available. We prefer the long narrow tuberculin type special syringe, but if an automatic injector (a spring with a push button to plunge the syringe in) is used, the short type is the only one that will fit. If more than 80 units are needed, larger-size syringes are available.

The actual injections should be rotated from side to side using the arms, legs, and abdomen. The injections are given subcutaneously by pulling up the skin and

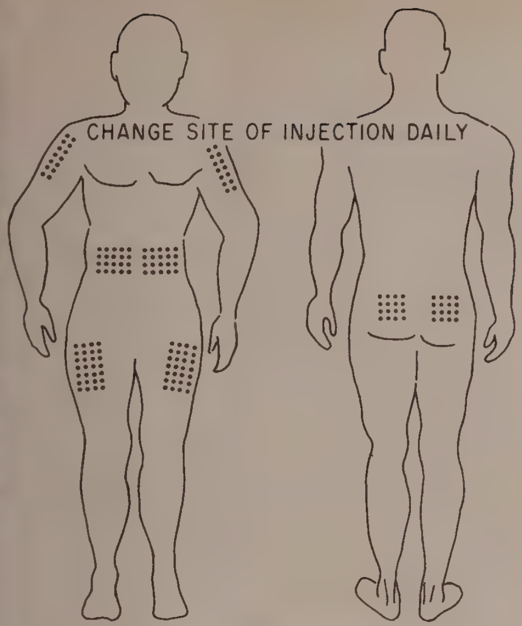


FIGURE 2. Sites of injection.

swiftly inserting the needle, pulling back on the plunger to see if any blood is aspirated, and then injecting the insulin. Practice makes this procedure simple and painless. The sites for injection are illustrated in Figure 2.

Since localized areas of tissue atrophy (loss of tissue) at sites of injection may be less common with insulin at room temperature, it is advisable to keep the bottle of insulin in current use at room temperature. Extra bottles of insulin should be refrigerated and should not be used beyond the expiration date. Needles are numbered according to the bore (diameter) of the needle; the higher the number, the smaller the bore. Usually number 25 and number 27 needles are used with a length of $^1/_2$ inch. The number 27 needle is especially useful when two doses of insulin daily are required. If there is trouble with leakage of insulin through the hole left from the injection, the needle should be inserted at a right angle to the skin and a longer needle used.

Oral hypoglycemic drugs

In 1942 a Frenchman named Janbon, while trying out new sulfa drugs for the treatment of typhoid fever, found a group known as sulfonylurea compounds which lowered the blood sugar in normal people. It was later found that they also lowered the blood sugar in some diabetic patients.

These sulfonylureas acted by stimulating the release of endogenous (the patient's own) insulin from the pancreas. They also had an effect on the liver. Unless the pancreas contained insulin, they were ineffective. As might be expected, they were of no value in juvenile diabetic patients, since these patients have no insulin in their pancreas. The sulfonylurea drugs are not forms of oral insulin. Insulin given orally is destroyed in the stomach.

The two sulfonylurea compounds available in this country are tolbutamide (Orinase) and chlorpropamide (Diabinese). Tolbutamide is available in 500-mg. tablets in bottles of 50. Since the drug is inactivated by the liver, it works over an eight-hour period and is best given in divided doses, usually before breakfast and supper. The usual range of dose is from 2 to 6 tablets daily. The occurrence of hypoglycemia is infrequent. A problem with tolbutamide or any of the oral drugs has been that after a period of time, they fail to work. In most cases this is caused by improper diet and failure to eliminate obesity. Sulfonylurea therapy has often led to better regulation than was possible with insulin in those patients who respond to the drug.

Chlorpropamide is available in two strengths: 100- and 250-mg. tablets in bottles of 100 and 60 respectively. Since this derivative is more slowly excreted than tolbutamide and is not inactivated by the liver, higher levels of the drug in the blood are possible. The usual dose range is from 100 to 500 mg., given as a single dose before breakfast. Since the drug tends to accumulate, it may have a profound blood sugar-lowering effect. If hypoglycemia develops, it is important to continue a high glucose intake over a several-day period, since the drug stays in the body for at least that length of time.

There is another oral hypoglycemic drug, phenformin hydrochloride (DBI), which is chemically unrelated to the sulfonylureas and acts in a different way. This drug lowers the blood sugar by changing certain enzymes (chemical regulators) to allow glucose to enter the tissues. Since phenformin only lowers the blood sugar and does not correct other disturbances in metabolism, insulin must be present either in exogenous (given by injection) or endogenous form.

Phenformin is supplied in 25-mg. tablets in bottles of 100 or in 50-mg. delayed-action capsules. Since the drug tends to cause gastric irritation at high dose levels, it is given in divided doses after meals. It usually is given after breakfast and supper, and the dose range is from 50 to 200 mg. per day. Although it can be used in adult diabetic patients who have endogenous insulin available, it is usually not as smooth in action as are the sulfonylurea drugs. It cannot be used alone in juvenile diabetic patients, but in this group it often is very helpful.

Phenformin in conjunction with insulin frequently leads to a more normal blood sugar and less glycosuria in children than was possible on insulin therapy alone. It also is occasionally useful in combination with sulfonylureas. One uncommon side-effect which may occur after several months of therapy is muscular weakness. The cause for the muscular weakness is not known, but reduction or stopping of the drug will eliminate this side-effect. Remember that these drugs are not interchangeable. One drug should never be substituted for another, and the dose should not be altered except on the advice of the patient's physician.

Exercise

Exercise lowers the blood sugar in all diabetic patients. The exact reason for this is not apparent, but at least in certain laboratory animals a substance of unknown nature is released from working muscle into the blood stream, causing the blood sugar to fall. No matter what the reason, in the diabetic patient regular daily exercise is helpful in maintaining a normal blood sugar.

Especially important is that exercise can lead to hypoglycemic reactions. On a given diet and a standard dose of insulin hard exercise can produce a far lower blood sugar than would be present ordinarily. When vigorous exercise is anticipated (for example, a tennis game) one or two meat sandwiches taken before the match, over and above the normal diet, should be administered. In addition, extra carbohydrate may be needed if the exercise is prolonged. Soft drinks serve very well for this purpose, since they are readily available sources of sugar. When two doses of insulin are used, the night dose of insulin can be reduced if there has been vigorous exercise during the day.

The effect of exercise in children is so profound that, as has been pointed out earlier, an afternoon feeding is essential. Children are often better managed with two doses of insulin than with one dose, since the second dose can be adjusted when needed. For some reason, we have observed that swimming has a more profound effect in children than other forms of exercise, and extra caution must be used in this event.

Complications

To pursue a way of life that demands adherence to a diet, the administration of insulin or oral agents, and other inconveniences when there may be absolutely no symptoms requires more than mere faith in one's physician. An understanding of the major problems in diabetes today is necessary. There are three major complications of diabetes: diabetic involvement of the eye, diabetic changes in the kidney, and diabetic abnormality of the nervous system.

The first of the complications is called diabetic retinopathy, and it affects the small blood vessels in the back of the eye (the retina). These vessels become weakened, and hemorrhages and exudates (debris from destroyed tissue) accumulate in the eye. Vision is frequently affected but not to a severe degree unless the hemorrhages are into the vitreous humor (the chamber of the eye). In New York State approximately 12 per cent of all causes of blindness are due to diabetes.

The second complication involves the kidney and is referred to as diabetic nephropathy. The damage is in the filtering system of the kidney, the glomerulus. Initially it causes no symptoms other than the appearance of albumin in the urine which is detected by special testing (the standard urine tests for sugar do not detect albumin). As the condition progresses, hypertension (high blood pressure), swelling of the body (edema), and progressive kidney failure (uremia) develop. This form of kidney damage is often associated with a superimposed kidney infection (pyelonephritis) which makes the kidney damage progress more rapidly. For this reason all urinary tract infections must be treated thoroughly in any patient with diabetes.

The third and last complication is diabetic neuropathy, a nonspecific degenerative process which can affect various portions of the nervous system. The neuropathy most commonly involves peripheral nerves and causes pain in the legs, especially at night, often associated with cramps. A loss of feeling is common with a "pins and needles" sensation, such as occurs when the hands and feet "fall asleep." The sympathetic (involuntary) nervous system is frequently involved, with gastrointestinal symptoms and bladder difficulties predominating. The main gastrointestinal symptom is diarrhea, especially at night, and the bladder symptom is an inability to urinate despite the presence of a large distended bladder (urinary retention). Other areas of the nervous system may also be involved and imitate a variety of other nervous system disorders which are not due to diabetes.

These diabetic complications are particularly serious since we have little understanding as to why they arise, and we have no satisfactory form of therapy once they develop. Diabetic neuropathy is an exception from the standpoint of treatment, since this condition frequently improves with careful diabetic regulation. Until our knowledge is better developed, we are left with prevention as our main goal of therapy.

Experience has shown that the best single way to prevent, or at least reduce, these complications is to control the diabetes carefully. It is not enough to obtain symptomatic regulation. Freedom from glycosuria, and as normal a blood sugar as possible must be achieved to constitute truly good control. The discovery of diabetes in its prediabetic or early diabetic state may result in a better record in preventing these complications.

Insulin reactions

When the blood sugar drops to low levels (hypoglycemia), characteristic symptoms develop. These symptoms are of two types: first, those symptoms due to the low blood sugar itself affecting the brain or nervous system (cerebral); and second, those symptoms due to a discharge of epinephrine by the adrenal gland in response to the low blood sugar in an effort to overcome it. The cerebral symptoms are: headache, usually on arising; mental confusion; blurred vision; unconsciousness (coma); and convulsions.

The adrenal symptoms usually are more prominent than the cerebral ones and come on more rapidly. These symptoms are: marked sweating, trembling, jitteriness, great hunger, rapid pulse, and pallor.

There is a special situation, usually occurring at night, when the blood sugar drops too low, triggering this adrenal response; since the patient is sleeping, the symptoms go unnoticed. The following morning a high blood sugar and marked glycosuria are found. It is important to be aware of the situation, since an increase in insulin would only tend to make it worse. Since the reason for the high blood sugar and heavy glycosuria is actually an insulin reaction which occurs during the night, it is necessary actually to reduce the insulin rather than to increase it. It is also important to emphasize that in children insulin reactions often occur abruptly and may be manifested principally by a sudden change in behavior. A sudden change in behavior accompanied by pallor in a child should always be treated first as an insulin reaction and questions should be asked later.

The treatment for an insulin reaction is simple—a rapid administration of glucose. A readily available source of glucose is orange juice. Table sugar and candies have to be converted to glucose in the body, resulting in a slight delay in raising the blood sugar. But the delay is negligible and fruit juice, candy, soft drinks, sugar lumps, and so forth are all satisfactory forms of therapy.

The standard treatment of an insulin reaction is one glass (8 oz.) of orange juice sweetened with from 1 to 2 tablespoons of table sugar. This can be repeated at from five- to ten-minute intervals until the patient's condition is back to normal. If the reaction is a severe one with unconsciousness, it is common for the patient to have no recollection of the episode.

What should be done in the unconscious patient who cannot swallow? If glucagon is available, it should be administered (see section on glucagon). Otherwise, it is best to take the patient to the nearest hospital emergency room where intravenous glucose is always available for administration. Your physician may give you special instructions to follow, but it is important to remember that no matter where you are, the emergency room at any hospital is prepared to treat a patient with a severe insulin reaction.

Glucagon

Glucagon is a hormone derived from certain cells in the pancreas which causes a profound discharge of glucose from the liver into the blood stream. It has recently become available for commercial use as a powder, containing 1 mg. of glucagon, together with fluid for dissolving it (diluent). The diluent is injected into the small vial containing the glucagon powder, causing it to dissolve. The solution is then drawn into a standard insulin syringe to the 1 cc. mark which would be the 40-unit mark in a U-40 syringe or 80-unit mark in a U-80 syringe. The fluid is injected in exactly the same way as insulin. Glucagon has its main use in the treatment of the patient who is unconscious owing to an insulin reaction. It can be given at home and usually awakens the patient in from five to ten minutes.

Since the effect is transitory, oral glucose must be given as soon as the patient is able to swallow. Any patient who has a history of severe reactions with unconsciousness or convulsions should have glucagon at home for use when needed. Glucagon should not be used if the patient is awake and able to swallow unless vomiting is present. The powder will not deteriorate, and a given vial is good for four years.

Diabetic acidosis

When carbohydrate cannot be utilized because of a relative or absolute lack of insulin, the body burns fat to supply calories for its needs. As more and more fat is burned, ketone bodies accumulate beyond the normal cellular ability to dispose of them. These ketones are organic acids, and as they pile up, the body acidity increases. In an effort to get rid of these acids, the respiratory rate increases with deep rapid respirations (Kussmaul breathing). If the situation goes on unchecked, coma develops, and then death.

The common denominator is a lack of insulin. This lack may be due to failure to take insulin or a severe infection which greatly increases the need for insulin. Often, when there is nausea or vomiting, as with a gastroenteritis, the patient omits his insulin because he has no desire for food and thinks he will not need the insulin if he does not eat. This is a serious mistake, since an ordinary gastroenteritis also increases the need for insulin, and the omission of a dose hastens the development of diabetic acidosis.

Unlike an insulin reaction which comes on rapidly, diabetic ketosis develops more slowly over a period of hours (from six to twelve hours). The initial symptoms are usually nausea, vomiting, deep rapid breathing, and drowsiness. The mouth and skin become very dry, and without appropriate treatment the situation can become critical rapidly. Since ketone bodies must accumulate for the condition to develop, if they can be detected at an early stage, the patient can recognize that he is getting into difficulty and prevent the condition from progressing. There is a simple urine test for ketones called the "Acetest." This test consists of a small white tablet which turns a purple color in thirty seconds when a drop of urine containing ketones is placed on it. Ketone bodies may be present when the dietary intake has been poor or after a severe insulin reaction, but a strongly positive test result for acetone combined with the patient's illness are warning signals of diabetic acidosis. The combination of nausea and vomiting and strongly positive ketone test results demands immediate attention. The patient's physician should be contacted promptly, and the dose of insulin should not be omitted. While the patient is at home, the urine can be checked every two hours, and additional doses of from 20 to 30 units of

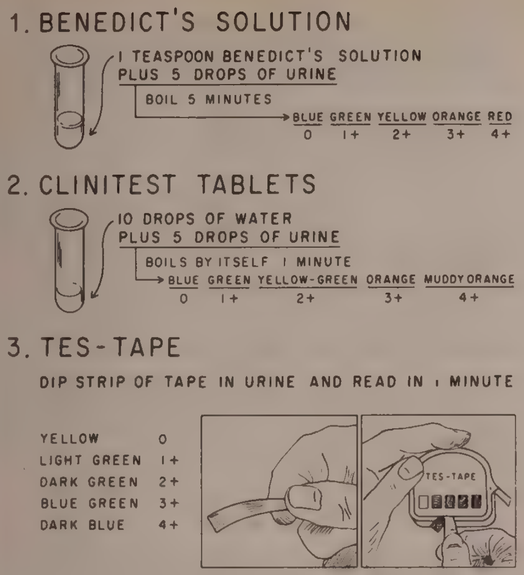


FIGURE 3. Urine testing.

regular insulin can be administered until the acetone clears. Clear broth and ginger ale are often the only nourishment which can be tolerated when there is nausea or vomiting. Above all, insulin should not be stopped, and there should be no delay in contacting the physician in charge. If you are in a strange city, remember again that the emergency room of any general hospital is prepared to handle diabetic acidosis.

Urine testing

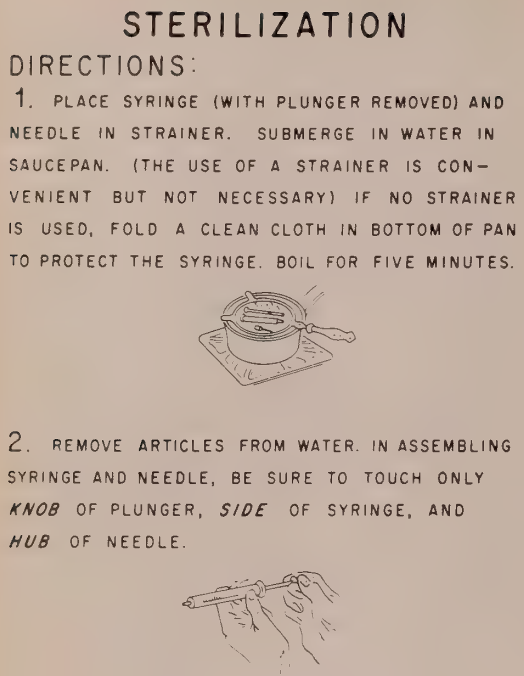
Urine testing for glucose is a useful guide in achieving diabetic regulation. In the severely diabetic patient the urine should be tested before each meal and at bedtime. A heavy spill of glucose should call for an additional test for acetone. In the mildly diabetic patient one test per day taken two hours after the heaviest meal, either lunch or supper, is sufficient. In the in-between group individual programs can be worked out, but one that is often satisfactory is a daily fasting urine test together with a full day of four tests once weekly. The results of these tests should be recorded, and on the same record any insulin reactions should be noted. This chart should be taken with the patient when he consults his physician.

There are three commonly used tests for sugar in the urine: Benedict's solution, reagent tablets (Clinitest), and urine sugar analysis paper (Tes-tape). The Benedict's and reagent tablet methods measure all reducing substances and are not specific for glucose. Urine sugar analysis paper measures only glucose and is preferred if the patient has delivered a baby and plans to breast feed, since sugar excreted by the lactating (nursing) mother or pregnant woman will cause a positive Benedict's or reagent tablet test result, but gives a negative test result with urine sugar analysis paper. For routine use we prefer the reagent tablet or urine sugar analysis paper test method, since they are convenient and reasonably accurate. The methods are illustrated in Figure 3. Bottles of reagent tablets must be kept tightly stoppered to prevent deterioration, and they must be kept out of easy reach of children, since accidental swallowing can result in severe burns or perforation of the esophagus (food tube).

Syringes and needles

The proper care of insulin syringes and needles will simplify therapy, help to avoid insulin reactions, and prolong the useful life of the equipment. We recommend keeping the syringe and needle in a metal container with a cover. Cotton is laid on the bottom, with the syringe and needle resting on the cotton. The cotton is saturated with rubbing alcohol, and enough alcohol is used to cover the syringe and needle. When ready for use, the syringe is plunged back and forth several times to get rid of the excess alcohol. It is then ready for use. Once weekly the metal container, syringe, and needle should be boiled for from five to ten minutes and the alcohol should be changed. When the needle becomes dull, it is best to replace it, although some clever patients have been able to resharpen the point. If the syringe becomes caked on the inside with debris from hard water deposits, soaking for several hours in vinegar will often redissolve the deposits. Some patients still prefer to boil their syringe daily. This can be accomplished by placing a strainer over a pot with boiling water. The syringe and needle are left in the strainer which is lifted out after five minutes of boiling (Fig. 4).

A plastic disposable syringe with an at-



STERILIZATION

DIRECTIONS:

1. PLACE SYRINGE (WITH PLUNGER REMOVED) AND NEEDLE IN STRAINER. SUBMERGE IN WATER IN SAUCEPAN. (THE USE OF A STRAINER IS CONVENIENT BUT NOT NECESSARY) IF NO STRAINER IS USED, FOLD A CLEAN CLOTH IN BOTTOM OF PAN TO PROTECT THE SYRINGE. BOIL FOR FIVE MINUTES.

2. REMOVE ARTICLES FROM WATER. IN ASSEMBLING SYRINGE AND NEEDLE, BE SURE TO TOUCH ONLY *KNOB* OF PLUNGER, *SIDE* OF SYRINGE, AND *HUB* OF NEEDLE.

FIGURE 4. Sterilization.

tached needle is now available. This is completely sterile and comes wrapped in a sterile plastic bag. The syringe is used once and is then discarded. These are convenient for trips, and it is hoped that eventually the price may become low enough to allow regular use of new ones every day.

Foot care

The diabetic patient faces a unique problem after many years of diabetes. Because of neuropathy, he has a decreased sensation in his feet and may not be able to feel heat and cold or small objects in his shoes. The lack of sensation, coupled with a susceptibility to infection, can convert a casual injury to the feet into a serious infection which may progress to gangrene (dead tissue). The gangrene usually leads to the loss of a toe, the foot, or even the entire leg. Careful foot care can almost always prevent this train of events from developing. Proper foot care entails the following:

1. Wash feet daily in warm soapy water (never hot) and dry carefully. Athlete's foot, corns, and calluses should be treated appropriately by your doctor or podiatrist, not yourself.

2. Cut nails carefully with a sharp, special toenail clipper. Cut straight across and do not dig into the corners. If the nails become very thickened, they should be ground by a podiatrist.

3. Never walk barefoot.

4. Carefully break in any new shoes. If you are in hazardous work, wear safety shoes. Do not wear tight shoes.

5. Look at your feet each day. Use a mirror if necessary. If the vision is poor, have someone else look at your feet. Remember that you may not feel a sore or an infected area. Usually it is easier to see an infected area than to feel it.

Identification tags

All diabetic patients should carry some form of identification, stating their name, address, phone number, medication program, responsible relative, and physician. This is of great value in the event of an insulin reaction or an accident which renders the patient unconscious. The usual identification form is a wallet card which is readily available and is generally satisfactory. For women and children other forms of identification are preferable. An identification bracelet or necklace is more suitable, since women and children are not likely to have wallets. At the present time the Medic Alert Foundation in Turlock, California, makes such bracelets and necklaces available for $5, together with registering all the pertinent clinical data on the individual patient. Their records are available twenty-four hours a day by a collect call from anywhere in the country. The bracelet or necklace is made of stainless steel or sterling silver and has a red emblem with the words "Medic Alert" on the medallion. On the back of the medallion the disorder and treatment program are engraved permanently. Similar medallions are now available in many drug stores and through local health associations.

Physician relationship

Your physician is your lifelong guide to the proper management of your disease. He is available to you at all times. If you have a question, call him. He would rather be called at supper time than be called out for an insulin-reaction case after he has gone to bed. See him regularly. There is no such thing as self-care. If you are doing very well, so much the better, but regular supervision of your program is essential.

Be honest with your doctor. If you have been off your diet, be frank. We are all aware of what is ideal and strive for it, but to err is human. If you do not feel at ease with your physician, discuss this fact with him. It is better to appraise him of your feelings than to make a switch to another physician with whom the same problem is likely to develop. The desire for consultation or visits to remote medical centers may crop up from time to time. Make the arrangements through your own doctor. He can best arrange for consultation, and his feelings will not be offended by a request from you for an opinion from someone else. When your own physician makes the arrangements, you will benefit since the recommendations of either the consulting physician or the distant medical center will be returned to him. Choose a physician who is well versed in diabetes and stay with him. Remember, he is trying to help you and by treating him with consideration, you will ensure that he will do the same for you.

ANNUAL CONVENTION: Medical Society of the State of New York
Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963,* and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Recent Advances in the Physiology of Acquired Heart Disease

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ACQUIRED HEART DISEASE is a very broad subject in which tremendous strides have occurred in recent years. Much of our knowledge during this period has been derived from the development of new concepts of diseases and treatment combined with the application of the latest technics. It has been necessary to train personnel to use new modalities first in the laboratory, followed by the more important clinical application. Examples of the employment of these advances in applied physiology would seem to be the most valuable manner in which to cover the subject briefly.

The era of closed-heart surgery ended with the successful clinical application of the heart-lung machine. By the addition of a heat exchanger to the circuit the patient's temperature is under fingertip control. Hypothermia provides prolonged safe periods of working time with a dry field for difficult intracardiac surgical procedures. Low oxygen demands by the vital centers at temperatures of from 5 to 10 C. result in a considerable reduction in the required extracorporeal flow rate. Less damage occurs to the blood elements. The advances in the knowledge of hematology and body chemistry have vastly improved postoperative care and contributed to the improved results of open-heart surgery. The progress mentioned has been accompanied by the development of new clinical products, equipment, instruments, and technics. These are used daily by the appropriate members of the cardiac team.

The most important aspect of these advances in knowledge can be reviewed by considering (1) coronary artery disease, (2) valvular heart disease, and (3) congestive heart failure.

Coronary artery disease

Coronary heart disease remains the nation's number one medical problem and the nation's number one killer. Approximately half a million persons die annually of this disease alone. This disease is the twentieth century plague. The etiologic background is apparently as baffling to our generation as the black death of medieval times was to the physicians of that era. However, the physiologic effects of this disease are mechanical before they become electrical, and therefore a mechanistic approach to the problem would seem logical.

The segmental distribution of the atheroma is apparent readily to the pathologist studying the pattern of the process. The disease characteristically involves the epicardial portion of the coronary arteries early in its course, while toward the end stages the diffuse small intramural arteries also contain atheromas. The early, partially occluding lesion producing angina pectoris is potentially lethal. By one of several basic pathologic processes it suddenly may become completely occlusive, producing a disproportion of oxygenation between adjacent areas of the myocardium. Such a state leads to ventricular fibrillation and death.

By the proper selection and study certain of these lesions now can be successfully

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removed surgically. The unobese patient of less than fifty years of age with angina and electrocardiographic evidence of coronary artery disease should be considered for coronary arteriography. With the present radiographic apparatus, high-density contrast media, and catheter technics one is rather consistently capable of demonstrating the intraluminal coronary arterial tree. The visualization of the lesions by cinearteriography is the single most important finding in cases selected for coronary endarterectomy.

This diagnostic study is so important that each case considered for any type of coronary surgery should have a coronary arteriogram done. The questionable case of coronary artery disease certainly should warrant this investigation before being branded with such a serious diagnosis. Several patients who had undergone some type of coronary operation elsewhere without relief were found to have a normal coronary bed. In a few instances psychiatric care was indicated.

MUCH PROGRESS *has recently been made in understanding the physiology of acquired heart disease and in the development of diagnostic and treatment technics. In coronary artery disease the development of coronary arteriography has enabled surgical removal of the lesions in certain cases. In acquired valvular disease many of the advances are the result of the adoption of open-heart technics and the application of advanced patho-anatomic knowledge in such operations as mitral commissurotomy. In patients with congestive heart failure ultrafiltration renal dialysis offers a means of treating intractable heart failure and decompensation when there is an excess of fluid.*

Acquired valvular disease

Recent significant advances have occurred with the growing abandonment of closed methods of treatment and the adoption of open-heart technics. The wider acceptance of cardiac surgery within the profession naturally has led to operations performed earlier with improved results from the physiologic standpoint. Effective operations with acceptable mortality rates are performed daily for stenotic or regurgitant lesions of the heart valves. Clinical laboratory technics have reached a high state of perfection in the diagnosis and physiologic study of these patients. The results of surgery are subject not merely to an opinion but also to physiologic confirmation.

Important improvement in physiologic results has been achieved by the application of basic anatomic and pathologic concepts. For example, it is general knowledge that a congenital aortic bicuspid valve will give an aortic systolic murmur without a physiologic impediment to the forward flow of blood. In certain cases of aortic regurgitation it is now possible to convert the diseased tricuspid valve to a bicuspid one with the restoration of the cardiovascular dynamics to an essentially normal state. To keep the operative risk low these subjects should be operated on before all of the natural compensatory mechanisms have passed their limits and the patient is in congestive heart failure.

The present operation for mitral stenosis is an excellent example of the physiologic application of advanced patho-anatomic knowledge. The shape of the valve is now generally appreciated as being truncated with a large septal leaflet and a small mural leaflet. The rheumatic process converts the valve to a cone-shaped fishmouth with a calcium deposition occurring in a small percentage of cases. If the commissurotomy is limited to the anatomic boundaries, a physiologic obstruction may remain because the incision has not been extended into flexible valve tissue. However, such results are no longer justified. Under direct vision the clot and calcium can be removed effectively, while reformation with embolization can be avoided postoperatively by the administration of heparin and/or fibrinolysin. More important, the septal leaflet is incised along its commissures with the extension of the incision well back into flexible (essentially uninvolved) valve tissue and along the line of subvalvular supporting structures. With the restoration of competent valve mobility, diastolic pressures on either side of the mitral valve are restored to normal values routinely.

Congestive heart failure: relief by ultrafiltration renal dialysis

Patients suffering from hypertensive, rheumatic, or arteriosclerotic heart disease commonly die in intractable congestive heart failure. A clinical defeatist attitude is frequent in these cases. With the development of technics capable of supporting the circulation while a definitive operation is performed, a means by which competency of the cardiovascular-renal mechanism can be restored becomes of paramount importance. If normal dynamics can be restored, a physiologic investigation may be performed safely, and corrective surgery may salvage such individuals. In dealing with these very sick patients usual small risks become large ones, although the hazards of artificial renal dialysis are low.

In the event that the patient has a nonsurgical condition producing intractable heart failure, we are now able to perform long-term venous-arterial cannulations for weekly or biweekly ultrafiltration renal dialysis. While not in use, the cannulae are connected to each other so that a small arterial venous shunt exists. This small shunt is of no physiologic importance.

The employment of the artificial kidney requires a trained team and excellent laboratory facilities and is time-consuming and expensive. Obviously only those subjects who have reached the limits of medical therapy should be considered for ultrafiltration dialysis. The patient who grows progressively less responsive to vigorous diuretic therapy with a weight gain, falling urinary output, and physical findings of congestive heart failure should be considered a potential candidate for dialysis. An elevated blood urea nitrogen is not considered a necessary requisite.

Once the patient is "on the kidney," several mechanisms are used simultaneously to eliminate the excess fluid. First, the filtration bath may be made hypertonic by adding extra glucose or invert sugars. Recently I have found low-molecular weight dextran to be more effective for this purpose. Second, the filtration pressure in the semipermeable membrane-type kidney coil can be elevated safely by a partially occluding clamp on the inflow line to the patient. Last, the kidney coil flow may be increased by the variable finger-type pump in the circuit which in turn elevates the lateral pressure within the coil, thereby further ultrafiltrating the blood.

In addition to removing several pounds of water from a patient during a period of dialysis, the plasma electrolytes are restored to normal values, and dialyzable waste products are eliminated.

The most dramatic result from the procedure occurs over the following four or five days. During this period the patient receives supplementary sodium chloride and potassium chloride by mouth while the daily diuretic medication is administered. Careful electrolyte control is essential. Within seven days the patient has returned to his dry weight. Occasionally a second dialysis may be indicated to "dry out" the subject completely. If there is a suspected surgically correctable lesion, a proper investigation may be carried out.

We have found this to be a reliable, safe, and effective method of treating intractable plus decompensation heart failure, that is, where there is an excess of fluid.

Summary

A very brief review of some of the recent important physiologic advances in acquired heart disease has been presented. Emphasis has been placed on the clinical application of these advances in the treatment of coronary arterial disease, valvular lesions, and congestive heart failure.

1500 Vine Street, Philadelphia 2

Phenothiazine Subgroups

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THE PHENOTHIAZINE *derivatives vary greatly, and are commonly grouped according to the side chain found at the number 10 position into the aliphatic, piperidine, and piperazine categories. They may also be categorized according to substitutions at the number 2 position of the hydrogen, chloride, fluoride, sulfur, oxygen, and carbon molecules. The more potent derivatives have a greater incidence of extrapyramidal symptoms and are longer lasting. Those which do not incorporate the piperazine ring cause prolonged sleeping time when used with barbiturates. The analgesic effects of the phenothiazines fall into three categories: analgesic, slightly antianalgesic, and definitely antianalgesic. The choice of derivative should be based on the specific purpose and desired duration of action, and the dosage should be individualized according to the age, sex, and physical status.*

THE PHENOTHIAZINE DERIVATIVES represent the largest group of tranquilizers in use today.[1] There are almost twenty of these derivatives on the market now, and new ones are regularly being offered to the public. While some never quite manage to justify their existence and pass out of the picture almost as quickly as they enter it, there is a never-ending search for newer ones with fewer undesirable side-effects.

Not all tranquilizers are phenothiazines. But what many physicians fail to realize is that the phenothiazines themselves vary greatly from one derivative to another and require different dose schedules. Aside from their tranquilizing capacities, certain desirable and undesirable side-effects are more pronounced in some of these drugs than in others. It is just as important to know the correct dosage for a specific purpose as it is to choose the proper phenothiazine for your patient. The dosage generally prescribed is usually that recommended for psychiatric treatment.[2] The use of the same drug for some other properties, such as its antiemetic value or its additive effect to sedatives, would, of course, require smaller doses.

New subgroup method

Commonly the phenothiazines are subgrouped according to the side chain found at the number 10 position or "tail."[3] These subgroups fall into the (1) aliphatic, (2) piperidine, and (3) piperazine categories. Figure 1 illustrates a new way to subgroup the phenothiazines. Its purpose is to acquaint the user of a contemplated drug with its potency and characteristics in relation to other phenothiazines with which the physician may be more familiar. This helps formulate the dosage and forewarns of possible complications with the newer derivatives. The inclusion or absence of the piperazine molecule in the number 10 side chain is also commented on.

The phenothiazine nucleus is illustrated at the top of the chart. Note that the substitutions occur only at the numbers 2 and 10 positions. The subgrouping in this chart is based only on substitutions occurring at the number 2 position instead of the more generally employed method of categorizing them according to the changes at the number 10 position.

In addition to the hydrogen, chloride, fluoride, and sulfur molecules described

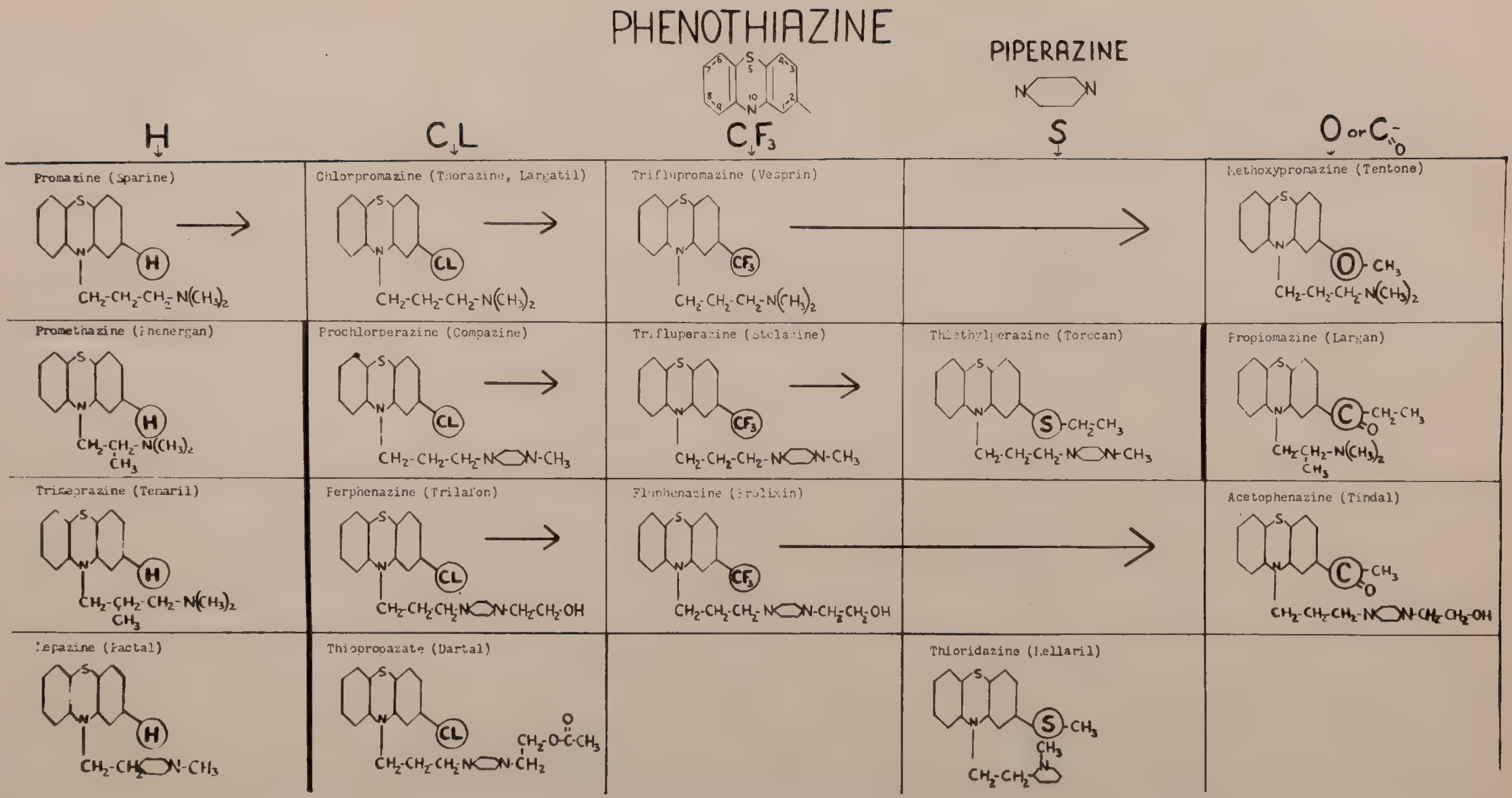
PHENOTHIAZINE
PIPERAZINE
H
CL
CF3
S
O or C=O
Promazine (Sparine)
Chlorpromazine (Thorazine, Largatil)
Triflupromazine (Vesprin)
Methoxypromazine (Tentone)
Promethazine (Phenergan)
Prochlorperazine (Compazine)
Trifluperazine (Stelazine)
Thiethylperazine (Torecan)
Propiomazine (Largan)
Trimeprazine (Temaril)
Perphenazine (Trilafon)
Fluphenazine (Prolixin)
Acetophenazine (Tindal)
Mepazine (Pactal)
Thiopropazate (Dartal)
Thioridazine (Mellaril)

FIGURE 1. New way to subgroup phenothiazines, showing potency and characteristics of contemplated drug in relation to other phenothiazines.

here, newer derivatives have appeared with an oxygen or carbon molecule at the number 2 position. Examples of these are methoxypromazine maleate and levomepromazine (Nozinan), as well as propiomazine hydrochloride and acetophenazine.

You will notice that wherever arrows point from one column to the next, the drugs are identical except for changes in the number 2 position. The top line of the chart illustrates that promazine, chlorpromazine, and triflupromazine have the identical side chain at the number 10 position; yet, with single changes occurring at the number 2 position, triflupromazine is twice as potent as chlorpromazine and four times as powerful as promazine[2]; and thus, the greater the halogenation of the derivative, the greater is its potency. But as halogenation increases, so does the possibility of extrapyramidal symptoms. It naturally follows that a smaller dose is required with the more powerful drugs.

Interpretation

A sulfur molecule in the form of a thiomethyl group at the number 2 position radically changes many properties of the phenothiazines. Thioridazine has little, if any, effect on the autonomic nervous system or temperature-regulating system. It also has practically no antiemetic effect and causes almost no extrapyramidal side-effects. It cannot be given parenterally, and therefore its usage is restricted to cooperative patients.[4]

When the piperazine nucleus, also shown at the top of the chart, is included in the number 10 side chain, potency is also greatly increased. For instance, prochlorperazine with the piperazine nucleus is many times as potent as chlorpromazine hydrochloride, while both have a chloride in the number 2 position. Less hypotension and tachycardia is associated with any phenothiazine derivative when the piperazine nucleus is included in the number 10 side chain. Needless to say, many of the newer phenothiazines incorporate this piperazine ring, although extrapyramidal effects are more common when this nucleus is included.[5] Chlorpromazine, one of the original phenothiazines, does not include it and is noted for the hypotension and tachycardia associated with its usage.[6,7]

Various other potential benefits and complications of the phenothiazine derivatives can also be better understood if this chart is followed.

Greater potency goes hand in hand with a greater incidence of extrapyramidal symptoms. Increased halogenation and the piperazine nucleus will cause greater potency; and the newer drugs such as trifluperazine and fluphenazine include both of these.

The more potent drugs are longer lasting and generally need to be administered no more than once a day. The less potent drugs (with the "H" at the number 2 position) will require more frequent dosage. Should extrapyramidal symptoms occur and be severe despite minimal dosage, diphenhydramine hydrochloride (Benadryl hydrochloride) can be given parenterally to alleviate these symptoms.[8] For mild reactions, antiparkinson agents can be given concurrently with the phenothiazines.

Generally those phenothiazines which do not incorporate the piperazine ring will cause prolonged sleeping time when used with barbiturates. This must be taken into consideration when the physician is deciding whether he wants the patient well sedated or alert.

The analgesic effects of the phenothiazines may be divided into three basic categories. Trimeprazine, chlorpromazine, promazine, and methotrimeprazine have some analgesic action. Perphenazine, trifluperazine, triflupromazine, and prochlorperazine show slight antianalgesic effects, while promethazine hydrochloride and pecazine have definite antianalgesic activity.[9,10]

Comment

Not all the indications for use or the complications which may arise from their use have been discussed here; but a careful perusal of the chart will help in choosing the specific phenothiazine for the specific purpose and desired duration of action. The parenteral dose should always be less than the oral dose. The oral route is the method of choice when possible, and amounts should be increased only if needed. The physician must realize that the dosage should be highly individualized according to age, sex, and physical status.

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Bronchoscopy in Treatment of Chronic Bronchitis, Asthma, and Emphysema

IN CHRONIC BRONCHITIS *bronchoscopy enables the following: removal of obstructing secretion at periodic intervals which permits adequate oxygenation and restores ventilatory function; visualization of underlying pathologic changes in the bronchial tract; exploration of the secondary bronchial orifices and removal of any plugging from inspissated mucus or granulation tissue; accurate bacteriologic examination, culture-sensitivity studies, and the making of autogenous vaccines; and direct instillation of antimicrobial and bronchodilating drugs into the bronchial tract. In bronchial asthma bronchoscopy enables diagnosis of bronchial obstruction and aspiration of the obstructive secretion. In chronic obstructive emphysema bronchoscopic aspiration of retained secretion, dilatation of stenosed areas, and direct instillation of decongestive and antimicrobial medication for the control of infection are important adjuncts in treatment.*

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IN THE RAPID progress of medical science during the past decade, bronchoscopy has come to play an important role in the diagnosis and treatment of pulmonary disease. As Chevalier Jackson, my former teacher of bronchoscopy, has said, "Look and see is the order of the day. In every accessible region of the body, the aid of direct vision is called upon to contribute to diagnosis and treatment."*

In the diagnosis of thoracic diseases, the internist, by means of external inspection, percussion, and auscultation, usually obtains sufficient information to establish a tentative diagnosis. His findings may be further corroborated by the roentgenologist, who, by means of fluoroscopy and radiologic examination, has an opportunity to look through the chest. But it remains for the bronchoscopist, employing direct visual inspection, to look inside the bronchial tree and observe the underlying pathologic condition. When there is a close association between the internist, the roentgenologist, and bronchoscopist, the diagnosis and treatment of bronchial pulmonary conditions is, of course, greatly facilitated.

Chronic bronchitis

Chronic bronchitis, often referred to as the "English disease" because of its high incidence in Great Britain, is one of the most common of all bronchial disorders. Due to man's increasing life span and possibly to his greater opportunity to inhale potentially noxious material such as smoke and industrial gases, there is a marked upswing in the incidence of chronic bronchitis. Unquestionably, the increase in cigaret smoking, with inhalation of toxic volatile tar products and the constant, daily inhalation of carbon particles from car exhausts are important causes of this condition.

Presented at the 155th Annual Meeting of the Medical Society of the State of New York, Rochester, New York, Section on Chest Diseases, May 9, 1961.

* Jackson, C., and Jackson, C. L.: Bronchoscopy, Esophagoscopy and Gastroscopy, Philadelphia, W. B. Saunders Co., 1934, p. 17.

The bronchoscopic findings in chronic bronchitis usually reveal a marked inflammatory change in the tracheal bronchial mucosa, with heavy retention of obstructing purulent secretion. The mucosa is markedly congested and may show evidence of ulceration, which may explain why hemoptysis during episodes of coughing is a common symptom. It is difficult to dislodge the heavy secretion by coughing, possibly because of defective ciliary drainage and weakened diaphragmatic action. If bronchial obstruction with infection is allowed to continue, bronchial stenosis and bronchiectasis may soon follow. The bronchoscopic removal of obstructing secretion at periodic intervals will permit adequate oxygenation and restore ventilatory function. This, in conjunction with measures to control infection, may prevent serious complications and restore the patient to comfortable health.

Aside from the removal of the obstructing bronchial secretion, the bronchoscopist by direct visual inspection can note the underlying pathologic changes in the bronchial tract within the field of endoscopic vision. If there is tumor-like tissue, he will be able to take a biopsy specimen. Moreover, he can explore the secondary bronchial orifices and remove any plugging from inspissated mucus or granulation tissue. Also, since the bronchoscopically aspirated secretion is free from oral contamination, a more accurate bacteriologic examination can be done; and it can be used for a culture-sensitivity study and for the making of autogenous vaccines. Bronchoscopy also makes possible direct instillation of antimicrobial and bronchodilating drugs into the bronchial tract. By means of intrabronchial lavage with normal saline, cytologic study of exfoliated cells for the detection of early carcinoma can be carried out.

Bronchial asthma

No chapter on bronchial asthma should ever be written unless it be prefaced by the quotation from the late Dr. Jackson, "All that wheezes is not asthma." If possible, every patient with bronchial asthma, particularly if adult, should undergo a diagnostic bronchoscopy. Time and again, bronchoscopic examination of patients undergoing treatment for this condition has revealed that the underlying cause of bronchial wheezing and dyspnea was tracheal or intrabronchial disease, in the form of neoplasm, bronchial strictures, localized bilateral atelectasis, rupture of tracheal and hilar tuberculous glands, various forms of bronchitis, nonopaque foreign bodies, laryngeal papillomata, and pressure on the trachea and bronchi from extrinsic causes.

It has been stated that in the United States bronchial asthma affects 2 per cent of the population and that approximately half of the cases are of the extrinsic type; that is, they result from allergy to external antigens from foods, all kinds of dust, pollens, molds, drugs, and so forth. Cases in which no evidence of hypersensitivity to specific antigens can be found are classified as intrinsic and result from infections of the respiratory tract. It has been my experience that practically every case of chronic asthma, including those which at first were considered allergic in type, showed evidence of organic structural changes in the bronchial tract due to superimposed infection. In a number of patients undergoing allergenic therapy, the endoscopic examination revealed a bronchial obstruction due to a swollen bronchial mucosa to which a viscid glairy secretion adhered. In a number of these patients emergency bronchoscopy, with removal of the obstructing secretion, immediately resulted in a symptomatic relief of their dyspneic condition. In several patients emergency bronchoscopy proved to be a life-saving measure.

The endoscopic findings in chronic bronchial asthma are mainly those of bronchial obstruction. The mucosa is usually congested, swollen, and edematous, more markedly so in the lower portions of the bronchial tract, where gravity further complicates the coughing-up of the glairy mucinous secretion. As a rule, bronchospasm is seldom seen in the major bronchi; it is largely confined to the peripheral, noncartilaginous bronchi. It is apparent that if the bronchial obstruction is not removed, obstructive irreversible emphysema may soon be established. The continuing superimposed bronchial infection further increases the bronchial obstruction. If the process continues,

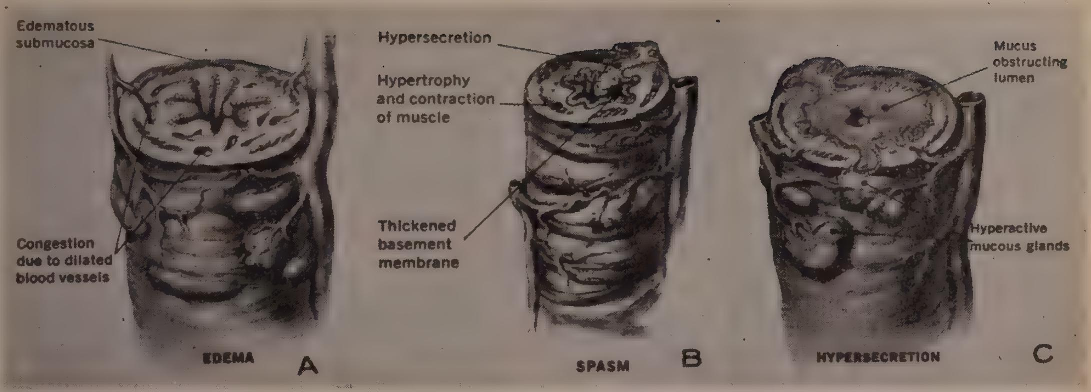
Edematous submucosa
Congestion due to dilated blood vessels
EDEMA
A
Hypersecretion
Hypertrophy and contraction of muscle
Thickened basement membrane
SPASM
B
Mucus obstructing lumen
Hyperactive mucous glands
HYPERSECRETION
C

FIGURE 1. Bronchial factors involved in pathogenesis of chronic obstructive emphysema. (A) Edema. (B) Spasm. (C) Hypersecretion. (Courtesy Winthrop Laboratories, New York City.)

serious bronchial changes will rapidly develop which may lead to severe pulmonary damage from which the patient will not recover.

The great difficulty in patients suffering from bronchial asthma is their inability to clear out the obstructing viscid sputum in spite of violent coughing. The diaphragm, depressed as a result of the obstructive emphysema, no longer has the forceful, piston-like action to expel the tenacious secretion. At this point the bronchoscopist can play a major role by aspirating the obstructive secretion, thus bringing about an immediate relief of the dyspneic condition.

Chronic obstructive emphysema

The treatment of advanced chronic obstructive emphysema, with symptoms of respiratory acidosis due to prolonged carbon dioxide retention, makes up one of the gloomy chapters in medical treatment. Although the exact cause of emphysema is not known, there is substantial evidence to show that bronchial infection and subsequent obstruction play a major role in its development. As the bronchial infection and obstruction increases and continues, pulmonary ventilation is greatly hampered. Then, too, some patients with obstructive emphysema have a spasmodic type of unproductive cough which raises the intra-alveolar pressure as air is forced against a closed glottis. As this process is repeated countless times, the elasticity of the alveoli becomes diminished, and the emphysematous process is hastened (Fig. 1).

It is not within the scope of this paper to discuss the various types of chronic emphysema, particularly those caused by pneumoconiosis, with direct structural changes in the alveoli and associated with diffuse pulmonary fibrosis. The emphysema which is of therapeutic importance to the bronchoscopist is the so-called "obstructive" form which is characteristically associated with some underlying bronchial infection. As has been previously stated, the genesis of chronic obstructive emphysema is still not completely clear. However, it is definitely known that its development is favored by circumstances which allow greater interference with expiration then with inspiration. This mechanism of bronchial obstruction with trapping of air in the distal portion of the bronchial tract is often referred to as an expiratory check-valve obstruction. The normal movements of the bronchi are as follows: During the phase of inspiration, with the descent of the diaphragm the bronchi elongate and widen; during expiration, with the ascent of the diaphragm the bronchi become shortened and narrowed. From this it is clear that if there is any bronchial obstruction due to swollen mucosa and retained secretion, the bronchial occlusion will be greatest during the phase of expiration.

It is evident that any form of treatment for the prevention of chronic obstructive emphysema must be directed to the relief of the bronchial obstruction. The bronchoscopic aspiration of the retained secretion, dilatation of stenosed areas, and the direct instillation of decongestive and antimicrobial medication for the control of infection are important adjuncts in treatment. In some patients with severe dyspnea and hypoxia who may not tolerate a bronchoscopic procedure, I have used bedside catheter suctioning. A number 16 or 18 catheter is passed into the larynx, trachea, and bronchi by the intranasal route. This is a very simple procedure. If necessary, the catheter may be reintroduced several times daily. Tracheostomy is another procedure which in the past two years has met with some success. The opening in the trachea makes possible the constant catheter suctioning of tracheal and bronchial secretions and opens an avenue for the administration of detergent agents, nebulized bronchodilating drugs, antimicrobial drugs, and oxygen therapy.

The procedures described should be used early in treatment in conjunction with other required therapy before there is a marked impairment of pulmonary ventilation due to destruction of alveolar septa. Somewhere along the pathway in the development of chronic obstructive emphysema, procedures developed to facilitate bronchial drainage, if used early, will prevent the serious complications and sequelae of bronchial obstruction.

Summary

In this brief review of the role of bronchoscopy in recent advances in the treatment of chronic bronchitis, asthma, and emphysema, I have attempted to emphasize the following:

1. Bronchoscopy has come to play an important role in the diagnosis and treatment of bronchopulmonary diseases.
2. Close cooperation between the internist, allergist, radiologist, and bronchoscopist, will in many instances facilitate the diagnosis and prove of invaluable aid in the treatment of bronchopulmonary disease.
3. Bronchoscopy, since it can remove obstructing secretion, is an indispensable aid in the prevention of serious pulmonary complications.

Stomach Freezing Successful In 86 Ulcer Patients

Stomach freezing as a method of treating duodenal ulcers has now been used successfully in 86 patients, according to an article in the September 1 issue of the *Journal of the American Medical Association.*

The technic consists of lowering the temperature of the stomach to around zero for an hour. A balloon is inserted into the stomach through which cold alcohol is circulated to achieve stomach temperatures from four below zero to 10 above zero. The procedure is well tolerated and appears to depress the secretion of digestive juice. The digestive juice containing hydrochloric acid is believed to be an irritant which, when suppressed, allows the ulcer to heal.

The majority of patients continued asymptomatic and found it unnecessary to observe dietary strictures or to take medication. The patients ranged from twenty-six to eighty-two years of age, with the majority in the fourth, fifth, and sixth decades of life. Most patients had been seriously considering an operation for relief.

So far there has been limited experience in treating patients with stomach ulcers with the freezing technic, but it is planned to explore the possibility of using the method to prevent recurrences of ulcers in the stomach once they have healed.

Primary Melanoma of the Meninges

PRIMARY MELANOMA *of the meninges is a rare condition which may occur at any age. In the reported cases the ratio of males to females is 2 to 1; the presenting symptoms were usually those of increased intracranial pressure; frequently the only other detectable abnormality was increased protein in the cerebrospinal fluid; and the cause of death was usually increased intracranial pressure due to blockage of absorption of cerebrospinal fluid by tumor. The tumor consists either of a diffuse, brown-black thickening of the meninges of variable density which may extend down the cord, of discrete pigmented spots, or of both these forms.*

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VERY FEW cases of primary melanoma of the meninges have been reported. The exact number which are definitely primary in this location is in some doubt because of varied nomenclature and criteria or inadequate description. A detailed study on the subject of pigmentation of the meninges was published in 1949 by Touraine,[1] who reviewed 66 cases of abnormal meningeal pigmentation. The present report is of 2 cases that are believed to be primary melanomas of the meninges.

Case reports

CASE 1. The patient, a seventy-two-year-old man, was admitted to St. Luke's Hospital complaining of progressive muscular weakness and having symptoms and signs typical of Parkinson's disease. After admission his condition deteriorated steadily. The spinal fluid was at normal pressure at first, but contained 129 mg. per cent of protein and later, 270 mg. per cent. Three weeks after admission he had increased intracranial pressure, and a ventriculogram showed enlarged lateral and third ventricles. While he was being anesthetized for a craniotomy, he died.

Gross autopsy findings. There was evidence of increased intracranial pressure. Over the base of the brain, the leptomeninges showed scattered pigmented spots 1 to 3 mm. in diameter (Fig. 1). Similar spots were seen over the parietal lobes and in the septum pellucidum. The ventricular system, especially the third ventricle, was dilated.

Microscopic autopsy findings. The dark nodules in the meninges were caused by focal invasion by plump tumor cells, some of which contained dark brown pigment. Lines of these cells followed the meninges into fissures and also penetrated into the cortex by perivascular cuffing. Similar tumor cells were present in the meninges covering the pars tuberalis of the hypophysis.

Other findings included glial satellitosis. Changes in the basal ganglia were not sufficiently marked to be diagnostic of Parkinson's disease There was general congestion of internal organs, pulmonary emphysema, and terminal acute bronchitis.

CASE 2. This ten-year-old boy had had congenital abnormalities, consisting of a cleft palate and defects of the abdominal wall repaired during the first five years of his life. He also had bilateral cryptorchidism and minor congenital malformations of the ribs. He was admitted with symptoms and signs of increased intracranial pressure and developed right-sided Jacksonian seizures after admission. Ventriculograms, carotid arteriograms, and dural sinus venograms were normal. Repeated lumbar punctures showed increasing intracranial pressure. Soon after admission the spinal fluid protein increased from normal to 118 and later

Presented at the New York Pathological Society Meeting, May 10, 1961.

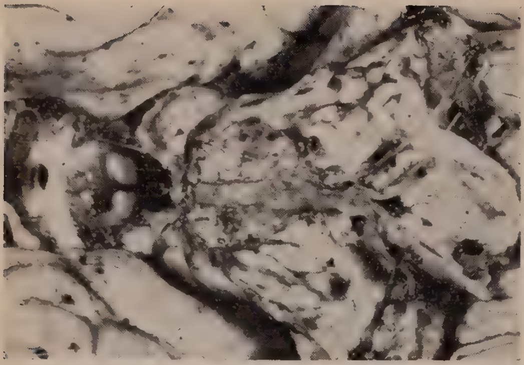

FIGURE 1. Case 1. Base of the brain showing scattered, discrete pigmented spots over pons, medulla, and medial parts of both temporal lobes.

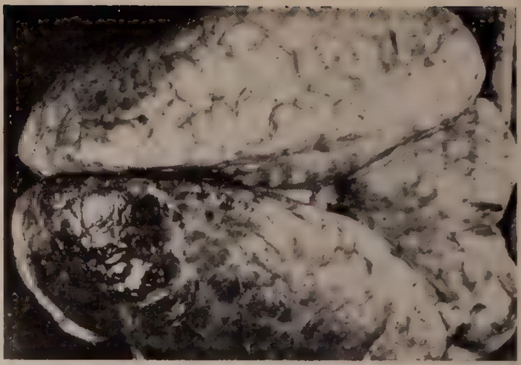

FIGURE 2. Case 2. Superior surface of brain showing thickening and pigmentation of meninges, most marked over the left frontal lobe and decreasing posteriorly, with more scattered pigmentation over right frontal lobe.

to 230 mg. per 100 ml. A spinal-peritoneal shunt was created to relieve the intracranial pressure, but after several weeks it became blocked. The patient's condition deteriorated, and he died three months after admission.

Gross autopsy findings. The brain showed signs of increased intracranial pressure, with flattening of the gyri. The leptomeninges were brown-black and thickened up to 6 mm. The pigmentation was thick and diffuse over the left frontal and temporal lobes, gradually and irregularly thinning out posteriorly (Fig. 2). Over the right hemisphere and the base, the pigmentation was in the form of 1- to 4-mm. spots, mostly widely scattered, but sometimes becoming confluent. The medulla and upper part of the cord were diffusely but less heavily pigmented.

Microscopic autopsy findings. The meninges were infiltrated and thickened by a sheet of fairly uniform cells with oval nuclei containing prominent nucleoli and vesicular cytoplasm; some contained pigment (Fig. 3). The tumor cells tended to be concentrated around blood vessels and invaded the cortex of the brain by perivascular cuffing as well as by occasional direct spread from sulci, which were widened by tumor (Figs. 4 and 5). The upper part of the spinal cord and the lower cranial nerves were individually surrounded, and some were invaded by similar tumor. The parenchyma of the pituitary gland was partly replaced by invading tumor.

Comment

On analysis of Touraine's review,[1] it appears that up to 1949 there were 18 reported cases of primary melanomatous infiltration of the leptomeninges. Since then, 5 other cases have been reported by Forbes and Maloney,[2] King, Chambers, and Garey,[3] Russi, Robinson, and Nagler,[4] Bouton,[5] and Uranova and Volodin.[6] An additional 2 in the present paper makes a total of 25. This number is less than that quoted in previous reports,[1,4–8] since patients with melanotic tumors not in the meninges have been excluded, as have those with prominent skin nevi, which may have contained malignant melanomas with secondary meningeal involvement.

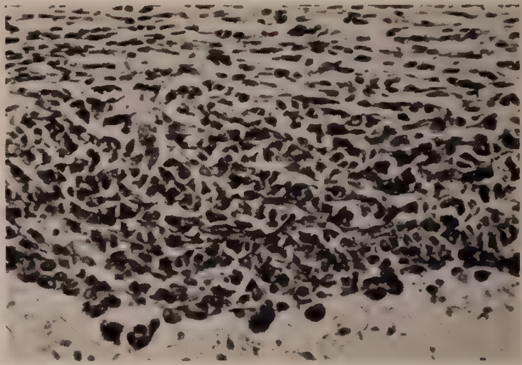

FIGURE 3. Case 2. The melanomatous pattern of growth of the tumor cells is seen. Many of the cells contain pigment.

In these 25 cases, males predominated over females in the ratio of about 2 to 1. There is insufficient mention of race and color for comment. Ages ranged from five to eighty-two years, the greatest number being between thirty and forty years. The presenting symptoms were usually those of increased intracranial pressure; the only abnormal

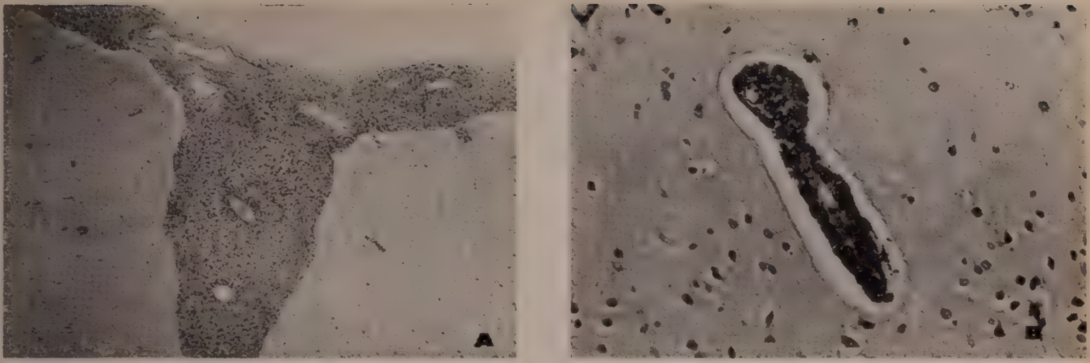

FIGURE 4. Case 2. Invasion of cortex of brain. (A) Section of frontal lobe showing tumor cells in meninges widening the sulcus and invading the cortex by perivascular cuffing. (B) Invasion of cortex of the brain by perivascular cuffing by tumor cells.

physical findings, those consistent with this. Frequently, the only other detectable abnormality was increased protein in the cerebrospinal fluid. When primary melanoma of the meninges was suspected, a melanogen test on the spinal fluid was occasionally revealing.[8]

Whether the tumor is potentially metastatic is not definitely established, although there is no doubt that histologically it appears malignant. In the cases reported the cause of death almost invariably was increased intracranial pressure due to a blockage of absorption of cerebrospinal fluid by tumor. The criteria employed here to determine primary origin in the meninges precludes the tumors in these cases having metastasized.

The increased skin pigmentation which may occur in pregnancy, Addison's disease, and other conditions of hyperpituitarism is now thought to be due to increased pituitary secretion of alpha and beta melanocyte-stimulating hormones,[9,10] although the exact mechanism of their action is unknown. Many authors have noted the presence of numerous lentigos, nevi, or generalized increase in pigmentation in association with meningeal melanomas.[5,7] It is also recognized that previously quiescent junctional nevi may become activated in the presence of a cutaneous melanoma,[11] but it is not known whether or not increased circulating melanocyte-stimulating hormone is present in these circumstances.

Although controversy concerning the histologic origin of cutaneous melanoma still exists,[11,12] there is more general agreement on the origin of meningeal melanomas.[12–14] Rawles[15] has shown that in mice only tissue containing neural crest elements can produce pigment. She has also demonstrated the migration of neural crest tissue to the epidermis, iris and choroid of eye, and leptomeninges. Masson,[14] Lerner,[16] and others believe that the Meissner sensory nerve endings in the meninges, derived from the neural crest, are the pigment cells which give rise to melanomas.

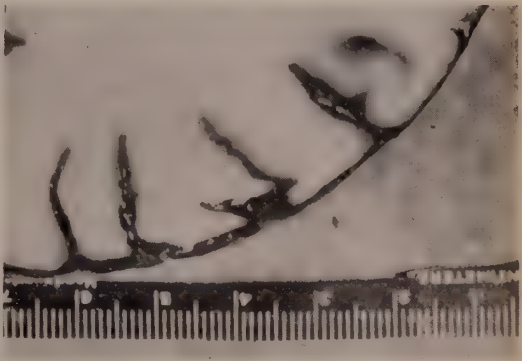

FIGURE 5. Case 2. Coronal section through left frontal lobe showing thickened pigmented meninges dipping into and widening the sulci.

Apart from any possibly demonstrable differences which may exist between meningeal and epidermal melanomas,[17] it is interesting to note differences in behavior. In our second case and in one of Kessler's cases reported by Touraine,[1] the patients were prepubertal, but the histologic appearance of the tumors and their behavior were similar to those of adult patients. This is unlike the great majority of epidermal juvenile melanomas, suggesting that there may be some difference in the response to hormonal stimulation between the meningeal and epidermal tumors.

Summary

Primary melanomas of the meninges, although rare, may occur at any age. Grossly, the tumor consists either of a diffuse, brown-black thickening of the meninges of variable density which may extend down the cord, of discrete pigmented spots, or of both these forms. Microscopically, in either case there is a sheet of fairly uniform, sometimes pigmented, melanoma cells, which may be carried into the cortex of the brain by perivascular cuffing or by direct spread.

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New light on fallen arches

New help may be on the way for the majority of Americans who suffer from fallen arches or who have tendencies toward arch difficulties, according to an address by Dr. Milton Lewis at the American Podiatry Association meeting, August 16, 1962.

An x-ray technic has been developed which makes it easier to diagnose the arch condition, to prescribe corrective treatment, and to measure the progress toward recovery. By using this method, the foot specialist can see more clearly certain bone and muscle relationships in the foot, among them, that between the heel and ankle bone. This has been called one of the most important factors in determining how the body weight is transferred to the foot proper.

Once the extent of the arch condition is determined, the patient is fitted with corrective shoes. He returns periodically for x-ray checkups which enable the podiatrist to study his progress and make any indicated changes in treatment.

While there is still considerable disagreement as to the causes of weakfoot, or fallen arches, an early diagnosis through an x-ray examination can mean a prompter return to normal foot health for many sufferers.

Hypnosis in Clinical Pediatrics

THE PROPER USE *of hypnosis can be a valuable tool in the treatment of emotional problems of children. A complete history is necessary, and the use of simple projective tests, such as the drawing of familiar family figures, may be helpful. Usually a light state of hypnosis is all that is needed for the acceptance of suggestions which relieve the anxiety and tensions of the patient, reassure him of the love of his parents, and bolster his feelings of self-esteem and self-confidence. This enables the child to pursue his natural goal: to gain mastery of his own abilities and to achieve a secure place, as an individual, in his environment.*

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IN 1777 MESMER USED hypnosis to cure a child of hysterical blindness. Elliotson, in 1831, using hypnosis, was "thus able to cure or relieve many of the diseases of children." Then we find a great silence in the literature which was broken by Ambrose of England with a series of reports from 1950 to 1956 which were finally gathered together in a text.[1] One also must pay tribute to the article of Solovey De Milechnin of Uruguay,[2] in which the use of hypnosis with children was explored further.

The phenomenon of hypnosis is noted soon after birth. When the newborn infant is put to the breast, the rhythmic sounds and vibrations of the maternal heartbeat are experienced by the infant. The crooning lullaby, the gentle cradling and rocking, the soothing and stroking, are all part of the tender loving care given to infants. And they all have potent hypnotic overtones, utilizing monotonous tactile and auditory stimulation.

If a child hurts itself, the mother will say "That's all right, don't worry, Mother will kiss it and make it all better. It won't hurt anymore." She kisses it, and miraculously, it stops hurting! The mother has produced hypnotic analgesia.

Hypnosis in the formal sense has a definite place in the armamentarium of any physician entrusted with the care of infants and children. We have been told that children are readily hypnotizable because their minds are less rigid, they are highly imaginative, and they spontaneously go off into a world of fantasy.[3] Because of the child's lack of maturity, his responses to stimuli and his psychologic defenses are not so fixed as are those of adults. It is this plasticity that makes it easier to work with children. In brief, they are perfect subjects for hypnosis.

The pediatrician occupies a unique position in medicine. He must be aware not only of the physical growth and development of his charges and with the variations resulting from genetic heritage, but also of the mental and emotional maturation. Because of the intimate relationship he has with parent and child, he has a knowledge of the home environment; the social, economic, and cultural patterns of the family; and most important, the attitude of the parents as related to each other and to the child.

For a comprehensive evaluation of his patient, the pediatrician must spend time with the child. He must adapt to the mentality of the child and learn to express himself in the language of the child. He must learn the peculiarities of each child's particular vocabulary and the meaning of these words to the child. The physician

Presented in part at the thirteenth annual meeting of the Society for Clinical and Experimental Hypnosis, October 5, 1961, Cleveland, Ohio.

must learn the child's likes and dislikes, his favorite games, sports, and so forth. He must learn how the child thinks, how he reacts, and if possible how he reacts within himself. All of this is necessary if one wishes to establish the rapport essential for the hypnotic relationship.

It is not within the scope of this paper to discuss the various "induction technics" used to obtain the hypnotic relationship. However, I should like to indicate some of the pitfalls which may arise. The selection of the proper context and precise verbalization often is the difference between a successful and an unsuccessful relationship. What does each word mean to the patient? For example: micturition, urinate, void, wee wee, sis, and so forth. Another pitfall is the use of the word "sleep," which often is misused during the induction procedure. This word must be omitted when one is working with children who have sleep difficulties. Many children equate sleep with death and horror, which situation is often being reinforced daily by prayers, movies, television, and fairy tales. More of this will be reported elsewhere.

To be truly meaningful, the care of the child entrusted to the pediatrician or the general practitioner must encompass not only the organic structural growth, but also the mental and emotional development and growth. The clinician with psychiatric orientation and a desire to practice "complete medicine" will find hypnosis a useful adjunct to the treatment of the emotional and behavior problems of children.

Case reports

CASE 1. A seven-week-old baby girl was seen by me because of "colic." The formula was taken with gusto only to be followed by intense crying, restlessness, and occasional vomiting. She would sleep only for short periods when she was completely exhausted.

It had been a planned pregnancy with a normal birth and neonatal history. Once the baby was home from the hospital, symptoms developed. Then followed a series of formula changes and feeding schedule changes without results. Sedatives and antispasmodic agents were of no avail.

Some three nurses and five pediatricians later she was referred to me.

The physical findings, including a neurologic evaluation, were entirely negative. The parents were both college graduates reared in an atmosphere of over-protection and indulgence. During the seventh month of pregnancy the death of one of their parents thrust the responsibility of the family business on the prospective father, who found this most taxing. They both felt themselves inadequately prepared for parenthood, and their anxiety was obvious.

A light stage of hypnosis was achieved simultaneously with both parents. It was suggested that they were intelligent individuals who loved each other and their baby. They would have complete confidence in their ability to care for the infant and the minor normal variations of the normal day-to-day behavior of their normal child would not bother or disturb them. They would have a happy, relaxed attitude regarding their child and would find pleasure and satisfaction in the care of the baby.

When aroused, they were instructed to stop all medication and continue the same formula. If any problem arose, they were to feel free to call me at any time.

The mother and baby were seen one week later, and the mother reported that everything was going along well. There had been only one short crying episode. Another examination of the baby showed her to be normal, and the mother was complimented for the fine job she was doing. Under hypnosis the previous suggestions were repeated to the mother.

An uneventful month passed, and the baby was seen again. The infant had gained two pounds. The mother and baby were doing well. The mother remarked, "I guess the trouble was all my feelings of guilt and tension, and I had no confidence in myself."

This evidence of her understanding of her problems and the manifested ability to adjust to her responsibilities in an intellectual and emotionally mature manner indicated that she had "grown up" to her status as a mother. Therefore, no further hypnosis was used, and routine instructions were given in the usual manner with the constant reassurance that she was doing a wonderful job and we would always be ready to help with any problems.

Comment. I do not propose that all cases of "colic" are due to anxieties of the parents and parent attitudes. I merely cite this example to show that the possibility exists and that a careful history must be taken with a sympathetic, understanding approach.

Young parents, many of whom have lived lives of dependency, are faced suddenly with life's most important function, to propagate and rear their young. This challenge and responsibility is not met readily by some parents. They must be helped first to understand the problem and then how to cope with it. They must be trained and guided by their physician in a kindly, understanding, and yet authoritative manner. As physicians, we must realize that the treatment of a case of "colic" calls for more than a change of formula and antispasmodic or sedative medications. It calls

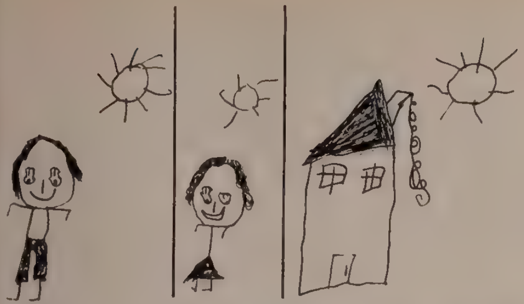

FIGURE 1. Case 2. This shows several drawings of the patient. Notice that in each instance a large sun, radiating light, is graphically presented. There must be no darkness!

for a study of the home environment, an evaluation of the needs and drives of the parents, and an appreciation of what the child means to the parents.

Case 2. A six-year-old girl had been afraid of the dark since the age of three years. She refused to go into any room in the small three-room apartment without the company of an adult. This became aggravated one year before she was seen by me and much worse the past four months.

The family and past history were irrelevant.

When she was three years old a female sibling was born. Two months later the parents noted that the patient's sleep pattern had changed. She would not go to bed at night unless her mother went into bed with her. She became "nervous and high strung," withdrawn, unhappy, and moody. She refused to stay in any room alone and was very demanding in her wants. This made her mother "nervous," and she would cry and shout at the child.

About one year before I saw her, the child was trapped in the elevator, which broke down between floors. Several weeks later she witnessed an armed robbery of their apartment. Since these two experiences she had refused to ride in an elevator, and she and her mother walked up and down the six flights of stairs to their apartment. She would fall asleep only in a room in the presence of her father and mother.

Four months later the patient started school. This put additional demands on her mother, who took her to school and waited in the back of the classroom during the entire session.

Three months later the child was hospitalized for an adenotonsillectomy. After returning home from the hospital she required the constant company of her mother.

The child had displayed no overt evidence of sibling jealousy. Indeed, her mother had no opportunity to give the sibling care or attention.

The physical findings, including a neurologic survey, showed entirely normal findings. She was cooperative and attentive, although shy, reserved, and apprehensive. It is interesting to note that she drew very well. Her faces were all smiling, but each picture had a large sun with lines radiating light over the picture (Fig. 1).

A moderate degree of hypnosis was achieved readily by means of visual hallucinations. Suggestions were given that her parents loved her very much and wanted her to be happy. They would always see that she was comfortable and safe. She was told she would be happier and would feel herself getting braver and stronger, like "Popeye" and "Mighty Mouse."

The child was seen three weeks later, at which time the parents said that great improvement had been noted. She went up and down in the elevator alone and went to school with children from her building. She no longer required the presence of her parents to go to sleep. At this visit a moderate depth of hypnosis was achieved again, and the previous suggestions were repeated and reinforced.

The patient was next seen six weeks later. Two days before she had watched a horror film on television. She was again afraid to go into a room alone and once more demanded constant attention.

The child was given another session of suggestions following the general theme of her two previous visits.

At the time of this writing, some two and one-half years later, the parents have reported that the patient is doing well in school. She has many friends and seems carefree and happy. There have been no more references to being afraid of the dark.

Comment. This highly suggestible child had suffered a series of episodes of psychic trauma and a feeling of rejection dating back to the birth of a sibling. Her insecurity became more marked after being accidentally trapped between floors in an elevator and then being present while the household was robbed. Next came the start of school and with it the crowning blow, a visit to the hospital for an adenotonsillectomy.

This was a series of unusual episodes in dramatic sequence, all adding up to anxiety, fears, and a feeling of insecurity. Being highly imaginative and very suggestible, she responded just as dramatically after three spaced sessions of hypnotherapy.

Case 3. A six and one-half-year-old female was brought in with a chief complaint of wetting, day and night.

The family history was irrelevant except that the patient is the third of five children, all girls, all planned pregnancies. The mother complained that she felt overworked and distraught and complained that the child "wets all the time, and I took her to a psychologist for treatment, going twice a week for nine months. But she still wets day and night and is always so unhappy. I really think that she is very jealous of my wonderful relationship with my husband.

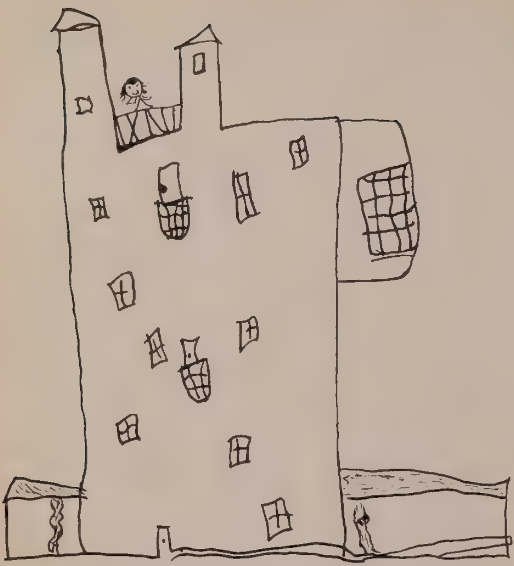

FIGURE 2. Case 3. "My room will be like the queen's room. I will have everything shiny and gold. I will live alone and sleep alone, like Lynn (oldest sister) and like Mommy and Daddy, who sleep alone, together" (April 1, 1960).

She often tells me that I don't love her, and wishes she had another mother who would give her more love and attention."

The child's developmental history and a urologic investigation produced normal findings. She was trained for bowel control by two years of age. She had never achieved urine control in spite of threats, punishments, restricted fluids, reward systems, being awakened every hour at night, being made to void every hour during the day, taking tranquilizers, and so forth.

There had been no serious illnesses or operations. She was good in sports, seemed happy in school, and got along well with children, except her own sisters.

The physical and neurologic examinations showed negative findings. The patient was happy and well coordinated, but when we started a conversation she became quiet and withdrawn and remarked, "I guess you are going to start in on my wetting. I just don't want to discuss it." She was immediately assured that I had no intention of doing anything more than have her show me how well she could draw. She first drew a picture of a castle with a parapet, with a woman on it (Fig. 2). She remarked, "That is mother watching the dogs. She doesn't worry about the children." Her drawings of her father, mother, and sisters were remarkable in detail except for the omission of noses in all of them (Figs. 3 and 4).

Through the use of visual hallucinations she achieved a light stage of hypnosis. Simple suggestions were given that both parents loved her very much; that she was pretty, smart, and could learn things so easily. It would be such fun to learn new things, and when she did, she would feel so happy. There was a final suggestion that it had been such fun playing this game and that she would want to play it again with me sometime soon.

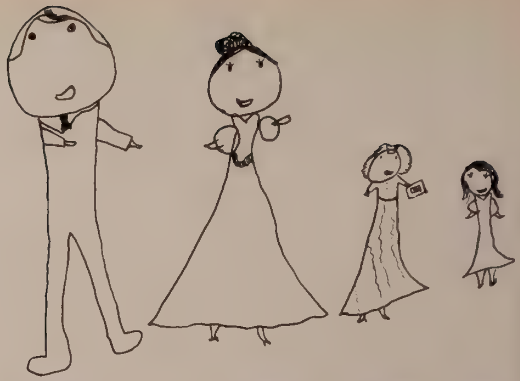

FIGURE 3. Case 3. Drawings of father, mother, grandmother, and maid (April 1, 1960).

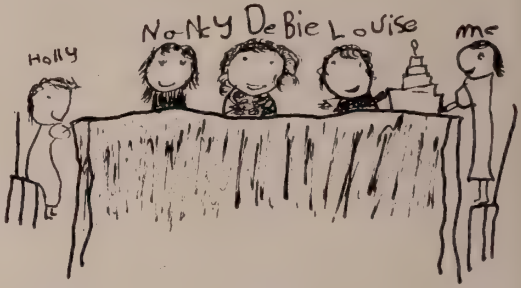

FIGURE 4. Case 3. Drawings of all five children at the table. Note that in Figures 3 and 4, in spite of the detail, no figure has a nose. Obviously, so that no one can smell her!

The mother was instructed to ignore the child's wetting and to instruct others in the family to ignore it also.

The child came to see me one week later with a note from the mother which stated that the patient "seemed so happy this week and wanted to see you. She has been looking forward to her visit with you."

Thus, it was evident that rapport with the child, possibly helped by posthypnotic suggestion, had been established.

A light stage of hypnosis was achieved rapidly, and the previous suggestions were repeated with the additional suggestion that she would learn a "signal" when her bladder was full. I had her experience this "signal" while under hypnosis. I emphasized that if she didn't always get the "signal," it would not

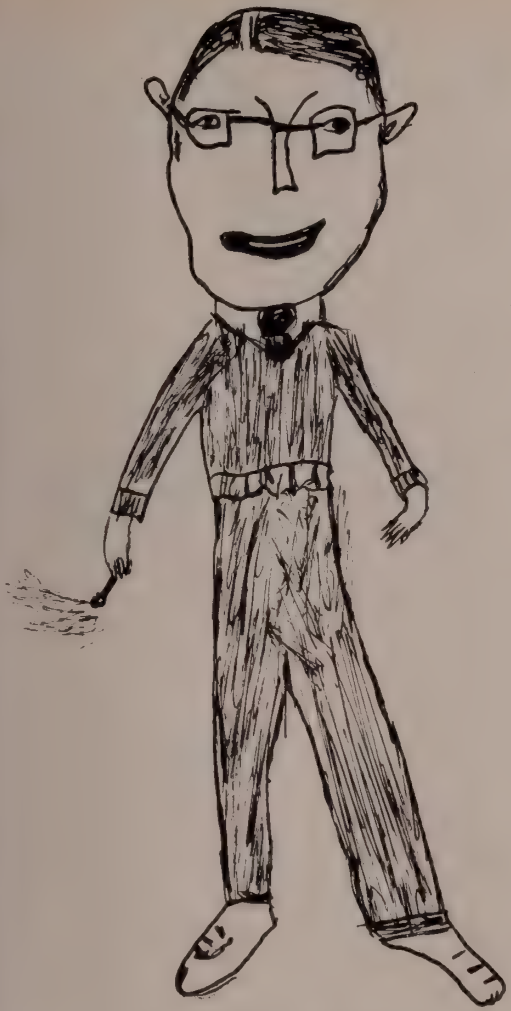

FIGURE 5. Case 3. Father, with prominent nose, and happy.

bother her, since her parents loved her just as much, but she would feel so much happier when she learned the "signal."

About eight weeks later I received a phone call from the mother, who reported that the child seemed much happier and no longer soiled herself during the day. She was fine at night until that week when she had an "accident" twice.

The child made her third visit to me a few days after this, greeted me with a big kiss, and told me how proud she was to have learned the "signal."

A light stage of hypnosis was achieved again, and all of the previous suggestions were reinforced with the additional suggestion that she would learn how to get the "signal" at night.

The mother was instructed to put the child to bed at night herself, to hold her and kiss her, tell her what a good girl she was and how much they all loved her, and how easy it would be to remember the "signal," a reinforcement of my suggestions.

I next saw this mother and child one month later, when I was told that the child had been fine until one week previously, when she started to wet again at night. The mother said that her husband had met temporary financial losses, and "I'm overworked and distraught. I guess I have shouted at my daughter and have spanked her often. If I've caused psychic trauma, I'm sorry."

On this fourth visit the child was induced again into a medium trance state. The same suggestions were repeated regarding the love of her parents, confidence in herself to learn the "signal," being happy, and so forth.

At the time of this writing, some twenty months later, the child has not regressed and is happy and outgoing.

Comment. Several months ago, at my request, the child sent me some recent drawings of her parents and herself (Figs. 5, 6, and 7). The improvements of the sketches indicate the rapid and mature technical advance she has made, and most important, a well-defined nose is prominent in each figure. Our patient is no longer fearful of smell because she no longer soils herself. Most graphic, however, is the sketch of herself (Fig. 7). Here we see the fantasy of an outgoing, self-confident, self-assured young child of eight years, picturing herself on the stage, the attractive center of everyone's attention.

Summary

These case presentations were selected not for reason of the presenting complaint but rather to illustrate some fundamental considerations on the use of hypnosis in children.

We note the necessity of a complete history to give us a family background and an insight into the attitude of the parents. We next evaluate the feelings of the child, expressed or overt, toward the parents and the home environment. We note how tension from the presenting symptoms, with its social implications and the fear of parental displeasure, sets up a vicious cycle in the child's mind. Each therapeutic effort which results in failure makes the child and the parent more frustrated and more anxious. Every failure reduces self-confidence and lowers self-esteem.

Another important aspect is that any brief, quickly forgotten emotional flare-up

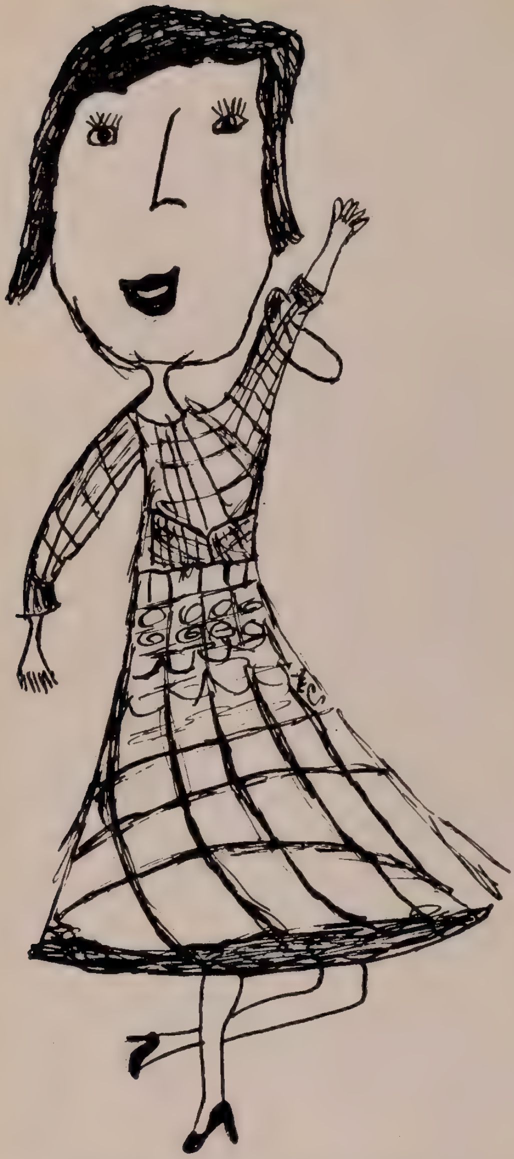

FIGURE 6. Case 3. Mother, with prominent nose, and happy.

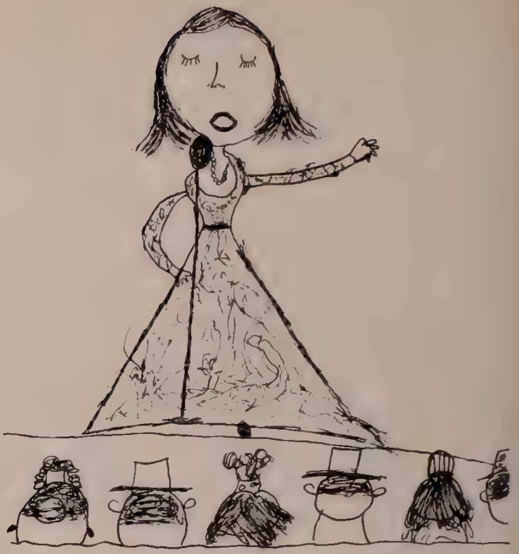

FIGURE 7. Case 3. The patient, glamorous, self-assured, and the center of attention. She is far superior to her rather poorly constructed audience!

of a parent may cause lasting psychic trauma in a child, who simply cannot understand a parent's dark mood. The child considers this more as a result of some direct, personal hatred. The parent no longer loves him!

The use of simple projective tests, such as the drawing of familiar family figures, may give us insight into the problems facing the patient. Moreover, while the patient is physically occupied with sketching, opportunities are present to observe such things as coordination, frustration, and so forth. One also can utilize this time, by tactfully asked questions, to accumulate a more intimate knowledge of the child's feelings.

Obviously, the history and evaluation take time, patience, and understanding, and some psychiatric orientation. This is the price that must be paid by anyone who undertakes and is entrusted with the care of children.

At the risk of over-simplification, the child's emotional problems are the result of some loss, or fear of loss, with its many ramifications, and this is usually the loss of the love of the parents, loss of self-esteem, and loss of self-confidence. All of these factors interfere with the child's natural goal: to gain mastery of his own abilities and to achieve a secure place, as an individual, in his environment. We relieve the anxiety and tensions of our patients by simple suggestions to reassure them of the love of their parents and to bolster their feelings of self-esteem and self-confidence.

Conclusion

Hypnosis offers a means of shortening the course of treatment. It has been my clinical experience with young children that a light state of hypnosis is all that is needed for the acceptance of suggestions. There is no necessity to probe deeply into the psyche. Rapport is established quickly. The relief of anxiety and tension factors is accomplished rapidly. Self-confidence and self-esteem are increased. There is an easier acceptance of the situation, and resistance is reduced. We can suggest and help the motivation for improvement.

The physician himself should be well adjusted, well trained, and psychiatrically oriented. He must maintain, as Raginsky said, "a state of balanced judgement, which is achieved when sufficient knowledge and experience have been gained. He must reconcile hypnosis with the broader dynamic concepts of interpersonal relationship and then use hypnotic techniques in their properly limited scope"[4] and always within the sphere of his own capabilities.

The proper use of hypnosis can be a valuable tool in the treatment of emotional problems of children.

ACKNOWLEDGMENT. Acknowledgment is gratefully made to my wife, Jean Jacobs, for her aid and helpful suggestions in the preparation of this report.

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Neurologic Complications Observed in Bronchogenic Carcinoma

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THE INCIDENCE of bronchogenic carcinoma has been increasing rapidly in the male population of the United States for the last twenty-five years.[1] The frequency with which this disease is now encountered is reflected in the increasing involvement of the nervous system. Symptoms related to the nervous system often herald the presence of an unsuspected carcinoma of the lung. This paper will report on nervous system involvement in 295 patients with bronchogenic carcinoma seen at Roswell Park Memorial Institute between January 1, 1957, and July 1, 1961. These patients were primarily the responsibility of the Thoracic Surgery Unit at this institution, but because of their various other complaints were seen frequently by the Neurosurgical Service.

Clinical material and results

Case histories and physical and laboratory studies of the 295 patients with bronchogenic carcinoma in this series showed that in 175 the nervous system was involved. In 120 patients there were no data to indicate nervous system involvement. In general, the diagnosis of bronchogenic carcinoma was made by the following means: sputum studies and bronchial washings, scalene-node biopsies, lung biopsy, pulmonary resection, and autopsy.

Pain was the most frequent complication of bronchogenic carcinoma and was encountered in isolated instances in 74 patients; 71 noted multiple sites of pain. Chest pain was most frequently encountered (in 70 patients). Forty-two complained of upper extremity and 17 of lower extremity pain. Pain related to the spinal column or midline in character was encountered in 40 instances, but in only 7 of these were signs of spinal cord compression noted. Twenty-eight patients had evidence of intracranial involvement. Vocal cord paralysis was found in 12, and a Horner's syndrome in 3.

Postmortem examination performed on 32 patients in this series disclosed that 23 had intracranial lesions. Of these, 16 had two or more metastatic tumors, while 7 had single lesions. Death in these 7 patients was related in each instance to the presence of the lesion and occurred from two weeks to two months after the development of central nervous system symptoms. One patient, however, survived six months after the development of the initial changes. Five of the spinal cord lesions were located in the cervical and high dorsal area and 1 in the lumbar area. In the group of patients listed as having central nervous system involvement, 19 (10.8 per cent) were living as of July 1, 1961. In those patients without evidence of involvement of the nervous system, 24 patients were alive, totaling 20 per cent of their over-all number.

Comment

No attempt has been made to group the patients by cell type of their tumor or by the mode of therapy. It should be noted, however, that in the majority of the patients seen at the Institute, the disease is well advanced.

The unexpected finding of 7 patients with single isolated metastatic lesions of the brain deserves comment. It is always difficult to resolve the therapeutic problem of a patient with both lung and brain tumor involvement. The question of whether

IN 295 PATIENTS *with bronchogenic carcinoma the nervous system was involved in 175. Pain was the most frequent complication and occurred in isolated instances in 74 patients and in multiple sites in 71, the most frequent site being the chest. Postmortem examination performed on 32 patients showed that 23 had intracranial lesions, of whom 16 had two or more metastatic tumors while 7 had single lesions. The treatment of choice for patients with pain resulting from nervous system involvement has been contralateral cordotomy and an ipsilateral high cervical posterior rhizotomy, with bilateral prefrontal lobotomy used in patients with far-advanced disease in which pain is the primary nursing problem.*

or not the central nervous system lesion is related to the lung lesion can be answered only at autopsy or by double surgical procedures. Usually, it is expensive and generally ineffectual to subject a patient to a thoracotomy as well as a craniotomy. Thus, the procedure of choice is to give such patients so-called "conservative" therapy, in which nothing is done. It may be that in light of the findings presented here, craniotomy should be resorted to more often, especially when death may result from rapid central nervous system damage. This therapeutic dilemma will become more pressing as more effective drugs are found for the control of the bronchogenic tumor, since death from brain involvement may occur before the expected effects of such a drug.

Since the majority of nervous system problems were related to pain, the therapeutic importance of this fact should be emphasized. It is our experience that pain in the majority of these patients can be controlled with narcotics for a limited time. Since the majority of our patients had pain above the umbilicus, surgical control was complicated. Pain of an upper extremity is difficult to handle by cordotomy alone.[2] Consequently, in this situation the procedure of choice at Roswell Park has been a contralateral cordotomy and an ipsilateral high cervical posterior rhizotomy. The involved extremity is not made useless by these procedures since the fifth, sixth, seventh, and eighth posterior cervical nerve roots are spared. We have found that bilateral prefrontal lobotomy has been effective in the patients with far-advanced disease in which pain is the primary nursing problem.[3] This is most effective in those patients with vague or poorly localized pain in the thoracic or abdominal areas. We have tried to restrict this procedure to those patients in whom life expectancy is measured in months. It can be performed under local anesthesia, and if the patient is ambulatory before surgery, ambulation is again possible within a matter of hours following the operation.

The fact that 10 per cent of those with nervous system involvement are surviving versus 20 per cent in the noninvolved group is significant only in that the former figure measures a more advanced state of the disease. If the tumor has spread sufficiently so that nervous tissue has become involved, life expectancy is reduced.

Summary

In a group of 295 patients seen over a three-and-one-half-year period at Roswell Park, over half complained of some form of nervous system involvement. The majority were pain problems, but in 23 of 32 postmortem examinations, brain involvement was found. The point of interest here is that 7 of these patients had isolated lesions. Had surgical intervention been elected as an approach to the intracranial disease, then life might have been prolonged.

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Effect of Allergens on Fungi: Growth of Mucor in Presence of Protein Derivative of M. Tuberculosis

Preliminary Note

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THE ADDITION *of the PPD (purified protein derivative) of tubercle bacilli to the surface of Sabouraud agar plates produced an increase in the in vitro growth of Mucor species.*

A STUDY of the effect of bacterial products on the in vitro growth of various fungi has been made possible by the availability of the PPD (purified protein derivative) of the tubercle bacillus, a naturally occurring allergenic material. An observation on Mucor species reported in this preliminary note has prompted the further study of symbiotic relationships between fungi and other organisms.

Materials

The materials used were Sabouraud dextrose agar (polypeptone 10, dextrose 40, agar 15) and tuberculin, PPD, second strength (Parke Davis & Co.).

Method

One drop of PPD was placed over a one-half inch transfer of the fungus on Sabouraud plates with and without coverslips. Controls of distilled water, peptone-protease solution, and fungus alone were employed with and without coverslips. Culture plates were grown at room temperature for from one to two weeks.

Results

Each of 21 fungi were found to form normal mycelia in the presence of the PPD and in controls, with comparable growth in experimental groups and controls. An increased growth of Mucor species was noted with mycelial growth approximately two to three times as great in the plates receiving the PPD. The possibility that the PPD might permit earlier spreading of the transferred spores and the availability of more abundant nutrient material was tested by using more distilled water in one control, which produced earlier spreading but no increase in the mycelial growth over other controls. The increased growth of the PPD plates became apparent macroscopically on the third day and remained consistently greater for the ten-day period during which the plates were observed. The fungus produced a white cottony mycelium through which light could be transmitted. A sufficiently profuse growth at the center of the colony prevented the transmission of light, enabling a clear pictorial presentation of the difference in growth.

Summary

An increase in the in vitro growth of Mucor species was obtained by the addition of the PPD (purified protein derivative) of tubercle bacilli to the surface of Sabouraud agar plates.

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Pain—Psychic or Physical?

A test that can show whether pain is physical or psychosomatic has been described by Leo Alexander, M.D., a Boston psychiatrist, in the September 8 *Journal of the American Medical Association.*

Through tests of various psychiatric patients Dr. Alexander has found that the galvanic skin responses of patients suffering physical pain were "strikingly different" from those suffering from psychogenic pain when the natural fluctuations were compared with those evoked by deliberate painful stimulation. To test the validity of this observation, he studied 20 patients whose chief complaint was pain which could be diagnosed definitely as either physical or psychogenic and, for comparison, an additional 14 patients who were free from pain.

Patients with psychogenic pain were found to have a low rate of natural fluctuations of skin resistance as well as a low level of responses to deliberate stimulation. This suggests that psychogenic pain may represent a state to which the nervous system has become conditioned and that, like depression, it may represent an inhibitory state.

Patients who suffered physical pain showed marked spontaneous fluctuations of skin resistance that corresponded to the waxing and waning of the physical pain while responses to induced stimulation were uninhibited. The natural fluctuations of skin resistance among pain-free patients did not differ from the psychogenic pain group but was significantly different from the organic pain group.

Clinicopathologic Conference

MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D., Editors

Knickerbocker Hospital
New York City
June 27, 1962

Conducted by MICHAEL S. BRUNO, M.D., and
WILLIAM B. OBER, M.D.

Discussed by MICHAEL S. BRUNO, M.D.

Jaundice at the End of Pregnancy

Case history

Frank Breech, M.D.: A thirty-three-year-old white gravida 4, para 3 was admitted at eight months gestation with a history of a cold, sore throat, stuffiness in the ears, and a nonproductive cough which had begun about one week previously. She had been treated symptomatically for a few days without relief. Three or four days before her entry to the hospital she gradually developed moderate epigastric distress, anorexia, and nausea, but there was no vomiting. She also complained of feeling weak and drowsy for about this period of time.

Her antepartum course had been uneventful up to this time. There had been no excessive weight gain. Her three previous pregnancies also had been uneventful. She had never had any illness suggesting gallstones or hepatitis. She had not been exposed to known liver toxins.

A physical examination revealed a well-developed, well-nourished white female who seemed slightly dehydrated and who was also lethargic. The temperature was 99 F., pulse 100, respirations 25, and blood pressure 132/60. The tongue was dry, and there was a sweetish odor to the breath. Coarse breath sounds were heard at the bases of both lungs. The heart rate was regular with a slight sinus tachycardia, and there was a soft systolic murmur at the apex. There was no tenderness in the abdomen, but there was slight costovertebral angle tenderness. The intra-abdominal organs could not be outlined because of the uterus, which was enlarged to an eight-months size. The fetal heart sounds were of good quality on admission. An examination of the extremities showed no edema or discoloration. A neurologic examination was unrevealing, and there was no peripheral lymphadenopathy, icterus, cyanosis, or lividity.

A urinalysis shortly after her admission revealed a pH of 5, a specific gravity of 1.010, 1 plus albumin, no sugar or acetone, and 4 to 6 white cells and 3 or 4 red cells per high power field. The hemoglobin was 10.7 Gm. per 100 ml., red cell count 3.6 million, hematocrit 32, and the white cell count 13,000 with 69 per cent polymorphonuclear leukocytes and 31 per cent lymphocytes. The day after the patient's entry the fasting blood sugar was 86 mg. per 100 ml., and the blood urea nitrogen was 22 mg. per 100 ml. Roentgenography of the chest showed the heart to be of normal size and the lungs well aerated with no evidence of infiltration.

She was treated with intravenous fluids and Achromycin, and her condition seemed stable. About thirty-six hours after admission she went into spontaneous labor. Shortly after the onset of labor the fetal heart sounds disappeared, and she delivered a stillborn male fetus which weighed $5^1/_4$

pounds. Early maceration of the fetus was noted. There was no excessive bleeding at or after delivery.

Within a few hours of the delivery it was apparent that she was "toxic" and overtly jaundiced. She remained somewhat lethargic. At this time the white cell count was 19,000 with 77 per cent polymorphonuclear leukocytes, 5 per cent band forms, 14 per cent lymphocytes, and 4 per cent monocytes. The serum bilirubin was 15.3 mg. per 100 ml. The thymol turbidity was 4.5 units, transaminase 106 units, and total protein 4.9 Gm. per 100 ml. with 2.3 Gm. albumin and 2.6 Gm. globulin. The serum sodium was 155 mEq., potassium 5.8 mEq., and chlorides 127 mEq. per liter, and the carbon dioxide was 58.4 volumes per cent. The blood pressure fluctuated between 124/70 and 103/54, and the pulse ranged from 90 to 100. The temperature was 99.4 F., and it never rose over 100 F. during the succeeding three days.

An examination of the chest showed slight dullness at the left lung base and coarse breath sounds in both bases. The abdomen, now emptied of the gravid womb, was essentially normal. The liver could not be felt nor could the spleen. There was no tenderness over the liver or in the epigastrium. No abnormal masses were felt. There was no fluid. The uterus was of normal size, and the lochia was not excessive or abnormal in character.

Her lethargy persisted and deepened. Treatment with intravenous solutions and vitamins was continued. The urine output was adequate. She vomited small amounts of fluid on two occasions. A representative urine specimen gave a positive test reaction for bile. Despite therapy, she continued to decline. On the third postpartum day the serum bilirubin was 25 mg. per 100 ml., transaminase 79 units, thymol turbidity 1.6 units, and alkaline phosphatase 1 unit. She vomited a moderate amount of reddish-brown material. The blood pressure declined to 80/30.

Gastric suction yielded 1,300 cc. of coffee-ground material. The blood pressure declined further despite pressor agents, and she became stuporous, dying later that day, five days after entry and three days after delivery.

Discussion

Michael S. Bruno, M.D.*: The problem deals with a young woman who developed jaundice during the eighth month of her fourth pregnancy and died after an illness of about two weeks duration. There is every reason to believe that she was perfectly well until one week before she was admitted to the hospital. In fact, most of the information we are given consists of significant negative observations. She had not had hyperemesis, hypertension, edema, unusual weight gain, albuminuria, or convulsions. Her state of nutrition was excellent. She had no history of gallbladder disease or biliary colic. She had not taken any medication of significance, and there was no exposure to known hepatotoxins. Of course, any pregnant woman does run the risk of exposure to the hepatitis virus from hypodermic needles used in the routine hematologic and serologic tests which are part and parcel of good prenatal care.

The outstanding features of this patient's illness were the vague, nonspecific, prodromal symptoms followed by the development of clinical icterus at about the time of delivery. The icterus deepened rapidly, and she died in hepatic decompensation three days after delivery. In attempting to analyze the nature of this disease we again find many significant negative observations. She was anicteric on admission. She was afebrile and remained so. The liver was not enlarged or tender, even when it could be better examined after the delivery.

We are given little positive help from an evaluation of the laboratory studies. The fact that the serum bilirubin rose to 25 mg. in three days is probably an index of the severity of her liver damage and the rapidity of her clinical course. The other parameters of "liver function" were either within normal limits or only slightly altered. They certainly do not point to any specific type of damage. Indeed, the degree of icterus and the clinical course are disproportionate to the remainder of the laboratory data.

There was a significant leukocytosis on admission, and it increased subsequently.

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There was a shift to the left in the differential count. There was no anemia, and no hemorrhagic phenomena were seen. Lymphocytosis and abnormal lymphocytes or monocytes were absent. The most significant urinary finding was bilirubinuria.

Can we relate the terminal illness and rapid demise to her pregnant state, or is this purely a matter of coincidence? I think that the differential diagnosis must pivot about this point. I shall attempt to answer this question later on, but logical reasoning, often the deceiver of the unsuspecting clinician, forces me to suppose that the fact that she was pregnant was decisive in the development of her disease and its fulminating course.

I already have stressed the negative findings in her past history, her excellent nutritional state, three prior uneventful and fruitful pregnancies, and the absence of any suspicion of chronic liver disease, such as cirrhosis or protracted hepatitis. There is no clue to suggest the presence of a systemic illness with prominent hepatic complications, such as disseminated lupus with "lupoid" hepatitis. The possibility of antecedent acute hepatic necrosis from any cause with the persistence of activity based on autoimmune mechanism or other antigen-antibody mechanism cannot receive serious consideration.

I cannot entertain seriously the possibility that this illness was the result of a known toxic substance. There was no history of exposure to or ingestion of such a toxin. The relatively normal renal function rules out toxins of the carbon tetrachloride type which produce necrosis in both the liver and the kidneys. The fulminating course and the lack of evidence of intrahepatic cholestasis are not consistent with the effects of Thorazine, steroids, and the whole range of compounds which produce this relatively mild, slowly progressing type of liver damage.

We can safely exclude hemolysis as the mechanism for the development of jaundice or liver damage. There were no laboratory parameters to support it. In fact, the few laboratory values given tend to exclude it. For the same reason I am willing to exclude the possibility of intrahepatic or extrahepatic obstruction. This is clearly a case of parenchymatous jaundice.

Could this be an example of viral hepatitis, either endemic or serum in type, which pursued a rapidly fatal course, killing a previously healthy pregnant woman in two weeks? It most certainly could be! The mortality rate of acute hepatitis increases markedly in pregnancy for reasons that are not clear, and cases of acute fulminating hepatitis, formerly called acute yellow atrophy, are more common in pregnant women.[1,2] On purely statistical grounds, acute hepatitis of the overwhelming type is the most likely explanation for the patient's demise.[3] In spite of this acknowledgment, statistics can be misleading if they are followed invariably as dicta and are not evaluated in the light of the total clinical picture.

I do not really believe that this patient had acute hepatic necrosis, and there is evidence to support this idea. First, although she was critically ill from overwhelming liver disease, she was afebrile from beginning to end. Her temperature never rose above 100 F. This would be remarkable in itself, since a spiking fever is an important feature of fulminating hepatitis. Second, persistent polymorphonuclear leukocytosis with a shift to the left in the differential count would be extremely rare in acute viral hepatitis. Leukopenia or a normal white cell count with lymphocytosis and immature mononuclear cells is the usual picture. Third, the liver was not enlarged or tender. I would not be disturbed if the liver were merely not enlarged; not all patients with viral hepatitis have large livers; indeed, the liver may be smaller than normal at autopsy in fulminating cases. However, I cannot imagine a serious infectious or necrotizing process that would not produce some tenderness in the liver region. Fourth, the laboratory data are not consistent with massive hepatic necrosis. Neither transaminase nor thymol turbidity values were significantly elevated on admission, and they fell to near normal levels after delivery. The alkaline phosphatase was only 1 Bodansky unit. Therefore, in spite of its statistical probability, because of these four reasons, I cannot interpret this case as one of infectious hepatitis, and I shall have to look elsewhere for the diagnosis.

I feel very strongly that the liver disease was related to her pregnancy in some way. If so, what pathologic entity can be incriminated as the cause, and what are the possible mechanisms?

Hepatic necrosis associated with fatty degeneration and hemorrhage is sometimes seen in instances of severe hyperemesis gravidarum.[4] Bile stasis and thrombosis in branches of the portal vein also may be present. In addition, degeneration of the renal tubular epithelium also may be found. Such cases are not common, and when they do occur are found in the first trimester, usually beginning in the second or third month. I mention this only to stress a point that internists may not be familiar with, namely, the severity and potentially fatal outcome of occasional cases of hyperemesis gravidarum. However, the present patient had passed through the first and second trimesters without difficulty and cannot be placed in this category.

In rare instances of toxemia of pregnancy, liver necrosis sufficient to cause liver failure may be found.[5] The hepatic lesion originally was thought to be due to a toxin, but at present circulatory factors and alterations of the blood coagulation appear more important in their pathogenesis. Fibrin thrombi obstructing the sinusoidal blood flow may result in focal lobular ischemia and necrosis. Fibrin thrombi in other organs, such as the kidney, pituitary, and adrenal may produce comparable lesions and clinical effects. The consumption of fibrinogen by the formation of these thrombi may explain the fibrinogenopenia and hemorrhagic phenomena seen in some of these patients. There is a poor correlation between the severity of toxemia and the degree of hepatic destruction. The presence of icterus in preeclampsia or eclampsia is an ominous sign. However, in the absence of hypertension, albuminuria, edema, or frank convulsions, we cannot consider this patient as having any variety of the toxemias of pregnancy.

There is one syndrome, apparently peculiar to pregnancy, which does seem to correspond very well with the features of the present case. In 1940, Sheehan[6] described a condition under the term "obstetric acute yellow atrophy" and summarized 6 cases from the files of a maternity hospital. His summary is startlingly close to what is described in this case. He states, ". . .clinically the condition is very suggestive of acute yellow atrophy. The usual course. . .is as follows: At thirty-six to forty weeks there was a sudden onset of severe vomiting and epigastric pain, followed in a few days by jaundice. These symptoms progressed very rapidly, the vomiting becoming intense, vomitus of coffee ground appearance and headache sometimes being present. After seven to twelve days the patient was delivered of a stillborn fetus, became comatose, and died three days after delivery. At autopsy the liver was yellow and rather small (1,040 to 1,300 Gm.). Its lobular pattern was not lost. Microscopically all the cases showed an identical lesion: There was gross fatty change affecting the entire lobule except for a sharply defined rim of normal cells about the protal tracts. The affected cells were bloated by a fine foam of tiny fatty vacuoles throughout the cytoplasm so that they resembled cells of the suprarenal cortex. The nuclei were normal, and there was an entire absence of necrobiotic change; cellular infiltration was lacking."

In 1955, Ober and LeCompte[7] reported 3 additional cases in considerable detail. They, too, showed a striking similarity to the present case. The patients died in hepatic failure following the onset of jaundice after a brief prodrome in the last month of pregnancy. The patients were essentially afebrile, and all had significant leukocytosis with white cell counts ranging from 17,000 to 33,000. The lesion is histopathologically distinctive. The absence of frank necrosis and inflammatory infiltration serves to distinguish it from viral hepatitis. The lesion does not resemble the conventional form of nutritional fatty metamorphosis in which there is usually a single, large, intracytoplasmic fat vacuole that pushes the nucleus to one side; rather, the nucleus is central, and the cytoplasm is swollen by a myriad of fine, fatty vacuoles separated from each other by delicate eosinophilic strands of cytoplasm. Binucleate parenchymal cells are common. There seems to be no increase in the Kupffer cells.

The lesion bears some resemblance to the effects of an exotoxin or an endotoxin, somewhat analogous to that produced by ethionine, a chemical analogue of methionine, which enters into metabolic competition with it. In the absence of specific pathogenetic data, the lesion has been interpreted as being the result of a metabolic injury to the liver, possibly related to a nutritional deficiency. Nature grants a nutritional priority to the developing fetus, and a diet barely sufficient in protein, amino acids, certain vitamins, and lipotropic substances, such as choline, can become relatively deficient for the mother in the pregnant state. In general, a normal liver is able to function without difficulty in a normal pregnancy. However, certain minor clinical phenomena suggest that in pregnancy there may be a decreased hepatic reserve. For example, spider angiomas and palmar erythema, often a hallmark of liver disease, are seen frequently in normal, healthy, pregnant women. One interpretation of such phenomena is that the liver, although not diseased, is unable to conjugate estrogens at the rate that they are being produced. It has been shown that an adequate level of certain vitamins is necessary for complete estrogen inactivation and that the impairment of the estrogen-inactivating mechanism may occur in the absence of morphologic changes.

Another explanation might be that the physiologic failure is the result of some humoral agent which is either specific to pregnancy, or, if not, is abnormally destructive during pregnancy. Whether or not such a hormone exists is purely speculative; it certainly has not been demonstrated. Whatever the mechanism, it is apparent that the metabolic alteration that results prevents the liver from converting and metabolizing fat either by inhibiting an enzyme system or by biologic antagonism to a necessary metabolite, or both.

To recapitulate, I decline to make a diagnosis of fulminant viral hepatitis in the absence of fever, hepatic tenderness, the presence of leukocytosis, and the lack of laboratory evidence of massive liver destruction. Given the fact that the disease took place in the eighth month of a previously normal pregnancy, I can exclude hepatic complications of hyperemesis gravidarum. In the absence of hypertension, albuminuria, edema, or convulsions I can safely exclude hepatic complications of pregnancy toxemia. Although the entity described by Sheehan is rare, I will be surprised if Dr. Ober does not demonstrate the distinctive lesion of acute fatty metamorphosis of the liver in pregnancy.

MARCEL TUCHMAN, M.D.: A somewhat similar picture occurs both clinically and pathologically in patients with kwashiorkor, a disease of nutritional deficiency found chiefly in Africa.

DR. BRUNO: The hepatic lesion of kwashiorkor more closely resembles the usual fatty metamorphosis seen in nonpregnant patients. The fat vacuole is usually single and is composed chiefly of neutral fat. The nucleus is eccentrically placed, and there is often some liver cell destruction.

THOMAS SILVERBERG, M.D.: Are these cases invariably fatal?

DR. BRUNO: No. There are a few reported cases that recovered, and some of these have been documented by liver biopsy, so we must accept them. In fact, if the possibility of this entity is considered, a needle biopsy of the liver is indicated for a confirmation of the diagnosis, and we must hope that prompt and vigorous therapy will salvage a greater number of these young women.

DR. BREECH: I noticed that you did not mention either Weil's disease or yellow fever as possible liver infections which might produce a comparable picture.

DR. BRUNO: From an epidemiologic point of view, such contingencies are remote, but I am glad someone mentioned them for the sake of completeness. The absence of fever, rash, or renal involvement militates against Weil's disease. As for yellow fever, I think it is geographically impossible. Besides, it is notoriously a disease characterized by a high fever.

VINCENT VINCI, M.D.: Do you think that the diagnosis is missed in some of these cases, even at autopsy?

DR. BRUNO: That is wholly possible. The entity is very rare, and unless one has had either first hand experience with it or has read about it, the lesion can be misdiagnosed.

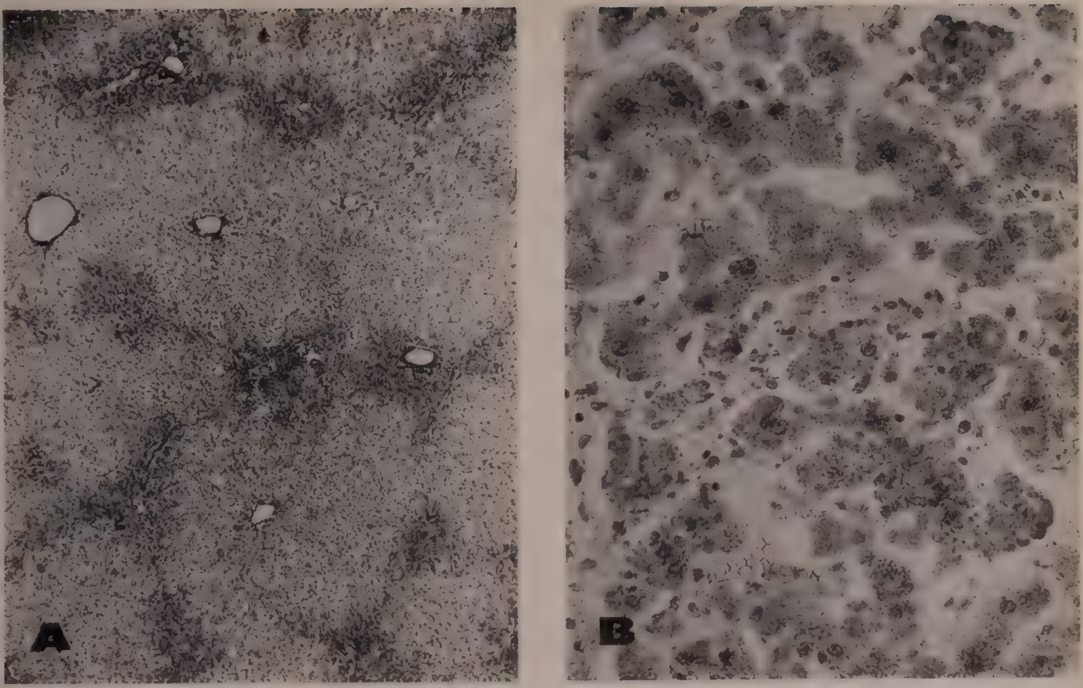

FIGURE 1. (A) Low-power view of liver showing preservation of lobular architecture. Most of the lobules are pale. There is a normally dark-staining rim at the peripheral and portal areas. (B) Fat stain of liver shows parenchymal cells honeycombed with multiple small droplets of fat.

Clinical diagnosis

Acute viral hepatitis, fulminant

Dr. Bruno's diagnoses

1. *Acute fatty metamorphosis of the liver associated with pregnancy*
2. (*Hepatic insufficiency*)

Pathologic report

William B. Ober, M.D.: It is always difficult to select a problem case for the director of the Medical Service that he is not already acquainted with. Therefore, when I received the sections of liver in this case from a colleague at another institution, I thought I would be able to set a trap for Dr. Bruno. But, with his customary penetrating analysis, he has eluded the snare and come up with the right answer. The material in this case was graciously furnished by Leslie Lukash, M.D., medical examiner of Nassau County, and I am very grateful to him for the opportunity to present it.

The fundamental lesion was that of acute fatty metamorphosis of the liver associated with pregnancy as was described previously.[6, 7] The liver was somewhat larger than average, weighing 1,820 Gm., in contrast to most of the reported cases in which there appears to have been a moderate reduction in size. It was soft, and on section the surface had a yellowish cast. The lobules appeared swollen and somewhat blurred. There was no overt necrosis or scarring. A microscopic examination revealed the characteristic lesion as described by Sheehan and later observers (Figs. 1 and 2). Although most centrilobular areas showed no loss of cells and had a normal reticulum pattern (Fig. 3A), occasionally one could demonstrate areas where the reticulum framework had collapsed partially and condensed (Fig. 3B), presumably indicating that parenchymal cells had fallen out without a trace. There was no inflammatory reaction in such sporadic foci. Possibly such observations can explain the loss of liver substance without overt necrosis. Sections stained for collagen did not show any fibrosis.

Dyson[8] has summarized the cases of this

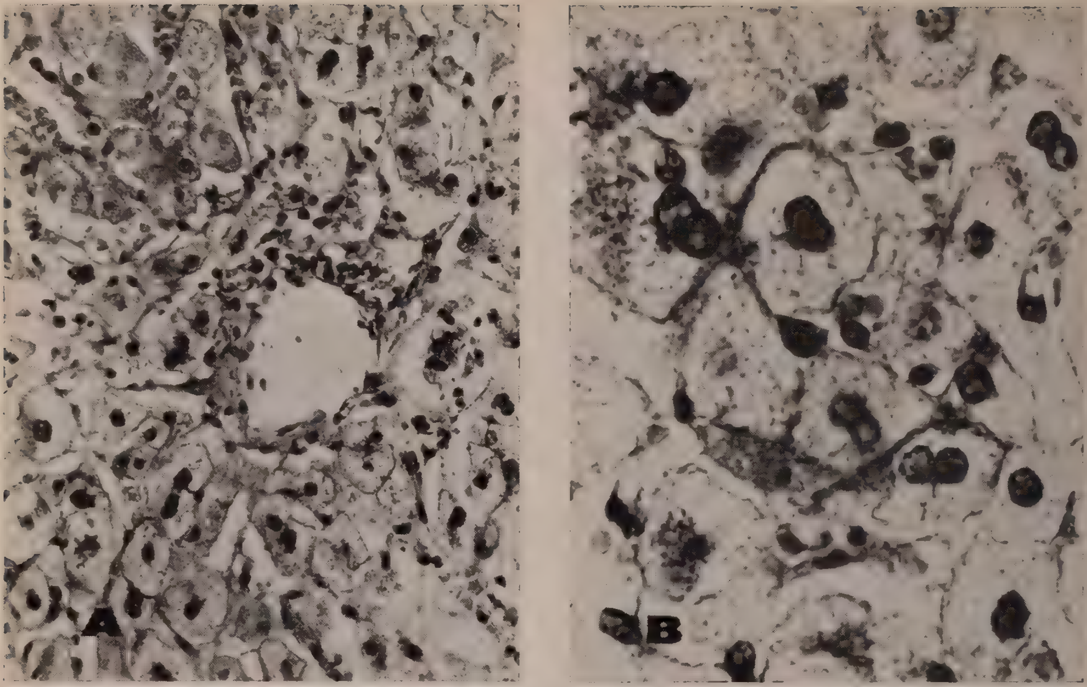

FIGURE 2. (A) Medium-power view of central vein in liver lobules showing a few lymphocytes in paracentral location. This was the maximal degree of inflammatory reaction. (B) High-power view of liver parenchyma showing fine fatty vacuolation of cytoplasm, many binucleate cells, and some variation in nuclear size and chromatin pattern.

entity in the literature. The maternal mortality is 86 per cent, and the fetal mortality is 74 per cent. Most of the deliveries result in stillbirths; occasionally the child will survive for a few hours. There is a paucity of information regarding the histopathologic findings in the children.

I have had the opportunity to study 5 unreported fatal cases including the present one, and 3 of these patients have had the additional finding of acute pancreatitis. The present case is one of these, and sections from the pancreas showed a conventional, acute, inflammatory exudate with fat necrosis (Fig. 4A). Microscopic observations on the pancreas included observations which would support two of the theories of pathogenesis of acute pancreatitis now current. In one area (Fig. 4B) there was inspissation of secretions within the pancreatic ductal system, and the wall of the duct was inflamed. In another area (Fig. 4C) there was fibrin thrombosis of an intralobular blood vessel with surrounding inflammatory exudate. This patient also had a slightly thickened gallbladder and many small gallstones, but the common bile duct was clear. She is the only patient with this form of liver disease to have had concomitant cholelithiasis, and I am willing to ascribe a mild degree of portal pleocytosis to it, but I do not think it played any role in the pathogenesis of the hepatic lesion. Neither of the other 2 patients who had acute pancreatitis had gallstones, and both of them showed a more extensive, more hemorrhagic pancreatic lesion.

There are many things about this entity that we cannot explain. Such basic questions as how the fat gets into the liver and why the patients die so rapidly remain unsolved. Also, just why 3 out of 27 patients, or 11 per cent, should have an associated pancreatitis remains unaccounted for. It is a small comfort to say that many patients with pancreatitis have fatty livers and/or biliary calculi. The mechanism is not understood.

Last, in the present case there is one observation which I offer with some reserva-

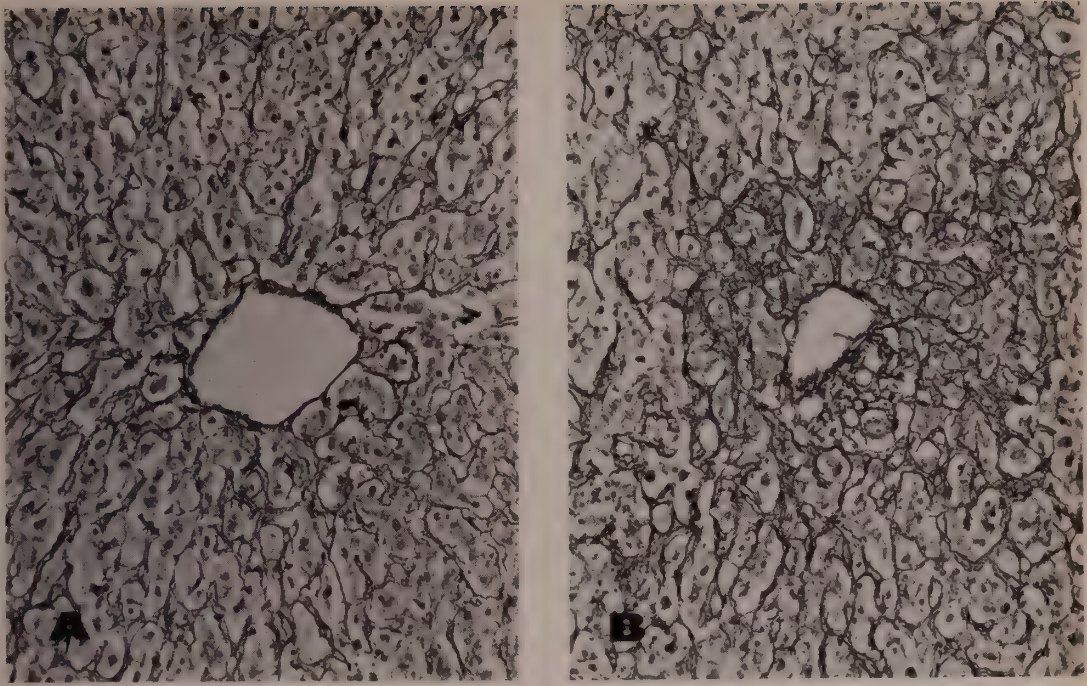

FIGURE 3. (A) Reticulum stain of centrilobular area of liver showing normal pattern. This was present in well over 80 per cent of the lobules. (B) Reticulum stain of liver showing collapse of silver-staining fibers with presumptive loss of liver cells in the absence of inflammation or overt necrosis. Same magnification as (A).

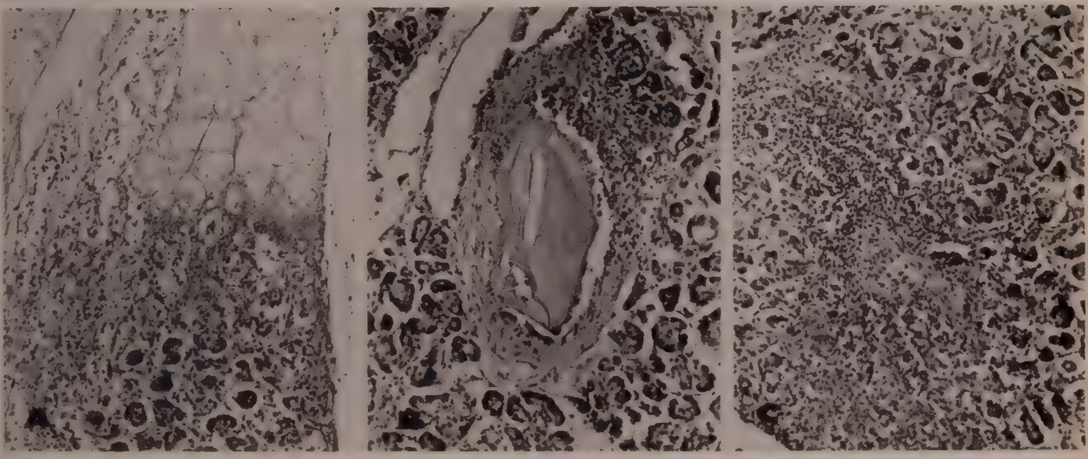

FIGURE 4. (A) Peritoneal surface of pancreas showing acute inflammatory exudate and fat necrosis. (B) Interlobular pancreatic duct with inspissated secretions in lumen and inflammatory exudate extending through its wall into the exocrine parenchyma. (C) Area of inflammation in a pancreatic lobule. The exudate surrounds a thin-walled vascular structure which is occluded by a fibrin thrombus.

tions. In an occasional liver cell nucleus I was able to detect a round, dense structure which resembled an inclusion body (Fig. 5). Also, I was able to identify less dense structures in certain nuclei which might be early or transitional forms of an inclusion body. Whether or not these structures are true inclusions awaits further study. It is really

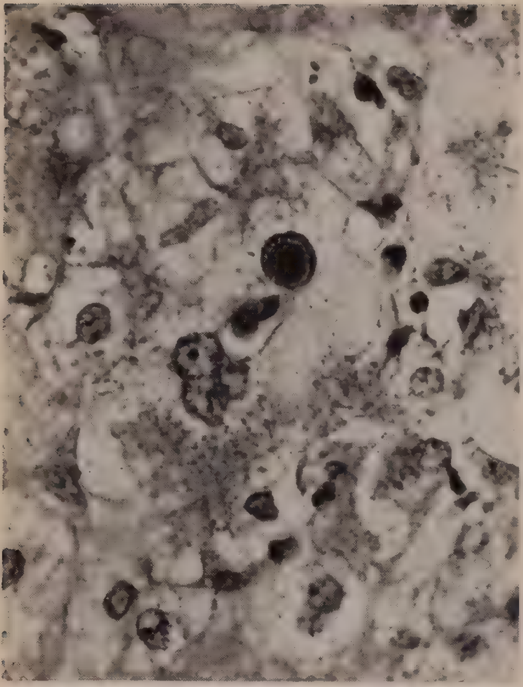

FIGURE 5. A fat-laden liver cell exhibits a dense, dark-staining intranuclear structure reminiscent of an inclusion body.

premature to guess their nature or to imply that they are viral, either in nature or effect, but such observations indicate the need for closer scrutiny of the lesion and its pathogenesis.

Anatomic diagnoses

1. *Acute fatty metamorphosis of the liver associated with pregnancy*
2. *Acute pancreatitis*
3. *Chronic cholecystitis and cholelithiasis*
4. *Bronchopneumonia*
5. *Status postpartum, three days*

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Broken foot bone no bar to army duty

Army podiatrists at Fort Leonard Wood and other posts have developed a way to keep soldiers on the job even after they have broken one or more small bones in the foot. Such breaks, in the past, almost automatically called for a plaster cast and up to a month on the shelf.

Now, according to a paper delivered at the meeting of the American Podiatry Association, August 16, 1962, by Lt. Richard H. Lanham, a small steel bar inserted in a regular combat boot will keep the fracture immobilized so that the soldier can perform all but the most strenuous combat training.

These minor foot fractures occur far more frequently among military personnel than among civilians. They are caused primarily by long marches, jumping, and other forms of extraordinary physical activity.

If soldiers, especially recruits, are placed in a cast following the discovery of one of these breaks, they are lost to the command for at least three weeks. In the case of recruits who serve on active duty for only six months and then enter the reserve, this often meant they would lose most of their basic training time and have to start over again.

But by wearing the combat boot with the steel bar fitted under the fracture, the soldier can be placed on limited duty, attend all regularly scheduled classes, and lose little actual training time. He will miss only marches and physical training that exert pressure on the affected part of the foot.

During the three to four weeks of this program, callous forms and healing takes place just as if the soldier was immobilized in a cast.

To date it has not been necessary to order any of the soldiers so treated to bed during the recovery period.

Nutrition Excerpts

Prepared with the cooperation of the faculty
of the Graduate School of Nutrition,
Cornell University, Ithaca, New York

DAPHNE A. ROE, M.D., Editor

Metabolic Obesity

J. L. GAYLOR, PH.D.
Ithaca, New York

CONSIDERABLE EMPHASIS is being given to studies of obesity, cardiovascular disease, and the nutritional properties of lipids. Regardless of whether or not abnormal lipid metabolism is basic to various syndromes, or whether or not the participation of lipids in cardiovascular disease is of paramount importance, a large body of information about lipid metabolism is being collected. A limited number of reports about lipid metabolism in human beings have appeared, as well as some initial experiments dealing with the biochemical aspects of human obesity. This brief review summarizes some of the current information about lipid metabolism and relates it to those cases in which lipid metabolism in obese subjects may differ from that in normal subjects.

Significance of adipose tissue metabolism

Before 1948, adipose tissue was assumed to be a storage depot of lipid which was utilized only during starvation or physiologic stress. Present evidence indicates that adipose tissue has three important functions: to synthesize triglycerides from serum lipids and glucose; to store the triglycerides; and to release the triglycerides into the plasma in the form of albumin-bound, free fatty acids.* The biochemical reactions by which these processes occur are normal, well-characterized reactions that have been described in recent reviews.[1,2] Hence, the net biochemical contribution of adipose tissue to the animal is the conversion of serum glucose to serum free fatty acids. When a subject is in caloric balance of intake and expenditure, the rate of formation and release of fatty acids in adipose tissue are also in balance. In times of caloric expenditure, the rate of release of free fatty acids exceeds formation; in times of caloric excess, the rate of synthesis exceeds the rate of release with resulting weight gain.

The unique property of adipose tissue is that the synthesis and release of free fatty acids occur at a rapid rate during all nutritional states. Indeed, it has been observed that the half-life of the plasma free fatty acids in dogs is approximately two minutes.[3] Similar values have been reported for other species including man. This rate of turnover, with no regard to the recyclization of fatty acids, is equivalent to 1,000 to 2,000 calories per day in adult human beings, or a very significant portion of one's daily caloric expenditure. Hence, because much of our caloric expenditure is mediated via rapidly metabolizing adipose tissue, minor changes in the metabolism of this tissue may significantly affect fat deposition. The retention of 1 per cent or 20 calories per day would result in a weight gain of at least 2 pounds per year.

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* Various authors refer to the free fatty acids (FFA) as nonesterified fatty acids (NEFA) or unesterified fatty acids (UFA). These terms equivalently describe the albumin-bound, free fatty acids of plasma.

Samples of lipids from human adipose tissue were analyzed by Hirsch *et al.*[4] with as little as 30 mg. of tissue obtained by aspiration. The gross composition of fatty acids was the same in both normal and obese subjects. Most of the differences observed between the fatty acid composition of adipose tissue from various individuals were ascribed to intakes of different dietary fats.[5] Therefore, chemical analysis alone does not indicate an altered adipose tissue metabolism in obese subjects. More refined metabolic studies are needed.

Human metabolic obesity

Certain lines of evidence indicate the possibility of an inheritable obesity. The inborn abnormality must be manifest as a metabolic lesion which may be determined with studies of fat metabolism. Although earlier studies were limited by the lack of an appropriate experimental animal, a genetically obese mouse was found to be particularly suited for such investigations. In addition to bearing obese offspring, this mouse also produced normal offspring in the same litter. Fat metabolism was studied in such mice and compared with normal littermates or littermates rendered obese by hyperphagia. The rate of synthesis of fatty acids in adipose tissue from the genetically obese mouse was 5 to 10 times greater than that in the littermate.[6] In similar studies the adipose tissue of the genetically obese mouse appeared to differ enzymatically both from normal mice and from mice rendered obese by hyperphagia.[7] Appropriately, this genetic difference has been called metabolic obesity.[7]

Others have observed that human obesity may be similarly classified. A small fraction of obese patients have been differentiated from excessive overeaters by lipid tolerance tests,[8] by the rate of turnover of plasma free fatty acids,[9] and by the clinical responses of obese individuals to diets that are either low or high in calories.

Further supporting evidence for a biochemical lesion that results in metabolic obesity in human beings is suggested by the carry-over of childhood obesity into adult life. For example, Abraham and Nordsieck[10] observed that twice as many overweight boys became obese men as did normal or underweight boys; similarly, five times as many overweight girls as normal-weight girls became overweight adults. Whereas a certain percentage of these increases were the result of psychologic and emotional disturbances, and of long-established food habits, this incidence of childhood and adult obesity is great enough to suggest a biochemical lesion in at least a portion of obese children who remain obese. Indeed, one would expect a biochemical lesion to appear in both the child and adult. It is likewise the practical experience that in individuals who have been obese since childhood, reduction of weight is more difficult to effect with low-calorie diets.

Site of a biochemical lesion

The actual site of a biochemical lesion in metabolic obesity appears obscure. Presumably because obese subjects are more refractory to weight reduction by low-calorie diets, a metabolically obese individual must have a more efficient utilization of dietary calories. There are relatively few biochemical alternatives whereby animals may derive more metabolic energy from a given number of dietary calories. One possible biochemical lesion was discussed by Gordon.[9] In his studies metabolically obese people had a lower respiratory quotient (RQ), indicating a greater combustion of lipid than that in people of normal weight. With no regard to the various metabolic pathways, the two general reactions that describe the conversion of carbohydrate (glucose) to carbon dioxide and water either directly (1) or via a fatty acid (palmitic acid) (2) are given in the following equations:

$$(1)\quad 12\ C_6H_{12}O_6 + 72\ O_2 \rightarrow 72\ CO_2 + 72\ H_2O,\ RQ = 1.0$$

$$(2)\quad a.\quad 12\ C_6H_{12}O_6 + 3\ O_2 \rightarrow 3C_{16}H_{32}O_2 + 24\ CO_2 + 24\ H_2O$$

$$b.\quad 3\ C_{16}H_{32}O_2 + 69\ O_2 \rightarrow 48\ CO_2 + 48\ H_2O$$

$$\text{Sum}\quad 12\ C_6H_{12}O_6 + 72\ O_2 \rightarrow 72\ CO_2 + 72\ H_2O,\ RQ = 1.0$$

If the carbohydrate is first converted to palmitic acid before combustion to carbon dioxide and water, as in (2) a and b, the sum of the reactions still yields an RQ of

1. Therefore, it is difficult to reconcile the reportedly low RQ in obese human beings because oxidation of glucose to carbon dioxide and water must consume the same amount of oxygen regardless of the pathway. Oxygen may not be generated by animals for use in these reactions. Essentially all of the oxygen consumed and carbon dioxide released must be via pulmonary exchange. In addition, no substantial difference is observed in the calculated amount of biochemical potential energy (adenosine triphosphate) that is formed.

Another alternative that may indicate a greater efficiency of caloric expenditure is reflected in the especially high tolerance of obese individuals for high-fat, ketogenic diets. Reportedly, diets containing as much as 90 per cent of the calories as fat result in no apparent ketonemia in many obese subjects.[9] However, the concentrations of ketones in the serum of normal individuals are greatly increased by such diets. Such increases may indicate a more rapid oxidation of the ketones in the obese subject. The obese subject appears to retain more ketones and be more efficient than normal human beings who presumably lose a certain amount of ketones in the urine. In a similar experiment Mayes[11] recently demonstrated that ketonemia in calorie-deficient, fat-fed rats was lowered by additional dietary fat. An analogous experiment may be designed for the metabolically obese human subject who apparently is burning a larger amount of fat.

Comment

Considerable advance has been made in the study of basic lipid metabolism. Simultaneously, research on the biochemistry of human obesity is developing. The following lines of evidence suggest that certain types of obesities in man may be metabolic in origin: the rapid rate of adipose tissue metabolism, experiments with genetically obese mice, lipid tolerance tests with human subjects, the concentration of plasma free fatty acids, and the apparent carry-over of a metabolic obesity from childhood to adult life. It is suggested that although these studies attempt to classify all types of obesity in human beings as either hyperphagic or metabolic, various degrees of metabolic obesity may be apparent within a population. Present studies may soon reveal whether or not a lesion in fat metabolism may chemically differentiate these obese human subjects.

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Number thirty-three in a new series of Nutrition Excerpts

Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by
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Prochlorperazine Dimaleate Poisoning

INCIDENT 1

Toxic Agent	*Age*	*Sex*
Prochlorperazine Dimaleate	8 years	Female

This eight-year-old child became ill on the day of her admission to the hospital. She was febrile, nauseated, and she had vomited. She also complained of a sore throat. A physician had prescribed prochlorperazine dimaleate suppositories. After the administration of 12 suppositories the patient became stuporous and developed convulsive seizures. The diagnosis on admission was prochlorperazine dimaleate intoxication and scarlet fever. The drug was withdrawn immediately, and after six days of hospitalization the patient made an uneventful recovery.

INCIDENT 2

Toxic Agent	*Age*	*Sex*
Prochlorperazine Dimaleate	8$^1/_2$ years	Female

The child's father, a pharmacist, called the Poison Control Center stating that his child had a severe reaction from syrup of prochlorperazine dimaleate. According to the Public Health Nurse who visited the home, the mode of onset was as follows: The child became ill with nausea, vomiting, abdominal pains, loose stools, and a temperature of 101 F. The family physician prescribed syrup of prochlorperazine dimaleate, 1 teaspoon (5 mg.) four times daily.

After two days on this medication the child became rigid with her head turned to the side and the tongue protruding, was unable to swallow, and presumably had excruciating pains at the base of the skull. The upper extremities were rigid. The child was taken to a nearby hospital.

On admission to the hospital, five days after the onset of the acute illness and on the third day since the medication was started, the patient had a spasm of the left masseter muscle, "accoucher's position" of the right hand, generalized hyperreflexia, and a bilateral Babinski sign. There was no nuchal rigidity and no fever. About one-half hour following the admission to the hospital the patient's mouth was drawn to the left side in a spasm, she was unable to speak and drooled saliva, and both arms were extended in rigidity. The patient was coherent at all times. The spasms were intermittent, and after two hours the patient also had a laryngotracheal spasm, slight cyanosis, hyperpnea, and drawing of the head to the left side. The eyes also were turned to the left. The laboratory findings on admission were: Hemoglobin 14.5 Gm. per 100 ml.; hematocrit 42.3; white blood cell count 4,000;

73 polymorphonuclear leukocytes; 4 basophils; 18 lymphocytes; and a urine specific gravity of 1,028.

On the day following admission the seizures subsided, and the patient's neurologic test results were negative. The temperature was still elevated at 101 F., but otherwise the patient presented no problems.

After a period of hospitalization and supportive therapy the patient made an uneventful recovery.

Comment

Prochlorperazine dimaleate is a widely used tranquilizer and antiemetic and is a phenothiazine derivative.

Prochlorperazine 2-chloro-10-[3-(1 methyl-4 piperazinyl]-propyl) phenothiazine is available in tablets, spansules, suppositories, ampules, and as a syrup.

It has been claimed that prochlorperazine dimaleate is more potent than chlorpromazine hydrochloride and less toxic, but admittedly some of the side-reactions, particularly the extrapyramidal manifestations, are accentuated. The alarming extrapyramidal seizures including, as in our cases, a spasm of the masseter muscles, are not uncommon in children and cause grave concern to families and attending physicians. Other side-effects noted include drowsiness, dizziness, dermatitis, dysphagia, protrusion of the tongue, hypotension, insomnia, dystonia, muscular twitchings, central nervous system depression, weakness, torticollis, excessive salivation, carpopedal spasm, opisthotonos, ataxia, laryngospasm, jaundice, and liver, kidney, and hematopoietic disturbances. In the cases reported to the Poison Control Center most of the symptoms which were encountered abated with supportive and symptomatic therapy. Several cases, however, have been reported in the literature in which the extrapyramidal reactions resulting from prochlorperazine dimaleate were potentially life-threatening, causing laryngospasm with acute respiratory distress and requiring heroic therapy.[1]

It is believed that prochlorperazine dimaleate acts on the higher neural centers in the diencephalon, in the hypothalamus, and in the reticular substance. The tranquilizing effect is said to be due chiefly to its activity on the diencephalon, including the basal ganglia, and its antiemetic effect to be due to a medullary activity.

The therapeutic dose of prochlorperazine dimaleate is 5 mg. three times daily. When the spansule is used, a 10- to 15-mg. spansule is recommended for once-a-day administration. The usual dose of the syrup is 5 to 10 mg., one or two teaspoons, three times daily.

When prescribing for children, the lowest recommended dose should be administered, and the dosage should be based on weight and not on the age of the child. It never should be prescribed for children weighing less than 20 pounds. It never should be administered in comatose states or during states of depression because of its additive depressant effect. It also should be pointed out that the antiemetic action of prochlorperazine dimaleate may mask signs of an overdosage of some toxic drugs.

The recommended dosage for children is between 5 and 15 mg. per day depending on the child's weight. It should not exceed 7.5 mg. in children weighing between 20 and 30 pounds and not more than 10 mg. per day for children weighing between 30 and 40 pounds. In children weighing between 40 and 90 pounds, the daily total dose should not exceed 15 mg. per day.

A useful, simple test to detect as little as 0.031 mg. per liter of prochlorperazine dimaleate in the urine has been described by Heyman, Almudevar, and Merlis.[2] A drop of urine containing metabolized prochlorperazine dimaleate will give a yellow to violet or red color on a sulfuric acid resin paper which has been impregnated with a 2 per cent ferric chloride solution. The color and the intensity of the color varies with the amount of the drug ingested. Unmetabolized prochlorperazine dimaleate also may be detected in the gastric contents and the urine.

Treatment

In the main, the treatment is supportive and symptomatic. Gastric lavage may be helpful if it is done before six hours after the ingestion. Picrotoxin should not be administered. Levophed may be of value for the hypotension. Neo-Synephrine also has been of value. As a general stimulant, caffeine sodium benzoate has been found to be helpful. Epinephrine should not be administered, since it may cause a vasomotor reversal and a lowering of the blood pressure. Stimulants which may cause convulsions, such as Metrazol, should be avoided. Short-acting barbiturates may be of value in the control of convulsions. For the neuromuscular reactions, anti-Parkinson drugs, such as Cogentin, Pagitane hydrochloride, Kemadrin, and Artane hydrochloride have been reported as useful and effective.

For mild reactions small doses of phenobarbital may be given. Benadryl, 25 mg. intravenously, also has been reported to afford prompt relief from the extrapyramidal reactions. Intramuscular Demerol administration also was reported to afford "amazingly fast and complete relief of symptoms" in several patients, although no explanation could be given for the amazing effect.

Waugh and Metts[1] report a case of severe extrapyramidal motor activity induced by prochlorperazine dimaleate and its relief by the intravenous injection of diphenhydramine hydrochloride. This patient developed a severe reaction with life-threatening respiratory distress and laryngospasm. This grave situation was controlled promptly by the intravenous administration of an antihistaminic drug, 25 mg. of diphenhydramine hydrochloride.

The authors suggest that in some extrapyramidal reactions parenteral forms of anti-Parkinson drugs should be used for prompt therapeutic relief and that there are several such ingestible antihistaminic drugs available for such use.

It is well to point out that the side-reactions obtained following the use of prochlorperazine dimaleate and the other phenothiazines are not without danger, and the utmost care must be devoted to their treatment and prevention. Despite some unwarranted claims that the neuromuscular reactions are only "occasionally" encountered and will abate merely by reassuring the patient that the symptoms are transitory and reversible, the over-all incidence is about 15 per cent, and the side-effects are not all transitory. The symptoms may be very severe, alarming, and life-threatening, requiring heroic, prompt, therapeutic measures.

Physicians must be made aware of the potential hazards of these drugs, to use them judiciously, and to alert parents to the need for the careful handling and storage of these potent agents so that they may not be ingested accidentally by children.

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Number one hundred three in a series of Accidental Chemical Poisonings

Case Reports

Fatal Hepatic Necrosis Associated with Zoxazolamine Therapy

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Reports of hepatic toxicity manifested in patients being treated with zoxazolamine (Flexin) have recently appeared in the literature.[1-3] A similar case came under observation on the Neurological Service of the Brooklyn Veterans Administration Hospital in 1959, in which a patient with a chronic, spastic neurologic disease[4-6] received zoxazolamine, a muscle relaxant, with fatal outcome. The case report follows.

Case report

A twenty-seven-year-old Negro male was admitted to the Neurological Service of the Brooklyn Veterans Administration Hospital. At age twenty-two the patient had noticed the onset of a progressive loss of vision of the right eye and moderate difficulty in speaking clearly. One year later the right leg began to "drag." By the age of twenty-six blurred vision in the left eye, progressive right-sided weakness, and left lower extremity weakness developed. The symptoms were progressive and not marked by remissions.

At the time of admission a physical examination revealed a well-developed and well-nourished male. Indistinct speech with scanning was present. There was no impairment of mental faculties, and the general physical examination showed normal findings.

Neurologically, the gait could not be tested as the patient could not walk. There was marked weakness of the lower extremities, and the right upper extremity was weaker than the left. There was no evidence of atrophy or fasciculations. The deep tendon reflexes were hyperactive. A Babinski toe sign was present on the right, and abdominal and cremaster reflexes were absent. Finger-nose and heel-knee tests revealed a moderate intention tremor bilaterally. The modalities of sensation were intact. The visual field on the right was contracted by gross confrontation, and there was pallor of the right disk. Horizontal nystagmus was present on gaze both to the right and to the left. The right pupil was slightly larger than the left, and both pupils reacted poorly to light. The ocular motility was normal. The remainder of the cranial nerves were not grossly involved.

An x-ray examination of the chest and skull showed normal findings. A serologic test for syphilis gave negative results. Other laboratory data showed normal findings, as did an electroencephalogram. A spinal fluid examination revealed negative results of a cardiolipin complement fixation test, 4 polymorphonuclear cells per cubic centimeter, and a total protein of 37 mg. per 100 ml. The diagnosis of multiple sclerosis was made at the time of admission.

The patient was referred to the Department of Physical Medicine and Rehabilitation for treatment, but there was essentially no improvement in the neurologic condition. After about two years, physical and occupational therapy was discontinued as the patient became extremely passive and withdrawn.

Because of increasing spasticity, mainly of the lower legs, the patient was given zoxazolamine, 250 mg. four times daily, starting on December 19, 1958. There was some relief of the spasticity. In addition, in January, 1959, as part of a general study of a new drug, the patient began to receive sodium succinate (Soduxin) 1.5 Gm. intravenously three times weekly. There was no objective improvement in the neurologic condition. The patient continued to have a coarse intention tremor and marked difficulty in speaking.

It was noticed on April 29, 1959, that the patient was deeply jaundiced. He had no other complaints. The liver was palpable 3 fingerbreadths below the right costal margin, and the stool was brown. The urine was strongly positive for bile, and a two-hour, 90-ml. sample contained 0.3 Ehrlich units of urobilinogen. On May 1, 1959, the following studies were obtained: total serum bilirubin, 30.4 mg. per 100 ml.; direct serum bilirubin, 7.6 mg. per 100 ml.; prothrombin time, 10.5 per cent; total serum protein, 7.9 Gm. per 100 ml.; serum albumin, 4.8 Gm. per 100 ml.; serum globulin, 3.1 Gm. per 100 ml.; cephalin flocculation, 3 plus; alkaline phosphatase, 11.2 King-Armstrong units; bleeding time, 4 minutes; Lee-White clotting time, 16 minutes, 40 seconds; white blood cell count, 10,000 per cubic milliliter; hematocrit, 52; hemoglobin, 16 Gm. per 100 ml.; and erythrocyte sedimentation rate (Wintrobe), 5 mm. per hour.

On May 2, 1959, the patient refused to eat. On the next morning he was noted to be agitated and disoriented. At this point the administration of zoxazolamine and sodium succinate was stopped. During the afternoon the patient lapsed into a profound coma from which he never recovered. Shortly thereafter a generalized spasticity and hyperreflexia developed. Twenty per cent glucose in water was given via a venous cutdown, and the patient also received neomycin orally (2 Gm. every six hours) and cleansing enemas. Hydrocortisone was administered intravenously, 300 mg. daily for the first five days with a gradual reduction thereafter. Because the patient was febrile he received chloramphenicol, 1 Gm. every six hours intramuscularly. Two days subsequent to the onset of the coma the patient was given 25 mg. of sodium-potassium glutamate for three successive days. There was only a transient return of pupillary reflexes. The SGOT (serum glutamic oxalacetic transaminase) was 305 units (normal less than 40 units) on May 5, 1959. The next day the serum ammonia was 200 gamma per 100 ml. After five days in coma, chemosis of the conjunctiva developed as well as edema of the hands and feet. Steroids were gradually reduced from that time on. Repeat studies revealed: total serum bilirubin, 34.1 mg. per 100 ml.; total serum protein, 6.5 Gm. per 100 ml.; serum albumin, 3.4 Gm. per 100 ml.; and serum globulin, 3.1 Gm. per 100 ml.

Slowly the urinary output began to fall, and the blood pressure required vasopressors for maintenance. Edema of the hands and feet increased, and a moderate amount of ascites developed. The liver was no longer palpable, and on percussion there was practically no liver dullness.

The blood urea nitrogen rose to 88 mg. per 100 ml. as the urinary output fell. The urinary electrolytes as well as the serum sodium were low. The patient expired on May 11, 1959, eight days after lapsing into coma.

The postmortem examination was limited to an abdominal incision. Grossly the liver was flabby and shrunken with the capsule wrinkled, and it weighed 700 Gm. The cut surface was pale yellow-brown and showed a loss of normal architecture. The photomicrographs (Fig. 1) illustrate the histology. There is an almost complete loss of parenchymal cells. The periportal structures can be identified. The high-power study of the periportal fields reveals extensive, mainly mononuclear cell infiltration and cholangioles plugged with inspissated bile (Fig. 1B). The anatomic diagnosis was acute hepatic necrosis with recognition that the pathologic differentiation of the probable etiologic agent, virus or hepatotoxic drug, was not possible.

Comment

The fatal acute hepatic necrosis in this case can be attributed to one of two etiologic factors. First, the patient could have developed a viral hepatitis. However, although the patient had received medication by injection, there were no known cases of homologous serum jaundice in the hospital, and the patients with infectious hepatitis would have been isolated on an infectious

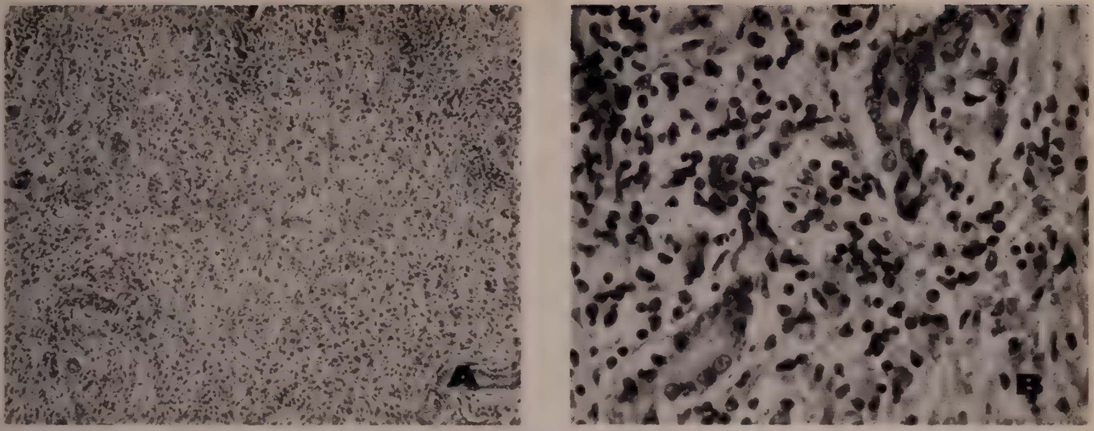

FIGURE 1. (A) Low-power photomicrograph of liver showing complete loss of parenchymal structure. Periportal structures and central vein (in center) are recognizable. (B) High-power photomicrograph of periportal area showing predominant mononuclear infiltration and bile plugs in cholangioles.

disease ward. It was also unlikely that the patient was in close contact with a carrier of infectious hepatitis. The absence of a prodromal period prior to the onset of jaundice with symptoms such as anorexia, weight loss, fever, headache, arthralgia, or urticaria also speaks against a primary viral cause in this case.

Second, the patient was receiving two drugs, sodium succinate and zoxazolamine, each of which might reasonably be suspected of being hepatotoxic. Sodium succinate has been used clinically since about 1948 in the study of the treatment of barbiturate poisoning.[7–9] Also sodium succinate has been used as an objective test of circulation time.[10] A review of the literature reveals no report of hepatotoxicity.

On the other hand, zoxazolamine, which has been in clinical use for several years both as a muscle relaxant and as a uricosuric agent,[11] has been noted to have mild side-effects such as gastrointestinal symptoms, rashes, dizziness, and drowsiness.[4,12] These reactions usually can be controlled by administering the drug with meals, reducing the dosage, or discontinuing it entirely.

However, other more serious complications have also been reported with the use of zoxazolamine. Cohen[13] and Streitz[14] reported cases of transient nephropathy developing shortly after the administration of small amounts of zoxazolamine. Hypersensitivity was the most likely mechanism here, although the deposition of urate crystals in the tubules owing to the uricosuric action of the drug may have been a contributing factor.

Finally, zoxazolamine has also been implicated in fatal liver necrosis. Hoffbauer *et al.*[1] described 2 cases of death from acute hepatic necrosis in patients receiving zoxazolamine for neuromuscular disorders. The first patient became jaundiced following a short period of anorexia after having taken the drug for thirty-five days. Coma developed rapidly. A postmortem examination revealed a liver weighing 1,100 Gm. with a shrunken capsule and showing diffuse hemorrhagic centrolobular necrosis. The second patient became jaundiced about one and a half months after taking zoxazolamine, 250 mg. three times daily. Death in coma ensued two weeks later. At the postmortem examination the liver was small and partially flabby, grossly revealed acute red and yellow atrophy, and microscopically showed diffuse necrosis. It was felt that fulminant viral hepatitis could not be excluded, but the possibility of a drug idiosyncrasy was more likely. Popper and Schaffner[2] reviewed these cases of Hoffbauer *et al.*[1] and included zoxazolamine in their list of drugs capable of inducing acute hepatic necrosis. More recently Carr and Knauer[3] have reported another case of fatal hepatic necrosis in a patient receiving zoxazolamine.

The case presented here is essentially the same as those of Hoffbauer *et al.*[1] and Carr and Knauer,[3] the only difference being that here the patient received zoxazolamine for about four months before showing any symptoms. Sudden intense jaundice developed and was followed shortly by rapidly deepening coma. No therapeutic regimen was found to be effectual. The reason for this became clear when at postmortem an examination of the liver revealed a picture of acute necrosis which was indistinguishable from acute necrosis of viral origin.

Although definitive proof that this patient did not succumb to viral hepatitis cannot be shown, the bulk of the clinical evidence indicates that zoxazolamine can be implicated as the agent responsible for the acute hepatic necrosis. At the present time our knowledge does not permit a clear delineation of the pathogenesis of this lesion. However, the mechanism appears to be unrelated to that responsible for the intrahepatic cholestasis which is seen typically, for example, with some tranquilizers. The occurrence rate of drug-induced hepatic necrosis is characteristically very low, but it is well to keep in mind, as illustrated by this case, that treatment with presumed innocuous medications is not without potential risk.

Summary

A fatal case of acute hepatic necrosis developing in association with the administration of zoxazolamine is presented. The patient was also receiving sodium succinate intravenously; no report of hepatic toxicity has ever been recorded with the use of this drug.

Zoxazolamine has been implicated in cases of mild nephrotoxicity and in 2 cases of fatal acute massive hepatic necrosis. Although an outside possibility exists that in the present case liver disease was secondary to a hepatotrophic virus, it seems more reasonable to conclude that the acute hepatic necrosis was caused by zoxazolamine.

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High Serum Alkaline Phosphatase*

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SERUM ALKALINE PHOSPHATASE levels beyond those known to such an experienced observer as Bodansky[1] must be rare indeed. An alkaline phosphatase value ranging between 400 and 500 Bodansky units was found in the serum of a patient with pancreatic carcinoma. Because of these extraordinarily high values, this case is recorded.

Case report

A sixty-eight-year-old white male was hospitalized elsewhere on February 28, 1959, because of suspected carcinoma of the liver. Five weeks previously his abdomen had become distended, and the distention had progressed. Three weeks before his admission to the hospital he noted darkening of the urine and, thereafter, anorexia, nausea, and vomiting. His past history indicated a possible myocardial infarction in 1949 and the incision and drainage of a rectal abscess in 1954. A history of alcoholic intake of possible significance was noted. A weight loss had occurred in the past thirteen months.

Ascites was present at the time of the initial hospitalization, and an irregular liver edge was felt 3 cm. below the costal margin. Slight jaundice had been present. A cell block made from the peritoneal fluid showed carcinoma.

On March 11, 1959, the patient was transferred to the Naval Hospital where he was seen to be emaciated and very ill. The vital signs were not remarkable. The scleras were icteric. The abdomen was soft and moderately distended. The firm, nontender liver edge was felt 5 cm. below the costal margin. The spleen was thought to be felt 3 cm. below the left costal margin. Two days after this last admission a diagnostic tap of the peritoneum yielded yellowish, cloudy fluid. A cell block revealed carcinoma. The laboratory studies are given in Table I. X-ray films of the chest and upper gastrointestinal series were not available for review, but the radiologist's reports on these studies mentioned no bony lesions. The ascites increased, and the patient deteriorated rapidly, expiring on the fifteenth hospital day.

The principal findings at necropsy were related to a neoplasm which was found in the midportion of the pancreas. The tumor presented signs of a very dense, sclerosing mass extending into the surrounding peripancreatic soft tissues and into the base of the mesentery, including the adjacent lymph nodes. The mass was adjacent to and undoubtedly compressed the bile duct, although this structure was not involved directly by an invasion by the tumor. In addition to the direct extension of the tumor, there were innumerable tiny tumor implants and metastases over all the omental, peritoneal, and mesenteric surfaces. Most of these were small, and there was no evidence of massive tissue destruction caused by the implants. Associated with the tumor implants over the serosal surfaces there were 1,500 cc. of cloudy, thin, ascitic fluid and numerous fibrous bands between the loops of the small bowel.

Histologically, the neoplasm was found to consist of well-differentiated, glandular-type cells which had invoked a marked scirrhous reaction. These well-differentiated neoplastic cells were of the type characteristically associated with pancreatic ductal carcinoma and were found throughout the sclerosing tissue previously described and in the lymphatic spaces in the immediate area. The tumor implants were composed of identical sclerosing carcinoma tissue.

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* The opinions and statements of the authors are personal and do not necessarily reflect those of the Naval Service at large.

Secondary findings included a marked degree of coronary arteriosclerosis with the residua of an old myocardial infarction and coronary thrombosis. The liver showed a mild degree of chronic passive congestion as well as probably early biliary cirrhosis. The latter was indicated by increased perilobular fibrosis, chronic and acute inflammatory cells, and inspissated bile in the ducts as well as in a rare canaliculus. There were no metastatic deposits in the liver on gross or microscopic examination. In the colon were several small polyps, all of which proved to be histologically benign. The spleen contained an old infarct. The gastrointestinal tract exhibited no gross abnormalities other than the serosal tumor implants. There were no areas of destruction of the bowel mucosa by a tumor or other process which would explain the markedly increased level of alkaline phosphatase. The kidneys exhibited a moderate degree of nephrosclerosis.

Comment

The most interesting clinical feature in this case was the remarkably high level of alkaline phosphatase which ranged between 400 and 500 Bodansky units. These high levels were found on consecutive specimens and were confirmed in three separate laboratories. No clear cause for the finding was evident at the postmortem study, although the compression of the bile duct, coupled with an elevated serum cholesterol, suggest hepatic obstruction as the mechanism.

The serum alkaline phosphatases are nonspecific phosphomonoesterases with an optimum pH of 9. Most of the enzyme activity appears in the gamma globulin with some in the beta globulin fractions of the serum. These nonspecific phosphatases, unlike specific phosphatases, such as glucose-6-phosphatase, which are more selective in substrate, act on the orthophosphoric esters of a variety of phenolic, alcoholic, sugar, and other compounds. Two types of activity can be demonstrated: hydrolase and phosphotransferase. At very low concentrations of substrate, such as might be encountered intracellularly, the optimum pH of the alkaline phosphatase of the intestinal mucosal cell is 7.35.[2] The enzymes are globulins of a low molecular weight and are found in every tissue in the body, being noticeably present in bone, liver, kidney, and the mucosa of the small bowel. They are found in blood, thoracic duct lymph, bile, and feces, but not in the urine.[3] They are normally detectable in a low concentration in a minority of polymorphonuclear leukocytes.[4]

The methods commonly in use for the measurement of serum alkaline phosphatase include those of Bodansky and of King and Armstrong. The Bodansky method employs beta-glycerophosphate, and the King-Armstrong method employs phenylphosphate as substrates. The normal range in the Bodansky method is 1.5 to 4 units and in the King-Armstrong method 3 to 13 units. The level of the enzyme in the serum represents a dynamic balance between the rate of entry into the circulation and the rate of disposal by excretion, degradation, or deposition in the tissues. The consensus at the present time is that changes in activity, such as those found in disease, represent genuine changes in enzyme concentration.[2]

The theories concerning the origin of alkaline phosphatase in the serum include the proposals that it comes primarily from bone or, alternatively, that it comes primarily from the liver.[2] As a matter of fact, the site of the origin of the enzyme is not established.

The function of the enzyme appears to vary with the tissue in which it is found. One hypothesis assumes that the alkaline phosphatase of the osteoblast is concerned with the formation of the fibrocollagenous framework or matrix of bone, rather than with the impregnation of that framework with calcium salts.[5] In many hepatic obstructive diseases, the alteration in serum proteins suggests that alkaline phosphatase may be related to the synthesis of protein.[3]

The serum alkaline phosphatase may be elevated in a variety of bony and hepatic

TABLE I. Laboratory studies at Naval Hospital, 1959

Procedure	March 12	March 16	March 20	March 21	March 25
Serum alkaline phosphatase (Bodansky units)	...	440	>500	...	...
Serum bilirubin, total (mg. per 100 ml.)	...	11.7	...	...	...
Serum bilirubin, direct (mg. per 100 ml.)	...	7.6	...	...	...
Serum cephalin flocculation (forty-eight hours)	...	2+	...	...	...
Serum thymol turbidity (MacLaglen units)	...	1.8	...	...	...
Serum cholesterol, total (mg. per 100 ml.)	...	375	...	...	...
Serum albumin (Gm. per 100 ml.)	...	3.4	...	...	3.3
Serum globulin (Gm. per 100 ml.)	...	2.5	...	...	2.2
Prothrombin activity (per cent)	...	45	...	...	...
Hemoglobin (Gm. per 100 ml.)	13.2	...	...	13.2	...
Hematocrit	48	...	...	42	...
Blood urea nitrogen (mg. per 100 ml.)	...	...	...	...	98
Peritoneal fluid-total protein (Gm. per 100 ml.)	...	...	...	...	4.8
Peritoneal fluid-specific gravity	...	...	...	...	1.021
Peritoneal fluid-alkaline phosphatase (Bodansky units)	...	...	...	...	17*

*Specimen stored two days before determination done. See text for discussion of low values.

diseases. The former group is characterized by the overactivity of substantial numbers of osteoblasts and includes Paget's disease, hyperparathyroidism on occasion, rickets and osteomalacia, osteoblastic sarcoma, and carcinoma metastatic to bone. Hepatic disorders with an elevated alkaline phosphatase generally are characterized by an element of obstruction at some point in the biliary drainage system from the canaliculus forward. The disorders in this group include extrahepatic biliary obstruction by a tumor, stricture, or stone; intrahepatic cholestasis produced by intrahepatic masses or infiltrative lesions; drug-induced hepatotoxicity of the cholestatic type; primary biliary cirrhosis; and viral hepatitis with cholestasis.[2,3,6,7]

Levels of 200 Bodansky units have been recorded in florid rickets and up to 100 Bodansky units in biliary cirrhosis, values considerably below those noted in the present report.[2]

Although the ordinary alkaline phosphatase in routine serum examinations is fairly stable to freezing, the enzyme in this case fell to levels of 35 units after freezing. A possible explanation for the finding of a decrease in the alkaline phosphatase value after freezing was suggested by Bodansky,[1] who noted that in carcinoma of the pancreas, particularly with metastases, there frequently may be associated a high proteolytic activity of the serum. He suggested that such proteolytic activity might destroy the alkaline phosphatase during the period of storage.

Summary

A case is presented with the finding of a remarkably elevated serum alkaline phosphatase, confirmed in three separate laboratories, in a case of carcinoma of the pancreas.

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Sarcoma of the Pancreas

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SARCOMA OF THE PANCREAS is a rare disease. From 1931 to 1961 at the Maria Hospital in Helsinki, Finland, there has been 1 proved case of sarcoma of the pancreas. During this approximately thirty-year period a total of 6,367 autopsies were performed, and 37,696 roentgenologic examinations of the upper portion of the gastrointestinal tract were done. The paucity of reports in the literature also indicates that the tumor is quite infrequent.[1-5]

Poppel[6] collected the points of interest in the reported cases and found that the macroscopic appearance of the tumor is nearly always the same. It appears to be smooth, regular, often fluctuating, and resembles a cyst. Only rarely does it appear nodular and hard. The cystic appearance must be attributable to the action of the pancreatic ferments. The microscopic appearance likewise varies little, for most of the tumors described were of a spindle-cell type.

The clinical symptomatology does not differ from that of a pancreatic cyst, since in most instances the sarcoma constitutes the degeneration of a cyst. Perhaps the more marked pain, the more rapid increase in the volume of the tumor, the presence of ascites, and the marked loss of weight direct the attention toward the suspicion of a sarcoma.

The diagnosis is based chiefly on the roentgen appearance, although here, too, the signs of a pancreatic cyst will dominate the picture entirely. If the tumor is localized to the head of the pancreas, an enlargement of the duodenal loop, modifications of the site of the duodenal bulb, the absence of the mucosal fold markings, a diminution of peristalsis with gastric residue, and deformities of the stomach will constitute the most important signs. However, if the tumor is localized to the tail of the pancreas, the deformities of the stomach and colon, consisting chiefly of the displacement or pressure effect, will appear more in the foreground.

Case report

A forty-six-year-old male was admitted to the Maria Hospital on August 22, 1955. His family history revealed that his mother had died of carcinoma of the uterus and an aunt of carcinoma of the stomach. The past history revealed that he had suffered from dyspepsia for the past fifteen years, and a tonsillectomy had been done at the age of sixteen.

The patient was admitted to another hospital because of abdominal colic. A laparotomy performed on April 26, 1955, disclosed in the retroperitoneum a mass larger than two fists, which were attached firmly to the pancreas and to the aorta. The tumor was inoperable, and a specimen for histologic examination showed fibrosarcoma (Fig. 1). The patient was referred for radiation therapy, and he received a tumor dose of 2, 184 r in a period of seventeen days by a 190-kv. unit (target skin distance 60 cm., opposing two anterior and two posterior fields of 10 by 15 cm.). The treatments were discontinued because of abdominal colic and anemia. (The hemoglobin was 5.7 Gm. per 100 ml.). An exploratory laparotomy disclosed a hemorrhage from a tumor. Blood transfusions were given, and the patient continued to be observed in the outpatient department.

When the patient was admitted to the Maria Hospital, he appeared emaciated and cachectic. The pulse was 72, and the blood pressure was 150/90. An abdominal mass was palpable below the left costal margin. There was no clinical jaundice.

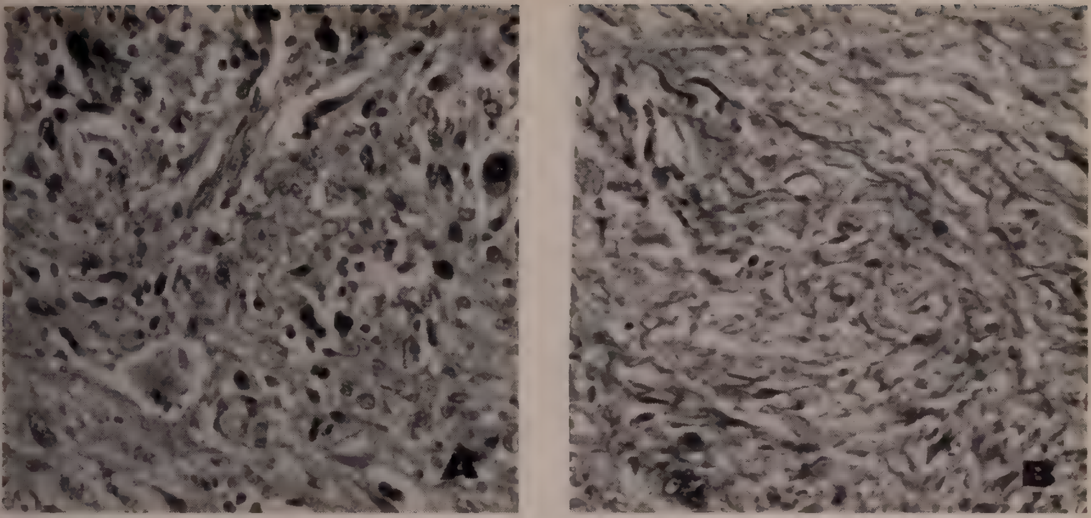

FIGURE 1. (A) Photomicrograph from a section of the pancreatic tumor. The biopsy specimen was taken at laparotomy on April 26, 1955, that is, before commencement of radiation treatment. Tumor appears medium-cellular and is composed of spindle and round cells that show considerable variation in size and shape with occasional giant cells. There is much production of collagen (Masson's trichrome stain). (B) Photomicrograph from a section adjacent to that in (A). The diastase periodic acid leukofuchsin stain shows a distinct PAS (para-aminosalicylic acid)-negative appearance. (×160)

A laboratory examination showed a hemoglobin of 11.3 Gm. per 100 ml.; red blood cell count of 3,400,000; and white blood cell count of 4,700. The blood sedimentation rate was 28 mm. in one hour (Westergren), and the Wassermann and Kahn tests produced negative findings. The blood sugar was 129 mg. per 100 cc. of blood. A gastric analysis showed no free acid and 12 degrees of total acid. The feces showed positive findings for occult blood. A urinalysis showed findings within normal limits.

A roentgen examination of the upper portion of the gastrointestinal tract on September 6, 1955, showed extrinsic pressure on the greater curvature aspect of the stomach (Fig. 2). The outline of the defect was smooth, and the mucosal pattern was normal. The finding was similar to that of a pancreatic cyst. A repeated course of radiation therapy was commenced, but the patient was too weak to continue the treatments after having received a tumor dose of 1,722 r in nine days (200 kv. convergent beam unit; single anterior port). The patient died on October 22, 1955.

An autopsy which was performed by

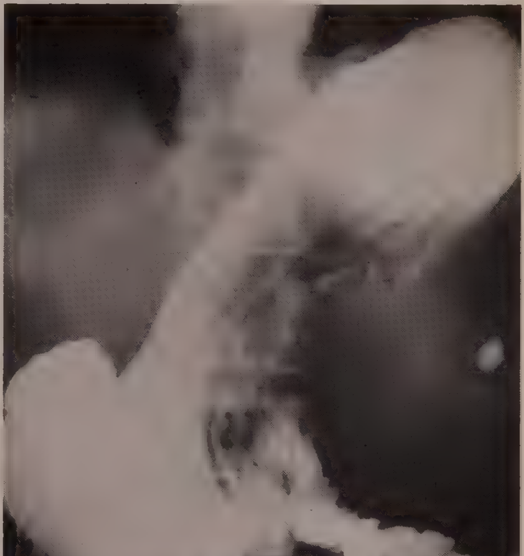

FIGURE 2. Roentgenogram of barium-filled stomach, supine position, shows a large extrinsic pressure defect on the greater curvature aspect. The outline of the defect is smooth and the mucosol pattern normal.

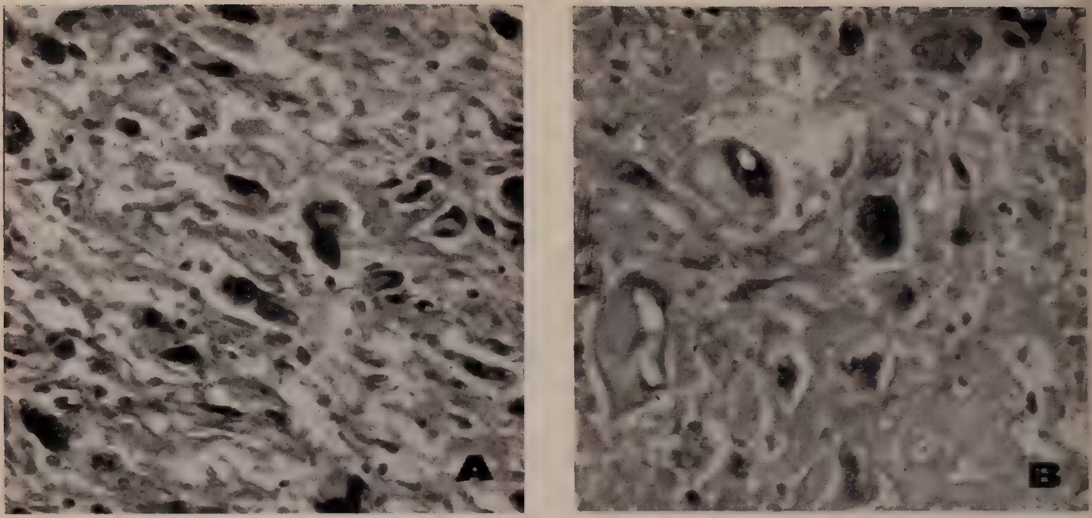

FIGURE 3. (A) Photomicrograph from a section of the pancreatic tumor. The biopsy specimen was obtained at autopsy on October 25, 1955, that is, after roentgen ray treatment of 3,906 r. The general histologic appearance resembles, in principle, that in Figure 1A. In addition, various types and degrees of retrogressive alterations, characteristic of the effect of radiation, are evident (Masson's trichrome stain). (B) Photomicrograph from a section adjacent to that in (A). Various types of cellular alterations characteristic of the radiation effect. At places there are signs indicating some recovery from the radiation damage. The diastase periodic acid leukofuchsin stain indicates that the tumor tissue is distinctly PAS-negative, whereas the ground substance depicts a weak PAS-positive nuance. (×160)

Prof. I. Wallgren revealed a cystlike hole containing fibrous masses between the spleen and the left kidney. The pancreas, particularly the tail, was infiltrated by a tumor. Metastatic nodules were found in both lungs. Microscopic sections of the pancreas and a lung nodule showed fibrosarcoma (Fig. 3).

Conclusion

A case of sarcoma of the pancreas is presented with special emphasis on the roentgenologic findings. This entity should be considered in the differential diagnosis of a pancreatic cyst.

Preoperatively it is impossible to differentiate between a benign cyst and a sarcoma of the pancreas. Therefore, keeping a patient under observation to follow the course of enlargement of "a pancreatic cyst" evidently is not adequate as treatment.

APOLLONKATU 23

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Histiomonocytic Leukemia Occurring in Patient with Hodgkin's Disease

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THE OCCASIONAL OCCURRENCE of acute leukemia complicating the course of the various types of lymphoma has been reported previously. Zeffren and Ultmann[1] reported that approximately 5 per cent of patients with reticulum cell sarcoma terminate with an acute leukemia, with the dominant cell type described as a myeloblast, monocytoid granulocyte, or immature reticulum cell. Lymphosarcoma is known to terminate in acute lymphoblastic leukemia.[2-5] Acute myeloblastic leukemia has been reported in a single case of giant follicular lymphoma.[6]

Leukemia occurring in patients with Hodgkin's disease has rarely been observed. Samwick, Cohn, and Swiller[7] reviewed the literature on this subject and reported a case of chronic granulocytic leukemia associated with Hodgkin's disease. Skworzoff[8] reported a case of acute myeloblastic leukemia and Hodgkin's disease occurring coincidentally in an eight-year-old girl. In both of these cases the presence of Hodgkin's disease was first recognized at the postmortem examination. Craver[9] described the case of a nineteen-year-old girl who developed acute monocytic leukemia one and one-half years after spray irradiation was given as therapy for Hodgkin's disease.

We have observed a patient with Hodgkin's disease who terminally developed acute histiomonocytic leukemia which was diagnosed clinically and by biopsy ante mortem and confirmed by autopsy.

Case report

HISTORY. A forty-four-year old white male was first seen at the Wadsworth General Hospital on July 5, 1960, on referral for an evaluation of fever and fatigue of three weeks duration.

From July, 1938, until May, 1939, he was hospitalized at the San Diego Naval Hospital with a diagnosis of pulmonary tuberculosis and was treated with phrenic nerve crush and pneumothorax. Sputum cultures were negative for acid-fast bacilli at the time of his discharge.

In February, 1953, he was admitted to the Long Beach Veterans Hospital because of enlarging axillary and supraclavicular lymph nodes. A biopsy of a right supraclavicular node was reported as showing Hodgkin's granuloma. Cultures of the biopsied material failed to reveal acid-fast bacilli; however, sputum cultures were positive. The treatment consisted of isoniazid (INH), PAS (para-amino salicylate), and streptomycin, and in May, 1953, his sputum became negative. Isoniazid and PAS were continued after his discharge in June, 1954, and maintained until the present admission.

In April, 1956, he was rehospitalized because of fever and chills and was given radiation therapy equal to a tumor dose of 1,280 r to the left axilla and left and right cervical areas. There was rapid regression in adenopathy and disappearance of fever. Because of recurring adenopathy an additional tumor dose of 1,000 r was administered in March, 1957, to both axillas and cervical areas, again with good results.

In March, 1960, the chills and fever recurred, and he was noted to have generalized adenopathy and moderate hepato-

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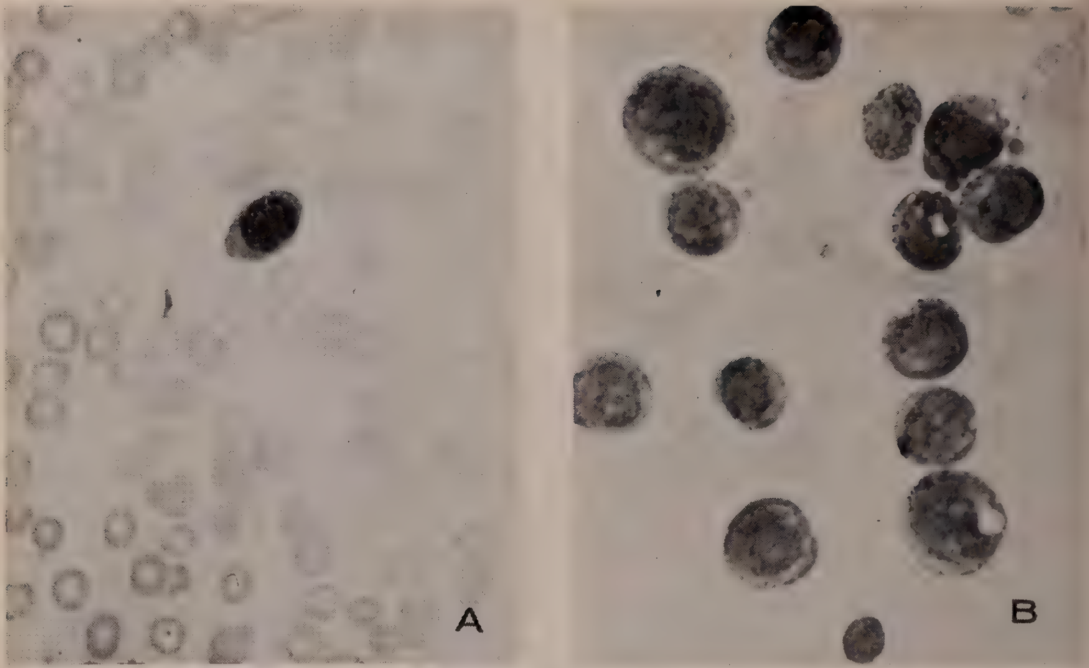

FIGURE 1. (A) Peripheral blood smear showing circulating monoblast and thrombocytopenia. (B) Bone marrow from sternal puncture showing infiltration with large blast cells with vacuolated cytoplasm.

megaly. On his readmission to the Long Beach Veterans Hospital a sternal marrow biopsy was performed. This showed a myeloid, erythroid ratio of 4 : 1 with normal cellularity and differentiation of all elements. Nitrogen mustard was administered intravenously on April 17, 1960, 0.4 mg. per kilogram of body weight. His fever disappeared during the next three days, and he was discharged.

Two to three weeks before the final admission his chills and fever recurred. He was referred to us for these complaints.

Physical examination. The patient appeared to be a cachectic white male. His blood pressure was 120/70, pulse, 96, and temperature, 98 F. Petechiae were present over both legs. There were numerous 0.5-cm.-square papules scattered over the trunk and lower extremities. A 3-cm.-square left infraclavicular rubbery node was present as well as bilateral enlarged axillary nodes. There was marked sternal tenderness. The lungs showed increased resonance. Fine crepitant rales were heard in the left apex. The liver was felt 2 fingerbreadths below the right costal margin. No spleen was palpable. The rest of the physical examination was unremarkable.

Laboratory findings. The white blood cell count on admission was 6,000, with 10 per cent blast cells, 2 per cent metamyelocytes, 78 per cent neutrophils, 8 per cent lymphocytes, and 2 per cent monocytes. The hemoglobin was 10.1 Gm., with a packed cell volume of 33 per cent. Platelets appeared markedly diminished on peripheral smear. Repeated leukocyte counts ranged between 4,000 and 8,000 with 5 to 40 per cent blast cells (Fig. 1A). A sternal marrow aspiration revealed an increased cellularity, with blast cells representing 90 per cent of the cells seen. These were large, immature cells with abundant vacuolated basophilic cytoplasm containing azurophilic granules (Fig. 1B). The histologic diagnosis was acute histiomonocytic leukemia. A chest x-ray film showed pulmonary emphysema and fibrosis with no evidence of active tuberculosis.

A biopsy of an enlarged axillary node again showed the presence of Hodgkin's disease (Fig. 2A). A biopsy of one of the multiple skin lesions revealed a dermal infiltrate

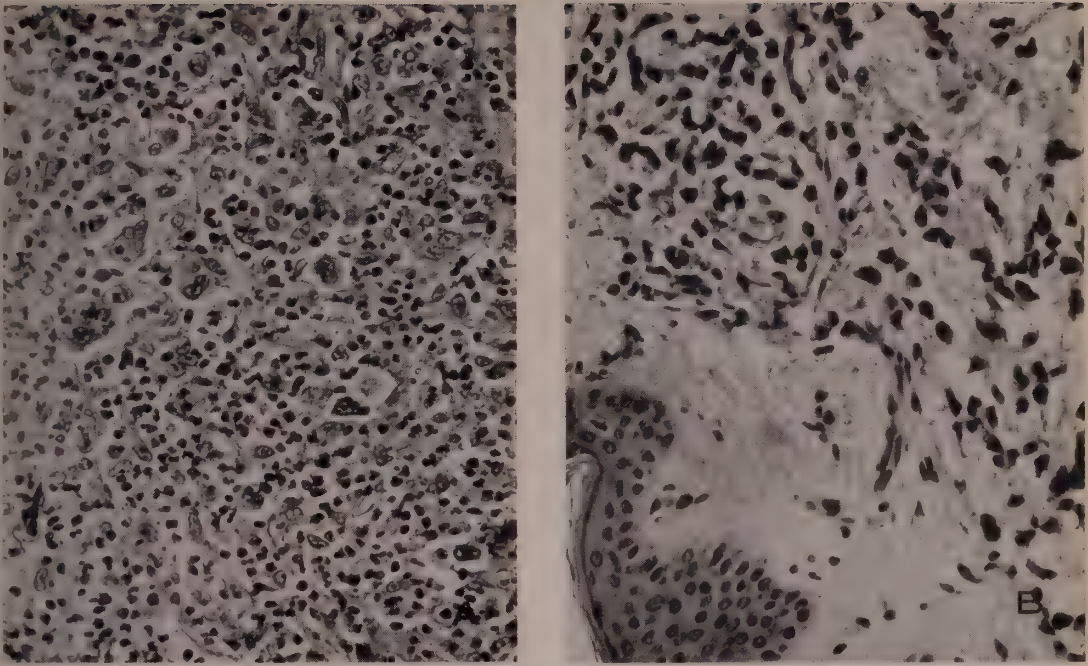

FIGURE 2. (A) Lymph node biopsy showing Hodgkin's disease. (B) Biopsy of skin nodule showing dermal infiltration with leukemic cells.

composed of large, immature cells similar to those found in the bone marrow (Fig. 2B). Concentrated sputum smears were negative for acid-fast bacilli.

COURSE. On July 12, 6-mercaptopurine therapy was instituted, 125 mg. a day. Five days later the leukocyte count was 2,800 and the hemoglobin 8.4 Gm., and the patient was weaker. There was some improvement after a transfusion with 4 units of packed cells. On August 1, the white count had fallen to 1,000, and a peripheral smear showed only blast cells. There was no change in adenopathy, skin lesions, or sternal tenderness. The patient's condition continued to deteriorate, and on August 6 he became hypotensive and expired in spite of supportive therapy.

A postmortem examination confirmed the coexistence of acute leukemia and Hodgkin's disease.

Comment

Although leukemoid blood pictures have been described in both Hodgkin's disease[10] and tuberculosis,[11] there can be little doubt that this patient developed acute histiomonocytic leukemia as a terminal event. The autopsy revealed extensive infiltration of the liver, bone marrow, and lungs with leukemic cells (Fig. 3). The spleen showed involvement with Hodgkin's disease (Fig. 4). In addition there were enlarged periaortic and perihilar lymph nodes which were replaced by Hodgkin's tissue. There was no evidence of active pulmonary tuberculosis.

There is convincing evidence that ionizing radiation is potentially leukemogenic for human beings. A definite increase in the incidence of leukemia was observed in atomic bomb survivors at Hiroshima and Nagasaki. Leukemia has been found in increased incidence in patients treated with radiotherapy for thyroid diseases, thymic tumors, and rheumatoid spondylitis. Our patient received extensive radiation therapy for his Hodgkin's disease during the four years prior to the onset of his leukemia. This four-year period coincides well with the modal latent period of five years between the exposure to irradiation and the development of leukemia which was found in atomic bomb survivors. It may well be that our patient's leukemia was related to his radiation therapy. On the other hand, 3 of Zeffren and

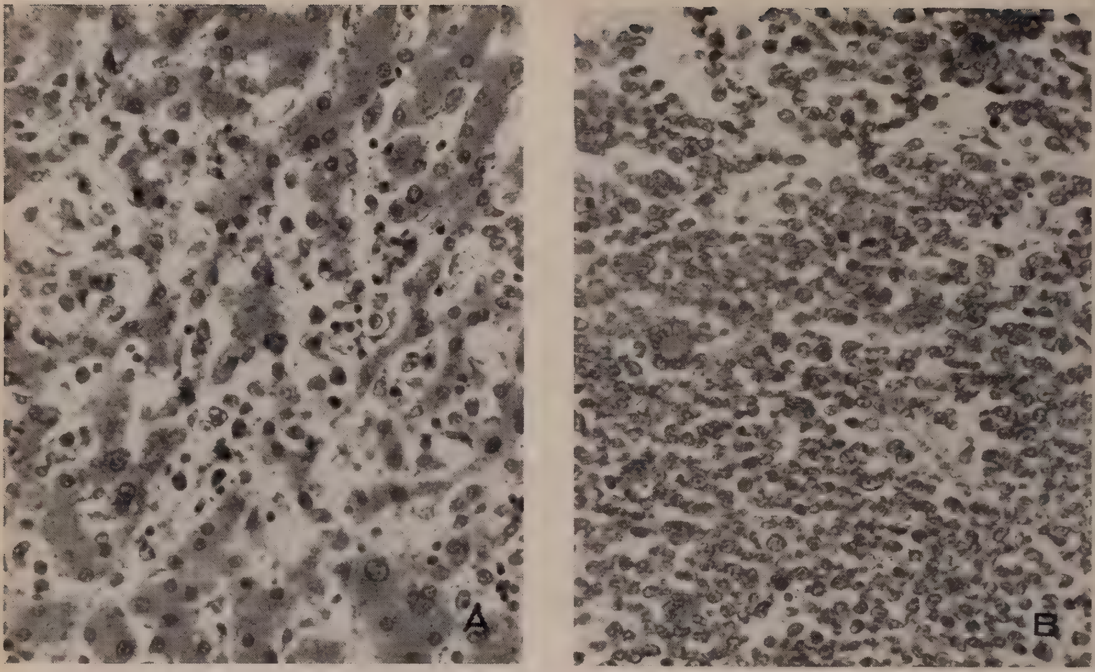

FIGURE 3. Leukemic infiltration of (A) liver and (B) bone marrow (×270).

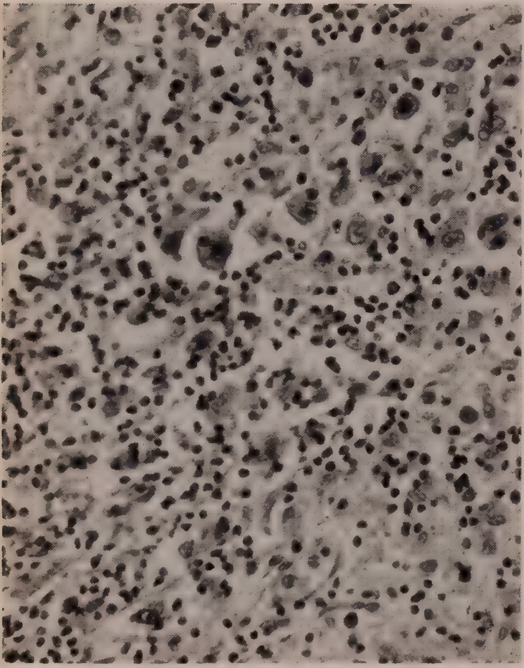

FIGURE 4. Hodgkin's disease of spleen (×270).

Ultmann's[1] 6 patients who developed acute leukemia during the course of reticulum cell sarcoma received no x-ray therapy.

Dameshek and Gunz[12] have stated that reticulum cell sarcoma and histiomonocytic leukemia may belong to the same closely knit group of neoplasms. They feel that the same relationship exists between reticulum cell sarcoma and monocytic leukemia as exists between lymphosarcoma and lymphatic leukemia and that the monocytic leukemia represents the leukemic counterpart of reticulum cell sarcoma. There is accumulated evidence that Hodgkin's disease and reticulum cell sarcoma are very closely related disorders, that is, the Sternberg-Reed cell is a modified reticulum cell.[13] Furthermore, Hodgkin's-like lesions occasionally are noted in patients with monocytic leukemia.[14] The finding of monocytic leukemia in our patient with Hodgkin's disease would tend to support Dameshek and Gunz's[12] theory.

Summary

A case of histiomonocytic leukemia occurring in a patient with proved Hodgkin's disease and pulmonary tuberculosis is presented. The possible causal relationship of radiation therapy is briefly discussed.

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Present Surgical Management of Portal Hypertension

Apart from liver failure, the chief cause of death among patients with cirrhosis is hemorrhage from a group of veins surrounding the junction of the esophagus and the stomach, according to M. Judson Mackby, M.D., San Francisco, California, at the recent meeting of the International Congress of International College of Surgeons in New York City.

This bleeding is due to scarring within the liver which produces blockage of blood flow through the portal vein carrying blood from the intestines to the liver. The resultant tremendous increase of pressure in this venous system is transmitted to the thin-walled veins in the wall of the esophagus which rupture with disastrous consequences. Surgical connection of the portal vein with the inferior vena cava, which carries the bulk of the venous blood from the lower extremities to the heart, will almost always decompress the high pressure portal system and prevent further bleeding.

Dr. Mackby advocates a side-to-side communication, when feasible, as the best and safest method of decompression, particularly if the patient has accumulated large quantities of ascites as the result of cirrhosis. Many patients with ascites do not bleed but may be incapacitated due to a greatly distended abdomen. In these cases a new drug, Spironolactone, has proved useful in the elimination of the excess fluid. However, surgery is occasionally necessary, and the operation of choice is the eversion and isolation of a segment of small intestine which is exposed to the abdominal fluid and which acts as an absorbent membrane. Reduction of portal pressure by portacaval junction will help or cure the remainder.

Segmental Ulcerative Colitis with Carcinoma in Octogenarian

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ALTHOUGH THERE is great satisfaction in the confirmation of the preoperative diagnosis at operation, the high point is the actual removal of a peculiar lesion or specimen from a patient.

The presence of segmental ulcerative colitis in an octogenarian is quite unusual, and the presence of an early carcinomatous plaque superimposed on one of the lesions is of particular interest. The following case report is of special interest for the following reasons:

1. For eighty-two years the patient had never had any gastrointestinal complaints until six weeks before entering the hospital.
2. The lesions found at operation were typical of segmental ulcerative colitis, a condition more commonly found in people between forty and fifty years of age.
3. A small malignant plaque was present in one of the involved segments without any evidence of any polypoid degeneration.
4. The clinical course of the disease was fulminating in this patient.

Case report

An eighty-two-year-old white female was admitted to St. Vincent's Hospital, New York City, on November 1, 1961, complaining of abdominal pain, fever, and arthritis of six weeks duration. Four days before admission gross rectal bleeding was first noticed. Her appetite was poor, she was losing weight, and becoming weak. The patient had been suffering from diabetes mellitus for fifteen years, and her electrocardiogram showed evidence of an old coronary infarct.

A physical examination revealed a pallid, obese female who did not appear particularly ill. The blood pressure was 160/90; the pulse rate, 86; and the temperature, 102 F. on the day of admission to the hospital. The abdomen was slightly distended, and tenderness could be elicited over the transverse colon. Rectal and sigmoidoscopic examinations indicated negative findings except for the presence of blood in the lower colon.

Laboratory examinations of the blood revealed a hemoglobin of 10.7 Gm. per 100 ml. and a hematocrit of 35. The white blood cells were 12,200, with 79 per cent polymorphonuclear cells and 21 lymphocytes. Stool examinations indicated negative findings for Amoeba or other parasites, but the examinations always showed positive findings for blood. A barium enema revealed a segmental ulcerative colitis involving the transverse colon in two areas, with the proximal lesion presenting a stenotic segment suggesting carcinoma (Fig. 1). A roentgen examination of the chest and upper gastrointestinal tract showed negative findings.

The patient was treated with transfusions, the large bowel was prepared with antibiotics, and on November 6, 1961, a laparotomy was performed. Two distinct and separate areas of segmental ulcerative colitis were found in the transverse colon. The proximal one measured about 10 cm. in length and contained a rather hard firm plaque 1.5 cm. in diameter at the site of the stenosis. The second lesion was closer to the splenic flexure and measured about 9 cm. in length. There was an area of normal colon between the two involved areas. The remaining abdomen showed negative findings. A segmental resection of the transverse colon including both lesions was performed, and an end-to-end anastomosis was accomplished without difficulty.

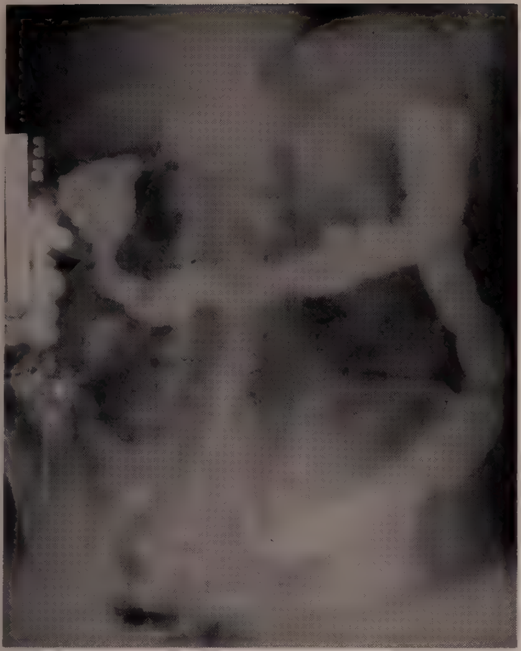

FIGURE 1. Barium colon roentgenogram demonstrating two separate lesions with arrow pointing to stenotic area containing malignant plaque.

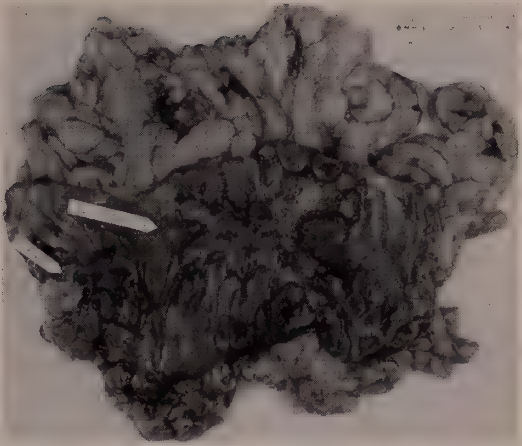

FIGURE 2. Proximal specimen of transverse colon with area of ulceration and malignant plaque.

The abdomen was closed with drainage. Her recovery was uneventful, and the patient was discharged on the fourteenth postoperative day without complaints. The pathologic diagnosis was segmental ulcerative colitis (active), with ulceration in both segments and adenocarcinoma in the plaque in the proximal lesion (Fig. 2).

Follow-up. This patient has been entirely well to date. She has had no further bleeding from the rectum and has one normal bowel movement a day. She has had no fever and has regained some of the weight which she lost prior to her operation.

Comment

It has been estimated that segmental colitis constitutes from 4 to 10 per cent of all cases with ulcerative colitis, and that segments of the transverse colon were involved most frequently.[1] The segments of the right colon were involved more than those of the left half.

Most of our knowledge about segmental colitis has been acquired since 1930 when Bargen and Weber[2] reported 23 cases and called the disease "regional migratory ulcerative colitis." In 1938 Crohn and Berg[3] reported a series of 17 cases and described them as "right-sided regional colitis."

It seems that segmental ulcerative colitis occupies a midposition, both clinically and pathologically, between diffuse ulcerative colitis and regional ileitis which was first described by Crohn, Ginzburg, and Oppenheimer in 1932.[4] The peak incidence for both diffuse ulcerative colitis and regional ileitis is in the third decade.

The most frequent symptoms present are bloody diarrhea, abdominal pain, fever, and some weight loss. There is usually evidence of anemia, and abdominal tenderness is quite often present. Malignancy, which is a definite hazard in diffuse ulcerative colitis, is encountered rarely in the segmental lesions. Barbosa, Bargen, and Dixon[5] report only 1 case in a series of 140 patients.

Segmental colitis is migratory in nature and usually begins in the transverse colon according to Neuman, Bargen, and Judd[1] and then may extend in either direction. There may be skip areas in which segments are involved discontinuously. If untreated, eventually the disease may involve the rectum which is rarely, if ever, involved in the early course of the disease.

The diagnosis is usually made on the basis of the clinical picture and the positive findings of an x-ray examination of the colon and the absence of ulceration of the rectum and sigmoid during an examination by sigmoidoscopy. Early diagnosis is important since it simplifies the treatment.

While the treatment may be either medical or surgical, it would appear from the study of the course of the disease that the early surgical approach should be considered primarily in most cases unless serious contraindications for surgery should exist. The following reasons are given:

1. Colonic surgery has been made relatively safe for such procedures today, and bowel continuity can be re-established without difficulty.
2. Excellent long-term results have been reported with surgery.
3. The recurrence rate is much greater following medical management.
4. The ever-present treatment of carcinoma should always be considered, and procrastination would eventually make a curable condition inoperable.

Summary

1. A case of segmental ulcerative colitis with carcinoma in an octogenarian has been presented.
2. It is anticipated that the result will be gratifying because of early surgical intervention.

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Fatal injuries caused by public accidents

Public accidents other than motor vehicle mishaps account for one fifth of all fatal injuries each year in the United States. Four out of every 5 victims in such public accidents are males, according to statisticians of Metropolitan Life Insurance Company.

Falls, the leading cause of fatal injuries in public places, claimed 4,900 of the nearly 18,000 lives lost in public accidents during 1959. Most of the falls occurred among older people. As much as one fifth of all the fatal falls happened on streets and highways.

Drownings, mainly among child and young adult bathers, ranked a close second with about 4,300 deaths during the year, while water transportation claimed an additional 1,600 lives.

Accidents involving aircraft, railways, firearms, and fire and burns by other means followed in decreasing numerical importance as major causes of public accidental deaths.

A great many of the deaths in public accidents are associated with sports and other recreational activities. In a study made by the company of its policyholders, it was found that more than two fifths of such fatalities resulted from water sports, exclusive of boating. Pleasure boating caused one sixth of all the deaths sustained in sports and recreation. Many of these stemmed from overloading of boats, occupants shifting positions, and the use of small boats in rough waters.

BILLSBORD

In this modern world of plenitude and progress Man needs so much. Peace. Health. Happiness. But if given a choice of a single gift for each and every person, I would select—Faith.

Whatever the depth of knowledge or extent of wisdom, none of us can foretell the future. As we face this unknown tomorrow, anxiety and apprehension beset us. When we attempt to forestall any possible contingency and neutralize each imaginary mishap, we find this search for absolute security a road to frustration and failure. For every hole we plug, every barrier we erect, and every protection we devise results in the discovery of new areas of weakness, a vista of new dangers.

Some, overwhelmed by a dread of illness, devote their lives to the search for reassurance as to the state of their health, only to die without ever knowing "a well day"; without ever freeing themselves from the chains of their hypochondriasis. Others, overcome by the spectre of need, hoard their wealth as a bulwark against the misfortune of a penniless future, only to die of malnutrition on some Skid Row while the newspaper reports as to the thousands of dollars found in their rags.

This frantic search for security is a race to nowhere, as round they go in a vicious circle doomed to the pursuit of a wraith that exists only in their own imagination. No accident is it that in a time of health insurance, workmen's compensation benefits, unemployment insurance, and old age pensions we are so insecure as to require unbelievable amounts of tranquilizers, to be addicted universally to sleeping pills, to seek reassurance in the distiller's handiwork or the psychiatrist's couch.

Only Faith can enable us to face the future. Psychologically it makes little difference as to the basis. One finds assurance in a lucky amulet, a personal horoscope, or in adherence to some objective of the world we inhabit as well as in the supernatural. This is Russia's secret weapon, for while openly waging destructive war on faith in God, they have succeeded in the inculcation of faith in the state and in an objective of a "heaven on earth" if not for men today, certainly for his children and their children.

With Faith one can face the hardships of the present with courage and daring, secure in the belief that whatever the cost, it is a step toward a desirable and worth-while objective. The catastrophic possibilities of the unknown future, while they may frighten him, cause no anxiety or worry, for whatever the handicap he must tolerate, or the pestilence he must endure, it is the price he must pay, a challenge he will meet to reach the promised land and not an ogre before which he trembles and runs. For Faith provides no escape from disaster—only the fortitude to meet it and the strength to face it. Faith does not prevent pain but provides the patience to endure it. Faith does not enable one to elude death but gives one the serenity to face the inevitable. Only Faith can manufacture martyrs, foster courage, give peace of mind, and find security.

When we put it aside and search for a guaranteed security, we find only cowardice, magnification of pain and suffering by a thousandfold in the anxiety of contemplation. Once we put it away life becomes meaningless, and then when suddenly we glimpse the Exit Door of life, we are overcome with the realization of our own mortality.

So it is that modern man presents a forlorn and pitiful spectacle as one notes his fear when facing the future or his revulsion and remorse as he looks backwards.

True it may be that contemplation of the present provides some temporary assurance. Bemused by the abundance of production, the elegance of his women, the height of his buildings, the fracture of the atom, and the sophistry of the "intellectuals," he readily accepts the concept—there is no God greater than man, and life is merely a problem of adjustment, not salvation.

Alas, this belief in man as God, although strong enough to destroy his faith in God the man, still lacks the vitality to fill the void, leaving him insecure and uneasy.

Tormented by doubts as to the origin and purpose of life, he vacillates between a feeling of futility with a "Why go on?" attitude and a gnawing, questing hope he can regain faith in the supernatural. Thus he crowds the churches and packs the tents of the evangelist, not through faith but searching for it. He seeks desperately for factual proof of the miraculous, that he might, as did Thomas, find consolation in the security of incontrovertible truth.

Some are so fortunate as never to doubt. Some succeed in their search for personal assurance. But if the majority are to find an answer, they must find it in the commonplace rather than the miraculous.

One wonders if everyone could gain a working knowledge of his physical self and then were to compare the economical construction, the graceful symmetry, and the functional competence of an anatomic structure or system to the contrived, awkward, bulky, and limited functioning counterparts designed by man—' would he not find it difficult, indeed, to escape an awareness of the fundamental gap existing between the created and the manufactured?

And so, if given a choice of a single gift for myself, I would select—Faith. For with it a man can move a mountain, without it he sits quivering in the corner of some dank cavern.

WRC

Indication of congenital limb deformities on birth records

Birth certificates should indicate the presence of congenital limb deformities to facilitate research into their cause and frequency, according to an article by Cameron B. Hall, M.D., Milo B. Brooks, M.D., and Jeannine F. Dennis, O.T.R., in the August 18, 1962, issue of the *Journal of the American Medical Association*.

The prevention of disease in general and of malformations in particular requires the detection of the causes, and finding the causes often depends on accurate knowledge of their frequency.

The frequency of congenital limb deficiency is unknown. Present birth certificates do not provide for the recording of such information, and it has been included in only a few medical centers.

A method for classifying congenital limb deficiencies provides a simple description of seemingly complex and unrelated malformations and should be used in initial birth records. Until the rate of occurrence is known, the role of the many factors implicated in these deformities, such as heredity, diet, irradiation, hormones, chemicals and injuries, cannot be evaluated.

Necrology

Henry Clinton Becker, M.D., of West Hartford, Connecticut, formerly of New York City, died on October 17 at West Hartford at the age of eighty-five. Dr. Becker graduated in 1904 from Cornell University Medical College. He was formerly chief attending physician at the Home for Aged and Infirm Females and chief of staff of the Bloomingdale Clinic. Retired, Dr. Becker was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Arthur Seymour Broga, M.D., of Oneida, died on October 8 at Syracuse Memorial Hospital at the age of sixty-three. Dr. Broga graduated in 1923 from Syracuse University College of Medicine. He was an attending physician at Syracuse City Hospital. From 1941 to 1944 he was physician to the Oneida public school system, from 1946 to 1950 coroner of Madison County, and at his death was serving as city health officer. Dr. Broga was a member of the American Academy of General Practice, the Syracuse Academy of Medicine, the Madison County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harold J. Constantine, M.D., of Buffalo, died on August 3 at Millard Fillmore Hospital at the age of sixty-five. Dr. Constantine graduated in 1924 from the University of Buffalo School of Medicine. Retired, he was a member of the Flying Physicians Association, Inc., the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Clarence Catlin Coryell, M.D., of New York City, died on October 23 at his home at the age of eighty-three. Dr. Coryell graduated in 1903 from Cornell University Medical College. He was an honorary attending physician at St. Elizabeth's Hospital. Before World War I when the City was combating diphtheria he was chief intubationist of the Board of Health for Manhattan, the Bronx, and Staten Island. Retired, Dr. Coryell was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Martin A. Furman, M.D., of the Bronx, died on October 15 at Jewish Memorial Hospital at the age of sixty-eight. Dr. Furman graduated in 1919 from Columbia University College of Physicians and Surgeons. In 1957 he became an associate compensation examining physician for the New York State Workmen's Compensation Board. Dr. Furman was a Diplomate of the American Board of Otolaryngology, a Fellow of the American College of Surgeons, and a member of the American Otorhinologic Society for Plastic Surgery.

Abraham Greenberg, M.D., of New York City, died on October 21 at his home at the age of fifty-four. Dr. Greenberg graduated in 1940 from the School of Medicine of the Royal Colleges, Edinburgh, Scotland. He was vice-president of the L. W. Frohlich Advertising Agency and president of the Science Information Bureau. Dr. Greenberg was a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph Hajek, M.D., of New York City, died on October 12 at St. Luke's Hospital at the age of seventy-two. Dr. Hajek graduated in 1918 from Long Island College Hospital Medical School. He was a consulting physician and cardiologist at St. Luke's Hospital and St. Luke's Hospital Outpatient Department. From 1926 to 1932 he taught at the College of Physicians and Surgeons and from 1951 to 1952 served as president of the St. Luke's Hospital Alumni Association. Dr. Hajek was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Karlis Karklinsh, M.D., of the Bronx, died on October 10 at his home at the age of sixty. Dr. Karklinsh received his medical degree in 1931 from the University of Latvia, Riga, where he had also served as an assistant professor of surgery. During World War II he became a pathologist for the United States 97th General Hospital, Frankfurt, Germany. Dr. Karklinsh was a member of the Bronx County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Mark A. Kraft, M.D., of New York City, died on October 17 at the New York Polyclinic

Hospital at the age of seventy-three. Dr. Kraft received his medical degree from the University of Odessa in 1914. He was a member of the American Thoracic Society, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Robert Henry Lyman, M.D., of Fillmore, died on September 7 at his office at the age of sixty-three. Dr. Lyman graduated in 1927 from the University of Pennsylvania School of Medicine. Town health officer of Hume for twenty years, he was a member of the Allegany County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Alphonse Mammana, M.D., of Buffalo, died on September 12 at his home at the age of sixty-five. Dr. Mammana graduated in 1920 from the University of Buffalo School of Medicine. He was an attending physician in general practice at Columbus Hospital. Dr. Mammana was a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Freeman Stanislaus O'Brien, M.D., of Wappingers Falls, died on September 9 at Castle Point Veterans Administration Hospital at the age of seventy-six. Dr. O'Brien graduated in 1908 from the University of Michigan Medical School. He was a member of the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Arthur Joseph O'Connor, M.D., of Scarborough, died on September 20 at his home at the age of seventy. Dr. O'Connor graduated in 1916 from Columbia University College of Physicians and Surgeons. He was a Fellow of the American College of Surgeons and a member of the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph William Puerner, M.D., of Niagara Falls, died on July 3 at the age of fifty-two. Dr. Puerner graduated in 1937 from the University of Pennsylvania School of Medicine. He was president of the medical staff and chief otolaryngologist at Mount Saint Mary's Hospital. Dr. Puerner was a Diplomate of the American Board of Otolaryngology and a member of the Niagara Falls Academy of Medicine, the Buffalo Academy of Medicine, the Niagara County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Nathan Sobel, M.D., of New York City, died on October 17 at Beekman-Downtown Hospital at the age of sixty-seven. Dr. Sobel graduated in 1918 from Columbia University College of Physicians and Surgeons. He was with the City of New York Department of Health and from 1950 to 1960 was medical and technical supervisor of the social hygiene division of the bureau of preventable diseases and bureau chief for the last three years. He was an attending physician in dermatology and syphilology at the Beekman-Downtown Hospital and chief of dermatology at the Beekman-Downtown Hospital Outpatient Department. Dr. Sobel was a Diplomate of the American Board of Dermatology, Inc., and a member of the Bronx Dermatological Society, the American Academy of Dermatology, the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Herman Sturcke, M.D., of Brooklyn, died on October 10 at Lutheran Medical Center at the age of seventy-two. Dr. Sturcke graduated in 1914 from New York University and Bellevue Hospital Medical School. He was an adjunct physician in ophthalmology at the Brooklyn Eye and Ear Hospital and a consulting ophthalmologist at the Lutheran Medical Center. Dr. Sturcke was a Diplomate of the American Board of Ophthalmology and a member of the Brooklyn Ophthalmological Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

J. Parker Talmadge, M.D., of Brooklyn, died on October 19 at Long Island College Hospital at the age of eighty-four. Dr. Talmadge graduated in 1902 from Albany Medical School.

Paul Zackheim, M.D., of Buffalo, died on September 20 at Buffalo General Hospital at the age of fifty-three. Dr. Zackheim graduated in 1933 from the University of Buffalo School of Medicine. He was an attending radiologist at Lafayette General Hospital. Dr. Zackheim was a Diplomate of the American Board of Radiology (Diagnostic Roentgenology) and a member of the Buffalo Radiological Society, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Medical News

Papers invited for A.M.A. meeting

The American Medical Association's Council on Scientific Assembly invites physicians to submit titles and brief abstracts of scientific papers they wish to deliver at the 1963 annual meeting of the Association which will be held in Atlantic City, June 16 through 20. Deadline for submission is December 15.

The Third Multiple Discipline Research Forum will also be an important part of the A.M.A. scientific assembly. It will be held for three days and will be limited to reports, eight minutes in length, of original investigation of fundamental problems in medicine and medical practice. The deadline for Forum abstracts is February 1, 1963.

The deadline for space in the scientific exhibits at the Atlantic City meeting is January 9, 1963. The deadline for receipt of application forms for the presentation of films on the motion picture program is January 9.

For information write to: George R. Meneely, M.D., Secretary, Council on Scientific Assembly, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Position for physician in Indiana

The Public School System of Gary, Indiana, has announced that the position of supervisor of health services is available to a qualified male or female physician.

In addition to the $15,000 yearly salary, benefits include: regular office hours; sick leave allowance cumulative to 135 days at full pay; state teacher's retirement benefits and Social Security benefits; group life insurance; leave for study or maternity; and sabbatical leaves.

For additional information contact: Dr. Thaddeus P. Kawalek, Assistant Superintendent, Personnel, School City of Gary, 620 East 10th Place, Gary, Indiana.

False claims for "air purifiers"

The Food and Drug Administration has launched a new enforcement drive against false claims that so-called "air purifiers" are good for treating or preventing diseases.

Consumers are warned not to expect the devices to be beneficial for hay fever, asthma, colds, sinus trouble, migraine, allergies, lung cancer, pneumonia, and a long list of other conditions.

One hundred eighty-seven units of five different brands of "negative ion generator air purifiers" were seized by the F.D.A. during a one-month period.

Seized were: Tribotron Negative Ion Generator; Tubin Ion-O-Matic Air Improver; Vornado Auto Air Conditioner; Dustronic Air Purifier; and Vita-Aire Units.

Deaths of asbestos workers investigated

The Health Research Council of the City of New York has announced that the deaths of approximately 200 asbestos workers in New York City over a ten-year period will be investigated for a possible link between asbestos dust and lung cancer. In addition, more than 800 current members of the Asbestos Workers Union, Local 12 (AFL-CIO) will cooperate in the study to uncover any suspicious signs of occupational disease, particularly a condition known as asbestosis. The 200 deaths to be investigated occurred among members of this labor union.

Announcement of the study came in connection with a Health Research Council grant of $60,835 to The Mount Sinai Hospital to conduct the study over a two-year period. The project will be supervised by Irving J. Selikoff, M.D., of the hospital's thoracic diseases division, and Jacob Churg, M.D., research pathologist at the institution.

Award offered for paper on drugs

The Revere Publishing Company, publishers of *The Journal of New Drugs,* have announced the second annual $1,000 Revere award for the best clinical paper published in its journal for the year ending June 30, 1963. The award will be made to the senior author of the best paper dealing with the clinical effects of a new drug or pharmaceutical preparation.

For information concerning the award write to: McKeen Cattell, M.D., Editor, The Journal of New Drugs, 660 Madison Avenue, New York 21, New York.

Certification in occupational medicine

The American Board of Preventive Medicine has announced that the next examination for certification in occupational medicine will be held March 16 through 18 at the Sheraton-Park Hotel in Washington, D.C., preceding the annual meeting of the Industrial Medical Association which will be held at the same hotel March 18 through 21.

Applications for certification should be sent to: Tom F. Whayne, M.D., Secretary-Treasurer, American Board of Preventive Medicine, 4219 Chester Avenue, Philadelphia 4, Pennsylvania.

Fellows inducted into American College of Surgeons

At a recent meeting the following New York State physicians were inducted as fellows of the American College of Surgeons:

Albany: John H. Carter, M.D., John H. P. Holden, M.D., and Harold F. Welch, M.D.; *Amityville:* E. George Heus, M.D.; *Auburn:* Charles Blaich Ryan, M.D.; *Bethpage:* William Douglas Brandon, M.D.; and *Brooklyn:* Randall D. Bloomfield, M.D., Richard J. Calame, M.D., William S. Calem, M.D., Robert M. Cavallaro, M.D., Solomon Ciprut, M.D., Richard J. Ciuzio, M.D., Jerome G. Davis, M.D., Fuad Dirbas, M.D., Herbert Harris, M.D., John J. Ippolito, M.D., Joseph L. Kostecki, M.D., Samuel Lichtig, M.D., Charles J. Monestere, M.D., Hubert S. Pearlman, M.D., Gerald W. Shaftan, M.D., and Lloyd A. Watts, M.D.

Also: *Buffalo:* Louis C. Cloutier, M.D., Bernie P. Davis, M.D., Duane H. Dougherty, M.D., Maurice J. Gonder, M.D., F. Stanley Hoffmeister, M.D., Donald J. Kelley, M.D., Guy Owens, M.D., and Herbert Berman, M.D.; *Dunkirk:* Maj. Edward S. Konwinski, MC, USA; *Elmira:* William H. Burke, M.D.; *Flushing:* Charles W. Stark, M.D.; *Freeport:* William G. McGuinness, M.D.; *Glen Cove:* Henry H. Bard, Jr., M.D.; *Hamburg:* Henry L. Pech, Jr., M.D.: *Hempstead:* Peter H. Ballen, M.D., and Anthony J. Barbaccia, M.D.; *Islip Terrace:* Nathaniel B. Messinger, M.D.; *Jamaica:* Harold Alfonso Garnes, M.D., and David Leisten, M.D.; *Jamestown:* Robert B. Wright, M.D.; *Kenmore:* Sayde A. Taheri, M.D.; *Middletown:* John B. Ellison, M.D.; *Montrose:* Herbert Hershey, M.D.; *New Hyde Park:* George J. Paul, M.D., Herbert Rothenberg, M.D., and Marvin Shapiro, M.D.; and *New Rochelle:* Lester J. Blatt, M.D.

Also: *New York City:* Rafael Alvarez, M.D., Ira M. Barash, M.D., Lt. Col. Alexander M. Boysen, MC, USA, Arnold S. Breakey, M.D., David M. Carberry, M.D., Elizabeth V. D. Coryllos, M.D., Stanley Edelman, M.D., Stanley C. Fell, M.D., Mark E. Fox, M.D., Victor H. Frankel, M.D., Emanuel A. Friedman, M.D., George Gorin, M.D., William D. Graham, M.D., Anwar J. Hanania, M.D., Byron A. Hero, M.D., Oliver O. Holder, M.D., Robert C. Knapp, M.D., Donald R. Krawitt, M.D., Russell W. Lavengood, Jr., M.D., Robert S. Litwak, M.D., James R. Malm, M.D., Thomas A. McGraw, M.D., Anthony C. Milea, M.D., Maj. Dwight W. Newton, MC, USAF, Ralph A. Olson, M.D., Herzl Ragins, M.D., Howard Richman, M.D., Myron S. Roberts, M.D., Joseph J. Rovinsky, M.D., Aaron M. Schwartz, M.D., Daniel Shapira, M.D., James F. Sullivan, M.D., Lawrence E. Taylor, M.D., George Truchly, M.D., David S. Werman, M.D., Robert D. Wickham, M.D., Joseph R. Wilder, M.D., and Milton M. Zaret, M.D.

Also: *Niagara Falls:* Joseph P. Mallo, M.D.; *Oneonta:* Tompkins G. Watson, M.D.; *Ossining:* Richard C. Ames, M.D.; *Patchogue:* Milton Tuerk, M.D.; *Plattsburgh (AFB):* Capt. LaMar S. McGinnis, Jr., MC, USAF; *Poughkeepsie:* Edward R. De Ramon, M.D., and Constantine J. Papastrat, M.D.; *Rochester:* Harold W. Bales, M.D., William C. Caccamise, M.D., Lester M. Cramer, M.D., Edward T. Mulligan, M.D., and Charles G. Rob, M.D.; *Rockville Centre:* Joseph J. Ferrari, M.D.; *Schenectady:* Glen E. Cooley, M.D.; *Spring Valley:* Sheldon B. Adler, M.D.; *Syosset:* Kenneth J. Kerwin, M.D., Harold W. Mayberger, M.D., and John H. Ray, III, M.D.; *Syracuse:* George C. Heitzman, M.D., Harold D. Kletschka, M.D., Stanley D. Leslie, M.D., and James B. Wray, M.D.; *Tonawanda:* Frank A. Pfalzer, Jr., M.D.; *Upton:* John E. Jesseph, M.D.; *Utica:* Charles W. Brady, M.D., and Melvin A. Smalley, M.D.; *Valley Stream:* Jerome B. Abelman, M.D.; *Wantagh:* Arnold R. Robbins, M.D.; *Watertown:* John G. Atkinson, M.D., and Warren W. Daub, M.D.; *Westbury:* Milton Eichler, M.D.; *White Plains:* Richard J. Neudorfer, M.D.; *Yonkers:* Harold Friedman, M.D., and Stanley Martin Rubin, M.D.; and *Yorktown Heights:* Richard T. Carr, M.D.

Essay contest on chest diseases

The Council on Undergraduate Medical Education of the American College of Chest Physicians is offering three cash awards to be given for the best contribution prepared by an undergraduate medical student on any phase of the diagnosis and/or treatment of chest diseases (heart or lungs).

The first prize will be $500; second prize, $300; and third prize, $200. A certificate of merit will also be given.

The winning contributions will be selected by a committee of chest specialists and will be announced at the twenty-ninth annual meeting of the American College of Chest Physicians to be held in Atlantic City, June 13 through 17. All manuscripts become the property of the American College of Chest Physicians.

For application forms and additional information write to: Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Calendar of overseas medical meetings

The Scandinavian Airlines System is offering a comprehensive calendar of overseas medical congresses and allied events during the period from December, 1962, to December, 1963. The calendar lists all known medical events in areas served by the airline. A brochure which outlines the program of the American Medical Society of Vienna is also available.

For information and brochures write to: Mr. A. John Harrison, Secretary, Medical Travel Section, Scandinavian Airlines System, 138–02 Queens Boulevard, Jamaica 35, New York.

Course in medical uses of radioactive isotopes

A four-month course in the medical uses of radioactive isotopes will be offered at the Queens Hospital Center by the Radiation Medicine Department. The course will begin on Tuesday, February 5, 1963, and will consist of weekly five-hour sessions covering lectures, laboratory exercises, and clinical management of patients.

For information write to: Philip J. Kahan, M.D., Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, New York.

Awards offered to young doctors and students

Three award programs in the field of medical communications for medical students, interns, and residents have been announced by the Student American Medical Association.

The awards, for medical photographs and art, scientific papers, and scientific exhibits, consist of cash prizes, trophies, and nationwide recognition. The programs are designed to stimulate students and young physicians to engage in scientific research and to develop their skills in communicating their knowledge to other members of the medical profession.

For information write to: Executive Director, Student American Medical Association, 333 North Michigan Avenue, Chicago 1, Illinois.

Speakers on nutrition available

The National Vitamin Foundation has announced that any group of physicians, surgeons, or dentists that can assure an audience of at least fifty persons is eligible to apply for qualified speakers, without cost, who will discuss the various aspects of "Nutritional and Metabolic Aspects of Disease."

With available subjects covering such categories as "Nutrition and Alcoholism," "Nutrition and Adolescence," "Calory and Protein Deficiencies," "Nutrition and Cancer," "Nutrition and Mental Health," "Vitamins and Deficiency Diseases," "Nutrition and Oral Health," and "Nutrition and Pregnancy," a panel of fifty-one leading physicians has been carefully chosen as speakers so that qualified men might be made available to discuss nutrition problems and their management in relation to all the branches of medicine in which they occur.

For information write to: National Vitamin Foundation, 149 East 78th Street, New York, New York.

Improved care for mentally disabled

Governor Nelson A. Rockefeller has announced a seven-point program to carry out the second phase of the State's comprehensive master plan for care of the mentally disabled.

The plan, which the Governor announced last January, has received wide acclaim and national recognition. Its purpose is to provide for maximum use of new therapies and to develop the full range of integrated services required for modern community-based treatment of mental disability.

The seven steps proposed by the Governor as the program's second phase include: (1) Complete removal of the ceiling on State aid to localities for their mental health services; (2) opening of the last five units for retreatment of chronic patients so that all State hospitals will have such units; (3) establishment of two additional units in the Downstate area for the treatment of emotionally disturbed blind children; (4) further expansion of an aftercare program for those narcotic addicts who have been hospitalized under the State's new program to insure their continued progress toward rehabilitation; (5) creation of two new special units, one Upstate and one Downstate, for the treatment of the mentally ill deaf; (6) decentralization of the treatment and care programs of two large State hospitals into smaller hospital units; and (7) continuation of the State's building program for new State schools.

Course in fractures and dislocations

The New York and Brooklyn Committee on Trauma of the American College of Surgeons is sponsoring a course on fractures and dislocations to be presented by Sir Reginald Watson-Jones in cooperation with Alexander P. Aitken, M.D., Brookline, Massachusetts, and Preston A. Wade, M.D., Harrison L. McLaughlin, M.D., Charles S. Neer, M.D., and Edwin F. Cave, M.D., New York City, December 12 through 14, in the auditorium of Alumni Hall, New York University Medical Center, 550 First Avenue, New York City.

For information contact: Rolla D. Campbell, Jr., M.D., 55 East 72nd Street, New York 21, New York.

Postgraduate course in urologic pathology

Columbia University, College of Physicians and Surgeons, is offering its annual postgraduate course in urologic pathology to be held on Mondays and Thursdays, January 3 through 31, from 8:00 to 10:00 P.M., under the direction of Meyer M. Melicow, M.D., and Dr. A. C. Uson.

For information contact: Melvin D. Yahr, M.D., Assistant Dean, Columbia University, College of Physicians and Surgeons, 630 West 168th Street, New York 32, New York.

Repeated warnings against arthritis drug

The Arthritis and Rheumatism Foundation has again warned physicians and patients not to use or consent to the use of a Canadian drug preparation, Liefcort, in the treatment of arthritis.

Supplies of the liquid formula brought into the country before the Food and Drug Administration's ban are still available. The F.D.A. has warned that many arthritis victims have suffered serious reactions from the preparation, and at least one death has been attributed indirectly to the use of the drug.

The formula, which was prepared in the home of Dr. Robert Liefmann, an unlicensed Canadian physician, contains at least ten times the therapeutic dose of prednisone, testosterone, and estradiol.

New State school for mentally retarded

The transfer in October of the first patients to the new West Seneca State School for the Mentally Retarded marked another in a series of steps that the State of New York has taken to meet the problems of mental retardation.

The school, the first new State institution to be built since the 1930's, will provide much needed service for the western part of the State. For many years residents from this area of the State have depended on the State School at Newark, New York, for services to the retarded.

The first children, all educable, were transferred from Newark, and additional patients will be transferred as trained personnel become available. New patients will be accepted at the school at a later date.

A full program of care and treatment will be provided. An educational program will be carried on during the current year in classrooms in existing buildings. A new school building will be ready for the next school year. The program will include training for the severely retarded, for educable children, and vocational training for young adults.

Course on rehabilitation

The Department of Physical Medicine and Rehabilitation of the New York Medical College-Metropolitan Medical Center will hold a course on rehabilitation of the chronically ill patient April 22 through May 3, 1963. The course has been designed for registered nurses, occupational therapists, physical therapists, and social workers.

For information write to: Coordinator, Postgraduate Education, Department of Physical Medicine and Rehabilitation, New York Medical College-Metropolitan Medical Center, 1 East 105th Street, New York 29, New York.

Personalities

Retired. Kenneth Lewis, Sr., M.D., New York City, as director of the First (Columbia) Surgical Division at Bellevue Hospital, New York City, after forty years of service.

Elected. Alan A. McLean, M.D., New York City, as a director of the Mental Health Association of Westchester County.

Awarded. Leon D. Hankoff, M.D., Brooklyn, half of the Revere Publishing Company's annual $1,000 award made to the senior author of the best clinical paper published in *The Journal of New Drugs* . . . Howard A. Rusk, M.D., New York City, the "Orden Nacional de Merito" by the government of Ecuador in appreciation of his work in the field of rehabilitation . . . Abner Wolf, M.D., New York City, a scientific award from the National Multiple Sclerosis Society in the form of a golden hope chest and a $500 cash prize for his work on the study of allergic encephalomyelitis.

Appointed. B. Edward Heckmann, M.D., Buffalo, as associate compensation examining physician in the Buffalo office of the Workmen's Compensation Board . . . Jean K. Weston, M.D., Ann Arbor, Michigan, as director of medical affairs of Burroughs Wellcome & Company, Tuckahoe.

Speakers. George E. Ehrlich, M.D., New York City, on September 5 in Detroit, Michigan, at a symposium on psychosomatic medicine sponsored by the Michigan and Wayne County Academies of General Practice on the subject "Musculoskeletal Disorders," and on October 25 at a postgraduate teaching day in Toledo, Ohio, sponsored by the Toledo and Lucas County Chapter of the Ohio Academy of General Practice and Roche Laboratories on the subject "Complications of Corticosteroid Therapy in Rheumatoid Arthritis and Their Treatment" . . . Richard H. Lyons, M.D., Syracuse, September 5, at a symposium on psychosomatic medicine sponsored by the Michigan and Wayne County Academies of General Practice on the subject "Cardiovascular Manifestations" . . . Bernard L. Pacella, M.D., New York City, at a meeting of the Suffolk County District Branch of the American Psychiatric Association held at the Veterans Administration Hospital, Northport, Long Island, on October 16 on the subject "Dreams and Dreaming" . . . Arthur Q. Penta, M.D., Schenectady, on October 8 before the French Congress of Laryngology and Bronchoesophagology, in Paris on the subject "The Removal of Metallic and Magnetic Foreign Bodies from the Air and Food Passages with the Aid of Alnico Magnets.',

Medical Schools

Albany Medical College

Honorary lectureship award. Allen O. Whipple, M.D., emeritus professor of surgery, Columbia University College of Physicians and Surgeons, was chosen by the College to receive its sixth annual Honorary Lectureship Award. The lecture and award ceremonies were held at the College on November 1. The Honorary Lecture Award is Albany Medical College's highest citation and consists of an inscribed silver plaque and a cash prize. The award is given in recognition of "distinguished service to mankind in the fields of science, medicine, and teaching."

Albert Einstein College of Medicine

Symposium on addiction. A symposium on addiction to narcotics, alcohol, and tobacco was held at the College October 4 and 5. Participating in the symposium were Israel Zwerling, M.D., associate professor of psychiatry, who spoke on "Addiction: an Interdisciplinary Problem"; Louis Lasagna, M.D., associate professor of pharmacology and experimental therapeutics and associate professor of medicine, Johns Hopkins School of Medicine, "Determinants of Addiction"; Gerald Deneau, M.D., assistant professor of pharmacology, University of Michigan, "Pharmacological Studies of 'Addicting' Drugs"; Conan Kornetsky, M.D., associate professor of pharmacology and psychiatry, Boston University School of Medicine, "Some Aspects of the Nature of Tolerance to Morphine"; J. Wayne McFarland, M.D., Division of Health Education, Atlantic Union Conference of Seventh-Day Adventists, South Lancaster, Massachusetts, "The Smoking Habit"; Judge John Murtagh, administrative judge of the Criminal Court of the City of New York, "Narcotics and the Law." Murray Jarvik, M.D., associate professor of pharmacology, was the sponsor of the symposium which was presented by the College's Interdisciplinary Program.

Epilepsy Foundation grant. The Epilepsy Foundation, Washington, D.C., has presented a grant of $2,500 to Robert Katzman, M.D., associate professor of neurology, and Elliott Weitzman, M.D., associate in neurology, both members of the Department of Neurology, who will attempt to find out how much of an effect water, salt, and certain hormones in the body have on the seizure pattern of epileptics.

Columbia University College of Physicians and Surgeons

Research gift. The Columbia University Psychoanalytic Clinic for Training and Research has awarded $21,750 from its Adele R. Levy Research Gift to 16 faculty members participating in the work of eight research projects. The grants will enable some projects to be carried to completion and will permit sufficient progress on those remaining so that applications may be submitted to private and government sources for continued financial support.

Those projects and faculty members included are "The Evaluation of Ego Strength," Arnold Cooper, M.D., Max Cohen, M.D., B. Ruth Easser, M.D., H. Lee Hall, M.D., Aaron Karush, M.D., Stanley Lesser, M.D., and Bluma Swerdloff, D.S.W.; "Eskimo Basic Personality and Social Homeostasis," Joseph Lubart, M.D.; "Psychoanalytic Interview as a Research Tool with Nonpatients," Willard Gaylin, M.D., and Herbert Hendin, M.D.; "Psychosomatic Research," Leon Moses, M.D.; "Evaluation of Psycotherapy with Physiologic Criteria (Ulcerative Colitis)," John F. O'Connor, M.D.; "Selection of Candidates for Psychoanalytic Training," Henriette R. Klein, M.D.; "Interview Technic in a Group Setting: Implications as a Teaching Method," George S. Goldman, M.D., Alvin Polatin, M.D., and Daniel Shapiro, M.D.; and "Suicide Motivation: Cross Cultural Approach," Herbert Hendin, M.D.

Cornell Medical College

Child health group formed in honor of Samuel Z. Levine, M.D. The Samuel Z. Levine Foundation for International Child Health has been organized in honor of Dr. Levine who has retired as professor and chairman, Department of Pediatrics and Pediatrician-in-Chief. The private, voluntary, nonpolitical, and nonsecretarian organization aims to promote the health and well being of children the world over, with particular emphasis on the emerging countries of Asia, Africa, and Latin America. Among those serving on the medical advisory board are a number of pediatricians who took at least a part of their training at The New York Hospital and include: Wallace W. McCrory, M.D., professor of pediatrics at the College; Leona Baumgartner, M.D., who was, until her recent appointment to a Federal post, Commissioner of Health of New York City; Henry L. Barnett, M.D., professor of pediatrics, Albert Einstein College of Medicine; Lewis Fraad, M.D., professor of child health, also at Albert Einstein; Norman Kretchmer, M.D., professor of pediatrics, Stanford; William M. Schmidt, M.D., professor of maternal and child health, Harvard School of Public Health; Irving Schulman, M.D., professor of pediatrics, University of Illinois; and Milton J. E. Senn, M.D., professor of pediatrics, Yale. Present faculty members also on the board are Milton I. Levine, M.D., and Carl Smith, M.D.

Dedication of new library. The Samuel J. Wood Library and Research Building was dedicated in October. Principal speaker was Dean W. Malott, president of the University. Others participating in the ceremonies were: John E. Deitrick, M.D., dean of the College; E. Hugh Luckey, M.D., chairman, Department of Medicine at the College and physician-in-chief, The New York Hospital; Dr. Joseph C. Hinsey, director, The New York Hospital-Cornell Medical Center, and David P. Barr, M.D., professor emeritus of medicine.

Students sponsor lecture series. "Challenge in Medicine" was the first of a series of lecture-discussions sponsored by students in the College, held on October 22. "The AMA—Pro and Con!" was the topic and the panel consisted of Gerald Dorman, M.D., member of the Board of Trustees of the American Medical Association, and Caldwell Esselstyn, M.D., a member of the President's Committee for Medical Care to the Aged. August H. Groeschel, M.D., associate director for professional services of The Hospital and assistant professor of public health, was the moderator.

New York Medical College

Visiting lectureships fund. The Herman Goldman Visiting Lectureships Fund, established through the efforts of Lothar B. Kalinowsky, M.D., has made possible a lecture series by four internationally-renowned scientists. Dr. Hans Hippius, professor of psychiatry, University of Berlin, began the series on October 26 with his talk on "Psychiatric Complications of Pharmacotherapy." On November 12, 13, and 14, Dr. N. S. Vahia, psychiatrist, Medical College of Bombay, lectured on "Witchcraft in India," "Value of Biologic Treatment in Psychiatry in a General Hospital in Bombay," and "Clinical Studies on a New Indigenous Tranquilizer." Dr. W. Linford Rees, Maudsley Hospital, England, presented the third in the series, November 29 and 30, and discussed "An Over-all Review of the Psychosomatic Aspects of Asthma," and on December 13 and 14, Dr. Stjepan Betlheim, professor, School of Medicine, Zagreb, Yugoslavia, will end the current series with talks on "Social Importance of the Neurosis and Their Treatment in Yugoslavia."

State University of New York Downstate Medical Center

New faculty members. Blanche A. Borek, M.D., Bernard S. Levowitz, M.D., assistant professors, Perry Katzen, M.D., senior lecturer, and Joseph L. Kostecki, M.D., clinical assistant professor, are new members in the Department of Surgery. In the Department of Medicine, Selahattin Kologlu, M.D., of Turkey, visiting assistant professor, and Emanuel E. Mandel, M.D., clinical associate professor, have been appointed. In the Department of Psychiatry, Albert L. Deutsch, M.D., clinical assistant professor, and Viola L. Wiegand, M.D., lecturer, have been appointed, and in the Department of Pathology as clinical assistant professors, Phillip G. Cabaud, M.D., and Victor Ginsberg, M.D.

Other appointments made are: Dr. Samuel W. Bloom, associate professor in administration; Kenneth G. Jennings, M.D., clinical professor, Department of Pediatrics; Dr. William Langan, assistant professor in physiology; and Dr. William T. West, assistant professor in anatomy.

National conference. A national conference on "The Fundamentals of Vascular Grafting" was held at the Center on November 5 and 6. The conference consisted of four sessions and was sponsored by the Department of Surgery. Chairmen of the sessions were: Clarence Dennis, M.D., chairman, Department of Surgery; Ralph A. Deterling, Jr., M.D., Tufts University School of Medicine; Michael E. DeBakey, M.D., Baylor University College of Medicine; and Charles A. Hufnagel, M.D., Georgetown University Medical Center.

State University of New York Upstate Medical Center

Hilda F. Silverman lecture. Myron E. Wegman, M.D., dean, University of Michigan School of Public Health, delivered the ninth annual Hilda F. Silverman Lecture on October 24. Dr. Wegman discussed "Child Health in a Changing World."

MEND. Richard Lindenberg, M.D., director of neuropathology and legal medicine, State of Maryland Department of Mental Hygiene, spoke on "Clinical Pathologic Aspects of Head Injuries" at the October MEND lecture

Lectures. "Mechanism of the Stimulation of Aldosterone Secretion" was discussed by James O. Davis, M.D., chief, section on experimental cardiovascular disease, National Heart Institute, Bethesda, Maryland, on October 16. While in Syracuse, Dr. Davis also spoke before the State assembly of the American Academy of

General Practice at the Onondaga County War Memorial.

At a meeting sponsored by the Association of Childhood Education International, Julius Richmond, M.D., professor and chairman, Department of Pediatrics, was one of nine selected national authorities to attend. The conference proceedings will be published at a later date.

Frank B. Rogers, M.D., director, National Library of Medicine, Bethesda, Maryland, discussed "Mechanized Information Retrieval Systems for Medical Literature" on October 17. The system, called MEDLARS (Medical Literature Analysis and Retrieval System), is being developed at the National Library and will be ready for use in 1964. The National Library since 1949 was called the Armed Forces Medical Library. Dr. Rogers is also president of the Medical Library Association for 1962–1963 and general chairman of the Second International Congress on Medical Librarianship to be held in Washington, D.C., next June.

University of Rochester School of Medicine and Dentistry

Medical Alumni Association annual meeting. The eighteenth annual meeting of the Medical Alumni Association was held October 11 to 13. A highlight was the dedication of the expanded and renovated Medical Library on October 12 at which the speakers were: William M. Allen, M.D., a 1932 graduate, now chairman, Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, on "The Medical Student and the Library"; Frederick G. Kilgour, librarian, Yale University School of Medicine, on "Information Dissemination in the Medical Library of the Next Decade"; and John M. Russell, president, The John and Mary R. Markle Foundation of New York City, "The New Foundations." George W. Corner, M.D., first professor of anatomy at the University and now historian of the Rockefeller Institute, talked on "Books We Never Return to the Shelf."

Donald G. Anderson, M.D., dean, and Priscilla L. Cummings, M.D., president of the alumni association, extended greetings.

The annual Karl M. Wilson lecture was given by Dr. Corner who discussed "Exploring the Placental Maze."

Gold Medal winner. Ralph F. Jacox, M.D., associate professor of medicine, was the winner of the Gold Medal of the University of Rochester Medical Alumni Association. The Gold Medal is given annually to a member of the University's medical faculty for "high integrity, distinguished contribution to students, and inspired teaching."

Acting chairman. Harry L. Segal, M.D., clinical professor of medicine, left in November for Lagos where he is serving a three-month faculty position as acting chairman of the Department of Medicine, of the University of Lagos Medical College, Nigeria.

Reading Habits Analyzed

In an analysis of medical communications, *Patterns of Disease*, a monthly Parke, Davis & Company publication for physicians, reports that it would take a physician three years and one hundred sixty-one days to read all the physiologic literature published in 1960, assuming he read at a rate of one page every two minutes during an eight-hour day.

Abstracts

Dube, A. H.: Diabetes teaching manual for patients and hospital personnel, NEW YORK STATE J. MED. **62:** 3754 (Dec. 1) 1962.

Diabetes mellitus, a hereditary disease due to a relative or absolute lack of insulin which results in inability to utilize carbohydrate properly for normal body energy, may be of the adult type, which usually is accompanied by obesity and responds to the oral drugs, or the juvenile type, in which obesity is uncommon, diabetic ketosis occurs readily, and insulin administration is necessary. Prediabetes often may be detected during pregnancy. Although there is no cure for diabetes, remission may occur. Good treatment means the maintenance of normal weight, normal activity, absence of glycosuria, and as normal a blood sugar as can be achieved without hypoglycemia; it consists of diet, insulin, exercise, and oral hypoglycemic drugs. Complications of diabetes include: diabetic retinopathy, nephropathy, and neuropathy. Insulin reactions may cause cerebral and adrenal symptoms; the treatment is rapid administration of glucose, or glucagon if the patient is unconscious. Diabetic acidosis may occur as the result of failure to take insulin or of severe infection which greatly increases the need for insulin, and the patient's physician should be contacted immediately. Urine testing for glucose is useful in achieving diabetic regulation. Proper care of syringes and needles, careful foot care, and identification tags are essential in patients with diabetes.

Lemmon, W. M.: Recent advances in the physiology of acquired heart disease, NEW YORK STATE J. MED. **62:** 3766 (Dec. 1) 1962.

Much progress has recently been made in understanding the physiology of acquired heart disease and in the development of diagnostic and treatment technics. In coronary artery disease the development of coronary arteriography has enabled surgical removal of the lesions in certain cases. In acquired valvular disease many of the advances are the result of the adoption of open-heart technics and the application of advanced patho-anatomic knowledge in such operations as mitral commissurotomy. In patients with congestive heart failure ultrafiltration renal dialysis offers a means of treating intractable plus decompensation heart failure when there is an excess of fluid.

Archer, J. S., and Hicks, R. G.: Phenothiazine subgroups, NEW YORK STATE J. MED. **62:** 3769 (Dec. 1) 1962.

The phenothiazine derivatives vary greatly, and are commonly grouped according to the side chain found at the number 10 position into the aliphatic, piperidine, and piperazine categories. They may also be categorized according to substitutions at the number 2 position of the hydrogen, chloride, fluoride, sulfur, oxygen, and carbon molecules. The more potent derivatives have a greater incidence of extrapyramidal symptoms and are longer lasting. Those which do not incorporate the piperazine ring cause prolonged sleeping time when used with barbiturates. The analgesic effects of the phenothiazines fall into three categories: analgesic, slightly antianalgesic, and definitely antianalgesic. The choice of derivative should be based on the specific purpose and desired duration of action, and the dosage should be individualized according to the age, sex, and physical status.

Penta, A. Q.: Bronchoscopy in treatment of chronic bronchitis, asthma, and emphysema, NEW YORK STATE J. MED. **62:** 3773 (Dec. 1) 1962.

In chronic bronchitis bronchoscopy enables the following: removal of obstructing secretion at periodic intervals which permits adequate oxygenation and restores ventilatory function; visualization of underlying pathologic changes in the bronchial tract; exploration of the secondary bronchial orifices and removal of any plugging from inspissated mucus or granulation tissue; accurate bacteriologic examination, culture-sensitivity studies, and the making of autogenous vaccines; and direct instillation of antimicrobial and bronchodilating drugs into the bronchial tract. In bronchial asthma bronchoscopy enables diagnosis of bronchial obstruction and aspiration of the obstructive secretion. In chronic obstructive emphysema bronchoscopic aspiration of retained secretion, dilatation of stenosed areas, and direct instillation of decongestive and antimicrobial medication for the control of infection are important adjuncts in treatment.

Spens, N., Parsons, H., and Begg, C. F.: Primary melanoma of the meninges, NEW YORK STATE J. MED. **62:** 3777 (Dec. 1) 1962.

Primary melanoma of the meninges is a rare condition which may occur at any age. In the reported cases the ratio of males to females is 2 to 1; the presenting symptoms were usually those of increased intracranial pressure; frequently the only other detectable abnormality was increased protein in the cerebrospinal fluid; and the cause of death was usually increased intracranial pressure due to blockage of absorption of cerebrospinal fluid by tumor. The tumor consists either of a diffuse, brown-black thickening of the meninges of variable density which may extend down the cord, of discrete pigmented spots, or of both these forms.

Jacobs, L.: Hypnosis in clinical pediatrics, New York State J. Med. **62:** 3781 (Dec. 1) 1962.

The proper use of hypnosis can be a valuable tool in the treatment of emotional problems of children. A complete history is necessary, and the use of simple projective tests, such as the drawing of familiar family figures, may be helpful. Usually a light state of hypnosis is all that is needed for the acceptance of suggestions which relieve the anxiety and tensions of the patient, reassure him of the love of his parents, and bolster his feelings of self-esteem and self-confidence. This enables the child to pursue his natural goal: to gain mastery of his own abilities and to achieve a secure place, as an individual, in his environment.

Owens, G., Belmusto, L., and Ross, C. A.: Neurologic complications observed in bronchogenic carcinoma, New York State J. Med. **62:** 3788 (Dec. 1) 1962.

In 295 patients with bronchogenic carcinoma the nervous system was involved in 175. Pain was the most frequent complication and occurred in isolated instances in 74 patients and in multiple sites in 71, the most frequent site being the chest. Postmortem examination performed on 32 patients showed that 23 had intracranial lesions, of whom 16 had two or more metastatic tumors while 7 had single lesions. The treatment of choice for patients with pain resulting from nervous system involvement has been contralateral cordotomy and an ipsilateral high cervical posterior rhizotomy, with bilateral prefrontal lobotomy used in patients with far-advanced disease in which pain is the primary nursing problem.

Zucker, H. S.: Effect of allergens on fungi: growth of Mucor in presence of protein derivative of m. tuberculosis; preliminary note, New York State J. Med. **62:** 3790 (Dec. 1) 1962.

The addition of the PPD (purified protein derivative) of tubercle bacilli to the surface of Sabouraud agar plates produced an increase in the in vitro growth of Mucor species.

New athlete's foot remedy

A preparation which helps keep the British Army on its toes may prove to be the answer to a common foot problem which plagues most Americans—athlete's foot.

Intensive testing, reported by Dr. Morton H. Walker at the American Podiatry Association meeting, August 16, 1962, showed that the new medication, chloroxylenol, when used regularly, clears up most cases of athlete's foot and prevents its recurrence. It is as convenient to use as toothpaste according to the testers.

Following testing on laboratory animals, unmarked bottles of chloroxylenol were given to 325 patients who complained of a variety of foot ills, including athlete's foot.

The results showed that in patients with athlete's foot who had used the preparation as prescribed, the fungus condition and accompanying itching disappeared within two weeks in most cases. In addition, chloroxylenol apparently stimulated the growth of new tissue, helped to evaporate perspiration, and invigorated the muscles.

While it adequately controlled chronic fungus conditions, chloroxylenol proved to be most effective against newly developed growth.

Medical Meetings

Israel S. Wechsler Lecture

The Israel S. Wechsler Lecture will be given at The Mount Sinai Hospital on Friday evening, December 7, at 8:30 P.M., by Seymour S. Kety, M.D., chief, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland. His subject will be "Amino Acids, Amines, and Behavior."

The lecture will be delivered at the Blumenthal Auditorium of The Mount Sinai Hospital, entrance through the hospital gardens, Fifth Avenue at 99th Street, New York 29, New York.

Bronx Pediatric Society

The Bronx Pediatric Society will present a "resident's night" at Morrisania Hospital, 168th Street and Gerard Avenue, the Bronx, at 8:30 P.M., on December 12.

The program will be as follows: *Bronx Hospital*—"Intractable Abdominal Pain Complicating Cystic Fibrosis of the Pancreas," presented by Reuben Wasserman, M.D., and discussed by Murray Davidson, M.D.; *Jewish Memorial Hospital*—"Introgenic Female Pseudo Hermaphrodism," presented by Elizabeth Montalban, M.D., discussed by Nathan Greenstein, M.D.; *Fordham Hospital*—"Infantile Pyknocytosis," presented by Robert E. Lukas, M.D., discussed by Julian Schorr, M.D.; and *St. Francis Hospital:* "Ectodermal Dysplasia of the Anhidrotic Type in Prolonged Fever in an Infant," presented by Jose Gabatin, M.D., discussed by Rosario Drago, M.D., and Theodore Ehrenreich, M.D.

Division of Dermatology, Downstate Medical Center

The Division of Dermatology of the Department of Medicine, State University of New York Downstate Medical Center, will present a discussion on "Office Dermatologic Surgery" on January 4, 1963, from 10:00 to 11:30 A.M., in the E Building Auditorium, Kings County Hospital, 451 Clarkson Avenue, Brooklyn 3, New York.

George Popkin, M.D., assistant clinical professor of dermatology and syphilology, New York University Post-Graduate Medical School, will be the speaker and Lawrence Frank, M.D., professor of dermatology, State University of New York Downstate Medical Center, will be the moderator.

American Society of Facial Plastic Surgery

The American Society of Facial Plastic Surgery will hold a meeting on January 18, 1963, at the Hotel Elysee, New York City, during the course in rhinoplasty which will be given by Irving B. Goldman, M.D., and his staff at The Mount Sinai Hospital, January 12 through January 25.

The program will be as follows: "Chemobrasion vs. Dermabrasion," Milton Reisch, M.D., and Norman Orentreich, M.D., New York City; "Correction of Baggy Eyelids," Morris Feldstein, M.D., New York City—discussion, Maury Parkes, M.D., Beverly Hills, California; "Use of Silicone in Correction of Facial Depressions," Maury Parkes, M.D.

For information contact: Samuel M. Bloom, M.D., Secretary, American Society of Facial Plastic Surgery, 123 East 83rd Street, New York 28, New York.

Heart Association of Southeastern Pennsylvania

The Heart Association of Southeastern Pennsylvania is sponsoring a two-and-a-half day symposium on the basic science aspects of genetics and their significance to medical care, especially as related to heart disease. The symposium will be held January 24 through 26, 1963, at the Hotel Sheraton, Philadelphia.

For further information write to: Albert N. Brest, M.D., Heart Association of Southeastern Pennsylvania, 318 South 19th Street, Philadelphia 3, Pennsylvania. Deadline for registration is January 11.

International Medical Assembly of Southwest Texas

The twenty-seventh annual session of the International Medical Assembly of Southwest Texas will be held in San Antonio, Texas, January 28 through 30, 1963, at the Granada Hotel. The subject of the meeting will be all aspects of cancer.

Two New York City physicians, Bronson S. Ray, M.D., and George T. Pack, M.D., will be among the speakers.

For further information write to: Mr. S. E. Cockrell, Jr., Executive Secretary, International Medical Assembly of Southwest Texas, 202 West French Place, San Antonio 12, Texas.

A.M.A. medicolegal symposium

The American Medical Association will hold a medicolegal symposium at the Americana Hotel in Miami Beach, Florida, Friday and Saturday, March 8 and 9, 1963.

Symposium on pediatric surgery

The Greater New York Chapter of The National Foundation is sponsoring a symposium on pediatric surgery to be held at The New York Hospital-Cornell Medical Center, March 18 through 20, 1963. Participants will include pediatric surgeons and pediatricians from various medical centers in the United States and Canada.

For information contact: S. Frank Redo, M.D., 525 East 68th Street, New York 21, New York.

Pan-Pacific Surgical Association

The Pan-Pacific Surgical Association has announced that the Association will hold its ninth congress on November 5 through 13, 1963, in Honolulu, Hawaii, and the first Pan-Pacific mobile educational lecture seminar, November 13 through December 10, 1963, in New Zealand, Australia, Thailand, the Philippines, Hong Kong, and Japan.

For further information write to: F. J. Pinkerton, M.D., Director General, Pan-Pacific Surgical Association, Suite 236, Alexander Young Building, Honolulu 13, Hawaii.

International conference on tetanus

An international conference on the prevention and treatment of tetanus will be held November 8 through 10, 1963, in Bombay, India. Free accommodation will be provided by the Society of the Study Group of Tetanus, sponsoring organization of the conference, for those authors whose papers are accepted to be read at the meeting.

Those wishing to submit papers should write to: Dr. J. C. Patel, Organising Secretary, International Conference on Tetanus, K. E. M. Hospital, Parel, Bombay 12, India.

Mortality From Blood Transfusions

There are more deaths annually in the United States from blood transfusions than from appendicitis, according to Max M. Simon, M.D., Poughkeepsie. Speaking at the thirteenth biennial congress of the International College of Surgeons in New York City, Dr. Simon said that reports from the Department of Health, Education, and Welfare showed that the annual mortality from three major complications of blood transfusion was computed to be 16,500. He listed the three major complications as reactions between the donated blood and that of the patient, overloading the circulation with too much blood, and serum hepatitis.

Other surgeons agreed with Dr. Simon that blood transfusions sometimes were given too lightly. Although indisputably lifesaving when they are really needed, the speakers agreed, transfusions can be a source of unnecessary hazard to the patient when they are given prophylactically, or just to "play it safe."

Abstracts in Interlingua

Dube, A. H.: Manual de instruction in diabete pro patientes e personal de hospital (*anglese*), NEW YORK STATE J. MED. **62:** 3754 (1 de decembre) 1962.

Diabete mellite, un morbo hereditari causate per le relative o absolute manco de insulina resultante in le incapacitate de utilisar hydrato de carbon efficacemente pro le normal economia de energias corporee, pote esser del typo adulte, que es usualmente accompaniate de obesitate e responde al drogas oral, o del typo juvenil, in que obesitate es incommun sed in que cetosis diabetic occurre prestemente e in que le administration de insulina es indispensabile. Prediabete pote frequentemente esser detegite durante le pregnantia. Ben que nulle cura es cognoscite pro diabete, le occurrentia de un remission es possibile. Un bon tractamento significa le mantenentia de peso normal, de activitate normal, de un stato de non-glycosuria, e del plus normal nivello possibile de sucro sanguinee (sin risco de hypoglycemia). Illo consiste del uso de un regulate dieta, de insulina, de exercitio, e de oral pharmacos hypoglycemic. Le complicationes de diabete include retinopathia, nephropathia, e neuropathia. Reactiones insulinic pote esser le causa de symptomas cerebral e adrenal. Le tractamento es le rapide administration de glucosa, o de glucagon si le patiente es inconscie. Acidosis diabetic pote occurrer como resultato del suspension de insulina o de un sever infection que grandemente augmenta le requirimento pro insulina. In iste situation le medico del patiente debe esser appellate immediatemente. Tests del urina pro deteger le presentia de glucosa es utile in le effortio de effectuar un stabilisation del diabete. Le correcte manutention del syringas e agulias, meticulose pedicultura, e le uso de medalias de identification es essential in patientes con diabete.

Lemmon, W. M.: Recente progressos in le physiologia de acquirite morbo cardiac (*anglese*), NEW YORK STATE J. MED. **62:** 3766 (1 de decembre) 1962.

Multe progressos ha in recente tempores essite facite in le comprension del physiologia de acquirite morbo cardiac e in le disveloppamento del technicas de diagnose e therapia. In morbo de arteria coronari, le disveloppamento de arteriographia coronari ha rendite possibile le excision chirurgic del lesiones in certe casos. In acquirite morbo valvular, multes del progressos es le resultato del adoption de technicas de chirurgia a corde aperte e del application de avantiate cognoscentias patho-anatomic, lo que vale particularmente in casos requirente commissurotomia mitral. In patientes con congestive disfallimento cardiac, dialyse renal con ultrafiltration offere un methodo pro tractar "intractabile" discompensation cardiac in le presentia de un excesso de liquido.

Archer, J. S., e Hicks, R. G.: Subgruppos phenothiazinic (*anglese*), NEW YORK STATE J. MED. **62:** 3769 (1 de decembre) 1962.

Le derivatos phenothiazinic varia grandemente e es communmente gruppate—secundo le catena lateral trovate in position numero 10—in phenothiazinas aliphatic, piperidinic, e piperazinic. Illos pote etiam esser categorisate secundo le substitutiones in position numero 2 de moleculas de hydrogeno, chloruro, fluoruro, sulfure, oxygeno, e carbon. Le derivatos plus potente es associate con un incidentia plus grande de symptomas extrapyramidal, e lor efficacia es plus durative. Le derivatos que non contine le anulo de piperazina causa prolongate tempores de somnio quando illos es usate con barbituratos. Le effectos analgesic del phenothiazinas se divide in tres categorias secundo que illos es positivemente analgesic, levemente antianalgesic, e definitemente antianalgesic. Le selection del derivato a usar in le caso particular debe esser determinate per le objectivo specific e le desirate duration del action. Le dosage debe esser individualisate secundo le etate, le sexo, e le stato physic del patiente.

Penta, A. Q.: Bronchoscopia in le tractamento de chronic bronchitis, asthma, e emphysema (*anglese*), NEW YORK STATE J. MED. **62:** 3773 (1 de decembre 1962.

In chronic bronchitis, bronchoscopia rende possibile le sequente processos: Elimination de secretion obstructori a intervallos periodic pro obtener un adequate oxygenation e pro restaurar le function ventilatori; visualisation de subjacente alterationes pathologic in le vias bronchial; exploration del orificios bronchial secundari e elimination de omne obstruction per inspissate muco o per tissu granulatori; accurate examination bacteriologic, studios de sensibilitate in cultura, e production de vaccinos autogene; e instillation directe de pharmacos antimicrobial e bronchodilatatori ad in le vias bronchial. In asthma bronchial, bronchoscopia rende possibile le diagnose de obstruction

continued on page 3842

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continued from page 3840

bronchial e le aspiration del secretion obstructive. In chronic emphysema obstructive, le aspiration bronchoscopic de secretion residue, le dilatation de areas de stenose, e le directe instillation de pharmacos decongestive e antimicrobial pro le elimination de infection es importante adjunctos al tractamento.

Spens, N., Parsons, H., e Begg, C. F.: Melanoma primari del meninge (*anglese*), New York State J. Med. **62:** 3777 (1 de decembre) 1962.

Melanoma primari del meninge es un condition rar que pote occurrer a non importa qual etate. In le hic-reportate casos le proportion de masculos a femininas es 2 a 1. Le symptomas de presentation esseva usualmente illos de un augmento del pression intracranial. Frequentemente le sol altere detegibile anormalitate esseva un augmento del proteina in le liquido cerebrospinal. Le causa del morte esseva usualmente un augmentate pression intracranial in consequentia de un blocage del absorption de liquido cerebrospinal per un tumor. Le tumor consiste de un diffuse spissification del meninge de color brunastro-nigre, variabile in densitate, que pote extender in basso al longo del medulla dorsal, o de discrete maculas pigmentate o etiam de ambe iste formas.

Jacobs, L.: Hypnose in le pediatria clinic (*anglese*), New York State J. Med. **62:** 3781 (1 de decembre) 1962.

Le intelligente uso del hypnose pote esser un instrumento de grande utilitate in le tractamento de problemas emotional de patientes pediatric. Un complete historia casuistic es necessari, e le application de simple tests de typo projective—per exemplo le designar de cognoscite figuras del familia—pote esser de assistentia. Usualmente non plus que un leve stato de hypnose es necessari pro le acceptation de suggestiones que allevia le anxietate e le tensiones del patiente, que reassecura le del amor de su parentes, e que reinfortia su emotiones de auto-respecto e auto-confidentia. Isto permitte al juvene individuo persequer su objectivo natural: attinger le complete maestria de su capacitates e establir se securmente, como individuo, in su ambiente.

Owens, G., Belmusto, L., e Rose, C. A.: Complicationes neurologic observate in carcinoma bronchogenic (*anglese*), New York State J. Med. **62:** 3788 (1 de decembre) 1962.

In un gruppo de 295 patientes con carcinoma bronchogenic, 175 monstrava evidentia de affection del systema nervose. Dolor esseva le complication le plus frequente. Illo occurreva in sitos isolate in 74 patientes e in sitos multiple in 71. Le sito le plus frequente esseva le thorace. Examines post morte esseva effectuate in 32 casos, con le constatation de lesiones intracranial in 23. Dece-sex de iste 23 patientes habeva duple o multiple tumores metastatic; in 7 le lesion esseva simple. Le tractamento de election pro patientes con dolor in consequentia de un affection del systema nervose esseva chordotomia contralateral e un rhizotomia postero-alticervical ipsilateral, con bilateral lobotomia prefrontal in patientes con morbo avantiatissime in que dolor es le primari problema de nosotrophia.

Zucker, H. S.: Le effecto de allergenos super fungos; le crescentia de Mucor in le presentia de purificate derivato proteinic de bacillos de tuberculosis; nota preliminari (*anglese*), New York State J. Med. **62:** 3790 (1 de decembre) 1962.

Le addition de purificate derivato proteinic de tuberculosis al superficie de placas de agar de Sabouraud resultava in un augmento del crescentia in vitro de species de Mucor.

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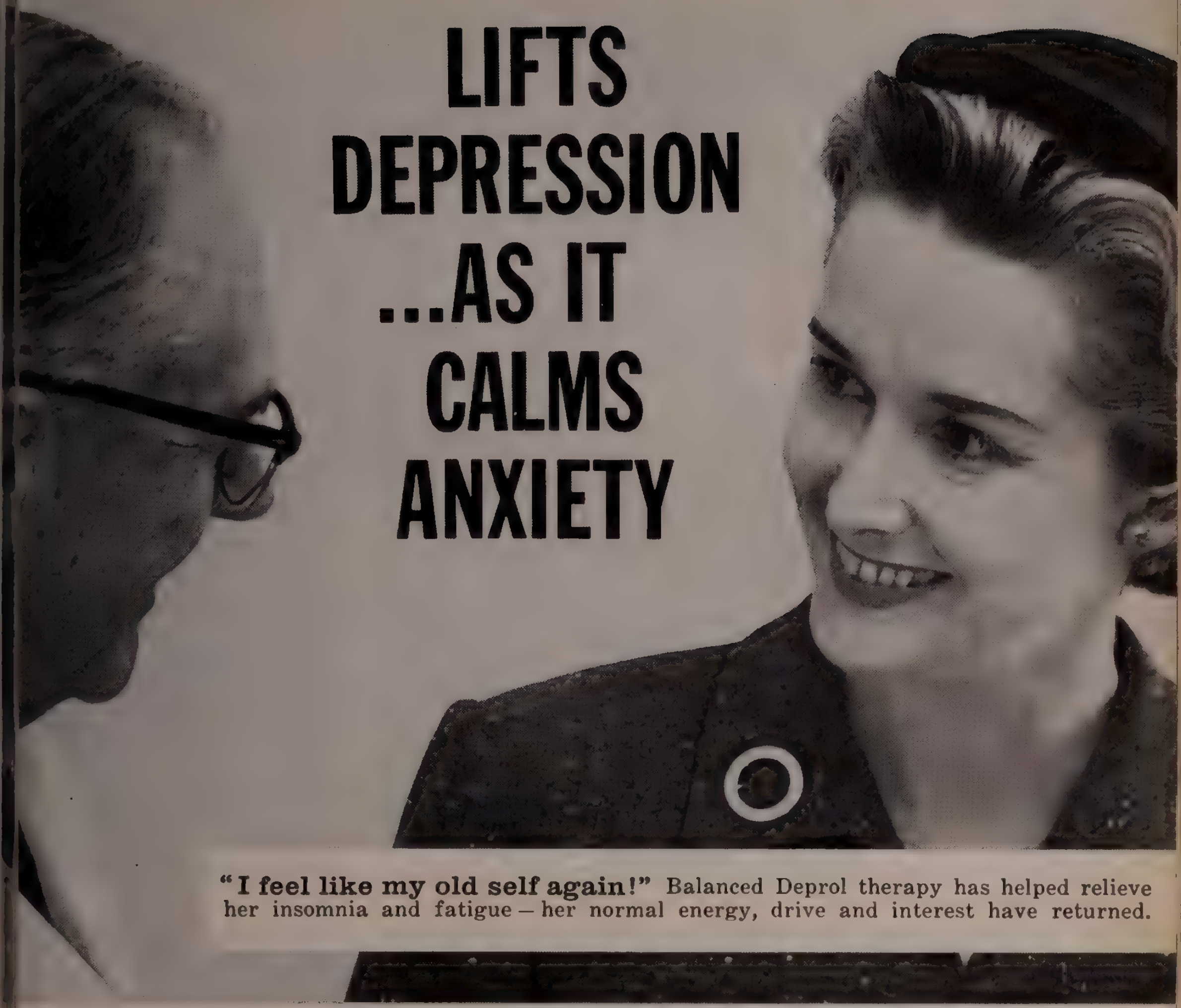

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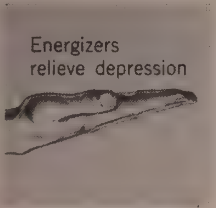

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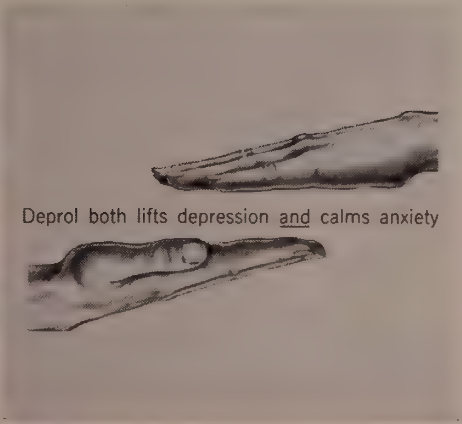

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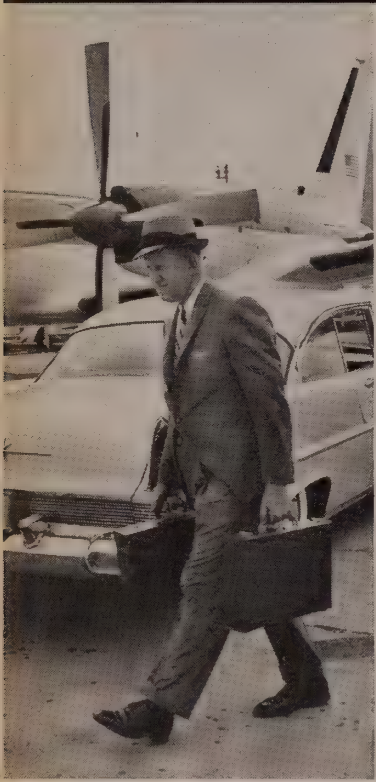
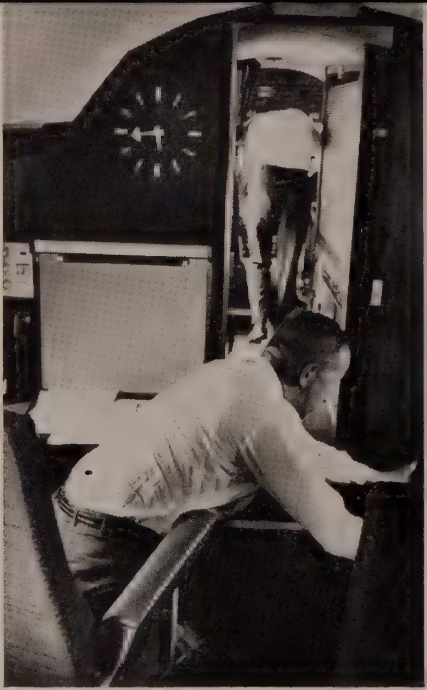
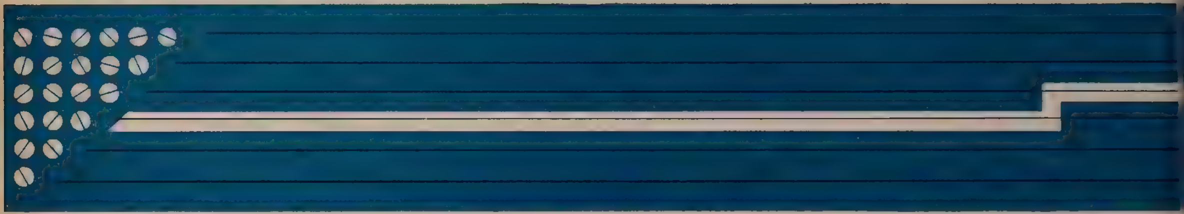




Orinase dosage 1 Gm. = ⊘⦸



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*Schwartz, I. R.:
Current Therap. Res. 3:29, Feb., 1961.

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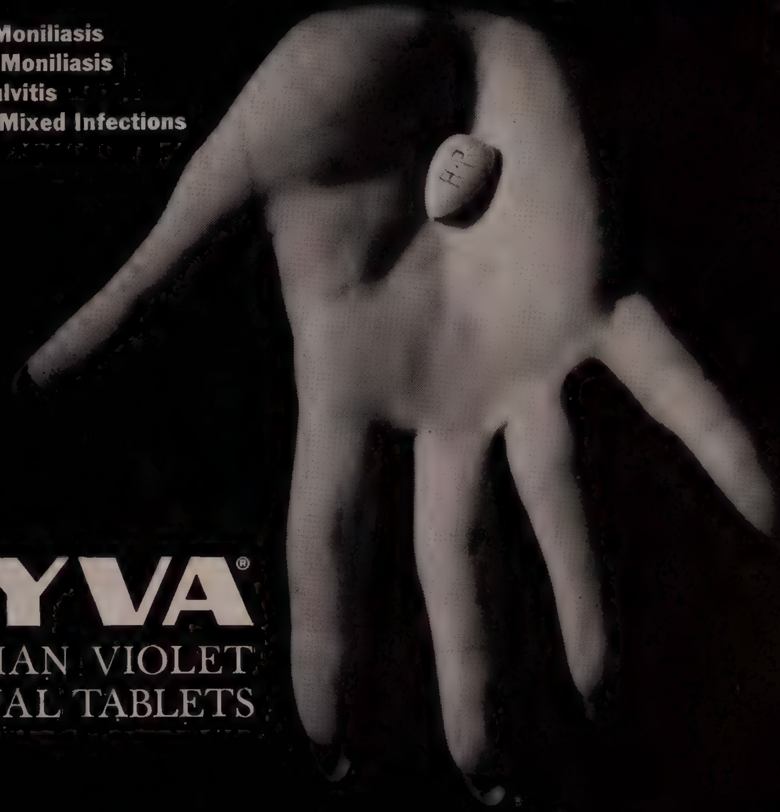

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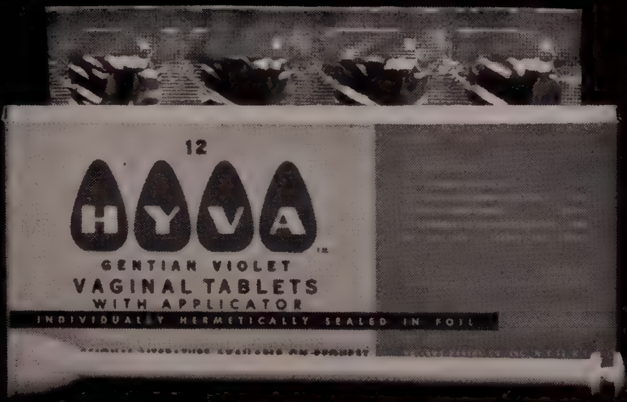
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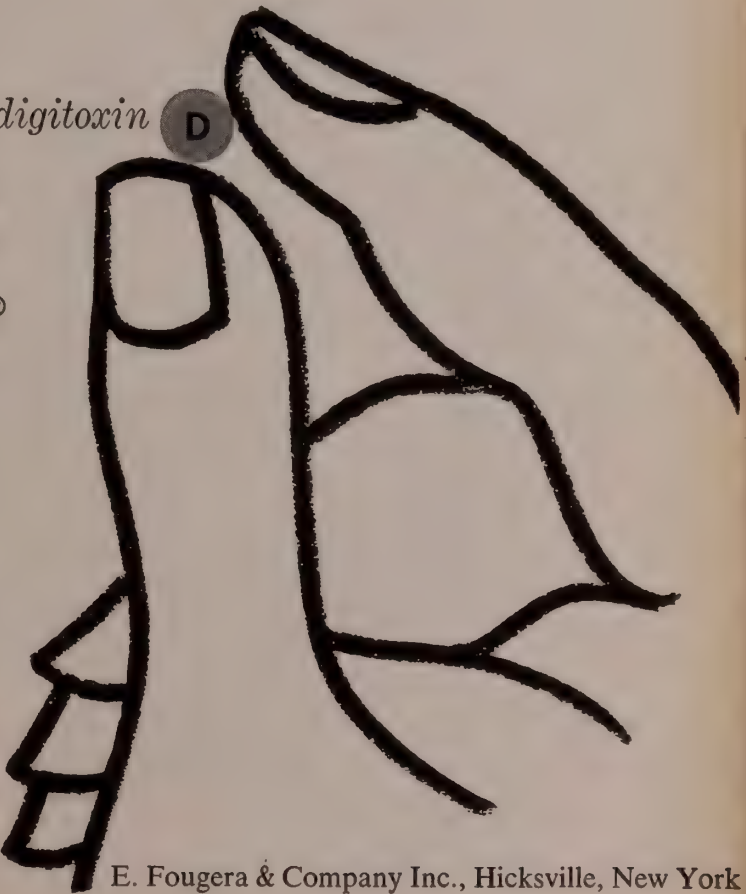

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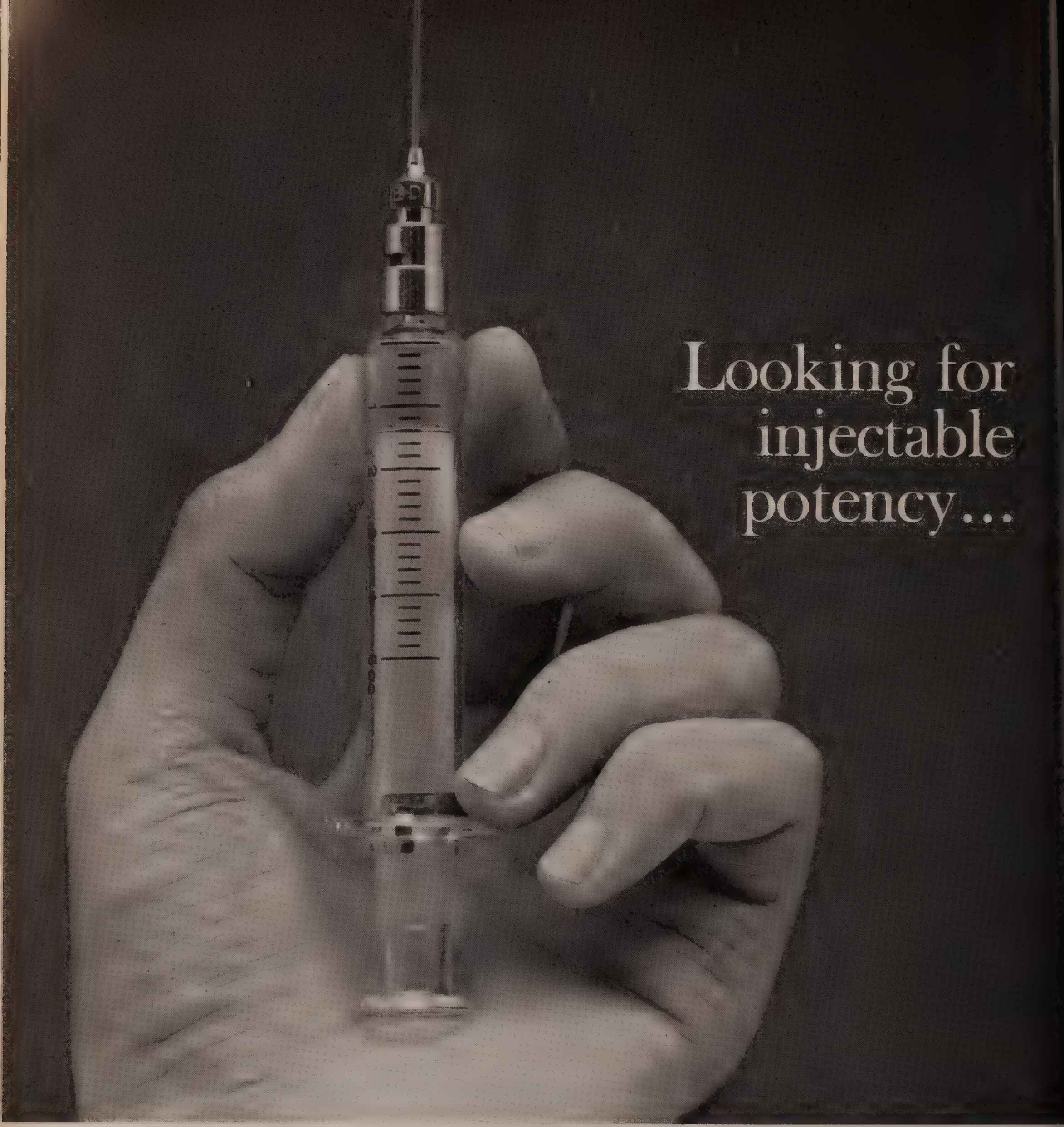
*Roseman, E.: Neurology 11:912, 1961.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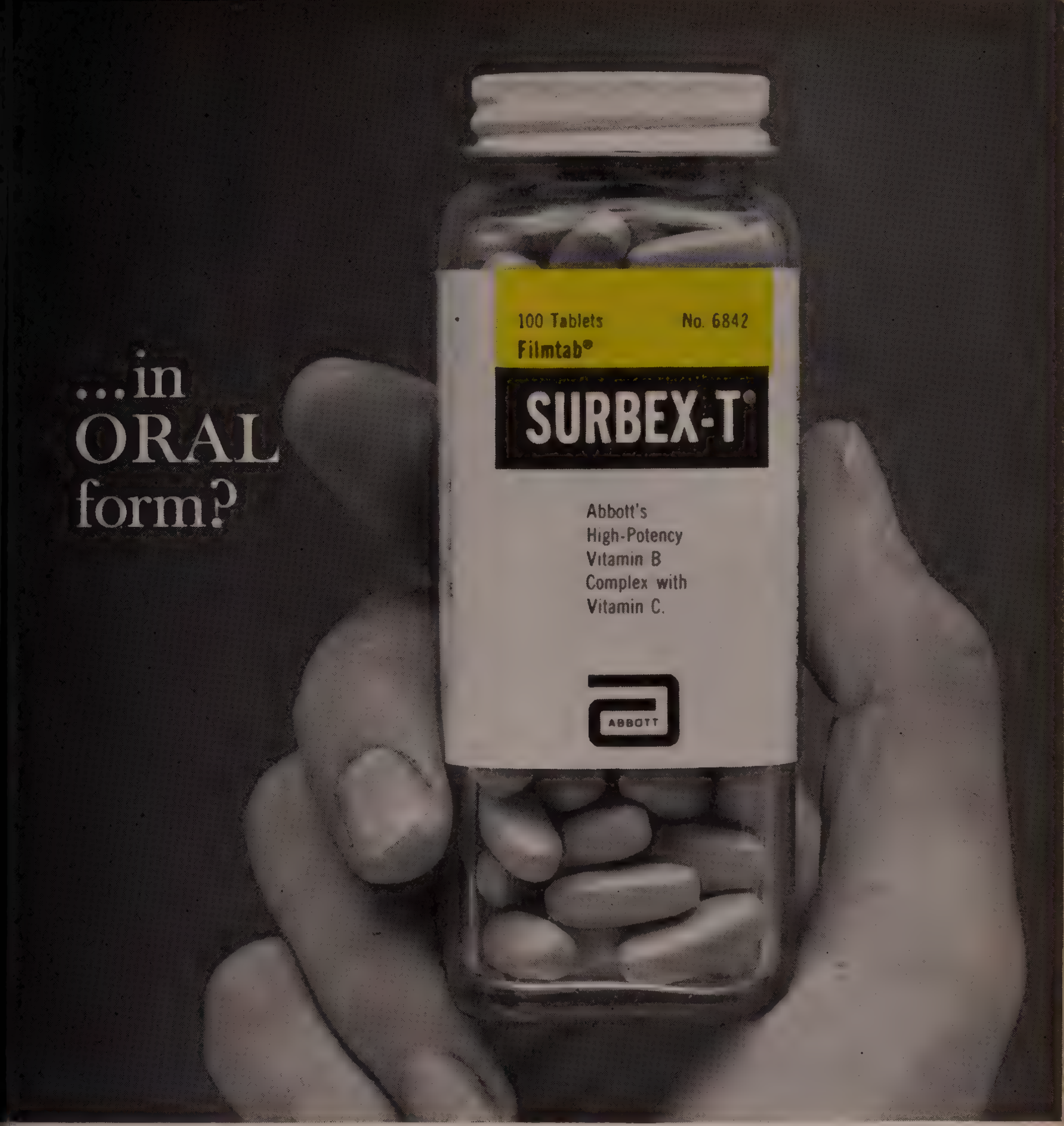
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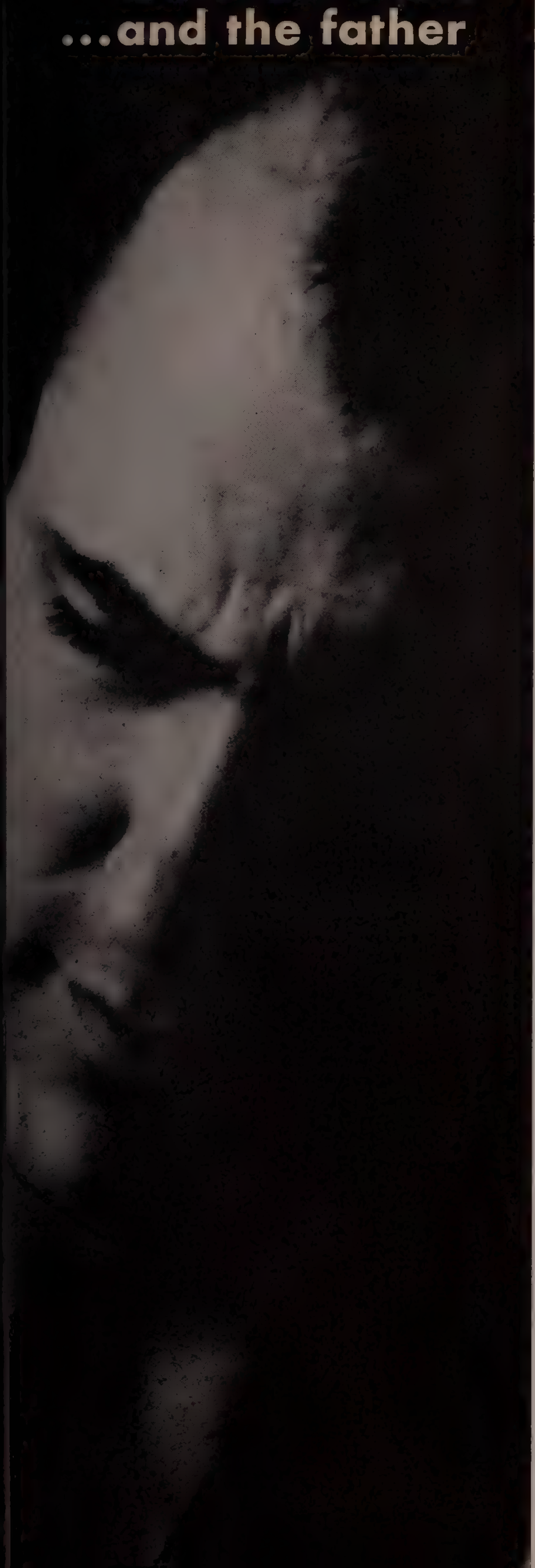

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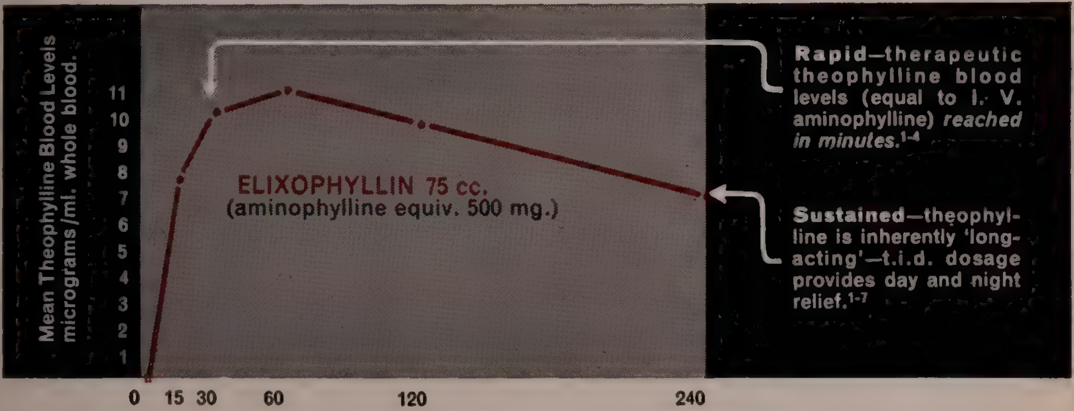

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References: (1) Kessler, F.: Connecticut S.M.J. *21*:205 (March) 1957. (2) Burbank, B.; Schluger, J., and McGinn, J.: Am. J. Med. Sci. *234*:28 (July) 1957. (3) Spielman, A.D.: Ann. Allergy *15*:270 (June) 1957. (4) Greenbaum, J.: Ann. Allergy *16*:312 (May-June) 1958. (5) Kessler, F.: Medical Times *87*:1298 (Oct.) 1959. (6) Bickerman, H.A., and Barach, A. L., in Modell, W.: Drugs of Choice 1960-1961, St. Louis, The C. V. Mosby Company, 1960, p. 516. (7) Wilhelm, R. E. in Conn., H. F.: Current Therapy—1961, Philadelphia, W. B. Saunders Company, p. 417. (8) Schluger, J. McGinn, J. T., and Hennessy, D. J.: Am. J. Med. Sci. *233*:296, 1957.

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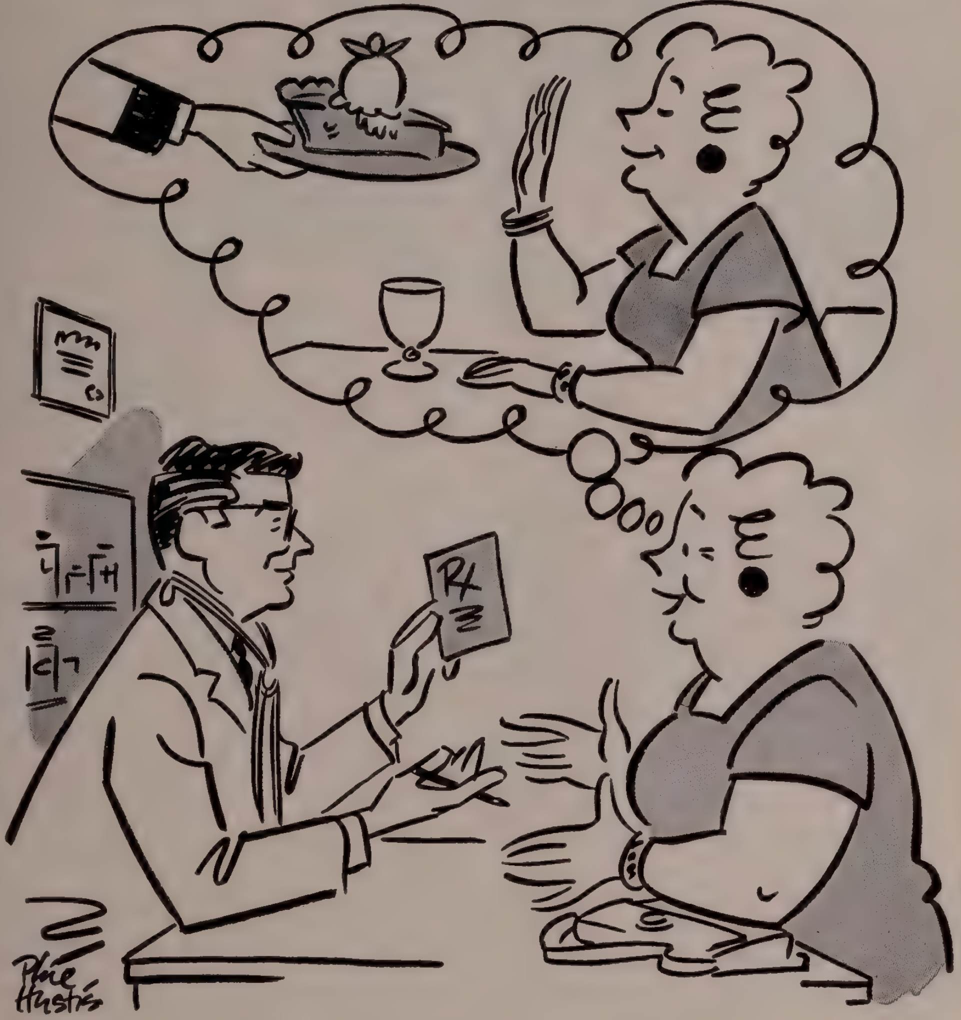

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1. Berger, R.A., Clinical Medicine, Sept. 1961.

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*Feinblatt, T. M., and Ferguson, E. A., Jr., Phenobarbital idiosyncrasy, avoidance by use of phenobarbital-niacin, *New York State J. Med.* Vol. 62: 221-223, 1962.

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[1] Ford, R. A., and Blanchard, K.: Journal-Lancet 78:185, 1958

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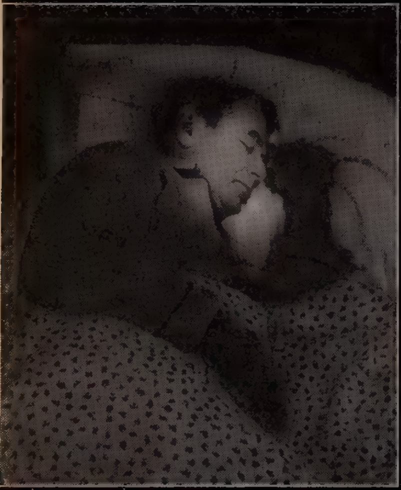

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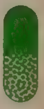

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References: (1) Malone, F. J., Jr.: *Mil. Med.* **125**:836, 1960. (2) Martin, W. J.; Nichols, D. R., & Cook, E. N.: *Proc. Staff Meet. Mayo Clin.* **34**:187, 1959. (3) Ullman, A.: *Delaware M. J.* **32**:97, 1960. (4) Petersdorf, R. G.; Hook, E. W.; Curtin, J. A., & Grossberg, S. E.: *Bull. Johns Hopkins Hosp.* **108**:48, 1961. (5) Jolliff, C. R.; Engelhard, W. E.; Ohlsen, J. R.; Heidrick, P. J., & Cain, J. A.: *Antibiotics & Chemother.* **10**:694, 1960. (6) Lind, H. E.: *Am. J. Proctol.* **11**:392, 1960.

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New York State Journal of Medicine

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Editorials

Christmas, 1962

In the opening scene of *Hamlet,* the watch at Elsinore says of the atmosphere of the Christmas season "so hallow'd and so gracious is the time."

Hallowed indeed because this humble birth was to renew for all men the ancient Hebraic ideal that man is individually responsible to God. The prophets had pounded home this thought year after year, generation after generation. Where this was ignored men suffered the external misfortune of tyranny but more importantly the internal degradation of purposelessness.

Hallowed indeed because this birth in a stable puts the pretensions of wealth and power and the trappings of success in perspective.

At this season men put aside pride, envy, and selfishness and for a time turn outward their hidden resources of humility, understanding, and generosity. The graciousness of open homes and open hearts abounds. Parties and gaiety encrusted by tradition run their accustomed way, but deeper still runs the strong current of spiritual renewal. This is the core of Christmas. It is as if men finally become aware that they are children of God and act like it.

May your Christmas be a happy one.

The art and joy of writing*

Writing is a doing or a giving activity, in contradistinction to reading or thinking which can be listening or receiving activities. Nonetheless, writing, reading, and thinking are interrelated and interdependent for it is difficult to conceive how one may write without having exposed oneself to a good deal of reading, and it is equally difficult to draw a line showing where one process ends and another begins. Yet it is so easy to write without thinking.

Science and art

There is an art in writing which one probably develops after having mastered the fundamentals of its science. There is joy in writing, and those who write—principally because their professional obligations demand it and represent the coin of prestige and recognition—may as well find and experience the delights and joys therein. It makes writing less of a chore; it also allows one to experience the joys of creation, vicarious though they may be.

Writing presupposes that the writer has something to say. But that assumption may be unwarranted; one is frequently exposed to writings which say nothing new, but which would have redeemed themselves fully had they been couched interestingly. The moral: if you have nothing startlingly new to say but you must say it, say it interestingly. This is where the art of writing comes into use.

Originality

To be sure, the art of writing comes into play when one has something new to say. But let us honestly assess the business of newness, or originality. It appears that men put great weight and value upon newness or originality per se. Yet, are they per se, of such value? Is newness alone of greater value than the old? Truly new concepts are rare—when they appear they are fundamental and tend to be revolutionary. Much of the so-called new is a rearrangement of the old—an old view reiterated, an old theme clarified, an old concept given a different and perhaps more valid interpretation. In the last named alternative lies much of what passes for new. The moral: let us not deprecate a theme merely because it is not new.

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* Reprinted, with permission, from The New York Journal of Dentistry **32:** 220 (June-July) 1962.

Lasting values reside in the old, which the art of writing can verbalize and convey, and can make a worth-while contribution. How often can we, in utter candor, recall having a truly new thought—daily? weekly? monthly? yearly? every ten years? ever? For example, very few plays of lasting value—philosophies that guide, concepts that have established new polities—are new; they have brilliantly rephrased older themes and thereby made substantial contributions.

Art

What is the art of writing?: to be sure, the rudiments of an art can be taught (after its basic science or mechanism has been explained). But the process of learning the art comes from within. It is learned by doing and drawing from the reservoir within. This presupposes that the reservoir is being continuously replenished by reading, by writing, by thinking.

Yet, it is not a one-to-one correspondence, that is, it does not mean that merely a great deal of experience of doing assures that the doer will have well learned the art. We hear experience prized as if it guarantees adequacy. But this old truth is ever new: a person with a great deal of experience in doing the wrong thing is in a much worse position than the less experienced person whose mind and heart are open to learn.

It is not our intention to make the business of the art of writing a mysterious one, or to imply patronizingly that "if-you-don't-have-it-you-can't-learn-it." Some hold that view—with which we do not necessarily agree. An example from another area will explain: the science of painting deals with colors—their compatibility, their physical properties, which in turn condition their behavior on canvas or on paper. The art lies in the mixing, in the development of shades and notes and the behavior of the nuance of shades in light and dark. One must know the science: but in order to have more than a wooden picturization one must learn the art, as well as the intangibles of the art. And one must practice the art to perfect it. One can learn something about an art didactically, but the full development of the art comes from within, from a warm or passionate devotion to it.

Language

Similarly, in writing, its science deals with structure of language and the requirements for conveying a thought. But the art, which makes clear or brilliant prose possible, which hits rather than merely conveys, comes from practice of writing, drawing upon a rich experience of reading, but more particularly in the exposure to sensation and imagination. One cannot have mastered the art of writing unless one has also the feel for words—their elasticity, their permutations and transmutations, their reappearance in different forms under different conditions.

Joy

Those who have mastered the art of writing, by being at one with words, derive a joy from its activity. Whether this is akin to the joy of creation or the joy in constructing something is immaterial. Many believe that the joy of writing resides partially in being able to express or convey articulately that which was in more or less shapeless form in their thoughts; others believe that the joy in writing arises from the ability to communicate with others, from the sharing and the communicating. Perhaps the truth lies in man's need to communicate.

The desire to communicate and the joy that one derives from it may be incidental. The motive for communication may be the need to communicate on the part of all men, and the joy experienced in it may be an incidental reward. But even the need to communicate is a manifestation of an upper layer—the core lies in the need among men for intercommunication. Except for those whose compulsion is satisfied by talking or by pontificating or for those who are psychologically blocked, intercommunication is the compelling need among men of various callings, cultures, interests, or activities. They need the give and take of exchange and interchange. Similar to the basic need of love and affection, people need to love as well as to be loved, rather than to give unilaterally or to receive unilaterally.

Words

Writing consists of words, but these are only the mechanical fixtures of writing—the tools of intercommunication—and are not an end in themselves. The use of big words does not make good writing, it stilts and frequently stultifies it. Simple words, arranged with insight producing clarity of meaning fructify our language and produce the most glowing prose in our language.

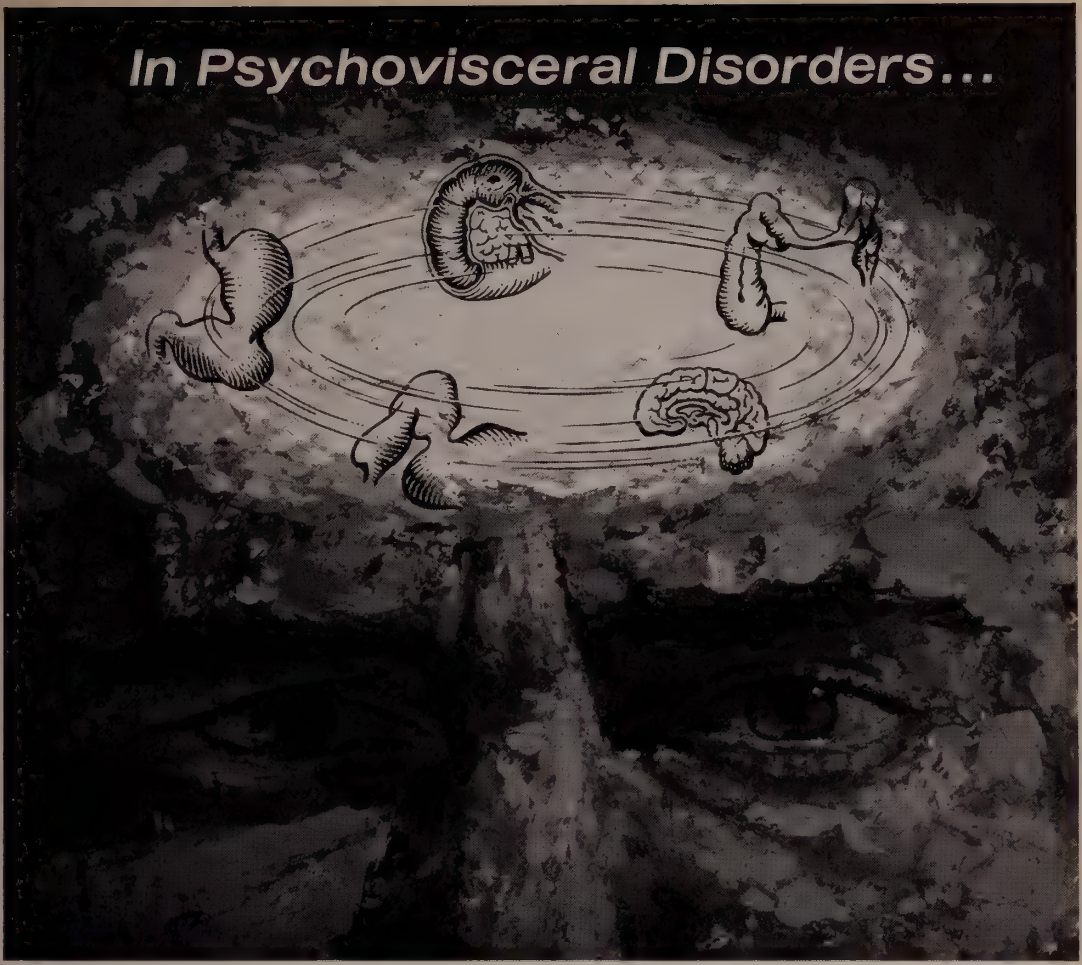
Few of us have the gift—only a master can use big words effectively, and then uses them sparingly. They serve a purpose when they say things succinctly but clearly. For example, it is manifestly simpler to say that the old gentleman's intentions with the aspiring actress were avuncular, rather than to explain that his relation was not that of a brother nor of a lover but that of an uncle. Or, in attempting to describe the figures in the segment of an arch that makes the interior curve—not in the framelike square but in the over-all inside surface—it is simpler to use the proper word in explaining that part of the arch, that is, the intrados, which is precisely the word we lumbered verbosely to convey and never hit.

How will the reader understand an uncommon word? Provided the writer did not in a pedantic spell convert simple words into bigword monstrosities, depend on the reader to look up an unfamiliar word. If the reader invests his time to read an article he would be thoughtless not to pay the small premium in time and effort to look up an occasional unfamiliar word; else he loses the principal of his investment in reading.

The difference between similar yet simple words, well applied, enhances clarity without the use of the formidable, heavyhanded big words. For example, the difference between fictitious—something which does not exist, and factitious, something which does exist but is a fake—tells a story plainly, clearly, and sharply. English is replete with such expressive similarities. (Parenthetically, it should be remembered that as a reader one must evaluate meanings and not succumb to persuasive and emotive words by those who plead special causes and thereby manipulate and enslave minds. Words like democracy, honor, goodness, Americanism, truth, are highly charged with emotion. Demagogues are aware of their skillful use, and labeling a reprehensible act with a high sounding phrase, they pass off counterfeit ideas with a genuine label.)

Writing offers the joys that arise from the dimensions within man, different from and surpassing the joys that are commonly catalogued as fun. But then, a propensity for a new thrill must be developed, and the art of writing enlarges that horizon of sensations.

—ERWIN DI CYAN, PH.D.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Radiation Hazards from the Standpoint of the Practicing Physician

HANSON BLATZ, E.E.*
New York City

From the New York City Office of Radiation Control

IN GENERAL USE *of radiographic x-ray equipment and its installation, the operator of the equipment should be provided with a well-shielded control booth. Adequate shielding should be provided in the floor and in the wall behind the film holder. The patient should be given maximum protection from unnecessary radiation. A fluoroscope should never be used if the same examination could be performed by an x-ray film. The eyes should be well dark-adapted before a fluoroscopic examination. If a fluoroscopic screen is more than fifteen years old, or if it has been subjected to heavy use or abuse, it should be replaced.*

IN THE PAST DECADE much has been said and volumes have been written regarding the exposure of individuals and of the entire population as the result of the medical and dental use of radiation, particularly x-rays. The National Committee on Radiation Protection and the American College of Radiology have made literally hundreds of recommendations as to the means for reducing the exposure of physicians and their assistants, as well as patients and neighbors. It is no wonder that most nonradiologist physicians are confused as to just what steps they should take to assure a reasonable degree of safety for themselves and their patients. Recent public debates about the possible effects of radiation exposure resulting from atomic weapons testing fallout has served further to add confusion and uncertainty regarding the significance of radiation exposure.

Background

To approach an understanding of the problem, it is important to have some basic information about radiation and radiation sources. How much radiation is the American public exposed to from natural and man-made sources, and what are some of the known and suspected biologic effects of radiation? Although radiation and its biologic effects often are spoken of as unknowns or mysteries, there is probably more known about radiation and its effects than about any other comparable toxic substance or influence to which modern civilized people are exposed. Many millions of dollars have been spent on scientific studies and the results have been highly publicized.

Let us look at what we now know about radiation and its sources. Man always has been exposed to significant amounts of radiation, and his exposure has varied considerably from place to place. We all are exposed to cosmic radiation from the skies as well as to radiation from radioactive materials, such as uranium and radium, in the ground and in the building materials that we take out of the ground. Our ancestors also have been exposed to this radia-

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* By invitation.

TABLE I. Radiation exposure in the United States

Sources	Millirems per Year to Gonads
Natural	
External	
Cosmic	50
Terrestrial	50
Internal	
K-40, C-14, RA-226	25
	125
Man-Made	
X-Rays	150
Occupational	5
Miscellaneous	5
	160
Fallout	
Gonad	1 to 3
Bone marrow	3 to 10

tion from the beginning of time. In the past sixty-five years there has been added to the natural radiation, man-made radiation which has more than doubled man's original exposure.

Table I gives an approximate comparison of the amounts of radiation to which the average American is exposed from all the known sources. As you can see, the single largest source is the medical and dental use of x-rays. It is not only the largest single source, but it is also the one that can be reduced most readily.

Biologic effects of x-ray

Before discussing the relative importance of reducing the radiation exposure from x-rays, let us consider what is known about the biologic effects. When x-rays first were used, there were many reports of burns and other damage to the fingers of the early investigators. Most such damage was experienced when little was known of the harmful effects of radiation. Today there should be no excuse for anyone receiving sufficient exposure to show any visible effects. Nevertheless, we still occasionally find dentists who hold dental x-ray films in patients' mouths with their own fingers.

Over the years, as more has been learned about radiation and its effects, there has been a series of breakthroughs in our knowledge about radiation effects. This resulted in a step-by-step reduction in the recommended permissible exposure. It was first recommended that levels of exposure be kept below that which would result in visible skin damage. Then a drastic reduction was recommended when it was learned that the blood-forming organs could be affected. Later we learned more about the properties of radiation. There was evidence that radiation had an aging effect that could shorten the lifespan and also could increase the incidence of leukemia, and a further reduction was recommended to keep well below the levels suspected of causing such effects on workers.

About thirty-five years ago, Muller* gave evidence of the genetic effects caused by relatively low levels of radiation exposure. For his study he received the Nobel Prize. Since that time, there has been further study by many investigators, and there is increasing evidence that small radiation exposures to large segments of the population are likely to result in genetic damage in future generations. It appears now that there is no threshold for genetic damage and that even the smallest additional exposure will increase the chances of such damage. We should not overlook the fact that man has always been exposed to significant amounts of radiation and that in some parts of the world there have been large populations exposed to much more radiation than have the citizens of this country. It is generally accepted in the scientific community, however, that radiation exposure should always be kept at the lowest practical minimum and that there should be no deliberate exposure without first balancing the benefits against any possible risk.

Regulation of exposure

Both The National Committee on Radiation Protection and the Federal Radiation Council appointed by the President have made certain basic recommendations regarding radiation exposure. They may be summarized quite briefly as follows:

1. The exposure of every radiation worker should be kept below 5 r a year on the

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* Muller, H. J.: Artificial transmutation of the gene Science **66**: 84 (1927).

average and as much below that as is practicable.

2. The exposure of those people not normally working as radiation workers, including those in the environs of radiation installations, should be kept below a level of $^1/_2$ r a year and as much below that amount as is practicable.

3. The exposure of every patient subjected to radiation should be kept at the lowest amount necessary to perform the required procedure.

The New York City Health Code, as well as similar codes administered by the State of New York Department of Health and all agencies attempting to control radiation exposure, is based on these basic criteria. In attempting to administer such regulations, the limitations on the exposure of physicians and their coworkers as well as the exposure of neighbors and nearby workers are quite straightforward, easily interpreted, and readily checked.

The operator of every x-ray machine should be provided with a shielded enclosure in which he must remain when he is making an exposure. The only exceptions to this rule are in the case of fluoroscopy, where specified protective aprons and gloves are required, and in the use of bedside or portable x-ray equipment. In each of these 3 cases the shielding offered is marginal and a compromise with convenience. For that reason, fluoroscopy and bedside and portable radiography never should be done except when necessary. Dental x-ray equipment, because of the low power involved, is also generally exempt.

The specifications for structural shielding in floors and walls, and in some cases ceilings, were established many years ago, and it is unfortunate to find that even today some physicians are not familiar with the requirements which for many years have been endorsed by organized medicine. One of the most common deficiencies in structural shielding has been found to result from an ignorance of the nature of human occupancy either on the other side of the wall of an x-ray room or in a space below. These considerations are quite important when we consider the extent to which x-ray beams are directed in a downward direction when one is examining a patient on a table and in a horizontal direction when an examiner is taking chest x-ray films. This is particularly important in apartment houses and in office buildings.

We have found many cases of neighbors being subjected to much higher radiation than the limits recommended because x-ray equipment has been installed, for example, in a building directly above a superintendent's maintenance room, a children's bicycle storage area, or an automatic laundry room located in an apartment house basement. In each case, the physician responsible was completely unaware of the fact that such activities were being carried out directly below his x-ray room. The legal responsibility in such cases is serious. Malpractice insurance covers only patients, and most liability insurance policies exclude radiation injuries. For these reasons, it is particularly important for every physician to make certain that irrespective of the legal requirements under the Health Code, he make certain he is not overexposing his neighbors without being aware of the fact. The City and State of New York Departments of Health expect to inspect for such conditions, but with so many installations in use (over 17,000 x-ray units in the city alone), it will take years to complete the inspections.

The most important aspect of radiation control and the most difficult one to administer is the elimination of unnecessary exposure of the patient. There is much evidence today that most patients are receiving many times the exposure necessary to perform a particular examination. Perhaps the most common cause of excessive exposure is the failure to limit the radiation beam to the area of clinical interest. If physicians were attempting to limit the beam, there would be much more evidence of corners of x-ray films showing the cutoff from a collimating cone. X-ray inspections have shown that in chest x-ray examinations more than two thirds of the equipment checked in New York City was provided with cones that exposed a much greater part of the body than was necessary to cover the x-ray film. In many cases the entire body, including the reproductive organs of the patient, was being exposed, thereby resulting in a gonad exposure many hundreds of times more than was actually necessary to make a satisfactory radiographic examination of the chest.

Another common source of excessive radiation exposure results from the use of a fluoroscope when an x-ray film could have been used. Fluoroscopes were designed primarily for observing the motion of internal organs. Their use may be justified in a few other instances, but they never should be used as a substitute for radiography.

There is not a clear understanding by many physicians of why it is necessary to minimize the dose to any particular patient. The discussion of such matters often results in the introduction of arguments concerning the possible harm to the patient himself. In terms of our most conservative criteria, we are not concerned primarily with the likelihood of injury or harm to the patient who is being examined, but we are very much concerned about the undetectable radiation damage to his genes which subsequently may be contributed to the population in reproduction. The question is not what harm any x-ray exposure can do to the exposed individual but what harm to the population as a whole can result from many such small additional doses. Such arguments always emphasize the difficulty in distinguishing between those patients who are likely to be the parents of children in the future and those who are unlikely to be. There are no certain methods of placing most individuals in either of these categories. The safest procedure then, is to assume that any individual still can be a parent unless there is some conclusive evidence that he or she cannot be. There are many matters concerning the use of x-ray equipment that are generally not considered in terms of minimizing the radiation dose of the patient.

The failure to adapt the eyes properly prior to fluoroscopy can result in a very much increased dose to the patient and to the operator. The same holds true for the use of a fluoroscopic screen that is not relatively new and well cared for. A fluoroscopic screen that is more than fifteen years old certainly should be discarded and replaced with a new one.

It is not generally recognized that poor technics, particularly in the processing of films, can result in marked increases in the patient dose. Some physicians have told us of technics which they employ in which it is necessary to develop the x-ray film for a period of only one or two minutes. Many x-ray operators do not rely on the recommended time and temperature method of developing films but develop them by inspection. This means that the film is placed in the developing solution and looked at occasionally until its density appears to be satisfactory. We are told by the manufacturers of x-ray films that both of these technics can result in an increased dose to the patient by a large factor. The use of exhausted developing solutions also results in excessive exposure.

Use of fluoroscopy

It appears that many physicians perform routine chest x-ray examinations with fluoroscopes rather than with radiographic units employing films. Such an examination generally involves about one hundred times as much radiation as if a film were to be used. In addition, the observed image is much less satisfactory in detail and may not be retained for further study or comparison. In addition to the excessive exposure of the patient, this is the greatest source of radiation exposure to the examining physician.

The general practice of fluoroscopy as we have been able to observe it often involves many shortcomings, all of which tend to expose both the patient and the operator to unnecessarily high amounts of radiation. The screens used on fluoroscopes to display the image are perishable items and should be replaced from time to time. The fluoroscopic screens available today are from two to three times as sensitive as those which were manufactured fifteen years ago. We find, however, that many fluoroscopes, perhaps as many as 50 per cent of those in use in New York City, have the original screens which were installed over fifteen years ago. This undoubtedly results in a radiation exposure of both the patient and the operator to as much as five times the radiation dose that would be experienced if a new screen were to be installed.

We also find that many physicians are

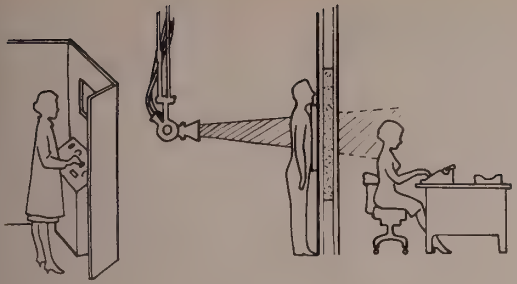

FIGURE 1. Shielded control booth protects operator of equipment, and shield in wall protects persons in room beyond.

not aware of the importance of good dark-adaptation of the eyes before the use of fluoroscopy. Those who have conducted studies insist that at least ten minutes of complete dark-adaptation before an examination is necessary to minimize exposure. The use of dark red dark-adaptation goggles can shorten the necessary time of complete darkness to a few minutes, but tests have shown that if the eyes are not properly dark-adapted, the ability of the eye to see the faint image properly is unsatisfactory. The usual result is for the physician to turn up the power sufficiently to obtain a brighter image that can be seen properly with his unadapted eyes. This also results in additional exposure to himself and to the patient. The fact that there are more fluoroscopes than radiographic units employing films registered in New York City gives some indication that the use of fluoroscopy is excessive.

Summary

Let me summarize my remarks by recommending a few basic rules in the use of a fluoroscope.

1. Never use a fluoroscope if the same examination can be performed by employing an x-ray film.

2. Make certain that the eyes are well dark-adapted before a fluoroscopic examination is attempted. This, of course, requires facilities for completely darkening the room without light leaks around the cracks of shades or under doors. Such leaks have been found to impair dark-adaptation significantly.

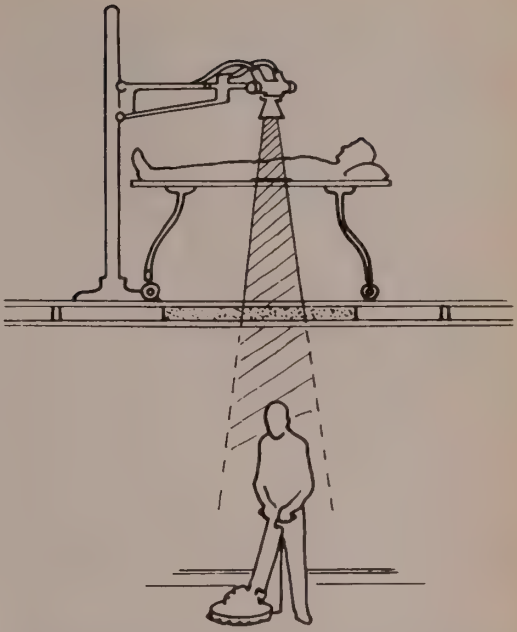

FIGURE 2. Shielding in floor protects persons in area below.

3. If a fluoroscopic screen is more than fifteen years old or if it has been subjected to heavy use or abuse, such as not covering it when it is not in use, it should be replaced by a new fluoroscopic screen.

Regarding the general use of radiographic x-ray equipment and its installation, there are also a few basic rules (Figs. 1 and 2):

1. Make certain that the operator of the equipment is provided with a well-shielded control booth provided with a protective window for observing the patient. The controls should be located so that the operator cannot operate the machine while looking around the edge of the control booth. This is now a legal requirement, and if such a condition does not exist, its correction is mandatory.

2. In radiography where the x-ray beam is directed downward, adequate shielding should be provided in the floor to protect any persons who may occupy the space below.

3. In chest radiography the wall behind the film holder should be shielded adequately to protect any persons in the room beyond.

4. In any radiographic exposure the patient should be given the maximum

protection from unnecessary radiation. This includes the use of the recommended aluminum to filter out unnecessary radiation and the use of a sufficiently small x-ray cone so that only the area of the film being used is covered. Any radiation that does not ultimately reach the film is of no use and exposes the patient unnecessarily.

Conclusion

As a result of inspecting over 15,000 x-ray machines in New York City it has been our experience that by far the large majority of physicians are most anxious to take whatever steps are necessary to comply with the Health Code and minimize the dose to their employes, their neighbors, and their patients. It is unfortunate that a few outspoken physicians have attempted to minify the effects of radiation in contradiction to the vast mass of scientific evidence available today. It appears evident that if all of the basic rules are followed, the cumulative radiation exposure of the population can be reduced drastically, and there should be no need for concern.

Perhaps the most important and most frequently misunderstood aspect of radiologic safety is that today we are not concerned primarily with the likelihood of harm to any patient being examined by the use of x-rays even under relatively poor conditions. We are, on the other hand, very much concerned with the multiplicity of slight but unnecessary overexposures to hundreds of thousands of patients every day because of the predicted radiologic impact on future generations.

ANNUAL CONVENTION: Medical Society of the State of New York

Statler Hilton, New York City / May 13 to 17, 1963

Prize Essays

The Lucien Howe Prize and the Merit H. Cash Prize will be open for competition at the next Annual Convention of the Medical Society of the State of New York, May 13 to 17, 1963, in New York City.

The *Lucien Howe Prize* of $100 will be presented for the best original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York.

The *Merit H. Cash Prize* of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State.

Essays shall be typewritten or printed with the name of the prize for which the essay is submitted, and the only means of identification of the author shall be a motto or other device. The essay shall be accompanied by a sealed envelope having on the outside the same motto or device and containing the name and address of the writer.

If the committee considers that no essay or contribution is worthy of a prize, it will not be awarded.

Any essay that may win a prize automatically becomes the property of the Medical Society of the State of New York, "to be published as it may direct."

All essays must be presented not later than *February 1, 1963*, and sent to the Chairman of the Committee on Prize Essays of the Medical Society of the State of New York, 750 Third Avenue, New York 17, New York.

Alfred A. Angrist, M.D., *Chairman*
Committee on Prize Essays

Alterations in Chronic Staphylococcal Furunculosis by Use of Gamma Globulin[*]

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A STUDY WAS MADE of 15 patients with chronically persisting, active staphylococcal skin disease to whom gamma globulin was given. Ten patients had an abrupt and favorable change in the course of their disease; 2 noted some improvement; and no benefit was noted in 3. Although the coincidence of therapy with improvement was striking, it is impossible to conclude that the gamma globulin played any role in altering the natural course of this remitting infection. Studies of the serum of the patients failed to show any change in antibody titers against staphylococci or in the construction of their protein pattern before, during, or after therapy.

NEITHER THE TREATMENT nor the prevention of chronic staphylococcal disease of the skin in the adult has enjoyed notable success. The management of single acute episodes of furuncles includes the use of various local antiseptics and antibacterial agents, incision and drainage, soaks, vaccines, and a number of other potions or nostrums. Despite cleanliness and care with all or some of these, recurrences of boils, abscesses, and even carbuncles, are expected. Although the affliction is common, its natural course is not well described in standard dermatologic and medical texts. This may be so because the disease generally is self-limited and eventually, after a year or longer, the skin without apparent reason resists further infection for an indefinite period. Later, however, a relapse frequently occurs, and the pattern of recurrent or continuous infections is repeated. Certain facts about the disease are apparent. Rarely is the presence of multiple, active, and large boils or furuncles associated with systemic symptoms, nor do distant metastatic lesions develop; the infection usually remains local. Any part of the skin can be involved, although most frequently recurrences develop in areas which were involved previously. Finally, antibacterial agents and vaccines, commercial and autogenous, have no dependable preventative effect, albeit some may shorten, or even abort, the natural course of an acute abscess.

Staphylococcal skin disease appears in a variety of forms, from the involvement with necrosis of all the layers of epidermis and subcutaneous tissue to superficial excoriations; from small areas of ulcerations and tissue destruction but with little exudation to large pus-filled abscesses and major dermatonecrosis. Often after the development of a single boil satellite lesions appear nearby, with each area undergoing its own natural course so that in a single individual all varieties of infections, in different stages of development and resolution, are observed. Consequently, local therapy directed toward the control of one diseased area may not necessarily influence other lesions. Indeed, the disease is discouraging to both the patient and the physician.

Because the vast majority of patients with staphylococcal skin disease are es-

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[*] This work was supported by a grant from Parke Davis Company, Detroit, Michigan.

TABLE I. Staphylococcal skin disease treated with gamma globulin

Kind of Lesion Before Gamma Globulin	Number of Patients	Results		
		Excellent	Minimal Improvement	None
Large abscesses and/or carbuncles	8	6	. . .	2
Multiple draining ulcerations	6	3	2	1
Draining sinuses thigh (old osteomyelitis)	1	1	. . .	. . .
TOTALS	15	10	2	3

sentially healthy people and because systemic complications rarely develop, one thesis to explain the infection is that the skin alone is deficient in some measure or substance which deficiency of local defense permits disease. Despite this, the tissue remains an effective first line of protection against generalized infection, and spread from it does not often happen.

The present study was undertaken to evaluate the course of staphylococcal skin disease as influenced by repeated doses of gamma globulin. We speculated that a globulin containing high concentrations of staphylococcal antibody might contribute sufficient amounts of the material presumed to be lacking in the skin of the subjects and that favorable alterations of the local infection might evolve if it were given in large amounts. Efforts to improve the response to staphylococcal disease by the use of gamma globulin have been described by others.[1-3] The kinds of infection in these series are appreciably different from the skin disease being studied here singularly, and thus general conclusions reported about the efficacy of gamma globulin in systemic infections may not necessarily apply to local disease. This report summarizes the clinical and laboratory observations made on a series of 15 patients with recurring staphylococcal disease of the skin who were given gamma globulin.

Materials and methods

Two boys, aged ten and twelve, 5 females, aged twenty to forty-one, and 8 men, aged twenty-two to fifty-eight, were included in the study. None had acne vulgaris or suppurative hidradenitis. Eight of the 15 patients had had recurring abscesses or boils for over six months with no period of freedom from at least one active lesion (Table I). Six of the 15 patients had multiple, shallow, ulcerating infections of the skin, continuously active for over two years. In 1 of these 6 patients, a boy aged twelve, the arm, leg, and facial lesions had been present and acutely inflamed for over seven years without a single remission. A detailed study of his globulins three months before his first dose of gamma globulin had failed to reveal any abnormality. The remaining patient had had acute osteomyelitis of the left femur for five years. There had been multiple acute exacerbations about every three months for the eighteen months prior to this study, each bout requiring hospitalization because of the acute morbidity of the relapse. He had two continuously draining sinuses, both on the lateral aspect of his thigh, for a year before the study. He was not acutely ill when he was admitted to the study. None of the others had systemic toxicity from their local infections at any time through the study period.

Isolated staphylococci

Coagulase-positive staphylococci, var. aureus, were isolated in a pure culture from every patient prior to the administration of gamma globulin. The measurement of susceptibility of isolated strains to six antibacterial agents—penicillin G, dimethoxyphenyl penicillin, erythromycin, chloramphenicol, novobiocin, and streptomycin—was performed. Phage typing was not done. Fourteen of the 15 strains isolated produced penicillinase. Recultures were performed whenever new draining lesions developed.

TABLE II. Influence of gamma globulin on course of staphylococcal skin abscesses

Results	Number of Patients
Complete remission	
No new lesions after second dose of globulin	3
Marked improvement	
Less number of new lesions	
Smaller size of new lesions	
Less pus formation in new lesions but not complete cure	7
Some improvement	
(Mostly subjective)	
Number of new lesions slightly less	
Size of new lesions slightly smaller	2
No change	3

TABLE III. Reappearance of new staphylococcal skin lesions within ninety days after last dose of gamma globulin*

Type of Original Disease	Number of Patients
Large abscesses with pus	3
Shallow ulcerations with small amount of pus	2

* On each occasion new lesion was similar to original disease but generally smaller in extent and in amount of tissue destruction.

Treatment program

When they were present, acute abscesses were treated with soaks, single antibacterial agents, incision, drainage, and other measures. These treatments were not different from those that had been practiced prior to the study.

The sole change in the patients' program to control the skin infection was the administration of gamma globulin.* Six single intramuscular doses were given at four-week intervals for five months. Subsequently, after the termination of the prescribed course, repeat single doses were given if a relapse developed, as occurred in 5 patients. The dose of the material was approximately 28 mg. of globulin nitrogen per kilogram of body weight (0.15 ml. per kilogram). Each lot of the gamma globulin had a high order of mouse protective antibody (±10,000 mouse protective units per milliliter and a high titer of agglutinating antibody as measured by the Boger technic (±1:32,000 per milliliter).

Tests performed

As a routine, serum was drawn from the patients before each dose of gamma globulin. Following the last dose, follow-up blood samples were obtained at one- and three-month intervals. Weekly specimens of blood were secured from a few patients. Each sample of serum was tested for the following: free electrophoresis (Tiselius method), total antistaphylococcal agglutinating antibody (technic of Boger), and a determination of the total nitrogen content (micro Kjeldahl). Selected samples taken periodically from 5 patients were sent to Dr. Fisher in Detroit for his determination of mouse protective staphylococcal antibody titers. Detailed technics for each of these procedures are described in the English literature, and our minor modifications need not be added to this report.[1-4]

Clinical observations

Each patient was examined at least every four weeks during the period of observations and more often as required by the appearance of new abscesses. On occasion, blood counts, urinalyses, total proteins, blood sugars, and repeat cultures were included in the routine examinations. None of the patients had diabetes as determined chemically; all the patients were well. At no time was the patient advised that the six doses of gamma globulin would cure his infection.

The clinical observations were continued for from twelve to twenty-four months after the last dose of gamma globulin.

Controls

Blood from 5 normal adults was drawn on the same schedule as that of the treated patients, and each was subjected to the same battery of tests. These 5 individuals were not given gamma globulin. Five patients with active, chronic pulmonary tuberculosis but with no skin or other staphylococcal disease were placed on identical schedules of gamma globulin. Their blood sera were drawn and tested in a similar fashion.

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* All the gamma globulin used was graciously supplied by J. K. Weston, M.D., William Kitto, M.D., and M. W. Fisher, Ph.D., of the Parke Davis Company, Detroit, Michigan.

The titers of agglutinating antibody were controlled by the determination of that antibody in the various lots of gamma globulin used throughout the clinical program.

Results

Clinical. Ten of the 15 patients had an abrupt and favorable change in the course of their disease (Tables I to III). Two others noted some improvement as measured by a decrease in the number of new abscesses and/or their characteristics. No benefit was observed in 3 patients. Five of the 12 patients who were benefited by the first course of gamma globulin had a recurrence of their abscesses from two to four months after the last dose of gamma globulin. In each patient the relapse was associated with the appearance of lesions similar to those which were present initially. A single repeat injection was given at the time of the relapse. In each instance there was a prompt subsidence of the disease, and the remission persisted for some months thereafter.

In a majority of those patients who showed appreciable improvement (7 of 10), the sequence of events was quite predictable. Each had had recurring boils and/or ulcerations present for at least six months prior to the first dose of gamma globulin. New ones continued to appear in an identical pattern for from four to six weeks after the first dose. Two to three weeks subsequent to the second dose a striking change in the skin was noted. When new lesions appeared, they were smaller, little if any pus was formed, and each resolved without adjuvant therapy.

Another kind of response was seen in 3 patients. Large single abscesses continued to appear between the third and fourth doses of globulin. These were as large and as symptomatic as those which had been present before the program was instituted, and accessory therapy was required for their control. Abruptly thereafter, however, lesions stopped forming, so that the over-all favorable response permitted their inclusion into the "marked improvement" category (Table II).

Two patients were impressed that the course of their miserable infections was definitely subdued during the five-month period. They considered that the improvement seemed to be in the lessening of the size of newly developing shallow abscesses and the amount of pus that was formed. In our evaluation, on the other hand, the kind of change noted was not appreciable, although it was probably true that fewer lesions developed during the five months of treatment. Mainly because of the patients' opinions we did finally classify the results as improvement (Table II).

Among the 10 patients who had objective and subjective improvement during and after the administration of gamma globulin, 6 originally had large boils, abscesses, or small carbuncles. Three others had multiple, shallow, infected ulcerations, and the last patient's two draining sinuses have remained closed for more than twelve months after the last dose, the first freedom from pus formation in over a year.

Among the 10 patients with excellent results there were three apparently permanent "cures" with the first course of treatment; no further infections were noted for from twelve to twenty-four months. The subsequent courses in the 7 other patients in this category were difficult to evaluate. In general, the patients claimed that permanent help had been given, but each has had recurrences of single lesions, usually appearing first six or seven months after the last dose of gamma globulin. Since exacerbations and remissions in the natural course of staphylococcal skin disease are anticipated, and since our long-term follow-up is no longer than twenty-four months, we cannot be certain that we have altered favorably the inevitable course of the disease in these 7 patients.

The staphylococcal skin disease of 3 patients was not improved by the administration of gamma globulin for five months. Two of the 3 had large recurring boils of

TABLE IV. Free electrophoretic patterns of serum proteins in two sets of controls in this study and in normal subjects as published by others[2,4]

Patients	Albumin (Per cent)		Alpha-1 Globulin (Per Cent)		Alpha-2 Globulin (Per Cent)		Beta Globulin (Per Cent)		Gamma Globulin (Per Cent)	
	Range	Average	Range	Average	Range	Average	Range	Average	Range	Average
Normal adult subjects (no gamma globulin)	46 to 63.7	56.8	2.8 to 7.3	4.7	7.6 to 13.9	10.1	11.9 to 26.7	18.8	6.3 to 11.9	9.5
Patients with chronic tuberculosis receiving gamma globulin	48.6 to 52.9	50.6	5 to 6.5	5.5	10.2 to 12.2	11.0	19.1 to 24.2	21.3	11.8 to 12.5	11.5
Normal subjects (published)[3]	53 to 63	58.0	4 to 8	5.0	8.2 to 10.4	9.0	10.8 to 14.7	14.0	8.5 to 14.7	14.0

TABLE V. Changes in values of free electrophoresis before and after administration of gamma globulin

Concentration	Number of Patients		
	Albumin	Beta Globulin	Gamma Globulin
Same*	3	4	7
Increased after gamma globulin	7	2	5
Decreased after gamma globulin	5	9	3

* Within 10 per cent of initial determination.

the face and/or buttocks, and the other had shallow ulcerations and weeping pus on the arms and chest. In each case the individual lesions subsided during the observation period by the use of an orally administered antimicrobial agent; in addition, many of the lesions had to be drained surgically. The appearance of large new lesions occurred during every month of the globulin administration, and each new lesion was no different from former ones, nor were there fewer of them. One patient, because she and her physician were so discouraged by the sequence, received weekly injections of gamma globulin for two months in the same dosage as was used initially. The extra amount did not alter the course of her disturbing disease. Nor, in fact, were the skin lesions different in appearance, frequency, or course when the gamma globulin was finally discontinued. These three failures were impressive.

In summary, 12 of the 15 patients were gratified and 10 of them exceedingly so; there were three striking failures.

LABORATORY (Tables IV and V, Fig. 1). *Tiselius.* The successive patterns of protein constituents in the 5 control subjects and in the 5 patients with tuberculosis who were given five doses of gamma globulin changed little or not at all during the five months of observations (Table IV). In brief, with few exceptions the normal cases fell within the distribution patterns which have been published in standard works on the subject.[3] The average levels of the various fractions in the patients with tuberculosis were somewhat different, but during the five months observation period they showed no change. Our normal gamma globulin concentrations were somewhat less than most other series report: 9.5 versus 14 per cent. In contrast, beta globulin fractions varied in the opposite direction: 18 versus 14 per cent. One explanation for this latter observation rests with the fact that we photographed the fractions on the descending limb, and frequently the so-called beta globulin abnormality was high enough to alter the over-all averages. The results with our technics, however, were consistent and not variable. Whatever variations were observed occurred equally in the patients with tuberculosis who received gamma globulin and in the normal subjects who were given nothing.

The patients with staphylococcal disease who received gamma globulin showed considerably more variations than the control subjects in the five months of observation and thereafter (Table V). There were no recognizable trends to the monthly changes, and as shown in the table, there

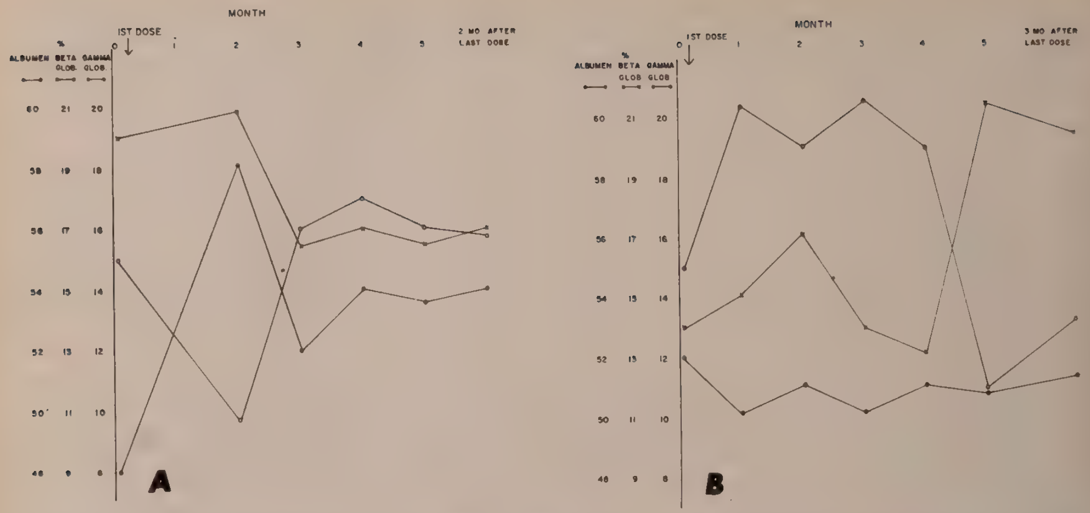

FIGURE 1. (A) Monthly variations in forty-year-old female patient with staphylococcal skin disease receiving monthly injections of gamma globulin. (B) Monthly variations in twenty-five-year-old female patient with staphylococcal skin disease receiving monthly injections of gamma globulin.

TABLE VI. Mouse protective staphylococcal antibody titers in control subjects*

Gamma Globulin	Reciprocal of 50 Per Cent Protection Dilution of Serum
None	80
None	4
Monthly injections	2
Monthly injections	3

* This work performed in toto by M. W. Fisher, Ph.D., in his Detroit laboratories. Titers as given are subject to ±20 per cent error.

is little meaning to the various increases and decreases from the beginning to the end. Figure 1 shows the monthly variations in 2 patients. Trends in their albumin, beta globulin, and gamma globulin fractions appear almost to go in completely opposite directions. The 2 patients had very similar disease processes—recurring painful large boils, on the neck in 1 patient and on the thighs and buttocks in the other, and impressive and favorable changes in both patients with gamma globulin. In other subjects with more ulcerating lesions of the face and neck, similar unpredictable changes in the successive pattern of protein were observed. Some showed stability in albumin and great variations in other fractions. There were no predictable changes in those patients who improved and contrariwise.

A few events did happen to the patterns of protein in some patients which are of interest.

1. Five patients with gamma globulin concentrations that were below average initially, that is, 8 per cent or less of the total protein, showed increases to normal levels during the period of observation. Generally, the increase to 10 per cent was gradual over a period of from two to three months. In 3 of the 5 patients no appreciable change in the course of their skin disease was apparent in this period. It must be pointed out that the amount of globulin given these 5 could not have contributed enough protein to account for the rise that was seen.

2. Seven patients had concentrations of albumin below 50 per cent in the pretreatment blood. Each of these concentrations rose to more normal levels within four weeks, and again the change could not be correlated with the clinical courses. No explanation for the low albumin levels can be proffered.

3. Initial beta globulin fractions in 11 of the 15 patients exceeded 18 per cent (average was 18.9 per cent). Most of these fell somewhat more than 10 per cent to an average of 16.5 per cent at five months.

TABLE VII. Mouse protective staphylococcal antibody titers in patients*

Condition of Patient	Pretreatment	After One Month	After Three Months	After Five Months
Shallow lesion	55	70	40	30
Multiple boils	22	18	18	17
Carbuncles	5	5	12	15
Large abscesses	12	32	28	15
Shallow lesions	2	2	2	2

* This work performed in toto by M. W. Fisher, Ph.D., in his Detroit laboratories. Titers as given are subject to ±20 per cent error.

TABLE VIII. Titers of serum agglutinating antibodies against staphylococci

	Titers in Serum			
	Before Period of Observation		After Doses of Gamma Globulin	
Patients	Range	Average	Range	Average
Normal subjects	1:400 to 1,600	1:800	1:400 to 1,600	1:800
Patients with chronic tuberculosis receiving gamma globulin	1:400 to 3,200	1:800	1:400 to 3,200	1:800
Patients receiving gamma globulin	1:800 to 6,400	1:1,600	1:800 to 1:3,200	1:1,600
Gamma globulin	1:25 to 600	1:32,000		

This trend was gradual and was not correlated with clinical alterations particularly. (It should be emphasized that our beta globulin levels uniformly were greater than the published averages.) The amount of beta globulin in the commercial gamma globulin used was less than 5 per cent. We cannot elucidate on this change either.

Changes in the alpha 1 and 2 globulins showed no trend and in general remained within average levels throughout. The variations from month to month did not vary more than 10 per cent in the majority of the patients.

In summary, the changes in the pattern of proteins of patients with staphylococcal skin disease who received repeated injections of gamma globulin were frequent, unpredictable, uninterpretable, and, at the moment, have no meaning. There surely was no correlation between the generally improved condition of the skin and these definite changes.

Mouse protection tests (Tables VI and VII). Single blood samples from 4 control subjects and serial ones from 5 patients revealed no essential change in the ability of the serum portion to control predictable staphylococcal infections in mice during the five months of observation. In general, however, and with only one exception as noted in Table VII, there were appreciable concentrations of protective substances in the serum of the patients before they received the globulin. One control, not ill with staphylococcal disease nor a carrier of same, similarly had a high titer; this also was unexplainable and unexpected.

Serum agglutinating antibodies (Table VIII). Serial blood samples from both the control subjects and from 4 of the 15 patients were tested for the presence of agglutinating antibodies against whole staphylococci. In general, the normal subjects and those with tuberculosis uniformly had titers of 1:800 or 1:1,600. These remained essentially unchanged throughout the period of observation. Occasionally a one-tube difference was noted. Patients with staphylococcal skin disease averaged, before treatment, one tube higher than the controls, that is, 1:1,600 to 1:3,200. As was true with all of the other tests, these concentrations did not change individually more than one tube throughout the same period, and in fact the over-all averages were exactly the same.

Comment

There is a paradox. Clinical observations clearly suggest that in 10 of 15 patients with long-standing, active, and discouraging staphylococcal skin disease, the repeated administration of gamma globulin altered favorably their previously unchanging or progressive disease states. Contrariwise, there is no evidence from the many tests performed that any significant, measurable immunologic change associated with staphylococcal infection occurred in the serum of these same patients.

It is recognized that very little specific antistaphylococcal antibody actually could have been added to the patients' humor by the dose of gamma globulin that was given, despite the fact that each lot used contained high levels of at least two such antibodies. In fact, it would have been inexplicable had changes in the gamma globulin pattern developed, for each dose given could have added little more than 2 per cent of the total body globulin nitrogen, an addition which probably could not be measured by the technics which were used. Rather, it was hoped that a small amount of artificially given antibody, in the form of gamma globulin, might be sufficient to boost the production of extra amounts by the host himself. It had been anticipated, foolishly perhaps, that the immune status of the host was so poised, and in certain ways adequate (systemic disease rarely develops in patients such as these), that a slight push would tip the balance heavily in his favor and that a change in that status would be demonstrable. It was not, and the presumption was not valid.

Serum antibodies which agglutinate staphylococci in vitro are not necessarily favorable or beneficial defense mechanisms developed by the host against actual staphylococcal disease, nor indeed has the presence of high titers protected the human being from becoming infected.[5] Neither, in fact, are the mouse protective antistaphylococcal materials, as described by Fisher,[6] necessarily effective ones for human beings. When they are present in the human being, it can be presumed only that the body has responded specifically to a bacterial invasion with a substance which, when administered to a mouse, protects that animal from a fatal staphylococcal infection. We had hoped to see a change in the concentration of one or both of these antibodies (they could be the same material, but this has not been described precisely) with the doses of gamma globulin used. Such conceivably could have been a lead to explain the beneficial clinical alterations in the infections. Since none developed, there must be some other explanation for the patients' improvements or failures, but none seems sensible at the moment.

Toxoidal materials and autogenous staphylococcal vaccines, on the other hand, have been shown to increase some kinds of antibody to staphylococci.[5,7–9] One can speculate that with more gamma globulin than was used in this study, given more often, the combination of globulin and a toxoid or whole organism vaccine would be a better stimulus to a number of staphylococcal antibodies in vivo. We did not attempt this; perhaps such an investigation is warranted.

Presuming that increases in circulating antibodies to staphylococci, whether they be mouse-protecting or agglutinating, or others not here measured, can be achieved artificially by some method, another very real problem arises. Will such increases benefit a patient with only staphylococcal skin disease? It is logical to suppose that a host with an inadequate skin defense against staphylococcal dermatonecrotic toxin probably does not need excess serum antibody of the antibacterial variety. He needs something added to the defense mechanisms in the skin itself, and perhaps that mechanism is neither antitoxic nor antibacterial. This would be a ticklish problem to study if it could be shown that increases in circulating antibodies are not correlated with skin improvement, as is implied in our study. Because we highly suspect that this is true, it is likely that the supply of the deficient substance can be increased only by the administration of some whole protein substance, not by a specific antigen from any part of a staphylococcus. At the moment there seems to be no lead as to what the deficient substance is.

The final comment in this report concerns recommendations about the use of gamma globulin in patients with chronically recurring skin abscesses. From the record it is obvious that the described program is not a therapeutic panacea—far from it—and it is just as logical to emphasize that ten times more gamma globulin probably would do little more. On the other hand, most of the patients were benefited, and the improvement was not psychologically induced, except that a great deal of added attention was given to each patient. They were promised nothing, but the favorable results were clearly evident to the clinician, and the personal testimonies of the 10 patients confirm the impression that benefit did in fact derive from the globulin. We doubt that the benefit experienced by this majority could have been only fortuitous; we deny that the therapeutic regimen has been witchcraft, for favorable responses occurred more frequently than was anticipated. Consequently, in selected patients we can indeed recommend that from 10 to 15 cc. of gamma globulin be given periodically for from four to six months as a trial prescription for the disease. With it a spontaneous remission in the natural evolution of staphylococcal dermatitis may be stimulated.

Summary

Fifteen patients with chronically persisting active staphylococcal skin disease received 0.15 ml. of commercial gamma globulin per kilogram of body weight for six doses given at four-week intervals.

Ten patients were benefited in marked and impressive fashion during the period of observation or perhaps coincidentally. Three showed absolutely no response, and the remaining had minimal improvements. It is impossible to conclude that the gamma globulin played any role in altering the natural course of this remitting infection, although the coincidence of therapy with improvement can be considered striking.

Detailed studies of the serum of these patients failed to show any change in antibody titers against staphylococci nor in the construction of their protein pattern before, during, or after the therapeutic regimen.

Acknowledgment. This paper was prepared with the technical assistance of Leonard Canarile, B.S.

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No Basis for X-Ray Treatment of Asthma

Any claim that asthma can be cured permanently by x-ray treatment or any presently known method is without scientific foundation, according to Jerome Glaser, M.D., Rochester, a pediatric allergist, in the September 1 issue of the *Journal of the American Medical Association*.

A recently publicized technic is purported to benefit asthma sufferers "by x-ray treatment of infected lymphoid tissue in the sinus cavities and the upper respiratory tract," according to a question submitted to the *Journal*. In reply, Dr. Glaser said that lymphoid tissue is not found in the sinuses.

X-ray treatment of a regrowth of adenoid tissue following the removal of the adenoids and tonsils is an accepted procedure for asthmatic children. This appears to be helpful in many instances by eliminating the source of infection which may trigger asthmatic attacks. However, such treatment is almost never indicated in adults because with advancing years such lymphoid tissue wastes away, Dr. Glaser pointed out.

Neurosurgery in Management of Patients with Cerebral Vascular Disease

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From the Upstate Medical Center

THE ROLE OF NEUROSURGEONS in the management of patients with cerebral vascular disease has been extended to consider many new clinical problems in recent years.[1-3] Some cases have been recognized as potentially amenable to surgery but have remained beyond the usual therapeutic considerations until improved diagnostic technics should become available. With the development of cerebral angiography, a critical technic was introduced. It was adopted slowly in this country and was not used frequently until after World War II. Improved seriographic equipment then was developed so that the arterial, intermediary, and venous phases of the cerebral circulation could be analyzed. The approximate rate of cerebral circulation, arteriovenous shunts, and tumor stains could be demonstrated with high quality x-ray visualization. Contrast media were introduced which had few side-effects. Automatic injectors for the delivery of a concentrated bolus of contrast material have contributed further clarity. This procedure has become relatively safe for patients of all ages and is a reasonably accurate technic with which to study the cerebrovascular system even in seriously ill patients.[4-6]

Technic

The contrast material for such studies may be introduced into the cerebral circulation from selected sites: direct carotid or vertebral artery puncture, direct puncture or catheterization of a brachial or femoral artery, or bilateral antibrachial vein injection for screening of the aortic arch. Such studies are performed in a progressive fashion and seek to demonstrate all of the arterial channels which contribute to the cerebral circulation. Rapid serial filming gives some index of changes in the rate of the cerebral blood flow and may reveal apparent blocks in cerebral circulation due to technical features of the angiogram.

Such studies may seem exhaustive at times but usually are essential if one is to plan appropriate and precise surgical procedures to correct abnormalities of the cerebral blood supply.

When an abnormality is demonstrated radiographically, the anatomic lesion must be considered in the light of detailed neurologic examinations and the clinical features of a patient's illness.

As angiographic technics improved and operative technics were added to our armamentarium, four major forms of cerebrovascular disease further challenged neurosurgery.

Congenital arteriovenous anomalies

Congenital arteriovenous anomalies are being removed under more and more adverse circumstances with improved prospects of achieving a satisfactory removal without a severe neurologic deficit. Many of these lesions manifest themselves initially with a spontaneous subarachnoid hemorrhage. They may bleed repeatedly without persistent impaired neurologic function. As a

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rule, however, with recurrent bleeding new and persistent symptoms appear.

These lesions also may be present initially with seizures which are frequently focal in origin. More rarely they may cause a slowly progressive or intermittent neurologic deficit. With serial cerebral angiography the primary arterial supply and the primary venous drainage from these lesions may be identified. This information is far more critical in determining the operability of the lesion than is its apparent size or location.

Berry aneurysms

A more common lesion responsible for a spontaneous subarachnoid hemorrhage is a congenital Berry aneurysm. From 5 to 10 per cent of these are found in the posterior fossa. The majority, however, cluster about the anterior portion of the circle of Willis. In the past fifteen years angiography has facilitated greatly the operative approach to these lesions. They were described first and some were localized on a clinical basis without angiography by Symonds in 1923.[7] As with the arteriovenous malformations, the precise location and the arterial blood supply to these lesions, rather than their particular size, are important elements in planning for their operative correction. With improved vertebral angiography, increasing numbers of these lesions have been identified and successfully operated on even in the posterior fossa.[8,9] Congenital aneurysms relating to the anterior part of the circle of Willis can be approached directly with an expected mortality rate reasonably estimated at 15 per cent as opposed to a probable mortality rate with the nonoperative management of these patients of about 50 per cent.[10-12]

Bleeding associated with many of these congenital lesions may introduce additional problems. An intracerebral hematoma which behaves as an expanding intracerebral mass may compound a patient's illness. Occasionally an aneurysm lying close to the arachnoid may bleed in part into the subdural space, causing an associated subdural hematoma. At the time of the angiography such mass lesions usually can be localized and treated primarily.

THE DEVELOPMENT *of cerebral angiography has made it possible to diagnose and determine the operability of such primary disorders of the cerebral vascular system as congenital arteriovenous malformations, congential Berry aneurysms, cerebral hematomas, and occlusive lesions of the aortic arch and carotid systems. Many of these lesions are associated with a low mortality and morbidity when the corrective procedures are planned on the basis of a careful clinical evaulation of the patient, selective angiography, and judicious use of newer surgical technics and adjuncts.*

Hematoma

A third lesion associated with cerebral vascular disease is the hematoma which follows an intracerebral hemorrhage. It has become apparent that little can be achieved by aspirating these lesions in the early hours following the onset of symptoms. The blood at this time is semisolid and is interspersed with white matter from the destroyed centrum ovale so that aspiration cannot be accomplished. If the hematoma is decompressed in the acute state, the evacuation of the cavity has an inconclusive end point, and bleeding continues.

Some patients, however, may not follow the usual course following an intracerebral hemorrhage. After the initial apoplectic onset they often will become less responsive for several hours and then their condition will stabilize gradually. As a rule these patients then will begin to improve and continue on a slow rise to maximum recovery.

However, when patients begin to attain a plateau at from two to five days from the onset of their cerebral vascular accident, or when during this interval they begin a secondary decline, it may be in association with the expansion of a localized clot rather than in association with primary cerebral damage, infarction, or cerebral edema. In this group, the aspiration of the hematoma may contribute materially to further improvement. Long-term considerations in this group of patients are not yet known, and their selection is still a matter of some difficulty. However, if a patient with an intracerebral cerebral hemorrhage begins to improve and then reaches a plateau or declines after from two to four days, cerebral angiography should be accomplished in considering the possibility of an expanding intracerebral hematoma which may be aspirated or removed.

Occlusive disease

One of the most recent areas in which operative intervention has been imposed for cerebral vascular disease is that of occlusive disease of the major vessels in the neck and in the thorax. I have used the word imposed intentionally, for our fundamental knowledge of these lesions in terms of their influence on cerebral function is incomplete in many ways. It is important to recognize that the mere identification of an anatomic abnormality does not necessarily imply that it contributes materially to a patient's symptoms, nor indeed does it imply that its correction will improve the patient's circumstance.

Such a lesion must correlate with a patient's symptoms or the present course of his disease before it can be attacked reasonably in a hope of correcting or ameliorating the future course of his difficulties. New collateral circulation demonstrable on angiography may be adequate in other patients to maintain cerebral circulation for many years without further incidence.

Many clinical entities may mimic the classical stuttering stroke of occlusive disease. An intracerebral glioma, meningioma, brain abscess, or hematoma may be responsible for the intermittent symptoms, yet the same patient may have a demonstrable partial or total occlusion of a primary cerebral vessel.[13]

Correction of defects

Perhaps the commonest form of occlusive disease which can be correlated with symptomatology of cerebral origin is that of partial or total occlusion of the internal carotid artery by a large atheromatous plaque near its origin. In evaluating the development of collateral circulation about such a lesion and planning for its correction, it is imperative that we obtain arteriographic information extending beyond the mere demonstration of the lesion in the internal carotid artery. The collateral circulation may remain quite adequate from the other carotid for many years as has been well demonstrated by patients who have had an internal carotid artery ligated for a cerebral aneurysm. It appears to be true that symptoms occur in this circumstance as the arteriosclerotic process proceeds in smaller and more distal cerebral vessels also. Herein lies the real difficulty in determining the appropriate measures to be taken in patients with this disorder. Despite the local preponderance of a large plaque in the proximal internal carotid, the disease is generalized. Occlusive changes in distal cerebral vessels as well as in the large vessels of the neck and aortic arch, which are more easily demonstrated, may be responsible for a cerebral infarction. These patients require extensive angiography to determine the probable lesion responsible for the symptoms and to determine the optimum course to follow in correcting one or more of these lesions.

Not all of these patients require operative intervention.[14] The posture of the cervical and suboccipital regions may contribute materially to the onset and alleviation of the symptoms.[15,16] One telephone company employe has worn a cervical collar for two and one-half years to avoid hyperextension. He had fainted nine times in the previous eighteen months when he looked toward the top of a telephone pole. This was presumably because of an occlusion of the vertebral artery at the atlanto-occipital junction. He has had no further attacks of this type despite having had two coronary occlusions and an occlusion of a major arterial vessel in the left lower extremity since then.

In other patients the intermittent attacks of cerebral ischemia may subside "spontaneously" as the collateral cerebral circulation is established. Such a development can be influenced favorably on occasion by the manual compression of the carotid artery for increasing periods.[17] Initially, such compression may be tolerated for only a few seconds when the patient is in the prone position, but with repeated testing the tolerance may increase to more than a minute with the patient sitting. Frequently the intermittent attacks will stop. Whether the patient's tolerance for carotid compression increases because the collateral circulation is developing slowly but independent of the compressions or whether the repeated compression may contribute to a degree in establishing new channels of collateral circulation is not known. Conservative measures sometimes can be found which will alleviate the patient's symptoms even though the disease is generalized.

For a time some investigators advocated thrombendarterectomy or bypass graft procedures rather enthusiastically for occlusive disease of the internal carotid and vertebral arteries. The selection of patients for these procedures even after angiography is difficult if one wishes to avoid intervention without a reasonable hope of influencing the patient's neurologic deficit. Most physicians agree that a young patient without hypertension or diabetes and a localized stenosing plaque in the proximal internal carotid artery without hemiplegia is an excellent candidate for thrombendarterectomy. It is probable, however, that patients with stenosis of the proximal internal carotid artery but with multiple or additional large plaques in the distal carotid branches and patients with total occlusion and the abrupt onset of severe hemiplegia are not candidates for such a procedure.

A bruit may be heard at the angle of the jaw in many patients with internal carotid stenosis. The bruit may relate to turbulence during systole near a small plaque or angular bifurcation. As the degree of stenosis increases the bruit may change from a systolic to a systolic plus a diastolic component. Whether or not operative intervention at this point is reasonable in an older person is not known. In a young person with little evidence of widespread atherosclerosis one might wish to consider thrombendarterectomy as a reasonable if not an established prophylactic procedure.

Summary

Since the advent of safe cerebral angiography, it has been possible to diagnose and more clearly understand the problems of many patients with primary disorders of the cerebral vascular system. A number of these disorders have become recognized as lesions amenable to operative intervention. The selection of patients for such procedures depends heavily on the information acquired from cerebral serioangiography. Congenital arterial venous malformations, congenital Berry aneurysms, cerebral hematomas, and occlusive lesions of the aortic arch and carotid systems are among those most frequently amenable to operative intervention and correction. Many of these lesions are favored with a low mortality and morbidity when the corrective procedures are planned on the basis of a careful clinical evaluation of the patient, selective angiography, and the judicious use of newer surgical technics and adjuncts.

150 Marshall Street

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TABLE I. Results of arterial surgery in 431 patients by the type of stroke

Type of Stroke	Number of Patients	Good Flow Established	Postoperative Course — Asymptomatic	Objectively Better	No Change	Died
Incipient or transient	294	284	195	66	32	1
Progressing	64	36	15	12	29	8
Completed	73	42	17	32	20	4

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Discussion

Charles Rob, M.D., *Rochester*. I shall concentrate on only one aspect of cerebral vascular disease, and that is atherosclerosis of the carotid and vertebral arteries in the neck.

It is now known that approximately 25 per cent of apoplectic strokes are caused by stenosis or thrombosis of the cervical portions of the carotid and vertebral arteries. The striking thing is the localization of the atherosclerotic process in the extracranial as compared with the intracranial cerebral arteries.

Yates and Hutchison* reported on 100 patients who died with a diagnosis of cerebral thrombosis. Detailed autopsies revealed that 14 of these 100 patients had a complete thrombosis of an intracranial artery, and 6 of the 14 had an extension from an extracranial thrombosis.

Fifty-eight of the 100 patients had a significant disease of an extracranial artery. Eighteen of these had a disease of the carotid only, 7 of the vertebral only, and 33 of the carotid and vertebral arteries. There were 28 wrong diagnoses made. These included cerebral hemorrhage and tumor.

Once the fact was established that stenosis and thrombosis of the carotid and vertebral arteries in the neck was much more common than thrombosis of the intracranial cerebral arteries, a new therapeutic approach became possible because these arteries are readily accessible by surgery. To date we have reconstructed the carotid and vertebral arteries in more than 400 patients, and the results have been satisfactory.

In our view the best results occur in patients with transient attacks or incipient strokes. A follow-up of patients with severe hemiplegia shows that many of them suffered from transient attacks before the major catastrophic hemiplegia. At this state these patients have an operable lesion, and efficient surgery can prevent a major hemiplegia.

In patients with severe hemiplegia surgery may be successful, particularly if it is performed soon after the onset, but as Table I shows, the results of surgery in patients with progressing or completed strokes are inferior to those with transient or incipient attacks.

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* Medical Research Council Report. Cerebral Infarction: The role of stenosis of the extracranial cerebral arteries, H.M.R. Stationery Office, London, England, 1961.

Rational Therapy of Acute Sore Throat

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IN EXPERIENCE WITH *1,420 cases of acute sore throat seen over three years, Staphylococcus aureus was present in 47 per cent of all cultures, beta hemolytic streptococcus in 28 per cent, and both Staph. aureus and beta hemolytic streptococcus in 9 per cent. No pathogens were isolated in 34 per cent. A correlation between suspected bacteriologic diagnosis and laboratory findings was poor. In therapy penicillin is given (1) when beta hemolytic streptococcus is isolated; (2) when the patient is obviously in a toxic condition, has had a history of rheumatic fever, nephritis, and previous severe suppurative complications, or has a pre-existing disease such as diabetes mellitus or congestive heart failure; and (3) if the attack is one of repeated episodes. Broad spectrum antibiotics are given only if there is definite evidence of penicillin allergy.*

THE REASONABLE and proper management of the "acute sore throat syndrome," consisting of a painful throat, a moderately high fever, headache, nausea, often vomiting, beefy swollen tonsils with varying amounts of exudates, and cervical adenitis, has been a vexing and provocative problem to those of us who are engaged in general practice in a community of approximately 6,000 people. What to many people is an extremely simple clinical problem has, by its prevalence, severity, disastrous sequelae, and socioeconomic ramifications, raised several questions in the authors' minds as to the proper management. The purpose of this report is to delineate the problems and to suggest a method of management.

Methods and materials

The 1,420 consecutive and unselected cases comprising this study were seen by us during the years 1958, 1959, and 1960, and we completed the standard histories, physical examinations, urinalyses, and often white blood counts. Each case was studied bacteriologically by obtaining a throat swab of the affected area, streaked on a slanted surface of Löffler's agar in a small tube, and processed by the Bender Laboratory, Albany, New York. Processing included the inoculation of pathogens after twelve hours of incubation at 37 C. Photographs of representative lesions were obtained. Representative case histories were selected for presentation. Repeat cultures were not included.

Results

Of the 1,420 cases cultured, all age groups were affected, but, as in other studies, school children were affected principally.[1] The results of the throat cultures are presented in Table I, revealing the per cent of cultures positive for beta hemolytic streptococcus alone, micrococcus or Staphylococcus aureus* alone, both beta hemolytic streptococcus and Staph. aureus, and those cultures where no pathogens were isolated. Staph. aureus was present in 47 per cent of all cultures, beta hemolytic streptococcus in 28 per cent, and both Staph. aureus and beta hemolytic streptococcus in 9 per cent. No pathogens were isolated in 34 per cent.

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* Throughout this report M. aureus may be used synonymously with Staph. aureus. The Bender Laboratory, which processed the cultures, used the term M. aureus.

TABLE I. Bacteriologic classification of throat cultures

Type of Culture	Number of Cultures	Per Cent of Cultures
Staph. or M. aureus alone	. . .	38
Beta hemolytic streptococcus alone	. . .	19
Staph. or M. aureus with beta hemolytic streptococcus together	. . .	9
No pathogenic organisms	. . .	34
TOTALS	1,420	100

The monthly incidence of Staph. aureus and beta hemolytic streptococcus which was observed is presented graphically in Figure I. The highest rates were noted, as expected, in the winter-spring months of February-March-April of each year. Significant secondary peaks were noted in the late summer months, principally in August and September.

It became apparent early in the study that a correlation between the suspected bacteriologic diagnosis and the laboratory findings was poor. In a group of 100 patients this correlation was approximately 50 per cent. It seemed that when one of the observers was convinced that an individual case was a classic "Strep. throat," the bacteriologic report inevitably came back as Staph. aureus or having no pathogen. Examples of this dilemma are presented in the following case histories and accompanying illustrations.

Case reports

Case 1. A nineteen-year-old female complained of a sore throat of four days duration, chills, and fever. An examination revealed a temperature of 101.8 F. (oral), cervical adenitis, and acute exudative tonsillitis and pharyngitis (Fig. 2). A laboratory examination revealed Staph. aureus only.

Case 2. A twenty-two-year-old female had a sore throat and fever. An examination revealed a temperature of 102.6 F. (oral), cervical

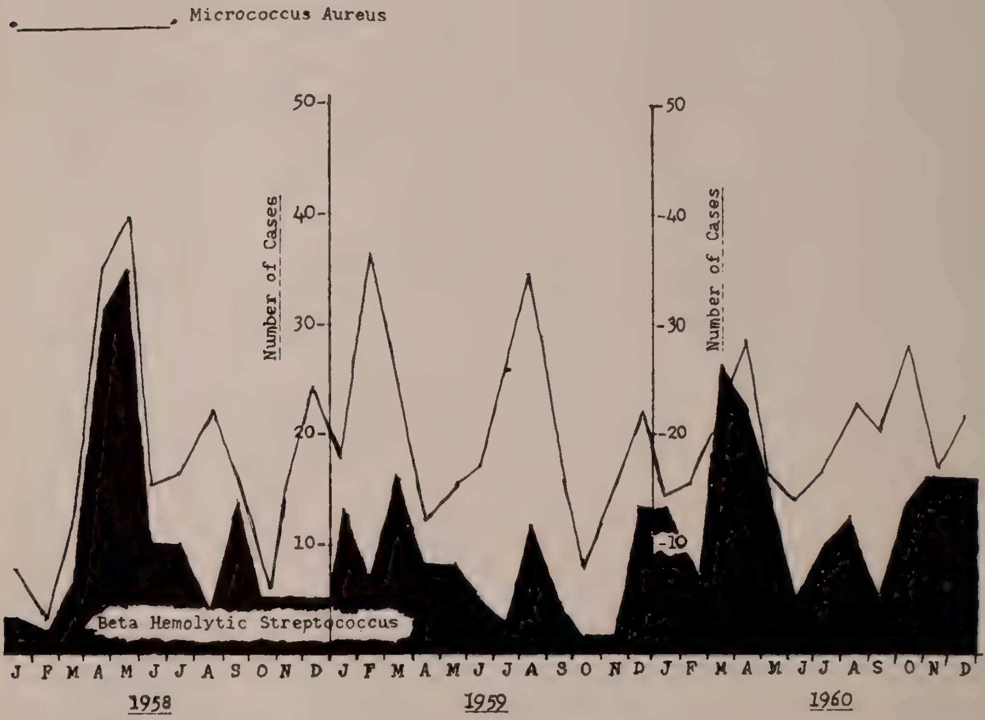

FIGURE 1. Monthly recovery rate of beta hemolytic streptococcus and M. aureus by throat culture (1958 to 1960).

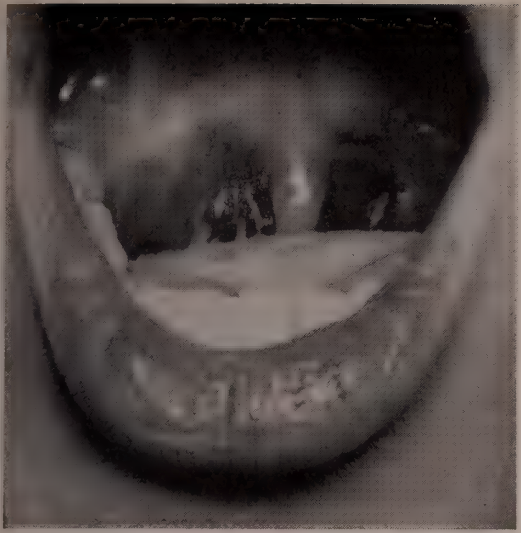

FIGURE 2. Case 1. Bacteriology: M. aureus only.

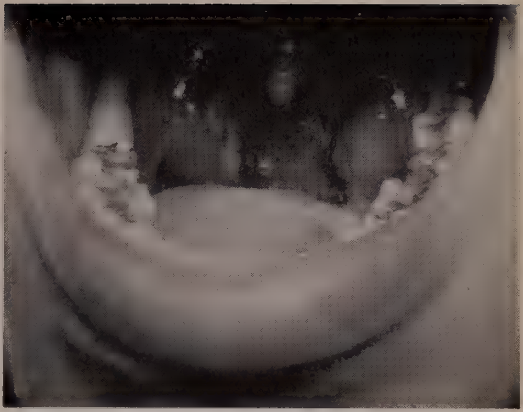

FIGURE 3. Case 2. Bacteriology: hemolytic streptococcus only.

adenitis, and acute exudative tonsillitis and pharyngitis (Fig. 3). A laboratory examination revealed hemolytic streptococcus.

Case 3. A twelve-year-old male had fever, chills, and a painful sore throat. An examination showed cervical adenitis and tonsillitis and pharyngitis with exudate (Fig. 4). A laboratory examination revealed both Staph. aureus and hemolytic streptococcus.

Comment. It is our impression that the bacterial agent cannot be reasonably suspected on the basis of clinical examination, as demonstrated by the cases presented. One case of definite acute rheumatic fever was seen during the three years in question. In contrast, 10 cases of acute glomerulonephritis were seen during the same period. All were male patients. The age varied between five and thirty-nine years, with an average of 13.2 years. The onset of nephritis followed from six to twenty-seven days after the acute sore throat, averaging 14.7 days. Hemolytic streptococcus was recovered in 6 of 10 cases during the initial pharyngitis, and in 4 of these Staph. aureus was recovered in addition. Two cases terminated fatally. Eight recovered without clinical evidence of sequelae.

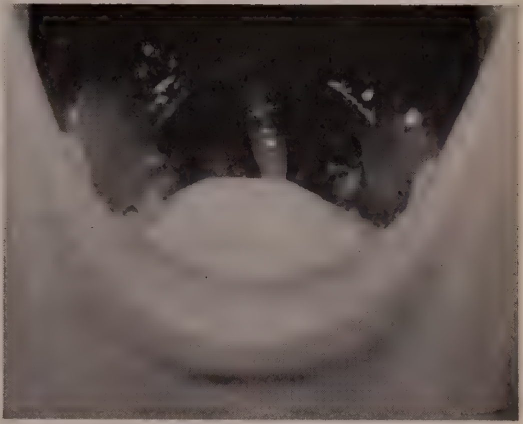

FIGURE 4. Case 3. Bacteriology: both M. aureus and hemolytic streptococcus.

Comment

Most authorities consider the hemolytic streptococcus pathogenic when it is recovered from an "acute sore throat." Classically Staph. aureus is not regarded as pathogenic when it is isolated from the pharynx.[2] The organism is recoverable from the nasopharynx in approximately 50 per cent of all people and in approximately 20 to 30 per cent from the pharynx in some studies.[3] And yet, when an organism as destructive as the coagulase positive Staph. aureus is the one most frequently recovered from the patient with the acute exudative tonsillitis and pharyngitis, is it justifiable to dismiss this organism as nonpathogenic, on the basis of studies on the flora of healthy people?

Both Staph. aureus and hemolytic streptococcus were isolated in 9 per cent of the cases. What significance is this combination of organisms? Is there any evidence of synergy? There is no real evidence that the infections in which both organisms were isolated were any more severe than when only one pathogen was recovered or when no pathogens were recovered. In our experience there was little correlation between the bacteriologic findings and the suspected causative organisms. Other observers feel that the accuracy of diagnosis is more certain.[4]

The scarcity of acute rheumatic fever is interesting. This has been noted by Bland[5] and is no doubt related to multiple factors such as improved standards of living, antibiotics, and possibly the natural mutation of the disease itself. By contrast, acute glomerulonephritis remains a serious problem. The mortality rate of 20 per cent in our series attests to this. The significance of the presence of Staph. aureus in the 4 of the 6 cases in which hemolytic streptococcus was recovered from the initial throat culture is unknown.

Should all cases be treated with antibiotics? We have the distinct impression that the course of the syndrome under discussion is generally the same, regardless of the organism obtained in the throat culture and whether antibiotics are given or not, except for the streptococcal throat which usually responds promptly to adequate therapy. There is a suspicion that there are less suppurative complications when antibiotics are used, but no evidence is presented to substantiate this.

Should cases only of hemolytic streptococcus be treated antibiotically? Mortimer and Rammelkamp,[6] other sources,[7] and Catanzaro, Rammelkamp, and Chamovitz[8] have shown that rheumatic fever and glomerulonephritis can be reduced by adequate treatment of streptococcal infections. We feel that streptococcal infection cannot be recognized for certain by clinical examination, and a delay of up to three days occurs before the bacteriologic report is obtained.

What effect has antibiotic therapy on the development of immunity to hemolytic streptococcus? There is an increasing body of evidence to suggest that prompt antibiosis aborts the usual development of immunity, and thus the recurrence of streptococcal episodes, particularly in adults, is increasingly common.[4,9]

The problem of which patients should be treated is so complex as to be nearly insoluble. However, the rationale of therapy utilized by us will now be presented for consideration. Since this program is flexible and individualized, no statistical presentation of results is possible.

Rationale of therapy of acute sore throat syndrome

1. Cultures are taken from all throats. Those patients in which beta hemolytic streptococcus is isolated are given ten days of penicillin therapy in therapeutic amounts and then cultures are taken again. Recurrences are treated in similar manner. Periodic urinalyses are made.

2. Penicillin therapy is started on the initial visit when the patient is obviously toxic or has had a history of rheumatic fever; nephritis; and previous severe suppurative complications, such as otitis media, abscess, and so forth. Penicillin treatment is also instituted if there is a pre-existing disease such as diabetes mellitus, congestive heart failure, and so forth, which can be worsened significantly by the acute illness.

3. If the attack represents one of repeated episodes, penicillin or another antibiotic to which the offending organism is found sensitive is given in an attempt to break the cycle.

4. If the patient is otherwise healthy and not severely ill or toxic, antibiotics are withheld, pending results of the culture. If Staph. aureus or no pathogen is obtained, antibiotics are not given unless the infection has persisted or worsened after from forty-eight to seventy-two hours.

5. Siblings are not given prophylactic penicillin unless there is a definite history of rheumatic fever or nephritis, in contrast to the other workers.[1]

6. Broad spectrum antibiotics generally have been less effective and are not used unless there is a definite evidence of penicillin allergy.

Summary

Experience with 1,420 cases of the acute sore throat syndrome seen in general practice over three years (1958 to 1960) has been described. The bacteriologic flora and seasonal variation have been presented. Evidence has been presented to demonstrate the authors' opinion that there is little

correlation between the bacteria discovered and the bacteria suspected. Experience with the nonsuppurative complications has been given. Questions have been raised as to the pathogenicity of Staph. aureus which is recovered in the acute sore throat syndrome; the problem of synergy between hemolytic streptococcus and Staph. aureus, and the possibility of Staph. aureus being etiologic in acute nephritis. Finally, questions have been raised as to which patients with the acute sore throat syndrome should receive antibiotic treatment. A rationale of therapy of this syndrome has been presented.

Acknowledgments. We are grateful to John K. Miller, M.D., and John J. Garrett, M.D., for their comments, and to Miss C. Mountain, bacteriologist, for her assistance.

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Clinical Evaluation of a New Analgesic in Obstetrics and Gynecology*

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THE SEARCH CONTINUES for the ideal analgesic for the mother in labor. This ideal drug would provide the prompt and potent relief of pain and apprehension for the mother without side-effects and without endangering the fetus.

For years morphine, alone or in combination with other drugs, has been used effectively for the relief of pain but with a relatively high incidence of side-effects as well as with more than occasional respiratory depression of the newborn infant.

Within the past two decades the naturally occurring opiates have been largely supplanted by synthetic agents of which meperidine hydrochloride has been the most popular. This drug is unrelated to morphine structurally but for the most part incorporates many of its pharmacologic properties. When meperidine is used alone or in combination with barbiturates, the results have generally been good without causing a marked increase over morphine in the respiratory depression of the infant. The side-effects of nausea and vomiting with meperidine as well as its decreased potency in comparison with morphine, however, leave it somewhat less than ideal. When it is used intramuscularly, its onset of action is frequently delayed. With intravenous administration, its margin of safety is reduced, and nausea and vomiting are much too common.

The use of meperidine in the gynecologic surgical patient is accompanied too frequently by poor control of postoperative pain. In addition, the hypotension, nausea, vomiting, and delayed onset of action do not permit one to classify meperidine as an ideal analgesic agent.

Meperidine has been used extensively on the obstetric-gynecologic service of St. Vincent's Hospital for the past several years and, in many instances, with satisfactory results. Because of the many inherent disadvantages of meperidine, we were anxious to study one of the newer synthetic agents in our obstetric and gynecologic patients. In view of its reported prompt onset of action and lower incidence of major side-effects in nonobstetric patients, oxymorphone† was chosen for a clinical appraisal of its usefulness in labor and its effects on the mother and the baby.

During our work, Resnick *et al.*[1] published their findings on the respiratory effects of oxymorphone. Respiratory depression was not clinically significant in healthy young subjects receiving a 1.5-mg. dose. However, in older and debilitated patients with cardiovascular, pulmonary, or hepatic disease, oxymorphone depressed respiration almost entirely at the expense of tidal volume without a change in the

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* The contents of this article are the personal views of the authors and are not to be construed as a statement of official Air Force policy.

† Oxymorphone is l-14-hydroxydihydromorphinone, available as Numorphan. The supplies of oxymorphone used in this study were provided by Endo Laboratories Inc., Richmond Hill, New York.

TABLE I. Statistics concenring 300 parturient patients given oxymorphone

Classification	Number	Per Cent
Parity		
Primigravida	140	47
Multipara	132	44
Grand multipara	28	9
Age (Years)		
Under 18	40	13
18 to 35	237	79
Over 35	23	8
Analgesia		
Excellent	112	37
Good	156	52
Fair	10	3
Poor	22	8
Length of labor		
Normal	269	90
Prolonged		
Primigravida	18	6
Multipara	13	4

A STUDY *was made of the use of oxymorphone (Numorphan) in 300 patients in labor and 100 postoperative gynecologic patients. In the former group the analgesia obtained was good to excellent in 89 per cent. The onset of action was extremely rapid and the average duration of pain relief, from three to four hours. The drug lacks deep sedative properties, and the side-effects were minimal. Labor was considered prolonged in 10 per cent of the patients, and contractions were weakened in 5 per cent following administration of oxymorphone. There was a greater incidence of respiratory depression in the newborn infants in those mothers who received oxymorphone less than thirty minutes before delivery, and general anesthesia seemed to account for a threefold increase in the number of severely depressed infants. In the surgical-gynecologic group analgesia provided by oxymorphone was uniformly satisfactory with few side-reactions and a lesser incidence of nausea and vomiting than is usually seen with meperidine.*

respiratory rate. In our study, we paid particular attention thereafter to the respiratory status of the newborn infant.

Oxymorphone is closely related structurally to morphine and to the synthetic dihydromorphinone hydrochloride. It is said to possess fifteen times the potency of morphine on a weight-to-weight basis with only one and a half times more toxicity.[2] Clinical studies reveal that 2 mg. of oxymorphone are equivalent to 16 mg. of morphine or 100 mg. of meperidine.[3] In clinically applicable doses, oxymorphone has been reported as a potent analgesic with low toxicity, a wide margin of safety, and a notably lowered incidence of side-effects.

Materials and methods

Our early experience with oxymorphone was gained from a pilot study which included over 200 patients. Because of the lack of published data on the clinical use of this agent in obstetrics, we felt that several months should be spent in becoming familiar with the actions of the drug prior to a formal investigation. Our total experience, then, has been with over 500 obstetric patients of whom the last 300 were studied formally and form the subject of this report. For the most part, the cases represent unselected consecutive patients on the ward service who were admitted to the labor suite.

The clinic population at this hospital is composed of between 70 and 80 per cent Puerto Ricans. The percentage figure of primigravidas in the study (Table I) is weighted by the fact that a number of unwed mothers are delivered by referral from two agencies. This also accounts for the relatively large proportion of patients below the age of eighteen (13 per cent) (Table I).

On admission, every patient received a complete physical examination. When they were not contraindicated, an enema was administered, and 100 mg. of either secobarbital or pentobarbital were given orally unless labor was far advanced.

Oxymorphone was ordered parenterally in doses which varied from 0.75 to 1.5 mg. depending on the patient's weight and the estimated time remaining prior to delivery. The initial dose was administered when the relief of pain seemed indicated, but efforts were taken to be certain that active labor existed. Twenty-seven per cent of the patients received oxymorphone before the cervix had dilated to 4 cm. The medication was repeated in 0.75-mg. doses at varying intervals depending on the severity of the pain but usually three to four hours following the last injection. Atropine was given concomitantly when indicated and in all cases in which general anesthesia was contemplated. The use of scopolamine was avoided in the patients under study.

Varied modalities of anesthesia were employed for delivery. The choice was based on patient or physician preference or on obstetric indication when such was present. General anesthesia consisted in all instances of either a gas-oxygen-ether sequence or cyclopropane and oxygen. Patients receiving nitrous oxide and oxygen alone were classified in a separate group. Fifty-five per cent of the patients were delivered under conduction anesthesia, which was either caudal or saddle block.

The patient was observed closely during labor for the onset of action of oxymorphone, the degree and duration of pain relief, maternal side-effects, aberrations of the fetal heart tones, and frequency and quality of uterine contractions. One minute following birth, the infant was evaluated using the Apgar scoring system.

In addition, 100 surgical patients who received oxymorphone postoperatively on the gynecologic service were studied. This group was composed primarily of ward patients plus several private patients. The patients were evaluated for the relief of pain, the duration of effect of the drug, and the side-effects or complications.

Results

For the purpose of convenience, the results obtained during this study are placed into four groups: (1) effects of oxymorphone on the mother, (2) effects on labor, (3) effects on the fetus, and (4) results in gynecologic surgical patients.

EFFECTS OF OXYMORPHONE ON THE MOTHER. The analgesia obtained with oxymorphone was rated as excellent in 37 per cent, good in 52 per cent, fair in 3 per cent, and poor in 8 per cent (Table I). If the first two categories are combined, we note that analgesia was satisfactory in 89 per cent of the patients.

Varying dosage schedules, for example, (*a*) 1.5 mg., (*b*) 1.5 mg. followed by 0.75 mg., (*c*) 0.75 mg. alone, or (*d*) 0.75 mg. repeated at intervals, all seemed to give comparable analgesic results in this clinical study. In addition, the total amount of oxymorphone administered during labor did not appear to influence the over-all analgesic result.

In contrast to the studies of Coblentz and Bierman,[3] our experience indicated that for the obstetric patient in labor, 1 mg. of oxymorphone is approximately equivalent in analgesic action to 100 mg. of meperidine. This is based, however, on our clinical evaluation and not on controlled pain-tolerance data.

The onset of action of oxymorphone was extremely rapid. Following the intramuscular administration of the drug, most of our patients experienced noticeable analgesia within five to ten minutes and obtained the maximum analgesic effect in fifteen to twenty minutes.

The average duration of pain relief with oxymorphone during labor was between three and four hours following intramuscular injection. The drug appears to have a slightly but distinctly shorter duration of action than meperidine.

A definite advantage of oxymorphone is its lack of deep sedative properties. Although our patients slept between contractions, they were easily roused to alertness. They were able to cooperate with anesthetic procedures and with obstetric maneuvers such as assisted breech delivery which required patient participation.

The side-effects with oxymorphone were minimal. With the doses of oxymorphone which were employed, no instances of hypotension or maternal respiratory depression occurred. Nausea and vomiting were seen so infrequently, even with the intravenous administration of the drug, that they were considered probably coincidental in the 2 or 3 cases in which they were observed. No allergic phenomena were encountered in the obstetric series.

EFFECTS OF OXYMORPHONE ON LABOR. Labor was considered to be prolonged if it exceeded twenty-four hours in primiparas or fourteen hours in multiparas. Of the patients in this series, 10 per cent exhibited labors so defined as prolonged (Table I).

TABLE II. Apgar scores and time interval between last injection of oxymorphone and birth of 300 infants

Apgar Score	Number of Births by Time Interval (Minutes) Less Than 30	30 to 60	60 to 120	More Than 120	Totals Number	Per Cent
8 to 10	22	47	70	106	245	82
5 to 7	4	8	12	14	38	13
Less than 5 (including 5 stillbirths)	5	1	4	7	17	5

Contractions were considered to be weakened if, following the administration of the drug, the intensity or duration of the contractions was decreased or the time interval between successive pains increased.

Contractions were weakened in 5 per cent of our patients following the administration of oxymorphone. When oxymorphone was administered before the cervix had reached 4 cm. of dilatation, there was no increase in the incidence of weakened contractions.

Eighty per cent of the patients whose contractions were noted to be weakened went on to labors of normal length.

There were, however, 3 documented cases in which a definite slowing of labor followed immediately on the administration of oxymorphone and could be explained by no other cause.

Effects of oxymorphone on the fetus. Of the 300 infants delivered during this study, there were 5 stillbirths and 2 neonatal deaths for a total perinatal mortality of 2.3 per cent. Oxymorphone is not incriminated in these 7 cases as a causal or responsible factor.

Seventeen infants showed Apgar scores of less than 5 (Table II). Five of these babies were stillborn. Of the remaining 12 babies there were 5 in whom there were obstetric factors present which are known to depress fetal reaction time.

Thirty-one mothers received oxymorphone less than thirty minutes before delivery. Five of these mothers (16 per cent) gave birth to infants scoring less than 5 on the Apgar scale. This is opposed to an incidence of 2 per cent, 5 per cent, and 5 per cent for other groups who were given the drug at longer intervals before delivery. When larger doses (1.5 mg.) were used within a short interval before delivery, there seemed to be no increase in the depressing effect over that seen with 0.75 mg.

Of the 76 patients who were delivered under general anesthesia, 13 per cent had infants scoring under 5 on the Apgar score. In contrast, when nitrous oxide-oxygen, conduction, or no anesthesia was employed, the percentages of severely depressed infants dropped to 3 per cent, 3 per cent, and 4 per cent respectively. The mothers of the low-scoring babies who were delivered by means of general anesthesia had been given oxymorphone at varying intervals before delivery, with no preponderance of them being medicated late in labor.

The vast majority of the infants studied showed rapid reaction times, 82 per cent of them rating a score of 8 to 10 on the Apgar scale. An additional 13 per cent were scored between 5 and 7, while the infants discussed previously whose Apgar scores were below 5 comprised only 5 per cent of the total series.

Results in surgical-gynecologic patients. The analgesia provided by oxymorphone for an unselected group of postoperative patients recovering from all types of pelvic and vaginal surgery was uniformly satisfactory. Many patients previously had received meperidine with poor results and manifested a marked increase in pain relief when oxymorphone was substituted. The usual dose of oxymorphone was 1 mg. intramuscularly, although the first postoperative dose was halved.

A rapid onset of effective pain relief was noted in these postsurgical patients, but, in contrast to the obstetric group, the duration of analgesia was more prolonged, lasting in most cases from four to six hours.

Nausea and vomiting in the postoperative patient may be related to many etiologic factors. It was our definite impression that with oxymorphone its incidence was markedly less than is usually seen with meperidine.

Other side-reactions were rare but did include 1 case of generalized pruritus that did not recur when the medication was discontinued. Two cases of transient hypotension were seen in the immediate postoperative period following the administration of oxymorphone. There was 1 patient whose respiratory rate was decreased owing to an overdosage.

Comment

The results obtained in this study indicate that the ideal analgesic for the laboring patient still eludes us. The synthetic opiates, however, offer important gains in progress in this field. Oxymorphone represents a significant advance in the relief of pain in both the parturient and the postoperative gynecologic patient because it provides rapid onset of analgesia coupled with a low incidence of side-effects.

Care should be exercised in the administration of oxymorphone late in labor with regard to the anticipated time of delivery to avoid respiratory depression of the newborn infant. It has a potent pain-relieving effect. The great majority of patients received either 1.5 mg. or 0.75 mg. of oxymorphone. Eighty-nine per cent of these two classes obtained good to excellent pain relief. In labor, the average duration of the effect of oxymorphone was between three and four hours; in gynecologic surgery patients, it was four to six hours in most instances.

Oxymorphone offers the advantage over most other potent analgesics in providing only a mild sedative effect. Its analgesic properties permitted patients to sleep between contractions, but they were easily roused and cooperated with anesthetic procedures and obstetric maneuvers.

In this series general anesthesia, regardless of when the analgesic was administered, seemed to account for a threefold increase in the number of severely depressed infants.

There was no increase in the incidence of weakened contractions when oxymorphone was administered before the cervix had reached 4 cm. of dilatation; weakened contractions occurred in only 10 per cent of the patients in whom labor was recorded as prolonged and in 5 per cent of the patients whose labors were normal in length.

Conclusion

Our report on the evaluation of a new analgesic, oxymorphone, is based on clinical experiences gained first from a pilot obstetric study of more than 200 patients and from a formal study of 300 additional patients in labor and 100 postoperative gynecologic patients.

Oxymorphone appears to provide distinct advantages over other commonly used analgesic agents and warrants a further definitive evaluation including double-blind studies.

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Immediate Laparotomy in Penetrating Wounds of the Abdomen

A STUDY WAS MADE *of 100 consecutive cases of suspected penetrating wounds of the abdomen in which immediate laparotomy was performed. In 85 cases the wounds were found to penetrate the peritoneum, and in 71 the liver or other viscera were injured. The hospital stay averaged 14.1 days for the penetrating group and 11.3 for the nonpenetrating. Complications were infrequent, and it would seem that prompt surgical intervention and the use of antibiotics played a part in the low infection rate. There were no deaths in the nonpenetrating group.*

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IT HAS LONG BEEN a surgical axiom that all suspected penetrating wounds of the abdomen be explored. In 1959 Shaftan* reported on 182 such patients among whom it was elected to perform no surgical procedure in 125 instances. This report led us to review critically our experience for the six-year period of 1955 through 1960. During this time there were 100 consecutive cases admitted through the emergency department of Knickerbocker Hospital which fell into this category, and they form the basis of this report (Table I).

It is the practice at this hospital to explore as an emergency all patients admitted with wounds which, either by their location or by the nature of the wounding agent, could possibly have penetrated the abdomen, regardless of the presence or absence of abdominal findings. The diagnosis is not dependent on x-ray findings, and in most cases x-ray films are taken only to rule out or confirm associated injuries. The preoperative work-up consists of a history and physical examination, a complete blood count and urinalysis, cross matching of the blood, and a hematocrit if there is moderate blood loss. Tetanus antitoxin is administered to all patients who have not had previous active immunization and who are not allergic to the antiserum. Tetanus toxoid is administered to all patients who have had previous immunization. Desensitization is carried out only if the wounds are likely to be contaminated with tetanus spores or if there is soft-tissue maceration. The patients are taken to the operating room as soon as the work-up is completed and they can be safely operated on.

All but 13 patients in this series received antibiotics. Penicillin and streptomycin were used for the most part. The tetracyclines or chloramphenicol were employed in those patients in whom there was an allergy to penicillin or whose wound cultures showed resistance of the organisms to penicillin and/or streptomycin. There were no wound infections in the 13 who received no antibiotics.

Technics

The operations were performed by both attending physicians and residents, and no uniform suture materials or closure methods were employed. Postoperative evisceration occurred in 4 cases. All lacerations of the bowel were closed in two layers, and anas-

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* Shaftan, G. W.: Indications for operation in abdominal trauma, Am. J. Surg. **99**: 657 (May) 1960.

TABLE I. Statistics on 100 cases of suspected penetrating wounds of the abdomen

Wound	Number of Cases	Average Age (Years)	Sex		Hospitalization (Days)	
			Male	Female	Average	Mean
Nonpenetrating	15	30.2	10	5	11.3	9.4
Penetrating	85	27.5	61	24	14.1	11.0

tomoses were performed in similar fashion. Only 1 patient developed a fistula. Clean lacerations of the liver which were not bleeding at the time of the surgical procedure were not sutured. There were no cases of recurrent bleeding from the liver. Wounds of the intraperitoneal large bowel were treated by primary closure without proximal colostomy or exteriorization. This, of course, is a peacetime hospital procedure which would not be applicable to wartime battle conditions in which exteriorization or at least proximal colostomy would be performed. There were 16 instances of colonic wounds, some multiple, which were treated with primary closure without complication. Proximal colostomy was employed for wounds of the colon below the peritoneal reflexion.

Analysis of cases

The 100 cases have been divided into two main groups: penetrating and nonpenetrating. In 85 the peritoneum was penetrated, and in 15 it was not (Table I). The average age was 28.3 years, ranging from fourteen to sixty-seven years with the majority in the third and fourth decades. Males outnumbered females by a ratio of more than 2 to 1. In 69 there was some notation on the chart that the patient either was intoxicated or had alcohol on the breath. Eighty-two patients were wounded by a knife, 11 by a bullet, and the remainder by objects varying from a knitting needle to the hood ornament of an automobile. With few exceptions the wounds were dispersed uniformly over the anterior lower chest and abdomen.

Two of the patients with nonpenetrating wounds were given blood transfusions of 500 cc. Transfusions were given to 42 of the patients with penetrating wounds, 18 receiving 500 cc. of blood and the remainder from 1,000 to 2,000 cc.

In computing the average hospital stay, those patients who died and those whose hospitalization was prolonged because of associated injuries were excluded. The mean hospital stay excludes only those patients who died. The associated injuries are broken down into two main groups: major and minor (Table II). Under minor injuries are included lacerations, minor fractures, and cerebral concussion. The major injuries include fractures of the weight-bearing bones, open fractures, tendon lacerations, and penetrating wounds of the thorax.

The penetrating wound cases have been subdivided further for the purpose of evaluating physical findings into (1) those patients in whom the peritoneum only was lacerated; (2) those in whom a clean non-bleeding laceration of the liver was found and in which exploration and aspiration of blood and bile from the peritoneal cavity were performed; and (3) those in whom more extensive visceral damage necessitated more definitive treatment (Table III).

In the nonpenetrating wound group, the prime physical finding was local tenderness, with some abdominal wall spasm occurring in 4 cases. In the penetrating wound group the physical findings became progressively more marked as the severity of the injury increased.

Shock occurred in 3 cases in which only the peritoneum was lacerated, in 1 case in which the liver was lacerated, and in 29 cases in which there was bowel and other visceral involvement.

Evisceration of the omentum and/or bowel occurred in 3 cases in which only the peritoneum was lacerated as well as in 13 cases with visceral involvement.

In the group in whom only the peritoneum was lacerated, 5 patients required transfusions, 2 receiving 500 cc. of whole blood and the other 3 receiving 1,000 to 2,000 cc.

TABLE II. Findings in 100 cases of suspected penetrating wounds of the abdomen

Finding	Nonpenetrating		Penetrating	
	Number	Per Cent	Number	Per Cent
Associated injuries	8	53.2	30	35.3
Major	1	6.6	12	14.1
Minor	7	46.6	18	21.2
Complications	2	13.3	12	14.1
Deaths	0	0.0	4	4.7
Cardiac arrests	0	0.0	2	2.3
Blood in abdomen (cc.)	..	...	85	...
500	...	...	46	...
1,000	..	...	31	...
1,000+	..	...	8	...
Blood replacement (cc.)	2	13.3	42	49.4
500	2	13.3	18	21.2
1,000	..	...	13	15.3
1,500	..	...	6	7.1
2,000	..	...	1	1.2
2,000+	..	...	4	4.7

TABLE III. Abdominal findings in 100 cases of suspected penetrating wounds of the abdomen

Abdominal Finding	Nonpenetrating Wound (15 Cases)	Peritoneum Only (14 Cases)	Liver Laceration (8 Cases)	Bowel and Other Visceral Involvement (63 Cases)
None	1	2	2	6
Local tenderness	10	5	5	12
Tenderness, spasm	4	4	1	16
Tenderness, spasm, rebound	..	2	..	10
Tenderness, spasm, rebound, distention, or absent bowel sounds	..	1	..	19
Shock	..	3	1	29
Evisceration	..	3	..	13

In each case bleeding was from the epigastric vessels with drainage into the abdominal cavity. In the group in whom only the liver was lacerated, 2 patients were transfused, receiving 500 cc. and 1,000 cc. respectively. In the 63 cases in which bowel and other viscera were involved, 38 required transfusions, 2 receiving 500 cc. of blood and the remainder receiving from 1,000 to more than 2,000 cc. The frequency of injury to various organs in 71 of the 85 cases of penetrating wounds was: liver, 18; spleen, 6; diaphragm, 8; stomach, 10; omentum, 8, pancreas, 2; mesentery, 11; small bowel, 22; colon, ascending, 6, transverse, 8, and descending, 2; rectum, 2; and bladder, 1.

Complications

There were 3 complications in the nonpenetrating group: 1 wound dehiscence, 1 superficial thrombophlebitis, and 1 instance of postoperative pneumonia.

There were 18 complications, including 4 deaths, which occurred in 12 patients in the penetrating group. Two of the deaths were from cardiac arrest. In 1 of these, inadequate blood replacement was a contributing factor. In the other anoxia appeared to play a major role. A third death was due to severe multiple injuries with a superimposed pneumonia. The fourth death was in a patient who had sustained lacerations of the vena cava and right iliac artery. Despite the repair of the vessels and massive blood replacement, the patient remained in shock and died.

The other complications included 2 of evisceration, 6 of wound infection (5 of the wound and 1 subphrenic), and 1 each of fistula, thrombophlebitis, recurrent bleeding, jaundice, and delirium tremens.

Comment

The age, sex, or wounding agent seemed to have little bearing on the morbidity or mortality. These were directly proportional to the number and severity of the organs which were involved. Alcohol likewise did not appear to influence these factors, although 69 per cent of the series either were intoxicated or had been drinking. This group withstood anesthesia and surgical procedures well with the exception of 1 case of delirium tremens.

The relative lack of infection as a complication (6 per cent for the entire series) was rather surprising. We do not intend to enter into the argument over the routine use of antibiotics, and we neither condone nor condemn this practice; we merely state a conclusion drawn from the data at hand: It would seem that prompt surgical intervention and the use of antibiotics both must have played a part in the low infection rate.

Only one bowel fistula occurred in the entire group. This was a small bowel fistula which required secondary closure. No large bowel fistula developed, despite the fact that all the perforations were closed primarily without proximal colostomy and instead of being exteriorized. The only subphrenic abscess developed in a patient who had sustained a laceration of the jejunum. None occurred in a patient who had an injury to the large bowel. It would seem that in peacetime hospital conditions, exteriorization and/or proximal colostomy are not required in the treatment of most penetrating wounds of the intra-abdominal large bowel. A proximal colostomy is still mandatory, however, for wounds of the colon below the peritoneal reflexion.

The fact that 49.4 per cent of the patients in the penetrating group received from 1 to 12 units of blood is alarming. Eighteen, or 21.2 per cent, received 500 cc. of blood, which perhaps was not absolutely required. There were no transfusion reactions. We know of no cases of serum hepatitis, but since a follow-up after the wounds were healed was almost impossible in this group, we can make no definite statement as to its occurrence.

In 18 of 63 cases (28.6 per cent) of serious intraperitoneal injury, there were either no abdominal signs or only local tenderness. This emphasized the lack of early signs in many cases. It must be stressed that wounds in the lower chest must be considered as suspected penetrating abdominal wounds and treated as such. This is especially true of those over the splenic area.

Summary

One hundred patients with suspected penetrating wounds of the abdomen who underwent emergency laparotomy are reviewed. In 85 cases the wounds were found to penetrate the peritoneum; in 71 cases the liver or other viscera were injured.

The physical findings are not a reliable index either of the penetration or of the extent of the pathologic condition. The hospital stay is not long, averaging 14.1 days for the penetrating group and 11.3 days for the nonpenetrating. Complications were infrequent, and in the nonpenetrating group there were no fatalities.

The findings justify the practice of emergency laparotomy for these cases.

Evaluation of Amblyopia Problem in the Child

THE DIAGNOSIS *before the age of six years of amblyopia, which affects the central vision only and may or may not be accompanied by a "turned eye," is not customary. However, early diagnosis and treatment are necessary for a favorable prognosis. Therefore a specific amblyopia screening program, to begin at about four years of age, and a thorough elucidation of all aspects of amblyopia, involving general physicians, pediatricians, private and public health nursing personnel, teachers, health counselors, and public health officials, are recommended.*

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AMBLYOPIA IS A REDUCTION in the acuteness of vision which cannot be relieved by glasses and which is not due to any visible pathologic changes in the eye. It is usually unilateral except for those instances where extreme bilateral refractive error plays a role.

At present well-baby care programs, as conducted by pediatricians and general practitioners in clinics and private practice, are excellent. The health records of children are noted carefully insofar as weight, height, teeth, and bones are concerned. By contrast, even at the best institutions and private offices the eyes are completely neglected and the vision is rarely recorded. Pediatricians and parents are content to "wait until the child attends school, they will examine his sight."

Milton Levine, M.D., Chief of Pediatrics, New York Hospital, has stated that he does not believe eye examinations are done routinely in pediatricians' offices outside the hospital.[1] The evaluation of the visual status in the child concerns the early detection of eyes which are "turned," as well as eyes which have an optical defect (hyperopia, myopia, or astigmatism), particularly when only one of the eyes is involved. The end result in either case is the permanent loss of useful central vision in one eye, if the condition is undiscovered and untreated.

Central vision develops gradually throughout the first six years of life. An infant cannot fixate because sharp vision is not present at that time. This process which is so important for reading, at a distance or near, consists of only a few degrees in the central portion of the visual field. Without adequate central vision of both eyes, parallel or straight eyes may eventually "turn." The visual mechanism cannot be expected to maintain permanent alignment in the absence of two distinct, identical pictures which can then be fused into a single picture in the brain. The youngster develops central vision by constant use whenever he is concentrating on small objects.

Peripheral vision develops at or immediately after birth. It is this function which permits an infant to follow lights and moving objects. The peripheral fields of the two eyes overlap partly, thus permitting the development of binocular vision.

Central vision only is affected in amblyopia. It can be considered "an island of central blindness in a sea of vision." Thus, in amblyopia the peripheral vision is perfect and only the small important central area is defective, as revealed by a perimeter or tangent screen study.

Normally, each eye receives a picture. Two grossly similar pictures reach the brain and are blended into one image, a single binocular image resulting in stereopsis. In the event that the eyes are not absolutely straight, two entirely different pictures are presented to the brain, and these pictures cannot be fused into a single image. This results in diplopia or double vision which the brain will not tolerate. A reflex is then developed involuntarily, whereby in young children the brain suppresses one of the pictures that it is receiving. The eye whose picture is suppressed involuntarily gradually loses its ability to see clearly, since the macula is not being stimulated and therefore does not continue to develop. This is known as amblyopia ex anopsia and may or may not be accompanied by a "turn" of the involved eye.

When a large uncorrected refractive error is present in only one eye, its retina receives a picture which is blurred. This unclear picture, on arriving in the brain, cannot be fused with the clear picture which the brain receives from the fellow eye. In the same way, the image is suppressed involuntarily, and central vision does not develop further. This type of amblyopia is caused by anisometropia, wherein the involved eye has an uncorrected optical error which has been ignored in the child and its presence undiscovered because the other eye has good vision.

Both forms of amblyopia can usually be corrected if they are discovered early. Glasses can be prescribed and worn easily by very young children. The defective eye can be improved by an occlusion of the better eye. If occlusion is begun the first two or three years of life, it is usually rapidly successful because the amblyopia is not as yet deep enough to be irreversible. Corrective glasses, patching of the good eye, and surgery, whenever indicated to further straighten crossed eyes, may result in normal binocular vision before school age. However, when treatment is unknowingly delayed until the age of seven years, the amblyopia may be so established that only a prolonged continuous patching can result in any improvement at all.

Leavenworth, in 1960,[2] reported that the good eyes of 19 children with amblyopia were occluded for sixteen weeks. Among 10 of these children who were six years of age or younger, the final corrected vision was 20/20 in 9 and 20/25 in 1. In all but 2 of the remaining 9 children who were older than six years of age, the final corrected vision fell short of 20/20.

The infant or preschool child with decided strabismus is usually referred immediately to an ophthalmologist or an eye treatment agency where treatment is begun and often the amblyopia is corrected completely before the child reaches school age.[3] The "problem" is the preschool child who has amblyopia accompanied by a slight or absent strabismus. Often when no strabismus is present the amblyopia case is missed entirely, or, when the strabismus is slight, it is not referred for treatment. Among pediatricians and general physicians, it is felt that in cases with small deviations of the eye the child will "grow out" of the deformity,[4] or that the child is "too young for the ophthalmologist to do anything with." Another favorite quote by the physician is, "When the child goes to school, they will check him (or her) there."

The question of ocular screening and vision recording appears to be a basic necessity in the evaluation of the visual status in young children. In 1958 Wood[5] stated that "It is difficult to visualize the optic fundus in children . . . and that this examination is not necessary in all patients." There was no mention made of recording the vision or some attempt at an evaluation of a possible squint in a pediatric examination.

Bettman and Fellows,[6] commenting on the Orinda Vision Study, state that routine school eye examinations fail to discover most serious ocular conditions until it is too late. It is for this reason that some of the statistics of the Eye Program of the Bureau for Handicapped Children have been recorded, in an effort to demonstrate clinically some of the foregoing facts.[7]

Statistical findings*

The findings at some of the health centers utilized in this evaluation were as follows:

Of 1,680 children examined in a ten-month period (September, 1959, to June, 1960) at the Red Hook Health Center, 77 or

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* Studies at these health centers have been maintained since this report was submitted for publication. The statistics have remained relatively unchanged.

4.58 per cent had amblyopia. Of 625 children examined in a three-month period (September, 1959, to December, 1959) at the Red Hook Health Center, 29 or 4.64 per cent had amblyopia. Of 681 children examined in a three-month period (September, 1959, to December, 1959) at the Fort Greene Health Center, 35 or 5.13 per cent had amblyopia.

Of the cases discovered at the Red Hook Health Center in the ten-month period, 69 out of 77 were in children seven years of age or over at the time of the first visit to the eye clinic (89.4 per cent). Of the cases discovered at the Red Hook and Fort Greene health centers in a three-month period, 58 out of 64 were in children seven years old or over at the time of the first visit to the eye clinic (90.6 per cent).

Comment

Discussion of findings. 1. The findings reveal that the usual age of the amblyopic child at the time of the first visit to the Department of Health Eye Clinic is seven years or more.

2. Inasmuch as the condition of amblyopia ex anopsia develops at a very young age, it indicates that some children have passed the annual vision screening test in the first year of school who should otherwise have been failed and reported to the school nurse. In short, the amblyopic eye was undiscovered.

3. The established treatment for amblyopia is occlusion of the good eye, forcing the poor eye to be employed and stimulating the vital macular zone of the retina. Authorities have proved that this treatment must be instituted before six years of age. It is well established that treatment will be more successful the earlier the discovery of this condition is made. It is apparent, therefore, from the previously mentioned material that the present system of vision screening in the New York City school system cannot be depended on to discover the amblyopic child at a sufficiently early age. Increased emphasis, therefore, must be placed on preschool vision screening, beginning at approximately three to four years of age. An evaluation of the vision of the young child by the general practitioner and pediatrician is essential.

The pitfalls of amblyopia. 1. The absence of associated ocular muscle imbalance (turned eye) which does not preclude the presence of amblyopia. Amblyopia associated with "turned eye" seeks an ocular agency early. Amblyopia not associated with "turned eye" does not seek an ocular agency because the normal eye is almost always excellent and functions for the two eyes.

2. The absence of vision examinations in the preschool child by either the general practitioner or the pediatrician.

3. The questionable practice of the medical profession of relying on the present vision screening program in the various school systems, whereby teachers are required to screen large numbers of their students visually.

Recommendations toward combating the problem of amblyopia. *The preschool vision screening program.* 1. To take place in the office of a family doctor or pediatrician, beginning at the age of three years, with picture or E charts (not performed at present).

2. Acquainting physicians, parents, teachers, nurses, and public health workers with the amblyopia problem by way of ophthalmologic and public health literature and child health stations.

3. Acquainting physicians, parents, teachers, nurses, and public health workers with a technic in testing the preschool child's vision.

Vision screening beginning in kindergarten and continued in the first and subsequent grade, to be known as the amblyopia screening program. 1. The vision screening should be performed to specifically rule out the presence of amblyopia.

2. This can be accomplished satisfactorily by checking the vision of each eye carefully and being certain to occlude completely the fellow eye, so that subconscious cheating does not occur and thereby result in a failure to diagnose an amblyopic eye, if present. This screening must be performed by personnel who are specifically acquainted with aspects of amblyopia. (The presence of ocular pathologic conditions and some refractive error will, by necessity, be dis-

covered if the vision is less than 20/20.)

Annual vision screening for undetected amblyopia cases. 1. All grades including high school.

2. Vision screening to be performed by teachers specifically acquainted with good technic in this form of testing.

Summary

The definition of amblyopia, two of its more common etiologic factors, and aspects of its pathogenesis have been discussed. In addition, the necessity for early diagnosis and its specific relationship to a favorable prognosis, whenever treatment can be instituted before six years of age was demonstrated.

Statistics and case histories taken from the eye clinics of the Bureau for Handicapped Children of the City of New York Department of Health showed that the diagnosis of amblyopia before six years of age is not customary.

Recommendations toward eliminating the amblyopia problem in the child, include the following:

1. A specific amblyopia screening program, utilizing trained personnel, to commence at about four years of age.
2. A thorough elucidation of all aspects of amblyopia, involving general physicians, pediatricians, private and public health nursing personnel, teachers, health counsellors, and public health officials.

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No More Proof Needed of Smoking-Cancer Link

The collection of further scientific data linking cigaret smoking and lung cancer is not needed. Studies already completed are adequate and are available for re-evaluation if necessary, according to Howard C. Taylor, M.D., New York City, in the September 1 issue of the *Journal of the American Medical Association.*

"The evidence . . .is far more precise, in fact, than that which has been accepted by physicians as adequate to take action against the causes of other plagues," he said.

Authorities estimate that 75 to 90 per cent of the 40,000 annual lung cancer deaths may be attributed to the smoking habit. These 30,000 to 36,000 deaths are approximately equal to the annual motor vehicle traffic death toll about which "so much justifiable horror" is expressed, Dr. Taylor said.

There is definite evidence that the life expectancy of men who are cigaret smokers is less than that of nonsmokers. Recent data indicate that the risk of dying in the "prime of life" (before age sixty-five) is almost twice as great for American men who are heavy cigaret smokers as for nonsmokers.

There is evidence that cigaret smoking has declined substantially among physicians over the past several years, and physicians are urged to examine the facts and act in accordance with their implication.

Inferior Mesenteric Artery Injury

A Complication of Translumbar Aortography

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TWO CASES *of inferior mesenteric injury following translumbar aortography are presented, 1 with a fatal outcome and 1 with complete recovery attributable partly to prompt diagnosis and therapy. Most of the complications of translumbar aortography and the contrast media employed arise as a consequence of breaks in the accepted standardized technic. Other factors include needle penetration, needle position, injection of radiopaque material, and a combination of two or more of these factors. A low translumbar approach is preferred, with a second needle at a different level used only when necessary.*

INTEREST was aroused in 1929 by the communication of Dos Santos, Lamas, and Caldas[1] regarding a method of translumbar aortography. It was not until 1942, mainly after the independent works of Nelson[2] and Doss, Thomas, and Bond[3] that the procedure acquired widespread application in the United States. In commenting on a total of about 100 cases in 1931, Dos Santos, Lamas, and Caldas[4] reported having encountered no complications. With the vivid interest in this procedure as a diagnostic tool the incidence of complications has increased considerably. Unfortunately, these complications occasionally are fatal and sometimes lead to permanent injury. Refined technics and the use of organic contrast media have failed to reduce considerably the over-all incidence of complications. A more cautious approach to translumbar aortography has limited its use generally to those cases in which the applicability of surgical therapy is assured.

In this paper 2 cases of complications following translumbar aortography are presented. Both complications developed as an injury to the inferior mesenteric artery. The first case had a fatal outcome, and, although an autopsy was not performed, surgery provided ample evidence as to the extent and severity of the damage. The second case had a favorable outcome partly, we think, because of a prompt diagnosis and therapy.

Case reports

CASE 1. A fifty-seven-year-old white male was admitted to the hospital on December 26, 1956, because of bilateral progressive intermittent claudication for about two years. There was a history of previous cardiac decompensation. A physical examination revealed a somewhat obese white male in no distress. The blood pressure was 145/85. A physical examination produced negative findings except for those in the lower extremities. The right femoral pulse was palpable and strong. The left femoral pulse was weak. Below this, the pulses on the right were weak. On the left they were absent. A chest x-ray film showed negative findings, and an electrocardiogram suggested myocardial damage. The serology, blood, and urinalysis showed negative findings.

On the sixth day after admission a translumbar aortogram under combined spinal and thiopental sodium (Pentothal sodium) anesthesia was performed unsuccessfully because of extravasation in the left para-aortic area. Twenty cc. of 70 per cent iodopyracet (Diodrast) and 20 cc. of 80 per cent potassium iodide were used. A left femoral arteriogram was then done using a total of 40 cc. of 70 per cent iodopyracet. There were no immediate untoward reactions. The review of the x-ray films thus obtained revealed a complete occlusion of the left femoral artery at about the junction of the middle and distal one-third involving a 4-cm. segment. Delayed films also showed an accumulation of large amounts of contrast medium in the region of the right lumbar area with evidence of moderate excretion by the left kidney.

At about 7 P.M. the same day the patient complained of a slight pain in the lower left quadrant of the abdomen, and one episode of vomiting occurred. The patient passed a fair night, but by the following morning anorexia, nausea, and vomiting had ensued, and the abdomen was markedly tender with rigidity over the left lower quadrant. No peristaltic sounds were heard. The rectal temperature rose to 102.2 F., and the pulse was 128 per minute and regular. A scout film of the abdomen revealed considerable distention of the small and large intestines without definite evidence of an intestinal obstruction, there being no evidence of fluid levels when the patient was in the upright position, nor was there any evidence of residual contrast medium from the previous examination. These findings were interpreted as being compatible with an ileus, secondary to retroperitoneal extravasation.

On the second day after the procedure the abdomen was found to be diffusely distended with tenderness and rebound tenderness present in all quadrants, especially so over the left lower quadrant where frank rigidity was noted. There was occasional vomiting and no passage of gas. The rectal temperature was 101 F., and on rectal examination melena was found to be present. The clinical impression at this point was that a mesenteric thrombosis was present. A Cantor tube was passed, giving exit to a large amount of gas and greenish fluid. A urinalysis showed 2 plus albumin, 2 or 3 white blood cells, and occasional casts. The hemoglobin was 12.5 Gm. per 100 ml., red blood cells 4,400,000; and white blood cells 17,000, with a differential of 80 segmented polymorphonuclear leukocytes, 2 nonsegmented polymorphonuclear leukocytes, 14 monocytes, and 4 lymphocytes. The electrolytes were within the normal range. Penicillin and streptomycin were given in doses of 1 million units and 0.5 Gm. respectively, followed by 600,000 units and 0.5 Gm. respectively three times a day. A surgical exploration was decided on. Accordingly, under combined spinal and thiopental sodium anesthesia, the abdomen was entered through a left paramedian incision. A moderate amount of cloudy fluid was found within the peritoneal cavity, a specimen of which was taken for culture and sensitivity tests and later was reported as showing no growth. The small bowel was distended considerably, and the large bowel from the distal transverse colon to the rectum at the peritoneal reflection was found to be gangrenous. A resection of the gangrenous segment of the large bowel followed by a transverse colostomy was performed. The rectal stump was closed. The retroperitoneal tissue at the level of the fourth and fifth lumbar vertebrae (left gutter) was found to be edematous. No extravasation of blood was found around the aorta or in any other location.

The patient's immediate postoperative condition was satisfactory. Antibiotics were continued as they had been preoperatively with the addition of tetracycline (Achromycin) 1 Gm. daily. The Cantor tube suction was maintained, and supportive measures were instituted. Tachycardia remained throughout the period of hospitalization. An electrocardiogram showed the tachycardia to be of sinusal origin with rare extrasystole.

On the first postoperative day the patient was afebrile, the abdomen remained distended, and the respiration was rapid. The patient looked somewhat cyanotic in spite of oxygen therapy, and also appeared to be slightly dehydrated. A chest x-ray film demonstrated segmental atelectasis in the lower lobe of the left lung. The hemoglobin and red cell count were at satisfactory levels. In addition to the previous antibiotic therapy, tetracycline 100 mg. three times a day was administered.

On the second postoperative day the colostomy was opened.

In spite of supportive and antibiotic therapy, the patient's condition followed a progressively downhill course, and he expired on the fourth postoperative day with a high blood urea nitrogen of 162 mg. per 100 ml. and a nonprotein nitrogen of 300 mg. per 100 ml.

The pathologic report on the surgical specimen was as follows: The gross description included a resected large bowel measuring 59 by 8 cm. The serosa was blackish-grey throughout. The vessels appeared to be occluded by friable red thrombi. On a cut section the mucosa in the proximal-most portion was edematous and injected. The wall was markedly edematous throughout. In the distal-most portion the mucosa appeared to be normal. The wall was firm, semitranslucent, and greyish-white. The intervening portion showed an ulcerated, necrotic, blackish-green mucosa. The wall was friable. In many areas the wall was necrotic, blackish-green, and typical of a gangrenous colon.

On microscopic examination the sections from the central portion showed complete necrosis of the bowel with diffuse, dense polynuclear cell infiltrate with thrombosis of the various vessels, especially those in the serosal fibrofatty tissue. There was also a dense polynuclear cell infiltrate of the latter. Sections from the better preserved areas showed marked edema and congestion of the wall with diffuse polynuclear cell infiltrate of the entire bowel and surrounding fibrofatty tissue.

The pathologic diagnosis was an infarction of the large bowel with superimposed acute, suppurative inflammation.

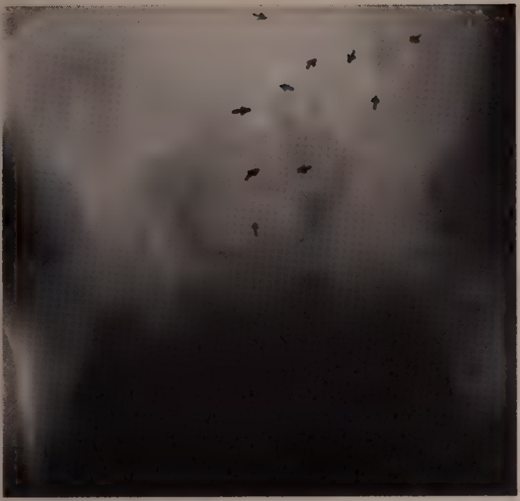

FIGURE 1. Note the sharp delineation of the inferior mesenteric artery and the very poor delineation of the abdominal aorta and iliac arteries, especially the left. This represents the first plate of the aortogram series.

Case 2. A sixty-five-year-old white male was admitted to the hospital on February 8, 1960, with a thirty-year history of bilateral intermittent claudication which had become considerably worse in the past two years.

His past history included a segmental resection of the transverse colon nine years before for carcinoma.

A physical examination revealed a well-nourished white male. The blood pressure was 165/70. The positive findings were limited to the lower extremities. The left femoral pulse was the only one palpable. Moderate ischemic changes were present in both feet. A chest x-ray film, an electrocardiogram, and blood and urinalysis showed negative findings except for a blood urea nitrogen of 22 mg. per 100 ml.

On the second hospital day a translumbar aortogram was performed under spinal anesthesia. Poor delineation of the aorta was obtained. The tip of the needle was above the cassette, but all the dye that could be seen outlined the lower aorta and both iliac arteries poorly. On the other hand, the inferior mesenteric and hemorrhoidal vessels showed good delineation (Fig. 1). Three successive injections of 70 per cent iodopyracet were made in an attempt to obtain better visualization. A total of 80 cc. was used. The aorta and the common iliac arteries were visualized very poorly. A flat plate of the abdomen taken about fifteen to twenty minutes later showed normal findings on the urogram and also an unremarkable gallbladder. There was contrast medium outlining the wall of the entire left portion of the colon. It was felt that this was due to the permeation of the bowel wall following a massive injection into the inferior mesenteric artery (Fig. 2).

The patient was placed immediately on the following therapeutic regimen: He was placed flat in bed; penicillin 300,000 units was administered every four hours; tetracycline 500 mg. was given immediately, and 250 mg. were given every six hours; narcotics were ordered withheld. An indwelling catheter was passed, and the patient was checked closely for the development of abdominal pain or other symptoms.

About four hours after the procedure the patient began complaining of crampy pains in the left lower quadrant of the abdomen and hypogastric pains which increased progressively in intensity. There was a 2 plus tenderness in the left lower quadrant, and 1 plus rebound tenderness appeared in the same area. Bowel sounds were present, and flatus was passed. A scout film of the abdomen seven hours after the procedure showed the disappearance of the dye. A rectal examination at the same time revealed no tenderness or melena. Nine hours after the procedure nausea and vomiting occurred. Ten hours after the aortogram a left splanchnic nerve block was performed using 2 per cent Xylocaine hydrochloride with the rapid and complete disappearance of pain. Two hours after the splanchnic block a rectal examination showed no blood or tenderness. There was no abdominal distention. Crampy pains in the left lower quadrant of the abdomen returned approximately two hours after the splanchnic nerve block, but although they increased, they remained moderate and never attained the severity of the initial ones. The patient remained afebrile throughout the day, and a white blood cell count failed to disclose any increase in the leukocytes. A Levin tube was passed and was connected with suction. The patient had a relatively comfortable night with only mild to moderate abdominal pains.

On the first day his rectal temperature rose to 100.6 F., and 2 plus tenderness and rebound tenderness were present on a somewhat more localized area in the left lower quadrant of the abdomen. The crampy pains subsided gradually, to a minimum in the late afternoon. Moderate flatus was passed. The abdomen remained soft. The sigmoid colon was tender and palpable as a sausage-shaped mass approximately 4 or 5 inches long. There were no bowel movements or evidence of melena following a rectal examination. The Levin tube drained moderately. Two white blood cell counts in the morning and evening respectively were as follows: In the morning the white blood cell count was 15,000 with the polymorphonuclear leukocytes 85 per cent (83 per cent segmented and 2 per cent nonsegmented); lymphocytes 11 per cent; monocytes 4 per cent; and no eosinophils. In the evening the white blood cell count was 15,800 with 88 per cent polymorphonuclear leukocytes (68 per cent segmented and 20 per cent nonsegmented); lymphocytes 10 per cent; monocytes 3 per cent;

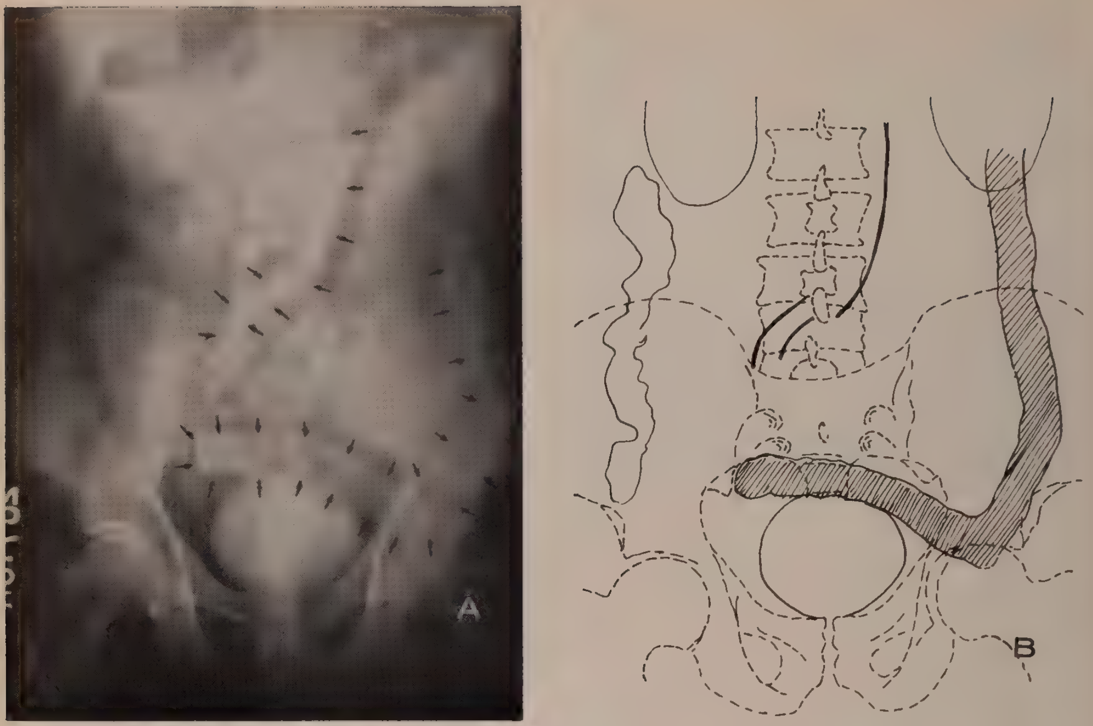

FIGURE 2. (A) Note the delineation of the splenic flexure, and descending and sigmoid colon by contrast medium. The outline of the kidneys and urinary bladder are visible as well. This plate represents a kidney, ureter, and bladder film taken approximately fifteen to twenty minutes after the first injection of dye. (B) Drawing emphasizes same features.

and eosinophils 1 per cent.

Streptomycin 0.5 Gm. twice a day was initiated.

On the second day the condition of the patient remained stationary. The same tenderness and rebound tenderness were present in the left lower quadrant of the abdomen, the abdomen was soft, and there were no bowel movements. The rectal temperature rose to 102 F., and the white blood cell count was 16,600 with a differential of 85 per cent polymorphonuclear leukocytes and 15 per cent lymphocytes. Intravenous supportive therapy and antibiotics were continued. Neomycin 1 Gm. every six hours orally was begun.

On the third day the abdomen was soft with minimal tenderness and rebound tenderness. The sausage-like sigmoid was not felt; there was a tarry stool during the night followed by a normal one about one-half hour later, both painless. The patient had a comfortable day. Toward the afternoon hyperperistaltic bowel sounds were heard. The left lower quadrant of the abdomen was still slightly tender to deep pressure. The temperature remained at 99.8 F.; the hemoglobin was 14.8 Gm. per 100 ml.; the hematocrit was 41; and the white blood cell count fell to 11,950 with the following differential: polymorphonuclear leukocytes 68 per cent, lymphocytes 25 per cent, monocytes 4 per cent, eosinophils 2 per cent, and bands 1 per cent. A scout film of the abdomen showed findings within normal limits. The Levin tube was removed, fluids were allowed by mouth, and the tetracycline was discontinued.

On the fourth day the patient felt well and remained afebrile. The patient had two bowel movements which were normal and were accompanied by mild, crampy pains with a slight episode of nausea in the early morning. There was a residual, very mild tenderness to deep pressure in the left lower quadrant of the abdomen.

On the fifth day the patient's condition was normal. The neomycin, penicillin, and streptomycin were discontinued, also because of incipient diarrhea. From that day on the patient's condition remained normal.

A sigmoidoscopy performed on the sixth day revealed no abnormal findings. A barium enema done several weeks later showed only moderate diverticulosis.

Comment

We concur with the widespread opinion voiced in the literature that although translumbar aortography and the contrast media employed are by no means harmless, most of the complications arise as a consequence of breaks in the accepted standardized technic.[5,6] Through the process of trial and error, certain steps of translumbar aortography as well as certain types of contrast media have been recognized and accepted as the safest. Certain differences in the procedure naturally exist, but these consist only of those which do not compromise the safety of the patient and which depend largely on the preference of the individual physician or school. Since all too often the complications produce such dreadful results, the practice of limiting translumbar aortography to those patients who would be considered for surgery has become accepted.

The analysis of the factors most commonly responsible for the occurrence of complications should take into consideration, apart from breaks in technic, four main points: (1) Injury produced by needle penetration, (2) needle position, (3) injection of radiopaque material, and (4) a combination of two or more of these factors.

INJURY PRODUCED BY NEEDLE PENETRATION. The insertion of the needle can produce a laceration of the vessel wall, elevation and possibly detachment of an atheromatous plaque, and partial needle penetration in the aortic wall. Furthermore, repeated punctures raise the incidence of lumbar pain and/or para-aortic hematoma to almost 100 per cent, according to some authors.[7]

NEEDLE POSITION. The factor of the needle position is important for two reasons: First, the penetration of the needle into structures other than the aorta, such as in renal vessels, the celiac axis, the superior and the inferior mesenteric arteries, and the inferior vena cava; and second, in the aorta itself the apposition of the distal end of the needle to the opening of one of the aortic branches is important. These occurrences are injurious generally only when they are in combination with factor 3 or less frequently with factor 1.

INJECTION OF RADIOPAQUE MATERIAL. Complications arising from the injection of radiopaque material alone have become a less frequent occurrence with the advent of organic types of contrast solution. Naturally, the concentration and amount of the administered solution are all-important variables in the occurrence of complications. In addition, systemic allergic and anaphylactic reactions to the contrast material are to be considered.[8]

COMBINATION OF THESE FACTORS. A lesion produced by the needle penetration into the aorta may become clinically significant if the injected contrast material is able to dissect along and between the aortic wall layers[9] or to act as an extravasated chemical irritant.[10-13] As for the contrast material, the less the concentration and duration of the action, the less the possibility of damage. In the patent aorta, due to its large caliber and to the velocity of the blood current, these conditions are met readily. Furthermore, the territory of the distribution of the contrast material is exceptionally ample. Should the radiopaque solution be discharged erroneously in locations other than the aortic lumen, either it will not be washed away at all or it will be distributed to a small area where, through insufficient dilution, it will be able to produce harmful effects.[11] This combination of needle displacement and chemical irritating action is one of the commonest sources of complications. Anesthesia, either general or spinal, is advisable to prevent the pain associated with an intra-aortic injection. A sudden motion by the patient during this phase could cause laceration of the aorta or the dislodgment of the needle with the extravasation of the dye. Also, anesthesia can mask the heraldic signs of ensuing complications in the hours immediately following translumbar aortography. The choice of local, spinal, or general anesthesia is a matter of personal preference, insofar as all of them present potentially the same risk.

It seems to us that, in view of the severity of the complications, a very judicious approach to translumbar aortography is necessary. This means not only a careful screening of patients as candidates for the procedure, the application of a strict technic, and the use of organic dyes only, but also, in carrying out the procedure itself, the avoidance of any steps not strictly necessary for the diagnosis of the case in question.[14-20]

It is probable that only a fraction of all the complications following translumbar aortography have been reported in the literature. McAfee[21] has made one of the most complete reviews of the subject. This author, considering 13,207 cases of translumbar aortography in the United States, found the rate of complications to be 1.02 per cent (135 cases) of which 0.28 per cent (37 cases) were fatal, and 0.74 per cent (98 cases) were nonfatal. Ten of the total 135 cases were gastrointestinal complications, 5 of which (50 per cent) were fatal. There were two direct injections of dye into the inferior mesenteric artery with left colon gangrene, 1 of which was fatal.

Vitt[22] and Wagner and Price[23] each recorded a death due to gangrene of the bowel following the direct injection of 80 per cent sodium iodide into the superior mesenteric artery.

Crawford *et al.*[7] reported 4 cases, summarized in Table I, in which death was due to superior mesenteric artery thrombosis and 1 case in which thrombosis of the inferior mesenteric artery was found incidentally at the time of an operation on the abdominal aorta for an aneurysm. In the 4-case group, 80 per cent sodium iodide was employed, while in the case of the inferior mesenteric artery thrombosis, 70 per cent sodium acetrizoate (Urokon sodium) was used. From clinical investigation[6] and as suggested by Crawford *et al.*,[7] it seems that the direct injection of inorganic compounds into the small aortic branches never has gone without thrombosis of the vessel and infarction or necrosis of the organ receiving the blood supply. Our own 2 cases herein reported seem to support this opinion.

Technic

In our institution a low translumbar approach has become preferred for the visualization of the terminal aorta and its branches, directing the needle at 90 degrees to the long axis of the body at the levels of the third and fourth lumbar vertebrae, unless it is deemed necessary to visualize the celiac axis, the superior and inferior mesenteric arteries, and the renal vessels. This is in essence the technic described by De Reus and Vink[24] for the examination of the lower abdominal aorta and iliac arteries. We usually use a short, beveled, 17-gauge, thin-walled needle, facing the needle bevel cephalad, and injecting a preliminary small dye dose of 5 to 7 cc. into the aorta to obtain information as to the needle position.

While it is true that arteriosclerotic changes are more severe below the level of the renal arteries, increasing the potential hazards of an arterial puncture at this level, we feel that with a low approach other organs and vessels are spared the unnecessary and potentially injurious action of the contrast material.[25] Other advantages are a better outline of the lower lumbar and iliac segments when using small amounts of dye and a greater safety when using larger amounts of radiopaque material. The technic described by Bruwer and Ellis,[26] advocating the simultaneous double needle penetration into the aorta at different levels, is objectionable to us on the same account of the production of unnecessary trauma.[27] We think that the introduction of one aortic needle and the injection of a small amount of dye will indicate whether or not a second needle placed at a different level is required. Should it become necessary, it can be introduced at this time. In our opinion this holds especially true since one has no means of knowing beforehand how extensive could be the damage, if any, directly or indirectly produced by the needle penetration. In other words, we prefer to follow the principle "when in doubt, abstain."

The cases mentioned previously, as well as our 2 cases, are summarized in Table I. We have included in the series cases of superior mesenteric artery damage following translumbar aortography because the modality of complications occurrence, the pathologic conditions, and the means of prevention and treatment are essentially the same.

The exact assessment of the beneficial effects produced by the various therapeutic measures instituted in Case 2 is difficult since it had a favorable outcome without surgery. Nonetheless, the radiologic evidence of contrast material in the wall of the sigmoid colon is a sufficient index of the high concentration of dye at this level; this is confirmed by the promptness and severity of the symptoms.

It seems most likely that the symptoms which otherwise would have appeared earlier were masked in the initial phase by the

TABLE I. Total cases of mesenteric artery thrombosis following translumbar aortograph reported in the literature

Author	Complication	Mesenteric Artery Involved	Contrast Media	Total Volume (Cc.)	Number of Injections	Operative Procedure	Outcome
Joyeaux *et al.*	Intussusception, partial gangrene of large intestine	Inferior	Tenebryl 411	16	1	None	Three gangrenous segments of intestine passed spontaneously
Wagner and Price[23]	. . .	Superior	80 per cent sodium iodide	10	1	None	Death
Doss, in Crawford, *et al.*[7]	. . .	Superior	80 per cent sodium iodide	Unknown	1	None	Death
Vitt[22]	. . .	Superior	80 per cent sodium iodide	Unknown	1	None	Death
Osius[27]	Necrosis distal portion of descending colon and rectum	Inferior	Unknown	Unknown	Unknown	Abdominoperineal resection and colostomy	Recovery
Trippel, *et al.*[27]	Gangrene of small intestine	Superior	Unknown	Unknown	Multiple	None	Death
Ferguson, in Crawford, *et al.*[7]	. . .	Inferior	70 per cent sodium acetrizoate	40	1	None	Recovery
Lord[28]	Edema of sigmoid and rectosigmoid	Inferior	70 per cent sodium acetrizoate	40	2	Exploratory laparotomy	Recovery
Fineberg, Schechter, and Barrick[18]	Gangrene of distal transverse, descending, sigmoid colon, rectum, and ovaries	Inferior; ovarian arteries	70 per cent sodium acetrizoate	35	2	Colectomy-colostomy, proctectomy, oophorectomy	Recovery
Sante[29]	. . .	Superior	80 per cent sodium iodide	Unknown	1	. . .	Death
Present study (Case 1)	Gangrene of distal transverse, descending, sigmoid colon and rectum	Inferior	70 per cent iodopyracet; 80 per cent sodium iodide	40	2	Left hemicolectomy and transverse colostomy	Death
Present study (Case 2)	. . .	Inferior	70 per cent iodopyracet	80	3	None	Recovery

anesthesia; the same impression is gained from other cases reported in the literature. For this reason we consider it useful to obtain flat plates of the abdomen shortly after the aortographic study and to assess the condition of the intra-abdominal organs. In this way complications can be foreseen to a certain extent, and prompt countermeasures can be applied. In Case 2 a preliminary study for the location of the needle was not done. The operator felt confident that his needle was placed properly. The injection of a small amount of dye showed the pelvic vessels, and a good flow of blood through the needle indicated that the tip was intravascular and in the aorta. This, in retrospect, was not necessarily true, and the tip of the needle probably was directed toward the orifice of the inferior mesenteric artery and partially impinged on the wall of the aorta within the lumen. The stream of dye was directed into the lumen of the inferior mesenteric artery. The dye then passed into the capillaries of the bowel wall. This patient probably did not have free anastomosis with the middle colic vessels (previous transverse colectomy). The fact that the dye was still visualized fifteen to twenty minutes after the procedure suggests that it had permeated the wall of the bowel. However, several hours later it disappeared completely.

The prime indication of this extravasation was the severe pain, tenderness, and rebound tenderness in the left lower quadrant of the abdomen. At this point surgery was considered seriously, but it was postponed. It was felt that the demarcation of the injury would not be present and possibly might be delayed for several days and that either too much or too little surgery might be performed. In regard to this it is interesting to note that in a very similar case reported by Lord,[28] this author proceeded to operate on the patient not less than twenty-four hours after translumbar aortography because of frank signs of mesenteric thrombosis and large bowel gangrene, and found only edema of the large bowel. It has to be noted that in this case the symptomatology was more severe than in our case, considering the six episodes of melena which occurred in the first twenty-four hours. Although 2 cases hardly constitute a statistical series, there are other cases in the literature in which symptoms were present and patients recovered without surgery.

The dramatic effect of the splanchnic block can be attributed either to the anesthetization of pain fibers or to the release of vasospasm, more likely the former.[30] Following the procedure, pain was present but never was as severe as it had been before.

From the analysis of the chronologic appearance of the symptoms, the occurrence of melena on the third day, followed shortly by the passage of normal stools, indicates the time at which the return of peristalsis in the descending sigmoid colon took place. The reappearance of peristalsis in the segment more directly damaged probably is well placed at the fourth day when a normal bowel movement was accompanied by crampy pains in the left lower quadrant of the abdomen.

An evaluation of the effectiveness of the antibiotic treatment is also difficult. Since we could not afford the risks entailed by the mechanical cleansing of the bowel, high dosages of antibiotics thereby were initiated parenterally in the hope of reducing the virulence of the pathogenic intestinal flora and thus affording some protection to the segment of the injured bowel.[31] The method, if not the rationale, is of course empiric. Neomycin was initiated when there was definite evidence of peristalsis in the presence of frank signs and symptoms. Antibiotics were discontinued when the threat of staphylococcic enteritis in the face of disappearing signs or symptoms did not justify their use any longer.

Summary

Two cases of inferior mesenteric injury following translumbar aortography are presented. The first case has a fatal outcome; surgery provided evidence of the extent of the injury and pathologic changes. An autopsy was not performed. The second patient recovered completely without undergoing surgery.

The technic of translumbar aortography employed by the authors for the visualization of the terminal abdominal aorta and its branches is outlined. Stress is laid on the fact that the best prevention of complica-

tions is the strict adherence to technic after the careful scrutiny of patients as candidates for the procedure.

The authors suggest that to diagnose complications at the earliest possible moment a flat plate of the abdomen should be taken at the end of the procedure so that the status of the intra-abdominal organs can be evaluated, and if complications are expected, prompt therapy can be instituted. An outline of the treatment is proposed in cases of complications consistent with an injury to the mesenteric arteries, and such treatment as was applied to Case 2 is discussed briefly. Also a review of the cases of superior and inferior mesenteric artery thromboses found in the literature is presented in the form of a table.

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Community Research for Solving Problems of Senior Citizens

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PHYSICIANS who serve on community public health and welfare agency boards often find themselves faced with questions about medical and other needs of older citizens. As they begin to seek solutions to these problems, it usually becomes obvious that insufficient information hampers attempts to assess unmet needs and to determine what might be done about these problems. If services are set up under these circumstances, they may be based on the feelings of a few persons or on exaggerated claims of some sort. Such programs run the risk of being geared to groups who have no need for them or of being unavailable, for all practical purposes, to many of those senior citizens who require assistance.

As some communities have already found out, a great deal of effort, to say nothing of funds, can be saved through an adequate measure of these needs by a scientific inquiry. Instead of rushing to organize services on a haphazard basis, it is both efficient and practical for community agencies to gather the necessary facts by a survey of the citizens themselves. This report exemplifies how such a survey can be made and its potential results, based on the work done in Albany County.

Function of survey

The whole process started simply enough. A cardiologist in private practice in the area who had become increasingly interested in geriatrics and the medical care needs of older citizens began discussing the subject with friends of his in the fields of medicine, engineering, cultural anthropology, and sociology. Before long, they were meeting periodically to talk over the problems of aging citizens. Almost invariably these sessions emphasized the necessity for interdisciplinary research and how this might be done. As a first step in this direction, a nonprofit research organization entitled the Center for the Study of Aging was formally incorporated through which funds for research might be channeled, with the group of friends comprising the board of directors.

Not long afterward there came an opportunity to carry out a study through the dual stimulus of the Committee on Aging of the Council of Social Agencies who wished to know more about its older citizens and of the Director, Bureau of Chronic Diseases and Geriatrics in the State of New York Department of Health.* The Department had pioneered in establishing small grants to encourage community programs and research on practical problems and had made one grant available for this work. With these funds it became possible to do a family interview survey which had five phases: constructing a sample, designing the interview questions, interviewing family representatives, analyzing data, and reporting results.

A sample of 1,200 households was selected on the basis of population distribution in the two small cities, six villages, and nine towns, as well as in the 26 census tracts of

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* At that time Frank W. Reynolds, M.D., was Director of the Bureau. The present Director is George M. Warner, M.D.

TABLE I. Percentage distribution of employment and social security status of people fifty years of age and over in Albany County

Status	Age (Years)											
	50 to 59		60 to 69		70 to 79		80 to 89		90 and Over		Total	
	Men N-219	Women N-230	Men N-142	Women N-163	Men N-66	Women N-87	Men N-19	Women N-33	Men N-4	Women N-2	Men N-450	Women N-515
Employment												
Working full time	85	38	55	15	14	1	5	3	...	...	62	22
Working part time	2	3	4	5	11	6	...	...	...	...	4	4
Self employed	6	1	6	2	2	...	...	...	25	...	5	1
Not working	7	57	35	77	72	88	95	97	75	100	29	71
Other responses	...	1	...	1	1	5	...	...	...	...	...	2
TOTALS	100	100	100	100	100	100	100	100	100	100	100	100
Social security												
Recipient	...	3	22	36	50	59	69	33	25	...	17	25
Nonrecipient	98	95	67	52	23	20	5	55	...	50	72	66
Not receiving it but have other pension	1	1	11	8	24	15	21	12	50	...	9	6
Status not obtained	1	1	...	4	3	6	5	...	25	50	2	3
TOTALS	100	100	100	100	100	100	100	100	100	100	100	100

Albany, the county's largest city. The size of the sample was determined by calculating the number of persons who were fifty years of age and over who were likely to be contacted in every 100 households according to the United States census tables. The actual households were selected after a careful assessment of all the existing records, as well as map making of newly built-up areas. This gave assurance that no households had been overlooked and that all of them had an equal chance of being chosen. The records consulted included the United States census block statistics, census tract data, recent population estimates of various departments of the state government, geologic survey maps which show rural dwellings, city hall records of buildings, and accounts from real estate offices.

Questions to be asked in homes were limited to those which would provide basic descriptive data on the population. Several pretests of the schedule were made before it was decided to ask in each of the sampled households the name, age, and sex of all members. For persons fifty years of age and over additional inquiry was made about their employment, social security status, and health.

Several hundred of the interviews were completed by a group of volunteer women who were interested in answers to the employment questions as a basis for a service they had proposed. The remainder of the interviews were done by two men, retired from responsible positions, who worked at a relatively small hourly rate, since this project was considered by them to provide an interesting and worth-while use of their time.

An analysis of the findings showed that 1,177 of the 1,200 household sample were contacted successfully, an exceptionally high rate of completion. It was learned that in these households there lived an average of 3.2 persons, slightly more women than men. The sex difference was particularly marked in the seventy-five to eighty-nine-year age range in which women outnumbered men by three to two. Ten per cent of the population were sixty-five years of age and over, and 26 per cent were over fifty years old.

As might be expected, persons fifty years of age and older lived in smaller-sized family units than did younger people, and men from sixty to eighty-nine years of age lived in smaller households than women of that age. It was interesting to note that more of the older group resided in the large city and fewer of them lived in the rural towns than would be expected if they had been divided between the two in numbers equal to their proportion of the total population. For residents in the large city an analysis of the socioeconomic level using census tract characteristics showed a higher proportion of persons beyond sixty years of age in the poorer areas, with more men than women.

When those persons fifty years of age and over in the whole county were asked if they were employed, looking for work, or retired, almost half of the men who were sixty years old and over were working, compared with 15 per cent of the women. Retirement levels increased sharply from fifty years on, being 1 per cent for the fifty to fifty-nine-year-old men, one third for those in their sixties, and over four fifths for the remainder. Two men and one woman over eighty-five years of age were still in gainful employment. With respect to the job-finding service that had been proposed by one of the community agencies, not much of a need was found for it. Only 1 person out of every 100 who was fifty years of age and older was looking for full-time work, and only 3 out of every 100 were seeking part-time employment.

In terms of financial resources, 25 per cent of the women and 17 per cent of the men received social security. An additional 6 per cent of the women and 9 per cent of the men had pensions from other sources. Beyond seventy years of age over one half of both men and women received social security. Table I contains employment and social security data in greater detail.

The interviews showed also that 10 per cent of the men and 13 per cent of the women, fifty years of age or older, had been sick during the week before they were contacted. As the age of men increased beyond sixty years, there was a tendency for the number who were ill to increase, while the trend was somewhat reversed for the women.

Medical significance of community survey

Before a survey of families is initiated by officers and board members of community health and welfare agencies, its possible contribution to their planning activities should be estimated. In addition to its immediate value to the women's organization in the community who could base their plans for a job-placement service for older citizens on these results, findings from this survey were reported at an annual community conference on aging and were published in the newspaper. Of equal, if not greater, value was the fact that once the communities' older citizens were located and some of their characteristics known, further knowledge about them could be gained quite easily.

A look at some everyday problems will illustrate the potentialities of a sample of families interviewed in this way for community planning. Deficiencies in the diets of older people cause concern to physicians, who see such patients in their offices, as well as to community agency workers. Data in this survey indicated that 1 out of 5 older people was living alone. This isolation means unsatisfactory meals, as other studies have shown, for part of that 20 per cent of persons who live by themselves. To know how seriously their nutritional status may be affected and what might best be done, those who are concerned can easily visit a sample of people with the characteristic that concerns them and make their decision on the basis of what they are eating and what their state of health actually is. Since the names, addresses, and other data can be punched on cards, it is a simple hand or machine operation to select all those persons over a selected age who live alone, as well as those in various sized families. Actual information can then be used in deciding whether private physician or public health nurse counseling can take care of possible needs or whether a special program such as "meals on wheels" is necessary.

Whether or not services which already exist in the community are known and are being used by older people often is debated by community action professionals. This basic survey showed where the majority of older people lived. To answer the question as to the extent of knowledge of and the actual use of facilities, such as the Sheltered Workshop and the Senior Citizens' Center, a sample of people with relevant characteristics could be selected and interviewed. Similarly, the need for various activities can be determined, as well as the difficulties older citizens have in taking advantage of community services. A survey of this nature with a sample of these people is now under way.

Housing is an area that interests many of us. The survey has shown how many people live alone at each age and the number of people in the households of others. But many other questions need answering in our communities, such as:

1. How are people making out sociologically, physiologically, and economically when they live alone, as compared to living with other people?

2. At what age and under what conditions are they giving up their independent residences to live with others or in institutions?

3. When and why are some of them going into residential or nursing homes?

4. At what age and under what circumstances do people move to other communities or to other states?

5. How many people are fairly secure economically and what are some causes of the problems of those who have difficulties?

6. How many still have marketable skills and what are they?

7. What is the extent of medical indigency and what factors are associated with ability or lack of ability to handle costs of medical care?

The functions in program planning of a sample of the families in a county have been discussed. Now, a few possibilities of this procedure will be presented.

Research significance of community survey

The questions researchers who are involved with this project would like to answer are these: What do people who are born and live out their lives in the slums die from and at what age? Is the pattern different for those in the wealthy areas? What is the pattern of illness and disease from birth to death for each type of area?

With regard to mental health, another essential question has been raised. Are there symptoms of senility occurring during early and middle adulthood which can be recognized prior to real senility? If there are, perhaps something can be done to delay the process. With the sample of families reported here, people can be studied at various ages to determine whether or not a scale of senility symptoms could be developed and validated. If this were successful, it then would be possible to experiment with a program to slow down the trend.

In considering the methods of answering these questions, the frequently used research designs that investigate the health or other problems of older people with the expectation that causation can be understood by studying the individual or older person at the time his condition comes to their attention are not adequate.

The human life span is a continual experience in which youth, adulthood, and old age merge rather than remain separate entities.[1,2] The fact that at a particular age, let us say sixty-five years, certain characteristics of people are associated with the occurrence of heart disease may not tell us very much. Perhaps those persons who are most subject to the disease because of what they ate, how they lived, or what they inherited are already dead from this cause or, scientifically as important, from other causes.

In essence, a basic sample of families, if kept up to date with changes in addresses, deaths, and births, would provide a fruitful laboratory in communities for program specialists, members of boards of agencies, and for medical and social scientists. By working together, program people, medical practitioners, and scientists can aid one another, can stimulate one another, and they can have a rewarding time doing it. It is suggested that this general type of plan, whereby a statistically sound panel of families is used to furnish up-to-date information for action and research, be tried in other communities. The establishment of a center for the study of aging, which was the means whereby the research reported here was carried out, can help focus the attention of scientists from several disciplines, but other means can be utilized about as well for carrying out community studies involving problems of senior citizens and the rest of the population.

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Day Hospital Rehabilitation of the Chronically Ill Patient

Preliminary Report of a Three-Year Experience in Schenectady, New York

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Day hospitals in the United States, Canada, and Great Britain have been utilized for the care of psychiatric patients since 1946. Experiences dating from 1930 are reported from the Soviet Union. Over 70 such day hospitals are said to be operating in Great Britain; the rapid growth of similar facilities in the United States led to a national day hospital conference sponsored by the American Psychiatric Association in 1958. There now seem to be several well-defined roles for day care in the total management of psychiatric patients. These activities seem closely related to the recent and rapid developments of interest in community psychiatry.

The day care approach in the rehabilitation of nonpsychiatric chronically ill and disabled patients may have been used prior to the demonstration herein reported. However, no systematic evaluation of the role of such a facility and of costs, results with patients, and so forth, is known to the authors. This report summarizes some of the results from a representative three of five years of experience with day hospital rehabilitation activities for chronically ill older adults. These data are preliminary only, are from hand tabulations, and are incomplete. Detailed analyses of complete information will be reported more fully later.

By definition, day hospital care is not to be confused with outpatient or clinic care. In the day hospital the patient spends all of the normal working day at the hospital receiving various forms of therapy. The patient leaves for the hospital after breakfast on weekdays, returns home in time for the evening meal, and spends his week end at home. Thus his social pattern is similar to that of the employed person rather than to the pattern of the institutionalized patient.

A true day hospital program requires that the hospital select only those patients who can benefit from daily full or part-day rehabilitation-oriented activity, combined with support and rest at the hospital. Also, the program implies that the medical care of the patient remains a direct and continuing responsibility of the hospital. The rehabilitation therapies available differ little from those offered to the institutionalized patient. The major differences are the near-elimination of the costly "hotel" portion of the hospital's functions and the closer integration of the hospital with the patient's family and with the community.

History

The Schenectady Rehabilitation and Day Hospital by strict definition did not operate solely as a day hospital. The majority of patients visited the hospital two or three times a week, and some received only a partial-day program; only a small group

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came in five days per week and spent the full day in rehabilitation activities. Thus the program provided a mixture of day care, outpatient, and day hospital services. Because of an antiquated physical plant and inefficient size, this hospital was closed in the summer of 1961. The Eastern New York Orthopedic Hospital, hereafter referred to as Sunnyview, also located in Schenectady, is developing similar programs in a much more desirable physical setting. Had the hospital been larger and continued operation, it is probable that the day hospital portion of the program would have become more standardized and the results, per se, more easily identifiable.

The Schenectady Rehabilitation and Day Hospital developed gradually more by circumstances and as community needs were recognized than by original design. The hospital formerly known as Schenectady City Hospital was operated as a bureau of the Health Department and had been utilized for years as a 33-bed contagious disease isolation facility. In the 1940's the incidence of the communicable diseases had decreased so markedly that the patient census fluctuated widely; much of the time the census was so low that the growing operational deficit precluded the continuance of the hospital unless some other use for the physical plant could be found. The hospital had been serving as a center for acute poliomyelitis cases from several surrounding counties, and, since patients with bulbar poliomyelitis were admitted, the logical step was to continue the care of these patients past the acute phase of the illness. In 1950 the facility became an "iron lung center" to which neighboring hospitals referred poliomyelitis patients with respiratory complications. Poliomyelitis patients having sequelae not of a respiratory nature were cared for by Sunnyview.

To meet the extensive long-term rehabilitation needs of these patients, necessary personnel were added so that by 1954 the staff consisted of two physical therapists, an occupational therapist, a psychiatric social worker, a recreational therapist, rehabilitation nurses, and aides. As the staff became available a natural extension of service was the rehabilitation of patients with physical disabilities other than respiratory paralysis. The program evolved slowly from 1950 until by 1954 it was developed more fully with the emphasis on the care and rehabilitation of older outpatients, adults, and many other patients with chronic illnesses. The emphasis on outpatients was in part due to a limited bed capacity, since in addition to those for the iron lung patients, beds had to be kept in reserve for patients with contagious diseases. The care of older adults was stressed because Sunnyview, the only other rehabilitation facility in the area, was largely an orthopedic center for the rehabilitation of children and did accept young adults, especially those who had the potential of returning to gainful employment, but admitted very few older adults with long-term rehabilitation problems.

A STUDY *was made of 80 day patients suffering from cerebral vascular accident and disorders of the central nervous and skeletal systems. The median age was sixty-two years and the median duration of disability prior to admission, six months. Fifty per cent required an evaluation and work-up on an inpatient basis before being transferred to the day program. The median of care was two and one-half days per workweek, generally for periods of up to ten weeks. Physical profiles were measured by five different scoring methods; the scores showed considerable improvement in a significant percentage of cases. Financing was handled privately in 50 per cent of the cases, by insurance with or without private payments in 26 per cent, and by public assistance in 21 per cent.*

The "day hospital" concept began to develop during the early months of 1956 when an interested physiatrist from Albany Medical College was added to the attending staff.

Regular weekly staff conferences were instituted almost from the very onset. At first these conferences (Screening Board meetings) were attended by a general practitioner, an orthopedic surgeon, a psychologist, and the hospital staff, with various other consultants being called in when indicated. By 1956 a physiatrist, a psychiatrist, and an appliance maker had been added, which along with the expanded hospital staff made for a very complete discussion of each patient's problems from the viewpoints of the different disciplines. The general practitioner always served as chairman. Members of the attending staff who were interested in serving on the Screening Board and who were donating their time were divided into four groups so that each man served for three consecutive months with his group each year. The physiatrist and the psychologist were paid modest salaries and attended all the sessions of the Screening Board. All "service" patients were screened before admission to the program and at periodic intervals as called for by their progress or lack of it. Private patients were screened at the attending physician's request.

In October, 1956, the State Health Department entered into a contract with the City of Schenectady for the purpose of refining and testing certain concepts regarding the rehabilitation of chronically ill patients. Under the provisions of this contract the State Health Department was to grant the city a sum of approximately $25,000 per annum over a period of from three to five years, while the city was to undertake a pilot day care program for the rehabilitation of disabled adults and older patients through the operation of a day hospital. The objectives were to determine the comparative results and costs of the treatment of patients at a day hospital and in the inpatient facilities of a primary rehabilitation center. It was thought that if a patient could live in his own home and be transported daily to the hospital for a full day of rehabilitation activities, important economies could be achieved without impairing the quality of service.

Analysis

In this preliminary report some experiences with 80 day patients admitted over the three-year period beginning January 1, 1958, and ending December 31, 1960, are analyzed. During this time the average daily day patient census was 7.6. There were 26 referrals and 24 admissions in 1958; 28 referrals and 26 admissions in 1959; and 36 referrals and 32 admissions in 1960. The 80 patients on whom data are reported include only those service patients who were evaluated and admitted by the Screening Board; 26 private patients admitted for day care are not included in these data.

The medical diagnosis on over one half (57 per cent) of the study patients was cerebral vascular accident, another 15 per cent had various disorders of the central nervous system, and still another 15 per cent had disorders of the skeletal system (bones and joints). One third of the 46 patients whose primary diagnosis was cerebral vascular accident had three or more other conditions, many of which were unrelated, and two-thirds had two or more other conditions. Of the noncerebral vascular accidents less than one-half had two or more other conditions. As might be anticipated, over one half of the disability diagnoses were hemiparesis, and another one-fourth had disabilities of the lower extremities resulting from fractures, amputations, and neurologic disorders.

The median age was sixty-two years with the largest number of patients falling into the fifty-five to sixty-four and sixty-five to seventy-four-year age groups. One-tenth were under age forty-five, and one-tenth were over seventy-five years. There was no significant difference in the age distribution between males and females. The median duration of disability prior to admission for all patients was six months. Only 2 patients were referred less than one month after the original incident, while 9 had had their disabilities for from seven to thirty years. Of the cerebral vascular accident group approximately one-third were referred less than three months after their vascular accidents, almost one-half had had their disabilities for six months prior to referral, and nearly one-fourth had been disabled for at least one year.

As has been indicated, physician referral was a prerequisite to admission to the program. At first only a handful of physicians utilized the day hospital program; however, it gradually caught on and was accepted widely by the profession. Forty-six physicians referred the 80 patients; three of these physicians resided outside

Schenectady County. Of the remaining 43, 32 were general practitioners, and 11 were specialists. The County Medical Society has 226 active members, approximately 80 of whom are general practitioners, so that about 40 per cent of the general practitioners referred patients. One third of the physicians who referred patients did so more than once so that one third of the referring physicians supplied nearly two thirds of the patients. Obviously understanding and cooperation by the physician community, especially the family physician, is a must if a program of this nature is to even "get off the ground."

One half of the patients required an evaluation and work-up on an inpatient basis before being transferred to the day program, a customary Screening Board recommendation when initial inpatient services seemed necessary. One third of these patients who were started as inpatients remained in the hospital less than twenty-five days; almost two-thirds stayed less than two months, while one-sixth were hospitalized more than three months. This last group was weighted by a couple of patients who stayed unusually long. These data would indicate that a day hospital program ought to be tied closely to an inpatient facility since a fairly large percentage of referrals cannot be evaluated fully solely on a day care basis.

Since day patients were not seen on week ends, only five workdays were counted in the day hospital workweek. On this basis, one third of the patients were day patients for a maximum period of five weeks, and two-thirds were day patients for up to ten weeks. However, one tenth of the patients were on day care for periods exceeding six months. Fifteen per cent required four or more days of care per week, 60 per cent of the patients required only two to three days care per week, and the median for the entire group was two and one-half days of care per workweek.

It was found that many patients lost their rehabilitation gains when they were discharged abruptly from day care. Therefore, a so-called "sustaining" category of service was developed. The sustaining patients came in less frequently, received fewer services, and came in for part days only, equivalent to outpatient services. Patients seemed to derive a psychologic benefit when the continued interest and concern of the staff with their maintenance of gains was assured and when they were afforded the social opportunity to meet and have luncheon with former patient acquaintances. Fifty-five per cent, or 43, of the day patients needed this kind of continuing supervision or sustaining program. One half of these sustaining patients needed a transition period of less than ten weeks from day hospital to discharged status, but one-fourth required continuing care for more than six months. More than one-half needed no more than one visit per week during this sustaining period.

There were 22 different categories of professional staff services available to the patients. Sixty-three per cent of the inpatients required seven or more different services at some time during their stay, whereas 45 per cent of the day patients and only 39 per cent of the sustaining patients required this many services. These are merely numbers of different services received. How much service was provided quantitatively is not yet analyzed.

Measurements of improvement

Five measurements of improvement were utilized. These were: PULSES, ADL (Activities of Daily Living), Self-Care, Locomotion, and Employability.

The PULSES measured the physical condition of the patient. P stood for general physical condition, U for upper extremity, L for lower extremity, S for sensory, E for excretory, and S for mental and emotional status. On each item the patients' abilities were scored on four grades ranging from no abnormalities to gross abnormalities. The total score might range from 6, indicating good condition, to 24, indicating the worst physical condition.

Self-Care status ranged in six steps from complete independence to complete or nearly complete dependence. Locomotion also was graded in six steps from being able to walk unaided or with a cane to the inability to walk without human assistance. In both Self-Care and Locomotion a score of 1 indicated good, and a score of 6 indicated the worst performance.

The ADL or Activities of Daily Living charted the ability to carry out each of 100 customary personal daily activities, such as turning a doorknob, brushing the teeth, using a knife and fork, and so forth. With ADL, the higher the score the better the performance, 100 being normal. Employability measurements were in four grades ranging from 1, or employable, to 4, or completely unemployable.

The day patients' abilities in each of these five areas were evaluated and recorded when they entered the program and when they were discharged. In this preliminary report only the changes occurring while the patients were in the day hospital category are analyzed. Prior marked gains occurred among the 50 per cent of patients who were hospitalized as inpatients before their transfer to the day hospital.

As measured by the PULSES, 30 per cent of the day patients were at a total score level of less than 10 when they were admitted as day patients. When discharged as day patients, 43 per cent were at a total score level of less than 10. In the Self-Care scoring, 45 per cent of the patients scored 2 or less initially. Seventy-one per cent scored 2 or less on discharge. In the Activities of Daily Living, 15 of the 80 patients had scores of less than 50 at the beginning, and only 9 had scores of below 50 at discharge. Only 2 patients were considered employable at full employment on day hospital admission, whereas 16 were so considered on discharge. The number of patients considered completely unemployable at the time of their admission was 66; this decreased to 46 at the time of their discharge.

Sixteen, or one fifth, of the patients were not able to complete the day hospital program for varying reasons, such as lack of transportation, lack of funds, insufficient motivation, family problems, and so forth. However, 18 did complete the program entirely, and another 36 were on their way to the completion of it as sustaining patients at the time of this analysis.

Per diem charges for inpatients' hospitalization were $14 plus extras, with an all-inclusive welfare rate of $20.23. The day patients were charged $6.50 per day, 50 cents of which was for the noonday meal. Per diem costs for inpatients' hospitalization were $25.48 and for day hospital patients were $17.25 in 1960.

Multiple sources of financing were used, but private payment alone, without third-party funds, accounted for 50 per cent of all the sources of financing. Twenty-one per cent, or 17 patients, supplemented their health and hospital insurance benefits with private payments; 5 per cent, or 4 patients, used insurance alone without private payments; and 21 per cent, or 17 patients, were receiving public assistance. Of the 22 patients whose care was paid partially by insurance benefits, 16 were beneficiaries of commercial insurance and only 6 of Blue Cross. The small number using voluntary insurance was due to the fact that Blue Cross Associated Hospital Service of Capitol District did not agree to reimburse for the day hospital care until March, 1960. Since that date this care has been included on an experimental basis with Blue Cross paying $4.00 of the $6.50 day hospital charge. Most of the deficit differences between charges and costs were underwritten by State Health Department demonstration monies and local tax funds.

Summary

1. The importance of a Screening Board or evaluation team cannot be overemphasized. It is through this technic that the patient's problems are discussed from the viewpoints of several different disciplines. The psychiatrist, psychologist, and psychiatric social worker are very valuable members of this team, since the mental and emotional aspects regarding both the patient and his family have great bearing on the patient's improvement.

2. The largest number of patients fell into the fifty-five to sixty-four and sixty-five to seventy-four-year age groupings and had disabilities of severe degree, many with serious unrelated but complicating illnesses. Dramatic improvement in any significant number of these patients was not anticipated. However, in many instances the improvement in the patients' functional abilities made the patients lesser burdens on their families and on the day hospital staff.

3. The understanding and cooperation of the medical profession of the community, especially the family physician, is a must if a program of this nature is to succeed.

4. The evaluation team found it necessary initially to hospitalize 50 per cent of the patients for evaluation and more concentrated service before the day hospital program was feasible. A day hospital program, therefore, should be tied closely to an inpatient rehabilitation facility.

5. Many patients will require a sustaining program following their discharge from the day hospital if they are to maintain their gains.

6. Physical profiles were measured by five different scoring methods: the PULSES, Self-Care, Locomotion, Activities of Daily Living, and Employability. The scores show considerable improvement in a significant percentage of cases. The total improvement recorded would have been greater had the inpatient improvements in function been incorporated in these data.

7. Financing was handled privately in 50 per cent of the cases; insurance with or without private payments was the source of financing in 26 per cent, and 21 per cent were paid by the Department of Public Welfare. By and large this was a group, many of whom could afford charges of $6.50 per day for the median two and one-half days of service per workweek but who would not have been able to manage a long period of inpatient hospitalization. The charges represented only a portion (estimated one third) of true per diem costs, and the deficits were financed largely out of demonstration and tax funds.

Tumor-leukemia link investigated

A commonly occurring tumor in African children may be a different manifestation of the same disease process that causes a common form of acute leukemia in children in the United States, according to Gilbert Dalldorf, M.D., of the Sloan-Kettering Institute for Cancer Research, New York City, in a recent issue of the *Journal of the American Medical Association*.

Although the symptoms of the diseases are different, both run a rapid, devastating course, and both respond similarly to radiation therapy and to various drugs. Both diseases represent roughly 40 per cent of all malignant tumors in children in each country, and in both countries boys are more frequently affected than girls. The disease found in Africa is termed malignant lymphoma since the tumor is made up of lymphoid tissue.

Lymphomas in North America and in most of the world are often associated with lymphoblastic leukemia. This is the most common malignancy of children in America and the least common in East Africa.

In a review of 130 lymphomas in children under fifteen years of age in Kenya, Dr. Dalldorf said, only 2 per cent were found to be associated with leukemia. In the United States all but about 5 per cent of the lymphomas in children are associated with leukemia. If both diseases are different expressions of childhood lymphoma, he said, the agents responsible must be assumed to exist in both continents, possibly in somewhat different form or subject to host or environmental factors that modify their characteristics.

Clinical Rehabilitation Conference

Prepared by the Department of Rehabilitation Medicine,
The Albert Einstein College of Medicine,
Bronx Municipal Hospital Center, New York City

EDWARD F. DELAGI, M.D., and
HEINZ I. LIPPMANN, M.D., Editors

Osteolytic Metastases from Breast Carcinoma

Edward F. Delagi, M.D.: Today we present a patient with a multiple metastatic disease of the bone who was referred to this department for possible ambulation. Will the student present the case.

Case history

This forty-eight-year-old female patient was admitted with swelling and loss of motion of the left knee. The history revealed a fall several weeks before. There was no history of weight loss or any other significant symptoms. Her social history revealed that she lived alone in a fourth floor walk-up apartment and that she has a twenty-four-year-old married daughter and three grandchildren. The patient had an education up to the eighth grade and had worked as a sewing machine operator.

On physical examination she appeared well developed, well nourished, and apprehensive and was in severe distress. Her blood pressure was 120/80. Her vital signs were normal. There were no palpable lymph nodes. An examination of her breasts showed inversion of the left nipple with retraction of the skin at the inferior aspect. The right breast was normal. No distinct masses could be felt. The rest of the physical examination, including a pelvic examination, showed normal findings. A neurologic examination showed normal findings. An examination of the extremities showed no edema, clubbing, or cyanosis. The left knee was rotated laterally. There was a prominent area of tenderness, swelling, heat, and redness at the lateral superior aspect of the left knee. There was no patella click. Percussion of the left greater trochanter revealed tenderness. Hip joint flexion and internal rotation were abolished. External rotation was possible to 20 degrees. There was no redness or warmth at the knee. The circumference of the suprapatellar area on the left was 41 cm. and 39 cm. on the right. There was tenderness and pain in the lumbar region.

Laboratory data showed a hematocrit of 45 and a white blood cell count of 16,000 with a normal differential count. A urine examination showed normal findings. The fasting blood sugar and blood urea nitrogen were normal. The blood calcium was 9.6 to 10.6 mg. per 100 ml. The calcium excretion in the urine was 68.3 mg. for twenty-four hours in a volume of 2,100 cc. The blood alkaline phosphatase during the time of hospitalization increased from 1.8 Bodansky units on January 5 to 5.3 Bodansky units on February 14. On February 16 it was 3.6 Bodansky units. The blood phosphate concentration ranged around 5 mEq. per 100 ml. Liver function tests were within normal limits. The total proteins were 6.9 Gm. per 100 ml. with a globulin of 4.3 and albumin of 2.6 Gm. per 100 ml.

A roentgenographic examination showed osteolytic metastases in the proximal portion of the left femur which had broken through the cortex. There was a pathologic fracture in the lower femur; there were metatastic lesions in the proximal tibia, patella, sacrum and pelvis, and left ankle. The intravenous pyelogram and skull x-ray films showed normal findings, and the right upper extremity, hands, and chest were normal. On December 18, 1961, an open biopsy was taken from the left femur which confirmed a pathologic diagnosis of adenocarcinoma consistent with metastasis with a primary tumor originating from the breast. On December 28, 1961, a left breast tumor was removed locally. During the operation, it became clear that an infiltrating carcinomatous lesion occupied the lower outer quadrant of the breast and invaded the chest wall, precluding a radical mastectomy. The pathologic diagnosis confirmed adenocarcinoma of the left breast. Chemotherapy and hydromethyl propyl testosterone were given. The left knee and greater trochanteric area and acetabulum were radiated with 580 r for eight days and the knee region with 1,500 r for fifteen days. Radiographic examinations on January 19 and 29 demonstrated some progression and a new pathologic fracture in the lateral condyle of the left femur. There was some decrease in the hip pain and the pain in the knee and some increase in the degree of motion. Her weight remained stable, and the appetite improved. The serum calcium ranged between 9.6 and 10.1 mg. per 100 ml. The hematocrit remained between 38 and 42. The platelet count remained from 200,000 to 300,000 per high-power field.

The patient was subjected to therapy in the Department of Orthopedic Surgery as follows: A Buck traction for symptomatic relief was instituted early in the hospital course. After a few days of traction the effect was lost, and traction was removed. Members of the surgical staff suggested that an intramedullary nail be inserted from the hip to the foot, immobilizing the knee but permitting ambulation in this fashion, or that a long leg brace would permit this patient to walk. It should be added that this patient in the course of her hospital stay has been told that she has carcinoma of the breast and metastases to the hip. She has expressed nervousness and worry about the burden she is imposing on her family. She desires very much to be ambulatory.

Dr. Delagi: Thank you. May we see the patient now. (The patient wheels herself into the conference room. The resident demonstrates that the main site of her pain is at the left knee. It is also demonstrated that the muscle strength of her knee extensors and flexors is good, that there is limitation of flexion of the knee, and that she can extend her knee completely). Does anyone want to ask this patient any question? If not, thank you. (The patient wheels herself out of the Conference Room.)

Dr. Barnaba, would you like to outline the problem as you see it?

Possible risks and benefits of ambulation

Vincent Barnaba, M.D.: I think the factors to be considered in deciding whether or not the patient should ambulate are as follows: First, would the patient derive any physiologic benefit from ambulating; second, would ambulating be hazardous because of possible pathologic fractures; and third, would it be justifiable to use ambulation to satisfy this patient's emotional needs? As you have heard, she desires very much to ambulate.

Alfred Ebel, M.D.: Answering the second question first, there is no doubt that there is some danger of further pathologic fractures here. Before proceeding with any other considerations, one should decide whether internal fixation or bracing are indicated.

Dr. Delagi: I would welcome a discussion on the question raised by Dr. Barnaba, wisely, as the first point, because I believe it is the most important: namely, why should one undertake to ambulate such a patient? It would be simpler to put her to bed in view of the danger of possible pathologic fracture or to keep her in a wheel chair. This would be justifiable from the standpoint of traditional management. However, I submit that a reconsideration of this principle is in order.

Bernard Stoll, M.D.: This patient is afflicted with a disease which represents a death sentence. Statistically, in a patient with an adenocarcinoma of the breast and multiple metastases, the life expectancy might be a year, a year and a half, or so. However, experience has taught us that the outcome of an individual case cannot be prognosticated reliably on statistical grounds. We have seen some patients with multiple metastases from adenocarcinoma of the breast survive functionally for many years. But even if this patient has only a short life expectancy, she has a right to live as full a life as possible, maybe especially because she has only a short time to live. I also submit that the more traditional management of similar cases is dictated, more often than not, by the fear of the physician of running into some additional difficulty.

Dr. Delagi: It is a generally accepted attitude in rehabilitation medicine that maintaining a patient at maximum function yields both physiologic and psychologic benefits. The specific question to be asked here is whether or not we are justified in maintaining such levels of activity that a pathologic fracture may result, which in itself may further immobilize the patient or may even produce severe neurologic complications if it should occur in the spine.

Dr. Stoll: Practically all therapy which is given in medicine, whether it is medical or surgical, implies risk, and I think the same criterion has to be applied here. We must weigh the risks of producing further complications against the physiologic and psychologic benefits of maximum activity.

Arthur S. Abramson, M.D.: This patient had been ambulatory until the day of her hospitalization, no diagnosis of metastases having been made up to that point. In my experience it is extremely unusual to see catastrophic complications arise from metastatic pathologic fractures. Actually, the most fearful complication would be the development of paraplegia due to the breakdown of a vertebra with a metastatic lesion. Paraplegia usually develops as a result of the expansion of the tumor and encroachment on the cord itself and not as a result of pathologic fractures, even though such a possibility cannot be denied. On the other hand, fractures elsewhere in the body such as those of the long bones can result from ambulation, and the chance of healing is just as good as the chance of healing in a normal bone. Immobilization is an evil in itself, and it makes no difference to the patient whether it arises from a prescription by the physician to prevent fractures or from the fracture itself. Also, we must consider that immobilization will lead to further osteoporosis and an increased tendency to fracture so that the turning in bed of such a patient may result in a fracture.

We should keep this patient as active as possible, and that means ambulation. Sometimes we come to think that activity and ambulation are withheld from such a patient out of a fear which is dictated by the x-ray findings.

Dr. Delagi: Dr. Cummings, you have had an opportunity to summarize your experiences with similar cases in a recent article.* May we have your comments.

General condition of patient

Victor Cummings, M.D.: This patient seems to be in good general condition in spite of extensive bony metastases. In general, in formulating the rehabilitation management in patients with extensive metastatic bone disease it is important not only to be aware of the anatomic site and mechanical implications of the actual bone lesion, but also to have an understanding of all the manifestations of systemic involvement. In the case of adenocarcinoma of the breast, essential data to be followed are the blood calcium, phosphorus, and alkaline phosphatase levels which reflect the activity of bone metastases. Alkaline phosphatase rises when bone repair prevails, while in the presence of more lytic activity the calcium level in the blood rises and often is associated with a general downhill course. In this patient this is not the case, and she is in good general condition.

Many other points arise. One of these is whether or not liver metastases are present. The negative findings of the liver function tests do not prove the point either way. Also, I would like to know more detailed information concerning the central and peripheral nervous system to rule out metastatic lesions in that area. A detailed survey of the whole skeletal system is advisable as well, because if we proceed to ambulate this patient, some sort of support by the upper extremities will be necessary, and we certainly should know whether or not metastases are present which might lead to pathologic fractures in the upper extremities. In view of her generally satisfactory condition and her desire, I would certainly do everything to help her to achieve ambulation.

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* Cummings, V., and Rosenthal, J.: Activation of the patient with skeletal metastatic neoplasia, J.A.M.A. **168:** 501 (Oct. 4) 1958.

I concur with Dr. Abramson that complications usually are more likely due to the expansion of the tumor than to ambulation per se. However, there are certain legal implications in allowing this patient to ambulate. It would be very difficult to prove that a pathologic fracture which occurs during ambulation prescribed by a physician would have occurred if the patient had not ambulated. Nevertheless, we have found it is possible to proceed with this kind of management if at least one responsible member of the family has been taken into full confidence regarding the condition of the patient and the risks and advantages that such management entails. I would sit down with this patient's husband and tell him that his wife has cancer with metastases and that it would be beneficial for her to ambulate in spite of the risks involved. If the patient should suffer a pathologic fracture this would be no worse a disaster than maintaining her at bed rest for the rest of her life. Of course, we would use all preventive measures to avoid complications.

Let me comment on how we can protect this patient against a pathologic fracture if she ambulates. May we see the roentgenograms again. A most obvious bone metastasis is in the left knee region and the lower and the upper end of the femur. It would appear that if bracing is indicated, only an ischial weight-bearing brace would do. On close inspection of these films, however, there is some involvement of the ischial bone, which would preclude this type of bracing (Fig. 1).

The next question is: Should the patient ambulate as a crutch walker? This will necessitate x-ray studies of her upper extremity. Of course, if the upper extremities are involved, this would militate against crutch walking. If one upper extremity is involved, maybe the other could be used for auxiliary weight bearing.

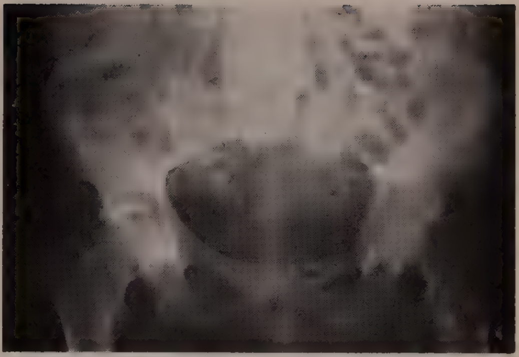
FIGURE 1. X-ray film showing involvement of ischial bone.

We have been impressed that many of these patients are young mothers who are highly motivated and want to be with their families and fulfill their duties as mother and housewife. Such patients have returned to their homes and ambulated as long as possible, even though with some pain, until shortly before they finally succumbed to the disease. If ambulation produces severe pain or if pain tolerance is very low, I would be reluctant to encourage such a patient to ambulate. The desire and motivation of the patient are both crucial indications for ambulation.

Dr. Delagi: In your article you mention internal fixation as a method of management when pathologic fractures do occur.

Dr. Cummings: Orthopedic management is the same as it is in patients without metastatic lesions in the bone. If difficulties arise later, they usually are caused by metastases elsewhere and not at the site of the previous fracture.

Dr. Abramson: Although prophylactic internal fixation may have merit in some similar cases, in this patient, because of extensive involvement of the lower end of the femur, such a procedure would be impossible. The proposal to insert a long nail from the hip to the ankle is not acceptable because it would create another disability.

Dr. Stoll: This patient's metastatic disease is obviously of very long duration, and I am sure that if skeletal x-ray films had been taken a year ago, we might have been having this same discussion just one year ago, and I would like everyone to realize what has happened in that year. This patient has had six months of practically painless full ambulation and two months in which she has been getting around with some pain in her knee. It seems to me that it would have been regrettable had we, because of fear, elected to limit this patient's activity one year ago, because this last year of hers would have been less full for herself and her family.

Dr. Cummings and his associate have done us a service by inserting into the literature their experience, which will help to develop an authoritative opinion which can be drawn on when such risks result in complications. Prior to this article, I am not aware of anything in the medical literature with which a practicing physician could justify his flying in the face of traditional management of such patients.

Summary

Dr. Delagi: In conclusion, I think the general opinion as expressed in this conference is that the rehabilitation principles of maximum functional activity are valid in patients with extensive metastatic bone disease, even in the presence of the risk of further pathologic fractures. In this patient the consensus is that we obtain x-ray studies of the patient's upper extremities, that we permit ambulation with as much protection of the involved extremities as possible, that prophylactic bracing or intramedullary nailing is not indicated at this time, and that immobilization of this patient because of the fear of fracture would be just as injurious as immobilization because of fracture.

Number eight in a series of Clinical Rehabilitation Conferences

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Alcoholic drinks enhance cleaning fluid danger

The consumption of alcoholic beverages has a potentiating effect on inhaled fumes of carbon tetrachloride, a widely used cleaning solvent, which can cause acute kidney failure, Peter S. New, M.D., Glenn D. Lubash, M.D., Lawrence Scherr, M.D., and Albert L. Rubin, M.D., of New York City, report in the September 8 issue of the *Journal of the American Medical Association.*

Nineteen cases of kidney failure associated with carbon tetrachloride poisoning since 1955 have been recorded by the authors. Seventeen of the patients were drinking alcoholic beverages at about the time they inhaled the fumes, and in 2 instances kidney failure followed the prompt use of carbon tetrachloride to clean clothes spotted at a cocktail party. The fact that only brief exposure to carbon tetrachloride can be damaging is not generally appreciated. The 2 other patients drank carbon tetrachloride, the physicians said. Eighteen of the 19 patients survived. The cause of the fatality was pneumonia.

Correlation Conferences in Radiology and Pathology

St. Luke's Hospital
New York City

Editors
NATHANIEL FINBY, M.D.
Director of Radiology
CHARLES F. BEGG, M.D.
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Pulmonary Schistosomiasis and Right Middle-Lobe Syndrome

Case history

A twenty-three-year-old Puerto Rican woman was admitted because of a second episode of pneumonia in the middle lobe of the right lung in a three-month interval. A severe upper respiratory infection had progressed in severity and became associated with right pleuritic chest pain during the week prior to admission. A fever of 104 F. occurred as an afternoon rise but diminished slowly during three days of penicillin therapy.

Her physical examination revealed normal findings except for increased bronchovesicular breathing over the right lateral and posterior lower chest. No rales were heard.

The laboratory studies showed normal findings except for a leukocytosis of 14,300 with eosinophilia varying between 1 and 6 per cent. A study of the stool for ova and parasites revealed Schistosoma mansoni and Trichuris trichiuria.

Bronchoscopy revealed purulent granulation tissue, which bled easily, at the orifice of the bronchus of the middle lobe. A biopsy of this area showed chronic inflammation. Radiographic and bronchographic studies (Figs. 1 and 2) showed an obstruction of the bronchus of the middle lobe of the right lung, with evidence of pneumonia distal to this obstruction.

Surgical exploration revealed enlarged lymph nodes about the middle-lobe bronchus. A small amount of caseous necrotic material was encountered when the bronchus was transected, and was positive on smear for acid-fast bacilli. The middle lobe of the right lung was removed.

Radiologic discussion

NATHANIEL FINBY, M.D.: Radiographically the appearance on routine chest radiography (Fig. 1A) and bronchography (Figs. 1B and 2) was that of a syndrome associated with pneumonia in the middle lobe of the right lung. The middle-lobe syndrome is often associated with bronchial compression by adjacent lymph nodes, which are enlarged because of tuberculosis or other infection. Enlarged lymph nodes were present in this patient in the region of the middle-lobe bronchus of the right lung, but there was also endobronchial disease.

Schistosomiasis is an extremely rare cause of the middle-lobe syndrome of the right lung, which was originally defined as a chronic suppurative process localized to an atelectatic middle lobe because of a mechanical obstruction of the middle-lobe bronchus by enlarged lymph nodes.[1] This same process has been described for other lobes of the

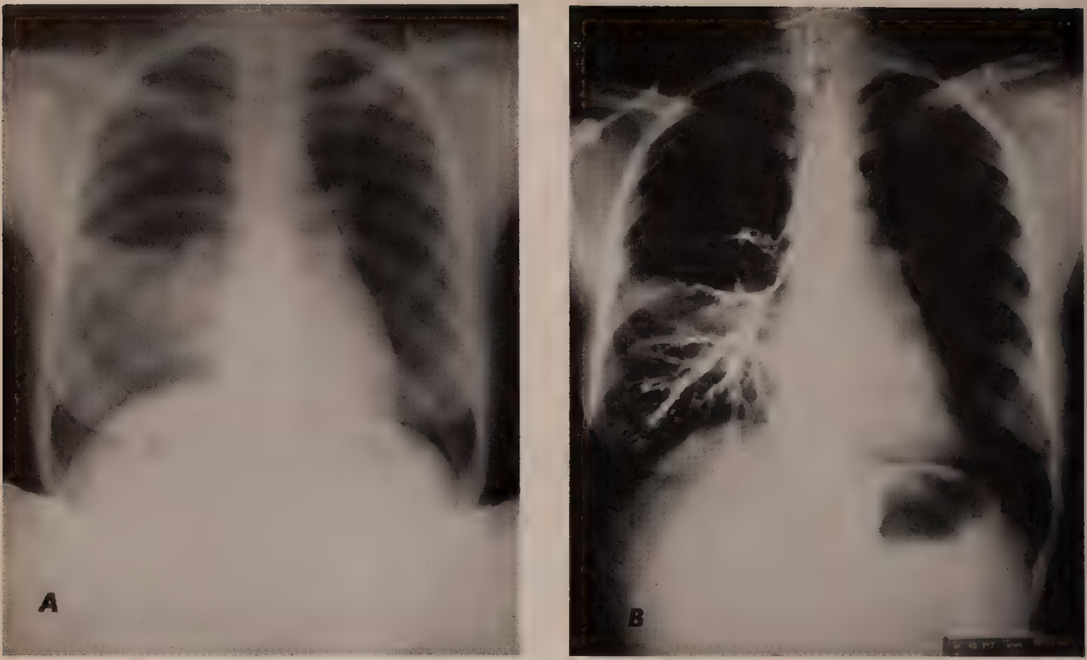

FIGURE 1. (A) Frontal chest film showing infiltration with some superimposed atelectasis of right middle lobe. (B) Bronchogram showing inability to fill right middle-lobe bronchus.

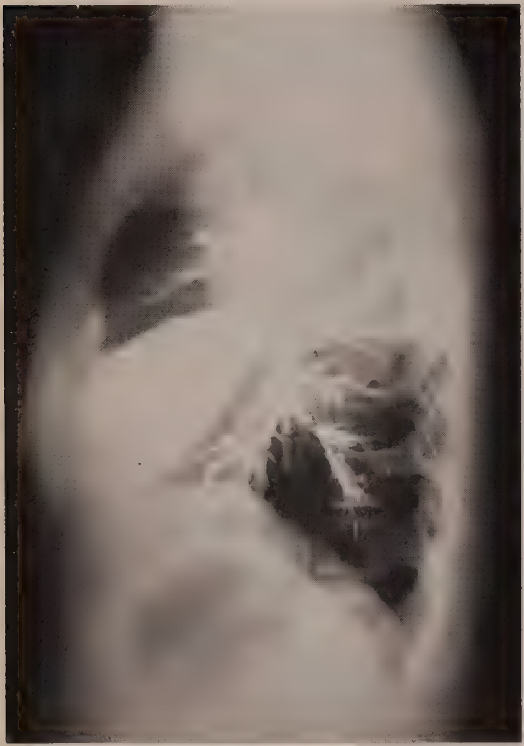

FIGURE 2. Lateral projection showing right middle-lobe infiltration and atelectasis with absence of filling of bronchus.

lung, although the length, pliability, and acute angle of emergence of the middle-lobe bronchus set the stage for obstruction uniquely because of its enlarged encircling lymph nodes.

S. mansoni has a wide natural distribution in the West Indies, with the incidence of schistosomiasis among Puerto Ricans estimated at 11 per cent.[2] The large Puerto Rican population in New York City thus necessitates consideration of schistosomiasis in the differential diagnosis of disease.

Radiographic manifestations of pulmonary disease due to schistosomiasis are infrequent. Occasionally, cor pulmonale can be recognized as a result of diffuse vasculitis and obliterative endarteritis due to Schistosoma ova. Schattner and Hill[2] report one patient who presented symptoms of middle-lobe syndrome due to schistosomal disease.

Pathologic discussion

Charles F. Begg, M.D.: The right middle lobe was firm, enlarged, and airless. Tenacious mucus occluded the visible portions of the bronchial tree (Fig. 3). This finding explains the failure of the middle-lobe bron-

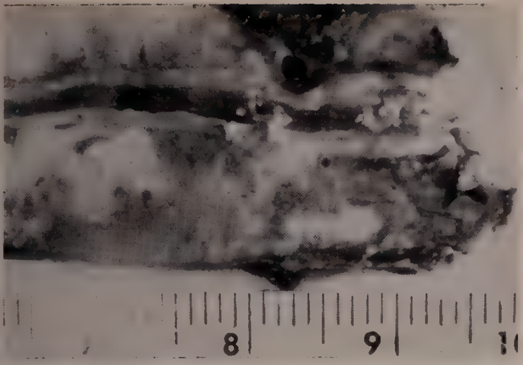

FIGURE 3. Transected middle lobe. Tenacious material occludes bronchial system. Adjacent parenchyma is consolidated.

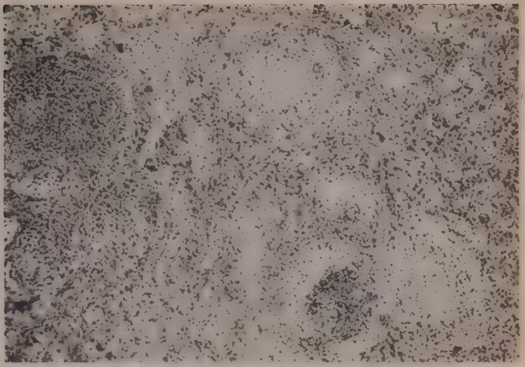

FIGURE 4. Heavy inflammatory exudate in parenchyma of lung. Numerous granulomata are present. Ova are not seen in this section but are found in other levels from this block.

chi to fill with contrast material. The cut surface was gray, bulging, moist, and firm.

Microscopically, there is a great variation in the reaction seen. The lumens of bronchi and bronchioles are occluded by a mixture of mucus, necrotic cellular debris, eosinophils, and neutrophils. In many places, bronchial and bronchiolar mucosa is ulcerated. Alveolar lumens are filled with an exudate of eosinophils, lymphocytes, and macrophages, with occasional neutrophilic polymorphonuclear leukocytes in the central portion of the lobe, and with a heavy protein precipitate and vacuolated macrophages in the more peripheral areas. Alveolar walls are not disrupted but are frequently thickened by cellular exudate.

Many granulomas are present (Fig. 4). They are composed of pale eosinophilic macrophages; fibrosis has occurred at the periphery of some; in others, there is a central pool of eosinophils. The granulomas are haphazardly distributed, some in the septa and some in alveoli. Intact S. mansoni ova, or fragments of them, are present within many of the granulomas (Fig. 5A). Fragments of ova are also seen in alveolar lumens, and in some of these alveoli swollen alveolar lining cells are seen engulfing them (Fig. 5B). Many of the pulmonary artery branches have thick, inflamed walls, with all layers involved (Fig. 6). Others exhibit cellular intimal fibrosis. There is no thrombosis. No ova are seen in the vessels.

An interesting feature of this case is the fact that the ova are strongly acid-fast when the sections are stained by the Ziehl-Neelsen method, which is used to demonstrate tubercle bacilli. When this was discovered, we re-examined the smear made from the material encountered at the time of the surgical intervention. The acid-fast particles which were interpreted originally as tubercle bacilli in this material are, in retrospect, minute fragments of ova. A culture of this material did not grow Mycobacterium tuberculosis.

Comment

Pulmonary disease caused by S. mansoni has been studied extensively by Lopes de Faria[3] who has also reviewed the literature. The involvement he describes is a necrotizing polyarteritis caused by a localization of Schistosoma ova in vessel lumens and walls. With sufficient infestation, pulmonary hypertension and right heart hypertrophy occur. He does not describe pneumonitis as a conspicuous feature of this disease. In the patient presented here there is a widespread inflammation with a vigorous reaction to the ova wherever they are seen. Polyarteritis and old fibrous thickening do occur in the vessels, but the ova are located in the parenchyma. Indeed, fragments of them are found in alveolar spaces with an inflammatory reaction to them. Despite these findings, we are loathe to ascribe the pneumonitis to schistosomiasis alone for the following reasons: (1) The clinical episodes were acute and febrile and responded well to penicillin; (2) there was no apparent involvement of other areas of the lung; and

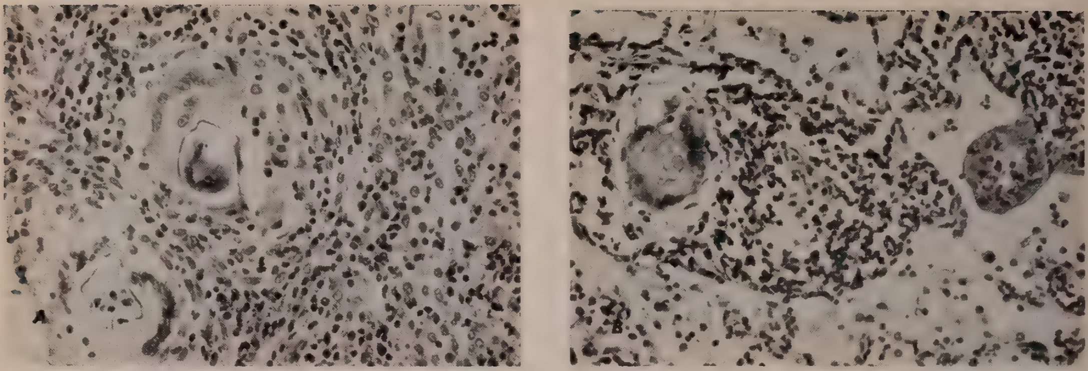

FIGURE 5. (A) Ova in centers of granulomata. Giant cells surround them. (B) Hyperplastic alveolar lining cells form protruding nodules. On left, fragment of ovum has been engulfed and chronic inflammatory cells fill alveolus.

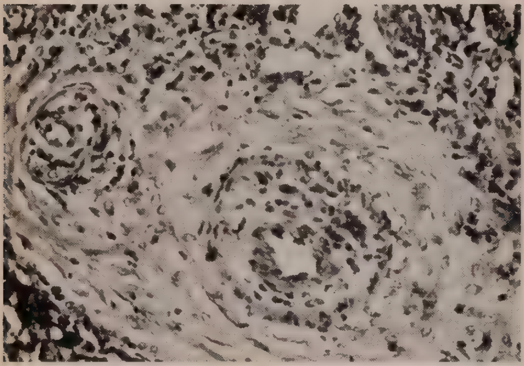

FIGURE 6. Artery with markedly thickened and cellular intima and reduction of lumen size.

(3) the subsequent course of this patient has indicated no similar involvement of other lung areas.

Our conclusion is that the middle lobe had indeed been damaged by schistosomiasis but that it was also involved in a secondary bacterial infection which, perhaps, broke down pre-existing barriers, causing a release of ova into the parenchyma where there was a further acute inflammatory reaction to them. The selection of the middle lobe by the secondary infection may be attributed to the anatomic peculiarities of the middle lobe which make it a favored locale for infection, plus the fact that prior injury by the ova had made the tissue more susceptible to infection. It is worth remembering that the chitinous shell of the S. mansoni ova is acid-fast, and one must remember that it is possible to misinterpret smears containing fragments of ova.

Histologic diagnoses

1. *Schistosoma mansoni infection*
2. *Secondary bacterial infection*

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Accidental Chemical Poisonings

From the Poison Control Center
The City of New York Department of Health

A series prepared by

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Mushroom Poisoning

TWO OUTBREAKS of mushroom poisoning were reported to the City of New York Department of Health in 1961.

One outbreak was reported in September in which 3 persons, a sixty-seven-year-old male and 2 females, sixty and thirty-one years old respectively, were involved. They were picking wild mushrooms at Pine Bush, New York. They cooked them and ate some of them. About three hours following the meal they experienced severe cramps, nausea, vomiting, and diarrhea.

Another outbreak was reported in October of the same year and involved a male and a female, both sixty-seven years of age. They picked some wild mushrooms outside of the city and ate these mushrooms. These 2 patients also developed cramps, nausea, vomiting, and diarrhea several hours after eating.

The mushrooms involved in both outbreaks were described as being orange in color and long-stemmed. All the patients recovered after a period of hospitalization and supportive therapy.

It is not generally appreciated that poisonous mushrooms may grow in the same locale as nonpoisonous mushrooms.

The most poisonous mushrooms are the Amanita muscaria (the fly agaric) and the Amanita phalloides (the death cup). Poisonings also occur from the Amanita pantherinia (the panther and the Gyromitra esculenta, or false morel). Although the Amanita group contains some edible species, it is safer not to eat any of the species belonging to this genus.

About 100 fatalities from mushroom poisonings occur annually in the United States. It has been reported that eating one or two mushrooms of the poisonous variety may prove fatal to an adult.

The Amanita muscaria contains an alkaloid, muscarine, which acts on the peripheral effector organs in the parasympathetic system. It also stimulates the smooth muscle fibers.

Amanita phalloides contains a toxic principle which is injurious to all body cells, and it causes liver, kidney, and brain damage. Amanita phalloides (the death cup) is distributed widely in nature. It is found growing in woods or cultivated land from spring until autumn.

The Amanita muscaria is found during the summer and fall occurring singly or in patches. It does not require a rich soil; on the contrary, it grows more abundantly in poor ground. It grows in cultivated soil, on partially cleared land, in wooded areas, and on roadsides. It has a variable color. The plant is brighter colored when it is young and fades as it matures. In the late autumn one finds a very pale colored variety. This species, like the phalloides, also is responsible for many deaths and many nonfatal but severe cases of mushroom poisoning.

Symptoms

Mushroom poisoning generally produces varied degrees of gastrointestinal disturbance, nausea, vomiting, abdominal pain, retching, thirst, and watery diarrhea. There is also a hypoglycemia present. In addition, there are symptoms which will vary with the type of mushroom ingested.

In poisonings caused by Amanita muscaria, there is also excessive lacrimation, salivation, profuse perspiration, slow pulse, diplopia, wheezing, muscular cramps, excitement, and delirium. All these symptoms may appear within two or three hours following the ingestion.

In mushroom poisoning caused by Amanita phalloides (the death cup) there is, in addition to the gastrointestinal symptoms, severe nausea, hematemesis, diarrhea which is usually bloody, jaundice, liver tenderness, nephritis, oliguria, anuria, hemoglobinuria, pulmonary edema, headache, central nervous system depression, mental confusion, convulsions, coma, and death. Mushroom poisonings from other species also may present the following symptoms: nausea, vomiting, diarrhea, muscle pains, jaundice, cyanosis, convulsions, coma, and death.

Laboratory findings

If kidney damage is present, the urine may contain albumin and red casts. There also may be oliguria or anuria.

If liver damage occurs, the liver function tests will be revealing. The blood chemistry also will show an increase in nonprotein nitrogen.

The prognosis varies with the type of mushroom ingested. It is reported that Amanita phalloides causes a 50 per cent case fatality rate. In the absence of liver and kidney damage the prognosis is much more favorable.

Prevention

Physicians should instruct their patients not to experiment with and not to eat any mushrooms regardless of where they may be found unless they are absolutely certain that they belong to the edible group and are nonpoisonous. It also may be emphasized that it is particularly dangerous to pick and eat young unopened mushrooms known as "buttons." It is extremely difficult to differentiate between poisonous and edible species in their early stages. A good and safe rule to follow is: never eat wild mushrooms.

The United States Department of Agriculture circular, *Some Common Mushrooms and How to Know Them*, states:

> Attention is called to the danger of depending on so-called tests for distinguishing poisonous and edible species. The assertions that mushrooms are poisonous if a silver coin placed in the utensil in which the mushrooms are cooked tarnishes, and that those which peel easily are edible, are wholly erroneous. The presence of insects on fungi is no guide as to their edibility, because insects infest both poisonous and edible mushrooms. The notion that soaking or boiling poisonous mushrooms in salt water will render them harmless has no foundation in fact.
>
> Although it is quite possible for a person to learn a few common and characteristic mushrooms, this circular in no way guarantees that the reader may be able to distinguish between all edible and poisonous species, for in order to become thoroughly familiar with the subject, continued study under a competent instructor is absolutely necessary.

Number one hundred four in a series of Accidental Chemical Poisonings

Case Reports

Primary Atypical Pneumonia

Unusual Therapeutic Problems

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WITHIN THE PAST twenty years the differentiation of bacterial pneumonia from nonbacterial infections of the lower respiratory tract has been studied extensively.[1] During this time, the term "primary atypical pneumonia" has been used widely; the disease has been considered a self-limited infection with pulmonary infiltration and constitutional symptoms. The careful documentation of such cases, the availability of more refined laboratory facilities, and the utilization of controlled groups such as the armed forces and college students have made the diagnosis one of exclusion.[2] Perhaps, as pointed out by Reimann,[3] the term primary atypical pneumonia should be dropped and viral pneumonia named according to etiology. Influenza and parainfluenza, Q fever, adenovirus infections, and psittacosis can simulate the clinical, roentgenographic, and laboratory findings. The Eaton agent[4] has been reported with increasing frequency and may be another cause of viral pneumonia.[2,5–8] RS virus, too, recently has been incriminated in the production of respiratory disease.[9]

However, more than one half of viral pneumonia cases defy specific etiologic classification, and there then remain a large number of cases many of which are associated with readily demonstrable serologic abnormalities (cold hemagglutination and agglutination of streptococcus MG). It is generally accepted that the fatality rate of these patients is low (from 0.1 to 0.2 per cent),[10] death usually occurs from respiratory embarrassment,[11] and therapy should be symptomatic and supportive. The following is the report of a case presenting an extremely ominous course and requiring extraordinary treatment.

Case report

CHIEF COMPLAINT. A seventeen-year-old white female student entered St. Mary's Hospital on September 15, 1959, for evaluation of a cough. The patient apparently was well until one week prior to admission when she experienced the insidious onset of nasal congestion and a nonproductive cough. These symptoms became more severe. For three days she had had chills and fever, and on the day of admission she complained of nausea and vomiting and was hospitalized.

HISTORY. The patient's family, social, and past medical histories were noncontributory.

PHYSICAL EXAMINATION. A physical examination revealed a flushed, well-nourished well-developed girl in no acute distress. Her temperature was 103 F., respirations 16, blood pressure 130/80, and pulse 110. Except for fine bilateral basilar rales, no other significant positive findings were present.

LABORATORY FINDINGS. Laboratory tests determined that the blood urea nitrogen was 9.5 mg. per 100 ml.; a urinalysis showed normal findings, and daily blood cultures yielded no growth. The hemogram results are given in Table I. Cultures of the nose and throat revealed no abnormal flora. The blood serology (Wassermann) showed negative results. An examination of the spinal fluid revealed normal protein and sugar and no cells. Roentgenograms of the

TABLE I. Hemogram results.

Elements	September										October
	15	17	18	22	23	24	25	26	29	30	3
Hemoglobin	11.4	12.1	11.1	...	8.6	8.6	9.9	...	11.4	11.1	11.1
Hematocrit	36	39	36	...	32	29	33	...	38	...	35
White blood cells	3,800	3,700	3,400	9,100	12,400	18,400	...	11,900	...	12,500	15,800
Polymorphonuclear leukocytes	65	82	83	90	...	...	...	...	...	92	86
Lymphocytes	35	14	15	7	...	...	...	...	...	8	12
Eosinophils	...	...	2	2	...	...	...	...	...	...	...
Monocytes	...	4	...	1	...	...	...	...	...	...	2
Cold agglutinin	...	Negative	...	...	1:512	1:4,096	...	...	1:2,048	...	1:2,048

chest indicated extensive bilateral pneumonia (Fig. 1). An electrocardiogram showed normal results.

Hospital course. After cultures were taken, the patient was given chloramphenicol (Chloromycetin) 250 mg. orally every four hours and Bicillin 600,000 units intramuscularly twice daily; she was also given parenteral fluids. On this regimen, her clinical condition worsened with increasing temperature, pulse, and respirations; her cough became more severe and remained nonproductive. A roentgenogram taken on September 23, 1959, indicated the rapid spread of the pneumonic process. Skin tests with old tuberculin 1:10,000 and 1:1,000 were negative after forty-eight hours. She was transferred to City Hospital for further study on September 23, 1959.

Course at Syracuse City Hospital. On admission to Syracuse City Hospital the patient's temperature was 104 F., her pulse 140, and respirations 62 per minute. She was dyspneic, flushed, and extremely apprehensive. There were fine rales audible throughout both lung fields. Laboratory data are included in Table I. A tracheostomy was performed immediately; there was no detectable clinical improvement. Cultures were taken on specimens from her trachea, nose, throat, and blood; all were sterile. She was maintained on intravenous fluids, oxygen, Alevaire aerosol solution, streptomycin 1 Gm. intramuscularly every twelve hours, and aqueous penicillin 1 million units in an intravenous drip every eight hours. Her condition deteriorated.

On the following day, her cold agglutinin titer was reported to be 1:512; there was a positive direct Coombs test; there were no detectable warm agglutinins; she was given 500 cc. of warmed whole (A+) blood. At this time, her condition was considered to be critical. Hydrocortisone 300 mg. was given intravenously in 1,000 cc. of 5 per cent dextrose and water; every eight hours thereafter she was given 1,000 cc. of 5 per cent dextrose and water with 100 mg. of hydro-

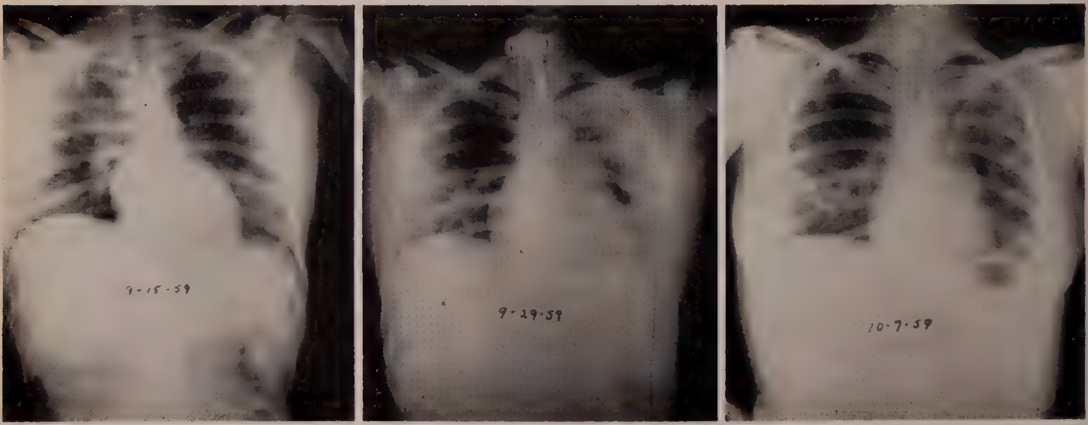

FIGURE 1. Dramatic clinical improvement followed the use of intravenous corticosteroids. Withdrawal of steroids precipitated temporary acute adrenal insufficiency.

cortisone and 1 million units of aqueous penicillin intravenously. Within six hours there was a dramatic fall in her temperature; she maintained a normal temperature after September 25, 1959. By that date there was also a fall in the pulse rate to 130 per minute and respirations to 36 per minute and a definite improvement in the patient's strength and morale. By September 29, 1959, her temperature, pulse, and respiration were normal; by this time she was raising moderate amounts of thin mucus and was able to take a soft diet. The rales were decreasing in distribution. The chloramphenicol was discontinued on September 28, 1959, streptomycin on September 29, 1959, and penicillin on October 3, 1959. The hydrocortisone was decreased gradually in dosage (Fig. 2). On September 28, 1959, she was given 50 mg. of hydrocortisone intravenously every eight hours, and that evening she was given the same dosage orally. On the following afternoon she complained of frontal headache and nausea. That evening she suddenly lost consciousness for a few seconds; she awakened and vomited her last dose of hydrocortisone tablets. She remained confused. At 3:00 A.M., on September 30, 1959, she experienced a generalized tonic and clonic convulsion. She remained unconscious and underwent seven distinct seizures that evening despite parenteral administration of Luminal and diphenylhydantoin (Dilantin). Except for coma and extensor plantar responses, an examination immediately after the first convulsion gave negative findings. A lumbar puncture revealed normal dynamics, no cells, and the protein to be 21 and the sugar 118 mg. per 100 ml. Eleven hours after her first seizure she was considered to be in acute adrenal insufficiency and was given 100 mg. of hydrocortisone in 5 per cent dextrose and saline intravenously every eight hours. Three hours later, the convulsions ceased. Two hours later her sensorium was normal and, except for a nonproductive cough, she felt well. On October 1, 1959, her temperature had risen to 104 F. but promptly returned to normal. On October 3, 1959, the tracheostomy tube was removed. The wound continued to drain for one week. Thereafter she received intramuscular injections of ACTH gel (40 units twice daily) as well as gradually decreasing amounts of intramuscular hydrocortisone and ACTH. She received her last dose of hydrocortisone on October 5, 1959, and her last ACTH on October 9, 1959. Diphenylhydantoin was discontinued on October 10, 1959. Her signs and symptoms of pneumonia had completely subsided by the time of discharge on October 11, 1959.

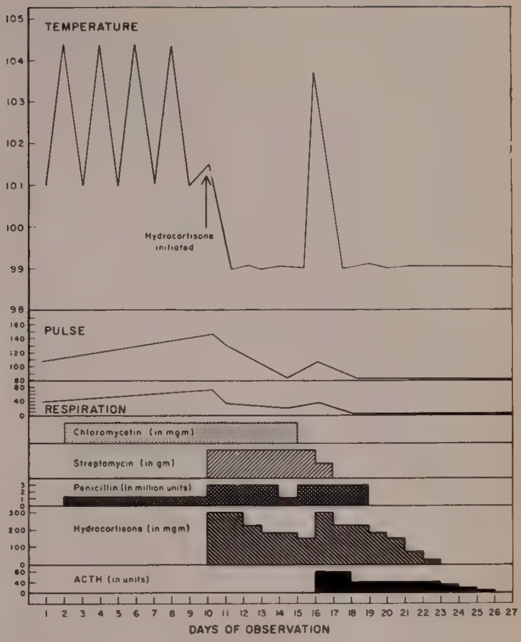

FIGURE 2. Extremely high cold agglutinin titers were present, aiding in diagnosis and therapy, but serving as a deterrent to the therapy of hyperpyrexia.

Since that time she has felt well and is now a college student majoring in physical education.

Complement fixation studies. Complement fixation studies taken on September 28, 1959, revealed no significant reaction for influenza types A and B. All routine cultures and acid-fast cultures were sterile. Serum electrophoretic studies done on September 30, 1959, were albumin 33.5 per cent (normal 44.72 per cent), alpha-1-globulin 6.1 per cent (normal 2 to 5 per cent), and alpha-2-globulin 17.6 per cent (normal 3 to 13 per cent), beta globulin 12.7 per cent (normal 6 to 19 per cent), and gamma globulin 30.2 per cent (normal 11 to 24 per cent).

Comment

Since 1943,[12] the identification of cold hemagglutinins in the sera of patients with viral pneumonia has been useful in establishing the diagnosis of primary atypical pneumonia; it is now accepted, as postulated by Finland *et al.*,[13] that the titer of cold agglutinins is often directly proportional to the severity of symptoms and extent of the pulmonary lesion.[14] The fears that antibiotic therapy might affect these titers[15] have not been realized. At present the test is considered nonspecific but extremely significant. Elevated titers are found in liver disease, trypanosomiasis, yaws, bronchiectasis, rubella, and blood dyscrasias.[13,16] However, a fourfold increase[14] or titers of 1:128 or more,[17] decreasing six to eight weeks after the onset of the disease, are rarely seen except in primary atypical pneumonia.

Because of the widespread pulmonary changes, initially absent cold agglutinins, and clinical deterioration, bacterial infection could not be excluded in this case. Cultures were taken, and chloramphenicol was administered. As the pneumonic process extended, penicillin and streptomycin were added to the regimen. The rise in the cold hemagglutinin titer made the diagnosis of viral pneumonia probable, and the question of continuing antibiotic therapy arose. Chloramphenicol may be effective in viral pneumonia,[2,18] but doubt remains regarding its efficacy.[1,19] No clinical improvement was observed in this patient so bactericidal drugs were utilized; streptomycin was given since tuberculosis could not be excluded, despite the negative results of the skin tests. This mimicking of pulmonary tuberculosis by viral pneumonia is not unusual.[15,20] Theoretically, penicillin was not indicated once the diagnosis was established, and it was maintained only because of a reluctance to alter a regimen that was succeeding in a critically ill patient. In retrospect, its use was unwise, since it has not a demonstrable beneficial effect in viral pneumonia,[19] and chemoprophylaxis is generally deplored.[21]

The utilization of adrenal steroids presented several points of interest. Of primary concern was their potential benefit. Certainly the judicious employment of steroids in infectious diseases is now an acceptable part of present therapy.[22] Their value presumably lies in the reduction of the undesirable effects of inflammation as well as in the contribution to the reversibility of vascular collapse due to infection.[23] However, the rationale for the use of steroids is not clear; in addition, the defense mechanism may be impeded, latent infections may be reactivated, and drugs have well-known side-effects.[22] A consideration of these various factors resulted in the use of steroids in our patient. There is no doubt that large doses of parenteral hydrocortisone lessened the evidences of toxicity within a matter of hours. In the opinions of several competent observers, corticosteroids permitted survival, but the limitation of observations pertaining to an infectious process in a single case are well known.[24] As expected, the healing of the tracheostomy wound was greatly delayed. A major unexpected complication of therapy did occur however. Contrary to the experience of Spink,[23] the gradual reduction of the dosage of steroids, their parenteral use, and the coincident administration of ACTH were necessary to prevent acute adrenal insufficiency and collapse. Attention to the detailed figures published by Spink indicates that, in some cases, he too utilizes a gradual reduction of dosage over several days. We believe our patient emphasizes clearly the recognized dangers of steroid therapy as well as the blind acceptance of generalized schemes of therapy applied to individual cases.

One more aspect of this case is of clinical importance, that is, the therapeutic problems resulting from high titers of cold hemagglutinins. Originally the elevated titers for these bodies were detected because of acute hemolytic anemias in 2 of the 3 patients with viral pneumonia;[12] it soon became clear that the hemolytic states were probably due to the presence of hemagglutinins rather than to sulfa therapy. In 1945 Finland *et al.*[25] warned that in severe cases of primary atypical pneumonia with high titers of cold hemagglutinins there may be hemolysis following the transient reduction of skin temperature, especially in the extremities, during chills, exposure to cold, or after the administration of antipyretics. These authors quote Ham as having produced hemoglobinuria in such patients by chilling an extremity. Shen, Castle, and Fleming[26] demonstrated that cohesion of the erythrocytes led to increased mechanical fragility and destruction while they were in motion in the circulation. Recently Jonsen and Kass[27] and Lewis, Szur, and Dacie[28] have produced evidence that complement fixation similar to an immune reaction is part of the hemolytic process. Besides the hemolytic phenomena, local gangrene has been reported in patients with high titer cold hemagglutinins and the extent of local reaction is reported to depend on the titer of cold agglutinins, critical temperature of cold hemagglutinins, viscosity of the blood, and the individual vascular response to cold.[29]

In our case these various theoretical considerations were of great importance during the episode of acute adrenal insufficiency and hyperpyrexia following the reduction in hydrocortisone therapy. Because of the convulsions, coma, and fever a cold water blanket or alcohol sponges were considered immediately as proper therapy to reduce hyperpyrexia; a consideration of the effects of hemolysis and local ischemia made such therapy contraindicated, however. Instead, treatment was directed entirely to the basic problem, adrenal insufficiency, and therapy with hydrocortisone and intravenous fluids proved efficacious.

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Angiosarcoma in Lymphedema Following Mastectomy

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ANGIOSARCOMA IS reported increasingly in the literature. Pack and Ariel, in 1958,[1] reported 200 cases of angiosarcoma of all types treated at Memorial Hospital in the previous ten-year period. In 55 per cent of the cases one of the extremities was involved, 20 per cent occurring in an upper extremity. In the majority of the cases with upper extremity involvement, the tumor occurred in a lymphedematous arm following a mastectomy. Stewart and Treves, in 1948,[2] were the first to report on angiosarcoma in so-called "elephantiasis chirurgica." They described this sequence: radical mastectomy, postoperative lymphedema, and then a long interval followed by the development of angiosarcoma as a separate primary lesion. Since this original paper, several investigators have reported isolated cases.[3-7] McSwain and Stephenson,[8] in a recent review of the literature, found 36 cases of lymphangiosarcoma following mastectomy and added 1 of their own. It is the purpose of this paper to report a typical case and to elucidate several aspects of the problem that have not been discussed recently.

Case report

HISTORY. A sixty-eight-year-old Italian female had undergone right radical mastectomy in 1952 for adenocarcinoma, followed by a full course of deep x-ray therapy. In 1956, she entered the hospital for treatment of congestive failure secondary to rheumatic heart disease of long standing. At the time, minimal edema of the right arm was noted. Her cardiac status was stabilized, and she was discharged. She re-entered in July, 1960, again in cardiac decompensation. In addition, in the two to three months immediately prior to this admission, she had noted increasing edema of the right arm as well as the appearance of a purplish discoloration on the medial surface of the upper arm. Angiosarcoma was suspected clinically, but the patient refused biopsy. She was discharged, only to be readmitted in August because of marked edema and pain and multiple bluish elevated nodules on the upper arm, which were very friable, ulcerated, and bled easily.

PHYSICAL EXAMINATION. The entire right arm and hand were markedly edematous. At the posterior medial surface of the upper arm there was a large 24 by 20 cm. area of bluish-yellow discoloration. Within this area were multiple bluish nodules ranging in size from 0.3 to 1 cm. and a large, friable, ulcerated mass measuring 6 by 3 by 2 cm. On the complete circumference of the forearm there were multiple small bluish-grey nodules in the skin (Fig. 1).

LABORATORY DATA. A skeletal survey indicated no abnormalities except for severe atrophy of the right humerus. A chest x-ray film showed marked cardiomegaly with bilateral pleural effusion. The alkaline phosphatase was reported as 8.7 units (1.4 to 4 units is normal). Laboratory tests revealed no other abnormalities.

TREATMENT AND PROGRESS. Because of the patient's cardiac problem, it was deemed advisable to perform the least amount of surgery necessary for good palliation. Accordingly, under regional anesthesia a disarticulation at the right scapulohumeral joint was done. The patient did well postoperatively. The alkaline phosphatase

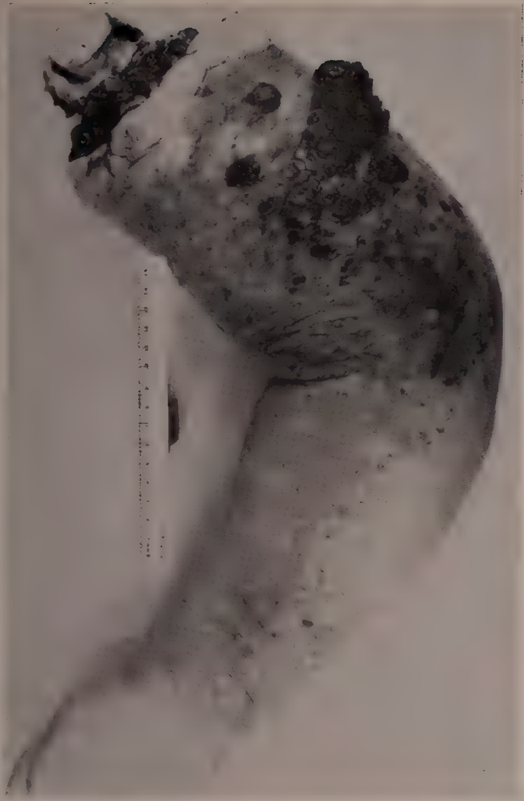

FIGURE 1. Resected right arm of patient who developed angiosarcoma eight years after mastectomy for adenocarcinoma.

returned to within normal limits, probably justifying the assumption that metastatic bone disease was present only in the humerus. The cardiac status once again stabilized, and the patient was discharged on the fourteenth postoperative day.

Pathologic examination. Histologically, there were aggregations of undifferentiated cells and of atypical vascular channels extending through the dermis into the subjacent fibroadipose tissue (Fig. 2). The striate muscle showed zones of degeneration, and in some areas permeations of atypical vascular channels were evident (Fig. 2).

Prognosis. No reliable statistics have been reported as to survival from the time of diagnosis to death from the disease itself. In a recent series, "In patients who died, the average duration of life following diagnosis in cases where the data are available was sixteen months."[8] However, of 37 patients, 31 were known to be dead, and on only 9 of these had autopsies been performed. It is therefore impossible to draw any meaningful conclusion unless one assumes that in all cases death was due to metastatic angiosarcoma (as opposed to metastatic mammary carcinoma and/or other unrelated causes). Since the procedure performed in our case was limited by the patient's cardiovascular status, we feel the prognosis is poor.

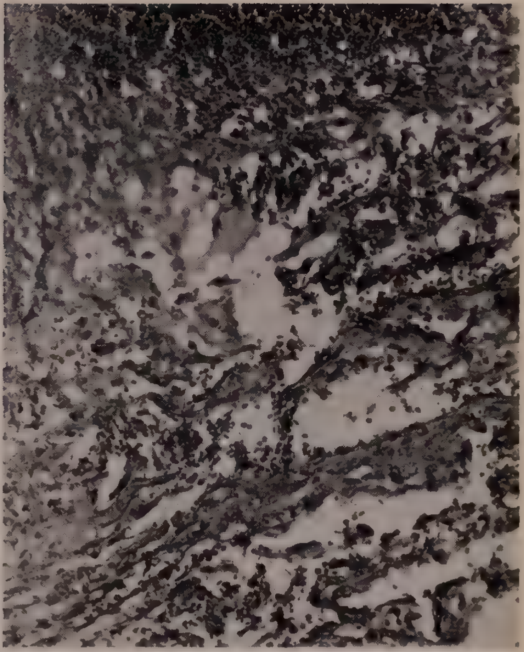

FIGURE 2. High-power photomicrograph of tissue from specimen in Figure 1. There is invasion of fibroadipose tissue underlying the dermis. Scattered erythrocytes are seen within atypical vascular channels.

Comment

In these cases of lymphadenosarcoma following mastectomy there has been a confusion of terminology and difficulty in classifying the type of malignant disease. Consequently it is not surprising that many theories as to the cause of this condition have been proposed. Some[7] have even considered the condition part of the original mammary carcinoma, in which the picture is that of a stromal response and/or an undifferentiated carcinoma rather than a new malignant condition.

Stewart and Treves[2] first advanced the possibility of a circulating carcinogen as a causative factor. They reported a case of angiosarcoma occurring in a lymphedematous arm of a patient on whom, unfortunately, a radical mastectomy had been performed for benign disease. A similar operation for carcinoma had been performed on the opposite side, with consequent development of lymphedema. The possibility of a circulating carcinogen, acting when it comes into contact with "modified human tissues," was postulated. Stewart and Treves believed that lymphedema was a predisposing factor, but that angiosarcoma was peculiar to the obstruction following radical mastectomy. However, McSwain and Stephenson[8] mention 4 cases occurring in congenital or post-traumatic lymphedema of the lower extremity in which there was no previous malignant tumor.

McCarthy and Pack[9] stated that trauma was a declared factor in 3 cases of angiosarcoma of their own and in 2 cases reported by Stout. A possible genesis from the "granulation tissue capillaries of traumatized areas" was hypothesized. The tumors in these cases, however, did not occur in the extremities following mastectomy.

Roentgen-ray irradiation has been implicated as a cause in other tumors, and this question has also been raised in angiosarcoma. But irradiation was not given either pre- or postoperatively in many of the reported cases. In addition, Herrmann and Gruhn[5] described a case of bilateral lymphedema (following radical mastectomies for asynchronous primary mammary carcinomas) in which angiosarcoma occurred only in one arm, namely, the side which had not been irradiated.

In reviewing the literature, we found that lymphedema as a causative factor appears to be the most popular theory. Martorell[10] went so far as to classify lymphedema as "tumorigenic." He believes that the phlebedemas, that is, those of venous origin, do not favor cellular proliferation. On the other hand, lymphatic stasis favors fibroblastic hyperplasia and subsequent degrees of elephantiasis. On rare occasions neoplastic proliferation may occur, leading to the formation of the multiple nodular tumors of angiosarcoma. In support of this, a case was reported of angiosarcoma occurring in a lymphedematous lower extremity with no preceding neoplasm. Although this theory seems attractive, angiosarcoma has not been reported in limbs with the massive chronic lymphedema secondary to filariasis.[2,5] Also, in some cases lymphedema did not appear in the involved extremity following radical mastectomy until many years postoperatively and then almost synchronously with the second primary, as in our case. We would suggest that in these cases angiosarcoma may actually be a cause of the lymphedema rather than vice versa.

Prompt amputation, including encompassing lymph nodes, that is, interscapulothoracic amputation, has been advised as the preferred treatment.[1,8] In one series 45 per cent of cases were found to have lymph node metastasis.[1] Unfortunately, early invasion of venous channels, probably on the basis of invasion of perivenular lymphatics, is characteristic of this tumor.[3-5] Present methods of treatment are therefore far from ideal.

Summary

Angiosarcoma in the lymphadematous arm following mastectomy is being reported with increasing frequency. A typical case is presented, and some bizarre facets of the disease are discussed. Theoretical considerations as to cause are abundant. It is our opinion that several factors are probably involved, and that further studies in this puzzling entity should be pursued.

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Antibody found in muscular disorder

Man's ability to produce antibodies to counteract invading germs is being investigated as a possible cause of myasthenia gravis, four researchers at the University of Buffalo School of Medicine reported in the October 6 *Journal of the American Medical Association.*

Previous investigators had found a factor with specific affinities for skeletal muscle in the blood of patients with the disease, according to the authors.

The Buffalo workers—Ernst H. Beutner, Ph.D., Ernest Witebsky, M.D., Dieter Ricken, M.D., and Richard H. Adler, M.D.—said they found additional evidence that the factor was an antibody and established that is was an autoantibody. There are actually two autoantibodies that seem to come into play. One antibody acts on skeletal and heart muscle, while the second acts only on skeletal muscle. Earlier investigators apparently found only the latter type. Final proof of the existence of these two antibodies depends on further extensive experiments.

Evidence of the antibody's presence was drawn from a comparison of 10 patients with myasthenia and 32 patients with other muscular and nonmuscular disorders, the researchers said. Among the 10 myasthenia patients, tests for antibody against skeletal muscle were strongly positive in 2, weakly positive in 3, doubtful in 8, and negative in 2. Among the other 32, no tests were positive, 3 were doubtful, and 29 were negative.

Even if it is assumed that myasthenia has an autoimmune cause, the triggering mechanism of the immunologic derangement remains unknown.

Hodgkin's Disease and Exfoliative Dermatitis

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THE REPORTED incidence of skin manifestations of the lymphogranulomatous group of diseases has been on the increase for the past half century. This can be attributed in part to Ziegler's report in 1911.[1] Cole[2] reported in 1917 that it was Ziegler's opinion that approximately 25 per cent of all cases of Hodgkin's disease exhibit skin involvement at some time or other. Ziegler stated that from 5 to 12 per cent of the cases manifested skin lesions as the first symptom. Bunting and Yates[3] quote Westphol as finding that in 10 per cent of his patients with Hodgkin's disease, the disease began with a lichenoid eruption; 15 per cent had skin eruptions. Jackson and Parker[4] state that skin lesions occur in approximately 30 per cent of Hodgkin's sarcoma cases. They are mostly papular, of dull red color, and often scaly. In Hodgkin's granuloma, they saw only one case of generalized exfoliative dermatitis.

Hence the skin has been reported to be involved specifically or nonspecifically in 15 to 25 per cent of patients with Hodgkin's disease. Cole[2] cited 13 cases with cutaneous manifestations in a series of 34. Two cases in this series had specific Hodgkin's involvement as noted by the presence of eosinophils, small mononuclear cells, and Sternberg-Reed cells. Cole did not divide his cases into types of involvement. In his 13 cases pruritis was the principal complaint, reported eight times. A pruritis-like exanthem was reported six times; a bronzelike pigmentation, four times; petechiae, twice; urticaria, once; and edematous swelling, three times.

For the past fifty years a variety of skin manifestations in the lymphomatous group have been reported. The lesions have ranged from tumorous infiltrations to exfoliations and papillomatous growths.[2,5,6] To date, there have been no reports of exfoliative dermatitis of the Brocq type in patients with Hodgkin's disease treated with nitrogen mustard. In a search of the literature with the aid of Merck Sharp & Dohme's recall system and Winthrop Laboratories' medical library, we failed to find any reports of nitrogen mustard as an etiologic agent.

Case report

A sixty-year-old white male was admitted to the Coney Island Hospital on January 1, 1961, with a chief complaint of intermittent fever, diffuse erythematous exfoliative rash, and generalized weakness (Fig. 1). The patient had first been seen in April, 1956, by one of us (M.M.) because of weakness and a mass in the left lateral area of the neck. The patient was hospitalized, and a biopsy revealed a histologic picture of Hodgkin's granuloma. From 1956 until this admission, the patient had been hospitalized four times. With each hospitalization he received a course of nitrogen mustard therapy consisting of two intravenous doses of 0.2 mg. of mechlorethamine hydrochloride (HN_2) per kilogram of body weight. The total amount given was 40 mg.

Just before the last hospitalization in June, 1960, the patient developed a mild, generalized exfoliative erythema. The last course of HN_2 had been given approximately eight months prior to that hospitalization. A chest x-ray of the patient during the June, 1960, hospitalization revealed a coin lesion of the anterior inferior segment of the right lower lobe. Seven days after

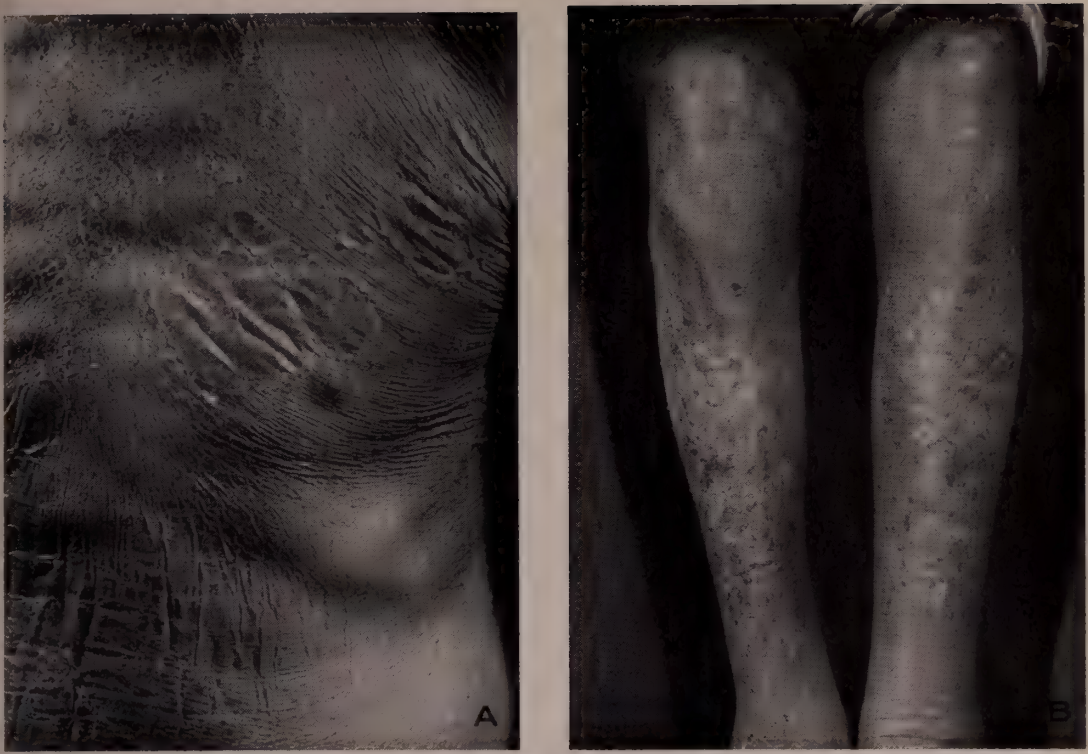

FIGURE 1. Erythematous exfoliative rash on (A) trunk and (B) legs of patient with Hodgkin's disease.

the HN_2 was given and prior to discharge, the coin lesion and the skin manifestations were gone.

In October, 1960, four months later, a rapid, progressive exfoliative dermatitis of the Brocq type developed. The patient was treated with ACTH and dexamethasone (Decadron). In spite of very energetic therapy, the skin eruption persisted, and the patient was admitted to the Coney Island Hospital.

An examination disclosed a small nodule about 0.5 cm. by 0.25 cm. of the left anterior triangle of the neck, generalized alopecia, and exfoliative erythema. The conjunctivas were pale. The vital signs were physiologic. An examination of the chest and abdomen revealed no abnormalities, and there was no pedal edema.

LABORATORY REPORT. The laboratory findings were as follows: white blood cells, 3,700; segmented neutrophils, 56; lymphocytes, 42; monocytes, 2; hemoglobin, 9.5 Gm. per 100 ml.; hematocrit, 30; blood urea nitrogen, 14 mg. per 100 ml.; fasting blood sugar, 81 mg. per 100 ml.; alkaline phosphatase, 8.5 units; total protein, 5.2 Gm.; albumin, 2.7 Gm.; globulin, 2.5 Gm. per 100 ml.; Coombs test, negative reaction; platelets, 160,000 per cubic millimeter.

The patient was given several blood transfusions. The white blood count ranged from 6,200 to 2,500. The bone-marrow study revealed no neoplastic cells. The skin biopsy showed stratified squamous epithelium with an intact basal cell layer and a focal mononuclear cell infiltrate underlying the corium. No eosinophils or Sternberg-Reed cells were noted.

A roentgen-ray examination of the spine revealed compression of the left half of the body of the fourth lumbar vertebra. An intravenous pyelogram showed slight displacement of the proximal third of the right ureter away from the midline.

While he was in the hospital the patient continued to receive steroid therapy. Approximately fourteen days before his death, the cervical mass had increased tenfold in size. He was then given local roentgen-ray therapy. Despite all the therapeutic measures taken, the patient ran a progressive downhill course and died on February 12, 1961.

AUTOPSY FINDINGS. Hodgkin's involvement of the mediastinal lymph nodes, liver, spleen, retroperitoneal nodes, lungs, wall of intestine, and peripancreatic nodes was seen on the microscopic sections. The normal architectural pattern was replaced by connective tissue. Within the connective tissue, lymphocytes, eosinophils, and Sternberg-Reed cells were seen. Skin sections showed a nonspecific fibrosis and infiltration of mononuclear cells, but no Sternberg-Reed cells were seen.

Comment

In addition to diffuse exfoliative dermatitis, disturbances of skin nutrition such as alopecia, dryness, and hyperkeratosis have been reported.[2,7,8] Urticaria and local and diffuse pigmentation similar to that in Addison's disease have been observed.[2] The pigmentation of Hodgkin's disease differs from that of Addison's disease in that the mucous membranes are not involved.

It is known that cases of exfoliative dermatitis occasionally persist for months with no evidence other than the lymph-node biopsy to demonstrate the true nature of the disease. The skin condition may disappear with roentgen-ray treatment. A remission may continue for months or even years. The patient may then present an acute exacerbation with enough clinical evidence to permit a specific diagnosis of leukemia, Hodgkin's disease, and so forth.[9]

Loveman[9] quoted Rulisan as stating that 25 per cent of all cases of Hodgkin's disease show skin manifestations, and that in 10 per cent the cutaneous lesion is the first symptom. Wile[6] has shown that the cutaneous lesions of the lymphadenoses may manifest themselves in three different ways:

1. True metastatic lesions may occur in the presence of a characteristic lymphadenotic blood picture.

2. The cutaneous lesions may antedate involvement of the blood picture and lymph nodes. Most of the cases of exfoliative dermatitis are in this group.

3. There may be scaly cutaneous eruptions, localized tumors, and so forth, in which transitory deviations from the normal blood composition as well as changes in the lymph nodes are found.

The cutaneous manifestations of Hodgkin's disease may be divided into two types: (1) Infiltrative or true lymphogranulomatosis cutis, in which there are definite plaques, nodules, or papular eruptions with a typical Hodgkin's histologic picture; (2) nonspecific, or a group of lesions set up by the general disturbances of metabolism; or excoriations, pigmentations, generalized exfoliative dermatitis, scarlatina, macules, papules, and so on (ids). This second group of lesions are usually toxic or metabolic and do not show the typical histologic changes of Hodgkin's disease.[2] The microscopic changes are variable.

Baxter, in 1879,[10] divided his cases in this manner, as did Loveman some fifty years later. Baxter stated that it was impossible to distinguish between the primary and secondary groups by clinical observation alone, and this also holds true today.

Examples of substances producing exfoliative dermatitis are mercury, gold, inorganic arsenic, phenobarbital, sulfonamides, potassium, thiocyanate, diethylstilbestrol, codeine, antibiotics, and so forth. Exfoliative dermatitis has been reported in association with hepatic and renal damage in a patient who was sensitive to para-aminosalicylic acid and streptomycin.[11]

The association between lymphomas and generalized cutaneous scaling is well known. The lesion has been reported in chronic lymphocytic leukemia, myeloid and monocytic leukemia, Hodgkin's disease, giant follicular lymphadenopathy, and polymorphous-cell (reticulum-cell) sarcoma.[5]

There are no reports in the literature to suggest that HN_2 can produce an exfoliative dermatitis. On one occasion the dermatitis cleared after a course of HN_2, but recurred four months later. Subsequent steroid therapy failed to modify the lesion. Little more can be added since we have had experience with only one case, but the occurrence should be recorded. One of us (M.M.) the senior author followed the case from the onset in 1956 to the patient's demise in 1961. The severity of the skin manifestations can be seen in Figure 1. In June, 1960, the skin lesions were of a similar nature, but not as confluent as those seen in Figure 1, taken before the patient's death in 1961.

Summary

A case of Hodgkin's disease associated with exfoliative dermatitis has been presented. The various associated cutaneous lesions have been discussed. To date, there have been no reports of HN_2 acting as a cause of the exfoliative dermatitis associated with Hodgkin's disease. Conversely, on one occasion there was mild improvement following the use of HN_2 in the case reported.

Exfoliative cutaneous lesions may or may not be histologically specific for Hodgkin's disease. The cutaneous lesion may antedate the disease and disappear with treatment, only to reappear later in association with other clinical manifestations of lymphoblastoma.

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Mortality rates slightly higher

Mortality among America's wage earners and their families was slightly higher in the first half of 1962 than in the corresponding periods of 1961 and 1960, it is reported by statisticians of the Metropolitan Life Insurance Company.

During the first half of this year, the mortality rate for all ages combined was 7.3 per 1,000, compared with 7.2 for each of the preceding two years.

Mortality from pneumonia and influenza increased about 10 per cent over that for the first half of last year, but was about 20 per cent below the rate of 28.3 per 100,000 recorded in the first half of 1960.

Little change occurred since last year in the death rate from the cardiovascular-renal diseases, which account for more than half of the total deaths. There was an increase of about 1 per cent in the mortality from cancer, while the death rate from respiratory cancer rose 4 per cent. Respiratory cancer now accounts for about one sixth of all deaths attributed to cancer.

Poliomyelitis accounted for only four deaths among Metropolitan's industrial policyholders. During the period only 202 cases of the disease were reported in the general population of the United States, or 15 per cent fewer than a year ago.

Progress continues to be made in the control of tuberculosis. The death rate from the disease established a new low of 5.2 per 100,000. It was 5.6 in the corresponding period of 1961 and 6.2 two years ago.

Accidental deaths increased slightly to 32.6 per 100,000, but there was a slight decrease in mortality from motor vehicle accidents.

Ramsay Hunt Syndrome Presenting Symptoms of Acute Pharyngitis

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THE SYNDROME of geniculate herpes zoster, although not originally described by Ramsay Hunt, was given a clinical classification by him that can still be applied today in the light of newer pathologic concepts.[1, 2] The classification is as follows: herpes oticus without neurologic signs, herpes oticus with facial palsy, herpes oticus with facial palsy and auditory manifestations, and herpes oticus with facial palsy and a Ménière's symptom complex.

Denny-Brown, Adams, and Fitzgerald[3] and Tschiassny,[1] Johnson and Zonderman,[4] and O'Neill[5] have expanded Hunt's original concept of geniculate ganglionitis to include the inflammation of portions of the seventh cranial nerve proximal and distal to the geniculate ganglion, as well as other contiguous cranial nerves.

The following is a case report that further ramifies this concept and demonstrates a unique presenting manifestation of this syndrome.

Case report

A thirty-eight-year-old white male chef entered the Rochester General Hospital on October 14, 1960, with the complaints of pain in the left ear and weakness of the left side of the face. The patient's illness apparently started two weeks prior to admission, with paresthesias over the left parietal scalp region followed soon after by coryza and sore throat. One week prior to admission a purulent pharyngitis was observed by his physician during an office visit. Soon after, he developed tinnitus and decreased hearing of the left ear and several days after that he experienced some nausea, vomiting, throbbing pain of the left ear, and hyperesthesia of the left side of the face. On the day prior to admission a temperature of 100 F. was noted together with a weakness of the left side of the face.

On examination the blood pressure was 120/80; the pulse, 84; and the temperature, 98.8 F. There was a left peripheral seventh cranial nerve paralysis with a flattening of the left nasolabial fold and an inability to close the left eyelid, wrinkle the left side of the forehead, or move the left-sided facial muscles of expression (Fig. 1A). The patient's taste was tested accurately and found bilaterally intact. The left tympanic membrane was erythematous, with several vesicles present on its surface. The pharynx was injected and had a white papular eruption over its left side. Pre- and postauricular lymph nodes were palpable on the left. There was no nystagmus. There was no rash, hypesthesia, or hyperesthesia over the face, external ear, or scalp. Although the tinnitus persisted, no decrease in hearing was detected.

Two days after admission a vesicular rash appeared over the left pinna, involving the antitragus and concha (Fig. 1B). Four days after admission the patient developed mild vertigo and a fine nystagmus on gaze to the right which persisted for two days. He did not complain of tearing in the left eye, nor was this observed.

The hematocrit was 47; hemoglobin, 15.6 Gm. per 100 ml.; and white blood cell count, 9,300 per cubic millimeter with 2 band forms, 64 segmented forms, 25 lymphocytes, and 9 monocytes. The sedimentation rate (Westergren method) was 15 mm. per hour. The urine had a trace of albumin and from two to five white cells per high-power field. Throat and ear cultures

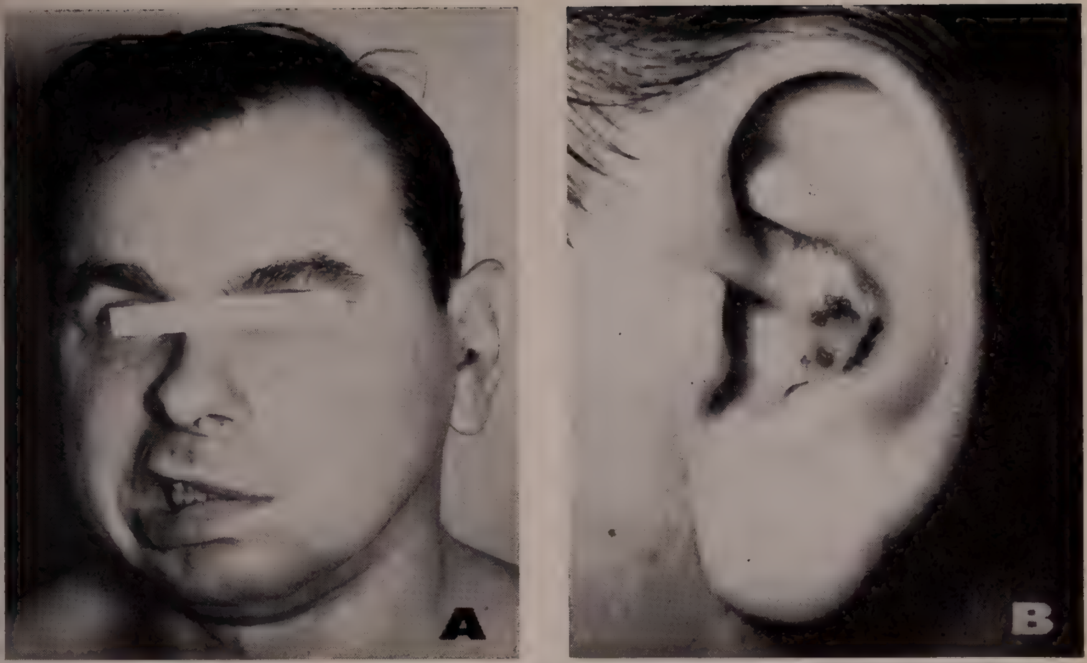

FIGURE 1. Patient with Ramsay Hunt syndrome. (A) Left peripheral seventh cranial nerve paralysis; (B) vesicular rash over left pinna, involving antitragus and concha.

grew no significant pathogens. A microscopic examination of vesicle fluid smears was noncontributory. Serum electrophoresis was normal, and neither serum cryoglobulins nor urinary Bence Jones proteins were demonstrated. A lumbar puncture demonstrated normal pressures and dynamics. The spinal fluid examination showed a protein of 68 mg. per 100 ml. and 62 mononuclear cells and 9 polymorphonuclear cells per cubic millimeter. The cultures were negative. An electrocardiogram and x-ray films of the chest, mandible, and mastoids indicated negative findings. No lymphoma or other malignant condition was demonstrated.

The patient was treated with Protamide (which affected his pain little), vitamin B complex, dexamethasone, and penicillin. The disease appeared to run its course despite therapy. The patient was discharged on October 28, 1960. He was without pain, the vesicles had disappeared, but the seventh cranial nerve paralysis persisted, having shown little improvement since admission. The patient went home on decreasing steroid doses and a weekly physical therapy program. He was again seen in January, 1961, and had a 40 to 50 per cent return of function to the left facial muscles.

Comment

The diagnosis of a herpes zoster infection is primarily a clinical one since culture technics are generally lacking. Serologic studies, although they are available in some laboratories, are not part of the usual clinical armamentarium.[6] Sachs and House[7] point out that only 5 cases of the Ramsay Hunt syndrome have come to postmortem examination. Two of these cases did not correlate with the usually expected clinical picture. Of the remaining 3 cases, only 2 were found to have changes of inflammation in the geniculate ganglion, while the last case showed the geniculate ganglion to have normal ganglionic cells with inflammatory changes proximal and distal to it. It is obvious that the clinicopathologic correlation has not been well defined.

Tschiassny[1] reviewed the anatomy of the seventh cranial nerve and devised the schema seen in Table I. He used the topognostic signs of the presence or absence of taste over the anterior two thirds of the

TABLE I. Location of lesion of seventh cranial nerve based on presence or absence of taste and tears

Location of Lesion	Presence of Taste	Presence of Tears
Infrachordal	Yes	Yes
Suprachordal	No	Yes
Transgeniculate	No	No
Suprageniculate	Yes	No

tongue and lacrimation as an indication of the site of inflammation in the peripheral portion of the facial nerve. This concept is foreign to Hunt's original thesis which placed the site of the inflammation entirely within the geniculate ganglion. The schema divides the facial nerve in its peripheral course into four regions (Fig. 2). Table I was derived from the observations that a lesion of the fibers carried in the chorda tympani may cause partial or complete loss of taste over the anterior two thirds of the tongue while trans- and suprageniculate lesions do not involve the nerves to Horner's muscle. Since Horner's muscle opens the lacrimal sac, a paralysis of this muscle produces epiphora. This schema, although apparently logical, has been questioned; not all observers agree that a suprageniculate lesion produces a loss of taste.[8]

Utilizing the previously mentioned criteria and Hunt's classification, the case presented here would probably be a herpes oticus with facial palsy and a Ménière's symptom complex with a suprageniculate lesion (presence of taste and absence of tears). Since the suprageniculate portion of the facial nerve lies in close proximity with the eighth nerve and the meninges, it is reasonable to postulate the involvement of the eighth nerve by way of an inflammatory edema or by a zoster infection through the communicating branch at this level. Inflammation involving the leptomeninges is demonstrated by the abnormal spinal fluid findings in this case and has been recorded by others.[4]

The term "herpes oticus" is properly reserved for a vesicular eruption which appears on the pinna, the tympanic membrane, and along the external auditory canal. These areas are supplied by the sensory portion of the seventh nerve. The so-called "zoster or geniculate zone" includes the tragus, antitragus, concha, part of the helix, antihelix, fossa, and a portion of the lobule. In addition to the seventh nerve, the external ear also receives sensory branches from the fifth, ninth, and tenth cranial nerves, as well as branches from the cervical plexus.[5] Herpetic lesions of these nerves have produced an eruption in the so-called "geniculate zone." Other reported areas of vesicular eruption with a geniculate herpes include the ipsilateral anterior two thirds of the tongue, the soft palate, and the fauces. Undoubtedly, the presenting manifestation of pharyngitis in this case represents a variation of this latter type of eruption. A presenting picture of this sort has not been recorded in the literature.

The signs and symptoms of this disorder include the classical triad of a vesicular cutaneous eruption, a radicular neuralgia, and a segmental palsy and sensory loss. The disease is usually unilateral and is heralded by a two-to-three-day period of headache, lassitude, and low-grade fever. Pain is frequently seen next in the general area of the affected ear, but is not localized to the ear alone. The pain may radiate into the scalp, down the neck, and into the jaw, and is described as neuralgic with paresthesias and hyperesthesias. Areas of anesthesia and hypesthesia are also found. The vesicular eruption is seen on the ear and rarely on the tongue, fauces, and soft palate. These same areas may become reddened, swollen, and tender. The facial palsy is of a lower motor neuron type and is usually complete. It has been reported that the palsy will follow the rash in a period of from one to ten days.[8] Paresis of the soft palate occurs rarely. Occasionally, however, there is a loss of taste over the anterior two thirds of the tongue on the affected side. Nerve deafness, tinnitus, and vertigo with vomiting may occur also.

The white blood cell count is usually normal. The spinal fluid shows a pleocytosis (as high as 450 cells per cubic millimeter[4]), predominantly mononuclear cells, and a moderately elevated protein if the meninges are involved. The spinal fluid pressure is normal.

The prognosis of the disease is favorable. There is little postherpetic pain, and taste

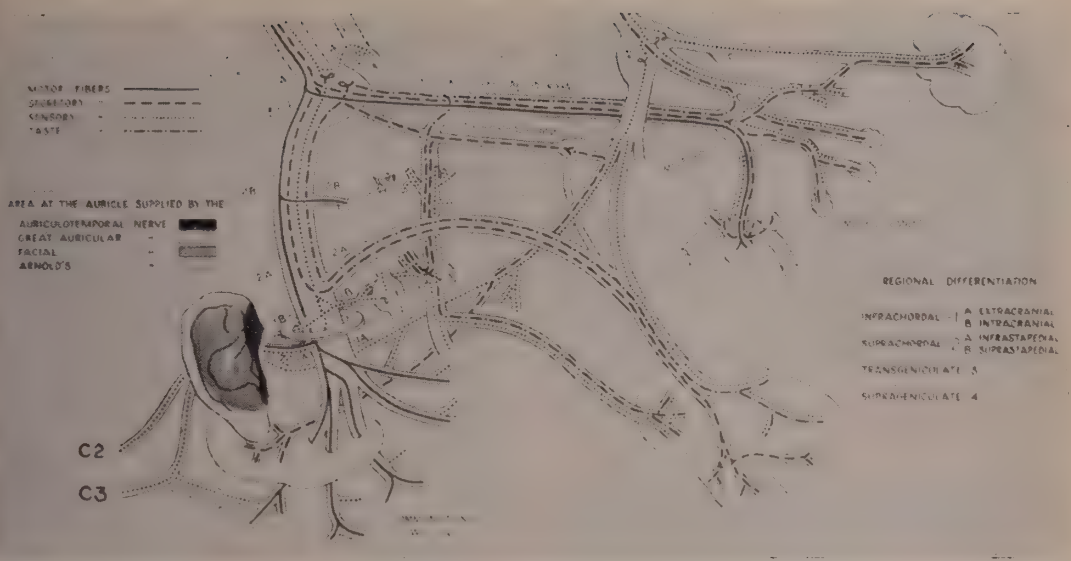

FIGURE 2. Distribution of afferent and efferent fibers of facial nerve for regional diagnosis of lesions. Schema divides facial nerve in its peripheral course into four regions: infrachordal = entire nerve distal to branching of chorda tympani; suprachordal = portion of nerve between branching of chorda tympani proximal to distal border of geniculate ganglion; transgeniculate = geniculate ganglion including branching of greater superficial petrosal nerve; and suprageniculate = portion of peripheral nerve proximal to branching of greater superficial petrosal nerve.

and balance return to normal in from weeks to months. About 50 per cent of those patients with deafness will manifest some recovery. The facial palsy has been reported to improve in a period of from six weeks to twelve months, and recovery is often complete.[9]

The treatment at present leaves much to be desired, and affects the prognosis little. With the exception of physical therapy to the weakened facial muscles, the treatment is essentially symptomatic. Protamide, antibiotics, steroids, and decompressive surgery have been used without notable success. The reported low incidence of this disorder is only apparent since it has been diagnosed incorrectly in the past as a number of conditions, among them Bell's palsy, otitis media, and dermatitis. An awareness of this syndrome will demonstrate its true frequency.

Summary

The signs and symptoms of the Ramsay Hunt syndrome (geniculate herpes zoster) have been reviewed, and a case demonstrating a unique presenting manifestation, pharyngitis, has been presented.

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A Dilated Tortuous Tributary Vein to the Hemiazygos Vein Seen First as an Unusual Inferior Posterior Mediastinal Mass

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When an inferior posterior mediastinal lesion appears on roentgen film, the differential diagnosis must include the following: schwannoma, ganglioneuroma, fibrosarcoma, bronchial cyst, and lipoma. Malignant neurogenic tumors, lymphangiomas, bronchial adenomas, diaphragmatic hernias, aneurysms, and esophageal lesions also should be considered.[1] Rarely, other lesions may present themselves.

The case to be presented in this paper is that of an unusual inferior posterior mediastinal lesion which was comprised primarily of a dilated tortuous aberrant vein passing over the anterior surface of the aorta and draining into the hemiazygos vein.

Case report

This forty-eight-year-old white male, Honduran National, was first noted to have a retrocardiac density on October 20, 1959, when films were taken while he was being studied for a fracture of the sixth, seventh, eighth, and ninth ribs on the left side. He originally had sustained these fractures when he was hit in the chest by a monkey wrench on August 19, 1959. Although he was asymptomatic except for some pain in the area of the rib fractures, because of the possibility of an aortic aneurysm he was admitted to the U.S. Public Health Service Hospital, Staten Island, New York, for further studies. His history revealed that he did not drink, but it was otherwise noncontributory.

The patient was a well-developed, small white male. His weight was 127 pounds, height 5 feet 7 inches, temperature 99.5 F., and blood pressure 152/105.

No venous distention was apparent. The chest was clear to auscultation and resonant to percussion. There were no enlarged organs or masses palpable.

Laboratory data. A few larvae of Strongyloides stercoralis were seen on a stool examination. The hemoglobin, hematocrit, and white cell count were normal, as was the differential blood count. Other laboratory findings included a prothrombin time of 90 per cent, cephalin flocculation 1 plus, thymol turbidity 1.8, total protein 7.6 Gm. per 100 ml. with 4.5 Gm. per 100 ml. albumin, and the alkaline phosphatase ranged from 2.5 to 3.8 Bessey Lowry units. The blood urea nitrogen was 24 mg. per 100 ml. and the glucose 113 mg. per 100 ml. There were no significant changes in the liver function studies one month postoperatively.

An electrocardiogram showed normal findings.

Roentgen findings. On admission a posteroanterior film (Fig. 1) taken with the patient in an upright position showed a double density behind the heart. There was a smooth bulge to the left of the ninth, tenth, and eleventh thoracic vertebrae extending 4 cm. from the midline and 7 mm. lateral to the margin of the descending aorta.

The retrocardiac mass was not identified definitely at the time of the fluoroscopy, on the oblique or lateral films, or on the lateral tomograms. Kymography did not help. The mass was seen best on postero-

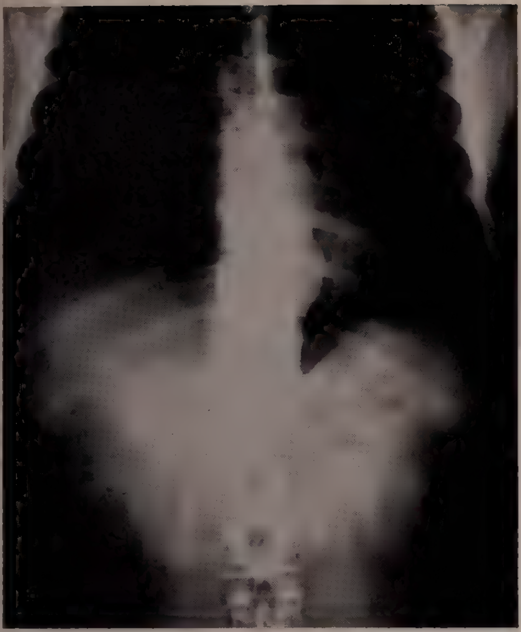

FIGURE 1. Posteroanterior film showing double density behind heart.

FIGURE 2. Posteroanterior tomogram showing mass.

anterior tomography at the 8-cm. cut (Fig. 2). An intravenous angiocardiogram was attempted but was not technically successful.

A barium swallow revealed that the mass was separate from the esophagus.

Retrograde aortography was effected through the left superficial femoral artery using a Lehman mechanical injector and a number 12 Lehman catheter. After the catheter was passed retrograde to the midthoracic area, 40 cc. of 85 per cent diatrizoate methylglucamine (Cardiografin) was injected. The descending thoracic aorta was visualized well, and no abnormality of it was seen (Fig. 3).

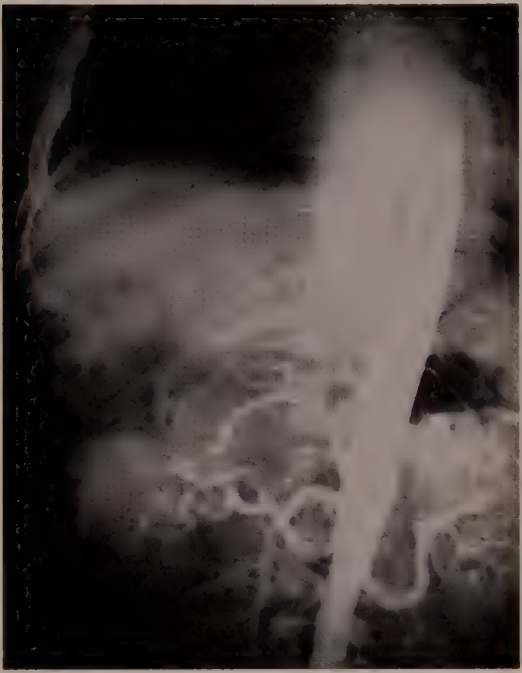

FIGURE 3. Retrograde catheter aortography reveals aorta to be apparently normal at the level of the mass.

COURSE. In view of the normal barium swallow and aortography studies a presumptive diagnosis of an inferior mediastinal tumor, probably neurogenic in origin, was made.

At surgery an inferior posterior mediastinal mass was found at the distal part of the descending thoracic aorta. This mass included areolar tissue, but consisted primarily of a dilated tortuous, aberrant vein which intercommunicated with itself. The vein ran primarily over the anterior left lateral wall of the aorta but was also present on the lateral wall of the esophagus. However, it was only very loosely adherent to the wall of the esophagus and was separate from the small plexus of esophageal veins, which appeared normal. The vein was readily visible over part of the aorta, but the veins over the inferior part of the thoracic aorta and esophagus were masked with areolar tissue and pleura and did not become apparent until they were dissected out.

Although the vein intercommunicated and had multiple dilations or varices up to 7 mm. in diameter, it came through the esophageal hiatus as a single smooth vein about 3 mm. in diameter and emptied into an apparently normal hemiazygos vein. At the point that it went through the esophageal hiatus it was quite separate from the esophageal wall. The esophagus itself was pulled up with tape to rule out any esophageal varices. No bruit was palpated.

When it was apparent that no significant esophageal varices were present and that the hemiazygos vein itself appeared normal, it was decided to ligate and excise the elongated and tortuous aberrant vein. This was accomplished after first clamping it without noting any proximal or distal distention.

On pathologic examination of the veins there was intimal thickening and fibrosis, and in a few regions adventitial and perivascular scleroses were noted. The smooth muscle component of the vein wall was thinned and at times markedly so. The impression was of phlebectasia and phlebosclerosis with marked aneurysmal dilatations of the vein.

Varices or aneurysms of the hemiazygos vein or its tributaries (symptomatic of a mass) should be included in the differential diagnosis of the posterior mediastinal masses.[2,3]

Comment

Although it may be necessary to do aortography studies and to do gastrointestinal series to rule out definitely an involvement of the aorta or the esophagus, certain preliminary tests may be carried out which will make one strongly suspect a varix of the hemiazygos system of veins.

Generally such a varix will change its shape and size with a change in the position of the patient and with changes in the intrathoracic pressure. Hence, such a varix may increase in size when the patient lies down and decrease in size when the patient stands,[4,5] or it may change with changes in the thoracic pressure, such as in the Valsava and Müller maneuvers. The size should decrease with the former and increase with the latter.[6,7]

Retrograde aortography has been proved to be a useful adjunct in the definitive demonstration of whether or not a lesion, particularly a mediastinal mass, communicates with the aorta. Although many radiopaque media have been used for such procedures, Lehman *et al.*[8] have found diatrizoate methylglucamine to be particularly satisfactory, and it has proved thus far to be satisfactory for us.

The diagnosis may be proved further by using the transosseous phlebography technic described by Tori[9,10] in which a radiopaque media is injected into the spinous process of the thoracic vertebra or into the posterior segment of the ribs. This radiopaque material then drains to the azygos and hemiazygos system.

Two previous cases of hemiazygos varices, or aneurysms, were reported by Campbell and Baruch in June, 1960.[3] Portal hypertension was believed to be the cause of two dilated areas of a hemiazygos vein. However, in our case there was nothing to support a diagnosis of portal hypertension. It has been noted that increased pressure in the supine or inferior vena cava may cause dilation of the azygos or hemiazygos system of veins. There was nothing to support this in our case.

The first case of an aneurysm of the hemiazygos system, presented by Leigh *et al.* in November, 1954,[2] also was a case of portal hypertension. Although previous authors[2,3] have referred to multiple aneurysms or an aneurysm of the hemiazygos vein or system, because of the multiplicity of the dilatation we prefer to refer to this as a tortuous tributary vein with multiple dilatations draining into the hemiazygos vein. It is noted that the word aneurysm has become so closely associated with arteries that its occurrence in veins is not recognized as a distinct entity by the Standard Nomenclature of Disease and Operation.[11]

Conclusion

Since there is nothing to support portal hypertension in our case, it must be assumed that the condition is secondary to a congenital anomaly—an aberrant vein passing through the esophageal hiatus and passing anterior to the aorta instead of posterior to it.[12]

Summary

A case of an unusual inferior posterior mediastinal mass consisting primarily of a dilated tortuous, aberrent, tributary vein to the hemiazygos vein has been presented. A brief review of other cases has been presented with a mention of diagnostic procedures that may be used in arriving at a diagnosis of a varix or aneurysm of a hemiazygos vein. Pertinent points are made relative to the significance of retrograde thoracic aortography as a diagnostic procedure.

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Cervical cancer deaths could be ended

Cervical cancer could be virtually eliminated as a major cause of death among women by repeated examinations at yearly intervals, a community-wide study has indicated.

More than 66,000 women in Louisville and surrounding Jefferson County, Kentucky, were screened for cancer of the cervix by the Pap smear test in the study begun in 1956, according to a report in the October 13 issue of the *Journal of the American Medical Association.*

The tests revealed abnormal cells in 883 women who then underwent biopsies, William M. Christopherson, M.D., James E. Parker, M.D., and James C. Drye, M.D., University of Louisville School of Medicine, said.

Preliminary analysis shows that 209 invasive cancers were detected, they said. Most of these were in the early stage, and should have a "relatively favorable" outcome.

A total of 288 localized cancers were found, they said, and these are "perhaps totally curable."

Another 210 possibly precancerous conditions were found, they said.

The over-all incidence of previously undiagnosed invasive cancer was 2.8 per 1,000 women and 3.7 per 1,000 women for localized cancer, the study showed.

The women who took part in the study were private patients, patients from a charity hospital, and women working in industries.

The rate of incidence of invasive and localized cancer was higher among the charity patients than the private patients. Among charity patients, invasive cancer occurred in 4.4 per 1,000 and localized cancer in 4 per 1,000, compared with an incidence among private patients of 2.5 per 1,000 for invasive cancer and 3.6 per 1,000 for localized cancer. These findings indicate that the socioeconomic implications of the disease are most interesting and deserving of further study.

Stevens-Johnson Syndrome

A Hypersensitivity Reaction in the Spectrum of Lupus Erythematosus

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ERYTHEMA MULTIFORME and its special variant, ectodermosis erosiva pluriorificialis, or Stevens-Johnson syndrome, has been regarded as a symptom complex with a characteristic clinical pattern and usually is self-limited. Various etiologic factors have been implicated, since the syndrome itself is apparently a vascular reactive pattern that is seen with systemic infection, medication, pregnancy, and endocrine and allergic disorders. In many cases specific etiologic factors cannot be identified.

Four cases of the Stevens-Johnson syndrome have been observed in a period of ten months with features strongly suggesting that this skin disorder is a reflection of a potentially reactive systemic hypersensitivity angiitis related to the symptom complex of disseminated lupus erythematosus.

Case reports

CASE 1. A ten-year-old white female with an excellent health record noted a bullous eruption on the skin of the trunk and extremities three days prior to her admission to the hospital. Her temperature ranged between 101 and 103 F. The past history revealed negative findings except for a convulsion associated with roseola at the age of one year. The patient had a strong familial history of atopy. The patient was given a long-acting sulfa preparation for a viral infection ten days prior to her admission. She was allegedly allergic to penicillin. A physical examination on admission revealed an acutely ill child with a fever of 103 F. A "butterfly rash" was noted over the malar prominences. Erythematous bullae and macular-papular lesions were scattered diffusely over the body, trunk, and extremities. Both eyes presented a purulent conjunctivitis. Mucosal erosions were noted in the mouth and the vagina. The white blood cell count on admission showed a leukocytosis of 16,800 per cubic millimeter which decreased eventually to 7,400 per cubic millimeter. The urine, blood chemistries, and chest x-ray film all showed findings within normal limits. L.E. (lupus erythematosus) cell preparations were not done. The patient was treated symptomatically and was discharged on the ninth hospital day, considerably improved.

CASE 2. An eleven-year-old white female had been placed on phenobarbital $^1/_4$ grain three times daily five years prior to the present admission because of symptoms diagnosed as "petit mal." Two weeks prior to her admission the patient had a major convulsion and was placed on diphenylhydantoin sodium (Dilantin sodium) 100 mg. twice daily. There was no family history of epilepsy or allergic diathesis. One day before her admission the patient developed a temperature of 100 F. and was unusually restless. Twelve hours prior to her admission she developed a generalized rash. An examination revealed a bullous and maculopapular eruption over the entire body. Her temperature on admission was recorded at 104 F. Severe conjunctivitis and erosive lesions were noted in the mouth and the vagina. No gross hematuria, hematemesis, or polyarthritis was noted. A laboratory examination revealed a leukocytosis of 5,200 per cubic centimeter with a normal differential, hematocrit of 42, and a platelet count of 3 plus. The sedimentation rate was 12. A urine examination showed a persistent albuminuria of 2 plus, a specific gravity of 1,020 to 1,030, many white blood cells per high power field, and yielded negative cultures. The stools showed negative guaiac findings. A Wassermann examination produced negative findings, and a chest x-ray film showed no abnormalities. All the viral studies gave negative findings. The blood chemistries were normal with the exception of a blood urea nitrogen of 25 to 31 mg. per 100 ml. An L.E. cell preparation showed negative findings on one examination. The patient was placed on Achromycin, 2 Gm. daily, Mycostatin 500,000 units three times daily, intravenous fluids, and 40 mg. of prednisone per day, with intravenous hydrocortisone supplemented up to 200 mg. per day. The patient deteriorated rapidly. On the fifth hospital day the patient lapsed into a coma with preterminal Cheyne-Stokes respirations followed by death. No autopsy was permitted.

Case 3. This thirty-year-old Negro female with numerous past hospitalizations entered the hospital because of an eye discharge of two weeks duration.

The patient had been a known grand mal epileptic patient for twenty years under treatment with diphenylhydantoin sodium and phenobarbital. In 1950 a blood examination disclosed a positive Wassermann test reaction without a history of chancre or rash. She was treated with penicillin. Her blood pressure at that time was noted to be 150/100 with no abnormality found in the urine. In 1956 the patient was admitted for an incomplete septic abortion.

In 1959 she developed bronchial asthma and a bilateral malar erythematous rash. In addition, she complained of pain in the right upper quadrant of the abdomen and in the right flank, dysuria, frequency, hematuria, and chills, with a recorded temperature of 105 F. A urine culture revealed Escherichia coli. Intravenous pyelogram studies showed normal findings. The pain and urinary symptoms subsided with antibiotic therapy. Abnormal liver chemistries (alkaline phosphatase of 13.8, transaminase of 92, sulfobromophthalein sodium (Bromsulphalein) of 20.4, and cephalin flocculation of 4 plus) prompted a liver biopsy which revealed areas of congestion in the sinusoids and round cell infiltration in the portal areas consistent with interstitial hepatitis. A hemoglobin was 7.5. L.E. cells were not found on repeated examinations. A renal biopsy revealed casts in the tubules and moderate arteriosclerosis with focal areas of fibrosis.

One week prior to the present admission in September, 1960, in addition to pain in the right eye, the patient noted numerous sores on the face and in the mouth, throat, nose, and vagina. On admission the patient was acutely ill with a temperature of 103 F. She had a generalized erythematous maculopapular eruption with occasional bullae and pustules over the face in a butterfly distribution. There was a purulent discharge from the right eye. The palate showed purplish discoloration and lesions with purulent exudate. A chest examination revealed inspiratory and expiratory wheezing diffusely over the thorax. The liver edge was palpable 3 fingerbreadths below the costal border.

A blood examination showed 10,000 white blood cells per cubic millimeter with a normal differential. The sedimentation rate was 27 mm. per hour, platelets 4 plus, and hematocrit 28. A urinalysis showed negative findings as did a serology test and a guaiac examination of the stool. The blood urea nitrogen was 7 to 11 mg. per 100 ml., fasting blood sugar 212 mg. per 100 ml., calcium 10, phosphorus 4.2, and total protein 7.8 mg. per 100 ml. with a globulin of 2.9 mg. per 100 ml. The sulfobromophthalein sodium revealed a 19.4 per cent retention. The thymol turbidity was 9 units, cephalin flocculation 4 plus, transaminase 13 units, and icterus index 5.8. A glucose tolerance test revealed a diabetic curve. An electrocardiogram revealed nonspecific S-T- and T-wave changes. L.E. cell preparations gave persistently negative findings. The patient was continued on diphenylhydantoin sodium and phenobarbital and treated with steroids, systemically and topically, to the skin and eyes with the gradual subsidence of the skin eruption.

Case 4. A twenty-five-year-old white female's condition was diagnosed as disseminated lupus erythematosus one year prior to her present admission because of a malar rash, polyarthritis, an elevated temperature, pleural effusion, pericardial fluid, skin nodules, palpable spleen, and leukopenia. L.E. cells were demonstrated repeatedly. She was placed on prednisone and eventually was maintained on 30 mg. daily. The chemistries at that time showed essentially negative findings with the urine showing only an occasional trace of albumin. A biopsy of the involved skin area revealed mild vasculitis with a perivascular inflammatory reaction.

Two days prior to her present admission the patient developed a rash over her hands which later involved the entire body, with sores in the mouth and burning on urination and around the anus. The temperature was noted to be 104 F. On admission the patient had bullae over the entire body with areas of denudation with marked surface weeping. Stomatitis, urethritis, and perianal erosions were noted. The patient had a very stormy course requiring massive doses of steroids and intensive nursing care to the skin. A secondary skin infection (80/81 phage-type staphylococcus) and lung abscesses were controlled with Staphcillin and chloramphenicol.

Chemistries revealed a blood urea nitrogen of 16 and normal serum electrolytes. The liver chemistries were normal except for a reversal of the albumin-globulin ratio of 2.4:3.8. A urine examination revealed an occasional red blood cell per high power field. A leukopenia of 2,750 per cubic millimeter persisted except for a count of 10,000 when the skin and lung abscesses were at their height. Signs of pericarditis occurred during a phase of her illness and were handled by an elevation of the steroid levels to 120 mg. of prednisone per day. An electrocardiogram revealed transient S-T- and T-wave changes. Eventually the patient recovered slowly. The steroid dosage was lowered gradually until she was sent home on 25 mg. of prednisone daily. The only residua were pigmentary changes of the skin, occasional complaints of pains in her wrists, and a low-grade temperature of 100 F.

Comment

The symptom complex of erythema multiforme that is seen fairly often in dermatologic practice has been known to affect other organs. Osler[1] described erythema multiforme and included examples of renal involvement. Costello in 1947[2] recorded renal involvement with arteriolar hyalinization and wire-loop involvement of the glomeruli in a man with severe erythema multiforme. There are innumerable papers on the systemic effects of erythema multiforme; a most recent paper by Comaish and Kerr[3] stresses again the protean and diffuse involvement of organs in erythema multiforme. In essence, the vascular involvement of the kidneys, liver, lungs, heart, and brain associated with severe erythema multiforme has been reported; a complete review is beyond the scope of this paper but can be found in several recent publications.[4–7] In addition, there are reports of joint involvement associated with erythema multiforme which may be a cause of "rheumatic activity" in adults.[8] The vascular changes, as described in erythema multiforme,[5] in allergic diseases,[9] and unclassified systemic vasculitis,[10,11] cannot be clearly delineated morphologically. In fact, the pathologic criteria which usually have been associated with systemic lupus erythematosus, namely, hematoxylin bodies, have been described in the Stevens-Johnson syndrome.[12] Indeed, subepidermal bullae seen in erythema multiforme have been described in systemic lupus erythematosus.[13]

Lupus erythematosus is a systemic disease with the widespread alteration of the connective tissue of many organs of the body. Its etiologic factors also have run the gamut of drugs, infection, endocrine imbalance, and allergic abnormalities. Autoimmune mechanisms have been proposed as a hypothesis to explain certain clinical features of this disease.[14]

The early presentation of systemic lupus erythematosus as idiopathic epilepsy has been emphasized.[15] The L.E. phenomenon and clinical picture have been reported in the hypersensitivity state induced by diphenylhydantoin sodium in epileptic patients.[16] Indeed, not only has the L.E. phenomenon been described with diphenylhydantoin sodium, but also there has been observed an increased incidence of allergic reaction associated with diphenylhydantoin sodium and trimethadione (Tridione) used in the treatment of convulsions occurring in disseminated lupus erythematosus.[17] Certain authors[18] have even suggested that the induced systemic lupus erythematosus syndrome caused by agents such as trimethadione or diphenylhydantoin sodium may indicate a pre-existing abnormality.

Agents such as these have been implicated as a cause of erythema multiforme with systemic organ involvement in several instances.[19-22] Therefore, we have a clinical syndrome, erythema multiforme, which may be difficult to separate from systemic lupus erythematosus in its vascular effects in distant organs and may be influenced by agents such as diphenylhydantoin sodium, trimethadione, and sulfa drugs.

Four cases have been observed which seem to reflect the spectrum of clinical manifestations cited previously. The first case revealed the classical Stevens-Johnson syndrome in a child who had a history of a febrile epileptic seizure at the age of one year with a history of familial atopy and who received a long-acting sulfa preparation.[23] The second case showed an epileptic patient with a malar butterfly eruption who received diphenylhydantoin sodium and who presented symptoms of the Stevens-Johnson syndrome, renal findings, and persistently negative L.E. cell preparations.

Case 3 was an epileptic patient on diphenylhydantoin sodium with a malar butterfly rash and involvement of the kidneys and liver, a history of positive serologic findings, and anemia. The Stevens-Johnson syndrome was manifested at her last admission. The fourth case was a patient with known systemic lupus erythematosus who, as part of her protean manifestation, revealed a clinical picture consistent with the diagnosis of the Stevens-Johnson syndrome.

In the first 3 cases the possible interplay of such factors as epilepsy, atopy, drug sensitivity, and systemic vascular involvement in the causation of a symptom complex prompted a comparison with the fourth case presented. A spectrum of autoimmune phenomena is suggestive with the vascular compartment capable of reacting to multiple etiologic factors. These observations would suggest that the altered host response, whether acquired or genetically determined, may be involved in "autoimmune" mechanisms.

It is concluded that certain clinical similarities have been witnessed in erythema multiforme and disseminated lupus erythematosus which suggest a hypersensitivity mechanism in both of them with an end organic response, such as vasculitis. This is in agreement with certain conclusions made by Rallison *et al.*,[24] further suggesting that erythema multiforme be viewed not as a benign disease, but as a strong suggestion for systemic involvement. A prolonged periodic observation is obligatory, as in the "chronic biologic false positive serologic reactor" or in patients having idiopathic positive heterophil antibodies, a positive Coombs test reaction, cold agglutinin titers of significance, hypergammaglobulinemia, leukopenia, anemia, thrombocytopenia, or the other manifestations of latent disseminated lupus erythematosus. The mechanisms for these closely related syndromes still are speculative. Newer work on the genetic nature of mesenchymal tissue diseases may be significant in elucidating common initiative events as well as observations of autoimmune phenomena.[25, 26]

Summary

Four cases of Stevens-Johnson syndrome are described which have in common certain anamnestic and clinical features. These when viewed in terms of the literature reports, support the concept that this vascular reaction of the skin should be considered as a reflection of a potentially reactive systemic angiitis found in the complex of disseminated lupus erythematosus.

119-05 80TH ROAD

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Study may lead to allergy avoidance

Studies of histamine-carrying cells have indicated a possible method of desensitizing persons allergic to such things as penicillin and insect bites.

Writing in the October 13 *Journal of the American Medical Association*, Walter B. Shelley, M.D., and William A. Caro, M.D., of Philadelphia, described the role of basophils and mast cells in the production of an allergic reaction.

When a person is challenged with a substance to which he is allergic, the authors said, both types of cells, the basophils in the blood and the mast cells in the skin, release histamine and disintegrate in the process. The release of histamine appears to be the basis for the primary signs of allergy.

Therefore, it might be possible to temporarily deplete what the researchers termed the "mastocyte-basophil" system and thus prevent the reaction. Individuals in "high hazard situations" in this way might be desensitized at will, and the authors feel that the possible role of histamine-releasing drugs deserves study in this connection.

Tracheoesophageal Fistula Without Atresia of the Esophagus

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TRACHEOESOPHAGEAL FISTULA without esophageal atresia has been dealt with only superficially in numerous writings on the general subject of esophageal atresia with tracheoesophageal fistula because of the apparent rarity of the lesion. This paucity of cases is more apparent than real, however, as is indicated by the series gathered from the literature by Lynn and Davis.[1] An awareness of this anomaly will lead to an early diagnosis with greater promise of successful treatment. A fistula should be suspected in the young infant who chokes on feedings and is subject to repeated pulmonary infections. The following case report is presented to illustrate these facts and to report a case which was successfully treated surgically.

Case report

An eleven-month-old male infant was admitted to the emergency room of the Lutheran Medical Center on July 1, 1954, in acute respiratory distress with marked dyspnea and cyanosis. He was born on August 3, 1953, in a private hospital in Brooklyn. He was the third sibling, born by a normal spontaneous delivery at term after an uneventful pregnancy. The infant was formula-fed and developed normally up to the fifth month at which time he developed repeated episodes of respiratory distress following feedings. These led to two admissions to other Brooklyn hospitals. The discharge diagnosis on both occasions was "acute laryngitis with bronchopneumonia." The infant was brought to the Lutheran Medical Center only a few hours after his discharge from the previous hospital. He had been given a feeding on arriving home and had choked on the feeding, with subsequent severe respiratory distress.

It is interesting to note that there was a history of several congenital anomalies on the maternal side of the infant's family and that a brother had died of a fulminating bronchopneumonia at the age of nine months.

A physical examination on admission revealed a normally developed infant of eleven months in obvious respiratory distress as evidenced by deep retraction of the intercostal and supraclavicular spaces. The nasopharynx was only slightly reddened, and no palpable cervical nodes were noted. On auscultation of the chest, moist rales were audible throughout both lung fields. The heart rate was rapid, but the sounds were normal with no audible murmurs. There were no obvious external congenital anomalies, and the remainder of the physical examination showed normal findings. A roentgenographic examination of the chest revealed bilateral infiltrative changes indicative of bilateral bronchopneumonia (Fig. 1).

The infant was placed immediately in an oxygen tent and started on antibiotics intramuscularly. On the second hospital day it was noted by the nurses that the infant started to cough when he was given oral fluids and soon thereafter was in acute respiratory distress. Further observation revealed the interesting fact that the infant would not cough when taking fluids lying on the right side or with the head turned to the left. The infant also assumed a characteristic position on his right side when he was given a bottle in bed and would turn his head to the left if he was given a bottle in the erect position.

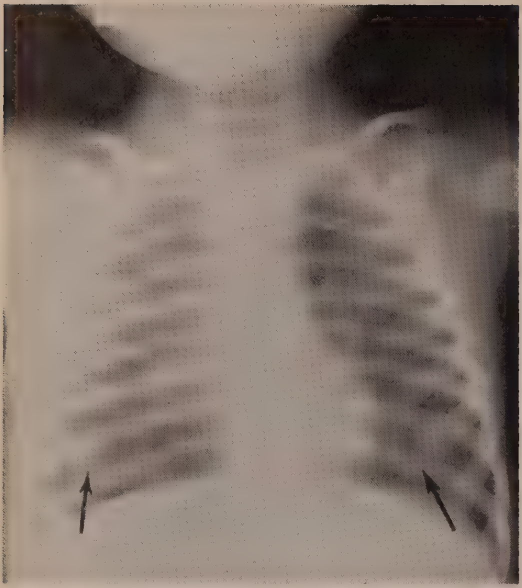

FIGURE 1. Admission x-ray film revealing bilateral bronchopneumonia.

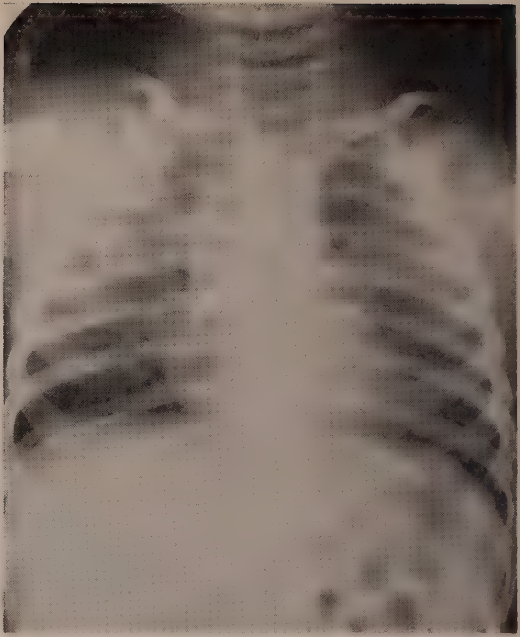

FIGURE 2. X-ray film revealing barium in right main bronchus.

Following these observations a tracheoesophageal fistula was strongly suspected, and therefore on July 6, 1954, the infant was given a small swallow of barium sulfate. X-ray films at this time revealed considerable barium in the trachea and in the right main bronchus (Fig. 2). The exact site of the fistula could not be determined on these films. Prompt postural drainage was instituted, and the barium was evacuated successfully, as indicated by subsequent x-ray films. On July 8, 1954, further efforts were made to localize the level of the fistula, atresia having been ruled out since barium had been seen passing into the stomach, and also on the original examination. A number 8 French catheter was passed into the esophagus without difficulty under fluoroscopic control to a level below the clavicles. A small amount of Iodochlorol was injected through the catheter and found to pass directly down the esophagus into the stomach with none evident in the tracheobronchial tree. The catheter was withdrawn to a point just below the cricopharyngeus, and more dye was injected. Now it passed not only down the esophagus into the stomach but also into the tracheobronchial tree (Fig. 3). It was concluded, therefore, that the fistula was in the cervical portion of the esophagus and not in the thoracic portion, so that the surgical approach to the fistula would necessarily have to be made through the neck rather than the chest.

By July 16, 1954, the infant's temperature had returned to normal with evidence of clearing of the original x-ray findings of bronchopneumonia. The infant's hydration and nutrition had been maintained without difficulty, and he was deemed adequately prepared for surgery. The cervical esophagus was explored through an incision along the anterior border of the sternocleidomastoid muscle on the left. The middle thyroid vein was divided for a better exposure of the esophagus. As the dissection approached the inferior cornu of the thyroid cartilage, a fistula approximately 2 to 3 mm. in diameter was encountered running from the trachea superiorly to the esophagus (Fig. 4). The fistulous tract was doubly ligated with fine silk sutures before it was divided, and a flap of areolar tissue was mobilized and placed between the trachea and the esophagus to prevent the recanalization of the

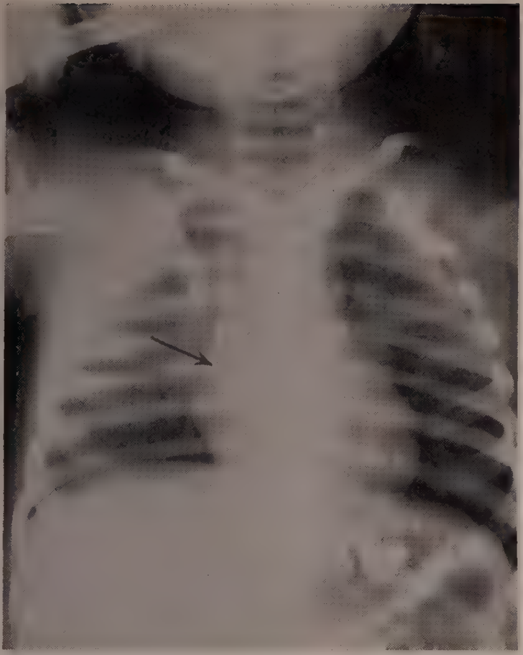

FIGURE 3. X-ray film showing radiopaque dye passing into tracheobronchial tree and into stomach.

fistula. The wound was closed in layers with fine silk sutures, without drainage.

Postoperatively the infant was fed through a polyethylene tube for five days, and the antibiotics were continued. There was no febrile reaction to the surgery. On the sixth postoperative day the infant was started on oral feedings. It was interesting to observe that he no longer assumed the characteristic preoperative position while drinking. Feedings were rapidly increased to a normal diet without evidence of respiratory distress. On August 18, 1954, a repeat esophagram was reported as showing entirely normal findings. The infant was discharged on September 12, 1954, having regained all of the weight which he had lost. A recent telephone conversation with the mother of the child established that he has remained well to date, except for occasional minor upper respiratory infections.

Comment

Although a search of the literature reveals only sporadic reports of successfully treated cases of tracheoesophageal fistula without atresia, it appears that more such cases are being reported because of the early recognition of this anomaly. The first successful closure of a tracheoesophageal fistula without atresia was reported by Imperatori in 1939.[2] It took two operations, however, to achieve closure in his six-and-one-half-year-old patient. Haight in 1948[3] reported the first successful closure of a tracheoesophageal fistula without atresia via the transthoracic route. His four-year-old patient had suffered seven bouts of pneumonitis before the anomaly was recognized. The third successful closure was reported by Helmsworth and Pryles in 1951.[4] Following this report there are increasing numbers of reported cases which were recognized early enough to be successfully treated surgically, as enumerated in the excellent reviews by Ferguson[5] and Lynn and Davis.[1]

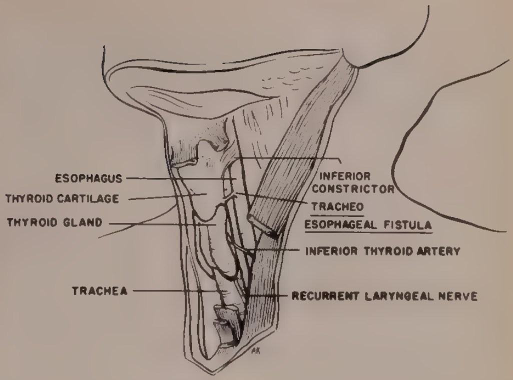

FIGURE 4. Illustration of tracheoesophageal fistula (connecting cricothyroid interval of trachea with esophagus).

Invariably these children choke on liquids with marked dyspnea, followed by severe coughing and cyanosis. Many of the children have repeated admissions to the hospital for pneumonitis. In addition, these children often have abdominal distention when crying because of an increased air intake into the gastrointestinal tract through the fistula, and on auscultation rales may be heard in the chest after the child is given liquids.

These fistulas are extremely difficult to demonstrate by x-ray film and even, at times, at the postmortem table. It is important to use a catheter in the esophagus to introduce a nonirritating opaque material such as 25 per cent Hypaque sodium at different levels for the selection of the proper surgical approach. A majority of the fistulas occur in the cervical esophagus, but some do occur below the level of the clavicles, and they necessitate a transthoracic approach. The films can best be taken in the right anterior oblique and in the lateral projections while the injection of the dye is continued after a fluoroscopic examination has demonstrated a fistula by the presence of dye in the tracheobronchial tree.

Esophagoscopy is of questionable value because of the small size of the infant esophagus, and, further, the small opening is often hidden in a longitudinal mucosal fold. It may possibly be used to identify methylene blue within the lumen of the esophagus after instillation high in the trachea via an endotracheal tube, if repeated attempts to visualize the fistula by x-ray film have failed. Occasionally the opening in the trachea can be seen on bronchoscopy if care is exercised in the examination of the posterior wall of the proximal trachea.

If all efforts to demonstrate the fistula fail, an exploration should be resorted to if the typical history can be obtained and there is evidence clinically or on the plain x-ray film that liquid enters the tracheobronchial tree when the infant drinks. The finding of bilateral pneumonitis should not contraindicate surgical correction of the defect since it is rarely fulminating and can be controlled easily with antibiotics.

In each case the fistula can be divided without difficulty after secure ligation of both ends of the tract. A flap of tissue may then be interposed between the severed ends to prevent recanalization of the fistulous tract.

Summary

A case of tracheoesophageal fistula without atresia of the esophagus, which was successfully corrected surgically, is presented to call attention to this anomaly which appears to be more common than is generally believed. Choking on the ingestion of liquids with coughing and cyanosis, abdominal distention on crying, and repeated episodes of pneumonitis should alert the pediatrician to be on the lookout for this anomaly. A prompt x-ray investigation should be undertaken with the instillation of radiopaque dye into the esophagus. If this fails to demonstrate the suspected fistula, surgical exploration should be resorted to in the presence of a typical history and clinical findings. When the fistula is demonstrated by x-ray examination or on endoscopy, surgery should be undertaken promptly even in the presence of pneumonitis, which is usually present in some degree when the fistula is demonstrated. A high index of suspicion on the part of the pediatrician, prompt efforts at the demonstration of the fistula, and early surgical correction of the anomaly will increase the number of cases which are treated successfully.

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Special Articles

The Australian Medical Care Plan

A Unique Partnership

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AUSTRALIA IS about as large as continental United States. Its Constitution and general governmental pattern has been derived from the same sources as our own. Its people are as freedom-loving and independent as Americans. The chief difference is in population. Australia has but 12 million as opposed to our 180 million people.

In spite of its size three quarters of Australia's population live in urban areas. Cities such as Melbourne, Sydney, Perth, Brisbane, and Adelaide might be Boston, Philadelphia, St. Louis, Minneapolis, or Rochester. An Australian or an American would feel equally at home in any of them.

Australia's medical schools and hospitals are of excellent quality. Its standards of health service rival ours. Medical literature from the United States is read by the doctors of Australia as though it were their own. The names of our distinguished doctors, hospital administrators, and health experts are well known to them.

If it is true that there are many similarities between the two nations it is also true that there are important differences. One of these differences is that like the citizens of nearby New Zealand, Australians have had to accept much more in the way of governmental control of wages and other economic aspects of their lives than we have in America. The present Australian Medical Care Plan devised by Sir Earle Page followed on the heels of the adoption of a governmental Welfare Plan which failed to deliver medical care although it was promised.

The central idea of the present Australian plan is to keep alive all of the local and individual incentives of doctors, hospitals, and citizens so that high-quality service is provided at the lowest possible cost. The origin and history of the plan and its present success may help us think through some of our problems, although they are somewhat more complex than those which faced Australia in 1952. Indeed it is the complexity of the medical, economic, social, managerial, and political factors in our situation which requires us to break them down into understandable components.

Medical care problem in the United States

MEDICAL CARE COSTS. A brief review of the broad outline of our problem as it relates to the United States reveals these facts about our national medical care costs. In 1948 the total private expenditure for medical care in the United States was $7,647,000,000. The cost of hospital care in short-term hospitals was $13 a day. Twelve years later in 1960, usage and cost had increased so that private medical care expenditure was $18.7 billion. During these eleven years hospital costs in the Middle Atlantic area went from $13 to $32 per day and in parts of the nation to as high as $50 a day.

Taken from another point of view the total cost of medical care, public and private, in the United States in 1948 was about $8 billion. By 1959 this had reached $22 billion and by 1960, $25 billion. Whereas in 1948 the total cost amounted to approximately 4 per cent of disposable personal income, in 1960 it was 5.4 per cent.

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* Deceased.

Read for the late E. A. van Steenwyk by Thomas S. Gates, Jr., at a meeting of the Medical Society of the County of Monroe, March 20, 1962, Rochester, New York.

These costs trends are dramatically illustrated in the experience of Philadelphia Blue Cross. The cost of hospital care for our present number of subscribers at the rate of utilization of days per 1,000 subscribers and the cost per day in effect for each of the three years—1940, 1950, and 1960, keeping all factors constant—for these years was respectively: 1940, $12 million; 1950, $21 million; and 1960, $60 million.

The trends in medical care costs make it clear why Blue Cross-Blue Shield have been subjected to public hearings on subscriber rates in all of the States. There is a limit to which such rates can go.

FACTORS IN MEDICAL CARE COSTS. What we do about the factors which affect medical care cost is a matter of utmost concern if our nation is to avoid transferring its medical care cost problem to government as has occurred in so much of the world. Such factors as controlled hospital expansion, to limit duplication of facilities so costly to maintain; extension of insurance coverage for medical expenses outside the hospital, to stop waste of hospital days; management and cost standards for health services, to give us proper guides in these matters; and acceptance by doctors of their part of the responsibility to control insured medical and hospital expenditures; all require collaborative work in every community to achieve a solid result.

I give you as an example of some local conflict on this a recent personal experience with our Physicians' Review Board and Hospital Administrators' Review Board. At a meeting with the Physicians' Review Board a doctor spoke up and said, "Of course, reasonable costs in hospital care will never be obtained until hospitals are operated on a seven-day-a-week basis, or at least six days, instead of the present four- or five-day basis." All of the doctors agreed. I then asked why this was so and was told that such was the way hospital management wanted it.

When I reported this discussion to the Hospital Administrators' Review Board, the Administrator members were uniformly of the opinion that the doctors did not want hospitals to be operated on a full scale on Saturday and Sunday. I hope that these two groups will come up with at least a partial solution to the waste in usage of hospital facilities, in Philadelphia, at least.

WHAT CAN BE DONE? On a common sense basis much can be done if those concerned in every community go to work on the aspects of the matter which are closest to hand. Progress may come in small bits and fractions, but these will add up to great community and national gains. Governmental authority could establish rules, but this creates more problems than it solves.

This is not to say that some governmental regulation may not be required or that governmental participation in solving the problem should be resisted. Once Sir Earle Page had created a program for Australia which assured the maintenance of private medicine and locally managed hospitals, Australian doctors and hospital and insurance people eagerly collaborated with their government.

Health care costs in the United States, in Australia, or anywhere in the modern world, are no longer solely a matter of the sick man's individual concern. All over the world this has now become a public issue on which some kind of public action may be expected. The question is what kind of public action could we in the United States support.

In this framework the Australian plan has significance to us even though there are important differences between our two nations. What works well in one country could fail in the other, what would be appropriate in one might not be in the other. In any case, an explanation of the partnership now existing between the Commonwealth government, doctors, hospitals, and voluntary insurance plans in Australia may help us get our own situation in better focus.

Development of Australia's program

Australia made a start toward a federal system of medical care in 1942. In that year the government imposed an income tax of about 7.5 per cent without limit to provide various welfare benefits including certain medical benefits and hospital service in wards. Ward service in hospitals was provided under this program for a time but the rates paid to the hospitals were so meager that other taxes had to be imposed to support hospitals. Medical benefits were never provided under this system. It was fortunate that the various private sick-benefit plans did not close up altogether when the governmental program was adopted because it was out of these voluntary medical and hospital care associations sponsored by trade unions, lodges, friendly societies, and other groups that Australia built its present system.

The full story on why medical benefits were not provided includes economic reasons, but a central consideration was a ruling of the High Court of Australia. Like our Supreme Court it is the arbiter of the Constitution. The court ruled that the requirements laid on physicians under the Welfare Plan amounted to civil conscription which is forbidden under the Constitution.

It was against this background of the failure of federal legislation to provide for medical care in Australia that Sir Earle Page became Minister for Health under the Menzies government. The people were in favor of a governmental system because no alternative had been proposed. Sir Earle met the desire of the people for protection against medical costs to everyone's satisfaction. He took it for granted that any program to be successful must assure all who needed care of prompt and efficient service. His philosophy, however, had also firmly imbedded in it the idea that the provision of care should be left in the "expert hands of the persons and the authorities who hitherto had handled them so well, the private doctor and the local hospitals."

To do this he proposed a program based on a partnership of the Commonwealth government, the hospitals, the medical profession, and voluntary health insurance organizations. Under this program the government safeguards the position of all members of the partnership through mutual agreements which can only be altered by common consent. The plan specifically provides that government will keep out of administrative responsibility for providing care or managing insurance.

The government supports preventive medicine through assistance in research. It also provides aid toward construction and improvement of medical schools and hospitals much as in the United States.

Under Page's program voluntary insurance plans receive a government subsidy in the form of a payment for each day of hospitalization or each item of medical service used by each insured person regardless of income. In effect the government says to the citizen, "It is your responsibility to enroll in a health insurance plan. When you do, the government, within limits, will match the insurance plan's payment for your care." This helps to keep the rates low, but it also assures the citizen of free choice of insurer, doctor, and hospital. Most important it keeps government out of the business of providing the service. On their part the voluntary insurance organizations administer the program without cost to the government. Every cent paid by government goes into medical or hospital care.

The Commonwealth also pays for certain "lifesaving" drugs dispensed by local drug stores or hospitals on the order of the physician. "Tonics" and common drug purchases are the individual's responsibility.

An all-out national campaign to eliminate tuberculosis in one generation is also supported by the government. Free diagnostic facilities are provided for all, and free treatment for those afflicted and cash allowances during the period of treatment for those with family responsibilities are also given so that normal family life will be maintained.

Free medical and hospital care is provided to pensioners. The doctors have cooperated in this by establishing lower fees for pensioners.

More recently the Commonwealth has adopted a system of Special Accounts which assures the voluntary plans that they will not lose by accepting certain risks if the government requests them to do so. For instance, the government has asked the plans to waive all waiting periods, even if a subscriber enrolls while on the way to the hospital. To the degree that this adversely affects a Plan's experience the government reimburses the Plan out of such a Special Account.

The subscription rates charged by cooperating insurance Plans are low compared with charges of Blue Cross and Blue Shield in America because the subsidy given by the Federal government is substantial.

The fact that pensioners' medical care costs are met by the government also relieves the insurance funds from the necessity of including a loading for this item in their subscription rates. This is now an important factor in the over-all rates needed by our Blue Cross-Blue Shield Plans.

The Australian system requires every insured person to pay some small charge for each medical service rendered or each day of hospital care received in addition to his modest subscription fee. It is believed that this small charge, never more than 10 per cent and often less, tends to reduce abuse. There appears to be no problem of double coverage under this system because no one can gain from such coverage.

One of the unique provisions of the legislation establishing the plan creates courts of doctors for various regions. These advise the Minister for Health as to penalties to be imposed on doctors who have wrongly taken advantage of the system. An unusual provision of this court is that lawyers may not represent the accused. The accused doctor appears before other doctors and is judged by them. If he is found guilty of wrongdoing he may be listed in medical publications as having been found guilty or may be delisted from receiving insurance funds for a month or longer. In extreme instances he may be delisted for life. It may be seen that the voluntary collaboration of doctors in Australia with government, hospitals, and the voluntary insurance plans has also been realistic. They have put teeth into their program and it is working. Action on all matters involving penalties is the responsibility of the Minister for Health.

The program has now enrolled more than 80 per cent of the population. Federal government spokesmen have often commented on its effective administration. While a master plan was created by Sir Earle Page, he had the foresight and wisdom to provide for the exercise of judgment of the partners in maintaining standards of service and economy thus freeing a tremendous reservoir of creative power within the partners. The government is also proud of the fact that not more than 20 persons on the Federal payroll are required to handle its responsibilities in the matter.

What Sir Earle set out to accomplish, to assure the nation that the matter of providing health services would be left in the hands of those who "hitherto had handled them so well—the private doctor and local hospitals"—has in fact been accomplished. Everyone is assured of necessary medical and hospital care at rates that are modest. Those who cannot pay even these rates are nonetheless assured of needed care.

A proposal for the United States

Whether or not we will learn from Australia and find our particular form of partnership with government depends on all of us who are involved, doctors, hospital people, and insurance and governmental leaders. The Blue Cross Association in January, 1962, made a practical proposal on the matter of hospital care for the aged which is now being widely considered. This is a national uniform contract for all persons over sixty-five years of age who desire it at uniform rates. Under this proposal subscription rates would be adjusted by levels of income, the government meeting the difference in premium for those with modest incomes or paying the premium altogether for those with little or no income instead of, as in Australia, matching payments made to every insured, regardless of income.

The advantage of local Blue Cross Plans federated for this purpose into a national instrument should be effective in the United States. More than this, the use of voluntary plans would keep a large part of present nongovernment funds going into care of the aged.

Earlier I referred to the fact that in 1960 total health care costs in the United States came to about $25 billion. It had not been noted that 20 per cent of this or $5 billion was used for the care of our 17 million aged individuals. Thus 9 per cent of our population, those over sixty-five years of age, are now using 20 per cent of all health dollars spent in the United States. The Social Security tax of one quarter of 1 per cent on employers and employees under the Administration Bill is expected to yield $1.4 billion the first year and nearly $2 billion by 1968. It is estimated that this will take care of benefits included for those covered under the program.

The Bill is of course only intended to cover those eligible under Social Security. The present Kerr-Mills Law will aid many older persons who are medically indigent. Nonetheless the question arises as to whether the money to be made available under the Administration Bill is new money or substitute money—substitute money for that which is now being paid by the aged themselves, their children, insurance organizations, and local governments. If it is new money more service will be given to our older citizens. If a substantial part of it is substitute money for that now being obtained from other sources the total service provided to the aged will not be increased. What I am trying to say is that if the Federal government would use the funds derived from this tax to supplement private sources more needed service could be provided.

Take for instance the subscriber who is over sixty-five years of age but who finds that present Blue Cross or other insurance coverage is beyond his means. He might be able to pay half the necessary subscription rate or a third. Why should he not continue to make modest payments even though the Social Security tax makes receipt of hospital care a right? The purpose of social insurance is to relieve a situation for those who need assistance most.

I do not mean to suggest that those who do not need assistance should be dealt out from receiving any benefits altogether. The taxpayer who has paid taxes for a hospital benefit should expect to receive something for his money. This could be done through a sliding scale which is suggested by the Blue Cross Association.

Assume for example, that the cost of providing adequate hospital, nursing home, and home care benefits for older persons is $12 per month per person, $24 per couple. Assume further, that every person receiving Social Security benefits regardless of income would be entitled to payment of half this cost. If a family man's income for tax purposes is over $6,000 per year he might pay $12 per month for coverage. If it were $5,000 to $6,000 he might pay less, $10 per month; from $4,000 to $5,000, $8 per month; from $3,000 to $4,000, $6 per month; from $2,000 to $3,000 he might pay $5 a month; and under $2,000 he would pay nothing. Under this concept much of the Social Security tax money collected for this purpose could be new money for medical care of those over sixty-five years of age. The government would thus make much of the money now being paid from private sources still available for care for the aged. It would increase the effectiveness of its dollars at the same time it created an effective partnership of voluntary and governmental agencies concerned with this problem. This would go a long way toward obtaining the necessary agreement of all concerned.

Comment

Anyone who has watched the succession of medical care bills considered by Congress for the past twenty years cannot help but conclude that governmental action of some kind may be expected. The mood of Congress is clearly that our ever enlarging number of the aged will not remain unprotected against medical care costs. On the other hand as present nongovernmental pension plans mature it may be expected that these programs and the basic old age benefits under Social Security will make it possible for more older people to participate modestly in meeting costs of private medical care insurance. This is therefore a good time for medicine, hospitals, and insurance to come forward with a program which will meet the need. If we can meet this need and if we can get to work on the control of medical care costs a new era in medical care will have arrived.

I do not believe that we can wait much longer on this matter. A responsible partnership with government which can capture the enthusiastic support of all can be created in America. Australia did it.

Drug Addiction Wave Among Adolescents

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Pharmacotherapy has never in the history of medicine assumed as prominent a role as it has in recent decades. This is true not only with respect to general medical practice but particularly with respect to the medical specialty dealing with mental and nervous diseases. The mounting use of pills, capsules, and injections has created the danger of misuse. Such misuse is becoming apparent in the form of a special kind of addiction among teen-aged youth which appears side-by-side with adult addiction to heroin and marihuana which today is a matter of such serious concern. Juvenile addiction has taken on the dimensions of a serious threat to juvenile health. It has been established that in some areas of New York City every seventh or eighth youngster indulges in uncontrolled and unselective self-administration of a large variety of drugs.

During the winter of 1961 to 1962, a group of medical and nonmedical child guidance specialists, including the writer, set out to collect some facts about habitual misuse of drugs by juveniles by surveying a number of areas in Greater New York and some suburban areas in Westchester County and Long Island. The following is a first report of the findings. Some reflections on prophylactic measures that might be taken to combat the problem are included.

Methods

The addiction manifests itself in four forms: (1) injection (intravenous and intramuscular); (2) drinking of certain patent medicines; (3) oral application of pills and capsules; and (4) inhalations by mouth or nose.

Injection. The drugs most frequently reported as taken by injection are ephedrine sulphate, Ritalin hydrochloride, Dilaudid hydrochloride, and cocaine. A few instances of heroin taken by injection were also reported.

Patent medicines. The drinking of "cod-cocks" (codeine "cocktails") was the most frequently reported misuse of patent medicines. The concoction consists of 8 to 12 ounces of one or more patent medicines containing codeine, of which a number are easily obtainable at drugstore counters. A case was reported of a sixteen-year-old boy who tried to make absinthe for himself from wormwood.

Pills and capsules. About 50 different hypnotic, tranquilizing, and stimulant drugs, taken indiscriminately in pill and capsule form, were reported. Among these were: LSD-25, atropine, P.A.D., Seconal sodium, Demerol, and Tuinal. Also reported were Benzedrine sulfate, Nembutal sodium, and Metamine, as well as the whole range of common tranquilizers and sleeping pills.

Inhalations. There have been reports in the press recently about addiction to gasoline and collodion. The present investigators found instances of the application of pharmaceutical agents which are used in anesthesia, chemicals which use ether as a base, and the excessive application of commercially sold inhalants such as Dristan. One boy possessed six containers of ether of the kind used in surgical anesthesia.

Process of addiction

An investigation of the reasons for taking these drugs revealed that they are dissimilar from the reason commonly reported by adult drug addicts: pathogenic irresistible craving. For most of the adolescents encountered in this survey who were "trying drugs," the reason given for doing so, for the most part, was to obtain a "thrill" or because "others do it." In some cases a youth wanted to appear "a good sport" among his clique. However, in quite a number of cases signs of habituation were found. The reasons given in these cases was enjoyment of the "otherness" of consciousness and being seen as a "hero" in the group. In some cases the youths were bound by secret pledges to the drug addiction group.

There is no doubt that quite a number of these youths will go from their playful taking of drugs to heroin and will eventually become real addicts.

There was little discrimination in the choice of drugs taken, although in some groups there was definite knowledge about the drugs being taken, especially those involving injection. In most instances there was a "big shot" who was able to get all kinds of drugs and who sold or distributed these without really knowing what they were or what their bad effects would be.

In some cases the entire social life of these adolescents, boys as well as girls, was centered around their addiction in a club-like pattern. In one instance, a club-like arrangement was found in a summer cottage section of outlying Brooklyn, where a group of youths, some of them truant from school, were spending days and nights indulging in cocaine. In one case, some youths were getting a "thrill" out of observing the others going into a state of unconsciousness or "getting high."

To the extent that it was possible to obtain information on this score, it appears that the drugs used were obtained by illegal means, mainly thefts from hospitals, doctors' offices, drug stores, and pharmaceutical distributing agencies. For the most part, those who stole the drugs were cleaning personnel and other low-grade employes who were paid little for these "goods." The actual sellers, suppliers, or "pushers" were apparently other youths, students, or "soda jerks"; there was also one instance of an addicted teacher who was a supplier. Most of the stolen goods are distributed in "five-" and "ten-cent" bags, for which the purchaser actually pays five or ten dollars.

The contents of the bags are in many cases unknown either to the seller or to the buyer. The writer was handed such bags, one of which contained aspirin and another Preludin. No doubt in many cases youths are defrauded by being sold placebo materials. Again and again the investigators were told that the only way the addicts had of determining what the "stuff" was by the color of the pills or the marking impressed on them, or simply by trying them out.

Some of the youngsters had books on toxicology and handbooks of drugs which are distributed freely. In many cases the young addicts were tragically misinformed about the nature of the drugs they were taking. Only in rare instances, when severe toxic conditions occurred, were parents, physicians, or guidance workers asked for help.

Comment

It appears that there are two aspects to the problem of dealing with this situation: first, by legal means to make it more difficult to obtain these pharmaceutical and chemical products; and second, by intensifying the guidance and control of the lives of our adolescents.

The threat of capital punishment has been a deterrent to kidnapping. It has been pointed out that drug addiction is a danger to health and safety serious enough to justify an increase in the punishment prescribed for "pushers" and other illegal distributors. A sentence of statutory life imprisonment for traffickers in drugs, while it would not stop such traffic, would no doubt greatly reduce it. It should be ruled a misdemeanor for physicians, hospital dispensaries, or drug stores to keep addictive products anywhere but in a safely locked place. Finally, certain drugs which attract addicts should not be distributed even in small doses without prescription. Prescription regulation should be more strictly enforced.

As for direct influence on adolescents themselves, parents and teachers should be alerted to the dangers of this type of addiction. We are now at a stage in educational development that calls for a considerable increase in guidance and psychologic services for adolescents. The wave of drug addiction discussed here is one evidence of how great the need for such services is and how urgent it is to make them available as quickly as possible.

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Abstracts

Blatz, H.: Radiation hazards from the standpoint of the practicing physician, New York State J. Med. **62:** 3893 (Dec. 15) 1962.

In general use of radiographic x-ray equipment and its installation, the operator of the equipment should be provided with a well-shielded control booth. Adequate shielding should be provided in the floor and in the wall behind the film holder. The patient should be given maximum protection from unnecessary radiation. A fluoroscope should never be used if the same examination could be performed by an x-ray film. The eyes should be well dark-adapted before a fluoroscopic examination. If a fluoroscopic screen is more than fifteen years old, or if it has been subjected to heavy use or abuse, it should be replaced.

Bunn, P. A., and Knight, R.: Alterations in chronic staphylococcal furunculosis by use of gamma globulin, New York State J. Med. **62:** 3899 (Dec. 15) 1962.

A study was made of 15 patients with chronically persisting, active staphylococcal skin disease to whom gamma globulin was given. Ten patients had an abrupt and favorable change in the course of their disease; 2 noted some improvement; and no benefit was noted in 3. Although the coincidence of therapy with improvement was striking, it is impossible to conclude that the gamma globulin played any role in altering the natural course of this remitting infection. Studies of the serum of the patients failed to show any change in antibody titers against staphylococci or in the construction of their protein pattern before, during, or after therapy.

King, R. B.: Neurosurgery in management of patients with cerebral vascular disease, New York State J. Med. **62:** 3908 (Dec. 15) 1962.

The development of cerebral angiography has made it possible to diagnose and determine the operability of such primary disorders of the cerebral vascular system as congenital arteriovenous malformations, congenital Berry-aneurysms, cerebral hematomas, and occlusive lesions of the aortic arch and carotid systems. Many of these lesions are associated with a low mortality and morbidity when the corrective procedures are planned on the basis of a careful clinical evaluation of the patient, selective angiography, and judicious use of newer surgical technics and adjuncts.

Mosher, J. F., Lefevre, I. D., and Yates, R. C.: Rational therapy of acute sore throat, New York State J. Med. **62:** 3913 (Dec. 15) 1962.

In experience with 1,420 cases of acute sore throat seen over three years, Staphylococcus aureus was present in 47 per cent of all cultures, beta hemolytic streptococcus in 28 per cent, and both Staph. aureus and beta hemolytic streptococcus in 9 per cent. No pathogens were isolated in 34 per cent. A correlation between suspected bacteriologic diagnosis and laboratory findings was poor. In therapy penicillin is given (1) when beta hemolytic streptococcus is isolated; (2) when the patient is obviously in a toxic condition, has had a history of rheumatic fever, nephritis, and previous severe suppurative complications, or has a pre-existing disease such as diabetes mellitus or congestive heart failure; and (3) if the attack is one of repeated episodes. Broad spectrum antibiotics are given only if there is definite evidence of penicillin allergy.

Klinges, K. G., Gibbons, J. M., Jr., and Pisani, B. J.: Clinical evaluation of a new analgesic in obstetrics and gynecology, New York State J. Med. **62:** 3918 (Dec. 15) 1962.

A study was made of the use of oxymorphone (Numorphan) in 300 patients in labor and 100 postoperative gynecologic patients. In the former group the analgesia obtained was good or excellent in 89 per cent. The onset of action was extremely rapid and the average duration of pain relief, from three to four hours. The drug lacks deep sedative properties, and the side-effects were minimal. Labor was considered prolonged in 10 per cent of the patients, and contractions were weakened in 5 per cent following administration of oxymorphone. There was a greater incidence of respiratory depression in the newborn infants in those mothers who received oxymorphone less than thirty minutes before delivery, and general anesthesia seemed to account for a threefold increase in the number of severely depressed infants. In the surgical-gynecologic group analgesia provided by oxymorphone was uniformly satisfactory with few side-reactions and a lesser incidence of nausea and vomiting than is usually seen with meperidine.

Klickstein, G. D., Edmunds, R. T., and Allen, P. D.: Immediate laparotomy in penetrating wounds of the abdomen, New York State J. Med. **62:** 3923 (Dec. 15) 1962.

A study was made of 100 consecutive cases of suspected penetrating wounds of the abdomen in which immediate laparotomy was performed. In 85 cases the wounds were found to penetrate the peritoneum, and in 71 the liver or other viscera were injured. The hospital stay averaged 14.1 days for the penetrating group and 11.3 for the nonpenetrating. Complications were infrequent, and it would seem that prompt surgical intervention and the use of antibiotics played a part in the low infection rate. There were no deaths in the nonpenetrating group.

Cholst, M. R., Cohen, I. J., and Losty, M. A.: Evaluation of amblyopia problem in the child, New York State J. Med. **62:** 3927 (Dec. 15) 1962.

The diagnosis before the age of six years of amblyopia, which affects the central vision only and may or may not be accompanied by a "turned eye," is not customary. However, early diagnosis and treatment are necessary for a favorable prognosis. Therefore a specific amblyopia screening program, to begin at about four years of age, and a thorough elucidation of all aspects of amblyopia, involving general physicians, pediatricians, private and public health nursing personnel, teachers, health counselors, and public health officials, are recommended.

Baum, V., and Eufrate, S. A.: Inferior mesenteric artery injury; a complication of translumbar aortography, New York State J. Med. **62:** 3931 (Dec. 15) 1962.

Two cases of inferior mesenteric injury following translumbar aortography are presented, 1 with a fatal outcome and 1 with complete recovery attributable partly to prompt diagnosis and therapy. Most of the complications of translumbar aortography and the contrast media employed arise as a consequence of breaks in the accepted standardized technic. Other factors include needle penetration, needle position, injection of radiopaque material, and a combination of two or more of these factors. A low translumbar approach is preferred, with a second needle at a different level used only when necessary.

Bouton, M. A., and Warner, G. M.: Day hospital rehabilitation of the chronically ill patient; preliminary report of a three-year experience in Schenectady, New York, New York State J. Med. **62:** 3944 (Dec. 15) 1962.

A study was made of 80 day patients suffering from cerebral vascular accident and disorders of the central nervous and skeletal systems. The median age was sixty-two years and the median duration of disability prior to admission, six months. Fifty per cent required an evaluation and work-up on an inpatient basis before being transferred to the day program. The median of care was two and one-half days per workweek, generally for periods of up to ten weeks. Physical profiles were measured by five different scoring methods; the scores showed considerable improvement in a significant percentage of cases. Financing was handled privately in 50 per cent of the cases, by insurance with or without private payments in 26 per cent, and by public assistance in 21 per cent.

High-altitude skiing found hazardous

High altitude skiing can be hazardous for certain susceptible individuals, according to an editorial in the September 29 *Journal of the American Medical Association.*

Published reports of two skiers who developed a potentially fatal lung condition while skiing at altitudes of from 6,000 to 10,300 feet were cited in the editorial.

The skiers, both physicians, aged forty-six and forty-eight, experienced difficulty in breathing, developed a cough, and turned blue from lack of oxygen. Their condition was diagnosed as pulmonary edema, a leakage of fluid into the air spaces and tissues of the lungs.

The forty-eight-year-old physician was near death when admitted to a hospital, but both patients recovered rapidly with oxygen therapy and bed rest.

These studies suggest that the syndrome is due to a transient constriction of the minute veins of the lung. There are also indications that susceptibility may be inherited.

Necrology

John Jaquelin Ambler, M.D., of New York City, died on November 7 at St. Elizabeth's Hospital at the age of fifty-seven. Dr. Ambler graduated in 1931 from the University of Virginia Department of Medicine. He was an attending neurosurgeon at Misericordia Hospital, chief of neurosurgery at St. Elizabeth's Hospital, and a consulting neurosurgeon at St. Vincent's Hospital, Staten Island. Dr. Ambler was a Fellow of the American Academy of Compensation Medicine, Inc., and a member of the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Earle Godfrey Brown, M.D., of Milltown, New Jersey, formerly of Garden City, retired, died on November 1 at the age of seventy-four. Dr. Brown graduated in 1913 from Northwestern University Medical School. Until 1937 he was commissioner of health for Nassau County. Dr. Brown was a Diplomate of the American Board of Preventive Medicine (Public Health) and a member of the American Public Health Association and the Association of Military Surgeons of the United States.

John Francis Xavier Cline, M.D., of New York City, died on October 3 at the age of thirty-three. Dr. Cline graduated in 1954 from New York Medical College.

Carl James De Sando, M.D., of Rochester, died on September 28 at St. Mary's Hospital at the age of forty-seven. Dr. De Sando graduated in 1938 from Georgetown University School of Medicine. He was assistant director of professional services at Monroe County Infirmary and a consulting physician in general practice at St. Mary's Hospital. Dr. De Sando was a member of the Rochester Academy of Medicine, the Monroe County Medical Society, and the Medical Society of the State of New York.

Desiderius Groszberg, M.D., of Northport, died on March 19. Dr. Groszberg received his medical degree from the University of Budapest in 1921. He was attending pathologist and chief of the laboratory at the Veterans Administration Hospital, Northport. Dr. Groszberg was a Diplomate of the American Board of Pathology, a Fellow of the American College of Physicians, and a member of the Association of Military Surgeons of the United States.

Edwin Horton Huntington, M.D., of Ossining, died on September 29 at Phelps Memorial Hospital, North Tarrytown, at the age of seventy-eight. Dr. Huntington graduated in 1914 from Albany Medical College. Former medical examiner of Westchester County, he was an honorary member of the medical staff of Phelps Memorial Hospital. Dr. Huntington was a member of the Westchester Academy of Medicine, the Westchester County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Edward Leder, M.D., of New York City, died on November 7 at his home in Brooklyn at the age of sixty-six. Dr. Leder graduated in 1920 from Long Island College Hospital Medical School. Retired in 1962 as principal examining physician for the New York State Workmen's Compensation Board, he was a consulting physician in occupational medicine at Columbus, and Holy Family, and St. Peter's Hospitals, a consulting physician in physical medicine and rehabilitation at Long Island College Hospital, and an associate attending physician in physical medicine and rehabilitation at St. Vincent's Hospital. Dr. Leder was a Diplomate of the American Board of Preventive Medicine, Inc. (Occupational Medicine), a Fellow of the American College of Gastroenterology, a Fellow of the American College of Chest Physicians, a Fellow of the American College of Preventive Medicine, a Fellow of the American Academy of Compensation Medicine, Inc., and a member of the American Board of Legal Medicine, the Industrial Medical Association, the New York Academy of Preventive Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Frank Pearlstein, M.D., of New York City, died on October 4 at the age of eighty. Dr. Pearlstein graduated in 1912 from Long Island College Hospital Medical School. He was a Diplomate of the American Board of Radiology (Diagnostic Roentgenology) and a member of the New York Academy of Medicine, the New York County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Samuel Harold Pohl, M.D., of Brooklyn, died on October 30 at Maimonides Hospital of

Brooklyn at the age of sixty-six. Dr. Pohl graduated in 1924 from Boston University School of Medicine. He was an associate attending pediatrician at Coney Island Hospital. Dr. Pohl was a member of the Kings County Medical Society and the Medical Society of the State of New York.

Frederick John Pratt, M.D., of Rome, died on September 22 at his home at the age of sixty-one. Dr. Pratt graduated in 1924 from Albany Medical College. He was a Diplomate of the American Board of Otolaryngology and a member of the Saratoga County Medical Society and the Medical Society of the State of New York.

Joseph Ricklin, M.D., of Brooklyn, died on November 7 at his home at the age of fifty-six. Dr. Ricklin graduated in 1936 from New York University Medical School. He was a member of the Kings County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Harvey C. Schneider, M.D., of Buffalo, died on October 1 at Buffalo General Hospital at the age of sixty-seven. Dr. Schneider graduated in 1919 from the University of Buffalo School of Medicine. He was an associate consulting physician at the Edward J. Meyer Memorial Hospital, a consulting internist at Buffalo State Hospital, and consulting physician at Buffalo General Hospital. Dr. Schneider was a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Joseph E. Vigeant, M.D., of Red Hook, died on November 8 at his home at the age of ninety. Dr. Vigeant graduated in 1896 from Albany Medical College. He was an attending physician at Northern Dutchess Health Service Center in Rhinebeck. A past-president of the Dutchess and Putnam Counties Medical Societies, Dr. Vigeant was a member of the Dutchess County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Erna Weil, M.D., of Merrick, died on September 1 at the age of fifty-five. Dr. Weil received his medical degree from the University of Munich in 1931. He was an attending psychiatrist at Meadowbrook Hospital Outpatient Department. Dr. Weil was a member of the Nassau Neuropsychiatric Society, the Nassau County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Wiley Merlio Wilson, M.D., of New York City, died on November 7 at The Mount Sinai Hospital at the age of eighty. Dr. Wilson graduated in 1918 from Howard University College of Medicine.

George Wineburgh, M.D., of Utica, died on October 19 at St. Elizabeth's Hospital at the age of fifty. Dr. Wineburgh graduated in 1937 from Cornell University Medical College. He was an attending surgeon at St. Elizabeth's Hospital and an attending surgeon in gynecology at Marcy State Hospital. Dr. Wineburgh was a member of the Utica Academy of Medicine, the Oneida County Medical Society, the Medical Society of the State of New York, and the American Medical Association.

Irving Zweifler, M.D., of Brooklyn, died on November 3 at the age of sixty. Dr. Zweifler graduated in 1926 from New York University and Bellevue Hospital Medical School. He was an associate attending physician at Kings County Hospital Medical Center and at Unity Hospital of Brooklyn. Dr. Zweifler was a Fellow of the American College of Cardiology and a member of the New York Cardiological Society, the Kings County Medical Society, and the Medical Society of the State of New York.

Abstracts in Interlingua

Blatz, H.: Riscos de irradiation ab le puncto de vista del medico practic (*anglese*), NEW YORK STATE J. MED. **62:** 3893 (15 de decembre) 1962.

In le uso general de un apparatura roentgenographic, le operator debe haber a su disposition un ben blindate cabina de commanda. Un adequate blindage debe esser installate in le solo e in le muro in retro del porta-pelliculas. Le patiente debe esser protegite maximalmente contra omne irradiation non necessari. Un fluoroscopio debe nunquam esser usate si le mesme examine es executabile per medio de un simple roentgenographia. Le oculos debe esser adjustate al obscuro ante un examine fluoroscopic. Si le ecran de fluoroscopia es ancian de plus que 15 annos o si illo ha essite fortemente usate o abusate, illo debe esser reimplaciate.

Bunn, P. A., e Knight, R.: Alterationes in chronic furunculosis staphylococcal per le uso de globulina gamma (*anglese*), NEW YORK STATE J. MED. **62:** 3899 (15 de decembre) 1962.

Esseva interprendite un studio de 15 patientes con chronicamente persistente active morbo cutanee a staphylococcos qui esseva tractate con globulina gamma. Dece del patientes experientiava un abrupte e favorabile alteration in le curso de lor morbo; 2 notava un certe grado de melioration; e nulle beneficio esseva notate in 3. Ben que le coincidentia del therapia con le melioration esseva frappante, il es impossibile asserer que le globulina gamma habeva un rolo in alterar le curso natural de iste remittente infection. Studios del seros del patientes non demonstrava ulle alteration in le titros de anticorpore anti staphylococcos o in le structura de lor configuration proteinic ante, durante, o post le therapia.

King, R. B.: Neurochirurgia in le tractamento de patientes con morbo cerebro-vascular (*anglese*), NEW YORK STATE J. MED. **62:** 3908 (15 de decembre) 1962.

Le disveloppamento del angiographia cerebral ha rendite possibile diagnosticar e determinar le operabilitate de disordines primari del systema cerebro-vascular como per exemplo congenite malformationes arteriovenose, congenite aneurysmas de Berry, hematomas cerebral, e lesiones occlusive del arco aortic e del systemas carotic. Multes de iste lesiones es associate con basse mortalitate e morbiditate, providite que le mesuras corrective es planate a base de un caute evalutation clinic del patiente, de angiographia selective, e de un judiciose use de moderne technicas e auxilios chirurgic.

Mosher, J. F., Lefevre, I. D., e Yates, R. C.: Therapia rational de acute mal de gurgite (*anglese*), NEW YORK STATE J. MED. **62:** 3913 (15 de decembre) 1962.

In 1.420 casos de acute mal de gurgite vidite in le curso de tres annos, 47 pro cento rendeva culturas de Staphylococcus aureus, 28 pro cento rendeva culturas de streptococco hemolytic beta, e 9 pro cento rendeva culturas con tanto Staph. aureus como etiam streptococco hemolytic beta. Nulle pathogenos esseva isolate in 34 pro cento del casos. Le correlation inter le suspicite diagnose bacteriologic e le constatationes laboratorial esseva pauco impressionante. Quanto al therapia, penicillina es usate (1) quando streptococco hemolytic beta es isolate, (2) quando le patiente es obviemente in un condition toxic, ha antecedentes de febre rheumatic, nephritis, o sever complicationes suppurative, o ha un pre-existente morbo como per exemplo diabete mellite o congestive disfallimento cardiac, e (3) quando le attacco es un in un serie de episodios. Antibioticos a large spectro es usate solmente in le presentia de definitemente evidente allergia a penicillina.

Klinges, K. G., Gibbons, J. M., Jr., e Pisani, B. J.: Evalutation de un nove analgesico in le practica obstetric e gynecologic (*anglese*), NEW YORK STATE J. MED. **62:** 3918 (15 de decembre) 1962.

Esseva interprendite un studio de oxymorphona (Numorphan) usate in 300 patientes in labores e in 100 patientes gynecologic postoperatori. In le prime de iste duo gruppos, le analgesia effectuate esseva bon o excellente in 89 pro cento del casos. Le accusation del efficacia esseva extrememente rapide, e le duration medie del alleviamento del dolores esseva tres a quatro horas. Le pharmaco es sin profunde effecto sedative. Le adverse effectos secundari esseva minime. Esseva judicate que le labores esseva prolongate post le administration de oxymorphona in 10 pro cento del patientes, e le fortia del contractiones pareva esser reducite in 5 pro cento. Esseva notate un augmento del incidentia de depression respiratori in neonatos ab matres tractate con oxymorphona minus que trenta minutas ante le parturition. Anesthesia general pareva resultar in un triplication del numero de severmente deprimite infantes. In le gruppo chirurgico-gynecologic, le analgesia providite per oxymorphona esseva uniformemente satisfacente con pauc adverse reactiones lateral e un plus basse incidentia de nausea e vomito que lo que es usualmente incontrate in le uso de meperidina.

Klickstein, G. D., Edmunds, R. T., e Allen, P. D.: Laparotomia immediate in vulneres penetrante del abdomine (*anglese*), NEW YORK STATE J. MED. **62:** 3923 (15 de decembre) 1962.

Esseva studiate 100 consecutive casos de suspicite vulneres penetrante del abdomine in le quales laparotomia immediate esseva effectuate. In 85 del casos il esseva trovate que le vulnere penetrava in le peritoneo. In 71 le hepate o altere visceres esseva lesionate. Le duration medie del sojorno al hospital esseva 14,1 dies in le gruppo con vulneres penetrante e 11,3 dies in illo con vulneres non-penetrante. Complicationes esseva infrequente, e il pare que prompte intervention chirurgic e le uso de antibioticos habeva un rolo in tener le infectiones a un basse nivello de incidentia. Nulle morte occurreva in le gruppo a vulneres non-penetrante.

Cholst, M. R., Cohen, I. J., e Losty, M. A.: Evalutation del problema de amblyopia in juveniles (*anglese*), NEW YORK STATE J. MED. **62:** 3927 (15 de decembre) 1962.

Non es costumari, a etates de infra sex annos, diagnosticar amblyopia que affice solmente le vision central e que pote sed non debe esser accompaniate de un "oculo tornate." Tamen, precoce diagnose e tractamento es necessari pro un favorabile prognose. Per consequente, es recommendate le establimento de un specific programma de detection pro amblyopia, comenciante al etate de circa quatro annos e comprendente un meticulose elucidation de omne aspectos de amblyopia con le cooperation del medico general, del pediatro, del personal de assistentia de hygiene public, de instructores scholari, de consulentes de hygiene, e de functionarios de hygiene public.

Baum, V., e Eufrate, S. A.: Vulneration del arteria mesenteric inferior; un complication de aortographia translumbar (*anglese*), NEW YORK STATE J. MED. **62:** 3931 (15 de decembre) 1962.

Es presentate duo casos de vulneration del arteria mesenteric inferior post aortographia translumbar. Un del casos se terminava in le morte del patiente. Le altere esseva sequite de un complete restablimento, attribuibile in parte al prompte diagnose e therapia. Le majoritate del complicationes de aortographia translumbar, incluse illos causate per le medios de contrasto usate, resulta de deviationes ab le acceptate technica standard. Altere factores include le penetration del agulia, le positionamento del agulia, le injection de material radio-opac, e un combination de duo o tres de iste factores. Un basse via de accesso translumbar es a preferer, con un secunde agulia a un altere nivello usate solmente in caso de necessitate.

Bouton, M. A., e Warner, G. M.: Rehabilitation al hospital de die pro le patiente chronicamente malade; reporto preliminari a base de tres annos de experientia in Schenectady, New York (*anglese*), NEW YORK STATE J. MED. **62:** 3944 (15 de decembre) 1962.

Esseva effectuate un studio de 80 patientes de die, suffrente de accidentes cerebro-vascular o de disordines del systemas nervose central o skeletic. Le etate median esseva sexanta-duo annos, e le duration median del invaliditate ante le admission al hospital esseva sex menses. Cinquanta pro cento del subjectos requireva studios evalutatori a base de hospitalisation total ante lor transferimento al programma de die. Le presentia median amontava a duo dies e medie per septimana, usualmente durante periodos de usque a dece septimanas. Profilos del stato physic esseva establite secundo cinque differente methodos de evalutation. Le cifras evalutatori reflecteva un considerabile melioration in un significative procentage de casos. Le expensas esseva coperite ex ressources private in 50 pro cento del casos, per assecurantia con o sin pagamentos private in 26 pro cento, e per assistentia public in 21 pro cento.

Medical Meetings

Albany Medical College seminar cruise

Albany Medical College of Union University announces its fourth postgraduate medical seminar cruise to be held January 4 through 16. The twelve-day cruise will be aboard the Swedish American Line vessel the *M. S. Gripsholm.* Ports of call are: St. Thomas, Virgin Islands; San Juan, Puerto Rico; Cap Haitien, Haiti; and Nassau, The Bahamas.

Members of the Medical College faculty will present a comprehensive postgraduate medical program, covering subjects in internal medicine, surgery, and obstetrics and gynecology. The seminar constitutes 23 hours of category I credit toward the postgraduate requirements of the American Academy of General Practice.

For information write to: Department of Postgraduate Medicine, Albany Medical College, Albany 8, New York.

Bronx Pediatric Society

Alfred Bongiovanni, M.D., acting chairman and professor of pediatrics of the University of Pennsylvania School of Medicine, will address the Bronx Pediatric Society on Wednesday, 8:30 P.M., January 9. Dr. Bongiovanni's topic will be "The Adrenogenital Syndrome." The meeting, which is sponsored by the Smith, Kline and French Laboratories, will be held in the auditorium of Morrisania City Hospital, 168th Street and Gerard Avenue, the Bronx. Nonmembers are cordially invited.

American Diabetes Association

The Committee on Professional Education of the American Diabetes Association in cooperation with the New England Diabetes Association will present a postgraduate course in diabetes January 16 through 18 at the Statler Hilton, Boston, Massachusetts. All aspects of the disease will be considered. Eighteen hours of category II credit will be given by The American Academy of General Practice.

For further information contact: American Diabetes Association, 1 East 45th Street, New York 17, New York.

Illinois Association for Maternal and Infant Health

The seventh Illinois congress for maternal and infant health will be held at the St. Nicholas Hotel, Springfield, Illinois, February 6 through 8. The congress will be sponsored by the Illinois Association for Maternal and Infant Health in cooperation with the American Association for Maternal and Infant Health.

For information write to: American Association for Maternal and Infant Health, 116 South Michigan Avenue, Chicago 3, Illinois.

West Virginia Academy of Ophthalmology and Otolaryngology

The West Virginia Academy of Ophthalmology and Otolaryngology will hold its sixteenth annual meeting at the Greenbrier Hotel, White Sulphur Springs, West Virginia, April 17 through 20.

For information write to: Worthy W. McKinney, M.D., Secretary, West Virginia Academy of Ophthalmology and Otolaryngology, Professional Park, Beckley, West Virginia.

International council of group psychotherapy

The third international congress of group psychotherapy will be held in Milano-Stresa, Italy, August 2 through 6, 1963. The congress is sponsored by the government of Milano, the University of Milano, and the International Council of Group Psychotherapy representing 77 countries.

This year the congress will deal with new developments of group psychotherapy and its influence on mental hygiene, psychiatry, and society at large.

For further information write to: Jacob L. Moreno, M.D., P.O. Box 311, Beacon, New York.

Medical News

The Dr. A. Charles Posner Alumni Club

The Dr. A. Charles Posner Alumni Club has been formed by colleagues, friends, and residents, both past and present, of Dr. Posner. Dr. Posner, who is soon to retire as director of obstetrics of Harlem Hospital and the Fulton Division of the Bronx Lebanon Hospital, was formerly chairman of District II, American College of Obstetricians and Gynecologists.

Membership is open to all obstetricians and gynecologists who have been or are associated with Dr. Posner. There are no dues. Applications may be obtained from: Murray Arnold, M.D., or Norman Fisk, M.D., Harlem Hospital, 137th Street and Lenox Avenue, New York, New York.

Course on bone and joint disease

A five-day, full-time lecture course to supply a formal context and a systematic approach to the pathology of bone and joint disease will be given by Lent C. Johnson, Jr., M.D., Washington, D.C., at the New York Medical College, 1 East 105th Street, New York City, January 1 through 5. The course is intended primarily for orthopedic surgery residents and as an advanced course for pathologists.

Applications may be obtained from: Arthur A. Michele, M.D., Department of Orthopedic Surgery, New York Medical College, 1 East 105th Street, New York 29, New York.

Postgraduate course on diseases of the blood vessels and thromboembolism

The American College of Physicians will present a postgraduate course on diseases of blood vessels and problems of thromboembolism, its diagnosis and treatment, January 21 through 25, at Cornell University Medical College and The New York Hospital. The course is especially directed to internists, cardiologists, and practitioners of general medicine.

For further information write to: The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pennsylvania.

Psychiatric problems in general practice

The Department of Postgraduate Medicine of the Albany Medical College announces an advanced course in psychiatric problems in general medical practice. A total of ten sessions will be given on Thursday afternoons from 12:30 to 3:00 P.M. beginning January 3 and concluding in June, 1963.

The course is limited in registration. Two instructors will be provided for each group of five physicians. Preference will be given to those who have had the basic orientation course or previous psychiatric training.

For further information contact: Chairman, Department of Postgraduate Medicine, Albany Medical College, Albany 8, New York.

Awards given for study of sterility

Michael Newton, M.D., chairman of the awards committee of the American Society for the Study of Sterility has announced that the following three awards will be presented at the annual meeting of the American Society for the Study of Sterility in New York City, April 19 through 21.

The Ortho Medal—The Ortho Medal and the sum of $1,000 will be awarded to a recipient selected on the basis of his contributions in the field of sterility and fertility or related subjects during the years 1960, 1961, and 1962. The money is to be used by the recipient for expenses in visiting medical and research centers of his choice.

The Rubin Award—The Rubin Award, consisting of a certificate of merit and the sum of $250 will be awarded to the author(s) whose paper is deemed to be the most significant contribution among papers appearing in the society's journal *Fertility and Sterility* during 1962.

The Carl G. Hartman Grant-in-Aid—The Carl G. Hartman Grant-in-Aid in the amount of $500 will be awarded to the most meritorious research project in fertility and sterility or related subjects. Applications for this grant should be sent to: Michael Newton, M.D., Chairman, Awards Committee, American Society for the Study of Sterility, 2500 North State Street, Jackson 6, Mississippi, before March 1. The applications should be accompanied by an original and one carbon copy of an outline of the proposed research. The outline should be brief but sufficiently detailed for the committee to evaluate.

Lectures at Maimonides Hospital

The Department of Pediatrics of Maimonides Hospital of Brooklyn, 4802 Tenth Avenue, Brooklyn 19, New York, is offering a series of conferences to be held on Tuesday mornings at 10:00 A.M. in the solarium of the Kronish Pavilion at the hospital.

The program is as follows: December 18—

"Dangers of Teratogenic and Other Agents for the Pregnant Woman," Sidney Q. Cohlan, M.D.; January 8—"Timing in Pediatric Surgery," Bertram Cohn, M.D.; January 15—"Pathogenesis of Hydrocephalus," Stanley Aronson, M.D.; January 22—"Proctologic Problems in the Juvenile Patient," Robert Turell, M.D.; February 5—"Differential Diagnosis of Hypocalcemia in Infancy and Childhood," Donald Gribetz, M.D.; February 19—"Protozoan Infections in Children—Prevalence, Clinical Manifestations, and Therapy," Howard B. Shookhoff, M.D.; March 12—"Medical Considerations of Pediatric Diseases of the Chest," Saul Starr, M.D.; March 19—"Rehabilitation Potentials of the Pediatric Patient with Long-Term Disabling Disease," Joseph G. Benton, M.D.; and April 2—"Differentiation of Pulmonic Stenosis, Ventricular Septal Defect with Normal Aortic Root from Tetralogy of Fallot," Robert Rosenblum, M.D.; April 23—"Specific Reading Disability," Archie A. Silver, M.D.; May 7—"Chronically Distended Bladder in Children," Keith Waterhouse, M.D.; May 14—"Hemolytic Disease in Infancy and Childhood," Marion Erlandson, M.D.

Personalities

Honored. Charles F. McCarty, M.D., Brooklyn, at a dinner given in his honor by the Coordinating Council of the First District Branch of the Medical Society of the State of New York, and the Medical Society of the County of Kings on November 15 at the Hotel St. George in Brooklyn . . . the late John J. Masterson, M.D., Brooklyn, as guest of honor at a testimonial dinner and dance on November 3 given by the Consultant Medical Advisors, Chairmen, and Board Members of the New York City Selective Service System.

Installed. Albert M. Betcher, M.D., New York City, as president of the American Society of Anesthesiologists.

Resigns. T. Campbell Thompson, M.D., New York City, as surgeon-in-chief of the Hospital for Special Surgery after twenty-eight years of service to the hospital.

Elected. Robert G. Hicks, M.D., New York City, re-elected as assistant treasurer of the American Society of Anesthesiologists . . . Allyn B. Ley, M.D., New York City, to the board of directors of the American Association of Blood Banks . . . M. Murray Peshkin, M.D., New York City, as president-elect of the Academy of Psychosomatic Medicine.

Appointed. James A. Brussel, M.D., as associate editor of *Psychiatric Quarterly* and *Psychiatric Quarterly Supplement* . . . Catherine B. Hess, M.D., Philadelphia, as Assistant Commissioner, and executive director of chronic disease services, the City of New York Department of Health . . . P. Peter Piliero, M.D., Bronx, as assistant medical director of the New York Telephone Company in charge of the Manhattan-Bronx-Westchester territory of the Company . . . William G. Thurman, M.D., White Plains, as attending pediatrician and chairman of the Department of Pediatrics at Memorial Hospital for Cancer and Allied Diseases, New York City . . . Harold M. M. Tovell, M.D., New York City, as director of the Department of Obstetrics and Gynecology at St. Lukes' Hospital, New York City.

Awarded. Anthony C. Cipollaro, M.D., New York City, the 1961 Clement Cleveland Award of the New York City Cancer Committee of the American Cancer Society for his "outstanding work in the campaign to control cancer" . . . Irving S. Cooper, M.D., New York City, the annual Barbara Shaskan Memorial Award . . . John H. Mulholland, M.D., New York City, an achievement award from New York University's University Heights Alumni Association.

Speakers. Richard D. Brasfield, M.D., New York City, on October 31 at a meeting of the Metropolitan New York Chapter of the American Medical Writers Association on the subject of his impressions of the practice of medicine in the Soviet Union gathered during his participation in the eighth international cancer conference in Moscow in July . . . Arthur Gerard DeVoe, M.D., on November 26 before the members of the Long Island Ophthalmological Society on the subject "Congenital Cataracts" . . . Paul H. Hoch, M.D., Commissioner, State of New York Department of Mental Hygiene at the first public meeting of the Federation of Mental Health Centers on November 4 . . . George James, M.D., Commissioner, City of New York Department of Health, on November 13 at a conference on the problems of venereal disease held at the Waldorf-Astoria Hotel . . . Gustav Machol, M.D., Brooklyn, on November 13 at a meeting of the Society of Medical Jurisprudence, New York City . . . Robert A. Nabatoff, M.D., New York City, on an extensive lecture tour through Japan, Formosa, Hong Kong, Thailand, and India, on the subject of recent advances in cardiac and vascular surgery . . . Theodore Rosenthal, M.D., Assistant Commissioner, City of New York Department of Health, on "We Must Eradicate V. D. in New York City" and Bruce P. Webster, M.D., New York City, on "V. D. Again Presents a Serious Challenge" at a conference on venereal disease at the Waldorf-Astoria on November 13 . . . Leo Wollman, M.D., Brooklyn, on October 26 before the New York Society of General Semantics on Hypnosis and Conditioning and also in October as a member of the faculty in the obstetrics and gynecology workshop which preceded the fifth annual meeting of the American Society of Clinical Hypnosis in Chicago.

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Sodium (dietetically sodium-free)	6 Mgs.
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Month in Washington

A Public Health Service study of possible links between cigaret smoking and lung cancer got underway with the appointment of a ten-member advisory committee including eight physicians from the academic field.

Luther L. Terry, M.D., Surgeon General of the P.H.S. and chairman of the committee, said he selected the members on the basis of geographic distribution and balance among professional disciplines, scientific objectivity, competence in special fields of interest, ability to think broadly outside of one particular field of interest, and ability to critically analyze a point of view.

In addition to being a committee member, Stanhope Bayne-Jones, M.D., also is serving as a special consultant to the committee staff. He is a former dean of the Yale School of Medicine and a former president of the American Society of Pathology and Bacteriology.

The Surgeon General has said that the committee is not merely an aggregate of ten men; it is a composition of specialists covering the broad range of medical sciences involved in evaluating the complex relationship between tobacco smoking and health.

The committee members were selected from a list of approximately 150 names submitted by Federal agencies, voluntary health organizations, and the tobacco industry.

In the first phase of its activity, the committee is making a comprehensive review of all available data on smoking and other factors in the environment that may affect health. It is expected that this review will be completed by next summer.

The second phase of the study will concern recommendations for action. No decision on how the second phase is to be conducted will be made until the first phase has been completed.

Soon after the appointment of the committee the National Cancer Institute, under the auspices of the P.H.S., issued a new booklet "Cancer Cause and Prevention" which referred to the conclusion reached by the P.H.S. in 1959 that smoking is the principal reason for the steep rise in lung cancer cases.

The booklet discusses cancer as a preventable disease. It describes environmental and personal factors involved in the causation of cancer and occupational cancer hazards that to some extent may be avoided. It goes into the problems of air pollution, radiation exposure, and food additives.

The booklet points out that as the older age group in the population increases, more people are living long enough to develop cancer induced by exposure to a causative agent earlier in life. Such cancers may take as long as forty years to appear, it says.

The publication concludes, "thus, mortality from malignant disease in the future can be reduced by continuous identification and eradication of cancer hazards."

* * *

The Food and Drug Administration was criticized as to both policies and operation by a Citizens Advisory Committee and some members of Congress.

A special advisory committee—appointed by the Secretary of Health, Education, and Welfare and headed by Dr. George Y. Harvey, a political science lecturer at the University of Missouri—said the F.D.A. had fallen short in carrying out its responsibility of protecting the American public against unsafe drugs, therapeutic devices, and foods.

The F.D.A. came in for even sharper criticism from Sen. Hubert H. Humphrey (D., Minn.) who indicated his Senate Government Operations Subcommittee would hold hearings in December on the agency. He charged that the F.D.A. lacks the ability and competence to carry out the new drug law effectively.

He accused the agency of failure to keep in touch with other governmental health projects and outside experts.

"Drugs have been approved which F.D.A. now admits should never have been approved," Humphrey said. "Drugs have been kept on the market long after F.D.A. admits they should have been eliminated from the market."

The sixteen doctors, educators, businessmen, and consumers on the advisory committee reported to H.E.W. Secretary, Anthony J. Celebrezze, after a year-long study of F.D.A. programs and procedures.

Making ten major recommendations for overhauling the F.D.A.'s approach to consumer protection, the panel said the Federal agency had been relying on "after-the-fact enforcement" of regulations rather than on taking more preventive action.

Celebrezze promised that the report would get a "most careful analysis." He said steps already were being taken to assure the public adequate protection through administrative action and under the new drug safety law recently passed by Congress.

"Although inspection and punitive action are vitally necessary," the committee said, "the time has arrived for a more constructive approach. After-the-fact enforcement is not always good consumer protection. Other approaches along preventive lines should be developed."

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INDICATION: *Accidental trauma*

INDICATED: Chymoral®

cuts healing time in accidental trauma

Whether the patient presents the simple edema and inflammation of a sprained ankle or the severe lacerations and bruising from a violent accident, immediate adjunctive use of Chymoral speeds resolution of traumatic manifestations. Chymoral modifies the inflammatory reaction to trauma, dissipates edema and blood extravasates, improves regional circulation, and thus aids the body's natural reparative activities. In other general practice areas, too, Chymoral cuts healing time. Excellent results have been achieved in acute sinusitis, bronchitis, bronchial asthma, emphysema, chronic pelvic inflammatory disease, and acute thrombophlebitis.[1-5]

Controls inflammation,
curtails swelling, curbs pain

1. Beck, C., *et al.*: Clin. Med. 7:519, 1960. 2. Teitel, L. H., *et al.*: Indust. Med. *29*:150, 1960. 3. Billow, B. W., *et al.*: Southwestern Med. *41*:286, 1960. 4. Clinical Reports to the Medical Department, Armour Pharmaceutical Company, 1960. 5. Taub, S. J.: Clin. Med. 7: 2575, 1960.

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CHYMORAL

Chymoral is an ORAL anti-inflammatory enzyme tablet specifically formulated for intestinal absorption. Each tablet provides enzymatic activity, equivalent to 50,000 Armour Units, supplied by a purified concentrate which has specific trypsin and chymotrypsin activity in a ratio of approximately six to one. ACTION: Reduces inflammation of all types; reduces and prevents edema except that of cardiac or renal origin; hastens absorption of blood and lymph extravasates; helps to liquefy thick tenacious mucous secretions; improves regional circulation; promotes healing; reduces pain. INDICATIONS: Chymoral is indicated in respiratory conditions such as asthma, bronchitis, rhinitis, sinusitis; in accidental trauma to speed absorption of hematoma, bruises, and contusions; in inflammatory dermatoses to ameliorate acute inflammation in conjunction with standard therapies; in gynecologic conditions such as pelvic inflammatory disease and mastitis; in obstetrics as episiotomies and breast engorgement; in surgical procedures as biopsies, hernia repairs, hemorrhoidectomies, mammectomies, phlebitis and thrombophlebitis; in genitourinary disorders as epididymitis, orchitis and prostatitis; in dental and oral surgery as fractures of the mandible or maxilla, difficult or multiple extractions, and alveolectomies. CONTRAINDICATIONS: None known. INCOMPATIBILITIES: None known. Antibiotics as well as generally accepted measures may be coadministered. SIDE EFFECTS: Mild gastric upsets, rarely encountered. DOSAGE: Recommended initial dose is two tablets q.i.d.; one tablet q.i.d. for maintenance. SUPPLIED: Bottles of 48 and 250 tablets.

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NO NEED TO ADD WATER
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*Brown, G. W.; Tuholski, J. M.; Sauer, L. W.; Minsk, L. D., and Rosenstern, I., J. Pediat. 56:391 (Mar.) 1960.

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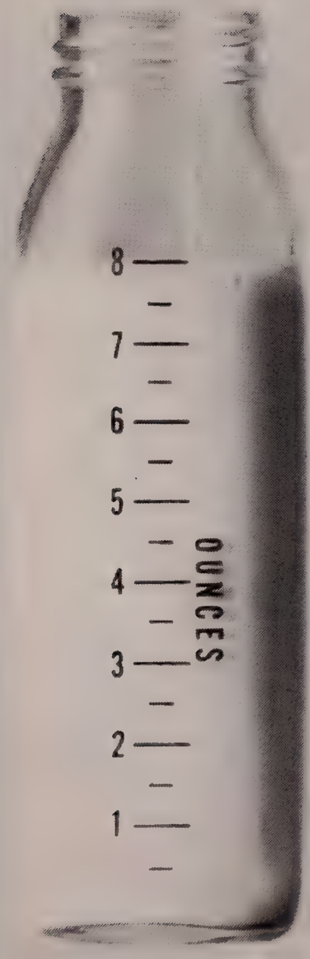

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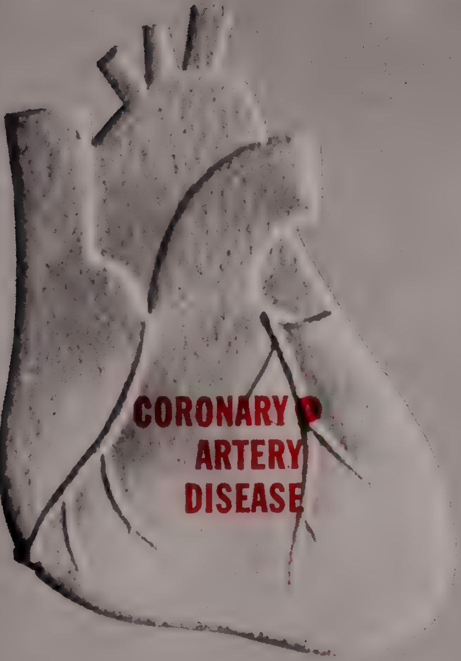

● "...now the leading cause of death in diabetic patients."[1]

Diseases of the cardiovascular-renal system account for about three-fourths of deaths among diabetic patients, with heart disease responsible for approximately one-half the total,[2,3] and coronary atherosclerosis the major cause of cardiac lesions.[1] While some feel that diabetics are predisposed, perhaps by heredity, to early onset of vascular disease, considered opinion is that vascular degeneration can be delayed or modified with "...careful and consistent control of diabetes from the time of diagnosis...."[4]

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References: (1) Root, H. F., and Bradley, R. F., in Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: The Treatment of Diabetes Mellitus, ed. 10, Philadelphia, Lea & Febiger, 1959, pp. 411, 437. (2) Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: *ibid.,* pp. 188-189. (3) Marks, H. H., *et al.:* Diabetes 9:500, 1960. (4) Marble, A., in Summary of Conference on Diabetic Retinopathy, Survey Ophth. (Part 2) 6:611-612, 1961.

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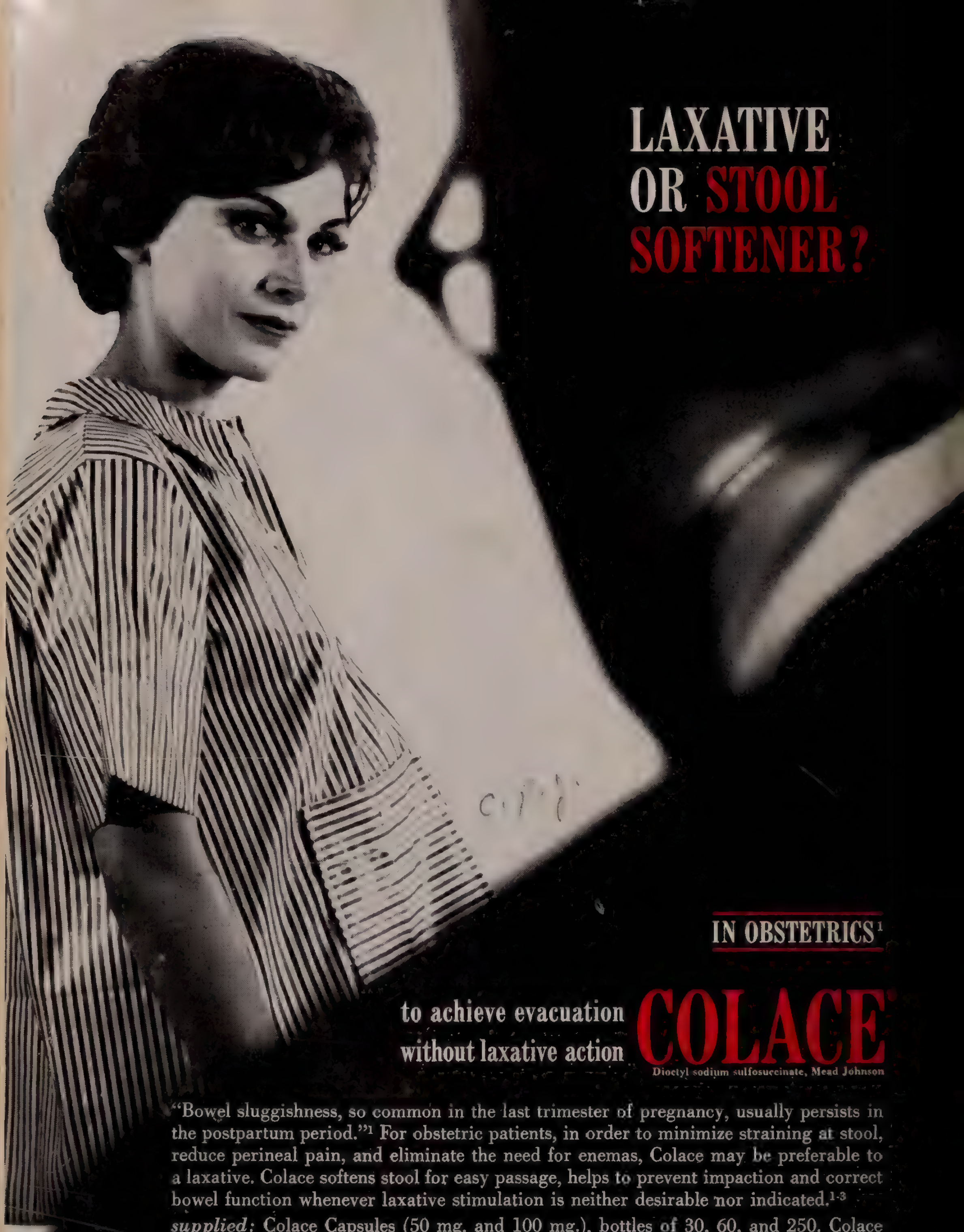

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references: (1) Schoenfeld, R. C.: Am. J. Obst. & Gynec. 74:1114-1115 (Nov.) 1957. (2) Smigel, J. O.; Lowe, K. J.; Hosp, P. H., and Gibson, J. H.: M. Times 86:1521-1526 (Dec.) 1958. (3) Turell, R.: A.M.A. Arch. Surg. 74:610-614 (April) 1957.

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